March 18, 2014

Ironwood Pharmaceuticals Initiates Phase II Clinical Study of IW-3718 in Refractory Gastroesophageal Reflux Disease

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) announced today that dosing has begun in its Phase IIa clinical study of its investigational compound IW-3718 in patients suffering from gastroesophageal reflux disease (GERD) who have not responded adequately to treatment with a proton pump inhibitor (PPI). Data are expected in the first half of 2015.

"There are an estimated 7 million patients in the U.S. who suffer regularly from symptoms of GERD - such as heartburn and regurgitation - despite receiving the current standard of care of treatment with a proton pump inhibitor to suppress stomach acid production. For many of these refractory GERD patients, research suggests reflux of bile acid from the intestine into the stomach and esophagus may play an important role in their ongoing suffering," said Michael Hall, MB. BCh., senior vice president, clinical development of Ironwood. "Refractory GERD is a significant unmet need among those suffering with gastrointestinal disorders, and we are investigating IW-3718 to assess whether it may help prevent bile acid reflux and provide relief for patients."

Preliminary findings from non-clinical studies conducted by Ironwood and collaborators have shown that bile acids can cause relaxation (opening) of the lower esophageal sphincter, which allows reflux of contents from the stomach into the esophagus. Bile and bile acids were also shown to cause increased activity of esophageal nerve fibers in related non-clinical studies. Importantly, these study data suggest that a bile acid sequestrant may be able to block these actions. Collectively, these and other data provide additional evidence to suggest that bile acids could play a role in the pathophysiology of refractory GERD, and that a targeted bile acid sequestrant could have therapeutic utility in the treatment of this disorder.

IW-3718 is a novel gastric retention formulation of a bile acid sequestrant, created by Ironwood, and co-developed with Depomed Inc. through incorporation of its proprietary Acuform® drug delivery technology. 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.

Ironwood is evaluating IW-3718 in a randomized, double-blind, placebo-controlled, multi-site Phase IIa clinical trial. The trial is expected to enroll approximately 90 patients with a confirmed diagnosis of gastroesophageal reflux disease who are taking a PPI and continuing to experience GERD symptoms. Patients will continue to take their PPI with the addition of either IW-3718 or placebo. The exploratory Phase IIa trial will evaluate a number of different GERD symptoms and efficacy endpoints as well as safety and tolerability of IW-3718. More information on the trial can be found here.

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, the European Union, 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 the size and scope of the clinical program for IW-3718, the completion of the Phase II clinical study and the date in which the data from the study will be available, the size of the potential patient population, and the cause of the symptoms suffered by the potential patient population. 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, without limitation, the risk that we are unable to enroll as many patients in the clinical study or on the same timeline as we currently anticipate; the clinical study needs to be discontinued for any reason, including safety, manufacturing or economic reasons; the data from such clinical study is not available when we currently anticipate it; the patient population is not as large as we presently estimate; and the data from non-clinical studies does not support the data from our clinical study. Applicable risks also include those listed under the heading "Risk Factors" and

elsewhere in Ironwood's Annual Report on Form 10-K for the year ended December 31, 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 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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