Crinetics Pharmaceuticals

CORPORATE PRESENTATION

J.P. Morgan 39th Annual Healthcare Conference January 2021

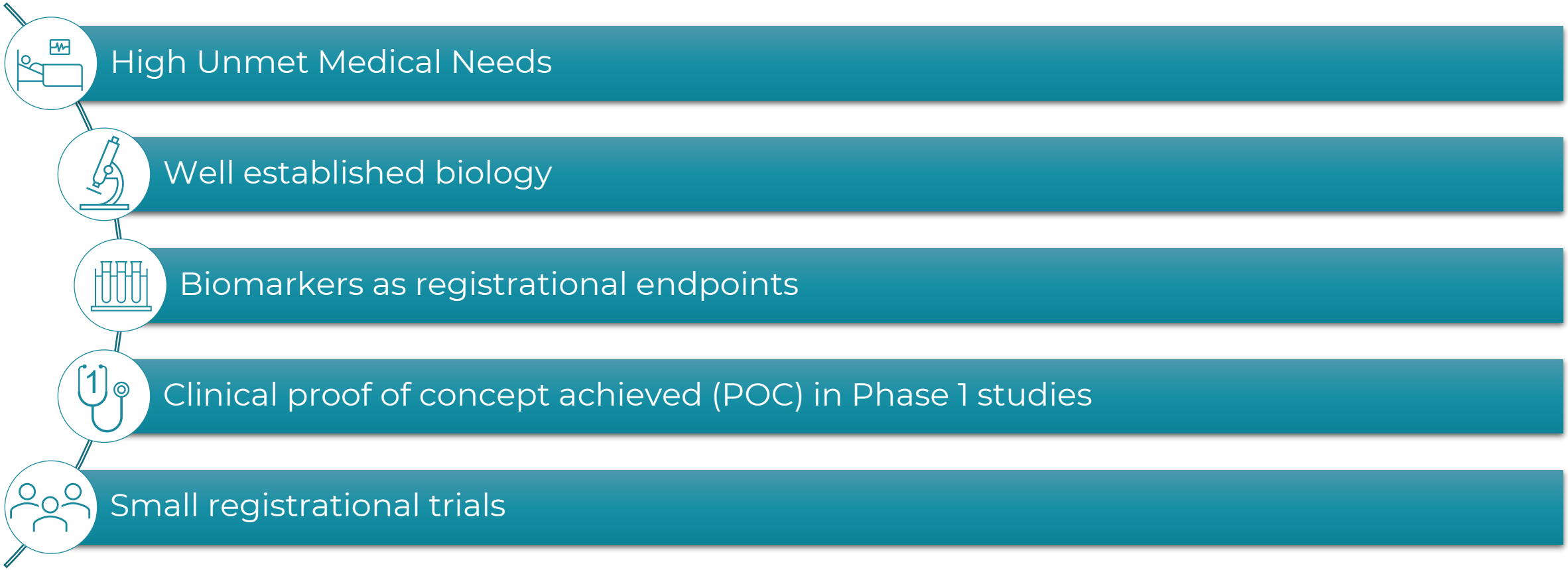
SAFE HARBOR STATEMENT

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 benefits of paltusotine for acromegaly patients and patients with carcinoid syndrome; the potential to initiate a pivotal Phase 3 trial of paltusotine in acromegaly and the expected timing thereof; our plans to meet with the FDA in the first quarter of 2021; the benefits of our improved tablet formulation of paltusotine; the potential to initiate a trial of paltusotine in patients with carcinoid syndrome due to NETs and the expected timing thereof; the potential benefits of CRN04894 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 CRN04894, report data therefrom, and the timing thereof; the potential benefits of CRN04777 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 CRN04777, report data therefrom, and the timing thereof; the potential for any of our ongoing clinical trials to show safety or efficacy; and our plans to identify and create new drug candidates for additional diseases, including hyperparathyroidism, nonfunctional pituitary adenomas and polycystic kidney disease, among other indications. 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 in acromegaly or a trial for carcinoid syndrome 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, CRN04894, CRN04777, 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.

Strategy: Drugs Built from Scratch for Purpose

We aim to discover, develop and commercialize drugs for endocrine indications with:



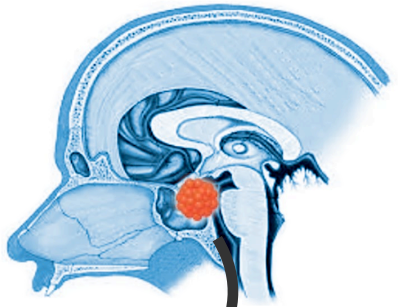
Pipeline Targets Indications with Unmet Need

Well established biology has the potential to allow for the use of biomarkers as registration endpoints

PROGRAM	Development Stage				Registrational Endpoint	Prevalence	
	Preclin	Phase 1	Phase 2	Phase 3		US Total	Global Range per 100,000
Paltusotine (SST2 agonist)							
Acromegaly				→	IGF-1 Levels	26K	2.8 – 13.0
Carcinoid Syndrome			→		Diarrhea & Flushing	33K	3.7 – 9.7
Nonfunctional NETs			→		Anti-tumor activity	138K	17 – 46
CRN04894 (ACTH antagonist)							
Cushing's Disease		→			Cortisol Levels	10K	2.5 – 3.8
Congenital Adrenal Hyperplasia (CAH)		→			Adrenal Androgens/ Glucocorticoid use	27K	6.7 – 10.0
CRN04777 (SST5 agonist)							
Congenital Hyperinsulinism (CHI)		→			Glucose Levels	2-4K	0.64 – 1.3
US TOTAL						**~236K**	

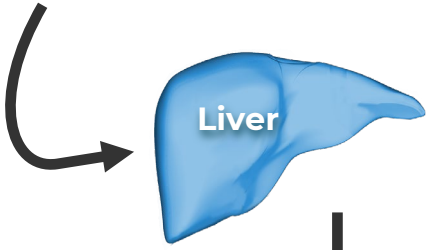
Endocrinology Invented Biomarkers! Clinical Proof-of-Concept in Phase 1 is Our Goal

Acromegaly



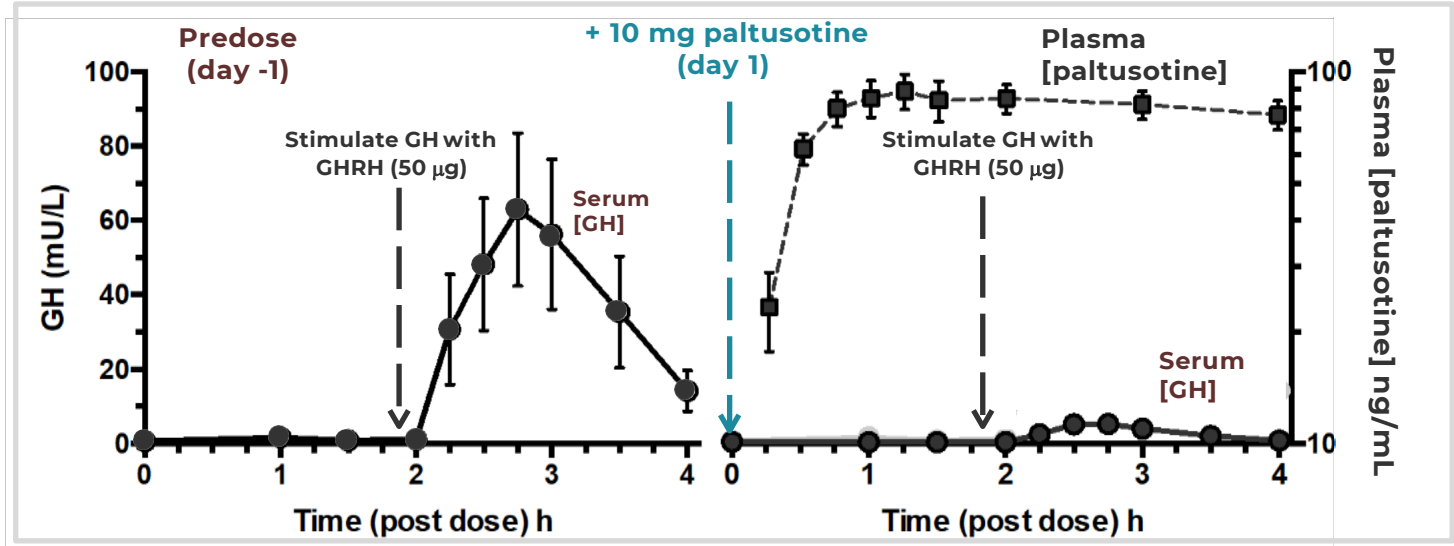
Paltusotine

GH

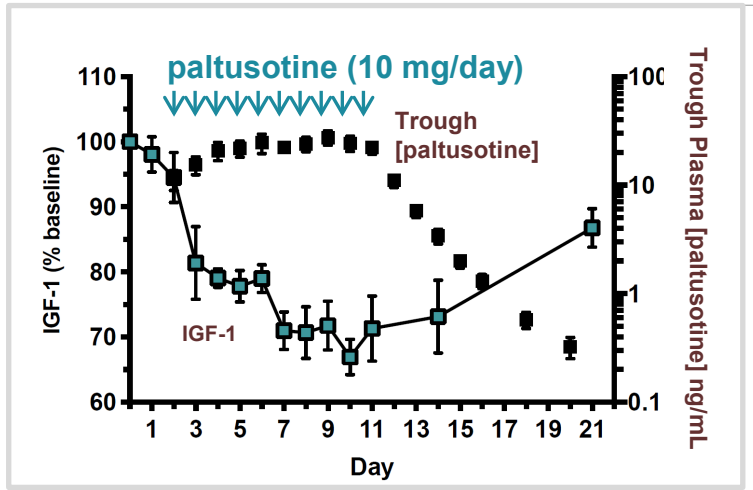


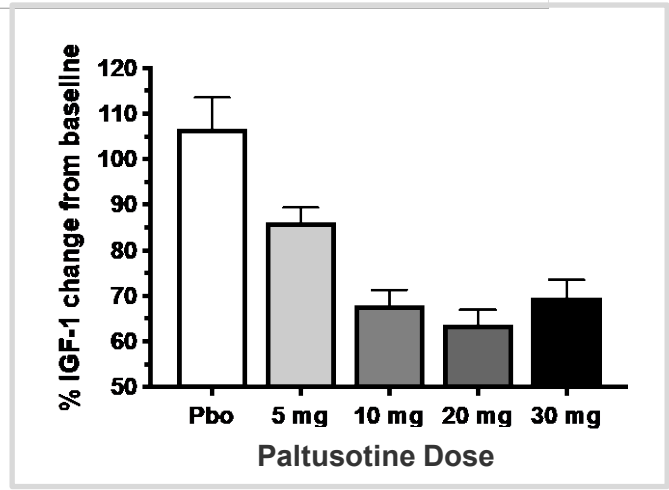
IGF-1
(1º Registration Endpoint)

Phase 1 SAD Data: Suppression of GH



Phase 1 MAD Data: Suppression of IGF-1





PALTUSOTINE: AN INVESTIGATIONAL, POTENTIAL FIRST-IN-CLASS, ORAL NONPEPTIDE SST2 AGONIST

Acromegaly

Carcinoid syndrome

Nonfunctional neuroendocrine tumors

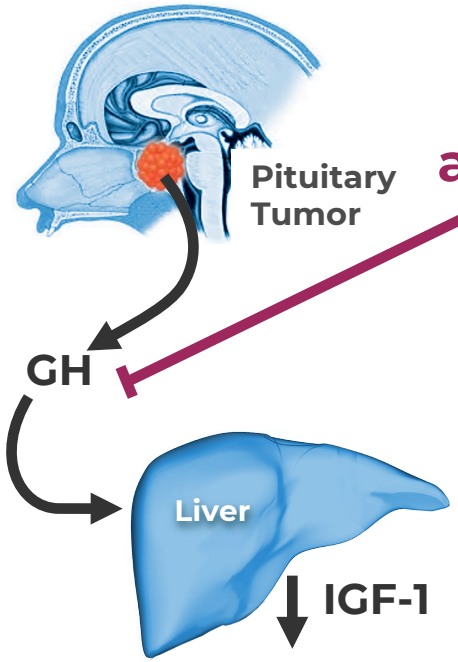
Acromegaly and NETS are Currently Treated with Injected SST2 Peptide Agonists

Acromegaly

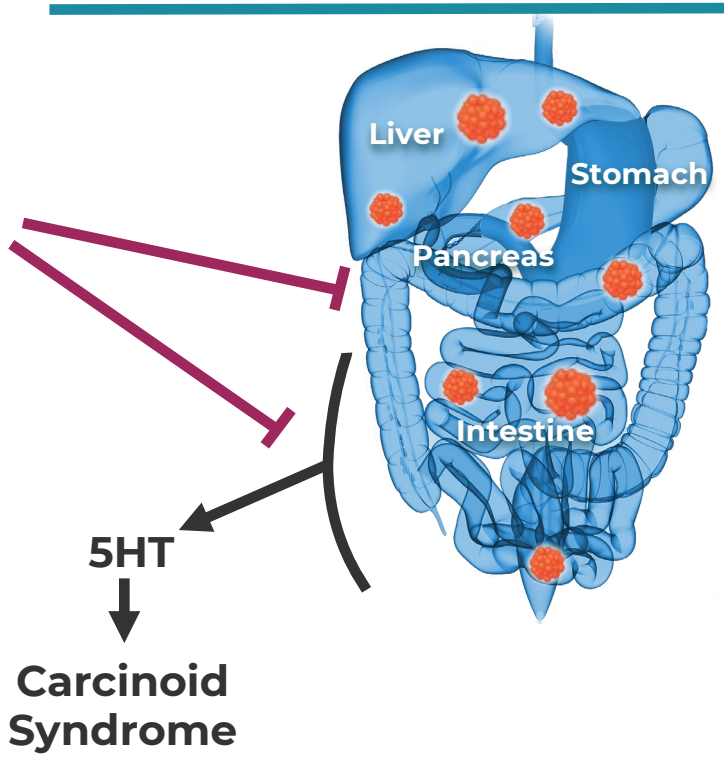
- Caused by benign pituitary tumor that secretes excess growth hormone (GH)
- Excess GH causes excess secretion of insulin-like growth factor-1 (IGF-1)

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



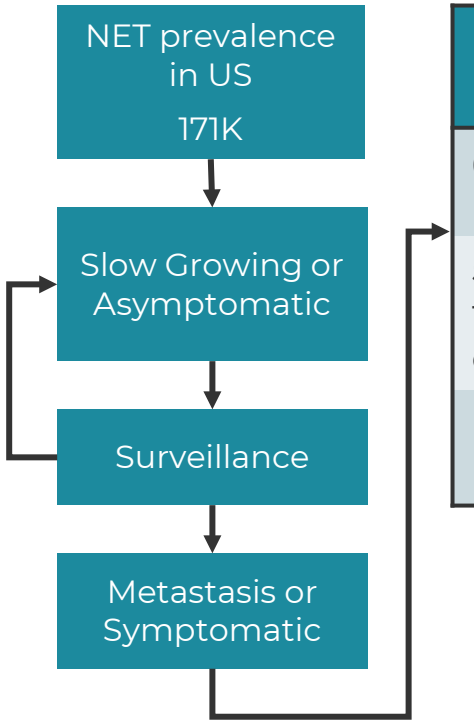
US Prevalence: **26,000**

Neuroendocrine Tumors (NETs)

- NETs arise from aberrant enteroendocrine cells in GI, pancreas or lungs
- In ~19% of cases, tumors are associated with excess secretion of serotonin and other hormones resulting in carcinoid syndrome
- Majority of tumors are "nonfunctional" and not associated with secretory syndrome
- Patients with grade 1 and 2 NETs and distant metastases have a 5-year survival ranging from 30-70%

US Prevalence	
Carcinoid Syndrome:	33,000
Nonfunctional tumors:	138,000
Total	**171,000**

NETs Treatment Considerations and Opportunities to Improve Current Standard of Care



First line intervention

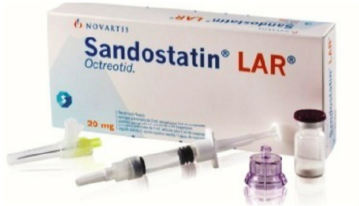
Tumor removal
62% eligibility (Grade 1 classification)
59% metastasis leading to limited surgery efficacy
Highly variable recurrence

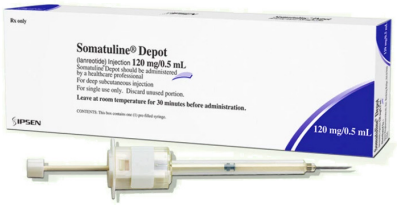
Common additional interventions

Symptom control (Carcinoid Syndrome)	Anti-tumor activity (Nonfunctional + CS)
19% occurrence of symptoms	PRRT: SST2 targeted radiotherapy
Symptoms shown to significantly decrease patient QoL	Everolimus & Sunitinib
90%+ SSA use and success controlling symptoms	Chemotherapy combinations ± SSAs
70% of patients report SSA injection site pain that lasts up to a week	SSA use significantly improves PFS of GEP-NETs

80-100% of GEP-NETs & P-NETs overexpress SST2 receptors

~$3B Market Despite Limitations of Current Therapies



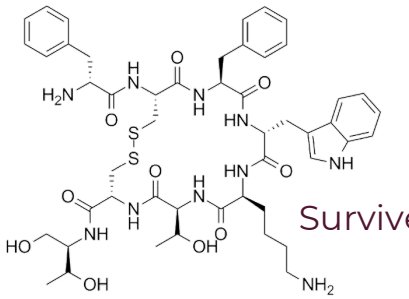


Sandostatin (octreotide)	Somatuline (lanreotide)	Somavert (pegvisomant)	MYCAPSSA (oral octreotide)
NOVARTIS $1.6B	IPSEN Innovation for patient care $1.2B	Pfizer $264M	CHIASMA
Monthly intramuscular 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous .2-.5ml; 18-gauge needle	Daily injections 1 ml; 28 – 31-gauge needle not supplied	Twice daily oral capsule
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	**Inconvenient.** Daily dose kits require refrigeration. Patients often must buy a second refrigerator for storage, making travel difficult.	**Food effect.** Cannot be taken <1 hour before eating or <2 hours after eating[1] **Limited efficacy**, as 42% of pivotal study patients did not maintain IGF-1 biochemical response after switching to MYCAPSSA from injectables[1] **Multiple drug-drug interactions**[1] **Cold chain distribution**[1]
Approval date: 1988, 1998(LAR)	**Approval date:** 2007	**Approval date:** 2003	**Approval date:** 2020

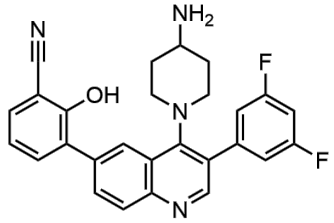
[1] MYCAPSSA Label

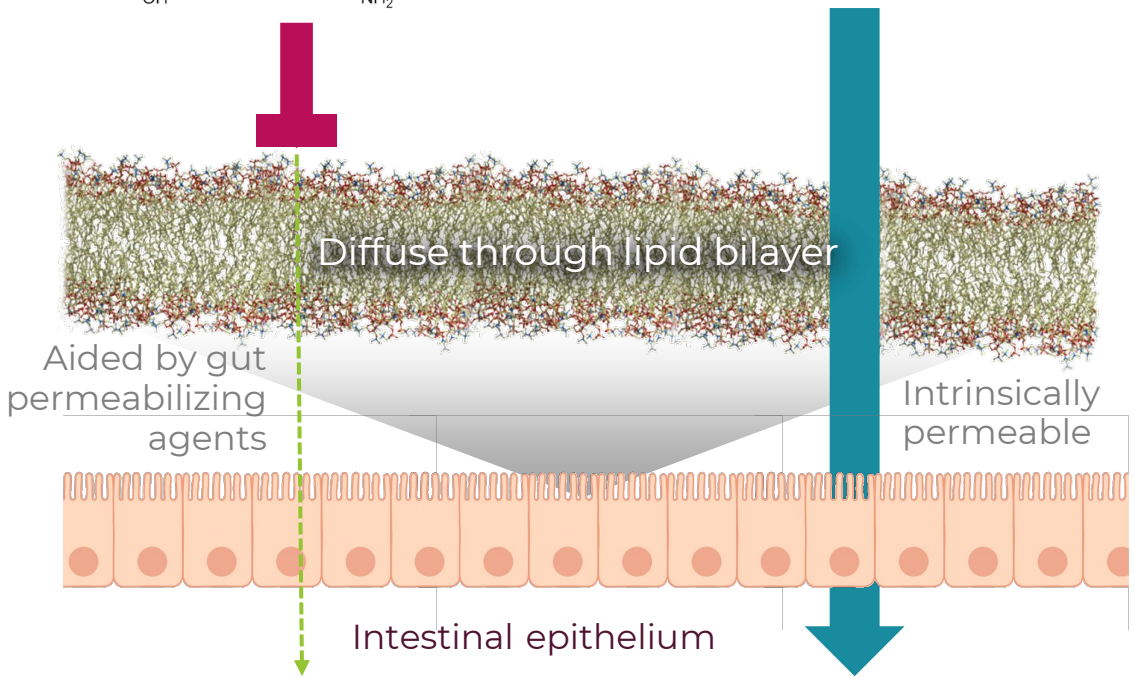
Paltusotine Showed High Intrinsic Oral Bioavailability

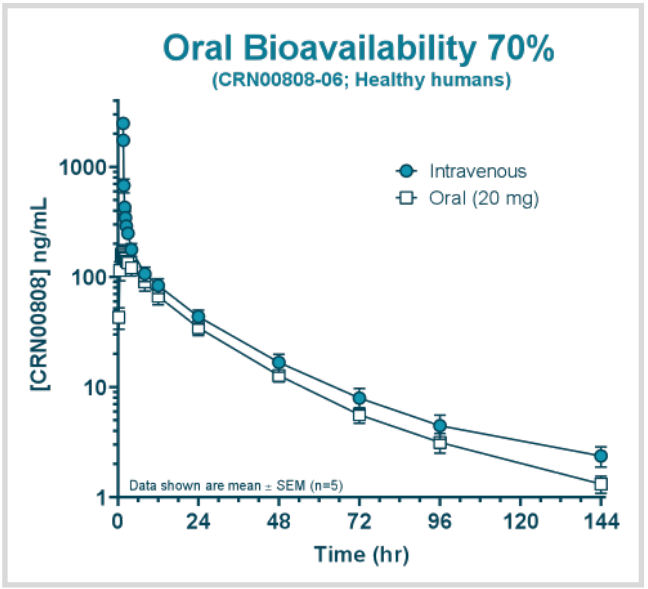
Peptide: Octreotide



Nonpeptide: paltusotine



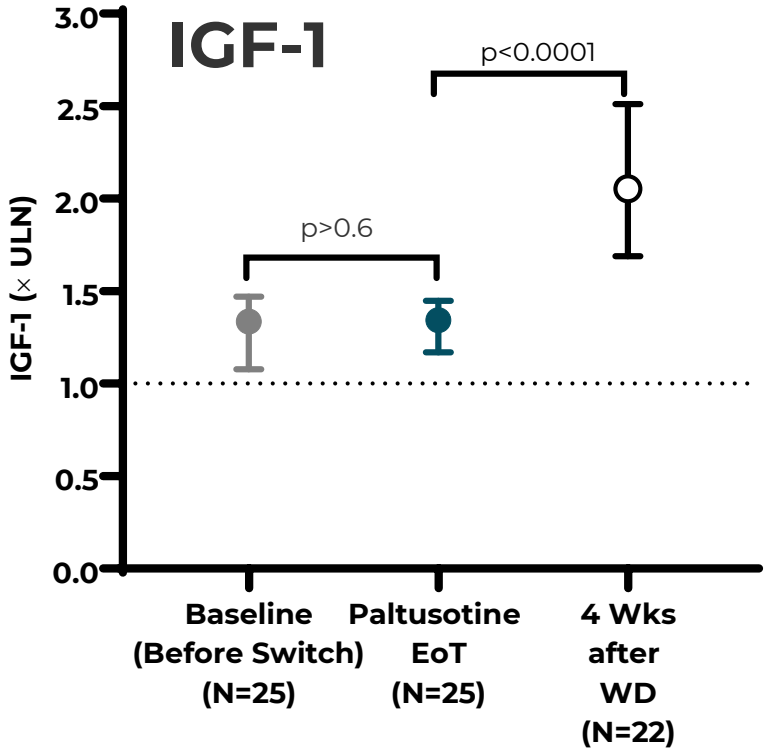


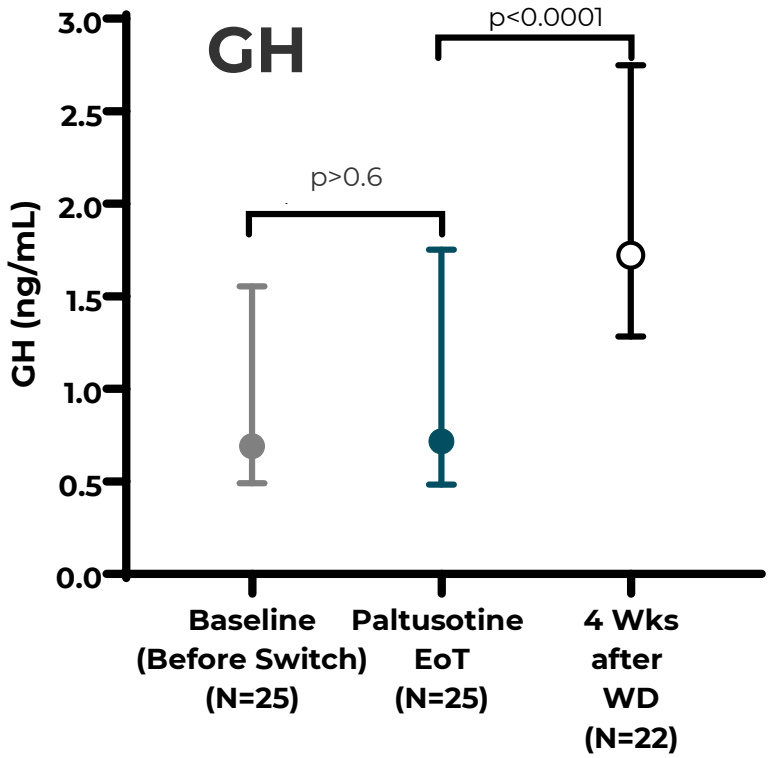


	Paltusotine (CRN00808)
Oral Bioavailability	70%
Observed Half Life	42-50 hr.

Phase 2 ACROBAT Edge Study Met Primary Endpoint

Hormone suppression maintained after switching from injected SOC to oral paltusotine

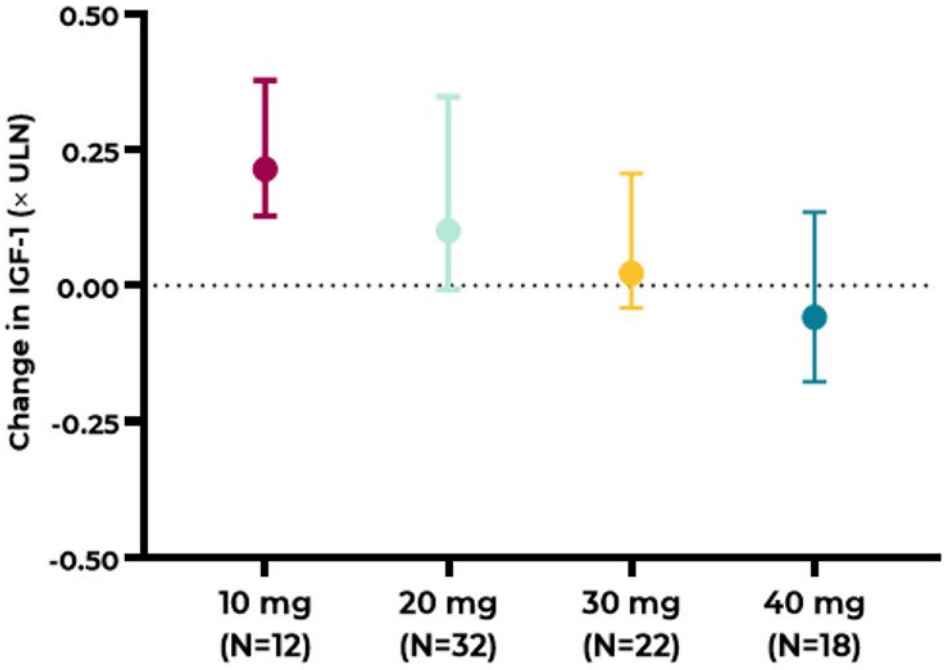




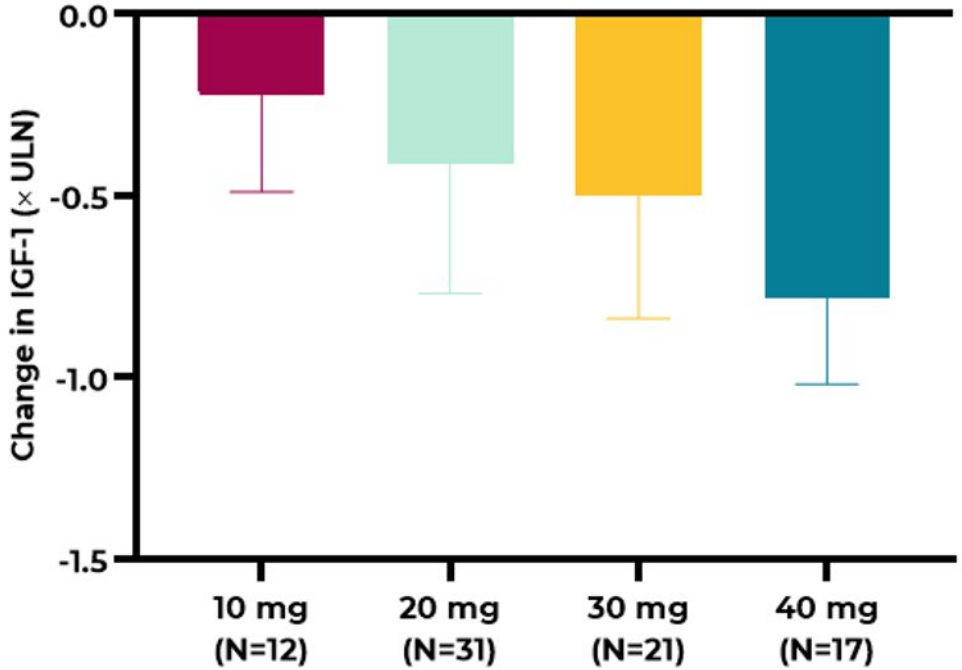
Data presented are median (Interquartile Range [IQR]: 25th percentile, 75th percentile) from the EDGE study's primary analysis population. EoT = End of Treatment defined as Week 13 (Visit 14) or last on treatment value carried forward (LOCF). Wks after WD is defined as Week 17 or result at least 22 days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

Evidence of Dose Response from Phase 2 Program

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

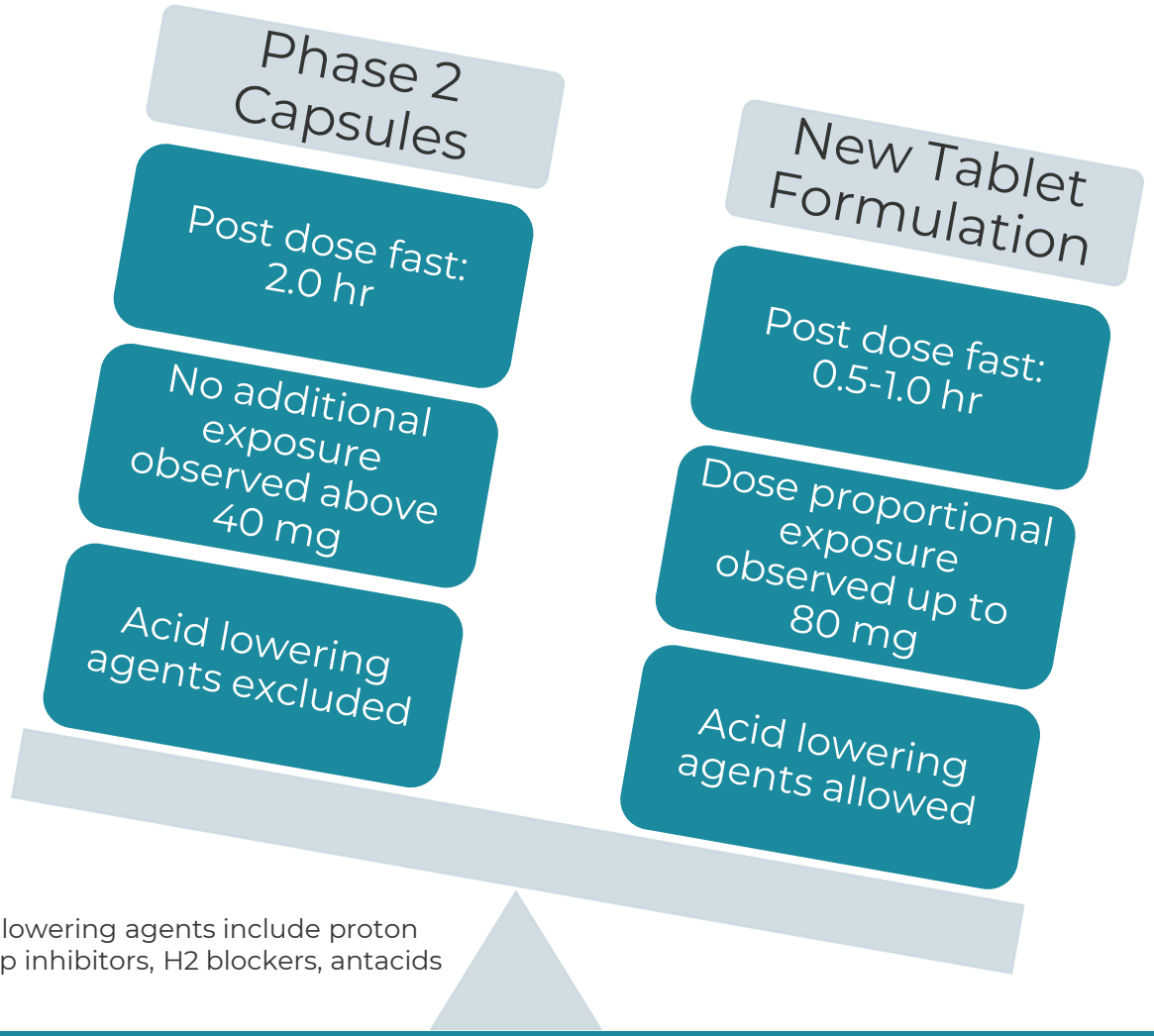


Magnitude of Paltusotine Activity: Change in IGF-1 from Steady State to 4 Weeks After Withdrawal



Post-hoc analysis of data from EDGE primary analysis population and EVOLVE patients
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 New Tablet Formulation Incorporates Multiple Improvements



Acid lowering agents include proton pump inhibitors, H2 blockers, antacids

New tablet formulation to be used in Phase 3 (and commercially, if approved)

Expected ambient shipping and storage

Data to be presented at ENDO (March 20-23, 2021)

Recent and Anticipated Paltusotine Milestones

1. New tablet formulation
   (ready for phase 3) ✓
2. End of Phase 2 meeting with the FDA
   (anticipated in 1Q 2021)
3. Initiation of Phase 3 acromegaly program
   (planned for 1H 2021)
4. Initiation of NETs trial in carcinoid syndrome
   (planned for 2021)

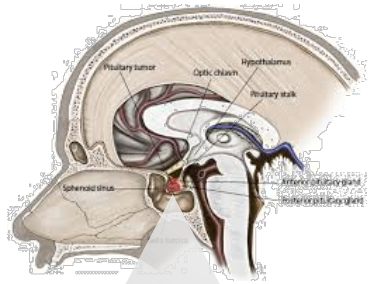
CRN04894: AN INVESTIGATIONAL, POTENTIAL FIRST-IN-CLASS, ORAL NONPEPTIDE ACTH ANTAGONIST

Congenital adrenal hyperplasia (CAH)

Cushing’s disease (CD)

Other conditions of ACTH excess

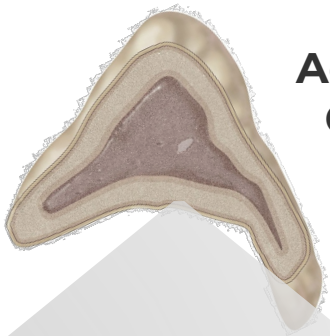
The Hypothalamic-Pituitary-Adrenal (HPA) Axis is the Body's Emergency Response System for Stress

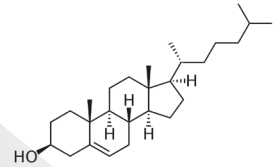


Stress

Adrenocorticotrophic hormone (ACTH)
is secreted by pituitary and acts at MC2 receptor on adrenal

Adrenal Gland





cholesterol

Hypothalamus

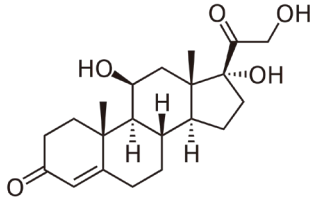
CRF

Optic Chiasma

Pituitary

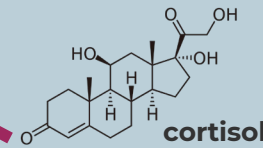
AVP

Cortisol



MC2/MRAP

Adrenal Cortical Cell



cortisol

21-hydroxylase

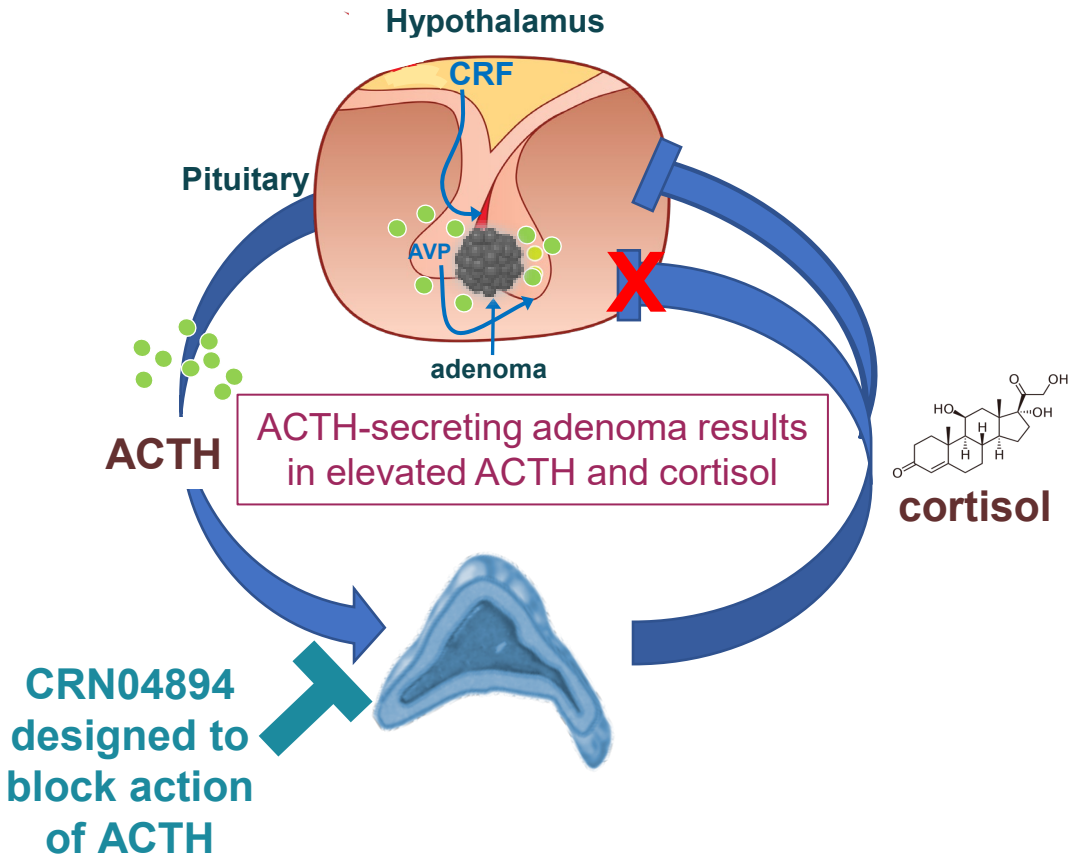
Adrenal Androgens (17-OHP, A_4)

mutated in CAH

(1) provides negative feedback to pituitary
(2) acts at peripheral target tissues (Glucocorticoid Receptor)

CRN04894, an ACTH Antagonist Designed to Treat Cushing's Disease at the Source

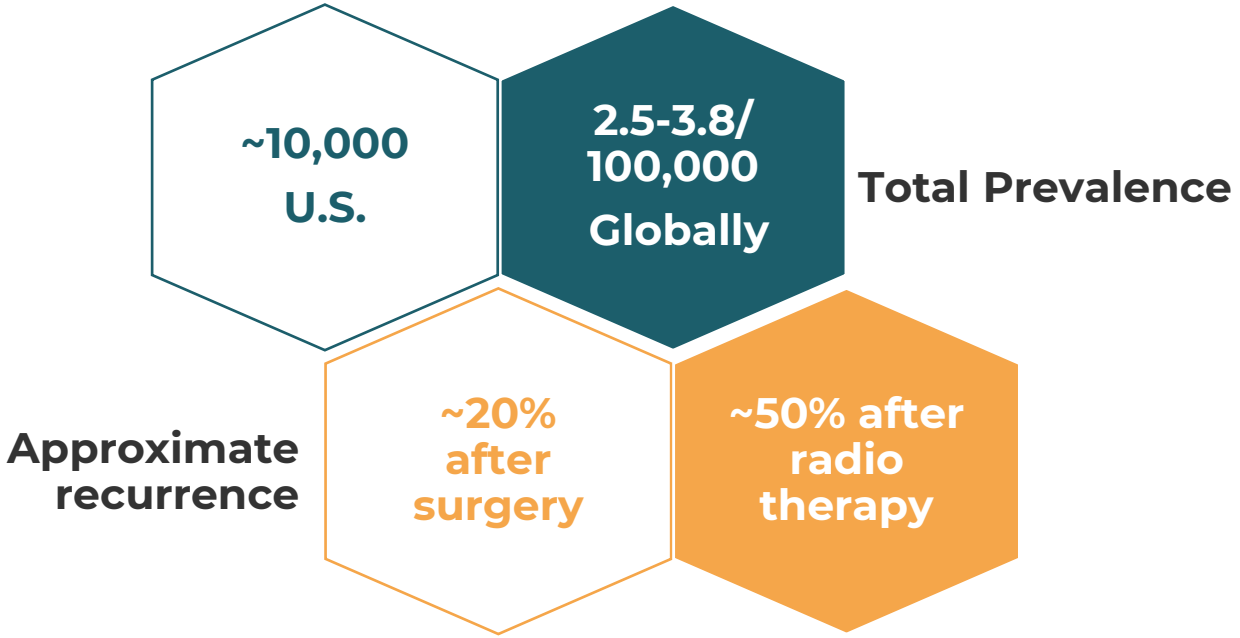
Cushing's Disease



Excess ACTH in Cushing's Disease patients results in:

1. Central obesity and round face
2. Dorsal and supraclavicular fat pads
3. Hypertension; Stretch marks; Bone loss; Hyperglycemia
4. Psychiatric disturbances

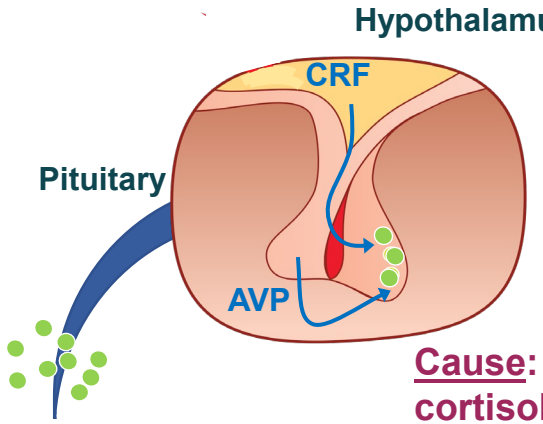
Biomarkers: Elevated ACTH, elevated Cortisol



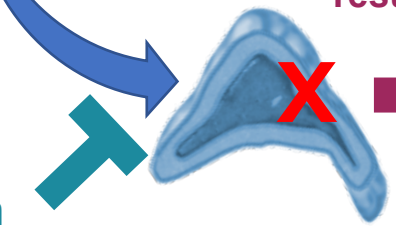
Korlym (2nd line Glucocorticoid Receptor antagonist) anticipated 2020 revenue = $355-365M

CRN04894, an ACTH Antagonist Designed to Provide Predictable Steroid Administration for CAH Patients

Congenital Adrenal Hyperplasia



Cause: Inability to produce cortisol due to genetic defect leads to loss of negative feedback to the pituitary, resulting in excess ACTH



CRN04894 designed to block action of ACTH

Effect: Elevated Androgens; Deficient Cortisol

27,000 U.S.

6.7-10/ 100,000 Globally

Total Prevalence of Classic CAH

No approved treatments

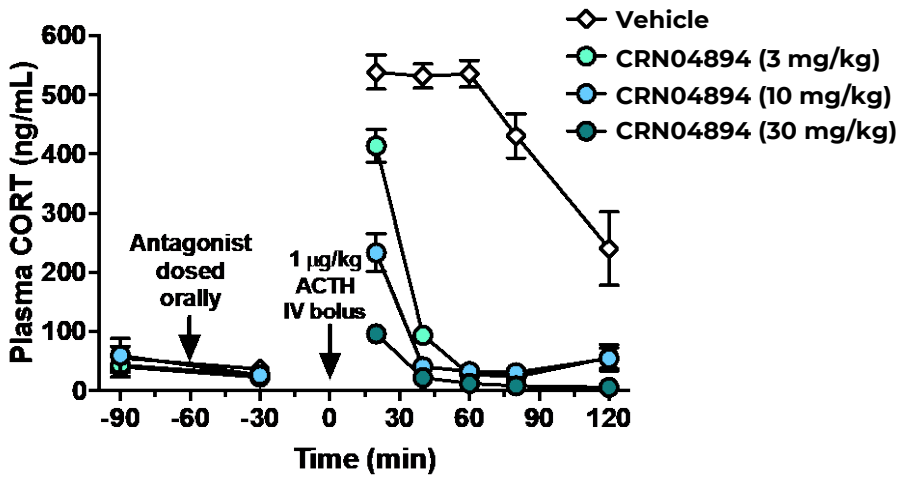
0

Current Therapies: Limitations and High Burden

Balancing glucocorticoid replacement and adrenal hormone suppression requires continuous oversight

CRN04894 Showed Activity in Preclinical Models

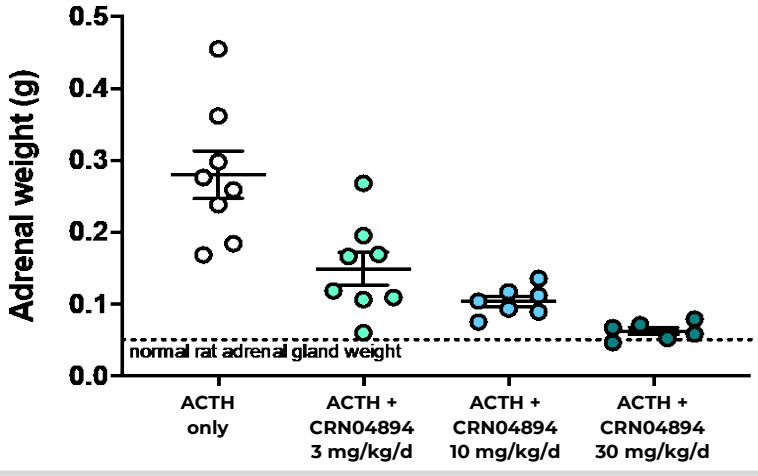
Acute suppression of ACTH-induced corticosterone observed in rats

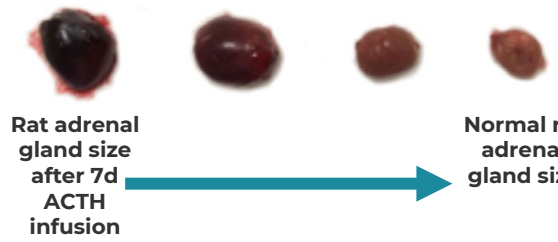


Experiment designed to mimic disease:

- CRN04894 orally administered
- Administer IV bolus of ACTH after 60 minutes
- Marked suppression of ACTH with increasing doses of CRN04894
- Analogous ACTH challenge in Phase 1 POC

Repeat CRN04894 dosing (7d) prevented adrenal hypertrophy from chronic ACTH infusion





Rat adrenal glands from analogous experiment with another Crinetics ACTH antagonist candidate. Photographs from CRN04894 experiment not taken.

Preclinical characterization of CRN04894 selected for oral presentation at ENDO (March 20-23, 2021)

CRN04894 Phase 1 Study Designed to Evaluate Clinical Proof-of-Concept

U.S. IND open

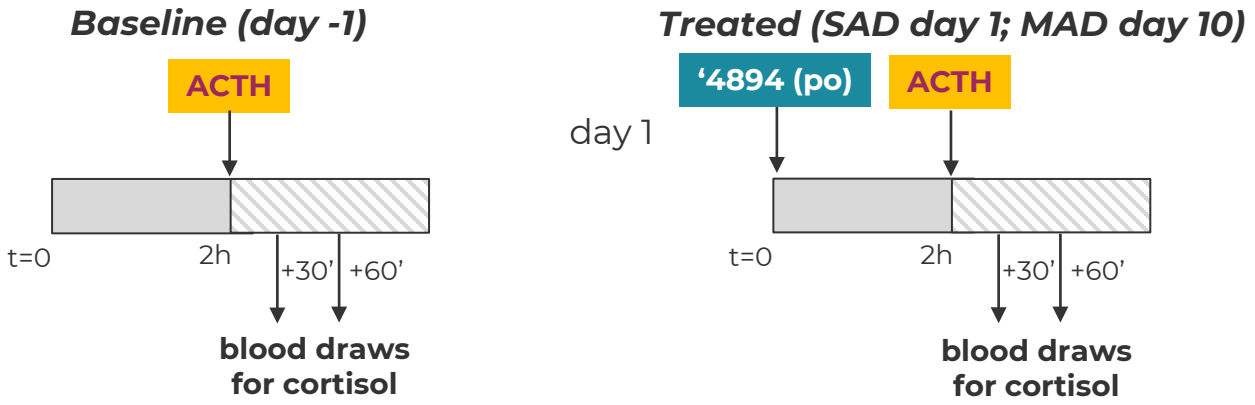
SAD (N=8/cohort)

- Starting dose 10 mg
- **Design: Administer ACTH with and without CRN04894**
- **Key Endpoint: ACTH stimulated peak cortisol day 1 vs. baseline (± CRN04894)**
- Additional Efficacy Endpoints:
  - Basal and ACTH stimulated 17-OHP, androstenedione, DHEA, aldosterone
- Safety/PK

MAD (N=9/cohort)

- **Design: Administer ACTH with and without CRN04894**
- **Key Endpoints:**
  - **Basal (8 am) cortisol Day 10 vs. baseline**
  - **ACTH stimulated peak cortisol Day 10 vs. baseline**
- Safety/PK

ACTH Challenge Test



Proof-of-Concept: Dose dependent suppression of ACTH-stimulated peak cortisol with CRN04894 vs baseline

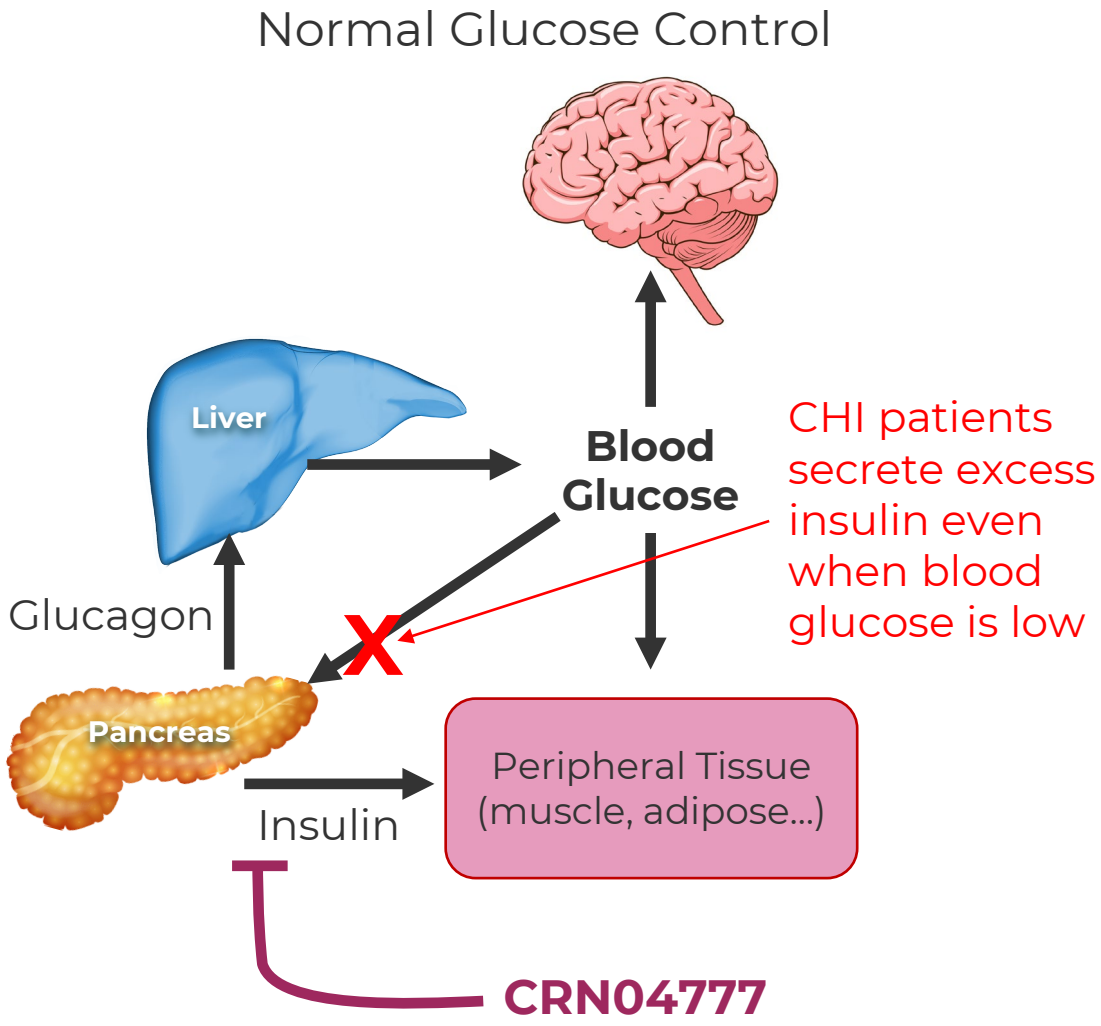
Recent and Anticipated CRN04894 Milestones

1. Open US IND ✓
   (complete)
2. Initiate Phase 1 FIH healthy volunteer POC study
3. Report Phase 1 SAD data
   (expected 1H 2021)
4. Report Phase 1 MAD data
   (expected 2H 2021)

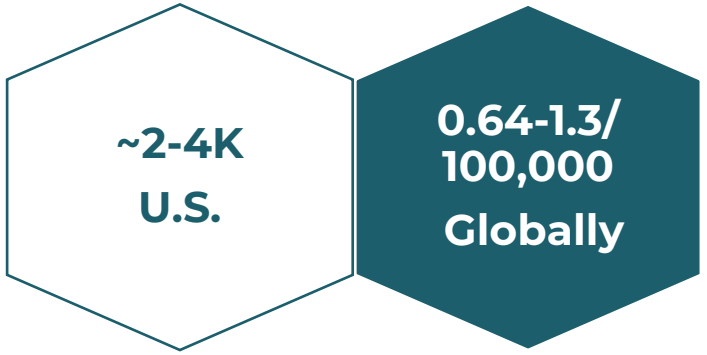
CRN04777: AN INVESTIGATIONAL, POTENTIAL FIRST-IN-CLASS, ORAL NONPEPTIDE SST5 AGONIST

Congenital hyperinsulinism (CHI)

Inappropriate Insulin Secretion Causes Life Threatening Recurrent Hypoglycemia in CHI



Congenital Hyperinsulinism



- Genetic defect results in excess insulin secretion when blood glucose is low
- Excess insulin causes hypoglycemia
- Untreated hypoglycemia can result in neurodevelopment disorders and death
- Early identification and intensive glucose management are critical

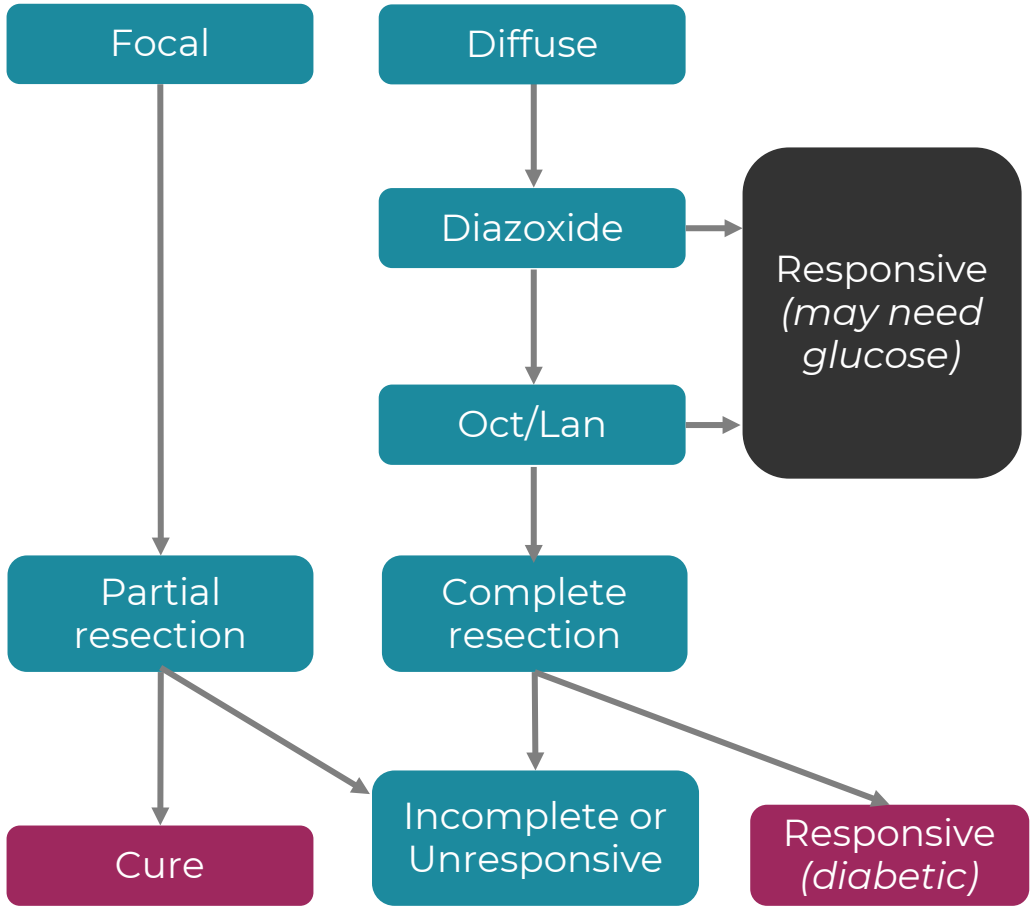
Robust global patient advocacy

- Congenital Hyperinsulinism International (www.congenitalhi.org)

Excruciating Unmet Medical Needs in CHI

Intensive 24h-glucose management (monitoring, feeding, glucose tube)

Current Standard of Care for CHI



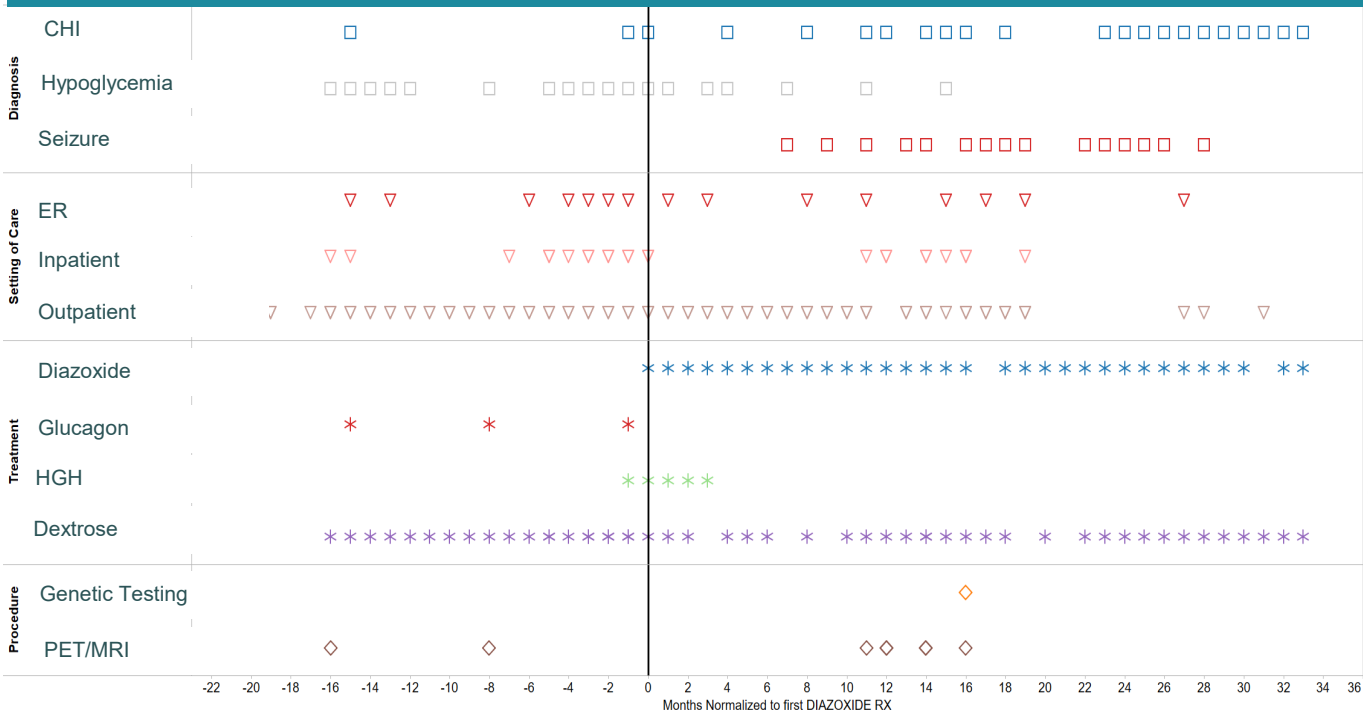
Patient & Parent Goals

- ✓ Put child to bed knowing they will wake up in the morning
- ✓ Avoid neurological damage
- ✓ Eliminate the glucose tube and backpack
- ✓ Reduce injections and glucose sticks
- ✓ Avoid pancreatectomy
- ✓ Medical management until HI resolves
- ✓ Be a kid not a patient

CHI Patient Care is a High Burden on Healthcare Systems

Healthcare utilization by a baby girl with CHI

Born 2014, Original CHI diagnosis 12/2014, First Diazoxide Tx 3/16[1]



Each shape and associated time stamp represents a medical claim over 5 years

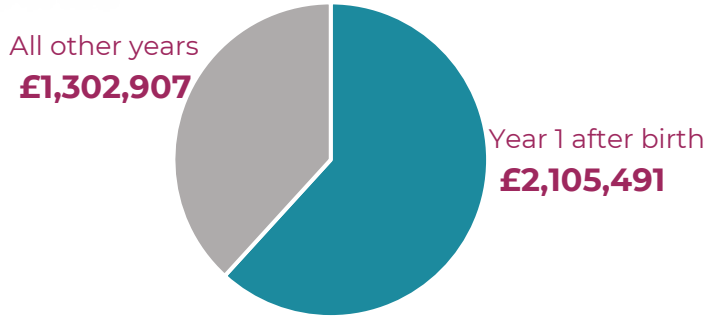
Current Challenges

- Variable time to diagnosis
- Constant dextrose infusion to maintain normal blood sugar levels
- Surgical removal of all or part of the pancreas – *Or*
- No surgical options
- Ineffective diazoxide treatment with multiple untoward effects

As a result:

- Hypoglycemic crises warranting repeat need for emergency services (can include seizure, loss of consciousness and death)
- Frequent and multi-day inpatient hospital stays
- Long-term consequences including neurodevelopmental impairment

Cost of Illness Estimate from the UK[2], £ 3,408,398 ($4,630,939): first 11 years of life

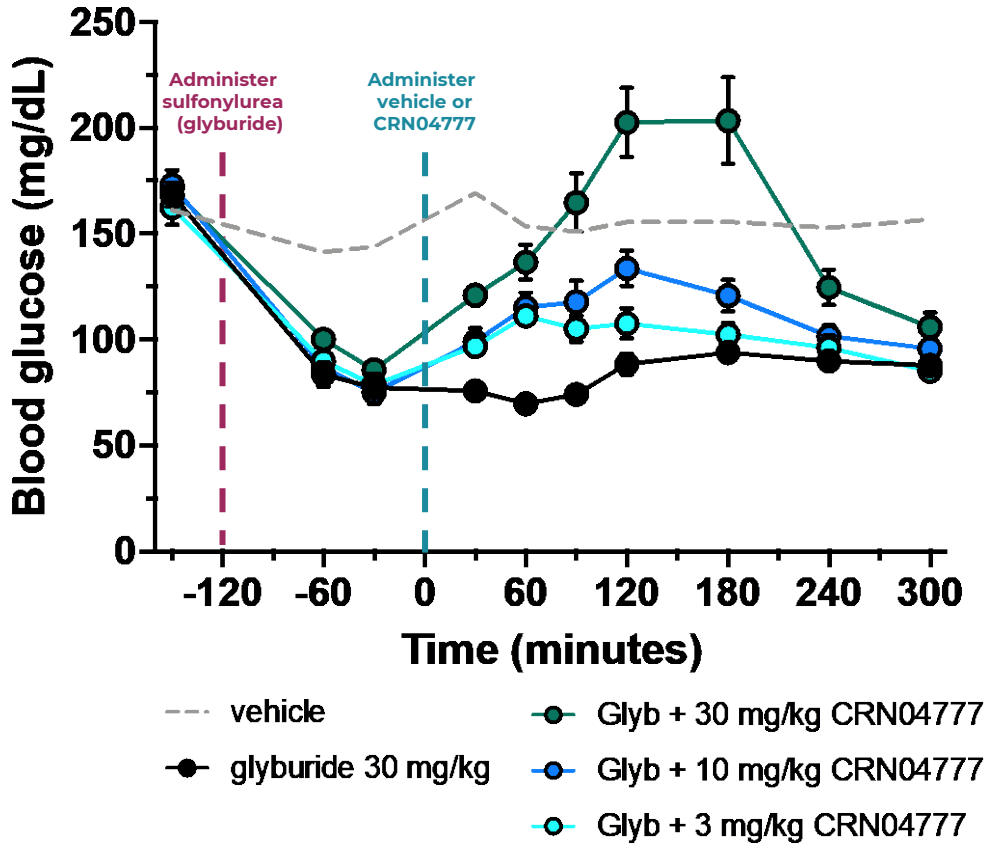


Patients unresponsive to first-line drug therapy (diazoxide) represented the greatest driver of costs

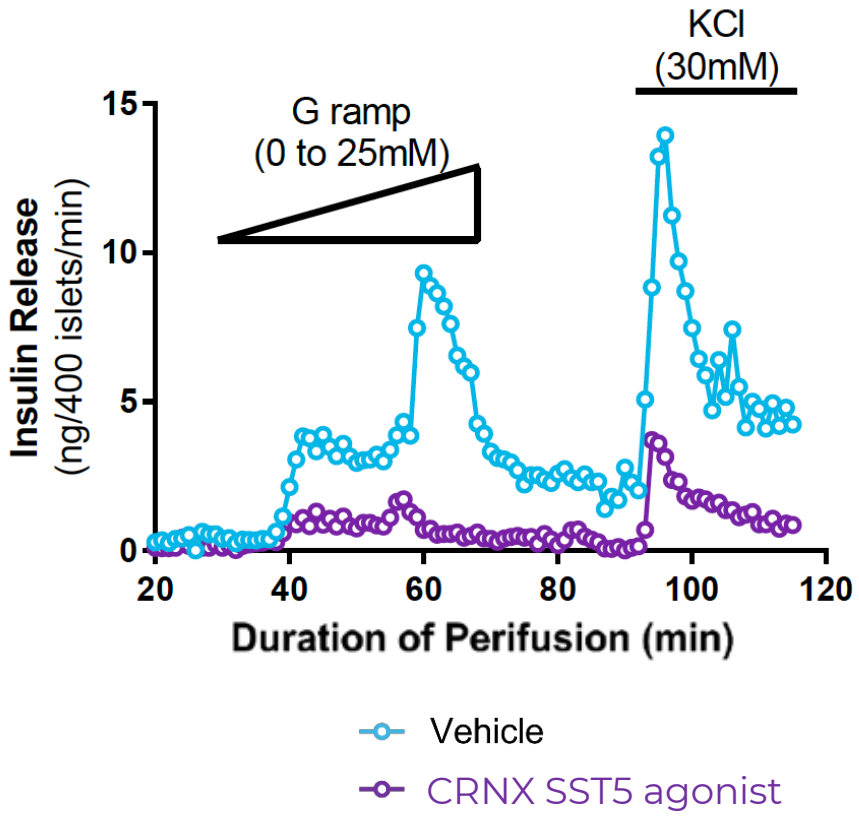
1. Claims data on file, 2013-2018 2. Eljamel, S et al The burden of congenital hyperinsulinism in the United Kingdom: a cost of illness study 2018

Proof of Mechanism Achieved in Animal Models and Patient Islets

CRN04777 rescued sulfonylurea-induced hypoglycemia in rats



CRNX SST5 agonist suppressed insulin from islets isolated from patient with Beckwith-Wiedemann Syndrome



Islet data was obtained using another Crinetics SST5 agonist candidate before CRN04777 had been selected for development

CRN04777 Phase 1 Study Designed to Evaluate Clinical Proof-of-Concept

SAD (3 parts)

SAD 1a (n=8/cohort, up to 6 cohorts)

- **IVGTT**: Measure plasma glucose, insulin, C-peptide AUC Day 1 vs baseline
- Measure fasting plasma glucose, insulin, C-peptide vs baseline

SAD 1b (n=8/cohort, 2 cohorts)

- **Sulfonylurea challenge using Glucose Clamp** Measure GIR, plasma glucose, and C-peptide during euglycemic Day 1 vs baseline

SAD 1c (n=6/cohort, 1 cohort)

- Food effect

Safety/PK

MAD (n=9/cohort, up to 5 cohorts)

Key Endpoints:

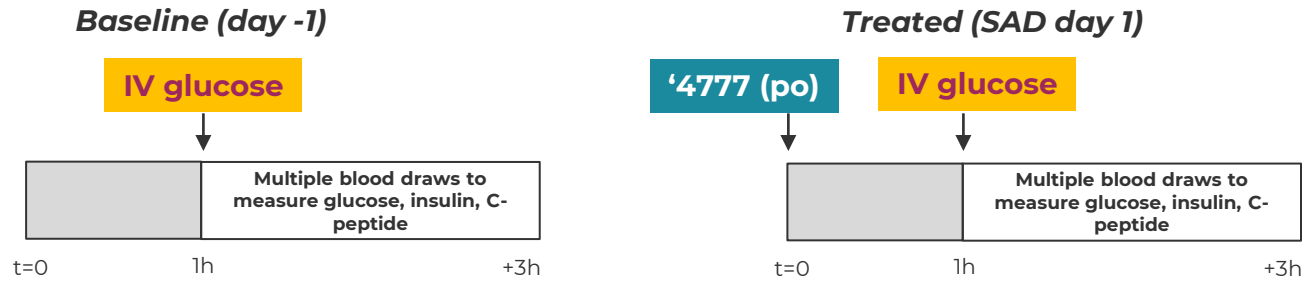
- **Sulfonylurea challenge using Glucose Clamp** Measure: GIR, plasma glucose, and C-peptide during euglycemic Day 1 vs baseline
- Mixed Meal Test: Measure plasma glucose, insulin, C-peptide, GLP-1 AUC Day 1 vs baseline

Safety/PK

Abbreviations: GIR: glucose infusion rate; SU: Sulfonylurea

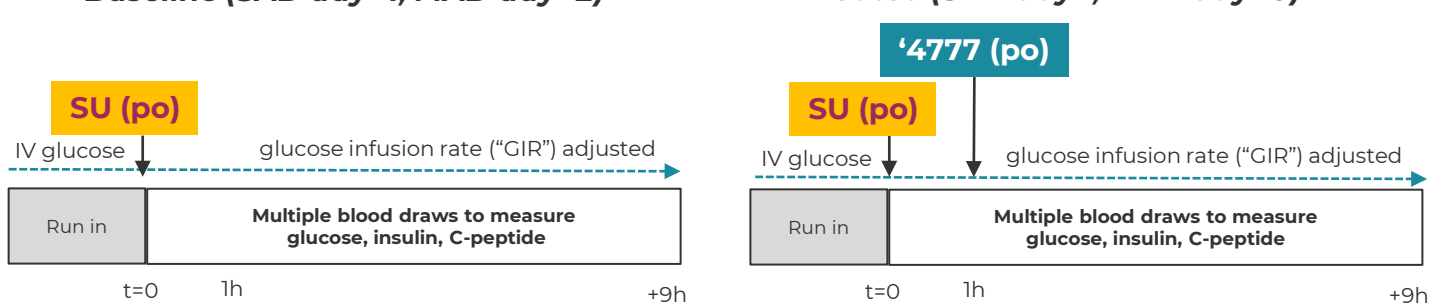
IV Glucose Tolerance Test (IVGTT)

Proof-of-Concept: Dose dependent suppression of glucose-stimulated insulin secretion with CRN04777 vs baseline



Sulfonylurea (SU) Challenge Test Using Glucose Clamp

Proof-of-Concept: Dose dependent suppression of sulfonylurea-stimulated insulin secretion with CRN04777 vs baseline



Recent and Anticipated CRN04777 Milestones

1. US Rare Pediatric Disease and EU Orphan Drug Designations ✓
   (received; CRNX may be eligible for priority review voucher in the US)
2. Initiate Phase 1 FIH healthy volunteer POC study
3. Report Phase 1 SAD data
   (expected mid-2021)
4. Report Phase 1 MAD data
   (expected 2H 2021)
5. Potential to Advance from Phase 1 directly into a Phase 2/3 study
   (anticipated in 2022)

2020 Accomplishments and Anticipated 2021-2022 Milestones

2020 Accomplishments	2021 Anticipated Milestones	2022 Goals
✓ Positive paltusotine acromegaly Phase 2 data	CRN04894 SAD POC data in 1H21	Paltusotine Phase 3 enrollment complete for acromegaly
✓ Improved paltusotine tablet formulation	CRN04777 SAD POC data in mid-2021	CRN04777 Phase 2/3 start
✓ CRN04894 (ACTH antagonist) IND open for FIH study	Paltusotine acromegaly Phase 3 start (1H21)	CRN04894 Phase 2 start
✓ CRN04777 (SST5 agonist) regulatory approval for FIH study in Germany	Paltusotine NETs program start (2021)	New Preclinical Candidates • Hyperparathyroidism • Nonfunctional pituitary adenomas • Polycystic kidney disease • Other