Crinetics Pharmaceuticals

Corporate Presentation

November 2024

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 potential for interim results to be consistent with final results, once available; the potential for any of our ongoing clinical trials to demonstrate safety or efficacy; the plans and timelines for the clinical development of atumelnant and paltusotine, including the therapeutic potential and clinical benefits or safety profile thereof; the potential benefits of paltusotine for carcinoid syndrome patients; the plans and timelines for the FDA response and the commercial launch of paltusotine if the NDA submission is approved; the expected timing of initiation of a Phase 3 program of paltusotine for carcinoid syndrome and FDA consultation; the expected timing of additional data and topline results from studies of atumelnant in CAH and Cushing's syndrome; the expected timing of announcing preclinical data for candidate on the NDC platform and the therapeutic potential thereof; and the potential and expected timing for IND-enabling studies in four different development candidates to transition to clinical development; the potential benefits of our PTH antagonist TSH antagonist, SST3 agonist, SST5 agonist, oral GLP-1 nonpeptide and oral GIP nonpeptide and our partner's nonpeptide radiotheranostics and SST2 agonist in patients across multiple indications and the expected timing of the advancement of such programs; and the company's anticipated cash runway. 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: 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 interim results of a clinical trial 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 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; the COVID-19 pandemic may disrupt our business and that of the third parties on which we depend, including delaying or otherwise disrupting our clinical trials 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 trials and nonclinical studies; regulatory developments 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. 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 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.

Crinetics Pharmaceuticals

Building a **Premier Endocrine-focused** Global 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

=

Paltusotine is an investigational drug candidate currently in clinical studies

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Deep Pipeline of **Transformative Drug Candidates**

Program	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Registrational	Anticipated Milestones
Paltusotine (SST2 agonist)	**Acromegaly**						Acromegaly NDA Acceptance (December 2024)
	Carcinoid syndrome						Initiation of Phase 3 (4Q2024)
Atumelnant (ACTH antagonist)	**Congenital adrenal hyperplasia**						Additional Phase 2 Data (Early 2025) and Phase 3 Initiation (1H2025)
	Cushing's disease						Later-stage development (2025)
PTH antagonist	**Hyperparathyroidism**						IND (2025)
Nonpeptide drug conjugate (CRN09682)	**NETs** and SST2-expressing solid tumors						IND (Early 2025)
TSH antagonist	**Graves' disease & TED**						IND (2025)
SST3 agonist	**ADPKD**						IND (2025)
Oral GLP-1 nonpeptide	**Obesity**						Candidate Selection (2025)
Oral GIP nonpeptide	**Obesity**						Candidate Selection (2025)
Nonpeptide radiotheranostics	**Multiple oncology indications**						Partner: Radionetics Oncology
SST2 agonist	**Extending lifespan of large and giant breed dogs**						Partner: Loyal

4 New Development Candidates

SST: somatostatin receptor type; ACTH: adrenocorticotropic hormone; PTH: parathyroid hormone; ADPKD: Autosomal dominant polycystic kidney disease.; TSH: thyroid-stimulating hormone; TED: thyroid eye disease; GLP-1: glucagon-like peptide-1 receptor agonists; GIP: gastric inhibitory polypeptide; NDA: New Drug Application; NETs: Neuroendocrine tumors

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World-class Development Leading to Global Commercialization

Paltusotine: Lead Clinical Candidate for Acromegaly and Carcinoid Syndrome

PATHFNDR-1 PHASE 3 RESULTS

PATHFNDR-2 PHASE 3 RESULTS

CARCINOID SYNDROME PHASE 2 RESULTS

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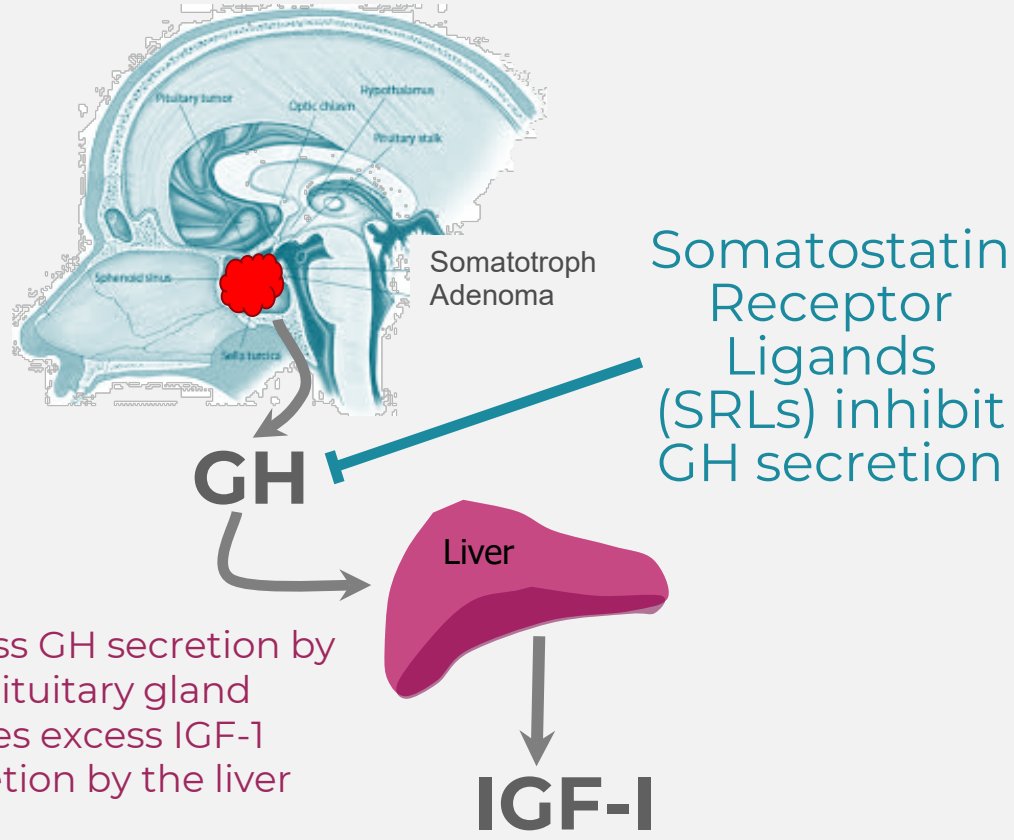
Paltusotine: New Drug Application for Treatment of Acromegaly Submitted to the FDA

Acromegaly is caused by a benign pituitary tumor secreting excess growth hormone (GH)



Acromegaly Symptoms/Complications

- Headache
- Hyperhidrosis/oily skin
- Bone and cartilage overgrowth
- Organ enlargement
- Cardiovascular disease/hypertension
- Changes in glucose and lipid metabolism
- Abnormal growth of hands and feet
- Alteration of facial features

Uncontrolled acromegaly is debilitating and increases risk of early death

Sources: http://www.fipapatients.org; Bex M, Abs R, T'Sjoen G, et al. Eur J Endocrinol. 2007;157(4):399-409; http://acromegalycommunity.com

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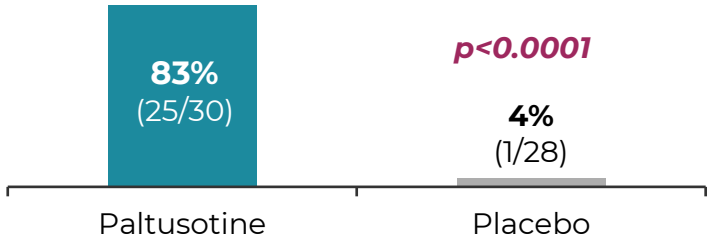
Acromegaly: Paltusotine **Positive Phase 3 Results** Provide Strong Footing for First Commercial Launch* in 2025

PATHFNDR-1

Patients switching from standard-of-care

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)

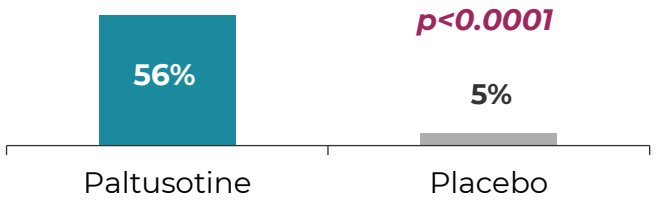
- Change from baseline in IGF-1 ($p < 0.0001$)
- Change from baseline in Acromegaly Symptoms Diary score ($p = 0.02$)
- Proportion of participants who maintained GH <1.0 ng/mL ($p = 0.0003$)

pathfndr-2

Non-pharmacologically-treated patients

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 ($p < 0.0001$)
- Change from baseline in Acromegaly Symptoms Diary score ($p = 0.004$)
- Proportion of participants who maintained GH <1.0 ng/mL ($p = 0.0001$)

*Paltusotine is an investigational drug. The safety and efficacy of paltusotine have not been established. In clinical studies, paltusotine was well-tolerated with no severe or serious adverse events or new safety signals. Commercial launch is dependent on regulatory approval.

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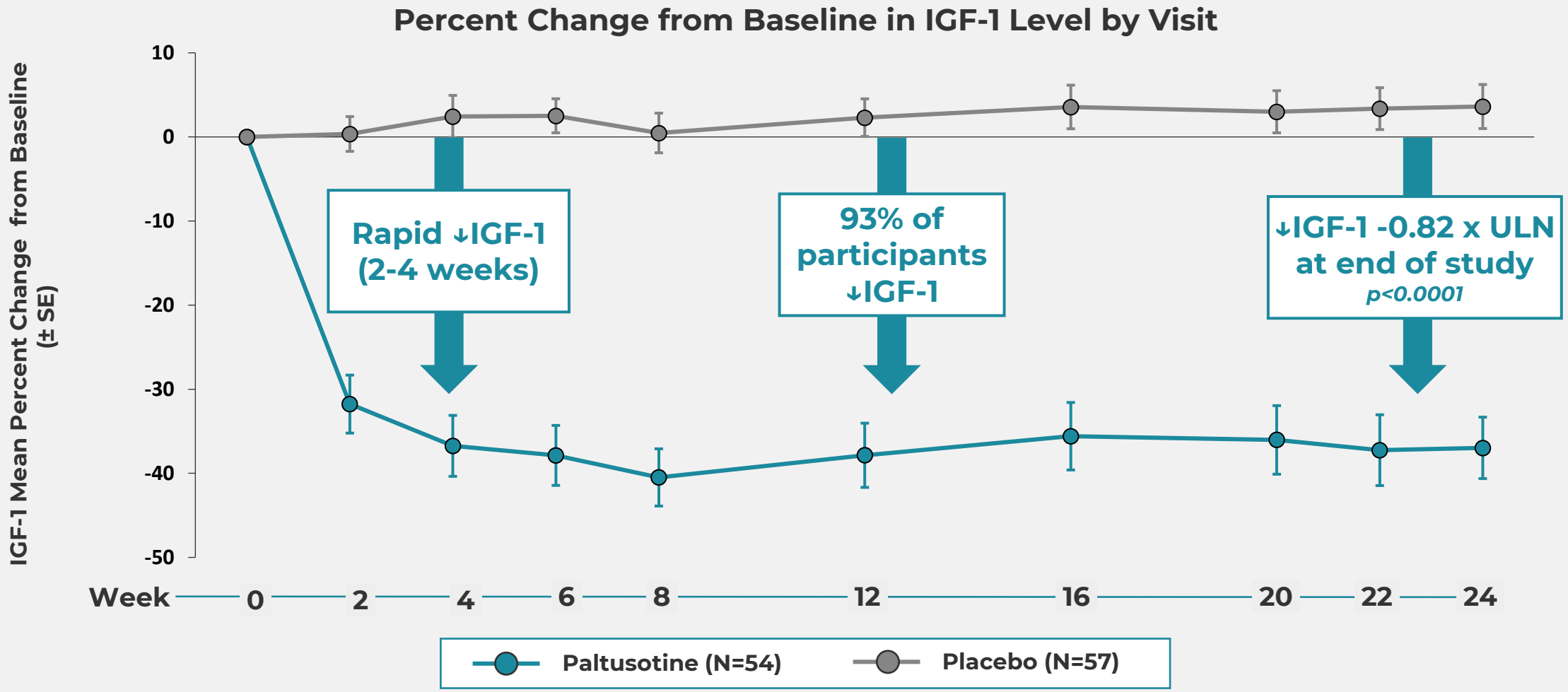
PATHFNDR-2: Paltusotine Treatment **Rapidly Decreased IGF-1 Levels in Almost 95% of Participants**



IGF-1 values measured prior to rescue or discontinuation are carried forward

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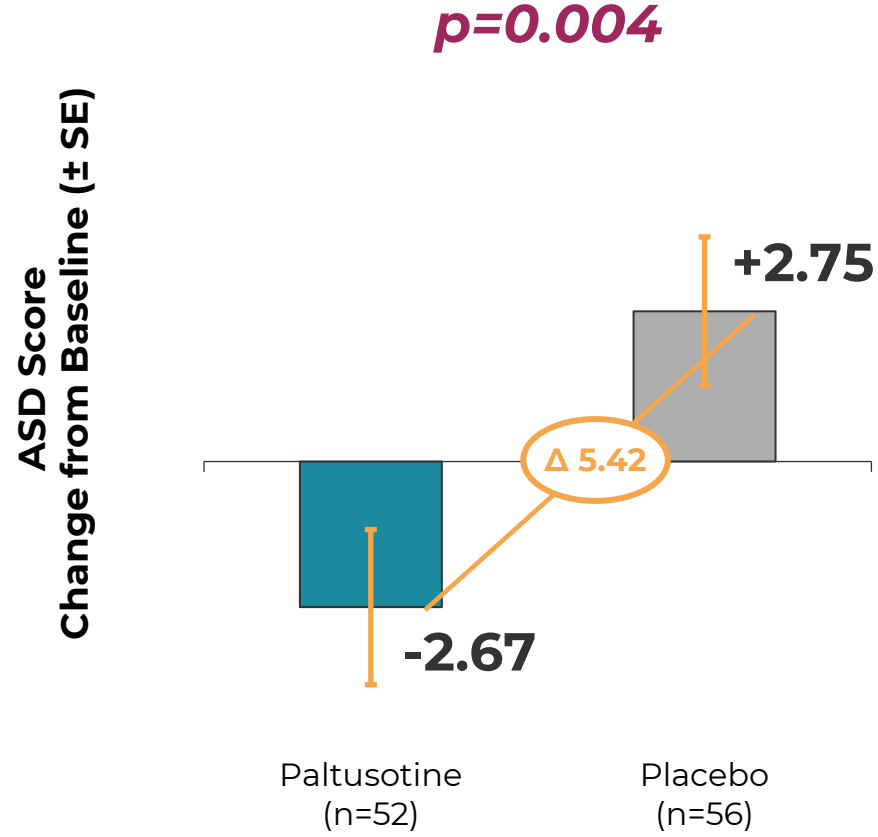
Acromegaly: Paltusotine Treatment **Improved Symptoms** as Reported in the Acromegaly Symptoms Diary (ASD)

- ASD was developed in accordance with FDA guidance to evaluate symptoms of acromegaly in clinical trials*
- Each symptom was rated from 0 (no symptom) to 10 (worst symptom), Total 0 to 70
- A daily symptom checklist was collected for participants prior to and during study treatment

Symptoms Evaluated in the ASD

Headache pain	Leg weakness
Joint pain	Swelling
Sweating	Numbness/tingling
Fatigue	

Change from Baseline to EoR in Total ASD Score



Martin et al. *Journal of Patient-Reported Outcomes* (2023) 7:15; https://doi.org/10.1186/s41687-023-00541-7.
Least Squares (LS) Mean is estimated based on an analysis of covariance.
EoR: End of Randomized control phase. ASD scores measured prior to rescue or discontinuation are used.

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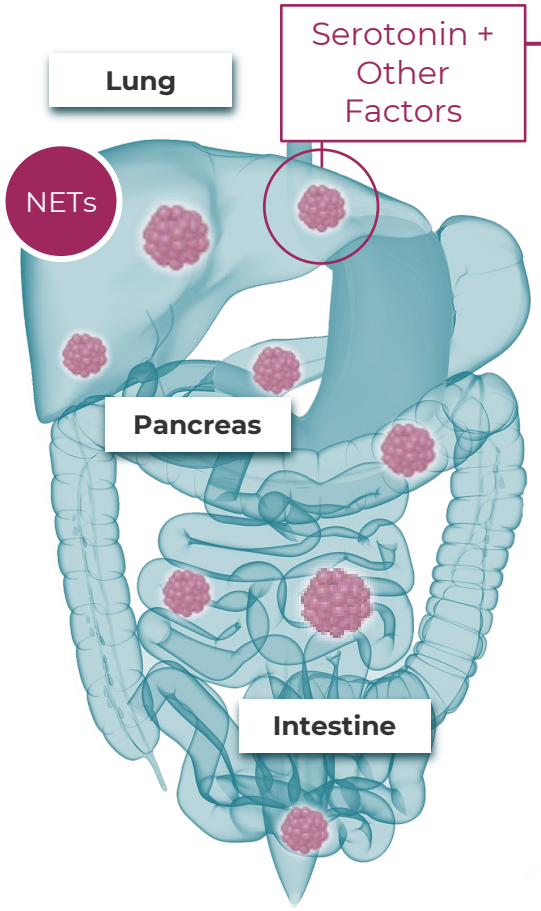
Paltusotine: Progressing Towards Phase 3 in **Carcinoid Syndrome**



Carcinoid Syndrome

Severe flushing episodes can be debilitating and potentially dangerous

Goal: *reduce frequency and severity (normal is < 1/day)*

Excess bowel movements (>3/day) are highly disruptive

Goal: *reduce frequency and urgency (normal is ≤3/day)*

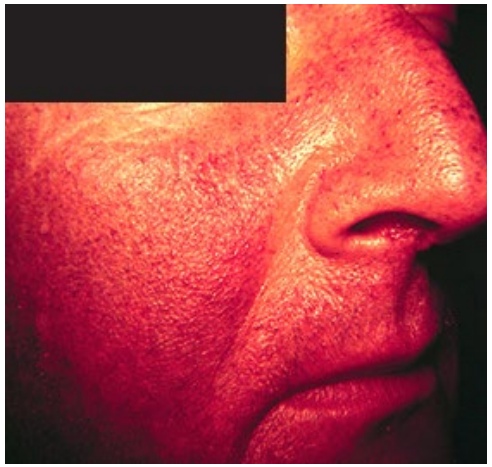
Severe and life-threatening complications: carcinoid heart disease (found in up to 50% of patients) & carcinoid crisis

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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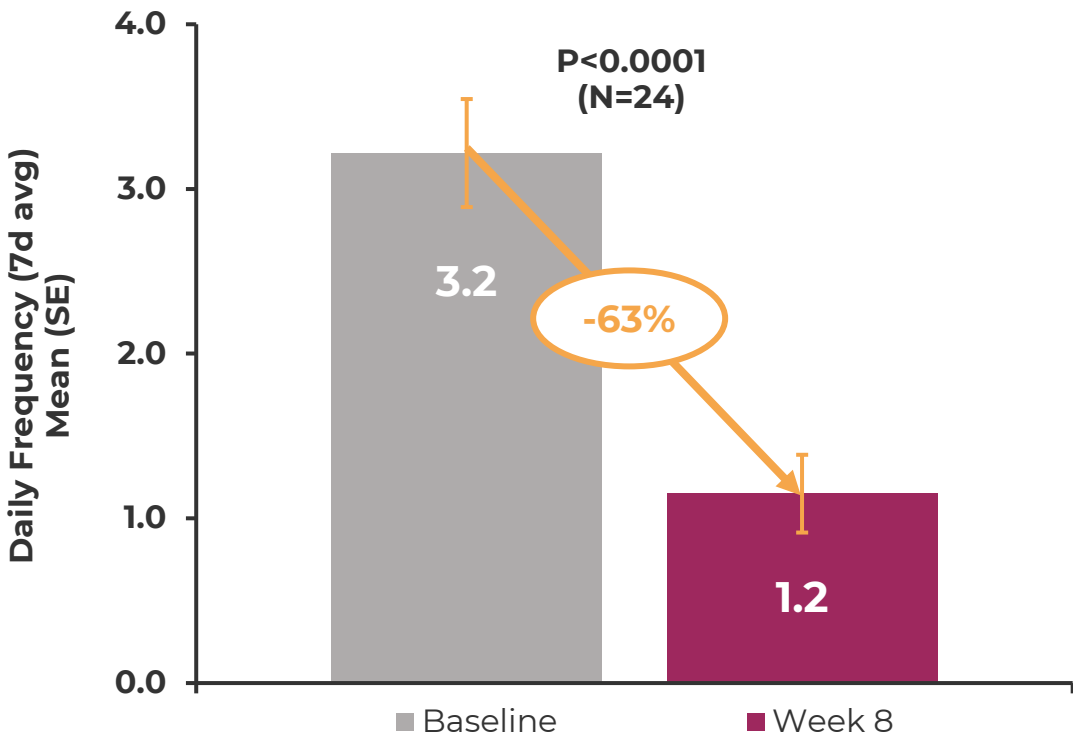
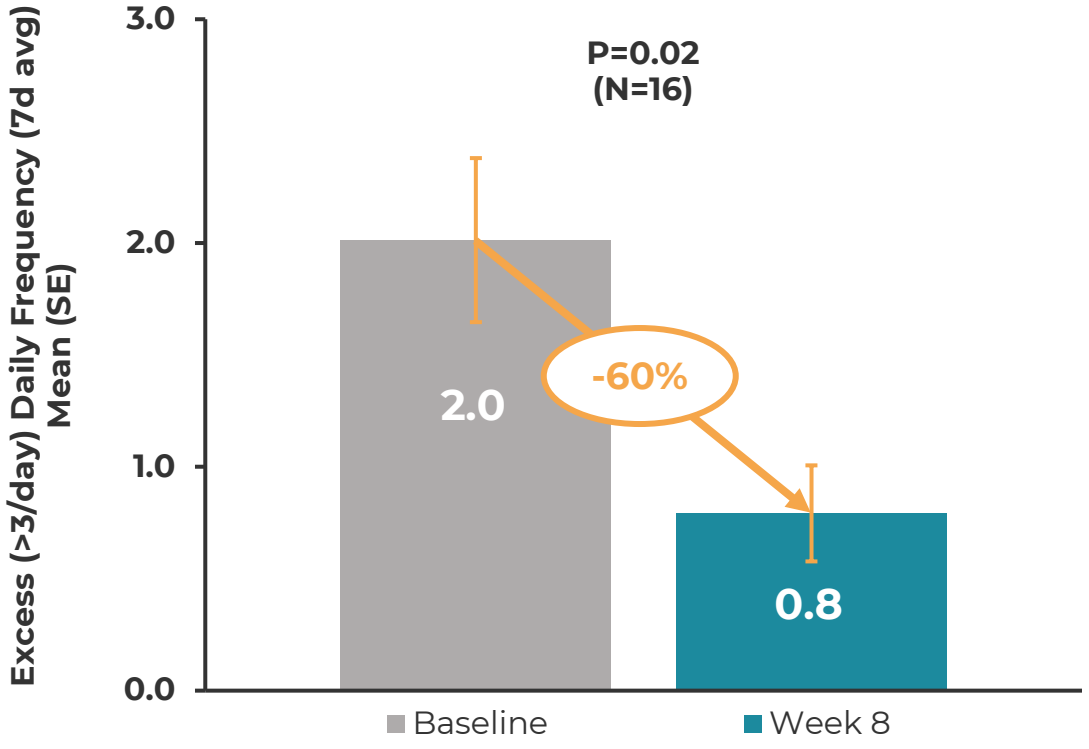
Carcinoid Syndrome: Paltusotine **Reduced Frequency of Key Symptoms**

Flushing Frequency For Patients with >1/day at Baseline



Excess Bowel Movement* Frequency For Patients with >3/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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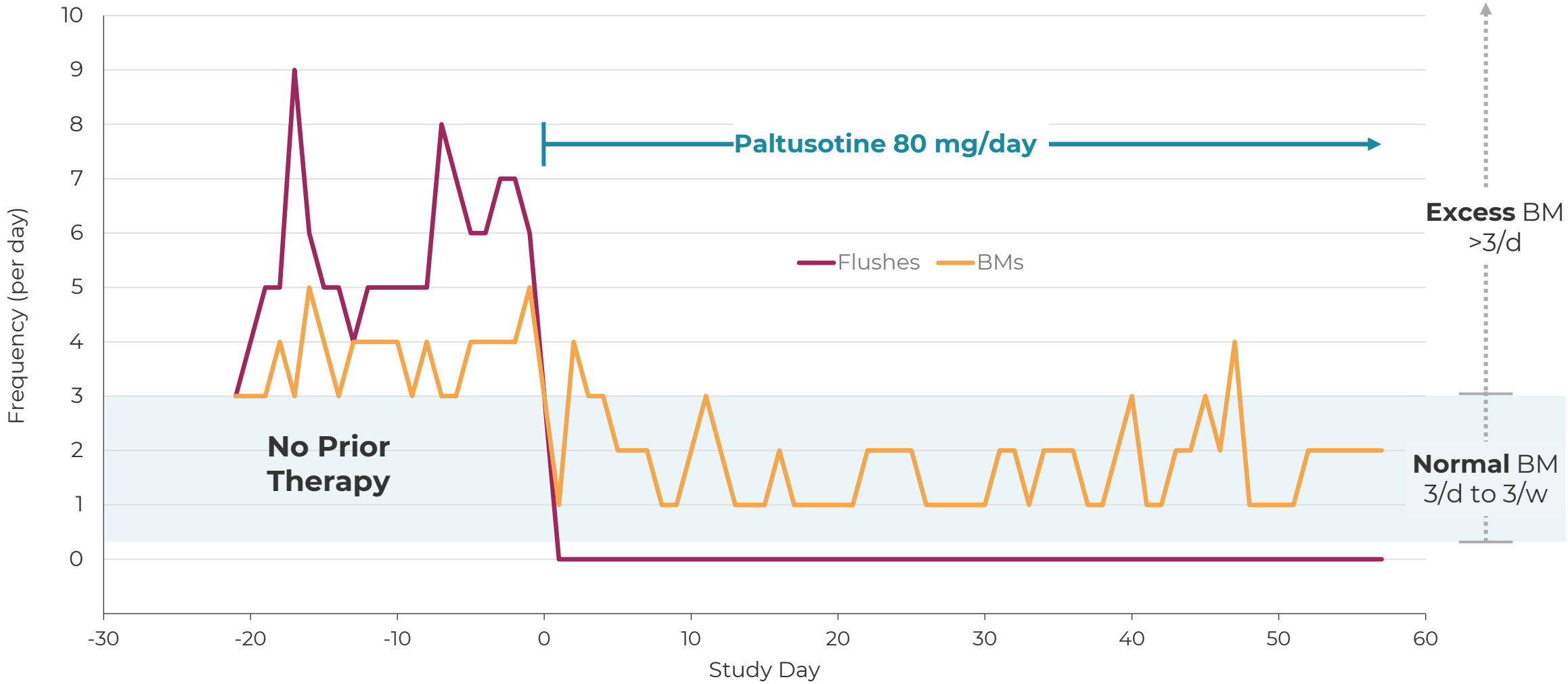
Carcinoid Syndrome: Example Study Participant Experienced **Elimination of Flushing and Normalization of BMs**



Study participant from Phase 2 clinical trial of paltusotine in carcinoid syndrome.
BM = bowel movement

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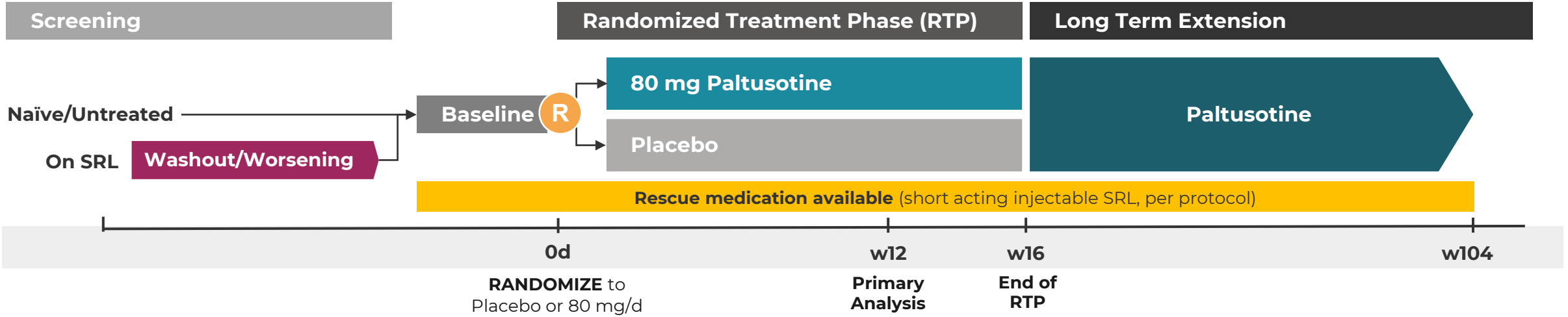
Carcinoid Syndrome: **CAREFNDR Phase 3 Study**

CARcinoid Syndrome Efficacy Study
CAREFNDR
Featuring a Noninvasive Daily Regimen

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, and other PROs

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

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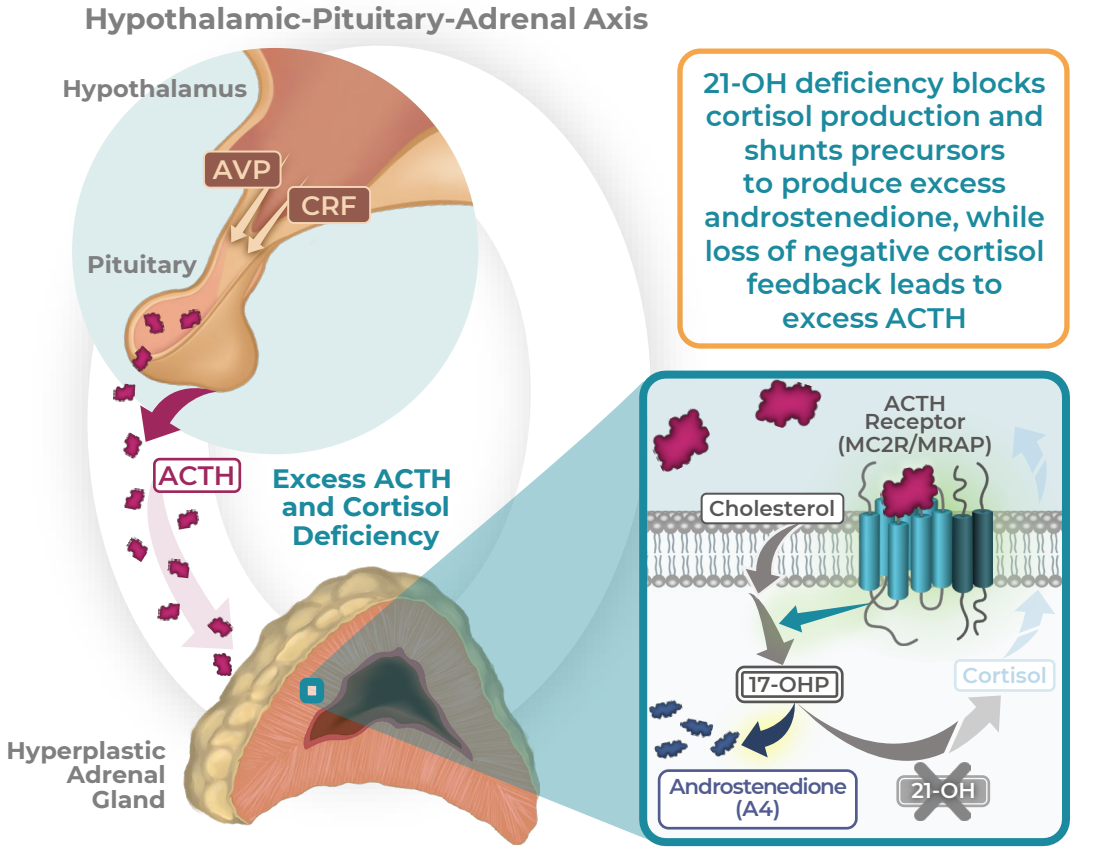
World-class Development to Grow the Late-Stage Pipeline

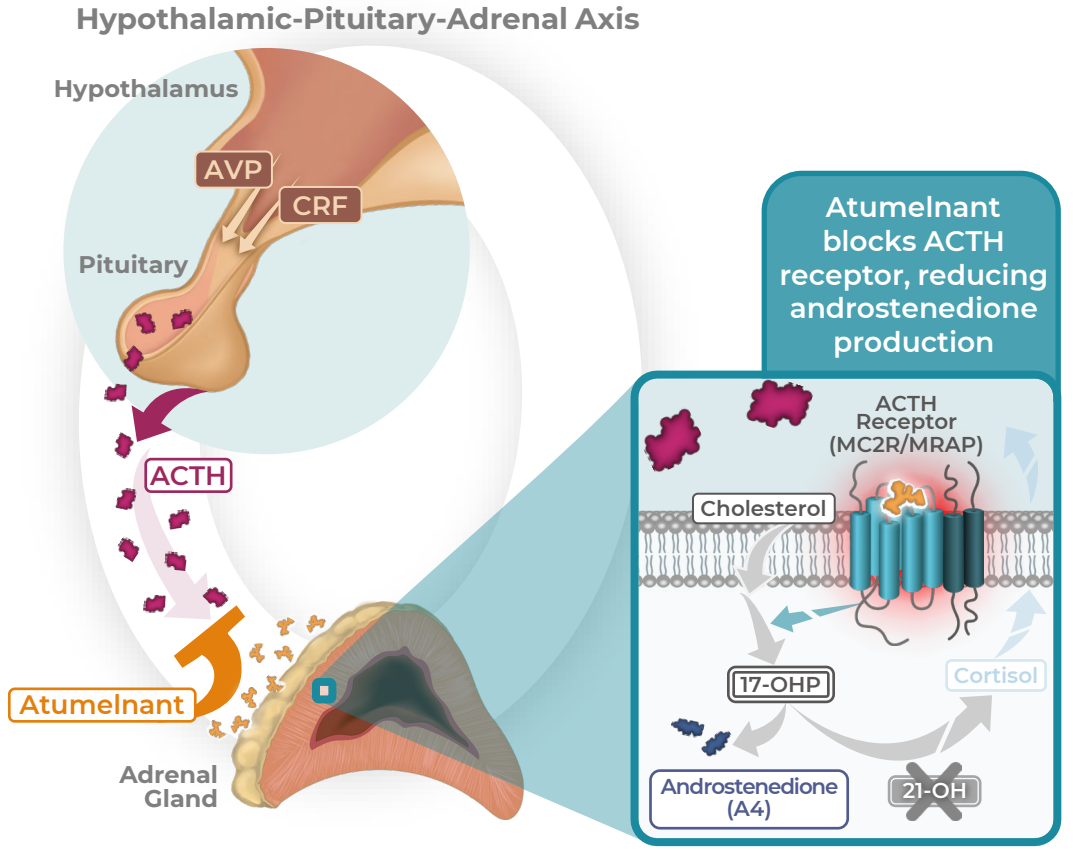
Atumelnant: In Development for Congenital Adrenal Hyperplasia and Cushing's Disease

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.

Atumelnant is an investigational drug being evaluated in clinical studies for CAH. Atumelnant has not been approved by any regulatory authority.

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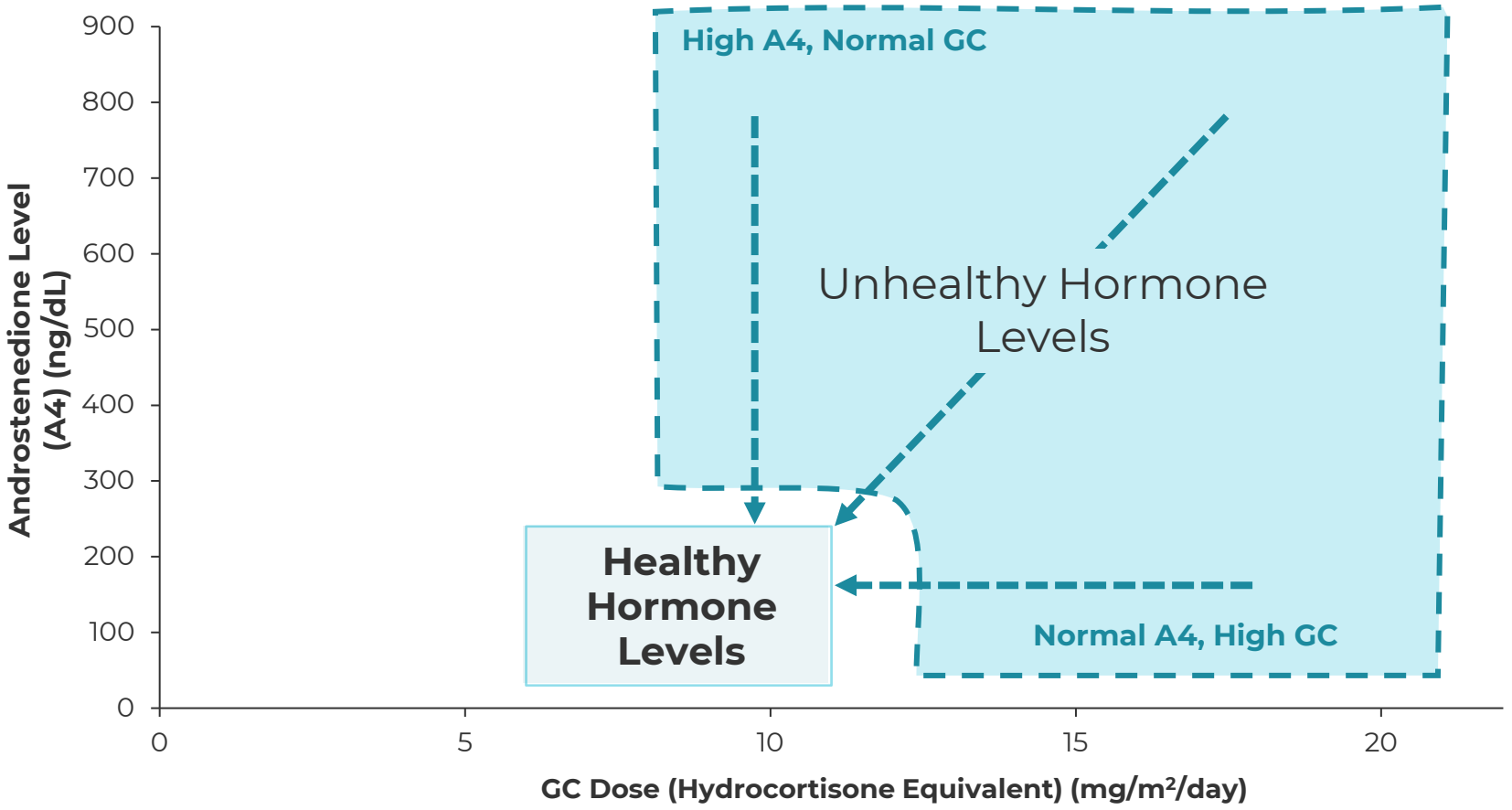
CAH: Goal of Treatment with Atumelnant is to Achieve **Healthy Levels of A4 and Glucocorticoids**



GC: glucocorticoid; A4: androstenedione. *Initial cut of data from Phase 2 study in a portion of patients with 80 mg atumelnant at 2 weeks..

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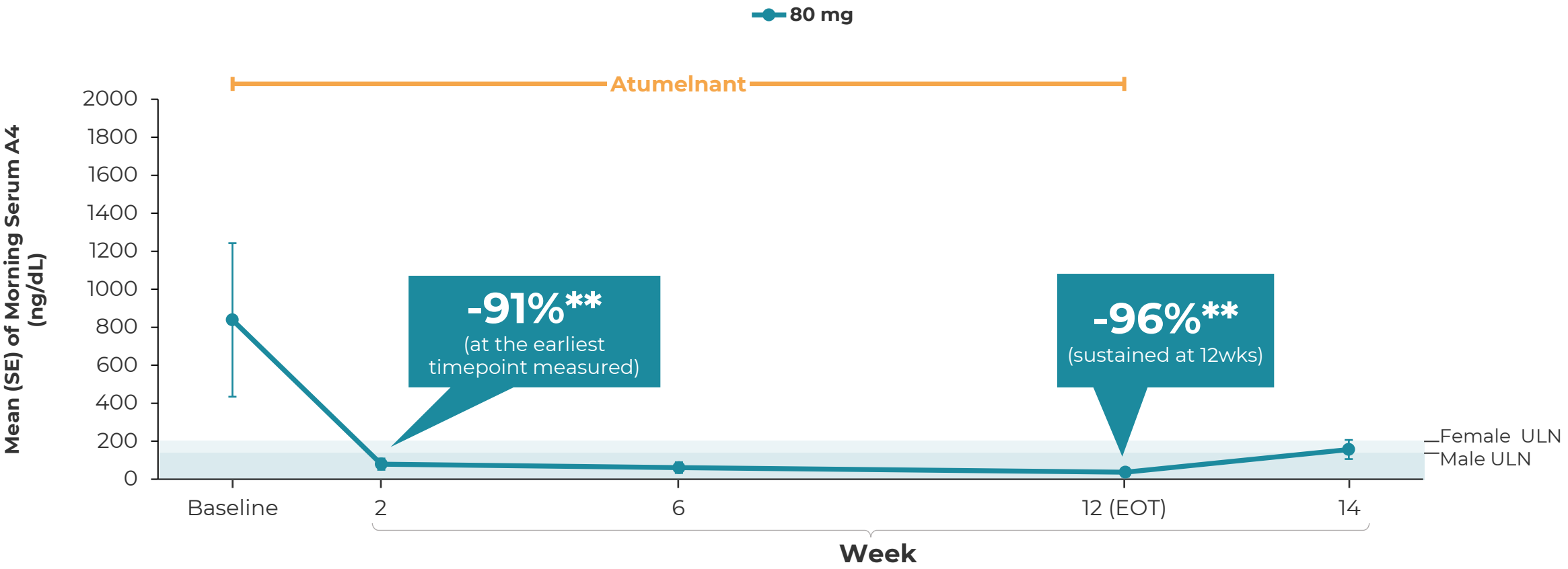
CAH: Atumelnant **Profoundly and Rapidly Reduced Mean A4**, Sustained at 12 Weeks*



Number of Participants:

80 mg	**6**	**6**	**6**	**4**	**4**

* Based on initial cut of data from the Phase 2 study
** Percent change between mean baseline and mean post-baseline value.
ULN: Upper limit of normal. EOT: End of Treatment
Data presented represents data cut off date of May 21st, 2024. Available data: 80 mg: n=4 for 12 weeks; n=6 for 6 weeks.

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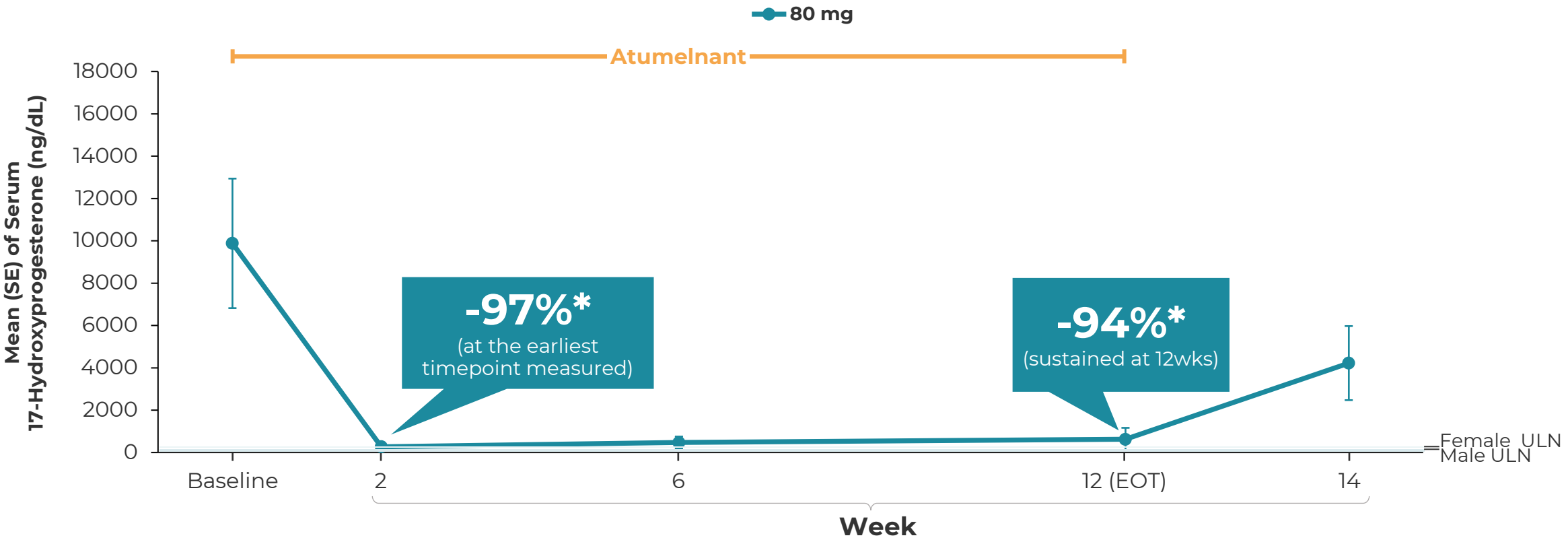
CAH: Atumelnant **Profoundly and Rapidly Reduced Mean 17-OHP**, Sustained at 12 Weeks



Number of Participants:

80 mg	**6**	**6**	**6**	**4**	**3**

* Percent change between mean baseline and mean post-baseline value.

ULN: Upper limit of normal, EOT: End of Treatment.

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CAH: Atumelnant Showed Profound, Rapid and Sustained **Reduction in Key Biomarkers** and **Improvements in Clinical Outcomes**

EFFICACY

- **100%** (n=6/6) of participants maintained androstenedione (A4) <ULN at all time points on atumelnant (80 mg)
  - A4 and related androgens are key drivers of disease pathophysiology
  - A4 is a potential endpoint in registrational trials
- **>90% reduction of A4** and **97% reduction of 17-OHP** on atumelnant (80 mg) beginning at 2 weeks and **sustained through 12 weeks**
- **Two female participants resumed regular menstrual cycles** on atumelnant (80 mg) after >2 years with no menstruation

SAFETY

Atumelnant was well-tolerated with no treatment-related severe or serious adverse events

More data from additional patients and dose levels expected in early 2025

Initiation of Phase 3 expected in 2025

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

ULN: Upper limit of normal. 17-OHP: 17-Hydroxyprogesterone. A4: Androstenedione.
Data presented represents data cut off date of May 21st, 2024. Available data: 80 mg: n=4 at 12 weeks; n=2 at 6 weeks; 40 mg: n=4 for 2 weeks.

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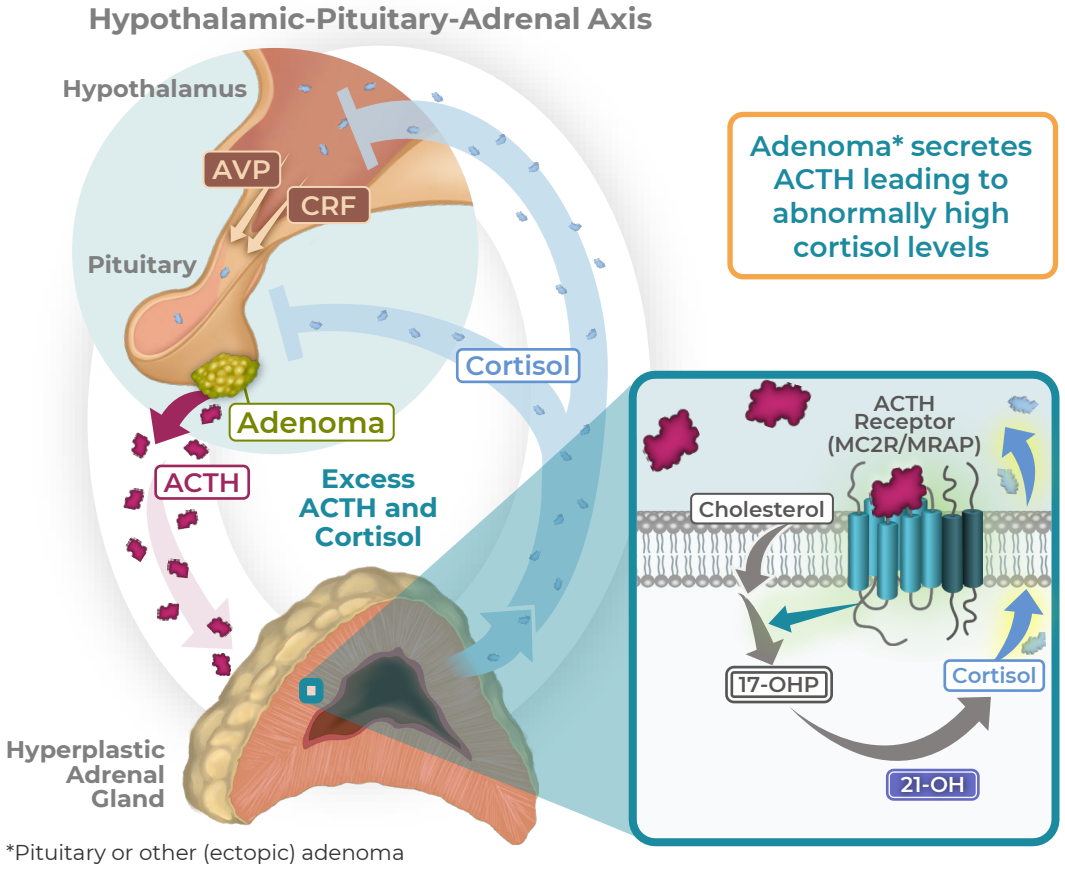
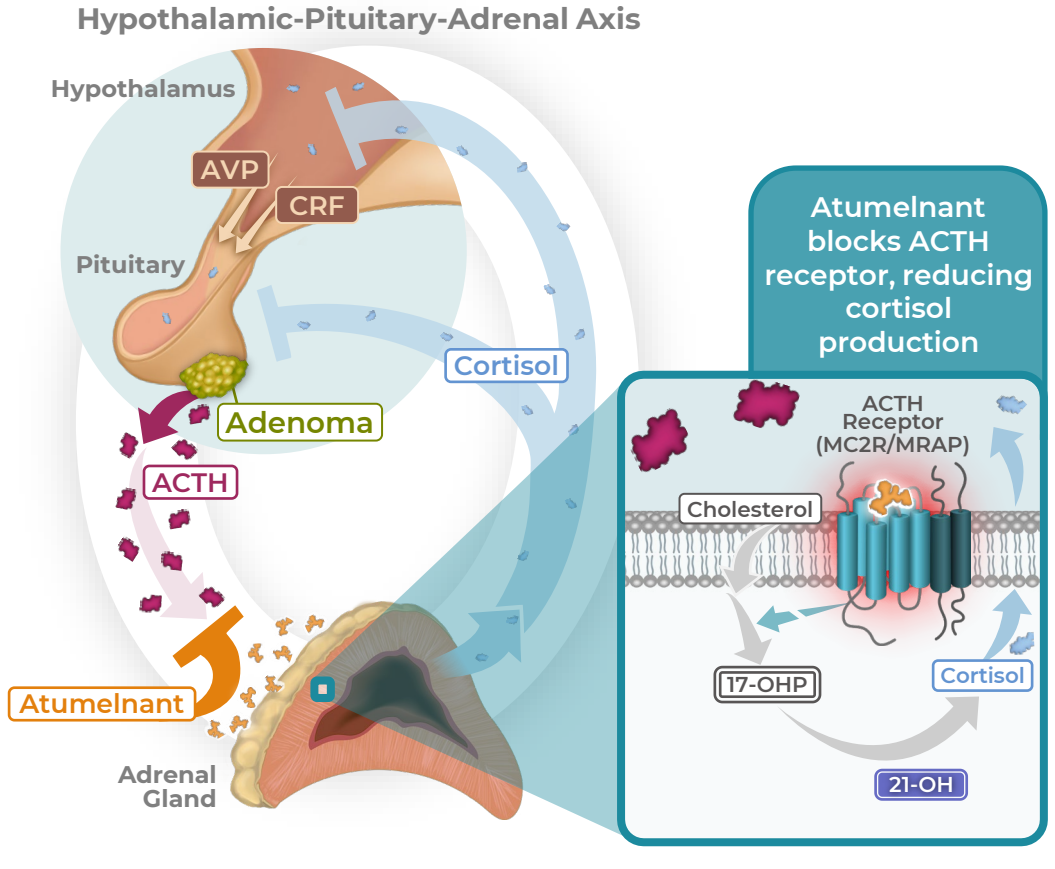
Atumelnant: Also in Development for **ACTH Dependent Cushing's Syndrome**

Disruptions in the HPA Axis Causing ADCS



*Pituitary or other (ectopic) adenoma

Atumelnant Mechanism of Action in ADCS



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Atumelnant is an investigational drug being evaluated in clinical studies for ADCS. Atumelnant has not been approved by any regulatory authority.

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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 µg/dL
- **24h Urine Free Cortisol:** Sustained at or Below the ULN and Maintained Control with Hydrocortisone (HC) Add Back
- **Every Participant Experienced Improvement in Multiple Clinical and/or Cushing's Lab Features**

SAFETY

Atumelnant was well-tolerated with no treatment-related severe or serious adverse events

Initiate later stage clinical development (2025)

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

ULN: Upper limit of normal. 17-OHP: 17-Hydroxyprogesterone. A4: Androstenedione.
Data presented represents data cut off date of May 21st, 2024. Available data: 80 mg: n=4 at 12 weeks; n=2 at 6 weeks; 40 mg: n=4 for 2 weeks.

Crinetics Pharmaceuticals

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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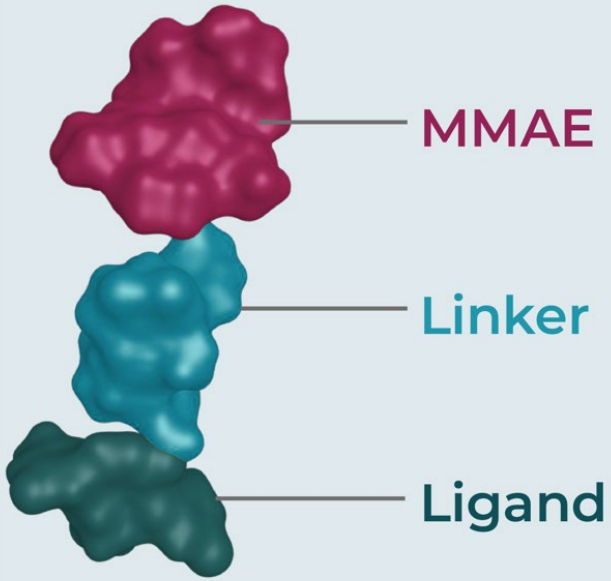
CRN09682: Designed to **Selectively Target and Deliver Cytotoxic Payloads** to SST2-Expressing Tumor Cells



CRN09682
nonpeptide drug conjugate targeting SST2 receptors

MMAE

- Non-cytotoxic when linked
- Highly potent when free

Cleavage Site

- Stable in plasma
- Cleaved intracellularly

Selective Nonpeptide SST2 Agonist

- High affinity
- High selectivity
- Optimized internalization
- Low molecular weight
- Traditional chemical synthesis

MMAE: monomethyl auristatin E; tubulin inactivator

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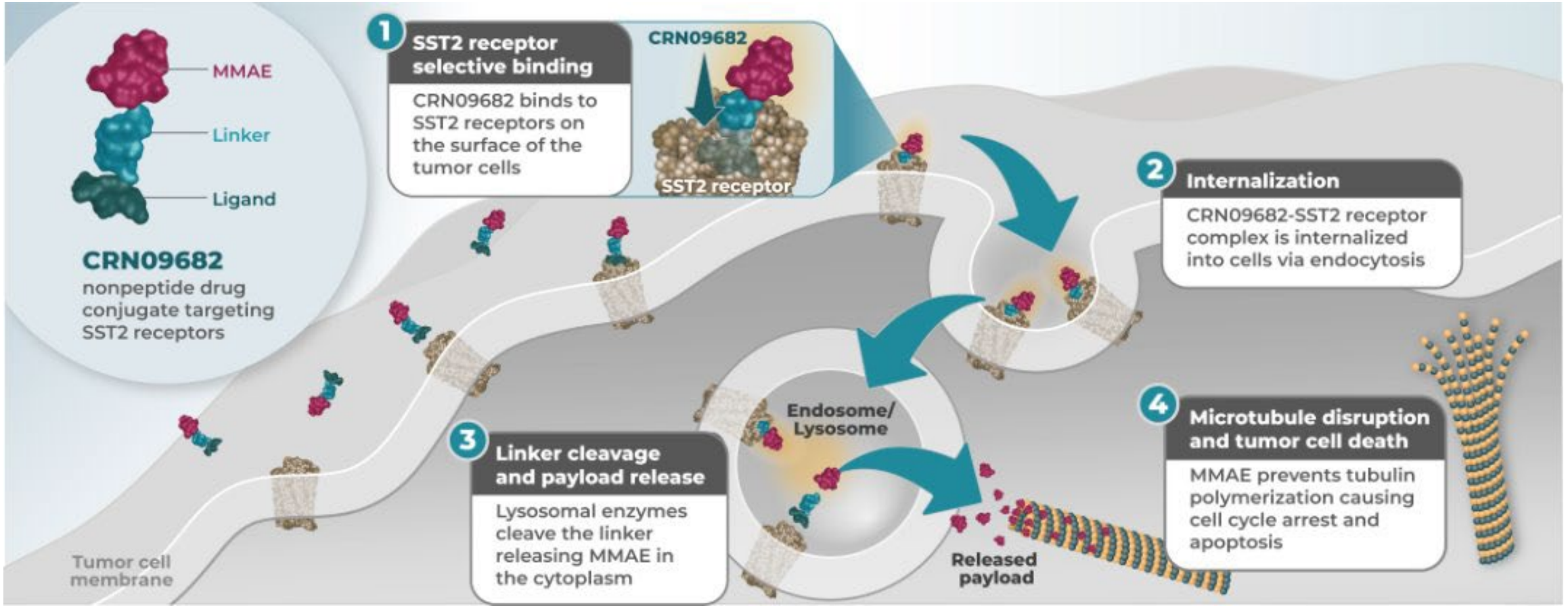
CRN09682: **Internalized Into Tumor Cells** and Releases MMAE to Trigger Microtubule Disruption and Apoptosis



MMAE: monomethyl auristatin E; tubulin inactivator

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Progress on **2H2024 Goals and Milestones**

Goal / Milestone	Timing	Progress
Initiation of IND enabling activities for SST3 candidate for ADPKD	3Q 2024	✓
NDA submission for paltusotine in acromegaly	3Q2024	✓
Raise capital to fund development of additional pipeline programs	4Q2024	✓
Nomination of TSH candidate for Graves' Disease / TED	4Q2024	✓
Initiation of Phase 3 activities for paltusotine in carcinoid syndrome	YE2024	•••
Additional data from Phase 2 study of atumelnant in CAH	Early 2025	•••
File IND for CRN09682 from novel NDC platform	Early 2025	•••

SST: somatostatin receptor type; ADPKD: Autosomal dominant polycystic kidney disease; NDA: New Drug Application; TSH: thyroid-stimulating hormone; TED: thyroid eye disease; IND: Investigational New Drug; NDCs: Nonpeptide Drug Conjugates; CAH: Congenital Adrenal Hyperplasia.

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Deep Pipeline of **Transformative Drug Candidates**

Program	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Registrational	Anticipated Milestones
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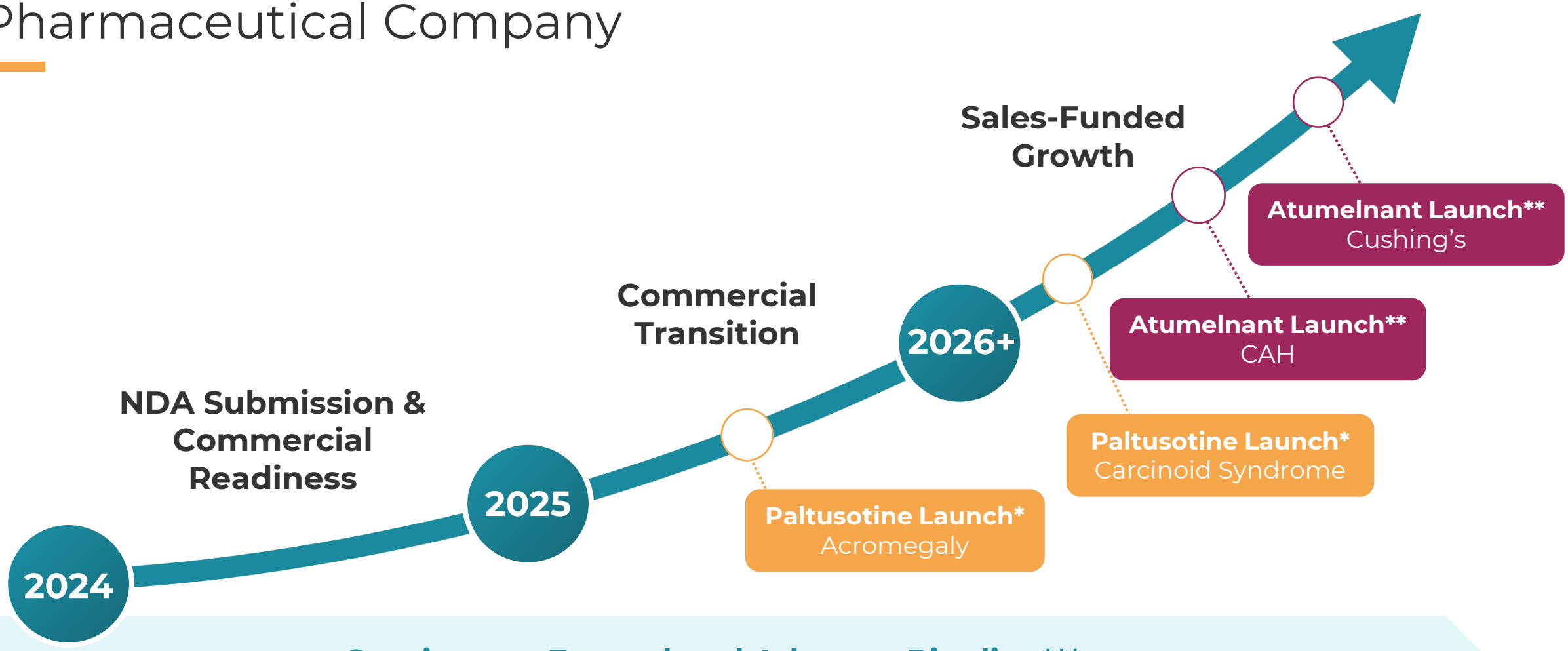
	Cushing's disease						Later-stage development (2025)
PTH antagonist	**Hyperparathyroidism**						IND (2025)
Nonpeptide drug conjugate (CRN09682)	**NETs** and SST2-expressing solid tumors						IND (Early 2025)
TSH antagonist	**Graves' disease & TED**						IND (2025)
SST3 agonist	**ADPKD**						IND (2025)
Oral GLP-1 nonpeptide	**Obesity**						Candidate Selection (2025)
Oral GIP nonpeptide	**Obesity**						Candidate Selection (2025)
Nonpeptide radiotheranostics	**Multiple oncology indications**						Partner: Radionetics Oncology
SST2 agonist	**Extending lifespan of large and giant breed dogs**						Partner: Loyal

4 New Development Candidates

SST: somatostatin receptor type; ACTH: adrenocorticotropic hormone; PTH: parathyroid hormone; ADPKD: Autosomal dominant polycystic kidney disease.; TSH: thyroid-stimulating hormone; TED: thyroid eye disease; GLP-1: glucagon-like peptide-1 receptor agonists; GIP: gastric inhibitory polypeptide; NDA: New Drug Application; NETs: Neuroendocrine tumors

Crinetics is Building the Premier Endocrine-focused Global Pharmaceutical Company



Continue to Expand and Advance Pipeline***

Hyperparathyroidism, Graves' Disease & TED, NETs, ADPKD, Obesity, New Platforms

NDA: New drug application; CAH: Congenital adrenal hyperplasia; TED: Thyroid Eye Disease.; NETs: Neuroendocrine tumors; ADPKD: Autosomal dominant polycystic kidney disease

*Pending NDA acceptance and regulatory approval. **Pending successful completion of registrational studies, NDA submission, acceptance and regulatory approval. ***Pending clinical development of new drug candidates for additional diseases

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