

Congenital Hyperinsulinism International
Family Conference

July 2020

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 for interim results to be consistent with final results, once available; the potential for any of our ongoing clinical trials to demonstrate safety or efficacy; the potential benefits of paltusotine for acromegaly patients; the potential to initiate a pivotal Phase 3 trial of paltusotine in acromegaly based on interim results to date and the timing thereof; the planned expansion of the paltusotine development program to include the treatment of patients with NETs and the expected timing thereof; the anticipated timing of topline data for Edge and timing for initiation of trials thereafter for its other development programs; the potential benefits of our ACTH agonist in patients across multiple indications and the expected timing of the advancement of such program; the potential benefits of our SST5 agonist in patients with congenital hyperinsulinism and the expected timing of the advancement of such program; and the company's anticipated cash runway. In some cases, you can identify forward-looking statements by terms such as "may," "believe," "anticipate," "could," "should," "estimate," "expect," "intend," "plan," "project," "will," "forecast" and similar terms. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, without limitation: the risk that interim results of a clinical trial do not necessarily predict final results and that one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, and as more patient data become available; potential delays in the commencement, enrollment and completion of clinical trials and the reporting of data therefrom; 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 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; we may use our capital resources sooner than we expect; and other risks described under the heading "Risk Factors" in documents we file from time to time with the Securities and Exchange Commission. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and, except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Crinetics: Who We Are and What We Do



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 PIPELINE

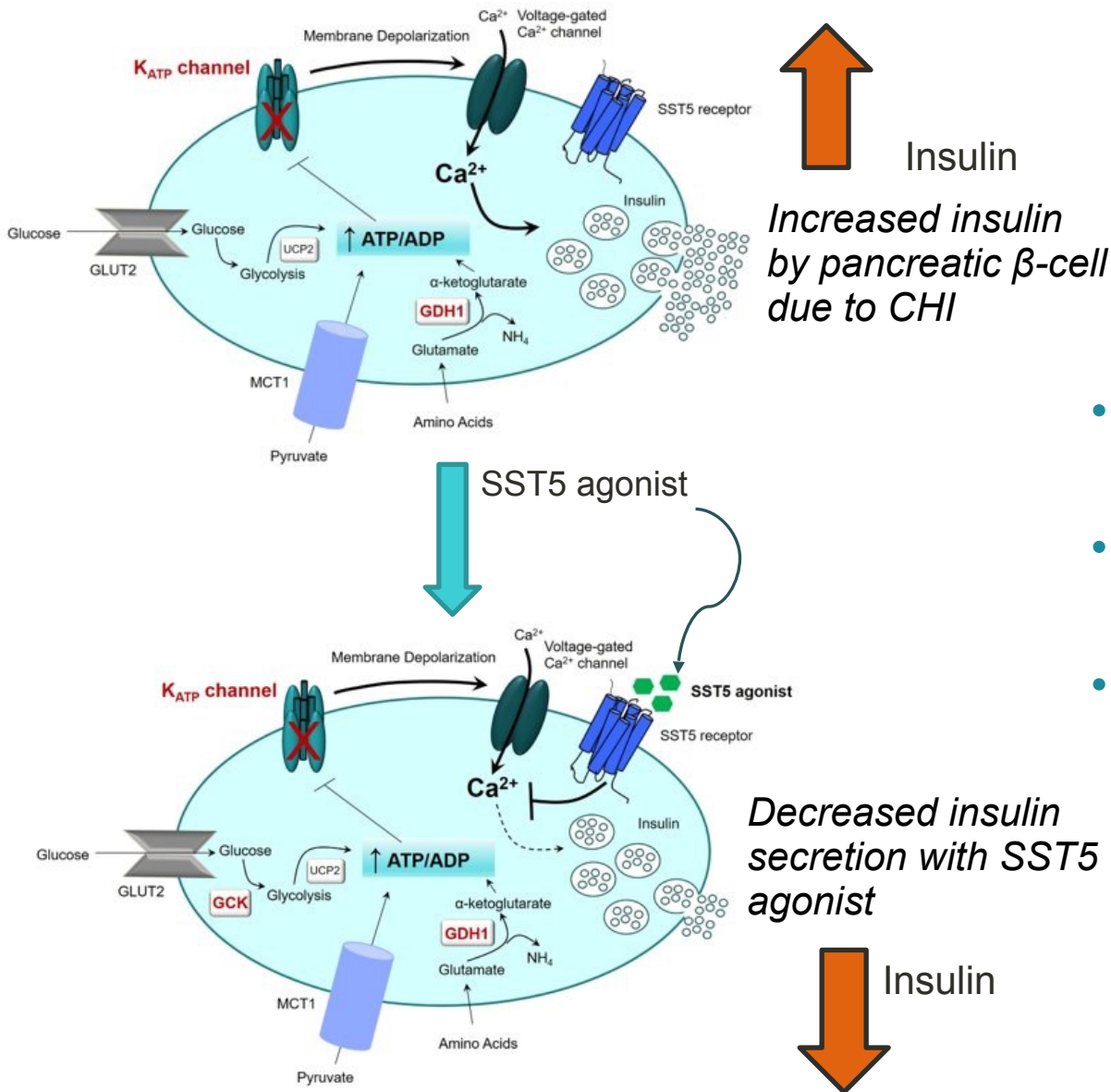


Building a rare disease franchise in endocrinology and endocrine oncology

PROGRAM	DISCOVERY	PRECLIN	PHASE 1	PHASE 2	PHASE 3	NEXT MILESTONE
Paltusotine Acromegaly						Topline data from Phase 2 acromegaly trials in 4Q 2020 Initiate acromegaly Phase 3 trial in 1H 2021
Neuroendocrine Tumors (NETs)						Initiate NETS Phase 2 trial in 2021
Oral ACTH Antagonist Cushing's Disease, Congenital Adrenal Hyperplasia						Initiate Phase 1 trial late 2020/early 2021
Oral SST5 Agonist Hyperinsulinism						Initiate Phase 1 trial late 2020/early 2021

All product candidates discovered and developed internally at Crinetics

Our hypothesis: An oral SST5 agonist may be a treatment for *all* forms of congenital HI



Increased insulin
by pancreatic β -cell
due to CHI

Rationale for SST5 Agonist

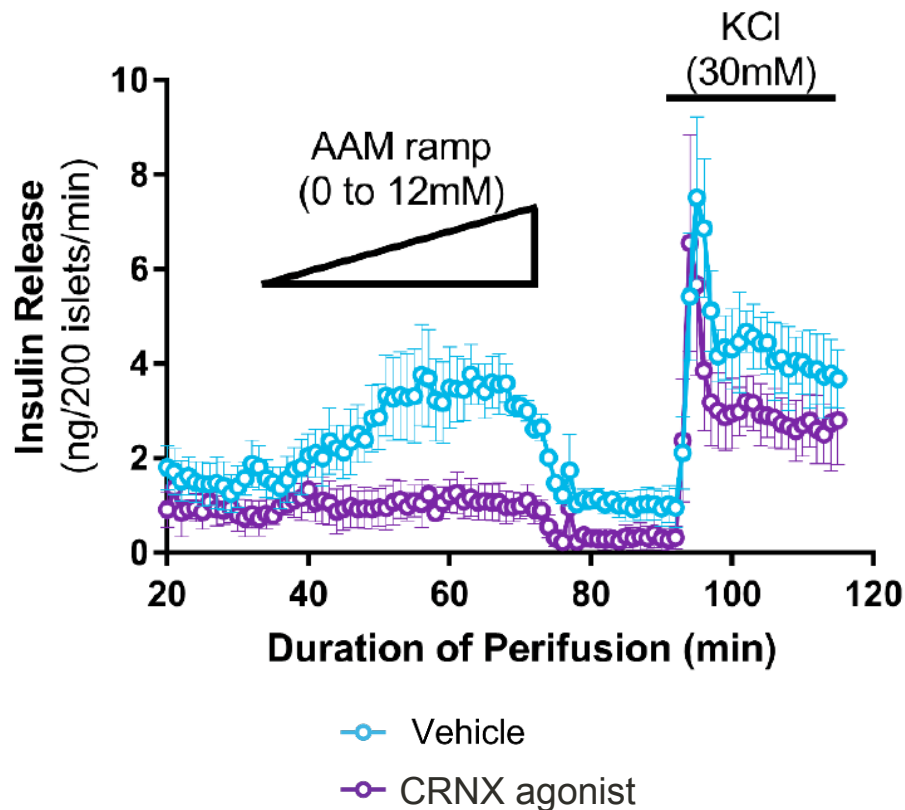
- Potent at suppressing insulin secretion
- Acts independently of K_{ATP} channel and other genetic mutation sites
- Oral administration (solution for young children, capsule/tablet for older children)

Decreased insulin
secretion with SST5
agonist

Crinetics SST5 agonists potently suppress insulin secretion in islet disease models and islets from potential patients

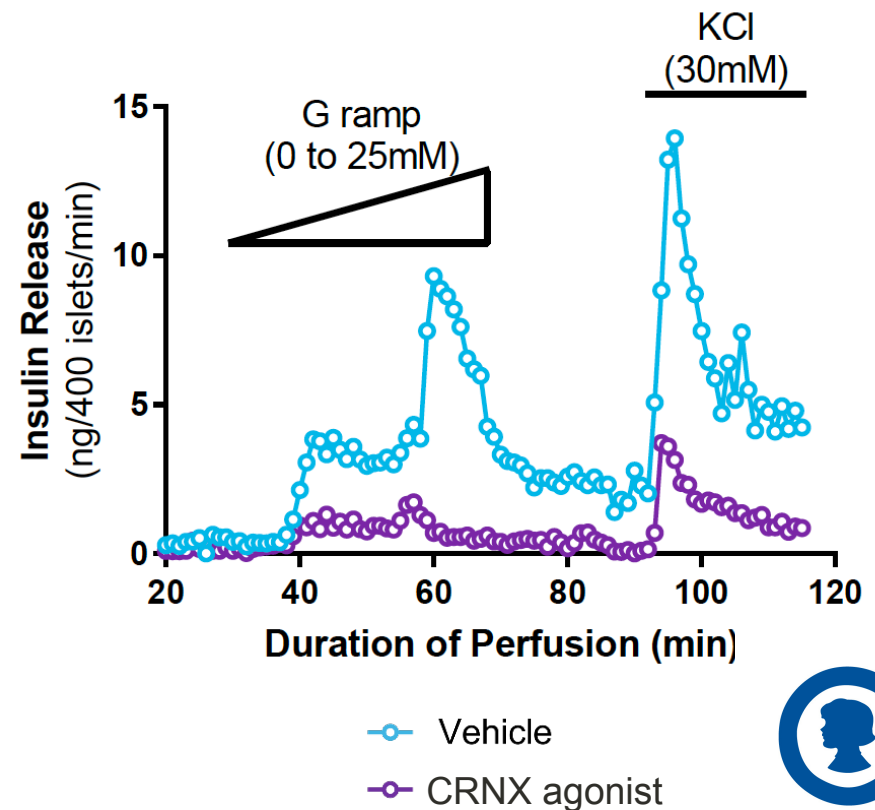
Mouse Model

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



Patient Islets

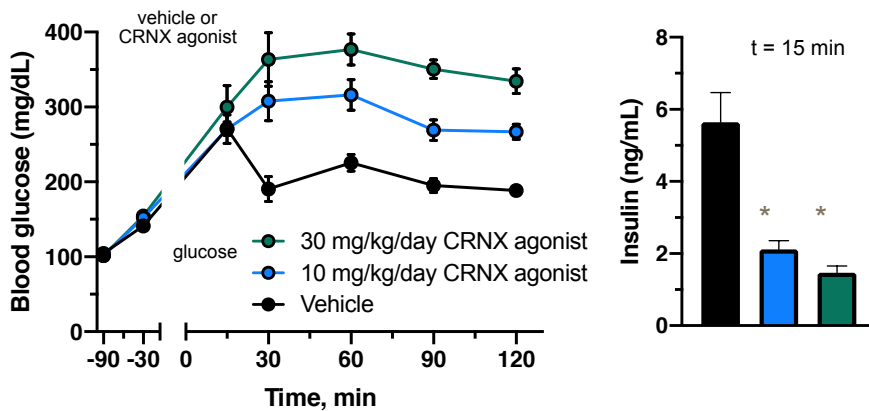
In isolated Beckwith Wiedemann Syndrome patient islets



Crinetics SST5 agonist candidate getting ready for clinical trials in humans

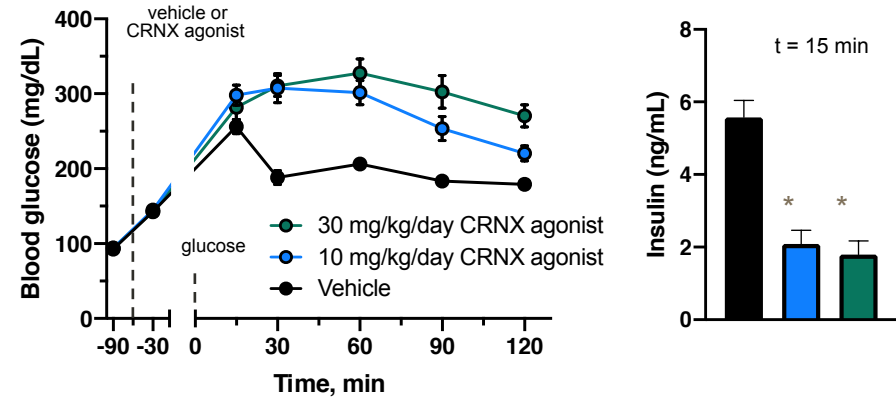
Day-1 OGTT

Glucose increased insulin suppressed in rats

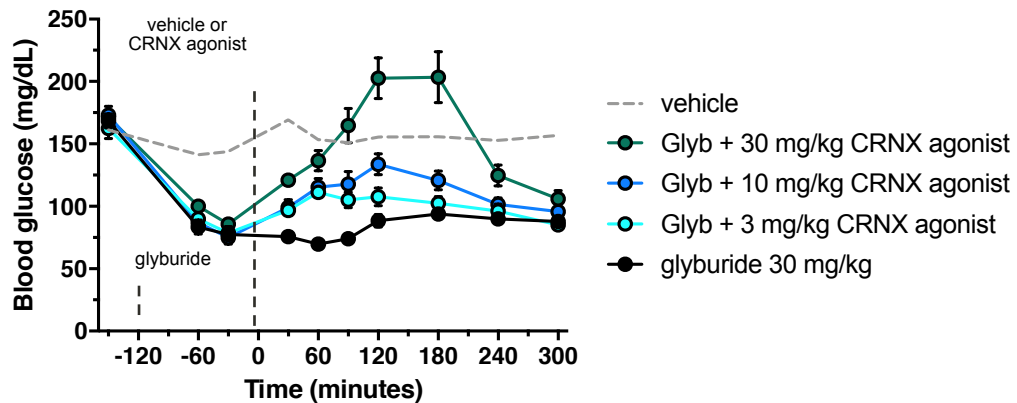


Day-7 OGTT

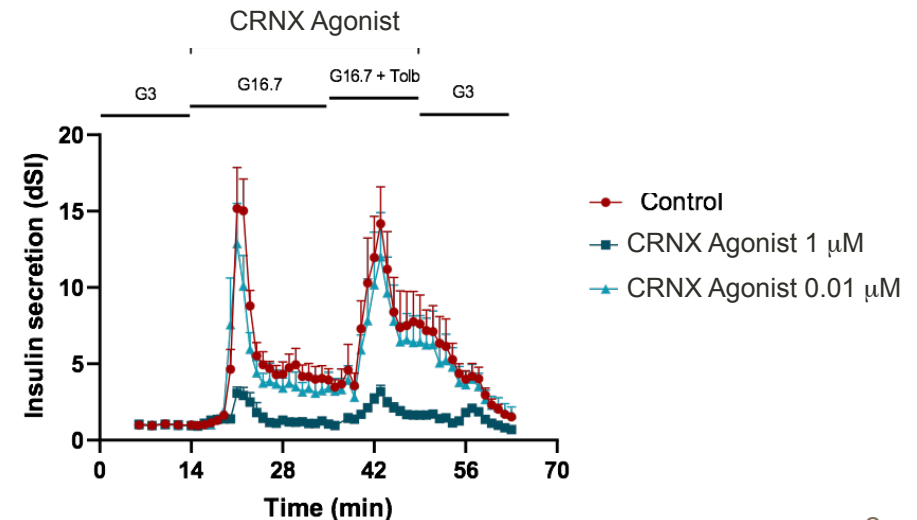
No loss of efficacy



Rescue of glyburide-induced hypoglycemia in rats



Insulin suppression from human donor islets



So, what's next??



- Finishing off all the manufacturing and animal safety studies to allow dosing in people
- Move into human studies
 - Phase 1 (healthy volunteers) early 2021
 - Phase 2 (patients with congenital HI) early 2022
- Collect more data!
 - We want to better understand the disease severity, duration, and patient/family concerns
 - We look forward to working with you