Crinetics Pharmaceuticals

CORPORATE PRESENTATION

September 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; 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.

Mission: ***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: 78
- Shares: 32.9 million*
- Cash & Investments: $205 million*
- Cash runway into 2023

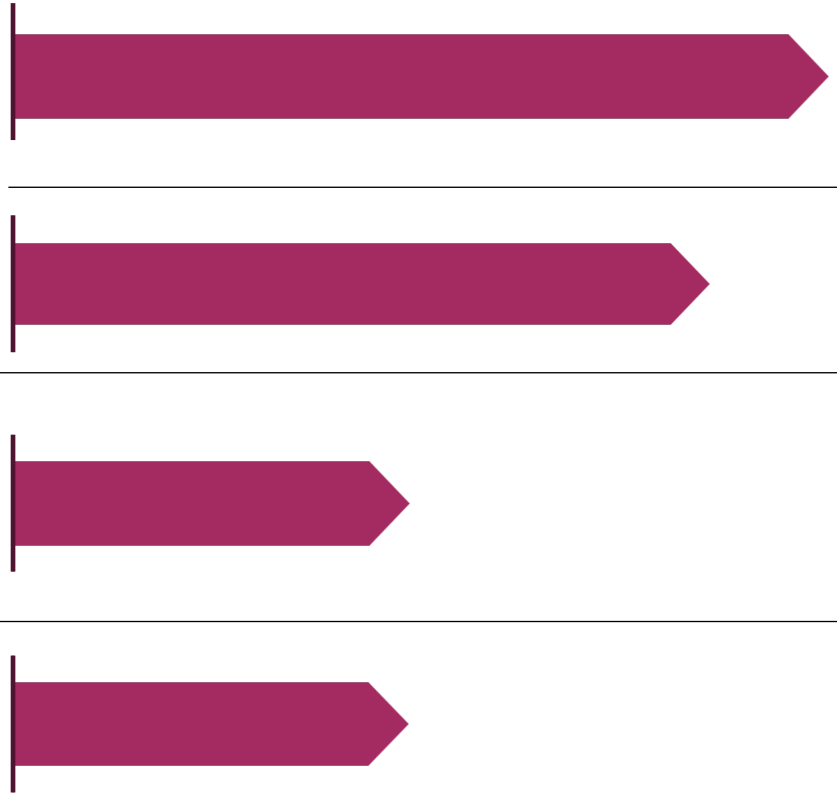
Our Strategy: Discover, develop and commercialize new drugs for multiple rare endocrine diseases and endocrine-related tumors with:

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

*As of June 30, 2020

Pipeline: Rare Disease Franchise in Endocrinology

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
Paltusotine Acromegaly						Phase 2 topline data in acromegaly - 4Q 2020 Initiate Phase 3 acromegaly - 1H 2021
Neuroendocrine Tumors (NETs)						Initiate Phase 2 in 2021
Oral ACTH Antagonist Cushing's Disease, Congenital Adrenal Hyperplasia						Initiate Phase 1 late 2020/early 2021
Oral SST5 Agonist Hyperinsulinism						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 SST2 Peptide Agonists

Acromegaly

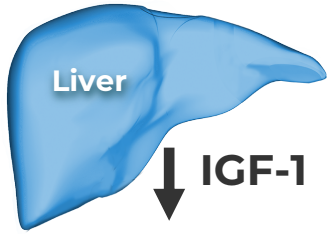
- Benign pituitary tumor
- Secretes excess growth hormone (GH)
- Excess GH causes excess secretion of insulin-like growth factor-1 (IGF-1)

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

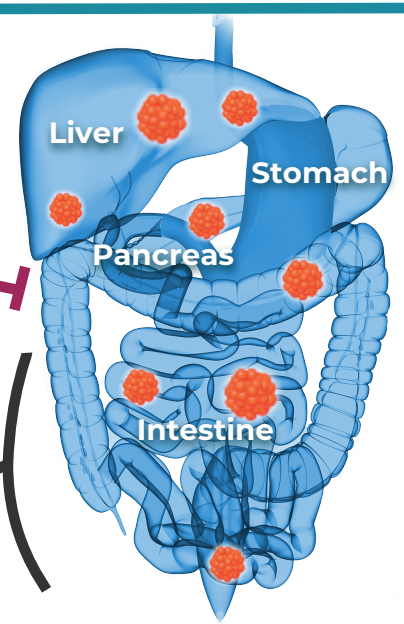
SST2 agonist

GH



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

Neuroendocrine Tumors (NETs)



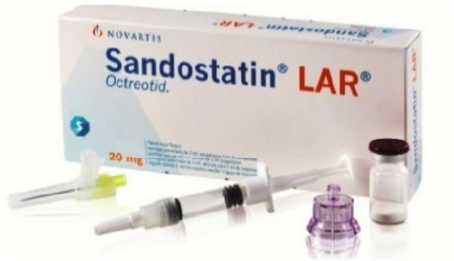
5HT

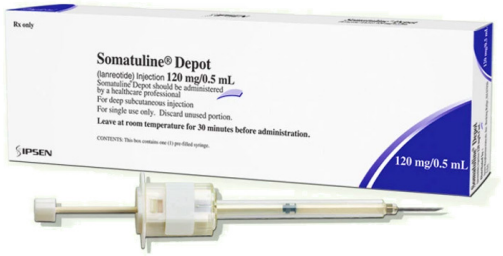
Carcinoid Syndrome

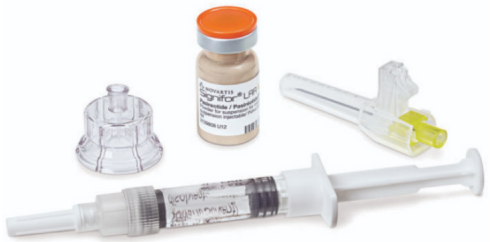
- NETs arise from aberrant enteroendocrine cells
- In ~10% of cases, tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome
- Patients with grade 1 and 2 NETs and distant metastases have a 5-year survival ranging from 30-70%

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

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



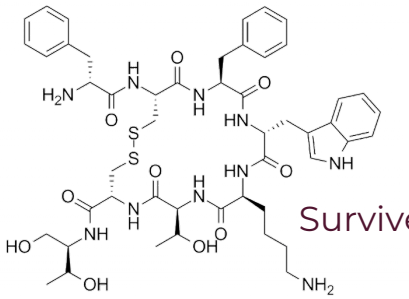




Sandostatin (octreotide)	Somatuline (lanreotide)	Somavert (pegvisomant)	Signifor (pasireotide)
NOVARTIS $1.6B	IPSEN Innovation for patient care $1.2B	Pfizer $264M	RECORDATI $75M
Monthly intramuscular 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous .2-.5ml; 18-gauge needle	Daily injections 1 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	***Approval date:*** 2007	***Approval date:*** 2003	***Approval date:*** 2014

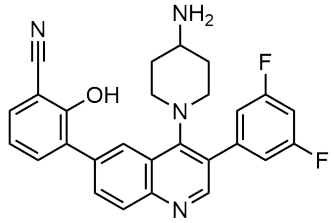
Paltusotine is Orally Bioavailable Just Like Other Traditional Oral Small Molecule Drugs

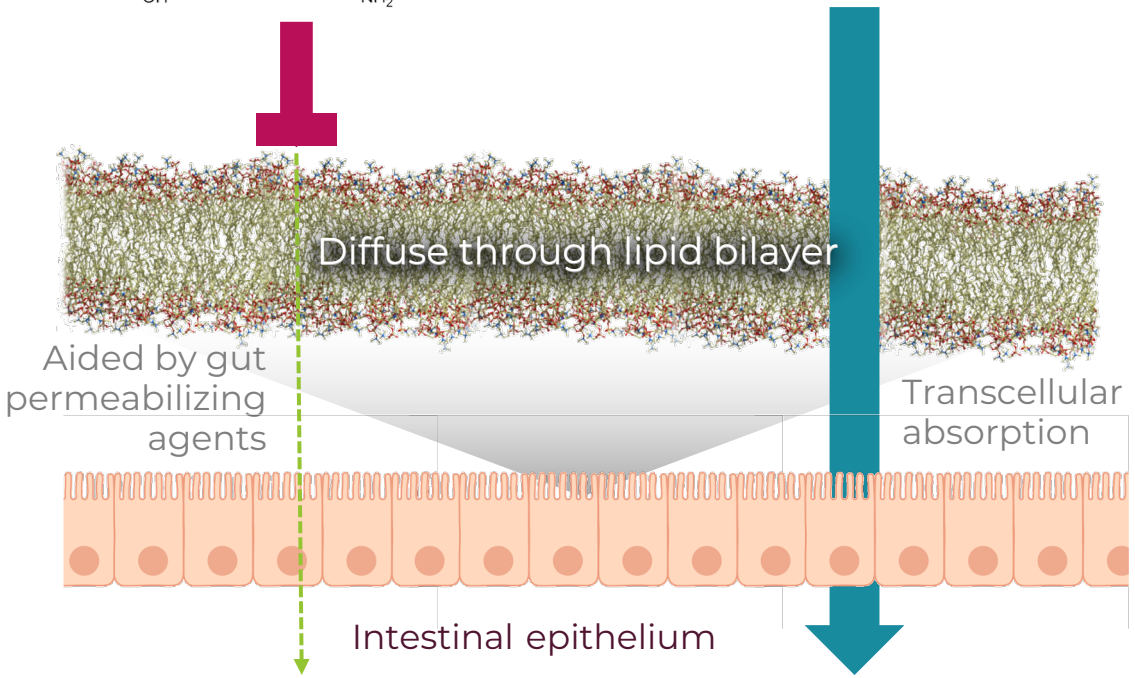
Peptide: Octreotide

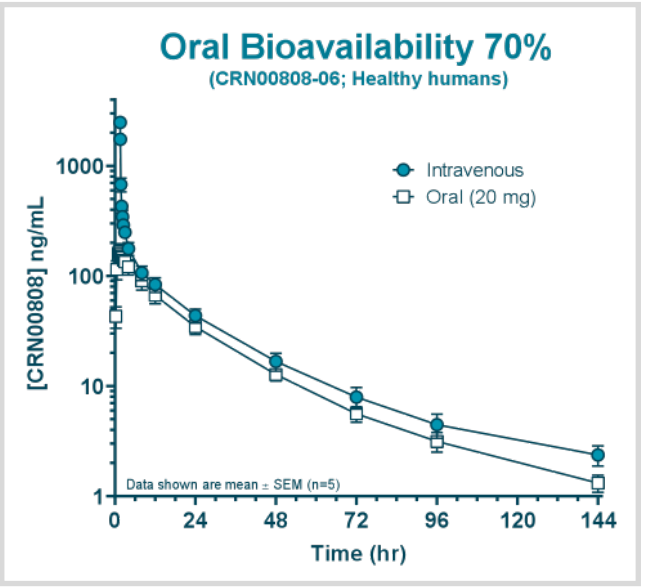


Survive proteolysis

Nonpeptide: paltusotine







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

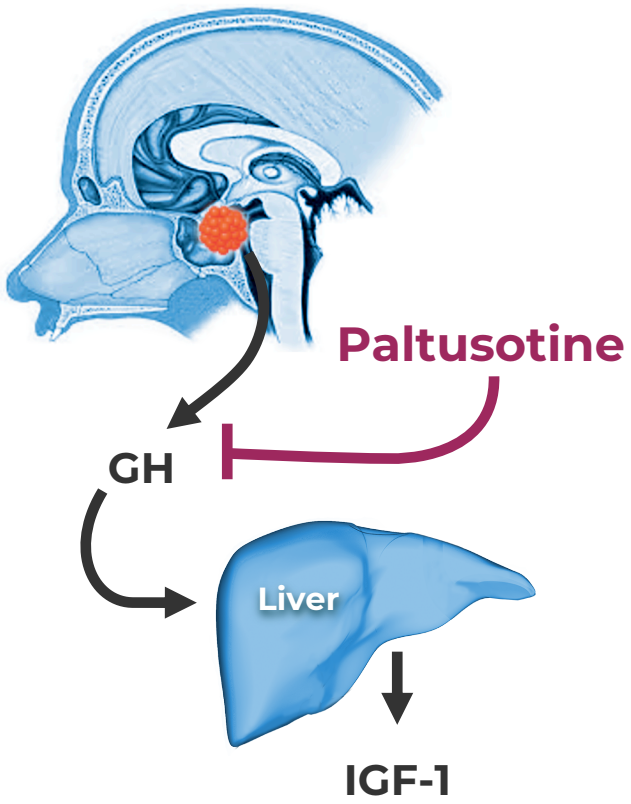
Paltusotine Target Profile

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

Suppression of GH and IGF-1 Determines Clinical Trial Success

Acromegaly



Study	Population	Goals	Success Criteria
Phase 1 FIH	Healthy Volunteers	Proof-of-concept Define PK/PD Preliminary safety	QD dosing GH/IGF suppression = peptide SSAs
ACROBAT EDGE	Patients not fully controlled on oct/lan monotherapy (>65% of patients)	Switch to oral and maintain IGF control Efficacy vs. washout	IGF on oral = prior IGF Treated IGF < washout IGF
ACROBAT EVOLVE	Patients fully controlled on oct/lan monotherapy (20-30% of patients)(1)	Switch to oral and maintain IGF control Efficacy vs. randomized withdrawal	Responder rate > placebo
ACROBAT ADVANCE	Edge & Evolve patients	Long-term safety	Durable safety and IGF suppression

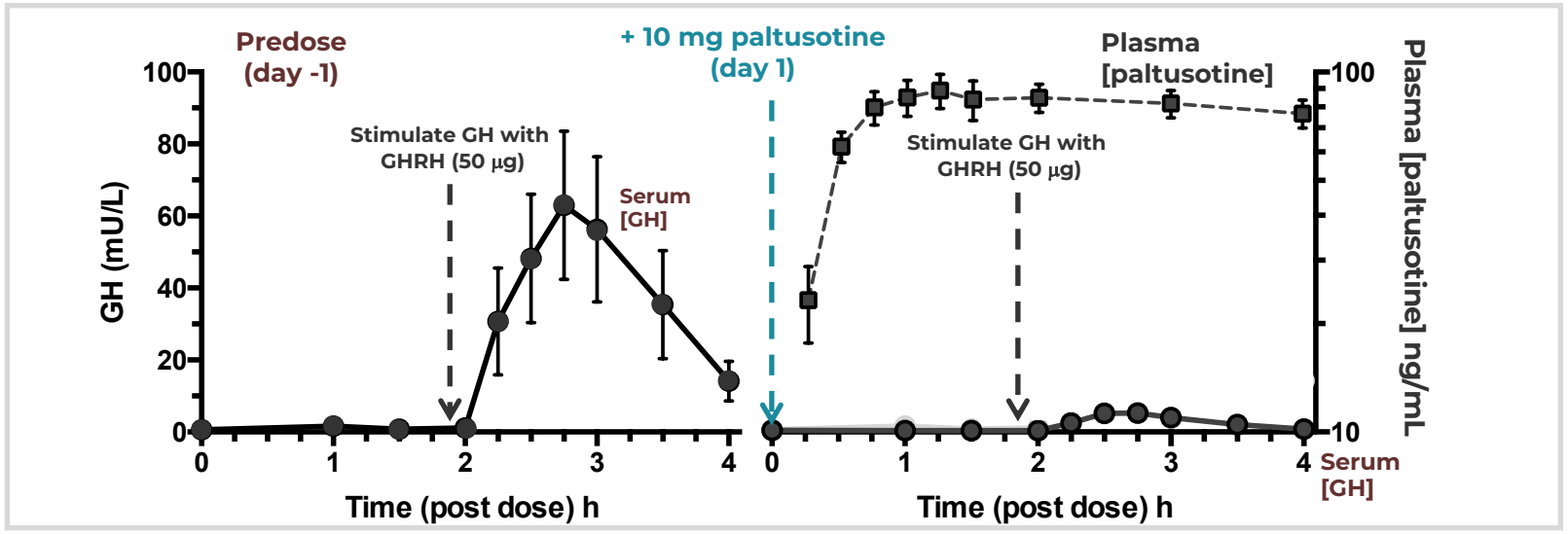
(1) New enrollment in the Evolve study has been discontinued. The 12 patients enrolled will continue in the study.

Colao et al, J Clin Endo Metab (2013); Strasburger et al, Eu J Endo (2016); Ezzat et al, Annals of Internal Medicine (1992)

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

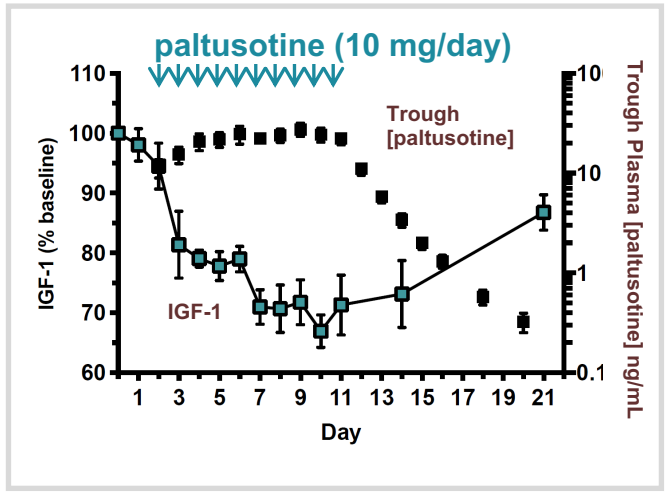
Single-ascending dose (SAD):

Demonstrated suppression of growth hormone

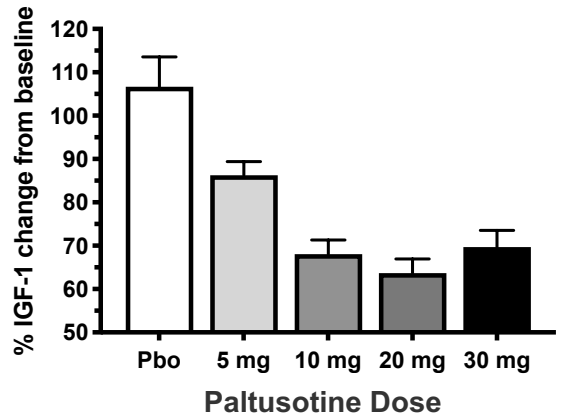


Multiple-ascending dose (MAD):

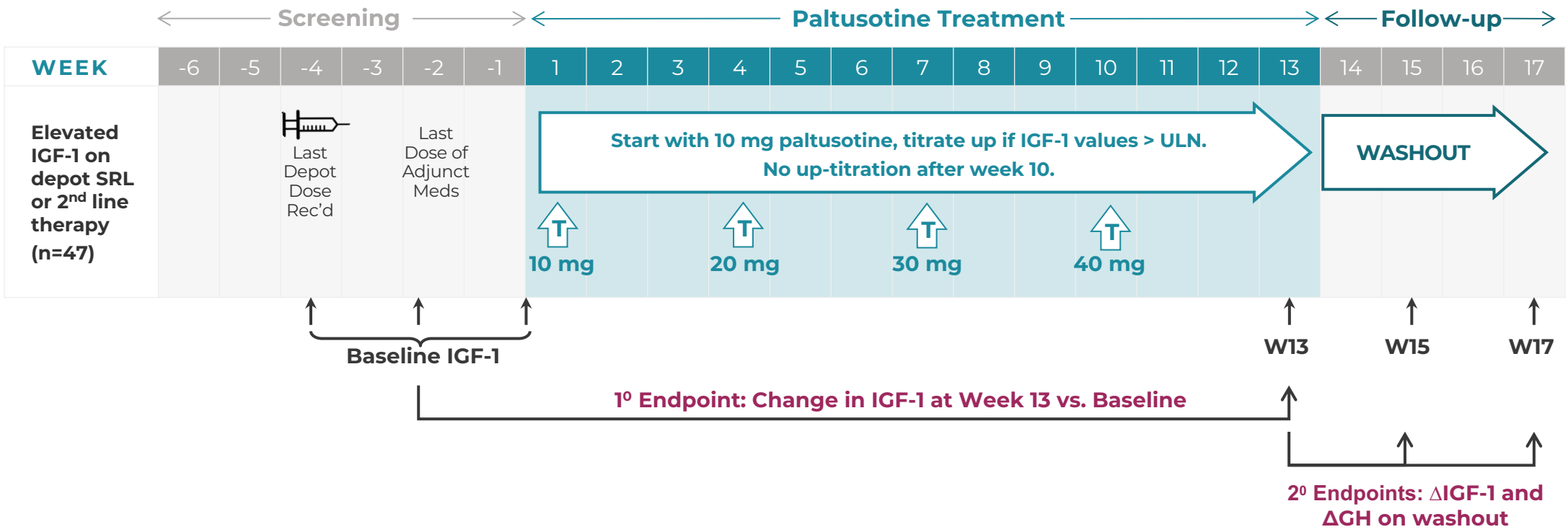
Demonstrated suppression of IGF-1



Dose response of IGF-1 suppression



Phase 2: ACROBAT Edge Design



Key eligibility criteria: Patients not fully biochemically controlled (IGF-1 > 1.0 x ULN) on octreotide or lanreotide monotherapy (Group 1)

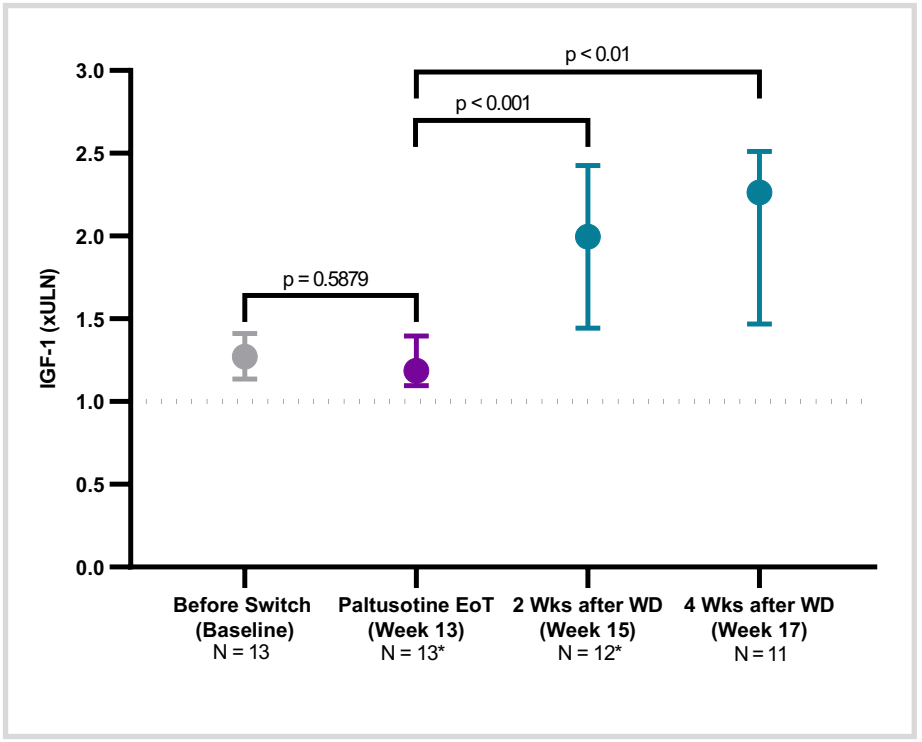
- Also investigating other subsets of patients who require add-on therapy to further suppress IGF-1 as well as pasireotide patients (Groups 2-5).

Profile of patients in Edge represent > 65% of acromegaly patients

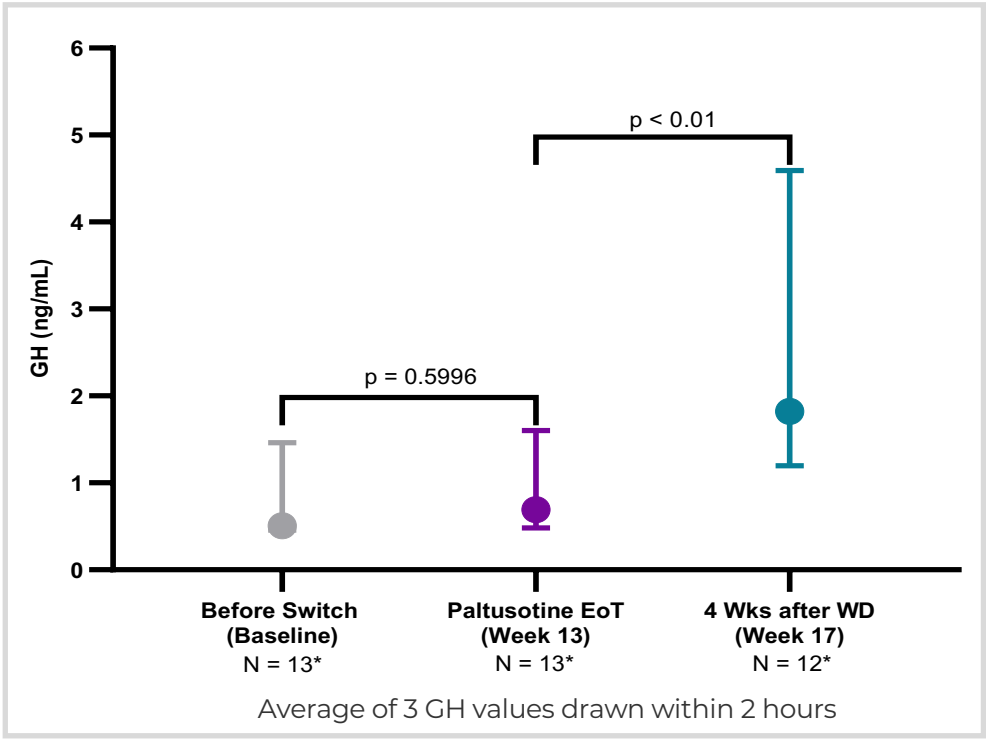
Edge Interim Results: Paltusotine Maintained GH & IGF-1

Both IGF-1 and GH levels promptly rose after withdrawal of paltusotine

Serum IGF-1 at EoT and after withdrawal



Serum Growth Hormone at EoT and after withdrawal



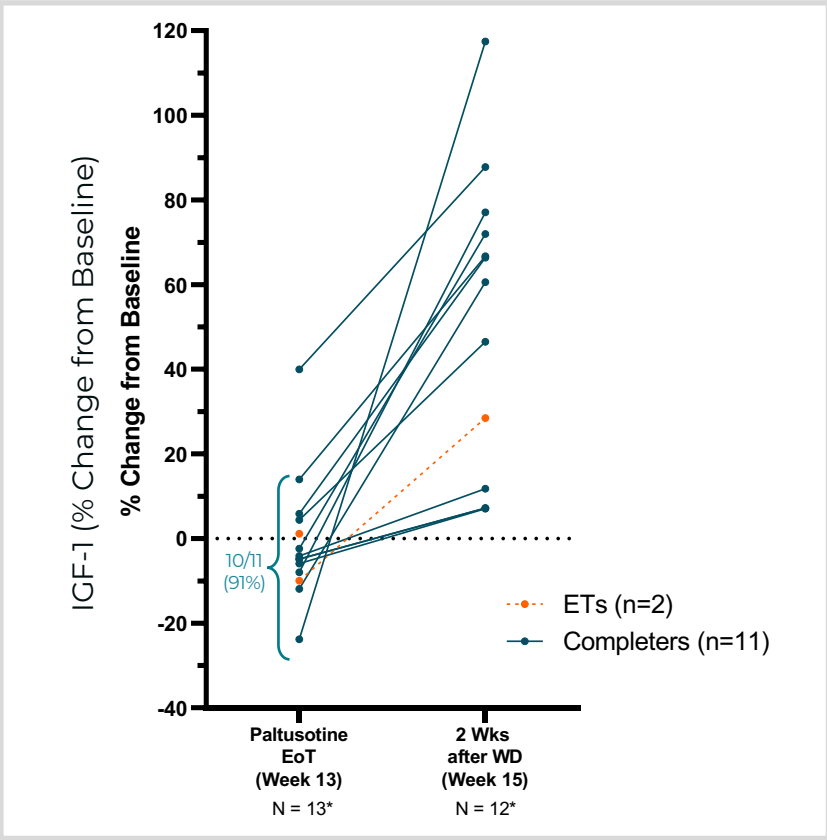
Data shown are median (25th percentile, 75th percentile) for Group 1 patients

- *Data includes two early termination (ET) patients who discontinued for non-study drug related reasons: (1) use of prohibited concomitant medication and (2) inability to complete study visits. Their final treatment values were used for EoT. The 2 ET patients had 16 days (~2 weeks) and 23 days (~3 weeks) of paltusotine exposure.
  One ET patient had final assessment 2 weeks after EoT (GH data from this subject was included in the 4 wk GH WD data), the washout data for the other was not available
- p-values are based on non-parametric Wilcoxon Sign Rank test of whether the median change is different from zero.
- EoT=End of Treatment; WD=Withdrawal

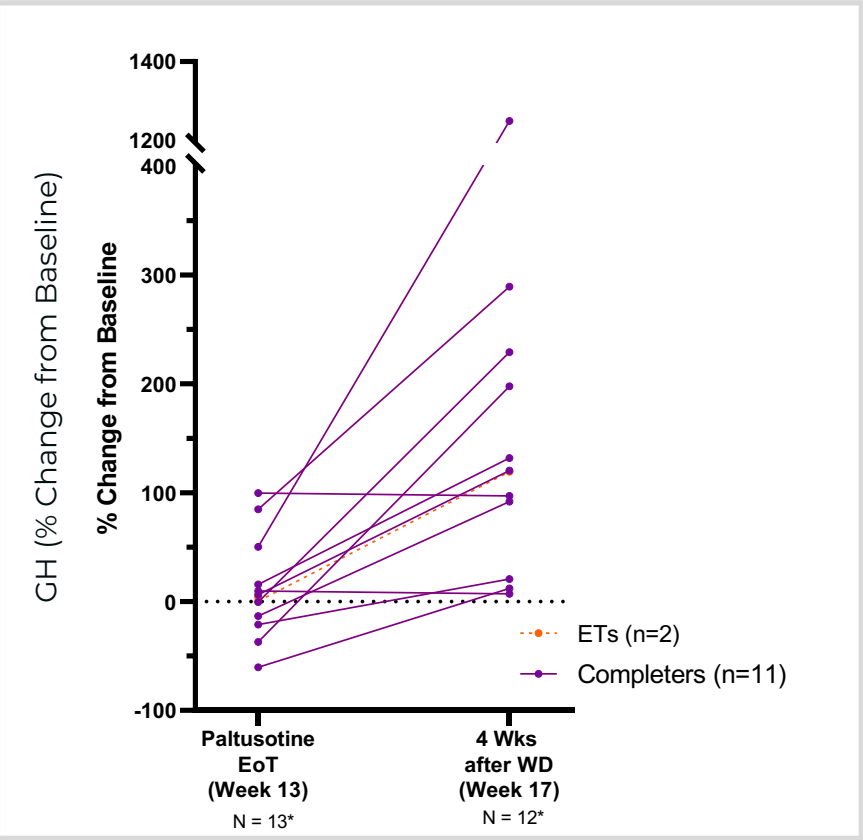
IGF-1 Maintained in > 90% of Group 1 Completers

IGF-1 and GH level changes after withdrawal were consistent with the approximately 2-day half-life previously measured in Phase 1 trial

Individual IGF-1 changes at end of treatment and 2 weeks after withdrawal of paltusotine



Individual GH changes at end of treatment and 4 weeks after withdrawal of paltusotine



- *Data includes two early termination (ET) patients who discontinued for non-study drug related reasons and had 16 days (~2 weeks) and 23 days (~3 weeks) of paltusotine exposure. 1 ET patient had final assessment 2 weeks after EoT (GH data from this subject was included in the 4 wk GH WD data), the washout data for the other was not available. These were not included in calculation of 91% who maintained IGF-1 levels within 15% of baseline values.
- Pre-trial therapy SRL median concentrations at W13 compared to baseline: [Lanreotide] ↓ by 70%; [Octreotide] ↓ by 100%; paltusotine median concentrations at W15 compared to W13 (last dose) were decreased by >99.9%
- EoT=End of Treatment; WD=Withdrawal

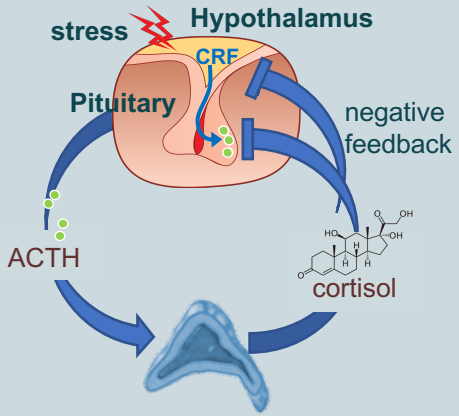
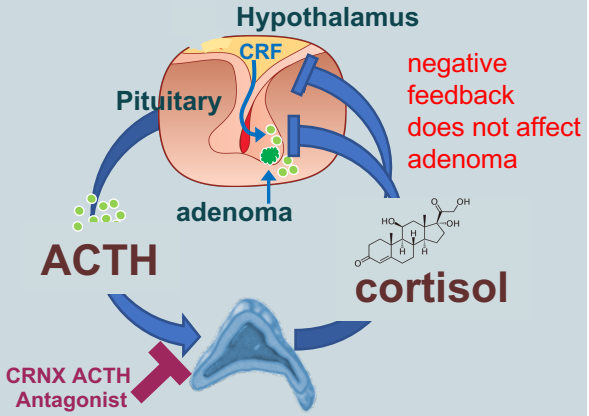
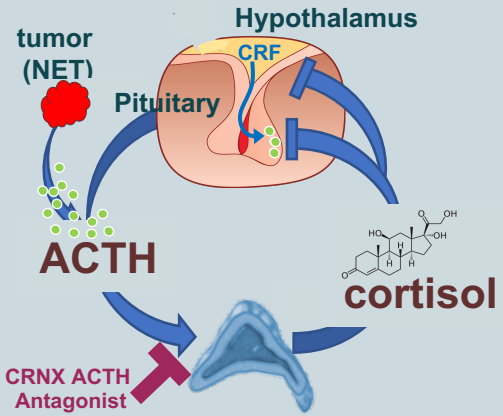
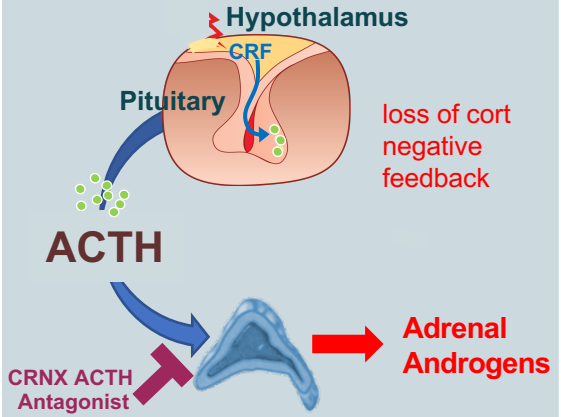
Paltusotine Clinical Program: Current Status

- Phase 2 ACROBAT Edge interim data from April 2020
  - Paltusotine maintained GH and IGF-1 levels after the 13-week dosing period that were previously attained by standard of care in the 11 acromegaly patients who completed the study
  - Upon cessation of dosing, GH and IGF-1 levels promptly rose as expected
- Phase 2 ACROBAT Edge and Evolve topline data expected in Q4
  - Edge enrolled 47 patients in 5 subgroups and Evolve enrolled 13 patients
  - Maintenance of GH and IGF-1 at 13 weeks is the efficacy endpoint
- Initiate Phase 3 acromegaly program in 1H21
  - Finalize study design with regulatory and KOL feedback using end of Phase 2 data
  - Hold end of Phase 2 meeting with FDA
  - Start P3 with to-be-marketed drug product formulation
- Initiate NETs (carcinoid syndrome) trial in 2021

NONPEPTIDE ACTH ANTAGONISTS

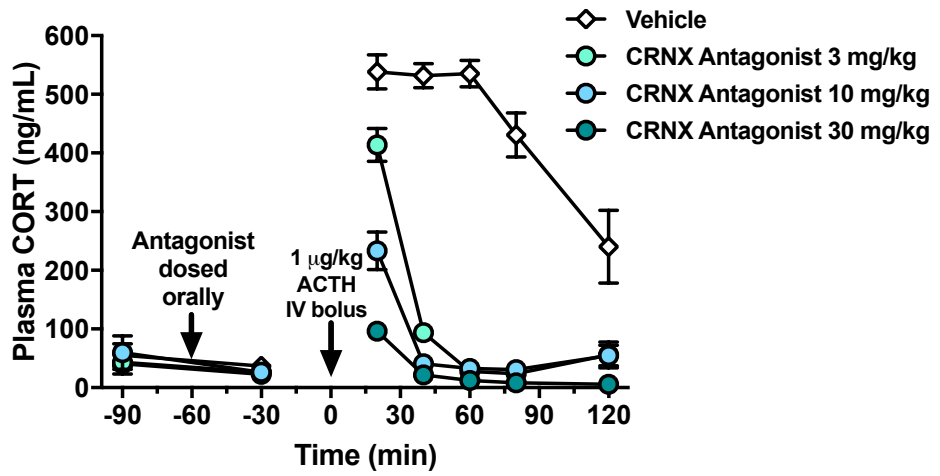
For the treatment of Cushing's Disease, congenital adrenal hyperplasia (CAH), and other conditions of ACTH excess

Indications for an Oral, Selective ACTH Antagonist

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

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

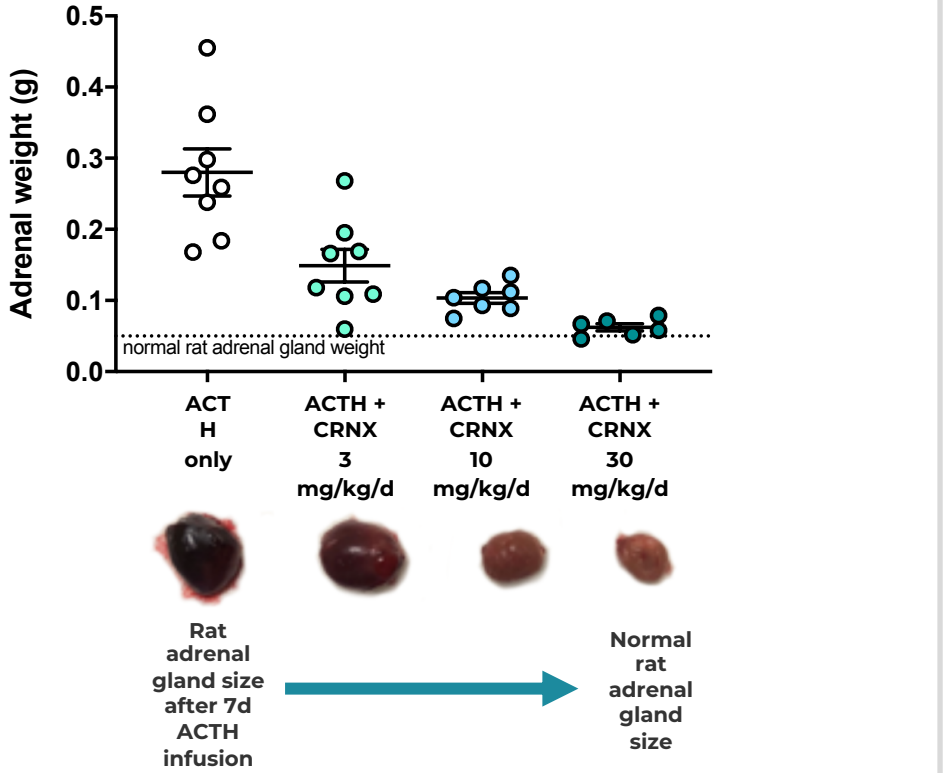
Acute suppression of ACTH-induced corticosterone observed in rats



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

- File IND Q4 2020
- 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)

NONPEPTIDE SST5 AGONISTS

For the treatment of congenital hyperinsulinism (CHI)

Congenital Hyperinsulinism (CHI) Disease Overview

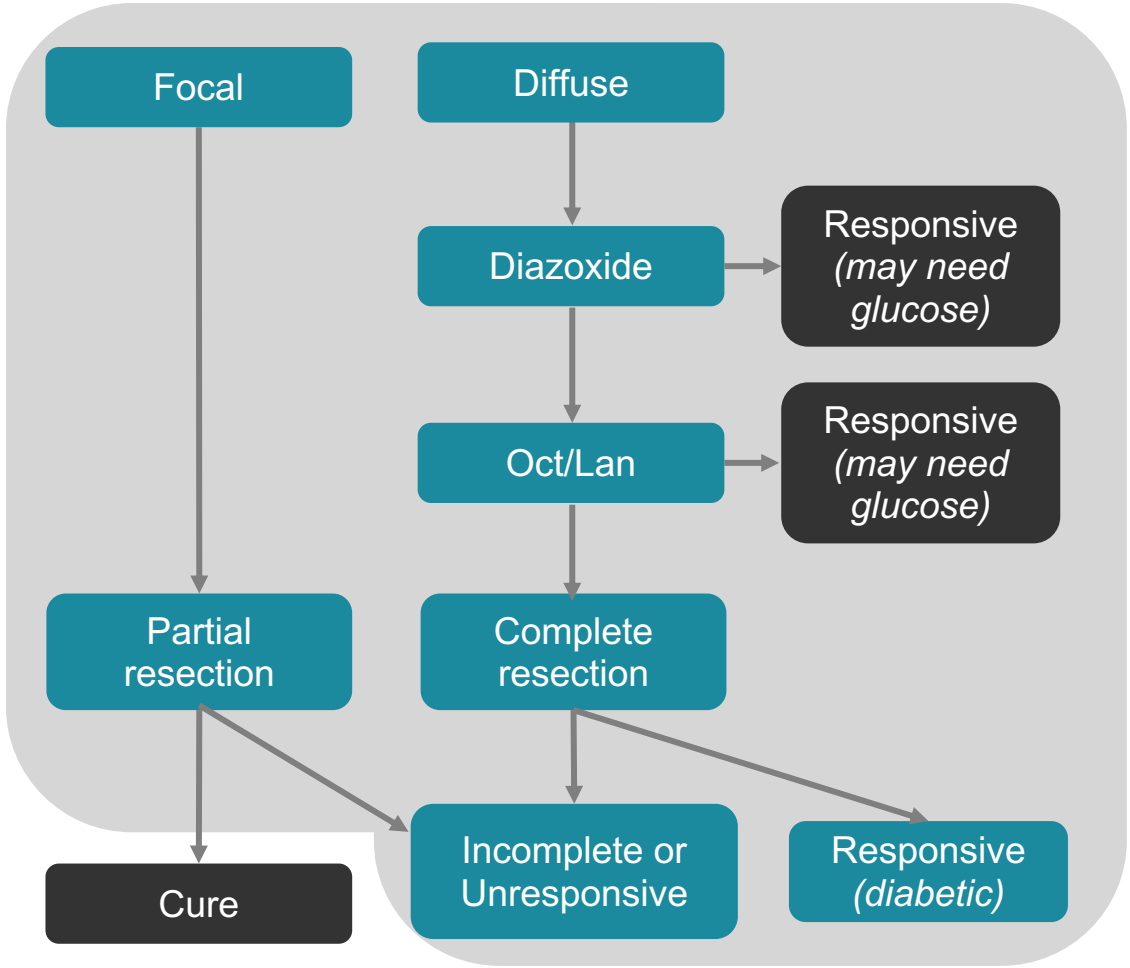
Disease

- 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)

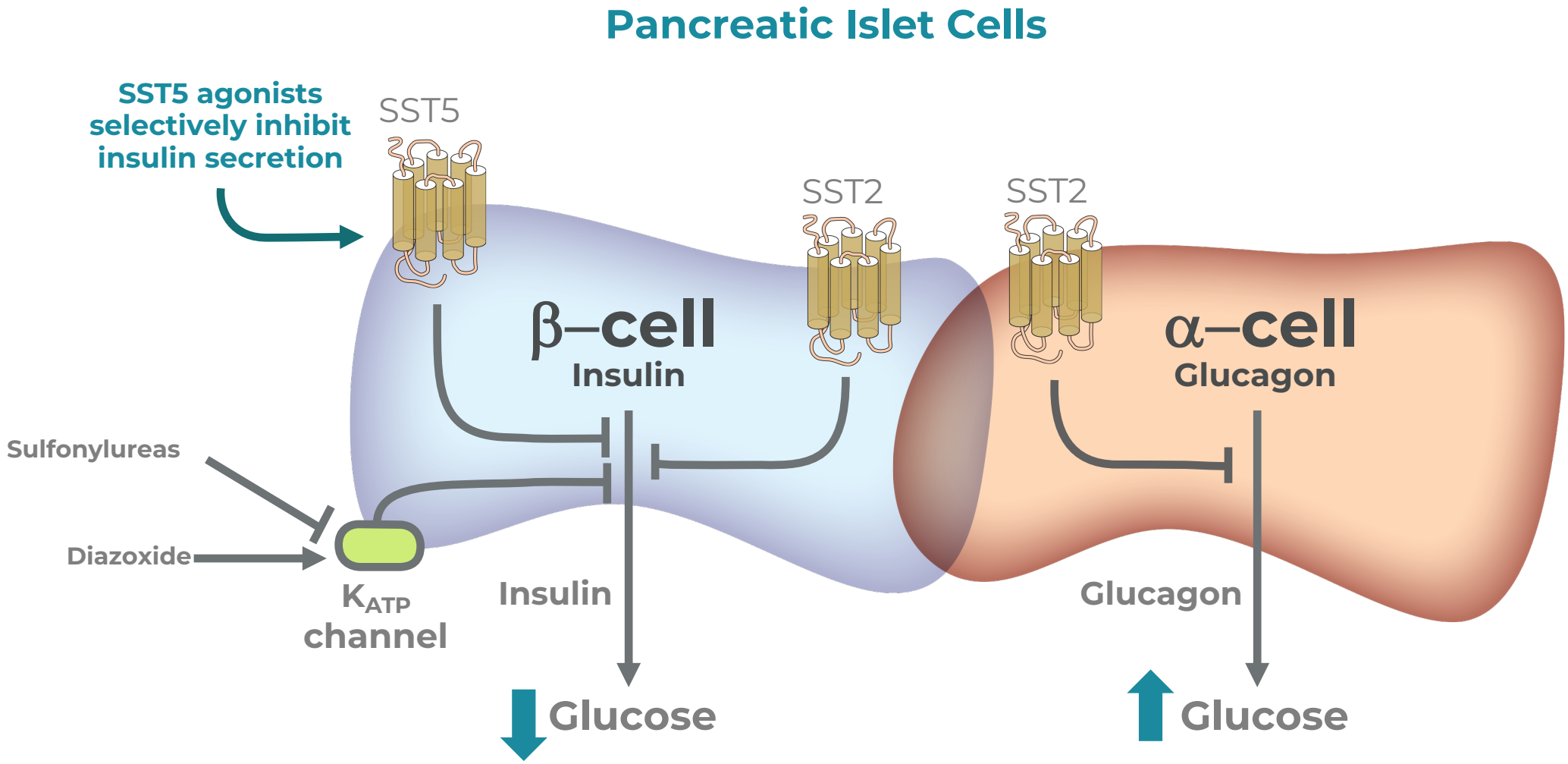
Patient and parent goals

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

Current Treatment Paradigm

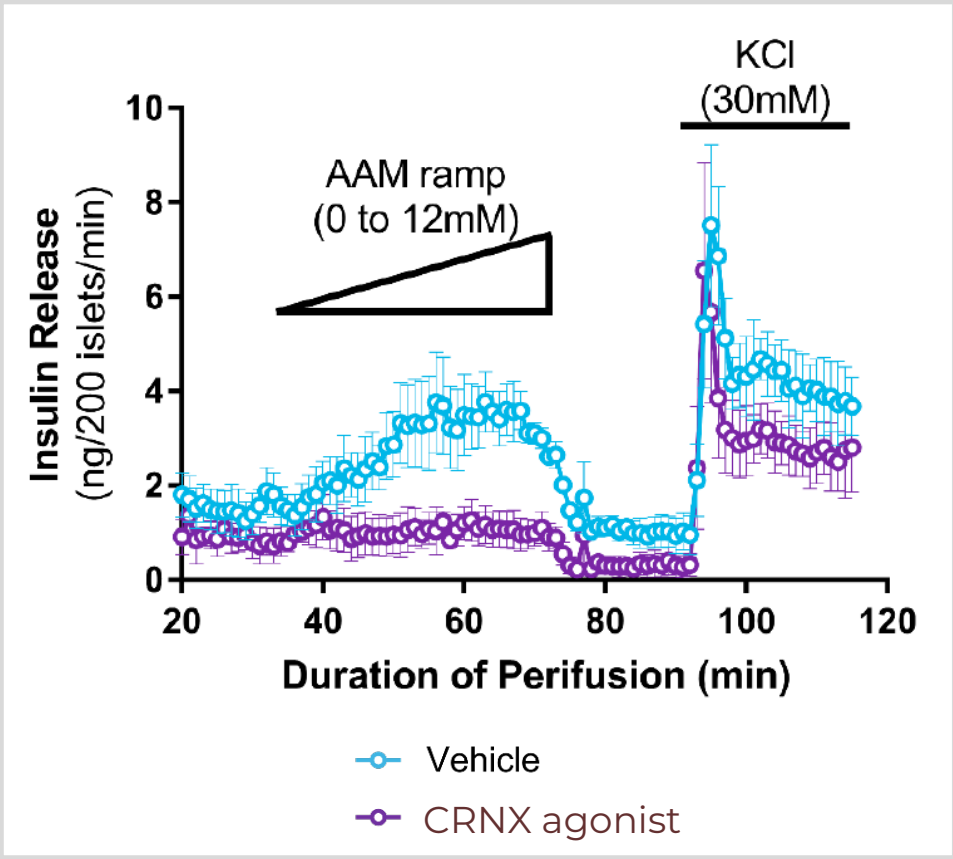


SST5 Agonists Inhibit Insulin Secretion Without Inhibiting Glucagon Secretion

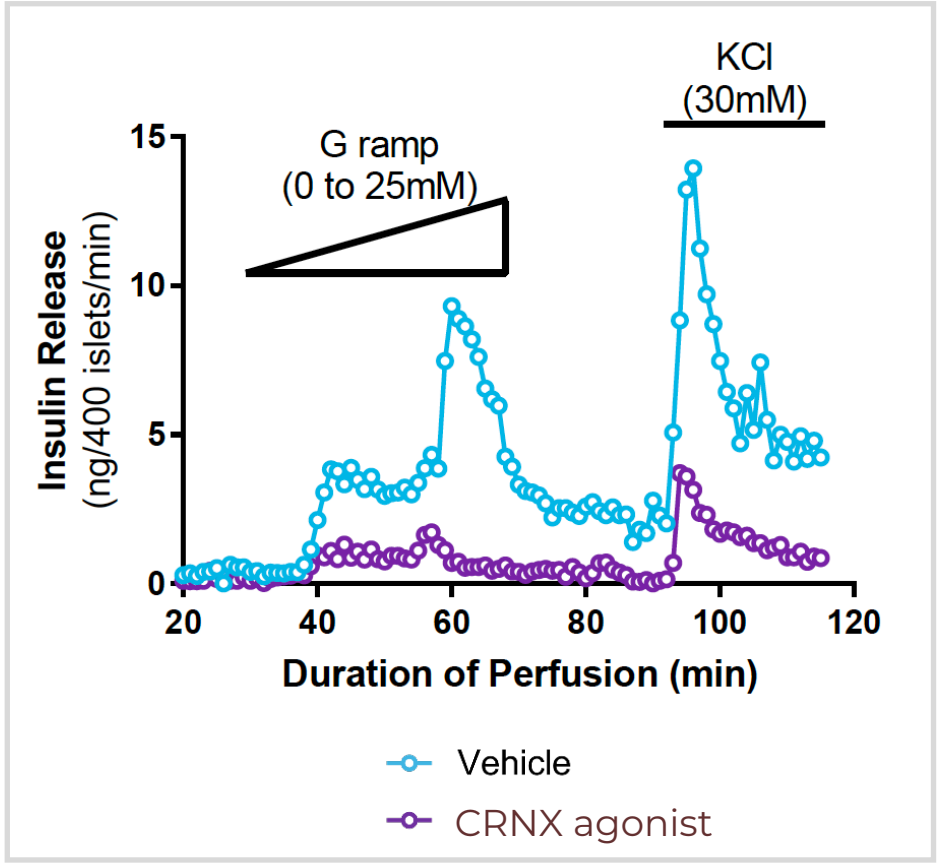


SST5 Agonists Potently Suppressed Insulin Secretion

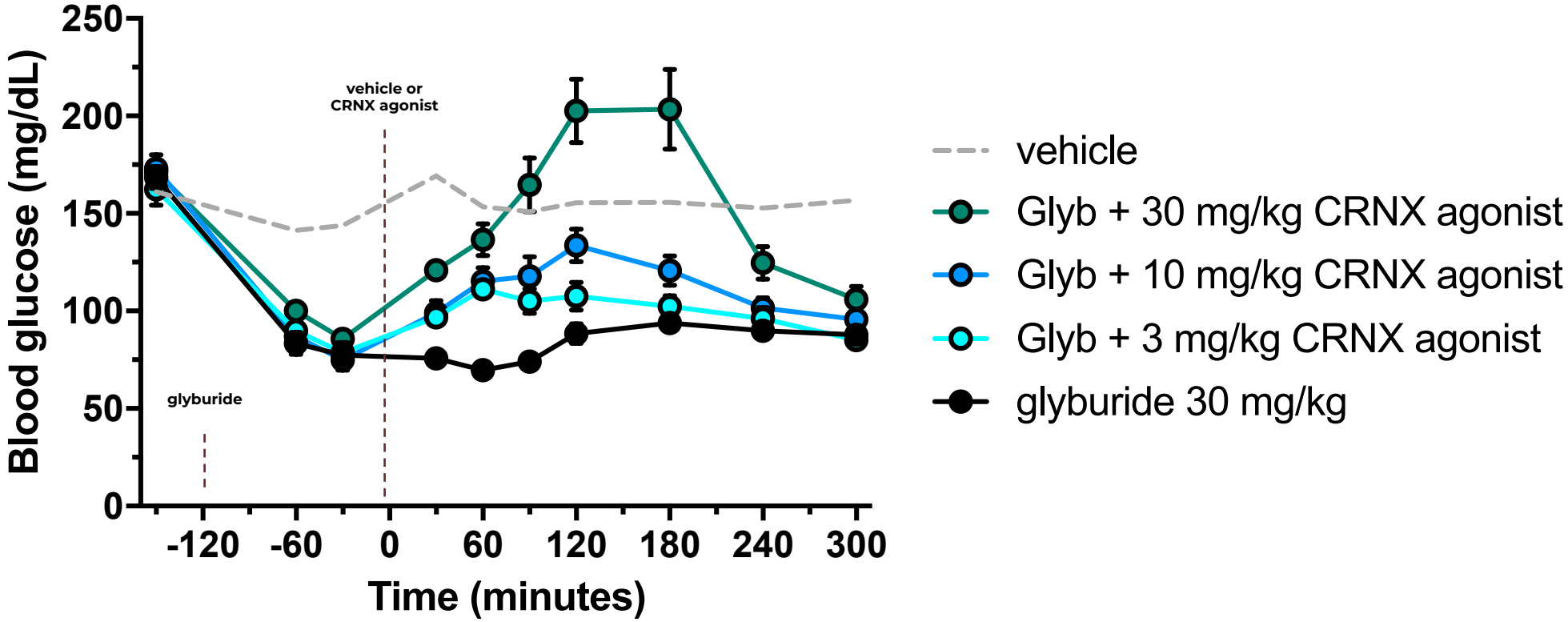
In isolated SUR1$^{-/-}$ knockout mouse islets (mimic genetic defect of ~50% of CHI patients)



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

Next Steps for SST5 Agonist Program

- File clinical trial application in Germany 4Q 2020
- 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	Topline data from Edge and Evolve acromegaly Phase 2 trials	4Q 2020
	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
Nonpeptide SST5 agonist	Initiation of Phase 1 clinical study	Early 2021

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

Edge interim data as of February 23, 2020

Data available for interim analysis

- As of February 23, 2020, 32 patients have enrolled in the study and either completed participation, or continue to receive paltusotine
- 17 patients have completed participation in the study.
  - 13 of these initial patients were treated with lanreotide depot (n=8) or octreotide LAR (n=5) monotherapy and entered the trial with IGF-1 above the upper limit of normal (Group 1)
  - 10 of the 11 (91%) patients in group 1 who completed paltusotine treatment maintained IGF-1 levels within 15% of their respective baseline levels at week 13
- Efficacy Evaluation Set (n=13)
  - All available data from Group 1 patients who completed participation in the trial as of February 23, 2020
- Safety Evaluation Set (n=32)
  - All patients dosed in all subgroups as of February 23, 2020 (n=32) including those that had not yet completed the study

Patient baseline characteristics

	Group 1 (N=13)	Total (N=32)
Median Age, years (Min, Max)	53.0 (34, 68)	51.5 (34, 70)
Sex		
Female	7 (53.8%)	19 (59.4%)
Male	6 (46.2%)	13 (40.6%)
Ethnicity		
Hispanic or Latino	0	6 (18.8%)
Not Hispanic or Latino	13 (100%)	26 (81.3%)
Race		
White	13 (100%)	29 (90.6%)
Black or African American	0	1 (3.1%)
Other	0	2 (6.3%)
Median Weight, kg (Min, Max)	97.9 (63, 155)	89.3 (57.3, 155)

Edge Interim Data: Paltusotine was well tolerated

Safety data in all patients dosed with paltusotine as of February 23, 2020 (n=32) in Edge

Adverse events on treatment regardless of causality in 2 or more patients

Preferred Term	Group 1 (N=13) n (%)	Total (N=32) n (%)
Number (%) of Patients with any TEAEs	9 (69%)	14 (44%)
Arthralgia	3 (23%)	6 (19%)
Headache	4 (31%)	5 (16%)
Abdominal discomfort	1 (8%)	3 (9%)
Peripheral swelling	2 (15%)	3 (9%)
Back pain	2 (15%)	2 (6%)
Diarrhoea	0	2 (6%)
Flatulence	0	2 (6%)
Hyperhidrosis	2 (15%)	2 (6%)
Palpitations	1 (8%)	2 (6%)

- No discontinuations due to adverse events
- No patients have required “rescue treatments” with standard acromegaly medications
- 1 SAE--Headache--non-treatment related (admission for diagnostic evaluation)
- No safety signals as of the interim data cut off date with vital signs, clinical safety laboratories (including amylase/lipase, fasting glucose, liver function tests), HbA1c, ECGs
- Safety and tolerability results have been generally consistent with those observed in >100 healthy volunteers dosed with paltusotine to date

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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