March 9, 2017

Ironwood Pharmaceuticals Showcases Progress Delivering Innovative Medicines to Patients and Building a Top-Performing Commercial Biotech at R&D Day 2017

- Commercial products expected to drive > 25% compound annual growth rate (CAGR) for Ironwood revenue between 2016 and 2020[1]; pipeline of innovative product candidates expected to accelerate high-margin revenue growth into late 2020s and beyond -

- Near-term catalysts highlighted for key programs including IW-3718, IW-1973 and linaclotide delayed release-1 -

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ:IRWD), a commercial biotechnology company, is hosting an R&D Day today, Thursday, March 9, 2017, beginning at 9:00 a.m. Eastern Time, at its headquarters in Cambridge, Mass. During the event, the company will present its progress delivering innovative medicines to patients and building a top-performing commercial biotech, with a focus on clinical and commercial strategies for three key pipeline programs: IW-3718 for uncontrolled gastroesophageal reflux disease (uGERD); IW-1973 for resistant hypertension (rHTN), heart failure with preserved ejection fraction (HFpEF) and diabetic nephropathy (DN); and linaclotide delayed release-1 (DR1) for irritable bowel syndrome with constipation (IBS-C).

This Smart News Release features an interactive multimedia capsule. View the full release here: http://www.businesswire.com/news/home/20170309005647/en/

"Ironwood's investments in innovation are delivering value for patients and shareholders: we expect to have one of the fastest-growing toplines in the biotech sector from 2016 through 2020," said Peter Hecht, chief executive officer of Ironwood. "Additionally, our mid- to late-stage pipeline is advancing, with a string of recent successes and with multiple near-term value-creating catalysts expected. We believe these next anticipated products will accelerate high-margin growth into the late 2020s and beyond."

Highlights of Key Programs

IW-3718 for Uncontrolled Gastroesophageal Reflux Disease (uGERD)

Ironwood has completed enrollment in a Phase IIb dose-ranging clinical trial of IW-3718, and data from this trial are expected in mid-2017. The company believes positive data would substantially reduce one of the more significant risks in the program, and that this potential medicine could generate greater than $2 billion in estimated U.S. annual peak sales.

- Unmet need: An estimated 10 million people in the U.S. suffer from uGERD, and many millions more suffer globally. This distinct population of patients is taking proton pump inhibitors (PPIs) and continues to experience heartburn symptoms. Data from physician surveys indicate a treatment offering a modest improvement in symptom relief over PPIs alone would be expected to result in physician adoption.
- Program rationale: IW-3718, an investigational gastric retentive formulation of a bile acid sequestrant, is being evaluated to assess its safety and efficacy - including its effect on heartburn severity - when used on top of ongoing PPI therapy in patients with uGERD. Data from a Phase IIa study demonstrated that approximately two-thirds of patients who underwent bile reflux monitoring tested positive for bile reflux into the esophagus, and that patients with ongoing or recent esophagitis indicating they were actively refluxing bile or gastric acid who received IW-3718 with their PPI demonstrated encouraging improvements in relief of heartburn.
- Next steps: The data from the Phase IIb trial expected mid-year will include two key analyses: 1) degree of reduction in heartburn severity for IW-3718 plus PPI versus PPI alone, and 2) define the level for a clinically meaningful improvement based on a patient-reported outcome measure incorporated into the study, and correlate with IW-3718 treatment effects. Given the severity of symptoms in this patient population, the lack of prescription treatment options, industry analogs and market research, Ironwood currently believes an improvement in heartburn severity of at least 15% for IW-3718 plus PPI versus PPI alone would be meaningful to patients and physicians.

IW-1973 for Resistant Hypertension (rHTN), Heart Failure with Preserved Ejection Fraction (HFpEF) and Diabetic

Nephropathy (DN)

In 2017, Ironwood expects to initiate Phase II clinical trials evaluating the investigational soluble guanylate cyclase (sGC) stimulator IW-1973 in three indications: rHTN, HFpEF and DN. The company believes IW-1973 could generate annual peak sales greater than $5 billion globally.

- Unmet need: rHTN, HFpEF and DN are estimated to impact 7 million, 3 million and 8 million patients in the U.S. alone, respectively, and many millions more globally. There are a limited number of treatment options available for these conditions, which are associated with significant morbidity and mortality.
- Program rationale: Dysregulation of the nitric oxide-soluble guanylate cyclase-cyclical guanosine monophosphate (NO-sGC-cGMP) signaling pathway is believed to be linked to multiple vascular and fibrotic diseases, such as rHTN, HFpEF and DN. IW-1973 modulated the NO-sGC-cGMP pathway and improved vascular function, vascular inflammation, fibrosis and metabolism in nonclinical studies.
- Next steps: Ironwood expects to initiate Phase II clinical trials with IW-1973 in all three indications during the second half of 2017.

Linaclotide Delayed Release-1 for Irritable Bowel Syndrome with Constipation (IBS-C)

LINZESS® (linaclotide) is on track to exceed $1 billion in annual U.S. net sales by 2020; LINZESS and linaclotide DR1, if approved, would be expected to co-exist in the market for more than a decade and achieve greater than $2 billion in U.S. annual peak sales.

- Unmet need: Market research has shown that abdominal pain is the most bothersome symptom for IBS-C patients and is what motivates them to seek treatment. Physicians and patients rate LINZESS highly for its effective relief of abdominal pain.
- Program rationale: Linaclotide DR1, an investigational medicine, is being studied to determine if it can provide delivery of linaclotide to the distal small intestine and colon, where the majority of the abdominal pain associated with IBS-C is believed to originate, and if it can improve abdominal pain relief in patients with IBS-C. Phase IIb data demonstrated that 300 mcg linaclotide DR1 resulted in numerically greater abdominal pain improvement compared to placebo and to the 290 mcg immediate release (IR) formulation of linaclotide.
- Next steps: Ironwood and Allergan intend to begin a Phase III program for linaclotide DR1 in adults with IBS-C in the second half of 2017, pending discussions with FDA.

Webcast Information

The R&D Day event will be accessible through the Investors section of the company's website at www.ironwoodpharma.com. To access the webcast, please log on to the Ironwood website at least 15 minutes prior to the start of the call to ensure adequate time for any software downloads that may be required. 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 75432701. The webcast will be available for replay via telephone starting March 9, 2017 at approximately 2:00 p.m. Eastern Time, running through 3:00 p.m. Eastern Time on March 16, 2017. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 75432701. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the webcast has completed.

About LINZESS (linaclotide)

LINZESS is the #1 prescribed brand for the treatment of adult patients with irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC), based on QuintilesIMS data. Since its FDA approval in August of 2012 and subsequent launch in December 2012, nearly 1.5 million unique patients have filled nearly 7 million prescriptions for LINZESS, according to QuintilesIMS.

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, straining and incomplete evacuation associated with CIC. The recommended dose is 290 mcg for IBS-C patients and 145 mcg for CIC patients, with a 72 mcg dose approved for use in CIC depending on individual patient presentation or tolerability. LINZESS should be taken at least 30 minutes before the first meal of the day.

LINZESS is contraindicated in pediatric patients less than 6 years of age. The safety and effectiveness of LINZESS in pediatric patients less than 18 years of age have not been established. In neonatal mice, linaclotide increased fluid secretion as a consequence of GC-C agonism resulting in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age

and older to develop severe diarrhea and its potentially serious consequences. In adults with IBS-C or CIC treated with LINZESS, the most commonly reported adverse event was diarrhea.

LINZESS is not a laxative; it is the first medicine approved by the FDA in a class called guanylate cyclase-C (GC-C) agonists. LINZESS contains a peptide called linaclotide that is structurally related to the naturally occurring peptides guanylin and uroguanylin, which activate the GC-C receptor in the intestine. Activation of GC-C is thought to result 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 the United States, Ironwood and Allergan plc co-develop and co-commercialize LINZESS for the treatment of adults with IBS-C or CIC. In Europe, Allergan markets linaclotide under the brand name CONSTELLA® for the treatment of adults with moderate to severe IBS-C. In Japan, Ironwood's partner Astellas received approval of linaclotide under the brand name LINZESS for the treatment of adults with IBS-C. Ironwood also has partnered with AstraZeneca for development and commercialization of linaclotide in China and with Allergan for development and commercialization of linaclotide in all other territories worldwide.

LINZESS Important Safety Information

INDICATIONS AND USAGE

LINZESS (linaclotide) is indicated in adults for the treatment of both irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC).

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS
LINZESS is contraindicated in patients less than 6 years of age. In nonclinical studies in neonatal mice, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration. Use of LINZESS should be avoided in patients 6 years to less than 18 years of age. The safety and effectiveness of LINZESS have not been established in patients less than 18 years of age.

Contraindications

- LINZESS is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions

Pediatric Risk

- LINZESS is contraindicated in patients less than 6 years of age. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. In neonatal mice, linaclotide increased fluid secretion as a consequence of GC-C agonism resulting in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age and older to develop severe diarrhea and its potentially serious consequences.
- Use of LINZESS should be avoided in pediatric patients 6 years to less than 18 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 years to less than 18 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction in LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. The incidence of diarrhea was similar in the IBS-C and CIC populations. Severe diarrhea was reported in 2% of 145 mcg and 290 mcg LINZESS-treated patients, and in < 1% of 72 mcg LINZESS-treated CIC patients. If severe diarrhea occurs, dosing should be suspended and the patient rehydrated.

Common Adverse Reactions (incidence ≥2% and greater than placebo)

- In IBS-C clinical trials: 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 trials of a 145 mcg dose: 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%). In a CIC trial of a 72 mcg dose: diarrhea (19% vs 7% placebo) and abdominal distension (2% vs < 1%).

Please see full Prescribing Information including Boxed Warning: http://www.allergan.com/assets/pdf/linzess_pi

About Uncontrolled Gastroesophageal Reflux Disease

An estimated 10 million people in the U.S. suffer from uncontrolled gastroesophageal reflux disease (uGERD); this distinct population of patients continues to experience symptoms such as heartburn and regurgitation despite receiving the current standard of care treatment with a proton pump inhibitor (PPI). While PPIs suppress production of stomach acid, research suggests reflux of bile from the intestine into the stomach and esophagus may play a role in the ongoing symptoms of uGERD. There are no FDA-approved prescription treatment options for these patients. If left untreated, uGERD can lead to serious complications including Barrett's esophagus and, in rare instances, esophageal cancer.

About IW-3718

IW-3718 is a novel, investigational gastric retentive formulation of a bile acid sequestrant, developed by Ironwood using the proprietary Acuform® drug delivery technology licensed from Depomed, Inc. IW-3718 is designed to remain in the stomach and duodenum (upper small intestine) over an extended period of time and to work in combination with a PPI to reduce the detrimental effects of bile and acid on the esophagus.

About Ironwood's sGC Program

Soluble guanylate cyclase (sGC), a central component of the NO-sGC-cGMP pathway, plays an important role in regulating diverse physiological processes such as blood flow, inflammation, fibrosis, and metabolism. Dysregulation of sGC may play a role in multiple vascular and fibrotic diseases with high unmet need such as diabetic nephropathy, resistant hypertension, heart failure, achalasia, sickle cell disease and vascular dementia. Ironwood established its expertise in this signaling pathway through the discovery and development of linaclotide, a guanylate cyclase C (GC-C) agonist. Stimulation of sGC is a clinically validated approach, and Ironwood leveraged its GC-C expertise to discover and develop multiple sGC stimulators. IW-1973 is currently being studied in diabetes patients with hypertension and IW-1701 is being studied in achalasia.

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is a commercial biotechnology company focused on creating medicines that make a difference for patients, building value for our fellow shareholders, and empowering our passionate team. We are commercializing two innovative primary care products: linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC), and lesinurad, which is approved to be taken with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with uncontrolled gout. We are also advancing a pipeline of internally and externally generated innovative product candidates in areas of significant unmet need, including uncontrolled gastroesophageal reflux disease and vascular and fibrotic diseases. Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. For more information, please visit www.ironwoodpharma.com or www.twitter.com/ironwoodpharma; information that may be important to investors will be routinely posted in both these locations.

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the development, launch, introduction and commercial potential of linaclotide, lesinurad, our product candidates and the other products that we promote and the drivers, timing, impact and results thereof (including near-term value-creating catalysts); reduction of a significant risk from IW-3718, if Phase IIb data is positive; market size, prevalence, growth and opportunity, including peak sales and the potential demand for linaclotide, lesinurad and our product candidates, as well as their potential impact on applicable markets; the potential indications for, and benefits of, linaclotide, lesinurad and our product candidates; the anticipated timing of preclinical, clinical and regulatory developments and the design, timing and results of clinical and preclinical studies; the potential for, and timing of, regulatory submissions and approvals for linaclotide, lesinurad and our product candidates, and the level of risk associated with the path to approval; expected periods of patent exclusivity; the strength of the intellectual property protection for linaclotide, lesinurad and our product candidates and our intentions and efforts to protect such intellectual property; our potential for sustainable, high-margin growth and shareholder returns; consensus expectations related to revenue growth for certain

commercial biotech companies; expectations concerning if and when we will become cash flow positive; and our financial performance and results, and guidance and expectations related thereto (including the drivers and timing thereof), including expectations related to Ironwood revenue CAGR, cash flow accretion, margin expansion and revenue growth, LINZESS U.S. net sales and growth, commercial margin and commercial costs, LINZESS profitability and Ironwood revenues. 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 those related to the effectiveness of development and commercialization efforts by us and our partners; preclinical and clinical development, manufacturing and formulation development; our reliance on AstraZeneca to provide critical support services related to lesinurad; the risk that findings from our completed nonclinical and clinical studies may not be replicated in later studies; efficacy, safety and tolerability of linaclotide, lesinurad and our product candidates; decisions by regulatory authorities; the risk that we are unable to successfully integrate lesinurad into our existing business, commercialize lesinurad or realize the anticipated benefits of the lesinurad transaction; the risk that we may never get sufficient patent protection for linaclotide and our product candidates or that we are not able to successfully protect such patents; the outcomes in legal proceedings to protect or enforce the patents relating to our products and product candidates, including ANDA litigation; developments in the intellectual property landscape; challenges from and rights of competitors or potential competitors; the risk that our planned investments do not have the anticipated effect on our company revenues, linaclotide, lesinurad or our product candidates; the risk that we are unable to manage our operating expenses or cash use for operations, or are unable to commercialize our products, within the guided ranges or otherwise as expected; and the risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Annual Report on Form 10-K for the year ended December 31, 2016, and in our subsequent SEC filings. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Ironwood undertakes no obligation to update these forward-looking statements.

[1] The > 25% Ironwood revenue CAGR calculation excludes any current or future revenue recognized in the period related to milestone payments to Ironwood, including approximately $39 million recognized in 2016.

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