January 21, 2014

Ironwood Pharmaceuticals Provides Fourth Quarter 2013 Investor Update

- Fourth quarter LINZESS® (linaclotide) net product sales of $51.0 million, as reported by Forest Laboratories, Inc., up 48% Quarter over Quarter -

- $118.8 million LINZESS net product sales in first full year of launch; $138.0 million LINZESS net product sales since December 2012 launch -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) today provided an update on its fourth quarter 2013 and recent business activities.

"2013 was a transformational year for Ironwood. LINZESS had a strong first full year in the market with greater than 200,000 unique adult patients filling a LINZESS prescription, more than 580,000 total prescriptions filled, over 50,000 healthcare practitioners gaining experience with LINZESS, approximately $119 million of net product sales for 2013 and approximately $138 million of net product sales since LINZESS launched in December 2012," said Peter Hecht, chief executive officer of Ironwood. "We are executing on our strategy to grow a leading GI therapeutics company by building on the success of LINZESS, leveraging our commercial capabilities and advancing a pipeline of multiple GI and guanylate cyclase programs. Through the prudent and efficient allocation of our capital across these priority growth platforms, we are working to maximize value for patients and for our fellow shareholders."

Fourth Quarter 2013 and Recent Highlights

LINZESS® (linaclotide)

- LINZESS net product sales, as reported by Forest Laboratories, Inc., were $51.0 million in the fourth quarter of 2013, an increase of approximately 48% quarter over quarter, and $118.8 million for the year ended December 31, 2013.
- More than 220,000 LINZESS prescriptions were filled in the fourth quarter of 2013, resulting in more than 24% growth in total prescriptions quarter over quarter, and over 580,000 LINZESS prescriptions were filled in 2013, according to IMS Health.
- In 2013, more than 50,000 healthcare practitioners prescribed LINZESS, including approximately 90% of high prescribing gastroenterologists and approximately 70% of other high prescribing healthcare practitioners, primarily primary care physicians. Physician prescribing continues to increase month over month.
- As of December 2013, approximately 75% of adult irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC) patients with commercial insurance had unrestricted access to LINZESS and approximately 80% of adult patients with commercial insurance had access to LINZESS at a copay of $30 per month or less through formulary coverage or the LINZESS Instant Savings Program.
- Ironwood and Forest continue to explore opportunities to enhance the clinical profile of LINZESS by seeking to expand its utility in its indicated populations, as well as studying linaclotide in additional indications and populations, new formulations and in combination with other products to assess its potential to treat various gastrointestinal (GI) conditions.

Linaclotide (Rest of World)

- Almirall, S.A., Ironwood's European partner, continues to launch CONSTELLA® (linaclotide) in Europe. CONSTELLA is currently available to adult IBS-C patients in nine countries in Europe, including the United Kingdom and Germany.
- 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. has completed enrollment in a Phase II double-blind, placebo-controlled, dose-ranging clinical trial of linaclotide in adult patients with IBS-C in Japan.

Research & Development

- Ironwood is leveraging its strong therapeutic expertise in GI disorders to advance up to seven GI development programs with multiple opportunities to generate proof of concept data over the next 24 months.
- Building on its pioneering research with linaclotide, guanylate cyclase-C (GC-C) and other guanylate cyclases, Ironwood is also advancing a second GC program targeting soluble guanylate cyclase (sGC), a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development.

Corporate and Financials

- **Total Revenues.** Revenues were approximately $5.0 million in the fourth quarter of 2013. This consisted of $2.9 million in collaborative arrangements revenue associated with its share of the net profits and losses from the sales of LINZESS in the U.S., $0.5 million in sales of active pharmaceutical ingredient (API), $1.5 million in the amortization of deferred revenue associated with consideration received from Ironwood's collaborations with Astellas and AstraZeneca, and $0.1 million in royalty payments based on sales of CONSTELLA in Europe from Almirall. For 2013, revenues were approximately $22.9 million. This consisted of $2.9 million in collaborative arrangements revenue associated with its share of the net profits and losses from the sales of LINZESS in the U.S., $12.2 million in sales of API, $5.7 million in the amortization of deferred revenue associated with consideration received from Ironwood's collaborations with Astellas and AstraZeneca, $1.9 million in milestone payments from Almirall as a result of the commercial launches of CONSTELLA in the U.K. and Germany, and $0.2 million in royalty payments from Almirall.
- **Operating Expenses.** Operating expenses were approximately $51.2 million in the fourth quarter of 2013. This consisted of $22.5 million in research and development (R&D) expenses, which included approximately $1.9 million in non-cash share-based compensation expense, and $28.7 million in selling, general and administrative (SG&A) expenses, which included approximately $2.6 million in non-cash share-based compensation expense. For 2013, operating expenses were approximately $225.6 million and consisted of $102.4 million in research and development expenses, which included approximately $9.2 million in non-cash share-based compensation expense, and $123.2 million in SG&A expenses, which included approximately $10.7 million in non-cash share-based compensation expense.
- **Collaborative Arrangements Revenue/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 as collaborative arrangements revenue or collaboration expense, as applicable. For the fourth quarter of 2013, Ironwood recorded the settlement payment from Forest as collaborative arrangements revenue and no collaboration expense was recorded. For 2013, collaboration expense was $42.1 million.
- **Interest Expense.** Interest expense was $5.3 million in the fourth quarter of 2013 in connection with the $175 million debt financing executed in January 2013. For 2013, interest expense was $21.0 million.
- **Net Loss.** Net loss was $52.0 million, or $0.43 per share, in the fourth quarter of 2013. For 2013, net loss was $272.8 million, or $2.35 per share.
- **Cash Position.** Ironwood ended 2013 with approximately $198 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $42 million of net cash for operations during the quarter and approximately $273 million of net cash for operations during the year ended December 31, 2013.
- **2013 Financial Guidance.** Ironwood provided financial guidance for its 2013 non-linaclotide R&D expenses to be in the range of $60 to $75 million. Total actual non-linaclotide R&D expenses in 2013 were $56.3 million. Additionally, Ironwood provided financial guidance for its 2013 marketing and sales expenses for LINZESS to be in the range of $250 to $300 million. Total actual 2013 marketing and sales expenses for LINZESS were $255.5 million.
- **2014 Financial Guidance.** Ironwood expects its 2014 total operating expenses 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 updated its financial guidance for the Forest and Ironwood total 2014 marketing and sales expenses for LINZESS, which it now expects 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, January 21, to discuss its fourth quarter 2013 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 30523527. 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 28, 2014. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 30523527. 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 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 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 was also approved by the European Commission for the treatment of adults in the European Union with IBS-C and is 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 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 in Europe by Almirall 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 Europe. 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 and our product candidates and programs in our pipeline; the anticipated timing of pre-clinical and clinical developments, including clinical trials (and their associated results); and our company's financial performance and results, including our projected 2014 operating expenses (including certain research and development 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, regulatory approvals, manufacturing, formulation development, intellectual property matters, efficacy, safety and tolerability, competition in disease states, and the commercial potential of LINZESS and our 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 Quarterly Report on Form 10‑Q for the quarter ended September 30, 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 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)

	December 31, 2013	December 31, 2012
Assets		
Cash, cash equivalents and available-for-sale securities	$ 197,602	$ 168,228
Accounts receivable, net	3,213	1,487
Inventory	22,145	6,699
Prepaid expenses and other current assets	6,168	8,026
Total current assets	229,128	184,440
Property and equipment, net	37,376	37,537
Other assets	12,458	7,930
Total assets	$ 278,962	$ 229,907
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 32,037	$ 48,561
Current portion of capital lease obligations	1,139	261
Current portion of deferred rent	2,790	2,735
Current portion of deferred revenue	5,074	3,381
Total current liabilities	41,040	54,938
Capital lease obligations	3,134	308
Deferred rent	8,822	11,593
Deferred revenue	11,416	18,024
Notes payable	174,672	—
Other liabilities	1,653	992
Total stockholders' equity	38,225	144,052
Total liabilities and stockholders' equity	$ 278,962	$ 229,907

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

	Three Months Ended December 31,		Year Ended December 31,	
	2013	2012	2013	2012
Revenue	$ 5,031	$ 26,980	$ 22,881	$ 150,245
Cost and expenses:				
Cost of revenue	533	965	7,203	965
Research and development (1)	22,516	28,273	102,378	113,474
Selling, general and administrative (1)	28,720	33,274	123,228	92,538
Collaboration expense	—	8,368	42,074	16,030
Total cost and expenses	51,769	70,880	274,883	223,007
Loss from operations	(46,738)	(43,900)	(252,002)	(72,762)
Other income (expense), net	(5,248)	45	(20,810)	138
Net loss	$ (51,986)	(43,855)	$ (272,812)	$ (72,624)
Net loss per share—basic and diluted	$ (0.43)	$ (0.41)	$ (2.35)	$ (0.68)
Weighted average number of common shares used in net loss per share —basic and diluted	120,929,271	107,439,026	115,851,875	106,402,639
(1) Non-cash compensation expenses reflected in the condensed consolidated statements of operations are as follows:				
Research and development	$ 1,904	$ 2,404	$ 9,178	$ 9,080
Selling, general and administrative	$ 2,634	$ 2,257	$ 10,651	$ 8,493

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

	Three Months Ended December 31,		Year Ended December 31,	
	2013	**2012**	**2013**	**2012**
LINZESS net sales	$ 51,044	$ 19,227	$ 118,753	$ 19,227
Commercial costs and expenses[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.	62,806	39,157	264,751	61,471
Net profit (loss) on sales of LINZESS	$(11,762)	$(19,930)	$(145,998)	$(42,244)
Ironwood's share of net loss	$ (5,881)	$ (9,965)	$ (72,999)	$(21,122)
Ironwood's selling, general and administrative expenses[3] Includes Ironwood's selling, general and administrative expenses attributable to the cost-sharing arrangement with Forest.	$ 8,795	$ 1,597	$ 33,839	$ 5,092
Ironwood's collaboration expense	$ —	$ 8,368	$ 39,160	$ 16,030
Ironwood's collaborative arrangement revenue	$ 2,914	$ —	$ —	$ —

[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 the Ironwood's share of net profit (loss) generated from the sales of LINZESS in the U.S. and the 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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