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Long-Term Follow Up of Patients with Carcinoid Syndrome Diarrhea Treated with Telotristat Ethyl: A Pooled Analysis of Phase 2 and 3 Trials

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BACKGROUND: Carcinoid syndrome (CS) secondary to metastatic neuroendocrine tumors (NET) is associated with increased morbidity and mortality. Tumoral serotonin secretion in CS can be associated with debilitating diarrhea, resulting in significant health risk and decreased quality of life. Telotristat ethyl (TE), a tryptophan hydroxylase inhibitor, has been shown in studies to be effective and well tolerated in the treatment of CS diarrhea, which is particularly important in a disease with median OS measured in years.

METHODS: The treatment-emergent adverse events (TEAEs) reported during 5 Phase 2 (n=2) and Phase 3 (n=3) clinical trials of TE in patients with CS were pooled. Overall survival was estimated based on a review of long-term safety data including causes of hospitalization and death.

RESULTS: Across the trials, 239 patients with CS were treated with at least 1 dose of TE (250 mg or 500 mg, mostly 500 mg). The mean time from diagnosis to enrollment was 6-8 years. As of January 2018, the mean duration of exposure was 1.6 years (1 week – ~ 6.4 years). Among these patients, at least 1 TEAE and at

least 1 serious TEAE were reported in 98% (n=234) and 49% (n=118) of patients, respectively. Depression-related TEAEs were all mild or moderate in intensity and generally did not limit treatment. The leading causes of hospitalization were gastrointestinal disorders and progression of underlying NET. Survival estimates at 1, 2, and 3 years were 93%, 89%, and 80% out of 125, 96, and 39 patients at risk, respectively (25 deaths in the first 3 years of follow-up). Nearly all deaths were due to progression or complication of underlying disease, with none attributable to TE.

CONCLUSION: The pooled long-term safety data of 5 Phase 2 and 3 clinical trials show safety and survival results that support treatment of CS diarrhea with TE.