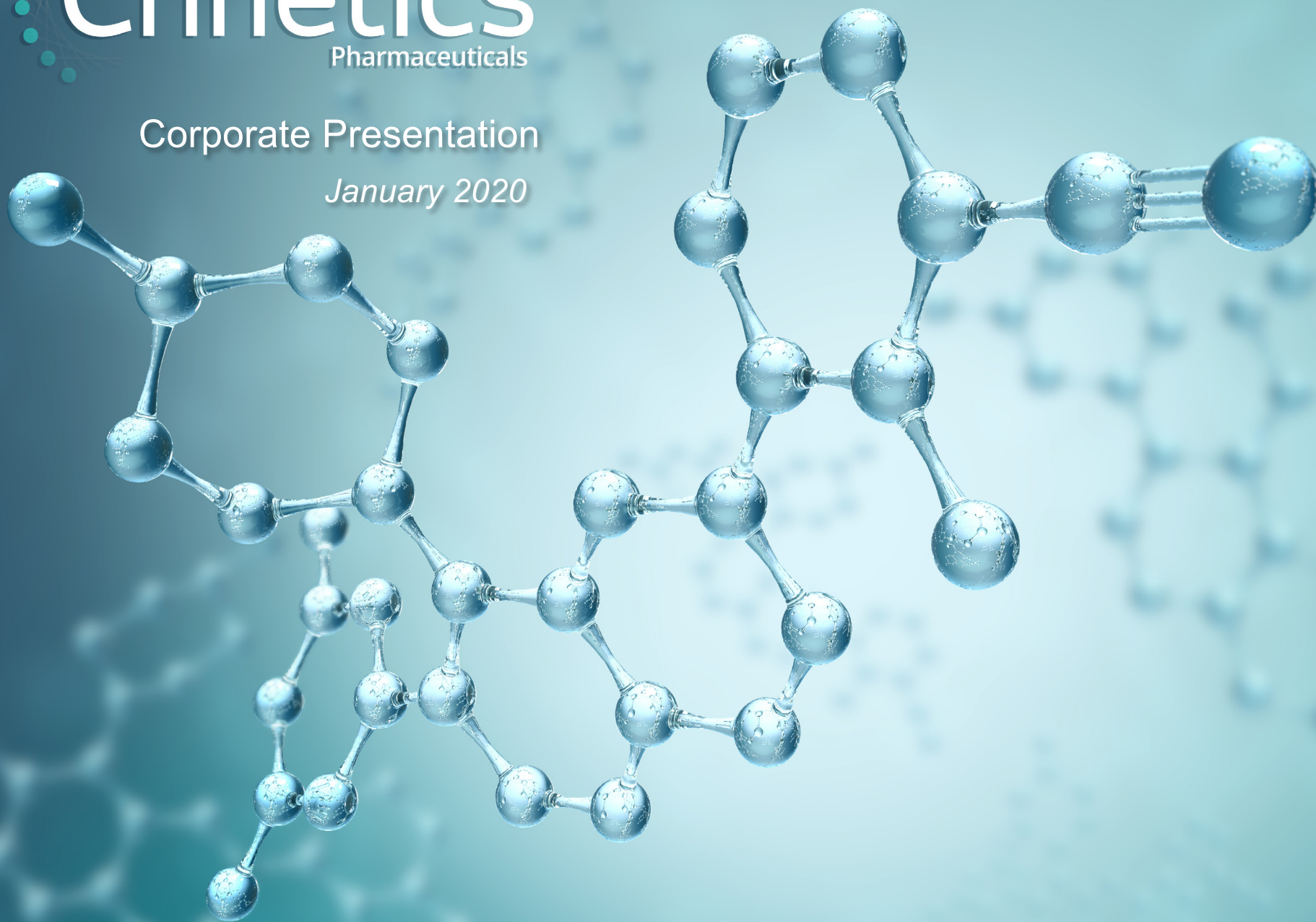




Corporate Presentation

January 2020



Safe harbor statement

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations, and future results of current and anticipated products, are forward-looking statements. 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. These known risks and uncertainties are described in detail in our filings made with the Securities and Exchange Commission from time to time. 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.

OUR VISION

To build the leading endocrine company that consistently pioneers new therapeutics to help patients better control their disease and improve their daily lives



Our strategy: Discover, develop and commercialize across multiple rare endocrine diseases and endocrine-related tumors

- Ongoing in-house discovery of novel drug-candidates
- Focus on endocrine diseases and related tumors with:
 - High unmet medical need
 - Established biology
 - Biomarker endpoints
 - POC in Phase 1
 - Small registration trials
- Rapidly advance clinical pipeline of multiple drug candidates in parallel
- Retain commercialization rights in core therapeutic areas and regions
- Nurture an entrepreneurial, scientifically rigorous, collaborative and inclusive company culture

The endocrine therapeutic area

Endocrine system:

Pituitary gland

Enteroendocrine cells

Hypothalamus

Pineal gland

Parathyroid glands

Thyroid gland

Thymus

Adrenal glands

Kidneys

Pancreas

Liver

Placenta

Ovaries (in female)

Testes (in male)

Multiple indications:

Acromegaly

Neuroendocrine tumors

Non-funct. pituitary adenomas

GH deficiency

Grave's disease

Hyperparathyroidism

Cushing's disease

Adrenal hyperplasia

Adrenal cancer

Hyperinsulinemia

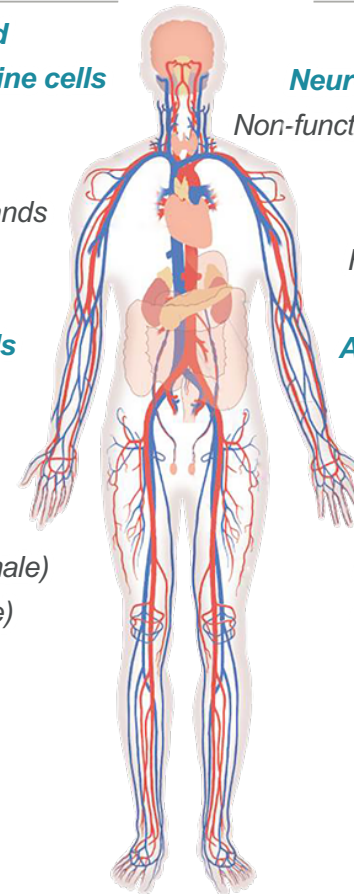
Insulinoma

Thyroid cancer

Hypoparathyroidism

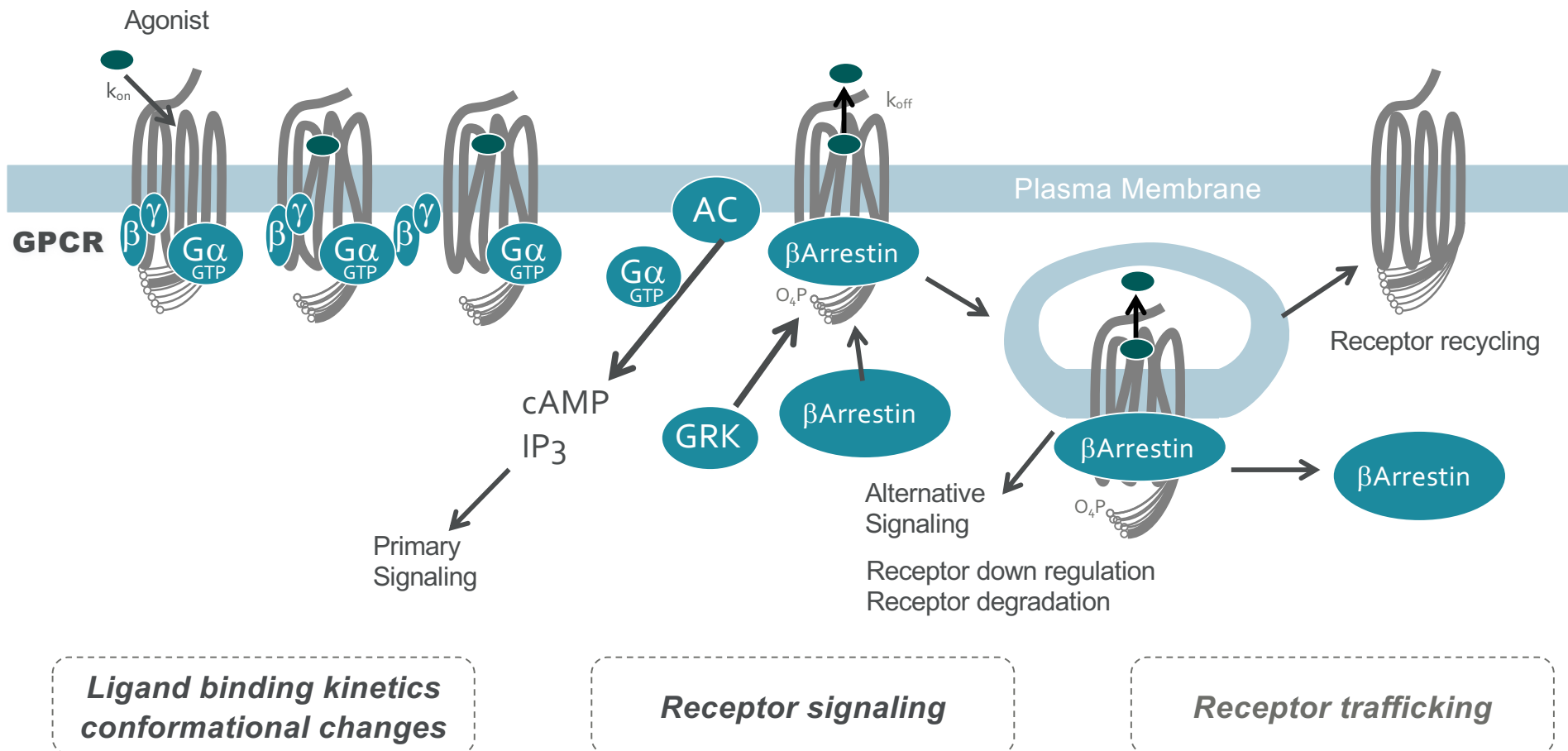
Androgen deficiency

Infertility



Targeting today / Future opportunity

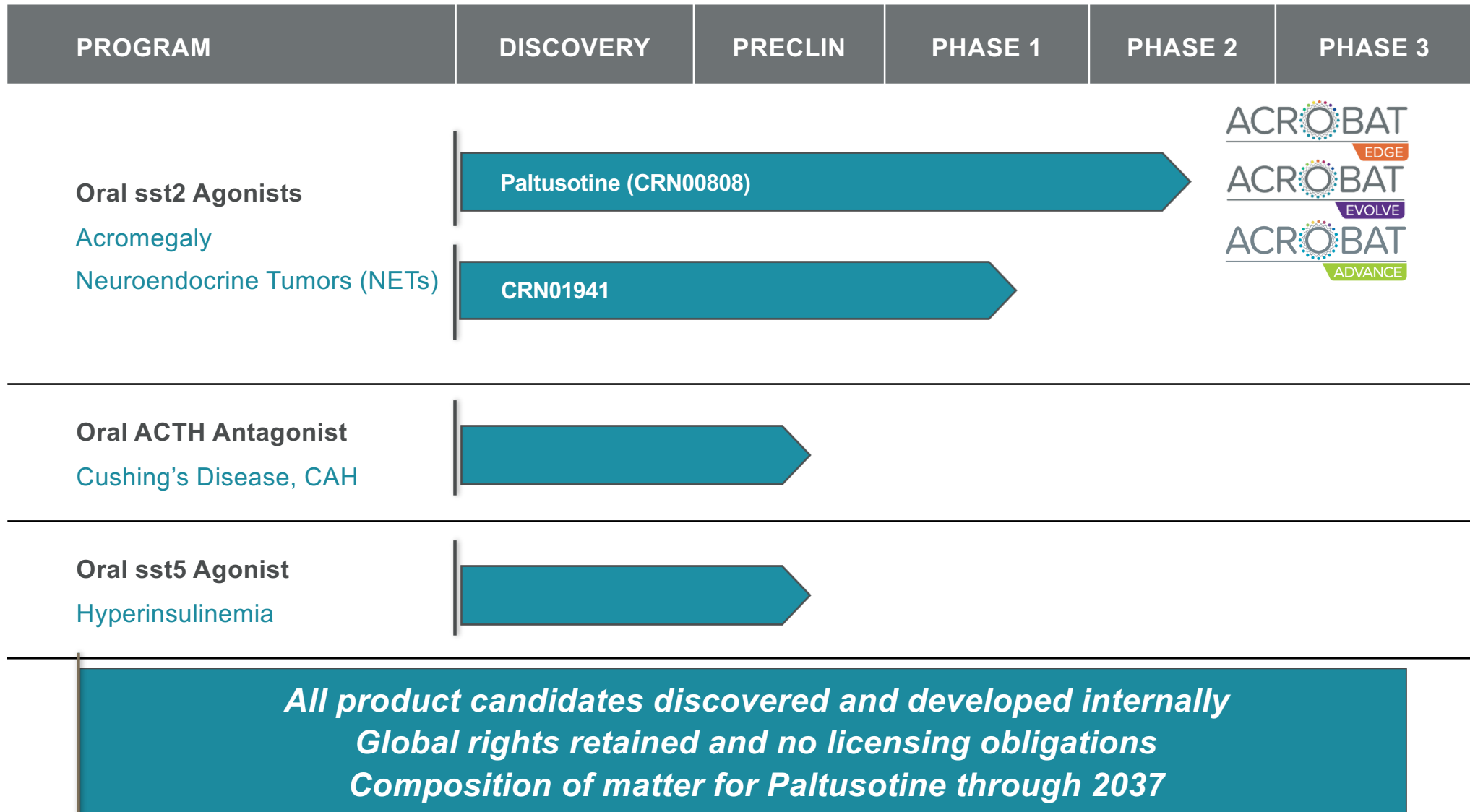
Our approach: Tailor ligands to regulate dynamic GPCR behaviors and ultimately improve patient outcomes

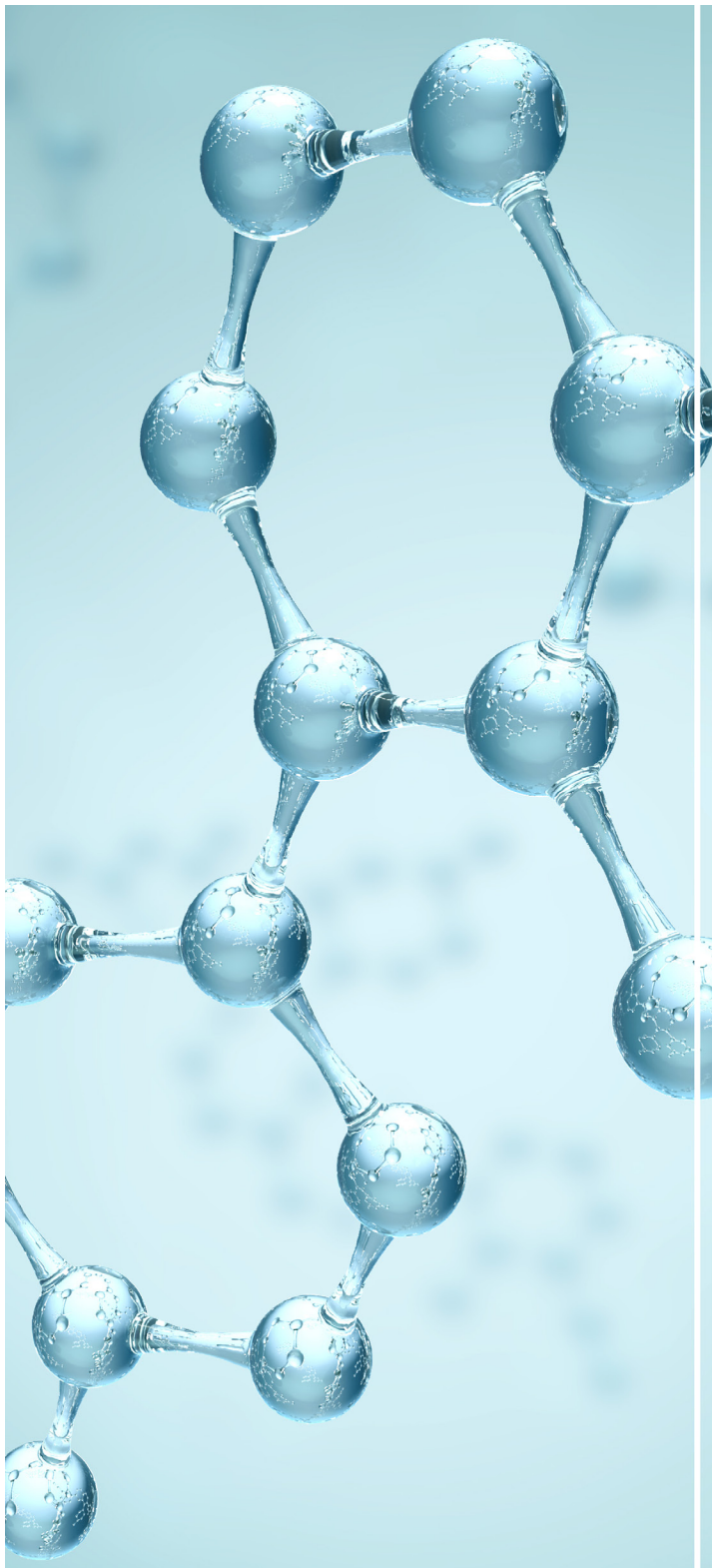


Our understanding of the complex GPCR signaling pathways enables us to develop oral, small molecule, product candidates that modulate GPCR dynamic behaviors

Pipeline

Building a rare disease franchise in endocrinology and endocrine oncology

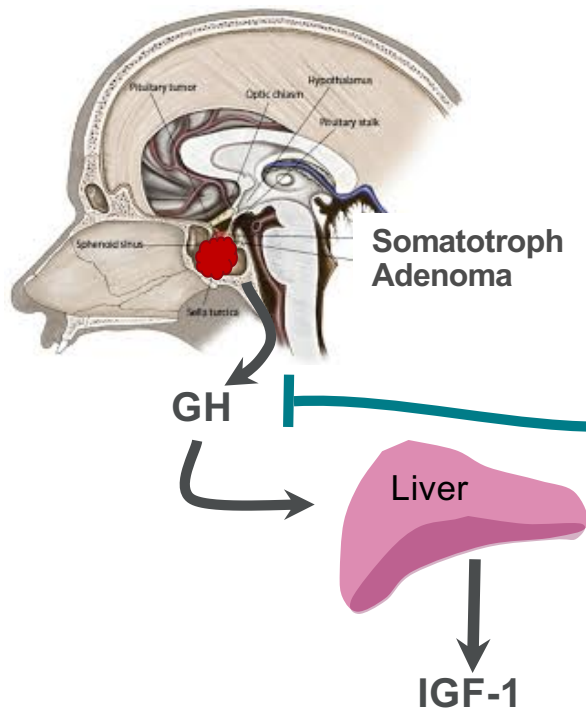




**Nonpeptide sst2 agonists
for the treatment
of acromegaly and
neuroendocrine tumors**

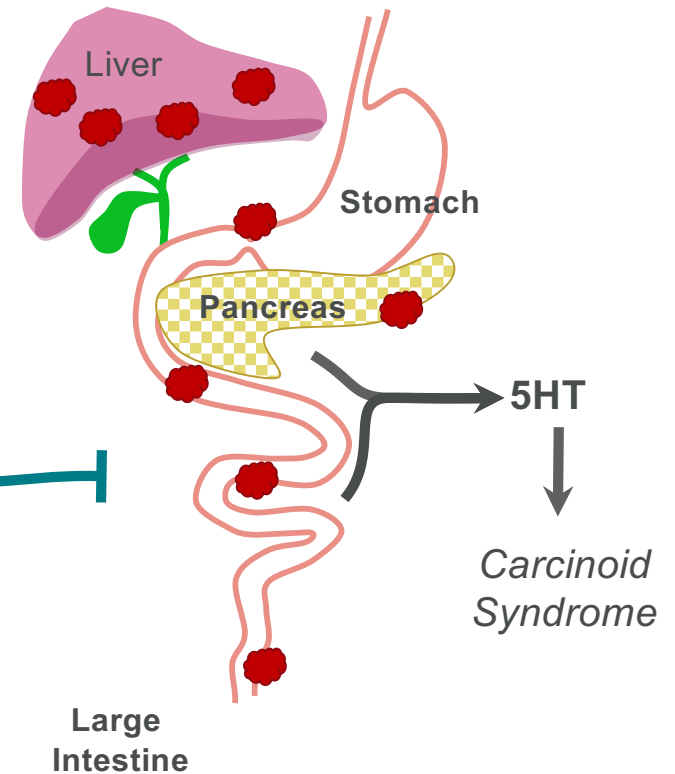
Somatostatin receptor type 2 (sst2) peptide agonists are the standard of care for acromegaly and NETs

Acromegaly



Prevalence: ~25,000 people with acromegaly in the US

Neuroendocrine Tumors (NETs)



Prevalence ~171,000 people with NETs in the US

Established commercial opportunity for injectable somatostatin peptides despite significant limitations

2018: \$2.9 billion in global sales*

High unmet need

Daily injections

- Patients buy a second refrigerator for storage
- Travel is difficult

Painful intramuscular/deep sc injections every month (octreotide, lanreotide)

- Hardness, bruising and swelling at injection site

Inconvenient

- Monthly visits to physician's office interrupts normal life

Limited efficacy

- Many patients do not achieve disease control
- Return of symptoms near end of the month



For most patients, acromegaly is not a solved problem

25-50% of IM injections are unsuccessful

Pancreas. 2013 Jul;42(5):878-82. doi: 10.1097/MPA.0b013e318279d552.

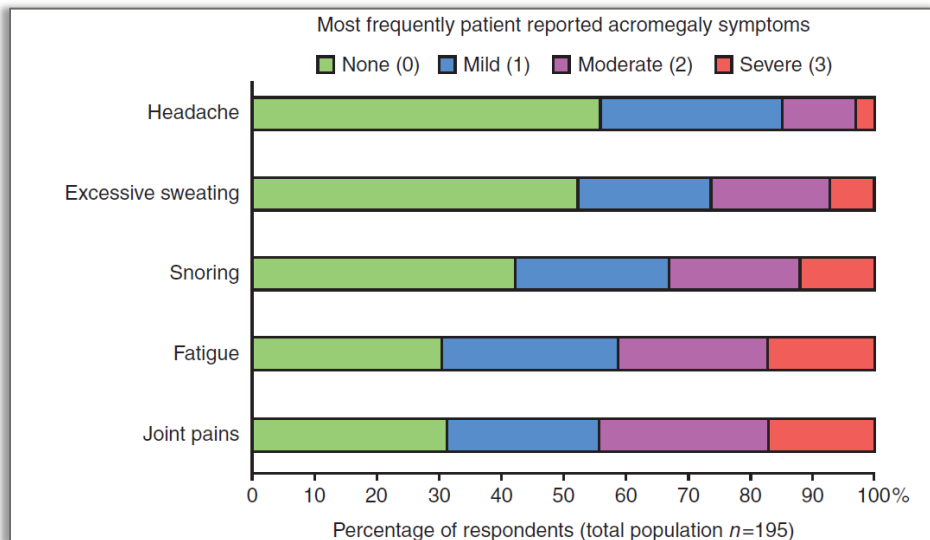
Improving the success rate of gluteal intramuscular injections.

Boyd AE¹, DeFord LL, Mares JE, Leary CC, Garriss JL, Dagohoy CG, Boving VG, Brook JP, Phan A, Yao JC.

Results: At baseline 52% of injections were successfully delivered....

After instruction, the success rate increase from 52 to 75%...
....Successful injection was associated with better control of flushing among those with carcinoid syndrome (P=0.005).

>70% of treated patients have symptoms



What patients are telling us

- “Not a day goes by when I ‘feel good’”
- “Mood disturbances, I would say *<are the most frequent symptom>*. Or inability to find the joy, I guess. You know, I start to have a difficult time processing emotions right before I get my injections.”
- “The doctor didn’t warn me about this.”
- “I had to schedule it [*injection*] sometimes after 3:30 because where I teach and where I was getting the injection was almost 40 minutes away. I had to make an appointment and my principal would let me leave early.”
- “Don’t plan on going someplace the next day because you may end up with diarrhea - I had diarrhea for three solid days. You don’t go anywhere. I got it [*injection*] last night and the hip that she gave it in hurts so bad.”

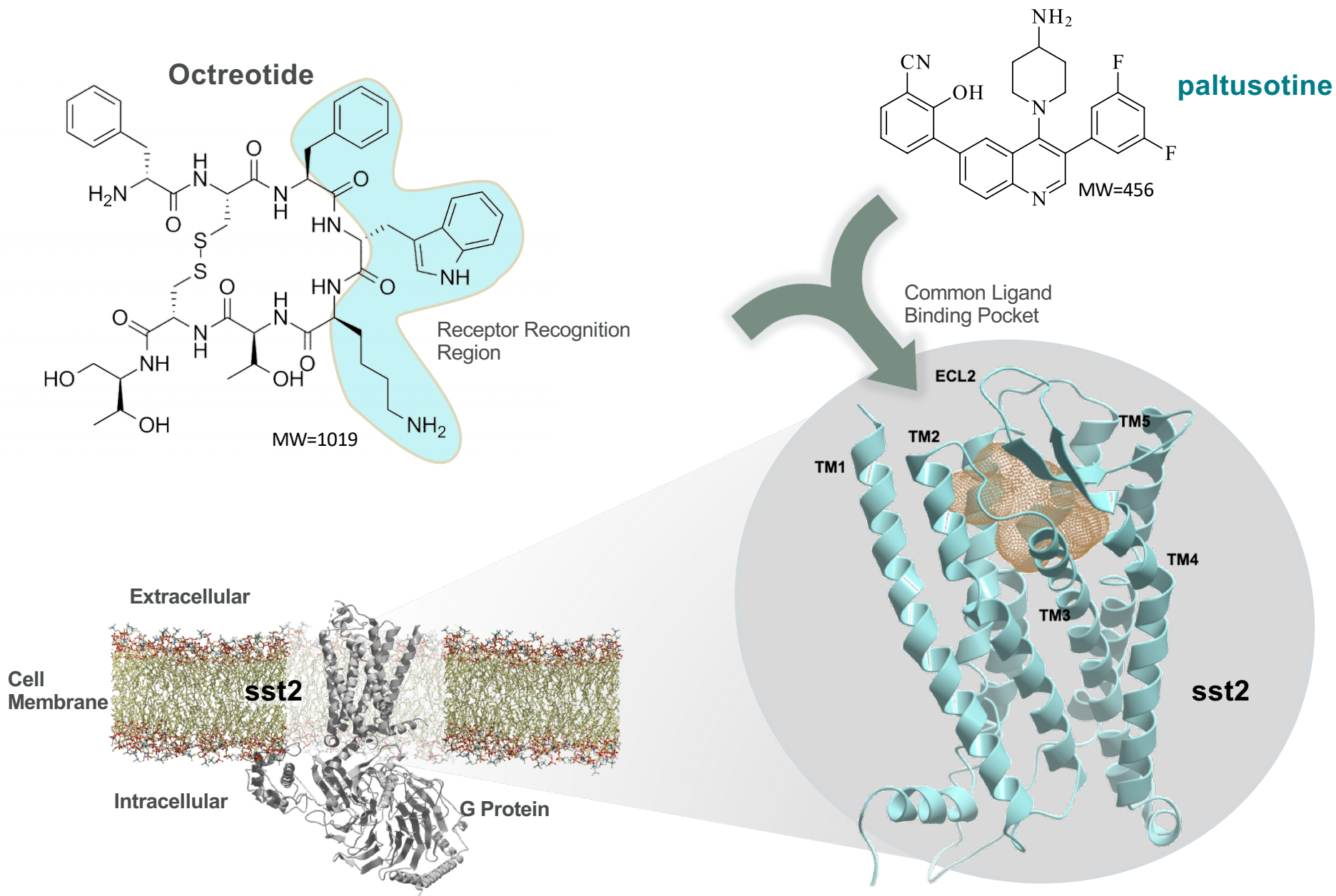
Paltusotine (CRN00808) – Target product candidate profile

- A new class of oral selective nonpeptide sst2 biased agonist designed for the treatment of acromegaly
- First agent in its class with reported clinical results

CHARACTERISTICS	PRIMARY BENEFITS
Orally bioavailable nonpeptide (small molecule)	Lack of injections/pain Administration at home Rapid dose optimization Consistent exposure over time Lower COGS and admin costs
Long half life (42-50 hrs.)	Once daily dosing
Reduced desensitization	Potential improved responder rates
Selectivity for sst2	Glucose control (avoid sst5 mediated hyperglycemia)

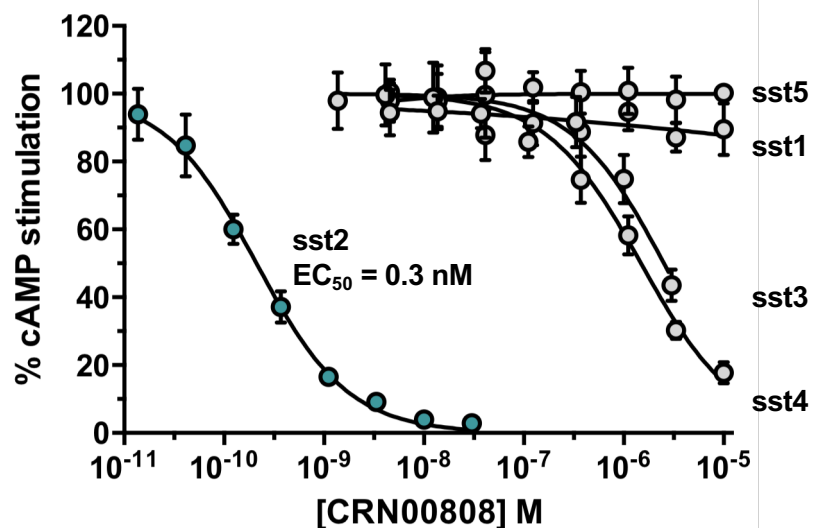
PRODUCT CANDIDATE TAILORED TO DELIVER KEY BENEFITS

Paltusotine (CRN00808) is a first-in-class nonpeptide



Paltusotine (CRN00808) overview

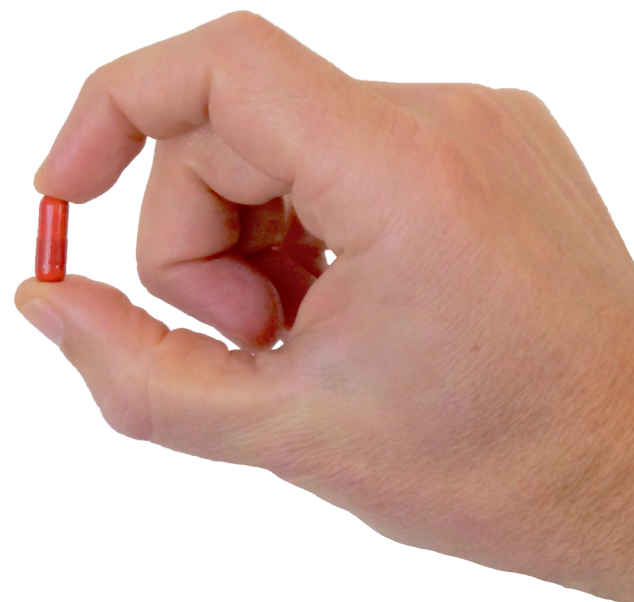
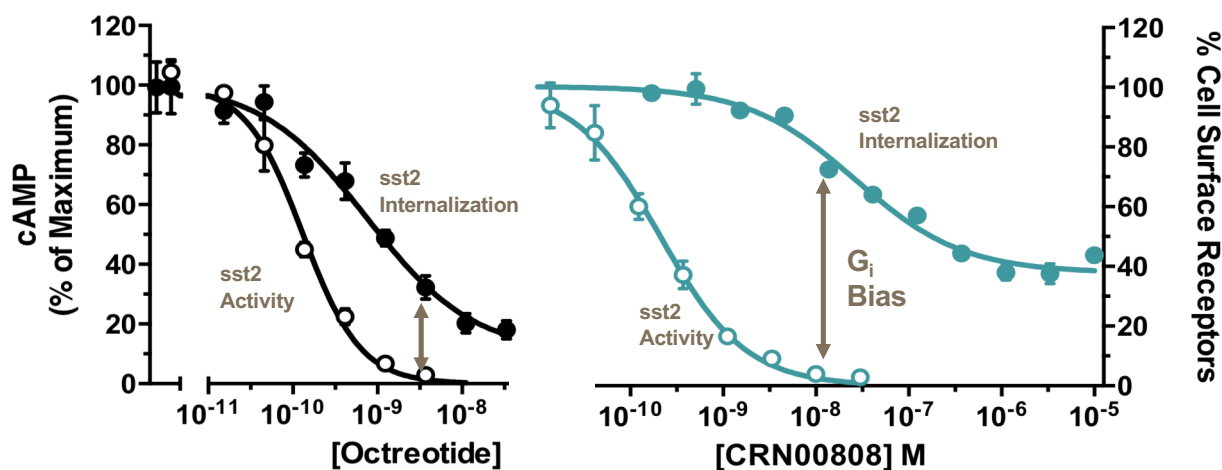
Selectivity for somatostatin receptor subtypes



Good “drug-like” pharmaceutical properties

- ✓ High oral bioavailability (F ~ 70%)
- ✓ Once daily dosing (t_{1/2} ~ 2 days)
- ✓ No drug-drug interactions
- ✓ Efficient API manufacturing
- ✓ Chronic toxicology studies complete (no DLT)

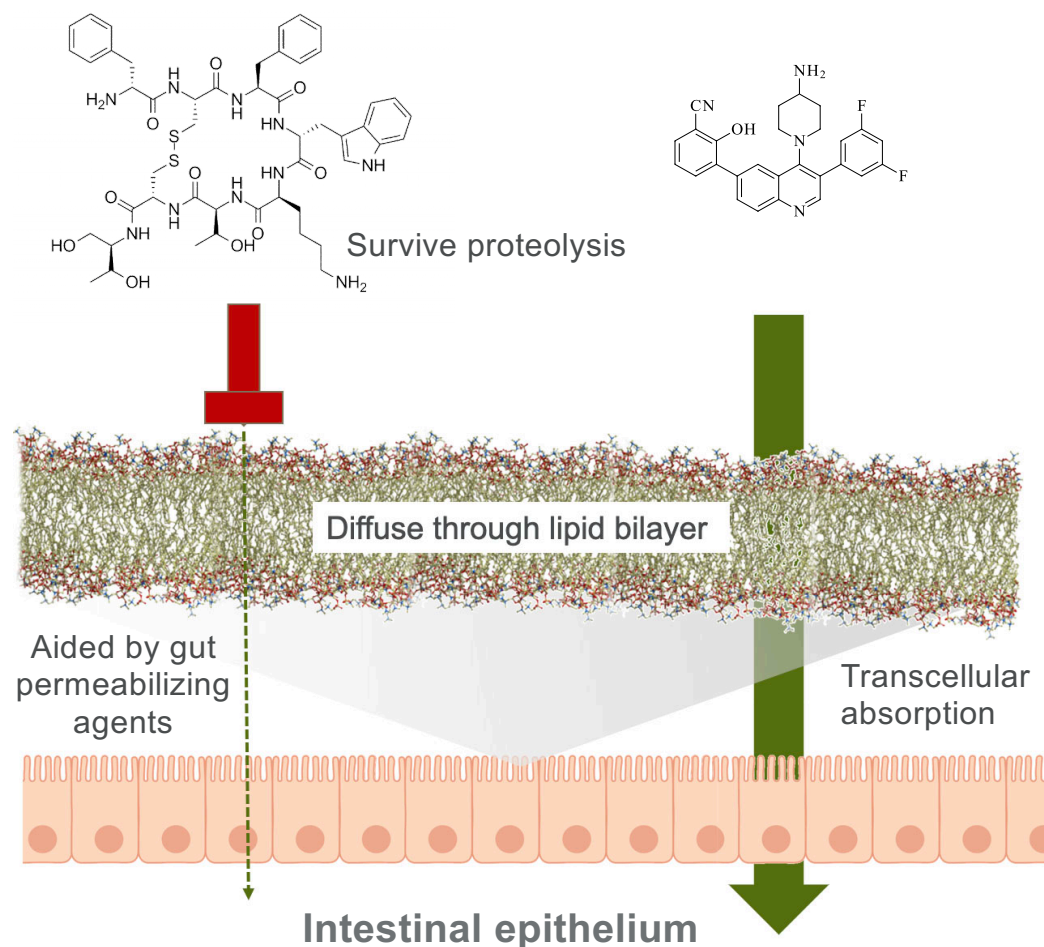
Agonist bias for G_i signaling over internalization



Paltusotine is intrinsically gut permeable just like other traditional oral small molecule drugs

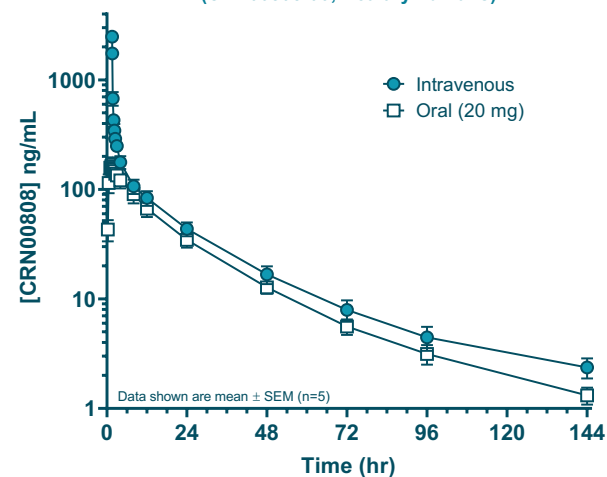
Peptide: Octreotide

Nonpeptide: Paltusotine






Oral Bioavailability 70%

(CRN00808-06; Healthy humans)



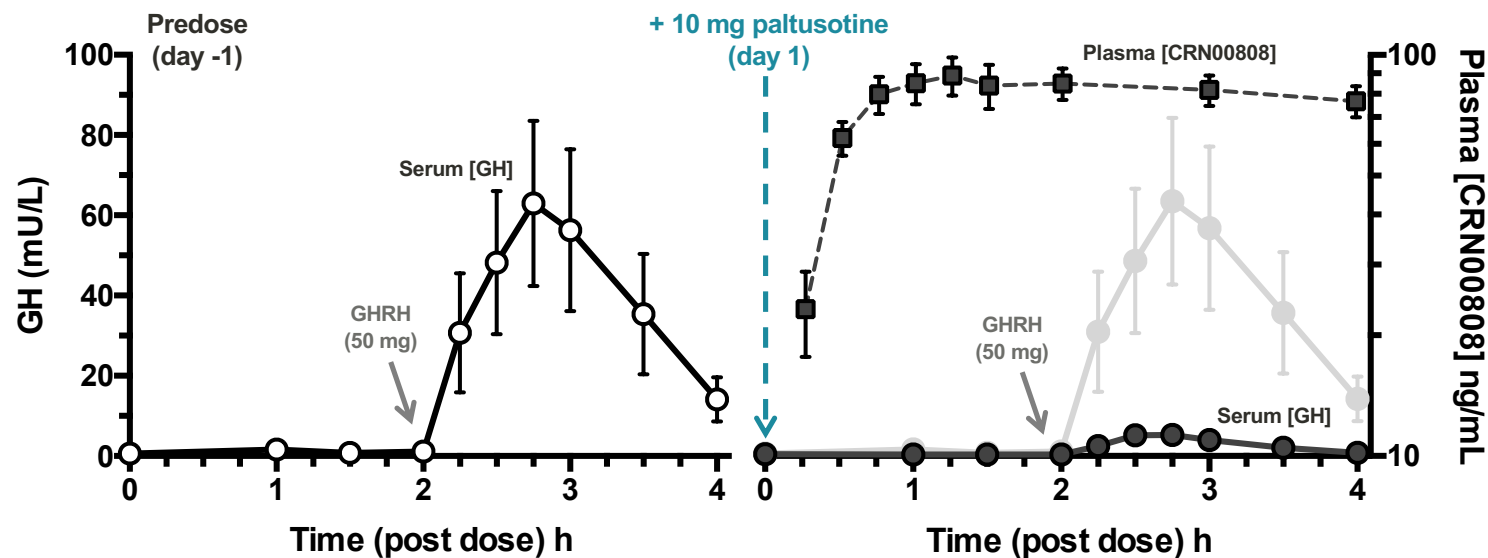
	Paltusotine (CRN00808)	Mycapssa® Tuvia et al., 2012
Estimated Oral Bioavailability	70%	~0.5%
Half Life	42-50 hr	2.4 hr

Acromegaly clinical development strategy: core studies so far

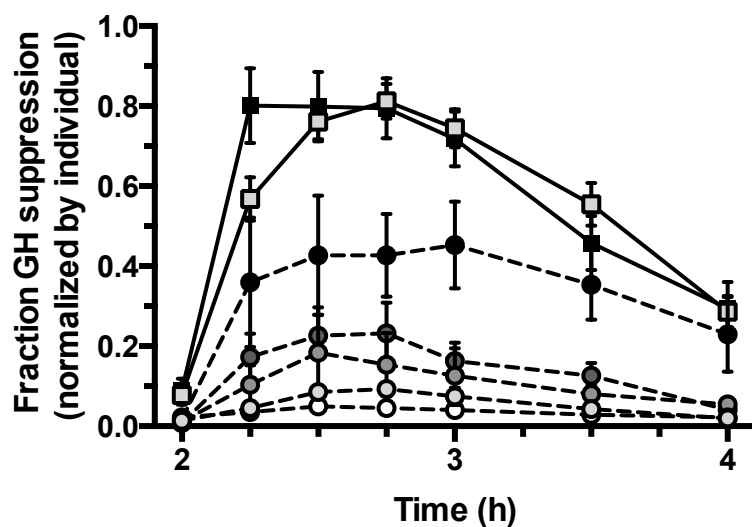
Study	Population	Goals	Success
Phase 1 FIM	Healthy Volunteers	Proof-of-concept Define PK/PD Preliminary safety	QD dosing GH/IGF suppression = peptide SSAs
	Patients not fully controlled on oct/lan monotherapy (>65% of patients)	Can patients switch to oral and maintain IGF control? Demonstrate efficacy vs washout	IGF control on oral = peptide SSAs Treated IGF < washout IGF
	Patients fully controlled on oct/lan monotherapy (20-30% of patients)	Can patients switch to oral and maintain IGF control? Demonstrate efficacy vs randomized withdrawal	Responder rate > pbo
	EDGE & EVOLVE patients + SSA naïve patients	Long-term patient experience for NDA submission Experience in newly diagnosed patients	Durable safety and IGF suppression

Phase 1 SAD arm: PK/PD analysis

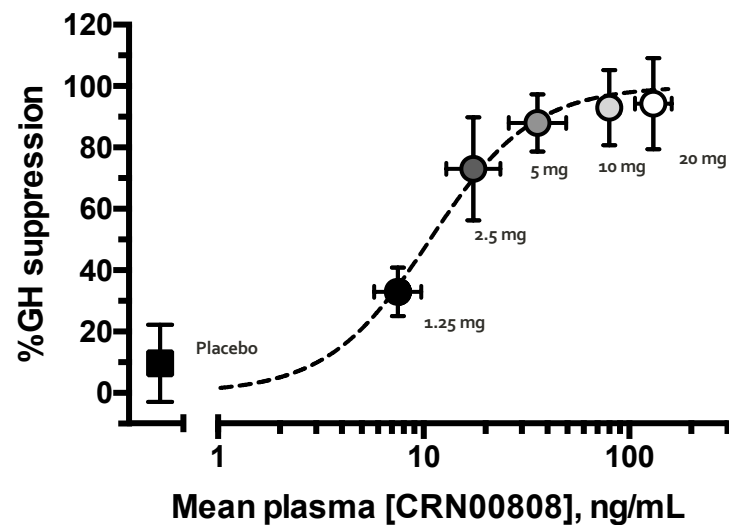
Suppression of GHRH stimulated GH secretion by 10 mg of paltusotine



Dose response of GH suppression

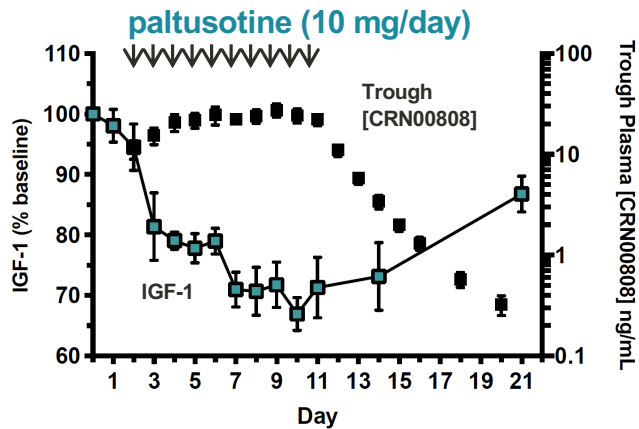


Exposure response of GH suppression

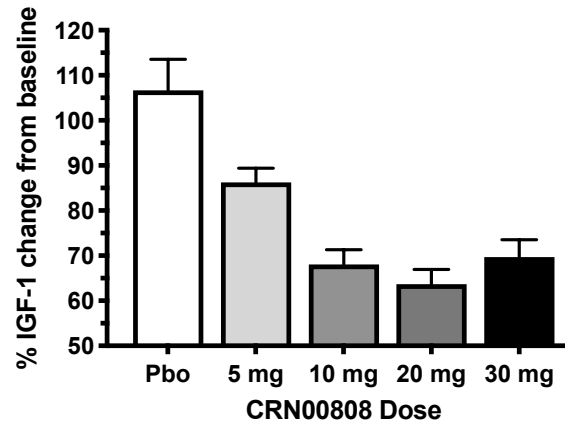


Phase 1 MAD arm: PK/PD analysis

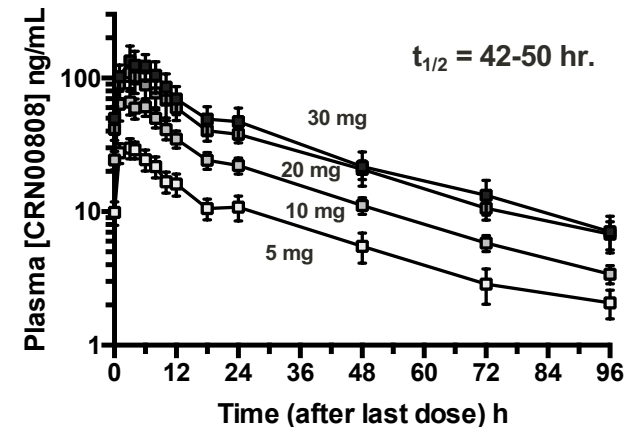
Time-course of plasma paltusotine trough and IGF-1 concentrations



Dose response of IGF-1 suppression



Plasma concentration on the last day of dosing



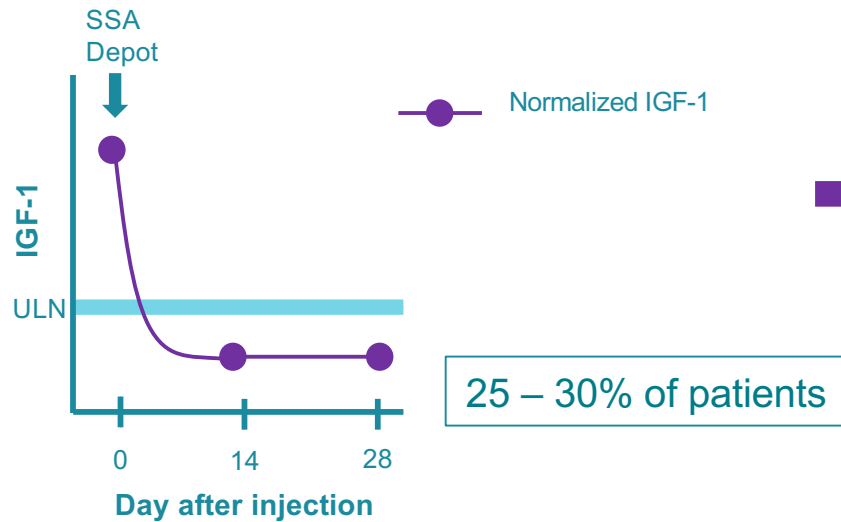
Safety & tolerability across phase 1

- Tolerability and AE profile was generally consistent with approved peptide somatostatin analogs (abdominal pain, flatulence, abdominal distension, and diarrhea in approximately 30% of subjects and mild elevations of pancreatic enzymes in approximately 10% of subjects)
- Additional adverse events included: headache, dizziness and cardiac rhythm abnormalities (including NSVT). One serious adverse event of moderate NSVT was observed following a single 1.25 mg dose and was considered unlikely to be related to paltusotine. These AEs were not dose dependent and were also observed in placebo subjects and/or prior to dosing.

10 mg selected as the initial dose in Phase 2 trials

Paltusotine targeted acromegaly market segments

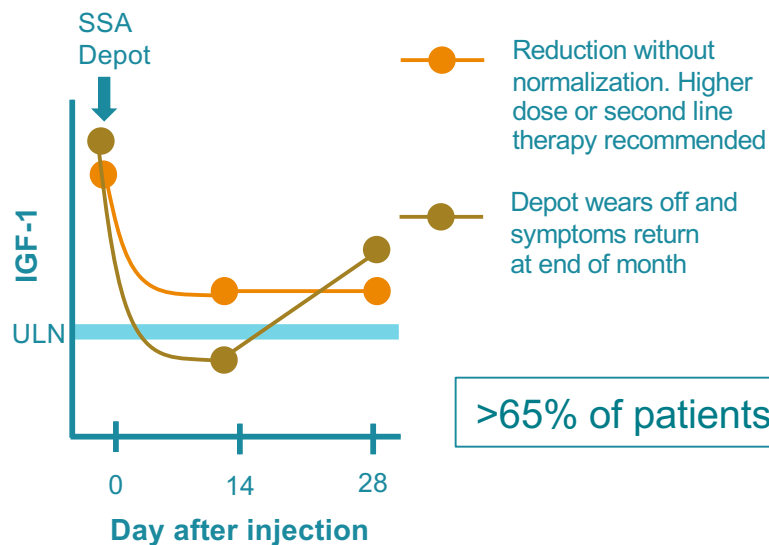
Patients Controlled by SSA Monotherapy



ACROBAT
EVOLVE

- Both studies at same centers
- Single screening process for both studies
- Regions: US, UK, Germany, Greece, Hungary, Italy, Poland, Romania, Serbia, Slovakia, Brazil, Australia, New Zealand
- Patients eligible for open label extension study (ADVANCE)

Patients Uncontrolled on SSA Monotherapy



ACROBAT
EDGE

← Screening → ← Paltusotine Treatment → ← Follow-up →

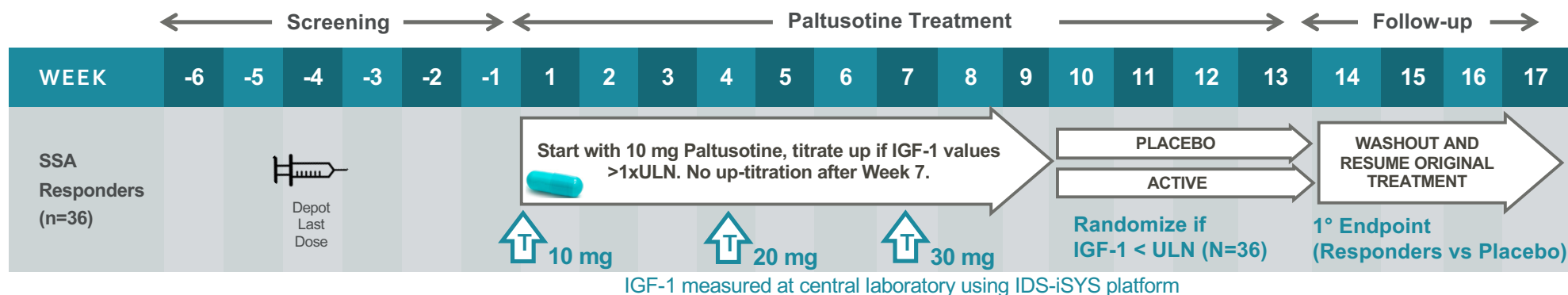


Key inclusion/exclusion criteria

- Patients on stable approved monthly dose of SSA for at least 3 mo.
- Can directly roll-over from EVOLVE screening if IGF-1 > 1.0x ULN
- 18 to 75 years of age

Acromegaly Phase 2 Trial for Patients Controlled on Injectable SSAs

Evaluation of Paltusotine vs placebo in patients controlled on injected octreotide/lanreotide monotherapy

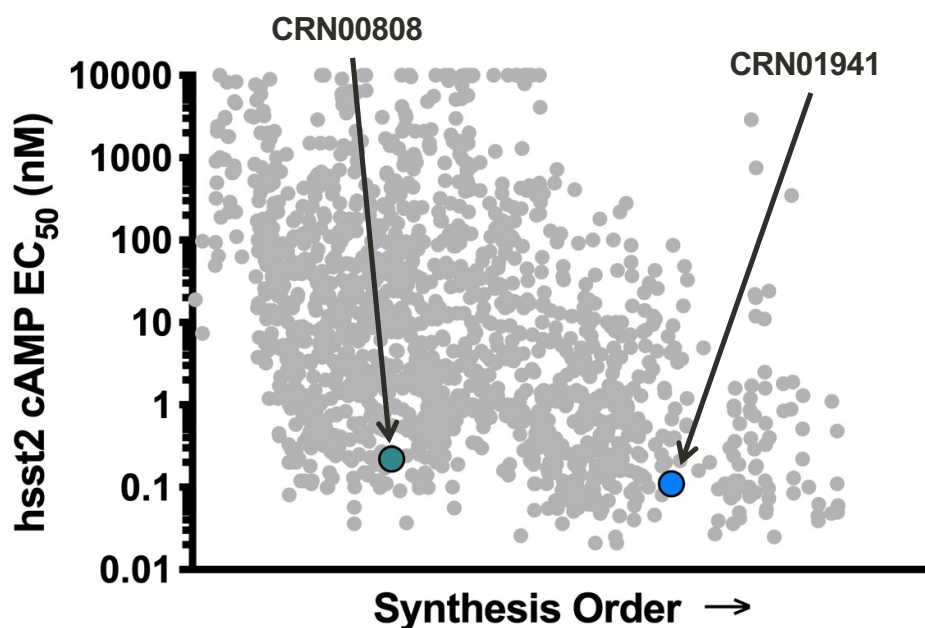


Key inclusion/exclusion criteria

- Mean IGF-1 $\leq 1.0 \times$ ULN during screening
- Patients on stable approved monthly dose of SSA for at least 3 mo.
- 18 to 75 years of age

CRN01941: Phase 1 human proof-of-concept clinical trial nearing completion

Results of sst2 chemistry effort



Part of an oral, sst2 agonist franchise

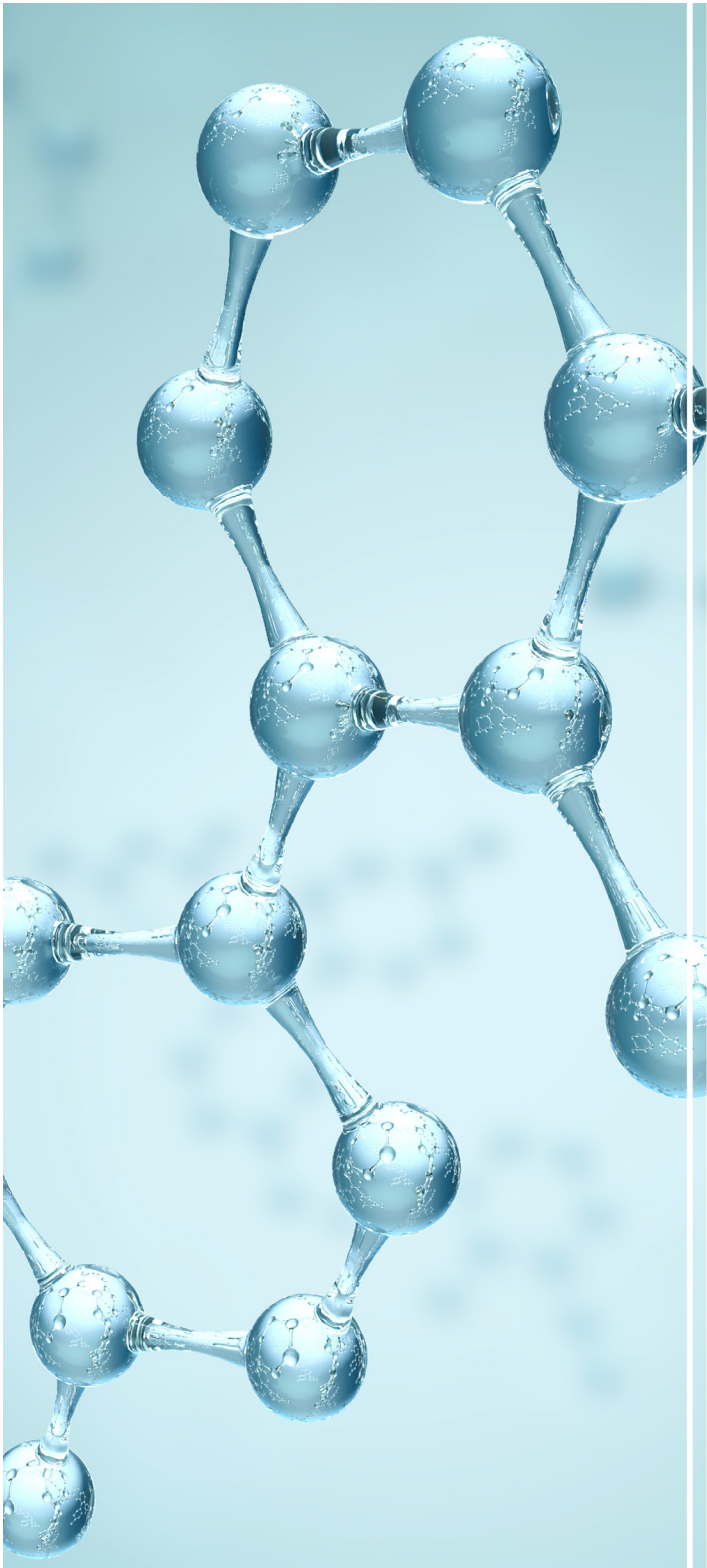
- Distinct chemical series from paltusotine and distinct patent family
- Phase 1 in-life complete, PK/PD being analyzed
- Phase 2/3 development planning underway guided by investigator/patient input and market opportunity analysis
- De-risked state of paltusotine could enable entry of NETs program into clinical trials sooner with nonclinical and CMC savings

We anticipate providing guidance on NETs development strategy 1H2020

sst2 Agonist Program Next Steps




- Complete enrollment in EDGE and EVOLVE and provide guidance to top-line data read-out
- Prepare for launch of paltusotine Phase 3 program:
 - Finalize study design for Phase 3 with regulatory and KOL feedback
 - Prepare drug product using final formulation for Phase 3
- Rat carcinogenicity studies progressing with results in 1H2022
- Initiate NETs clinical development

Crinetics is committed to a commercialization strategy that unlocks the full potential of oral sst2 agonists across multiple indications

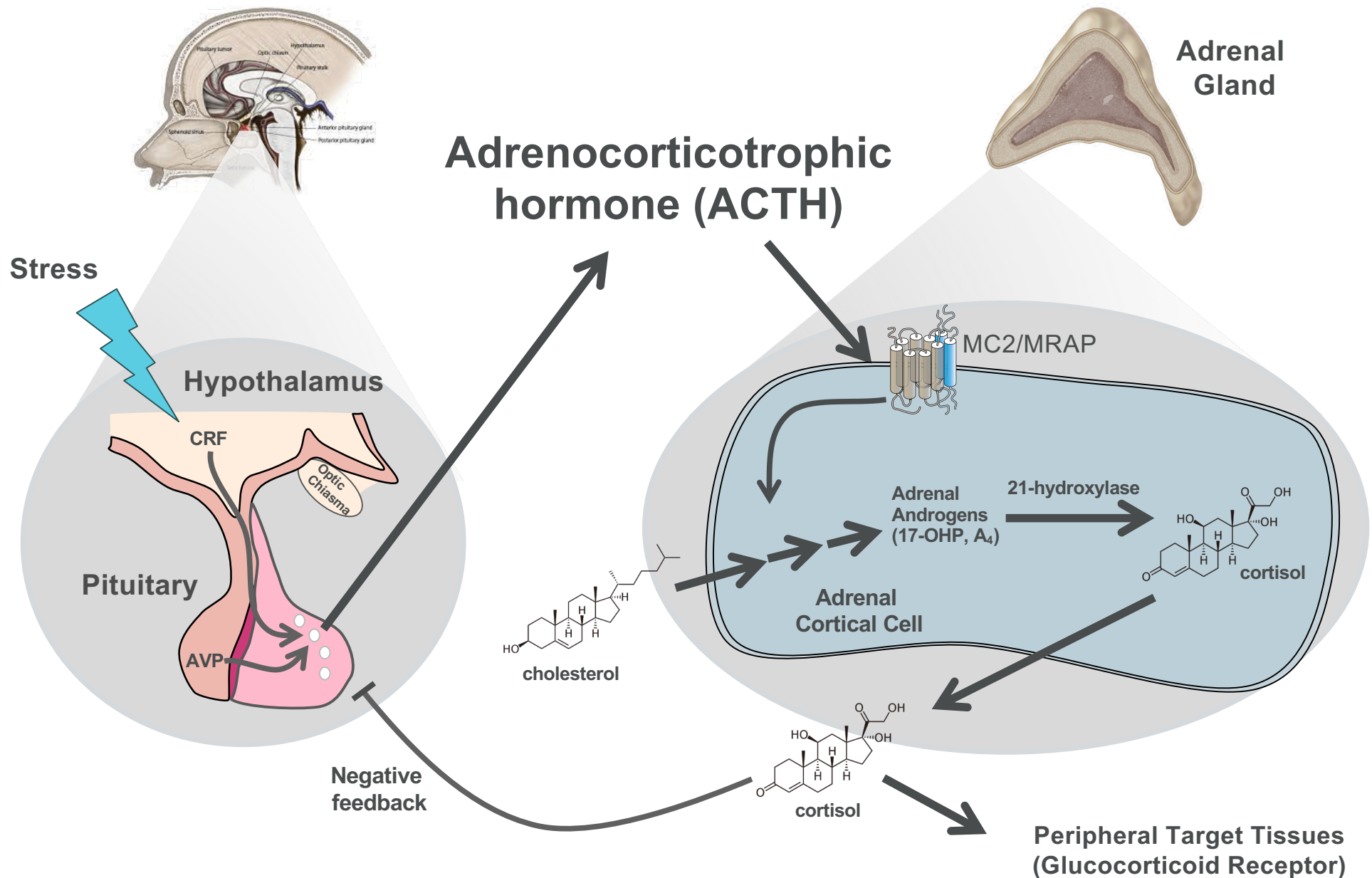


Nonpeptide ACTH Antagonists
for the treatment of Cushing's Disease,
Congenital Adrenal Hyperplasia (CAH),
and other conditions of ACTH excess

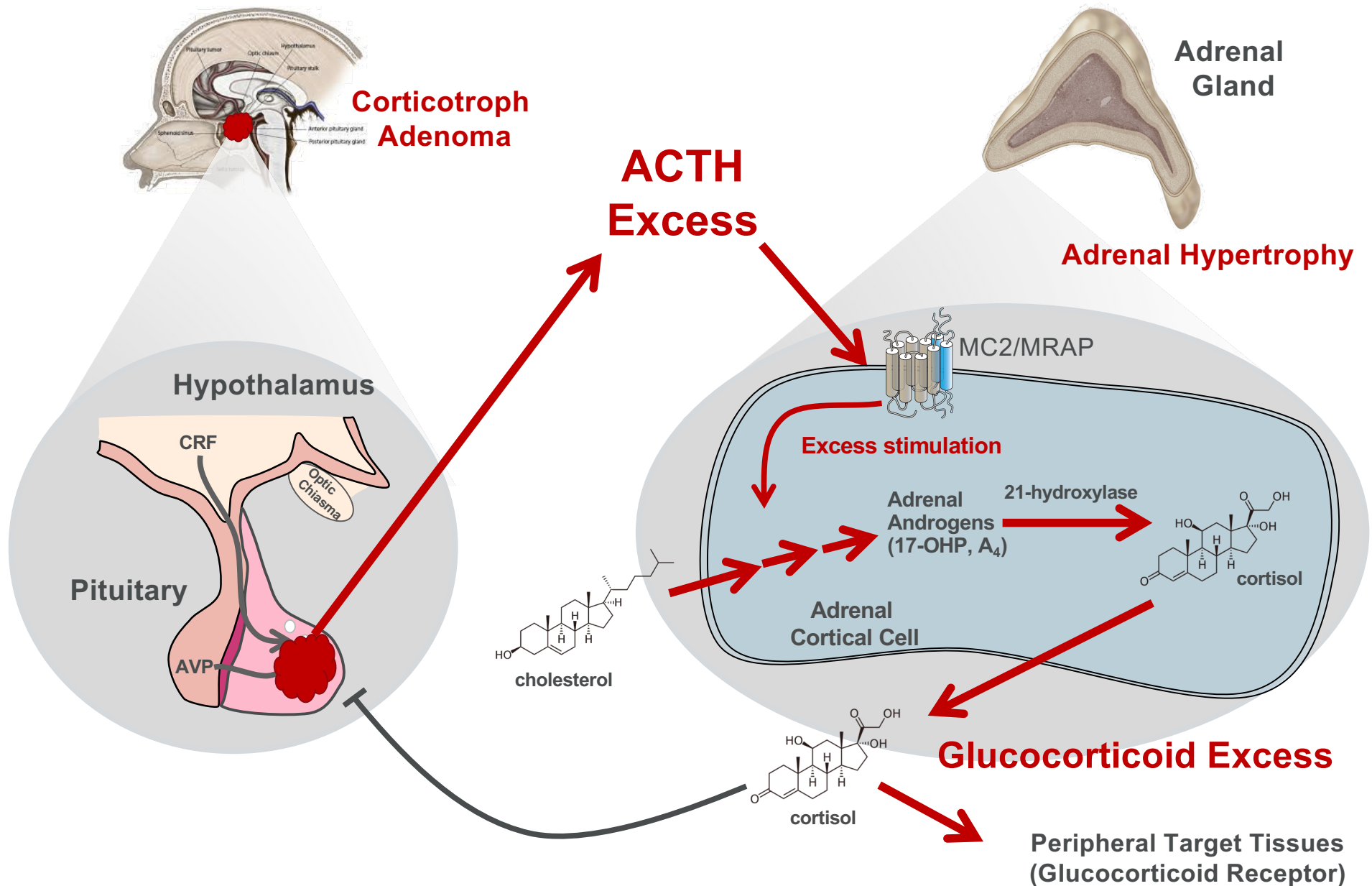
Multiple markets of entry are possible for an ACTH antagonist, all are areas of high unmet need

Condition	Defect	Impact	ACTH antagonist target
Congenital Adrenal Hyperplasia (CAH)	Genetic defects that prevent production of cortisol by the adrenal	Loss of negative feedback causes over production of ACTH from the pituitary and build up of steroid precursors	
Cushing's Disease (CD)	Pituitary tumor	Over production of ACTH leading to hypercortisolemia	
Ectopic Cushing's Syndrome	Non-pituitary tumor	Over production of ACTH leading to hypercortisolemia	

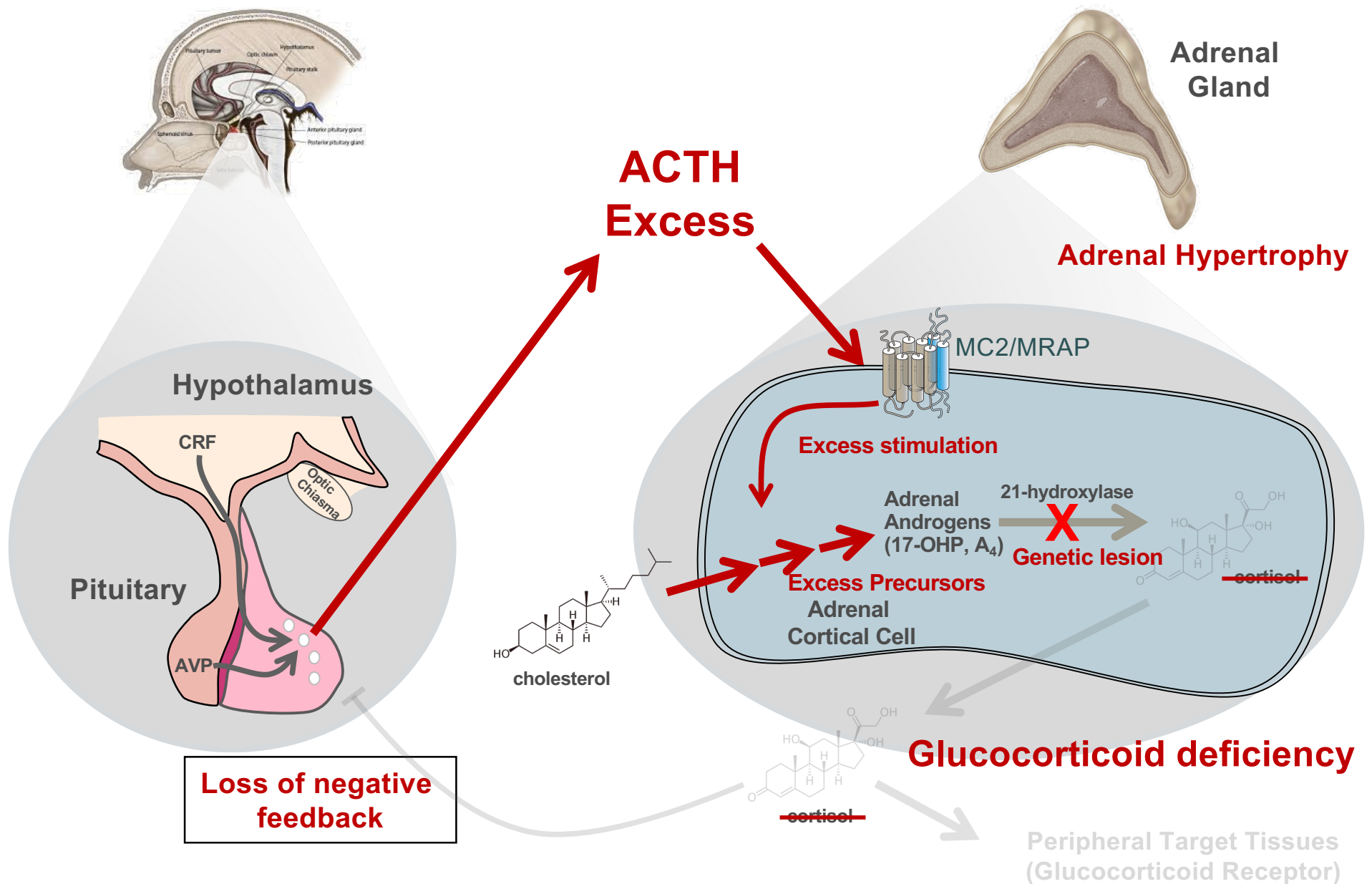
The hypothalamic-pituitary-adrenal (HPA) axis



Cushing's Disease Etiology

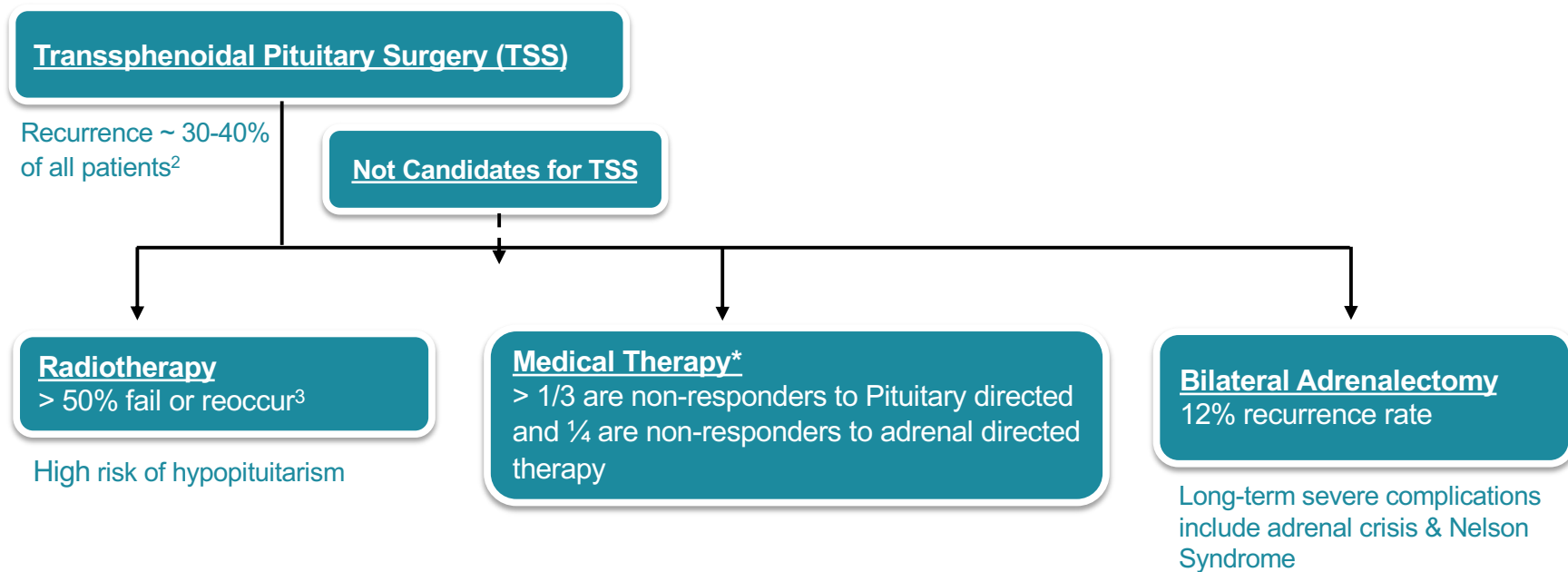


Congenital Adrenal Hyperplasia (CAH) Etiology



Current treatment paradigm of Cushing's Disease highlights Crinetics market opportunity

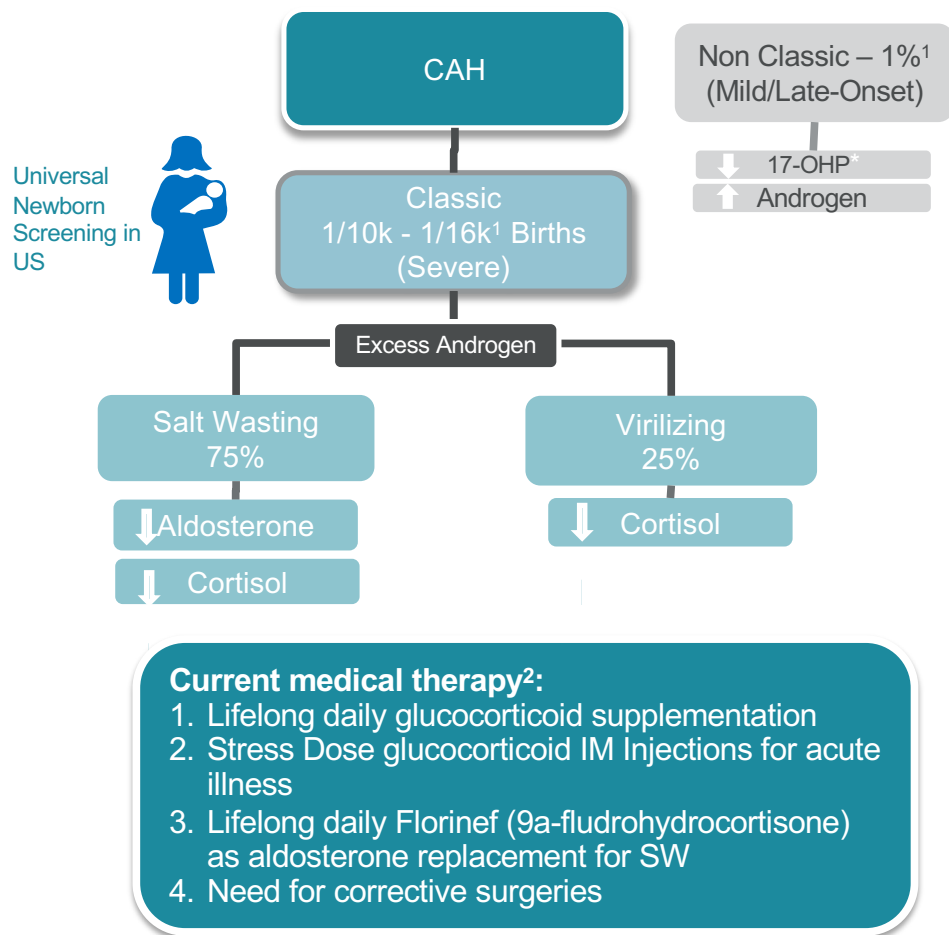
Of the approximately 16K diagnosed Cushing's Syndrome cases in the US, 80% are ACTH-dependent¹ ~ 12K. The majority (~70%) have Cushing's Disease



- Opportunity exists for Crinetics ACTH antagonist as post-surgical maintenance therapy
- Greater opportunity exists as 1st line medical therapy in delaying or preventing radiation and adrenalectomy

*Adrenal-directed: (ketoconazole, metyrapone, mitotane) Pituitary-directed: (cabergoline, pasireotide) Glucocorticoid receptor (mifepristone) †approved only for CS – \$285-315M expected 2019 revenue

Classic Congenital Adrenal Hyperplasia requires lifelong treatment



Long-term risk and outcomes of current options:

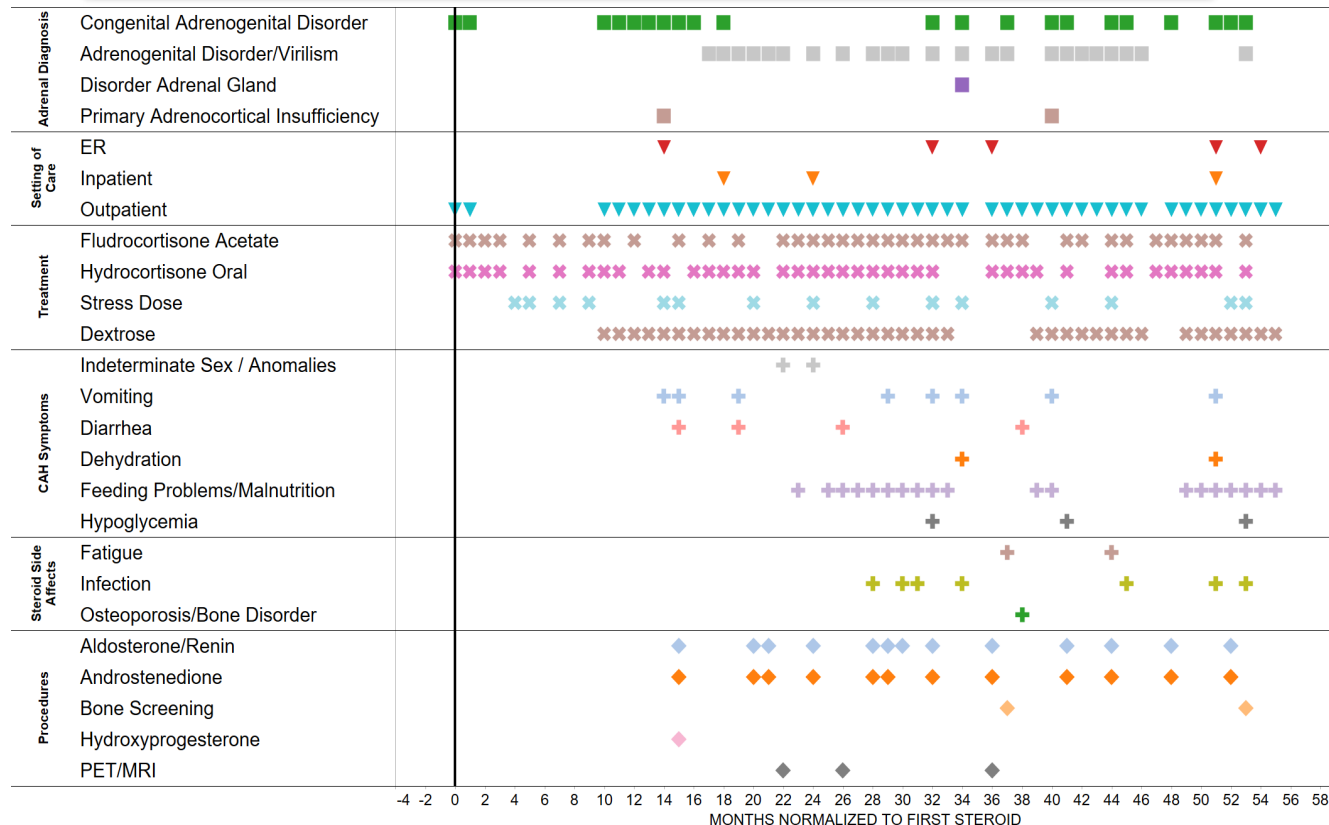
- Average 11 hospital visits for adrenal crisis³
- ~2X risk of bone fractures compared to general population²
- Adults with CAH will require stress doses on ~171 days over their lifetime³
- Adverse Metabolic Profile (hypercholesterolemia, insulin resistance, hypertension)
- Loss of 7 years of life compared to general population; >20% will die of a condition complicated by adrenal crisis³
- Women with CAH 6.2kg/m² greater BMI than general population of similar age³

There is an opportunity for Crinetics' ACTH Antagonist to replace existing therapies. Alleviating the need for excess glucocorticoids and associated risks of overtreatment.

*17-OH progesterone, chemical used to make cortisol

Treatment of CAH with excess steroids can lead to unintended health consequences

Baby girl: Born 2014, Original CAH diagnosis 5/2014, First Steroid Rx 5/14¹



Current Challenges

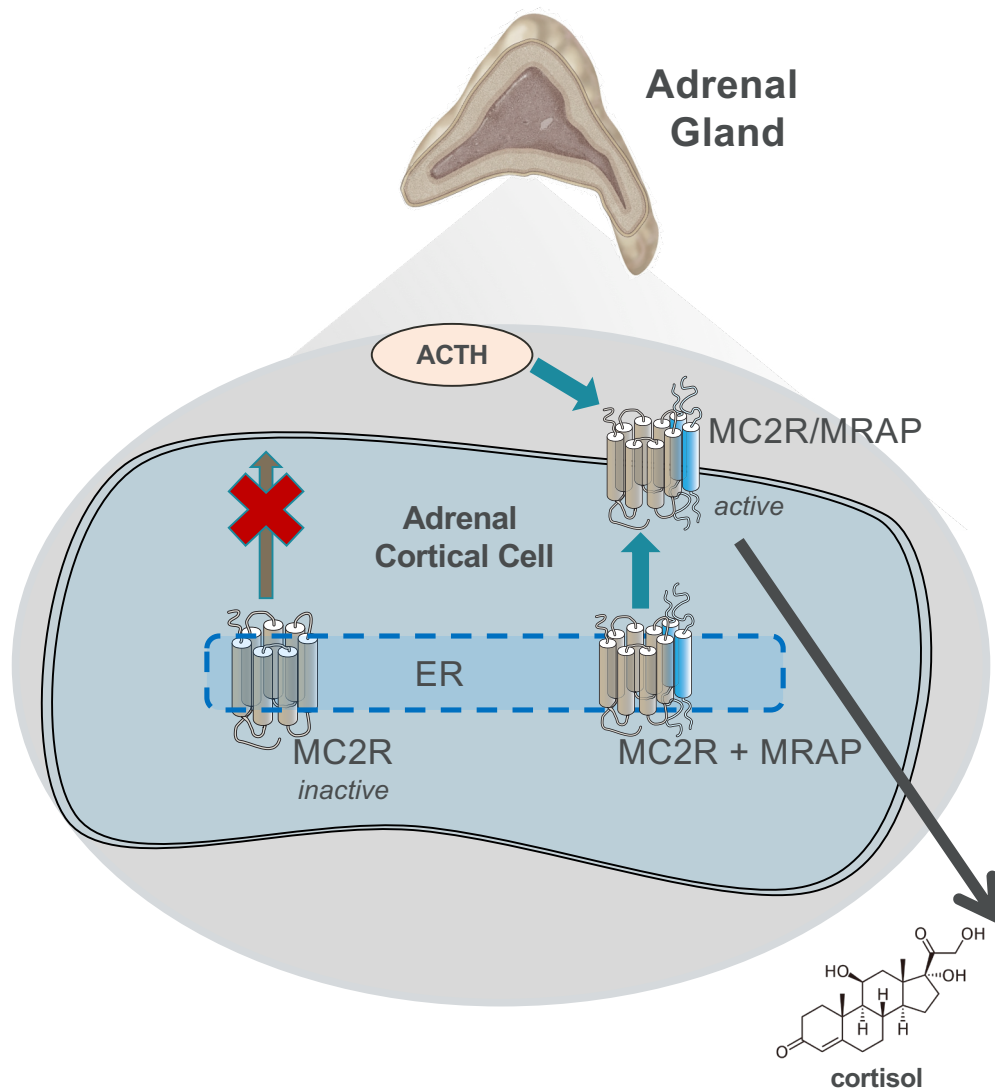
- Steroids introduced in the 1950s have extended the lives of many CAH patients beyond middle age
- While mortality can now be delayed, these patients and the healthcare system suffer treatment of
 - Repeat infections
 - Polycystic ovarian syndrome
 - Hirsutism
 - Hypertension
 - Obesity
 - Osteoporosis
 - Tumors

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

Crinetics' ACTH antagonist represents an opportunity to treat the underlying disease of CAH and avoid the pitfalls of excess steroid use that leads to costly medical care

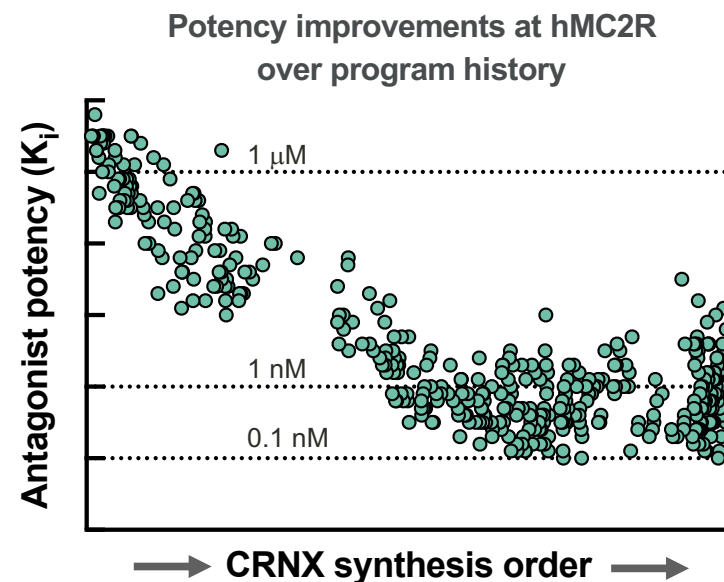
ACTH Antagonists: A potential breakthrough in endocrinology

Recent discoveries in peptide hormone GPCR regulation enabled discovery of first-in-class nonpeptide drug candidates



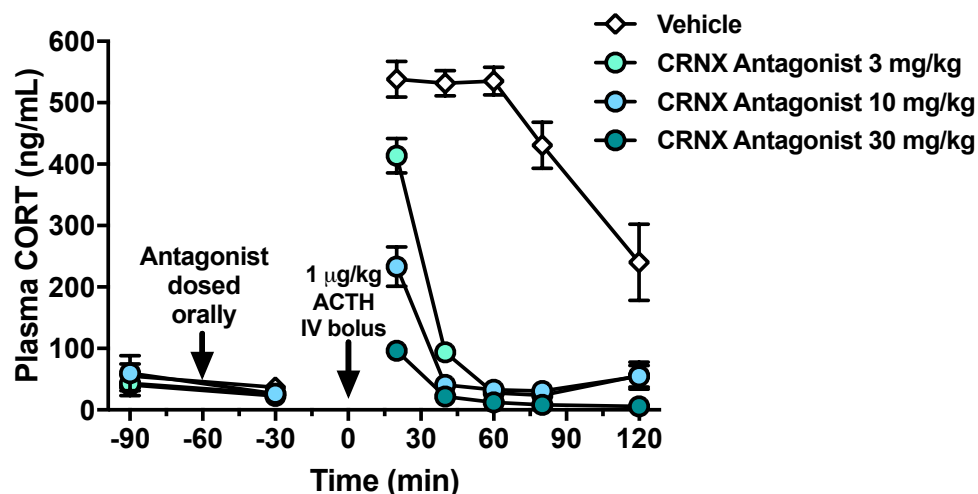
2005: First description of MRAP's role in MC2R expression and ACTH binding

2016: Crinetics initiates effort to create first nonpeptide ACTH antagonist

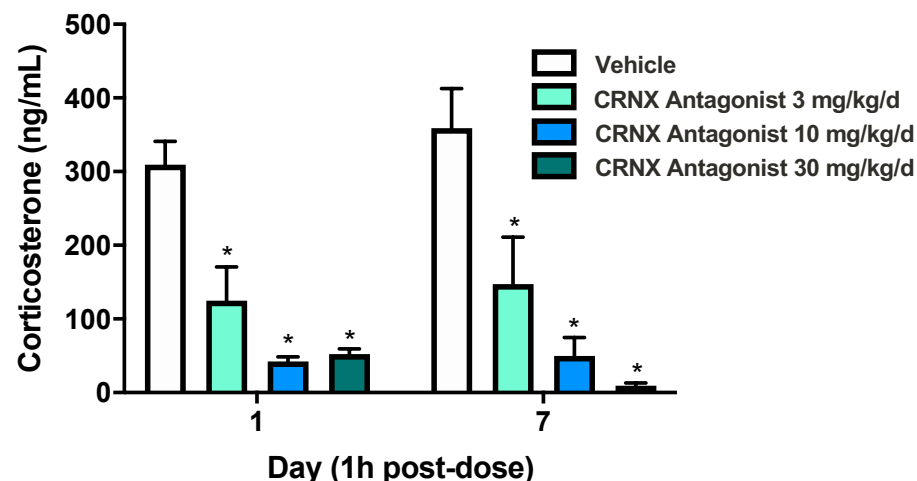


Nonpeptide ACTH antagonists are effective in rat models that mimic Cushing's and CAH

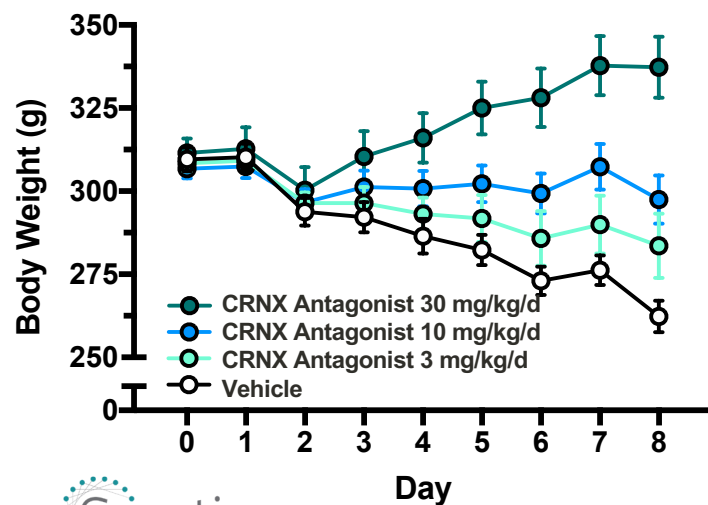
Acute suppression of ACTH-induced corticosterone in rats



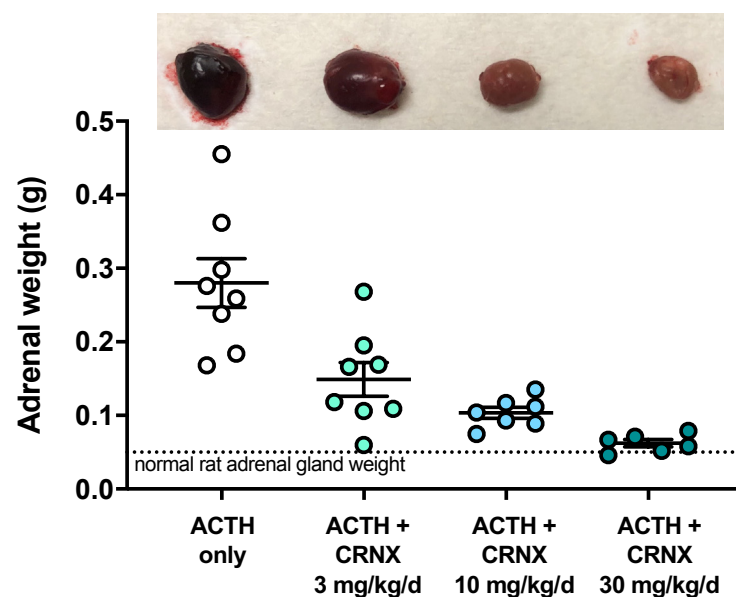
Repeat antagonist dosing (7d) suppresses corticosterone from chronic ACTH infusion



Repeat antagonist dosing (7d) rescues body weight loss from chronic ACTH infusion

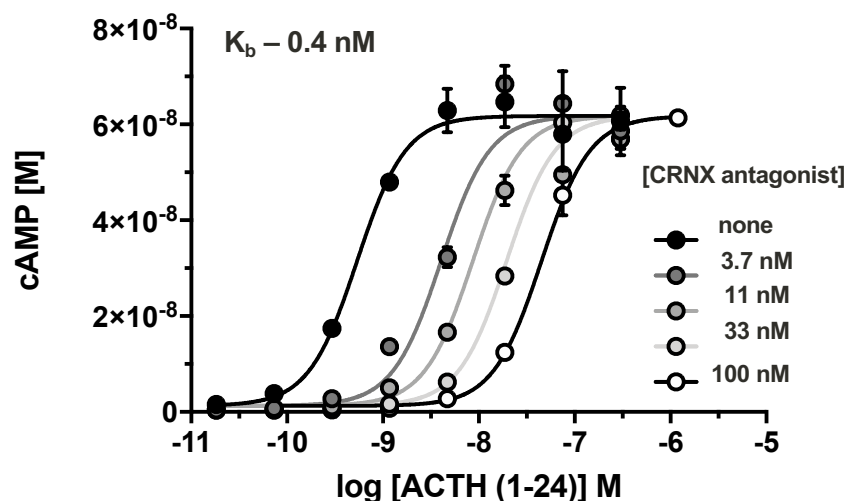


Repeat antagonist dosing (7d) rescues adrenal hypertrophy from chronic ACTH infusion



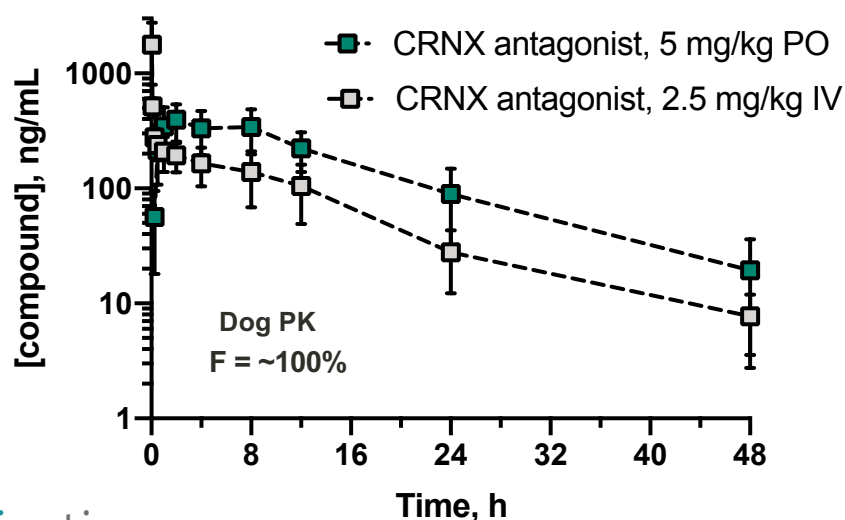
Crinetics ACTH antagonist lead compound now in preclinical development is a high-quality drug candidate

Potent in vitro pharmacology

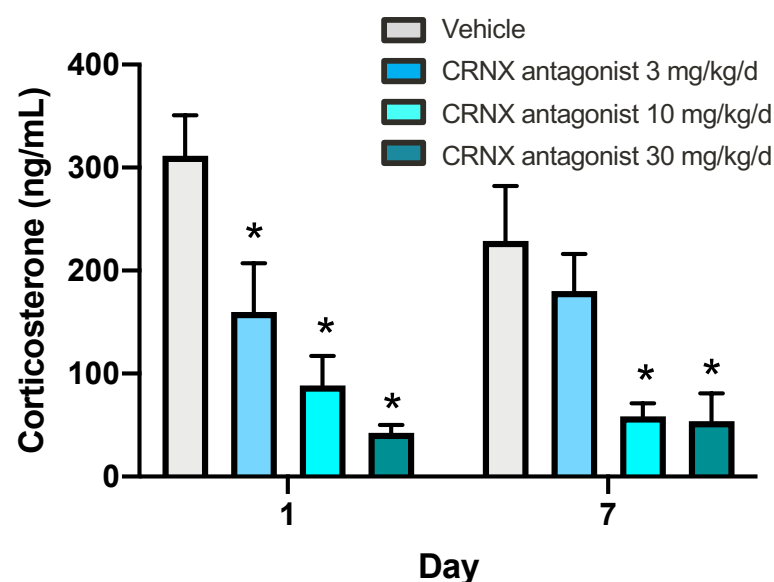


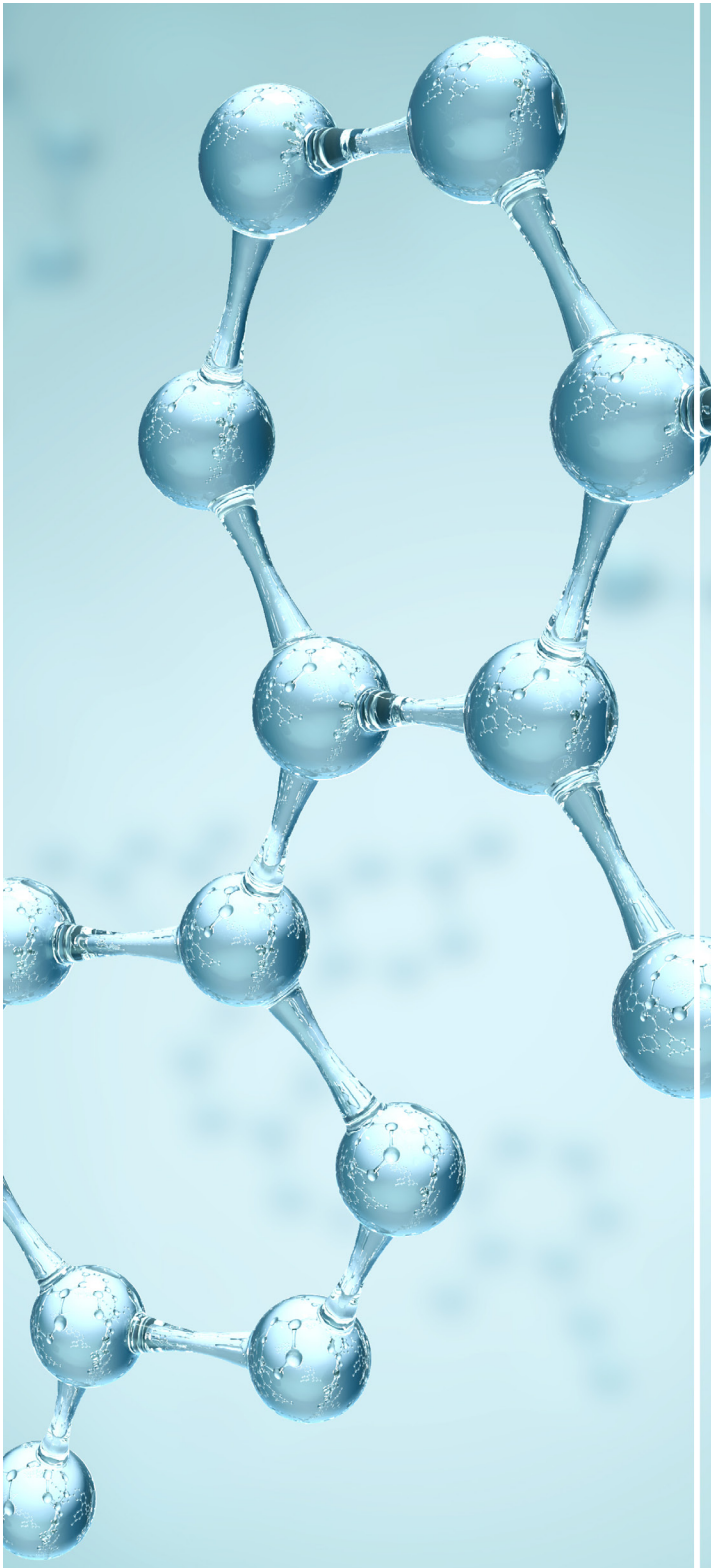
Property	CRNX ACTH Antagonist Candidate
MW	~600
Solubility @ pH 7.4	1 mg/mL
human MC2R [K_b]	0.4 nM
rat MC2R [K_b]	3.4 nM
hMC1,3,4,5 [K_i]	>1 μ M
CYP inhibition	No Inhibition
CYP induction	No Induction
Species differences in metabolism	No human unique metabolite
Rat PK	$t_{1/2} = 2.9$ h $F = 47$ %
Dog PK	$t_{1/2} = 8.7$ h $F = \sim 100$ %
Genotoxicity	Negative

Excellent Bioavailability



Potent in vivo efficacy





sst5 agonists for the treatment of
hyperinsulinism due to congenital
mutations, bariatric surgery,
and insulinoma

Congenital Hyperinsulinism (CHI): disease overview and treatment limitations

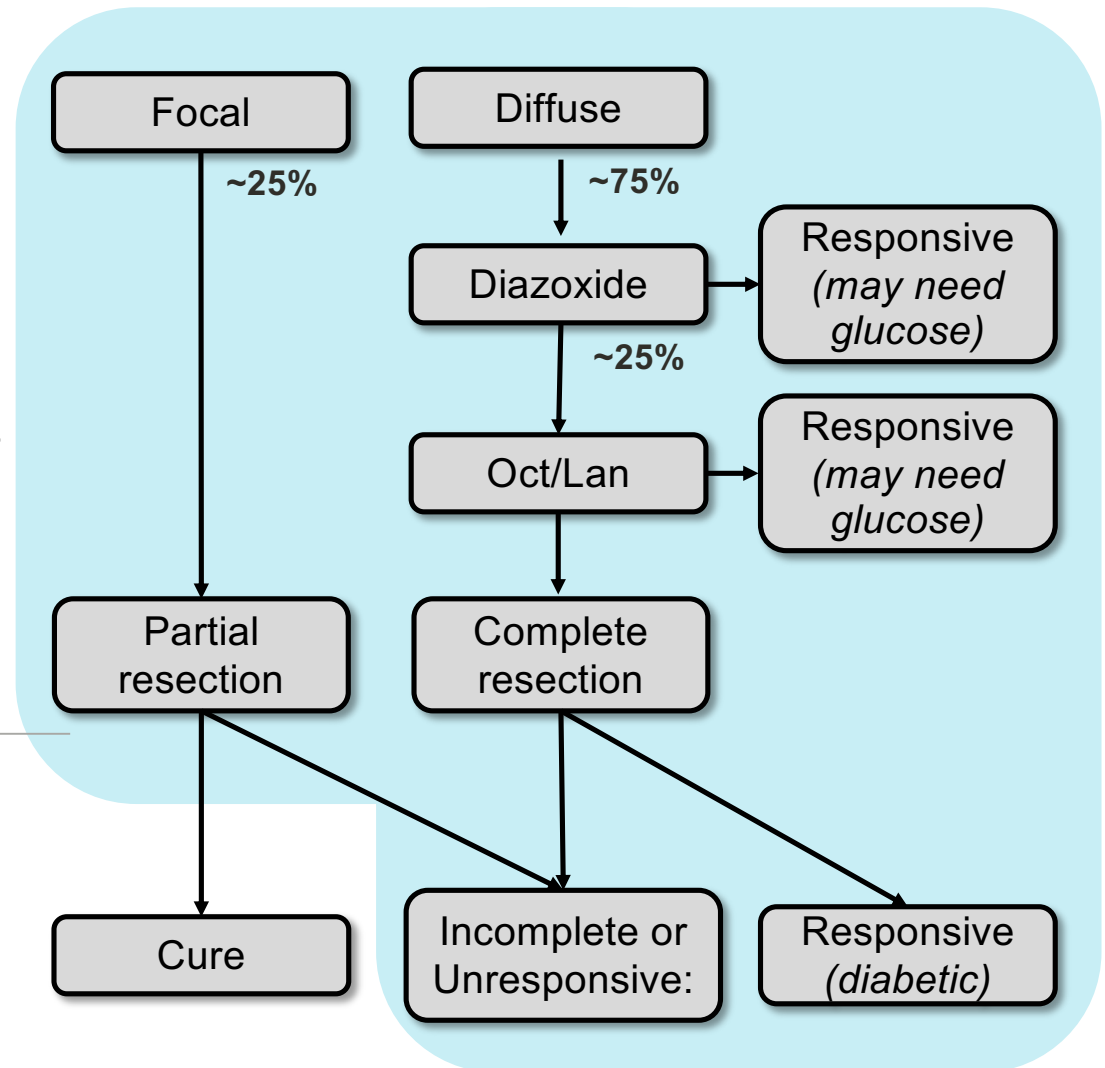
Indications

- Congenital hyperinsulinism (CHI)
 - Genetic defects (eg. K_{ATP} channel) results 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)

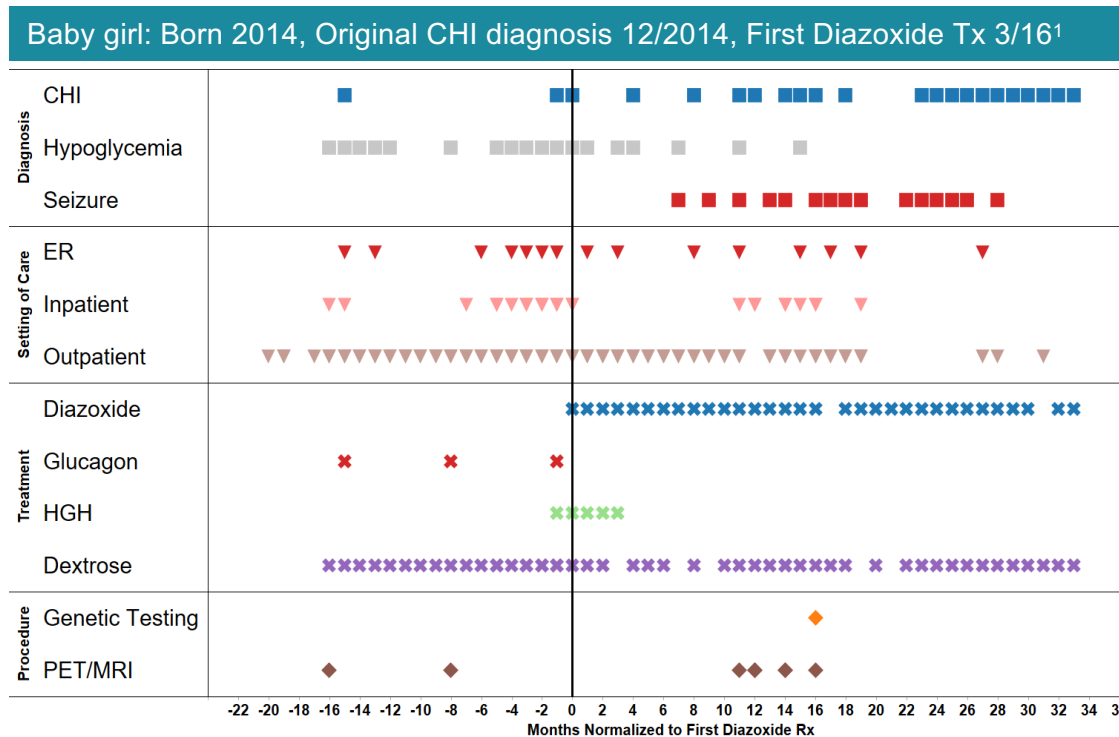
Patient and parent goals

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

Amenable to sst5 agonist



A typical CHI baby requires extreme use of healthcare resources with poor outcomes



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

Current Challenges

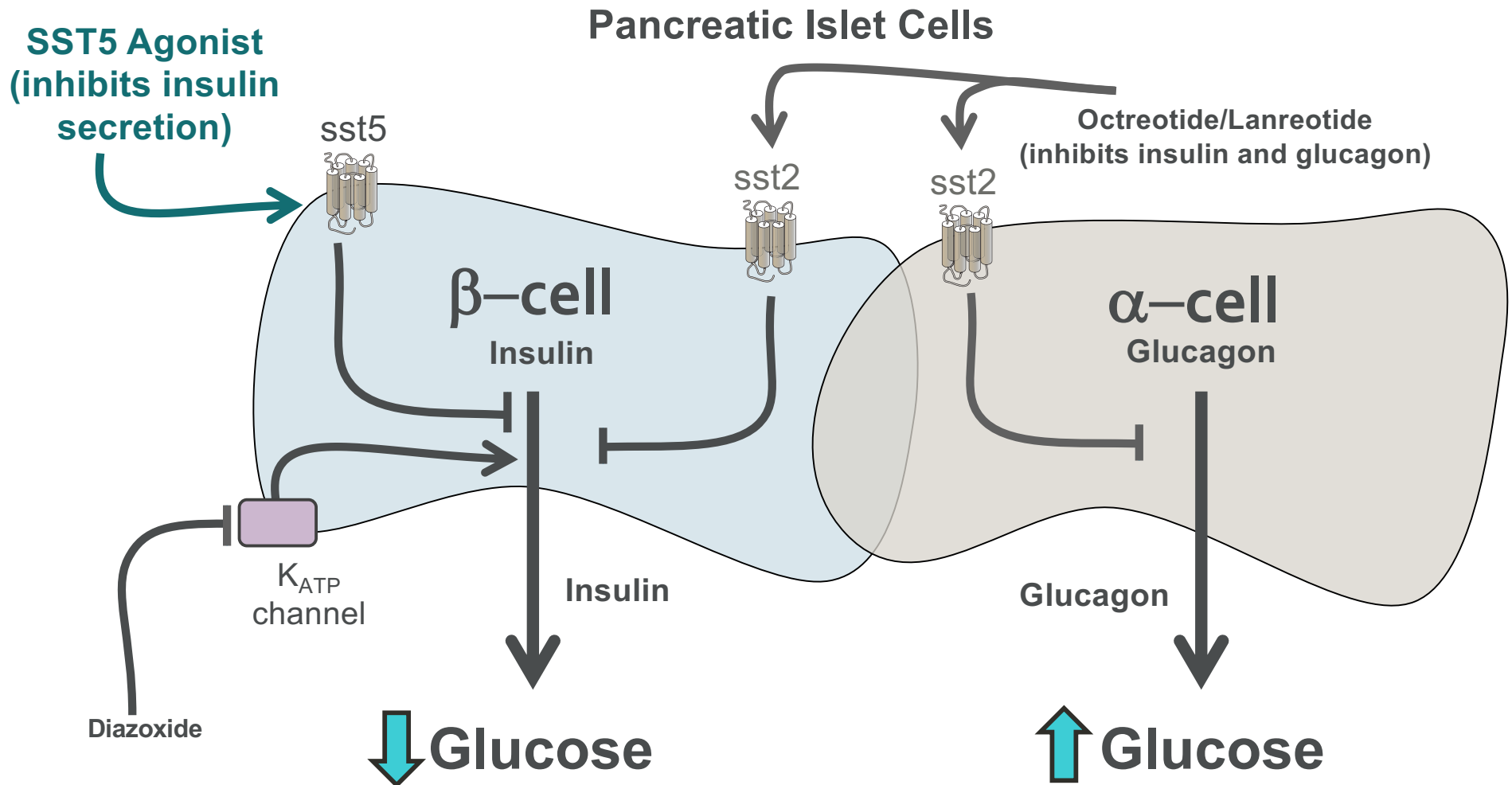
- Variable time to diagnosis
- Constant dextrose infusion to maintain normal blood sugar levels
- Surgical removal of all or part of the pancreas, *or*
- No surgical options
- Ineffective diazoxide treatment with multiple untoward effects

As a result:

- Hypoglycemic crises warranting repeat need for emergency services
- Frequent and multi-day inpatient hospital stays
- Long-term consequences including severe seizures, permanent brain damage, and further cerebral sequelae

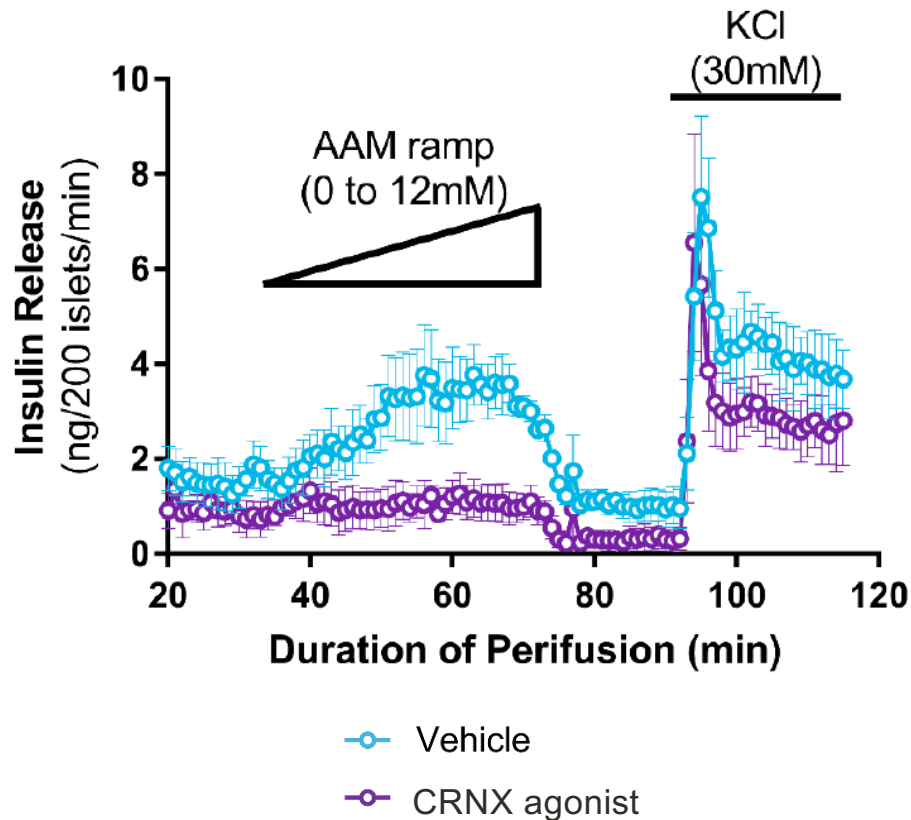
Crinetics' SST5 agonist represents an opportunity to address persistent hypoglycemia and perhaps change the paradigm of CHI treatment and healthcare burden it brings

Our hypothesis: an oral, selective sst5 agonist is the optimal strategy for treating all HI patients

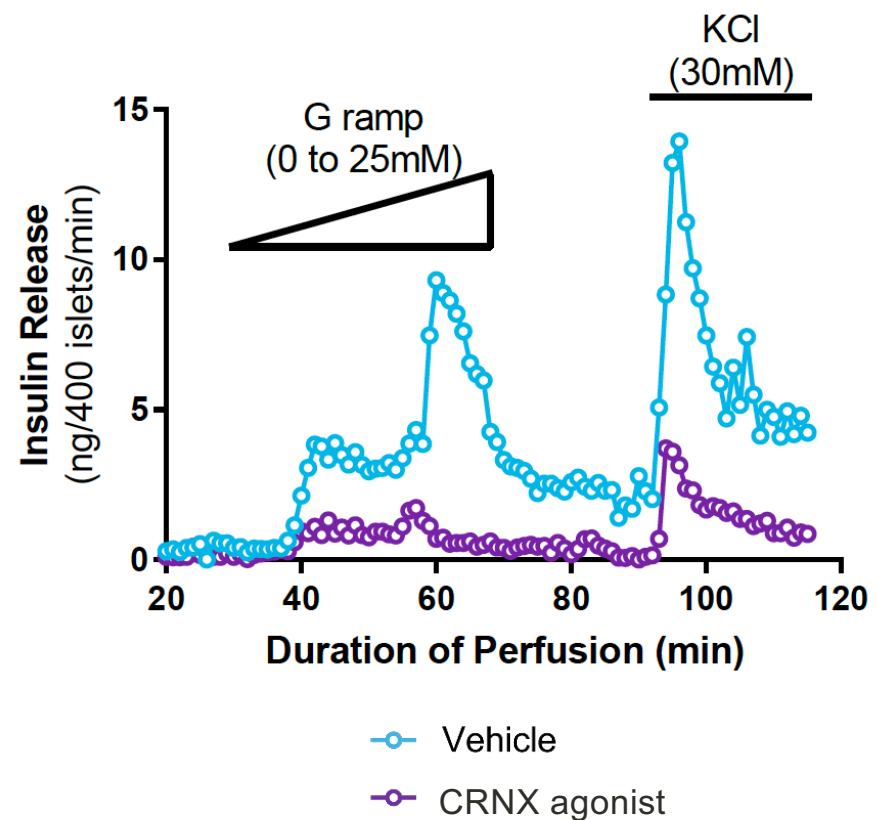


Mechanistic islet studies demonstrate CRNX sst5 agonists potently suppress insulin secretion in disease models

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

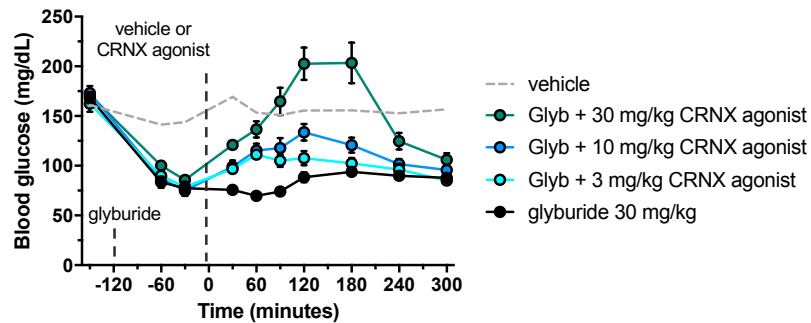


In isolated Beckwith Wiedemann Syndrome patient islets

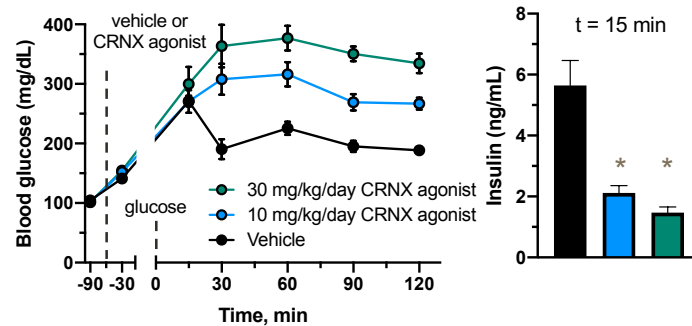


Crinetics sst5 agonist lead compound now in preclinical development is a high-quality drug candidate

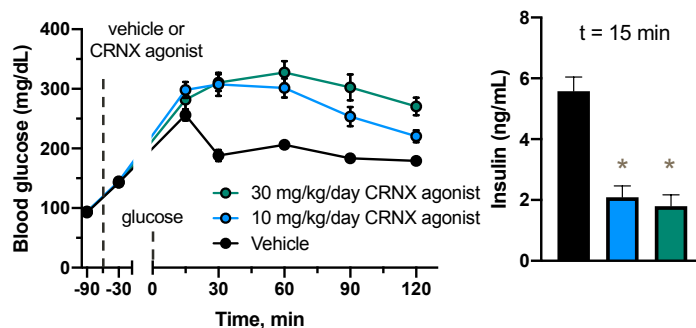
Rescue of
glyburide-induced
hypoglycemia



Day-1 OGTT
Glucose increased
insulin suppressed



Day-7 OGTT
Effects maintained



Property	CRNX sst5 Agonist Candidate
MW	< 500
Solubility @ pH 7.4	0.8 mg/mL
human sst5 [EC ₅₀]	0.4 nM
rat sst5 [EC ₅₀]	6.2 nM
hsst1 [EC ₅₀]	>10000 nM
hsst2 [EC ₅₀]	770 nM
hsst3 [EC ₅₀]	540 nM
hsst4 [EC ₅₀]	4700 nM
CYP inhibition	No Inhibition
CYP induction	No Induction
hERG [IC ₅₀]	>10 µM
Rat PK	t _{1/2} = 3.3 h F = 30 %
Dog PK	t _{1/2} = 9.9 h F = 57 %
Genotoxicity	Negative

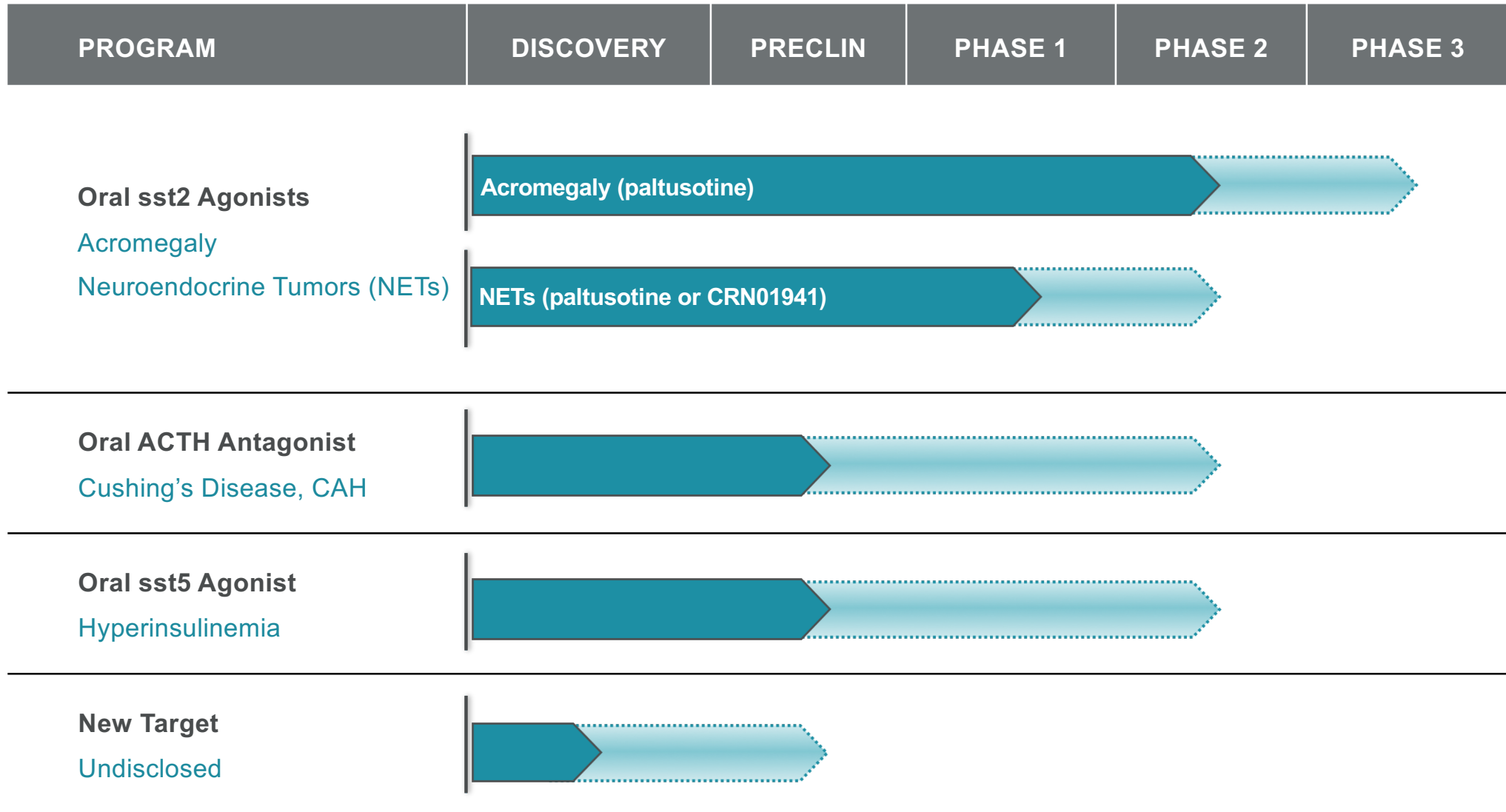
Financial Overview

As of September 30, 2019

- \$132 million cash and investments
- Strong balance sheet with cash runway into second half of 2021
- 24.2 million common shares outstanding

Pipeline: Looking forward towards 2021

...with a maturing rare disease franchise in endocrinology and endocrine oncology







Appendix



Leadership Team

Scott Struthers, PhD President & CEO, Founder



Frank Zhu, PhD VP of Chemistry, Founder



Steve Betz, PhD VP of Biology, Founder



Ajay Madan, PhD VP of Development



Marc Wilson Chief Financial Officer



Alan Krasner Chief Medical Officer



























Gina Ford VP, Corporate Strategy & Commercial Planning










Directors and Advisory Board

BOARD OF DIRECTORS

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Weston Nichols, PhD	Analyst, Perceptive Advisors					
Stephanie Okey, M.S	Former SVP, Genzyme Corporation					

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