Crinetics Pharmaceuticals

2021 CLINICAL STRATEGY AND 2020 FINANCIAL RESULTS

March 30, 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 to initiate Phase 3 trials of paltusotine in acromegaly, report data therefrom and the expected timing thereof; the potential for such Phase 3 program to support broad approval of paltusotine for all acromegaly patients who require pharmacotherapy; the potential to initiate a trial of paltusotine in patients with carcinoid syndrome due to NETs, report data therefrom and the expected timing thereof; the enrollment of a Phase 1 trial of CRN04894, the ability to report data therefrom, and the timing thereof; the enrollment of a Phase 1 trial of CRN04777, the ability to report data therefrom, and the timing thereof; and our future financial positions. 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: potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; the FDA or other regulatory agencies may require one or more additional clinical trials of paltusotine or suggest changes to our planned Phase 3 clinical trials prior to and in support of the approval of a New Drug Application or applicable foreign regulatory approval; advancement of paltusotine into a Phase 3 trial in acromegaly or a trial for carcinoid syndrome is 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.

Key 2020 and Early 2021 Accomplishments

1. Positive paltusotine acromegaly Phase 2 data and completed FDA meeting to inform design of upcoming Phase 3 program
2. Initiated Phase 1 study of CRN04894, an investigational ACTH antagonist being developed for Cushing's disease and congenital adrenal hyperplasia
3. Initiated Phase 1 study of CRN04777, an investigational SST5 agonist being developed for congenital hyperinsulinism
4. U.S. Orphan Drug designation for paltusotine in acromegaly
5. Rare pediatric disease designation for CRN04777 in congenital hyperinsulinism
6. Ended 2020 with over $170M in cash, cash equivalents, and investments

PATHFNDR Phase 3 Program: Designed to Support Potential for Broad First-Line Medical Therapy

Two double-blind, placebo-controlled studies planned to support broad labeling in the U.S. and Europe for use in all acromegaly patients who require pharmacotherapy

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*

PATHFNDR-2: Untreated Patients

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

PATHFNDR-1: Enabling Switching from SOC

Key Eligibility Criteria

Patients controlled on octreotide or lanreotide depot monotherapy

- IGF-1 ≤ 1.0x ULN

R

Placebo (n = 26)

Total 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

Endpoints

Primary:

- Percent responders vs. placebo
  - Responders: mean IGF-1 ≤ 1.0x ULN at weeks 32, 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 screening
- 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 2023
- Trial to be followed by an OLE for eligible patients

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

PATHFNDR-2: Enabling Use in Untreated Patients

Key Eligibility Criteria

Medication naïve
(or untreated ≥4 mo.)
OR
Washout of octreotide

R

- Placebo (n = 37)
  - Total Treatment Period: 12 weeks
- Paltusotine (n= 37)

- Starting dose: 20 mg QD or placebo
- Weeks 1-2: Initial **forced dose escalation to 40 mg**
- Increase to 60 mg QD if IGF-1 > 0.9x ULN
- Decrease by 20 mg if necessary, for tolerability
- IGF-1 samples taken periodically throughout treatment period

Screening/washout: 1-3 months → 1:1 Randomization → Titration Period: weeks 1-9 → 10 → 12 Endpoint Assessment: weeks 10-12

Endpoints

Primary:

- Percent responders vs. placebo
  - Responders: mean IGF-1 ≤ 1.0x ULN during weeks 10-12

Key Secondary:

- Change from baseline IGF-1
- Proportion of patients with GH < 2.5 or <1 ng/mL at endpoint assessment
- Change from baseline in total Acromegaly Symptoms Diary (ASD) score

Statistical powering:

- Power > 90%

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 2023
- Trial to be followed by an OLE for eligible patients

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

Anticipated Paltusotine Milestones

1. Initiate PATHFNDR-1: switching from SOC
(anticipated in 2Q 2021)

2. Initiate PATHFNDR-2: use in untreated patients
(anticipated in 2H 2021)

3. Initiation of Phase 2 NETs trial in carcinoid syndrome
(end of 2021)

4. Report topline data from PATHFNDR-1 & 2 trials
(expected in 2023)

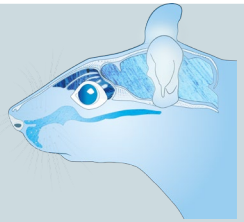
Endocrinology Development Strategy: Focus on Hormone Levels from Preclinical to Approval

Preclinical POC

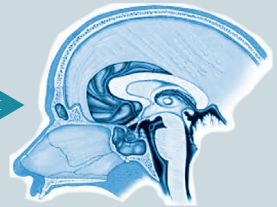
ΔHormones,
PK, Safety

Phase 2/3
Disease Efficacy

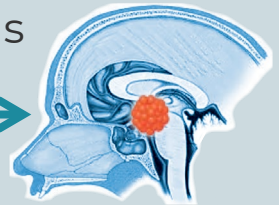
ΔHormones,
PROs, PK, Safety



Phase 1 Healthy Volunteers



Phase 2/3 Trials (Patients)



Phase 1 Healthy Volunteer POC

ΔHormones,
PK, Safety

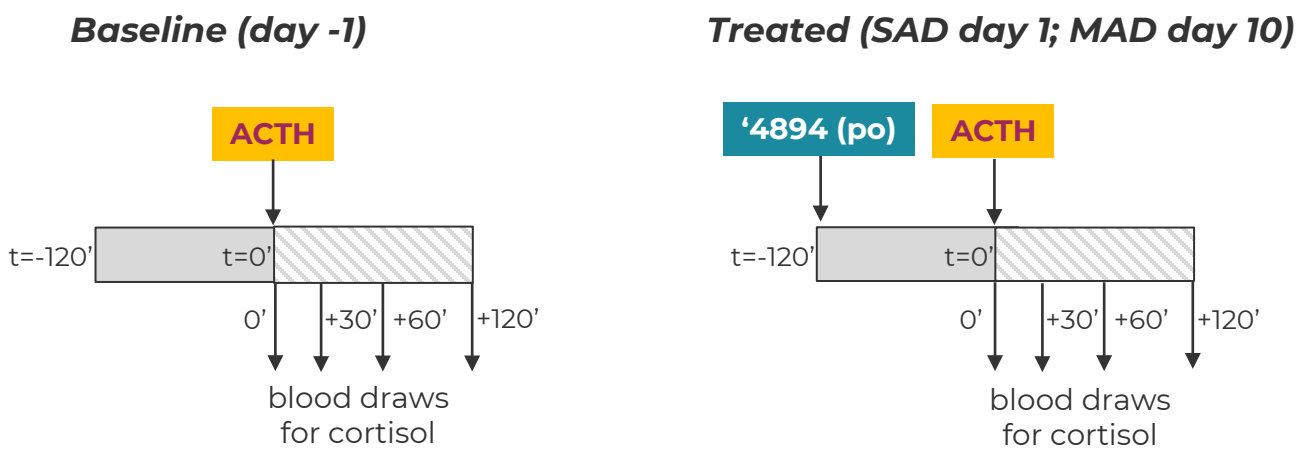
CRN04894 Phase 1 Clinical POC
Cushing's Disease and CAH – Adrenal Suppression

Healthy volunteers: SAD data expected 1H 2021; MAD data expected 2H 2021

Objectives

- Safety and tolerability
- Pharmacokinetics
- PK/PD for suppression of ACTH-induced adrenal activity
- Dose selection for patient studies

ACTH Stimulation Test



Proof of concept: dose dependent suppression of ACTH-stimulated peak cortisol with CRN04894

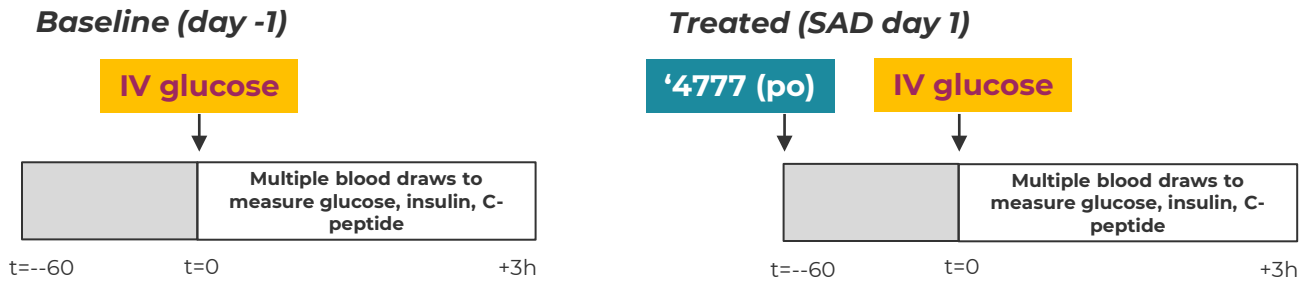
CRN04777 Phase 1 Clinical POC Congenital Hyperinsulinism – Insulin Suppression

Healthy volunteers: SAD data expected mid-2021; MAD data expected 2H 2021

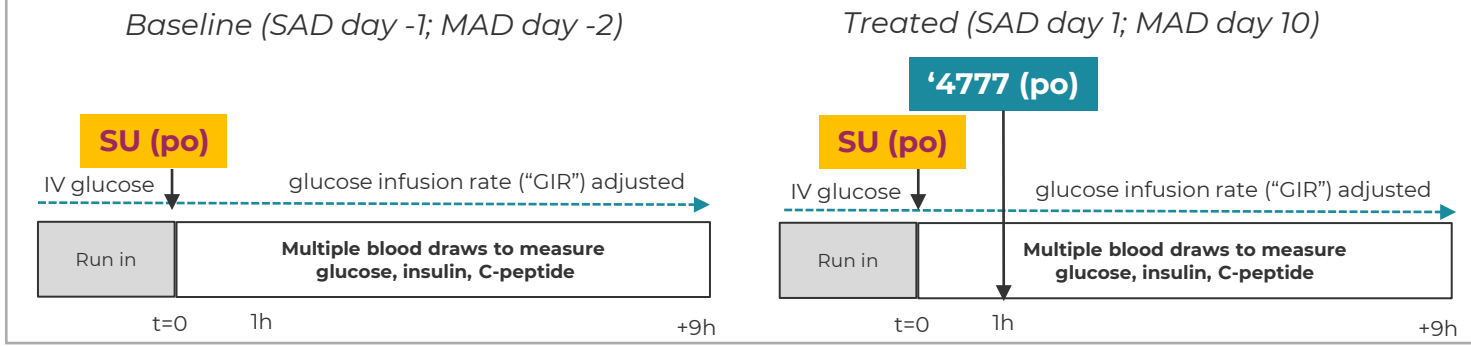
Objectives

- Safety and tolerability
- Pharmacokinetics
- PK/PD for suppression of stimulated insulin secretion
- Dose selection for patient studies

1. IV Glucose Tolerance Test (IVGTT)



2. Sulfonylurea (SU) Challenge Test (Glucose Clamp)



Proof of concept: dose dependent suppression of glucose- or sulfonylurea-induced insulin secretion with CRN04777

Financials

Funded into 2023 based on current projections

Cash Position and Outstanding Shares	
Cash, cash equivalents and investments	$170.9 million as of Dec. 31, 2020
Common shares outstanding	33,028,876 as of Feb. 28, 2021

Fourth Quarter and Full Year 2020 Financials		
	4Q 2020	Full Year 2020
Total OpEx	$21.8 million	$75.0 million
R&D Expenses	$16.8 million	$57.0 million
G&A Expenses	$5.0 million	$18.0 million
Net Loss	$21.6 million	$73.8 million

2021 Goal: Three Programs with Clinical POC

Poised for steady cadence of milestones in 2021

	Q1	Q2	Q3	Q4
Paltusotine SST2 Agonist for Acromegaly & NETs	Initiate PATHFNDR-1		Initiate PATHFNDR-2	
			Initiate Phase 2 NETs Trial in Carcinoid Syndrome	
CRN04894 ACTH Antagonist for Cushing's Disease & CAH	Initiate Phase 1	Phase 1 SAD Data	Phase 1 MAD Data	
CRN04777 SST5 Agonist for Congenital HI	Initiate Phase 1	Phase 1 SAD Data		
			Phase 1 MAD Data	

'4894 and '4777 programs follow our development strategy validated by paltusotine