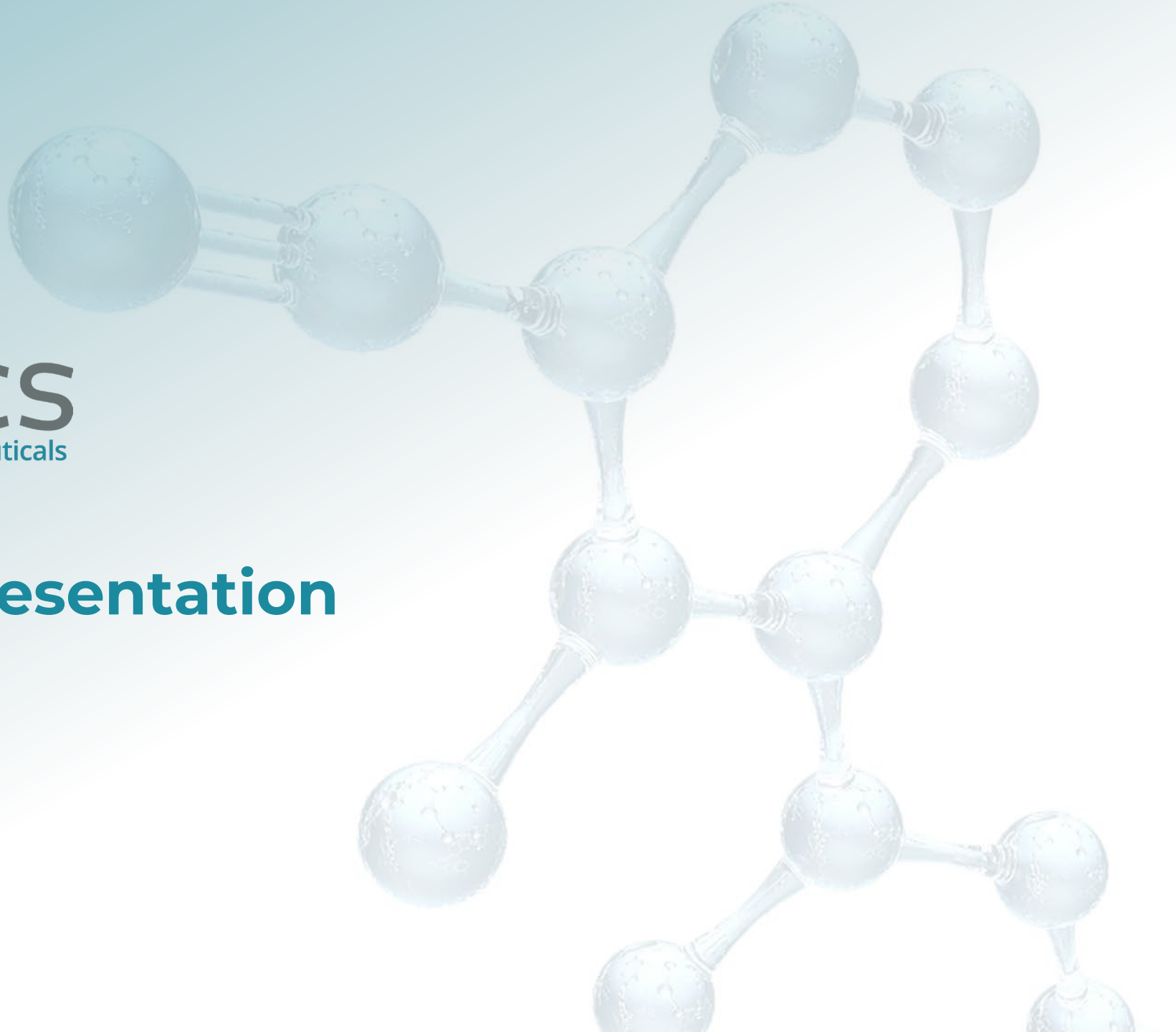
Crinetics Pharmaceuticals

Corporate Presentation

April 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 expected timing of initiation of a Phase 3 program in patients with carcinoid syndrome; 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 initial 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 studies; 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**

Crinetics Pharmaceuticals

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**

Program	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Paltusotine (SST2 agonist)	Acromegaly (PATHFNDR-1)					Acromegaly NDA Submission (2H24)
	Acromegaly (PATHFNDR-2)					
	Carcinoid syndrome					Initiation of Phase 3 (2H24)
CRN04894 (ACTH antagonist)	Congenital adrenal hyperplasia					Initial Phase 2 Data (2Q24)
	Cushing's disease					Initial Phase 2 Data (2Q24)
PTH antagonist	Hyperparathyroidism					Candidate Selection (2024)
SST3 agonist	Polycystic kidney disease					Candidate Selection (2024) (Exploring global partnership)
TSH antagonist	Graves' disease & TED					Candidate Selection (2024)
Oral GLP-1 nonpeptide	Diabetes/Obesity					Candidate Selection (2025)
Oral GIP nonpeptide	Diabetes/Obesity					

Expansion into highly prevalent indications

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

PATHFNDR-2
PHASE 3 RESULTS

CARCINOID SYNDROME
PHASE 2 RESULTS

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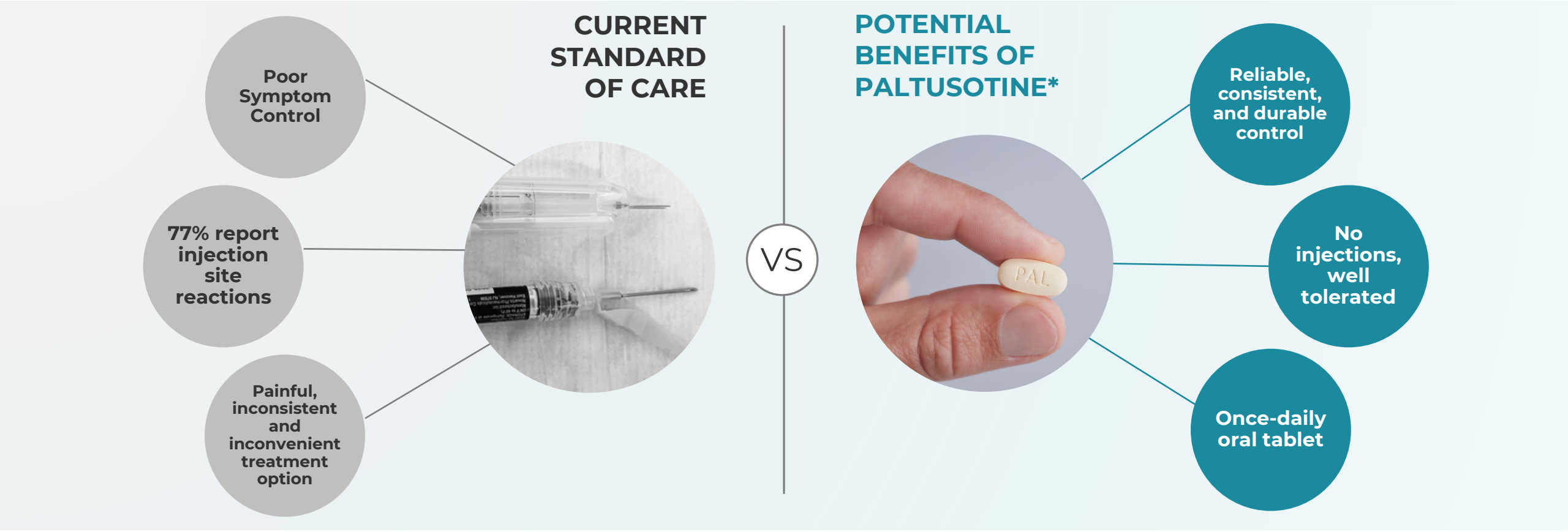
Paltusotine: Designed to Allow People with Acromegaly and Carcinoid Syndrome to Focus on Living



***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

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PATHFNDR-1 and PATHFNDR-2 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 ($p = 0.02$)

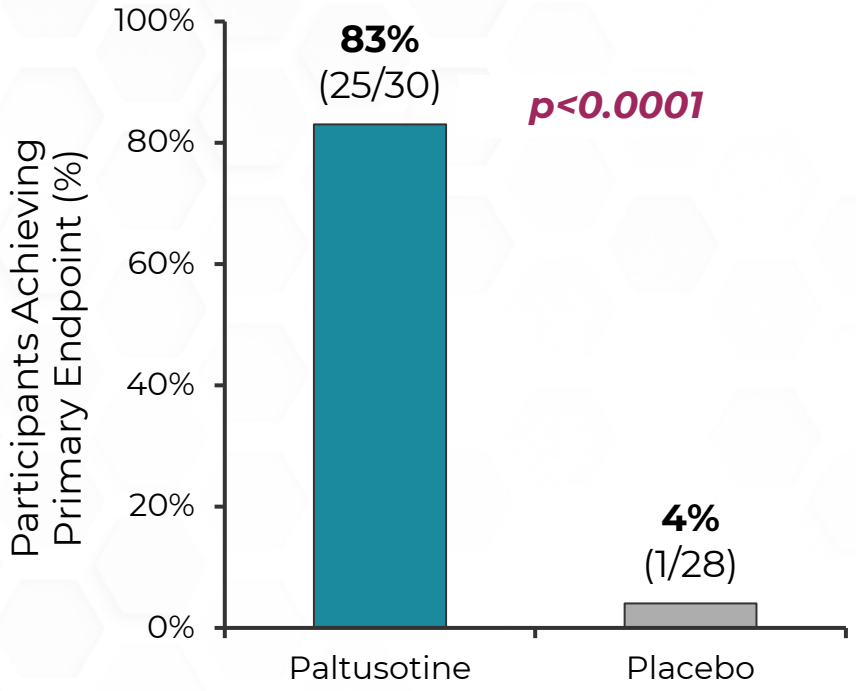
Proportion of participants who maintained GH <1.0 ng/mL ($p = 0.0003$)

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 Positive Phase 3 Results in Acromegaly

PRIMARY ENDPOINT

56% of participants on paltusotine achieved IGF-1 ≤ 1.0xULN vs **5%** on placebo ($p < 0.0001$)

SECONDARY ENDPOINTS
(paltusotine arm vs placebo)

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

67% of participants achieved IGF-1 <1.3xULN with paltusotine

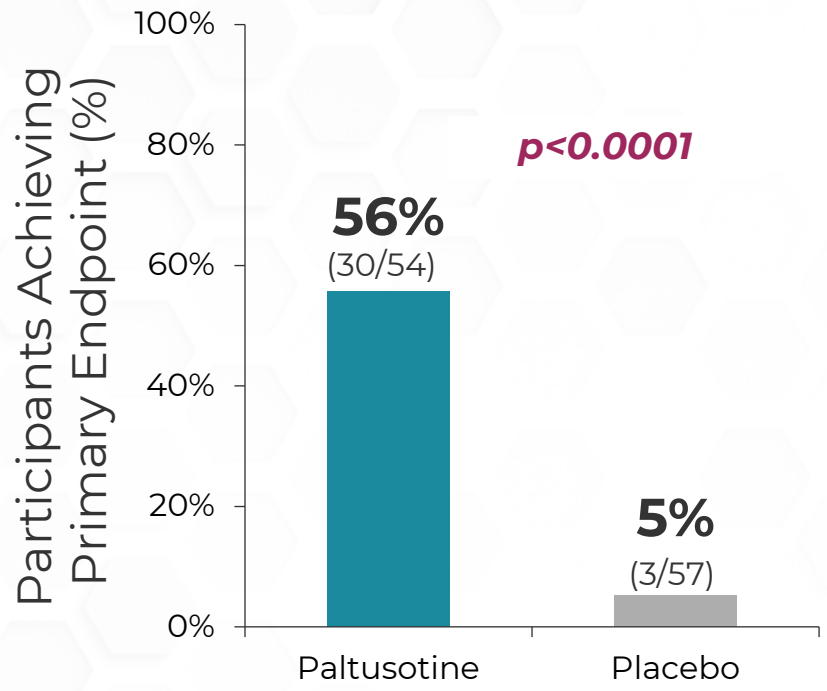
Change from baseline in Acromegaly Symptoms Diary score ($p = 0.004$)

Proportion of participants who maintained GH <1.0 ng/mL ($p = 0.0001$)

SAFETY

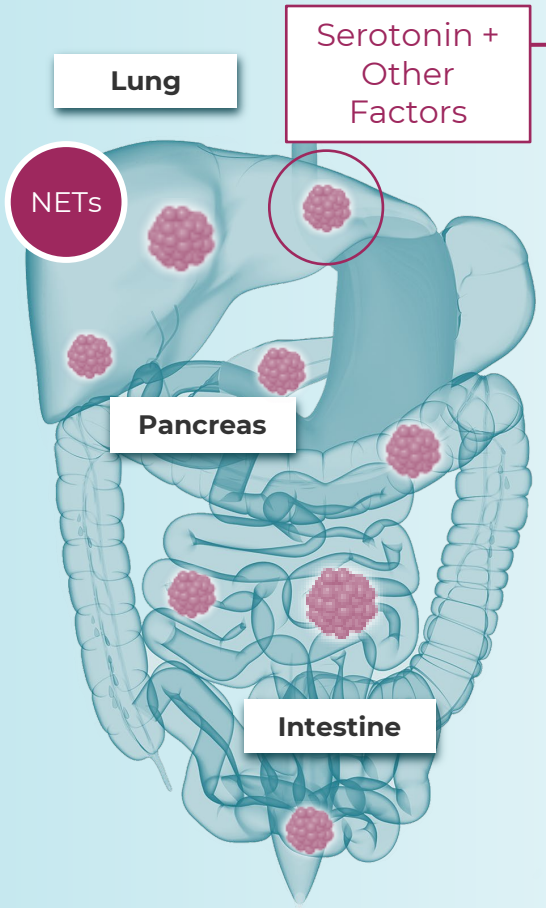
Paltusotine was well-tolerated with no severe or serious adverse events

Paltusotine demonstrated no new safety signals



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

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



Carcinoid Syndrome

~33,000 Patients Diagnosed with Carcinoid Syndrome (U.S.)

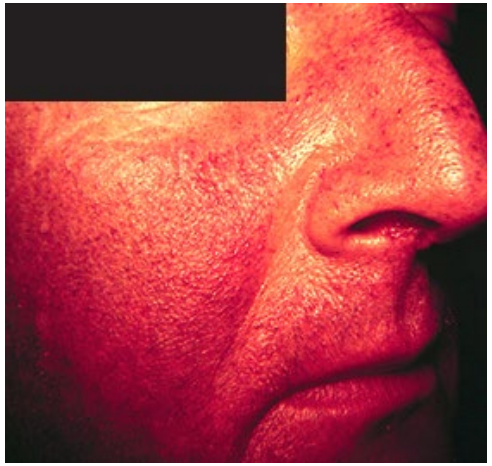
Excess bowel movements (>3/day) are highly disruptive
Goal: *reduce frequency and urgency (normal is ≤3/day)*

Severe flushing episodes can be debilitating and potentially dangerous
Goal: *reduce frequency and severity (normal is < 1/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®

 NETs = Neuroendocrine tumors; SRL = somatostatin receptor ligand

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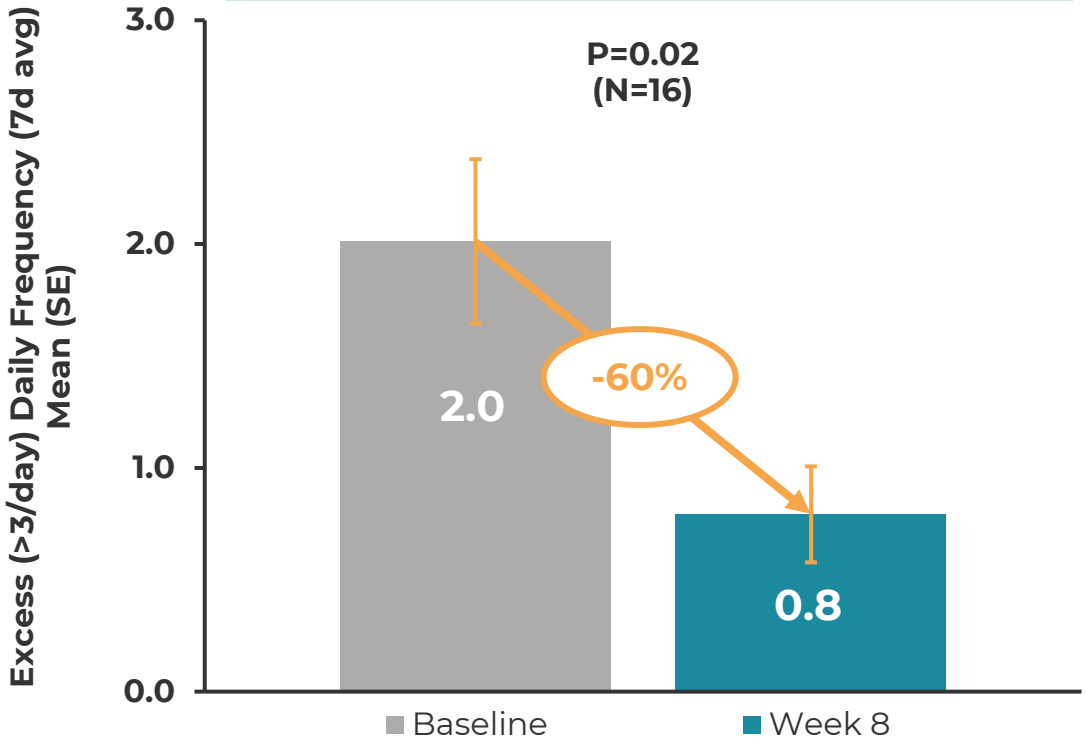
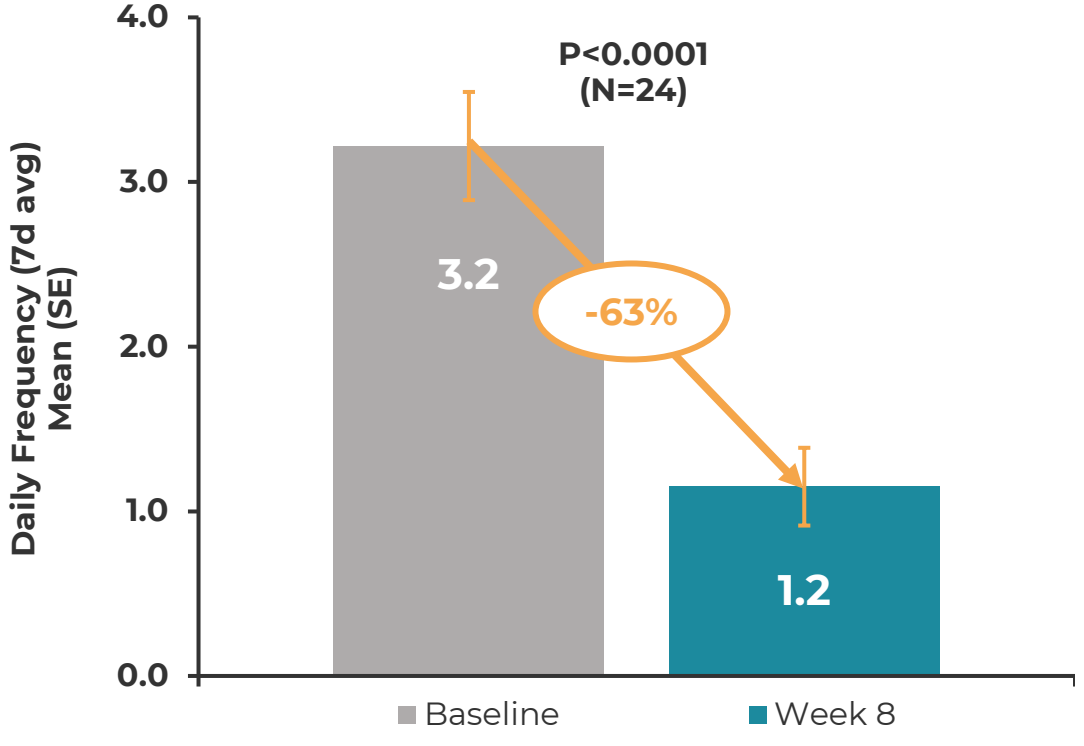
Paltusotine Reduced Frequency of Key Carcinoid Syndrome Symptoms: Excess BM and Flushing

Excess Bowel Movement* Frequency For Patients with >3/day at Baseline



Flushing Frequency For Patients with >1/day at Baseline



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

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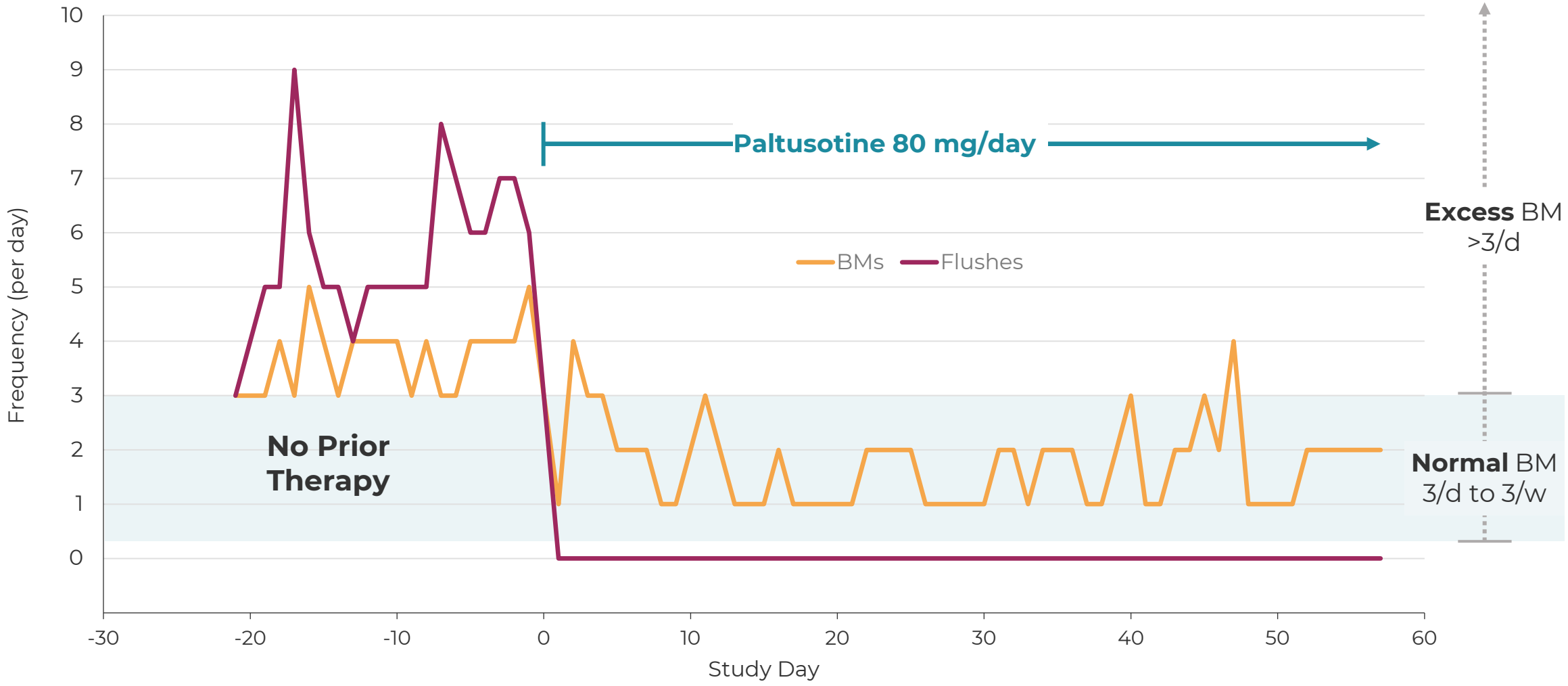
Example Carcinoid Syndrome Study Participant:
Elimination of Flushing and Normalization of BMs



BM = bowel movement

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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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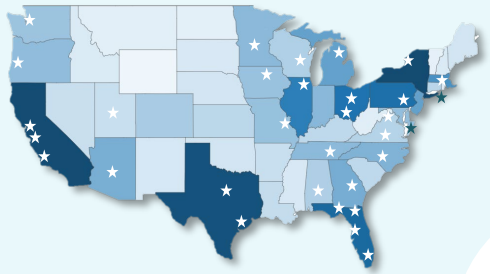
Building the Base for Commercial Success in Multiple Indications for Paltusotine

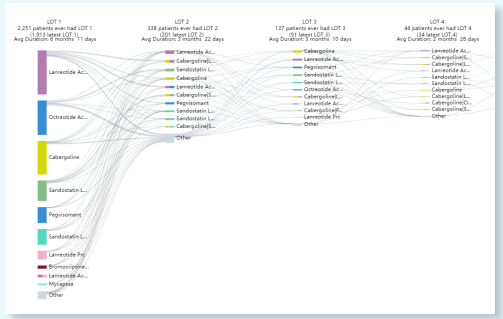
Complete Prescribers Map

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



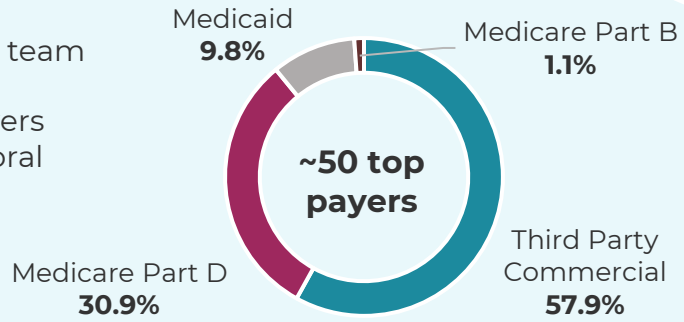
Market Research

- 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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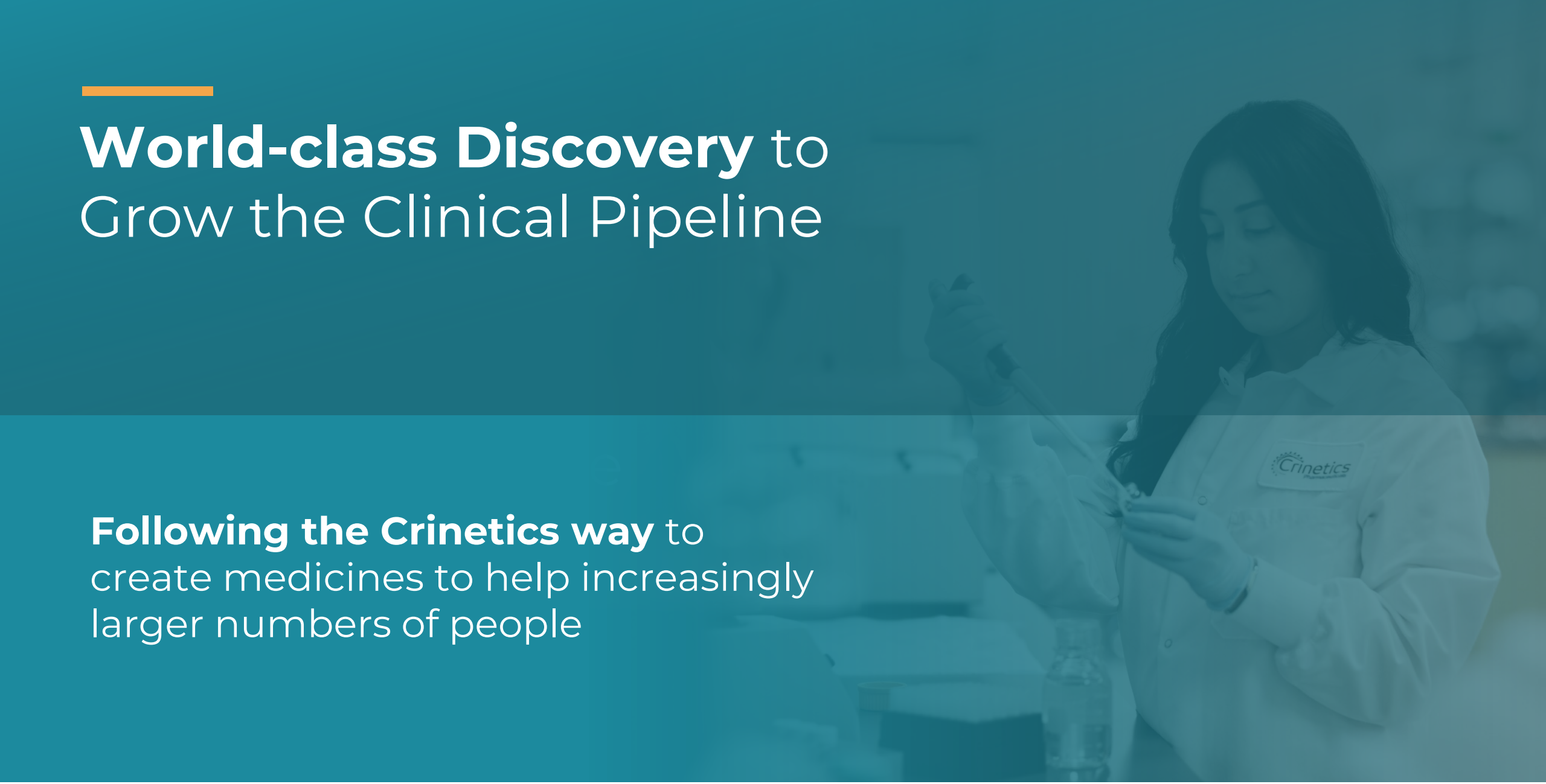
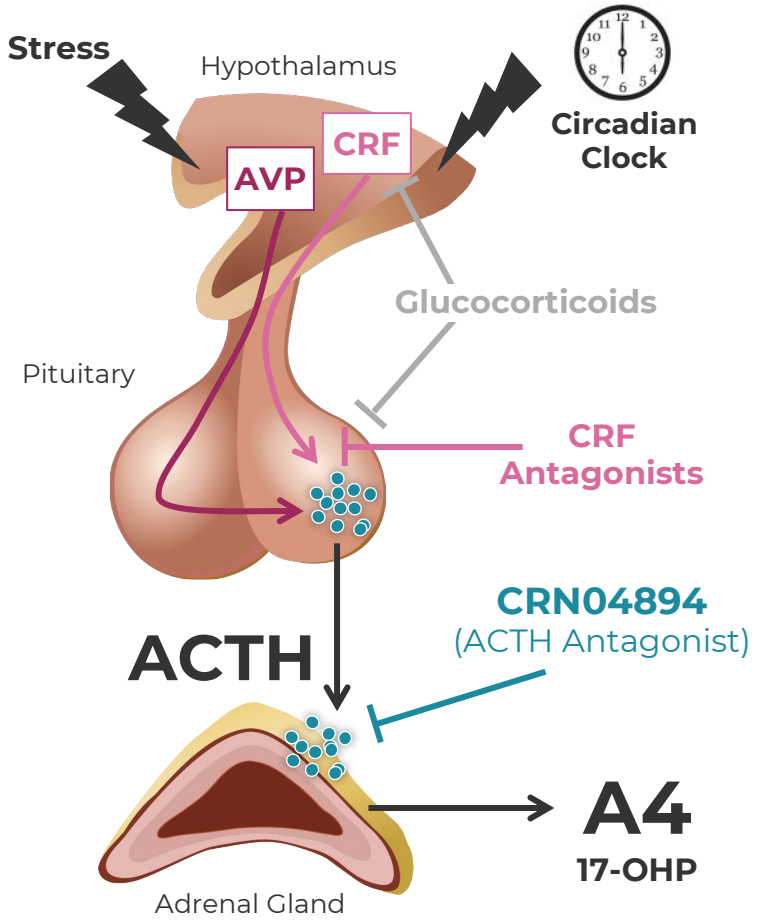
World-class Discovery to Grow the Clinical Pipeline



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

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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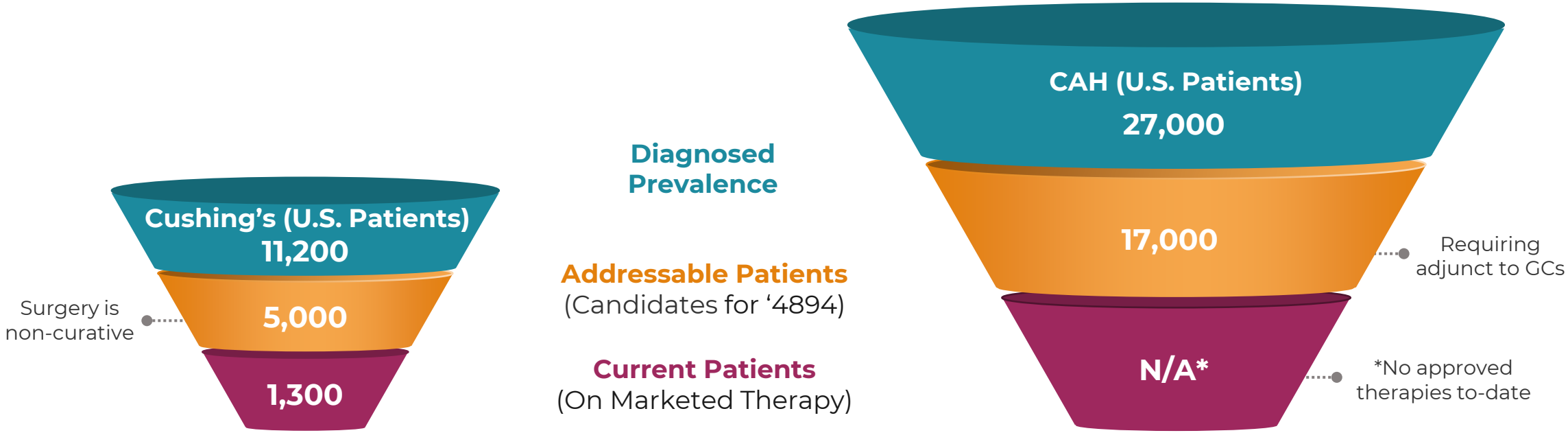
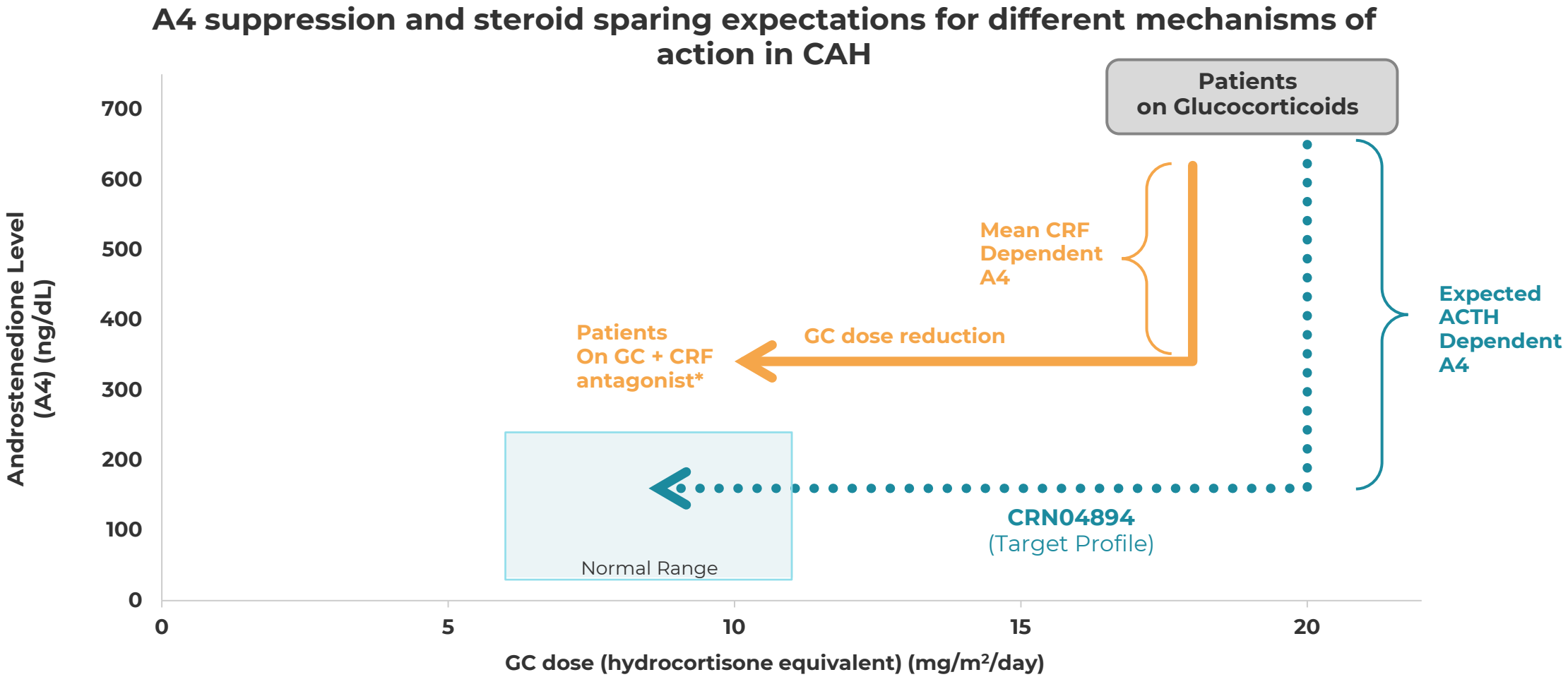
CRN04894: Initial Multi-Billion Dollar U.S. Market Opportunity in CAH and Cushing's Disease



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



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

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Open-Label Study of CRN04894 in Patients with Congenital Adrenal Hyperplasia (CAH)

Sequential Dose Cohorts of CRN04894 QD with Flexibility to Increase or Decrease Doses
GC therapy maintained through study

Key Eligibility Criteria

N = 18-30

Participants with CAH and high A4 (≥1.5xULN) at screening

Age: ≥16 years

Screening: 4 weeks

80 mg QD (n=6-12)

SRC review

QD Dose (n=6-12)

SRC review

QD Dose (n=6)

Optional cohort

Treatment Periods:

3 cohorts (one optional), each 12 weeks

SRC review of 3 patients at week 2 prior to dose changes in next cohort

Objectives: Collect information needed for Phase 3 Design

Primary Efficacy Assessment: Change from baseline in morning serum A4 at week 12

Secondary Efficacy Assessment: Change from baseline in morning serum 17 hydroxyprogesterone (17-OHP) at week 12

Primary Safety Assessment: Incidence of TEAEs

Timeline

- Initial Data from Subset of Patients in 2Q24
- Topline Data expected in 2024

SRC = Safety Review Committee

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Open-Label Study of CRN04894 in Cushing's Disease and EAS Patients

Sequential Dose Cohorts of CRN04894 QD with Flexibility to Increase or Decrease Doses

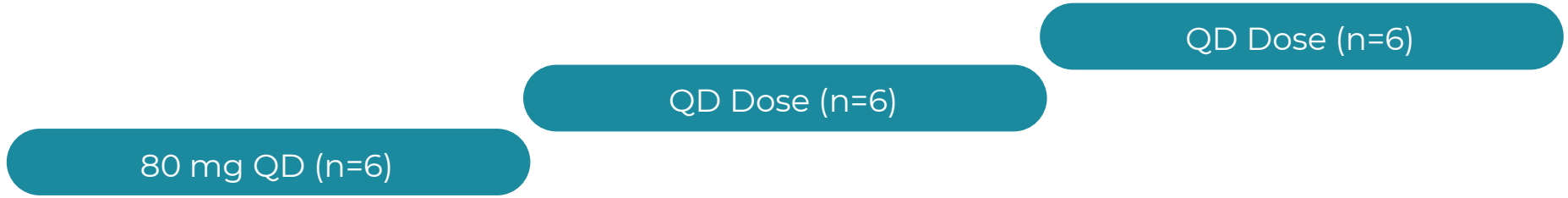
Key Eligibility Criteria

N = 18

ADCS:

- Cushing's disease
- Ectopic ACTH syndrome

Failed surgery or are awaiting surgery



Screening/Washout:
14 Days

Treatment Periods:
3 cohorts, each 10 days

Objectives: Collect information needed for Phase 3 Design

Primary Assessments: Safety and Pharmacokinetics Assessments

Secondary Efficacy Assessments

- 24-hour urinary free cortisol: Change from baseline to Day 11
- Percentage of patients who normalize 24-hour urinary free cortisol on Day 11
- Early morning and 24-hour serum cortisol: Change from baseline to Day 11

Collaborator & Timeline

- Company-sponsored study is being conducted in collaboration with the NIH Clinical Research Center
- Initial Data from Subset of Patients in 2Q24

EAS = Ectopic ACTH Syndrome

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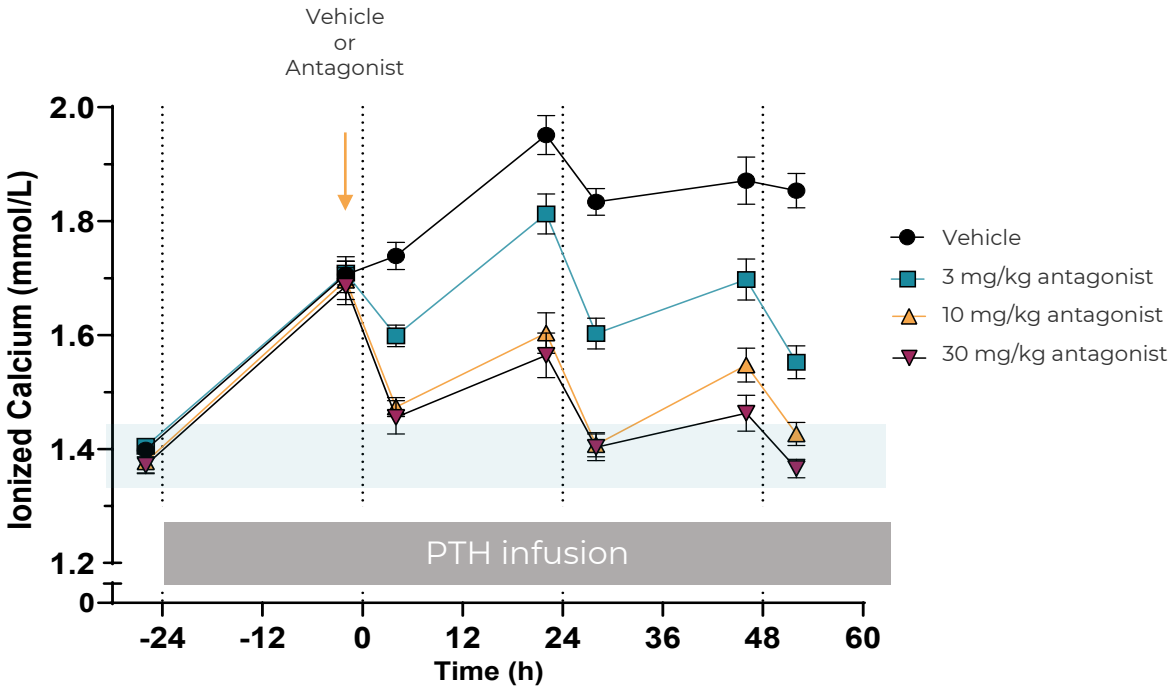
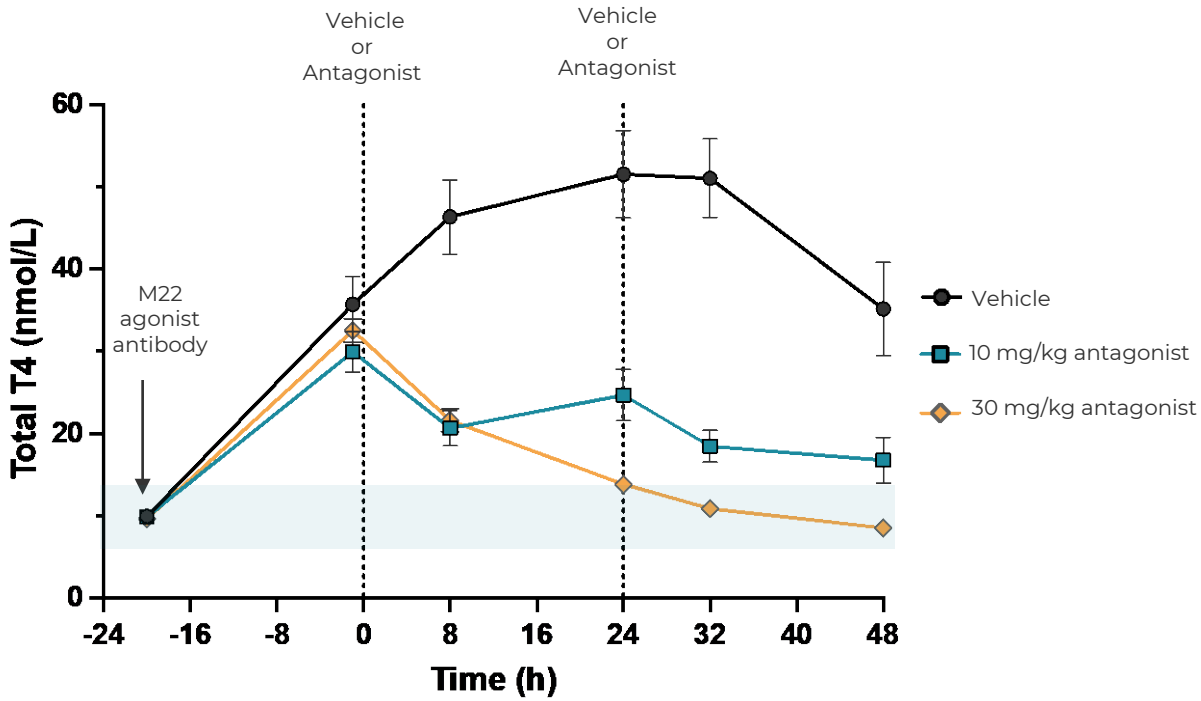
Two New Programs Anticipated to Begin First-in-human Enabling Studies in 2024

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

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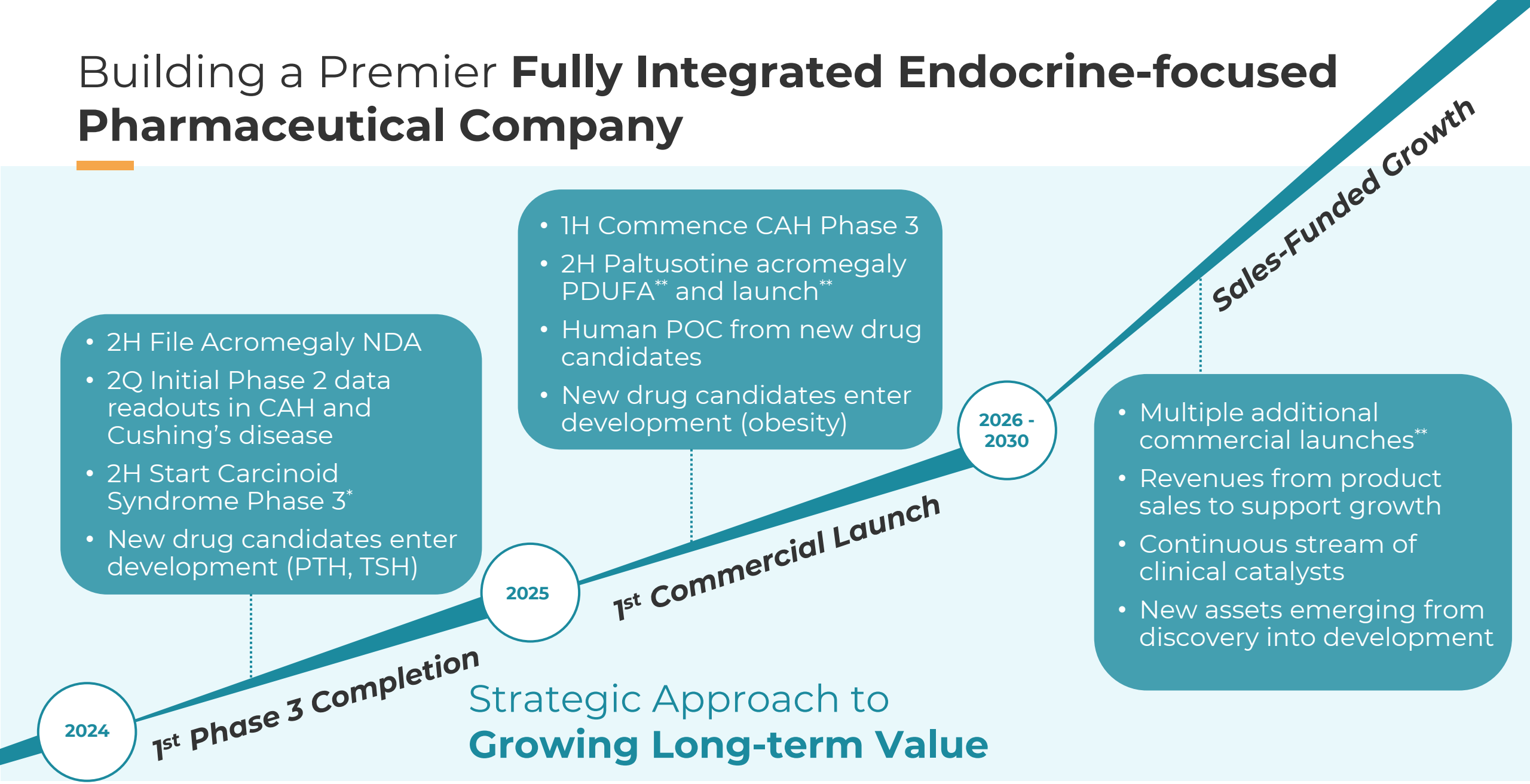
Building a Premier **Fully Integrated Endocrine-focused Pharmaceutical Company**



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

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

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