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Ironwood and Allergan Announce Supplemental New Drug Application for 72 mcg Linaclotide in Chronic Idiopathic Constipation Has Been Accepted for FDA Review

CAMBRIDGE, Mass. and DUBLIN, June 9, 2016 /PRNewswire/ -- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) and Allergan plc (NYSE: AGN) today announced that the U.S. Food and Drug Administration (FDA) has accepted for review the supplemental New Drug Application (sNDA) for the 72 mcg dose of linaclotide for use in the treatment of adults with chronic idiopathic constipation (CIC). The sNDA for the 72 mcg dose of linaclotide is based on efficacy and safety data from a double-blind, placebo-controlled Phase III clinical trial of 1,223 adult patients with CIC. The FDA Prescription Drug User Fee Act (PDUFA) target action date is expected to occur in early 2017.

If approved by the FDA, the 72 mcg dose of linaclotide would provide an additional treatment option for adult patients with CIC. Linaclotide is currently approved by the FDA for the treatment of adults with CIC as a 145 mcg capsule to be taken once per day. In addition, it is approved for the treatment of adults with irritable bowel syndrome with constipation (IBS-C) as a 290 mcg capsule to be taken once per day. Since FDA approval in December of 2012, more than 1 million unique patients have filled a prescription for linaclotide, according to IMS Health.

About Chronic Idiopathic Constipation

Chronic idiopathic constipation (CIC) is a functional gastrointestinal disorder estimated to impact as many as 35 million adult Americans. CIC is generally characterized by infrequent bowel movements (less than three times per week), but symptoms vary across this broad and heterogeneous patient population and may also include recurrent straining, lumpy or hard stools, and/or a sensation that the bowels are not fully empty. Results derived from responses to a web-based survey commissioned by Allergan and Ironwood suggest that only 12 percent of adult CIC sufferers are medically diagnosed. There are few available prescription treatment options for this condition.

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 also has partnered with Astellas Pharma Inc. for development and commercialization of linaclotide in Japan and with AstraZeneca for development and commercialization in China.

Important Safety Information

WARNING: PEDIATRIC RISK

LINZESS is contraindicated in pediatric patients under 6 years of age. In nonclinical studies, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration in young juvenile mice. Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. The safety and efficacy of LINZESS has not been established in pediatric patients under 18 years of age.

Contraindications

- LINZESS is contraindicated in pediatric patients under 6 years of age.
- LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions

Pediatric Risk

- LINZESS is contraindicated in children under 6 years of age. The safety and effectiveness of LINZESS in pediatric patients under 18 years of age have not been established. In neonatal mice, increased fluid secretion as a consequence of GC-C agonism resulted in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, children under 6 years of age may be more likely than older children and adults to develop significant diarrhea and its potentially serious consequences.
- Use of LINZESS should be avoided in pediatric patients 6 through 17 years of age. Although there were no deaths in older juvenile mice, given the deaths in young juvenile mice and the lack of clinical safety and efficacy data in pediatric patients, use of LINZESS should be avoided in pediatric patients 6 through 17 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction of LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. Severe diarrhea was reported in 2% of LINZESS-treated patients. The incidence of diarrhea was similar in the IBS-C and CIC populations.
- Patients should be instructed to stop LINZESS if severe diarrhea occurs and to contact their healthcare provider. The healthcare provider should consider dose suspension and rehydration.

Adverse Reactions

- In IBS-C clinical trials, the most common adverse reactions in LINZESS-treated patients (incidence ≥2% and greater than placebo) were diarrhea (20% vs 3% placebo), abdominal pain (7% vs 5%), flatulence (4% vs 2%), headache (4% vs 3%), viral gastroenteritis (3% vs 1%) and abdominal distension (2% vs 1%).
- In CIC clinical trials, the most common adverse reactions in LINZESS-treated patients (incidence ≥2% and greater than placebo) were diarrhea (16% vs 5% placebo), abdominal pain (7% vs 6%), flatulence (6% vs 5%), upper respiratory tract infection (5% vs 4%), sinusitis (3% vs 2%) and abdominal distension (3% vs 2%).

Please see full Prescribing Information including Boxed Warning: http://www.allergan.com/assets/pdf/linzess_pi

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), refractory gastroesophageal reflux disease, uncontrolled gout, 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

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

Allergan markets a portfolio of best-in-class products that provide valuable treatments for the central nervous system, eye care, medical aesthetics, gastroenterology, women's health, urology, cardiovascular and anti-infective therapeutic categories, and operates the world's third-largest global generics business, providing patients around the globe with increased access to affordable, high-quality medicines. Allergan is an industry leader in research and development, with one of the broadest development pipelines in the pharmaceutical industry and a leading position in the submission of generic product applications globally.

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.

This press release contains forward-looking statements. Investors are cautioned not to place undue reliance on these

forward-looking statements, including statements about the PDUFA target action date for the 72 mcg dose of linaclotide and the potential benefits of the 72 mcg dose of 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 the effectiveness of commercialization efforts by Ironwood and Allergan; efficacy, safety and tolerability of linaclotide; decisions by regulatory authorities; challenges from and rights of competitors or potential competitors; and those risks listed under the heading "Risk Factors" and elsewhere in Ironwood's Quarterly Report on Form 10-Q for the quarter ended March 31, 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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