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Once-Daily Oral Paltusotine in the Treatment of Patients With Biochemically Uncontrolled Acromegaly: Interim Results of the PATHFNDR-2 Open-Label Extension

Mônica R. Gadelha, MD, PhD[1]; Alessandra Casagrande, MD, PhD[2]; Atanaska Elenkova, MD, PhD[3]; Cesar L. Boguszewski, MD, PhD[4]; Raquel S. Jallad, MD[5]; Beibei Hu, MS[2]; Erika Hubina, MD, PhD[6]; Pouneh K. Fazeli, MD, MPH[7]; Maria Fleseriu, MD[8]; Peter J. Snyder, MD[9]; Christian J. Strasburger, MD[10]; Martin Bidlingmaier, MD[11]; Yining Zhao, MD[12]; Beatriz Soares, PhD, MD[13]; Peter J. Trainer, MD[2]; R. Scott Struthers, PhD[2]; Alan Krasner, MD[2]; Beverly M.K. Biller, MD[14]

[1]Neuroendocrinology Research Center/Endocrinology Division, Medical School and Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [2]Crinetics Pharmaceuticals, Inc., San Diego, CA, USA; [3]Department of Endocrinology, Medical University-Sofia, USHATE "Acad. Ivan Penchev", Sofia, Bulgaria; [4]Department of Internal Medicine, Endocrine Division (SEMPR), University Hospital, Federal University of Paraná, Curitiba, Brazil; [5]Neuroendocrine Unit, Division of Endocrinology and Metabolism, Clinics Hospital, University of São Paulo Medical School, São Paulo, Brazil; [6]2nd Department of Internal Medicine, Division of Endocrinology, Central Hospital of Northern Pest - Military Hospital, Budapest, Hungary; [7]Neuroendocrinology Unit, Division of Endocrinology and Metabolism, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [8]Pituitary Center, Departments of Medicine and Neurological Surgery, Oregon Health and Science

University, Portland, OR, USA; [9]Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Pennsylvania, Philadelphia, PA, USA; [10]Department of Medicine for Endocrinology and Metabolism, Charité Universitaetsmedizin, Campus Mitte, Berlin, Germany; [11]Medizinische Klinik und Poliklinik IV, Klinikum der Universität München, Munich, Germany; [12]Department of Neurosurgery, University Hospital Erlangen, Erlangen, Germany; [13]Department of Internal Medicine, Medical School of the Federal University of Minas Gerais, Belo Horizonte, Brazil; [14]Neuroendocrine and Pituitary Tumor Clinical Center, Massachusetts General Hospital, Boston, MA, USA

Presenting author: Mônica R. Gadelha, MD, PhD

Corresponding author: Alan Krasner, MD

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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-2 was a randomized, double-blind, placebo-controlled trial (24-week randomized controlled [RC] phase; single-arm, open-label extension [OLE; currently ongoing]) that evaluated the efficacy and safety of paltusotine in patients with biochemically uncontrolled acromegaly. The OLE is evaluating the efficacy and safety of longer-term treatment with paltusotine. Of 106 patients who completed the RC phase, 103 (97.2%) continued into the OLE (paltusotine in RC, n=51; placebo in RC, n=52). In addition, 11 patients who met eligibility criteria for the RC phase and were in the screening process when target enrollment was reached were directly enrolled in the OLE. At this interim analysis (data cutoff: September 1, 2024), 88 patients had efficacy data at Study Week 60 (OLE Week 36; efficacy analysis). The safety analysis included all 114 enrolled patients. Compared with OLE baseline, mean IGF-I was maintained in patients who received paltusotine in the RC

(Week 60 mean change, -0.01 xULN; n=40) and decreased in patients who received placebo in the RC (Week 26 mean change, -0.63 xULN; n=52; Week 60 mean change, -0.81 xULN; n=39) and directly enrolled patients (Week 60 mean change, -0.75 xULN; n=9). Mean Acromegaly Symptom Diary score was maintained in paltusotine RC patients (Week 60 mean change, 0.1; n=39) and decreased in placebo RC patients (Week 60 mean change, -1.8; n=39) and directly enrolled patients (Week 60 mean change, -1.1; n=8). As of this analysis, 13 patients (11.4%) had discontinued from the OLE: 9 investigator decision, 2 due to AEs, 1 withdrawal by patient, and 1 requiring prohibited medication. Paltusotine was generally well tolerated. In conclusion, IGF-I levels decreased rapidly in patients who had received placebo during the RC phase and patients with elevated IGF-I who were directly enrolled into the OLE, and the previously observed decrease was sustained in patients who continued on once-daily oral paltusotine. Paltusotine was well tolerated during long-term treatment.
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