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## **IRONWOOD PHARMACEUTICALS AND FOREST LABORATORIES ANNOUNCE PRESENTATION OF LINACLOTIDE PHASE 2B CHRONIC CONSTIPATION STUDY RESULTS**

— Data being presented today at Digestive Disease Week —

*CAMBRIDGE, Mass. and New York, May 20, 2008* — Ironwood Pharmaceuticals, Inc. (formerly Microbia, Inc.) and Forest Laboratories, Inc. (NYSE: FRX) today announced the presentation of data from a Phase 2b randomized, double-blind, placebo-controlled study assessing the safety and efficacy of linaclotide in patients with chronic constipation (CC). Analysis of these data indicate that linaclotide met its primary endpoint. The study results are being presented today at the Digestive Disease Week conference in San Diego by Anthony Lembo, M.D. of the Beth Israel Deaconess Medical Center in Boston.

In the four-week study, once-daily doses of linaclotide—75 mcg, 150 mcg, 300 mcg, or 600 mcg—were compared to placebo. The primary endpoint was the change from pre-treatment in weekly spontaneous bowel movement (SBM) frequency. During the two-week pre-treatment period, the mean baseline weekly SBM frequency rate for the intent-to-treat (ITT) population (n = 307) across all treatment groups was 2.3. Patients in the ITT population who received once-daily dosing of linaclotide demonstrated a statistically significant change in weekly SBM frequency of 2.6 (75 mcg,  $p < 0.05$ ), 3.3 (150 mcg,  $p < 0.01$ ), 3.6 (300 mcg,  $p < 0.001$ ), and 4.3 (600 mcg,  $p < 0.001$ ) compared to 1.5 for patients receiving placebo. Increases in SBM frequency were dose-related. At all doses above 75 mcg, linaclotide-treated patients also experienced statistically significant improvements in complete spontaneous bowel movement (CSBM) frequency, stool consistency, straining, bloating, abdominal discomfort, and severity of constipation. Linaclotide was well tolerated at all doses with no treatment-related serious adverse events in any patient during the treatment period. The most common adverse event was diarrhea, which occurred in 5 percent (75 mcg), 9 percent (150 mcg), 5 percent (300 mcg), and 14 percent (600 mcg) of linaclotide-treated patients compared to 3 percent of placebo-treated patients. Diarrhea resulted in the discontinuation of 3 percent of linaclotide-treated patients and none of the placebo-treated patients.

“Chronic constipation is an uncomfortable condition that can adversely affect a patient’s quality of life,” said Anthony Lembo, M.D. “These Phase 2b data indicate that linaclotide has the potential to significantly improve the symptoms associated with CC.”

This study is part of a larger Phase 2 program investigating the effect of linaclotide treatment on patients with CC and irritable bowel syndrome with constipation (IBS-C). Ironwood and Forest previously announced the top-line interim analysis from the IBS-C study. The companies intend to present the Phase 2B IBS-C study data at an appropriate scientific venue later this year. The companies plan to initiate Phase 3 trials in both IBS-C and CC patients in the second half of 2008.

### CC Trial Design

The U.S.-based Phase 2b study was designed to assess the safety, efficacy, and dose response of linaclotide in patients with CC. The primary efficacy endpoint was the change in the overall mean weekly frequency of SBMs from the pre-treatment baseline through the four-week treatment period. Following a no-drug washout period of 14–17 days, patients (n = 310, with equal randomization across treatment groups) were randomized to receive placebo or linaclotide once-daily in the morning at doses of 75 mcg, 150 mcg, 300 mcg or 600 mcg for 28 days. Following completion of the four weeks of double-blind treatment, patients were followed up for safety assessments for an additional two weeks. Bowel function measurements included the number of SBMs and CSBMs compared to baseline, stool consistency using the Bristol Stool Form Scale (BSFS), and straining. Patient-reported outcomes included measures of abdominal pain, abdominal discomfort, and bloating on a daily basis; and constipation severity and overall relief of constipation on a weekly basis. In addition, the use of rescue medication, end-of-treatment satisfaction, and disease-specific quality of life were assessed.

### Glossary of Terms

**Spontaneous bowel movement (SBM):** An SBM is a bowel movement that occurs in the absence of laxative, enema, or suppository usage within the preceding 24 hours.

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

**Bristol Stool Form Scale (BSFS):** A seven-point scale measuring stool consistency. BSFS is a surrogate marker of gastrointestinal transit time.

### About Linaclotide

Linaclotide is a first-in-class compound currently being evaluated for the treatment of IBS-C, CC, and other gastrointestinal disorders. Linaclotide is an agonist of guanylate cyclase type-C, a receptor found on the lining of the intestine. In preclinical testing linaclotide was shown to decrease visceral pain, increase fluid secretion into the intestine, and accelerate intestinal transit. Linaclotide was designed to exert its effect on the intestine with minimal systemic exposure. In Phase 2a trials, linaclotide improved bowel function as measured by both CSBMs and SBMs in patients with CC and IBS-C. An issued composition of matter patent for linaclotide provides

protection to 2025. In September 2007, Ironwood and Forest entered into a 50/50 collaboration to co-develop and co-promote linaclotide in United States.

### **About Chronic Constipation (CC)**

As many as 26 million Americans suffer from CC. 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. The discomfort of CC significantly affects patients' quality of life by impairing their ability to work and participate in typical daily activities.

### **About Irritable Bowel Syndrome (IBS)**

One out of six adults in developed countries suffers from IBS, a chronic condition marked by abdominal pain and disturbed bowel function. IBS accounts for 12% of adult visits to primary care physicians and is the most common disorder diagnosed by gastroenterologists. Health care costs associated with IBS exceed \$25 billion annually. IBS patients fall into three subgroups—constipation-predominant (IBS-C), diarrhea-predominant (IBS-D), and alternating (IBS-A)—and 30% to 40% of these patients suffer from IBS-C. There are currently few available therapies to treat the nine million U.S. patients diagnosed with IBS-C.

### **About Digestive Disease Week (DDW)**

DDW is the largest international gathering of physicians, researchers, and academics in the fields of gastroenterology, hepatology, endoscopy, and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases, the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy, and the Society for Surgery of the Alimentary Tract, DDW takes place May 17-22, 2008, at the San Diego Convention Center, San Diego, CA. The meeting showcases approximately 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. For more information, visit [www.ddw.org](http://www.ddw.org).

### **About Ironwood Pharmaceuticals**

Ironwood Pharmaceuticals (formerly Microbia) ([www.ironwoodpharma.com](http://www.ironwoodpharma.com)) is an entrepreneurial pharmaceutical company dedicated to the science and art of great drugmaking. The Company is advancing several clinical candidates—linaclotide for the treatment of irritable bowel syndrome with constipation, chronic constipation, and other functional gastrointestinal disorders; and novel, next-generation cholesterol absorption inhibitors for the treatment of hypercholesterolemia. Ironwood also has a growing pipeline of additional drug candidates in earlier stages of development. Microbia Precision Engineering, Inc., a majority-owned subsidiary of Ironwood, Inc., is an industrial biotechnology company developing and commercializing novel bioprocesses for the production of specialty chemicals. Ironwood has raised \$231 million in private equity financing and is located in Cambridge, Massachusetts.

### **About Forest Laboratories Inc. and Its Products**

Forest Laboratories is a U.S.-based pharmaceutical company dedicated to identifying, developing, and delivering products that make a positive difference in people's lives. Forest

Laboratories' growing product line includes Lexapro(R) (escitalopram oxalate), an SSRI indicated for adults for the initial and maintenance treatment of major depressive disorder and generalized anxiety disorder; Namenda(R) (memantine HCl), an N-methyl-D-aspartate (NMDA)-receptor antagonist indicated for the treatment of moderate to severe Alzheimer's disease; Campral(R)\* (acamprosate calcium), indicated in combination with psychosocial support for the maintenance of abstinence from alcohol in patients with alcohol dependence who are abstinent at treatment initiation; and Bystolic(R) (nebivolol), a beta-adrenergic receptor blocking agent indicated for the treatment of hypertension. For more information, visit [www.frx.com](http://www.frx.com).

\*Campral is a registered trademark of Merck Santé s.a.s., a subsidiary of Merck KGaA, Darmstadt, Germany.

*Except for the historical information contained herein, this release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements involve a number of risks and uncertainties, including the difficulty of predicting FDA approvals, the acceptance and demand for new pharmaceutical products, the impact of competitive products and pricing, the timely development and launch of new products, and the risk factors listed from time to time in Forest Laboratories' Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, and any subsequent SEC filings.*

Sources: Forest Laboratories, Inc. and Ironwood Pharmaceuticals

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