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Disease Control in Patients With Acromegaly Switching From Injected Somatostatin Receptor Ligands to Once-Daily Oral Paltusotine: Interim Results of the PATHFNDR-1 Open-Label Extension

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ABSTRACT

Paltusotine is a selective, non-peptide, SST2 receptor agonist in development as a once-daily oral treatment for patients with acromegaly or carcinoid syndrome. PATHFNDR-1 was a randomized, double-blind, placebo-controlled trial that evaluated the efficacy and safety of switching to paltusotine in patients whose acromegaly was controlled (IGF-I ≤1.0× ULN) with injected depot somatostatin receptor ligands (SRLs; octreotide LAR or lanreotide depot). PATHFNDR-1 includes a 36-week randomized controlled (RC) phase and a single-arm, open-label extension

(OLE; currently ongoing). At the end of the RC phase, IGF-I ≤1.0× ULN was maintained in 83.3% of paltusotine-treated patients versus 3.6% of patients in the placebo control group (P<0.0001). The OLE is evaluating the efficacy and safety of longer-term treatment with paltusotine. IGF-I and GH levels were measured at a central laboratory using validated immunoassays. The Acromegaly Symptom Diary (ASD) is a patient-reported outcome measure that consists of 7 core items (headache, joint pain, sweating, fatigue, leg weakness, swelling, numbness/tingling; score range, 0-70; higher scores indicate greater symptom burden). Fifty-eight patients enrolled in the RC phase (paltusotine, n=30; placebo, n=28); 53 of 58 (91.4%) continued into the OLE (paltusotine in RC, n=27; placebo in RC, n=26). As of the analysis cutoff date (15 Aug 2024), median (range) duration of exposure to paltusotine during the OLE was 72.6 (9.4-120.4) weeks. Fifty patients had efficacy data at Study Week 96 (OLE Week 60; efficacy analysis). Mean (SD) IGF-I was 0.93 (0.22)× ULN at OLE baseline (Week 36) and 0.81 (0.21)× ULN at Week 96 (mean change: -0.11; n=50). At Week 96, mean (SD) IGF-I was similar for patients who received paltusotine (0.82 [0.23]× ULN) or placebo (0.80 [0.20]× ULN) in the RC phase. Mean (SD) GH was 1.0 (1.0) ng/mL at OLE baseline and 1.1 (1.2) ng/mL at Week 96. Mean (SD) ASD score was 10.7 (10.5) at OLE baseline and 12.0 (10.3) at OLE Week 96 (mean change, 1.3; n=42). As of this analysis, the most common AEs during the OLE (reported in >3 patients, as of this analysis) were diarrhea (15.1%), nausea (9.4%), fatigue (7.5%), and urinary tract infection (7.5%). Serious AEs were reported in 6 patients, 1 of which was considered treatment-related (bile duct stone). There was 1 study discontinuation due to an AE: a fatal occurrence of acute combined drug intoxication, which was unrelated to study medication. In conclusion, once-daily oral paltusotine maintained biochemical and symptom control and was

well tolerated during long-term treatment in patients with acromegaly who switched from injected SRLs.

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Disclosures

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AC, BH, PJT, RSS, and AK are employees and shareholders of Crinetics Pharmaceuticals.

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MRG reports being a principal investigator (PI) of research grants from Crinetics and Recordati; an occasional consultant for Camurus, Crinetics, Ipsen, Novo Nordisk, and Recordati; and a speaker for Camurus, Ipsen, Novo Nordisk, and Recordati.