October 22, 2013

Ironwood Pharmaceuticals Provides Third Quarter 2013 Investor Update

— Third quarter LINZESS® (linaclotide) net product sales of $34.4 million, as reported by Forest Laboratories, Inc. —

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

"This quarter, we continued to make good progress across our key value drivers. LINZESS is performing well across the key leading indicators, reinforcing the significant opportunity we see ahead. Our scientists continue to advance the pharmacology of linaclotide and explore its utility more broadly while also progressing our broader pipeline, and our global partners are making important strides in bringing linaclotide to appropriate patients worldwide," said Peter Hecht, chief executive officer of Ironwood Pharmaceuticals, Inc.

Third Quarter 2013 and Recent Highlights

LINZESS® (linaclotide)

- LINZESS net product sales, as reported by Forest Laboratories, Inc., were $34.4 million in the third quarter of 2013.
- More than 178,000 LINZESS prescriptions were filled in the third quarter of 2013, resulting in more than 40% growth in total prescriptions compared to the previous quarter, and more than 539,000 LINZESS prescriptions have been filled since the launch of LINZESS on December 17, 2012, according to IMS Health.
- To date, more than 80% of high prescribing gastroenterologists and more than 50% of high prescribing primary care physicians have prescribed LINZESS; approximately 1,000 physicians are writing their first LINZESS prescription each week.
- As of September 2013, approximately 80% of adult irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC) patients with commercial insurance had unrestricted access to LINZESS and greater than 60% of adult patients with commercial insurance have access to LINZESS at a copay of $30 per month or less through formulary coverage or the LINZESS Instant Savings Program.
- Ironwood received positive top-line data from a Phase IIIb clinical trial conducted with Forest to evaluate the effect of LINZESS on abdominal symptoms in patients with CIC and prominent abdominal bloating. The average bloating score reported by these patients at baseline was 7.1 on a 0 to 10 point scale. Data from the clinical trial demonstrated that LINZESS dosed at 145 mcg in adult CIC patients resulted in a statistically significant increase in bowel movements, achieving the trial's primary endpoint. Data from the trial also indicate that all 27 pre-specified secondary endpoints, including a statistically significant reduction in abdominal bloating relative to baseline in adult patients suffering from CIC, were achieved. Diarrhea was the most commonly reported adverse reaction reported in the study. Data showed a diarrhea rate of 5.9% and 16.9% in patients treated with LINZESS at the 145 mcg and 290 mcg doses, respectively, versus 2.3% in placebo-treated patients, and a 1.3% and 5.0% discontinuation rate due to diarrhea in patients treated with LINZESS at the 145 mcg and 290 mcg dose, respectively, versus 0.6% in placebo-treated patients.
- Ironwood and Forest continue to explore additional development opportunities to work with the FDA to strengthen the clinical profile of LINZESS within its indicated population and to expand the product label for additional approved patient populations and indications, as well as to explore the potential for linaclotide-based combination products. The companies expect to initiate a Phase IIa clinical trial of LINZESS in adult patients with opioid-induced constipation during the first half of 2014, and to continue working with the FDA to establish an appropriate plan to study LINZESS in the pediatric population.

Linaclotide (Rest of World)

- CONSTELLA® (linaclotide) is currently available to adult IBS-C patients in multiple countries in Europe, and Ironwood's European partner, Almirall, S.A., will continue to launch CONSTELLA in additional European countries.
- Ironwood and AstraZeneca AB began enrolling 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 enrollment in a double-blind, placebo-controlled, dose-ranging Phase II clinical trial of linaclotide in adult patients with IBS-C in Japan.

Research & Development

- In addition to exploring additional linaclotide development opportunities, Ironwood is leveraging its pioneering understanding of linaclotide's pharmacology and mechanism of action, guanylate cyclase-C (GC-C) agonists, cyclic GMP, and symptomatic diseases to advance other programs in its pipeline, which include early development candidates and discovery research efforts focused on gastrointestinal disease, central nervous system disorders, allergic conditions and cardiovascular disease.

Corporate and Financials

- **Total Revenues.** Revenues were approximately $4.9 million in the third quarter of 2013. This consisted of $3.4 million in sales of active pharmaceutical ingredient (API) and $1.5 million in the amortization of deferred revenue associated with consideration received from Ironwood's collaborations with Astellas and AstraZeneca. LINZESS net product sales are recorded by Forest and are not included in Ironwood's total revenues (refer to the LINZESS U.S. Collaboration Expense Calculation at the end of this press release).
- **Operating Expenses.** Operating expenses were approximately $53.3 million in the third quarter of 2013. This consisted of $23.0 million of research and development expenses, which included approximately $2.3 million in non-cash share-based compensation expense, and $30.3 million of selling, general and administrative expenses, which included approximately $2.9 million of non-cash share-based compensation expense.
- **Collaboration Expense.** Ironwood reported $6.2 million in collaboration expense in the third quarter of 2013. 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.
- **Interest Expense.** Interest expense was $5.3 million in the third quarter of 2013 in connection with the $175 million debt financing executed in January 2013.
- **Net Loss.** Ironwood reported a net loss of $61.8 million, or $0.51 per share, in the third quarter of 2013.
- **Cash Position.** Ironwood ended the third quarter of 2013 with approximately $242 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $58 million of net cash for operations during the quarter.
- **Financial Guidance.** Ironwood today reiterated its financial guidance for the Forest and Ironwood total 2013 sales and marketing expense for LINZESS to be in the range of $250 to $300 million. Ironwood also reiterated its guidance for its 2013 non-linaclotide research and development expense to be in the range of $60 to $75 million.
- Ironwood will host an Investor Day on December 12, 2013 to further discuss its corporate strategy, including an update on the commercialization of LINZESS, a discussion around linaclotide opportunities in additional populations and indications, and its overall R&D efforts.

Conference Call Information

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time, on Tuesday, October 22, to discuss its third 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 75229614. 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 October 29, 2013. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 75229614. 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 committed to the art and science of making medicines, from discovery through commercialization. We're focused on three goals: transforming knowledge into medicines that make a difference for patients, creating value that will inspire the continued support of our fellow shareholders, and building a team that passionately pursues excellence. Our first product, linaclotide, is approved in the United States and Europe. Our pipeline priorities include exploring further opportunities for linaclotide, leveraging our deep expertise in functional gastrointestinal disorders, and advancing programs in other areas such as allergic conditions, cardiovascular disease, central nervous system disorders and other conditions defined by patient symptoms. 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 to learn more about Ironwood. Information that may be important to investors will be routinely posted in both these locations.

LINZESS® and CONSTELLA® are trademarks owned by Ironwood Pharmaceuticals, Inc.

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, the potential for LINZESS as a treatment option for adults in the United States suffering from IBS-C and CIC, the addition of new physicians who are prescribing LINZESS, Ironwood's and its partners' anticipated non-clinical and clinical development activities for linaclotide and their associated timelines, Ironwood's intended activities for the product candidates and early development programs in its pipeline, the anticipated launch timeline for CONSTELLA in Europe, Ironwood's and its partners' ability to bring linaclotide to appropriate patients worldwide, the amount Ironwood and Forest anticipate spending on sales and marketing expenses for LINZESS in 2013 and the amount Ironwood anticipates spending on non-linaclotide research and development expenses in 2013. 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 market acceptance of LINZESS in the U.S. is not as anticipated, Ironwood or its partners are unable to manufacture or distribute a sufficient commercial supply of linaclotide, the rate of new physician adoption of LINZESS begins to decrease, Ironwood and Forest increase or modify their plans for the sales and marketing campaigns for LINZESS in the U.S. and such modifications result in an increase or a decrease in the associated expenses, Almirall is unable to obtain sufficient pricing or reimbursement for CONSTELLA in countries in Europe or it chooses to launch CONSTELLA on a different timeline, serious adverse events arise in patients that are deemed to be related to linaclotide treatment, the incidence or severity of diarrhea in patients treated with linaclotide is higher than expected, efforts to strengthen the clinical profile of linaclotide within its indicated population and advancements in the further development of linaclotide in additional patient populations or indications or in linaclotide-based combination products do not proceed as expected, or 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 June 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. 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)

	September 30, 2013	December 31, 2012
Assets		
Cash, cash equivalents and available-for-sale securities	$ 242,390	$ 168,228
Accounts receivable, net	3,086	1,487
Inventory	20,561	6,699
Prepaid expenses and other current assets	9,789	8,026
Total current assets	275,826	184,440
Property and equipment, net	37,231	37,537
Other assets	12,786	7,930
Total assets	$ 325,843	$ 229,907
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 30,736	$ 48,561
Current portion of capital lease obligations	1,115	261
Current portion of deferred rent	2,776	2,735
Current portion of deferred revenue	5,074	3,381
Total current liabilities	39,701	54,938
Capital lease obligations	3,427	308
Deferred rent	9,519	11,593
Deferred revenue	12,684	18,024
Notes Payable	174,650	—
Other liabilities	1,653	992
Total stockholders' equity	84,209	144,052
Total liabilities and stockholders' equity	$ 325,843	$ 229,907

Condensed Consolidated Statements of Operations

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Revenue	$ 4,932	$ 96,413	$ 17,850	$ 123,265
Cost and expenses:				
Cost of revenue	2,021	—	6,670	—
Research and development (1)	23,016	23,453	79,862	85,201
Selling, general and administrative (1)	30,264	22,846	94,508	59,264
Collaboration expense	6,182	2,506	42,074	7,662
Total cost and expenses	61,483	48,805	223,114	152,127
Loss from operations	(56,551)	47,608	(205,264)	(28,862)
Other income (expense), net	(5,224)	27	(15,562)	93
Net income (loss)	$ (61,775)	$ 47,635	$ (220,826)	$ (28,769)
Net income (loss) per share—basic	$ (0.51)	$ 0.44	$ (1.93)	$ (0.27)
Net income (loss) per share—diluted	$ (0.51)	$ 0.42	$ (1.93)	$ (0.27)
Weighted average number of common shares used in net income (loss) per share —basic	120,768,893	107,266,823	114,140,821	106,036,522
Weighted average number of common shares used in net income (loss) per share —diluted	120,768,893	114,337,327	114,140,821	106,036,522

(1) Non-cash share-based compensation expenses included reflected in the condensed consolidated statements of operations are as follows:				
Research and development	$ 2,349	$ 2,648	$ 7,274	$ 6,676
Selling, general and administrative	2,850	2,487	8,017	6,236

LINZESS U.S. Collaboration Expense Calculation[1]

(in thousands)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
LINZESS net sales	$ 34,444	$ -	$ 67,709	$ -
Commercial costs and expenses[2]	63,276	7,420	201,945	22,314
Net profit (loss) on sales of LINZESS	$ (28,832)	$ (7,420)	$(134,236)	$(22,314)
Ironwood's share of net profit (loss)	$ (14,416)	$ (3,710)	$ (67,118)	$(11,157)
Ironwood's selling & marketing[3]	$ 8,234	$ 1,204	$ 25,044	$ 3,495
Ironwood's collaboration expense	$ 6,182	$ 2,506	$ 42,074	$ 7,662

[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 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 sales incurred by Forest as well as selling and marketing costs incurred by Forest and Ironwood that are attributable to the cost-sharing arrangement between the parties.

[3] Includes Ironwood's selling and marketing costs attributable to the cost-sharing arrangement with Forest.

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