Crinetics Pharmaceuticals

Corporate Presentation

October 2019

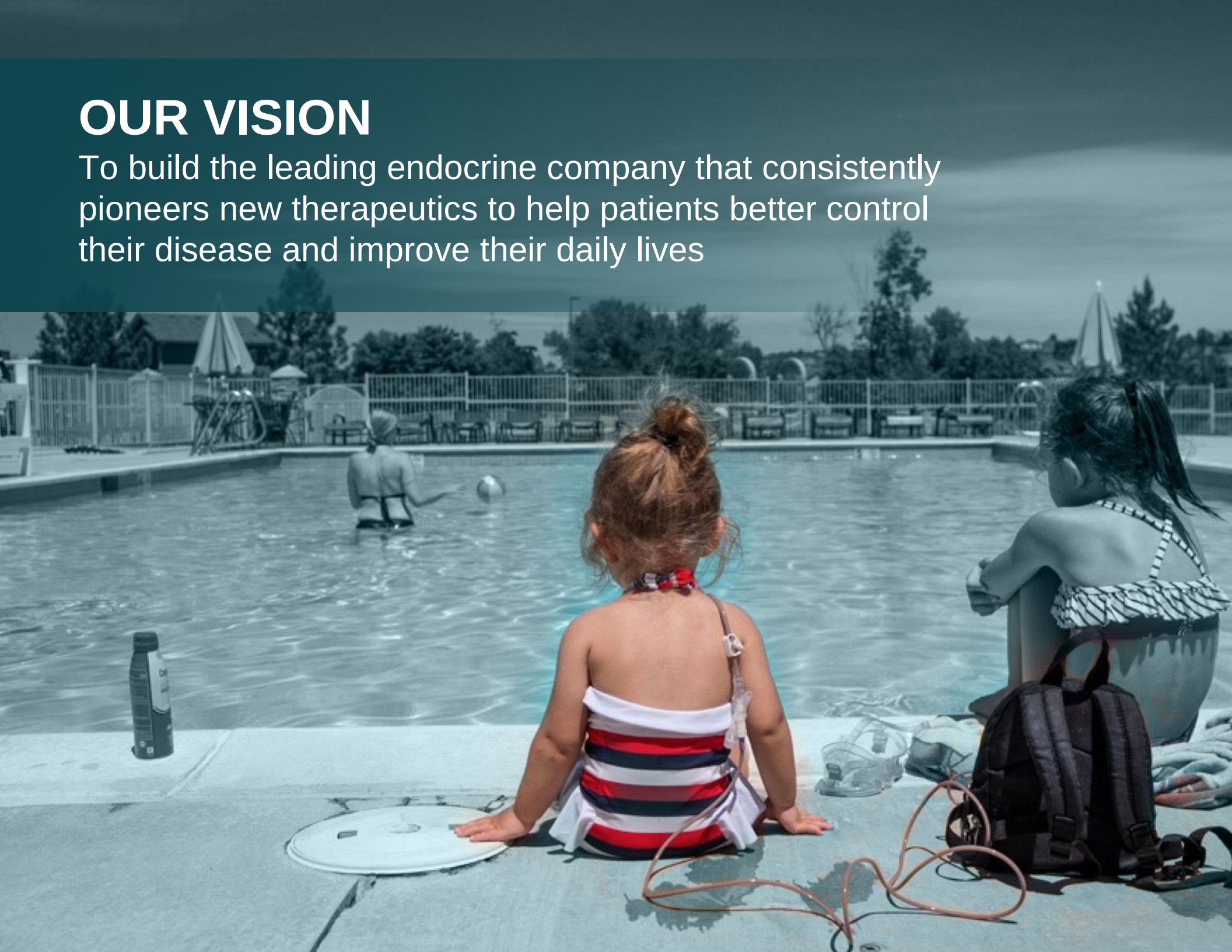
Safe harbor statement

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

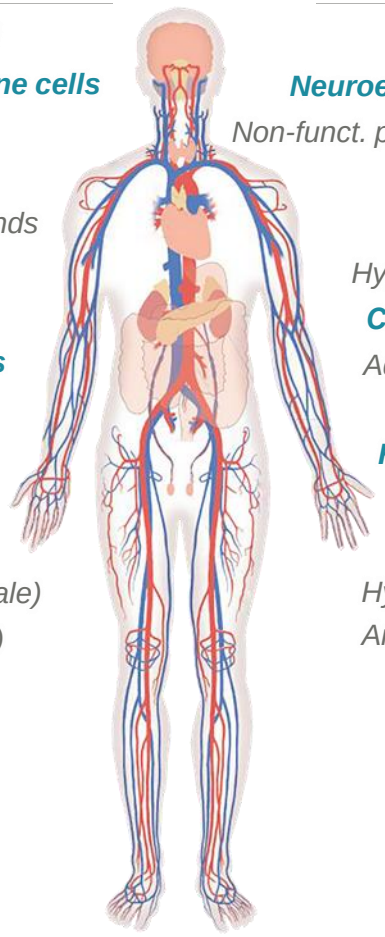


Our Strategy: Discover, develop and commercialize across multiple rare endocrine diseases and endocrine-related tumors

- 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

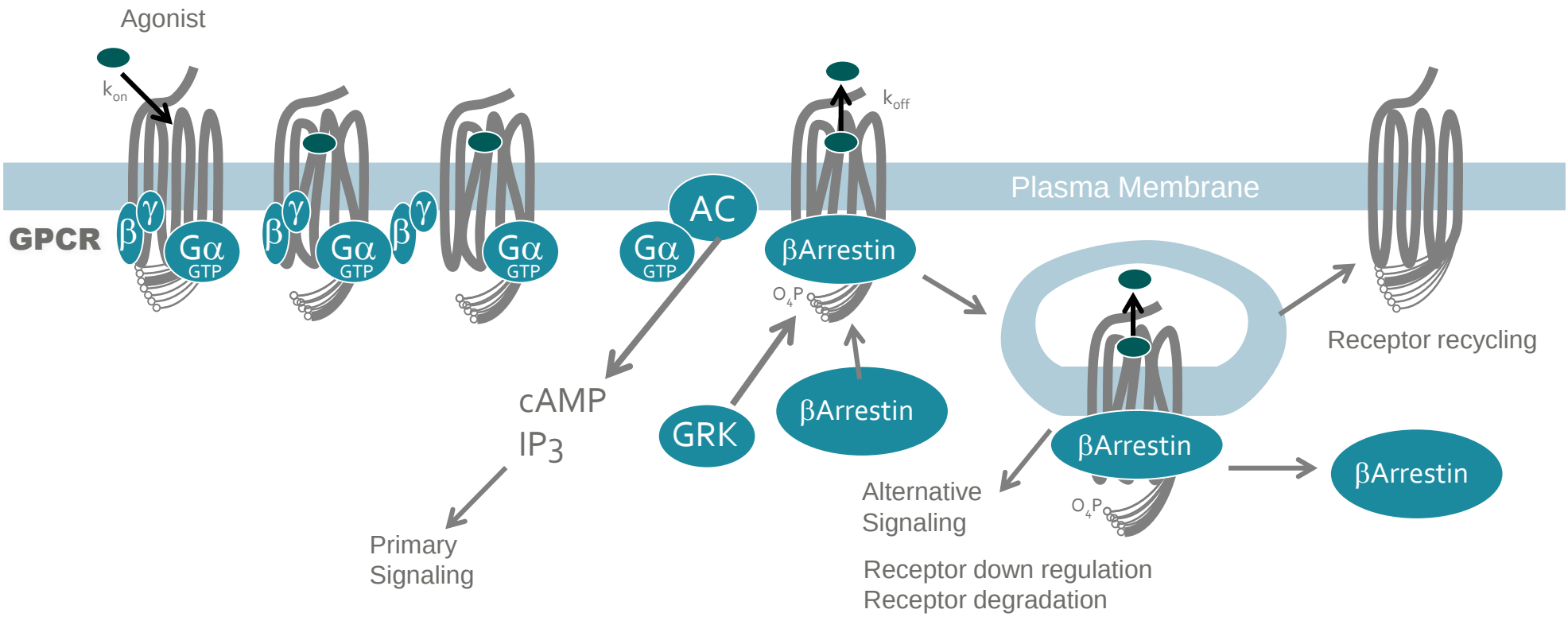
The endocrine therapeutic area

Endocrine system:	Multiple indications:
Pituitary gland	***Acromegaly***
Enteroendocrine cells	***Neuroendocrine tumors***
Hypothalamus	*Non-funct. pituitary adenomas*
Pineal gland	*GH deficiency*
Parathyroid glands	*Grave's disease*
Thyroid gland	*Hyperparathyroidism*
Thymus	***Cushing's disease***
Adrenal glands	*Adrenal hyperplasia*
Kidneys	*Adrenal cancer*
Pancreas	***Hyperinsulinemia***
Liver	*Insulinoma*
Placenta	*Thyroid cancer*
Ovaries (in female)	*Hypoparathyroidism*
Testes (in male)	*Androgen deficiency*
	Infertility



Targeting today / *Future opportunity*

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



Ligand binding kinetics conformational changes

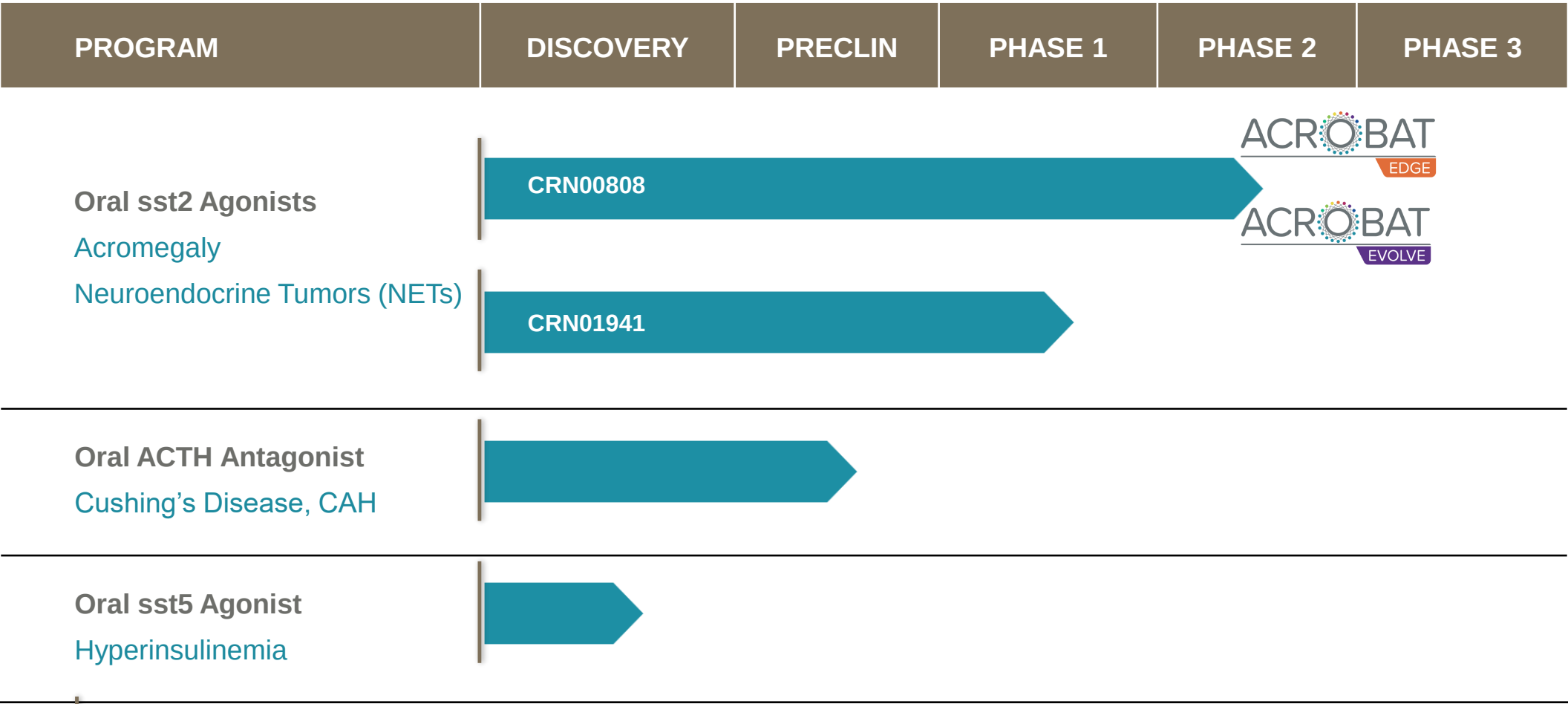
Receptor signaling

Receptor trafficking

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

Pipeline:

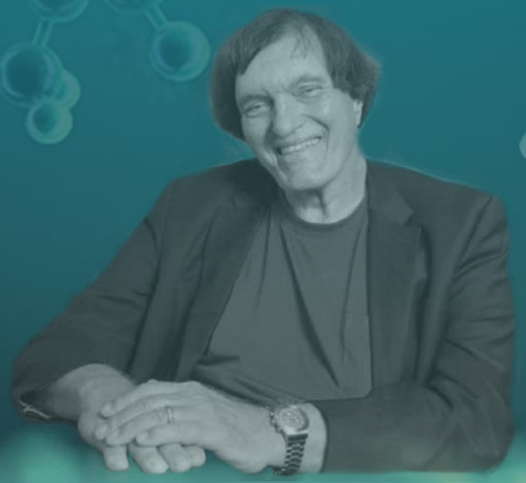
Building a rare disease franchise in endocrinology and endocrine oncology



All product candidates discovered and developed internally
Global rights retained and no licensing obligations
Composition of matter for CRN00808 through 2037

CRN00808 and CRN01941

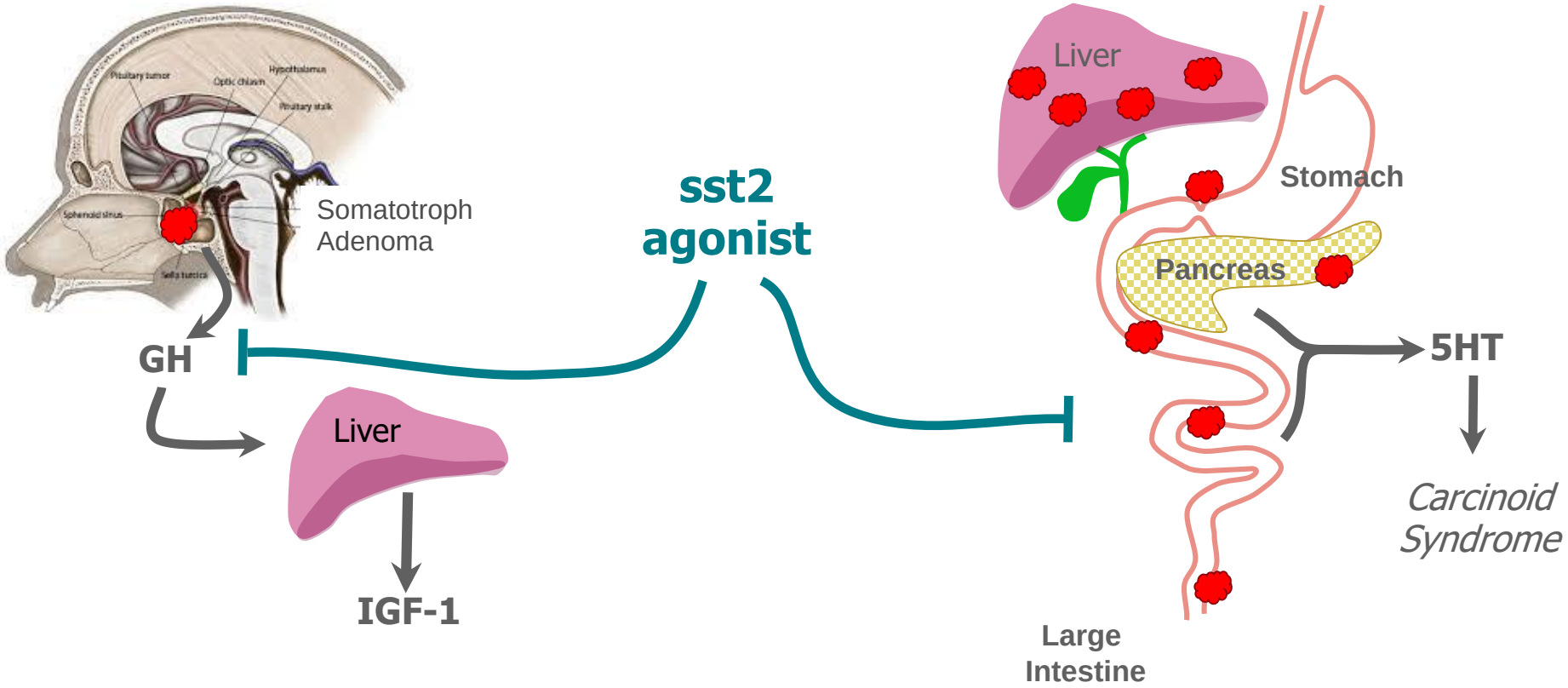
for the treatment of acromegaly and neuroendocrine tumors



Somatostatin sst2 agonists are standard of care for acromegaly and NETs

Acromegaly

Neuroendorine Tumors (NETs)



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

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*

RECORDATI
Signifor®
(pasireotide)
$72M

Pfizer
Somavert®
(pegvisomant)
$254M

IPSEN
Innovation for patient care
Somatuline®
(lanreotide)
$968M
(Ipsen #1 drug)

NOVARTIS
Sandostatin®
(octreotide)
$1.6B
(Novartis #5 drug)

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

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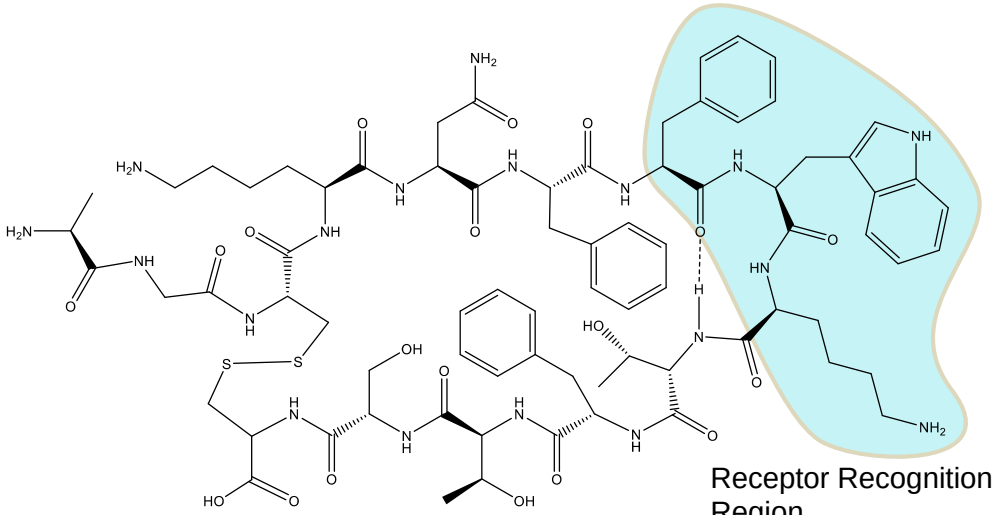
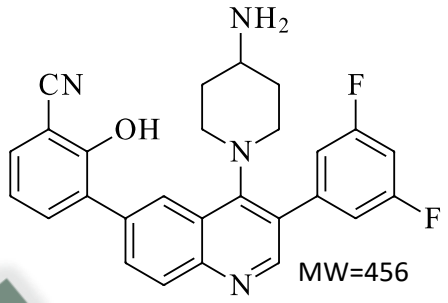
Sourc
[1] Inclu

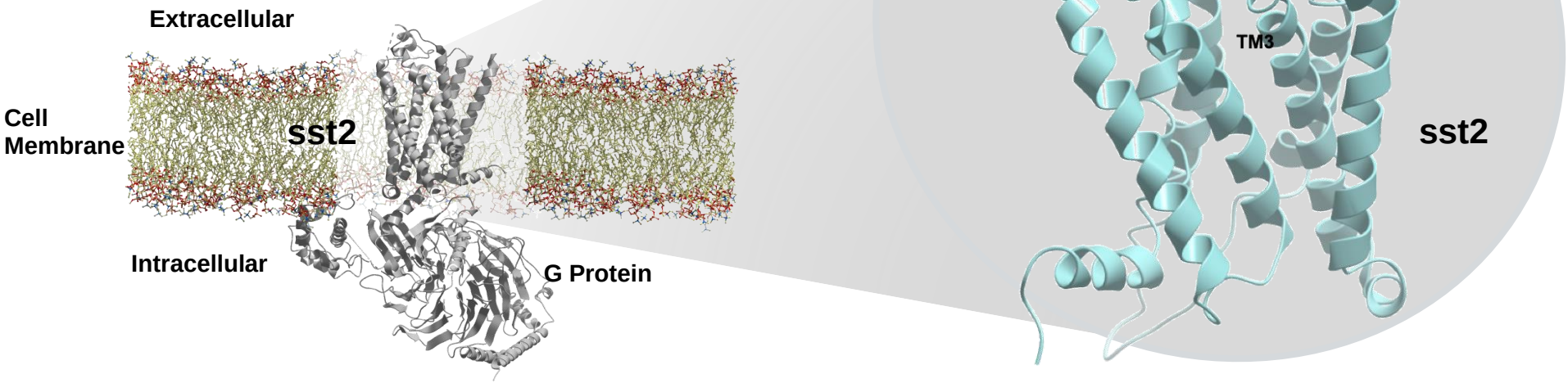
CRN00808 is a *nonpeptide*

Somatostatin-14:
H-Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys-OH



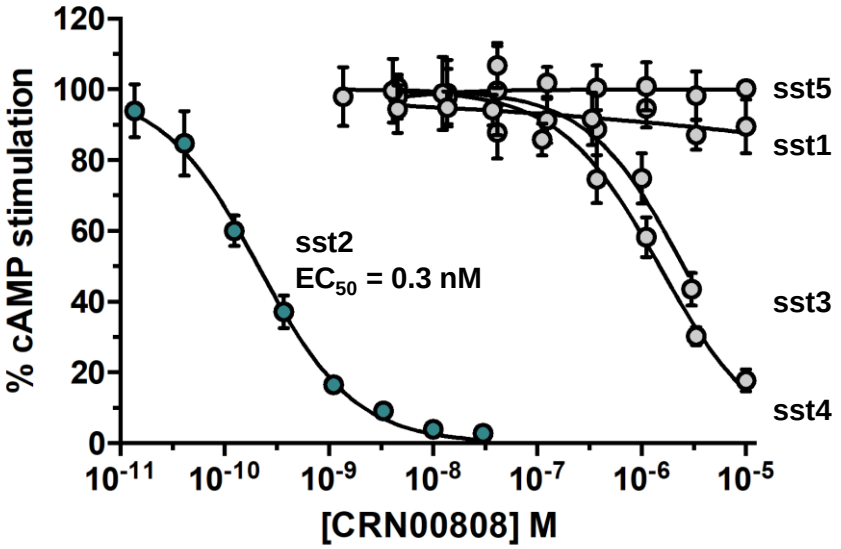
CRN00808





CRN00808 overview

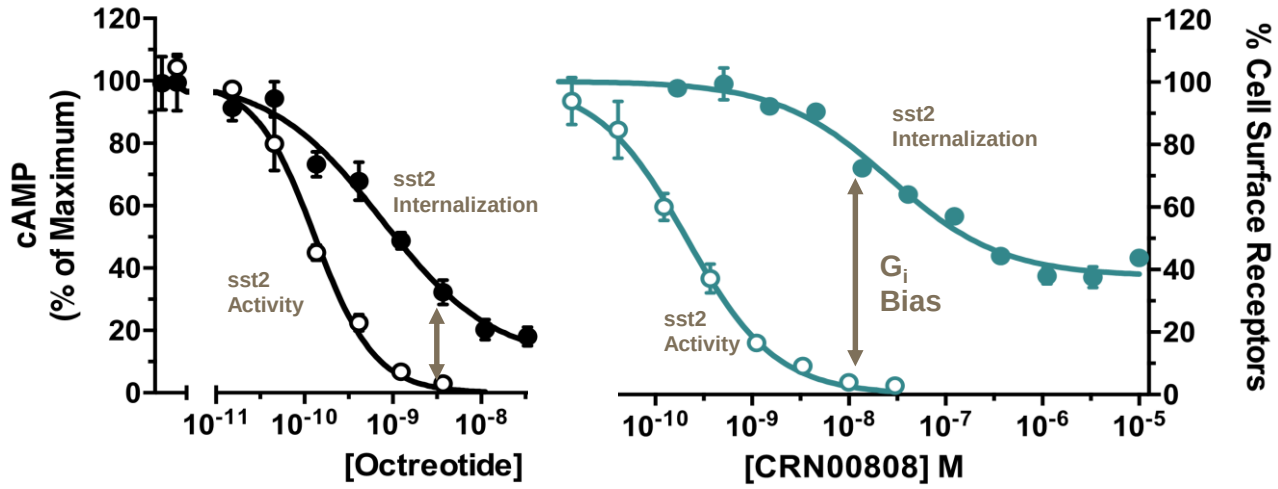
Selectivity for somatostatin receptor subtypes

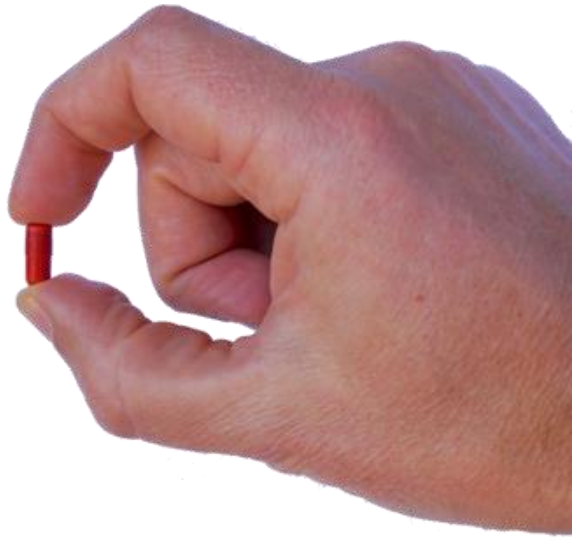


Good "drug-like" pharmaceutical properties

- ✓ High oral bioavailability
- ✓ 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





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

PRODUCT CANDIDATE TAILORED TO DELIVER KEY BENEFITS

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)

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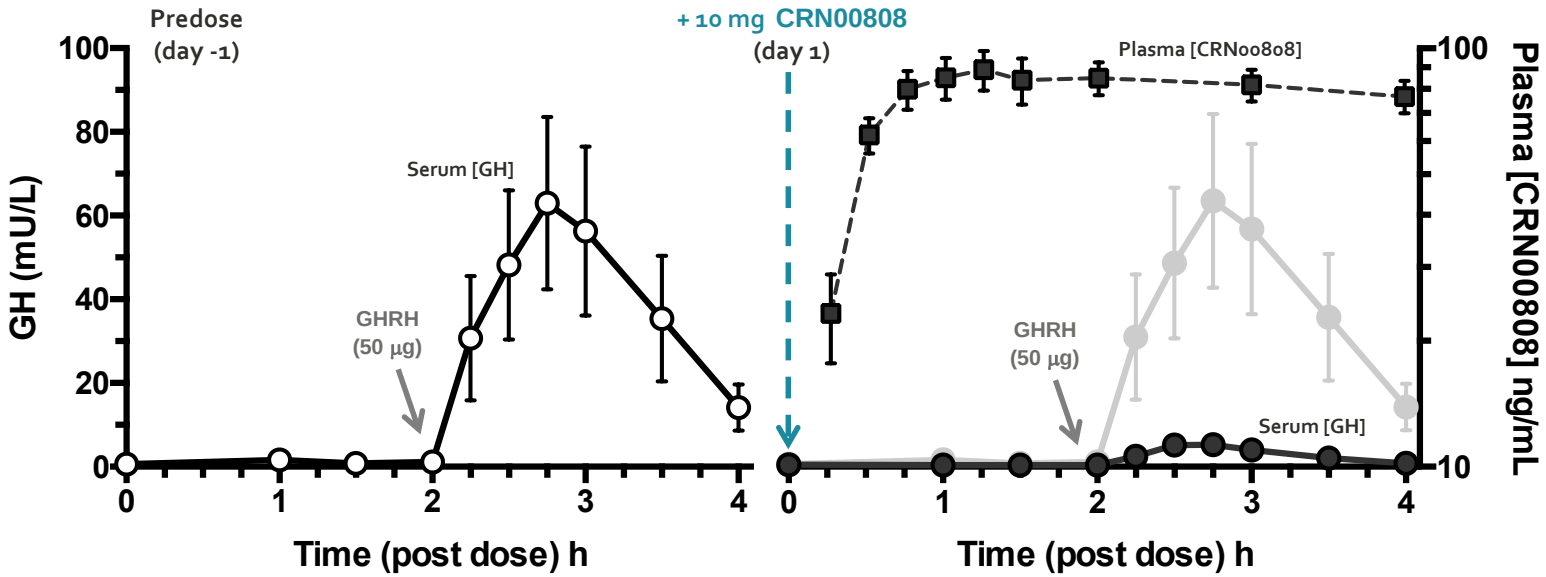
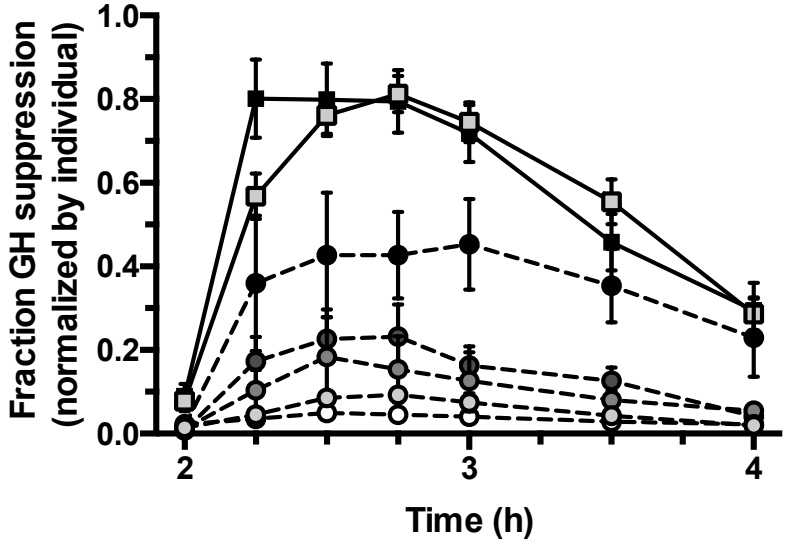
Phase 1 SAD arm: PK/PD analysis

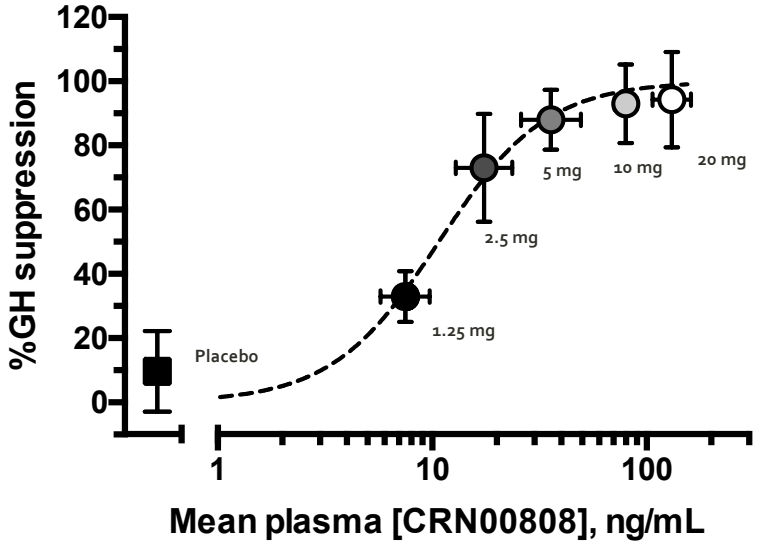
Suppression of GHRH stimulated GH secretion by 10 mg of CRN00808



Dose response of GH suppression

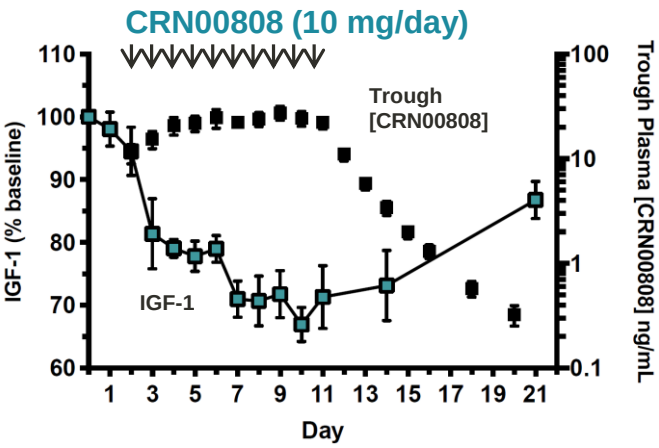


Exposure response of GH suppression

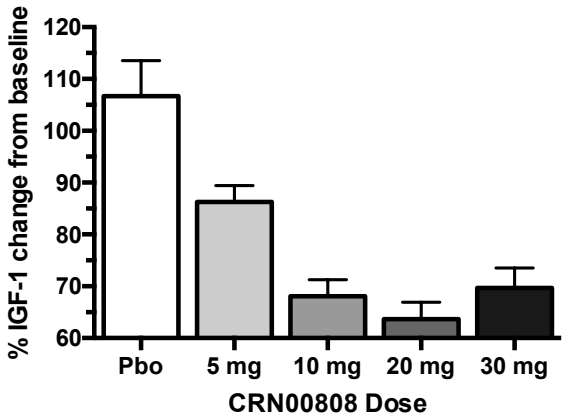


Phase 1 MAD arm: PK/PD analysis

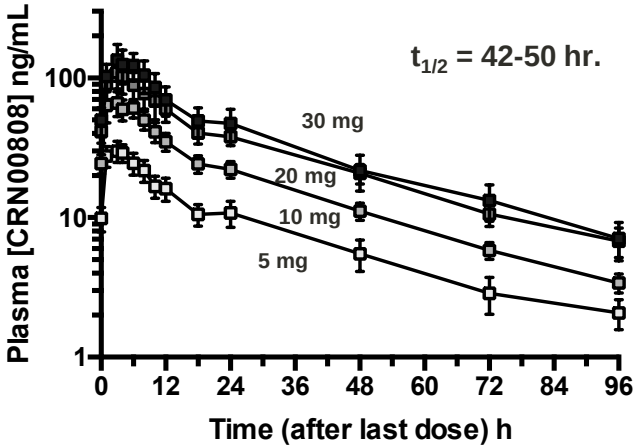
Time-course of plasma CRN00808 trough and IGF-1 concentrations



Dose response of IGF-1 suppression



Plasma concentration on the last day of dosing



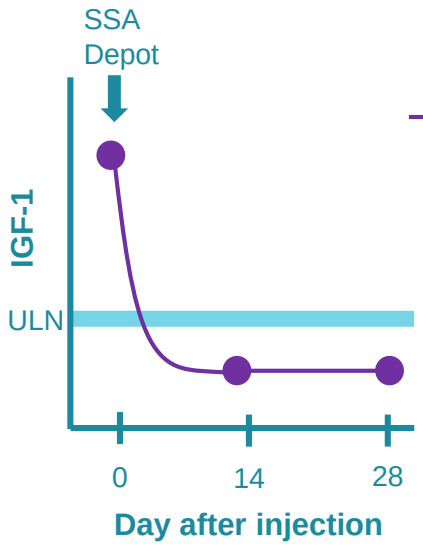
Safety & tolerability across phase 1

- 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 CRN00808. 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

CRN00808 targeted acromegaly market segments

Complete Responder (Controlled)

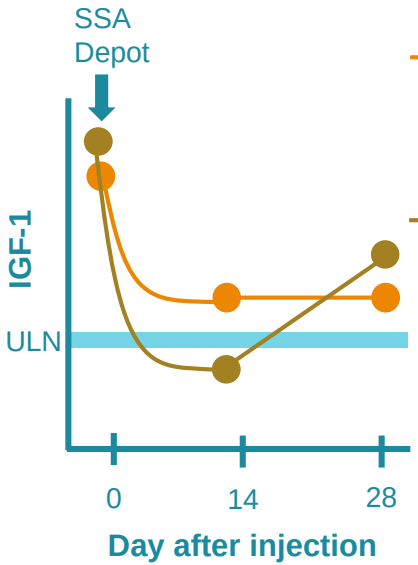


Normalized IGF-1

25 – 30% of patients

ACROBAT EVOLVE

Partial Responder (Uncontrolled)



Reduction without normalization. Higher dose or second line therapy recommended

Depot wears off and symptoms return at end of month

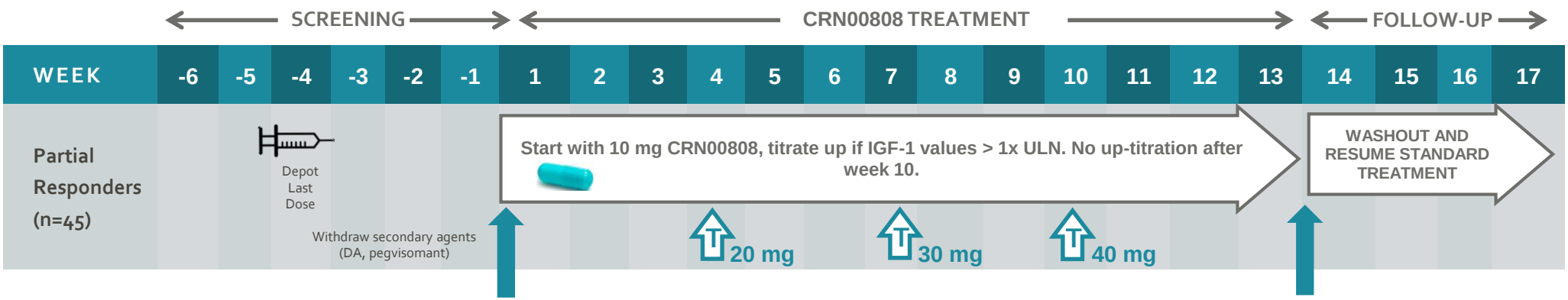
>65% of patients

ACROBAT EDGE

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

Acromegaly Phase 2 Trial for Partial Responders to Injectable SSAs

Exploration of CRN00808 in patients inadequately controlled on injected SSA monotherapy



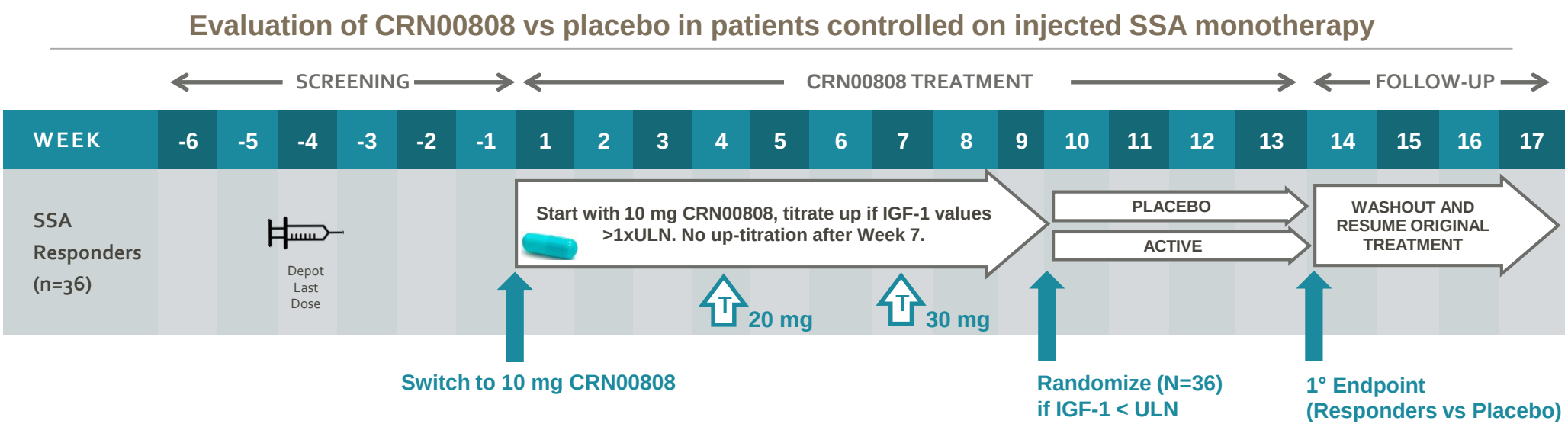
Group	Patient Groups	IGF-1 range	# of Patients
1	Octreotide LAR or lanreotide depot	> 1.0x ULN to ≤ 2.5x ULN	at least 30
2	Dopamine agonist + octreotide LAR or lanreotide depot	> 1.0x ULN to ≤ 2.5x ULN	
3	Dopamine agonist + octreotide LAR or lanreotide depot	≤ 1.0x ULN	Max 15
4	Pasireotide LAR	≤ 1.0x ULN	
5	Pegvisomant + octreotide LAR or lanreotide depot	≤ 1.0x ULN	

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

IGF-1 measured at central laboratory using IDS-iSYS platform

ACROBAT EVOLVE Acromegaly Phase 2 Trial for Patients Controlled on Injectable SSAs



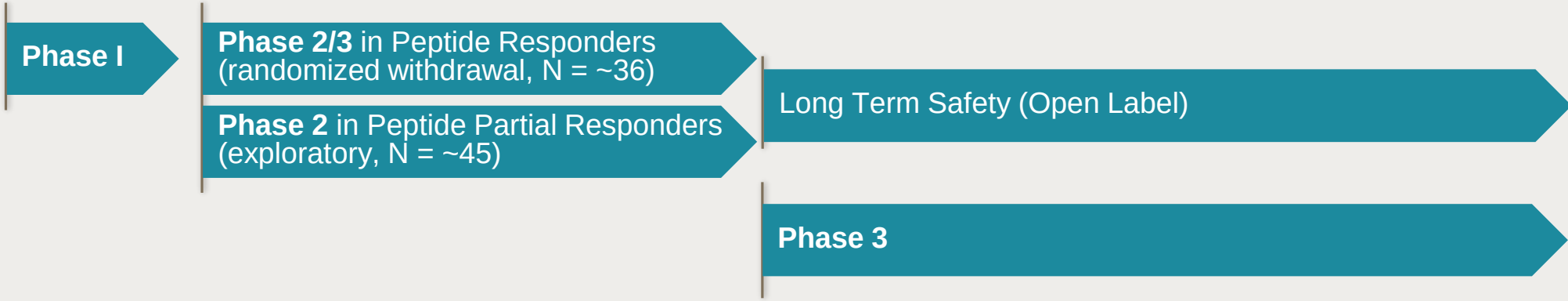
Key inclusion/exclusion criteria

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

IGF-1 measured at central laboratory using IDS-iSYS platform

CRN00808: Established clinical development strategy based on other approved products

Planned clinical development path outline

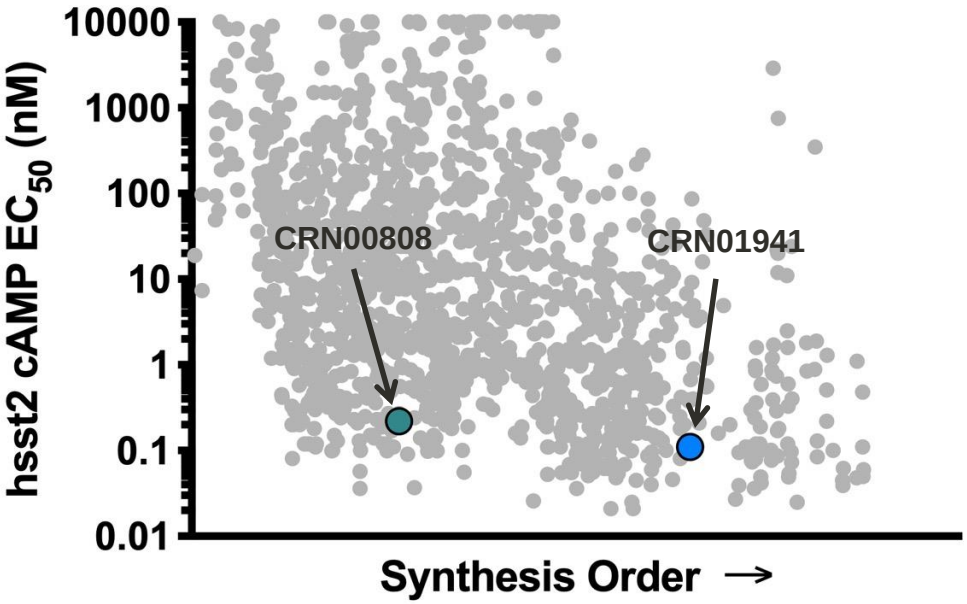


Summary of acromegaly registration trials for other products

DRUG (TRIAL)	COMPARATOR	N	PRIMARY ENDPOINT
Somatuline® Depot (lanreotide) Injection	placebo	107	50% GH ↓ @ 4 weeks
	none	63	IGF normalization @ week 48
Oral octreotide	baseline	155	IGF normalization @ month 7
	placebo	56	IGF normalization @ month 9
	octreotide/lanreotide	150	TWA IGF-1 over 9 months
Signifor (pasireotide) Injection 0.3 mg/mL, 0.6 mg/mL, 0.9 mg/mL	octreotide/lanreotide	198	GH + IGF normalization @ week 12
	octreotide	358	GH + IGF normalization @ month 12
SOMAVERT pegvisomant	placebo	112	IGF reduction / normalization @ week 12

CRN01941 overview

Results of sst2 chemistry effort



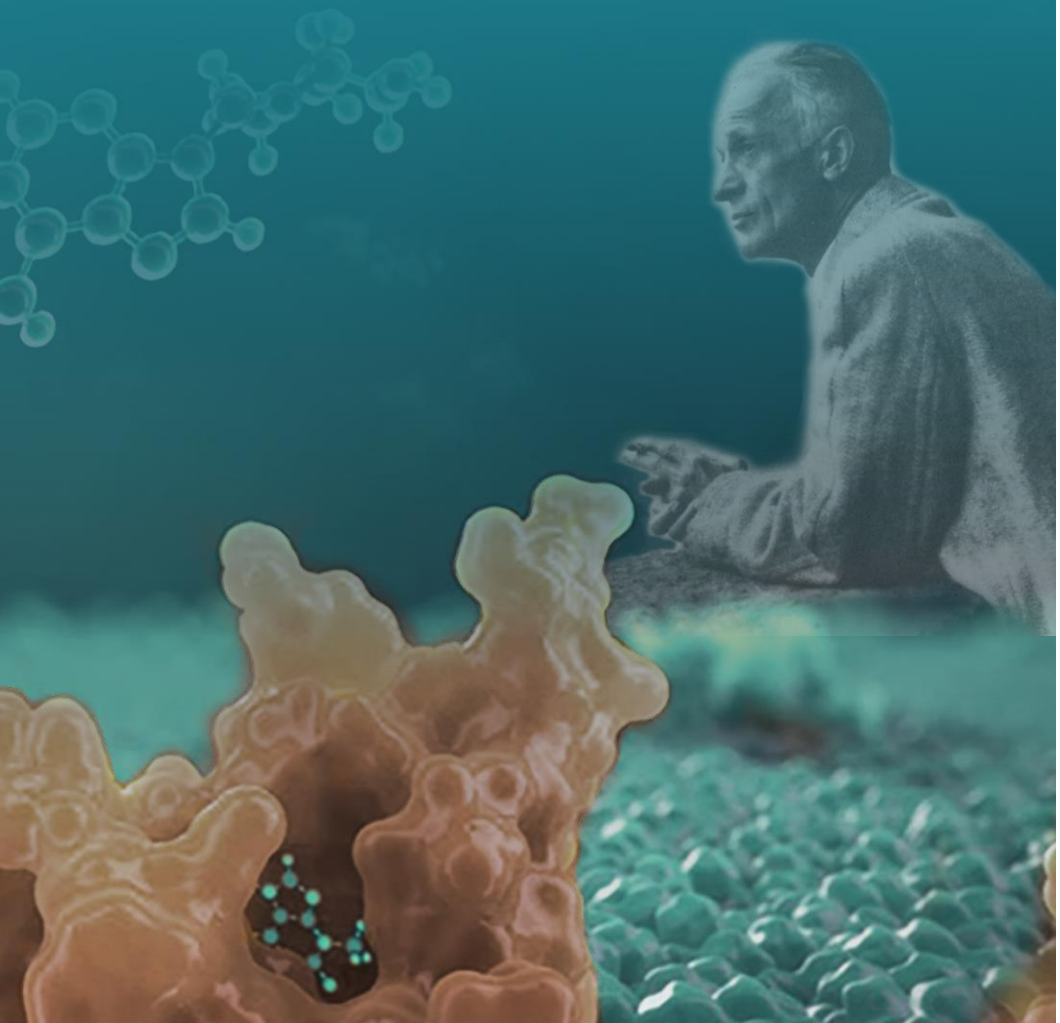
Creating business optionality

- Distinct chemical series from CRN00808
- Distinct patent family from CRN00808
- Potential backup to CRN00808
- Potential for independent NETs development
- Potential for independent pricing
- Potential for independent partnering

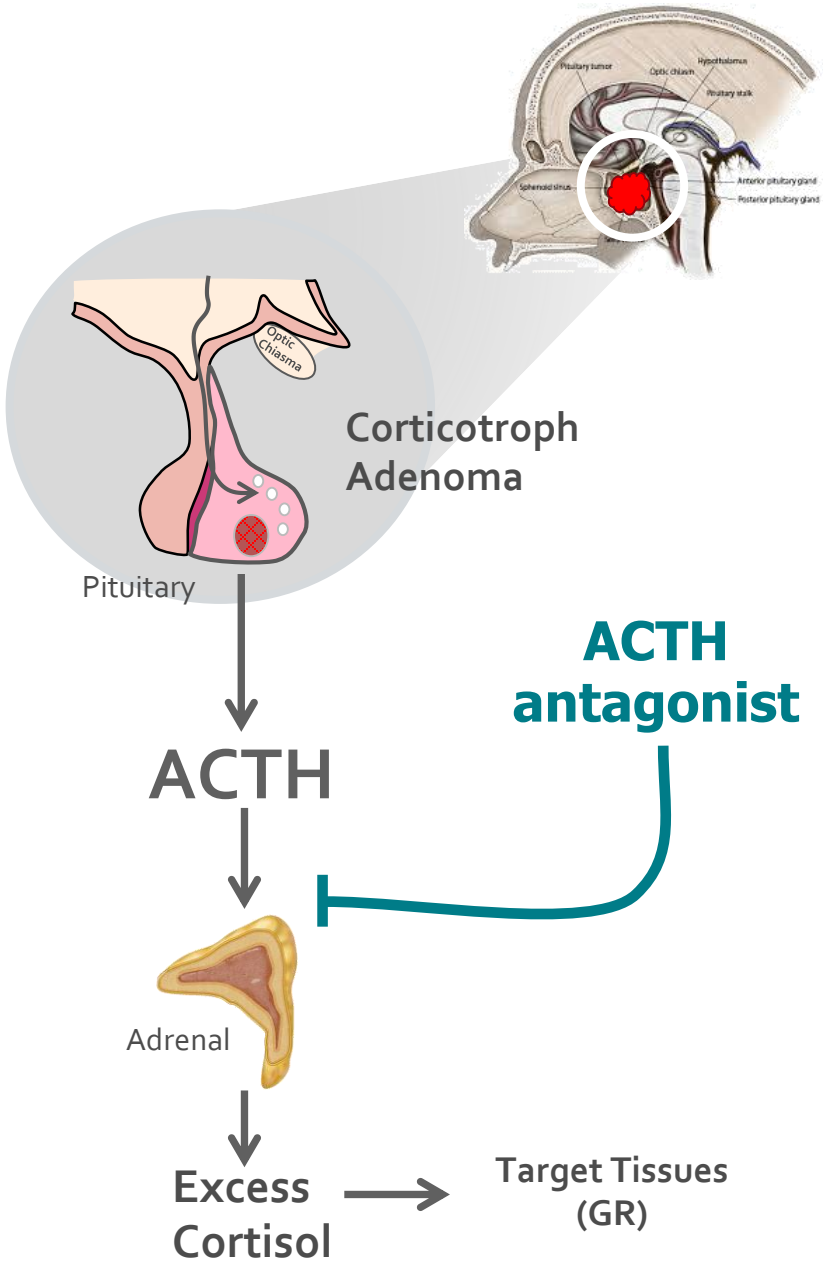
Phase 1 human proof-of-concept clinical trial ongoing with results expected in late 2019 / early 2020

ACTH Antagonists

for the treatment of Cushing's disease and other conditions of ACTH excess



Cushing's Disease Etiology

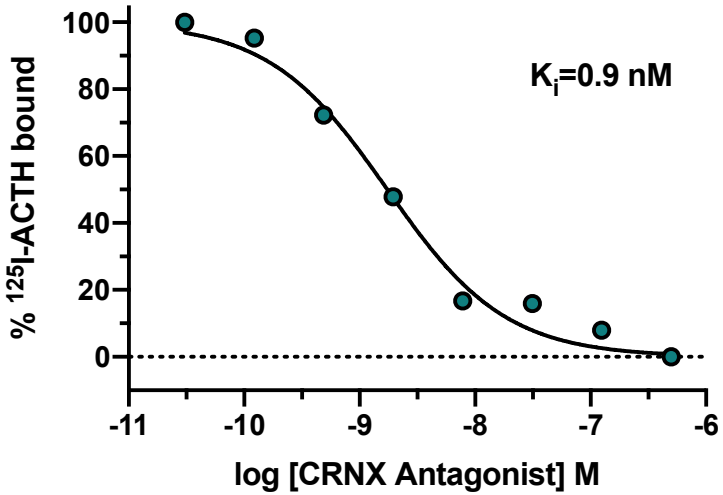


Cushing's Disease Standardized Mortality Ratio = 2.4 (95% CI, 1.2-3.9)

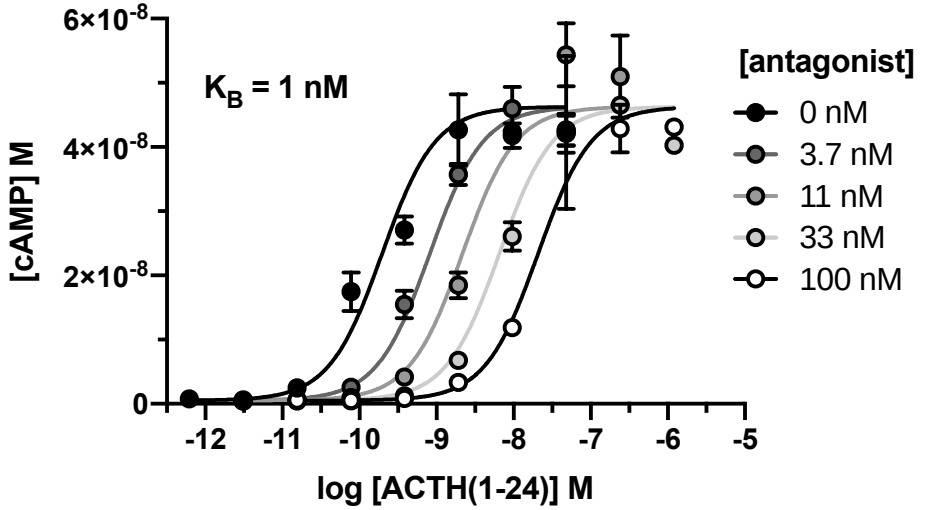
Source: Dekkers et al (2007) 1210, 2006-2012

An ACTH antagonist lead

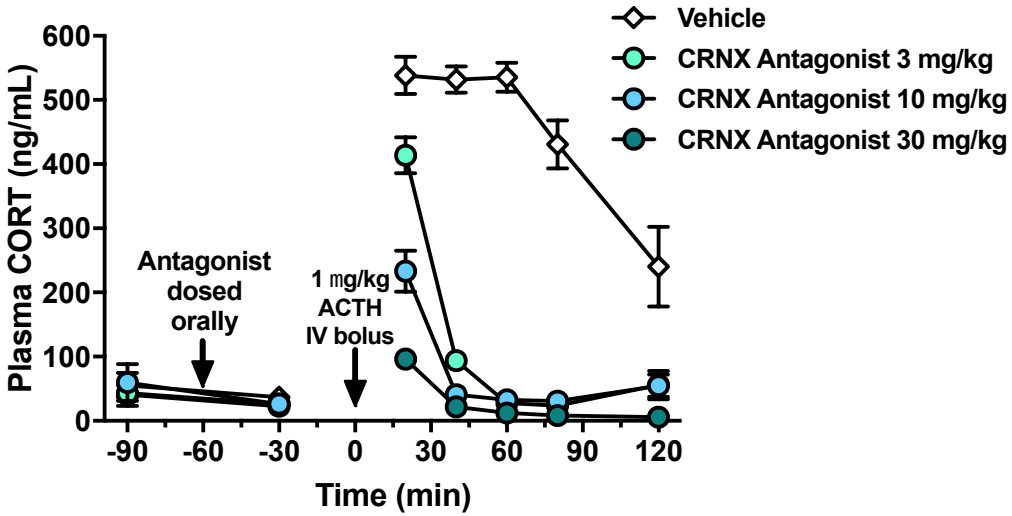
Competition radio-ligand binding assay



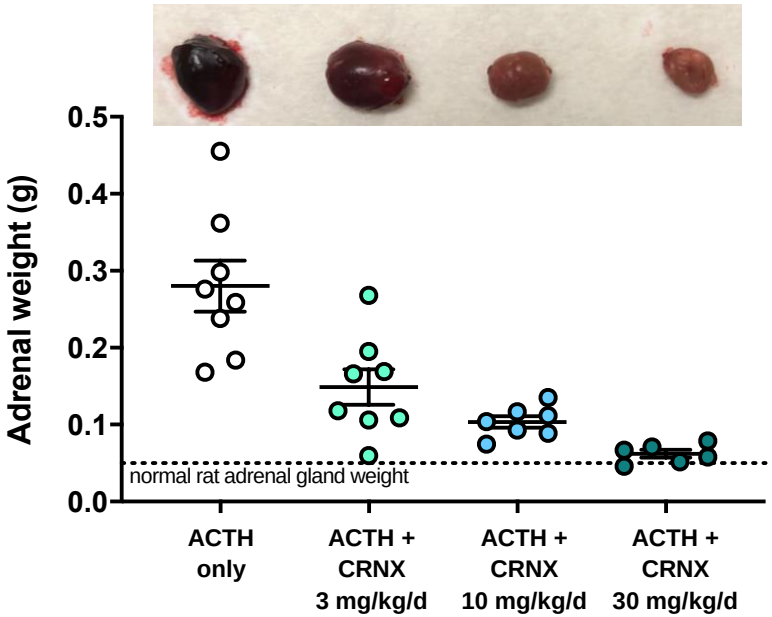
Schild analysis of functional antagonism



In vivo POC: acute suppression of ACTH-induced corticosterone in rats



In vivo POC: repeat antagonist dosing (7d) rescues adrenal hypertrophy from chronic ACTH infusion



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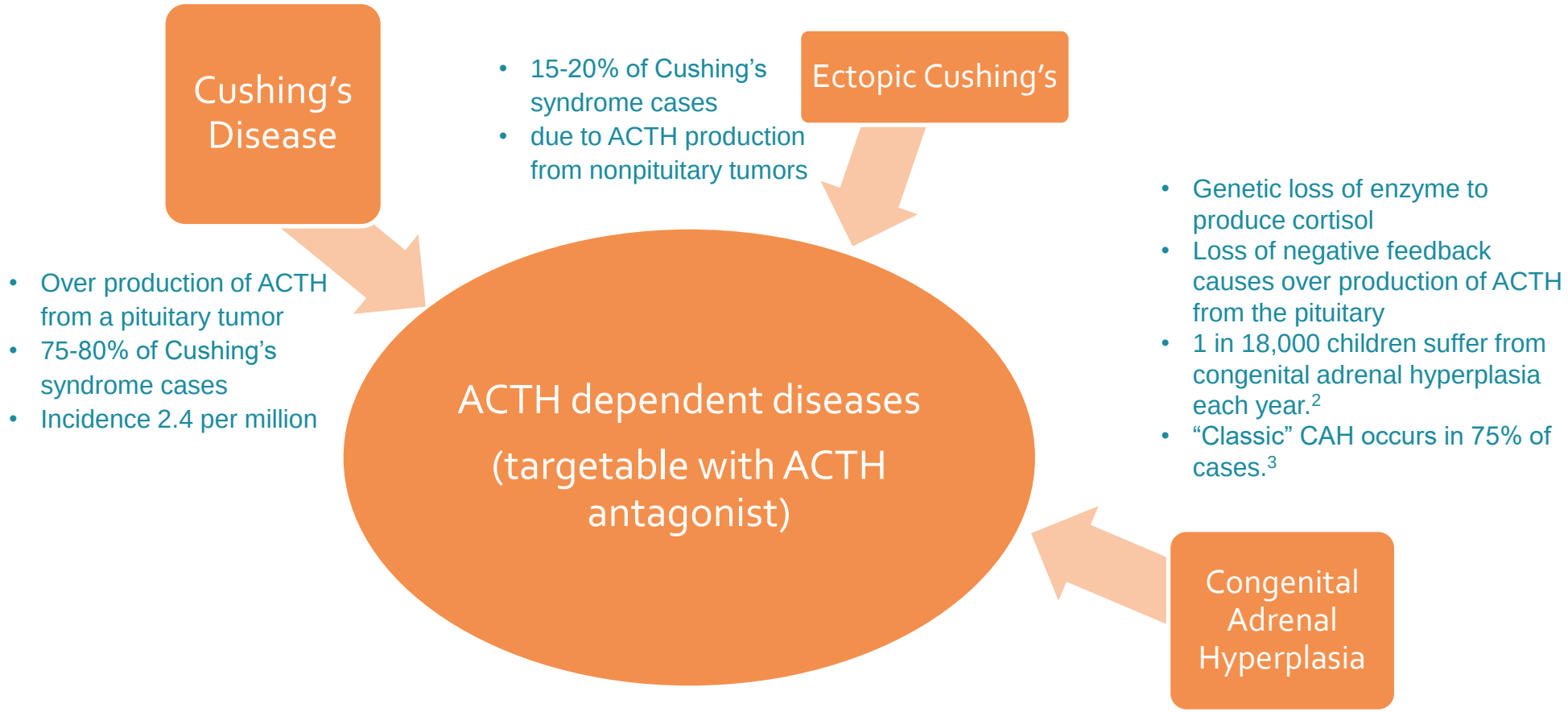
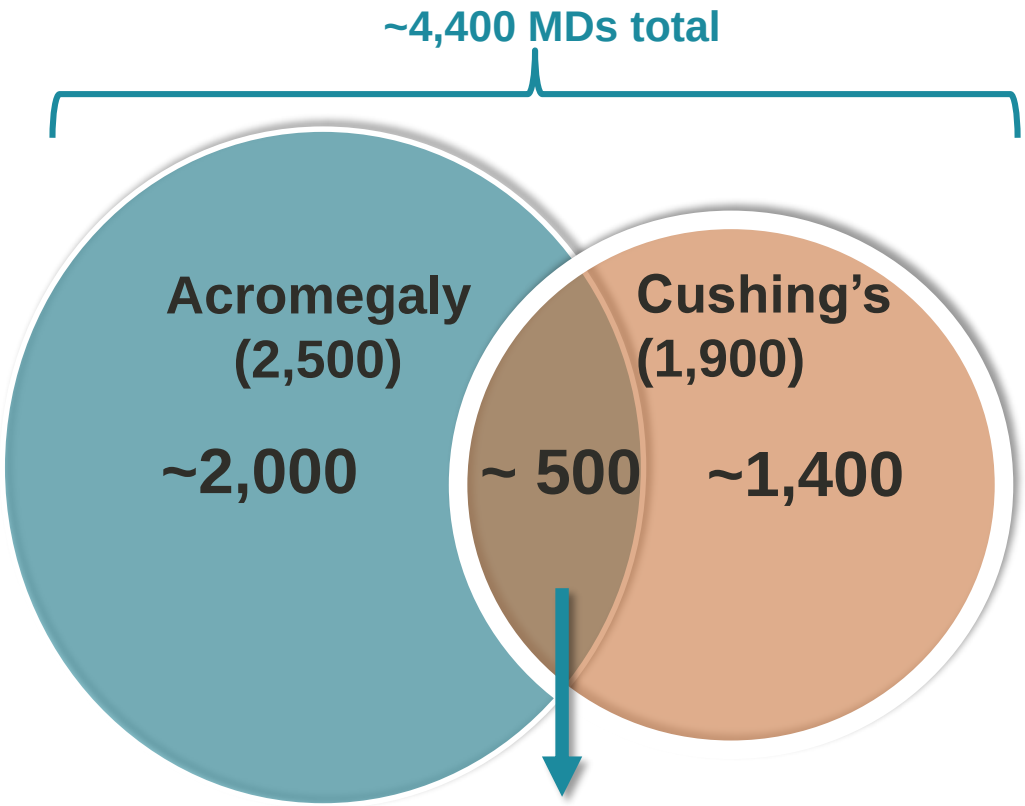
Multiple markets of entry possible for ACTH antagonist

All these indications have high unmet medical need



1. Sharma TS et al. Clin Epidemmiol. 2015;7;281-293 2. National Institute of Child Health and Human Development
3. Phyllis W. Speiser, M.D. Medical Management of CAH retrieved from www.caresfoundation.org

Approximately 4,400 Unique Physicians Treat Acromegaly or Cushing's Disease (CD) Patients



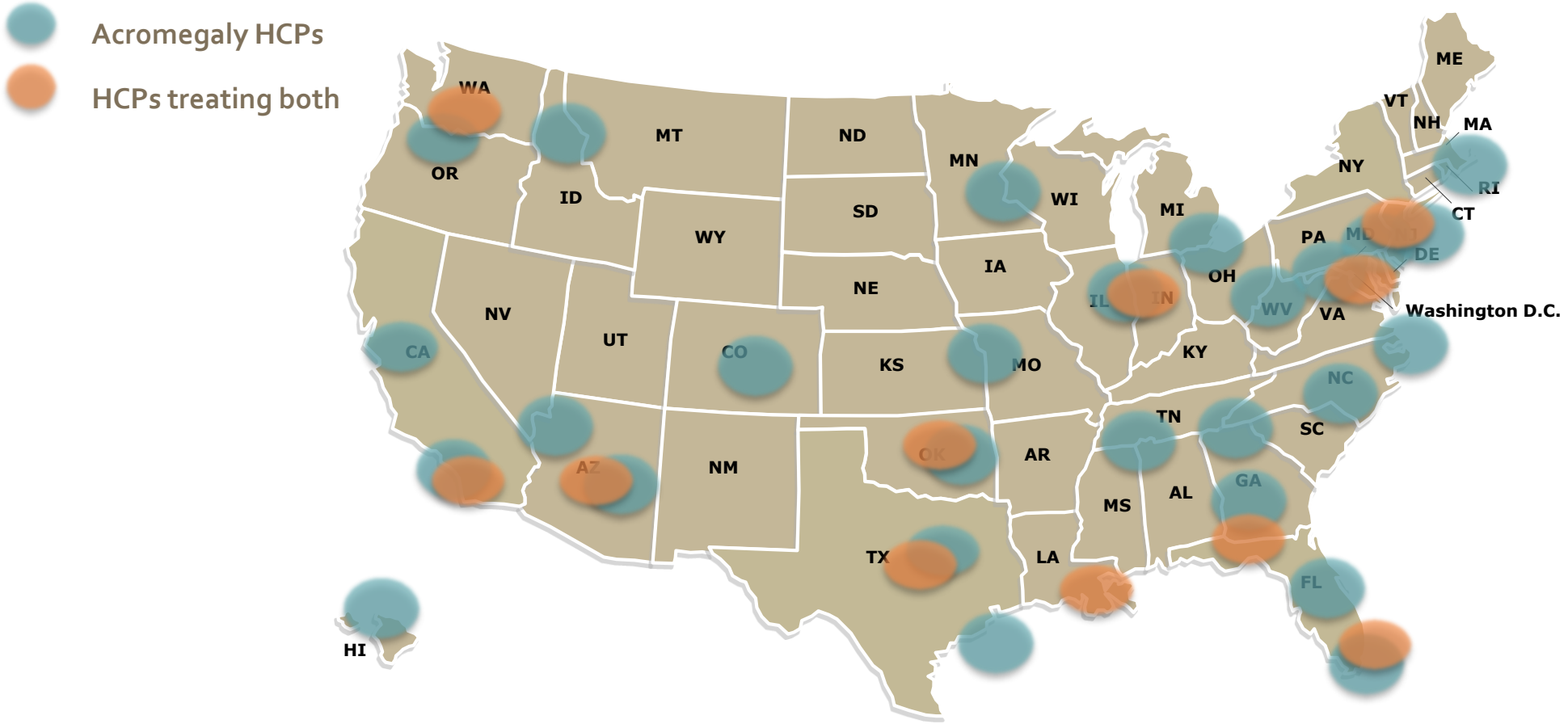
500 core neuroendocrinology specialists

- 55% Acromegaly treated patients and 40% of all acromegaly prescriptions
- 44% CD treated patients and 45% of all Cushing's prescriptions

Crinetics adult endocrine portfolio can initially focus on 500 physicians treating both acromegaly and Cushing's disease

1. Broder MS, et al Pituitary. 2015 Jun 18(3) 283-9 2. Data on file, US Health claims data 2017-18

Health care providers treating acromegaly and Cushing's disease are highly concentrated



Includes Acromegaly Rx Decile HCP 2-10

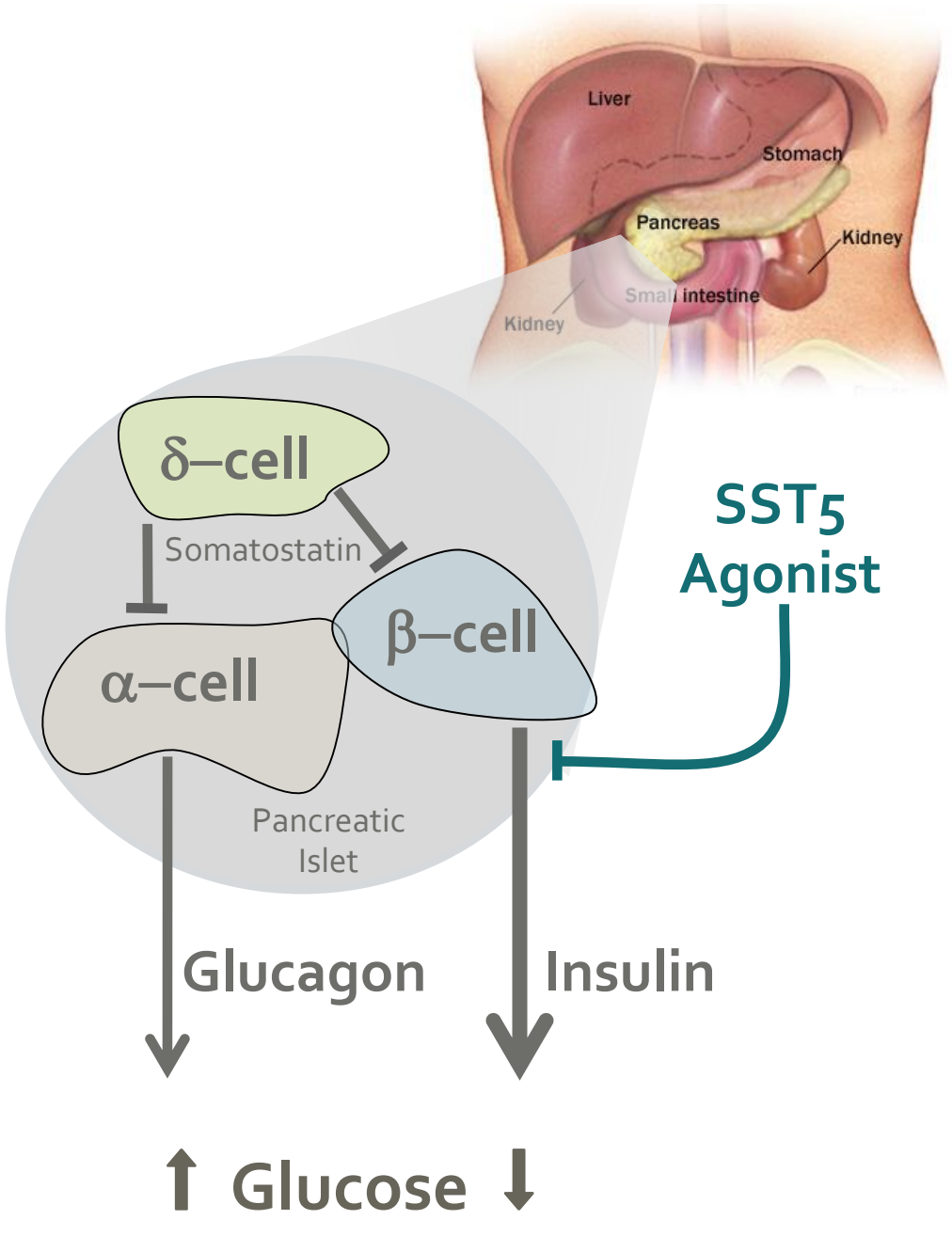
Approximately 1,200 health care providers treat 90% acromegaly patients[1] and overlap with those treating Cushing's disease patients

1. Data on file, US Health claims data 2017-18

sst5 Agonists

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

Hyperinsulinism and Hypoglycemia



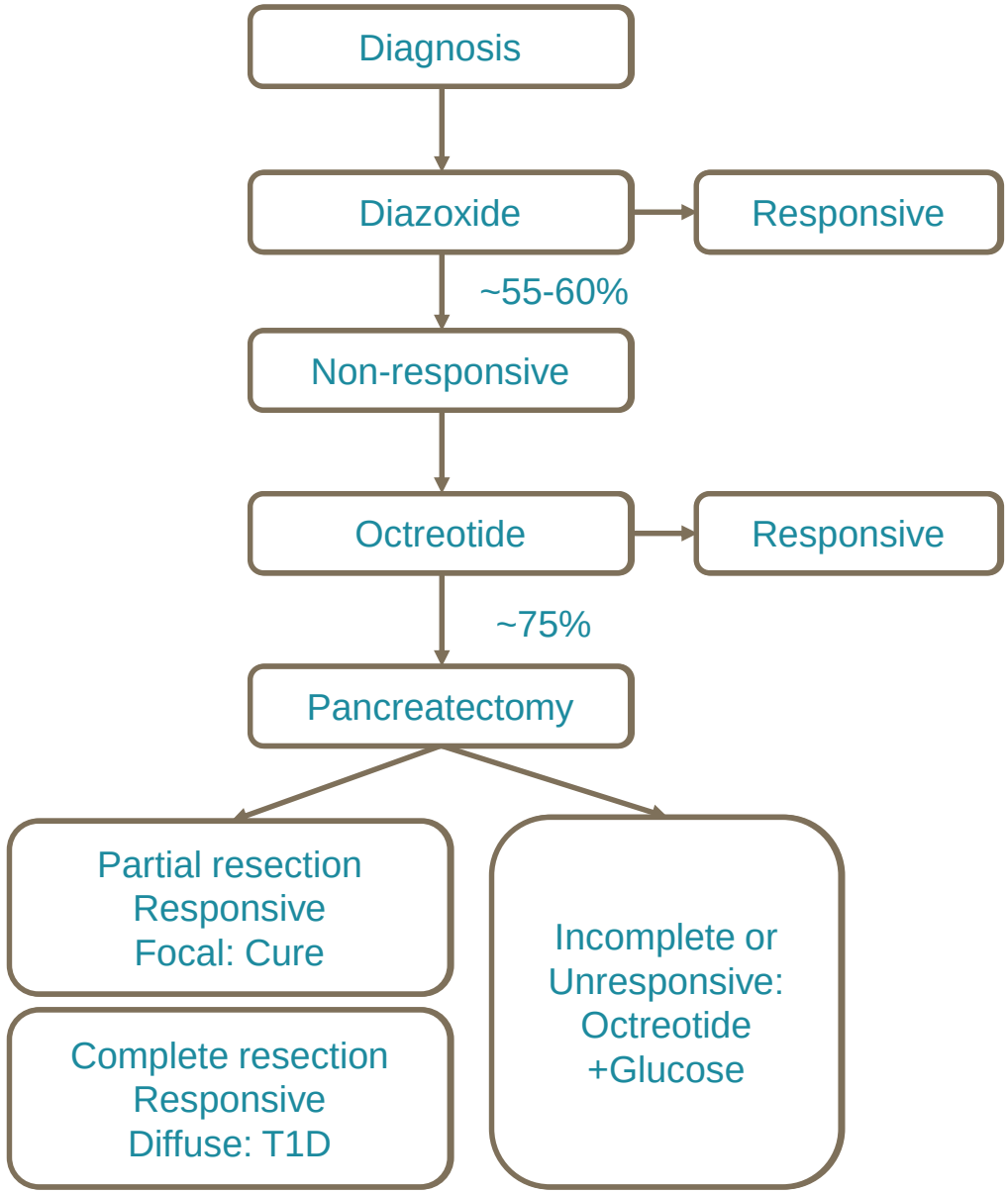
Congenital Hyperinsulinism (CHI): disease overview and treatment limitations

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)

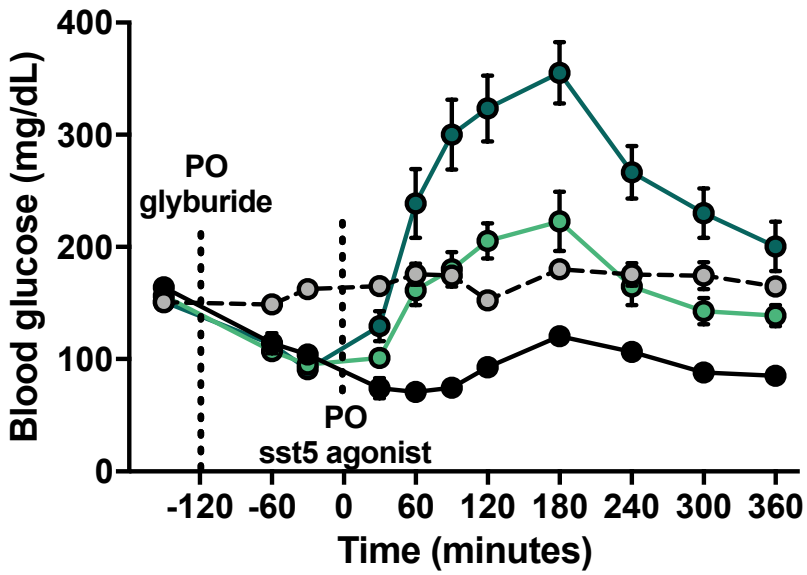
Patient and parent goals

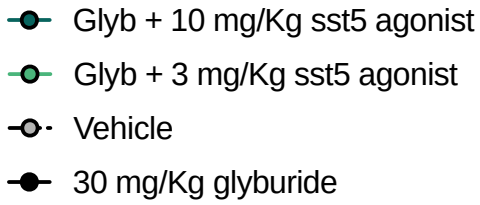
- Avoid pancreatectomy
- Prevent cognitive / developmental problems
- Reduce injections and glucose sticks
- Medical management until HI is resolved
- Live a normal life



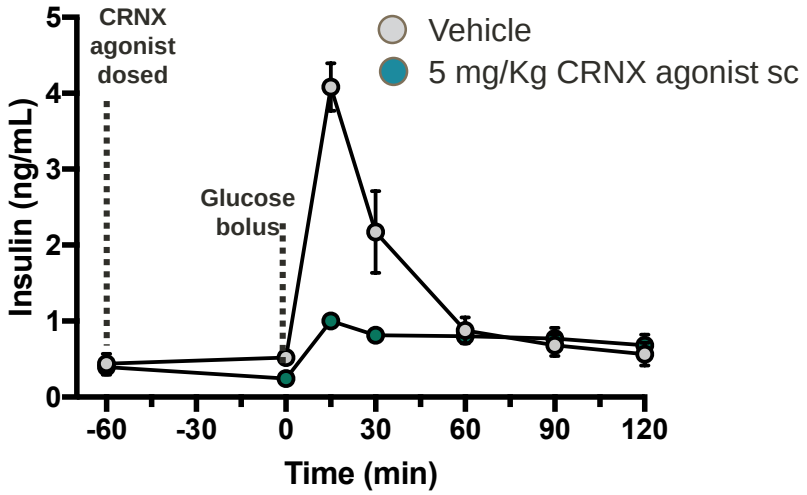
sst5 Agonists: Preclinical results

Rescue of hypoglycemia in rats induced by treatment with sulfonylurea glyburide

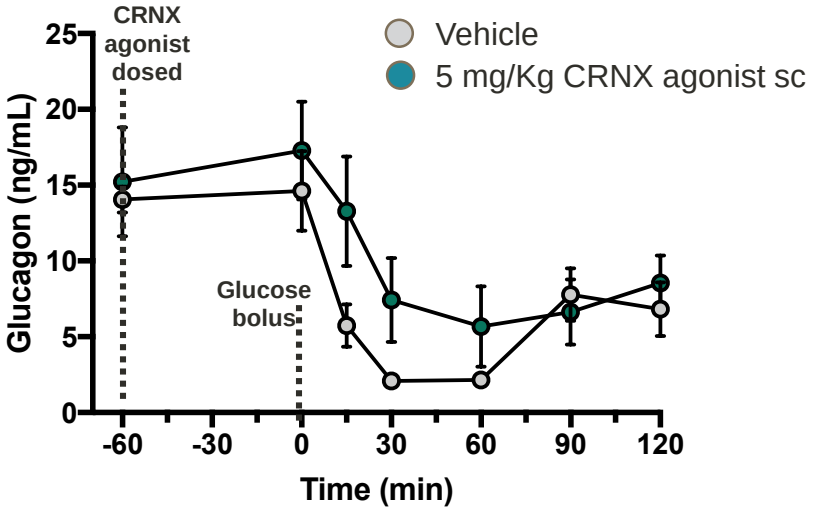




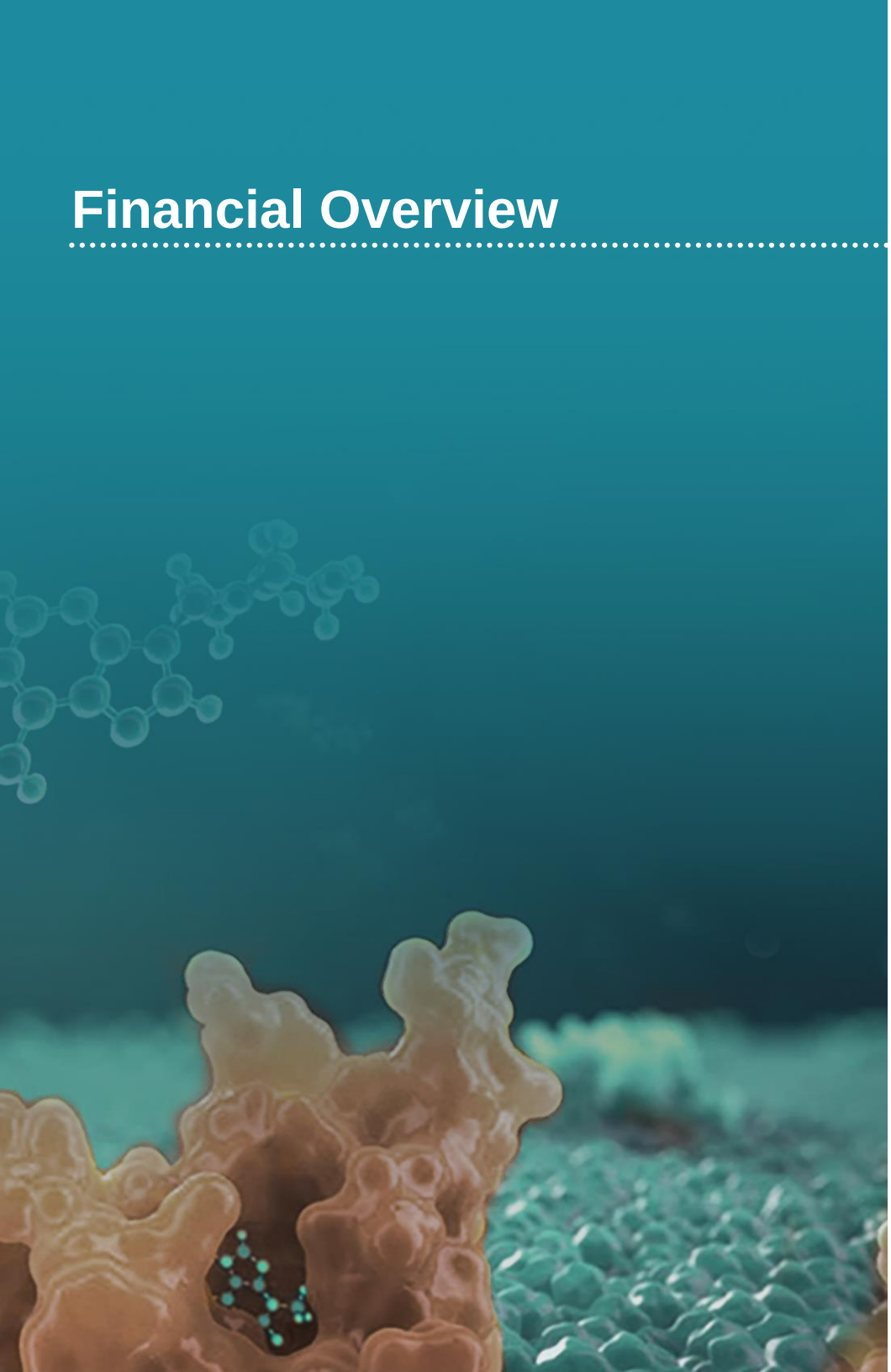
In an OGTT, CRNX agonist suppressed insulin…



…while maintaining glucagon levels



Financial Overview



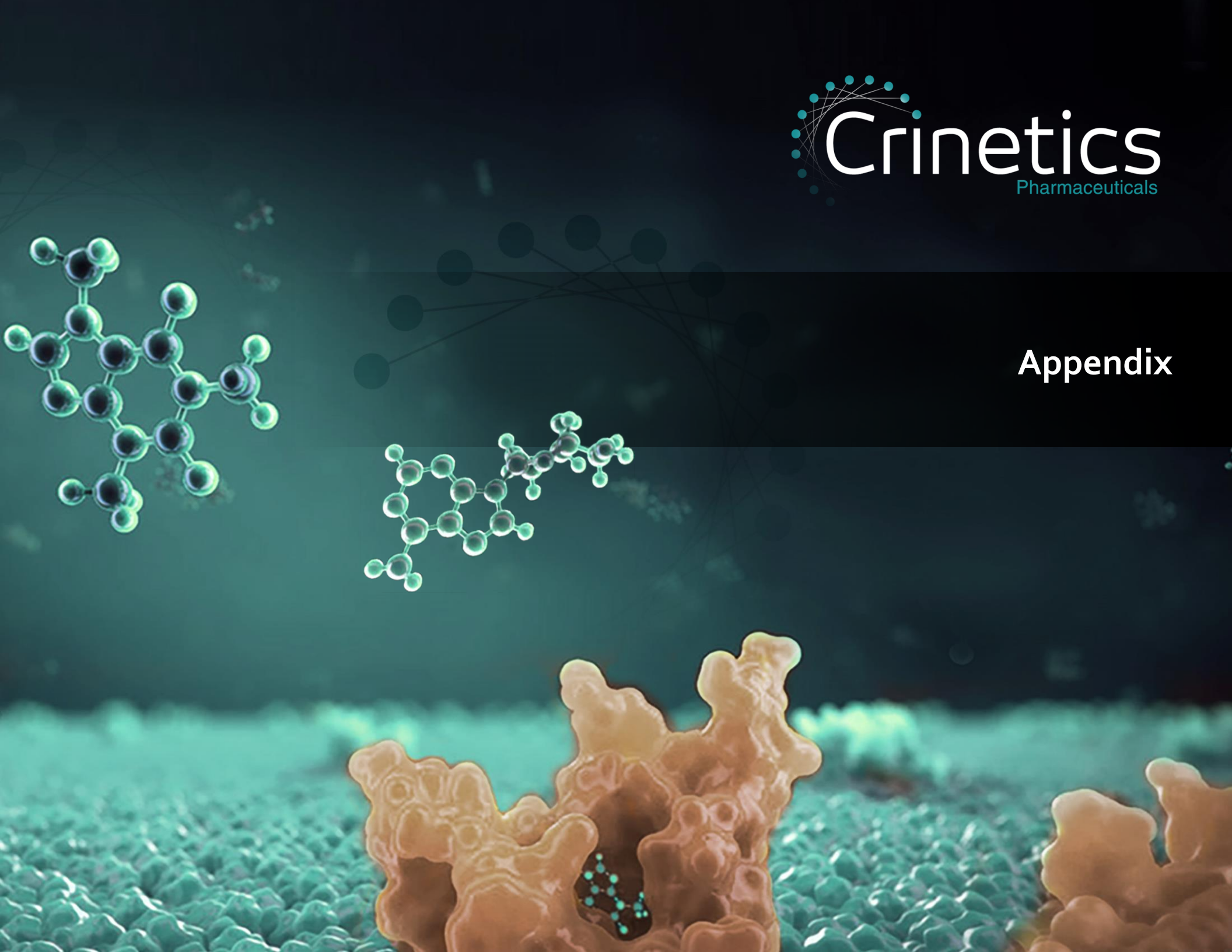
As of June 30, 2019

- $145.0 million cash and investments
- Cash runway through 2020
- 24.2 million common shares outstanding

Crinetics
Pharmaceuticals

Crinetics
Pharmaceuticals

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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Scott Struthers, PhD	Founder & CEO
Steve Kaldor, PhD	Former CEO, Quanticel
Matt Fust, M.B.A.	Former CFO, Onyx
Jack Nielsen, M.Sc.	Managing Director, Vivo Capital
Weston Nichols, PhD	Analyst, Perceptive Advisors
Stephanie Okey, M.S	Former SVP, Genzyme Corporation

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