August 4, 2014

Ironwood Pharmaceuticals Provides Second Quarter 2014 Investor Update

- 36% growth in total LINZESS® (linaclotide) prescriptions quarter over quarter -

- Second quarter LINZESS U.S. net product sales of $62.7 million -

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

"Demand for LINZESS grew 36% in the second quarter supported by the initiation of our direct-to-consumer efforts, which drove net product sales higher despite a two week decrease in wholesaler inventory during the quarter. We are eighteen months into the launch and LINZESS is now approaching profitability. With over 375,000 patients having initiated therapy with LINZESS since launch, millions of therapy-seeking patients still to be reached, and patent exclusivity expected to at least 2031, there is enormous opportunity for LINZESS ahead," said Peter Hecht, chief executive officer of Ironwood Pharmaceuticals. "At the same time, building off of linaclotide, and leveraging our deep understanding of the GI category and our research in guanylate cyclases, we are advancing a robust pipeline of product candidates targeting multi-billion dollar markets. As we execute on our strategy to build a leading gastrointestinal therapeutics company, we believe we have many opportunities to bring important new medicines to patients and create meaningful value for our shareholders."

Second Quarter 2014 and Recent Highlights

LINZESS® (linaclotide)

- LINZESS U.S. net product sales, as provided by Actavis plc, were $62.7 million in the second quarter of 2014, an increase of approximately 3% quarter over quarter. Wholesaler inventory levels decreased to approximately two to three weeks at the end of the second quarter of 2014, as compared to approximately four to five weeks at the end of the first quarter of 2014.
- Over 326,000 total LINZESS prescriptions were filled in the second quarter of 2014, according to IMS Health, representing 36% growth quarter over quarter. More than 1,000,000 LINZESS prescriptions have been filled by more than 375,000 unique 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 81,000 in the second quarter of 2014, according to IMS Health. This represents a greater than 50% increase in prescribers since the beginning of 2014.
- More than 70% of people with commercial insurance or Medicare Part D plans had unrestricted access to LINZESS as of June 2014. Additionally, in June 2014, approximately 75% of people with commercial insurance had a copay of $30 or less, through formulary coverage or the LINZESS Instant Savings Program.

Linaclotide (Rest of World)

- Actavis and Almirall, S.A. began commercializing linaclotide in Canada and Mexico, respectively. Actavis has exclusive rights to commercialize linaclotide in Canada as CONSTELLA® (linaclotide) and, through a sublicense from Actavis, Almirall has exclusive rights to commercialize linaclotide in Mexico as LINZESS. Ironwood will receive royalties in the mid-teens percent based on net sales in Canada and Mexico.
- Almirall continues to commercialize CONSTELLA in Europe, where it has been approved for adult patients with moderate to severe IBS-C. CONSTELLA is available in 10 European countries, including the United Kingdom, Italy, and most recently Spain, with additional country launches expected in 2014. Commercialization of CONSTELLA in Germany was suspended due to an inability to reach agreement with the German National Association of Statutory Health Insurance Funds on a reimbursement price. Almirall continues to evaluate possibilities to provide access to CONSTELLA to appropriate patients in Germany.

Research & Development

- Ironwood and Actavis continue to explore opportunities to evaluate linaclotide in potential additional indications such as opioid-induced constipation (OIC), colorectal cancer prevention, and pediatrics, as well as in a colonic delivery formulation. Ironwood is also leveraging its gastrointestinal and guanylate cyclase expertise to advance a pipeline of additional potential product candidates, including IW‑3718 which is being studied for refractory gastroesophageal reflux disease (GERD), IW-9179 which is being studied for functional dyspepsia and gastroparesis, and IW-1973 and IW-1701, two candidates in its soluble guanylate cyclase (sGC) program being studied for severe cardiovascular diseases. Research and development highlights for the quarter include:
    - Ironwood and Actavis initiated a development program for linaclotide in patients suffering from OIC, with enrollment in a Phase II clinical study anticipated to begin in the third quarter of 2014. Data are expected in the second half of 2015.
    - Ironwood and Actavis completed the nonclinical pediatric post-marketing requirement for LINZESS. The companies are now working with the FDA regarding plans to conduct clinical studies of LINZESS in pediatric patients.
    - Ironwood and Actavis have deprioritized and suspended efforts to develop linaclotide in a fixed dose combination with a proton pump inhibitor (PPI) pending clarity on the clinical and regulatory path.
    - Ironwood continues to enroll patients in a Phase IIa clinical study evaluating its investigational gastric retentive bile acid sequestrant, IW‑3718, for patients with GERD symptoms who have not responded adequately to treatment with a PPI. Data are expected in the first half of 2015.
    - Ironwood identified a second development candidate, IW-1701, in its sGC program. IW-1701 and Ironwood's first sGC candidate, IW-1973, have differentiated pharmacological profiles that may allow for targeting of multiple severe cardiovascular diseases. Ironwood expects to advance IW-1973 into clinical development in the first half of 2015 and advance IW-1701 into clinical development in the second half of 2015.

Corporate and Financials

- **Collaborative Arrangements Revenue.** Collaborative arrangements revenue was approximately $6.8 million in the second quarter of 2014 compared with approximately $14.6 million in the first quarter of 2014. Revenue consisted of $1.8 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 $5.0 million in sales of linaclotide active pharmaceutical ingredient (API), amortization of deferred revenue associated with consideration received from Ironwood's collaboration with Astellas Pharma Inc., revenue recognized under the collaboration with AstraZeneca AB, and milestone and royalty payments based on sales of CONSTELLA in Europe from Almirall.
- **Cost of revenue.** Cost of revenue is recognized upon shipment of linaclotide API to certain licensing partners outside of the U.S. Actavis records costs associated with linaclotide API in the U.S. In the second quarter of 2014, cost of revenue was approximately $10.5 million, as compared to $1.9 million in the first quarter of 2014. The increase in cost of revenue was primarily due to an $8.9 million write-down of linaclotide API to net realizable value, primarily attributable to lower projected sales in the European market, mainly due to the suspension of commercialization of CONSTELLA in Germany.
- **Operating Expenses.** Operating expenses were approximately $51.4 million in the second quarter of 2014, as compared to approximately $57.1 million in the first quarter of 2014. Operating expenses consisted of approximately $22.1 million in research and development (R&D) expenses, which included $2.3 million in non-cash share-based compensation expense, and approximately $29.3 million in selling, general and administrative (SG&A) expenses, which included $3.7 million in non-cash share-based compensation expense.
- **Interest Expense.** Interest expense was approximately $5.3 million in the second quarter of 2014 in connection with the $175 million debt financing executed in January 2013.
- **Net Loss.** Net loss was approximately $60.4 million, or $0.44 per share, in the second quarter of 2014, as compared to approximately $49.6 million, or $0.38 per share, in the first quarter of 2014. Net loss for the second quarter of 2014 includes $8.9 million, or $0.06 per share, due to the write-down of inventory to net realizable value.
- **Cash Position.** Ironwood ended the second quarter of 2014 with approximately $302 million of cash, cash equivalents and available-for-sale securities. Ironwood used approximately $36 million of cash for operations during the second quarter of 2014, as compared to approximately $58 million in the first quarter of 2014.
- **2014 Financial Guidance.** Ironwood today reiterated its financial guidance for 2014. Total operating expenses are expected to be in the range of $215 million to $245 million, consisting of $105 million to $120 million in R&D expenses and $110 million 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 Actavis and Ironwood total 2014 marketing and sales expenses for LINZESS, which it expects to be in the range of $240 million to $270 million.

Conference Call Information

Ironwood will host a conference call and webcast at 4:30 p.m. Eastern Time, on Monday, August 4, to discuss its second 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 67488246. 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 7:30 p.m. Eastern Time, on August 4, running through 11:59 p.m. Eastern Time on August 11, 2014. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 67488246. 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 under 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 due to dehydration in young juvenile mice. The safety and efficacy of LINZESS in pediatric patients under 18 years of age have not been established. In adults with IBS-C or CIC treated with LINZESS, the most commonly reported adverse event was diarrhea.

Ironwood and Actavis plc 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 under 6 years of age. In nonclinical studies, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration in young juvenile mice. Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. The safety and efficacy of LINZESS has not been established in pediatric patients under 18 years of age.

Contraindications

- LINZESS is contraindicated in pediatric patients under 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 children under 6 years of age. The safety and effectiveness of LINZESS in pediatric patients under 18 years of age have not been established. In neonatal mice, increased fluid secretion as a consequence of GC-C agonism resulted in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, children under 6 years of age may be more likely than older children and adults to develop significant diarrhea and its potentially serious consequences.
- Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. 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. The healthcare provider should consider dose suspension and rehydration.

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 and its impact; the launch and commercialization of linaclotide in additional countries and the timing thereof, as well as expectations regarding the commercialization of CONSTELLA in Germany; market size, growth and opportunity, and potential demand, for linaclotide and our product candidates, as well as their potential impact on applicable markets; the anticipated timing of pre-clinical and clinical developments; the timing and results of clinical and pre-clinical trials; the expected period of patent exclusivity; the 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; LINZESS profitability and the timing thereof; inventory levels, gross-to-net adjustments and the correlation between LINZESS net sales and total prescriptions; 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), cash burn, 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 our company revenues, LINZESS or our product candidates; 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, Actavis plc, 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 March 31, 2014, 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)

	June 30, 2014	December 31, 2013
Assets		
Cash, cash equivalents and available-for-sale securities	$301,978	$ 197,602
Accounts receivable, net	4,455	3,213
Inventory	12,989	22,145
Prepaid expenses and other current assets	6,338	6,168
Total current assets	325,760	229,128
Property and equipment, net	33,560	37,376
Other assets	11,744	12,458
Total assets	$371,064	$ 278,962
Liabilities and Stockholders' Equity		
Accounts payable and accrued expenses	$ 24,681	$ 32,037
Current portion of capital lease obligations	1,104	1,139
Current portion of deferred rent	2,817	2,790
Current portion of deferred revenue	6,447	5,074
Current portion of notes payable	6,577	—
Total current liabilities	41,626	41,040
Capital lease obligations	3,158	3,134
Deferred rent	7,431	8,822
Deferred revenue	8,879	11,416
Notes payable	168,139	174,672
Other liabilities	—	1,653
Total stockholders' equity	141,831	38,225
Total liabilities and stockholders' equity	$371,064	$ 278,962

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2013	2014	2013
Revenue	$ 6,840	$ 9,663	$ 21,445	$ 12,918
Cost and expenses:				
Cost of revenue	10,518	3,418	12,442	4,649

Research and development (1)	22,142	24,093	49,286	56,846
Selling, general and administrative (1)	29,299	30,870	59,223	64,244
Collaboration expense	—	11,162	—	35,892
Total cost and expenses	61,959	69,543	120,951	161,631
Loss from operations	(55,119)	(59,880)	(99,506)	(148,713)
Other income (expense), net	(5,238)	(5,269)	(10,477)	(10,338)
Net loss	$ (60,537)	$ (65,149)	$ (109,983)	$ (159,051)
Net loss per share—basic and diluted	$ (0.44)	$ (0.57)	$ (0.82)	$ (1.44)
Weighted average number of common shares used in net loss per share —basic and diluted	138,315	113,441	134,053	110,772

(1) Non-cash compensation expenses reflected in the condensed consolidated statements of operations are as follows:

Research and development	$ 2,271	$ 2,701	$ 4,961	$ 4,925
Selling, general and administrative	$ 3,741	$ 2,116	$ 7,125	$ 5,167

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2014	2013	2014	2013
LINZESS U.S. net sales	$ 62,746	$ 28,763	$123,558	$ 33,265
Commercial costs and expenses[2]	79,424	67,629	139,340	138,669
Net loss on sales of LINZESS	$ (16,678)	$ (38,866)	$ (15,782)	$(105,404)
Ironwood's share of net loss	$ (8,339)	$ (19,433)	$ (7,891)	$ (52,702)
Ironwood's selling, general and administrative expenses[3]	$ 7,806	$ 8,271	$ 15,805	$ 16,810
Profit share adjustment[4]	$ 2,311	$ —	$ 2,311	$ —
Ironwood's collaborative arrangement revenue (expense)	$ 1,778	$ (11,162)	$ 10,225	$ (35,892)

[1] Ironwood collaborates with Actavis 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 Actavis as well as selling, general and administrative expenses incurred by Actavis 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 Actavis.

[4] Ironwood or Actavis may incur additional expenses related to certain contractual obligations, resulting in an adjustment to the company's share of the net profits as stipulated by the collaboration agreement.

Media Relations
Trista Morrison, 617-374-5095
Director, Corporate Communications
tmorrison@ironwoodpharma.com
or

Investor Relations
Meredith Kaya, 617-374-5082
Director, Investor Relations
mkaya@ironwoodpharma.com

Source: Ironwood Pharmaceuticals, Inc.