

Corporate Presentation

May 2021 | Soleno Therapeutics



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Soleno Therapeutics (NASDAQ: SLNO)

Strategic Highlights

Orphan asset in Phase 3 Program for Prader-Willi syndrome

Topline data reported in June 2020

Significant commercial potential in PWS, an orphan indication with high unmet need.

No approved treatments for hyperphagia, the hallmark symptom of PWS

IP protection to mid-2030s

Protected by multiple layers of granted and pending patents

Provides composition of matter protection, as well as protection of formulations, and method of use

Substantial potential for patent term extension

Orphan Drug and Fast Track Designations

Orphan designation in the US and EU. Fast Track granted in US

Significant upside potential in other indications

Compelling product profile

Addresses hallmark symptoms of PWS

Clinically relevant improvements in hyperphagia, behaviors, and body composition with established decades-long safety profile

Financed by leading healthcare investors

Financed by

Leading HC-focused institutional investors, Abingworth, Oracle Partners and Jack Schuler

Leadership Team

- Anish Bhatnagar, M.D.

Chief Executive Officer



- Jim Mackaness

Chief Financial Officer



- Neil M. Cowen, Ph.D.

Senior VP, Drug Development



EPICYTE

- Kristen Yen, M.S.

VP, Clinical Operations

Essentialis



- Patricia C. Hirano, M.P.H.

VP, Regulatory Affairs

PRAHEALTHSCIENCES



Prader-Willi Syndrome (PWS)

- Complex genetic neurobehavioral/metabolic disorder due to the loss or lack of expression of a set of genes on chromosome 15
- Birth incidence ~1:15,000 live births
- Elevated mortality rates; average life expectancy ~30 years
- Highest unmet needs
 - Hyperphagia
 - Increases in lean body mass/reductions in fat mass
 - PWS-related behaviors
- PWS families have low quality of life
 - Non-PWS siblings show high rates of post traumatic stress syndrome



DCCR Once Daily Tablets

Daily Dosing Critical to Facilitate Independence and Compliance



Tablet formulation of choline salt of diazoxide
(diazoxide choline is an NCE)

DCCR allows for gradual absorption of diazoxide over 24 hours



Protected by multiple issued patents, including composition of matter



More than 330 subjects investigated, including more than 120 with PWS

Ongoing Phase 3 program in PWS

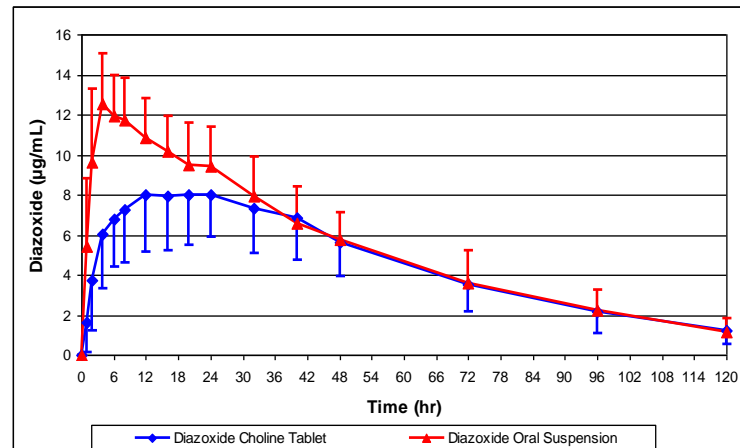
Diazoxide is Not Approved for Use in PWS

Use of diazoxide-based dosage forms in PWS blocked by issued Soleno patent claims

- Oral K_{ATP} channel agonist approved in 1976
- More than 40 years' chronic use in neonates/infants, children, and adults
- Only current use in ultra-rare condition of hyperinsulinism



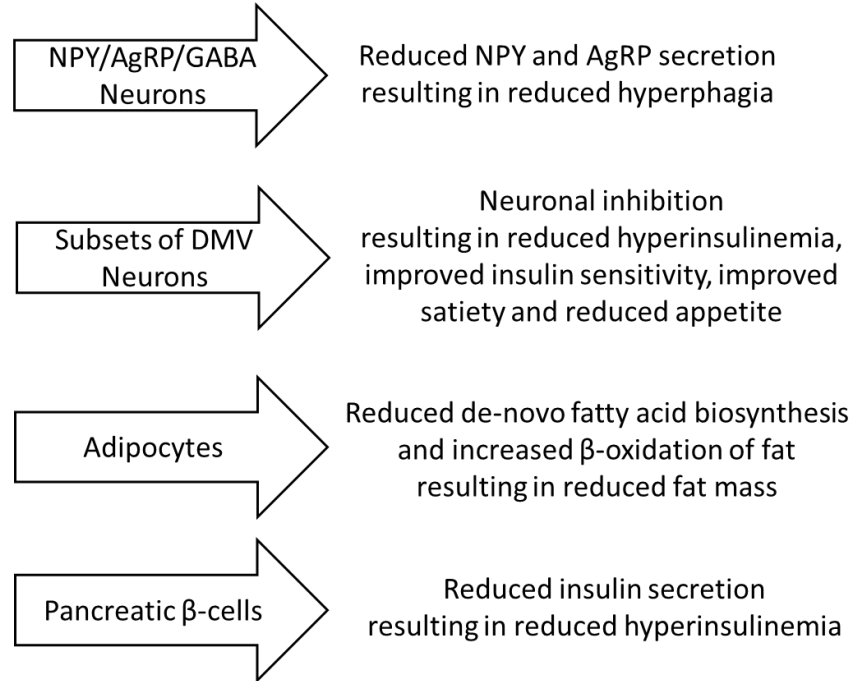
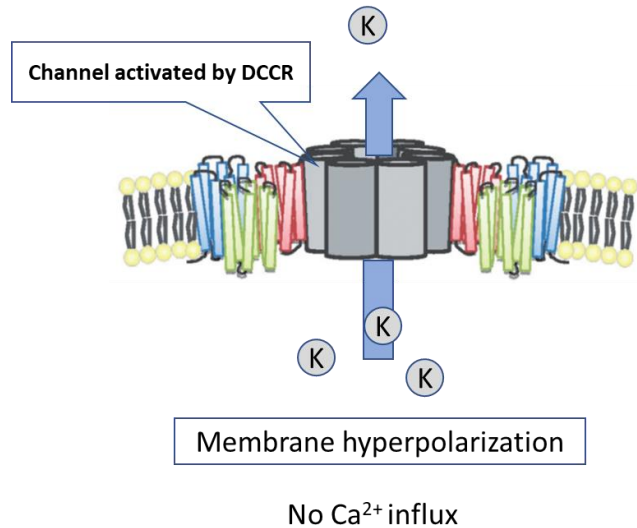
- Only oral suspension currently marketed in US
- Long, bitter aftertaste
- Problems with dose uniformity
- Rapid protein binding of diazoxide



- BID/TID dosing required
- Rapid absorption → high C_{max}
- Several of the most common adverse events C_{max} -associated



Mechanism of Action in PWS



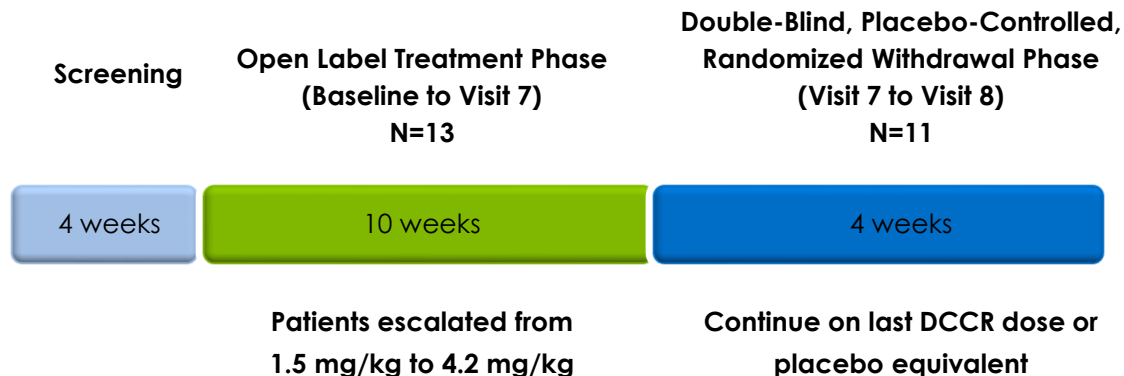
Genes, 11(4), 450. <https://doi.org/10.3390/genes11040450>.

Evidence of efficacy in multiple animal models of NPY-associated obesity with hyperphagia

Animal model	Model of	Significant positive effects on	Reference
MAGEL2 mouse	Prader-Willi syndrome	Hyperphagia, body fat, glycemic control, energy expenditure	Mol Genet Metab 2018 123(4):511-517
Zucker fatty rat	LepR deficient obesity	Hyperphagia, rate of weight gain, glycemic control and insulin sensitivity	Endocrinology 1999 140(7):3197-3202.
Zucker diabetic fatty rat	LepR deficient obesity	Hyperphagia, rate of weight gain, glycemic control, leptin, adiponectin, circulating lipids and hepatic lipid content	Endocrinology 2004; 145:5476–5484 and Med Sci Monit 2005 11(12):BR439-448.
Db/Db mouse	LepR deficient obesity	Completely eliminated hyperphagia	Life Sci 1981 28(15-16):1829-40.
OETF fatty rat	CCK1 receptor deficiency	Hyperphagia, rate of weight gain, body fat, glycemic control, hepatic lipid content	J Diabetes & Its Complications 2008; 22:46-55.
High fat diet induced obese mouse	Induced obesity with hyperphagia	Reduced caloric intake, weight loss, loss of body fat, circulating lipids, glycemic control	Mol Genet Metab 2018 123(4):511-517; Endocrin 2000 141(10):3630-3637
VMH lesioned rat	Hypothalamic obesity	Completely eliminated hyperphagia	Pharmacol Biochem & Behav 1978 9:717-720.
VMH lesioned chicken	Hypothalamic obesity	Hyperphagia	Physiol Behav 1983 30(3):325-329.

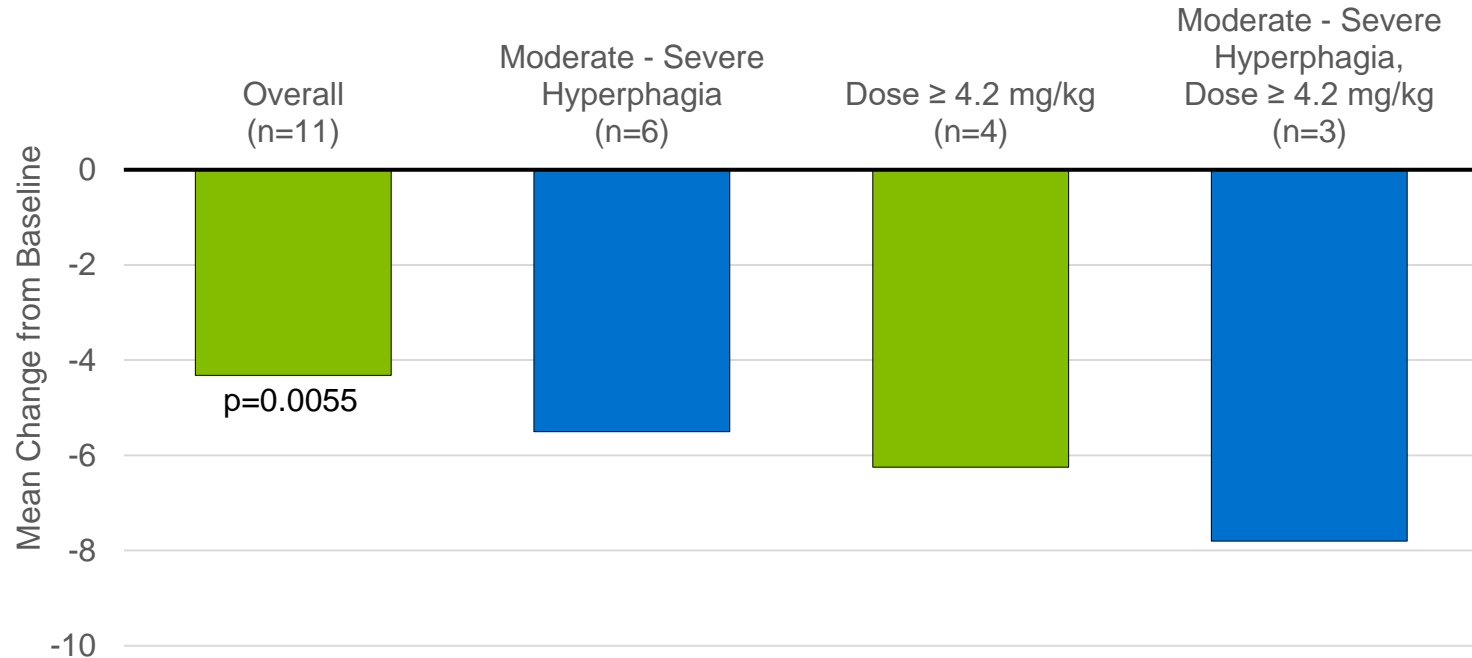
DCCR Pilot Study in PWS – Study PC025

- Randomized, Placebo Withdrawal, Single-Center Study of DCCR in obese, genetically-confirmed PWS patients ages 10 to 22 years
 - Included subjects with mild as well as moderate-to-severe hyperphagia
 - 5 subjects enrolled in a subsequent 6-month open-label extension study

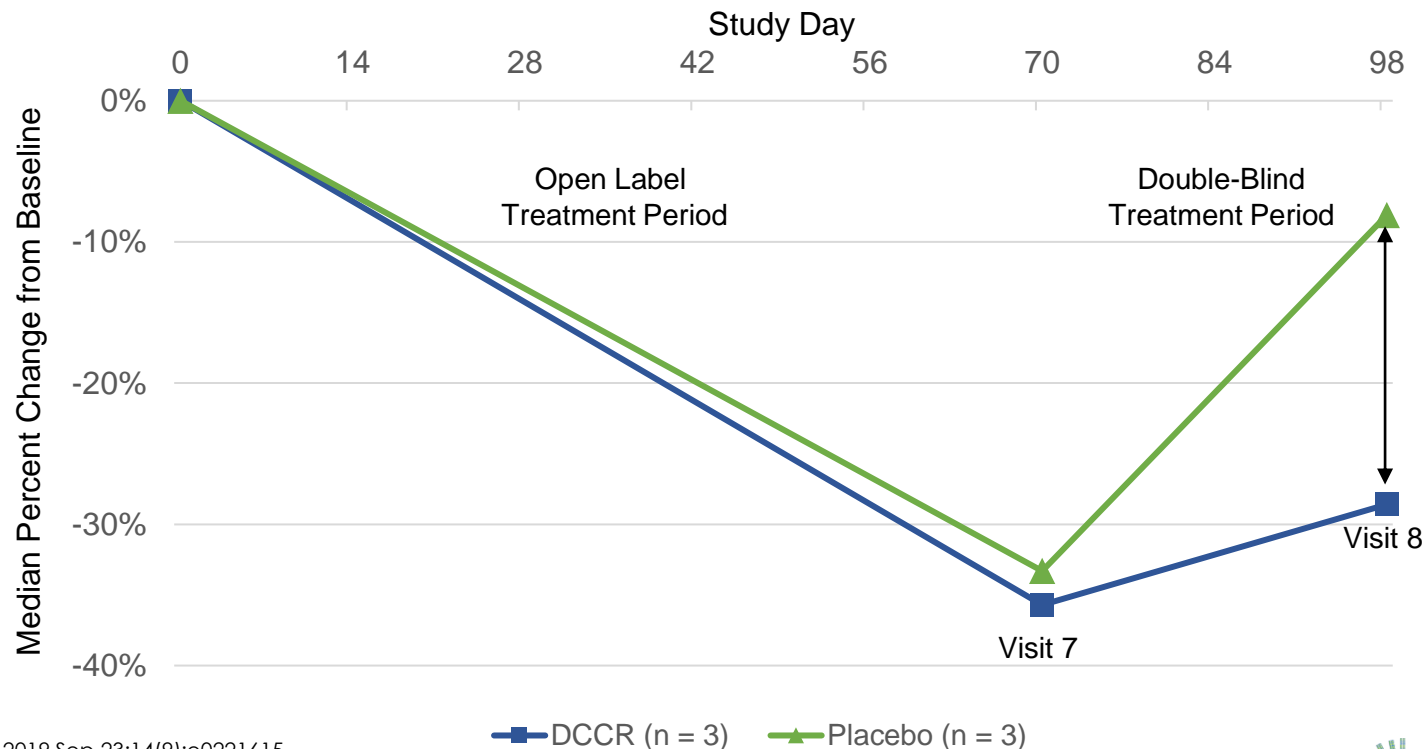


Study PC025 Reduction in Hyperphagia after 8 Weeks of Open-Label Treatment

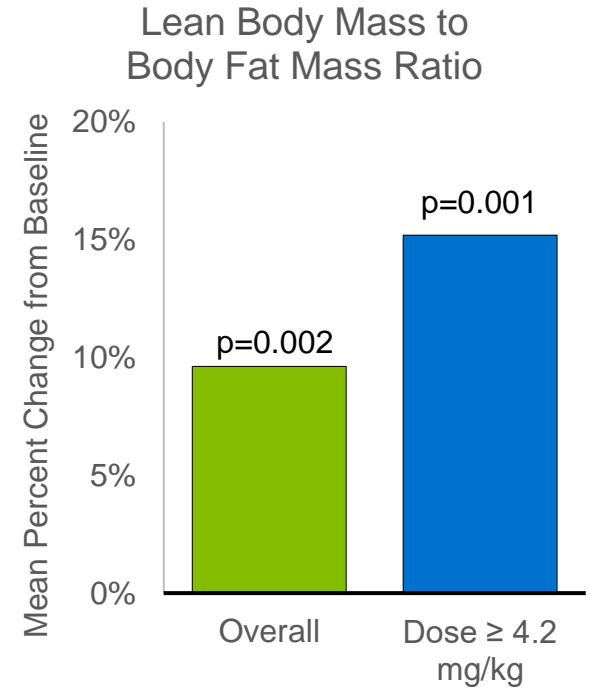
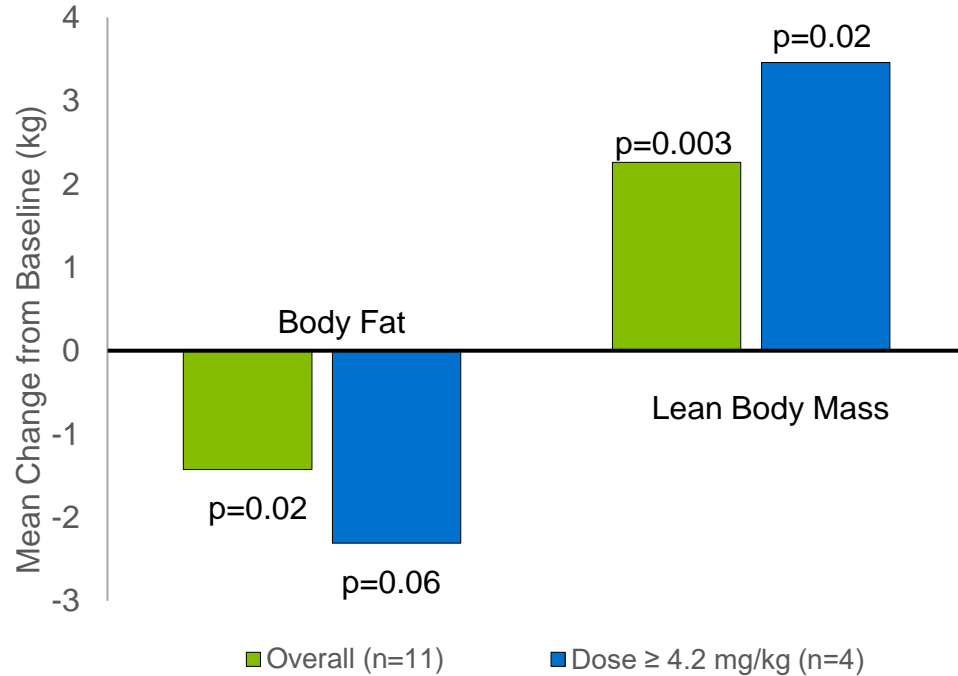
Greater Reductions at Highest Dose and Higher Baseline Hyperphagia



PC025: Changes in Hyperphagia in Subjects with Moderate to Severe Hyperphagia at Baseline

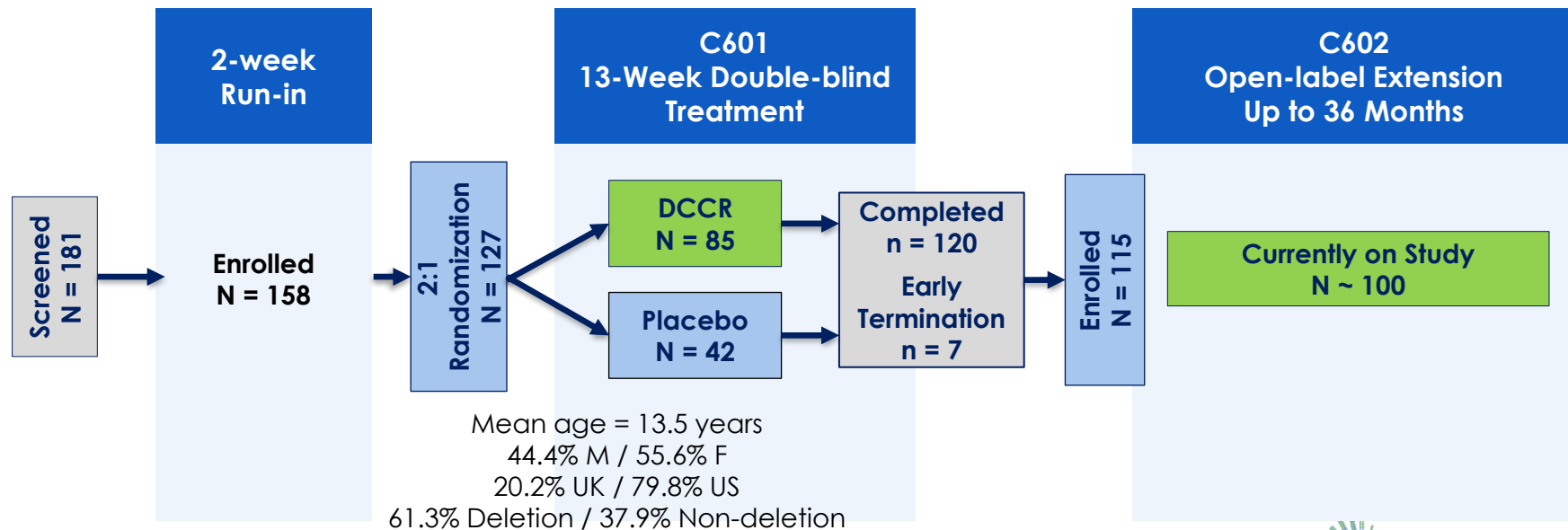


PC025: Changes from Baseline in Body Fat and Lean Body Mass



DCCR Phase 3 Clinical Program Design

- C601 (DESTINY PWS): Multi-center, randomized, double-blind, placebo-controlled, parallel arm study in patients with PWS (Phase 3)
- C602: Open-label safety extension study



C601 Primary and Key Secondary Endpoints

Primary Endpoint	DCCR (N = 82)	Placebo (N = 42)
Mean Change from Baseline in Hyperphagia at Visit 7	-5.94 (0.879)	-4.27 (1.145)
LS Mean Difference [DCCR-Placebo] (SE)	-1.67 (1.294)	
p-value	0.1983	
Key Secondary Endpoints		
Clinical Global Impression of Improvement at Visit 7 (CGI-I)	0.029	
Mean Change From Baseline in Body Fat Mass (DXA)	0.025	
Caregiver Global Impression of Change at Visit 7 (Caregiver GI-C)	0.409	

Impact of COVID-19 Pandemic on DESTINY PWS

- Comprehensive analyses undertaken based on
 - Published statistical guidance from the FDA and from industry publications^{1,2}
 - Published literature on impact of COVID-19 (COVID) pandemic on childhood psychiatric conditions³
 - FPWR Global Registry COVID Pandemic Impact survey⁴
- Expected that subjective endpoints more likely to be impacted
 - HQ-CT
 - Caregiver GI-C
 - PWS Profile (PWSP)
 - Others

¹ U.S. FDA. Guidance for Industry: Statistical Considerations for Clinical Trials During the COVID-19 Public Health Emergency. June 2020.

² Meyer et al. Statistical Issues and Recommendations for Clinical Trials Conducted During the COVID-19 Pandemic. *Statistics in Biopharmaceutical Research*. 2020;12 (4):399-411.

³ Aman MG, Pearson DA. Challenges for Child and Adolescent Psychiatric Research in the Era of COVID-19. *J Child Adolesc Psychopharmacol*. 2020;30(5):280-284.

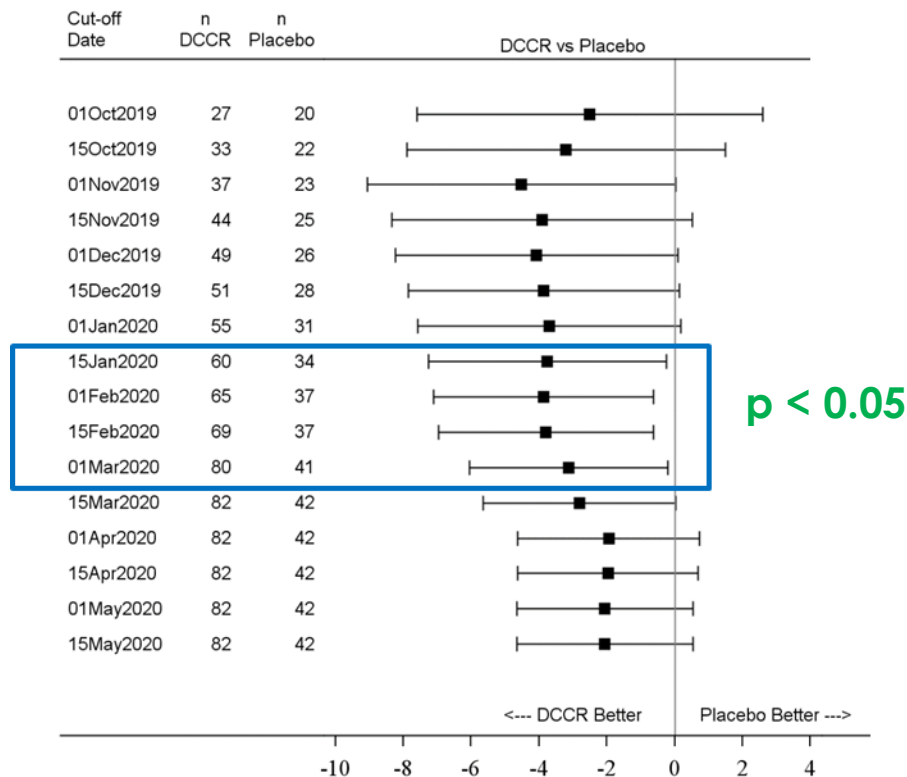
⁴ Foundation for Prader-Willi Research. PWS Registry Data: Impact of COVID-19 on PWS Families. <https://www.fpwr.org/blog/pws-registry-data-impact-of-covid-19-on-pws-families-infographic> and unpublished data, January 2021.

C601 Primary and Key Secondary Endpoints

Primary Endpoint	All Data		Data through March 1, 2020	
	DCCR (N = 82)	Placebo (N = 42)	DCCR (N = 80)	Placebo (N = 40)
Mean Change from Baseline in Hyperphagia at Visit 7	-5.94 (0.88)	-4.27 (1.15)	-6.64 (1.00)	-3.51 (1.28)
LS Mean Difference [DCCR-Placebo] (SE)	-1.67(1.29)		-3.13 (1.48)	
p-value	0.198		0.037	
Key Secondary Endpoints				
Clinical Global Impression of Improvement at Visit 7 (CGI-I)	0.03		0.015	
Mean Change From Baseline in Body Fat Mass (DXA) at Visit 7	0.03		0.004	
Caregiver Global Impression of Change at Visit 7 (Caregiver GI-C)	0.41		0.031	

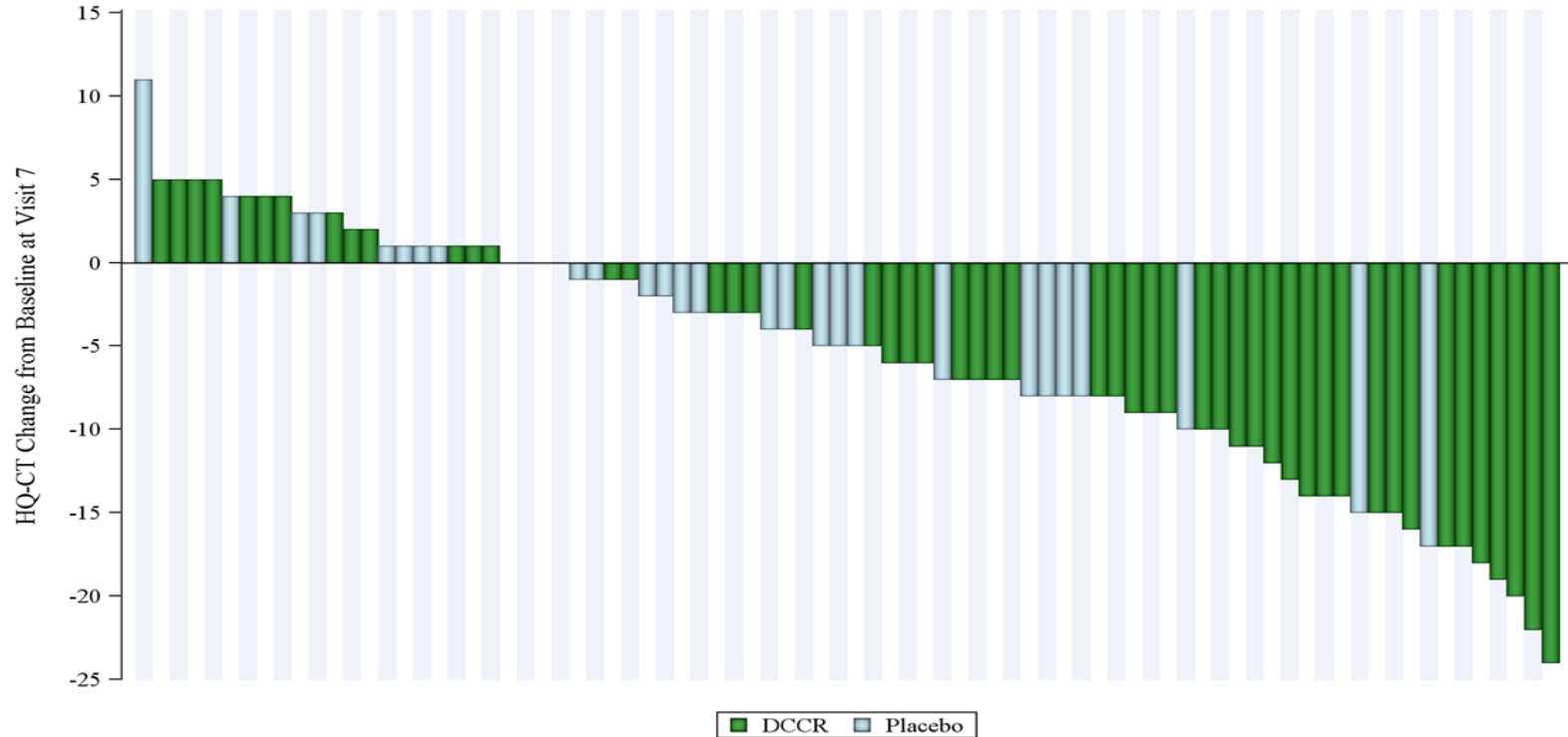
Analyses in this presentation are preliminary and may be subject to change.

C601 HQ-CT Changes in HQ-CT by Cut-off Date

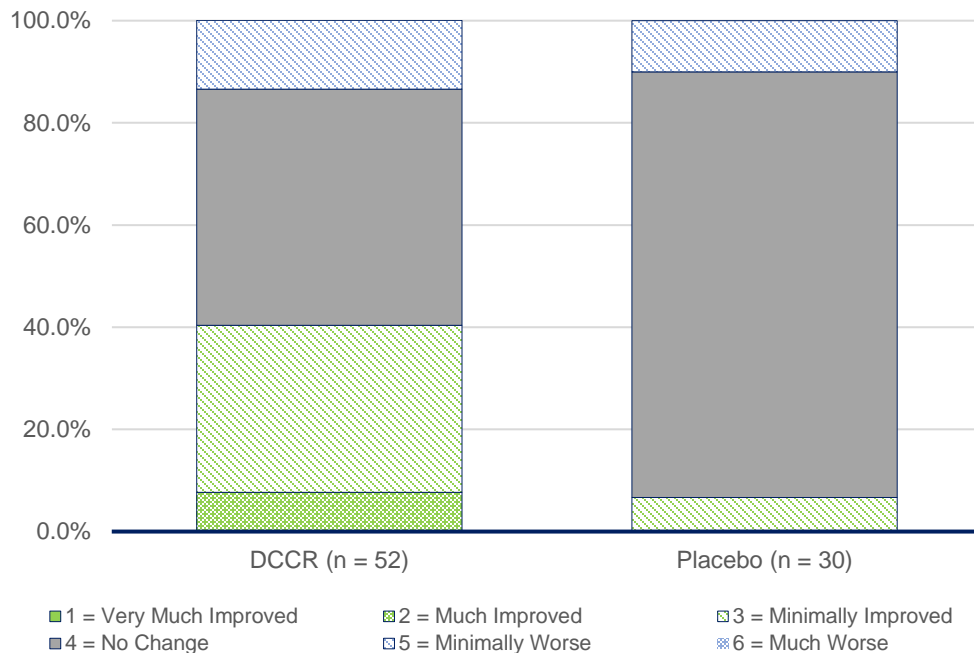


Data through March 1, 2020

HQ-CT Changes from Baseline Waterfall Plot through March 1, 2020



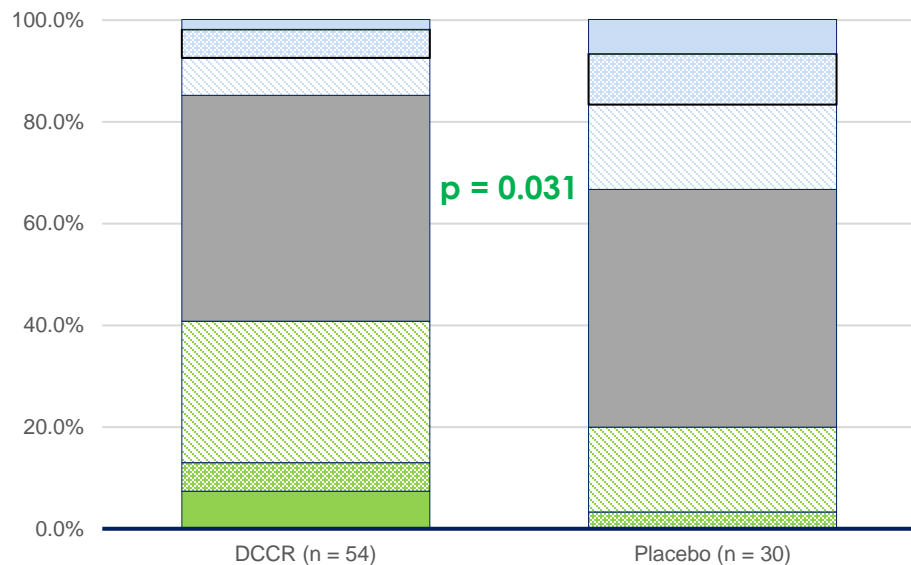
C601 Key Secondary Endpoint: CGI-I



CGI-I Rating	DCCR (n = 52)	Placebo (n = 30)
Improved	40.4%	6.7%
No Change	46.2%	83.3%
Worse	13.5%	10.0%

*p-value using CMH; all observed values through March 1, 2020
Using imputation for missing data $p = 0.037$*

C601 Key Secondary Endpoint: Caregiver GI-C

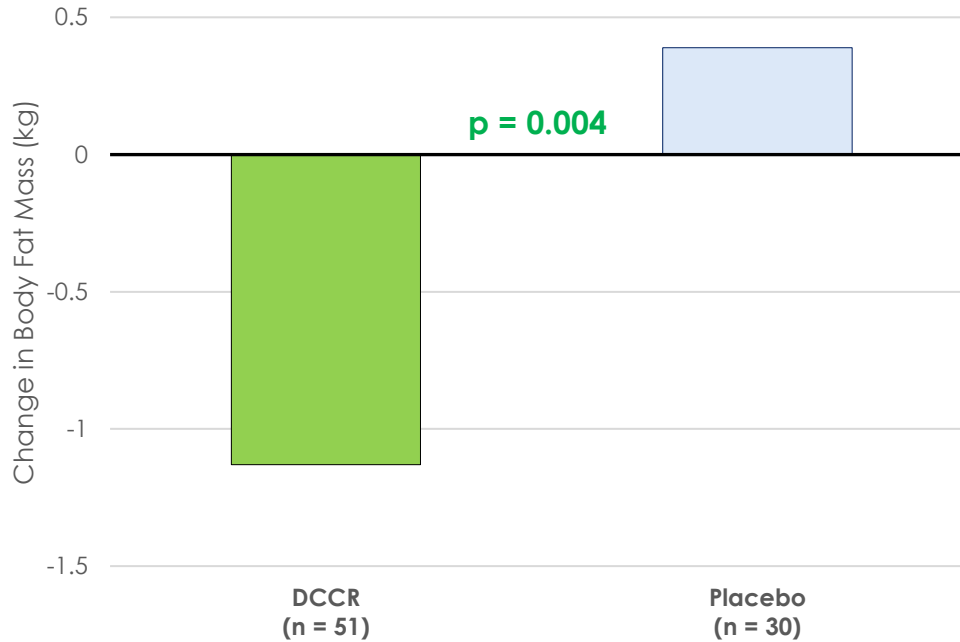


Caregiver GI-C Rating	DCCR (n = 54)	Placebo (n = 30)
Better	40.8%	20.0%
No Change	44.4%	46.7%
Worse	14.9%	33.4%

■ 1 = Very Much Better
 ■ 2 = Moderately Better
 ■ 3 = A Little Better
 ■ 4 = No Change
■ 5 = A Little Worse
 ■ 6 = Moderately Worse
 ■ 7 = Very Much Worse

p-value using CMH; all observed values through March 1, 2020
 Using imputation for missing data *p* = 0.086

C601 Key Secondary Endpoint: Body Fat Mass



Observed values through March 1, 2020
Using imputation for missing data $p = 0.005$

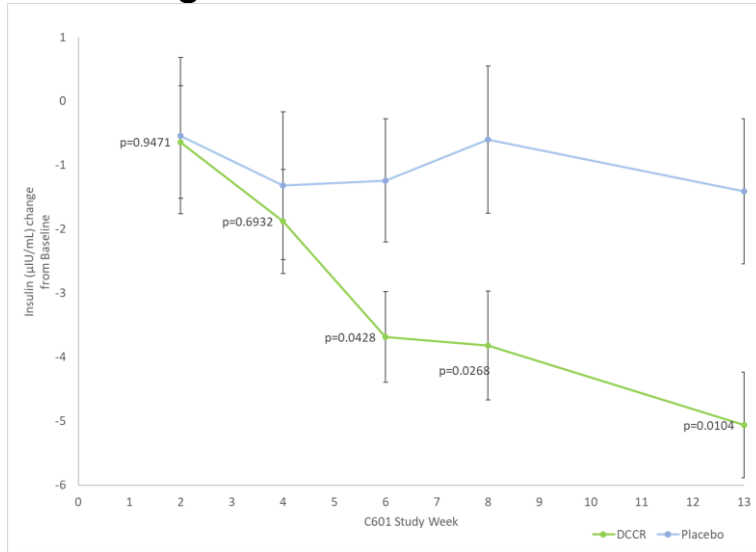
C601 Behavioral Endpoints, data through March 1, 2020

PWSP Domain	p-value DCCR vs Placebo
Aggressive Behaviors	0.048
Anxiety	0.018
Rigidity, Irritability	0.003
Compulsivity	0.008
Depression	0.185
Disordered Thinking	0.011
DBC-2	
Total Score	0.009
Communication Disturbance	0.003
Social Relating	0.008

Observed values through March 1, 2020

C601 Mean Changes from Baseline in Key Cardiometabolic Markers

Insulin Change from Baseline at Week 13



Source: Soleno Therapeutics Preliminary Analysis

Change from Baseline at Week 13 (through March 1, 2020)	DCCR vs Placebo p-value
Decreased Acylated Ghrelin (active form)	0.009
Decreased Leptin	<0.0001
Increased Adiponectin	<0.0001

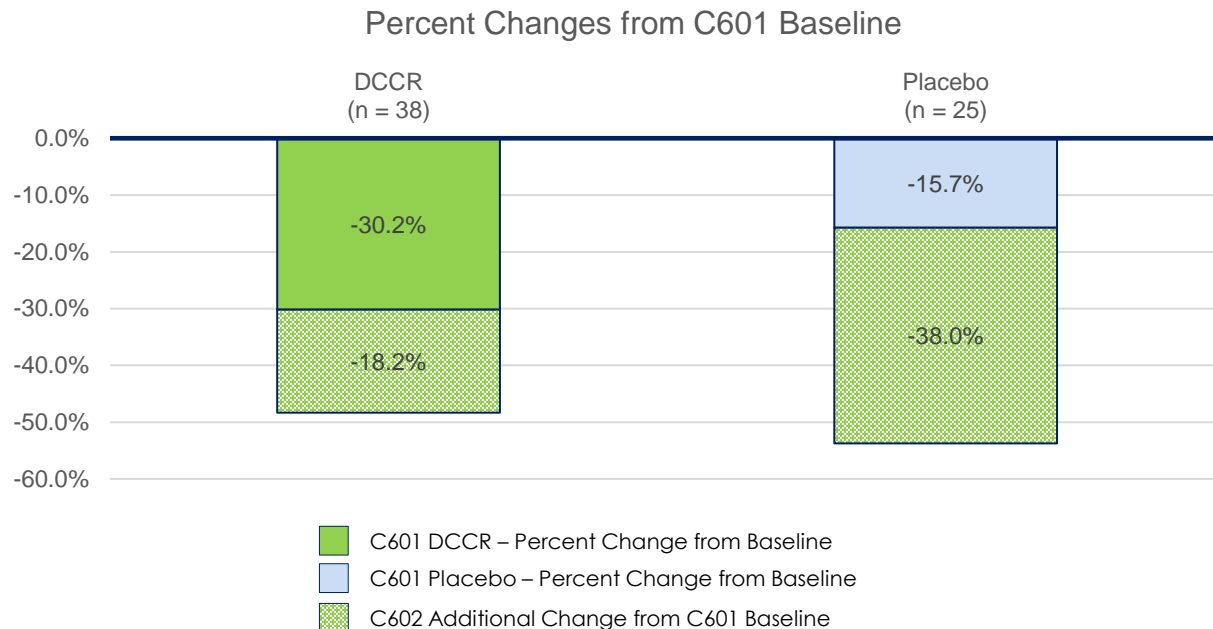
Conclusions from pre-COVID Analysis

- Clear impact of the COVID-19 pandemic on the results in DESTINY PWS
- Primary, subjective key secondary, and several other endpoints that were not significant in the topline analyses, are significant with pre-March 1, 2020 analyses
- No differences observed in the safety of DCCR compared to the profile seen in the topline analyses

C602 Interim Analysis

- Data includes those subjects who completed C602 Visit 6 (i.e., 13 weeks of open-label DCCR treatment)
 - N = 63
 - DCCR = 38
 - Placebo = 25
 - Demographics and baseline characteristics comparable to the ITT Population
 - Lower percent of subjects in UK compared to C601 ITT population due to later start of C601 compared to US
 - Interim analysis, partially verified data – conducted in parallel with topline analysis of C601

Changes in HQ-CT from C601 Baseline at Visit 7 and Further Changes in C602



DCCR Safety Profile

- The safety profile of DCCR was generally consistent with the known profile of diazoxide and prior experience with DCCR
- The most common adverse events reported were hypertrichosis, peripheral edema and hyperglycemia
- Most events were Grade 1 in severity
- No Grade 4 or higher events
- There were no serious unexpected adverse events (SUSARs) related to DCCR

DCCR Status

- Met with FDA Nov 2020, minutes issued Dec 2020
 - Discussed potential adequacy of data from completed and ongoing studies
 - Agreed to review plans for analyses comparing DCCR data to external data sources
 - FDA did not rule out possibility of an additional clinical trial
- Pre-COVID data submitted to FDA after Nov 2020 meeting
 - March 2021 FDA responded that additional controlled data are necessary to support an NDA submission

Support from Patient Advocacy Groups

- Significant support from patient advocacy organizations and the PWS community as a result of patients' and caregivers' experiences with DCCR
 - FPWR/PWSA USA combined petition submitted to the FDA requesting regulatory flexibility and review of an NDA for DCCR when submitted
 - Signed by 26,640 supporters
 - “Town Hall” organized by families to discuss personal experiences with DCCR during studies C601 and C602

Financial Highlights

- Cash balance at end of Q1 2021 \$41.6M
- No Debt

- Common shares outstanding at end of Q1 2021 79.7M
- Fully Diluted shares at end of Q1 2021 86.8M

Pipeline – Other Opportunities for DCCR

	Potential Upside Opportunities for DCCR	Estimated US Prevalence
Syndromic Obesity	Fragile X-PWS Phenotype	6,700 - 8,500
	Schaaf-Yang syndrome	200 - 300
	Smith Magenis syndrome	13,000 - 22,000
	MC4R deficiency	32,700 - 163,000
Other	Chronic Hyperinsulinism	820 - 1,100
	Glycogen Storage Disease Type 1	2,800 - 6,800

Extensive IP Protection

Three families of patents being prosecuted in all major pharma markets – primary cases on all three issued

Pharmaceutical formulations of K_{ATP} channel activators and uses thereof
PWS relevant claims:
treatment of hyperphagia

Salts of K_{ATP} channel activators and uses thereof
PWS relevant claims:
treatment of PWS +
Composition of Matter
coverage of DCCR

Methods for treating subjects with PWS or SMS
PWS relevant claims:
reductions in aggressive behavior + others

- Extensive protection of diazoxide choline, DCCR formulation and use, method of manufacture covering the treatment of PWS and more generally, in syndromic obesity expiring 2025 - 2035
- Composition of matter (potential for extension to 2034 in US and to 2031 in EU)
- Up to 6 patents are orange book listable (up to 3 expiring in 2035)

Key Takeaways

- PWS is a rare disease, US estimate of 10,000 – 20,000 people
- DCCR is focused on treating the highest unmet needs of PWS for which no approved treatments exist
- Once a day tablet formulation with orphan pricing
- Focused physician population that can be targeted by a small commercial footprint
- Substantial potential upside with other rare disease indications

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