January 15, 2013

Ironwood Pharmaceuticals Provides Fourth Quarter 2012 Investor Update

- Initiated Promotional Efforts for LINZESS™ (linaclotide) with Forest in December 2012; LINZESS Available to Patients in Pharmacies Across U.S.; Forest Reported $19.2 Million in Net Sales of LINZESS in Fourth Quarter 2012
- Almirall Received Approval from European Commission for Constella® (linaclotide) in E.U.
- Formed Strategic Collaboration with AstraZeneca to Co-Develop and Co-Commercialize linaclotide in China; Gained Rights to Co-Promote NEXIUM® (esomeprazole magnesium) in U.S.
- Advanced Pipeline of Early Development Candidates and Discovery Research Efforts, and Continued to Explore Development Opportunities to Broaden LINZESS Label, both within Current Indications and Potential Future Indications
- Ended 2012 with $168 Million of Cash, Cash Equivalents and Available-for-Sale Securities; Completed $175 Million Debt Offering in January 2013

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) today provided an update on its fourth quarter 2012 and recent business activities.

"The past several months have been a remarkable period of time for us at Ironwood — particularly with the commercial launch of LINZESS in the U.S. and the approval of Constella in the E.U.," said Peter Hecht, Chief Executive Officer of Ironwood. "In December, the joint Ironwood and Forest team stocked LINZESS in over 44,000 pharmacies across the U.S. and began educating over 85,000 physicians. Looking ahead, we will continue to focus on the LINZESS launch, while also exploring development opportunities to strengthen the clinical profile of linaclotide and broaden the product label in other indications and geographies. We will also continue to progress our other pipeline programs, including potential linaclotide-based combination products, IW-9179 for functional dyspepsia and IW-2143 for anxiety, among others. Through these activities, we continue to work towards our overarching goals of delivering differentiated medicines to patients and value to our shareholders."

Fourth Quarter 2012 and Recent Highlights

LINZESS (linaclotide)

- LINZESS net product sales, as reported by Forest Laboratories, Inc., were $19.2 million in the fourth quarter of 2012.
- In December 2012, Ironwood and Forest initiated promotional efforts for LINZESS in the United States, with more than 1,400 sales specialists now educating over 85,000 physicians. LINZESS is available in more than 44,000 pharmacies. The United States Food and Drug Administration (FDA) approved LINZESS in August 2012 as a once-daily treatment for adult men and women suffering from irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). LINZESS can help to relieve abdominal pain and constipation associated with IBS-C, as well as constipation, infrequent bowel movements, incomplete evacuation and hard stools associated with CIC.
- Ironwood and Forest are exploring development opportunities to strengthen the clinical profile of LINZESS within its indicated population and to expand the product label for broader patient populations and indications, as well as exploring the potential for linaclotide-based combination products. In July 2012, the companies initiated a Phase 3b clinical trial to further characterize the effect of LINZESS on abdominal symptoms in patients with CIC. Ironwood expects to report data from this trial in the second half of 2013.

Constella (linaclotide)

- In November 2012, Ironwood and Almirall, S.A. announced that Almirall received marketing authorization from the European Commission for Constella® (linaclotide 290mcg) for the symptomatic treatment of moderate to severe IBS-C in adults in the European Union. Initial launches in Europe are expected in the first half of 2013.

Linaclotide (Rest of World)

- In October 2012, Ironwood and AstraZeneca formed a collaboration to co-develop and co-commercialize linaclotide in

China. The two companies are jointly responsible for strategic oversight of the development and commercialization of linaclotide in China. AstraZeneca will have primary responsibility for local operational execution, including clinical development. In addition, as part of the arrangement, Ironwood's sales force will promote AstraZeneca's NEXIUM in the United States.

- In October 2012, Astellas initiated a double-blind, placebo-controlled, dose-ranging Phase 2 clinical trial of linaclotide in more than 500 Japanese adult patients with IBS-C.

Research & Development

- In addition to exploring further linaclotide development opportunities, Ironwood continues to advance its pipeline, which includes early development candidates and discovery research efforts focused on gastrointestinal disease, central nervous system disorders, allergy conditions and cardiovascular disease.
- In October 2012, the company advanced its second GC-C agonist, IW-9179, into a Phase 2 clinical trial designed to evaluate its safety in approximately 80 patients with functional dyspepsia. Functional dyspepsia is a condition characterized by upper gastrointestinal pain, fullness, early satiety and bloating, and is estimated to affect more than 35 million people in the United States. There are a limited number of approved treatment options for functional dyspepsia.
- In December 2012, Ironwood advanced its investigational anti-anxiety compound, IW-2143, into a Phase 1 clinical trial. IW-2143 was in-licensed from Bionomics Limited in January 2012.
- In December 2012, Ironwood expanded its research collaboration with Protagonist Therapeutics, Inc. The collaboration, originally announced in January 2011, leverages Protagonist's proprietary disulfide‑rich peptide (DRP) technology platform and is aimed at providing Ironwood with novel peptides against targets for potential development in therapeutic areas with significant unmet medical needs.

Corporate

- Ironwood ended 2012 with approximately $168 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $70 million of net cash for operations during the year ended December 31, 2012.
- In January 2013, Ironwood completed a debt offering of $175 million bearing an 11% interest rate.

Conference Call Information

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time, on Tuesday, January 15, to discuss its fourth quarter 2012 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 83300312. 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, running through 11:59 p.m. Eastern Time on January 22, 2013. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 83300312. The archived webcast will be available on Ironwood's website for 14 days.

About LINZESS (linaclotide)

LINZESS is the first and only guanylate cyclase-C (GC-C) agonist approved by the FDA 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 transit and a reduction in visceral pain, which is thought to be mediated by decreased activity of pain-sensing nerves. The clinical relevance of the effect on pain fibers in 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 was also approved by the European Commission for the treatment of adults in the European Union with IBS-C and will be marketed under the brand name Constella® through a license agreement between Ironwood and Almirall, S.A. Ironwood also has partnered linaclotide with Astellas Pharma Inc. for development and commercialization in Japan and certain other Asian countries and with AstraZeneca for development and commercialization in China.

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is an entrepreneurial pharmaceutical company dedicated to the art and science of great drugmaking. Ironwood is located in Cambridge, Mass. To learn more, visit www.ironwoodpharma.com.

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%).

Drug Interactions

No drug-drug interaction studies have been conducted with LINZESS. Linaclotide and its active metabolite are not measurable in plasma following administration of the recommended clinical doses; hence, no systemic drug-drug interactions or drug

interactions mediated by plasma protein binding of linaclotide or its metabolite are anticipated.

Linaclotide does not interact with the cytochrome P450 enzyme system based on the results of in vitro studies. In addition, linaclotide is neither a substrate nor an inhibitor of the efflux transporter P-glycoprotein (P-gp). Ironwood Pharmaceuticals, Inc.

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, the potential for LINZESS as a treatment option for adults in the United States suffering from IBS-C and CIC, the availability of LINZESS in pharmacies in the U.S., Ironwood's and Forest's intended non-clinical and clinical development activities for linaclotide and Ironwood's intended activities and associated timelines for the other product candidates and early development programs in its pipeline, the anticipated launch timeline for Constella in the European Union, the development and potential commercialization of linaclotide in China, and the potential for IW-9179 as a treatment option for adults suffering from functional dyspepsia. 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 the risks that the commercial launch of LINZESS in the U.S. is not executed as anticipated, Ironwood or its partners are unable to manufacture or distribute a sufficient commercial supply of LINZESS, adoption of LINZESS by physicians or patients is faster or slower than anticipated, Almirall is unable to obtain sufficient pricing or reimbursement for Constella in countries in the European Union, serious adverse events arise in patients that are deemed to be definitely or probably related to linaclotide treatment, the incidence or severity of diarrhea in patients treated with linaclotide is higher than expected, or advancements in the further development of linaclotide in additional patient populations or indications, or in the development of other products or early development programs in Ironwood's pipeline, do not proceed as expected, as well as risks related to the difficulty of predicting regulatory approvals and the acceptance of and demand for new pharmaceutical products. Applicable risks also include those that are listed in Ironwood's Quarterly Report on Form 10 - Q for the quarter ended September 30, 2012, 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 subsequent SEC filings. Ironwood undertakes no obligation to update these forward - looking statements to reflect events or circumstances occurring after this press release. 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)

	December 31, 2012	December 31, 2011
Assets		
Cash, cash equivalents and available-for-sale securities	$ 168,228	$ 164,016
Accounts receivable, net	1,487	652
Inventory	6,699	—
Prepaid expenses and other current assets	8,026	2,899
Total current assets	184,440	167,567
Property and equipment, net	37,537	33,625
Other assets	7,930	7,785
Total assets	$ 229,907	$ 208,977
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 48,561	$ 24,568
Current portion of capital lease obligations	261	233
Current portion of deferred rent	2,735	4,042
Current portion of deferred revenue	3,381	36,291
Total current liabilities	54,938	65,134
Capital lease obligations	308	422
Deferred rent	11,593	12,435
Deferred revenue	18,024	21,130
Other liabilities	992	—
Total stockholders' equity	144,052	109,856
Total liabilities and stockholders' equity	$ 229,907	$ 208,977

Condensed Consolidated Statements of Operations

(in thousands, except share and per share amounts)
(unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2012	**2011**	**2012**	**2011**
Revenue	$ 26,980	$ 32,154	$ 150,245	$ 65,871
Cost and expenses:				
Cost of revenue	965	—	965	—
Research and development	28,273	24,224	113,474	86,093
Selling, general and administrative	33,274	13,925	92,538	45,546
Collaboration expense	8,368	1,037	16,030	374
Total cost and expenses	70,880	39,186	223,007	132,013
Loss from operations	(43,900)	(7,032)	(72,762)	(66,142)
Other income (expense), net	45	58	138	1,293
Net loss before income tax expense	(43,855)	(6,974)	(72,624)	(64,849)
Income tax expense	—	—	—	3
Net loss	$ (43,855)	$ (6,974)	$ (72,624)	$ (64,852)
Net loss per share —basic and diluted	$ (0.41)	$ (0.07)	$ (0.68)	$ (0.65)
Weighted average number of common shares used in net loss per share —basic and diluted	107,493,026	100,394,800	106,402,639	99,874,790

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