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Ironwood Reports Positive Top-Line Data from Exploratory Phase IIa Trial Of IW-3718 in Refractory Gastroesophageal Reflux Disease

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) announced today that top-line data from an exploratory Phase IIa clinical study indicate IW-3718 improved heartburn and certain other symptoms associated with refractory gastroesophageal reflux disease (GERD). Based on these initial data, Ironwood intends to advance IW-3718 into a dose-ranging Phase IIb study.

Refractory GERD, which affects an estimated 8 million Americans, is characterized by the chronic presence of symptoms such as heartburn despite treatment with a proton pump inhibitor (PPI) to suppress stomach acid. Research suggests some refractory GERD patients may experience reflux of bile from the intestine into the stomach and esophagus. IW-3718 is a novel formulation of a bile acid sequestrant designed to bind over an extended period of time to bile that refluxes into the stomach and upper small intestine, potentially providing symptomatic relief in refractory GERD.

"This study explored the hypothesis that some refractory GERD patients experience bile reflux into the esophagus, and our initial data confirm that hypothesis. Approximately two-thirds or 33 of the 52 patients who underwent bile reflux monitoring tested positive for bile reflux into the esophagus during the pretreatment period of the study," said Mark Currie, Ph.D., senior vice president, chief scientific officer, and president of research and development at Ironwood. "Importantly, the subgroup of patients in this study who tested positive for bile reflux and received IW-3718 demonstrated encouraging improvements in relief of heartburn and certain other upper gastrointestinal symptoms often associated with refractory GERD, when compared to patients receiving placebo."

Heartburn was the most severe and most frequent symptom experienced by patients before starting study treatment. Average baseline heartburn severity among study participants was 3.5 on a 10-point scale, with 0 representing no heartburn and 10 representing very severe heartburn. The improvement in heartburn severity for IW-3718-treated patients was 1.7 points in the overall trial population and 2.1 points in the subgroup of patients who tested positive for bile reflux (versus 1.2 points and 1.1 points, respectively, for the placebo-treated groups in each comparison). In terms of frequency, patients entering the trial reported that only 13.7% of their days were free of heartburn. The percentage of heartburn-free days for IW-3718-treated patients increased by 30.3% in the overall trial population and 34.6% in the bile reflux-positive subgroup (versus 24.7% and 23.6%, respectively, for the placebo-treated groups in each analysis). Patients receiving IW-3718 also demonstrated encouraging improvements in regurgitation and in some upper GI symptoms that are often associated with GERD, including epigastric burning, early fullness and post-prandial fullness. Symptom improvements were greatest in the bile reflux-positive subgroup. Additionally, 45.7% and 56.3% of IW-3718-treated patients in the overall trial population and in the bile reflux-positive subgroup, respectively, were responders regarding degree of relief of overall GERD symptoms (versus 27.7% and 29.4%, respectively, for the placebo-treated groups in each analysis). Certain upper GI symptoms that did not appear to be impacted by treatment included nausea, epigastric pain and bloating. IW-3718 was generally well-tolerated with the most common adverse event being constipation.

The randomized, double-blind, placebo-controlled, multi-site, Phase IIa study enrolled 93 patients with a confirmed diagnosis of GERD who were taking a PPI and continuing to experience frequent GERD symptoms, including heartburn at least four days per week. The trial included a two-week pretreatment period during which baseline symptoms were assessed via an electronic diary, followed by a randomization period in which patients had the option to undergo 24-hour Bilitec® and pH monitoring to assess the extent of esophageal exposure to bile and acid reflux. Patients were randomized to receive either 1,000 mg of IW-3718 or placebo twice-daily for four weeks. Patients continued to take their PPI during the pretreatment, randomization and treatment periods. The exploratory study evaluated a number of GERD-related symptoms rather than specifying a primary endpoint, and as such was not powered to establish the statistical significance of a particular endpoint. Data presented for heartburn severity and heartburn-free days reflect change from baseline to week four. For the responder analysis, responders regarding degree of relief of overall GERD symptoms were defined as patients who reported scores of 1 (completely relieved) or 2 (considerably relieved) on a seven-point scale for at least two out of four weeks in the treatment period, or who reported scores of 1, 2 or 3 (somewhat relieved) for all four weeks.

Ironwood plans to further analyze data from the trial and present the findings at an upcoming medical meeting.

About IW-3718

IW-3718 is a novel, 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 deliver the bile acid sequestrant to the desired sites of action - specifically the stomach and duodenum (upper small intestine) - over an extended period of time. Data from non-clinical studies support the extended release profile of IW-3718.

About Refractory Gastroesophageal Reflux Disease (GERD)

An estimated 8 million Americans suffer from refractory gastroesophageal reflux disease (GERD), experiencing continued symptoms such as heartburn and regurgitation despite receiving the current standard of care treatment with a proton pump inhibitor (PPI) to suppress stomach acid production. There are a limited number of FDA-approved treatment options for these patients. Research suggests reflux of bile from the intestine into the stomach and esophagus may play a role in the ongoing symptoms of refractory GERD patients.

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.

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 top-line assessment of the data from the Phase IIa clinical trial of IW-3718 in refractory GERD and our plans for further analysis; our development plans for IW-3718, including the planned advancement of IW-3718 into a dose-ranging Phase IIb study; the design of the Phase IIa trial and its impact on the results thereof; the design and possible benefits of IW-3718 and its potential as a treatment for refractory GERD; and refractory GERD symptoms and the causes of such symptoms, as well as available treatments, prevalence and unmet need. 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, the risk that we are unable to effectively execute on our clinical program for IW-3718 and do so in a timely and cost-effective manner; those risks related to pre-clinical and clinical development; the risk that findings from our completed nonclinical studies may not be replicated in later clinical trials, or that our clinical trials may not be predictive of the results we may obtain in later-stage clinical trials; the risk that unfavorable findings may arise from new clinical data or additional analyses of existing clinical data; those related to the efficacy, safety and tolerability of IW-3718; those related to decisions made by regulatory authorities; the risk that we may never get sufficient patent protection for IW-3718; those related to intellectual property rights of competitors or potential competitors; the risk that the patient population is not as we presently estimate; and the risks presented by future business decisions made by us, our partners and our competitors or potential competitors. 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, 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.

Ironwood Pharmaceuticals, Inc.
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

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