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The Potential of Dextofisopam for Treatment of Irritable Bowel Syndrome and Inflammatory Bowel Disease

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Purpose: A series of nonclinical and clinical studies were conducted to determine the potential of dextofisopam, the R-enantiomer of the homophthalazine tofisopam, for treating irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD).

Methods: We tested dextofisopam in animal models of IBS and IBD, including the glass bead expulsion test (IBS), the balloon distension test (IBS), and the dextran sodium sulfate (DSS)-induced colitis test (IBD). We also tested the effects of dextofisopam on various aspects of GI function, including basal upper (the charcoal meal test) and lower (fecal output) GI motility, basal gastric acid secretion, and gastric irritancy.

Dextofisopam was also tested in randomized, placebo-controlled, double-blind, single- and multiple-dose Phase 1 clinical trials in healthy human volunteers, and is currently under investigation in a double-blind, placebo-controlled Phase 2 clinical trial in male and female patients with diarrhea-predominant or alternating IBS.

Results: In animal models, dextofisopam attenuated distension-induced contractile activity in the glass bead expulsion test and reduced abdominal contractions in the balloon distension test. In contrast, dextofisopam had little or no effect on basal upper or lower GI motility. Dextofisopam, administered orally, intraperitoneally, or intracolonically, also reduced the signs and symptoms of colitis in the DSS-induced colitis test. At pharmacologically relevant doses, dextofisopam had little or no effect on basal gastric acid secretion and did not cause gastric irritation.

In the two Phase 1 studies in healthy volunteers, single oral doses of up to 400 mg dextofisopam and multiple oral doses of up to 600 mg BID for 7 days were well tolerated, with no serious or severe adverse events and minimal impact on cognitive or motor function. Preliminary, blinded safety data from the ongoing Phase 2 study of dextofisopam in patients with IBS continue to support a favorable safety profile for the drug.

Conclusion: Preclinical data support the potential utility of dextofisopam for the treatment of IBS and IBD. Results from completed Phase 1 studies indicate dextofisopam is well tolerated at daily doses of up to 600 mg BID. Data from an ongoing trial of dextofisopam in patients with IBS continue to support a favorable safety profile for the drug. Additional clinical studies are planned.