



Ironwood and Forest Announce Positive Linaclotide Results from Phase 3 Trial in Patients with Irritable Bowel Syndrome with Constipation

-- Top-line Results Show Trial Met All Primary and Secondary Endpoints --

CAMBRIDGE, Mass. & NEW YORK, Sep 13, 2010 (BUSINESS WIRE) -- Ironwood Pharmaceuticals, Inc. (NASDAQ: IRWD) and Forest Laboratories, Inc. (NYSE: FRX) today announced positive top-line results from the first of two Phase 3 clinical trials assessing the efficacy and safety of the investigational drug, linaclotide, in patients with irritable bowel syndrome with constipation (IBS-C). Analyses of the data indicate clinically meaningful and statistically significant improvement was achieved for linaclotide-treated patients compared to placebo-treated patients for all four primary efficacy endpoints, which included two composite responder endpoints encompassing abdominal pain and complete spontaneous bowel movements (CSBMs), as well as individual responder endpoints for abdominal pain and CSBMs. Significant improvement was also achieved for linaclotide-treated patients compared to placebo-treated patients for all pre-specified secondary endpoints, which are measures of abdominal pain, abdominal discomfort, bloating, and bowel symptoms. The safety results were consistent with those observed in previous linaclotide trials, with diarrhea being the most common adverse event in linaclotide-treated patients. A second Phase 3 trial of linaclotide in IBS-C is ongoing with top-line results expected in Q4 2010.

"The results of this Phase 3 trial, combined with the previously reported positive IBS-C and chronic constipation trial results, further support our belief that linaclotide has the potential to improve abdominal pain and bowel symptoms, offering a promising treatment for more than 30 million individuals suffering from these chronic gastrointestinal disorders," said Peter Hecht, Chief Executive Officer of Ironwood.

"There are millions of patients suffering from IBS-C and limited treatment options to address both their abdominal pain and bowel symptoms, which were improved in this first clinical study," said Howard Solomon, Chairman and Chief Executive Officer of Forest Laboratories. "These results are very promising. We believe linaclotide will be a valuable treatment for these patients. We look forward to receiving the results of the second pivotal trial in Q4 2010."

This trial, LIN-MD-31, is part of Ironwood and Forest's Phase 3 program investigating the effect of linaclotide treatment on patients with IBS-C or chronic constipation (CC). Previously, Ironwood and Forest reported positive results of two Phase 3 trials in patients with CC. The companies expect to file a New Drug Application in mid-2011 in the United States. The IBS-C trials were designed to also support regulatory submission in Europe. Today, in a separate press release, Ironwood and its European partner, Almirall, announced top line results from LIN-MD-31 for the E.U. endpoints.

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 pretreatment baseline period, a 12-week treatment period with patients receiving either a 266 mcg once daily dose of linaclotide or placebo, and a four-week randomized withdrawal period. During the pretreatment 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, 76 percent of patients had no CSBMs. The results for the four primary endpoints are detailed below:

1. Composite responder endpoint 1: abdominal pain and CSBM

-- A greater proportion of linaclotide-treated patients compared to placebo-treated patients (12.1 percent vs. 5.1 percent, $p=0.0004$) had, in the same week, at least a 30 percent reduction in abdominal pain, at least three CSBMs, and an increase of one or more CSBMs. These criteria had to be met for at least nine of the 12 weeks of the treatment period for a patient to be considered a responder for composite responder endpoint 1.

2. CSBM responder endpoint:

-- A greater proportion of linaclotide-treated patients compared to placebo-treated patients (19.5 percent vs. 6.3 percent, $p<0.0001$) had, in the same week, at least three CSBMs and an increase of one or more CSBMs. These criteria had to be met for at least nine of the 12 weeks of the treatment period for a patient to be considered a responder and is a component of composite responder endpoint 1.

3. Abdominal pain responder endpoint:

-- A greater proportion of linaclotide-treated patients compared to placebo-treated patients (34.3 percent vs. 27.1 percent, $p=0.0262$) had at least a 30 percent reduction in abdominal pain. This criterion had to be met for at least nine of the 12

weeks of the treatment period for a patient to be considered a responder and is a component of composite responder endpoint 1.

4. Composite responder endpoint 2: abdominal pain and CSBM

-- A greater proportion of linaclotide-treated patients compared to placebo-treated patients (33.6 percent vs. 21 percent, $p < 0.0001$) had, in the same week, at least a 30 percent reduction in abdominal pain and an increase of one or more CSBMs. These criteria had to be met for at least six of the 12 weeks of the treatment period for a patient to be considered a responder for composite endpoint 2. This recently announced additional primary endpoint also reflects the FDA draft guidance published in March 2010 for evaluating the efficacy of IBS therapies.

All secondary endpoints measured in LIN-MD 31 demonstrated statistically significant (pless-than or equal to 0.0014) improvements for linaclotide-treated patients compared to placebo-treated patients. These endpoints include the individual components of composite responder endpoint 2 (abdominal pain responder and CSBM responder) as well as change from baseline measures of abdominal pain, abdominal discomfort, bloating, percent pain-free days, CSBM frequency, SBM frequency, stool consistency, and straining.

- For the abdominal pain component of composite responder 2, a greater proportion of linaclotide-treated patients compared to placebo-treated patients (50.1 percent vs. 37.5 percent, $p = 0.0003$) had at least a 30 percent or greater reduction in pain for at least six of the 12 weeks of the treatment period.
- For the CSBM component of composite responder 2, a greater proportion of linaclotide-treated patients compared to placebo-treated-patients (48.6 percent vs. 29.6 percent, $p < 0.0001$) had an increase of one or more CSBMs for at least six of the 12 weeks of the treatment period.

Additionally, there was no evidence of rebound worsening of abdominal pain 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 diarrhea (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 the linaclotide-treated patients and 3 percent for the placebo-treated patients.

Forest and Ironwood expect to present detailed results at appropriate scientific conferences.

Glossary of Terms LIN-MD-31

Spontaneous bowel movement (SBM): An SBM is a bowel movement that occurs in the absence of laxative, enema, or suppository usage during the current or preceding day.

Complete spontaneous bowel movement (CSBM): A CSBM is an SBM that is accompanied by the patient self-reporting a feeling of complete emptying of the bowel.

ROME II Criteria: A patient who reports abdominal discomfort or pain for two or more of the following three features for at least 12 weeks, which need not be consecutive, in the 12 months before the screening visit, or before starting chronic treatment with tegaserod or lubiprostone: (1) relieved with defecation; (2) onset associated with a change in frequency of stool; (3) onset associated with a change in form (appearance) of stool.

About Linaclotide

Linaclotide, an 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. Ironwood has out-licensed linaclotide to Amgen 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)

IBS-C is a chronic functional gastrointestinal disorder characterized by abdominal pain, discomfort, and bloating associated with altered bowel habits, and as many as 11 million people in the U.S. suffer from it. 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 Chronic Constipation (CC)

As many as 34 million Americans suffer from symptoms associated with CC and 8.5 million patients have sought treatment. Patients with CC often experience hard and lumpy stools, straining during defecation, a sensation of incomplete evacuation, and fewer than three bowel movements per week, as well as discomfort and bloating. This condition significantly affects patients' quality of life by impairing their ability to work and participate in typical daily activities. There is a high rate of dissatisfaction with currently available treatments.

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.

About Forest Laboratories, Inc.

Forest Laboratories (NYSE: FRX) is a U.S.-based pharmaceutical company with a long track record of building partnerships and developing and marketing products that make a positive difference in people's lives. In addition to its well-established franchises in therapeutic areas of the central nervous and cardiovascular systems, Forest's current pipeline includes product candidates in all stages of development and across a wide range of therapeutic areas. The Company is headquartered in New York, NY. To learn more about Forest Laboratories, visit www.FRX.com.

This press release contains forward looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and relating to the joint development efforts being undertaken by Forest and Ironwood with respect to the development of the pharmaceutical product linaclotide. 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 our filing of a New Drug Application with the FDA 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 joint linaclotide development activities do not progress, the difficulty of predicting FDA approvals, the acceptance of and demand for new pharmaceutical products, the impact of competitive products and pricing, and whether linaclotide will ever be commercialized successfully. In addition, each of Forest and Ironwood (and their respective contributions to the development of linaclotide) may be affected by the risk factors that are listed from time to time in their Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, and other SEC filings. Neither Forest nor Ironwood undertakes any obligation (and neither intends 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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