
**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 14, 2025

Crinetics Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction
of Incorporation)

001-38583
(Commission File Number)

26-3744114
(IRS Employer
Identification No.)

6055 Lusk Boulevard
San Diego, California
(Address of Principal Executive Offices)

92121
(Zip Code)

Registrant's Telephone Number, Including Area Code: (858) 450-6464

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	CRNX	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

On January 14, 2025 at 4:30 pm Pacific Time, Scott Struthers, Ph.D., Founder and Chief Executive Officer of Crinetics Pharmaceuticals, Inc. (the “Company,” “Crinetics,” “we,” “us,” or “our”), will present a Company update at the 43rd annual J.P. Morgan Healthcare Conference, which is taking place in San Francisco, CA from January 13-16, 2025. A live audio webcast of Dr. Struthers’ presentation may be accessed on the Events & Presentations section of the Company’s website or directly on the J.P. Morgan virtual meeting platform. During the presentation, the Company will reference the corporate slide presentation attached as Exhibit 99.1 to this Current Report on Form 8-K, which is incorporated herein by reference.

The presentation will feature an overview of Crinetics’ key priorities and anticipated milestones for 2025. These include:

- The continued efforts to further increase commercial readiness so that the Company can rapidly provide patients in the United States with acromegaly with broad access to once-daily oral paltusotine if the new drug application is approved, with the Prescription Drug User Fee Act Target Action Date of September 25, 2025.
- The continued development of atumelnant, an investigational adrenocorticotrophic hormone (ACTH) antagonist, for congenital adrenal hyperplasia (CAH) and Cushing’s disease, with Phase 3 initiation for adult CAH patients expected in the first half of 2025 and later-stage trial initiations for pediatric CAH patients and patients with Cushing’s disease expected in 2025.
- The continued advancement of Investigational New Drug-enabling studies of 4 development candidates for neuroendocrine tumors and somatostatin receptor type-2-expressing solid tumors, hyperparathyroidism, Graves’ disease, thyroid eye disease, and autosomal dominant polycystic kidney disease.

The Company’s updated corporate presentation has been posted to the Company’s website, www.crinetics.com. The Company plans to use its website to disseminate future updates to its corporate presentation and does not intend to file or furnish a Form 8-K alerting investors each time the presentation is updated.

The information contained in this Item 7.01, including in Exhibit 99.1 hereto, is being “furnished” and shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), is not subject to the liabilities of that section and is not deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the “Securities Act”), or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements other than statements of historical facts contained in this Current Report on Form 8-K are forward-looking statements, including statements regarding [statements regarding the NDA review process and the expected timing of the completion of the FDA’s review of the NDA for paltusotine for the treatment or maintenance of treatment of acromegaly in the United States, the therapeutic potential and clinical benefits or safety profile of paltusotine for patients with acromegaly, the plans and timelines for the commercial launch paltusotine for acromegaly, if approved, and of our commercial readiness efforts, the clinical development of atumelnant, including the therapeutic potential and clinical benefits or safety profile thereof, the plans for and the therapeutic potential of our development candidates, and the potential of our other research, discovery, and clinical trial programs.] These forward-looking statements speak only as of the date of this Current Report on Form 8-K and are subject to a number of 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, the risks and uncertainties described in the company’s periodic filings with the SEC. The events and circumstances reflected in the Company’s forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Additional information on risks facing Crinetics can be found under the heading “Risk Factors” in Crinetics’ periodic filings with the SEC, including its annual report on Form 10-K for the year ended December 31, 2023 and quarterly reports on Form 10-Q for the quarters ended March 31, 2024, June 30, 2024, and September 30, 2024. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by applicable law, Crinetics does 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Corporate Slide Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Crinetics Pharmaceuticals, Inc.

Date: January 14, 2025

By: /s/ R. Scott Struthers, Ph.D.
R. Scott Struthers, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)



January 2025

**J.P. Morgan Healthcare
Conference**



Safe Harbor Statement

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics," the "company," "we," "us," 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 plans and timelines for the clinical development of atumelnant, including the therapeutic potential and clinical benefits or safety profile in patients with CAH or Cushing's Disease and the expected plans and timing for ongoing clinical studies and related initiatives; the therapeutic potential and clinical benefits or safety profile of paltusotine for patients with acromegaly and carcinoid syndrome; the plans and timelines for a commercial launch of paltusotine for acromegaly, if approved, and potential launches of other product candidates; the plans and timing of investigative new drug (IND)-enabling programs and applications; the potential selection of additional product candidates for development; the potential benefits of CRN09682, and the timing of plans for its development and IND submission; the potential of our ongoing discovery efforts to target future indications for obesity, and other GPCR-driven oncology; the plans for global reach and infrastructure buildout. 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," "potential," "target" or the negative of or 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 completion or 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; 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 suggest changes to our planned clinical studies; 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; 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; clinical studies and preclinical studies may not proceed at the time or in the manner expected, or at all; the timing and outcome of research, development and regulatory review is uncertain, and our drug candidates may not advance in development or be approved for marketing; 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. 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 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



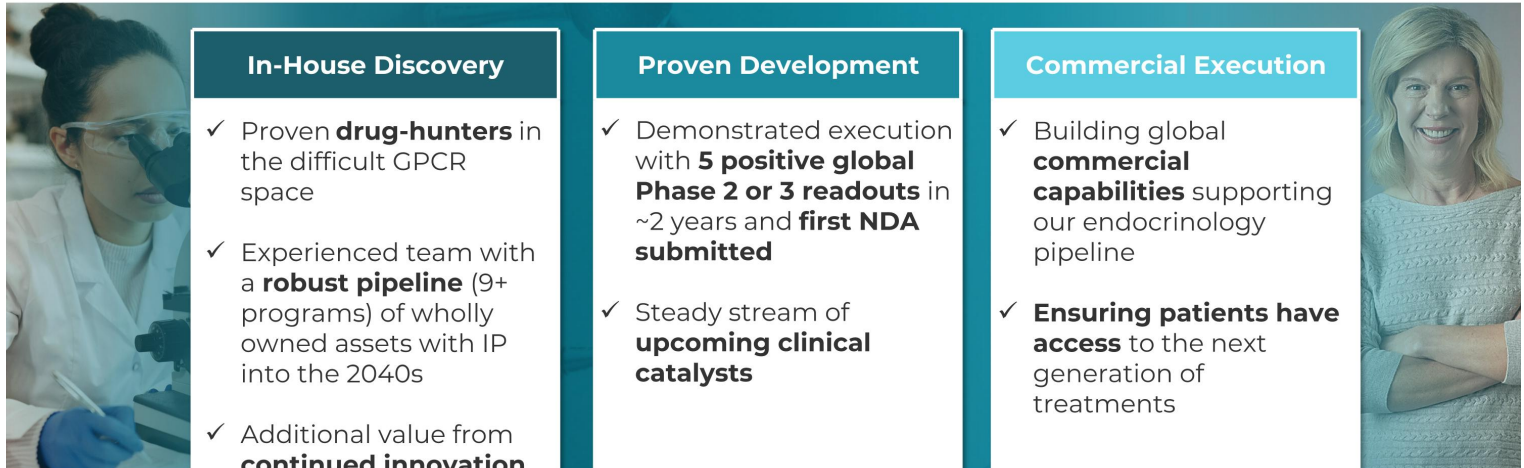
Strengthened Balance Sheet to ~\$1.4B Pro Forma Cash and Investments¹

4

¹ As of September 30, 2024, Pro forma cash and investments consists of \$863 million of cash and investments as of September 30, 2024, plus \$543 million of net proceeds from the public offering of \$575 million of common stock in October 2024. Paltusotine and atumelnant are investigational drugs. NDA: New Drug Application



Transforming Endocrine Disease Treatment from Discovery to Commercialization...



In-House Discovery	Proven Development	Commercial Execution
<ul style="list-style-type: none">✓ 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	<ul style="list-style-type: none">✓ Demonstrated execution with 5 positive global Phase 2 or 3 readouts in ~2 years and first NDA submitted✓ Steady stream of upcoming clinical catalysts	<ul style="list-style-type: none">✓ 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*



ELLEN
Living with
Acromegaly

Source: Crinetics interviews & market research

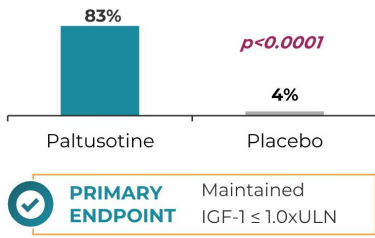
¹ Fliseriu M, Molitch M, Dreval A, et al. Disease and treatment-related burden in patients with acromegaly who are biochemically controlled on injectable somatostatin receptor ligands. *Front Endocrinol (Lausanne)*. 2021;12:627711.

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

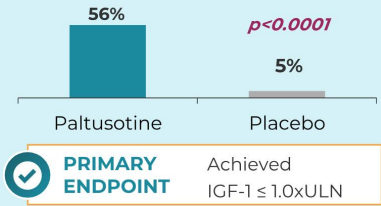
In Phase 3 Studies, Investigational Paltusotine Achieved Rapid, Reliable and Consistent **Biochemical Control** in Acromegaly



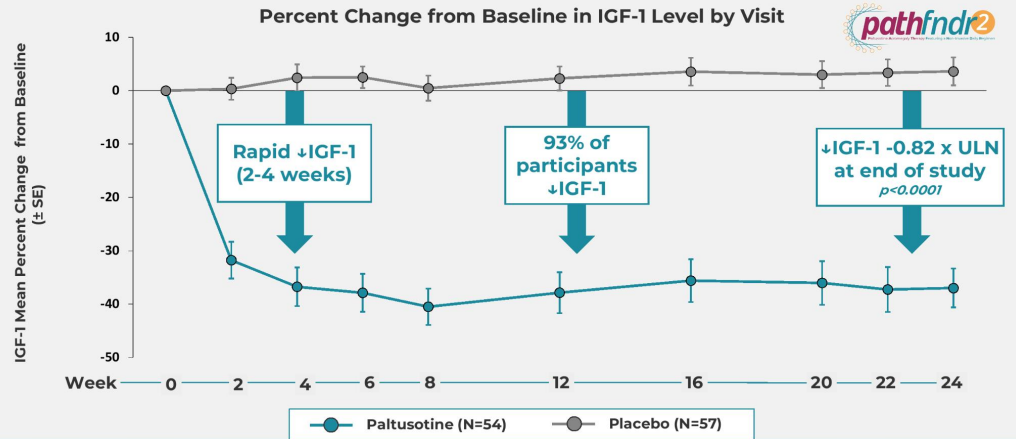
Patients switching from standard-of-care



Non-pharmacologically-treated patients



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



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



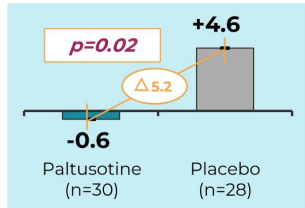
In Phase 3 Studies, Investigational Paltusotine Improved Acromegaly **Symptom Control**

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

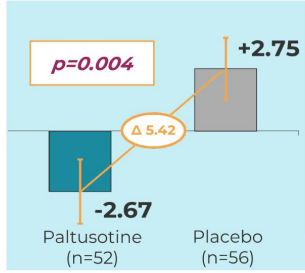
ASD Score Change from Baseline (± SE)



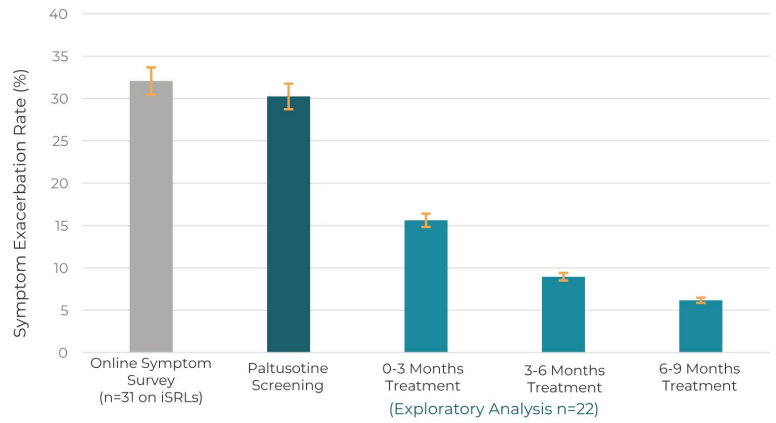
Average Baseline ASD Score in PF1 was 11-13



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



ACTIVATE

ADOPT

ACCESS

ADHERE

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



Abram
Living with
CAH

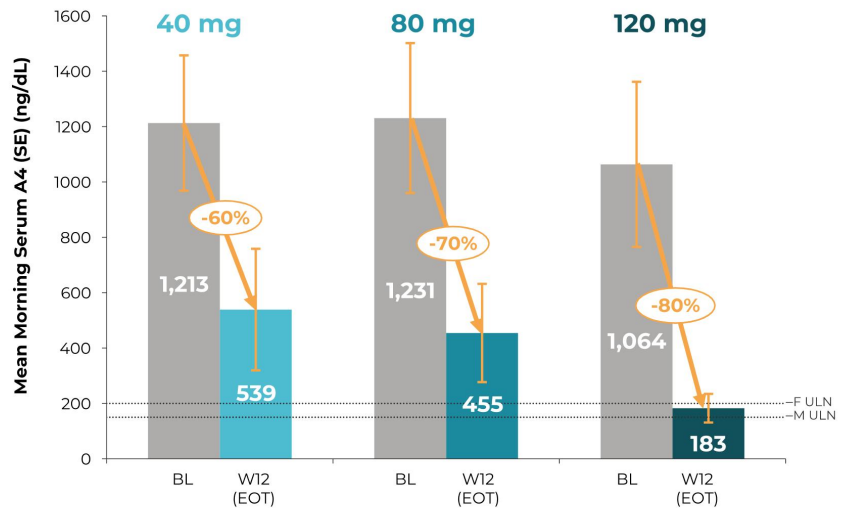
CAH Has a Range of Clinical Implications

"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	$p=0.0003$	$p<0.0001$	$p<0.0001$

11 Participants At Baseline: 40 mg N=11; 80 mg N=11; 120 mg N=6.
 Participants At Week 12: 40 mg N=10; 80 mg N=11; 120 mg N=6.
 CFB: change from baseline, LSM: Least-square-mean

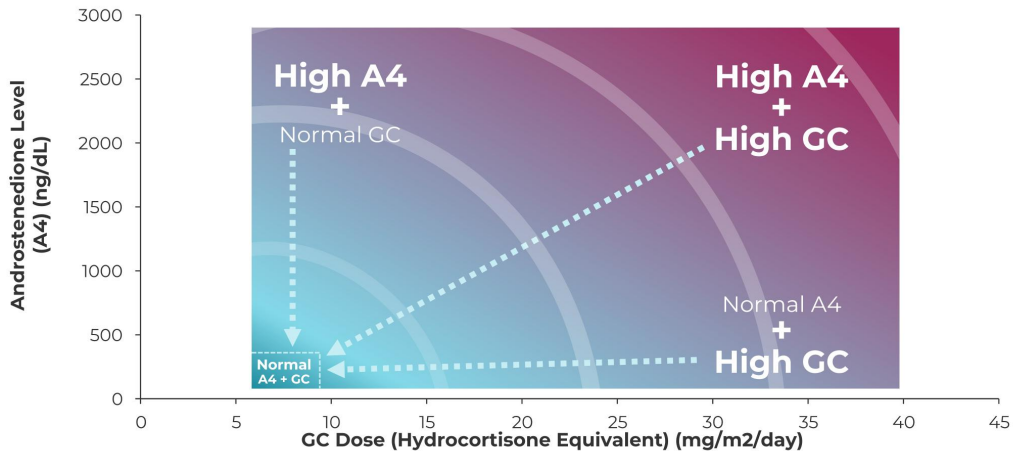


Significant **Clinical Improvements** Achieved with Atumelnant Treatment

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; 6/10 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



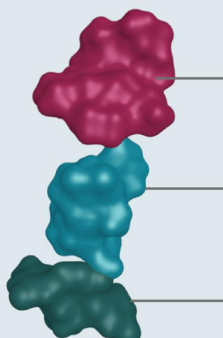
A single pill taken once a day, that eliminates excess ACTH driven adrenal activation and its clinical sequelae for people struggling with Congenital Adrenal Hyperplasia

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	ADPKD ¹
 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



CRN09682
nonpeptide drug conjugate targeting SST2 receptors

- 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*

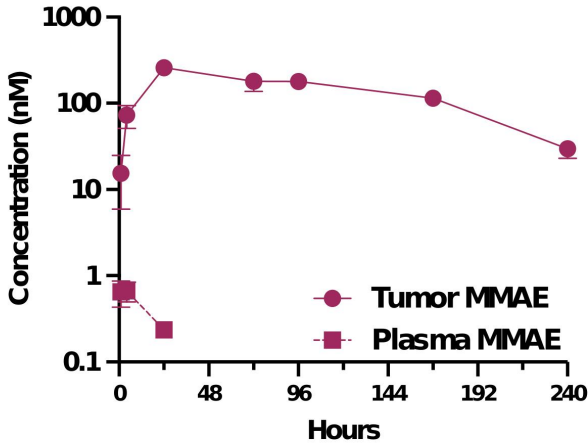
Differentiation vs. Current Modalities

- **Anticancer Agents**
(Chemotherapies, PROTAC)
 - ✗ Not tumor specific
 - ✗ Unfavorable PK/ADME
 - ✗ Narrow TI
- Y● **Antibody-Drug Conjugate**
 - ✗ Long half-life
 - ✗ Poor tumor penetration
 - ✗ Unspecific uptake
- ←● **Radioligand Therapies**
 - ✗ Limited number of cycles
 - ✗ Radionuclide supply
 - ✗ Treatment logistics
 - ✗ Radiation safety

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

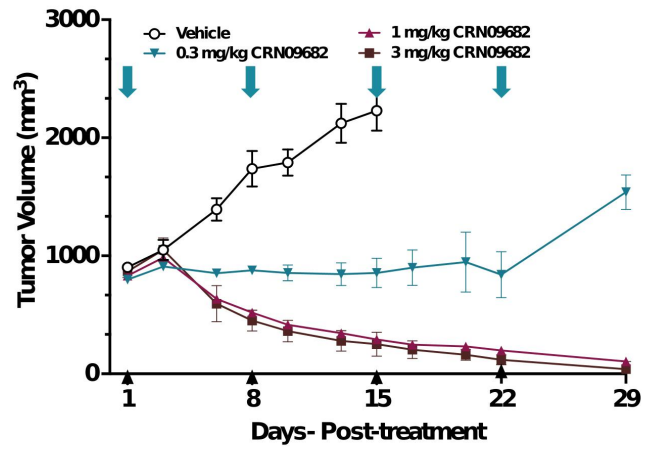
CRN09682 Selectively **Delivers MMAE to Tumors With Minimal Systemic Exposure to Free MMAE** in Mice

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)
	Carcinoid syndrome						Ongoing Phase 3
Atumelnant (ACTH antagonist)	Congenital adrenal hyperplasia						Phase 3 Initiation in Adult, Phase 2b/3 Initiation in Pediatric (2025)
	Cushing's disease						Later-stage trial Initiation (2025)
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

17 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; IND: Investigational New Drug Application; PDUFA: Prescription Drug User Fee Act



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**

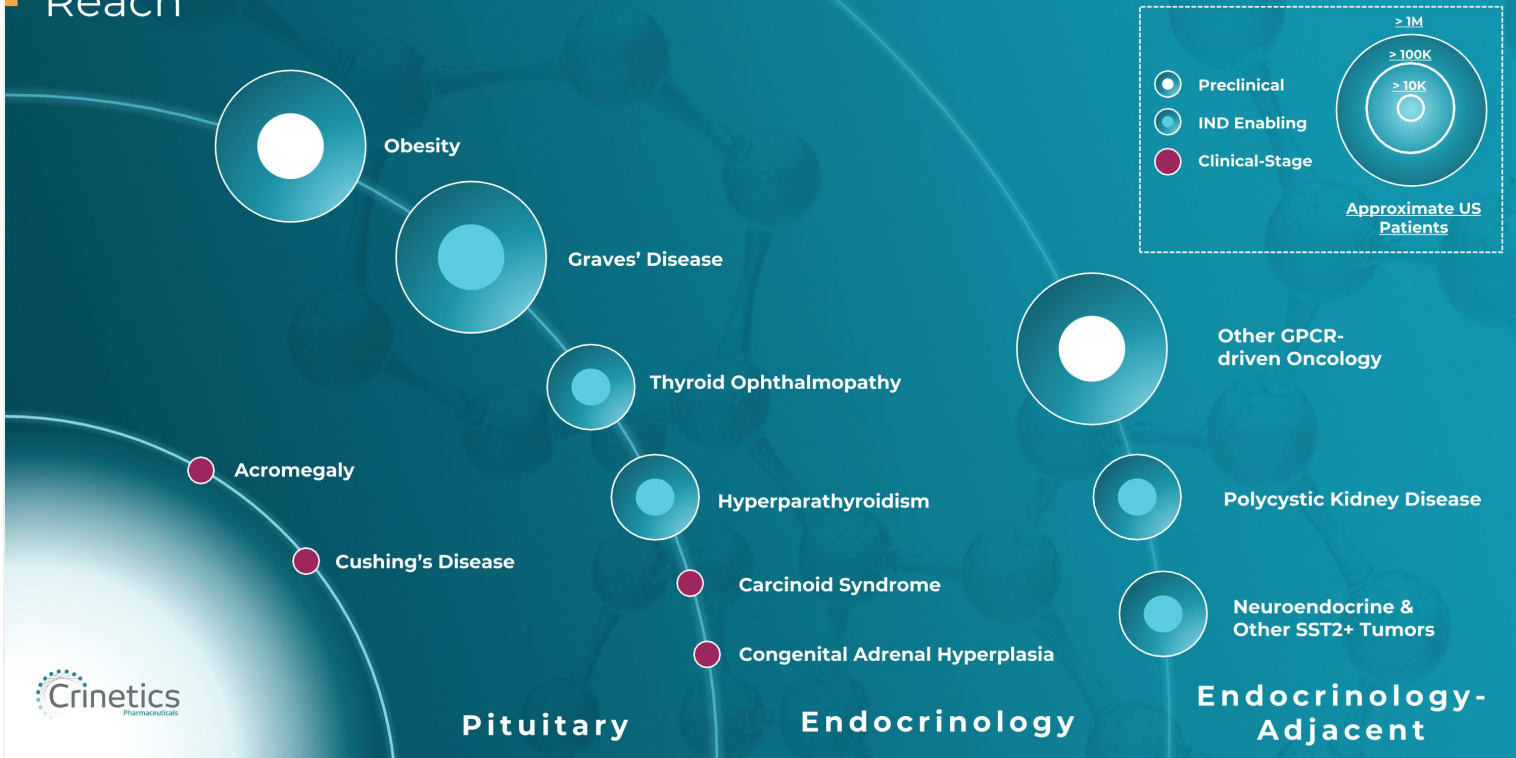
NDA: New drug application; CAH: Congenital adrenal hyperplasia; ADPKD: Autosomal Dominant Polycystic Kidney Disease; TED: Thyroid Eye Disease; NDC: Nonpeptide Drug Conjugate

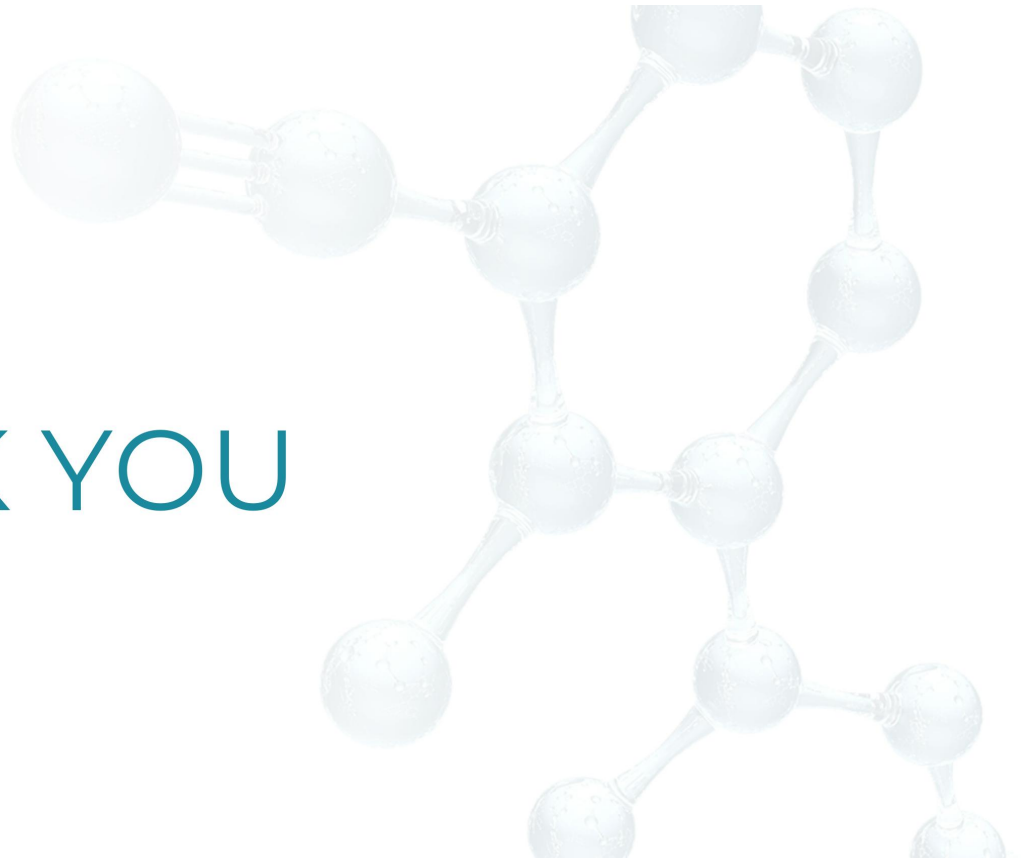
18 |

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



Exploring New Frontiers With Our Science to Expand Patient Reach





| THANK YOU

