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Astellas and Ironwood Report Positive Top-Line Data from Phase III IBS-C Trial Conducted in Japan

TOKYO & CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Astellas Pharma Inc. (TSE: 4503) and Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) announced today that the Phase III clinical trial of linaclotide conducted in Japan in adults with irritable bowel syndrome with constipation (IBS-C) met its primary endpoints. Astellas expects to submit a new drug application to the Ministry of Health, Labor and Welfare in Japan in 2016.

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

"I am really pleased to receive the positive top-line data from the Phase III IBS-C trial. Astellas expects linaclotide to provide a new therapeutic option for patients suffering from IBS-C," said Bernhardt G. Zeiher, M.D., President, Development at Astellas Group.

"Linaclotide has now met all primary endpoints in all eight of its Phase III/IIIb clinical trials, spanning two indications, three doses and multiple countries," said Mark Currie, Ph.D., Chief Scientific Officer and President of Research and Development at Ironwood. "Our recent positive Phase III data in China and now in Japan represent important achievements by Ironwood and our global partners toward bringing linaclotide to appropriate patients around the world, and we continue to innovate with linaclotide as part of our mission to address a broad spectrum of patient needs."

Top-line data from the Phase III trial in Japan indicate linaclotide-treated patients showed statistically significant improvement compared to placebo-treated patients for both of the two co-primary endpoints. Regarding the first primary endpoint, 34% of linaclotide-treated patients were Global Assessment of Relief of IBS Symptoms Responders, compared to 18% of placebo-treated patients ($p < 0.001$). Regarding the second primary endpoint, 35% of linaclotide-treated patients were Complete Spontaneous Bowel Movement (CSBM) Overall Responders, compared to 19% of placebo-treated patients ($p < 0.001$). Additionally, improvements were achieved in pre-specified secondary endpoints in this trial covering abdominal and constipation symptoms, including bloating and abdominal pain/discomfort. Diarrhea rates in this trial were 9.6% for linaclotide vs. 0.4% for placebo; all cases were characterized as mild or moderate in severity.

The double-blind, placebo-controlled Phase III clinical trial randomized 500 adults with IBS-C in Japan. Patients were randomized 1:1 to receive either 500 mcg of linaclotide or placebo for 12 weeks. The co-primary endpoints of the trial were (i) Global Assessment of Relief of IBS Symptoms Responder Rate, in which patients rated their improvement in IBS symptoms over each week compared to the baseline period and achieved significant or moderate relief for at least six out of 12 weeks, and (ii) CSBM Overall Responder Rate, in which patients reported experiencing at least three CSBMs per week and an increase of at least one CSBM from baseline in the same week, and achieved both of these measures for at least six out of 12 weeks. The trial also includes an additional 40-week, open-label follow-on study period, which is ongoing.

It is estimated that 2.9% of adults in Japan suffer from IBS-C, and there are no prescription products currently approved in Japan for the treatment of this condition. Ironwood and Astellas entered into a licensing agreement in 2009 to develop and commercialize linaclotide in Japan.

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), with more than 825,000 unique patients in the U.S. having filled more than 3.5 million linaclotide prescriptions since launch, according to IMS Health. Linaclotide is marketed by Allergan for the treatment of adults with moderate to severe IBS-C in Europe under the brand name CONSTELLA®. Ironwood also has partnered with Astellas for development and commercialization of linaclotide in Japan and with AstraZeneca for development and commercialization in China.

About Astellas

Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. We focus on Urology, Oncology, Immunology, Nephrology and Neuroscience as prioritized therapeutic areas while advancing new therapeutic areas and discovery research leveraging new technologies/modalities. We are also creating new value by combining internal capabilities and external expertise in the medical/healthcare business. Astellas is on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at www.astellas.com/en.

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. 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, which include, among other things, statements about the top-line assessment of the data from the Phase III clinical trial of linaclotide in adults with IBS-C; the development and regulatory plans for linaclotide in Japan, and the timing thereof, including the expected submission of a new drug application in Japan; the design of the Phase III trial and its impact on the results thereof; the design and possible benefits of linaclotide and its potential as a treatment for adult men and women IBS-C patients in Japan, as well as the ability of Ironwood and its partners to bring linaclotide to appropriate patients around the world; IBS-C prevalence and unmet need; and market size, growth and opportunity, and potential demand for linaclotide in Japan. 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 Astellas is unable to effectively or timely execute on the development and regulatory plan for linaclotide in Japan; the risk that findings from the completed linaclotide clinical trials may not be predictive of the product's performance, if it is commercialized; 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 linaclotide; those related to decisions made by regulatory authorities and the timing of those decisions; the commercial potential of linaclotide in Japan; the risk that Ironwood and Astellas may never get sufficient patent protection for linaclotide in Japan; those related to intellectual property rights of competitors or potential competitors; the risk that the patient population is not as presently estimated; and the risks presented by future business decisions made by Ironwood, Astellas and their competitors or potential competitors. Applicable risks also include those that are listed in Ironwood's Quarterly Report on Form 10‐Q for the quarter ended September 30, 2015, 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. Neither Ironwood nor Astellas undertakes any obligation to update these forward‐looking statements to reflect events or circumstances occurring after this press release. 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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