October 16, 2012

Ironwood Pharmaceuticals Provides Third Quarter 2012 Investor Update

— Received FDA Approval of LINZESS™ (linaclotide) for Treatment of Adult Patients with IBS-C or CIC; Prepared for Commercial Launch in December —

— Received Positive Opinion from CHMP Recommending Approval of linaclotide for Treatment of Adults with IBS-C in E.U. —

— Peer-Reviewed Publications of LINZESS Phase 3 IBS-C Data in American Journal of Gastroenterology —

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

Third Quarter 2012 and Recent Highlights

Linaclotide

- The U.S. Food and Drug Administration (FDA) approved LINZESS 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, and constipation and hard stools associated with CIC. Ironwood and Forest Laboratories, Inc. expect LINZESS to be available to U.S. patients in December 2012.
- Ironwood and Almirall, S.A. received a positive opinion from the European Committee for Medicinal Products for Human Use (CHMP), recommending approval of linaclotide for the symptomatic treatment of moderate to severe IBS-C in adults in the E.U. A decision by the European Commission is expected in 2012. If approved, the product will be marketed under the brand name Constella®.
- Astellas, Ironwood's linaclotide 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.
- Results from the two Phase 3 trials of linaclotide for the treatment of IBS-C in adults were published in the October 2012 issue of the American Journal of Gastroenterology (AJG).
- Ironwood and Forest will present 10 abstracts at the American College of Gastroenterology (ACG) 2012 Annual Scientific Meeting being held in Las Vegas from October 19-24, 2012. Data being presented include analyses of abdominal and bowel symptoms from Phase 3 trials of linaclotide in IBS-C and CIC, as well as data about the economic burden of IBS-C and CIC and data on the use of patient-reported outcomes to assess the symptoms of these conditions.
- Ironwood and Almirall will present six abstracts and two oral presentations at the 20th United European Gastroenterology Week being held in Amsterdam from October 20-24, 2012. Data being presented include analyses of abdominal and bowel symptoms from Phase 3 trials of linaclotide in IBS-C.

Research & Development

- In addition to the company's ongoing efforts to evaluate linaclotide's pharmacological potential in a variety of patient populations, Ironwood continues to pioneer the guanylate cyclase-C (GC-C) agonist space through the advancement of a second GC-C agonist, IW-9179. IW-9179 is currently being investigated in a Phase 2a clinical trial designed to evaluate its safety in approximately 80 patients with functional dyspepsia.
- Ironwood continues to advance its broader pipeline, which includes early development candidates and discovery research efforts focused on gastrointestinal disease, central nervous system disorders, respiratory disease, and cardiovascular disease.

Corporate

- Ironwood received an $85 million milestone payment from Forest for FDA approval of LINZESS.
- Including the $85 million milestone payment, Ironwood ended the third quarter of 2012 with approximately $193 million of

cash, cash equivalents, and available-for-sale securities and used approximately $47 million of net cash for operations during the nine months ended September 30, 2012.

Conference Call Information

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time, on Tuesday, October 16, to discuss its third 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 37414107. 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 23, 2012. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 37414107. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the call.

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 chronic abdominal pain and constipation associated with IBS-C and constipation and hard stools associated with CIC. The recommended dose is 290 mcg for IBS-C patients and 145 mcg for CIC patients.

LINZESS binds to the GC-C receptor locally in the intestine, with no measurable blood plasma concentrations, resulting in an increase in both intracellular and extracellular concentrations of cyclic guanosine monophosphate (cGMP). Elevations in intracellular cGMP are believed to stimulate secretion of intestinal fluid and accelerate gastrointestinal transit resulting in increased frequency of bowel movements. Elevations in extracellular cGMP are believed to decrease activity of pain-sensing nerves, which is thought to be responsible for a reduction in intestinal pain, according to nonclinical models.

Ironwood and Forest will co-promote LINZESS in the United States. Ironwood has outlicensed linaclotide to Almirall, S.A. for European development and commercialization and to Astellas Pharma Inc. for development and commercialization in Japan, Indonesia, Korea, the Philippines, Taiwan, and Thailand.

About Irritable Bowel Syndrome with Constipation (IBS-C)

Irritable bowel syndrome with constipation (IBS-C) is a chronic functional gastrointestinal disorder that affects as many as 13 million people in the United States and over 20 million people in Europe. IBS-C can have a negative impact on daily living; patients often experience recurring abdominal pain or discomfort, constipation, and bowel symptoms including hard or lumpy stools in more than 25% of bowel movements, and soft or watery stools in less than 25% of bowel movements. There are currently few available therapies to treat this disorder.

About Chronic Idiopathic Constipation (CIC)

Chronic idiopathic constipation (CIC) is a functional gastrointestinal disorder in which individuals experience infrequent bowel movements (less than three times per week) for at least three months. Patients who suffer from CIC may also experience a sensation of incomplete evacuation and hard stools. As many as 35 million Americans may suffer from symptoms associated with CIC.

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).

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is an entrepreneurial pharmaceutical company dedicated to the art and science of great drugmaking. LINZESS (linaclotide), Ironwood's guanylate cyclase-C (GC-C) agonist, is an FDA-approved drug for the treatment of adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). Ironwood also has a growing pipeline of additional drug candidates in earlier stages of development. Ironwood is located in Cambridge, Mass. To learn more, visit www.ironwoodpharma.com.

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 anticipated time period in which LINZESS will be available for IBS-C and CIC patients, linaclotide's potential as a treatment for IBS-C or CIC, the potential approval of linaclotide in the E.U. as a result of the positive CHMP opinion, Astellas's development plans for linaclotide in Japan, and our development plans for IW-9179 and our other pipeline programs . 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 we are unable to launch LINZESS in the U.S. as anticipated, we or our partners are unable to manufacture or distribute a sufficient commercial supply of LINZESS to enable a successful commercial launch, adoption of LINZESS by physicians or patients is not as rapid as anticipated, 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, the European Commission does not agree with the CHMP recommendation for approval of linaclotide in the E.U., or advancements in our development 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 our Quarterly Report on Form 10-Q for the quarter ended June 30, 2012, in addition to the risk factors that are listed from time to time in our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and any subsequent SEC filings. We undertake 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, 2012	December 31, 2011
Assets		
Cash, cash equivalents and available-for-sale securities	$ 193,323	$ 164,016
Accounts receivable, net	182	652
Inventory	965	—
Prepaid expenses and other assets	7,877	2,899
Total current assets	202,347	167,567
Property and equipment, net	36,470	33,625
Other assets	7,701	7,785
Total assets	$ 246,518	$ 208,977
Liabilities and Stockholders' Equity		
Accounts payable, net and accrued expenses	$ 27,636	$ 24,568
Current portion of capital lease obligations	280	233
Current portion of deferred rent	4,531	4,042
Current portion of deferred revenue	3,130	36,291
Total current liabilities	35,577	65,134
Capital lease obligations	361	422
Deferred rent	9,690	12,435
Deferred revenue	18,782	21,130
Total stockholders' equity	182,108	109,856
Total liabilities and stockholders' equity	$ 246,518	$ 208,977

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2012	2011	2012	2011
Revenue	$ 96,413	$ 12,218	$ 123,265	$ 33,717
Operating expenses:				
Research and development	23,453	22,905	85,201	61,869
General and administrative	25,352	10,929	66,926	30,958
Total operating expenses	48,805	33,834	152,127	92,827
Income (loss) from operations	47,608	(21,616)	(28,862)	(59,110)
Other income (expense), net	27	986	93	1,235
Net Income (loss) before income tax expense	47,635	(20,630)	(28,769)	(57,875)
Income tax expense	—	3	—	3
Net income (loss)	$ 47,635	$ (20,633)	$ (28,769)	$ (57,878)
Net income (loss) per share—basic	$ 0.44	$ (0.21)	$ (0.27)	$ (0.58)
Net income (loss) per share—diluted	$ 0.42	$ (0.21)	$ (0.27)	$ (0.58)
Weighted average number of common shares used in net income (loss) per share —basic	107,266,823	100,174,100	106,036,522	99,699,545
Weighted average number of common shares used in net income (loss) per share —diluted	114,337,327	100,174,100	106,036,522	99,699,545

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