

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

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## BACKGROUND

- Surgical resection of the causative pituitary tumor is the recommended first-line treatment for acromegaly<sup>1</sup> but fails to achieve remission in ~50% of patients<sup>2</sup>
- Some patients are not surgical candidates or refuse surgery, or surgery may be delayed<sup>1</sup>
- 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<sup>3,4</sup>

## 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 I; SRL = somatostatin receptor ligand; ULN = upper limit of normal.

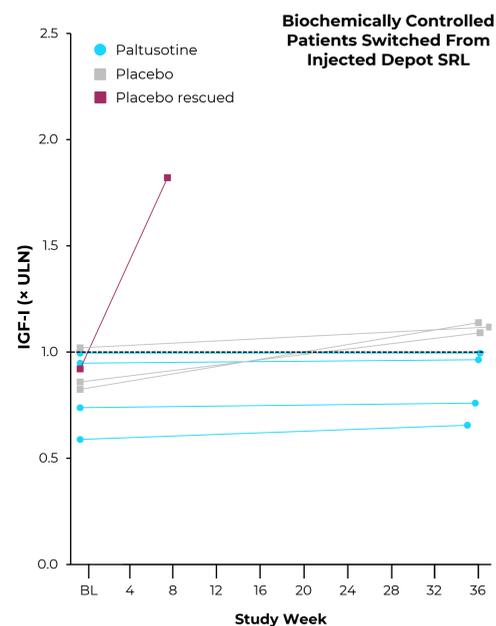
## RESULTS

### 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)

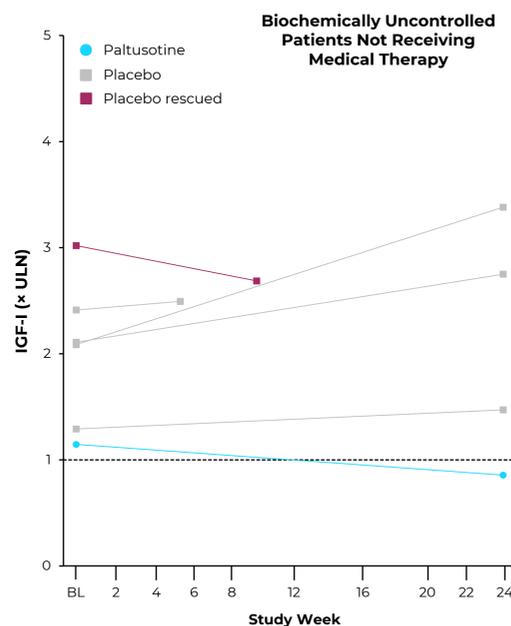
\*Mean (SD) for PATHFNDR-1 and PATHFNDR-2; median (range) at parent study baseline for ACROBAT Advance. IGF-I = insulin-like growth factor I; NE = not evaluable; ULN = upper limit of normal.

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



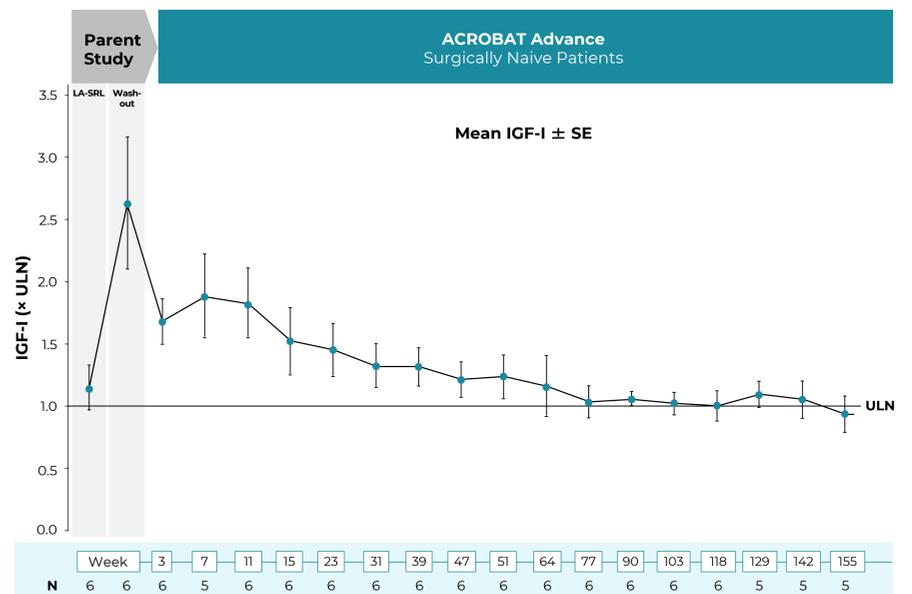
\*EOT (end of treatment) defined as Week 36 if no rescue medication administered or last assessment prior to rescue. BL = baseline; EOT = end of treatment; IGF-I = insulin-like growth factor I; ULN = upper limit of normal.

### 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 I; 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 I; LA-SRL = long-acting somatostatin receptor ligand; 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. Flešeriu 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.

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