Constella® (linaclotide), the first approved prescription therapy in a new class of treatments for adults with IBS-C, is now available in Europe

- Constella®, the first and only medicine approved by the European Commission for the symptomatic treatment of moderate to severe Irritable Bowel Syndrome with Constipation (IBS-C) in adult patients, is now available in Germany, UK and Nordic countries

- Constella® has received the recognition by the Scottish Medicines Consortium as adding value to the treatment of adults with IBS-C

Barcelona, June 13th 2013 – Almirall, S.A. (ALM:MC) and Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) announced the launch of Constella® (linaclotide 290mcg capsules once daily), the first approved prescription therapy in a new class of treatments for adults suffering from moderate to severe IBS-C¹, in Europe. Constella® is now available in Germany, the UK and Nordic countries and is expected to be launched in several other European countries in 2013.

Constella is the first and only product approved in the EU for the treatment of IBS-C in adults and has been demonstrated in clinical trials to improve abdominal pain – one of the hallmark symptoms of IBS-C, as well as to improve constipation-related symptoms. IBS is a functional, chronic and relapsing gastrointestinal disorder affecting over 10% of the European population, and it is estimated that one-third of IBS patients suffer from IBS-C² with different degrees of severity. Symptoms associated with IBS-C include abdominal pain and/or discomfort, bloating and constipation.

“The availability of linaclotide is excellent news for the one-third of adult IBS patients that have constipation. The symptoms associated with the condition can negatively impact the lives of patients. A targeted prescription treatment specifically for IBS-C is extremely welcome – for both appropriate patients and physicians alike who can now better manage this unpleasant, chronic condition”, said Professor Eamonn Quigley, Gastroenterologist.

The IBS-C Diagnosis

The diagnosis and management of IBS-C can be frustrating for both patients and clinicians alike³. 30% of gastrointestinal problems reported in general practice consultations are IBS⁴ but only 19% of patients are diagnosed during their first consultation⁴ with 56% of patients requiring up to five consultations before a diagnosis is made.

Adult patients with IBS-C have been shown to not only have a significantly lower level of health-related quality of life compared with healthy individuals, but also similar to patients with asthma, migraine, and other different disease states.³,⁵,⁶

Prior to the approval of Constella, IBS-C treatment options consisted mainly of therapies for individual symptoms such as antispasmodics or unlicensed antidepressants for pain and laxatives for constipation³.
“Thousands of adult patients are seeking help for IBS-C symptoms such as abdominal discomfort and constipation and, up until now, there was no specific prescription treatment available for their disease. Through the combined efforts of many people, we now have the ability to provide relief to many of these adult patients”, said Luciano Conde, Chief Operating Officer at Almirall. “This condition also causes significant distress and economic cost to patients and poses a considerable economic burden in Europe overall.”

“Bringing linaclotide to appropriate patients worldwide is an important aspect of Ironwood’s mission,” said Tom McCourt, Chief Commercial Officer at Ironwood. “Building on our strong initial launch of linaclotide in the U.S., we now hope to make a difference in the lives of adult European IBS-C patients suffering from this prevalent and very bothersome condition.”

The SMC Resolution

 Also, yesterday, the Scottish Medicines Consortium (SMC) recommended Constella® for adult patients with moderate to severe IBS-C who have not responded adequately to or cannot tolerate other suitable treatment options. The SMC clinical experts highlighted an unmet need in this patient group and accepted the use of Constella® within NHS Scotland. Experts welcome “an additional symptomatic treatment for IBS-C in an area where there is a lack of documented, reliable and licensed treatment options”.

Constella® was approved in November 2012 by the European Commission, and it is under registration for regulatory approval in Switzerland.

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Notes to editors

About Constella® (linaclotide)
Linaclotide is a Guanylate Cyclase-C receptor agonist (GCCA) with visceral analgesic and secretory activities. Linaclotide is a 14-amino acid synthetic peptide structurally related to the endogenous guanylin peptide family. Both linaclotide and its active metabolite bind to the Guanylate Cyclase-C (GC-C) receptor, on the luminal surface of the intestinal epithelium. Through its action at GC-C, linaclotide has been shown to reduce visceral pain and increase GI transit in animal models and increase colonic transit in humans. Activation of GC-C results in an increase in concentrations of cyclic guanosine monophosphate (cGMP), both extracellularly and intracellularly. Extracellular cGMP decreases pain-fiber activity, resulting in reduced visceral pain in animal models. Intracellular cGMP causes secretion of chloride and bicarbonate into the intestinal lumen, through activation of the cystic fibrosis transmembrane conductance regulator (CFTR), which results in increased intestinal fluid and accelerated transit.

Linaclotide was discovered by scientists at Ironwood and is marketed in Europe by Almirall through a license agreement between the two companies. Constella® is a trademark owned by Ironwood Pharmaceuticals, Inc.

About Irritable Bowel Syndrome with Constipation (IBS-C)
IBS is defined as a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel function and with features of disordered defecation. IBS-C is
one of four clinically different subtypes of IBS. One-third of patients with IBS are thought to have IBS-C\(^3\) and suffer chronically from both abdominal pain and constipation. The Rome III Diagnostic Criteria for Functional Gastrointestinal Disorders includes criterion for the diagnosis of IBS\(^3\) as:

- Recurrent abdominal pain or discomfort at least three days/month, in the last three months with symptom onset at least 6 months prior to diagnosis, associated with two or more of the following:
  - improvement with defecation
  - onset associated with a change of frequency of stool
  - onset associated with a change in form (or appearance) of stool

The estimated prevalence of IBS over 10% of the European population\(^2\). IBS can have a negative impact on daily living with considerable socio-economic and psychological consequences, and represents a major proportion of gastrointestinal workload in both primary and secondary care. Due to the complex, multimodal nature of the condition there is no cure for IBS and there are minimal therapeutic options.\(^10\)

**About Almirall**
Almirall is a pharmaceutical company committed to provide valuable medicines from its own R&D, external partnerships, licenses and collaborations. In 2012, Almirall invested over 23% of its sales in R&D. Through seeking innovative medicines we aim to become a relevant player in respiratory and dermatology diseases with also a strong interest in gastroenterology and pain. With around 3,000 employees in 22 countries, Almirall generated total revenues of 900 million Euros in 2012.

The company was founded in 1943 and is headquartered in Barcelona, Spain. The stock is traded in the Spanish stock exchange (ticker: ALM). For more information please visit www.almirall.com

**About Ironwood Pharmaceuticals**
Ironwood Pharmaceuticals (NASDAQ: IRWD) is committed to the art and science of making medicines, from discovery through commercialization. We're focused on three goals: transforming knowledge into medicines that make a difference for patients, creating value that will inspire the continued support of our fellow shareholders, and building a team that passionately pursues excellence. Our first product, linaclotide, is approved in the United States and Europe. Our pipeline priorities include exploring further opportunities for linaclotide, leveraging our deep expertise in functional gastrointestinal disorders, and advancing programs in other areas such as allergic conditions, cardiovascular disease, central nervous system disorders and other conditions defined by patient symptoms. 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 to learn more about Ironwood. 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, including, but not limited to, the potential for Constella as a treatment option for the symptomatic treatment of moderate to severe IBS-C in adult men and women, the anticipated launch timing of Constella in various European countries, and the potential for Constella to be approved in Switzerland. 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 the risks that Constella is priced at a point lower than anticipated, Almirall is unable to secure sufficient reimbursement for Constella in various European countries, physicians do not view Constella as an effective or safe treatment option for adult men or women who suffer from moderate to severe IBS-C, Constella is not widely adopted by patients in the E.U., and Almirall is unable to produce an adequate commercial supply of Constella, as well as risks related to the difficulty of predicting regulatory approvals, the acceptance of and demand for new pharmaceutical products, the potential prescribing habits of doctors, the impact of competitive products and pricing, and whether linaclotide will ever be commercialized successfully in a given country. Applicable risks also include those that are listed in Ironwood Pharmaceuticals’ Quarterly Report on Form 10-Q for the quarter ended March 31, 2013, in addition to the risk factors that are listed from time to time in Ironwood Pharmaceuticals’ Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and any subsequent SEC filings. We undertake no 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.

References