Ironwood Pharmaceuticals Announces Approval of LINZESS® (linaclotide) in China for the Treatment of Adults with IBS-C

January 15, 2019

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 15, 2019-- Ironwood Pharmaceuticals, Inc. (Nasdaq: IRWD), a commercial biotechnology company, today announced that the National Medical Products Administration (NMPA) approved the marketing application for LINZESS® (linaclotide) for adults with irritable bowel syndrome with constipation (IBS-C) in China. Ironwood anticipates that it will launch the drug with its partner in China, AstraZeneca, in the second half of 2019.

Linaclotide is a guanylate cyclase-C (GC-C) receptor agonist currently approved and available for the treatment of adults with IBS-C or chronic idiopathic constipation (CIC) in the United States and more than 30 other countries.

Tom McCourt, who will become president of Ironwood following completion of its planned separation into two companies, commented, “Today’s regulatory approval in China represents another important step in bringing linaclotide to millions of adult patients suffering from IBS-C in many countries around the world. With approximately 14 million adult patients suffering from IBS-C in China, this approval is incredibly important as it brings a new option to treat some of the bothersome recurring abdominal and constipation symptoms associated with IBS-C.”

Data from the Phase III trial in China indicated that patients treated with linaclotide showed a statistically significant improvement compared to placebo-treated patients for both co-primary endpoints. Regarding the first primary endpoint, 60.0% of linaclotide-treated patients were Abdominal Pain/Discomfort Responders, compared to 48.8% of placebo-treated patients (p=0.001).

Regarding the second primary endpoint, 31.7% of linaclotide-treated patients were IBS Degree of Relief Responders, compared to 15.4% of placebo-treated patients ($p < 0.0001$). Statistically significant improvements were achieved in all pre-specified secondary endpoints in this trial, including abdominal pain, abdominal discomfort, bloating, straining, frequency of complete spontaneous bowel movements, frequency of spontaneous bowel movements and stool consistency.

The most common adverse event reported in linaclotide-treated patients was diarrhea (9.4% for linaclotide vs. 1.2% for placebo). Discontinuation due to diarrhea was 0.7% for linaclotide vs. 0.2% for placebo. Overall rates of discontinuation due to adverse events were 1.7% for linaclotide vs. 1.4% for placebo.

The randomized, double-blind, placebo-controlled Phase III clinical trial randomized 839 adults with IBS-C in China, Australia, Canada, New Zealand and the United States. Patients were randomized 1:1 to receive either 290mcg of linaclotide, or placebo, for 12 weeks. The co-primary endpoints of the trial were (i) 12-Week Abdominal Pain/Discomfort Responder, which is defined as a patient who has at least a 30% improvement in his/her abdominal pain or abdominal discomfort level for at least half of the weeks in the 12-week treatment period, and (ii) 12-Week IBS Degree of Relief Responder, which is defined as a patient who rates their IBS symptoms as being "considerably relieved" or "completely relieved" for at least half of the weeks in the 12-week treatment period.

AstraZeneca and Ironwood are jointly responsible for the development and commercialization of linaclotide in China, with AstraZeneca primarily responsible for local operational execution.

About linaclotide

Linaclotide is a guanylate cyclase-C (GC-C) agonist that is thought to work in two ways based on nonclinical studies. Linaclotide 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. Linaclotide is marketed by Ironwood and Allergan plc in the United States as LINZESS® and is indicated for the treatment of adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). Linaclotide is marketed by Allergan for the treatment of adults with moderate to severe IBS-C in Europe under the brand name CONSTELLA®. Ironwood is partnered with AstraZeneca for development and commercialization of linaclotide in China, Hong Kong and Macau. Astellas also has the exclusive rights to develop and commercialize linaclotide in Japan.

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 discovered, developed and are commercializing linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC). Our pipeline priorities for linaclotide include a Phase IIIb trial evaluating its efficacy and safety on multiple abdominal symptoms, including abdominal bloating, pain, and discomfort in adult patients with IBS-C, as well as research into a formulation of linaclotide designed to relieve abdominal pain associated with IBS.

We are also advancing a pipeline of innovative product candidates in areas of significant unmet need, including persistent gastroesophageal reflux disease, diabetic nephropathy, heart failure with preserved ejection fraction and sickle cell disease. 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.

Forward-Looking Statements

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about Ironwood's business, leadership team, business strategy, pipeline advancement, productivity and the potential of its products and product candidates and their impact; and the completion and timing of the planned separation of Ironwood. 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 possibility that we may not complete the separation of our business on the terms or timeline currently contemplated, if at all, achieve the expected benefits of the separation, and that the separation could harm our business, results of operations and financial condition; the risk that the transaction might not be tax-free; the risk that we may be unable to make, on a timely or cost-effective basis, the changes necessary to operate as independent companies; Cyclerion's lack of independent operating history and the risk that its accounting and other management systems may not be prepared to meet the financial reporting and other requirements of operating as an independent public company; the risk that a separation may adversely impact our ability to attract or retain key personnel; the effectiveness of development and commercialization efforts by us and our partners; preclinical and clinical development, manufacturing and formulation development; the risk that findings from our completed nonclinical and clinical studies may not be replicated in later studies; efficacy, safety and tolerability of our products and product candidates; decisions by regulatory authorities; the risk that we may never get sufficient patent protection for our products 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 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 those risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Quarterly Report on Form 10-Q for the quarter ended September 30, 2018, 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.

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