Crinetics Pharmaceuticals

Developing GPCR-targeted oral small molecules for endocrine disorders and endocrine-related tumors

CORPORATE PRESENTATION

March 2023

SAFE HARBOR STATEMENT

This presentation contains forward-looking statements. Crinetics Pharmaceuticals, Inc. ("Crinetics") cautions you that statements contained in this presentation regarding matters that are not historical facts are forward-looking statements. These statements are based on the company's current beliefs and expectations. Such forward-looking statements include, but are not limited to, statements regarding: the potential benefits of paltusotine for acromegaly patients and patients with carcinoid syndrome; the potential for the PATHFNDR program to support registration of paltusotine for all acromegaly patients who require pharmacotherapy; the expected timing of topline data from the PATHFNDR-1 and PATHFNDR-2 studies and the Phase 2 study in patients with carcinoid syndrome; the potential benefits of CRN04894 in patients across multiple indications and the expected plans and timing of the initiation of Phase 2 programs; the potential benefits of CRN04777 in patients with congenital or syndromic hyperinsulinism and the expected plans and timing of the initiation of a Phase 2 program; the potential benefits of PTH receptor antagonists for patients with hyperparathyroidism, the potential benefits of TSH antagonist for Graves' Disease or Thyroid eye disease; the potential for any of our ongoing clinical studies to show safety or efficacy; the potential of our ongoing discovery efforts to target future indications for polycystic kidney disease, or diabetes/obesity; and our plans to identify and create new drug candidates for additional diseases. 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," "laying the foundation," "aspiring," "target" 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 preliminary results of preclinical studies or clinical studies 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 studies and the reporting of data therefrom; the FDA or other regulatory agencies may require additional clinical studies of paltusotine or suggest changes to our planned Phase 3 clinical studies prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; 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 studies 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 studies, nonclinical studies and preclinical studies for paltusotine, CRN04894, CRN04777, our discovery efforts for hyperparathyroidism, polycystic kidney, Graves' Disease & Thyroid eye disease or diabetes/obesity product candidates; regulatory developments or price restrictions 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 ("SEC"). 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.

Building the World's Premier Fully-Integrated Endocrine Company

Crinetics Today

- Leading GPCR drug discovery platform
- Global endocrinology clinical study capabilities
- First Phase 3 readout expected in 2023
- Pipeline: 3 product candidates with clinical POC

Crinetics Tomorrow

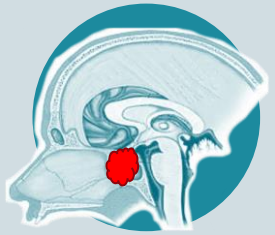
- Clinical POC in highly prevalent indications
- Global approvals for multiple products
- Fully integrated commercial capabilities
- Multiple programs in late clinical development

Building a sustainable company to bring product after product to market by continuously innovating from discovery to commercialization

GPCR: G protein-coupled receptor; POC: Proof-of-concept

De-risk and Accelerate Time to POC with Crinetics' Endocrine GPCR Discovery and Development Engine

Well-Understood Targets

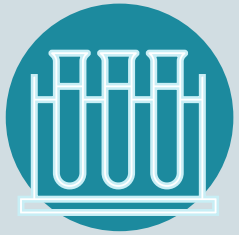


Identify endocrine indications with unmet needs and well-understood targets

Drug Discovery Expertise

Craft high quality, orally bioavailable, small molecule drug candidates

Highly Conserved Models



Select best candidates with predictive endocrine biomarkers in preclinical models

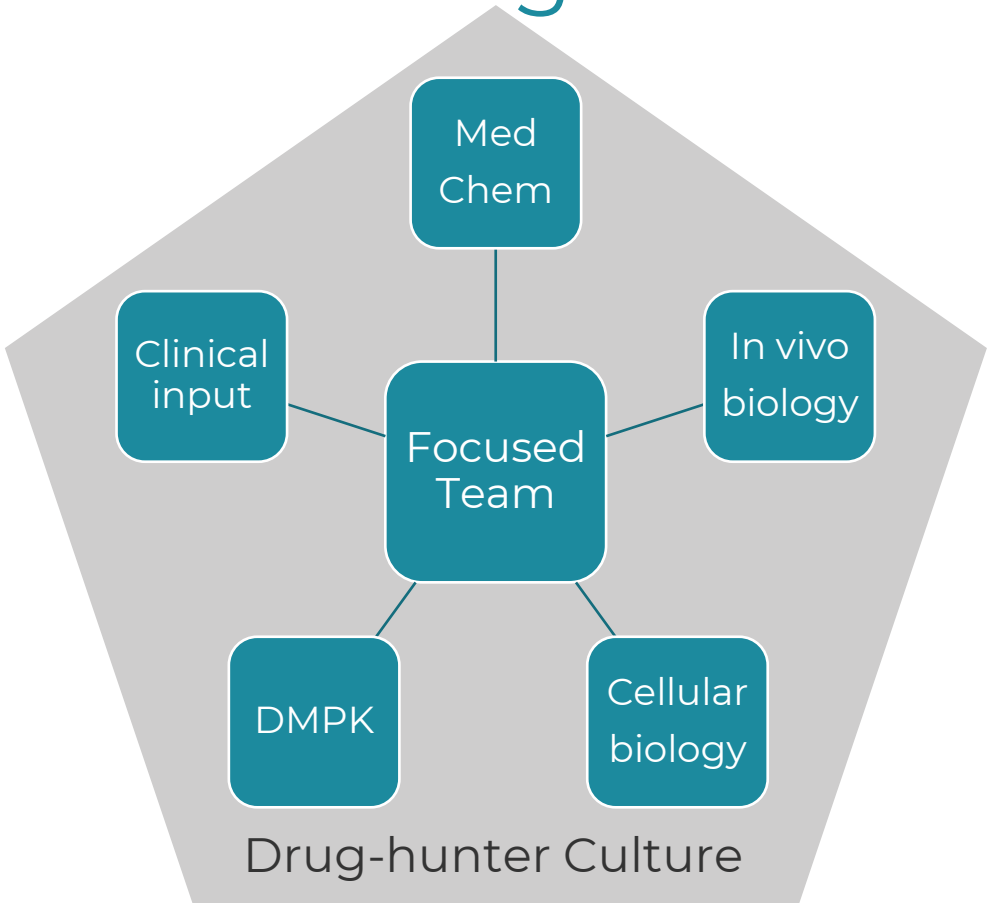
Biomarker Development

De-risk in healthy volunteers and then prove in patients with accepted hormone biomarker endpoints through registrational studies

A fully integrated and reproducible strategy for crafting drug candidates and de-risking development programs against important, difficult and high value drug targets.

POC: Proof-of-concept

Crinetics' Discovery Laboratory Has Reproducibly Crafted Drug Candidates That Work



Discovery Guiding Principle:
It's the Team, not just the Tools

- Understanding the biology and medicine is key
- Every GPCR is different
- Every assay cascade is different
- No one technique will solve every challenge
- No checklist can capture what makes a compound into a drug

Differentiation, speed and probability of success in drug discovery are determined by the teams operating these tools, the integrated strategies they employ, and the culture that drives them.

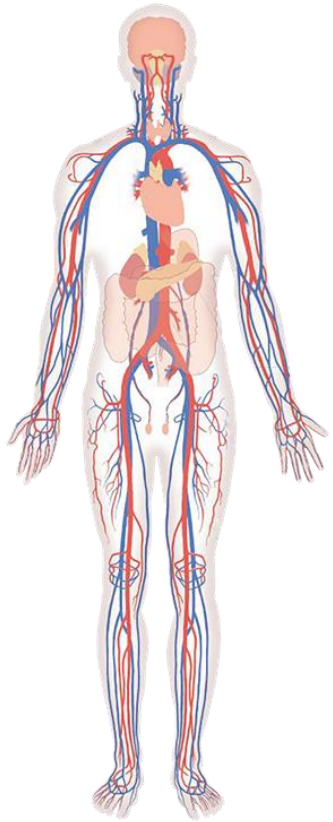
Endocrine GPCRs: Wide Open Field with Many High Value Opportunities

Approximately *one-third* of all approved drugs target GPCRs, but the majority of GPCR targets have been inaccessible.[1]

Many of these historically inaccessible endocrine GPCR targets possess:

- **High-probability biology** based on well characterized endocrine systems that are conserved across species, giving the ability to design early experiments that give highly translatable answers on both safety and efficacy (preclinical & clinical)
- **High-value opportunities** often addressing multiple highly prevalent indications

*CRNX Targeting Today / **Future***



Acromegaly
Neuroendocrine Tumors
Hyperinsulinism
Cushing's Disease
Congenital Adrenal Hyperplasia
Hyperparathyroidism
Polycystic Kidney Disease
Graves' Disease
Thyroid Ophthalmopathy
Diabetes
Obesity
Breast Cancer (RDNX)
Other Endocrine Cancers (RDNX)
Insulinoma
Hypoglycemia
Androgen Deficiency
Infertility
Thyroid Cancer
Growth Hormone Deficiency
Hypoparathyroidism
NASH
Nonfunctional Pituitary Adenomas
…

Source: 1. Hauser AS, Chavali S, Masuho I, et al. 2018;172(1-2):41-54.e19. doi:10.1016/j.cell.2017.11.033
RDNX: Targeted by Radionetics Oncology

Building a Synergistic Commercial Product Portfolio With Growing Stream of Catalysts

Program	Discovery	Preclin.	Phase 1	Phase 2	Phase 3	Anticipated Milestones
Paltusotine (SST2 agonist)*	Acromegaly (PATHFNDR-1)					Topline Results (3Q'23)
	Acromegaly (PATHFNDR-2)					Topline Results (1Q'24)
	Carcinoid Syndrome					Data (2H'23)
CRN04777 (SST5 agonist)	Congenital Hyperinsulinism					
CRN04894 (ACTH antagonist)	Cushing's Disease					Phase 2 Data (2024)
	Congenital Adrenal Hyperplasia					Phase 2 Data (2024)
PTH antagonist	Hyperparathyroidism					Candidate Selection (2023)
Undisclosed	Polycystic Kidney					Candidate Selection (2023)
TSH antagonist	Graves' Disease & TED					
Undisclosed (multiple)	Diabetes/Obesity					

NEW high prevalence indications

Crinetics is a known and trusted partner of the global endocrinology community who work with us on program after program

*Partnered with Sanwa Kagaku Kenkyusho for development and commercialization in Japan; SST: Somatostatin receptor type; ACTH: Adrenocorticotropic hormone; PTH: Parathyroid hormone; TSH: Thyroid-stimulating hormone; TED: Thyroid eye disease

Extending and Externalizing the Impact of our Discovery Engine to Novel Precision Targeted Radiopharmaceuticals

Radionetics Oncology

Crinetics Pharmaceuticals

5AM VENTURES

FRAZIER HEALTHCARE PARTNERS

Technology spun out of CRNX in 2021

- $30 million funding from 5AM Ventures and Frazier
- CRNX retains significant ownership
- Milestones in excess of $1B and single-digit royalties on net sales from technology license

Emerging broad clinical pipeline in oncology

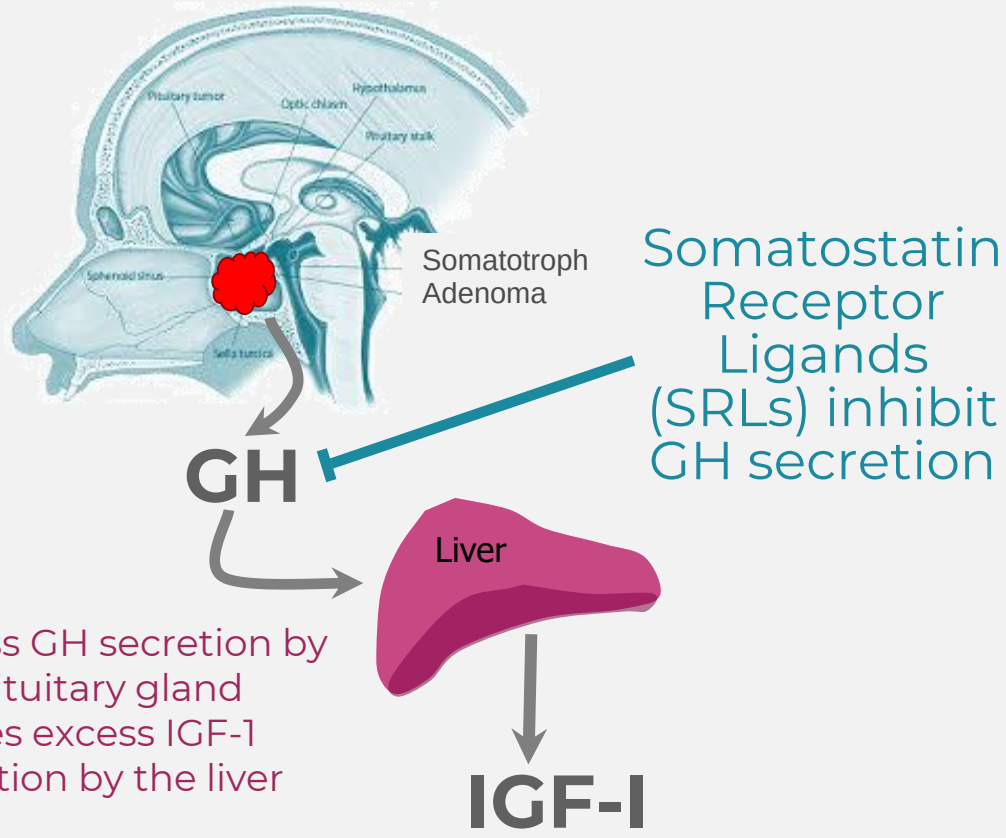
- Target 1: IND filing in an endocrine cancer in 1Q'23 with imaging POC in '23
- Target 2: IND filing in relapsed/refractory breast cancer in 4Q'23/1Q'24
- Potent leads against multiple additional targets for major cancers

PALTUSOTINE: A FIRST-IN-CLASS, ORAL SMALL MOLECULE SOMATOSTATIN RECEPTOR LIGAND FOR ACROMEGALY AND CARCINOID SYNDROME

Building Development and Commercial Capabilities

What is Acromegaly?

Acromegaly is caused by a benign pituitary tumor secreting excess growth hormone (GH)



Acromegaly Symptoms/Complications

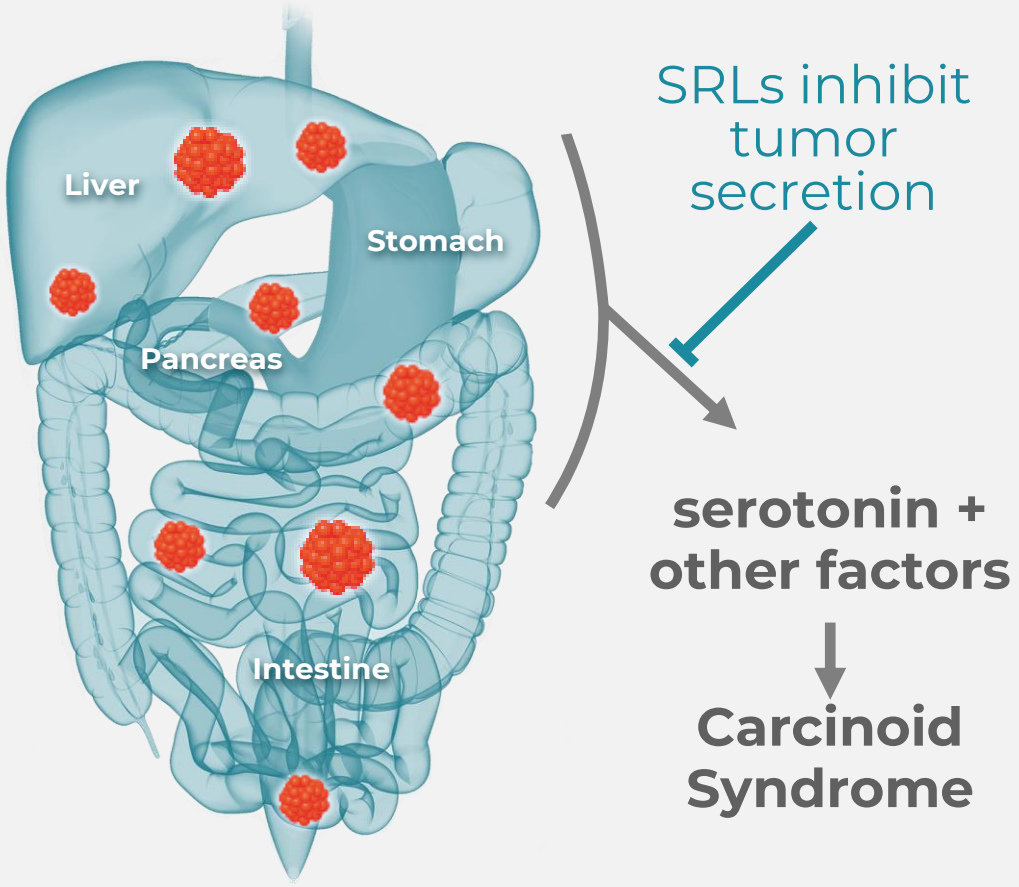
- Headache
- Hyperhidrosis/oily skin
- Bone and cartilage overgrowth
- Organ enlargement
- Cardiovascular disease/hypertension
- Changes in glucose and lipid metabolism
- Abnormal growth of hands and feet
- Alteration of facial features

Uncontrolled acromegaly is debilitating and increases risk of early death

Sources: http://www.fipapatients.org; Bex M, Abs R, T'Sjoen G, et al. Eur J Endocrinol. 2007;157(4):399-409; http://acromegalycommunity.com

What are Neuroendocrine Tumors (NETs) and Carcinoid Syndrome?

NETs arise from neuroendocrine cells in GI tract, pancreas or lungs

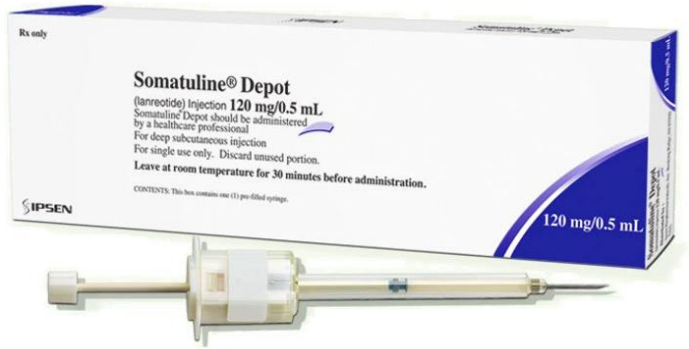


Carcinoid Syndrome Symptoms/Complications

- Diarrhea
- Flushing
- Difficulty breathing
- Tachycardia
- Carcinoid heart disease (valvulopathy)
- Carcinoid crisis (life threatening)

Carcinoid syndrome is caused by excess secretion of serotonin and other humoral factors secreted by NETs, resulting in severe diarrhea, flushing, and heart disease

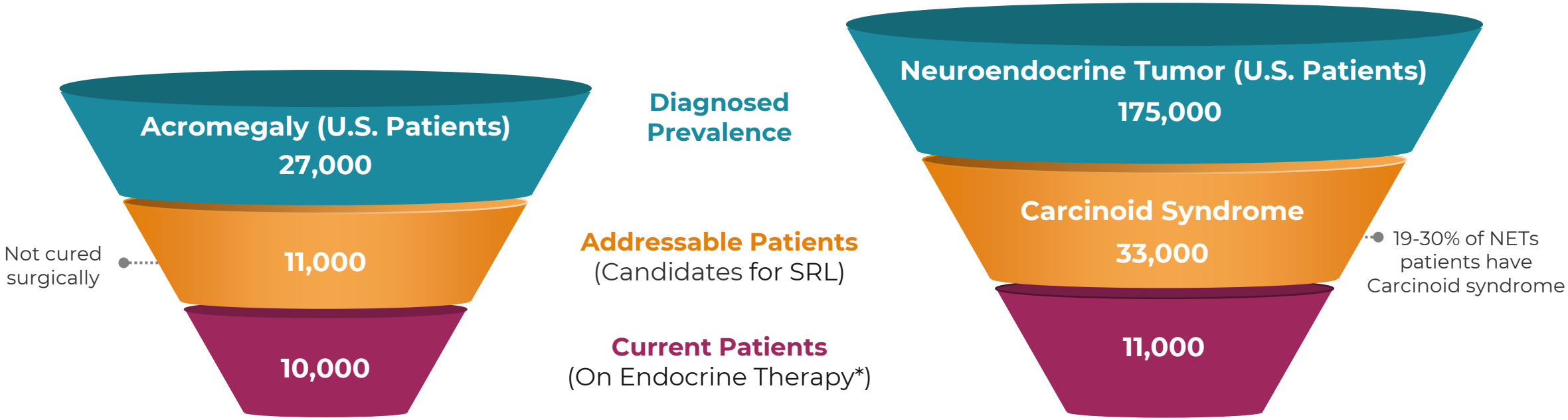
Somatostatin Receptor Ligands (SRLs) for Acromegaly and NETs are a $2.7B Established Market



	Sandostatin (octreotide)	Somatuline (lanreotide)
Sponsor	NOVARTIS	IPSEN Innovation for patient care
Administration	Monthly intramuscular injections 5-mL vial; 1½" 19-gauge needle	Monthly deep subcutaneous injections .2-.5ml; 18-gauge needle
Global Net Sales (2021)	$1,400M[1]	$1,300M[1]
U.S. Net Sales (2021)	$843M[1]	$893M[2]
Approval date(s)	1988, 1998(LAR)	2007

Sources: 1. Net sales sourced from sponsor earnings reports; 2. IQVIA reported U.S. Net sales

Paltusotine: Initial Multi-Billion Dollar U.S. Market Opportunity in Acromegaly and Carcinoid Syndrome



$70K	Average WAC for Monthly Injectables	$100K
$700M	Current Market for Endocrine Therapy (U.S.)	$1,100M
$800M	Total Addressable Market for Endocrine Therapy (U.S.)	$3,200M

*Endocrine therapy includes SRLs, dopamine agonists, and growth hormone antagonists
WAC: Wholesale acquisition cost; Sources: Company data on file

There are Treatment Challenges and a High Burden of Care with Currently Available SRLs

Efficacy

Poor symptom control: 33 – 55% of acromegaly patients on injectable SRLs (octreotide/lanreotide) report worsening of symptoms at the end of each injection cycle[1,2]

Poor disease control: 42% of participants in a pivotal study of oral octreotide did not maintain IGF-1 biochemical response after switching from injectables[3]

Tolerability

Treatment-related injection site reactions reported by 77% of patients on monthly SRLs[4]

Gastrointestinal side effects reported by 74% of patients after SRL injections[4]

Burden of Care

Monthly SRL injections are **painful and often are administered in a doctor's office**

Oral octreotide requires **two daily doses and fasting** 1 hour before or 2 hours after administration

SRL: Somatostatin receptor ligand; Sources: 1. Geer et al. BMC Endocrine Disorders, (2020) 20:117; 2. Strasburger et al. European Journal of Endocrinology, (2016) 174; MYCAPSSA label; 4. Fleseriu et al. Frontiers in Endocrinology; March 2021, Vol.12

Laying the Foundation for a Successful Paltusotine Acromegaly Launch

Aspiring to bring the only once daily oral SRL to patients as a trusted member of the global endocrine community

Properly Resourcing Commercial Functions

- Began building commercial team in Q1 2022
- Making continued investments to inform a targeted and nimble market access plan

Reducing the Burden on Patients*

- Once daily pill
- Consistent IGF-1 and symptom control
- Ship & store at room temperature
- Delivered to home
- Patient support services

Ease of Adoption for Physicians*

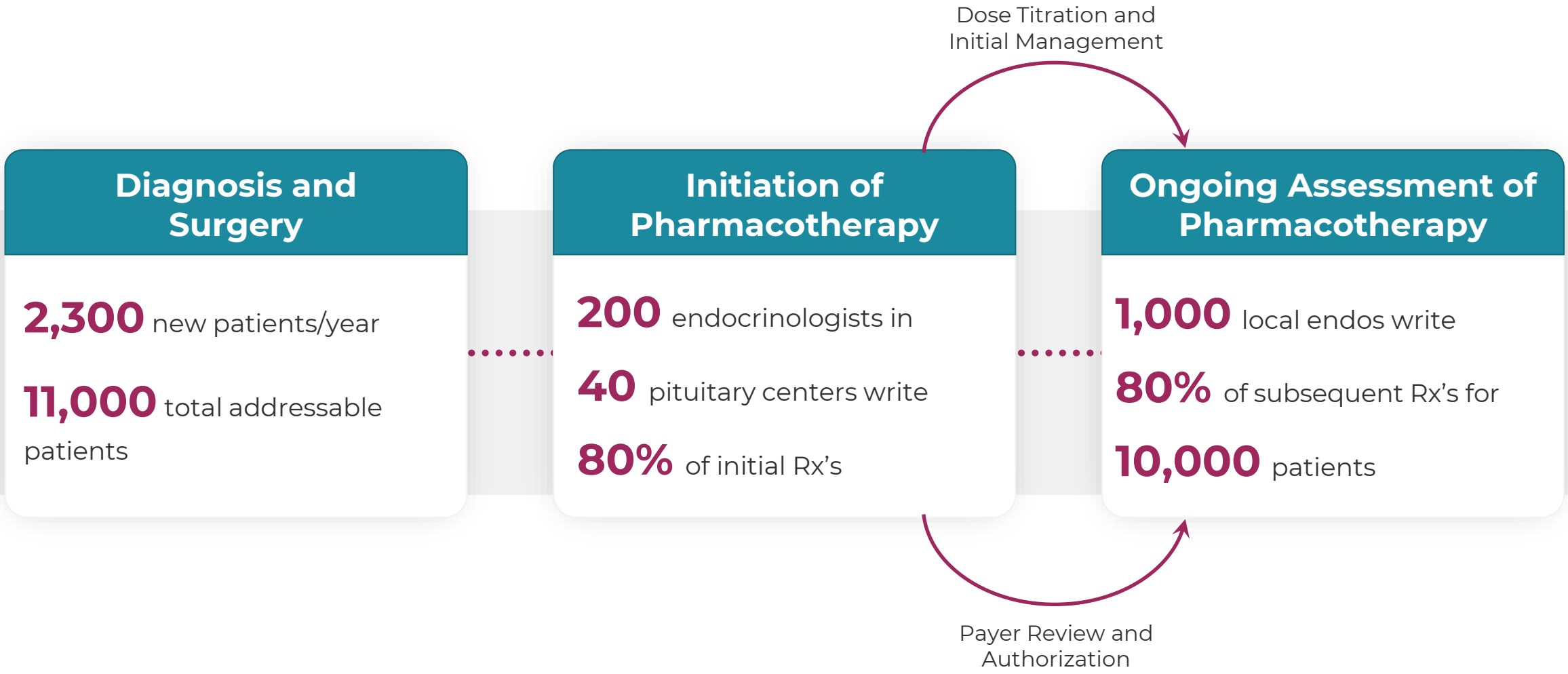
- Confident IGF-1 control
- Simple dose selection: 40 mg or 60 mg (if needed)
- Low drug interaction risk
- Extensive data on switching from injectables
- HCP support services

Providing Value to Healthcare System

- Potential for reduced patient out of pocket costs
- At-home option reduces costs for payers compared to in-office administration
- At-home option saves resources for HCPs that would otherwise administer injections in-office

*Based on target product profile and company plans if paltusotine receives regulatory approval (clinical studies intended to demonstrate target product profile and support applications seeking regulatory approval are ongoing)
HCP: Healthcare Provider

Concentrated Prescriber Bases at Key Stages of the Acromegaly Patient Journey in U.S.

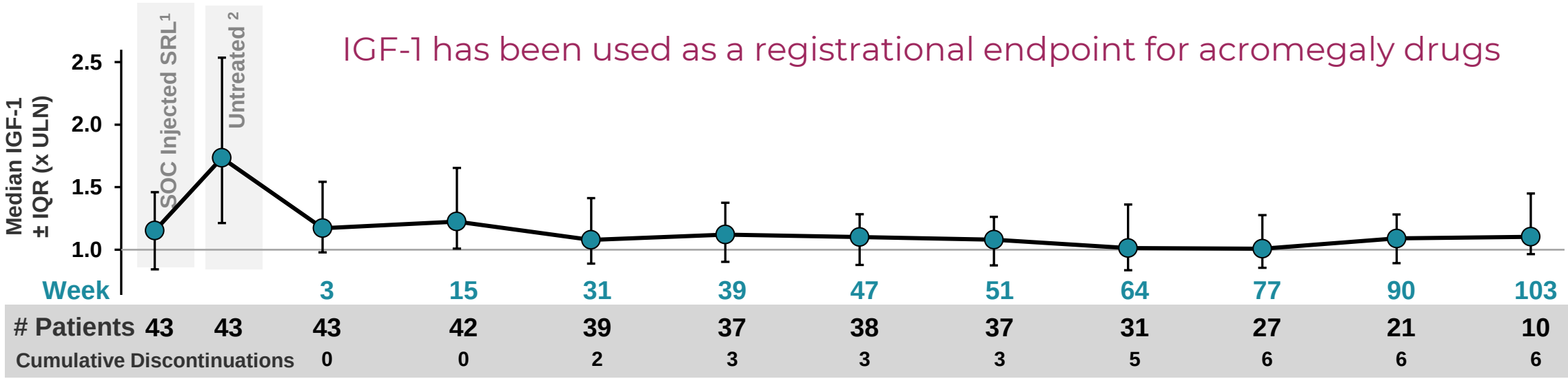


Source: Company data on file

Acromegaly Patients on Paltusotine Maintained IGF-1 Levels for Up to Two Years in Open Label Study for Phase 2 Patients

Phase 2 | Paltusotine Open Label Extension (OLE)

IGF-1 has been used as a registrational endpoint for acromegaly drugs



88% Eligible Phase 2 study participants opted to continue into the open label extension (OLE)

89% OLE participants selected once-daily oral paltusotine as their preferred treatment option over injected standard-of-care[1]

1. SRL: Long-Acting Injected SRL baseline therapy during screening from Evolve/Edge Phase 2 studies before switching to paltusotine; 2.Untreated period following the Evolve/Edge Phase 2 studies when patients were washed out of paltusotine prior to starting the open label extension study; Source: Oral presentation, Gadelha, M. at the 35th Brazilian Congress of Endocrinology and Metabolism

The Paltusotine Development Program Has Built a Global Development Capability for All Future Programs

The Paltusotine Acromegaly Phase 3 Program is Designed to Support Potential, Broad First-Line Medical Therapy Label. Underway at ~100+ sites in Countries Around the World

PATHFNDR-1: Switching from SOC

Evaluate safety and efficacy of paltusotine in acromegaly patients switching from injectable octreotide or lanreotide depots, who are currently *biochemically controlled*

(N=58, treatment duration 9 months, 1° endpoint: % responders vs. placebo)

PATHFNDR-2: Untreated Patients

Evaluate safety and efficacy of paltusotine in untreated acromegaly patients who are *biochemically uncontrolled*

(N=76, treatment duration 6 months, 1° endpoint: % responders vs. placebo)

PATHFNDR-1: fully enrolled with topline data expected in 3Q'23
PATHFNDR-2: enrollment ongoing with topline data expected in 1Q'24
NDA submission expected in 2024*

* Pending a successful outcome from the PATHFNDR program; SOC: Standard of care; NDA: New drug application

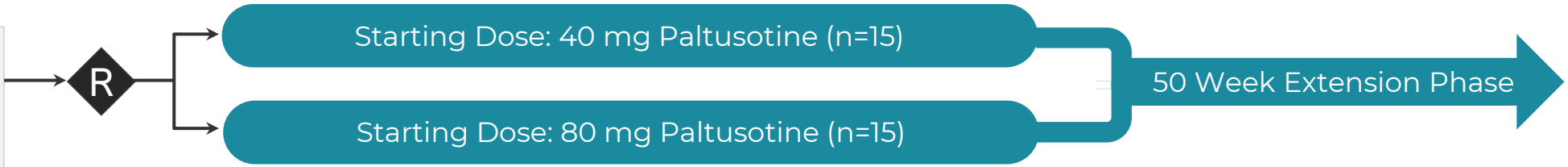
Carcinoid Syndrome: Label Expansion Opportunity for Paltusotine

Ongoing Open-Label, Randomized, Phase 2 Study in Patients with Carcinoid Syndrome

Key Eligibility Criteria

Naïve or treated with octreotide or lanreotide

Grade 1 or 2 NET



Randomized Treatment Period: 8 weeks

- Dose range: 40 mg, 80 mg, or 120 mg
- Paltusotine dose adjusted as required

Objectives: Collect information needed for Phase 3 Design

Primary: Safety and Pharmacokinetics Assessments

Secondary: Efficacy Assessments: Bowel movement frequency, flushing frequency, PRO measures, short-acting octreotide rescue use, 5-hydroxyindoleacetic acid (5-HIAA, serotonin metabolite) levels

Timelines

- Data expected in 2H 2023
- Study to be followed by a 50-week extension study for eligible patients

NET: Neuroendocrine tumor; QD: Once daily; PRO: Patient reported outcome

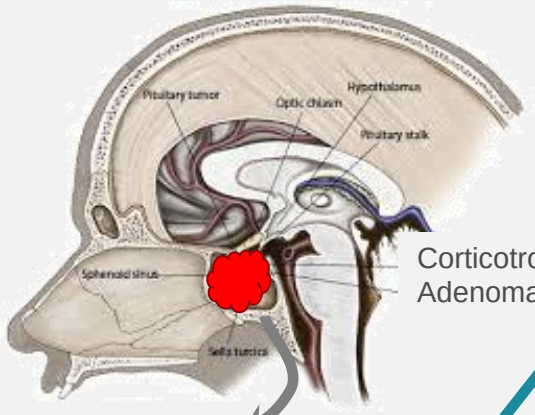
OUR ENDOCRINE FRANCHISE IS EXPANDING WITH ADDITIONAL PRODUCT CANDIDATES ENTERING PATIENT STUDIES

CRN04894: A First-in-Class, Oral Small Molecule ACTH antagonist for Cushing's Disease (CD) & Congenital Adrenal Hyperplasia (CAH)

CRN04777: A First-in-Class, Oral Small Molecule SST5 Agonist for Hyperinsulinism

What is Cushing's Disease?

Cushing's disease is caused by a benign pituitary tumor secreting excess ACTH



Corticotroph Adenoma

ACTH antagonist blocks the action of ACTH

ACTH

Excess ACTH secretion causes excess cortisol secretion by the adrenal

Adrenal

Cortisol

Cushing's Symptoms/Complications

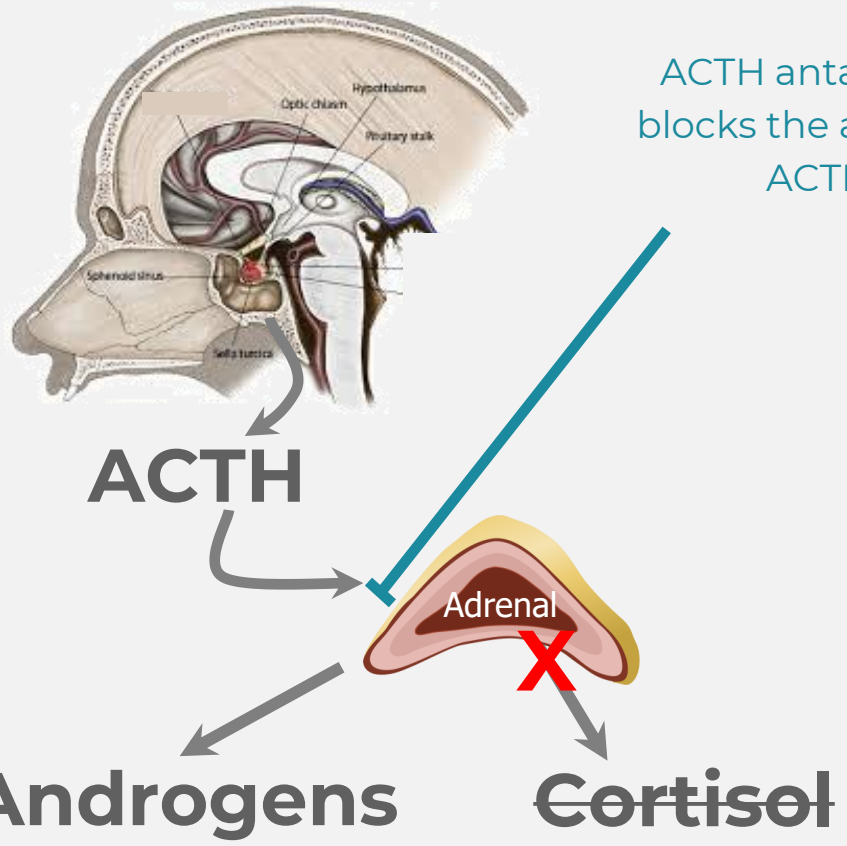
- Weight gain and fatty tissue deposits (midsection, face, shoulders)
- Stretch marks, thinning fragile skin, bruising, slow healing
- Reproductive dysfunction and hirsutism
- Fatigue, muscle weakness
- Emotional, cognitive or neuropsychiatric difficulties
- Hypertension
- Osteoporosis

Uncontrolled Cushing's disease is debilitating and increases risk of early death

ACTH: Adrenocorticotropic hormone

What is Congenital Adrenal Hyperplasia (CAH)?

CAH patients have too little cortisol resulting in excess ACTH and excess androgens



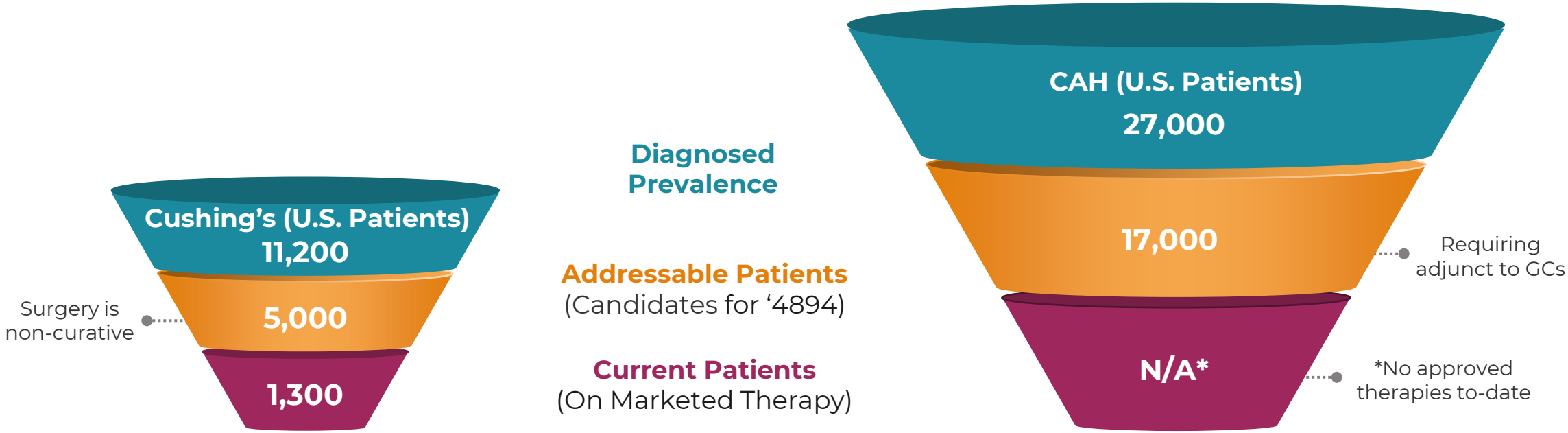
Classic CAH Symptoms/Complications

- Low Cortisol:
  - Low blood pressure, blood sugar, energy
  - Adrenal crisis can be life threatening
- Androgen Excess
  - Short stature, precocious puberty, acne
  - Females: hirsutism, atypical genitalia, sex misassignment, menstrual dysfunction, infertility, acne, hair loss
- Males: adrenal rest tumors
- Over-treatment with glucocorticoids can result in Cushing's syndrome symptoms and signs

Uncontrolled CAH is debilitating and increases risk of early death

ACTH: Adrenocorticotropic hormone

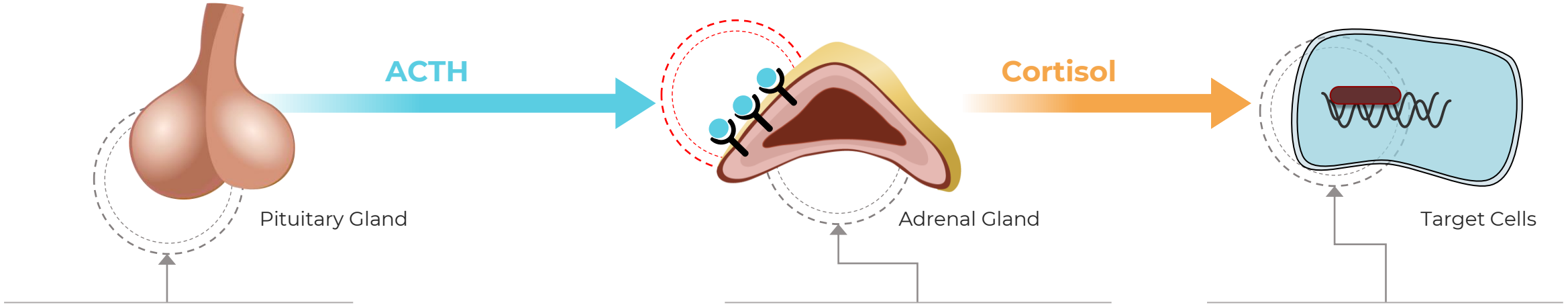
CRN04894: Initial Multi-Billion Dollar U.S. Market Opportunity in Cushing's Disease and CAH



$1,500M	Total Addressable Market for Branded Therapy (U.S.)	~$2,500M

Source: Company data on file.

Current Therapeutics Have Limited Efficacy and/or Safety Issues, Leaving High Unmet Need



Pituitary Directed Agents to Suppress ACTH Secretion

Available: glucocorticoids, pasireotide, cabergoline

- Limited efficacy
- Safety issues

Adrenal Steroidogenesis Inhibitors

Available: ketoconazole/ levoketoconazole metyrapone/osilodrostat,

- Limited Efficacy
- Safety Issues
- Low Adherence

Glucocorticoid Receptor Antagonist

Available: mifepristone

- Efficacy difficult to assess
- Safety issues

Sources: Felders et al. Lancet Diab Endo 7:300-12, 2019. Castinetti JCEM 99: 1623-1639, 2014. Castinetti JCEM 106: 2114-2123, 2021. ACTH: Adrenocorticotropic hormone

CRN04894 Target Product Profile: Normalize Adrenal Cortisol Levels and Symptoms

The only once daily oral ACTH receptor antagonist to normalize adrenal cortisol levels and get patients back to normal without toxicity monitoring requirements

Cushing's Disease

- Normalize cortisol levels (UFC) & symptoms
  - Body weight & central obesity
  - Hypertension
  - QoL and neuropsychiatric effects
- No increase in androgens, hirsutism, acne
- Low risk of hypoadrenalism

No toxicity monitoring requirements

- No expected QTc prolongation / monitoring
- No expected liver toxicity / monitoring

Congenital Adrenal Hyperplasia

- Reduce GC dosage to physiological levels
- Avoid body weight gain, hypertension, and neuropsychiatric effects
- Normalize adrenal androgens (e.g. A4) & symptoms:
  - Women: menstruation, infertility, hirsutism
  - Men: Reduce testicular adrenal rest tumor size, secondary gonadal failure

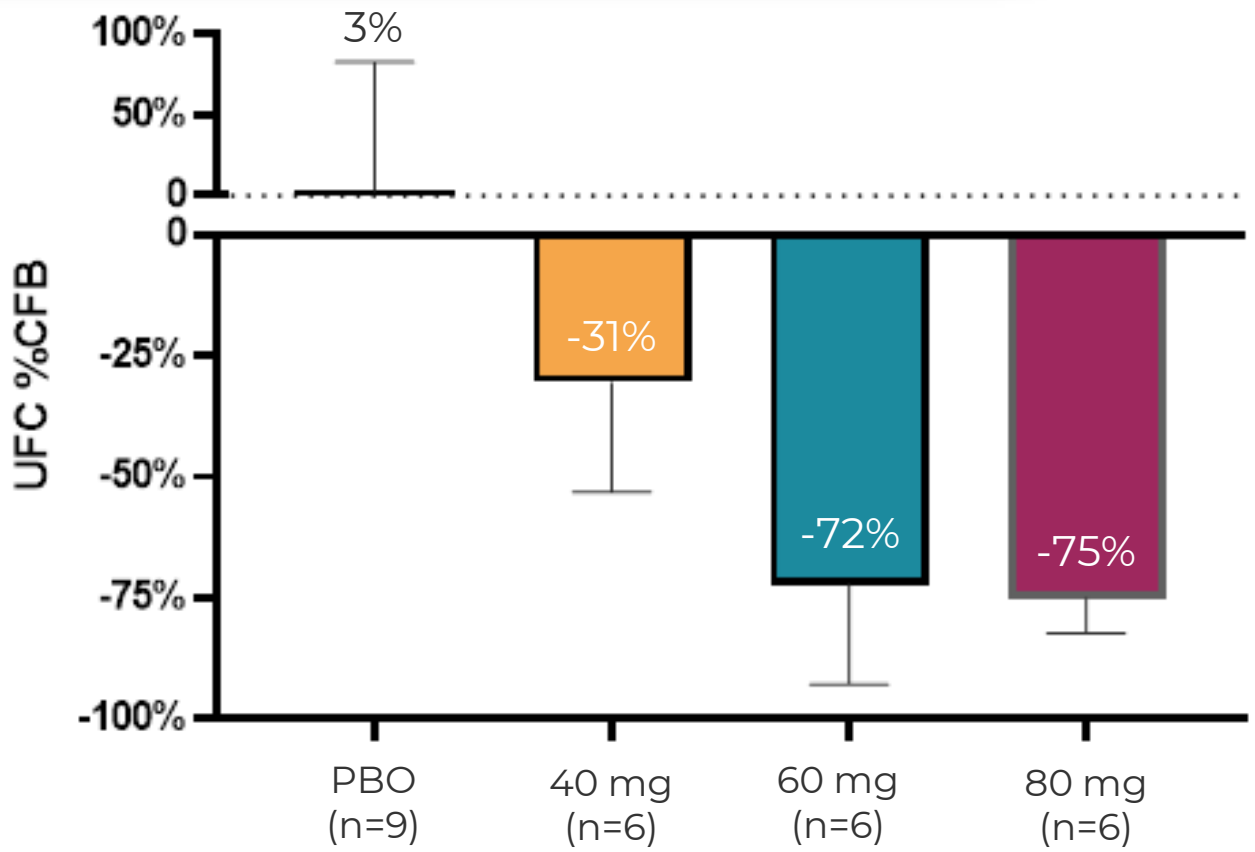
A once-daily oral medication

- Favorable profile for patient compliance

QoL: Quality of life; GC: Glucocorticoid

CRN04894 Potently Suppressed Adrenal Activity as Measured by Urinary Free Cortisol*

24-Hour Urinary Free Cortisol (day 9)



Normalization of 24-hour urinary free cortisol has been the registrational endpoint for Cushing's disease drugs

*Results from Phase 1 clinical study in healthy volunteers. Data shown are median ± IQR. Includes data from subjects receiving glucocorticoid rescue. UFC: Urinary free cortisol; CFB: Change from baseline; PBO: Placebo
Source: Oral presentation, Krasner et al. at ENDO 2022

Open-Label Study of CRN04894 in Cushing's Disease and EAS Patients

Sequential Multiple Ascending Dose Cohorts up to 160 mg QD

Key Eligibility Criteria

N = 18

ADCS:

- Cushing's disease
- Ectopic ACTH syndrome

Failed surgery or are awaiting surgery

Screening/Washout:
14 Days

80 mg QD (n=6)

120 mg QD (n=6)

160 mg QD (n=6)

Treatment Periods:
3 cohorts, each 10 days

Objectives: Collect information needed for Phase 3 Design

Primary Assessments: Safety and Pharmacokinetics Assessments

Secondary Efficacy Assessments

- 24-hour urinary free cortisol: Change from baseline to Day 11
- Percentage of patients who normalize 24-hour urinary free cortisol on Day 11
- Early morning and 24-hour serum cortisol: Change from baseline to Day 11

Collaborator & Timeline

- Company-sponsored study is being conducted in collaboration with the NIH Clinical Center
- Data expected in 2024

QD: Once daily

Proposed Open-Label Study of CRN04894 in Patients with Congenital Adrenal Hyperplasia (CAH)

Sequential Multiple Ascending Dose Cohorts up to 160 mg QD; GC therapy maintained through study

Key Eligibility Criteria

N = 18-30

Participants with CAH and high A4 (≥1.5xULN) at screening

Age: ≥16 years

Screening: 4 weeks

80 mg QD (n=6-12)

SRC review

120 mg QD (n=6-12)

SRC review

160 mg QD (n=6)

Optional cohort

Treatment Periods:

3 cohorts (one optional), each 12 weeks

SRC review of 3 patients at week 2 prior to dose escalation in next cohort

Objectives: Collect information needed for Phase 3 Design

Primary Efficacy Assessment: Change from baseline in morning serum A4 at week 12

Secondary Efficacy Assessment: Change from baseline in morning serum 17 hydroxyprogesterone (17-OHP) at week 12

Primary Safety Assessment: Incidence of TEAEs

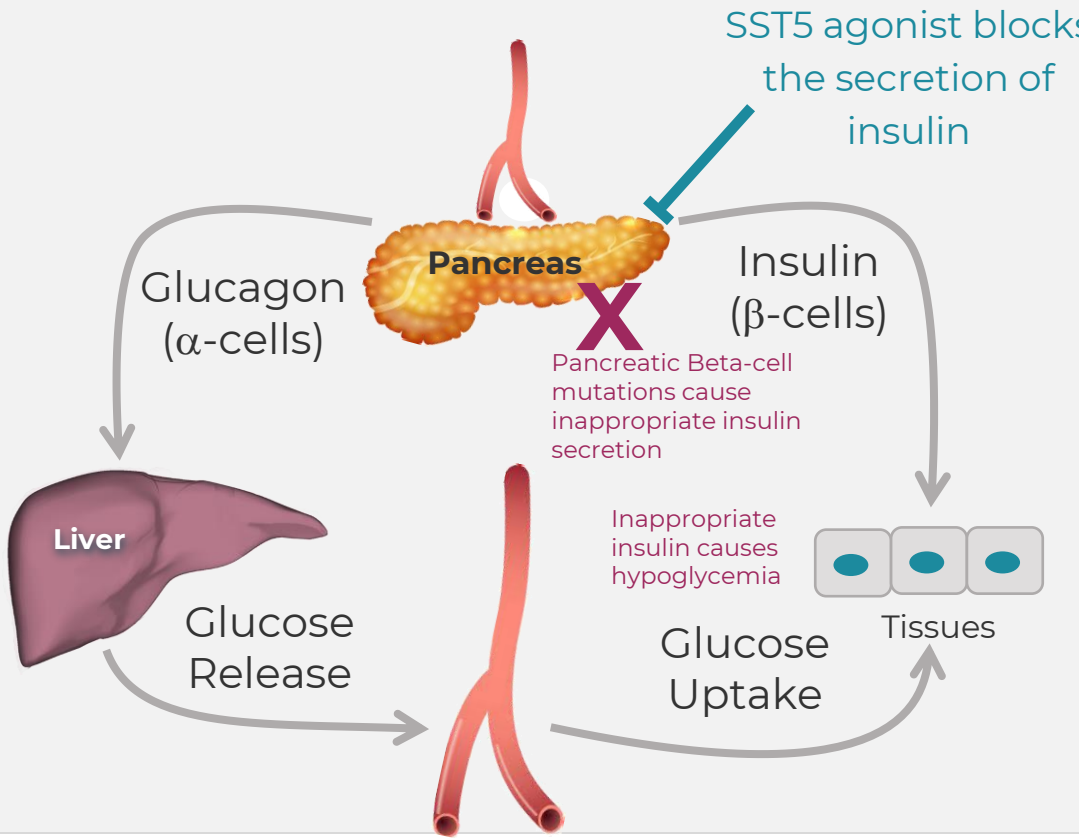
Timeline

- Data expected in 2024

GC: Glucocorticoid; A4: Androstenedione; ULN: Upper limit of normal; QD: Once daily; SRC: Safety review committee; TEAE: Treatment emergent adverse event

What is Congenital Hyperinsulinism (CHI)?

Excess insulin produces life-threatening hypoglycemia (low blood glucose)

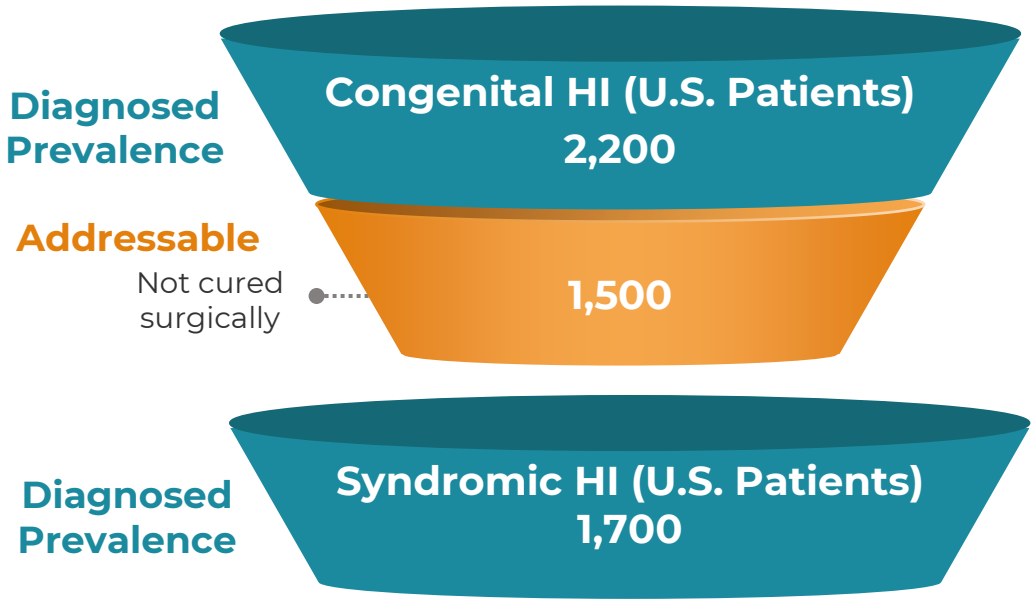


Recurrent hypoglycemia episodes lead to:

- Neurodevelopmental/behavior disorders (26-48% of patients)
- Epilepsy/seizures
- Severe hypoglycemia can lead to coma and death

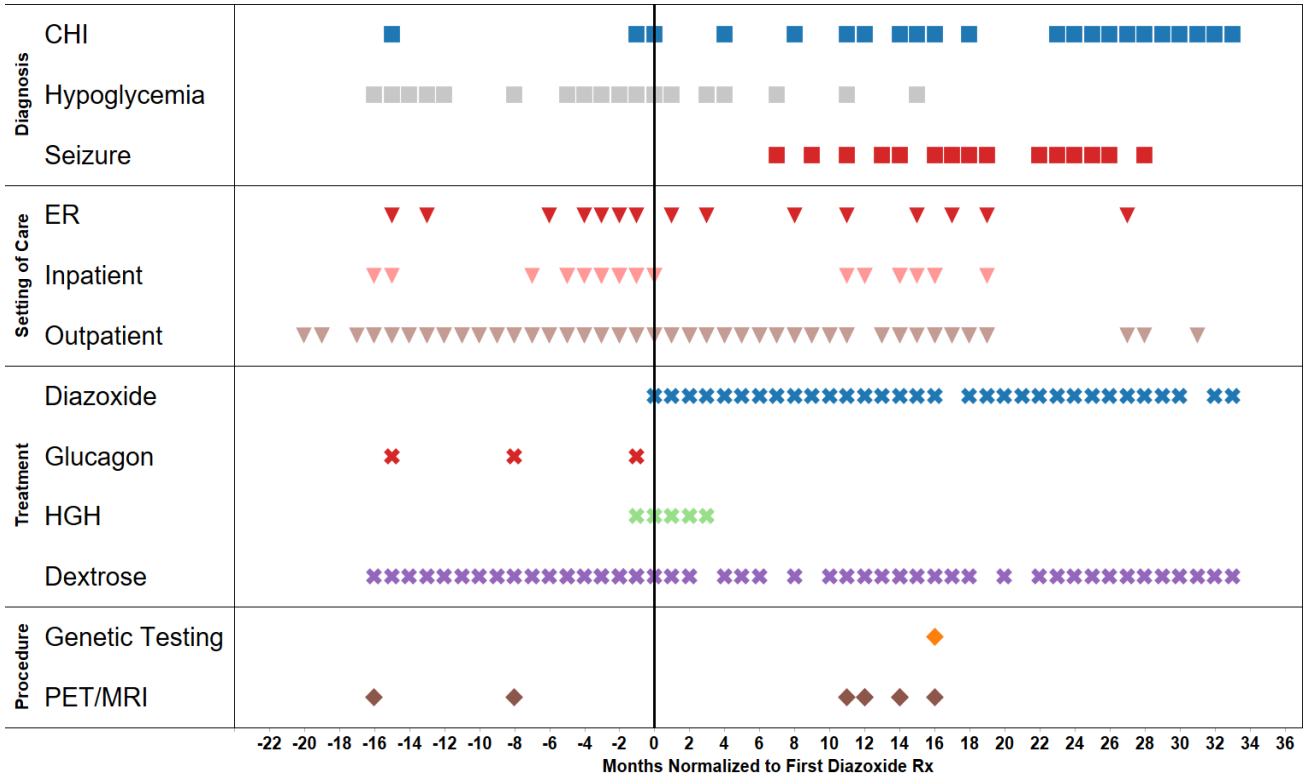
1. Meissner T, et al..2003. Eur J Endocrinol. 149(1):43–51.; 2. Menni F, et al. 2001. Pediatrics, 107: 476-79 3. Lord K, et al. 2015. High Risk of Diabetes and Neurobehavioral Deficits in Individuals With Surgically Treated Hyperinsulinism J Clin Endocrinol Metab.100(11):4133– 4139. SST5: Somatostatin receptor type 5

CRN04777: Initial Meaningful Market Opportunity in Congenital and Syndromic Hyperinsulinism



Total Addressable Market for Branded Therapy (U.S.) **~$960M**

High unmet medical need and high healthcare system burden remain with current standard of care



Claims history from baby girl born in 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

Source: Company data on file

Treatment Challenges and High Burden of Care with Currently Available CHI Therapies

Glucose Support

IV glucose

Enteral dextrose

Rescue

Injectable glucagon analogs

Safety, efficacy, & route of administration all need better options

Medical

Diazoxide

- Ineffective in ~50% of patients; black box warning

Injectable SST2 agonists

- Tachyphylaxis, no pediatric dosing guidelines, painful

Surgical

Pancreatectomy
(complete or partial)

- Type 1 diabetes likely if complete resection successful

SST2: Somatostatin receptor type 2

CRN04777 Target Product Profile Designed for Kids, Their Caregivers, and the Healthcare System

Bringing the only kid friendly, once daily oral therapy to patients as a trusted member of the global CHI community

Kid and Family Friendly

- Raspberry flavored sweetened syrup taken orally
- Take with breakfast once a day
- Minimize doctor visits
- Delivered to home
- Patient/caregiver support services

Ease of Adoption for Physicians

- Effective for all patients with hyperinsulinism
- Confident hypoglycemia prevention
- Simple dose adjustment based on glucose
- Minimal drug-drug interactions
- HCP support services

Providing Value to Healthcare System

- Potential for reduced patient out of pocket costs
- At-home option reduces costs for payers compared to in-office administration
- Prevent expensive hospitalizations
- Prevent life-long complications

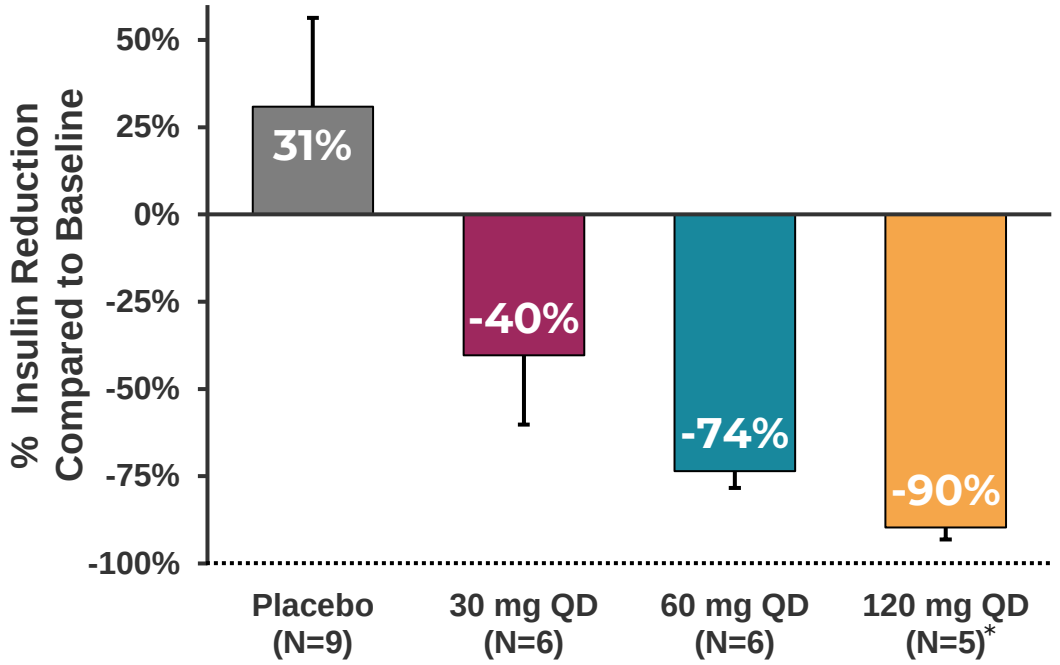
Laying Foundations for Global Access

- Strong engagement with global patient groups
- Strong engagement with global centers of excellence
- Global clinical development plan

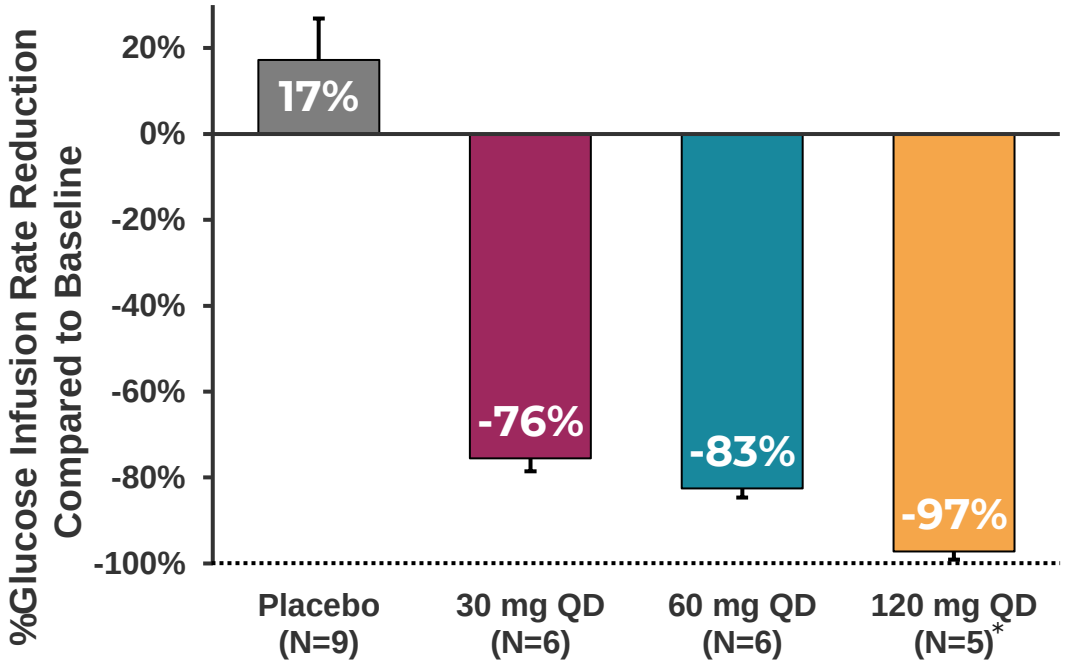
HCP: Healthcare provider

CRN04777 Reduced Insulin Secretion & IV Glucose Support in Healthy Volunteer Model of HI#

Change in Insulin



Change in Glucose Infusion Rate



#Data on file from a Phase 1 study in healthy volunteers; Data shown are mean ± SEM, reduction of each subject's AUC on Day 10 vs. baseline (Day -2); HI: Hyperinsulinism; QD: once daily; * n=1 subject withdrew consent (not treatment related);

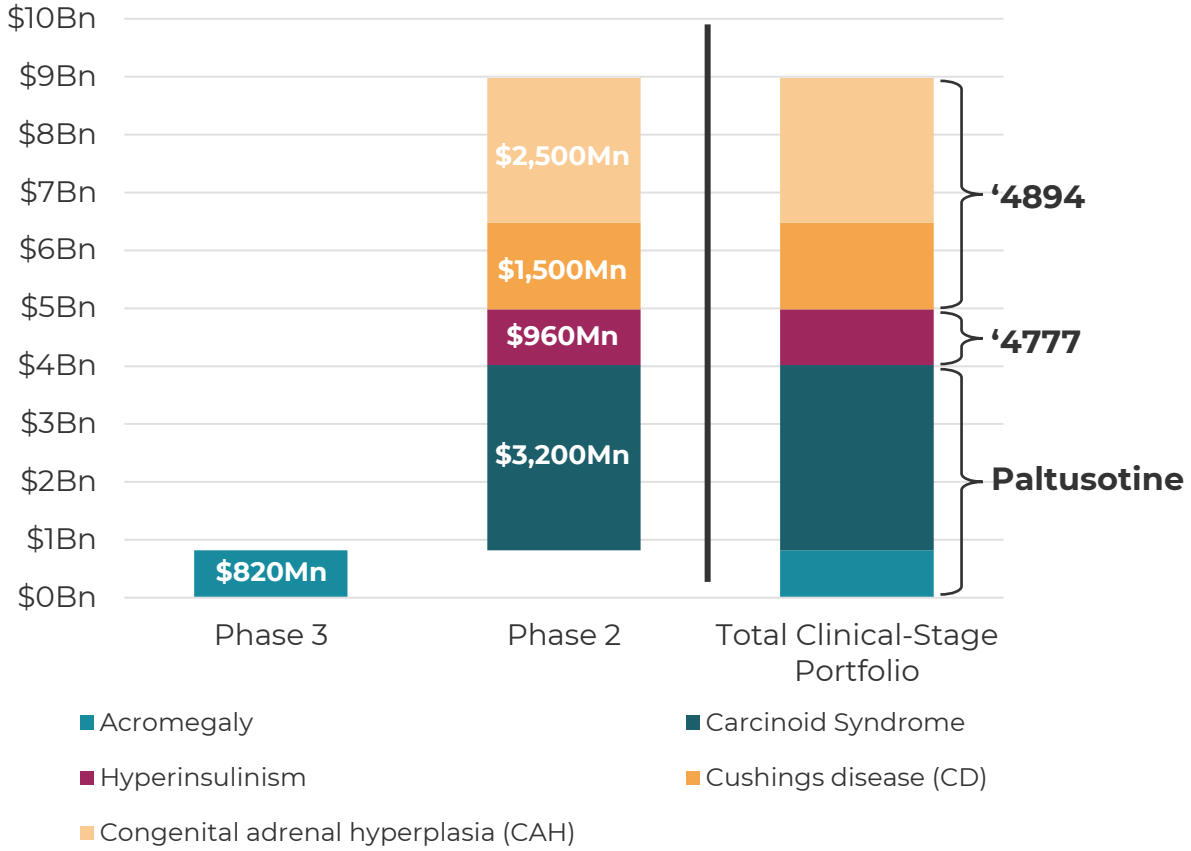
OUR GPCR DISCOVERY AND DEVELOPMENT ENGINE IS CONTINUING TO CRAFT AND ADVANCE NEW ASSETS

Targeting highly prevalent endocrine disorders with a favorable probability of success

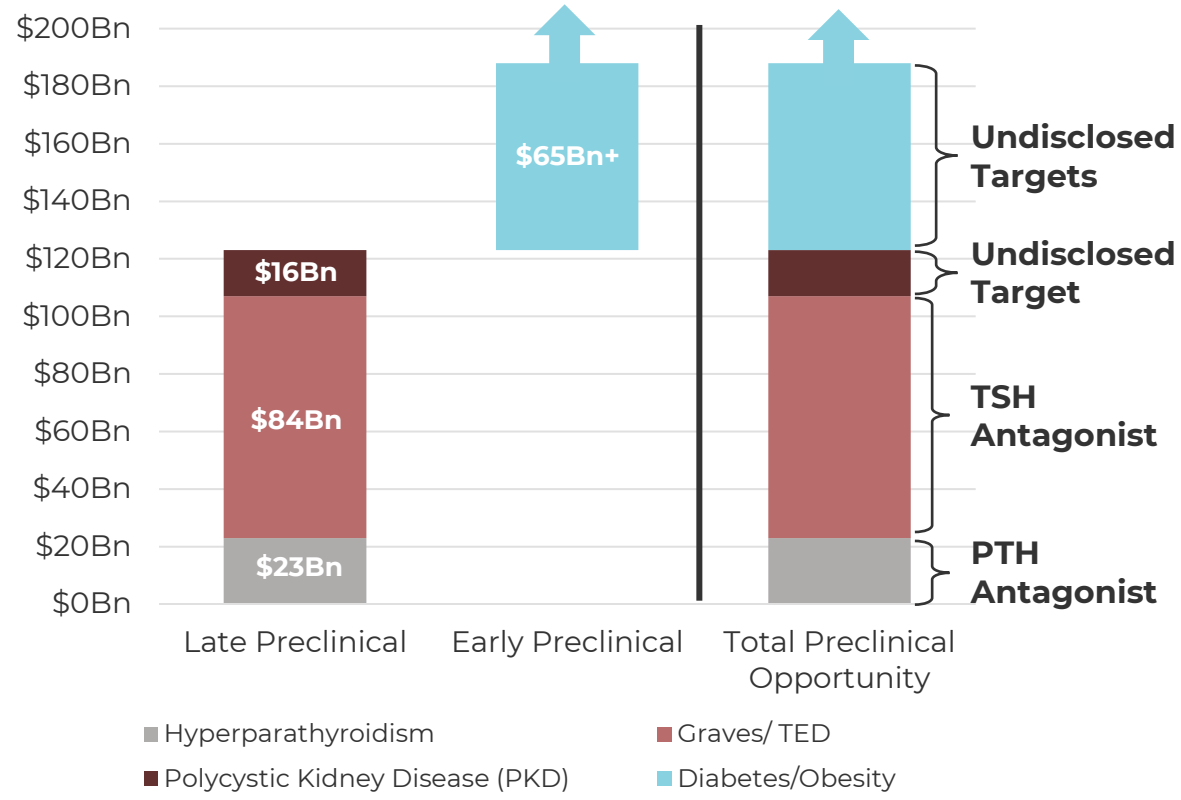
Growing Franchise Addresses Multi-Billion Dollar Market Opportunity Across Endocrinology

Current Clinical Pipeline → **Future Opportunity**

TAM by Asset Stage of Development



Total Preclinical Portfolio Market Opportunity *



* The portion of each market that could be addressable will depend on relevant indication subpopulations and clinical development plans pursued

Sources: Company data on file

Investment Highlights: Expected Milestones and Financial Position

2023

- **3Q23** PATHFNDR-1 Topline Data
- **2H23** Carcinoid syndrome P2 data
- **2023** New drug candidates from discovery efforts

2024

- **1Q24** PATHFNDR-2 Topline Data
- **2024** Acromegaly NDA Submission
- **2024** Cushing's Disease P2 data
- **2024** Congenital Adrenal Hyperplasia P2 data
- **2024** New drug candidates from discovery efforts

Strong Financial Position to Execute Through 2024

$334.4 million in cash & investments as of December 31, 2022

NDA: New drug application

REFERENCE

PATHFNDR-1: Enabling Switching from SOC

Key Eligibility Criteria

Acromegaly patients controlled on octreotide or lanreotide depot monotherapy

- IGF-1 ≤ 1.0x ULN

R

Placebo (n = 26)

Treatment Period: 9 months

Paltusotine (n= 26)

- **Start on 40 mg** QD or placebo
- IGF-1 assessments each month
- 6 months flexible dose titration; 3 months maintenance dose period
- Months 2-6: Increase to 60 mg QD if IGF-1 > 0.9x ULN
- Months 2-6: Decrease by 20 mg if necessary, for tolerability

Screening: 1-3 months → 1:1 Randomization → Titration Period: months 1-6 → 34, 36 Endpoint Assessment: Weeks 34, 36

Endpoints

Primary:

- Percent responders vs. placebo
  - Responders: mean IGF-1 ≤ 1.0x ULN at weeks 34, 36

Secondary:

- Change from baseline IGF-1
- Proportion of patients with GH < 1 ng/mL at endpoint assessment out of those <1 ng/mL at baseline
- Change from baseline in total Acromegaly Symptoms Diary (ASD) score

Statistical powering:

- Power > 90%

Rescue Criteria

Patient is rescued with an injectable and classified as a non-responder if following criteria are met at **60 mg dose**:

- Two consecutive IGF-1 ≥ 1.3x ULN

AND

- Exacerbation of acromegaly clinical signs/symptoms

Timelines

- Start Q2 2021
- Topline Data expected in 3Q'23
- Study to be followed by an OLE for eligible patients

ULN: Upper Limit of Normal; PBO: Placebo; QD: Once daily; OLE: Open label extension

PATHFNDR-2: Enabling Use in Untreated Patients

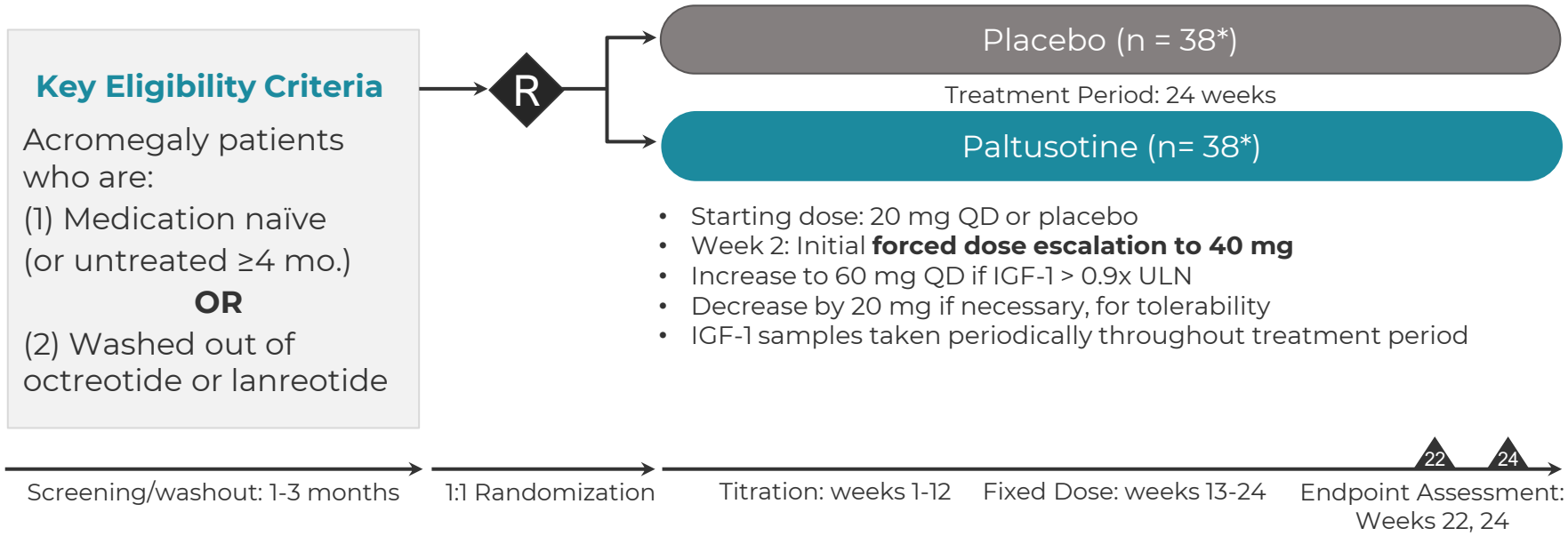
Key Eligibility Criteria

Acromegaly patients who are:

(1) Medication naïve (or untreated ≥4 mo.)

OR

(2) Washed out of octreotide or lanreotide



Endpoints

Primary:

- Percent responders vs. placebo
  - Responders: mean IGF-1 ≤ 1.0x ULN at weeks 22, 24

Key Secondary:

- Change from baseline IGF-1

Secondary:

- Proportion of patients with GH <1 ng/mL at endpoint assessment
- Change from baseline in total Acromegaly Symptoms Diary (ASD) score

Statistical powering:

- Power estimate = 90%

*Optional sample size re-estimation based on subgroup enrollment

Rescue Criteria

Based on assessments of:

- IGF-1 levels
- Clinical signs/symptoms

While on the 60mg dose

Timelines

- Start 2H 2021
- Topline Data expected in 1Q'24
- Study to be followed by an OLE for eligible patients

ULN: Upper Limit of Normal; PBO: Placebo; QD: Once daily; OLE: Open label extension

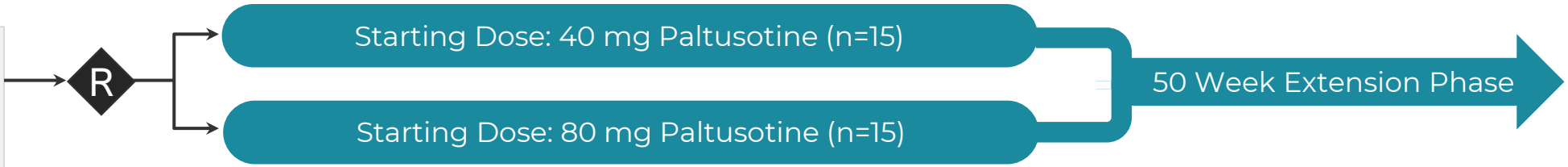
Carcinoid Syndrome: Label Expansion Opportunity for Paltusotine

Ongoing Open-Label, Randomized, Phase 2 Study in Patients with Carcinoid Syndrome

Key Eligibility Criteria

Naïve or treated with octreotide or lanreotide

Grade 1 or 2 NET



Randomized Treatment Period: 8 weeks

- Dose range: 40 mg, 80 mg, or 120 mg
- Paltusotine dose adjusted as required

Objectives: Collect information needed for Phase 3 Design

Primary: Safety and Pharmacokinetics Assessments

Secondary: Efficacy Assessments: Bowel movement frequency, flushing frequency, PRO measures, short-acting octreotide rescue use, 5-hydroxyindoleacetic acid (5-HIAA, serotonin metabolite) levels

Timelines

- Data expected in 2H 2023
- Study to be followed by a 50-week extension study for eligible patients

NET: Neuroendocrine tumor; QD: Once daily; PRO: Patient reported outcome

Robust Patent Portfolio

Patent Family Subject Matter	Estimated Expiration
Paltusotine Portfolio	
Compound	2037
Additional Filings	2039 - 2043
CRN04894 Portfolio	
Compound	2039
Additional Filings	2042
CRN04777 Portfolio	
Compound	2040
Additional Filings	2042
PTH Antagonist Portfolio	
Compound	2042

- Additional filings include salts, polymorphs, formulations, and treatment methods
- Patent portfolios are filed broadly, in the vast majority of global pharmaceutical markets
- Estimated expiration dates do not include any available patent term extensions or supplementary protection certificates, e.g., up to five years in U.S. and Europe