PK7-05

Paltusotine in the Treatment of Surgically Naive Patients With Acromegaly: Post Hoc Analysis From Three Clinical Trials

Manoel Ricardo Alves Martins, MD, PhD[1]; Cesar L. Boguszewski, MD, PhD[2]; Roman Junik, MD, PhD[3]; Pouneh K. Fazeli, MD, MPH[4]; Christian J. Strasburger, MD[5]; Martin Bidlingmaier, MD[6]; Mônica R. Gadelha, MD, PhD[7]; Beverly M.K. Biller, MD[8]; Beibei Hu, MS[9]; Alessandra Casagrande, MD, PhD[9]; Lise Kjems, MD, PhD[9]

BACKGROUND

- Surgical resection of the causative pituitary tumor is the recommended first-line treatment for acromegaly[1] but fails to achieve remission in ~50% of patients[2]
- Some patients are not surgical candidates or refuse surgery, or surgery may be delayed[1]
- Paltusotine (PALSONIFY™) is a nonpeptide selective somatostatin 2 receptor agonist approved by the US Food and Drug Administration as a once-daily oral treatment for adults with acromegaly who had an inadequate response to surgery and/or for whom surgery is not an option[3,4]

AIM

- To evaluate the effects of paltusotine in patients with acromegaly without a prior history of pituitary surgery

METHODS

- Post hoc analysis of 20 surgically naive patients

CONCLUSIONS

- In this limited sample of surgically naive patients, paltusotine treatment resulted in IGF-I responses similar to those in the overall study population (including patients with prior surgery)
- Paltusotine was well tolerated in surgically naive patients
- Future studies with larger sample sizes are required to confirm these initial findings

Surgically Naive Patients From Three Clinical Trials

	PATHFNDR-1	PATHFNDR-2	ACROBAT Advance
Study design	Randomized, placebo-controlled trial (phase 3)	Randomized, placebo-controlled trial (phase 3)	Single-arm, open-label extension study (phase 2, ongoing)
Patient population	Biochemically controlled (IGF-I ≤1.0× ULN) on injected depot SRL	Biochemically uncontrolled, no acromegaly medications at randomization	Biochemically controlled or uncontrolled on injected depot SRL ± adjunctive medication
Treatment	Switched (randomly assigned) to paltusotine or placebo	Randomly assigned to paltusotine or placebo	Paltusotine (switched from SRL-based regimen in parent study)
Treatment duration	36 weeks	24 weeks	Up to 3 years (this analysis)
Concomitant acromegaly medications	None	None	Add-on treatment with cabergoline or pegvisomant permitted

IGF-I = insulin-like growth factor 1; SRL = somatostatin receptor ligand; ULN = upper limit of normal.

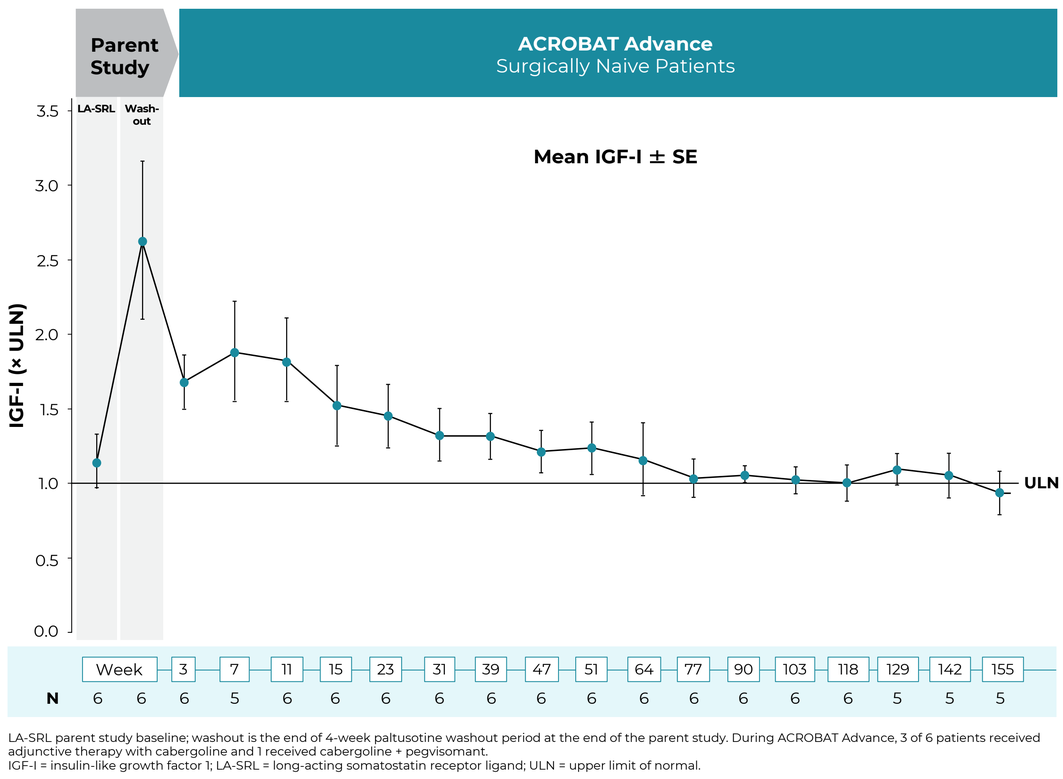
RESULTS

Patient Characteristics and Study Treatment

	PATHFNDR-1 (n=8)	PATHFNDR-2 (n=6)	ACROBAT Advance (n=6)
Age, years, mean (SD)	56.3 (13.1)	57.7 (11.9)	65.5 (4.4)
Female, n (%)	5 (62.5)	3 (50.0)	4 (66.7)
Paltusotine, n	4	1	6
Placebo, n	4	5	—
Baseline IGF-I, × ULN*			
Paltusotine	0.82 (0.19)	1.15 (NE)	1.09 (0.60-1.79)
Placebo	0.91 (0.09)	2.18 (0.62)	—
Paltusotine dose, n (%)			
40 mg/day	2 (50.0)	0 (0)	3 (50.0)
60 mg/day	2 (50.0)	1 (100)	3 (50.0)

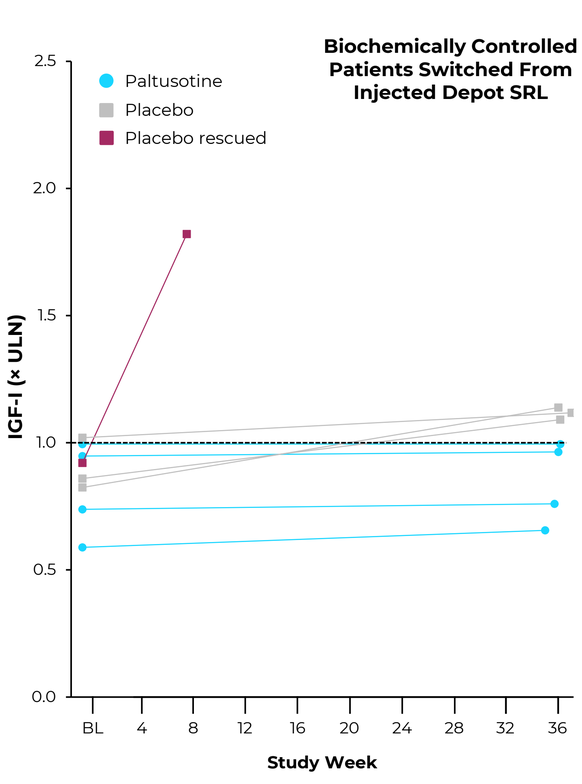
*Mean (SD) for PATHFNDR-1 and PATHFNDR-2; median (range) at parent study baseline for ACROBAT Advance. IGF-I = insulin-like growth factor 1; NE = not evaluable; ULN = upper limit of normal.

ACROBAT Advance: Mean IGF-I Level During Open-Label Treatment With Paltusotine



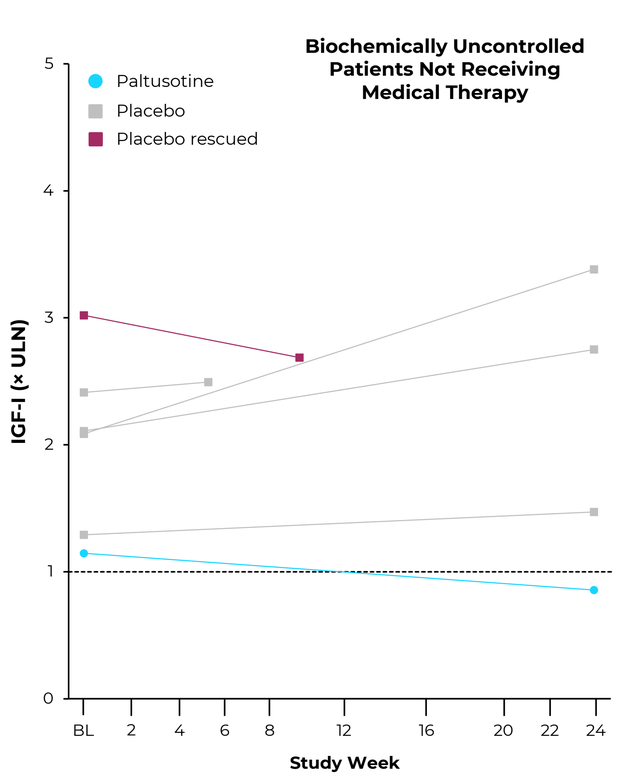
LA-SRL parent study baseline; washout is the end of 4-week paltusotine washout period at the end of the parent study. During ACROBAT Advance, 3 of 6 patients received adjunctive therapy with cabergoline and 1 received cabergoline + pegvisomant.
IGF-I = insulin-like growth factor 1; LA-SRL = long-acting somatostatin receptor ligand; ULN = upper limit of normal.

PATHFNDR-1: IGF-I Level at Baseline and EOT* for Each Patient



*EOT (end of treatment) defined as Week 36 if no rescue medication administered or last assessment prior to rescue.
BL = baseline; EOT = end of treatment; IGF-I = insulin-like growth factor 1; ULN = upper limit of normal.

PATHFNDR-2: IGF-I Level at Baseline and EOT* for Each Patient



*EOT (end of treatment) defined as Week 24 if no rescue medication administered or last assessment prior to rescue.
BL = baseline; EOT = end of treatment; IGF-I = insulin-like growth factor 1; ULN = upper limit of normal.

SAFETY

- 1 paltusotine-treated patient discontinued study participation (ACROBAT Advance) due to inability to fulfill study requirements and procedures
- 3 paltusotine-treated patients (ACROBAT Advance) experienced serious adverse events (osteoarthritis, worsening coronary artery disease, renal oncocytoma) that were considered not related to study medication
- Radiology assessments showed tumor size stability in paltusotine-treated patients

REFERENCES

1. Fleseriu M, et al. *Lancet Diabetes Endocrinol.* 2022;10(11):804-826. **2.** Starnoni D, et al. *Acta Neurochir.* 2016;158(11):2109-2121. **3.** Zhao J, et al. *ACS Med Chem Lett.* 2023;14(1):66-74. **4.** PALSONIFY™ (paltusotine) tablets, for oral use. Package insert. Crinetics Pharmaceuticals, Inc.; 2025.

ACKNOWLEDGMENTS

The authors thank the site investigators, study coordinators/nurses, clinical staff, and patients who participated in these studies.

For author affiliations, additional acknowledgments, and disclosures, please use the QR code.

Crinetics Pharmaceuticals

Deutsche Gesellschaft für Endokrinologie (DGE) 69th Deutscher Kongress für Endokrinologie • March 11-13, 2026 • Weimar, Germany

AUTHOR AFFILIATIONS
[1]Federal University of Ceará Medical School and Drug Research and Development Center, Fortaleza, Brazil; [2]University Hospital, Federal University of Paraná, Curitiba, Brazil; [3]Nicolaus Copernicus University, Collegium Medicum, Bydgoszcz, Poland; [4]University of Pittsburgh School of Medicine, Pittsburgh, PA, USA; [5]Charité Universitaetsmedizin, Berlin, Germany; [6]Klinikum der Universität München, Munich, Germany; [7]Medical School and Hospital Universitario Clementino Fraga Filho, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil; [8]Massachusetts General Hospital, Boston, MA, USA; [9]Crinetics Pharmaceuticals, Inc., San Diego, CA, USA

ACKNOWLEDGMENTS
The studies were funded by Crinetics Pharmaceuticals, Inc. Technical editorial and medical writing assistance were provided under the direction of the authors by Marie-Louise Ricketts, PhD, Crinetics Pharmaceuticals, Inc., and Synchrony Medical Communications, LLC, West Chester, PA, USA; funding for this support was provided by Crinetics Pharmaceuticals, Inc.

AUTHOR DISCLOSURES
MRAM reports serving as a PI of research grants from Crinetics Pharmaceuticals, Inc.; receiving consulting fees, honoraria, and meeting support from Ipsen and Novo Nordisk; and serving on advisory boards for Novo Nordisk and Recordati. CLB reports serving as a PI of research grants from Crinetics Pharmaceuticals, Inc.; having received consulting fees, honoraria, and meeting support from Crinetics Pharmaceuticals, Inc., Ipsen, and Recordati; and serving on an advisory board for Crinetics Pharmaceuticals, Inc. RJ reports serving as a PI of research grants from Crinetics Pharmaceuticals, Inc. PKF reports serving as a PI of research grants from Corcept and Crinetics Pharmaceuticals, Inc.; a consultant for Quest Diagnostics and Regeneron; and an occasional advisory board member for Camurus, Chiesi, Corcept, and Crinetics Pharmaceuticals, Inc. CJS reports serving as a PI of a research grant from Crinetics Pharmaceuticals, Inc., and an occasional consultant/speaker for Alexion, Amolyt Pharma, Crinetics Pharmaceuticals, Inc., Novo Nordisk, Pfizer, Recordati, and Sandoz-Hexal. MB reports serving as a PI of research grants from Amolyt Pharma, Camurus, Chiasma, Crinetics Pharmaceuticals, Inc., IDS, Ionis, Lumos, and OPKO; an occasional consultant for Crinetics Pharmaceuticals, Inc., Ionis, Novo Nordisk, Pfizer, Roche, and Sandoz; and a speaker for Euroimmun, Novo Nordisk, and Pfizer. MRG reports serving as a PI of research grants from Alexion, Crinetics Pharmaceuticals, Inc., Debiopharm, and Recordati; an occasional consultant for Camurus, Crinetics Pharmaceuticals, Inc., Novo Nordisk, and Recordati; and a speaker for Camurus, Crinetics Pharmaceuticals, Inc., Novo Nordisk, and Recordati. BMKB reports serving as a PI of research grants to Massachusetts General Hospital from Alexion, Crinetics Pharmaceuticals, Inc., and Debiopharm; and as an occasional consultant for Alexion, Camurus, Chiesi, Crinetics Pharmaceuticals, Inc., Pfizer, and Recordati. BH and AC are employees of Crinetics Pharmaceuticals, Inc. LK was an employee of Crinetics Pharmaceuticals, Inc., when this work was conducted.