December 22, 2016

Ironwood and Allergan Report Topline Phase IIb Data Supporting Further Investigation of Linaclotide Colonic Release-2 (CR2) for Abdominal Pain in Non-Constipation Subtypes of IBS

Data also support potential for broad opportunity to treat additional GI indications associated with abdominal pain

Companies separately announced Phase IIb data with linaclotide colonic release-1 (CR1) for IBS-C

Ironwood to host conference call today at 8:30 a.m. Eastern Time

CAMBRIDGE, Mass. & DUBLIN--(BUSINESS WIRE)-- Ironwood Pharmaceuticals, Inc. (NASDAQ:IRWD) and Allergan plc (NYSE:AGN) announced today topline data from a Phase IIb clinical trial evaluating an investigational linaclotide colonic release-2 (CR2) formulation in adult patients with irritable bowel syndrome with constipation (IBS-C). The data showed that CR2, as intended, numerically improved abdominal pain and other abdominal symptoms, such as bloating and discomfort, relative to placebo, with no apparent effect on bowel movement function. These findings support further investigation of CR2 in specific GI indications where patients experience abdominal pain but are not necessarily constipated, such as IBS-Mixed, IBS with diarrhea, ulcerative colitis and diverticulitis. The companies plan to engage with the U.S. Food and Drug Administration (FDA) to discuss next steps for advancing CR2 into a Phase IIb dose-ranging clinical trial in patients with non-constipation subtypes of IBS.

"There is increasing research into the mechanisms underlying pain and other abdominal symptoms in GI disorders, including IBS, as well as research highlighting the hypersensitivity of pain-sensing nerves in the lower GI tract in many patients suffering from these conditions," said Brennan Spiegel, director of Health Services Research at Cedars-Sinai Health System. "We currently have a limited number of treatment options for these patients, and a medicine that could address abdominal pain without impacting bowel function could represent a real advancement in care."

Linaclotide is currently FDA-approved and available in an immediate release (IR) formulation, LINZESS®, for the treatment of adults with IBS-C or chronic idiopathic constipation (CIC). Linaclotide is thought to work in two ways, based on non-clinical studies: by decreasing the activity of pain-sensing nerves and by increasing fluid secretion into the intestine. Linaclotide CR2 is designed to provide targeted delivery of linaclotide to the colon, where the majority of the abdominal pain associated with IBS-C is believed to originate. This clinical trial was designed to evaluate whether CR2 could further decrease the activity of key pain-sensing nerves in the colon with a minimal effect on fluid secretion. Ironwood and Allergan also announced topline results from the same Phase IIb trial with a second formulation, linaclotide colonic release-1 (CR1), in a separate press release issued today.

The double-blind, placebo-controlled, dose-ranging Phase IIb trial randomized 532 adult patients with IBS-C into one of eight possible treatment arms. This trial was exploratory in nature and comparisons to placebo were evaluated using nominal p-values. In the trial, the average weekly change in Bristol Stool Form Scale (BSFS) scores and frequency of complete spontaneous bowel movements (CSBM) from baseline to week 12 were comparable for CR2 and placebo (BSFS: 1.0 - 1.15 for CR2 compared to 0.94 for placebo on a 7-point scale; CSBM: 0.87 - 1.28 for CR2 compared to 1.11 for placebo), indicating no apparent effect on bowel movement function in this study. In contrast, the average weekly change in abdominal pain from baseline to week 12 ranged from -1.63 to -1.83 across the CR2 dose range studied versus -1.37 for placebo, using an 11-point scale. Reduction from baseline at week 12 in abdominal pain was -33.8% to -36.6% for the CR2 doses compared to -26.2% for placebo. Together these data suggest the potential for CR2 to reduce abdominal pain in GI indications not associated with constipation.

The most common adverse event in CR2 patients in this trial was upper respiratory tract infection/nasopharyngitis, which was reported in 3% of CR2-treated patients and 4.5% of placebo-treated patients. The rate of diarrhea reported in the trial ranged from 0%-3% for CR2-treated patients compared to 1.5% for placebo.

Additional data from the Phase IIb trial are expected to be shared at upcoming scientific meetings and via peer-reviewed publications.

"With the linaclotide colonic release program, our intent was to dial up or down the two components of the linaclotide mechanism of action - the effect on pain-sensing nerves and the effect on fluid secretion - by varying where the drug is delivered," said Mark Currie, Ph.D., chief scientific officer and president of research and development at Ironwood. "These initial data support our hypothesis that delivery in the proximal ileum and colon could allow us to better isolate linaclotide's ability to decrease the activity of pain-sensing nerves in the intestine, and we look forward to advancing CR2 from IBS-C into GI indications where patients experience abdominal pain but not constipation."

"The linaclotide colonic release program is a testament to the pioneering pharmacology work done by Mark Currie and the Ironwood team, which led to linaclotide being the first and only FDA-approved guanylate cyclase-C agonist, and is now continuing to raise the bar for innovation in this field," said David Nicholson, Ph.D., chief R&D officer at Allergan. "The encouraging data from this study warrant further investigation of CR2 and its potential to benefit the additional 20-25 million patients estimated to suffer from non-constipation subtypes of IBS."

Ironwood and Allergan are pursuing patent protection for CR1 and CR2 that, if issued, is expected to provide patent coverage into the mid-2030s.

Ironwood Conference Call Today at 8:30 a.m. ET:

Ironwood will host a conference call and webcast at 8:30 a.m. Eastern Time on Thursday, December 22, to discuss the results of the linaclotide colonic release Phase IIb clinical trial. 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 43363931. To access the webcast, please visit the Investors section of Ironwood's website at www.ironwoodpharma.com at least 15 minutes prior to the start of the call to ensure adequate time for any software downloads that may be required. The call will be available for replay via telephone starting at approximately 11:30 a.m. Eastern Time, on December 22, running through 11:59 p.m. Eastern Time on December 29, 2016. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) using conference ID number 43363931. The archived webcast will be available on Ironwood's website for 14 days beginning approximately one hour after the call has completed.

Study Design

Patients in the double-blind, placebo-controlled, dose-ranging Phase IIb clinical trial were randomized to one of eight groups: one group received placebo, one group received linaclotide 290 mcg (approved formulation), three groups received various doses of linaclotide CR1 (30 mcg, 100 mcg or 300 mcg), and three groups received various doses of linaclotide CR2 (30 mcg, 100 mcg or 300 mcg). The 290 mcg approved formulation was included as a reference group for this study. The trial was designed to evaluate the safety and efficacy of each linaclotide colonic release dose and formulation relative to placebo; the statistical power was based on a linear dose response. Additional objectives included assessing how the two colonic release formulations compared to each other and to the approved 290 mcg formulation of linaclotide. All doses were administered orally, once daily for 12 weeks.

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 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's partner Astellas received approval of linaclotide in Japan 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.

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 advancing a pipeline of innovative medicines in areas of significant unmet need, including irritable bowel syndrome with constipation (IBS-C)/chronic idiopathic constipation (CIC), uncontrolled gout, refractory gastroesophageal reflux disease, and vascular and fibrotic diseases. We discovered, developed and are commercializing linaclotide, the U.S. branded prescription market leader in the IBS-C/CIC category, and we are applying our proven R&D and commercial capabilities to advance multiple internally-developed and externally-accessed product opportunities. 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.

About Allergan plc

Allergan plc (NYSE: AGN), headquartered in Dublin, Ireland, is a bold, global pharmaceutical company and a leader in a new industry model - Growth Pharma. Allergan is focused on developing, manufacturing and commercializing branded pharmaceuticals, devices and biologic products for patients around the world.

Allergan markets a portfolio of leading brands and best-in-class products for the central nervous system, eye care, medical aesthetics and dermatology, gastroenterology, women's health, urology and anti-infective therapeutic categories.

Allergan is an industry leader in Open Science, the Company's R&D model, which defines our approach to identifying and developing game-changing ideas and innovation for better patient care. This approach has led to Allergan building one of the broadest development pipelines in the pharmaceutical industry with 65+ mid-to-late stage pipeline programs in development.

Our Company's success is powered by our more than 16,000 global colleagues' commitment to being Bold for Life. Together, we build bridges, power ideas, act fast and drive results for our customers and patients around the world by always doing what is right.

With commercial operations in approximately 100 countries, Allergan is committed to working with physicians, healthcare providers and patients to deliver innovative and meaningful treatments that help people around the world live longer, healthier lives.

For more information, visit Allergan's website at www.Allergan.com.

Forward-Looking Statement

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these forward-looking statements, including statements about the topline assessment of the data from the Phase IIb clinical trial of CR2; the development and regulatory plans for CR2, and the timing thereof, including further investigation and advancement of CR2, engaging with the FDA and advancing CR2 into a Phase IIb dose-ranging clinical trial; the design of the Phase IIb trial and its impact on the results thereof; the timing of additional Phase IIb data; the potential indications for, and benefits of, CR2; the design and possible benefits of CR2 and its potential as a treatment for patients; prevalence and unmet need; market size, growth and opportunity, and potential demand for CR2 in the U.S.; and the strength of the intellectual property protection for linaclotide. 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 preclinical and clinical development, manufacturing and formulation development; the risk that future clinical studies need to be discontinued for any reason, including safety, tolerability, enrollment, manufacturing or economic reasons; the risk that findings from our completed nonclinical and clinical studies may not be replicated in later studies; efficacy, safety and tolerability of linaclotide; the risk that the therapeutic opportunities for the CR formulations are not as we expect; decisions by regulatory authorities; those risks related to competition and future business decisions made by us and our competitors or potential competitors; 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; developments in the intellectual property landscape; and the risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, Allergan's Annual Report on Form 10-K for the year ended December 31, 2015 and in the subsequent SEC filings of each company. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Ironwood and Allergan undertake no obligation to update these forward-looking statements.

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