# 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

Presenter: Beverly M.K. Biller, MD

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# Author disclosures

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# Paltusotine in development for the treatment of patients with acromegaly

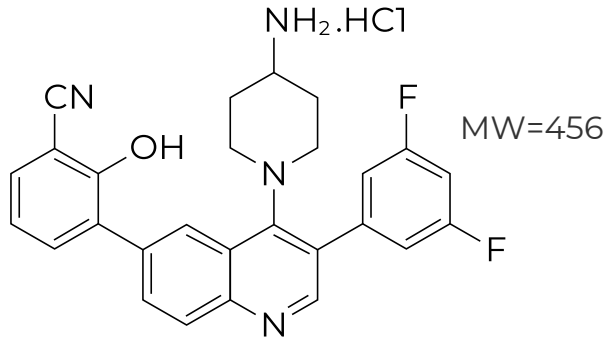
## BACKGROUND

- Paltusotine is a non-peptide, selective somatostatin 2 (SST2) receptor agonist in development as once-daily, oral treatment for patients with acromegaly or carcinoid syndrome[1]

## OBJECTIVE

- To evaluate the efficacy and safety of longer-term treatment with paltusotine in an open-label extension of PATHFNDR-1 study

### Paltusotine



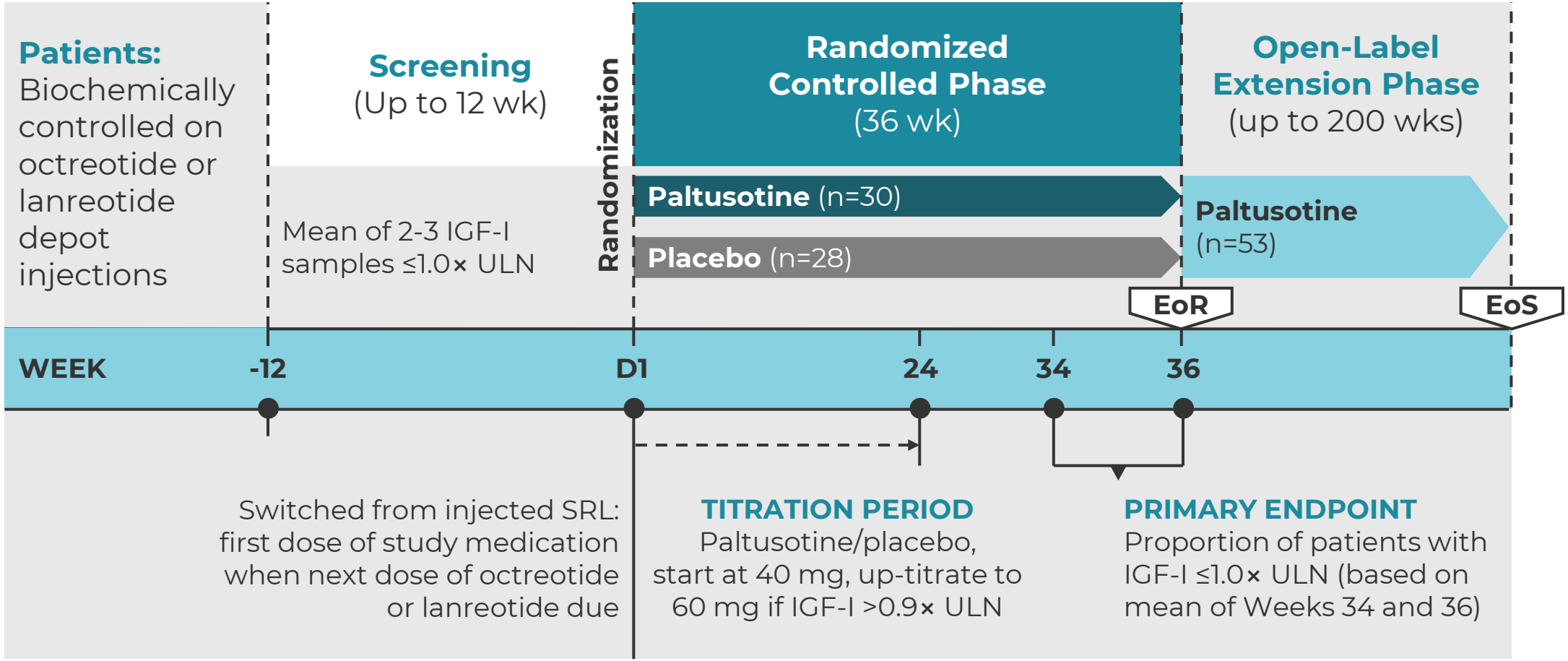

### Properties of the paltusotine molecule

| | |
|---|---|
| **Highly potent SST2 agonist[1]** | **EC50 = 0.25 nM** |
| **Selectivity for SST2 over other SST receptors[1]** | **>4000 fold** |
| **Oral solution bioavailability[2]** | **69%** |
| **Apparent terminal half-life[2]** | **28 hours** |
| **Administration[3]** | **On an empty stomach and 1 hour before a meal** |

1. Zhao J, et al. *ACS Med Chem Lett*. 2023;14(1):66-74. 2. Luo R, et al. [published online ahead of print March 5, 2025]. *Br J Clin Pharmacol*.
3. Luo R, et al. *J Endocrine Soc*. 2021;5(suppl 1):A524.

# Background

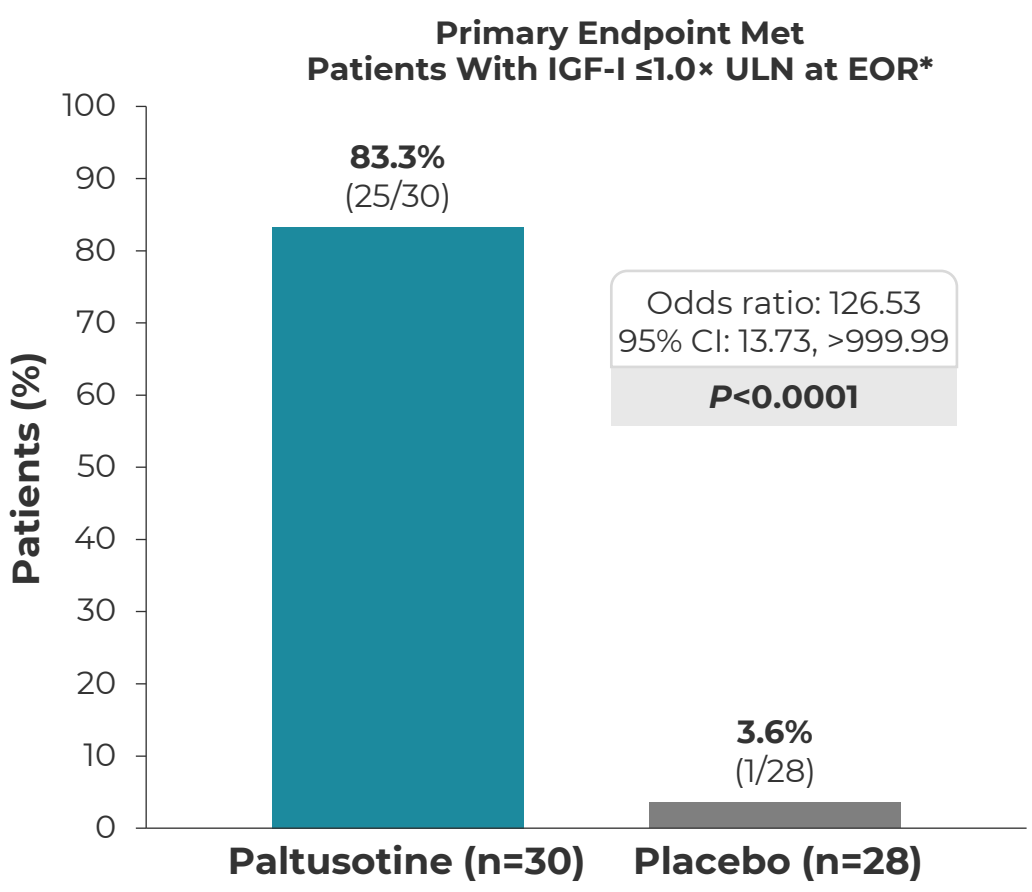
## PATHFNDR-1: phase 3 study in patients with acromegaly switched from injected SRL monotherapy to once-daily oral paltusotine

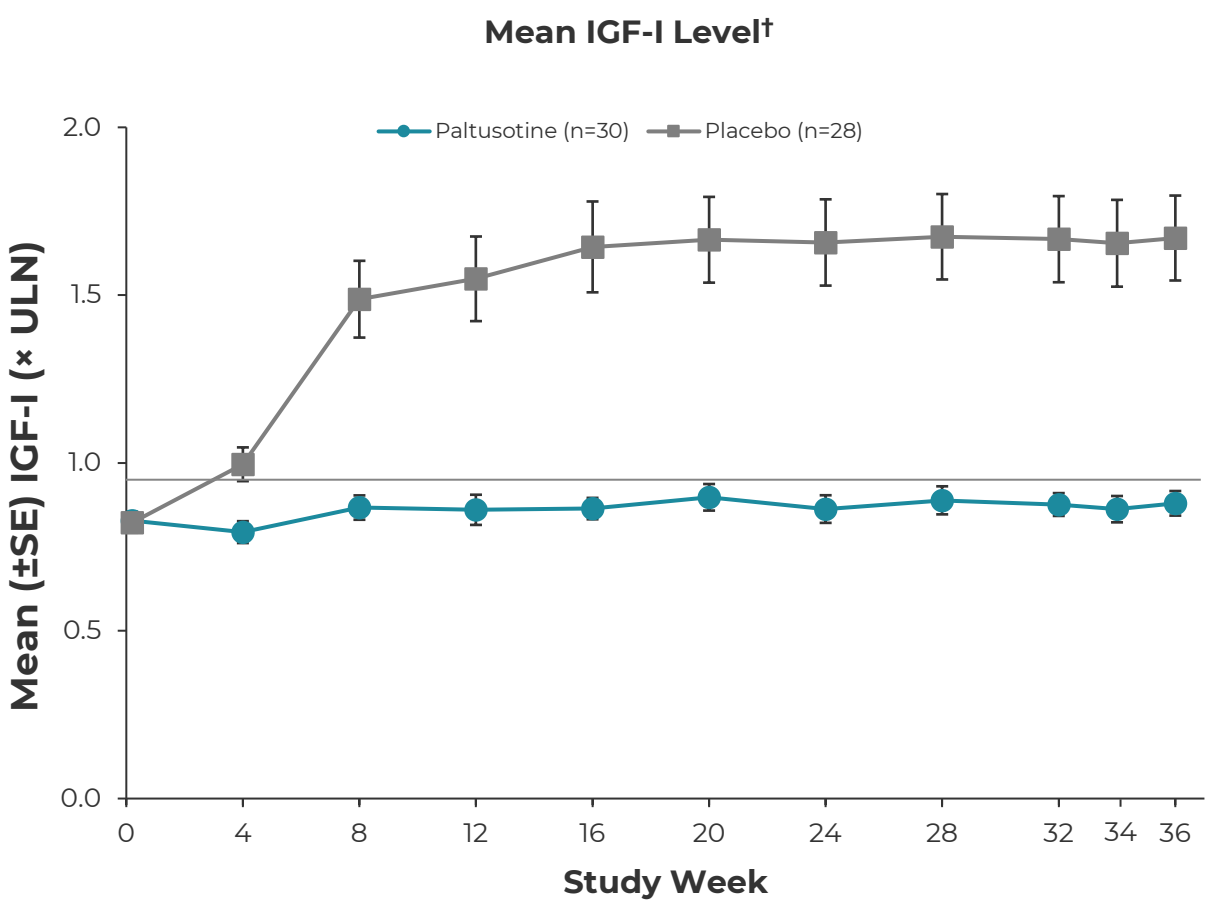



EoR = end of randomized controlled phase; EoS = end of study; SRL = somatostatin receptor ligand.

Results from the randomized controlled phase were published last year: Gadelha MR, et al. *J Clin Endocrinol Metab*. 2024;110(1):228-237.

# PATHFNR-1: randomized controlled phase

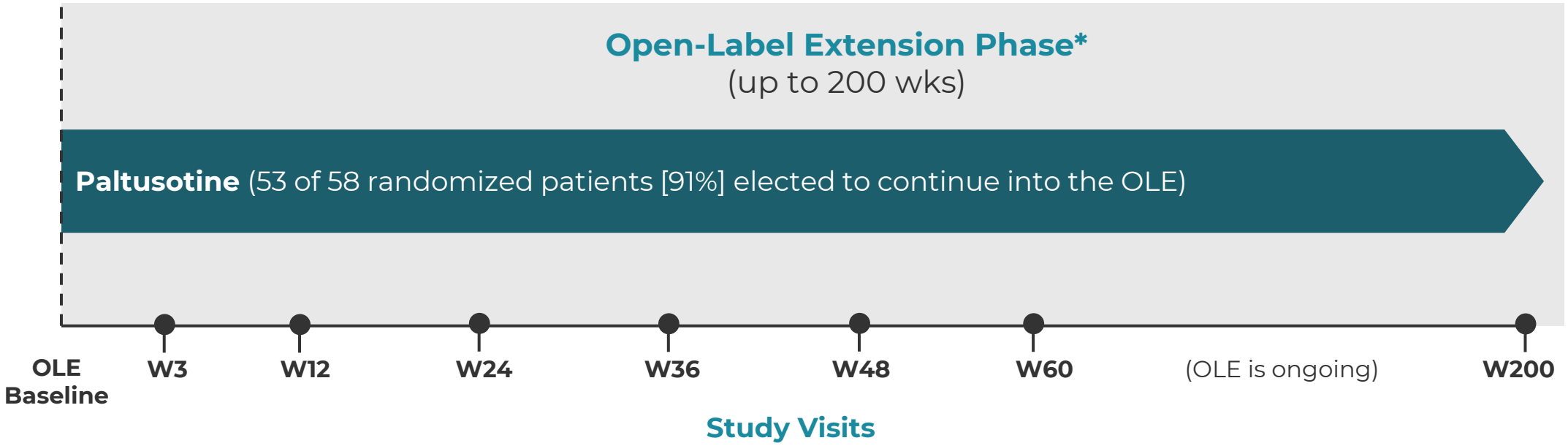



*Based on the mean of 2 measurements (Weeks 34 and 36) in the randomized controlled phase. †Week 36 or last visit before rescue. Last observation carried forward (LOCF) for patients who received rescue medication or discontinued from the study. EOR = end of randomized controlled phase.

*Bar graph figure reprinted with permission from* Gadelha MR, et al. *J Clin Endocrinol Metab*. 2024;110(1):228-237. https://creativecommons.org/licenses/by/4.0/

# PATHFNDR-1: open-label extension (OLE) phase




- Duration of treatment in the OLE: range, 9.4-120.4 weeks
- This analysis includes efficacy data through OLE Week 60 and safety data through the cutoff date

*Data cutoff for this analysis: August 15, 2024.

# Open-label extension (OLE) endpoints

## EFFICACY

- IGF-I levels and GH levels
  - Measured centrally using Immunodiagnostic Systems iSYS immunoassays
  - Single-measurement GH during OLE
- Acromegaly Symptom Diary
  - Developed in accordance with FDA guidance
  - Administered at study visits during OLE

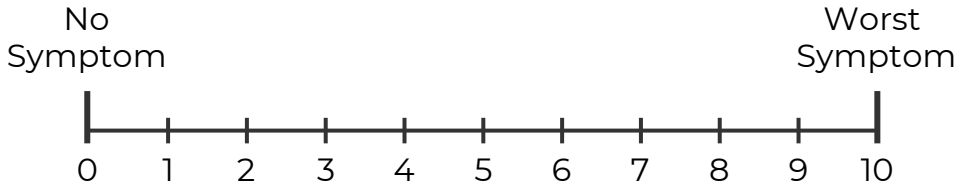
## SAFETY

- Adverse event monitoring
- Clinical laboratory tests, ECG, pituitary MRI (~every 1-2 years), biliary/gall bladder ultrasound (~every 2 years or if symptoms)

| Acromegaly Symptom Diary Core Symptoms |
|---|
| Headache pain |
| Joint pain |
| Sweating |
| Fatigue |
| Leg weakness |
| Swelling |
| Numbness/tingling |

**Total Score (0-70)**

**Numeric Scale (per symptom)**

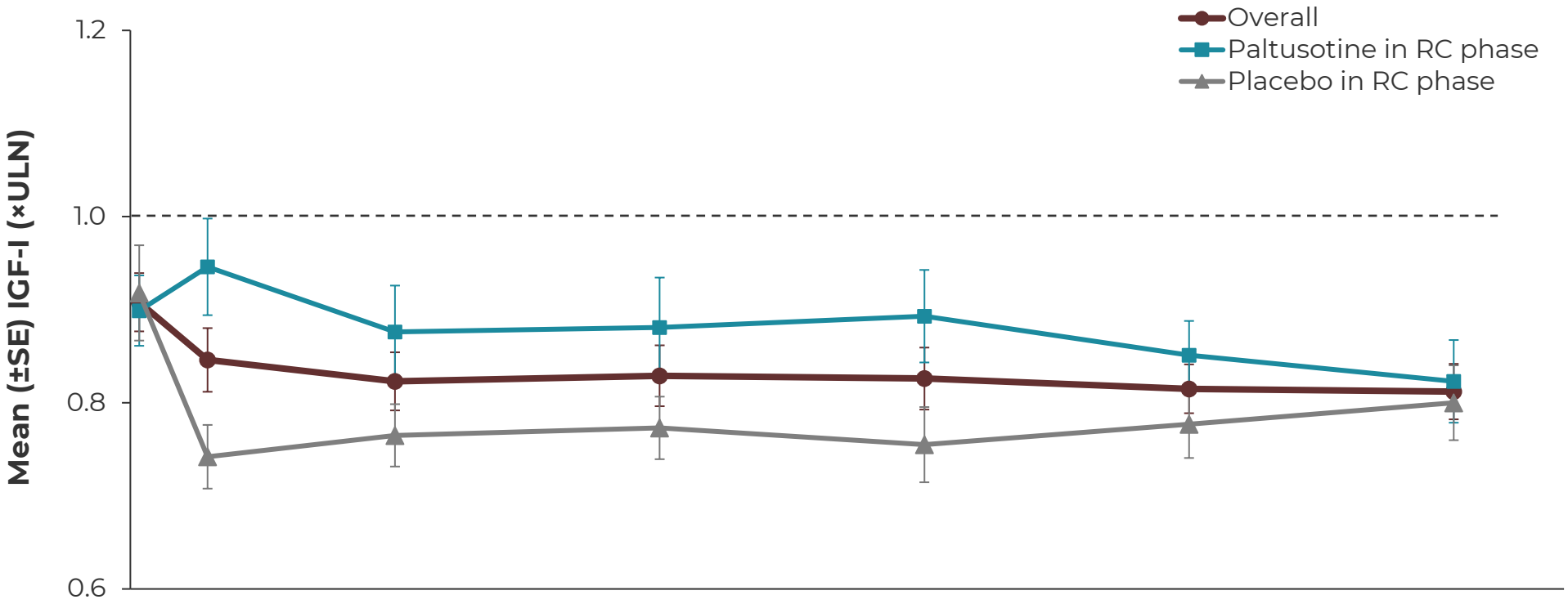



1. Martin S, et al. *J Patient Rep Outcomes*. 2023.;7(1):15.

# Open-label extension (OLE) population: patient characteristics

| OLE Population | Paltusotine (n=53) |
|---|---|
| Age, years, mean (SD) | 55 (13.0) |
| Female, n (%) | 30 (56.6) |
| Time since diagnosis, years, mean (SD) | 12.9 (7.5) |
| Prior pituitary surgery, n (%) | 45 (84.9) |
| Treatment during randomized controlled phase before the OLE, n | |
| Paltusotine | 27 |
| Placebo | 26 |
| Received rescue medication in randomized controlled phase, n | |
| Paltusotine | 1 |
| Placebo | 16 |

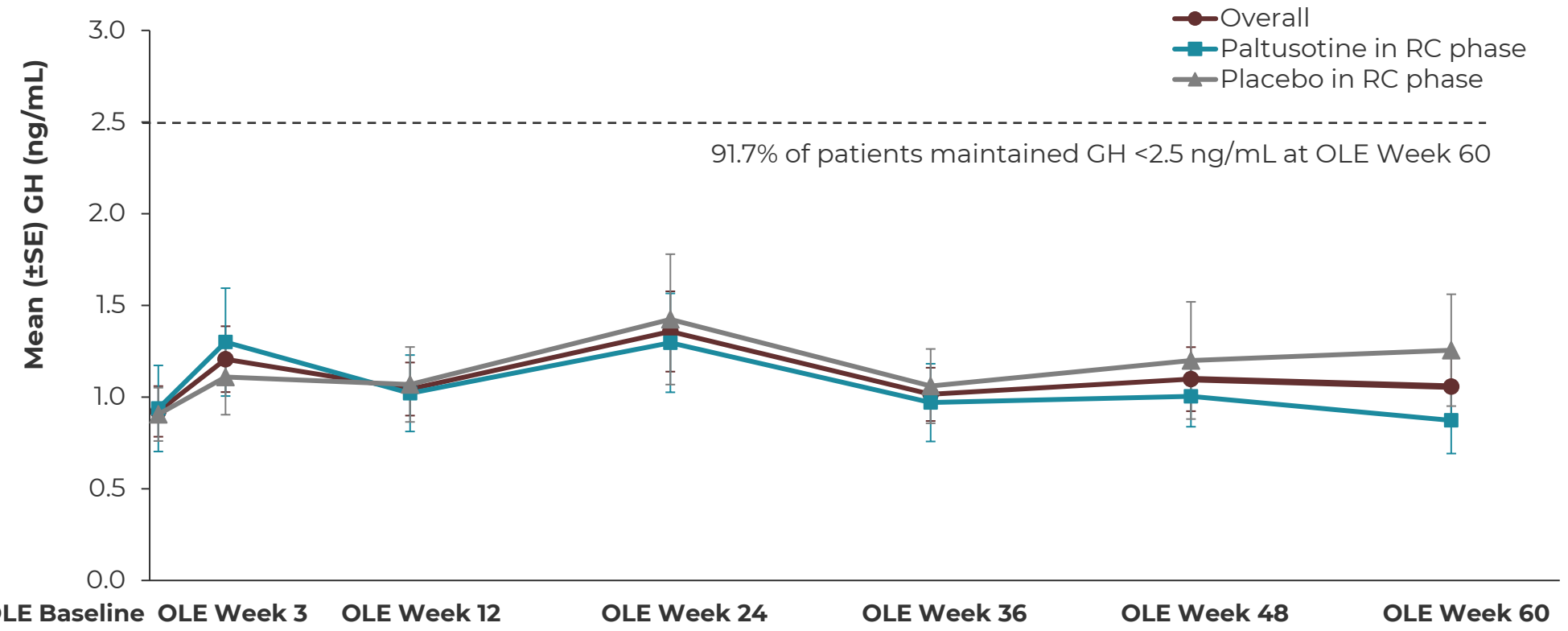
# IGF-I levels were maintained during >1 year of treatment in the open-label extension (OLE)




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Paltusotine in RC phase, n | 27 | 26 | 27 | 27 | 26 | 26 | 26 |
| Placebo in RC phase, n | 26 | 25 | 25 | 25 | 25 | 24 | 24 |

- Starting OLE dose of paltusotine 40 mg/day; optional titration to 60 mg/day based on IGF-I and downtitration to 20 mg based on tolerability
  - Paltusotine dose (last available assessment): 20 mg/day, n=2; 40 mg/day, n=33; 60 mg/day, n=18

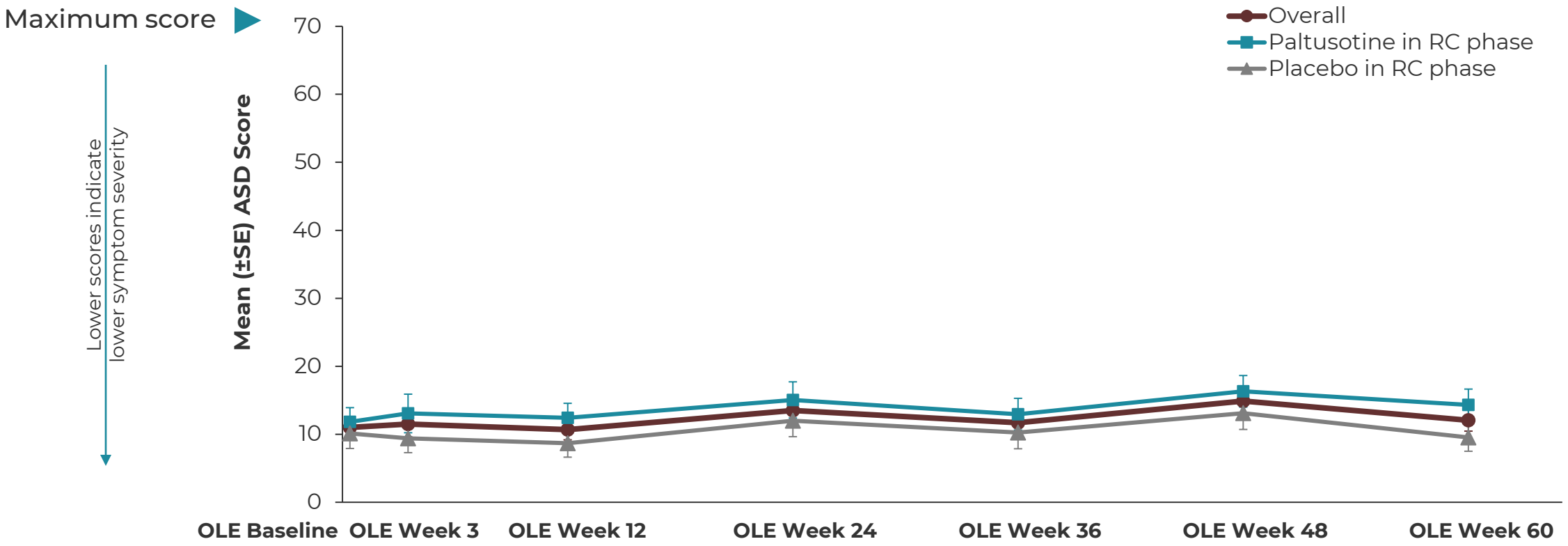
# Growth hormone levels were maintained during the open-label extension (OLE)




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Paltusotine in RC phase, n | 27 | 26 | 27 | 27 | 25 | 26 | 26 |
| Placebo in RC phase, n | 26 | 25 | 25 | 25 | 25 | 24 | 24 |

OLE baseline is 5-sample GH measurement at Week 34 of randomized controlled phase. Random (1-sample) GH measurements during OLE.

# Acromegaly Symptom Diary scores were stable throughout the open-label extension (OLE)




| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Paltusotine in RC phase, n | 25 | 16 | 22 | 20 | 22 | 25 | 22 |
| Placebo in RC phase, n | 22 | 12 | 19 | 21 | 19 | 20 | 20 |

# Open-label extension (OLE): summary of safety

| AEs During Open-Label Extension, n (%) | Patients (n=53) |
|---|---|
| Any AE | 47 (88.7) |
| Treatment-related serious AE | 1 (1.9)* |
| Treatment-related AE leading to discontinuation | 0 |
| Most common AEs (incidence >5%) | |
| Diarrhea | 8 (15.1) |
| Nausea | 5 (9.4) |
| Urinary tract infection | 4 (7.5) |
| Fatigue | 4 (7.5) |

| Paltusotine in RC (n=27) | Placebo in RC (N=26) |
|---|---|
| 1 (3.7) | 7 (26.9) |
| 1 (3.7) | 4 (15.4) |

*Bile duct stone.

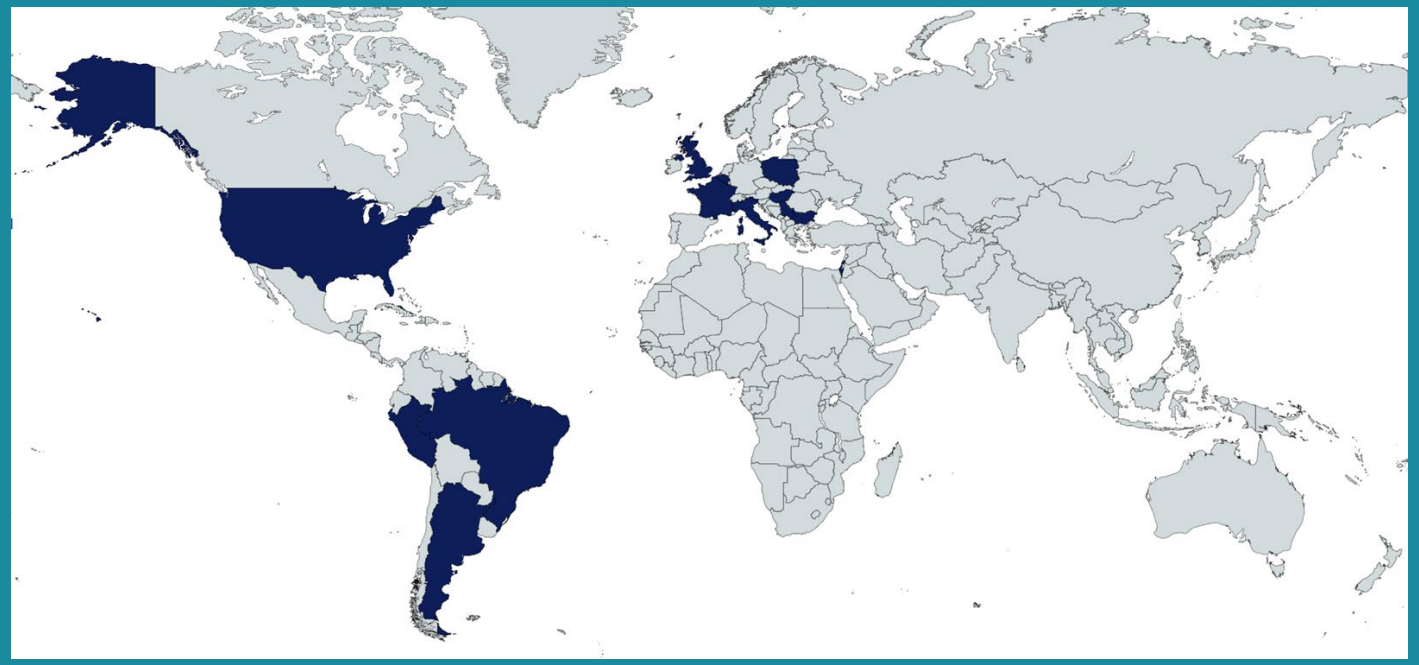
- Tumor volume remained stable in 32 patients with available MRI scans at OLE Week 48 (total of 84 weeks in 17 patients on paltusotine throughout the RC phase and OLE)

# Conclusions

- Of 58 patients who enrolled in the study, 53 patients (91.4%) opted to continue into the open-label extension
- Paltusotine demonstrated consistent disease control during more than 1 year of treatment
  - IGF-I and GH levels were maintained during >1 year of paltusotine therapy in the open-label extension
  - Scores on the Acromegaly Symptom Diary indicated stable symptom control
  - MRI scans showed stable tumor volume through 48 weeks of treatment in the open-label extension
- Paltusotine was well tolerated in patients with acromegaly who switched from injected depot SRLs
- Paltusotine may be an effective long-term treatment option for patients with acromegaly

SRL = somatostatin receptor ligand.

# THANK YOU!



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