Crinetics Pharmaceuticals

CORPORATE PRESENTATION

November 2020

SAFE HARBOR STATEMENT

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including 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 potential benefits of paltusotine for acromegaly patients; the potential to initiate a pivotal Phase 3 trial of paltusotine in acromegaly with our to-be-marketed formulation based on interim results to date and the timing thereof; the planned expansion of the paltusotine development program to include the treatment of carcinoid syndrome in patients with NETs and the expected timing thereof, including the initiation of a Phase 2 trial in these patients; the anticipated timing of topline data for Edge and PK/PD data for its other development programs and initiation of trials thereafter; the potential benefits of our ACTH antagonist in patients across multiple indications and the expected timing of the advancement of such program, including the potential to initiate a Phase 1 trial of our lead ACTH antagonist and the timing thereof; the potential benefits of our SST5 agonist in patients with congenital hyperinsulinism and the expected timing of the advancement of such program, including the potential to initiate a Phase 1 trial of our lead SST5 agonist and the timing thereof; the potential for any of our ongoing clinical trials to show safety or efficacy; 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," "forecast" and similar terms. These statements involve known and unknown risks, uncertainties 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 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; potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; advancement of paltusotine into a Phase 3 trial and our lead ACTH antagonist and SST5 agonist into Phase 1 trials are dependent on and subject to the receipt of further feedback from the FDA; 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 for paltusotine and our other product candidates; 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.

<u>Mission:</u> To build the leading endocrine company that consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives

Company Overview

Highlights

- Nasdaq listed: CRNX
- Headquarters: San Diego, CA
- Employees: 80
- Shares: 32.9 million*
- Cash & Investments: $187 million*

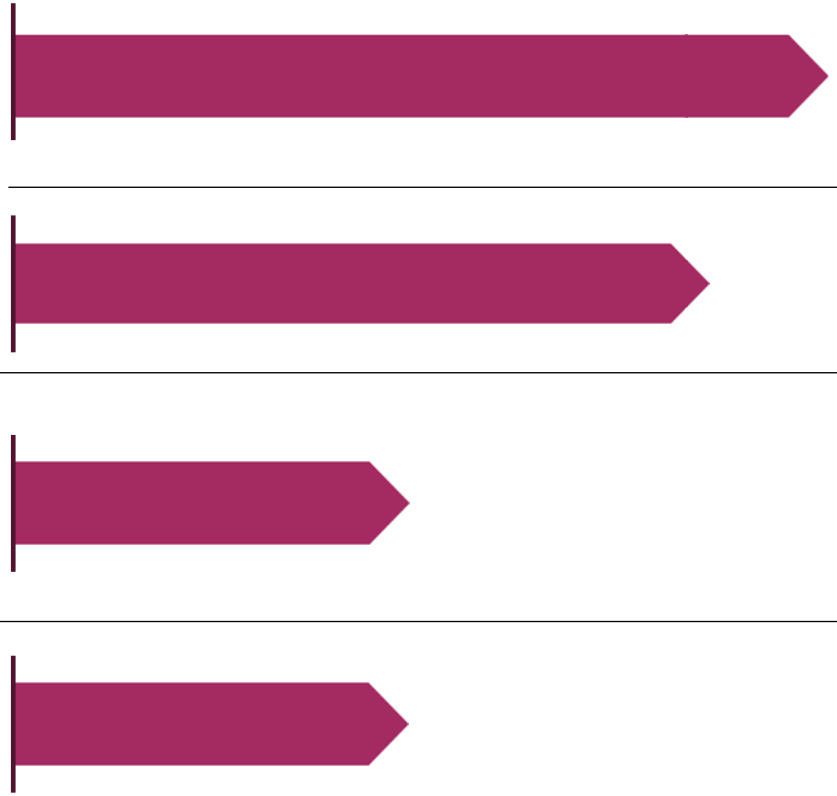
Our Strategy: Discover, develop and commercialize new drugs for multiple rare endocrine diseases and endocrine-related tumors with:

- High unmet medical need
- Established biology
- Biomarker endpoints
- POC in Phase 1
- Small registration trials

*As of September 30, 2020

Pipeline: Rare Disease Franchise in Endocrinology

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
Paltusotine Acromegaly						Initiate Phase 3 acromegaly - 1H 2021
Neuroendocrine Tumors (NETs)						Initiate Phase 2 in 2021
Oral ACTH Antagonist Cushing's Disease, Congenital Adrenal Hyperplasia (CAH)						Initiate Phase 1 late 2020/early 2021
CRN04777 Congenital Hyperinsulinism (CHI)						Initiate Phase 1 early 2021



All product candidates discovered and developed internally. Global rights retained and no licensing obligations.

PALTUSOTINE

An **oral nonpeptide SST2 agonist** for the treatment of acromegaly and neuroendocrine tumors

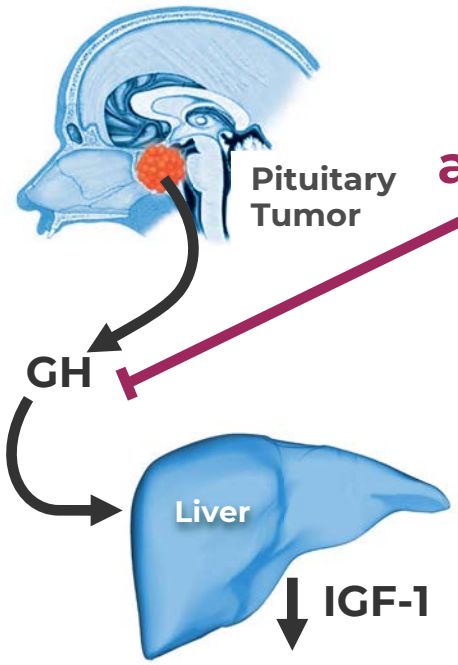
Acromegaly and NETS are Currently Treated with Injected Somatostatin Receptor Ligand (SRL) Depots

Acromegaly

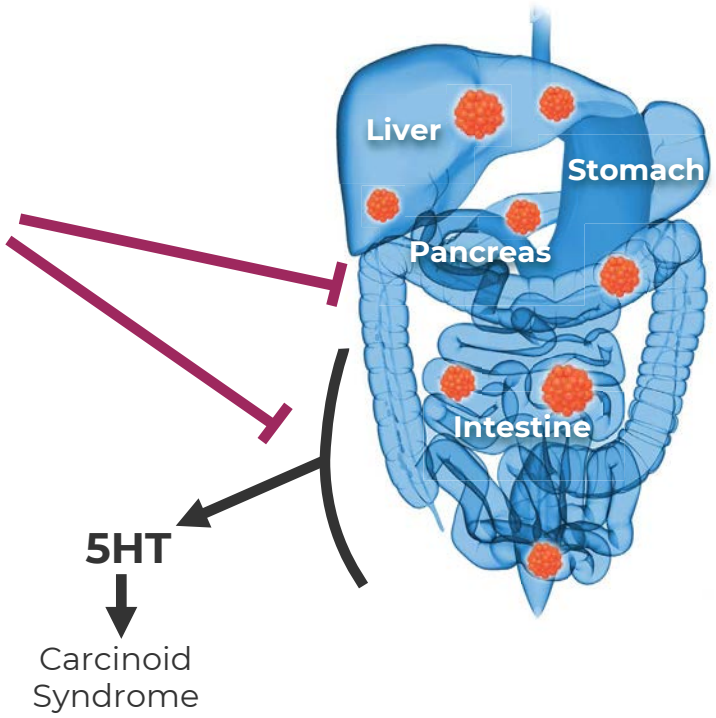
- Benign pituitary tumor
- Secretes excess growth hormone (GH)
- Excess GH causes excess secretion of insulin-like growth factor-1 (IGF-1)

Results in:

1. Bone and cartilage overgrowth
2. Organ enlargement
3. Changes in glucose and lipid metabolism
4. Abnormal growth of hands and feet
5. Alteration of facial features



SST2 agonist



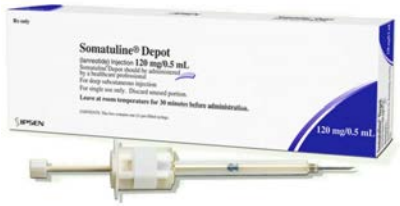
Neuroendocrine Tumors (NETs)

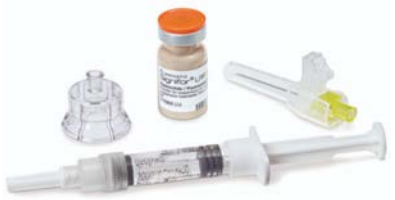
- NETs arise from aberrant enteroendocrine cells
- In ~10% of cases, tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome
- Patients with grade 1 and 2 NETs and distant metastases have a 5-year survival ranging from 30-70%

Prevalence: >25,000 in the U.S.

Prevalence: ~171,000 in the U.S.

~$3.1B (2019) Market, Despite Limitations of Injectables

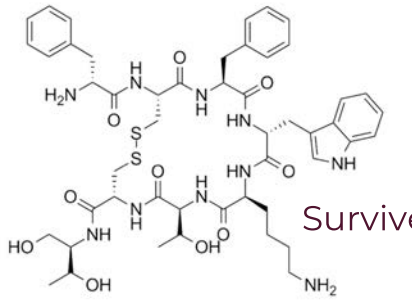




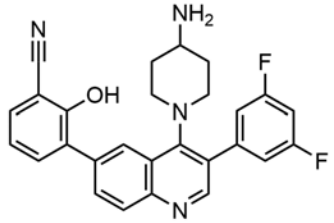
Sandostatin (octreotide)	Somatuline (lanreotide)	Somavert (pegvisomant)	Signifor (pasireotide)
NOVARTIS $1.6B	IPSEN Innovation for patient care $1.2B	Pfizer $264M	RECORDATI $75M
Monthly intramuscular 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous .2-.5ml; 18-gauge needle	Daily injections 1 ml; 28 – 31-gauge needle not supplied	Monthly intramuscular 1 ml; 20-gauge needle
Painful injections. Injection site reactions **Inconvenient monthly visits** to physician's office interrupts normal life **Limited Efficacy** as many patients experience return of symptoms near end of month	**Painful injections.** Injection site reactions **Inconvenient monthly visits** to physician's office interrupts normal life **Limited Efficacy** as many patients experience return of symptoms near end of month	Patients buy a second refrigerator for storage. Travel is difficult.	Impaired glucose control and risk of diabetes.
Approval date: 1988, 1998(LAR)	**Approval date:** 2007	**Approval date:** 2003	**Approval date:** 2014

Paltusotine is Orally Bioavailable Just Like Other Traditional Oral Small Molecule Drugs

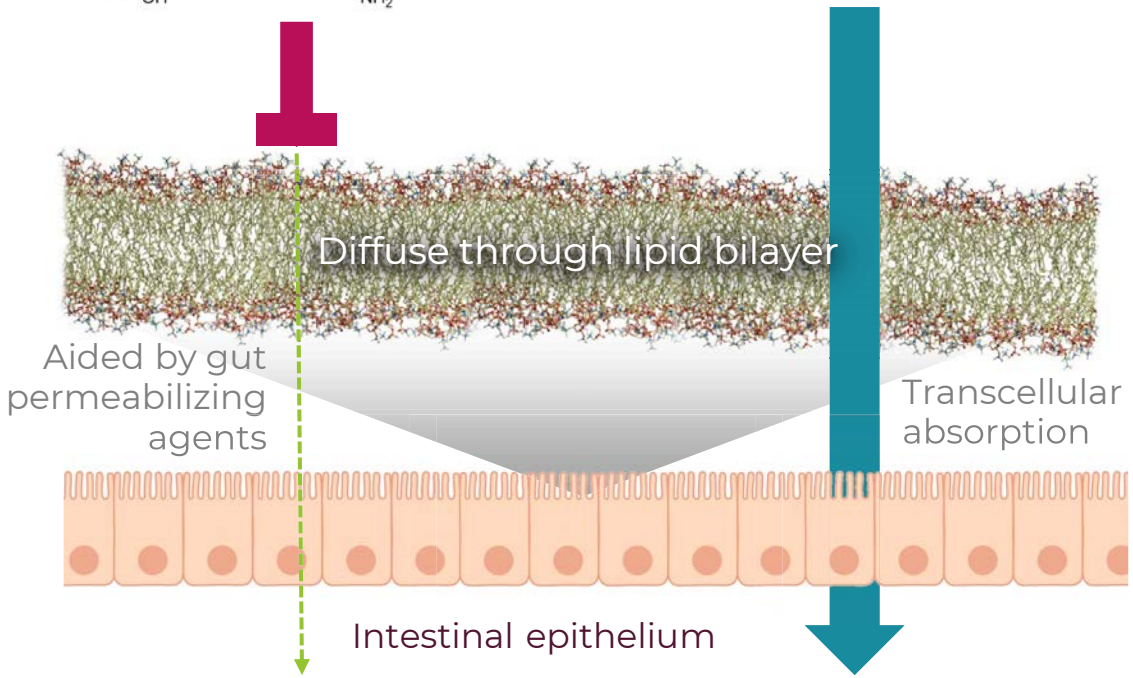
Peptide: Octreotide

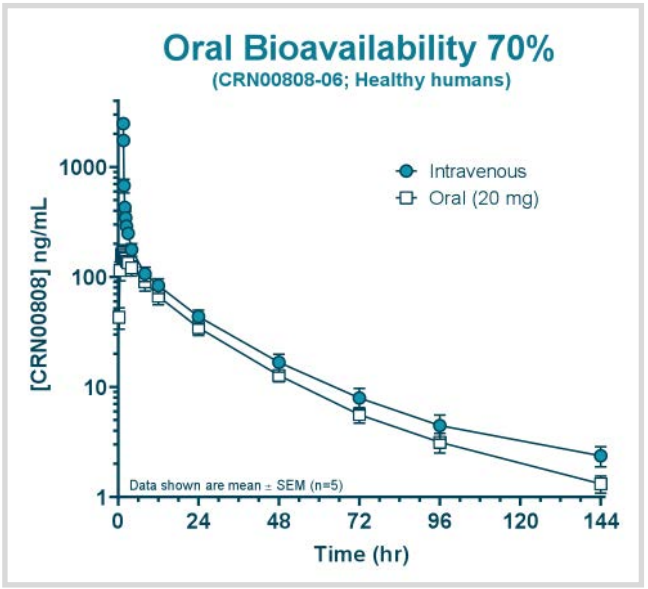


Nonpeptide: paltusotine



Survive proteolysis





	Paltusotine (CRN00808)
Oral Bioavailability	70%
Observed Half Life	42-50 hr.

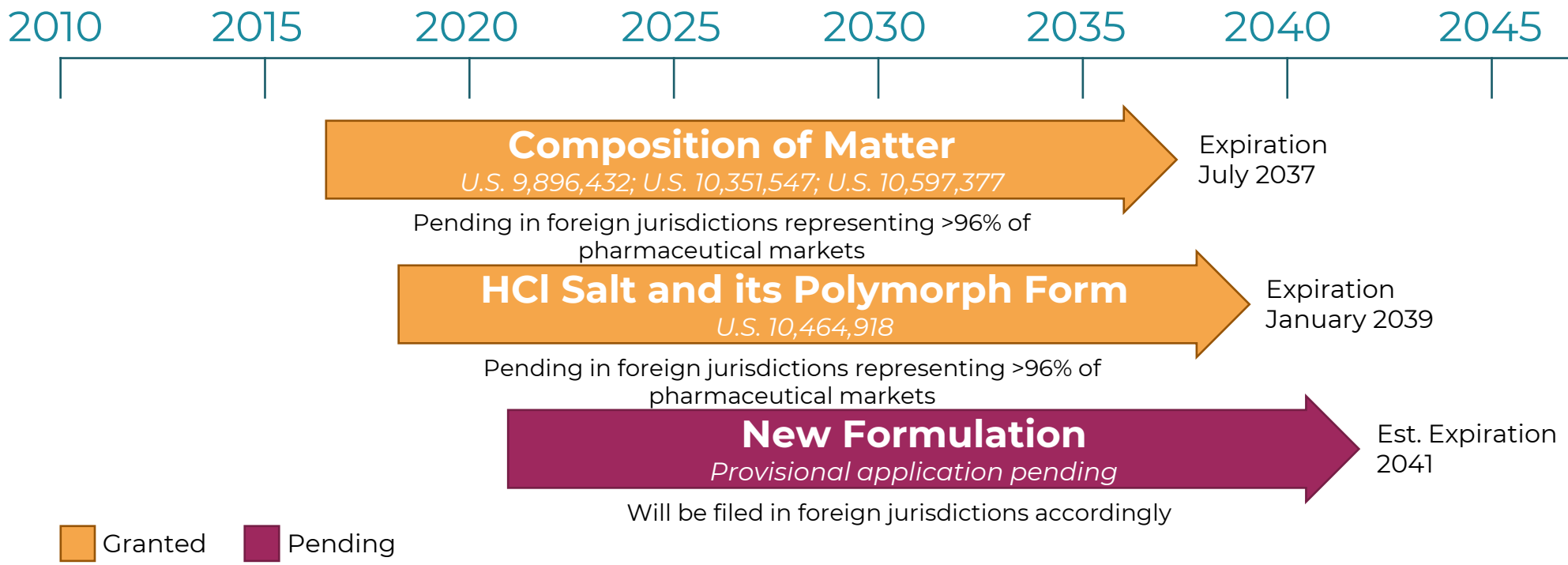
Paltusotine Target Profile

First-in-class oral nonpeptide SST2 agonist specifically designed for the treatment of acromegaly and NETs

ATTRIBUTE	POTENTIAL BENEFIT
Nonpeptide structure (small molecule)	Low COGS Ambient temperature supply chain
High SST2 potency/selectivity	Potent GH/IGF-1 suppression Low dose No increases in hyperglycemia
High oral bioavailability	Oral administration at home No injection pain or inconvenient office visits Low dose
Long half-life (42-50 hrs.)	Once daily administration Consistent exposure throughout month Forgiveness of missed dose
No drug-drug interactions	Easier prescribing for patients on other drugs No excipients that alter absorption of other drugs

Paltusotine is Protected by a Strong IP Portfolio

Multiple U.S. patents granted; national stage applications filed in 2017



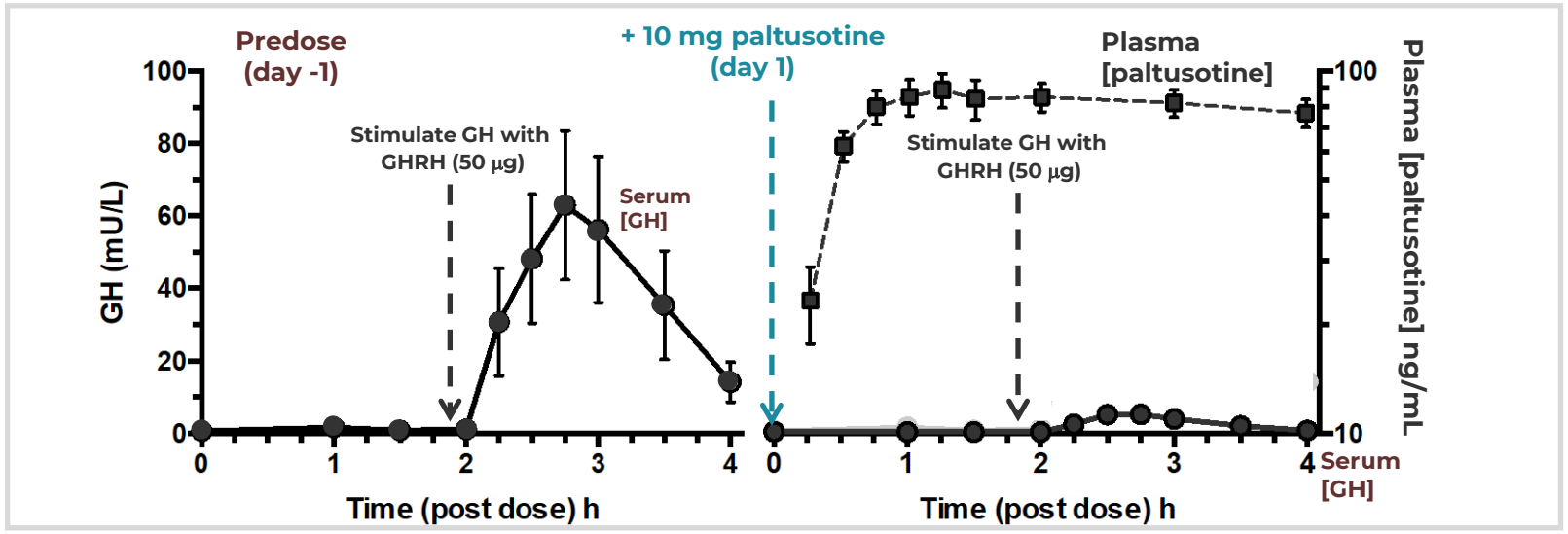
Additional intellectual property protection

- Crinetics holds U.S. composition of matter patents for 3 additional classes of SST2 agonists
- Paltusotine is eligible for 7 years of market exclusivity upon approval (independent of patents)

Phase 1: Clinical POC With Suppression of GH & IGF-1

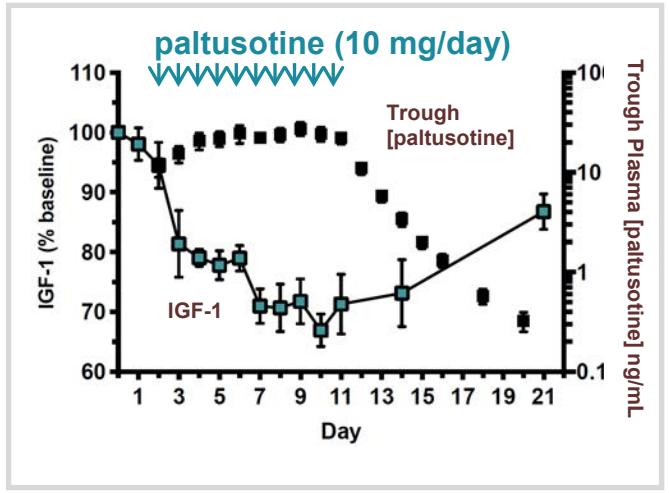
Single-ascending dose (SAD):

Demonstrated suppression of growth hormone

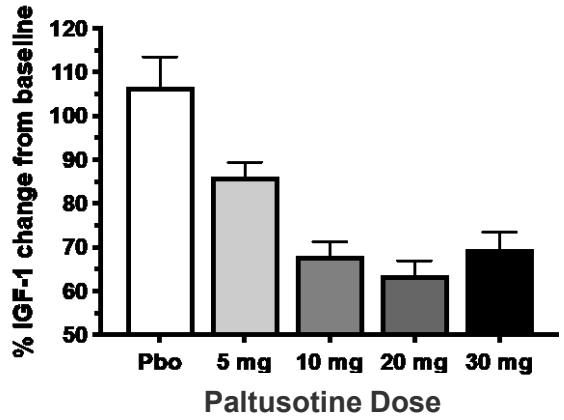


Multiple-ascending dose (MAD):

Demonstrated suppression of IGF-1

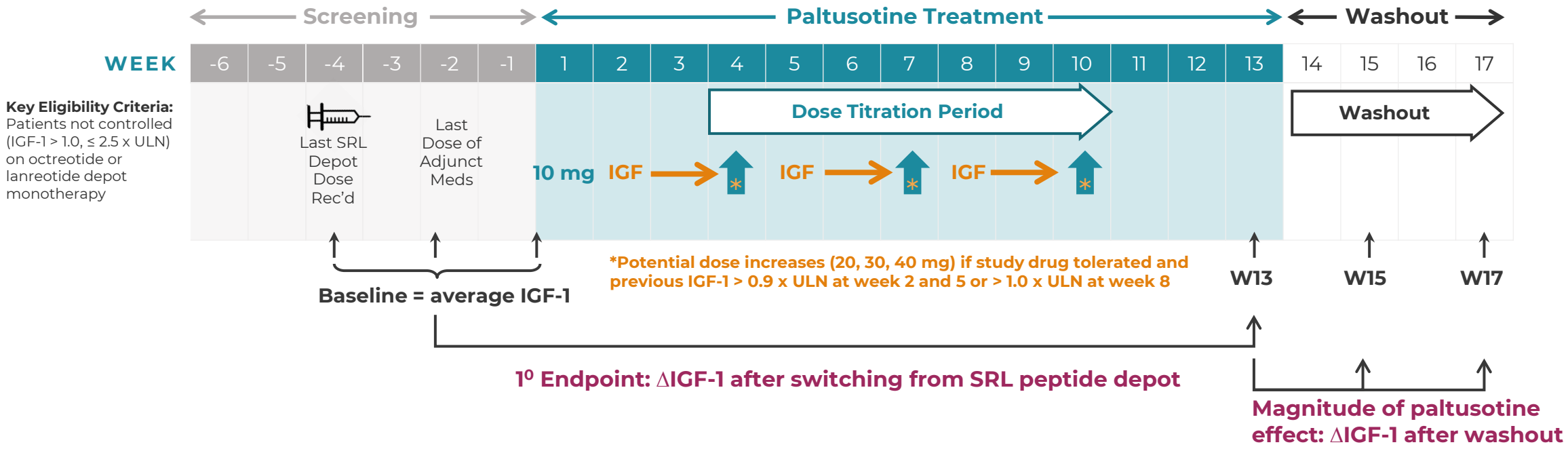


Dose response of IGF-1 suppression



ACROBAT Edge Study Design

A global clinical trial conducted at 45 clinical sites in 13 countries



Primary Endpoint: Change in IGF-1 at Week 13 vs. baseline (average of three IGF-1 screening values)
Primary Hypothesis was: No change in the median IGF-1 at Week 13 versus baseline
Primary Analysis Population: Group 1 patients (those previously on octreotide or lanreotide depot monotherapy)
Open Label Extension (-05 Advance Study): Available to patients who complete Edge and Evolve

ACROBAT Edge Patient Groups

Group	Pre-Trial Therapy	Baseline IGF-1 (x ULN)	Total Enrolled
1	SRL monotherapy (octreotide or lanreotide)	> 1.0 ≤ 2.5	25
2	SRL + cabergoline	> 1.0 ≤ 2.5	10
3	SRL + cabergoline	≤ 1.0	5
4	Pasireotide	≤ 1.0	4
5	SRL + Pegvisomant	≤ 1.0	3

Prespecified Primary Analysis Population

Exploratory Populations

Prespecified Primary Analysis Population (Group 1)[1]

- Patients treated with SRL (octreotide or lanreotide) with elevated IGF-1 at baseline—representing the majority of patients in clinical practice
- The primary hypothesis was that the group would show no change in the median IGF-1 at Week 13 versus baseline

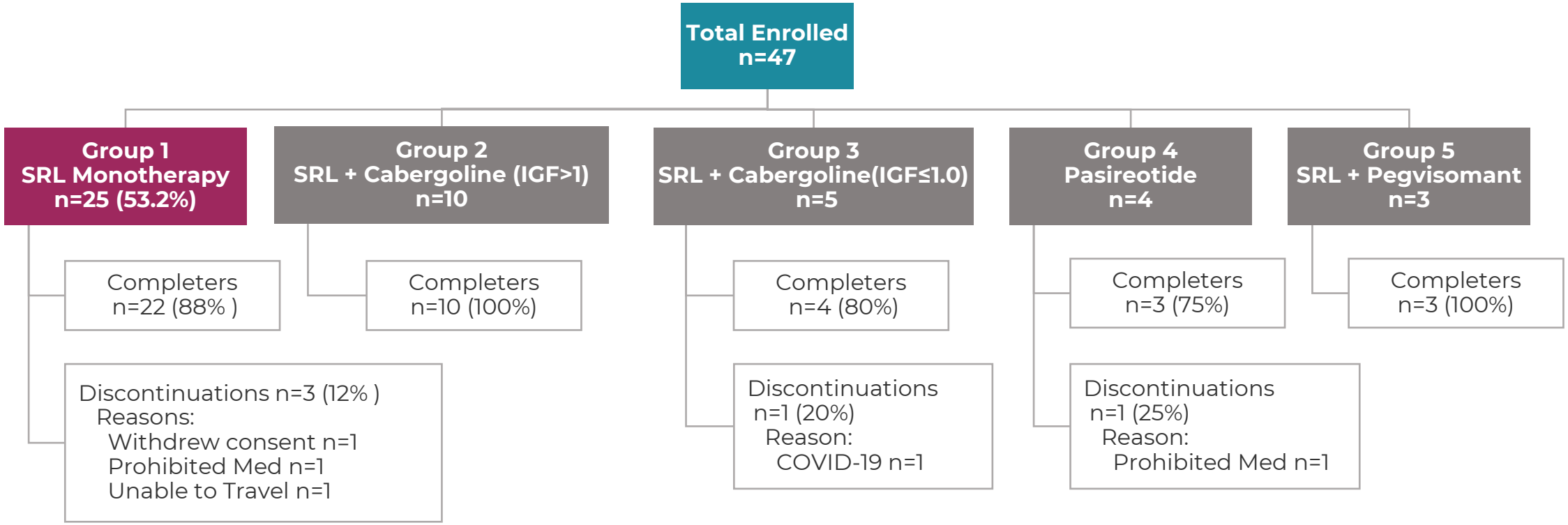
Exploratory populations (Groups 2-5)

The study also evaluated whether paltusotine can contribute to the care of patients treated with more intensive treatment regimens

[1]Prespecified in Edge Statistical Analysis Plan

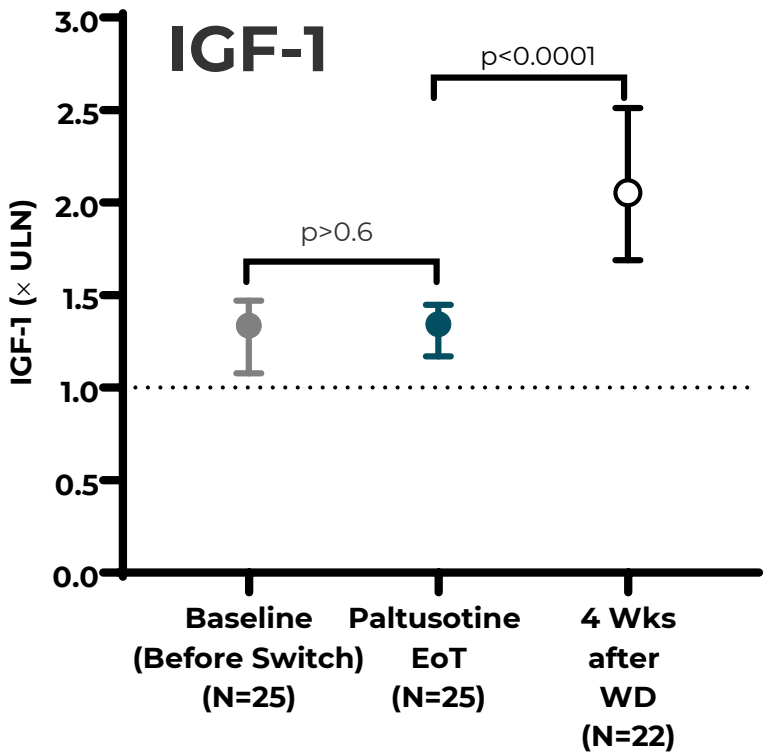
ACROBAT Edge Patient Disposition

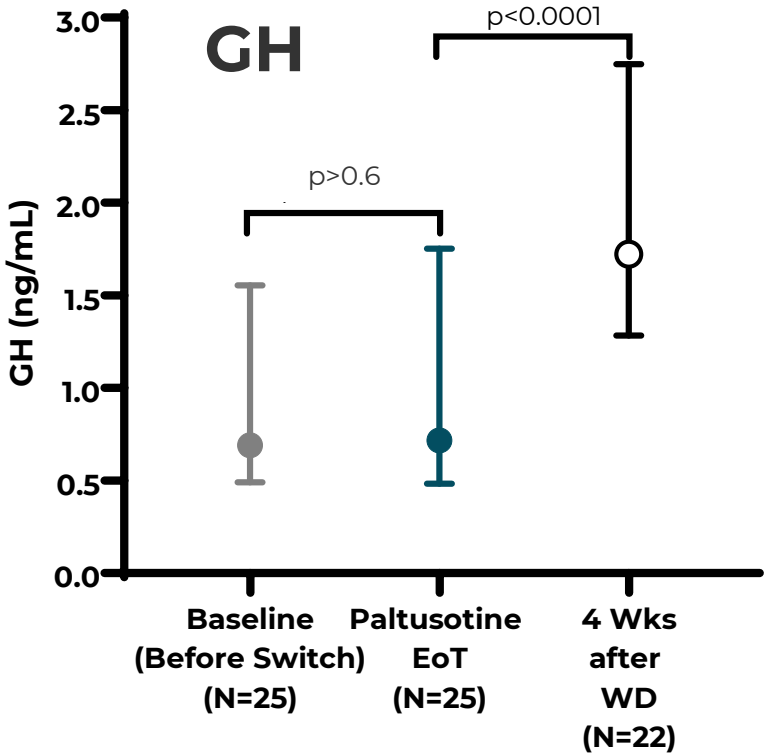
89% of patients completed the study



Paltusotine Maintained IGF-1 and GH Levels After Switching From Injected SRL Peptide Depots

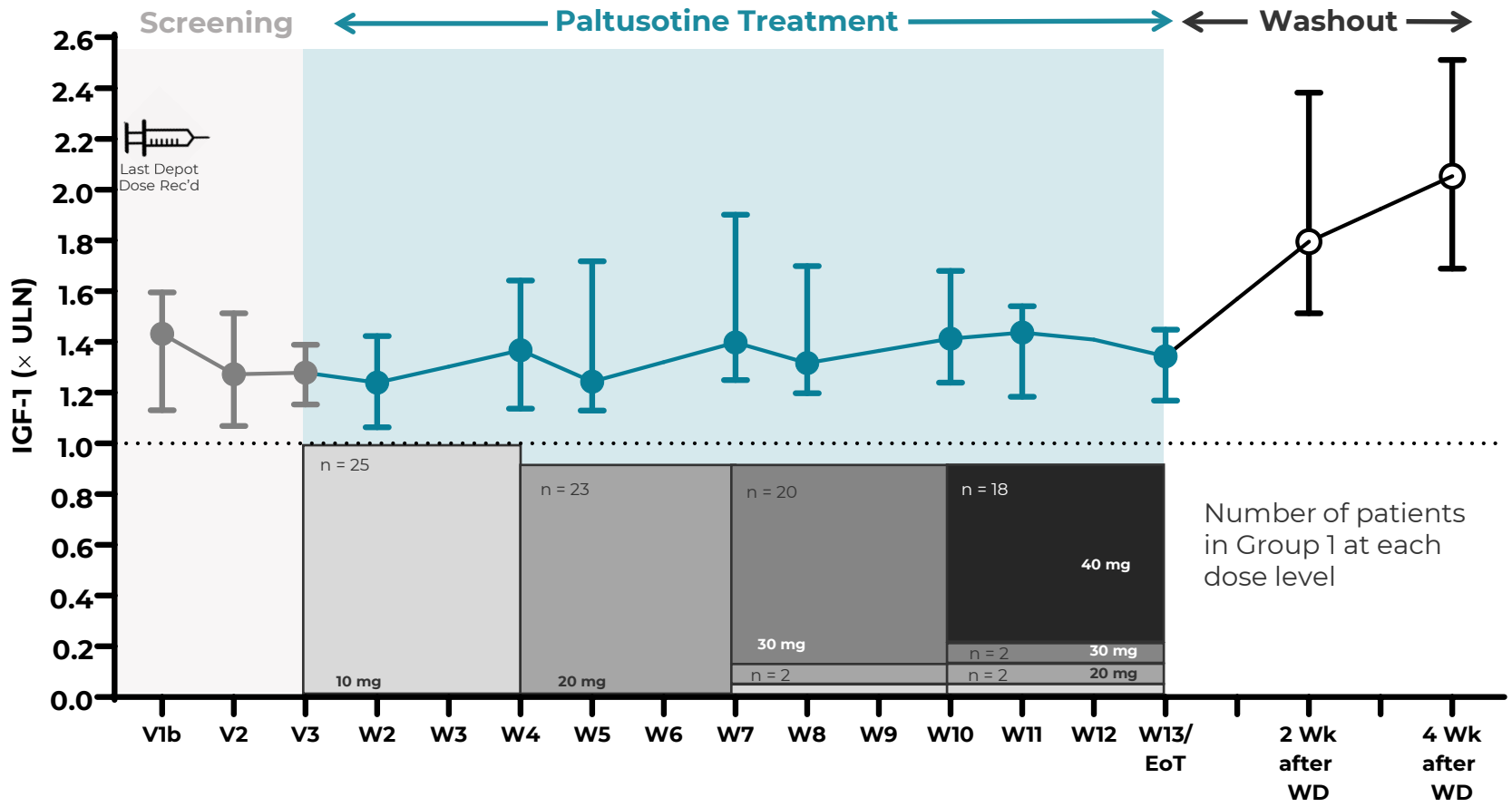
Hormone levels observed in primary analysis population (Group 1)





Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). Wks after WD is defined as Week 17 or result at least 22 days after last dose.
Note: p-values are based on non-parametric Wilcoxon Sign Rank test of whether the median change is different from zero.

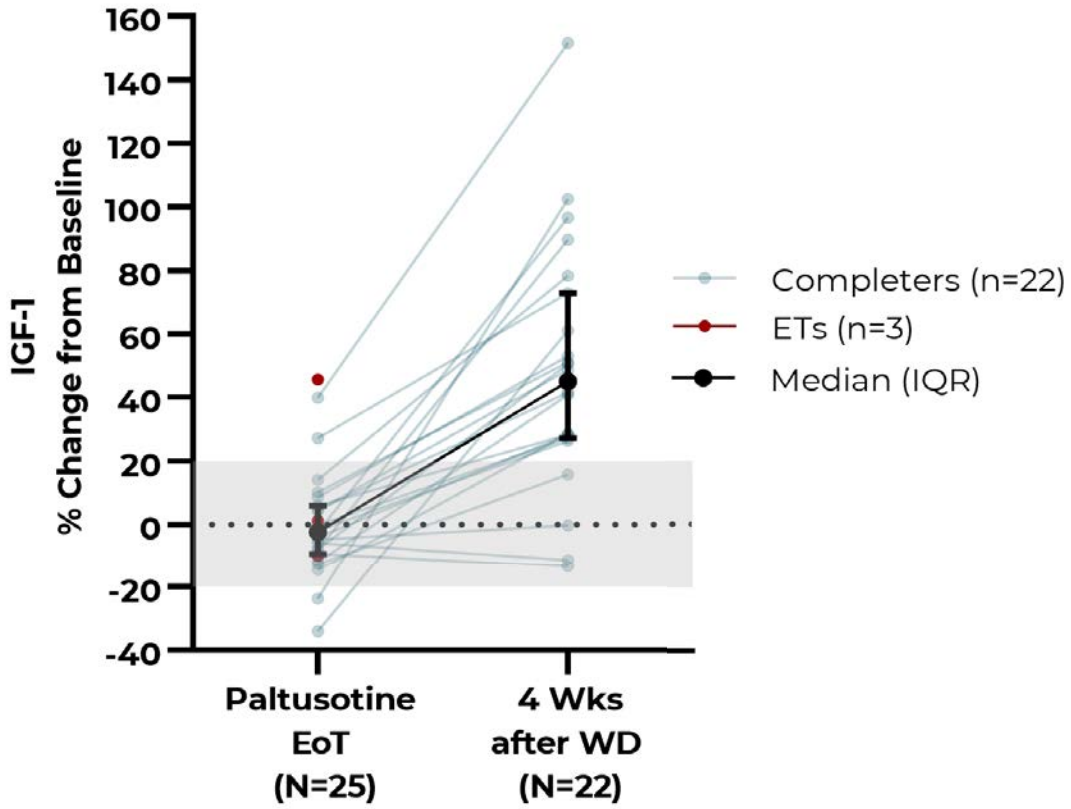
IGF-1 Levels Were Maintained After Switching to Paltusotine from Injected SRL Depots



Potential dose increases (20, 30, 40 mg) if study drug tolerated and previous IGF-1 > 0.9 x ULN at week 2 and 5 or > 1.0 x ULN at week 8
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) from Group 1 patients in Acrobat Edge; Screening Period could range from 4-6 weeks.
WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose.

Switching to Once Daily Oral Paltusotine Maintained IGF-1 Levels in 87% of Group 1 Patients

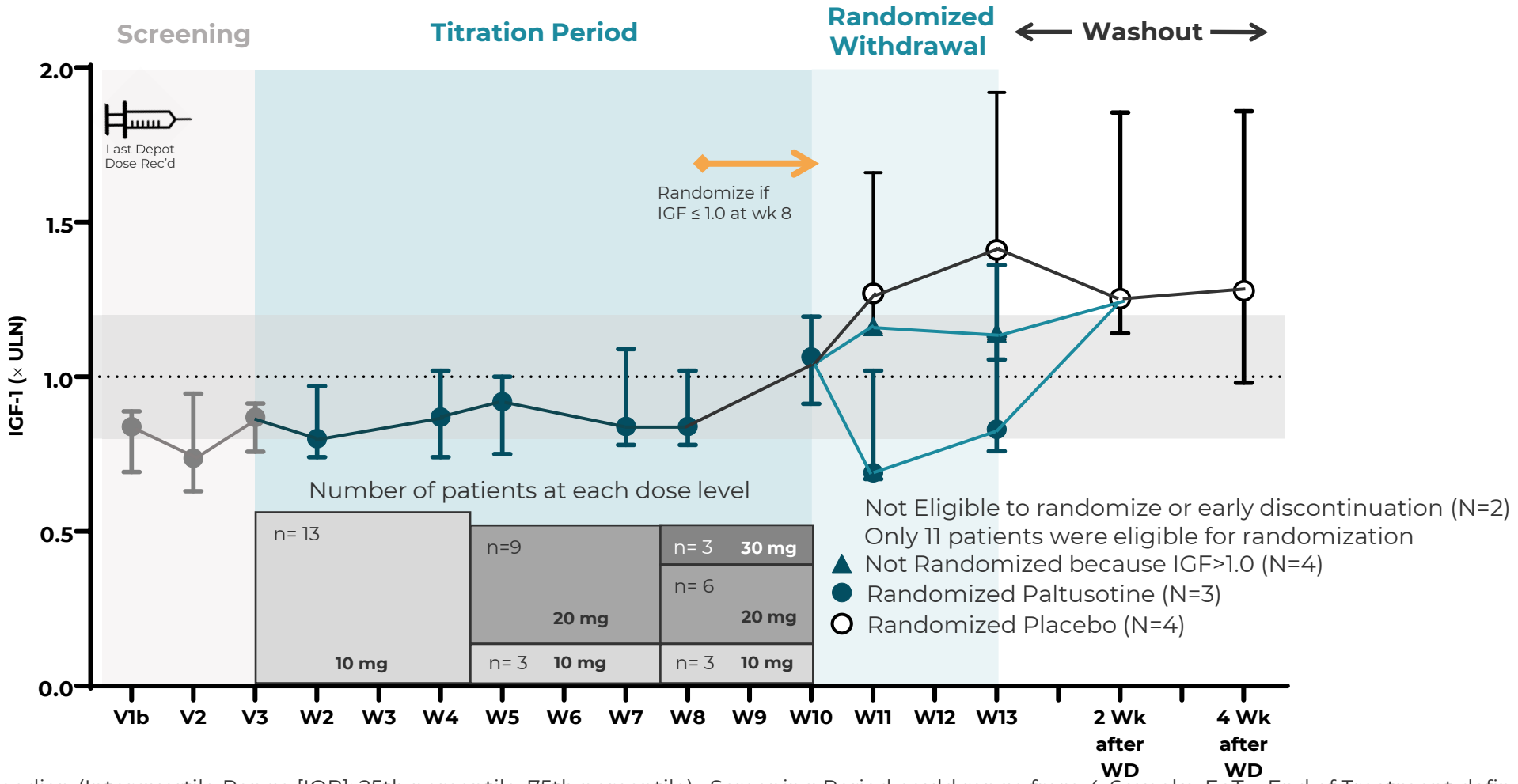
Individual patient percent change in IGF-1 at end of treatment vs. baseline and change at 4 weeks after withdrawal of paltusotine



- 20/23[1] patients (87%) who completed the dosing period achieved IGF-1 levels at EoT that were within 20% of baseline or lower
- 18/22[2] (82%) patients who completed the study showed a meaningful (>20%) rise from baseline in IGF-1 four weeks after withdrawal of paltusotine

[1]Two patients discontinued prior to the completion of the dosing period
[2]One patient discontinued during the washout period

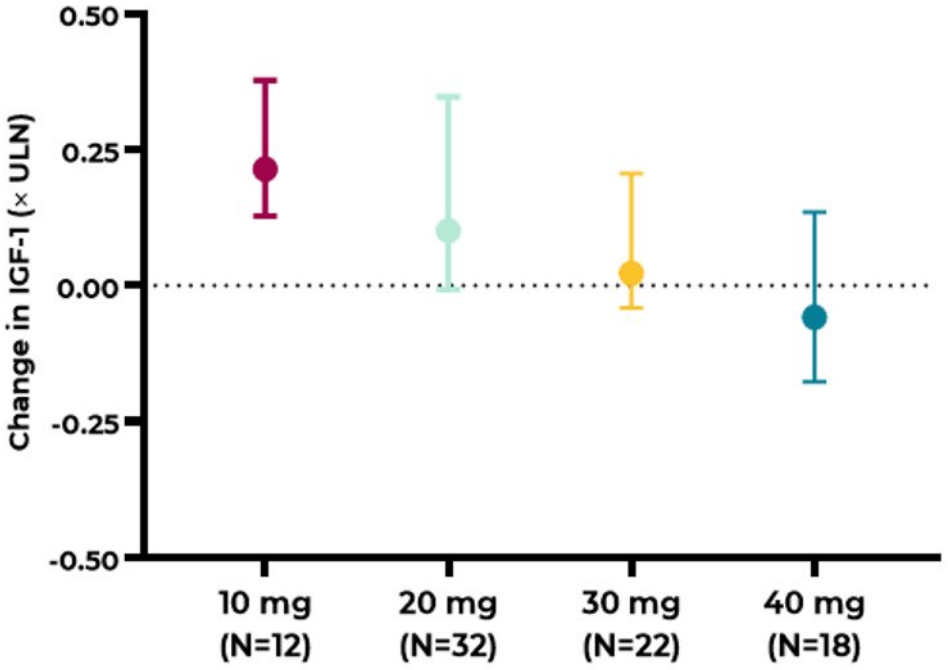
Evolve Patients Contributed to Dose Response Data, but Most Did Not Titrate to More Effective Dose Levels



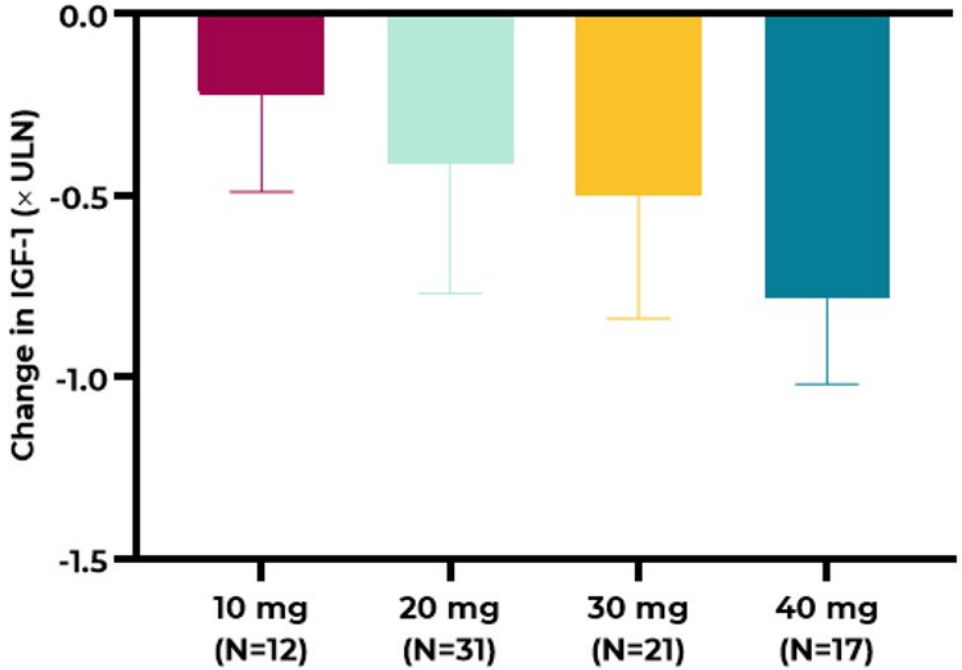
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile). Screening Period could range from 4-6 weeks. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose.

Post-Hoc Analysis of Edge (Group 1) and Evolve Provide Evidence of a Dose Response

Results from Switching to Paltusotine: Change in IGF-1 from Baseline to Steady State at Indicated Dose



Magnitude of Paltusotine Activity: Change in IGF-1 from Steady State to 4 Weeks After Withdrawal



Steady state IGF-1 at the indicated dose: Patients were on the indicated dose for at least 12 days. Data prior to Week 7 were excluded because of insufficient washout of depot injection during this window. Data are shown from Week 7, Week 10, and Week 13.
Data presented are median +/- IQR. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF).
WD = Withdrawal, where 2 Wks after WD is defined as Week 15 or result within 7-21 days after last dose and 4 Wks after WD is defined as Week 17 or result at least 22 days after last dose. One subject is missing 4 Weeks after withdrawal observation.
Octreotide and lanreotide concentrations were measured 17 weeks after depot dose (W13 of the treatment period). Octreotide was completely washed out. Lanreotide concentrations were >75% reduced from baseline.

Paltusotine was Generally Well Tolerated Across Clinical Trials

Treatment Emergent Adverse Events ≥ 5%*	Edge/Evolve Patients (N=60) n (%)	Healthy volunteers (N=128^) n (%)
Common Acromegaly Symptoms		
Headache	19 (32%)	23 (18%)
Arthralgia	15 (25%)	0
Fatigue	13 (22%)	6 (5%)
Peripheral swelling	11 (18%)	0
Paraesthesia	10 (17%)	1 (1%)
Hyperhidrosis	10 (17%)	0
Sleep apnoea syndrome	4 (7%)	0
Common SRL Side Effects		
Diarrhoea	5 (8%)	27 (21%)
Abd pain/Abd pain upper	5 (8%)/2(3%)	25 (20%)/6(5%)
Abdominal discomfort	4 (7%)	12 (9%)
Abdominal distension	3 (5%)	7 (6%)
Other		
Catheter site pain	0	9 (7%)
Nausea	0	9 (7%)
Back pain	5 (8%)	2 (2%)
Dyspepsia	3 (5%)	0
Urinary tract infection	3 (5%)	0

Acrobat Edge and Evolve

- No study discontinuations due to adverse events
- No patients required rescue treatments with standard acromegaly medications during treatment
- No safety signals seen with vital signs
- No safety signals seen in clinical laboratories, including no amylase/lipase elevations > 3x ULN, HbA1c, LFTs, ECGs
- No treatment related SAEs; 2 non-treatment related SAEs:
  1. Nephrolithiasis: lithotripsy for pre-existing kidney stone
  2. Headache: admission for diagnostic evaluation

*TEAEs include any AE that newly appears, increases in frequency, or worsens in severity following initiation of study drug through 28 days after last dose.
^ Treated with 1 or more doses of CRN00808.HCl as of 31 August 2020

Summary of ACROBAT Phase 2 Results

- *Primary endpoint achieved in Edge:* Once daily oral paltusotine maintained IGF-1 levels at week 13 after switching from injected somatostatin receptor ligand (SRL) depots of octreotide or lanreotide [ΔIGF-1 =-0.034 (-0.107, 0.107), median (IQR[1])]
- Both IGF-1 and GH levels promptly rose after withdrawing paltusotine which characterized the magnitude of therapeutic activity of oral paltusotine
- Paltusotine contributed to IGF-1 lowering in patients previously treated with injected SRLs + oral cabergoline combination therapy
- Post-hoc analysis of patients from both Edge (Group 1) and Evolve[2] provided evidence of a dose response with higher doses being more effective
- Paltusotine was well tolerated

[1]Interquartile Range: 25th , 75th percentile
[2]Enrollment in ACROBAT Evolve was discontinued in April 2020. Previously enrolled patients continued in the study. Data from the Evolve patients (N=13) are included safety and dose-response analysis.

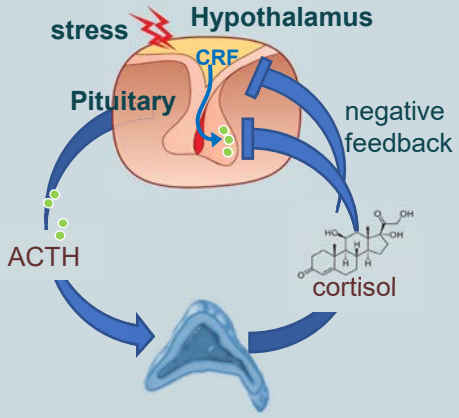
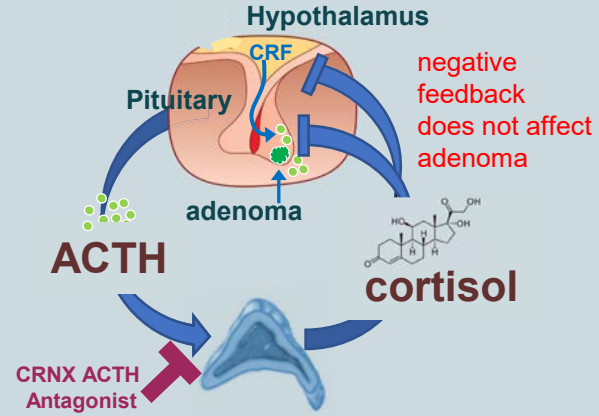
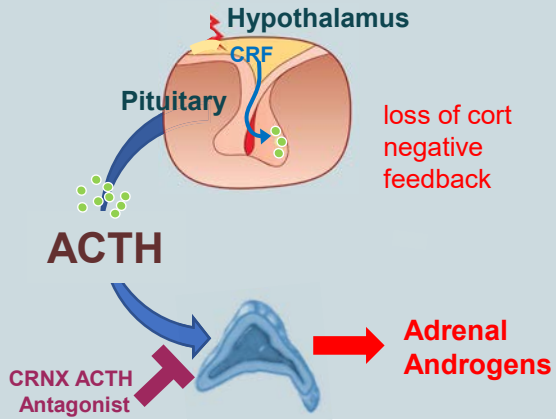
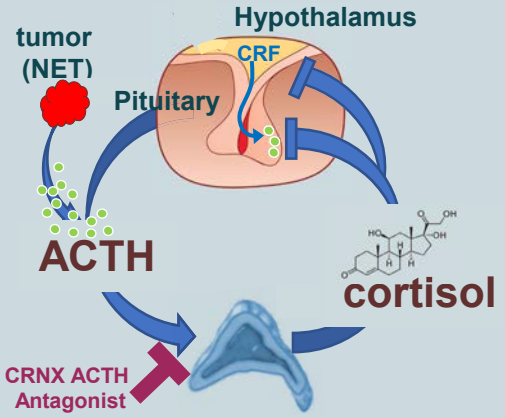
Paltusotine Development Program 2021 Plans

- End-of-phase 2 meeting with FDA anticipated in 1Q 2021
- Planned initiation of Phase 3 acromegaly program in 1H 2021 with to-be-marketed formulation
- Planned initiation of NETs trial in carcinoid syndrome in 2021

NONPEPTIDE ACTH ANTAGONISTS

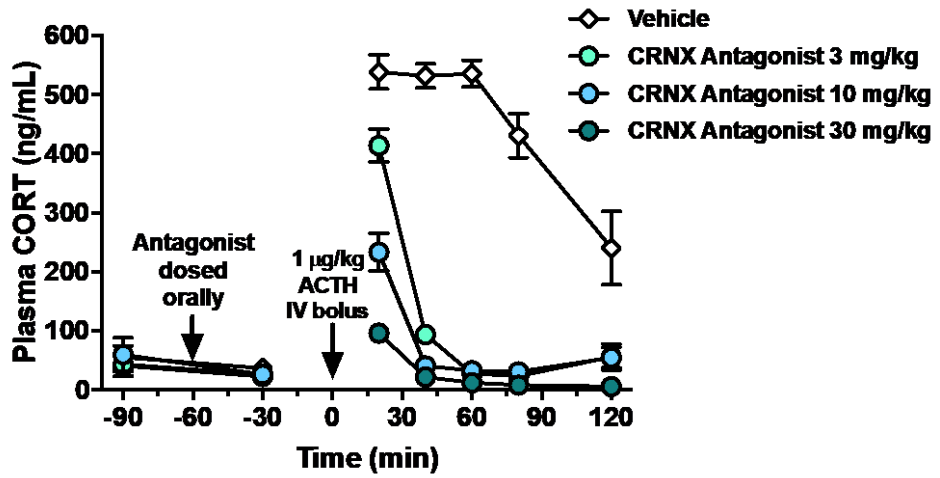
For the treatment of Cushing's Disease, Congenital Adrenal Hyperplasia (CAH), and other conditions of ACTH excess

Indications for an Oral, Selective ACTH Antagonist

Normal	Cushing's Disease (CD)	Congenital Adrenal Hyperplasia (CAH)	Ectopic ACTH Syndrome (EAS)
			
Defect/Etiology	ACTH-secreting pituitary tumor	Genetic defect prevents adrenal cortisol production	ACTH-secreting non-pituitary tumor
Symptoms	Central obesity and round face; Dorsal and supraclavicular fat pads; Hypertension; Stretch marks; Bone loss; Hyperglycemia; Psychiatric disturbances	Adrenal insufficiency; Infertility; Hirsutism; Short stature; Precocious puberty; Adrenal rest tumors	Muscle weakness, immobility; Weight loss; Severe hypertension, edema, hypokalemia; Severe hyperglycemia; Thromboembolism; Infection; Psychosis
Biomarkers	Elevated ACTH Elevated cortisol	Elevated ACTH Absent cortisol Elevated androgens	Extremely elevated ACTH Extremely elevated cortisol

Nonpeptide ACTH Antagonists Demonstrated Activity in Rat Models that Mimic Cushing's and CAH

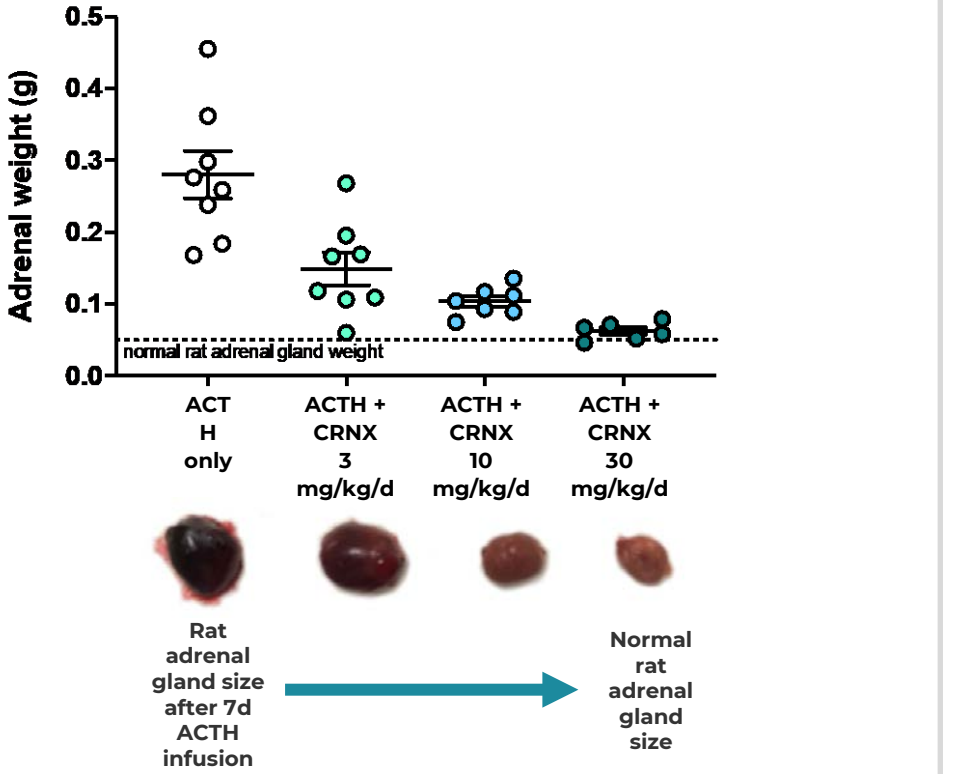
Acute suppression of ACTH-induced corticosterone observed in rats



Experiment designed to mimic disease:

- CRNX ACTH antagonist orally administered
- Administer IV bolus of ACTH after 60 minutes
- Marked suppression of ACTH with increasing doses of ACTH antagonist

Repeat antagonist dosing (7d) prevented adrenal hypertrophy from chronic ACTH infusion



Next Steps for ACTH Antagonist Program

- Initiate Phase 1 healthy volunteer study in late 2020 / early 2021
- Phase 1 study designed to provide clinical proof-of-concept
  - Study is expected to provide meaningful PK/PD data
  - Study incorporates ACTH stimulation test production in order to measure ability of CRNX candidate to suppress ACTH stimulated cortisol (reproduces preclinical paradigm)

CRN04777

An **oral nonpeptide SST5 agonist** for the treatment of congenital hyperinsulinism (CHI)

Congenital Hyperinsulinism (CHI) Disease Overview

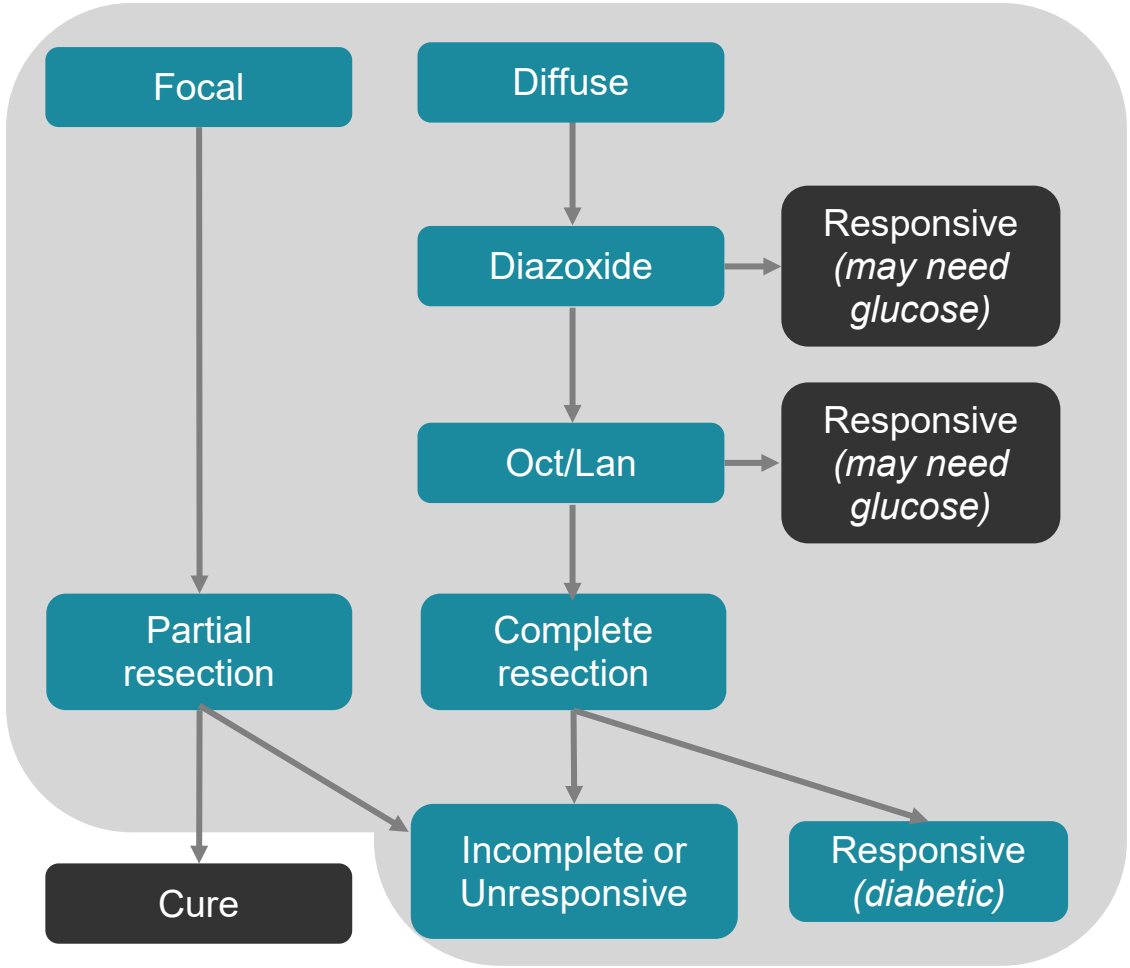
Disease

- Caused by genetic defects (e.g. KATP channel) that result in excess insulin secretion and profound hypoglycemia
- Incidence: 1:30,000 to 1:50,000 births (U.S.)
- Treated at a handful of specialty centers world-wide (e.g. Children's Hospital of Philadelphia)

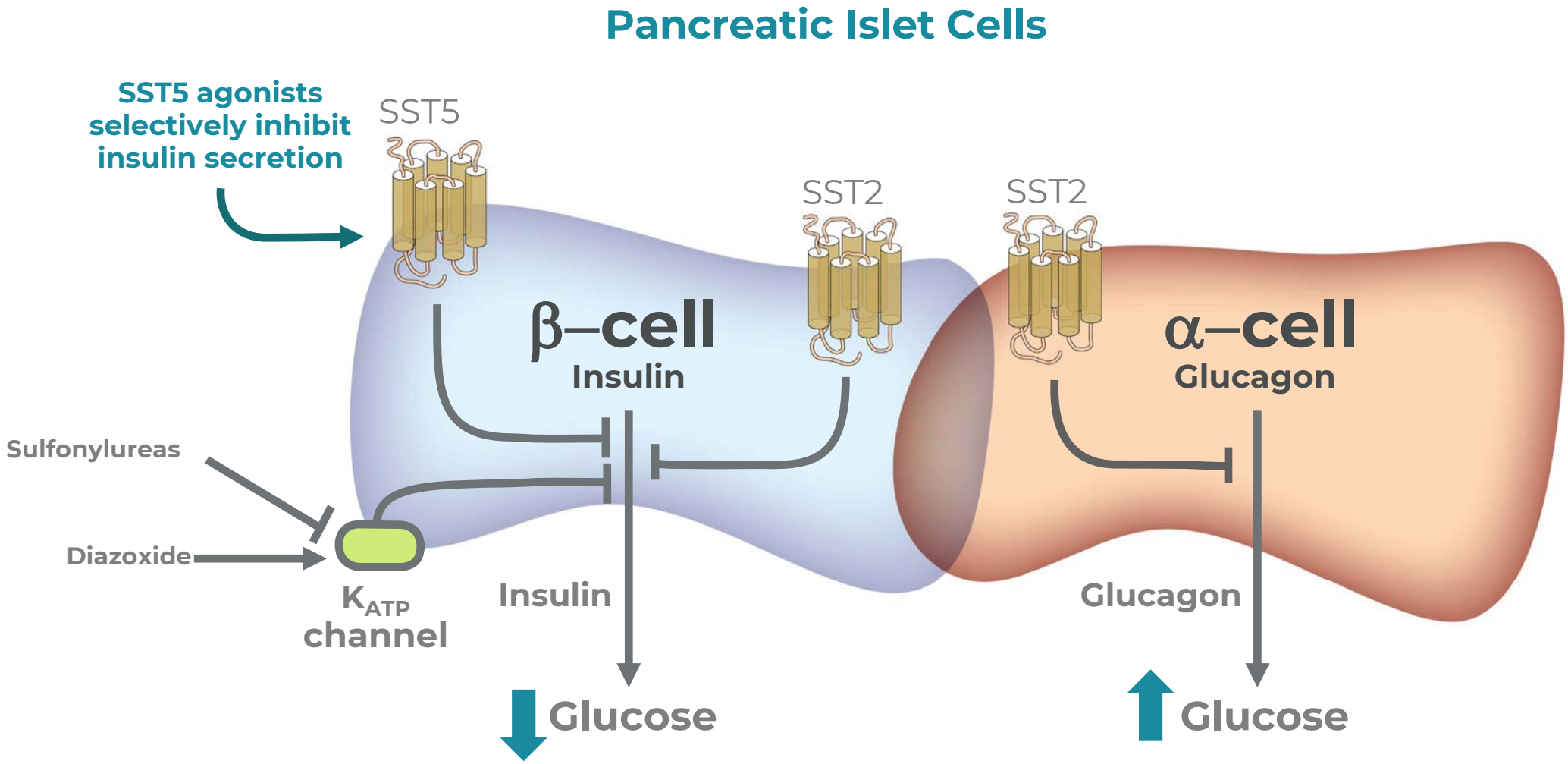
Patient and parent goals

- Avoid pancreatectomy
- Prevent cognitive / developmental problems
- Reduce injections and glucose sticks
- Medical management until HI is resolved
- Live a normal life

Current Treatment Paradigm

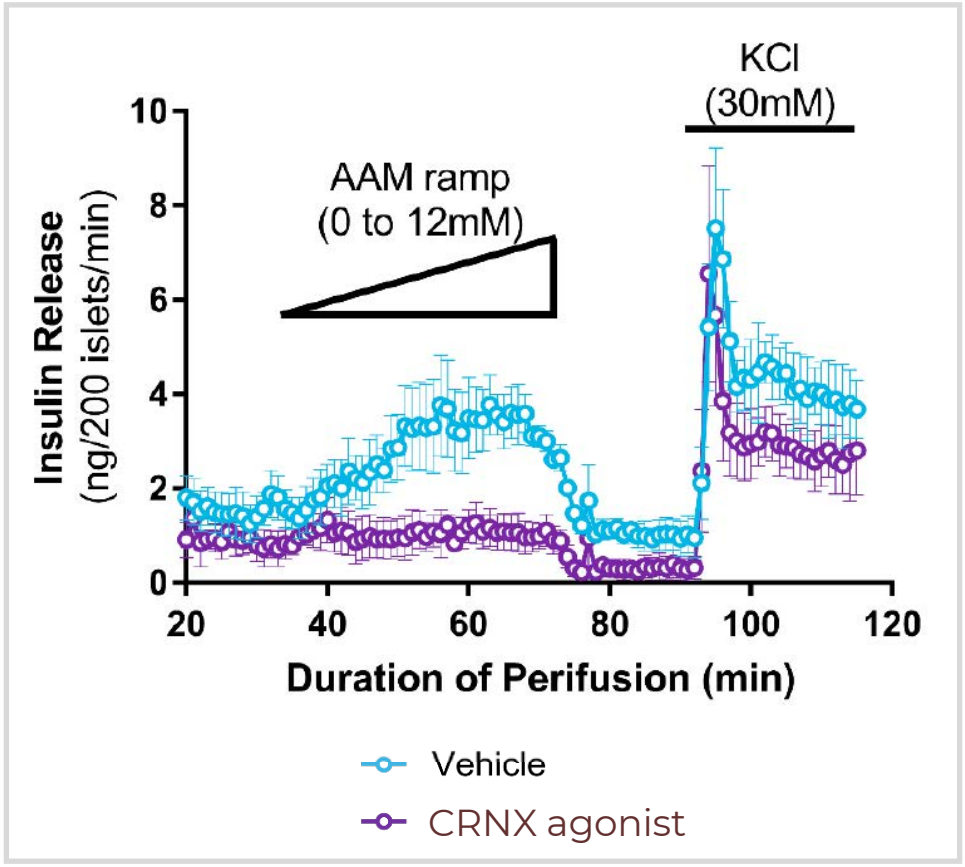


SST5 Agonists Inhibit Insulin Secretion Without Inhibiting Glucagon Secretion

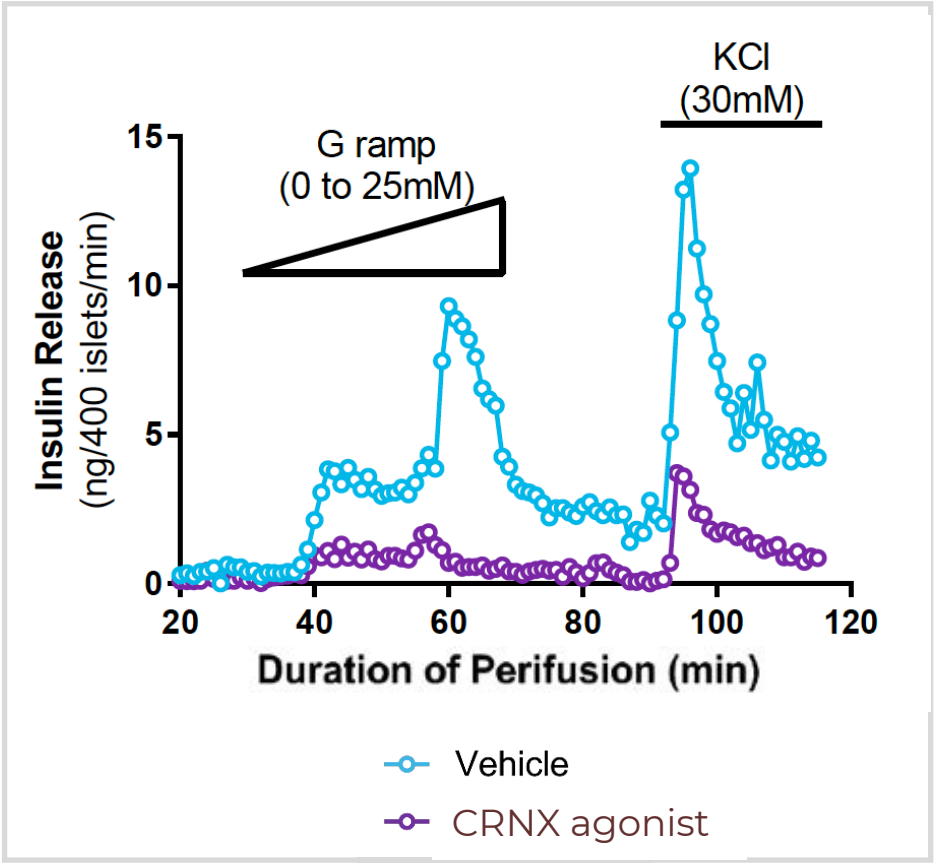


SST5 Agonists Potently Suppressed Insulin Secretion

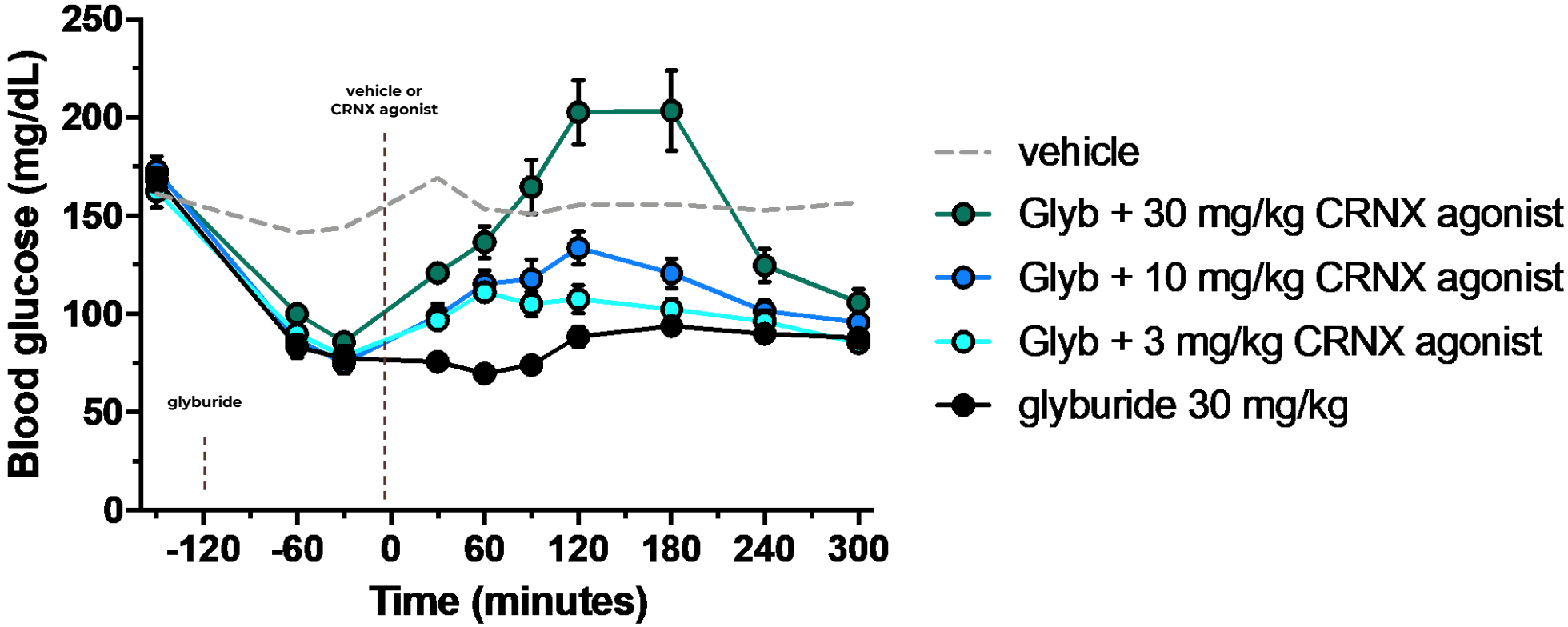
In isolated SUR1$^{-/-}$ knockout mouse islets (mimic genetic defect of ~50% of CHI patients)



In isolated islets from patient with CHI (Beckwith Wiedemann Syndrome) who underwent pancreatectomy



Proof of Mechanism: Rescue of Sulfonylurea Induced Hypoglycemia in Rats



Experimental design

- Administer glyburide (sulfonylurea) to induce hypoglycemia. This pharmacologically mimics the genetic defect of ~50% of kids with CHI
- CRNX SST5 agonist orally administered after 2 hours
- Rescue from hypoglycemia with increasing doses of CRNX SST5 agonist

CRN04777 Program

- Rare Pediatric Disease Designation received
- Initiate Phase 1 healthy volunteer study in early 2021
- Phase 1 study designed to provide clinical proof-of-concept
  - Study is expected to provide meaningful PK/PD data
  - Study designed to evaluate the ability of CRNX candidate to reverse sulfonylurea induced hyperinsulinism in specialized glucose-clamp study (reproduces preclinical paradigm)

Anticipated News Flow and Milestones

Program	Milestone	Expected Timing
Paltusotine Nonpeptide SST2 agonist	Initiation of acromegaly Phase 3 program	1H 2021
	Initiation of NETs Phase 2 program	2021
Nonpeptide ACTH antagonist	Initiation of Phase 1 clinical study	Late 2020 or early 2021
CRN04777 Nonpeptide SST5 agonist	Initiation of Phase 1 clinical study	Early 2021

Maturing pipeline of a rare disease franchise in endocrinology and endocrine oncology


Crinetics
Pharmaceuticals

APPENDICES

Key Patent Families Anchor a Robust IP Portfolio

Paltusotine Portfolio				
Patent Family Subject Matter	**Patent Nos.**	**Status**	**Priority Date**	**Estimated Expiration**
Composition of Matter	U.S. 10,562,884 U.S. 10,604,507 U.S. 10,766,877	**Granted in**: U.S. **Pending in**: EA, EP, AU, BR, CA, CN, IL, IN, JP, KR, MX, NZ, SG, ZA, TW, HK, ID, UA, VE	July 2016	July 2037
HCl Salt and its Polymorph Form	U.S. 10,464,918	**Granted in:** U.S. **Pending in:** EA, EP, AU, BR, CA, CN, IL, IN, JP, KR, MX, NZ, SG, ZA, TW, ID, UA, VE	January 2018	January 2039
New Formulation	N/A	Pending	Sep 2020	September 2041
ACTH Antagonist Portfolio				
Patent Family Subject Matter	**Patent Nos.**	**Status**	**Priority Date**	**Estimated Expiration**
Composition of Matter	U.S. 10,562,884 U.S. 10,604,507 U.S. 10,766,877	**Granted in:** U.S. **Pending in:** TW **To be filed in:** EA, EP, AU, BR, CA, CN, IL, IN, JP, KR, MX, NZ, SG, UA, ZA	June 2018	June 2039
SST5 Agonist Portfolio				
Patent Family Subject Matter	**Patent Nos.**	**Status**	**Priority Date**	**Estimated Expiration**
Composition of Matter	N/A	**Pending in:** PCT, U.S., TW, AR, VE	Aug 2019	Aug 2040

Leadership Team

Scott Struthers, PhD	President & CEO, Founder	Neurocrine Biosciences; ScienceMedia; BIOSYM Technologies; salk. Where cures begin.
Frank Zhu, PhD	VP of Chemistry, Founder	Neurocrine Biosciences; UC San Diego; Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences
Steve Betz, PhD	VP of Biology, Founder	Neurocrine Biosciences; Abbott; DU PONT MERCK
Ajay Madan, PhD	Chief Development Officer	Neurocrine Biosciences; UC San Diego; XenoTech, Uncommon Science | Uncommon Service
Marc Wilson	Chief Financial Officer	CIDARA Therapeutics; Trius Therapeutics; Neurocrine Biosciences; pwc
Alan Krasner	Chief Medical Officer	Shire; BIODEL; Pfizer; Johns Hopkins School of Medicine
Gina Ford	VP, Corporate Strategy & Commercial Planning	AcelRx Pharmaceuticals, Inc.; IPSEN, Innovation for patient care; SOLSTICE NEUROSCIENCES; élan
Adriana Cabré	VP, Human Resources	National University; MedImpact; AMYLIN; CooperVision

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