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LX1606 / LX1032: A Serotonin Synthesis Inhibitor in a Randomized, Double-Blind Phase 2 Clinical Trial in the U.S. as a Novel Approach for Managing Gastrointestinal (GI) Symptoms in Carcinoid Syndrome

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Background: Carcinoid tumors are mostly derived from EC cells of the midgut, and often produce and release large amounts of serotonin (5-HT). Excess of serotonin is believed to be responsible for many of the symptoms, such as diarrhea, in patients with carcinoid syndrome (CS). LX1606 (a.k.a. LX1032), an orally delivered peripheral tryptophan hydroxylase (TPH) inhibitor, represents a novel approach to potentially alleviate symptoms due to excess 5-HT in carcinoid patients. LX1606 is being developed under Fast Track designation from the FDA.

Methods: The ongoing Phase 2 trial in the U.S. is a 4-week, randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety, tolerability, and effects of a range of doses of LX1606 in patients with symptomatic carcinoid syndrome refractory to stable-dose octreotide LAR therapy. Upon completion of the 28-day blinded portion of the study, patients may continue on open-label treatment for up to 32 additional weeks.

Results: In Phase 1 clinical trials in healthy volunteers, LX1606 was well tolerated when given up to 500 mg 3 times daily. A dose-dependent reduction in urinary 5-HIAA levels was observed, achieving a 50-60% reduction, relative to placebo, by Day 14. Additionally, the 500 mg regimens showed a statistically significant decrease in blood 5-HT levels compared to placebo, confirming the compound's mechanism of action.

Conclusion: LX1606 is a novel, orally-delivered TPH inhibitor with a favorable safety profile in healthy volunteers. Significant reduction in peripheral 5-HT production in Phase 1 studies indicates that LX1606 could be a new approach to managing hyperserotoninemia-related complications of CS. A randomized,

double-blind Phase 2 clinical trial in the U.S. to evaluate the safety, tolerability and effect on symptoms of LX1606 in patients with symptomatic CS not managed by stable-dose long-acting octreotide therapy is ongoing.