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Ironwood Pharmaceuticals Details Strategy to Establish Leading Gastrointestinal Therapeutics Company

— Strong First Year for LINZESS® (linaclotide); Leading Indicators Reinforce Significant Opportunity Ahead —

— Detailing Seven GI Clinical Development Programs with Multiple Opportunities to Generate Proof of Concept Data over Next 24 Months —

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) will detail its strategy to establish a leading gastrointestinal (GI) therapeutics company during its Investor Day today in New York City. This strategy leverages Ironwood's strong development and commercial capabilities in addressing GI disorders as well as its pharmacologic expertise in guanylate cyclase (GC) pathways, all of which is based on Ironwood's pioneering work bringing forward LINZESS, the first FDA-approved product in a new class of GI medicines called GC-C agonists.

"At Ironwood, we've had the privilege to successfully discover, develop and commercialize LINZESS, a medicine that is already helping hundreds of thousands of adult patients suffering from IBS-C or CIC. Our commercial and R&D teams are both executing at a very high level: we are working closely with our U.S. partner Forest to drive strong uptake of LINZESS, and we are also building a robust pipeline of potential treatments for other highly symptomatic GI conditions," said Peter Hecht, chief executive officer of Ironwood Pharmaceuticals, Inc. "With LINZESS well on its way to becoming a leading GI brand, we have both the opportunity and the obligation to prioritize the areas of our business that we believe will maximize value for patients and shareholders. We will leverage our development and commercial expertise in an effort to address patient needs across the upper and lower gastrointestinal tract, and we will build on our deep pharmacologic expertise as we work to unlock value from our GC research platform, with a goal of advancing seven GI clinical development programs with multiple opportunities to generate proof of concept data over the next 24 months."

To execute on its strategy, Ironwood will:

- Maximize LINZESS
- Leverage strong commercial capabilities
- Advance robust GI pipeline and guanylate cyclase (GC) research
- Prioritize investments in key value drivers

Maximize LINZESS

Ironwood and Forest Laboratories, Inc. introduced LINZESS in December 2012 for the treatment of adult patients with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). In its first year on the market, LINZESS has delivered strong results across key leading indicators for commercial success, including physician adoption and prescription rates, payer uptake and patient persistency.

As of November 15, 2013, more than 48,000 healthcare practitioners had prescribed LINZESS since its launch, and prescribing is increasing month over month. Approximately 75 percent of LINZESS claims were being paid as of October 2013, with continued progress with the payer and with the companies' automated copay assistance program. Additionally, patient persistency is tracking 40 percent to 57 percent above that seen for certain other prescription products in this category at this stage of their launch. According to IMS Health, more than 190,000 unique patients had filled a prescription for LINZESS through October 2013, with more than 500,000 total prescriptions filled from launch through November 2013.

Ironwood and Forest believe LINZESS has the potential to continue to help more adult patients and build a new category of primary care products. The companies intend to:

- Further engage adult patients through optimization of the marketing mix and expanded direct-to-consumer education beginning in the first half of 2014, seeking to encourage greater patient/physician dialogue.
- Continue to engage with payers with the goal of further improving unrestricted access for commercial plans and

increasing the rate at which claims are paid to greater than 80 percent.

- Optimize the selling effort and maximize the efficiency of the sales force by focusing on the highest prescribing physicians to further accelerate product growth.
- Explore opportunities to strengthen the clinical profile of LINZESS by expanding its utility in additional labeled indications and populations. Ironwood and Forest are working collaboratively to:
    - Initiate a Phase II clinical trial to study linaclotide in opioid-induced constipation, which is expected to begin in the first half of 2014.
    - Initiate a co-administration study of linaclotide and a proton pump inhibitor, which is expected to begin in the second half of 2014, to explore the safety and efficacy of these two categories of drugs when used together and to further investigate the potential for a fixed-dose combination for symptoms of both gastroesophageal reflux disease and IBS-C or CIC.
    - Establish an appropriate plan with the FDA to study age-appropriate formulations of linaclotide in pediatric patients.
    - Continue their partnership with the National Cancer Institute (NCI) on an ongoing NCI-funded Phase I biomarker study to evaluate linaclotide's potential to prevent colorectal cancer.

Leverage Commercial Capabilities

Ironwood has built strong commercial capabilities across marketing, reimbursement, patient engagement and sales, with a highly-skilled team of clinical sales specialists who have built strong relationships with both gastroenterologists and primary care physicians across the U.S. These important Ironwood assets are a growth platform and are expected to generate value with internally and externally developed new products over time.

Advance Robust GI Pipeline and GC Research

Millions of patients suffer from highly symptomatic disorders of the upper or lower gastrointestinal tract and many of these patients are actively seeking care and new treatment options. Many GI disorders may share an underlying physiological cause characterized by visceral hypersensitivity and/or delayed motility — two key aspects that linaclotide's proposed mechanism of action may address.

In addition to working to maximize the utility of linaclotide, Ironwood is advancing multiple development programs aimed at leveraging its expertise in clinical GI disorders:

- **Linaclotide Colonic Delivery:** targeted delivery of orally-administered linaclotide to the distal small intestine and colon designed to potentially enhance lower abdominal symptom relief for IBS-C and CIC sufferers; providing the opportunity to investigate optimizing the clinical profile of linaclotide for multiple GI disorders with lower abdominal pain as a predominant symptom, including other IBS subtypes, ulcerative colitis, and diverticulitis, among others; plan to initiate Phase II clinical trial in mid-2015.
- **IW-9179:** GC-C agonist designed to target upper GI tract conditions; Phase IIa clinical trial to evaluate IW-9179 as a potential treatment for functional dyspepsia ongoing; plan to initiate Phase IIa clinical trial to evaluate IW-9179 in patients with gastroparesis in the first half of 2015.
- **IW-3718:** gastric retentive formulation of a bile acid sequestrant; plan to initiate Phase IIa clinical trial in first half of 2014 to assess utility in refractory gastroesophageal reflux disease.

Building on Ironwood's pioneering research with linaclotide, GC-C and other guanylate cyclases, the company is focusing its research efforts on GC-C agonists and on a second GC that Ironwood has been targeting for a number of years, soluble guanylate cyclase (sGC). sGC is a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development based on Ironwood's expertise in medicinal chemistry, formulation and modulating tissue distribution.

Ironwood expects to initiate an sGC clinical study in the first half of 2015. Priority potential indications for evaluation in the sGC program include pulmonary arterial hypertension and other cardiovascular indications.

Prioritize Investments Across Key Value Drivers

Ironwood is focusing its investments on its priority growth platforms. The company reduced the net cash used in operating activities from $93 million in the first quarter of 2013 to $58 million in the third quarter of 2013 and it expects this trend to continue through 2014 due to revenue growth and expense management. Ironwood reiterated that its projected 2014 LINZESS sales and marketing expenses with Forest are between $250 million and $300 million, as previously stated.

While Ironwood is focused primarily on commercializing its products within the U.S., the company is also establishing a strong global brand and is collaborating with high performing partners to lead the advancement of linaclotide in certain territories worldwide. Ironwood has established linaclotide partnerships in Europe, China, Japan, Canada and Mexico. Ironwood will continue to evaluate opportunities to establish partnerships in its un-partnered territories.

Webcast Information

Ironwood will host a live webcast of its Investor Day, beginning at 8:30 a.m. Eastern Time, on Thursday, December 12. 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 event to ensure adequate time for any software downloads that may be required. A replay of the webcast will be available on Ironwood's website for 90 days following the conference.

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 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 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 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 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, and the investments associated with those 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 anticipated increased operating efficiencies and our projected 2014 sales and marketing 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 and our partner, Forest Laboratories, Inc., are unable to commercialize LINZESS within the guided range of expenses; and the risk that we are unable to effectively reduce our operating expenses to a sufficient magnitude or for a sufficient period of time. 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 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.

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