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Pharmacokinetics, Pharmacodynamics, Safety, and Tolerability of DP1038, an Intranasal Formulation of Octreotide Acetate, in Healthy Volunteers

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BACKGROUND: Octreotide is a synthetic peptide analog of naturally occurring somatostatin, with similar pharmacological effects but longer duration of action. It inhibits the secretion of growth hormone (GH) from pituitary adenomas for the treatment of acromegaly, and of serotonin and other hormones in the treatment of neuroendocrine tumors (NETs). DP1038 is being developed for the treatment of acromegaly and NETs as a non-invasive alternative to injectable treatments.

METHODS: The Phase 1 trial was conducted in two parts in separate subject cohorts. In Part 1, the pharmacokinetics (PK), safety, and tolerability of DP1038 were assessed in a four-way crossover modified Latin square design, in which 12 subjects received three single intranasal administrations of DP1038 (each at a different dose level), plus a single subcutaneous (SC) administration of octreotide acetate. In Part 2, the pharmacodynamic effect of a single dose of DP1038 was evaluated in 20 subjects in a crossover design and compared to single-dose SC octreotide acetate. Subjects were administered DP1038 (1200 µg) or SC octreotide acetate (100 µg) followed by a GHRH-arginine challenge, a standard test to stimulate GH release, and serial blood sampling to measure GH concentrations over time was performed.

RESULTS: DP1038 was well tolerated, and exhibited a similar safety profile to SC octreotide acetate. Mild, local tolerability events, all grade 1 in severity, included

sneezing and nasal discomfort with occurrence rates per administration of 32.7% and 27.2%, respectively. DP1038 demonstrated a consistent, dose-proportional PK profile with significant nasal bioavailability. In Part 2, DP1038 showed comparable GH suppression to SC octreotide acetate.

CONCLUSION: Therapeutic doses of octreotide acetate can be successfully administered via intranasal delivery, are well tolerated, and efficiently suppress GH secretion during GHRH-arginine challenge. Current clinical results warrant additional testing in larger clinical trials.