



# Corporate Presentation

January 2026



# Safe Harbor Statement

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. (“Crinetics,” the “company,” “we,” “us,” or “our”) cautions you that all statements other than statements of historical facts contained in this presentation are forward-looking statements. Such forward-looking statements include, but are not limited to, statements regarding: the estimates relating to market size, our ability to optimize the launch or ensure broad access to Palsonify™ or our ability to drive diagnosis and treatment for undiagnosed patients; the plans and timelines regulatory filings or approval of paltusotine outside the US; the expected timing of patient enrollment in the Phase 3 program of paltusotine for carcinoid syndrome; the expected timing of patient enrollment in additional studies of atumelnant in CAH or our plans or timing for a phase 2/3 study of atumelnant in Cushing’s syndrome; the plans and timelines for the clinical development of our drug candidates, including the therapeutic potential and clinical benefits or safety profile thereof; and the expected timing for the initiation of clinical trials or the potential benefits of our development candidates in patients across multiple indications; the expected timing of additional research pipeline updates or the expected timing of the advancement of those programs; and the company’s anticipated cash runway or its operating cash burn guidance. In some cases, you can identify forward-looking statements by terms such as “may,” “believe,” “anticipate,” “could,” “should,” “estimate,” “expect,” “intend,” “plan,” “project,” “will,” “contemplate,” “predict,” “continue,” “forecast,” “aspire,” “lead to,” “designed to,” “goal,” “aim,” “potential,” “target,” or other similar terms or the negatives thereof.

These statements speak only as of the date of this presentation, involve known and unknown risks, uncertainties, assumptions, and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: estimates relating to market size and growth potential, which involve a number of assumptions and limitations, particularly about any projections, assumptions, and estimates of our future performance; the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk; the possibility of unfavorable new clinical data and further analyses of existing clinical data; potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical trials and nonclinical studies; regulatory developments or political changes, including policies related to pricing and pharmaceutical drug reimbursement in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization; our ability to obtain and maintain intellectual property protection for our product candidates; we may use our capital resources sooner than we expect or our cash burn rate may accelerate; and other risks described under the heading “Risk Factors” in documents we file from time to time with the Securities and Exchange Commission. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and, except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

# Our Mission:

To be **the world's leading endocrine company** that consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives



Tony



Ellen



Wendy



Brittany



Dee



Lesley



Claire

Acromegaly

Carcinoid Syndrome

Congenital Adrenal Hyperplasia

ACTH-Dependent Cushing's Syndrome

NETs and SST2-Expressing Solid Tumors

Hyperparathyroidism

Graves' Disease

ADPKD

Obesity

# Transforming Endocrine Disease Treatment from Discovery to Commercialization



## In-House Discovery

- ✓ Proven **drug-hunters** in the difficult GPCR space
- ✓ Experienced team with a **robust pipeline** (9+ programs) of wholly owned assets with IP into the 2040s
- ✓ Additional value from **continued innovation**

## Proven Development

- ✓ Demonstrated execution with **5 positive global Phase 2 or 3 readouts** in ~2 years and **first FDA approval** in 2025
- ✓ Steady stream of **upcoming clinical catalysts**

## Commercial Execution

- ✓ Building global **commercial capabilities** supporting our endocrinology pipeline
- ✓ **Ensuring patients have access** to the next generation of treatments



Partnering with patients every step of the way.

# Continued Value Creation with Deep Pipeline of Transformative Drug Candidates



SST: somatostatin receptor type; ACTH: adrenocorticotrophic hormone; NETs: Neuroendocrine tumors; TSH: thyroid-stimulating hormone; TED: thyroid eye disease; ADPKD: Autosomal dominant polycystic kidney disease; PTH: parathyroid hormone; GLP-1: glucagon-like peptide-1 receptor agonists; GIP: gastric inhibitory polypeptide; IND: Investigational New Drug Application; PDUFA: Prescription Drug User Fee Act; CHMP: Committee for Medicinal Products for Human Use.

# World-class Development Leading to Global Commercialization

**Paltusotine:** Lead Clinical Candidate for  
Acromegaly and Carcinoid Syndrome



PATHFNR-1  
PHASE 3 RESULTS



PATHFNR-2  
PHASE 3 RESULTS



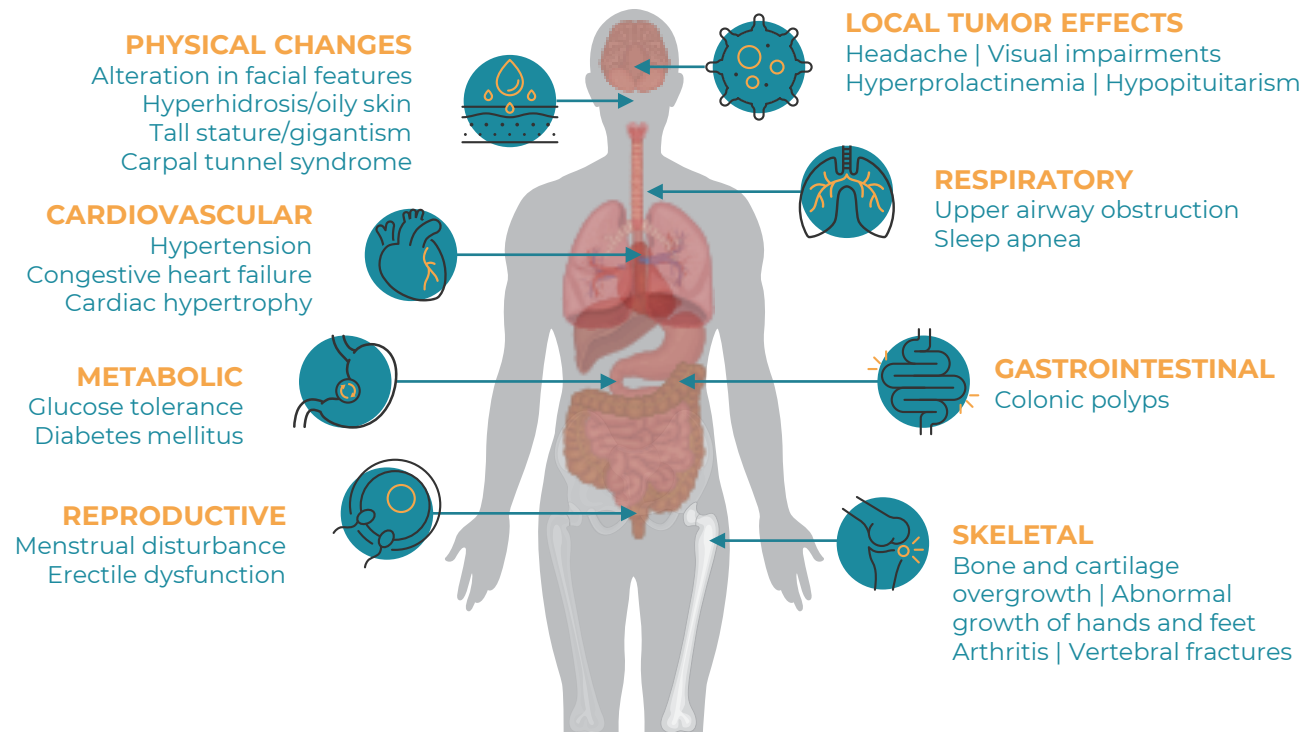
CARCINOID SYNDROME  
PHASE 2 RESULTS



# Acromegaly Symptoms Take a Toll on Patients

Acromegaly is a rare chronic disease caused by a pituitary adenoma that secretes excess GH, resulting in hypersecretion of IGF-I<sup>1,2</sup>

## Effects of Prolonged Exposure to IGF-I and GH<sup>1,2</sup>



## Patient Symptoms<sup>3-4</sup>

-  Enlarged hands, feet, lips, nose, tongue, and jaw
-  Skin changes: oily skin, thickened skin, excessive sweating
-  Headaches, which may be frequent and/or severe
-  Joint pain, vertebral fractures
-  Peripheral neuropathy, carpal tunnel syndrome

GHRH = growth hormone-releasing hormone; IGF-I = insulin-like growth factor I.

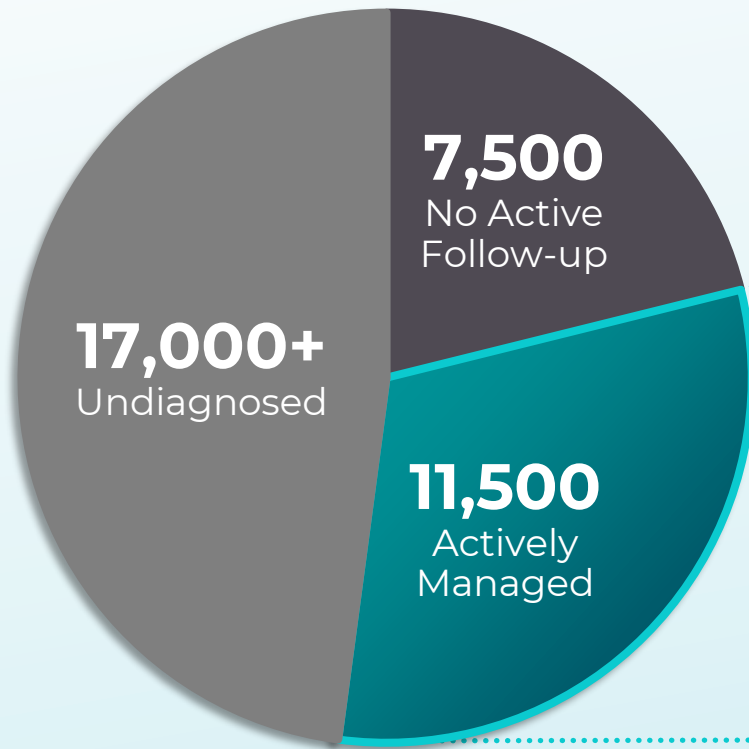
1. Colao A, et al. *Nat Rev Dis Primers*. 2019;5(1):20. 2. Gomes-Porras M, et al. *Int J Mol Sci*. 2020;21(5):1682.

Figure adapted with permission from Colao A, et al. *Nat Rev Dis Primers*. 2019;5(1):20. 3. Fleseriu M, et al. *Lancet Diabetes Endocrinol*. 2022;10(11):804-826.

4. Slagboom TNA, et al. *Pituitary*. 2023;23(4):319-332.

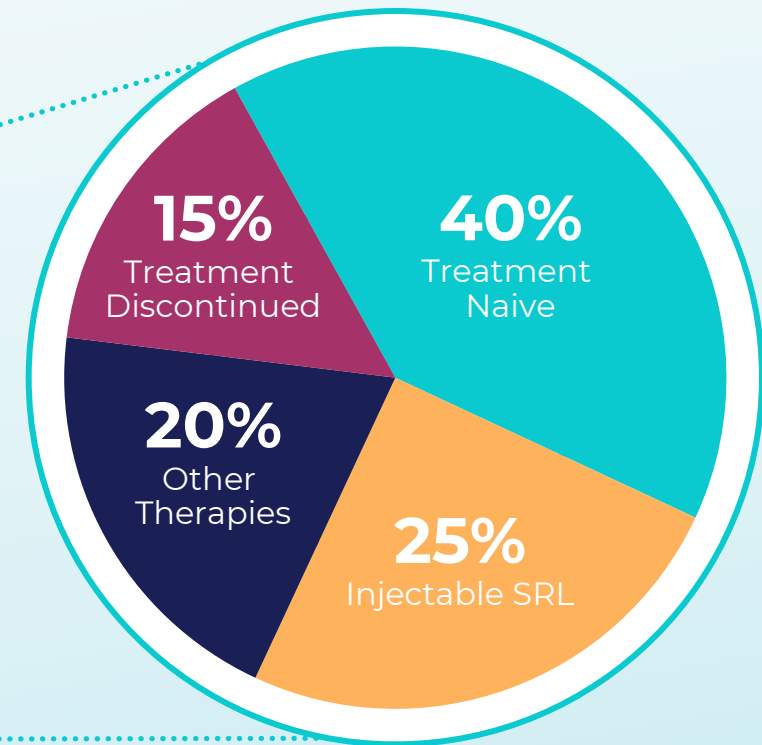
# Acromegaly Patient Reach

**36,000 People Living with  
Acromegaly in the US**



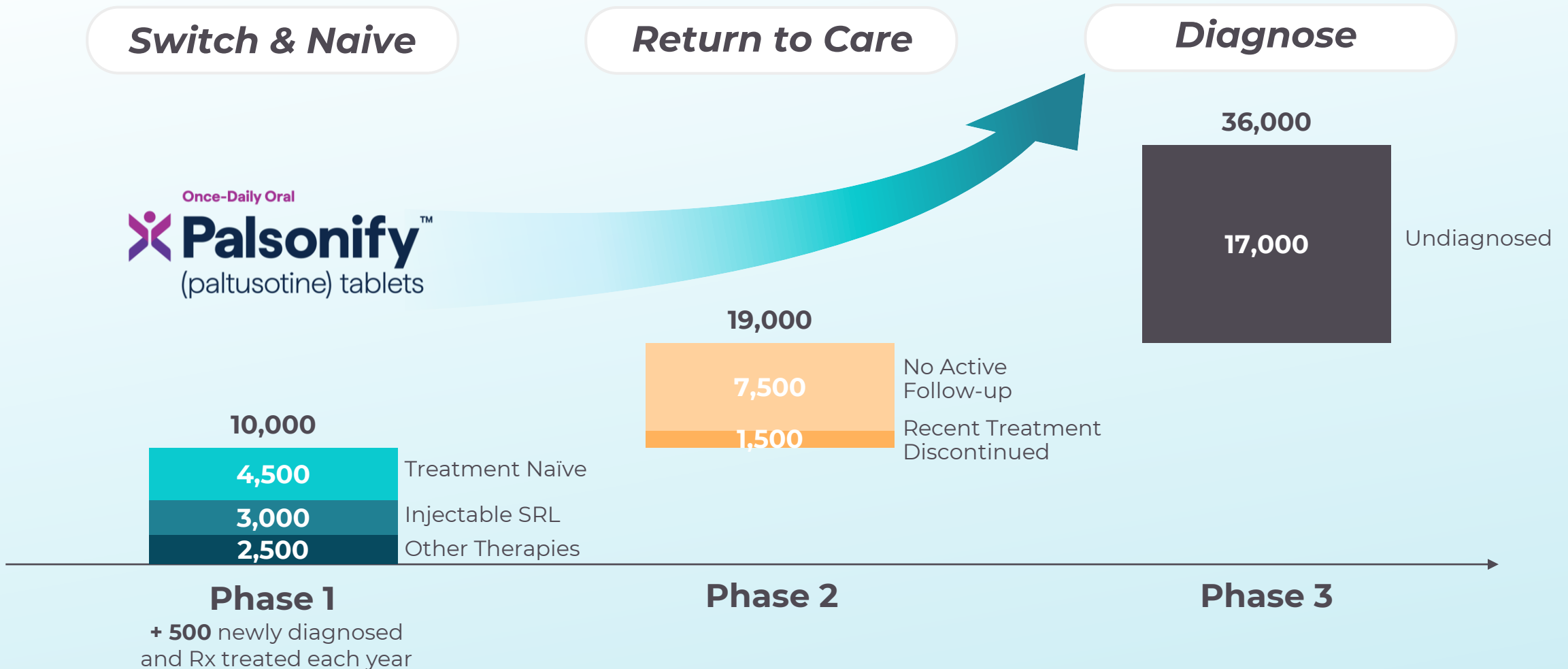
**1,500/yr diagnosed**

**11,500 Actively Managed and  
Addressable in Short-Term**



**500/yr initiating pharmacotherapy**

# Palsonify: Executing Phased Launch to Address Broader Acromegaly Patient Population



Abbreviations: SRL, Somatostatin Receptor Ligand.

Note: Market sizes are Company estimates based on a synthesis of Komodo Health claims analysis and analysis from Stratis Group and McKinsey & Company.

# Acromegaly Patients Face Significant Unmet Need, Presenting a Compelling Market Opportunity

77%

Reported injection site reactions after SRL treatment<sup>1</sup>

79%

Had acromegaly symptoms worsen at end of SRL injection cycle<sup>2</sup>

64%

Felt upset for being dependent on others for treatment<sup>1</sup>



“It's urgent because symptoms affect my quality of life, affect my relationships, affect my abilities to fulfill my responsibilities professionally, personally...I need to be functional.”

– *Patient living with acromegaly*

**ELLEN**  
Living with  
Acromegaly

**Source:** Crinetics interviews & market research

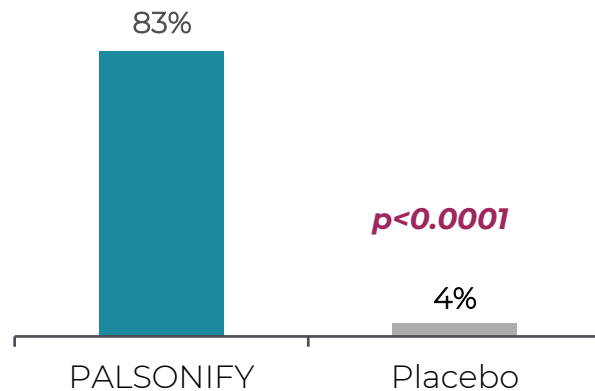
<sup>1</sup> Fleseriu M, Molitch M, Dreval A, et al. Disease and treatment-related burden in patients with acromegaly who are biochemically controlled on injectable somatostatin receptor ligands. *Front Endocrinol (Lausanne)*. 2021;12:627711.

<sup>2</sup> Liu S, Adelman DT, Xu Y, et al. Patient-centered assessment on disease burden, quality of life, and treatment satisfaction associated with acromegaly. *J Investig Med*. 2018;66(3):653-660.

SRL: Somatostatin Receptor Ligands

# In Phase 3 Studies, PALSONIFY Achieved Rapid, Reliable and Consistent Biochemical Control in Switch Patients

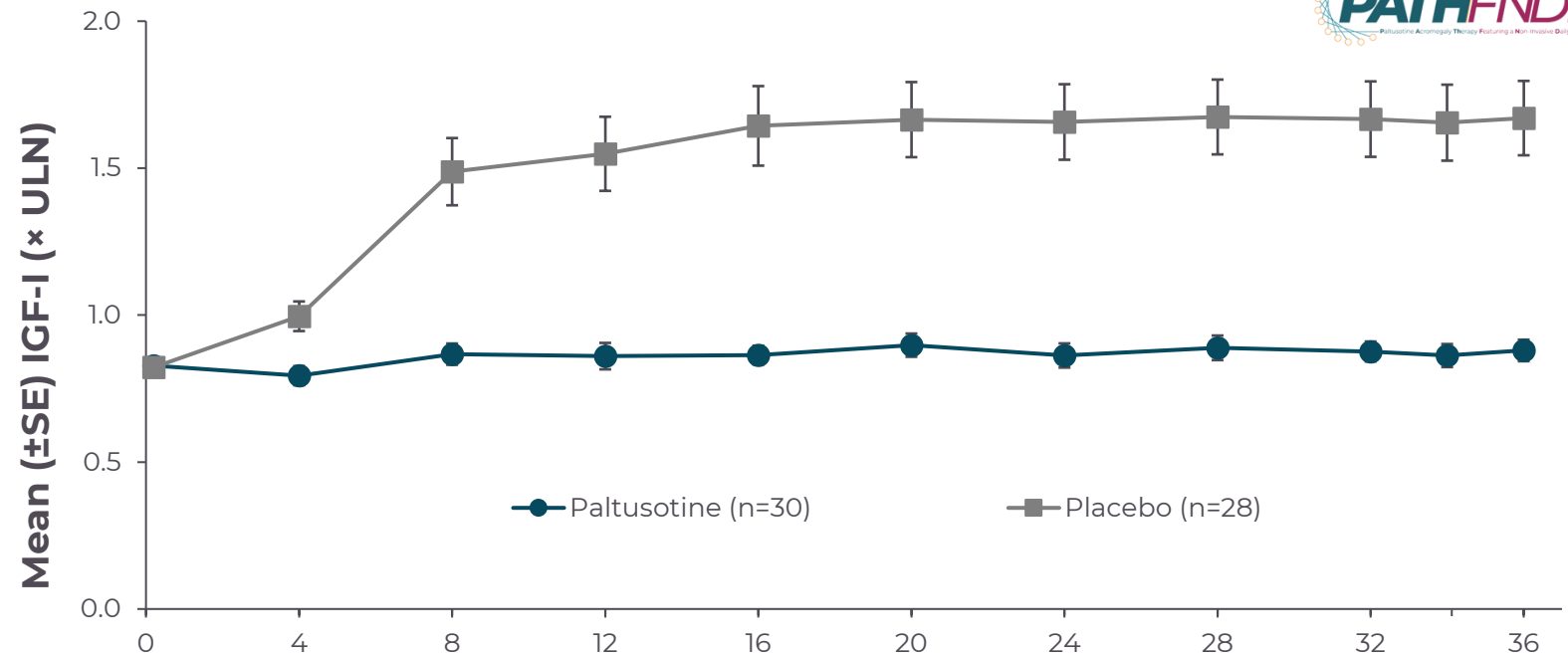
Patients switching from standard-of-care



**PRIMARY  
ENDPOINT**

Maintained  
IGF-1  $\leq 1.0 \times \text{ULN}$

PALSONIFY Treatment Maintained IGF-1 Control in Patients who Switched from SRL Injections



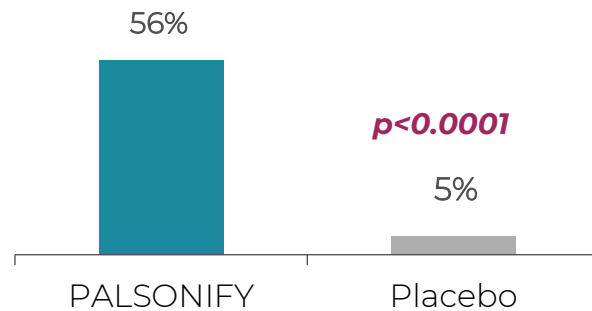
Only 1 patient taking PALSONIFY in PATHFINDER-1 had an IGF-1 above 1.1 x ULN at EOT<sup>1</sup>

\*Last observation carried forward for patients who received rescue medication or discontinued from the study.

EOT: end of treatment (week 36 or last assessment before rescue).

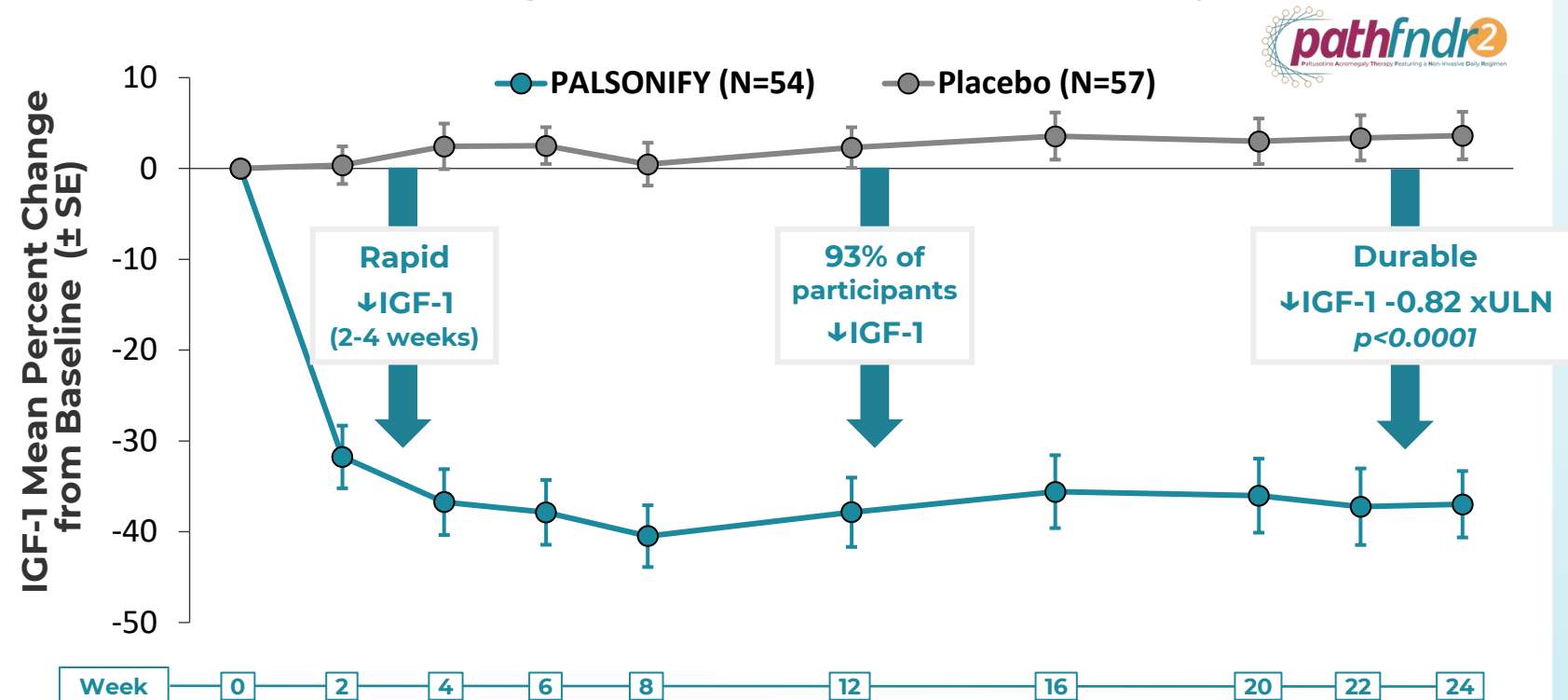
# In Phase 3 Studies, PALSONIFY Achieved Rapid, Reliable and Consistent Biochemical Control in Naïve Patients

Non-pharmacologically-treated patients

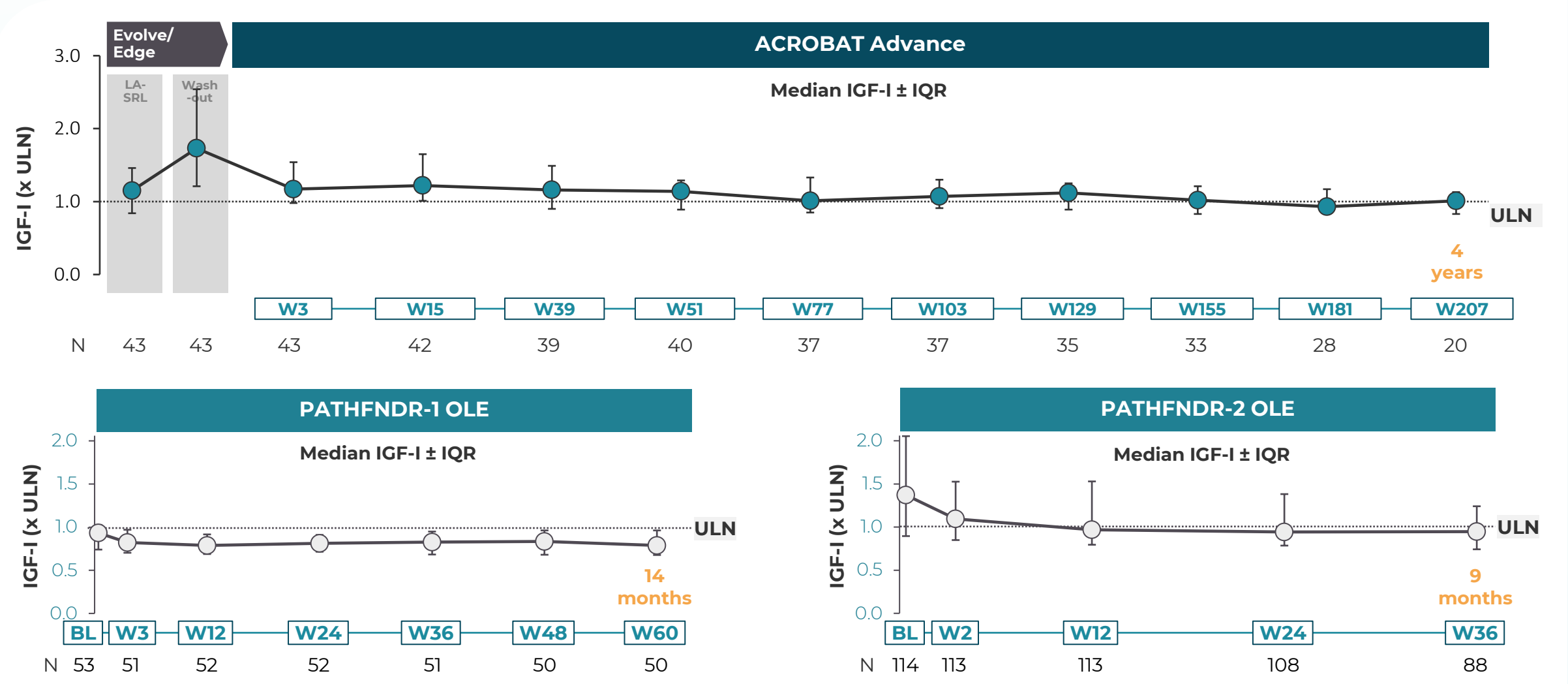


**PRIMARY ENDPOINT** Achieved IGF-1  $\leq 1.0 \times \text{ULN}$

Percent Change from Baseline in IGF-1 Level by Visit

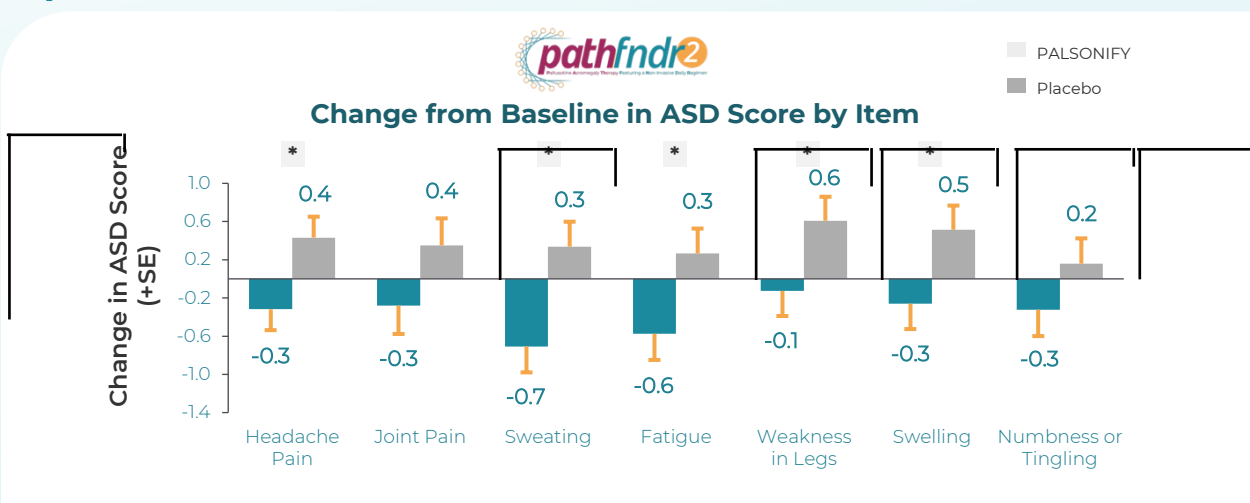
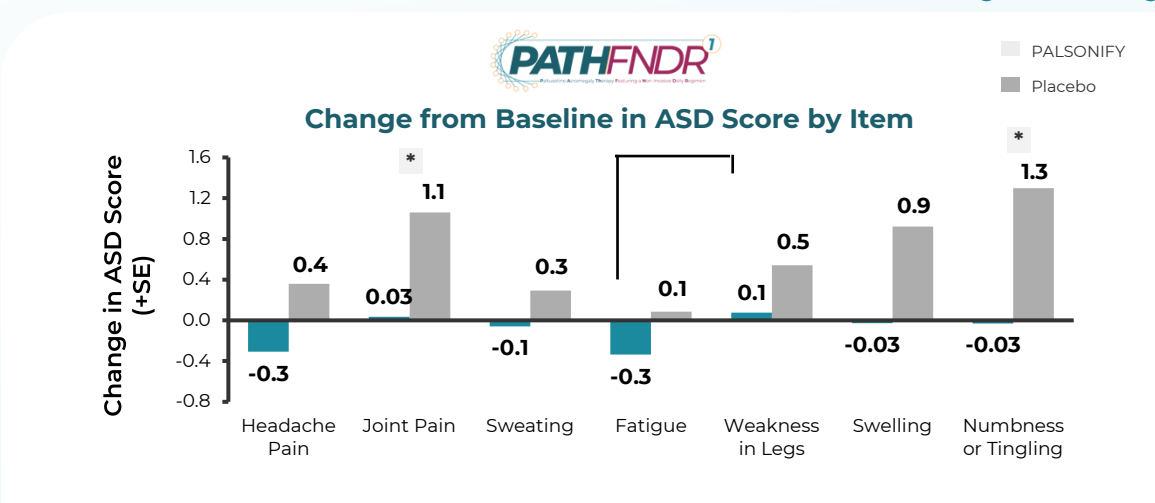


# PALSONIFY Treatment Results in Long-Term Stable Biochemical Control Across a Range of Acromegaly Patients

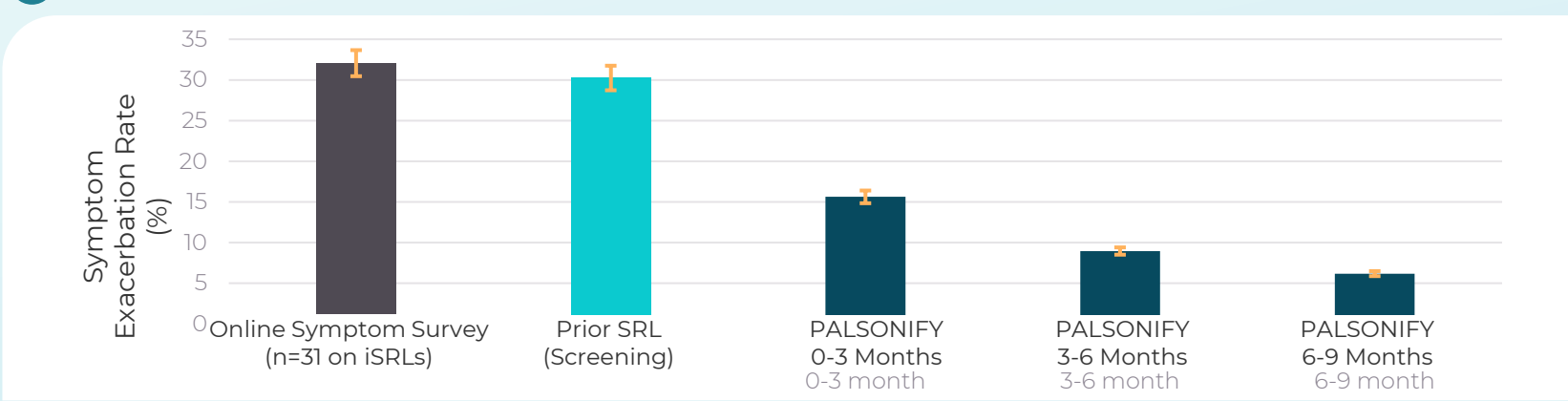


# In Phase 3 Studies, PALSONIFY Achieved Consistent Control of Symptoms and Reduced Frequency of Symptom Exacerbations

✔ Label includes trend towards reduced severity of 7 key symptoms in both randomized trials



✔ Symptom exacerbation frequency continued to decline throughout the 9-month study



## Exploratory Post-Hoc Analyses with Acromegaly Symptom Diary (ASD)

(Exploratory Analysis n=22, Exploratory post hoc analysis; should not be interpreted as establishing clinical significance)

# PALSONIFY was Well-Tolerated with No Severe or Serious Adverse Events

## Key safety outcomes from the randomized control period of Phase 3 studies

- **No serious adverse events**  
None occurred with PALSONIFY vs 2.4% with placebo
- **GI AEs resolved**  
Most GI AEs occurred within the first 2 months (median duration of 6 to 18 days), were generally mild to moderate and resolved without discontinuing PALSONIFY
- **Low discontinuation rate**  
<4% of patients taking PALSONIFY discontinued due to AEs
- **Stability or reduction in size of pituitary tumors**  
No patients receiving PALSONIFY had clinically significant increases in tumor volume, clinically significant decreases were observed in 4 patients taking PALSONIFY but not in any patients taking placebo



| Adverse Reaction   | PALSONIFY<br>N=30<br>n(%) | Placebo<br>N=28<br>n(%) |
|--------------------|---------------------------|-------------------------|
| Diarrhea           | 7 (23)                    | 3 (11)                  |
| Nausea             | 4 (13)                    | 1 (4)                   |
| Decreased appetite | 3 (10)                    | 0                       |
| Palpitation        | 2 (7)                     | 0                       |
| Gastroenteritis    | 2 (7)                     | 0                       |



| Adverse Reaction  | PALSONIFY<br>N=54<br>n(%) | Placebo<br>N=57<br>n(%) |
|-------------------|---------------------------|-------------------------|
| Diarrhea          | 18 (33)                   | 8 (14)                  |
| Abdominal pain    | 10 (19)                   | 3 (5)                   |
| Nausea            | 5 (9)                     | 1 (2)                   |
| Sinus bradycardia | 4 (7)                     | 0 (0)                   |
| Hyperglycemia     | 4 (7)                     | 1 (2)                   |

# Executing on Our Strategy to Make PALSONIFY the Foundation of Acromegaly Care

Leverage synergistic field teams and targeted marketing to educate on best-in-class profile and streamline access

## PATIENTS

Activate patients to start, switch, or resume treatment

## PROVIDERS

Make PALSONIFY the therapy of choice

## PAYERS

Demonstrate value proposition to facilitate access

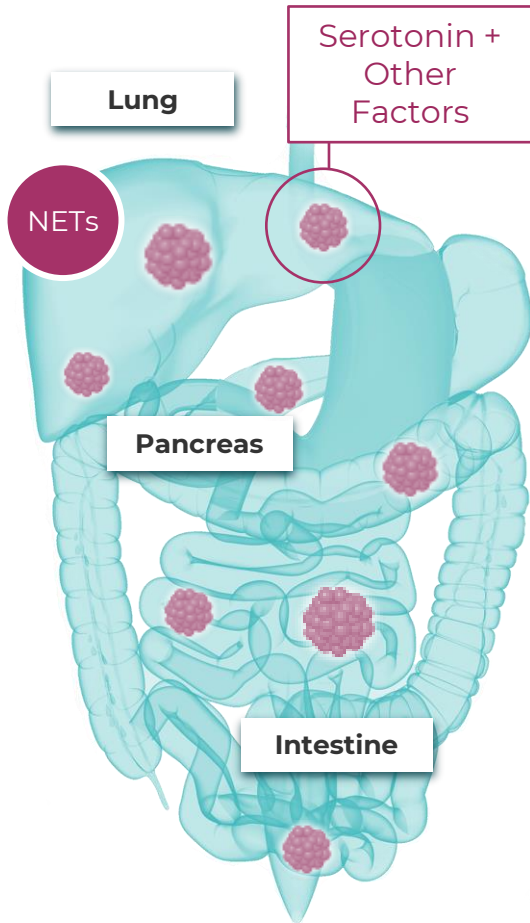
ACTIVATE

ADOPT

ACCESS

ADHERE

# Carcinoid Syndrome: Second Indication for Paltusotine



## Carcinoid Syndrome

**Severe flushing episodes can be debilitating and potentially dangerous**

**Goal:** reduce frequency and severity (normal is  $< 1/\text{day}$ )

**Excess bowel movements ( $>3/\text{day}$ ) are highly disruptive**

**Goal:** reduce frequency and urgency (normal is  $\leq 3/\text{day}$ )

**Severe and life-threatening complications: carcinoid heart disease (found in up to 50% of patients) & carcinoid crisis**

**Goal:** prevent severe complications

**Injected SRLs impose a high burden of care and frequently lose effectiveness before next injection**

**Goal:** eliminate depot and rescue injections and provide consistent control throughout the month

**Facial flushing in a patient with carcinoid syndrome**



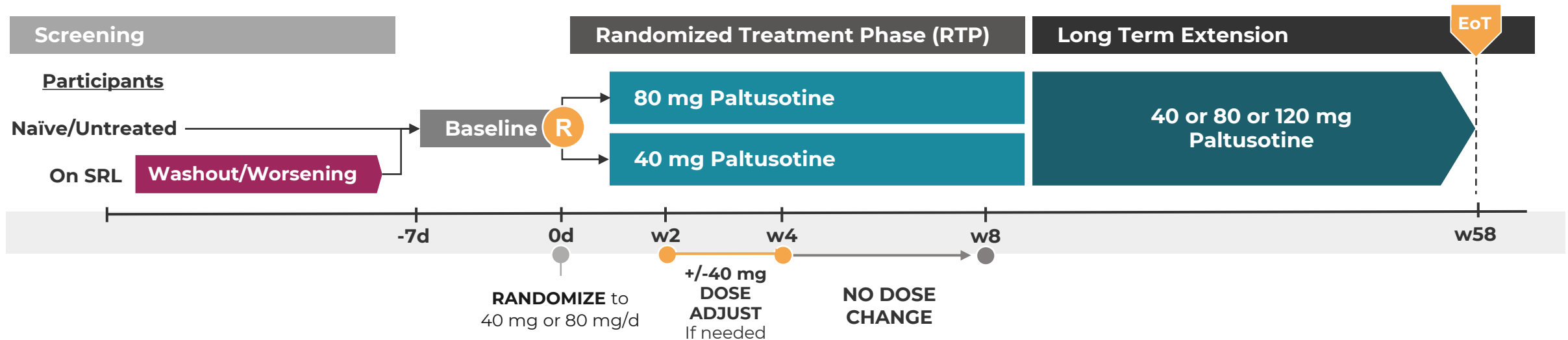
Courtesy of Stephen E Goldfinger, MD [UpToDate](#)

# Phase 2 Study Design: Evaluating Safety, PK and Efficacy of Paltusotine in Carcinoid Syndrome Patients

**Protocol:** 8-week, open-label, parallel, randomized 2-dose study followed by a Long Term Extension phase

## Key Eligibility Criteria:

- Treatment naïve or currently untreated and actively symptomatic –OR– controlled on SRL therapy and symptom worsening upon washing out of treatment
- Positive SSTR expression
- Grade 1 or 2 NET



## 1 Primary Endpoint

Safety and tolerability of Paltusotine

## 2 Secondary Endpoint

Pharmacokinetics of Paltusotine

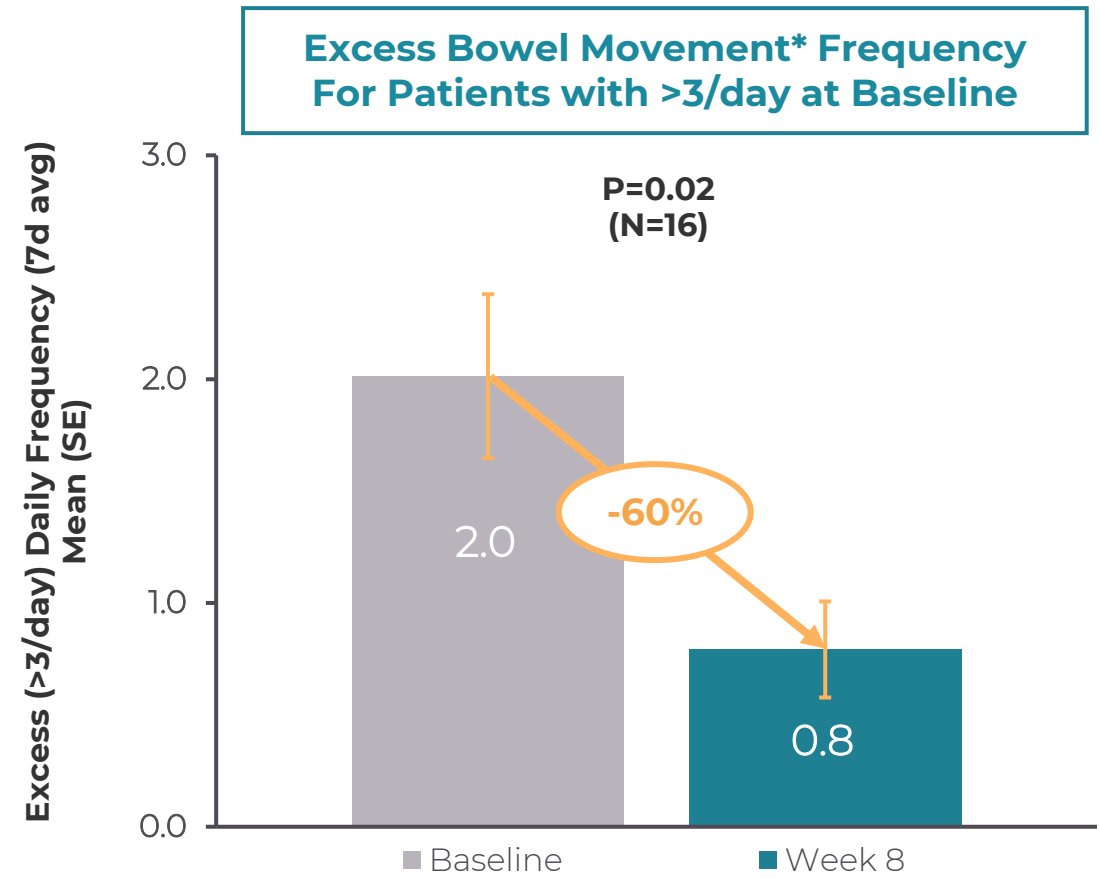
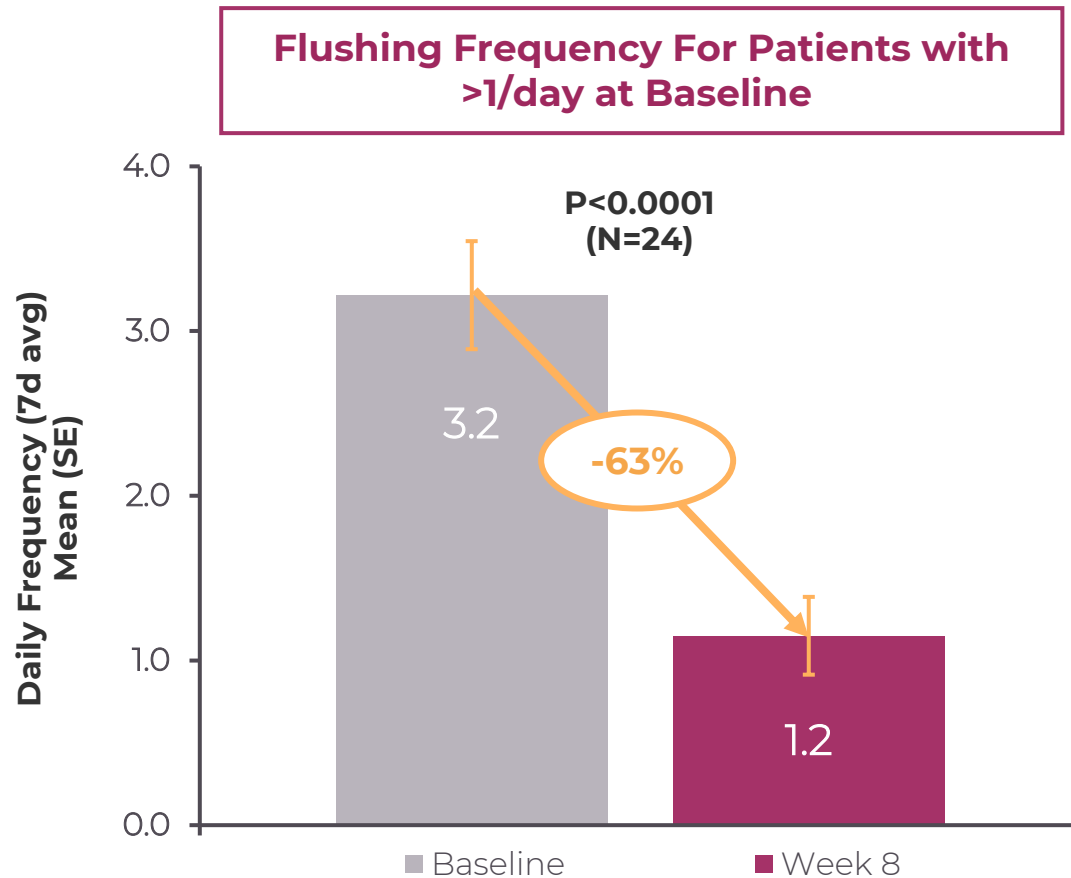


## Exploratory Efficacy Endpoints

Bowel movement and flushing frequency and severity markers, octreotide rescue use, biomarkers, PRO measures

EoT = end of treatment; NET = Neuroendocrine tumor; PK = Pharmacokinetics; PRO = patient reported outcome; SRL = somatostatin receptor ligand; SSTR = somatostatin receptor.

# Paltusotine Reduced Frequency of Key Carcinoid Syndrome Symptoms in Phase 2 Study



\*Excess bowel movements (BM) were defined as daily bowel movements above the upper limit of normal (3 per day).

# Paltusotine: Promising Potential for a Second Indication of Carcinoid Syndrome

## Substantial Patient Impact



**18-34K people**

with carcinoid syndrome in the U.S. treated with SRLs<sup>1</sup>

Patients on painful monthly SRLs injections often have breakthrough symptoms

## Positive Phase 2 Data

- ✓ Flushing frequency reduced by 63%
- ✓ Excess bowel movement frequency reduced by 60%
- ✓ Well tolerated, with safety profile consistent with other paltusotine clinical studies
- ✓ Preliminary investigator-assessed progression free survival (PFS) rate of 74% following one year of treatment

## Phase 3 Trial Underway

- ✓ First patient randomized in **November 2025**
- ✓ 20+ sites activated
- ✓ OLE to evaluate PFS and effect in real-world setting

Paltusotine is under investigation for the treatment of carcinoid syndrome.

CS = Carcinoid Syndrome

<sup>1</sup> SEER 17 & SEER 8 (Surveillance, Epidemiology, and End Results) Health Advances analysis, data on file

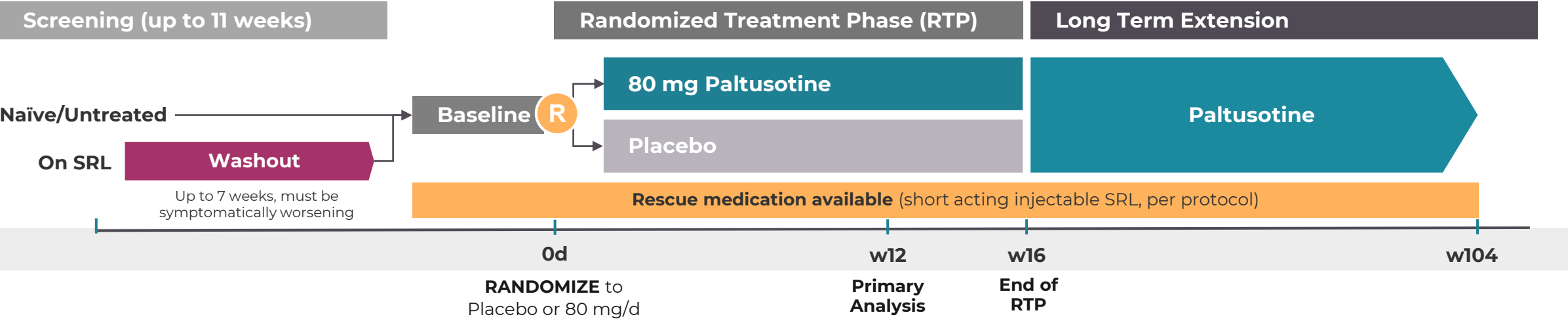
# CAREFNDR Phase 3 Study of Paltusotine in Carcinoid Syndrome

## Study Size:

141 patients, 2:1 randomization

## Key Eligibility Criteria:

- Treatment naïve or currently untreated and actively symptomatic –OR– controlled on SRL therapy and symptom worsening upon washing out of treatment
- Grade 1 or 2 NET, Positive SSTR expression



- 1 Primary Endpoint**

Change from baseline in frequency of flushing
- 2 Key Secondary Endpoint**

Change from baseline in bowel movement frequency
- Additional Efficacy Endpoints**

Flushing severity, bowel movement urgency, OLE to include assessment of tumor control (PFS)

# World-class Development to Grow the Late-Stage Pipeline

**Atumelnant:** In Development for Congenital  
Adrenal Hyperplasia and Cushing's Disease



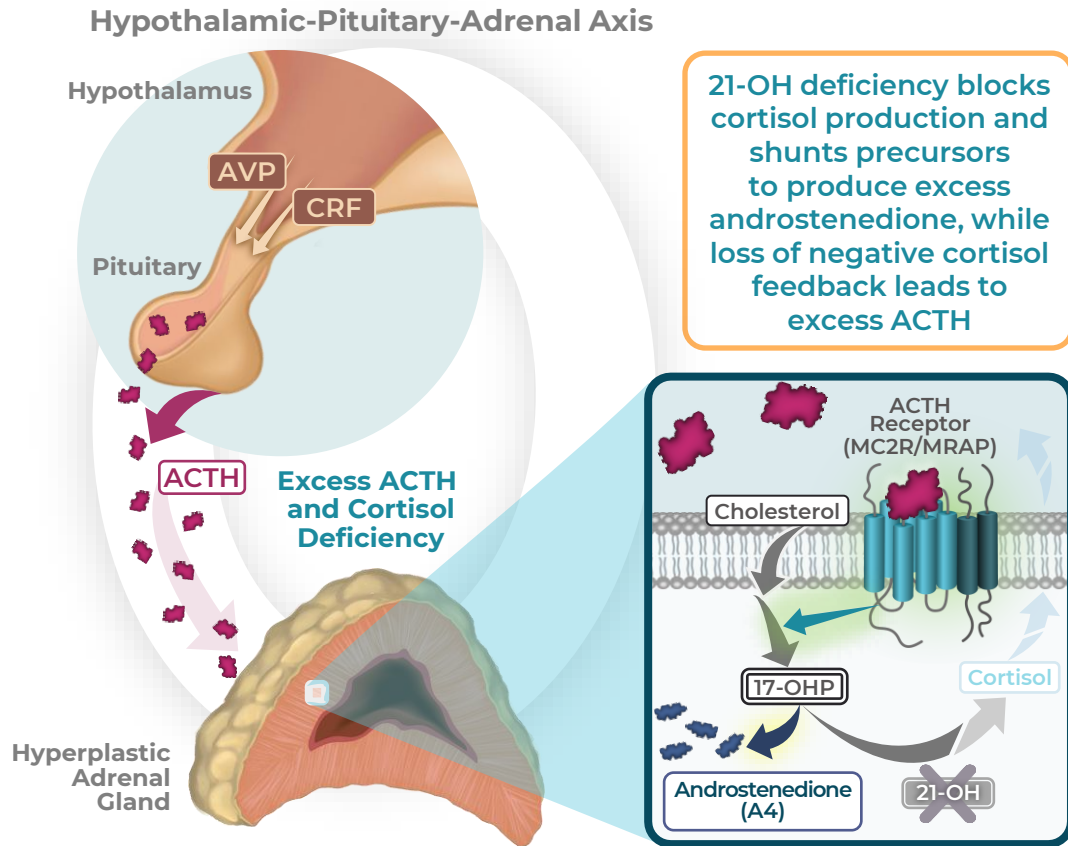
CUSHING'S DISEASE  
PHASE 2 INITIAL  
FINDINGS



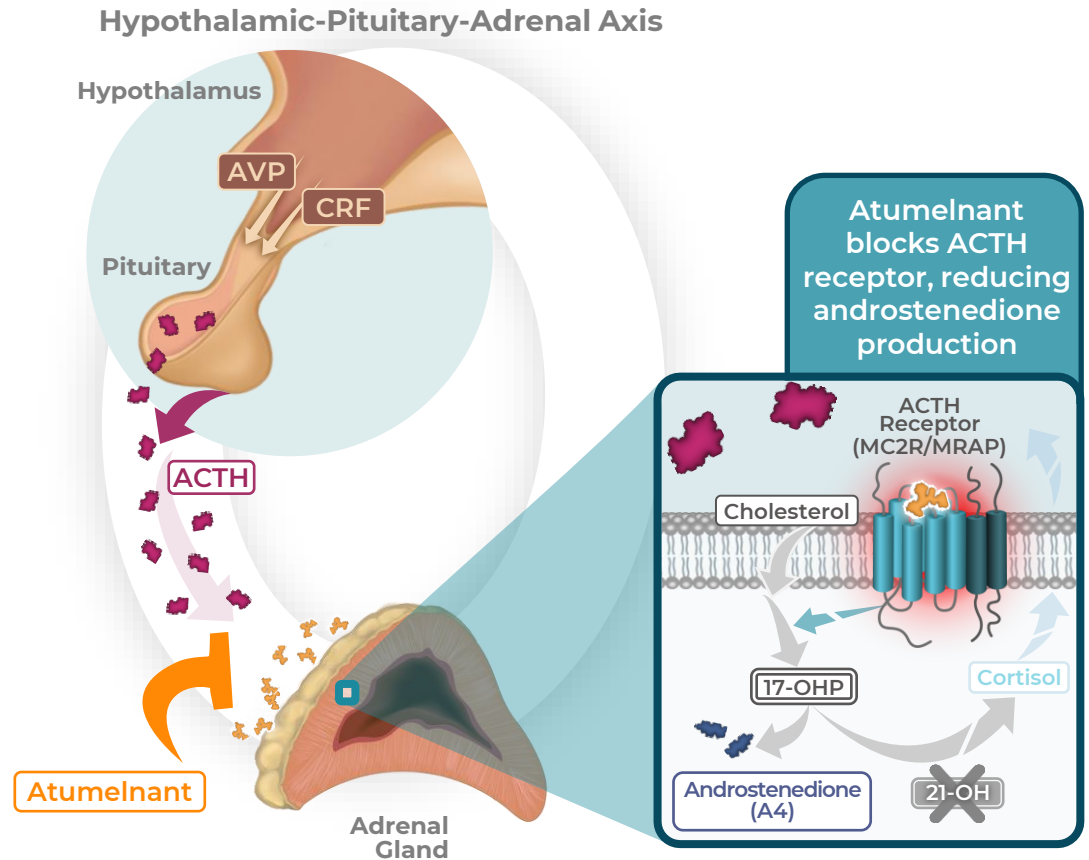
CAH PHASE 2  
TOPLINE RESULTS  
RELEASE

# Atumelnant: The First Oral, Daily ACTH Antagonist is in Development for Congenital Adrenal Hyperplasia

## Disruptions in the HPA Axis Causing CAH



## Atumelnant Mechanism of Action in CAH



**Reference:** Kim SH, Han S, Zhao J, et al. Discovery of CRN04894: A novel potent selective MC2R antagonist. *ACS Med Chem Lett.* 2024;15(4):478-485.

**Abbreviations:** ACTH, adrenocorticotrophic hormone; AVP, arginine vasopressin; CRF, corticotropin-releasing factor; 17-OHP, 17-hydroxyprogesterone; 21-OH, 21-hydroxylase; MC2R, melanocortin type 2 receptor; MRAP, melanocortin 2 receptor accessory protein.

# CAH Affects ~17,000 Addressable Adult and Pediatric Patients in the US

## Treatment Goals in Adults with CAH

- Reduction of A4 and other androgens to address hyperandrogenism, which can manifest as excessive facial hair, acne and polycythemia
- Restore normal menstrual cycles and fertility in women
- Shrink testicular adrenal rest tumors, alleviate pain and restore fertility in men
- Eliminate excessive exposure to glucocorticoids to minimize related adverse effects including weight gain, cardiovascular issues, diabetes, and osteoporosis



### CAH Has a Range of Clinical Implications

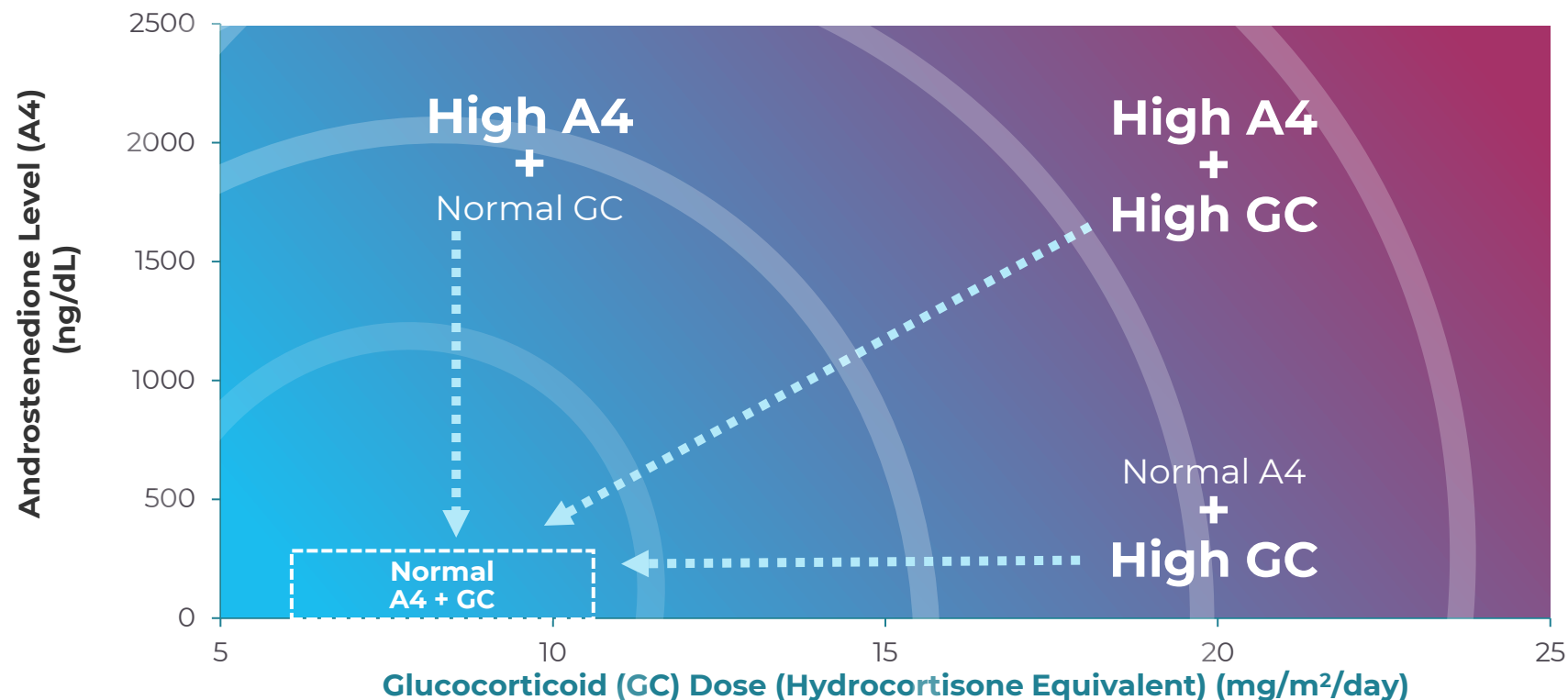
*"I have to keep my meds with me all the time and set alarms to take them...weight gain, fatigue, and mental health are all challenges."*

– Abram, Living with CAH



**Amanda's Daughter**  
Living with CAH

# Atumelnant Vision: Healthier Hormone Levels for People Living with CAH



A single pill taken once a day that eliminates excess ACTH driven adrenal activation *and its clinical sequelae* for people struggling with Congenital Adrenal Hyperplasia

# Phase 2 Study of Atumelnant in Congenital Adrenal Hyperplasia (CAH)

## Key Eligibility Criteria

**N=34-40**

- Male or female participants  $\geq 18$  to 75 years. Age:  $\geq 16$  years (US)
- Classic 21-hydroxylase deficiency
- On  $\geq 15$ mg Hydrocortisone equivalent daily dose
- A4  $> 1.5 \times \text{ULN}$

## Treatment Arms:

- 4 cohorts, each 12 weeks (N=6-12)

**80 mg Once Daily (PM Dosing) (n=11)**

**40 mg Once Daily (PM Dosing) (n=11)**

**120 mg Once Daily (PM Dosing) (n=6)**

**80 mg Once Daily (AM Dosing) + GC Reduction (n=6-12)**

**Open-Label Extension to Include Patients from All 4 Cohorts**

Pre-trial glucocorticoid therapy (dose and regimen) maintained throughout the study for first 3 cohorts

**Objectives:** Evaluate the Safety, Efficacy, and Pharmacokinetics of Atumelnant

**Primary Endpoint:** Change from baseline in morning serum A4 at week 12

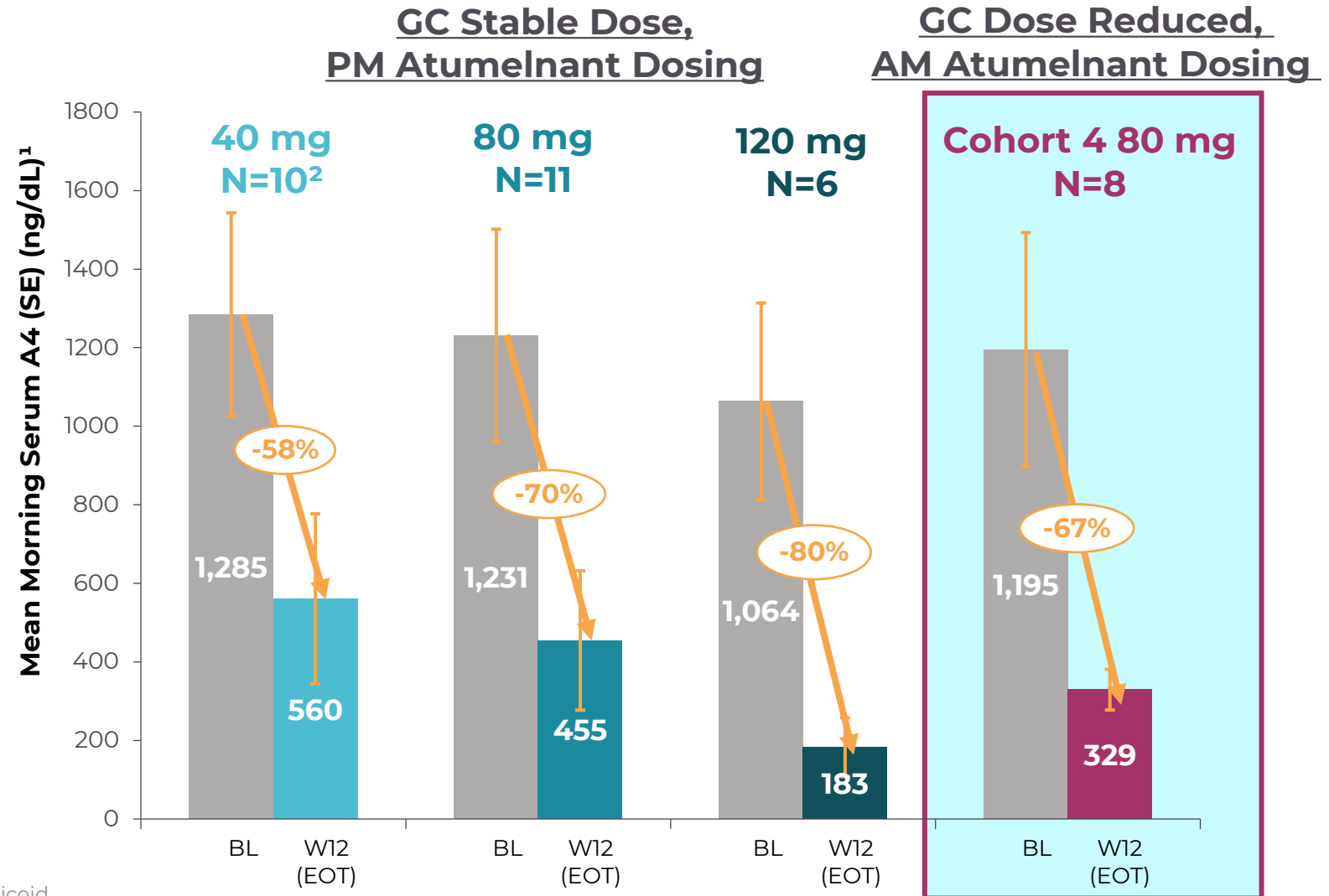
**Secondary Endpoint:** Change from baseline in morning serum 17-OHP at week 12

**Primary Safety Assessment:** Incidence of TEAEs throughout the study



# Rapid, Substantial and Sustained A4 Reductions, the Key Biomarker for CAH Disease Control

- All dose cohorts had substantial decreases vs. baseline, with the magnitude of response increasing with dose
- In Cohort 4, reducing glucocorticoid (GC) doses had no meaningful impact on magnitude of reduction in A4 levels
- Morning dosing of atumelnant in Cohort 4 also had no discernible impact on A4 reduction
- Additional data to be generated in ongoing open-label extension



BL = Baseline, W12 = Week 12; EOT = End of Therapy. GC = Glucocorticoid

<sup>1</sup> Percentage declines shown on chart represent the means of individual percentage declines observed

<sup>2</sup> 1 participant had a missing week 12 value (taken outside time window).

# Atumelnant Continues to be Well Tolerated with No Serious Adverse Events Reported

## Phase 2 (N=38<sup>1</sup>)

### Cohort 1 – 3 (N=28) (Stable GC doses)

- Well tolerated, no serious adverse events and no treatment-related severe adverse events
- No discontinuations
- 1 participant at 120 mg experienced AST/ALT increases without increases in bilirubin and with values reverting to baseline off study drug

### Cohort 4 (N=10<sup>1</sup>) (GCs reduced)

- Well tolerated, no serious adverse events and no treatment-related severe adverse events
- No discontinuations due to adverse events
- No hepatic transaminase adverse events

## OLE (N=25 to date<sup>2</sup>) (GCs reduced)

- 7 participants now have exposure ≥20 weeks, of which 1 participant has reached >40 weeks of treatment
- Well tolerated, no serious adverse events and no treatment-related severe adverse events
- No discontinuations
- No hepatic transaminase adverse events

- Over 750 weeks of cumulative CAH patient exposure from the Phase 2 and OLE
- >200 participants have received atumelnant to date across the clinical development program, including healthy volunteer, clinical pharmacology, Cushing's and CAH studies

<sup>1</sup> Two subjects withdrew consent in Cohort 4.

<sup>2</sup> As of December 31, 2025, N=25 participants enrolled. OLE data based on limited data snapshot as of December 12, 2025. Atumelnant is an investigational drug currently in Phase 3 studies for the treatment of CAH.

# Atumelnant Data to Date Show Promising Profile for the Treatment of CAH

## Substantial Patient Impact



~12K  
Adults



~5K  
Children

Currently Living with  
CAH in the U.S.

## Positive Phase 2 Data

- ✓ Rapid and sustained mean A4 reductions of up to 80% as soon as 2 weeks and sustained at 12 weeks across all cohorts
- ✓ A4 reductions maintained in Cohort 4 while GC doses reduced to physiologic levels in 7 of 8 patients
- ✓ Well tolerated, with favorable benefit/risk profile

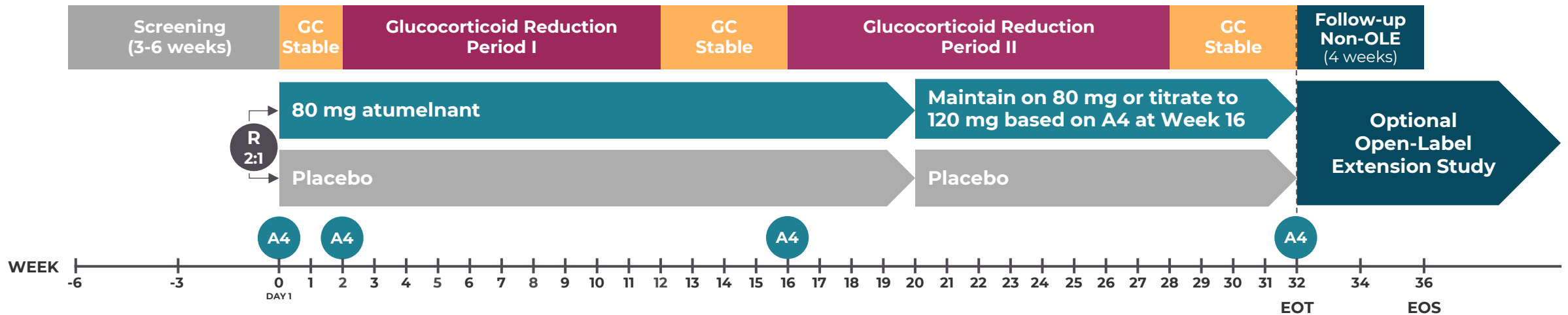
## Phase 3 Program Underway

- ✓ First patient randomized in **December 2025**
- ✓ Pediatric trial to initiate in 1H2026
- ✓ Phase 2 OLE ongoing to gather incremental data on longer duration of treatment, and will include patients rolling over from Phase 3

# Phase 3 Adult CAH Study Designed to Achieve Both A4 And GC Normalization

## Key Eligibility Criteria (N = 150):

- Male or female participants  $\geq 18$  to 75 years.
- Classic 21-hydroxylase deficiency
- Stable GC dose for 2 months
- A4  $>ULN^1$  with supraphysiologic GC dose ( $\geq 11$  mg/m<sup>2</sup>/day)
- A4  $>ULN^1$  with physiologic GC dose ( $<11$  mg/m<sup>2</sup>/day)
- Normal A4<sup>2</sup> with supraphysiologic GC dose ( $\geq 14$  mg/m<sup>2</sup>/day)



### 1 Primary Endpoint

Proportion of participants with morning **post-GC** A4  $\leq ULN$  who are on physiologic GC replacement at Week 32

### 2 Key Secondary Endpoints

- Percent change from baseline in serum morning **pre-GC** A4 at week 2
- Percent change from Baseline in serum early morning **pre-GC** 17-OHP at week 32
- Proportion of participants with morning **pre-GC** A4  $\leq ULN$  who are on physiologic GC replacement at Week 32
- Percent change from baseline in GC daily dose when **post-GC** A4  $\leq ULN$  at week 32

### 3 Other Secondary Endpoints

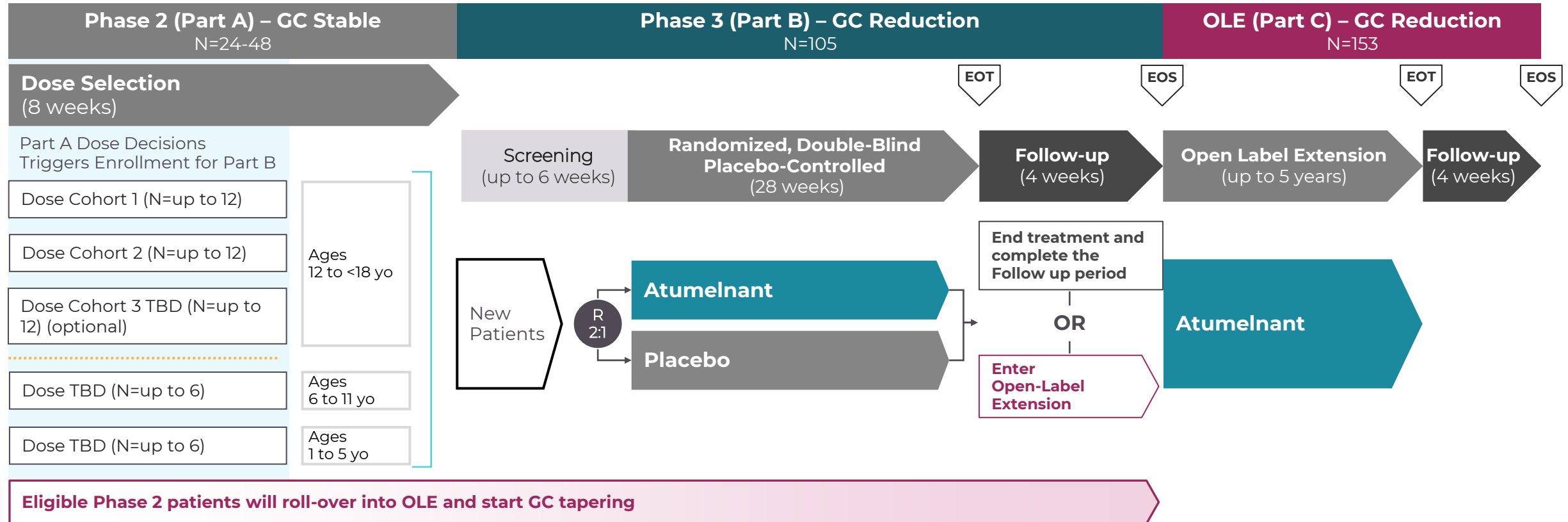
- Defined to evaluate the impact of atumelnant on the clinical signs, symptoms, co-morbidities and outcomes of CAH

<sup>1</sup>Approximate ULN is 150 ng/dL for males and 200 ng/dL for females.

<sup>2</sup>Normal A4 defined as above mid-range to  $\leq ULN$ .

A4: Androstenedione; GC: Glucocorticoid; ULN: Upper limit of normal; OLE: Open-label extension

# Pediatric CAH: Global Phase 2/3/OLE Operationally Seamless Study



## 1 Primary Endpoint

- Phase 2: Change from baseline in morning serum A4 at Week 8
- Phase 3: Percent change from baseline in GC daily dose at Week 28 while serum early morning A4  $\leq$  ULN
- OLE: Change from baseline in morning serum A4 over time

## 2 Key Secondary Endpoints (Phase 3)

- Change from baseline in morning serum A4 at Week 4
- Change from baseline in morning serum 17-OHP at Week 4
- Proportion of participants with physiologic GC dose while serum early morning A4 <ULN at Week 28

## Key Eligibility Criteria

- Male or female participants 1 to <18 years.
- Classic 21-hydroxylase deficiency
- Stable GC dose for 1 month
- A4 > ULN with supraphysiologic GC dose ( $\geq 11$  mg/m<sup>2</sup>/day)

# Establishing Uncompromising CAH Treatment Goals

## Androgen and GC Normalization



**Establishing the uncompromising treatment goal** of normal adrenal androgens (A4  $\leq$  ULN) with physiologic glucocorticoid replacement

## GC as Replacement, Not Treatment



Early and extended period for **glucocorticoid reduction** designed to achieve physiologic GC doses with the intent to **replace missing cortisol rather than to treat CAH**

## Tailored Therapy



**GC reduction periods** and **PD guided dose escalation** (80 to 120 mg) allows treatment to be tailored to the individual patient's needs

## Broad Patient Population



**Inclusive of patients who can benefit** from either androgen normalization, GC normalization or both

## Clinical Outcomes



**New disease-specific patient-reported outcomes tool** (CAHSIS PRO\*) and inclusion of metabolic parameters and other **signs and symptoms of CAH** (menses, BMI, blood pressure, glucose, lipids, bone density, polycythemia, etc.)

\* Exploratory

Atumelnant is an investigational drug in clinical studies. Its safety and efficacy have not been established.

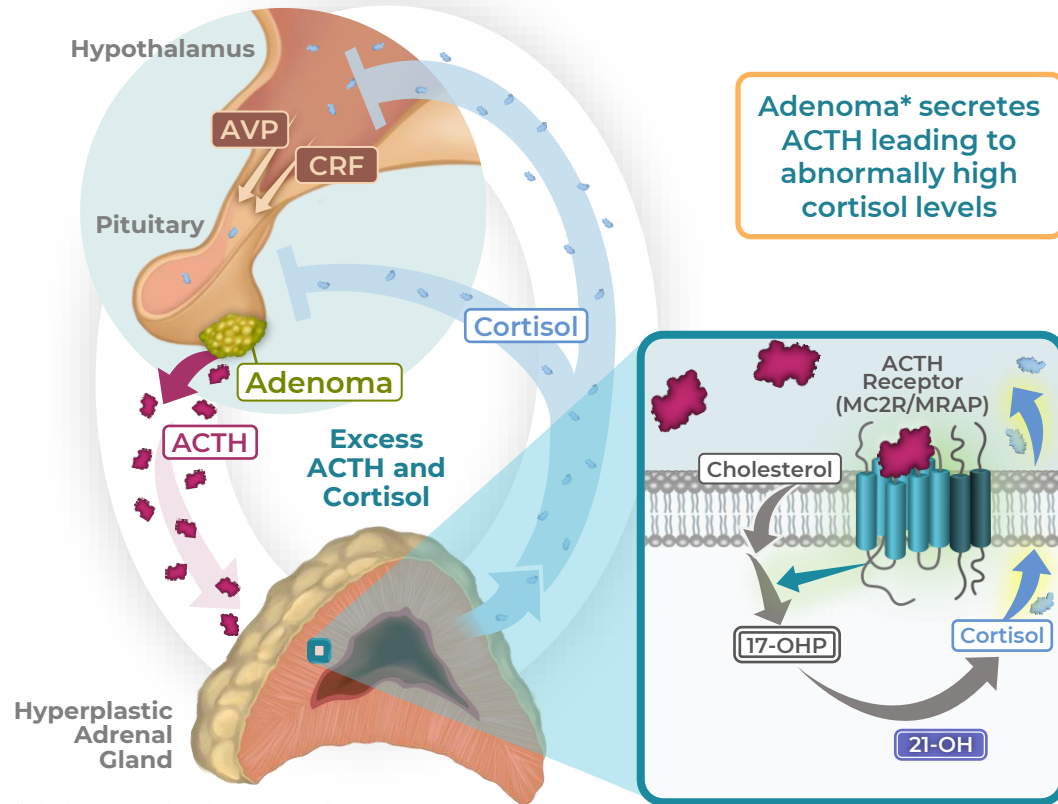
A4: Androstenedione; ULN: Upper limit of normal; PD: Pharmacodynamic; GC: Glucocorticoid; BMI: Body mass index; PRO: Patient-reported outcomes;

BMI: body mass index

# ACTH Dependent Cushing's Syndrome (ADCS): Second Indication for Atumelnant

## Disruptions in the HPA Axis Causing ADCS

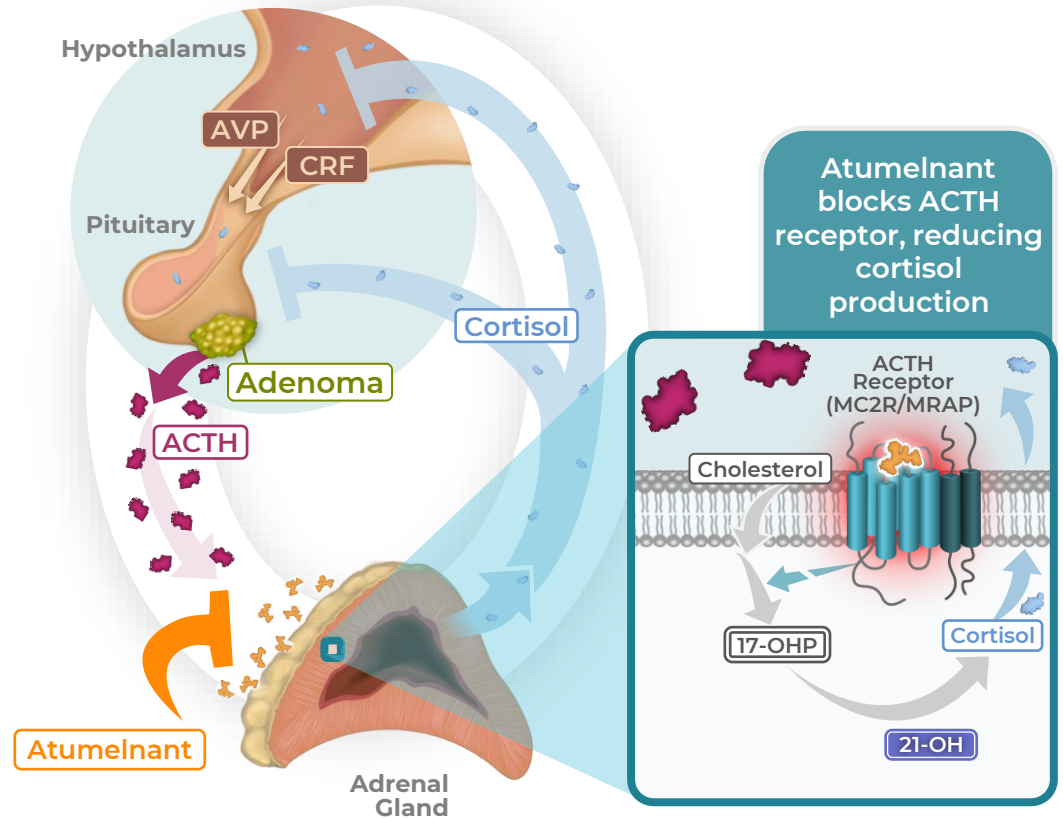
### Hypothalamic-Pituitary-Adrenal Axis



\*Pituitary or other (ectopic) adenoma

## Atumelnant Mechanism of Action in ADCS

### Hypothalamic-Pituitary-Adrenal Axis



Reference: Kim SH, Han S, Zhao J, et al. Discovery of CRN04894: A novel potent selective MC2R antagonist. *ACS Med Chem Lett.* 2024;15(4):478-485.

Abbreviations: ACTH, adrenocorticotrophic hormone; AVP, arginine vasopressin; CRF, corticotropin-releasing factor; 17-OHP, 17-hydroxyprogesterone; 21-OH, 21-hydroxylase; MC2R, melanocortin type 2 receptor; MRAP, melanocortin 2 receptor accessory protein.

Atumelnant is an investigational drug being evaluated in clinical studies for ADCS.

# ADCS Medical Treatment Remains a Significant Unmet Need for the Endocrinology Field



## Unpredictable outcomes with existing therapies

---

Goal is to control cortisol levels (serum and urine cortisol) and reduce associated complications  
~50-80% efficacy but with unpredictable adrenal insufficiency or hypercortisolism  
Therapies given multiple times daily



## Unacceptable delay to cortisol normalization

---

Titration every 2+ weeks or longer  
*“Change in treatment should be considered if cortisol levels are persistently elevated after 2–3 months on max tolerated doses”<sup>1</sup>*



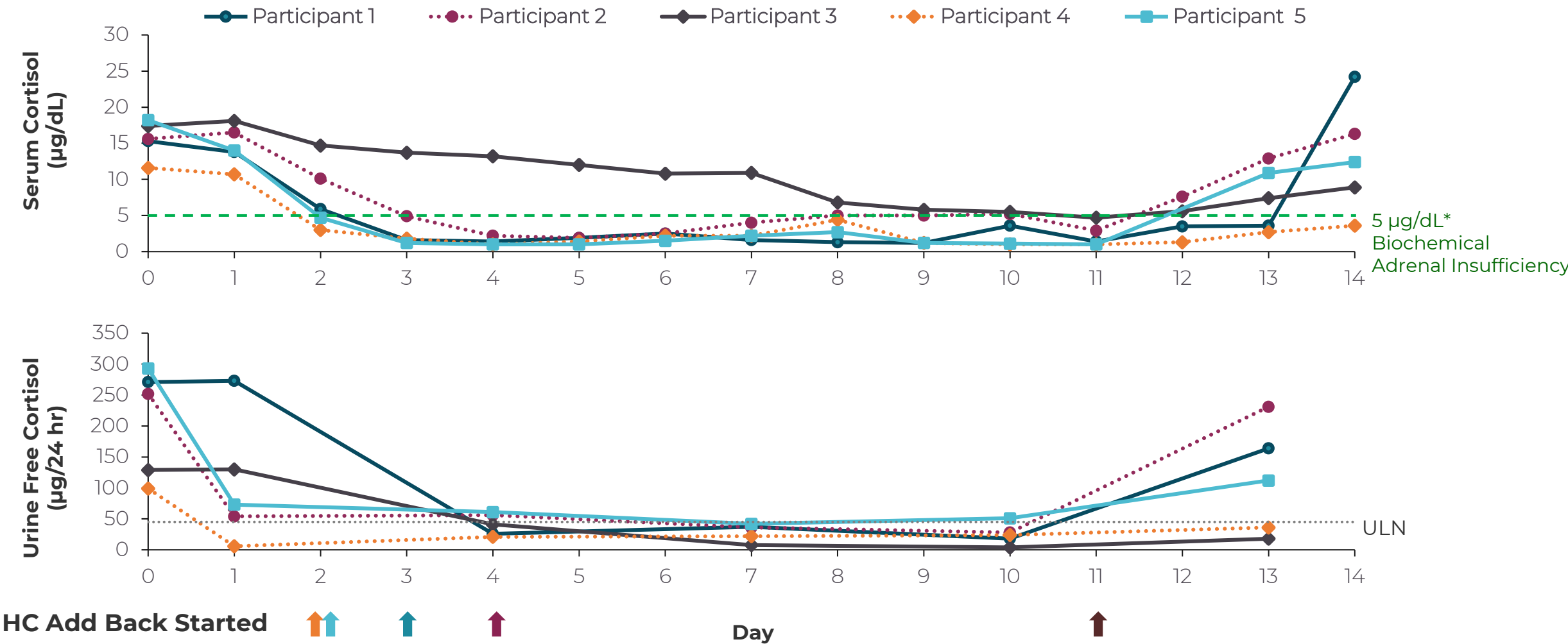
## Multiple Limiting Adverse events

---

- Hepatotoxicity
- Hypokalemia
- Hypertension
- Hyperandrogenism
- Hypogonadism
- QT prolongation

1. Fleseriu, Maria, et al. "Consensus on diagnosis and management of Cushing's disease: a guideline update." *The Lancet Diabetes & Endocrinology* 9:847-875, 2021.

# In Phase 1b/2a, Morning Serum Cortisol: All Participants Rapidly Achieved Cortisol Levels <5 µg/dL



Note: Data shown from initial participants in a single-center in-patient investigator sponsored trial.

# ACTH Dependent Cushing's Syndrome: Atumelnant Showed Profound, Rapid and Sustained Reduction of Excess Cortisol



## EFFICACY

- **Morning Serum Cortisol:** All Participants Rapidly Achieved Serum Cortisol Levels  $<5 \mu\text{g/dL}$
- **24-hour Urine Free Cortisol:** Sustained at or Below the ULN with Hydrocortisone Add-Back
- **Every Participant Experienced Improvement in Multiple Clinical and/or Cushing's Lab Features**



## SAFETY

Atumelnant was well-tolerated

**Initiate later stage clinical development in 2026**

Atumelnant is an investigational drug in clinical studies. Its safety and efficacy have not been established.

# World-class Discovery to Grow the Clinical Pipeline

**Following the Crinetics way** to create medicines  
to help increasingly larger numbers of people

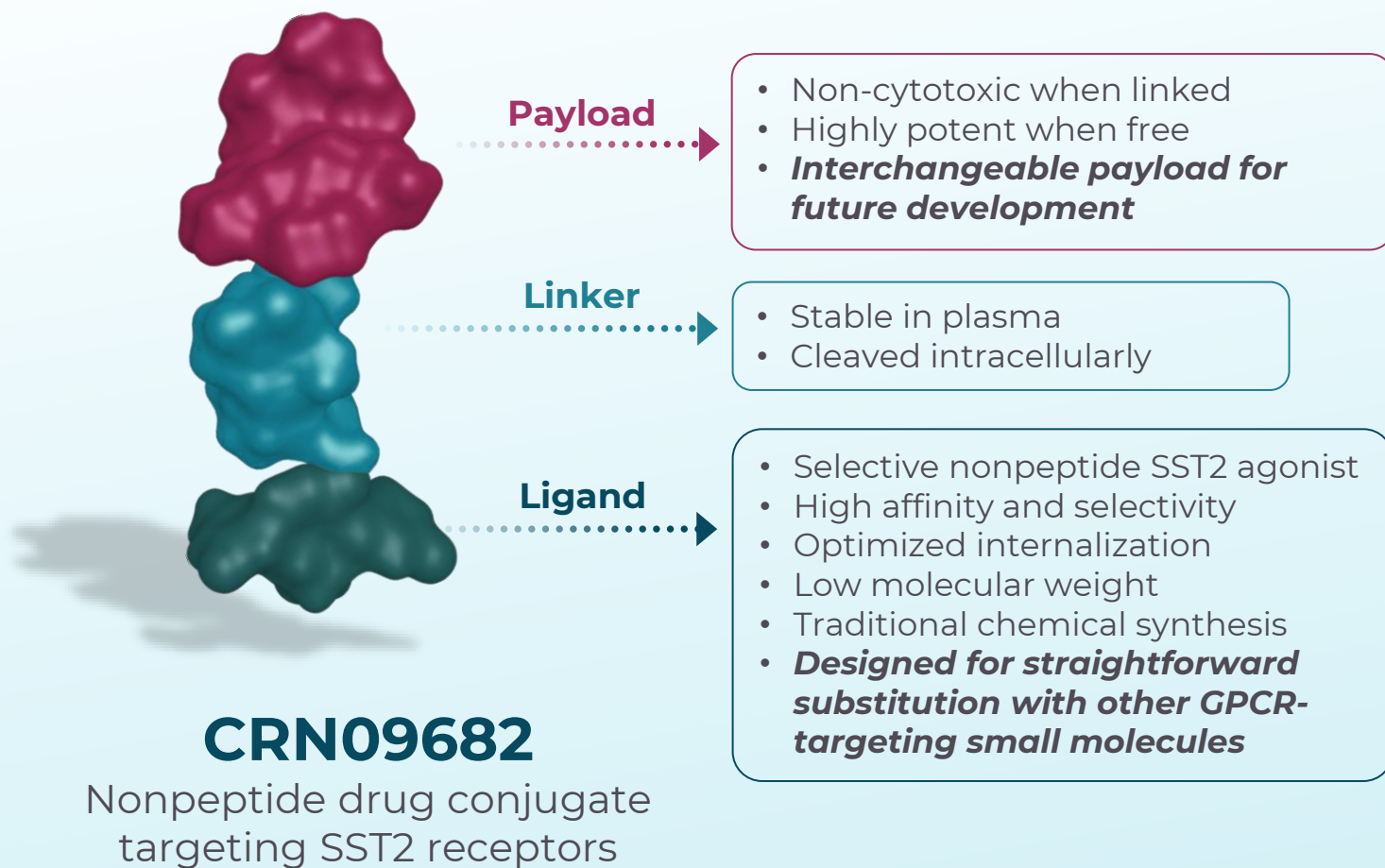


# Multiple INDs Driving Next Wave of Innovation

|                                                                                                                            |                                                                            |                                                           |                                                   |                                  |
|----------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|-----------------------------------------------------------|---------------------------------------------------|----------------------------------|
|  <b>Indication</b>                        | <b>Neuroendocrine Tumors (NETs)</b>                                        | <b>Hyperparathyroidism</b>                                | <b>Graves / TED</b>                               | <b>ADPKD</b>                     |
|  <b>Target</b>                            | SST2+ NDC (CRN09682)                                                       | PTH antagonist                                            | TSH antagonist                                    | SST3 agonist                     |
|  <b>Approximate US Patient Population</b> | <b>140K patients</b> with SST2+ NETs                                       | <b>200K incident cases</b> of primary hyperparathyroidism | <b>3M+</b> patients with Graves, many develop TED | <b>300K+</b> patients with ADPKD |
|  <b>Potential Indications to Explore</b> | SST2+ Tumors (HR+ Breast, Head & Neck, Thyroid, Metastatic Melanoma, etc.) | Hypercalcemia of Malignancy; Tertiary Hyperparathyroidism | Thyroid Cancer, Goiters, Pretibial Myxedema       | Other Ciliopathies               |

**Phase 1 Data Provides Multiple Opportunities for Value Creation**

# CRN09682: First Candidate from Crinetics' Nonpeptide Drug Conjugate Platform for SST2-Expressing Tumors



## Differentiation vs. Current Modalities

### ● **Anticancer Agents** (Chemotherapies, PROTAC)

- X Not tumor specific
- X Unfavorable PK/ADME
- X Narrow therapeutic index

### Y● **Antibody-Drug Conjugate**

- X Long half-life
- X Poor tumor penetration
- X Nonspecific uptake

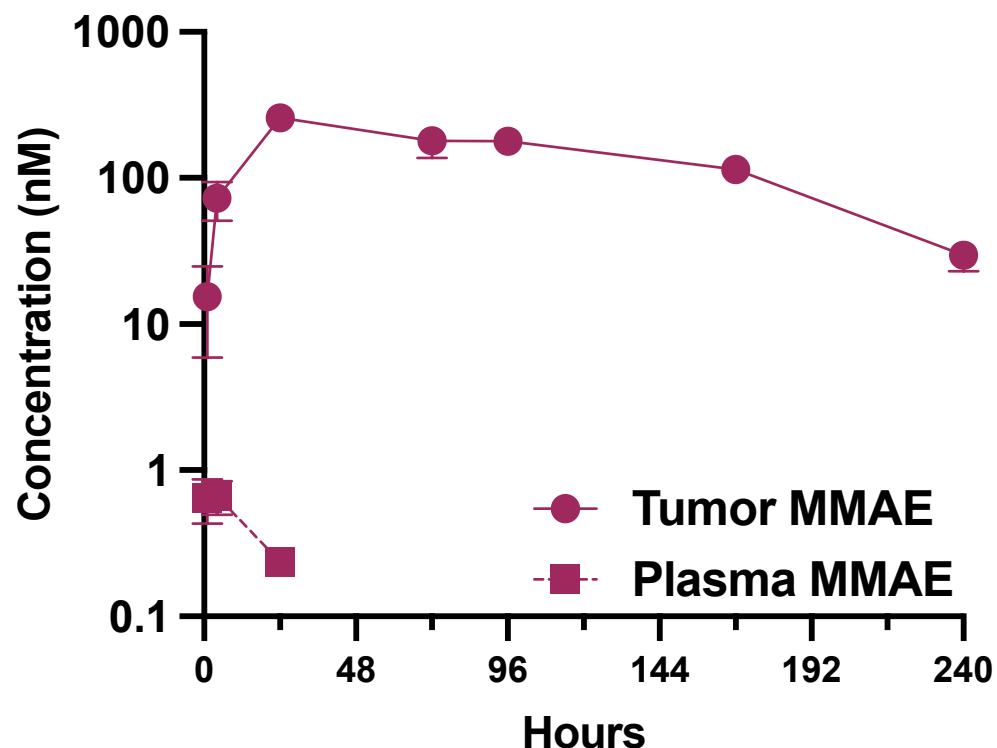
### ◀☢ **Radioligand Therapies**

- X Limited number of cycles
- X Radionuclide supply
- X Treatment logistics
- X Radiation safety

# IND Accepted for CRN09682, Phase 1/2 Initiated in NETs and SST2-Expressing Solid Tumors

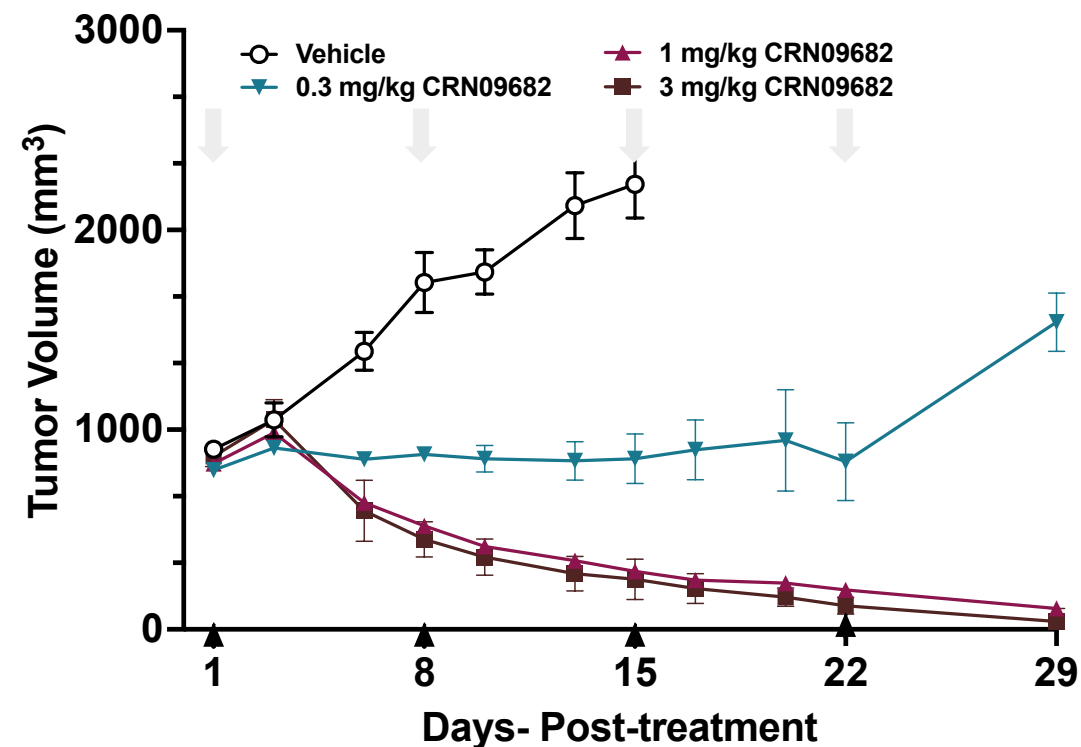
CRN09682 Selectively **Delivers MMAE to Tumors With Minimal Systemic Exposure to Free MMAE** in Mice

Concentrations of free MMAE in small cell lung tumor-bearing nude mice



CRN09682 Induces **Rapid Regression of SST2+ Small Cell Lung Tumors** in Nude Mice with High Tumor Burden

CRN09682 Efficacy study in NCI-H524 tumor model



# CRN09682: Promising Potential for Neuroendocrine Tumors and Other SST2+ Tumors

## Substantial Patient Impact



~11-21K people treated with antitumor agents for NETs<sup>1</sup> (U.S.)



And even more with other SST2+ tumors (U.S.)

## Promising Preclinical Data

- ✓ Selectively delivered MMAE into SST2+ SCLC tumor model with minimal systemic exposure to free MMAE
- ✓ Induced rapid tumor regression in SCLC preclinical cell-derived tumor model in a dose-dependent manner

## Phase 1/2 Program Underway

- ✓ First patient dosed in **November 2025**
- ✓ Phase 1 dose escalation study with Bayesian optimal interval design
- ✓ Phase 2 dose expansion study in SST2+ expressing neuroendocrine tumors, SCLC and other neuroendocrine carcinomas, and other solid tumors

# Exploring New Frontiers With Our Science to Expand Patient Reach



Obesity



Graves' Disease



Thyroid Ophthalmopathy



Hyperparathyroidism



Carcinoid Syndrome



Congenital Adrenal Hyperplasia



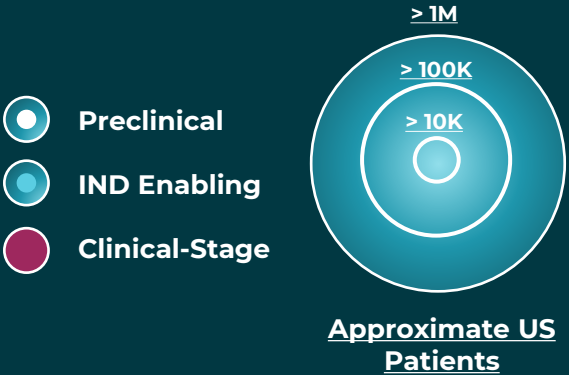
Other GPCR-  
driven Oncology



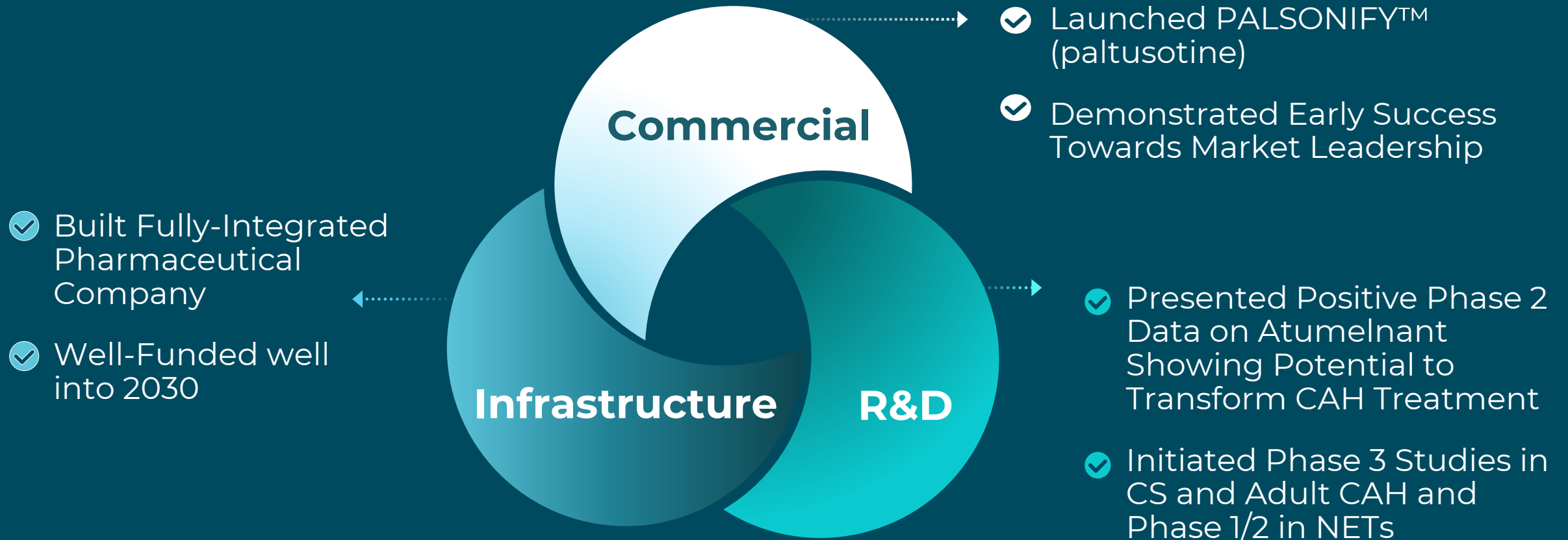
Polycystic Kidney Disease



Neuroendocrine &  
Other SST2+ Tumors



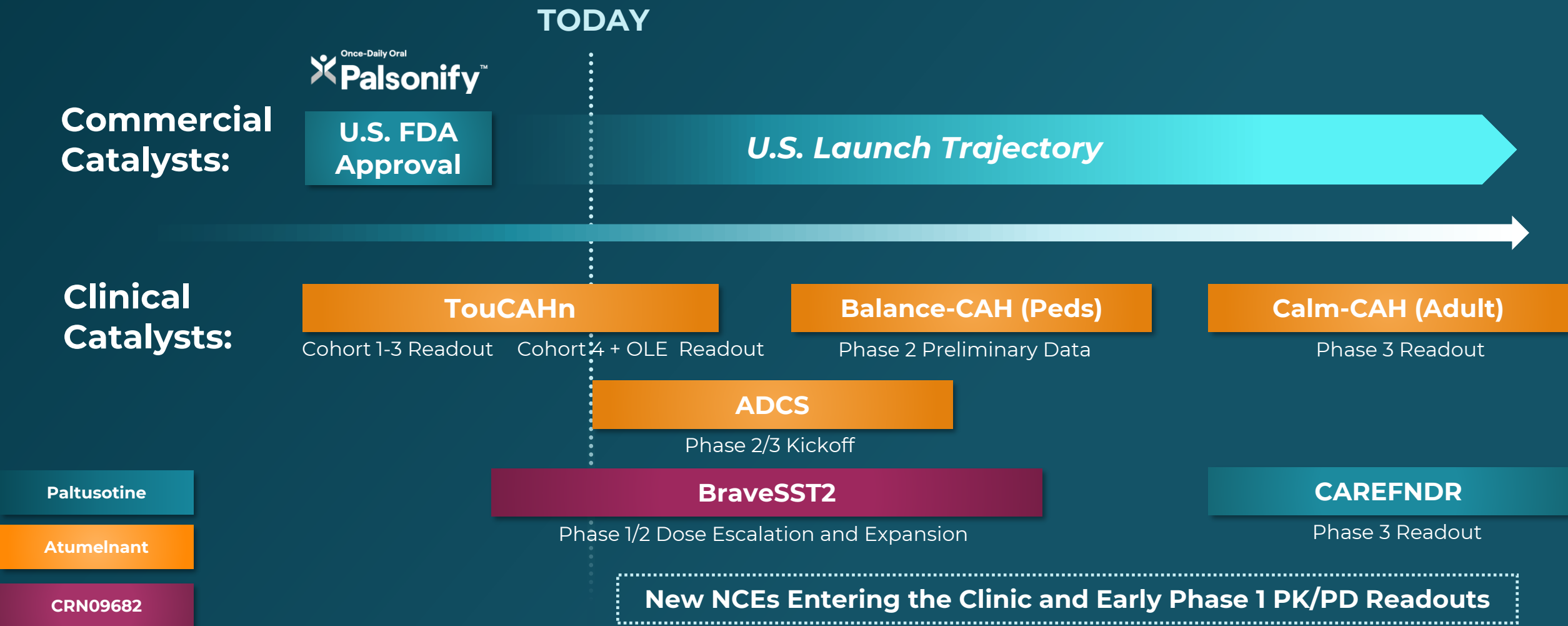
# 2025: A Breakout Year



**Preliminary and Unaudited ~\$1.4 Billion in Cash, Cash Equivalents, and Investments<sup>1</sup>**

<sup>1</sup> As of January 8, 2026; includes the net proceeds from our recent underwritten public offering of common stock that closed on January 8, 2026.

# Poised to Deliver Multiple Commercial & Clinical Catalysts in the Next 24+ Months



Abbreviations: ADCS, ACTH-dependent Cushing's Syndrome

# Vision 2030:

Emerging as the Premier  
Endocrinology Business



## **Sustainable Growth**

Funded by Revenue

**2**

**Marketed Products**

**4**

**Approved Indications**

**7+**

**Clinical Pipeline Candidates**



## **Pipeline Expansion**

Fueled by Internal Innovation

The vision for 2030 is aspirational and subject to significant risks, including the successful completion of ongoing and future clinical programs, regulatory review and approval by relevant authorities, and market conditions.