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Cumulative Safety Experience of Telotristat Etiprate in Clinical Trials Supports Advancement to Phase 3

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Background: Telotristat etiprate (TE) is a novel, oral inhibitor of serotonin synthesis. TE reduced carcinoid syndrome (CS) gastrointestinal (GI) and other symptoms in Phase 2 studies. We conducted a safety review from 3 Phase 1 studies of healthy subjects and 2 Phase 2 studies of patients with CS.

Methods: Databases were pooled and examined using: 1) 77 special MedDRA queries, 2) adverse events (AEs) by study day, 3) System-organ class (SOC) and preferred term, and 4) laboratory testing.

Results: 121 subjects were included in this analysis, as of 19 January 2013: 88 healthy subjects receiving single- or multiple-dose levels up to 1500 mg/day for up to 14 days; 33 were patients with CS treated with TE at dose levels up to 1500 mg/day for 4 or 12 weeks, depending on the study, with an option to continue into an open-label phase (total of 124 weeks). Of the 33 patients, 16 were on TE for ≥6 months, 11 were on TE for ≥12 months, and 6 were on TE for ≥24 months. There was no common AE theme in any study. All SAEs were assessed as unrelated with the exception of 1 event of nausea and vomiting (N/V) in a patient. Most AEs were assessed as mild-moderate intensity; most resolved spontaneously. In Phase 1 studies, mild increases in hepatic transaminase levels (mostly <2xULN) occurred; 1 subject discontinued therapy (500 mg bid). In Phase 2 studies, no signal for transaminase abnormalities has been observed to date. In all studies, the most common SOC was GI Disorders, particularly N/V; these events occurred relatively early in treatment, usually without recurrence.

Conclusions: This safety review supports advancement of TE to Phase 3 for treatment of CS. The most common events in patients were GI symptoms, consistent with the underlying disease.