Crinetics Pharmaceuticals

# Corporate Presentation

February 2024

# Safe Harbor Statement

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics," the "company," "we," or "our") cautions you that statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the potential benefits of paltusotine for acromegaly patients and patients with carcinoid syndrome; the potential for the PATHFNDR program to support registration of paltusotine for all acromegaly patients who require pharmacotherapy; the plans and timelines for commercial launch and clinical development of paltusotine and CRN04894, including the therapeutic potential and clinical benefits or safety profile thereof; the appropriateness of the power assumptions used for the PATHFNDR-2 study; the expected timing of topline data and full results from the PATHFNDR-2 study and the Phase 2 study in patients with carcinoid syndrome and sharing the results with the FDA to align on and design a Phase 3 program; the expected timing of the submission of a new drug application for paltusotine for the treatment of acromegaly and related open label extension studies, and potential regulatory approval; the potential benefits of CRN04894 in patients with Cushing's disease or Congenital Adrenal Hyperplasia and the expected plans and timing for data from ongoing clinical studies; the potential benefits of PTH receptor antagonists for patients with hyperparathyroidism, the potential benefits of TSH antagonist for Graves' Disease or Thyroid eye disease; the potential for any of our ongoing clinical studies to show safety or efficacy; the potential of our ongoing discovery efforts to target future indications for hyperparathyroidism, polycystic kidney disease, Graves diseases, Thyroid eye disease, or diabetes/obesity, and the expected plans and timing for candidate selection and clinical development of such candidates; our plans to identify and create new drug candidates for additional diseases; the direction or trajectory of the Company's potential future growth, and our expected plans and timing for commercialization of paltusotine and other product candidates pending regulatory approval, including efforts in connection with prescribers, market research, payer engagement, and distribution channels. 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," "laying the foundation," "leading to," "goal," "potential," "aspiring," "target," or the negative of and other similar terms.

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: topline and initial data that we report may change following a more comprehensive review of the data related to the clinical studies and such data may not accurately reflect the complete results of a clinical study, and the FDA and other regulatory authorities may not agree with our interpretation of such results; the risk that preliminary results of preclinical studies or clinical studies do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available; the appropriateness of the power assumptions used for the PATHFNDR-2 study; the possibility of unfavorable new clinical data and further analyses of existing clinical data; potential delays in the commencement, enrollment and completion of clinical studies and the reporting of data therefrom; the FDA or other regulatory agencies may require additional clinical studies of paltusotine or suggest changes to our planned Phase 3 clinical studies prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; international conflicts may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical studies and preclinical studies, manufacturing and supply chain, or impairing employee productivity; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical studies, nonclinical studies and preclinical studies for paltusotine, CRN04894, our discovery efforts for hyperparathyroidism, polycystic kidney, Graves' Disease & thyroid eye disease or diabetes/obesity product candidates; regulatory developments or price restrictions 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; and other risks described under the heading "Risk Factors" in documents we file from time to time with the Securities and Exchange Commission ("SEC"). 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.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to addressable patients and addressable market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

# Building a Premier **Fully Integrated Endocrine-focused Pharmaceutical Company**

## Strategic Approach to **Growing Long-term Value**



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# **The Crinetics Way:** Endocrinology for Health

**Deep roots** in endocrinology

+

**Commitment** to transforming people's lives

+

**World-class in-house R&D**

=

**Purposely crafted medicines**




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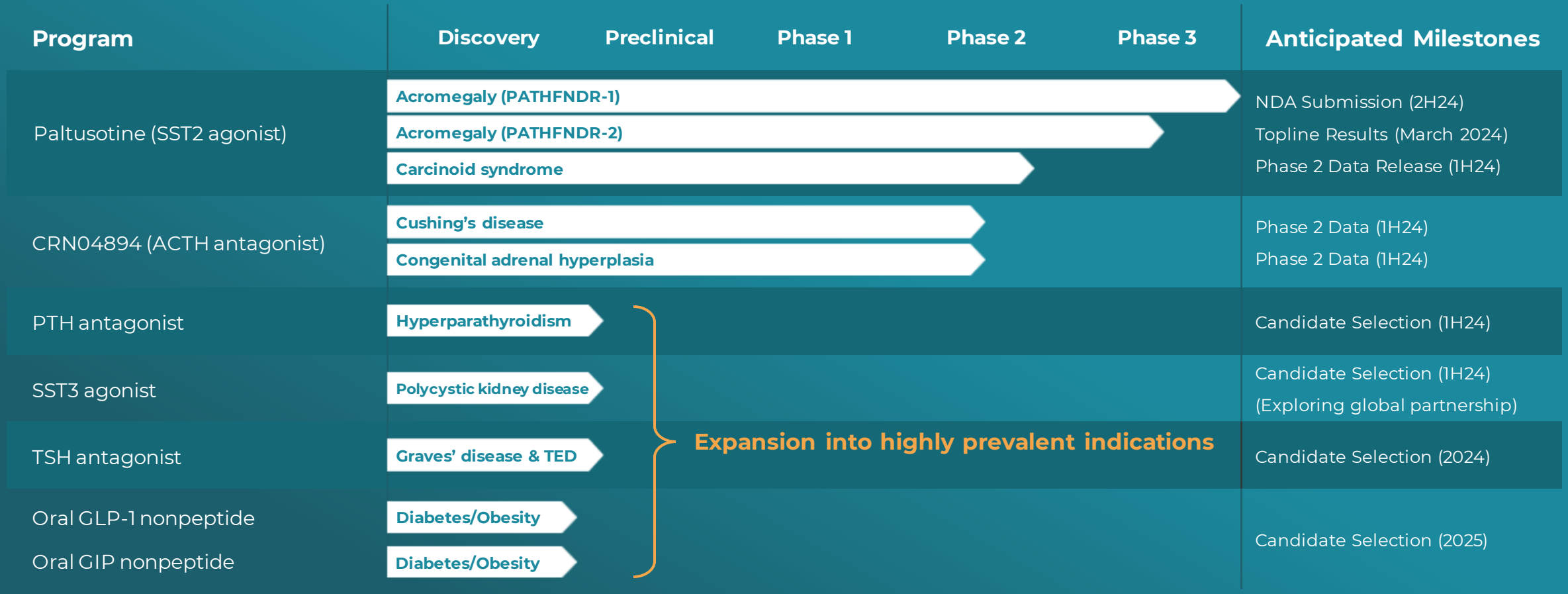
# Deep Pipeline of **Transformative Drug Candidates**




SST: somatostatin receptor type; ACTH: adrenocorticotropic hormone; PTH: parathyroid hormone; TSH: thyroid-stimulating hormone; TED: thyroid eye disease; GLP-1: glucagon-like peptide-1 receptor agonists; GIP: gastric inhibitory polypeptide



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# **World-class Development** Leading to Global Commercialization

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

**PATHFNDR-1**
**PHASE 3 RESULTS**

**CARCINOID SYNDROME**
**PHASE 2 RESULTS**



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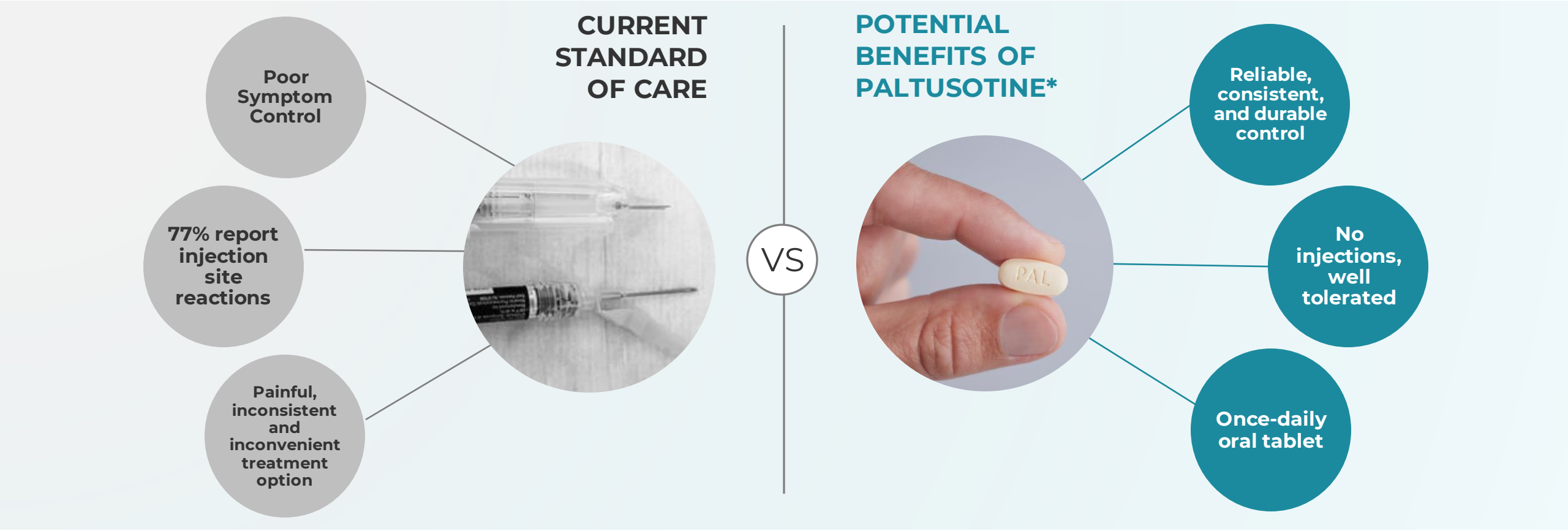
# **Paltusotine:** Designed to Allow People with Acromegaly and Carcinoid Syndrome to Focus on Living




***Pending receipt by paltusotine of regulatory approval. Clinical studies to support applications for regulatory approval are ongoing.**

**References** 1. Geer EB, Sisco J, Adelman DT, et al. Patient reported outcome data from acromegaly patients treated with injectable somatostatin receptor ligands (SRLs) in routine clinical practice. *BMC Endocr Disord*. 2020;20(1):117. doi:10.1186/s12902-020-00595-4; 2. Strasburger CJ, Karavitaki N, Störmann S, et al. Patient-reported outcomes of parenteral somatostatin analogue injections in 195 patients with acromegaly. *Eur J Endocrinol*. 2016;174(3):355-62. doi:10.1530/EJE-15-1042; 3. Fleseriu et al. Frontiers in Endocrinology; March 2021, Vol.12

# **PATHFNDR-1 Positive Phase 3 Results in Acromegaly** Provide Strong Footing for First Commercial Launch* in 2025

### PRIMARY ENDPOINT

**83%** of participants on paltusotine maintained IGF-1 ≤ 1.0xULN vs **4%** on placebo ($p < 0.0001$)

### SECONDARY ENDPOINTS
(paltusotine arm vs placebo)

Change from baseline in IGF-1 ($p < 0.0001$)

Change from baseline in Acromegaly Symptoms Diary score ($p = 0.02$)

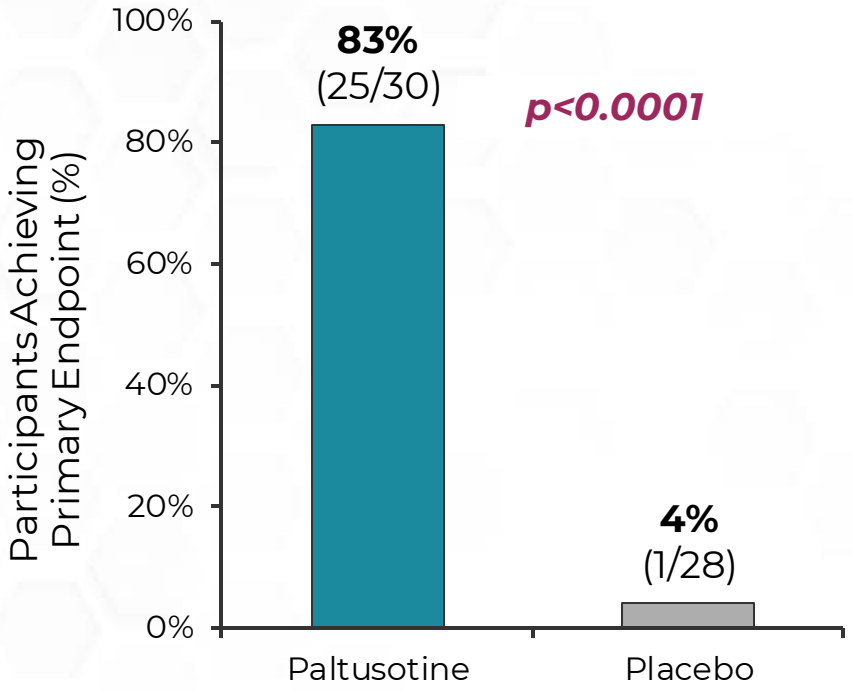
Proportion of participants who maintained GH <1.0 ng/mL ($p = 0.0003$)

### SAFETY

Paltusotine was well-tolerated with no severe or serious adverse events

Paltusotine demonstrated no new safety signals

***Paltusotine is an investigational drug in clinical studies for the treatment of acromegaly and carcinoid syndrome***



# PATHFNDR-2 STUDY

## Key Eligibility Criteria

Acromegaly patients who are:

(1) Medication naïve (or untreated ≥4 mo.)

**OR**

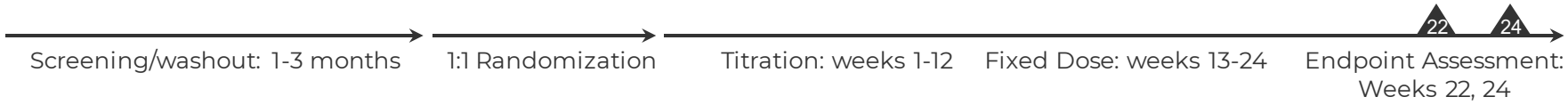
(2) Washed out of octreotide or lanreotide

R

- Placebo
- Paltusotine

Treatment Period: 24 weeks

- Starting dose: 20 mg QD or placebo
- Week 2: Initial forced dose escalation to 40 mg
- Increase to 60 mg QD if IGF-I > 0.9x ULN
- Decrease by 20 mg if necessary for tolerability
- IGF-1 samples taken periodically throughout treatment period
- Final study enrollment: 111 participants including treatment naïve (n=46), untreated ≥4 mo. (n=36), and washed out (n=29)




## Endpoints

**Primary:**

- Proportion of subjects who achieve IGF-I levels ≤ 1.0x ULN (mean of IGF-I at weeks 22, 24)

**Key Secondary:**

- Change from baseline IGF-I

**Secondary:**

- Proportion of patients with GH <1 ng/mL at endpoint assessment
- Change from baseline in total Acromegaly Symptoms Diary (ASD) score

**Statistical powering:**

- Power estimate = 90%

## Rescue Criteria

Patient is rescued with an injectable and classified as a non-responder if following criteria are met at **60 mg dose**:

- Two consecutive IGF-I ≥ 1.5x ULN

**AND**

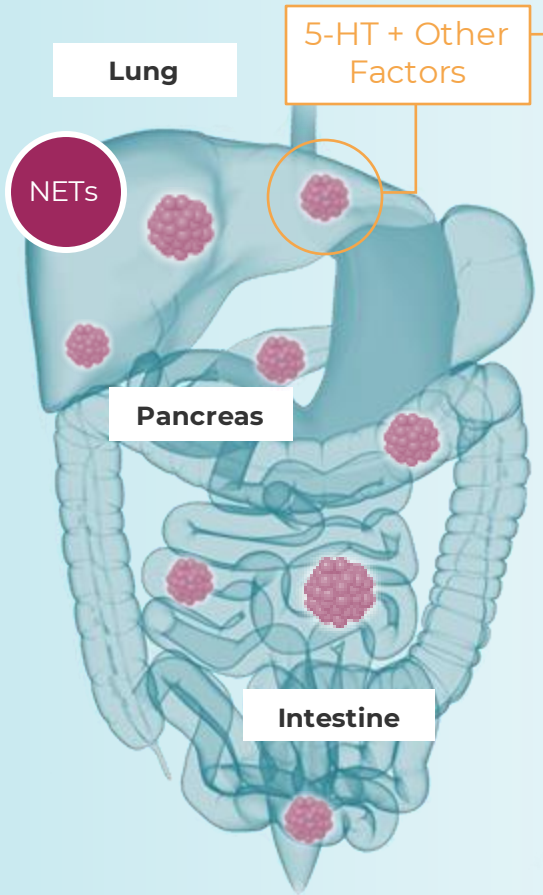
- Exacerbation of acromegaly clinical signs/symptoms

## Timelines

- Topline Data expected in March 2024
- Study to be followed by an OLE for eligible patients

ULN: Upper Limit of Normal; QD: Once daily; OLE: Open label extension

# **Paltusotine:** Progressing Towards Phase 3 in a Second, More Prevalent Indication



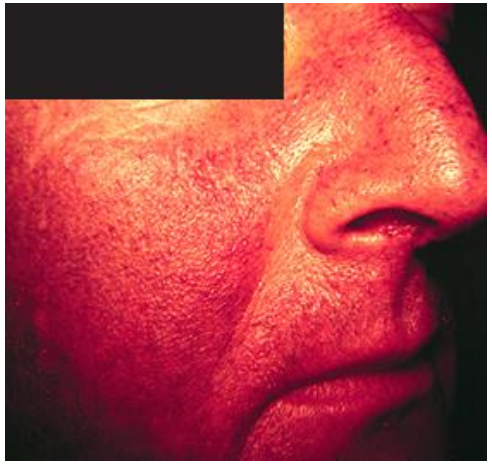

## Carcinoid Syndrome

~**33,000** Patients Diagnosed with Carcinoid Syndrome (US)

## Treatment Goals

- **Reduce frequency and urgency of highly disruptive excess bowel movements**
- **Reduce frequency and severity of severe flushing episodes which can be debilitating and potentially dangerous**
- **Prevent severe complications from carcinoid heart disease (found in up to 50% of patients) & carcinoid crisis**
- **Eliminate breakthrough of symptoms with injected SRLs and reduce a high burden of care**

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



*Courtesy of Stephen E Goldfinger, MD* UpToDate®

 5-HT = Serotonin; NETs = Neuroendocrine tumors; SRL = somatostatin receptor ligand

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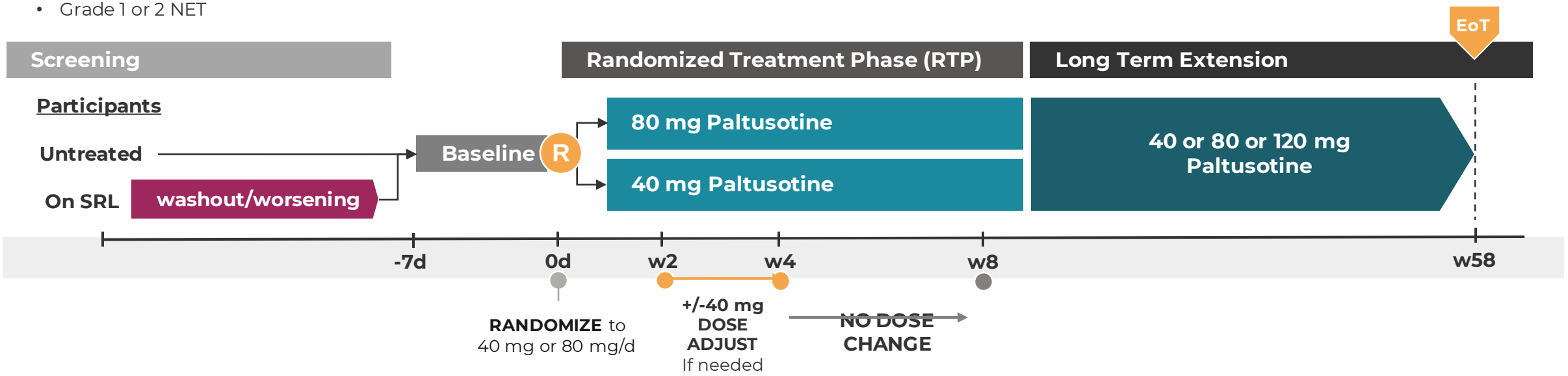
# Phase 2 Study Design: Evaluating Safety, PK and Efficacy of Paltusotine in Carcinoid Syndrome Patients

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

**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 at 40, 80 and 120 mg doses

**Exploratory Endpoints**

Bowel movement and flushing frequency, octreotide rescue use, biomarkers, stool consistency, abdominal pain, PRO measures



SSTR = somatostatin receptor; SRL = somatostatin receptor ligand
EoT = end of treatment; PRO = patient reported outcome

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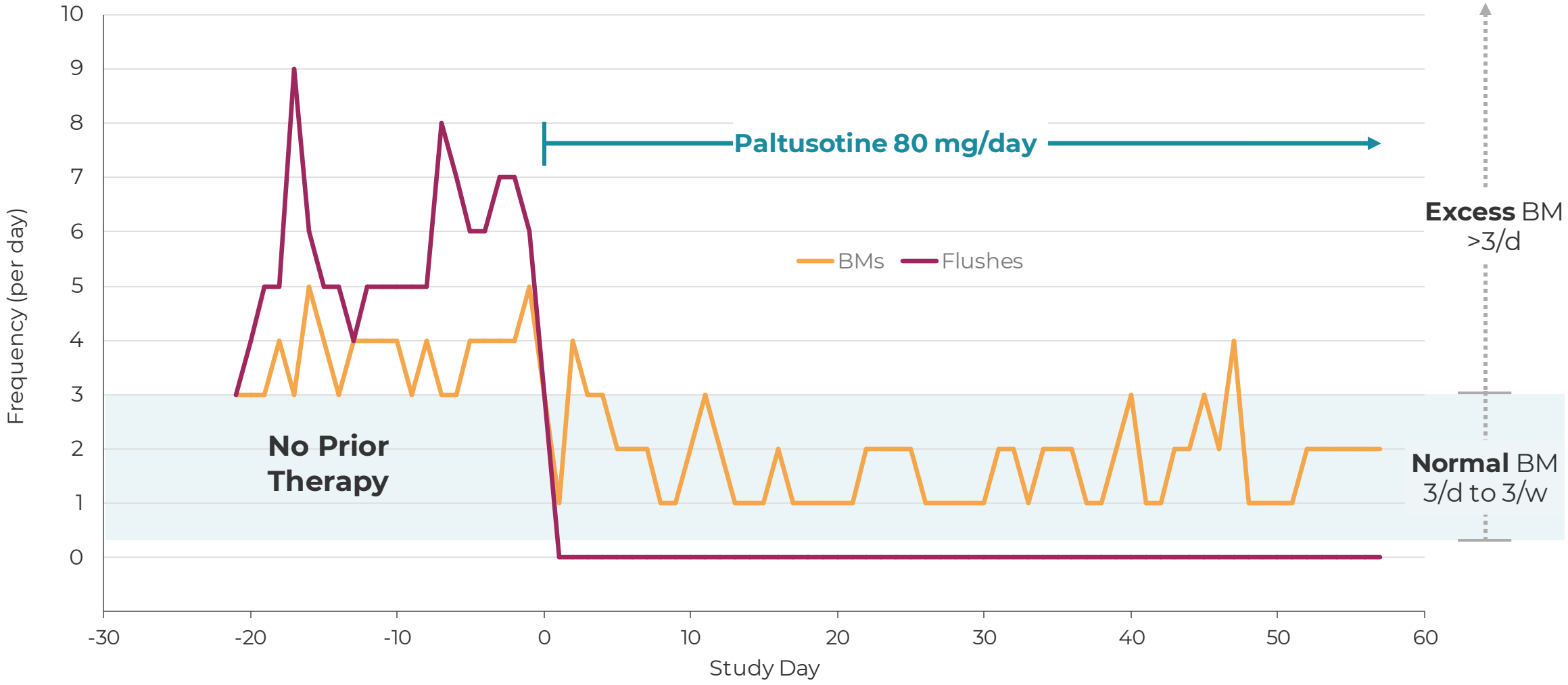
# **Example Carcinoid Syndrome Study Participant:**
## Elimination of Flushing and Normalization of BMs




**BM** = bowel movement



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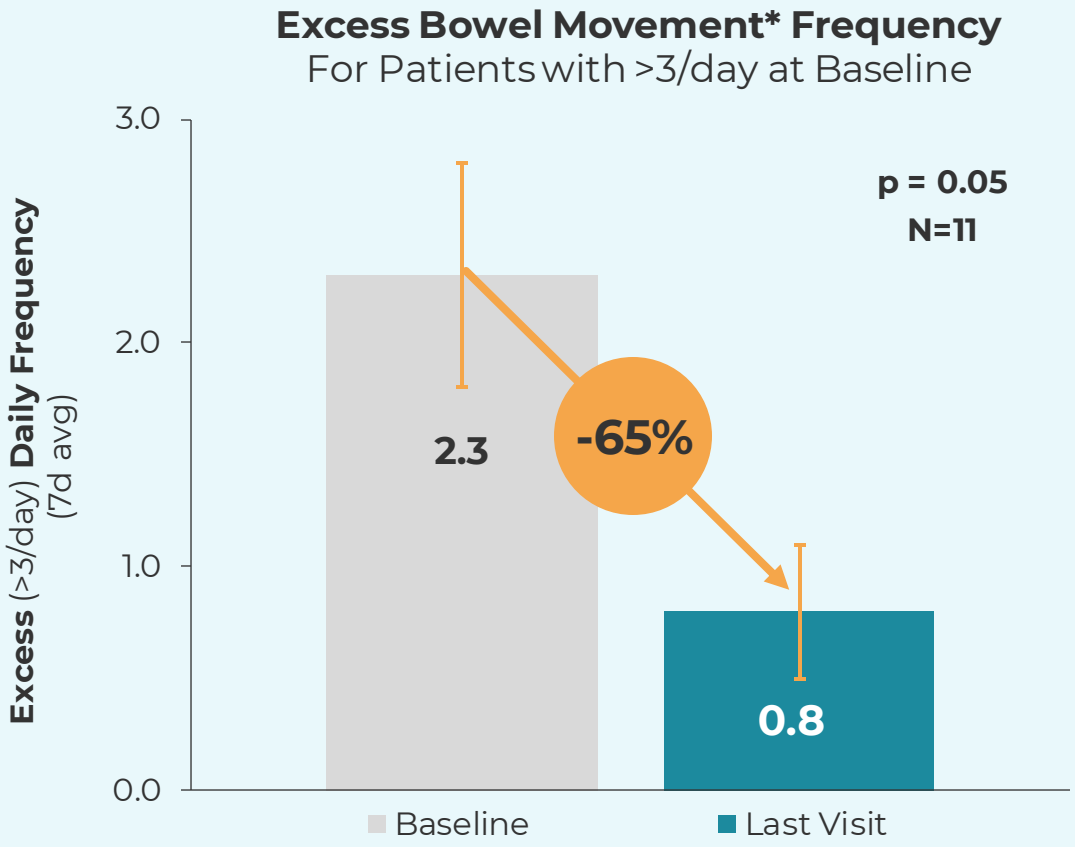
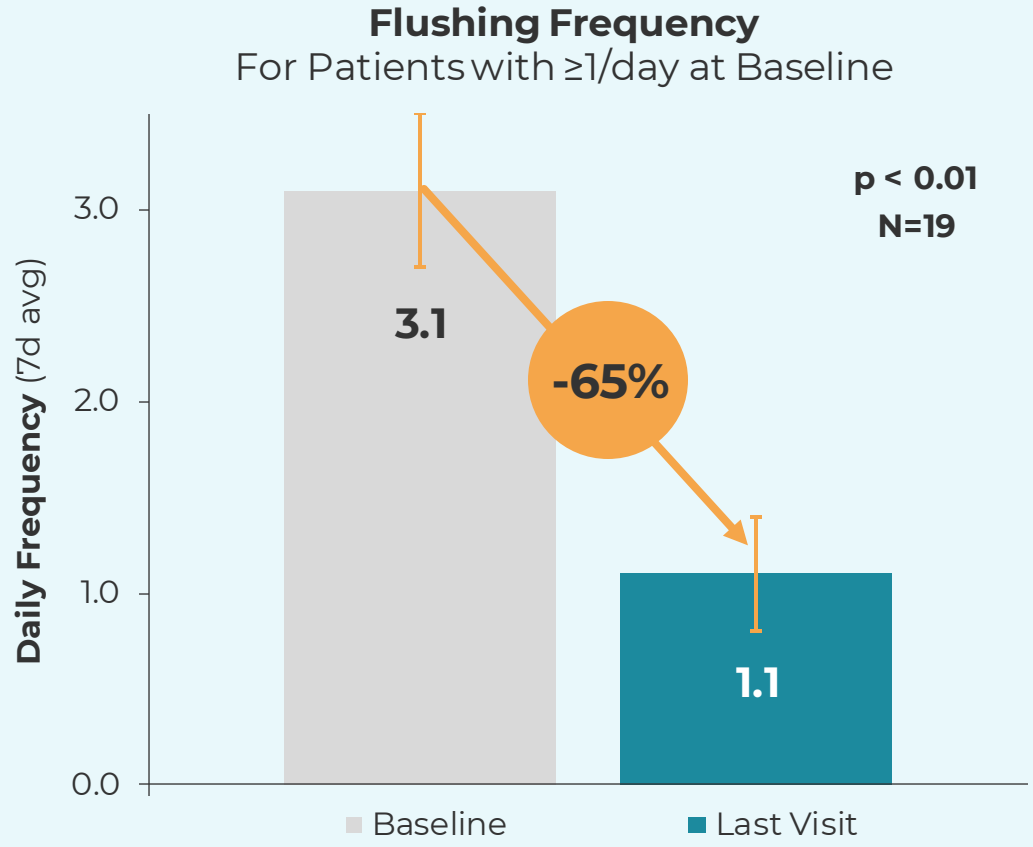
# **Paltusotine** Reduced the Frequency of Both Key Carcinoid Syndrome Core Symptoms: Excess BM and Flushing




*Excess bowel movements (BM) were defined as daily bowel movements above the upper limit of normal (3 per day)
Exploratory analysis of last visit prior to the preliminary data cut off includes 23 subjects: 15 subjects completed the week 8 visit, 4 subjects completed week 6 visit, 3 subjects completed week 4 visit and 1 subject completed week 2 visit.



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# **Paltusotine:** Initial Multi-billion Dollar U.S. Market Opportunity in Acromegaly and Carcinoid Syndrome

| **Diagnosed Prevalence** (U.S. Patients) | Acromegaly **27,000** | Carcinoid Syndrome **33,000** |
|---|---|---|
| **Addressable Patients** Candidates for SRL | **11,000** *Not cured surgically* | **33,000** |
| **Current Patients** On Endocrine Therapy* | **10,000** | **10,000** |
| **Average Annual WAC**** For Injectables | **$70K** | **$100K** |
| **Current Market** For Endocrine Therapy (U.S.) | **$700M** | **$1,000M** |
| **Total Addressable Market** For Endocrine Therapy (U.S.) | **$800M** | **$3,300M** |

*Endocrine therapy includes SRLs, dopamine agonists, and growth hormone antagonists.
**WAC: Wholesale acquisition cost; Sources: Company data on file



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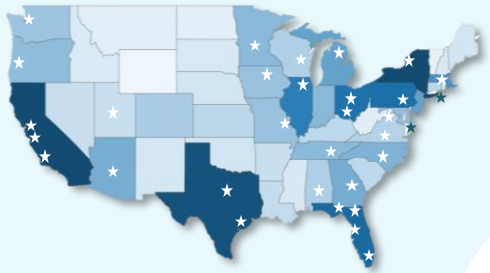
# **Building the Base for Commercial Success** in Multiple Indications for Paltusotine

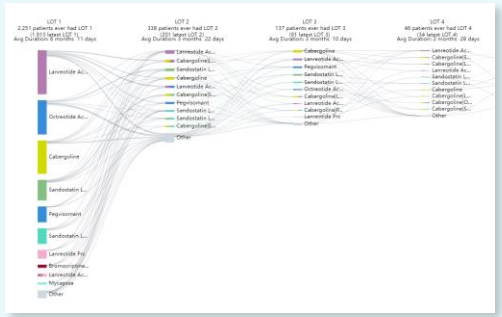
## Complete Prescribers Map

- 200 HCPs initiating 80% of acromegaly scripts
- 40 overlapping centers for both pituitary and NCCN
- Ad boards with top prescribers
- Expanding Med Affairs team



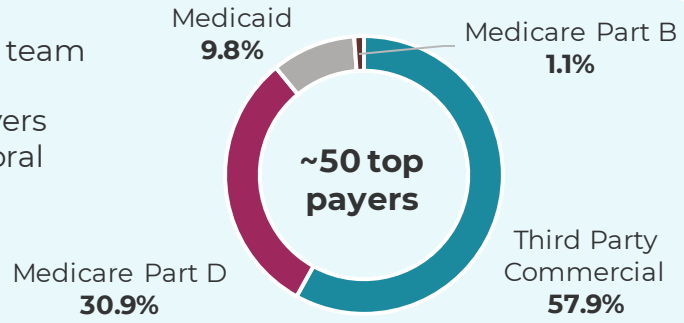

## Market Research

- Backbone of marketing group in place
- Market research indicates burden of care is key to overcome inertia
- Compelling PATHFNDR-1 data is strengthening awareness



## Payer Engagement

- Backbone of market access team in place.
- Engaged 50% of top US payers
- Payers appreciate value of oral option




## Distribution Channel

- Finalized third party logistics vendor contract
- Negotiating specialty pharmacy network contracts
- Building Crinetics' Provider & Patient Services Hub




**NCCN:** National Comprehensive Cancer Network
Source: Crinetics interviews & market research

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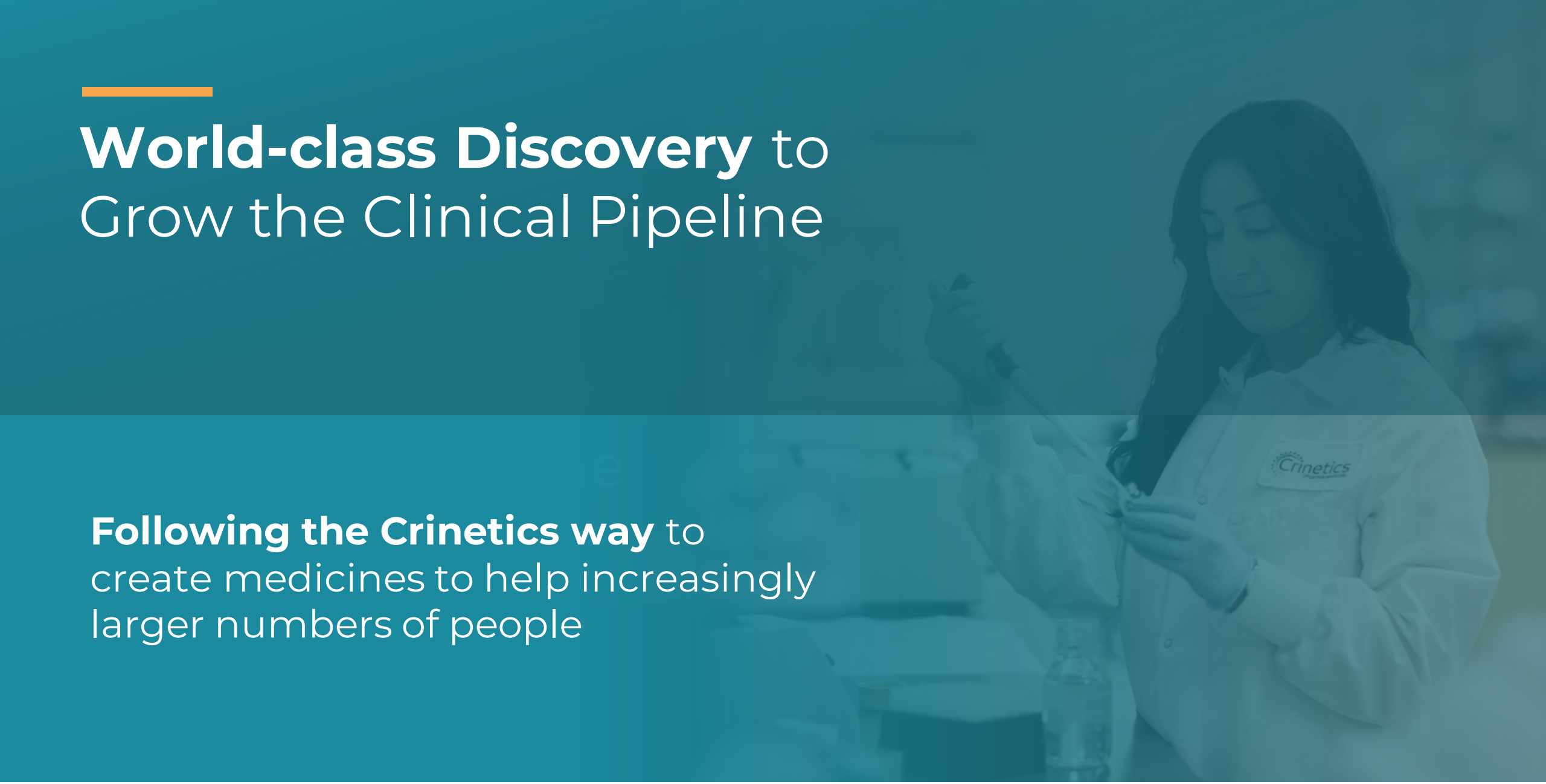
# **World-class Discovery** to Grow the Clinical Pipeline



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



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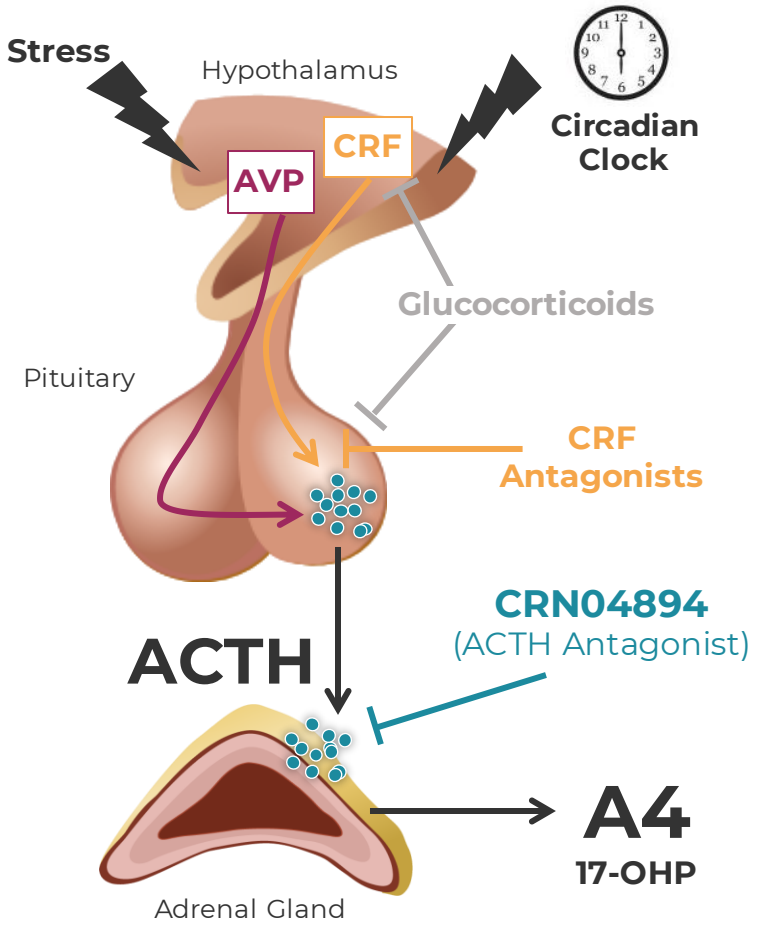
# **CRN04894:** Second Clinical Asset In Late-Stage Development Skillfully Crafted to Help Patients Reach Their Treatment Goals




## Lead Indication: Congenital Adrenal Hyperplasia (CAH)

**~27,000** Patients Prevalent/Diagnosed with Classical CAH (US)

## Treatment Goals:

- Normalize/eliminate adrenal androgen production
- ✓ Restore normal menstrual cycles and fertility in women
- ✓ Shrink testicular adrenal rest tumors, alleviate pain, restore fertility in men
- ⊗ Prevent consequences of excess androgens in children: atypical genitalia, precocious puberty, short stature, hirsutism
- ⊗ Avoid complications of glucocorticoid excess (weight gain, hypertension, bone disease…) and enable physiologic replacement levels



**AVP:** arginine vasopressin, **CRF:** corticotropin releasing factor; **A4:** androstenedione; **17-OHP:** 17-hydroxyprogesterone, **ACTH:** Adrenocorticotropic hormone

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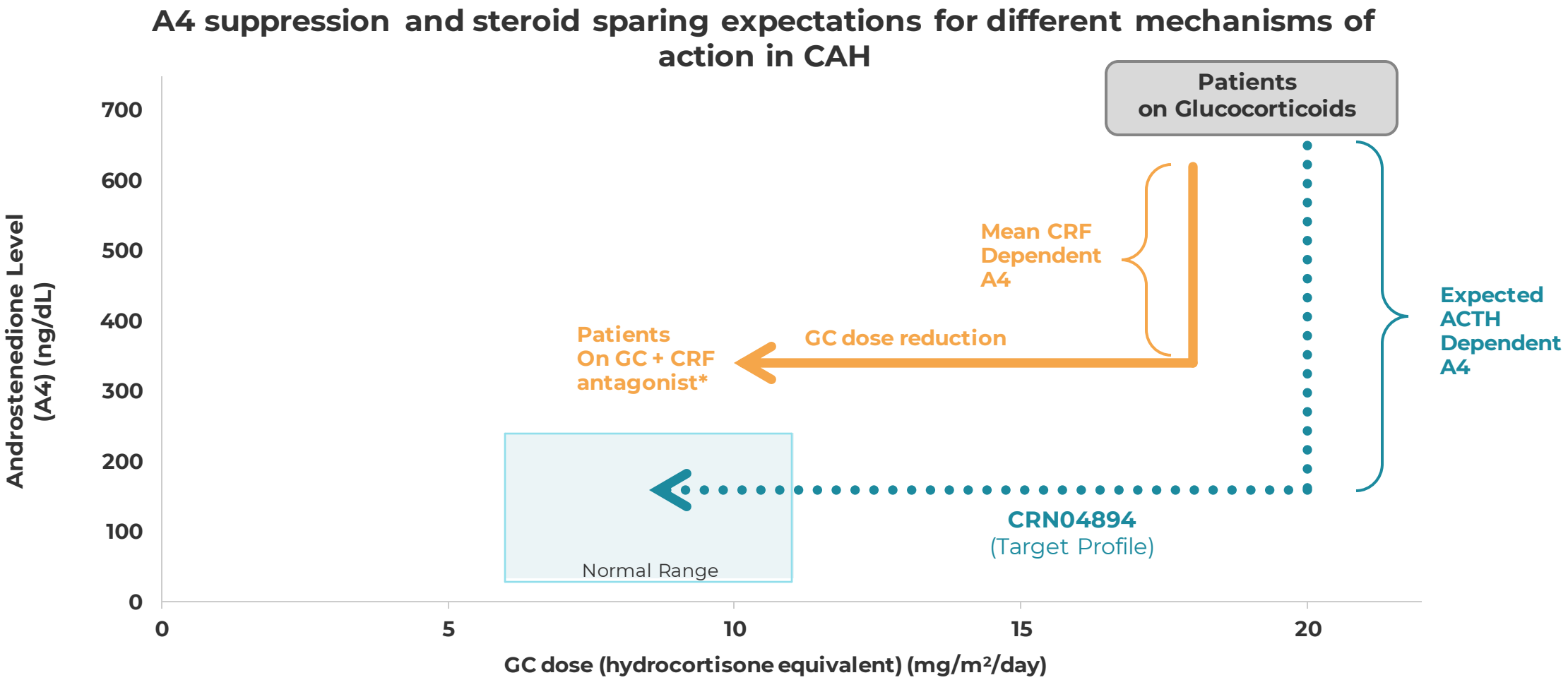
# **CRN04894**: Targeting Mechanism Designed to Provide Maximum A4 Suppression. Initial Data Expected 2Q24

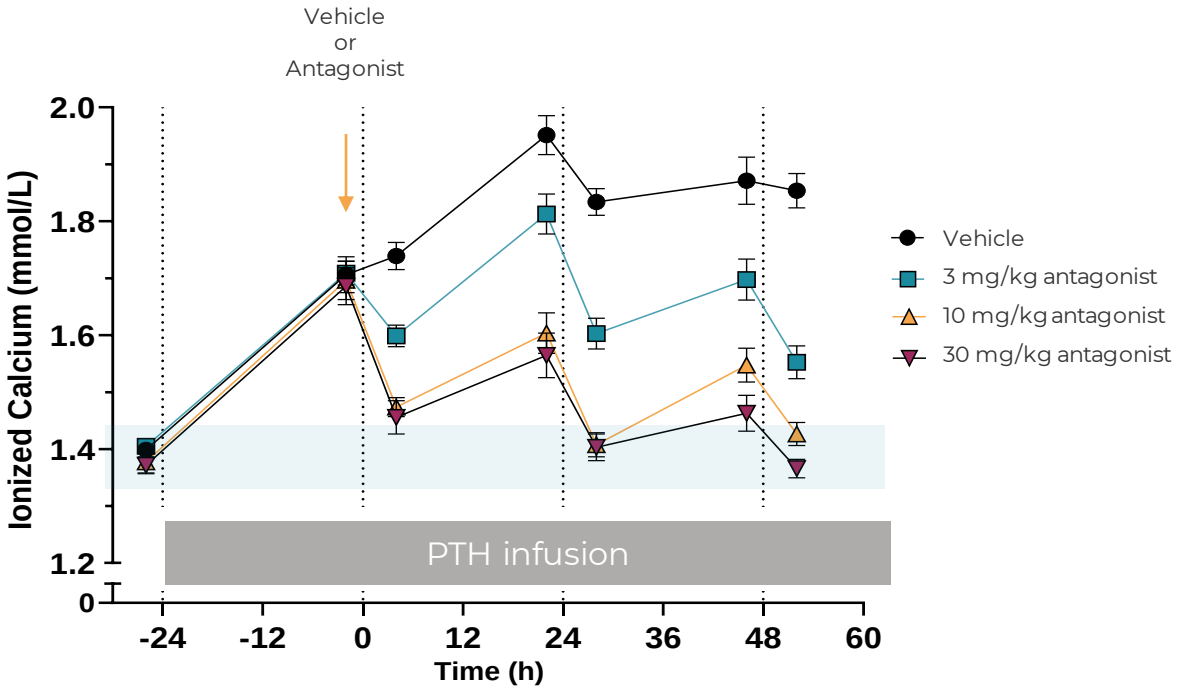





**CRF:** corticotropin releasing factor; **GC**: glucocorticoid; **A4**: androstenedione

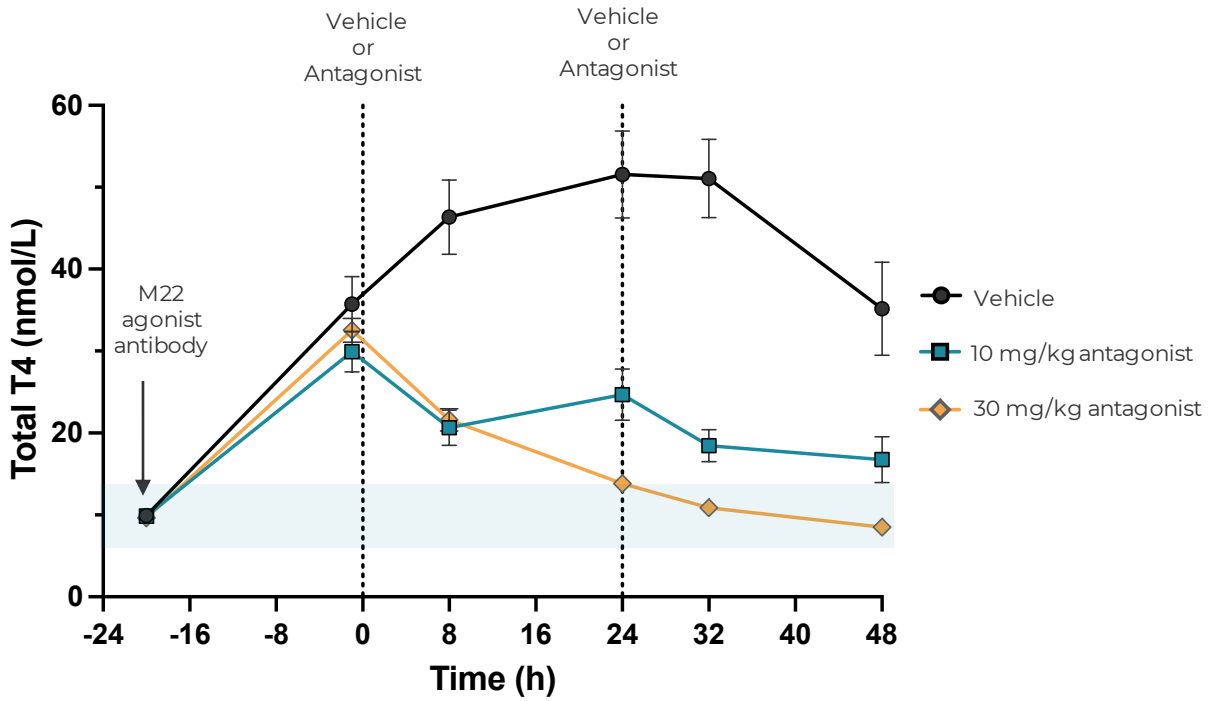
# Two New Programs Anticipated to Begin First-in-human Enabling Studies in 2024

## PTH Antagonist for Hyperparathyroidism




*Preclinical efficacy data for potential candidate*

## TSH Antagonist for Graves' Disease and TED*

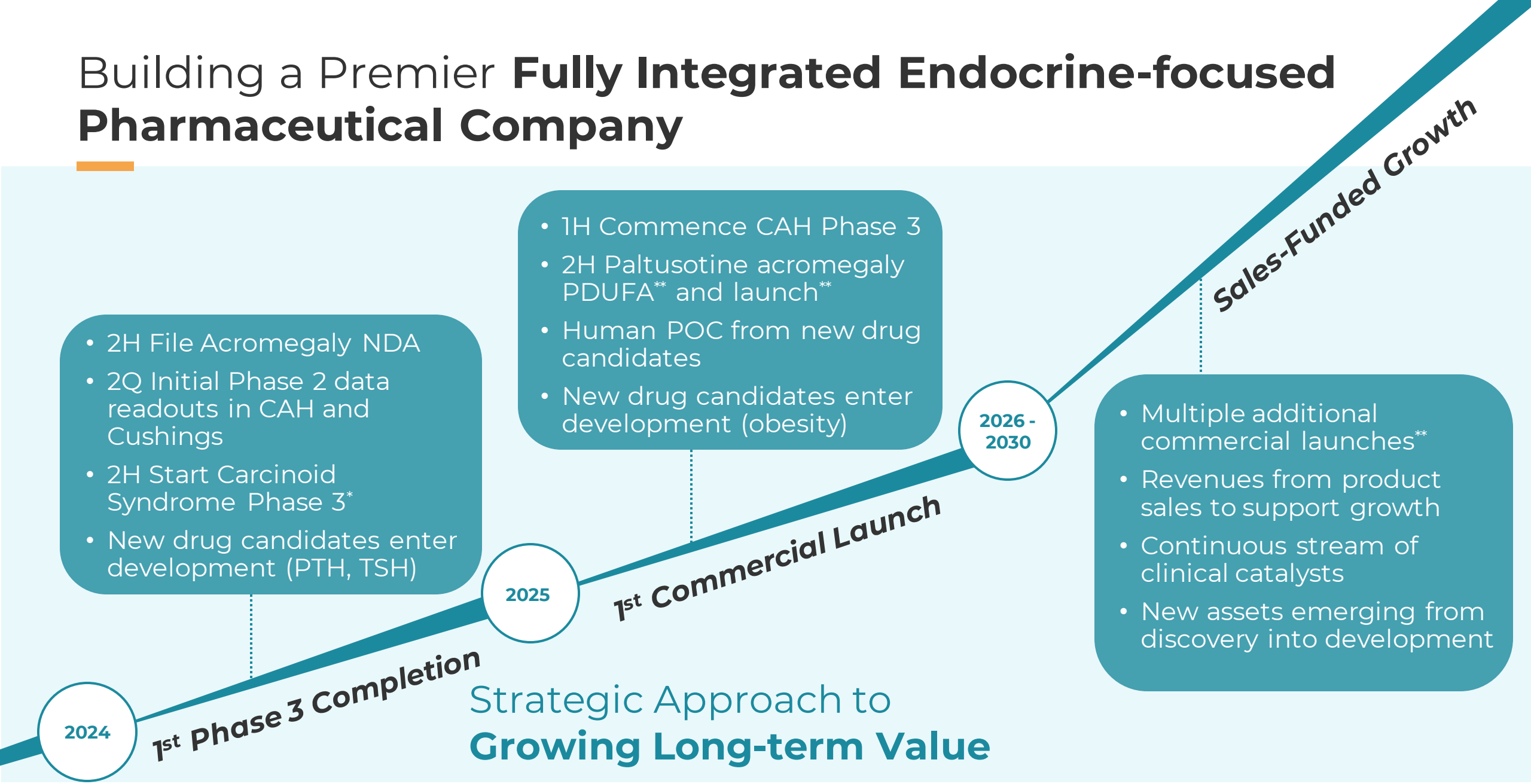



*Preclinical efficacy data for potential lead candidate*



**PTH**: parathyroid hormone; **TSH**: thyroid stimulating hormone; **TED**: thyroid eye disease

# Building a Premier **Fully Integrated Endocrine-focused Pharmaceutical Company**




## Strategic Approach to **Growing Long-term Value**



*Pending alignment with FDA
**Pending NDA submission and regulatory approval

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