Almirall and Ironwood announce positive results from a phase 3 trial with linaclotide in patients with irritable bowel syndrome with constipation

- Top-line results of the phase 3 study with linaclotide show that both primary and main secondary endpoints were met and was well tolerated.

- Irritable bowel syndrome with constipation (IBS-C) is a dehabilitating disease that impacts patient's quality of life.

Barcelona and Cambridge, Mass., September 13, 2010 — Almirall, S.A. (ALM:MC) and Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) today announced positive top-line results from a Phase 3 clinical trial assessing the efficacy and safety of a once-daily dosing of linaclotide 266 mcg in patients with irritable bowel syndrome with constipation.

The two co-primary endpoints required by the European Medicines Agency (EMA) were met in this study, showing statistical significance and clinically relevant improvement for linaclotide-treated patients both for abdominal pain/abdominal discomfort responder and IBS degree of relief responder over the three-month period. Significant improvement was also achieved for all pre-specified main secondary endpoints (stool frequency, stool consistency, straining, and bloating). The safety results were consistent with those observed in previous linaclotide clinical trials, with diarrhoea being the most common adverse event in linaclotide-treated patients.

"IBS is a disease that severely impacts the quality of life of patients and linaclotide is a specific treatment developed for the relief of symptoms in this condition," said Per Olof Andersson, Executive Director R&D, Almirall. *"These results are very promising and we believe linaclotide will be a valuable treatment in an area with such high unmet need. We look forward to the results of the second pivotal trial in Q4 2010 led by our partner Ironwood."*

"The results of this Phase 3 trial, combined with previously reported positive linaclotide trial results, further support our belief that linaclotide has the potential to improve abdominal pain and bowel symptoms, offering a promising treatment for individuals suffering from this chronic gastrointestinal disorder," said Peter Hecht, Chief Executive Officer of Ironwood.

LIN-MD-31, conducted in North America jointly by Ironwood and their U.S. partner Forest Laboratories, Inc., was designed to support regulatory submission in both Europe and the U.S. In a separate press release, Ironwood and Forest announce positive top-line results from this trial for the U.S. endpoints. The trial is part of a larger Phase 3 program investigating the effect of linaclotide treatment on patients with IBS-C. The companies expect the top-line results of the second Phase 3 trial to be available in Q4 2010, after which filing dates in Europe will be determined.

Ironwood has out-licensed linaclotide to Almirall for European development and commercialization. The companies expect to present detailed results of the studies at appropriate scientific conferences.

Phase 3 trial LIN-MD-31

Primary Efficacy Endpoint Results

Trial LIN-MD-31 was a multicenter, randomized, double-blind, placebo-controlled trial conducted in 803 patients meeting modified Rome II criteria for IBS-C. The trial included a two-week pre-treatment baseline period, a 12-week treatment period with patients receiving either a 266 mcg dose of linaclotide or placebo, and a four-week randomized withdrawal period. During the pre-treatment baseline period the mean abdominal pain score was 5.6 (on a 0 – 10 scale where 0 is no abdominal pain and 10 is very severe abdominal pain) with 88 percent of patients suffering from abdominal pain every day. The results for the co-primary endpoints are detailed below:

1. **12-week Abdominal Pain/Abdominal Discomfort Responder**

   A greater proportion of linaclotide-treated patients compared to placebo-treated patients (55 percent vs. 42 percent, p=0.0002) had an improvement from baseline of 30 percent or more in either the mean abdominal pain score or the mean abdominal discomfort score for at least six of the 12 weeks of the treatment period, with neither of these scores worsening from baseline for the same week.

2. **12-week IBS Degree of Relief Responder**

   A greater proportion of linaclotide-treated patients compared to placebo-treated patients (37 percent vs. 18 percent, p<0.0001) responded to the degree of relief of IBS symptoms question with an answer of “considerably relieved” or “completely relieved”, for at least six of the 12 weeks of the treatment period.

All main secondary endpoints measured in LIN-MD-31 (stool frequency, stool consistency, straining and bloating) were statistically significant (p<0.0001) for linaclotide-treated patients compared to placebo-treated patients. There was no evidence of rebound worsening of abdominal or bowel symptoms during the randomized withdrawal period.

The most common adverse events that occurred more frequently in linaclotide-treated patients compared to placebo-treated patients were diarrhoea (19 percent vs. 4 percent), flatulence (5 percent vs. 2 percent), abdominal pain (5 percent vs. 3 percent), and headache (5 percent vs. 4 percent). Overall rates of discontinuation due to adverse events were 8 percent for linaclotide and 3 percent for placebo.

About Almirall

Almirall is an international pharmaceutical company based on innovation and committed to health. Headquartered in Barcelona, Spain, Almirall researches, develops, manufactures and commercialises its own R&D and licensed drugs with the aim of improving people’s health and wellbeing. Almirall focuses its research resources in therapeutic areas related to the treatment of asthma, COPD (Chronic Obstructive Pulmonary Disease), rheumatoid arthritis, multiple sclerosis, psoriasis and other dermatological conditions. Almirall’s products are currently present in over 70 countries while it has direct presence in Europe and Latin America through 12 affiliates. For further information please visit the website at: www.almirall.com.

About Ironwood Pharmaceuticals

Ironwood Pharmaceuticals (NASDAQ: IRWD) is an entrepreneurial pharmaceutical company dedicated to the art and science of great drugmaking. Linaclotide, Ironwood's GC-C agonist, is being evaluated in a confirmatory Phase 3 program for the treatment of irritable bowel syndrome with constipation (IBS-C) and chronic constipation. Ironwood also has a growing pipeline of additional drug candidates in earlier stages of development. Ironwood is located in Cambridge, Mass. To learn more about Ironwood Pharmaceuticals, visit www.ironwoodpharma.com.

This press release contains forward looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. You are hereby cautioned not to place undue reliance on these forward-looking statements, including, but not limited to, our top-line assessment of our Phase 3 IBS-C clinical

trial data and its implications for the future development of linaclotide, linaclotide's potential as a treatment for IBS-C, the timing of our release of additional top-line results from a second linaclotide Phase 3 IBS-C trial, and the timing of the filing of a Marketing Authorization Application 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, among others, the risks that our other linaclotide development activities do not progress, the difficulty of predicting regulatory approvals, the acceptance of and demand for new pharmaceutical products, the impact of competitive products and pricing, whether linaclotide will ever be commercialized successfully and 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 and do not intend 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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About Linaclotide

Linaclotide, a first in class investigational drug, is an agonist of the guanylate cyclase type-C (GC-C) receptor located on the luminal surface of the intestine. In preclinical models, linaclotide has been shown to reduce visceral pain, increase fluid secretion, and accelerate intestinal transit. The effects on secretion and transit are mediated through cyclic guanosine monophosphate (cGMP), which is also believed to modulate the activity of local nerves to reduce pain. Linaclotide is an orally delivered peptide that acts locally in the gut with no measurable systemic exposure at therapeutic doses and is intended for once-daily administration. Linaclotide is in Phase 3 clinical development for the treatment of irritable bowel syndrome with constipation (IBS-C) and chronic constipation. An issued composition of matter patent for linaclotide provides protection to 2025.

Ironwood and Forest are co-developing and co-promoting linaclotide in the United States. Also, Ironwood has out-licensed linaclotide to Almirall for European development and commercialization, and to Astellas Pharma Inc. for development and commercialization in Japan, Indonesia, Korea, the Philippines, Taiwan, and Thailand.

About Irritable Bowel Syndrome with Constipation (IBS-C)

Irritable bowel syndrome (IBS), a functional gastrointestinal disorder, is a recognized complex symptom with abdominal pain and disturbed bowel action. It leads to a substantial reduction in the quality of life, accompanied by considerable socio-economic and psychological consequences[1-4] and represents a major proportion of gastrointestinal workload in both primary and secondary care[5]. The overall prevalence was 11.5% (6.2–12%); 9.6% had current symptoms, 4.8% had been formally diagnosed[6].

There are currently few available therapies to treat this disorder and there is a high rate of dissatisfaction with available therapies. Patients suffering from IBS-C can be affected physically, psychologically, socially, and economically.

About prior Phase IIb trials

Results communicated in this release are consistent with those from a Phase 2b study assessing linaclotide's safety and efficacy in 420 patients with irritable bowel syndrome with constipation (IBS-C). Analysis of the data indicated that once-daily oral dosing of linaclotide, across a range of doses, significantly reduced abdominal pain and significantly improved constipation symptoms in patients with IBS-C throughout the 12-week study period. Those results were presented at the 16th United European Gastroenterology Week in October 2008.

For further information, please refer to Ironwood's press release of March 4th, 2008.

1. Talley NJ, Gabriel SE, Harmsen WS, et al. Medical costs in community subjects with irritable bowel syndrome. Gastroenterology 1995; 109: 1732–41.
2. Longstreth GF. Irritable Bowel Syndrome — a multibillion dollar problem. Gastroenterology 1995; 109: 2029–31.
3. Whitehead WE, Burnett CK, Cook EW III, Taub E. Impact of Irritable Bowel Syndrome on quality of life. Digestive Dis Sci 1996; 41: 2248–53.
4. Jones RH. Clinical economics review — gastrointestinal disease in primary care. Aliment Pharmacol Ther 1996; 10: 233–9.
5. Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence, characteristics and referral. Gut 2000; 46: 77–8.
6. P. S. Hungin et al - The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects - Aliment Pharmacol Ther 2003; 17: 643–650.