



## **Ironwood Pharmaceuticals to Present New Data for Linaclotide, Linaclotide Delayed Release and IW-1701 at Digestive Disease Week® 2017**

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- [Ironwood Pharmaceuticals, Inc.](http://www.ironwoodpharm.com) (NASDAQ: IRWD), a commercial biotechnology company, today announced that the company and its collaborators will present clinical and preclinical data for linaclotide and linaclotide delayed release, as well as preclinical data for IW-1701, during Digestive Disease Week (DDW) in Chicago, May 6 through May 9, 2017.

Linaclotide and linaclotide delayed release are guanylate cyclase-C (GC-C) agonists which act by a mechanism pioneered by Ironwood scientists; IW-1701 stimulates soluble guanylate cyclase (sGC), which works through a pharmacologically related signaling pathway. Linaclotide delayed release and IW-1701 are investigational drugs. Researchers will present late-breaking clinical data focusing on the effect of linaclotide delayed release on abdominal pain in Irritable Bowel Syndrome with Constipation (IBS-C), as well as several key preclinical studies focusing on the effect of linaclotide on various models of chronic visceral hypersensitivity. Additional presentations will focus on treatment satisfaction and other analyses of linaclotide in Chronic Idiopathic Constipation (CIC).

The data will be presented via oral and poster presentations as follows:

### **Phase IIb Data on the Effect of Linaclotide Delayed Release on Abdominal Pain in IBS-C (Late-Breaker)**

- | *Targeted delivery of linaclotide to specific areas of the intestine affects clinical efficacy in patients with irritable bowel syndrome with constipation (IBS-C)* (poster presentation Tu2031), by William Chey, M.D., University of Michigan, Division of Gastroenterology, Department of Medicine, Michigan Medicine, Ann Arbor, MI, will be presented at the Clinical Science, Late-Breaking session on Tuesday, May 9, Noon to 2:00 p.m.

### **Treatment Satisfaction and Additional Clinical Analyses of Linaclotide in CIC:**

- | *Indirect treatment comparison: placebo-adjusted results from phase 3 trials of two GC-C agonists in patients with chronic idiopathic constipation - linaclotide and plecanatide* (poster presentation Su1532), by Philip Schoenfeld, M.D., University of Michigan School of Medicine, Ann Arbor, MI, will be presented at the Constipation and Other Functional Colonic Syndromes session taking place on Sunday, May 7, Noon to 2:00 p.m.
- | *The relationship of patient-reported treatment satisfaction with stool consistency and frequency in chronic idiopathic constipation (CIC) patients treated with linaclotide or placebo* (poster presentation Su1526), by Darren Brenner, M.D., Northwestern University Feinberg School of Medicine, Chicago, IL, will be presented at the Constipation and Other Functional Colonic Syndromes session taking place on Sunday, May 7, Noon to 2:00 p.m.
- | *Dose-finding of linaclotide for patients with chronic constipation in Japan: a phase II randomized, double-blind, and placebo-controlled study* (poster presentation Su1543), by Shin Fukudo, M.D., Ph.D., Tohoku University Graduate School of Medicine, Sendai, Japan, will be presented at the Constipation and Other Functional Colonic Syndromes session taking place on Sunday, May 7, Noon to 2:00 p.m.

### **Sustained Response and Additional Clinical Analyses of Linaclotide in IBS-C:**

- | *Intestinal, non-intestinal, and extra-digestive response to linaclotide in patients with irritable bowel syndrome with constipation: results at week 4 predict sustained response* (oral presentation 263), by Enrique Rey, M.D., Hospital Clínico San Carlos, Madrid, Spain, will be presented at the Irritable Bowel Syndrome session taking place on Sunday, May 7, 8:00 a.m. to 9:30 a.m.
- | *Linaclotide is effective and safe for patients with irritable bowel syndrome with constipation in Japan: a phase III randomized, double-blind, and placebo-controlled and long-term extension study* (poster presentation Mo1548), by Shin Fukudo, M.D., Ph.D., Tohoku University Graduate School of Medicine, Sendai, Japan, will be presented at the Irritable Bowel Syndrome: Clinical session taking place on Monday, May 8, Noon to 2:00 p.m.

## Similarities and Differences in Symptoms and Quality of Life for Patients with IBS-C or CIC:

- 1 *Differences in demographic and symptom-related characteristics among patients with irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC): Results from the CONTOR Study* (poster presentation Mo1666), by Jessica Abel, Allergan plc, will be presented at the Patient Reported Outcomes: IBD, GERD, Functional Disorders session taking place on Monday, May 8, Noon to 2:00 p.m.

## Effect of Linaclotide on Various Models of Visceral Hypersensitivity (Preclinical Data):

- 1 *Oral administration of gut-restricted guanylate cyclase-c agonist, linaclotide, reduces endometriosis-induced vaginal hyperalgesia* (poster presentation Mo1541), by Pei Ge, Ironwood Pharmaceuticals, will be presented at the Enteric Neurobiology: Pharmacology and Physiology session taking place on Monday, May 8, Noon to 2:00 p.m.
- 1 *Extracellular cGMP reduces the excitability of sensory dorsal root ganglion neurons via an extracellular mechanism* (oral presentation 723), by Stuart Brierley, Ph.D., SAHMRI, Flinders University, Adelaide, SA, Australia, will be presented at the Basic Mechanisms in Enteric Neurosciences session taking place on Monday, May 8, 4:00 p.m. to 5:30 p.m.
- 1 *Linaclotide attenuates visceral organ crosstalk: importance of guanylate cyclase c (GC-C) activation in reversing colonic hypersensitivity induced by urinary bladder hyperpermeability* (poster presentation Tu1602), by Ehsan Mohammadi, University of Oklahoma Health Science Center, Oklahoma City, OK, will be presented at the Irritable Bowel Syndrome session taking place on Tuesday, May 9, Noon to 2:00 p.m.
- 1 *Chronic oral administration of linaclotide inhibits nociceptive signaling in response to noxious colorectal distension in a model of chronic visceral hypersensitivity* (oral presentation 1098), by Stuart Brierley, Ph.D., SAHMRI, Flinders University, Adelaide, SA, Australia, will be presented at the Sensory Neurobiology, Visceral Nociception and Neuroimmunology session taking place on Tuesday, May 9, 2:00 p.m. to 3:30 p.m.

## Effect of IW-1701 on Relaxation of Lower Esophageal Sphincter (Preclinical Data)

- 1 *The soluble guanylate cyclase stimulator IW-1701 enhances nitric oxide-mediated relaxation of human lower esophageal sphincter ex vivo* (poster presentation Mo1504), by Yueh-Tyng Chien, Ironwood Pharmaceuticals, will be presented at the Functional GI and Motility Disorders session taking place on Monday, May 8, Noon to 2:00 p.m.

## About Linaclotide

Linaclotide is a guanylate cyclase-C (GC-C) agonist that binds to the GC-C receptor locally, within the intestinal epithelium, and is thought to work in two ways, based on nonclinical studies. Activation of GC-C results in increased intestinal fluid secretion and accelerated transit, as well as 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 nearly 1.5 million unique patients in the United States having filled nearly 7 million linaclotide prescriptions since launch, according to IMS Health. In Europe, Allergan markets linaclotide under the brand name CONSTELLA® for the treatment of adults with moderate to severe IBS-C. In Japan, Ironwood's partner Astellas markets linaclotide 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 and with Allergan for development and commercialization of linaclotide in all other territories worldwide.

## LINZESS INDICATIONS AND USAGE

LINZESS (linaclotide) is indicated in adults for the treatment of both irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC).

## IMPORTANT SAFETY INFORMATION

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### WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

LINZESS is contraindicated in patients less than 6 years of age. In nonclinical studies in neonatal mice, administration of a single, clinically relevant adult oral dose of linaclotide caused deaths due to dehydration. Use of LINZESS should be avoided in patients 6 years to less than 18 years of age. The safety and effectiveness of LINZESS has not been established in patients less than 18 years of age.

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## Contraindications

LINZESS is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.

LINZESS is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

## Warnings and Precautions

### *Pediatric Risk*

LINZESS is contraindicated in patients less than 6 years of age. The safety and effectiveness of LINZESS in patients less than 18 years of age have not been established. In neonatal mice, linaclotide increased fluid secretion as a consequence of GC-C agonism resulting in mortality within the first 24 hours due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than patients 6 years of age and older to develop severe diarrhea and its potentially serious consequences.

Use of LINZESS should be avoided in pediatric patients 6 to less than 18 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 years to less than 18 years of age.

### *Diarrhea*

Diarrhea was the most common adverse reaction in LINZESS-treated patients in the pooled IBS-C and CIC double-blind placebo-controlled trials. The incidence of diarrhea was similar in the IBS-C and CIC populations. Severe diarrhea was reported in 2% of 145 mcg and 290 mcg LINZESS-treated patients, and in < 1% of 72 mcg LINZESS-treated CIC patients. If severe diarrhea occurs, dosing should be suspended and the patient rehydrated.

### **Common Adverse Reactions** (incidence =2% and greater than placebo)

In IBS-C clinical trials: 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 trials of a 145 mcg dose: 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%). In a CIC clinical trial of a 72 mcg dose: diarrhea (19% vs 7% placebo) and abdominal distension (2% vs < 1%).

Please see full Prescribing Information: [http://www.allergan.com/assets/pdf/linzess\\_pi](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 commercializing two innovative primary care products: linaclotide, the U.S. branded prescription market leader for adults with irritable bowel syndrome with constipation (IBS-C) or chronic idiopathic constipation (CIC), and lesinurad, which is approved to be taken with a xanthine oxidase inhibitor (XOI) for the treatment of hyperuricemia associated with uncontrolled gout. We are also advancing a pipeline of internally and externally generated innovative product candidates in areas of significant unmet need, including uncontrolled gastroesophageal reflux disease and vascular and fibrotic diseases. Ironwood was founded in 1998 and is headquartered in Cambridge, Mass. For more information, please visit [www.ironwoodpharma.com](http://www.ironwoodpharma.com) or [www.twitter.com/ironwoodpharma](https://www.twitter.com/ironwoodpharma); information that may be important to investors will be routinely posted in both these locations.

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