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J.P. Morgan Healthcare Conference



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This presentation also contains information gathered from market research, estimates and other statistical data made by independent parties and by us relating to addressable patients, addressable market size and other data about our industry or the potential market opportunity for our drug candidates. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to the opinions gathered in market research or 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,
Endocrine-Focused** Global
Biopharmaceutical Company to
Improve the Lives of Patients

*Discovering, Developing, and Commercializing the Next Generation of
Therapeutics for Patients with Endocrine Diseases*



2024: Solid Track Record of Success

Paltusotine Milestones

- ✓ Completed Phase 3 Program in Acromegaly and FDA Accepted NDA
- ✓ Positive Phase 2 Results from Paltusotine in Carcinoid Syndrome and Initiation of Phase 3 Trial
- ✓ Built Commercial-ready Organization for Launch

Atumelnant Validation

- ✓ Positive Topline Results in Phase 2 Studies in Congenital Adrenal Hyperplasia and Initial Results in Cushing's Disease

Other Pipeline Achievements

- ✓ Discovery of Innovative Nonpeptide Drug Conjugate (NDC) Platform
- ✓ Advanced Four Internally-Discovered Candidates into IND-enabling Studies



Strengthened Balance Sheet to ~\$1.4B Pro Forma Cash and Investments¹

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 NDA submitted**
- ✓ 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.

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

77%

Reported injection site reactions after SRL treatment¹

79%

Had acromegaly symptoms worsen at end of SRL injection cycle²

64%

Felt upset for being dependent on others for treatment¹

“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 Testimonial*

Source: Crinetics interviews & market research

¹ 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.

² 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

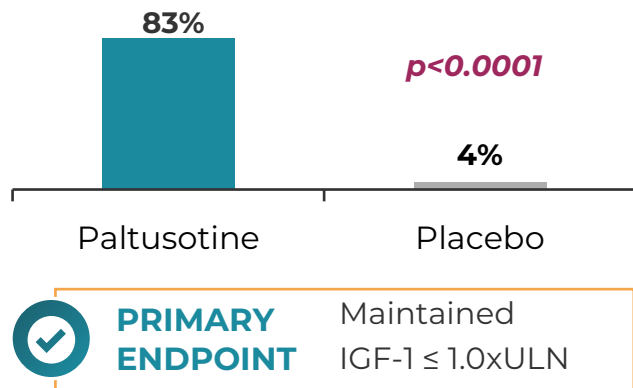


ELLEN
*Living with
Acromegaly*

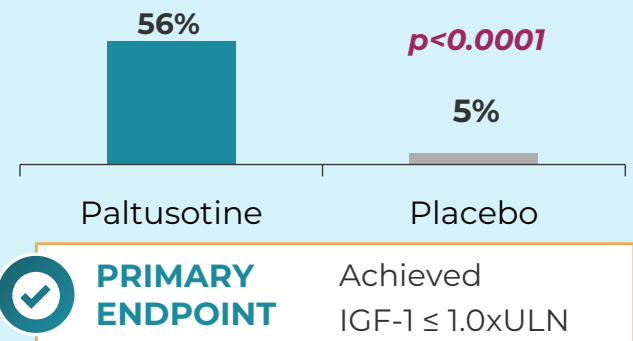
In Phase 3 Studies, Investigational Paltusotine Achieved Rapid, Reliable and Consistent **Biochemical Control** in Acromegaly



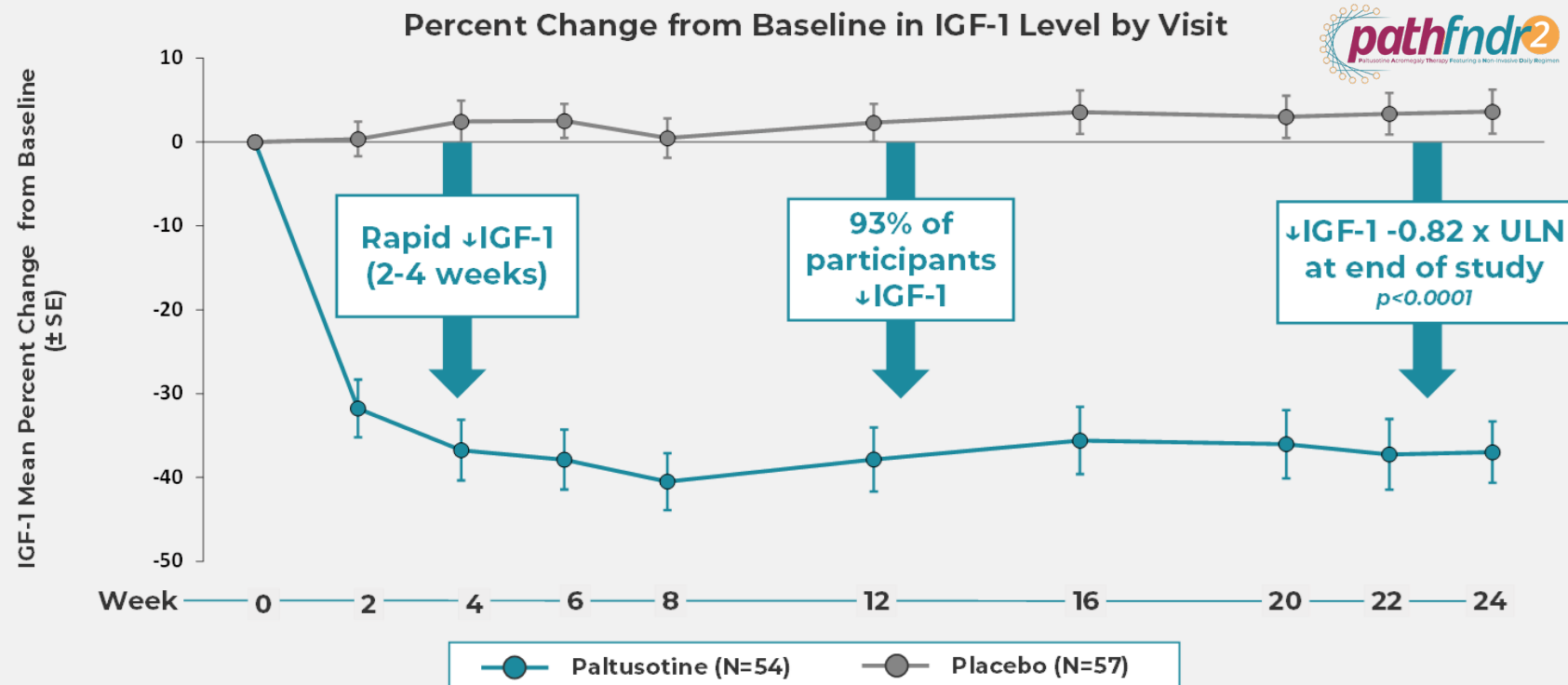
Patients switching from standard-of-care



Non-pharmacologically-treated patients



Paltusotine Treatment Rapidly Decreased IGF-1 Levels in Almost 95% of Participants



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

7 *Paltusotine is an investigational drug. Commercial launch is dependent on regulatory approval. In clinical studies, paltusotine was well-tolerated with no severe or serious adverse events or new safety signals.



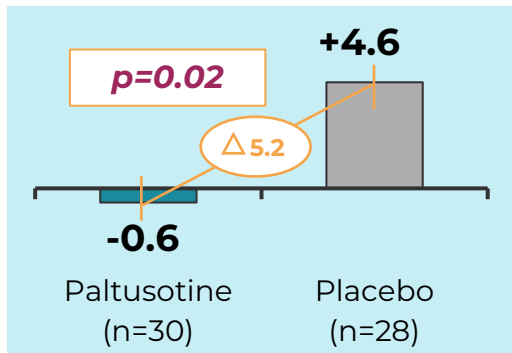
In Phase 3 Studies, Investigational Paltusotine Improved Acromegaly **Symptom Control**

✓ Total ASD Score Reduced in PATHFNRD-1 and -2

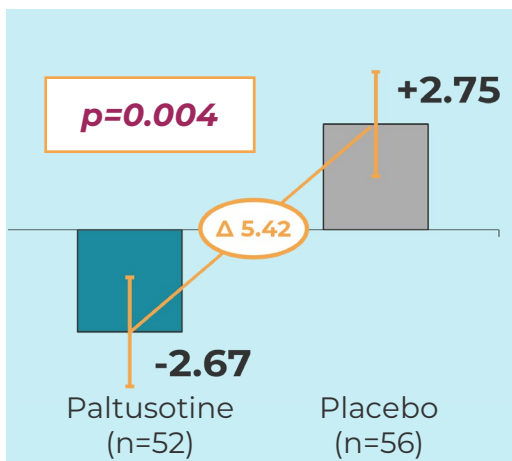
ASD Score Change from Baseline (± SE)



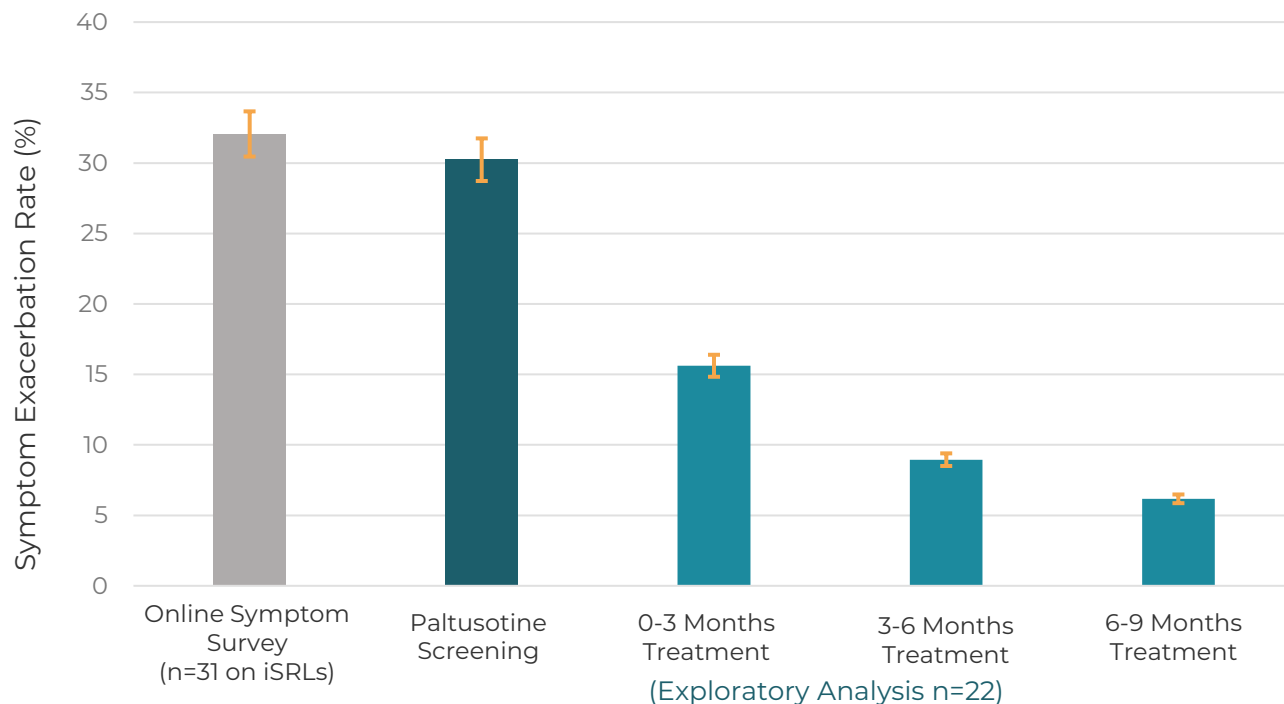
Average Baseline ASD Score in PF1 was 11-13



Average Baseline ASD Score in PF2 was 15-17



✓ Reduced Frequency of Breakthrough Symptoms¹



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

Data on File

iSRL = injectable somatostatin receptor ligands; ASD: Acromegaly Symptom Diary; EoR: End of Randomized control phase. ASD scores measured prior to rescue or discontinuation are used. **ASD Symptoms:** Headache pain, joint pain, sweating, fatigue, leg weakness, swelling, leg weakness, numbness/tingling. Each rated 1 (best) to 10 (worst). Total Score possible of 70. Exploratory analysis also included two additional symptoms on sleep and memory.

¹ Symptom exacerbation rate defined as % of days in which the 2-day average is 2 or more points higher than the previous 2-day average for any individual symptom



Paltusotine Mission:

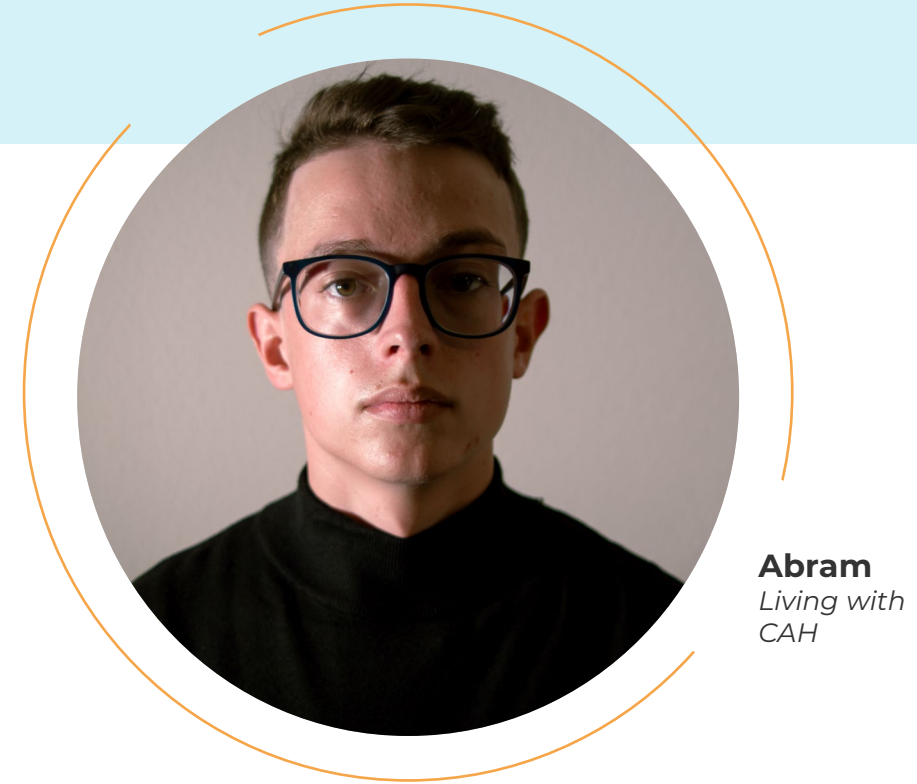
Deliver next generation care to people with acromegaly



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



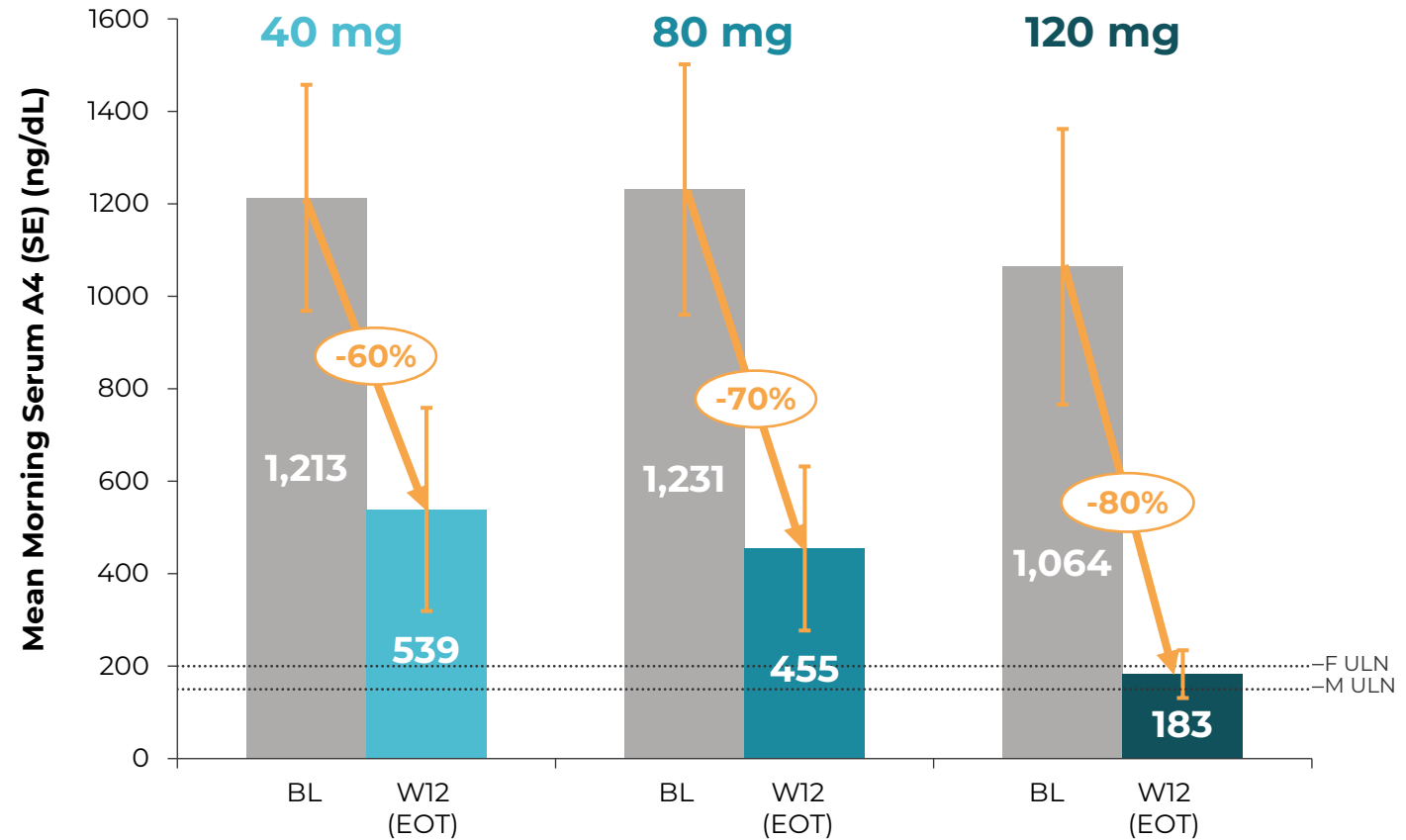
CAH Has a Range of Clinical Implications

"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

Atumelnant Demonstrated Rapid, Substantial and Sustained A4 Reductions, the **Key Biomarker** for CAH Disease Control

- Across each cohort, baseline A4 levels were significantly elevated (>1,000 ng/dL)
- All dose cohorts saw substantial decreases vs. baseline, with the magnitude of response increasing with dose
- The 120 mg cohort experienced the largest A4 reduction, with a mean decline of 80% at Week 12



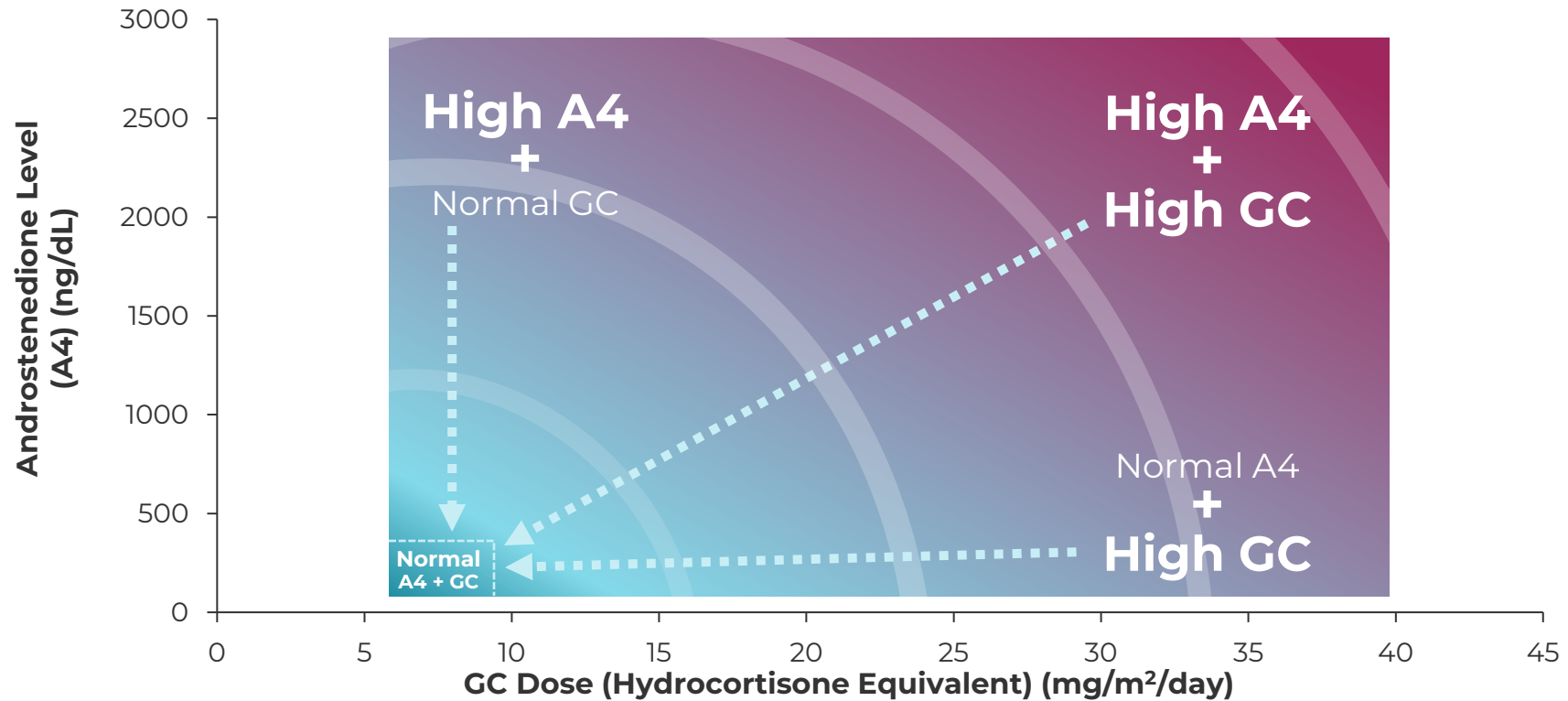
Primary Endpoint: CFB in pre-GC morning serum A4 at week 12			
A4 CFB (ng/dL) at week 12, LSM	-619	-774	-954
p-value	<i>p</i> =0.0003	<i>p</i> <0.0001	<i>p</i> <0.0001

Significant **Clinical Improvements** Achieved with Atumelnant Treatment

CAH Manifestations	Achieved following 12 weeks of treatment with atumelnant
Overproduction of androgens, and androgen precursors	✓ Normalization of A4 in many participants and substantial reduction in 17-OHP levels (across dose groups)
Females: <ul style="list-style-type: none">• Elevated testosterone levels• Absent/irregular menses	✓ Testosterone substantially reduced/normalized in the majority of participants; 6/11 participants resumed menses
Males: Elevated A4/testosterone ratio	✓ Clinically relevant reductions in many participants
Androgen mediated polycythemia (linked to increased cardiovascular risks)	✓ Resolution in 5/6 participants with polycythemia
Hirsutism and acne	✓ Improvements reported, longer treatment likely needed for full effects
Adrenal gland hyperplasia	✓ Consistent reductions in adrenal volume





Atumelnant was generally well tolerated with no severe or serious adverse events

Atumelnant Vision: Healthier Hormone Levels for People Living with CAH



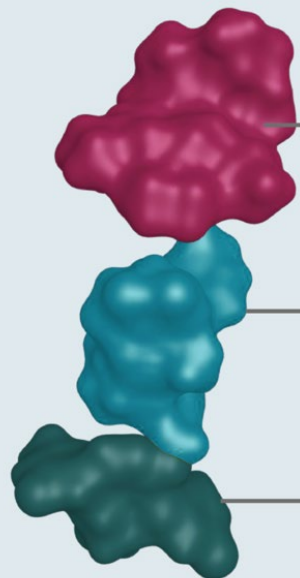
A single pill taken once a day, that eliminates excess ACTH driven adrenal activation and its clinical sequelae for people struggling with Congenital Adrenal Hyperplasia

Four INDs Expected in 2025 Driving Next Wave of Innovation to Address Unmet Needs in Large Patient Populations

 Indication	Neuroendocrine Tumors (NETs)	Hyperparathyroidism	Graves / TED	ADPKD¹
 Target	SST2+ NDC (CRN09682)	PTH antagonist	TSH antagonist	SST3 agonist
 Approximate US Patient Population	140K patients with SST2+ NETs	200K incident cases of symptomatic primary hyperparathyroidism	3M+ patients with Graves, many develop TED	300K+ patients with ADPKD
 Potential Indications to Explore	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 Provide Multiple Opportunities for Value Creation

CRN09682 is Designed to Selectively Target and Deliver Cytotoxic Payload to SST2-Expressing Tumor Cells



MMAE

- Non-cytotoxic when linked
- Highly potent when free
- **Interchangeable payload for future development**

Linker

- Stable in plasma
- Cleaved intracellularly

Ligand

- Selective nonpeptide SST2 agonist
- High affinity and selectivity
- Optimized internalization
- Low molecular weight
- Traditional chemical synthesis
- **Designed for straightforward substitution with other GPCR-targeting small molecules**

CRN09682

nonpeptide drug
conjugate targeting
SST2 receptors

Differentiation vs. Current Modalities



Anticancer Agents
(Chemotherapies, PROTAC)

- X Not tumor specific
- X Unfavorable PK/ADME
- X Narrow TI



Antibody-Drug Conjugate

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



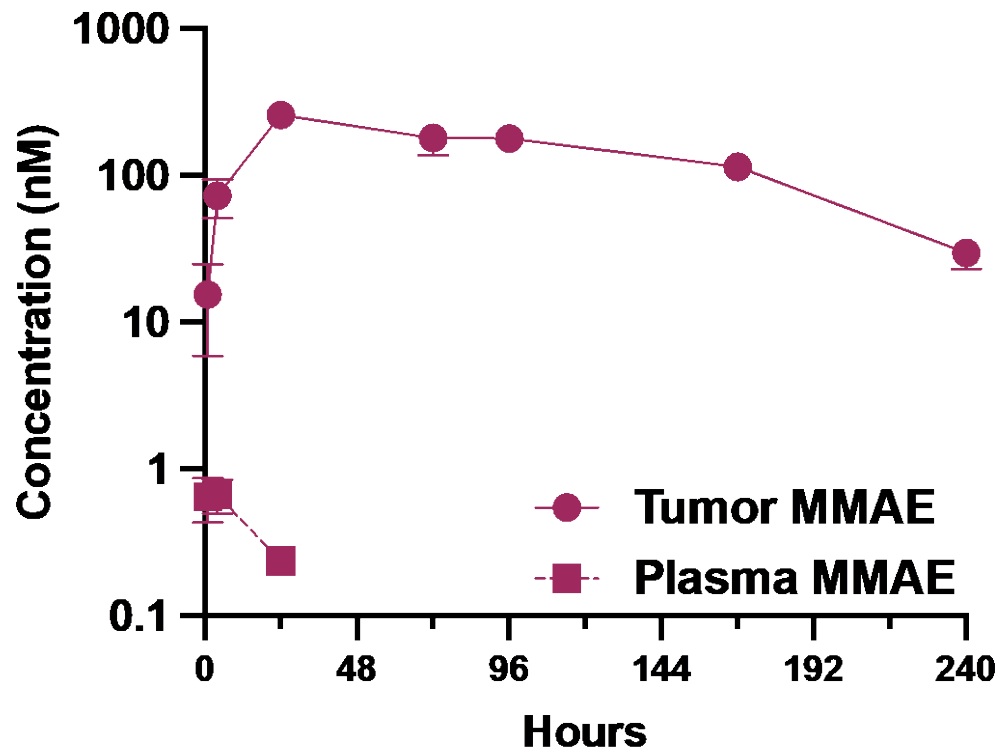
Radioligand Therapies

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

IND Submission for CRN09682 Expected Early 2025 Based on Promising Preclinical Data

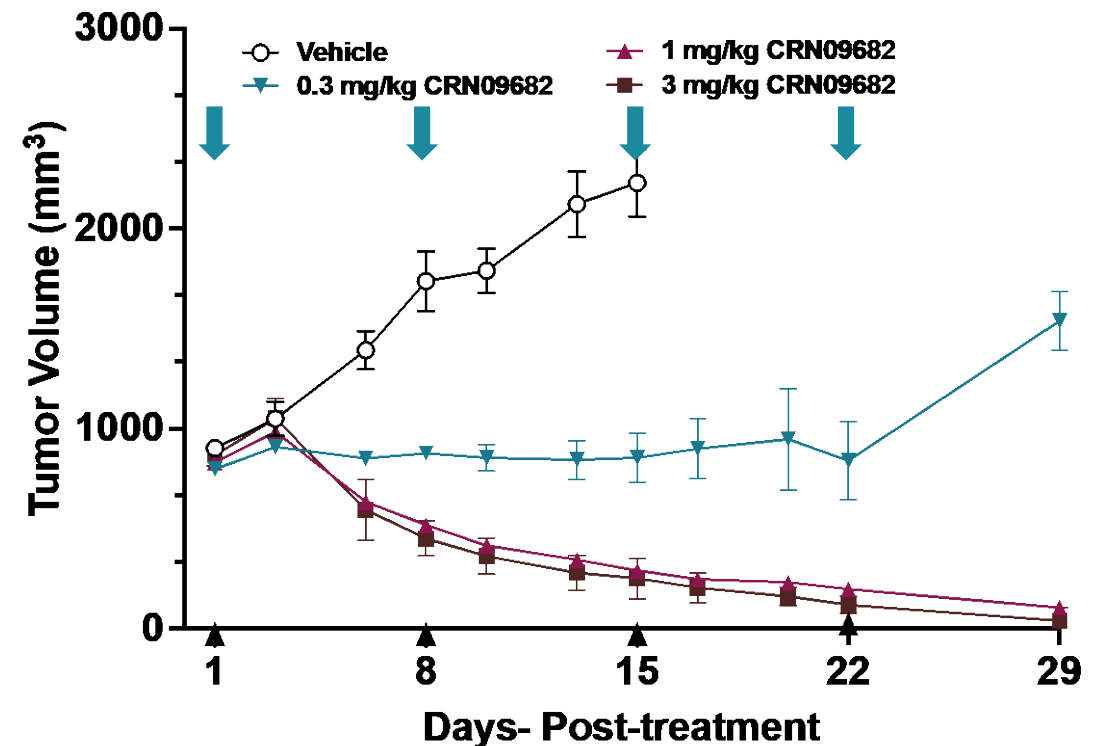
CRN09682 Selectively **Delivers MMAE to Tumors With Minimal Systemic Exposure to Free MMAE** in Mice

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



Continued Value Creation with Deep Pipeline of Transformative Drug Candidates

Program	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Registrational	Milestones / Partner
Paltusotine (SST2 agonist)	Acromegaly						PDUFA Date (September 2025) Ongoing Phase 3
	Carcinoid syndrome						
Atumelnant (ACTH antagonist)	Congenital adrenal hyperplasia						Phase 3 Initiation in Adult, Phase 2b/3 Initiation in Pediatric (2025) Later-stage trial Initiation (2025)
	Cushing's disease						
Nonpeptide drug conjugate (CRN09682)	NETs and SST2-expressing solid tumors						IND (Early 2025)
PTH antagonist	Hyperparathyroidism						IND (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: 
SST2 agonist	Extending lifespan of large and giant breed dogs						Partner: 

4 New IND-enabling Programs

Building a Premier Endocrine-Focused Global Biopharmaceutical Company

Plans for 2025: **ADVANCE**

Launch Paltusotine*

- PDUFA date September 25, 2025
- EU regulatory filing 1H2025

Start Four Pivotal Trials

- Carcinoid, Adult CAH, Pediatric CAH and Cushing's

Plan to File Four INDs

Announce Obesity Development Candidates

Pipeline for 2026+: **EXPAND**

Grow Commercial Engine

- Launch of paltusotine in **2nd** indication*
- Launch of atumelnant in **2** indications*
- Commercialization in global markets*

Execute Near-Term Clinical Catalysts

- Phase 3 data in **2** trials: Carcinoid and Adult CAH
- Phase 2/3 data in **2** trials: Cushing's and Pediatric CAH

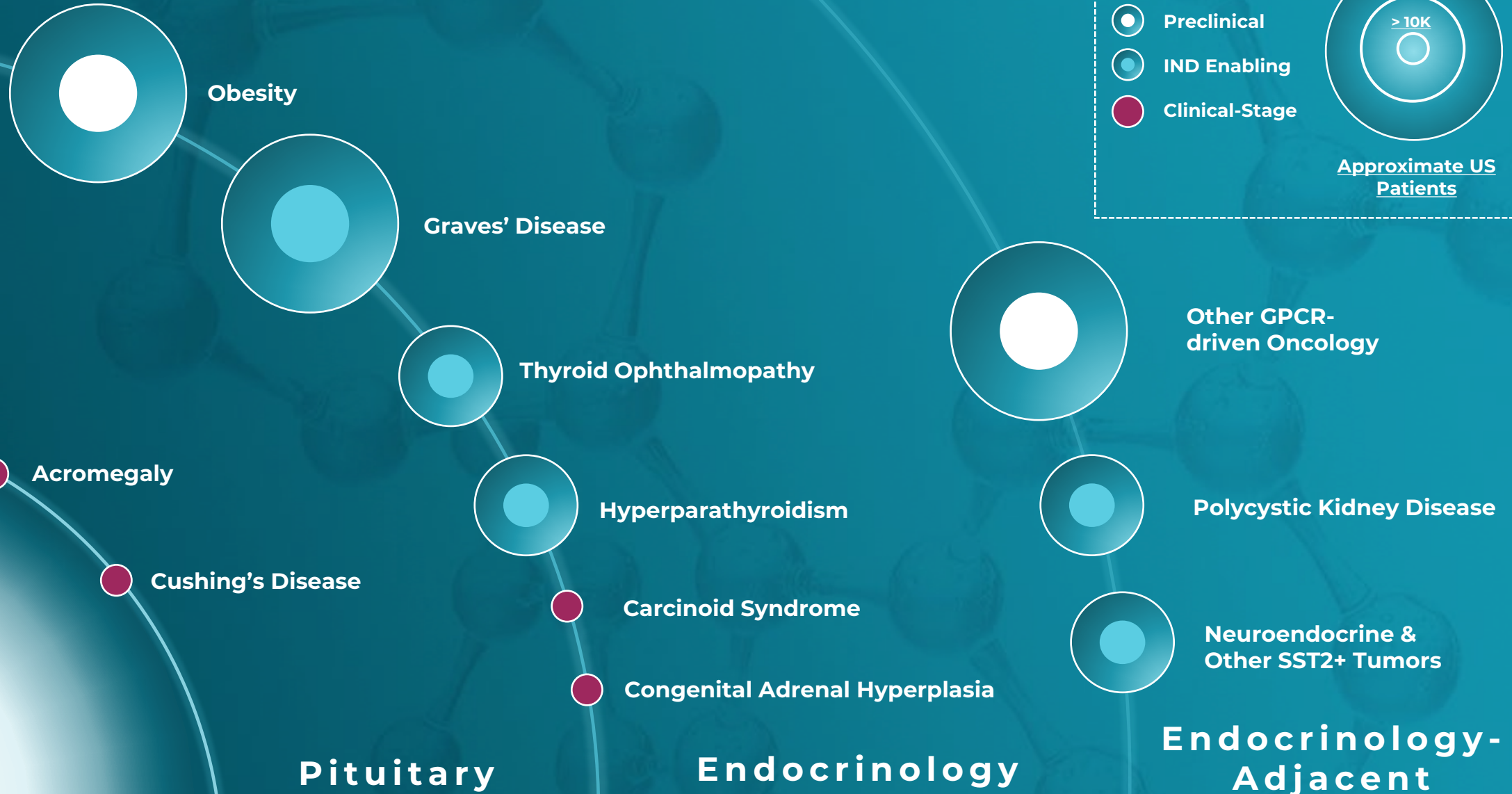
Bolster Pipeline in Long-Term

- Early clinical readouts on **4** 2025 INDs
- IND filings for obesity candidates and other NCEs from Discovery**

NDA: New drug application; CAH: Congenital adrenal hyperplasia; ADPKD: Autosomal Dominant Polycystic Kidney Disease; TED: Thyroid Eye Disease; NDC: Nonpeptide Drug Conjugate

*Pending regulatory approval. **Pending clinical development of new drug candidates

Exploring New Frontiers With Our Science to Expand Patient Reach





THANK YOU

