Corporate Presentation

September 2021 | Soleno Therapeutics

Certain Notices and Disclaimers

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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, long-term data in Sep 2021

Clinically relevant improvements in hyperphagia, behaviors, and body composition with DCCR supported by decades-long safety profile of active moiety

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 US and EU for PWS. Fast Track granted in US

Significant upside potential in other indications

Orphan designation granted for GSD1a in US

>$1bn PWS global market opportunity

Addresses hallmark symptoms of PWS

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

No approved treatments for hyperphagia, the hallmark symptom of PWS

Financed by leading healthcare investors

Financed by leading HC-focused institutional investors

Abingworth, Nantahala, Oracle Partners and Jack Schuler

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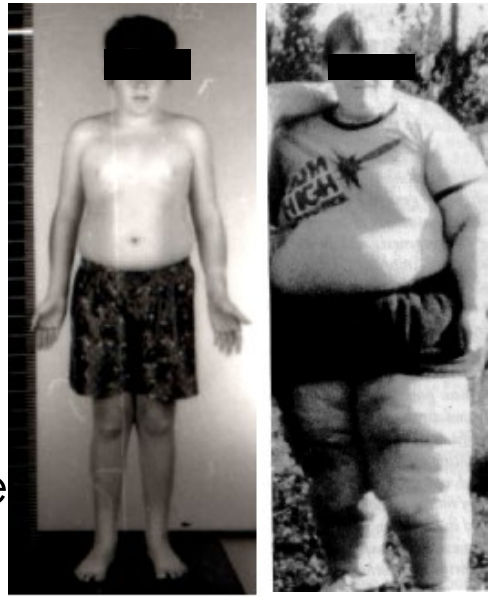
Leadership Team

- Anish Bhatnagar, M.D.
  Chief Executive Officer
- Jim Mackaness
  Chief Financial Officer
- Neil M. Cowen, Ph.D.
  Senior VP, Drug Development
- Kristen Yen, M.S.
  VP, Clinical Operations
- Patricia C. Hirano, M.P.H.
  VP, Regulatory Affairs

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
  - Low lean body mass/increased fat mass
  - PWS-related behaviors
- Families with a child with PWS have low quality of life
  - Non-PWS siblings show high rates of post traumatic stress syndrome



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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

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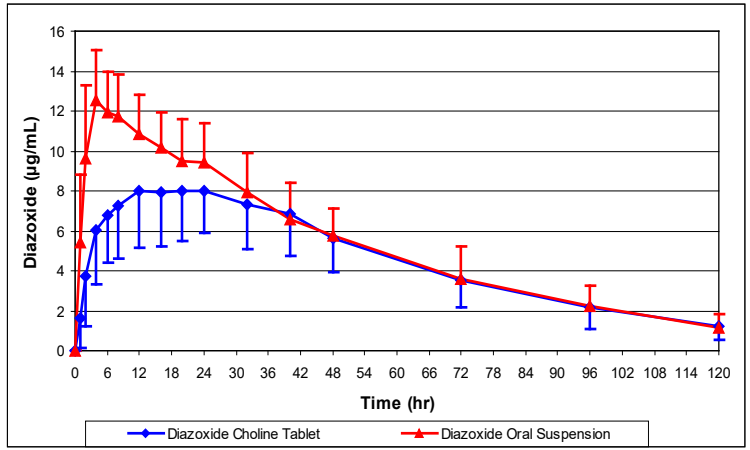
Diazoxide is Not Appropriate for Use in PWS

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

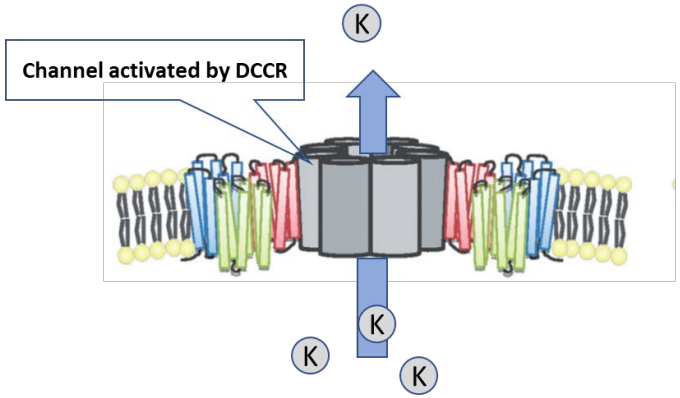
- Oral K_{ATP} channel agonist approved in 1976
- More than 40 years' chronic use in neonates/infants, children, and adults
- Only current use in ultra-rare condition of hyperinsulinism



- 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



Membrane hyperpolarization

No Ca^{2+} influx

NPY/AgRP/GABA Neurons → Reduced NPY and AgRP secretion resulting in reduced hyperphagia

Subsets of DMV Neurons → Neuronal inhibition resulting in reduced hyperinsulinemia, improved insulin sensitivity, improved satiety and reduced appetite

Adipocytes → Reduced de-novo fatty acid biosynthesis and increased β-oxidation of fat resulting in reduced fat mass

Pancreatic β-cells → Reduced insulin secretion resulting in reduced hyperinsulinemia

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

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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.
OLETF 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.

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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 13 subjects with mild as well as moderate-to-severe hyperphagia
  - Conducted at UC Irvine
- DCCR treatment resulted in
  - Significant reductions from baseline in hyperphagia score
  - Loss of body fat
  - Increases in lean body mass
  - Reductions in aggressive behaviors
  - Trends towards differences between DCCR and placebo during 4-week randomized withdrawal period

PLoS ONE 14(9): e0221615. https://doi.org/10.1371/journal.pone.0221615

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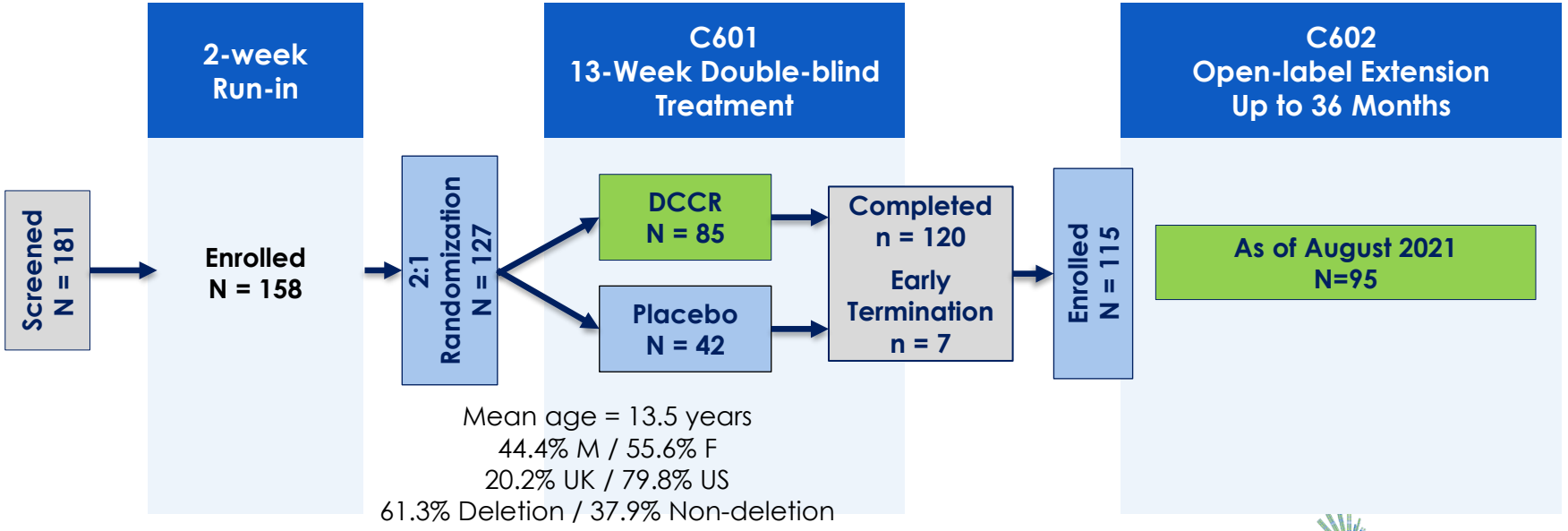
DCCR Phase 3 Clinical Program Design

- 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

	All Data		Data through March 1, 2020	
Primary Endpoint	**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.

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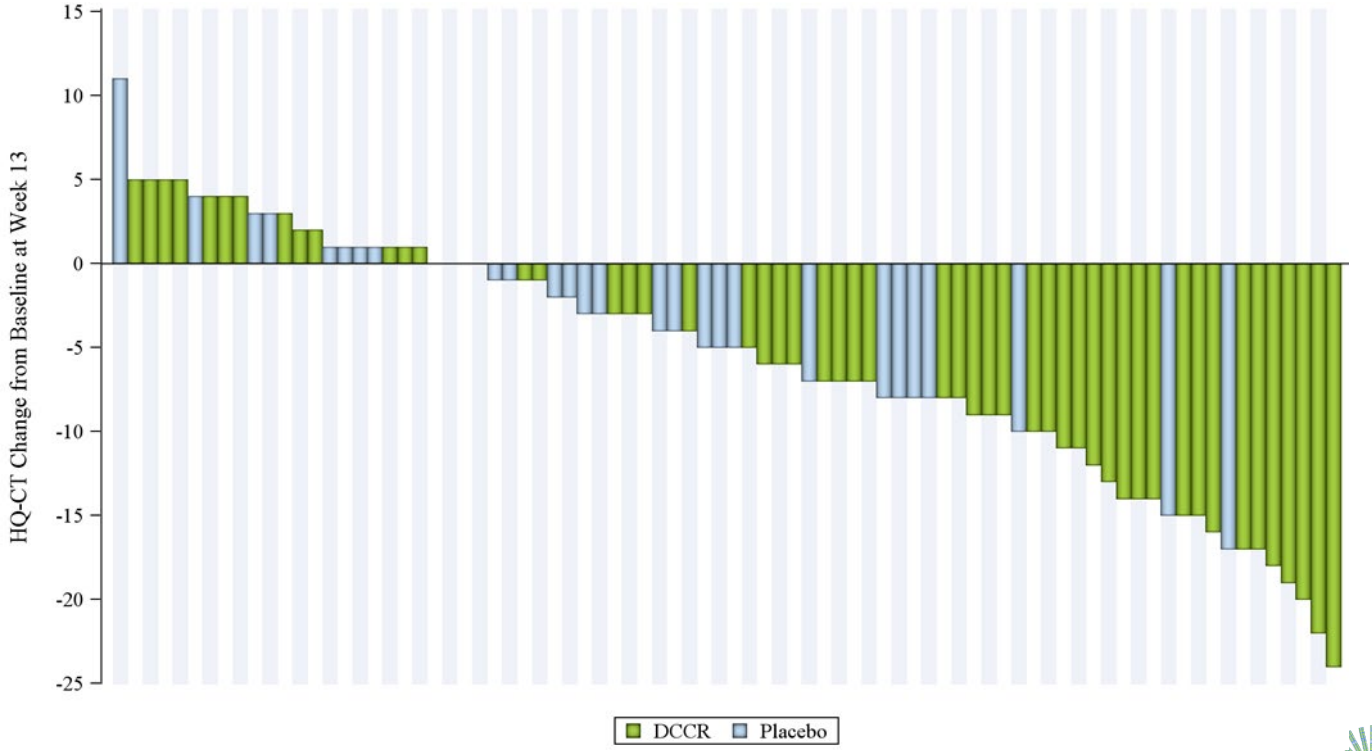
HQ-CT Changes from Baseline Waterfall Plot through March 1, 2020



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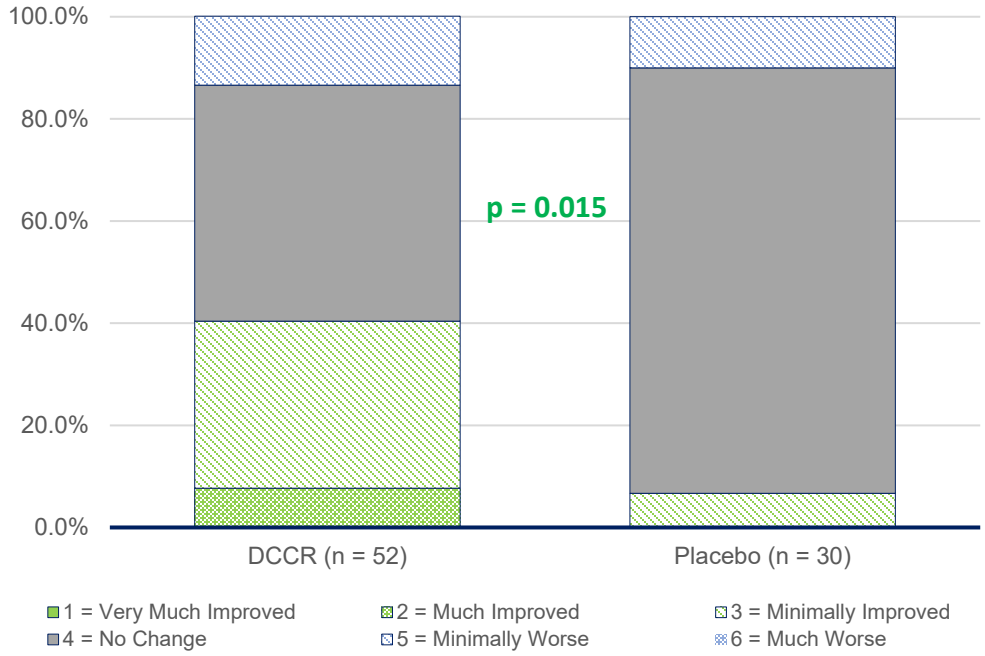
C601 Key Secondary Endpoint: CGI-I



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

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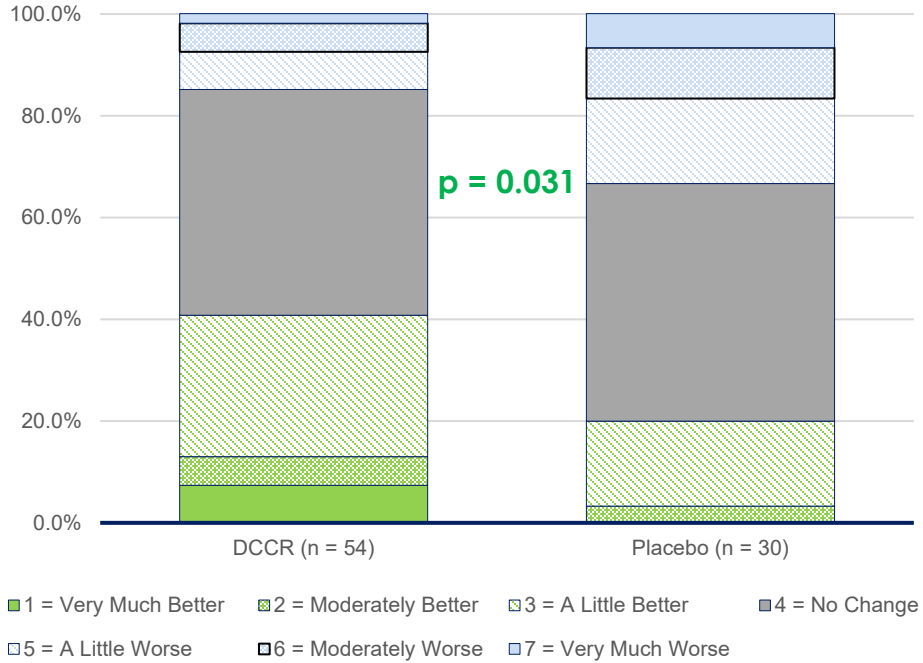
C601 Key Secondary Endpoint: Caregiver GI-C



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%

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

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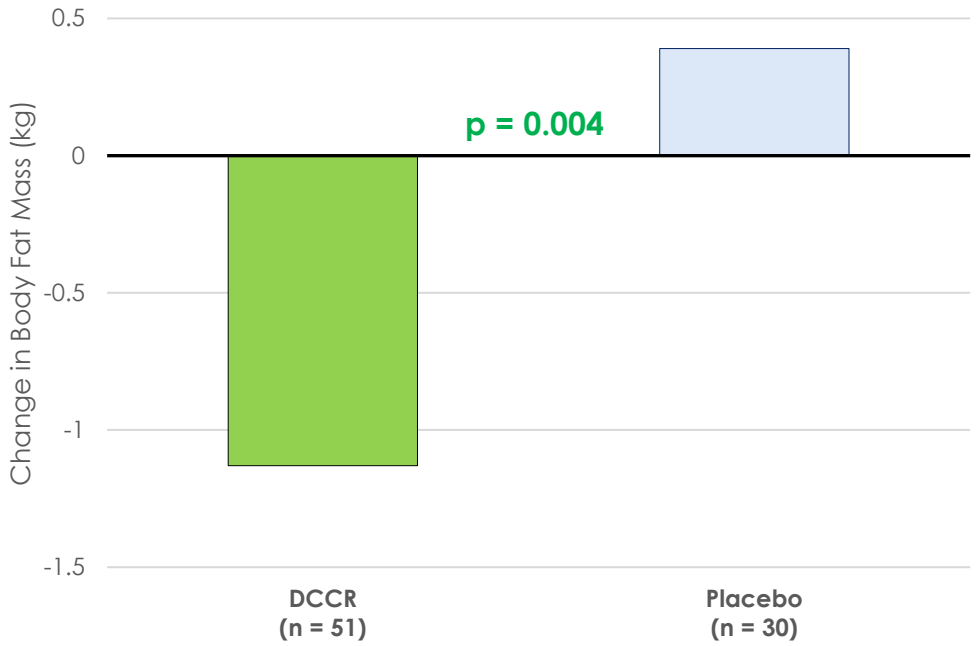
C601 Key Secondary Endpoint: Body Fat Mass



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

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C601 Behavioral Endpoints

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

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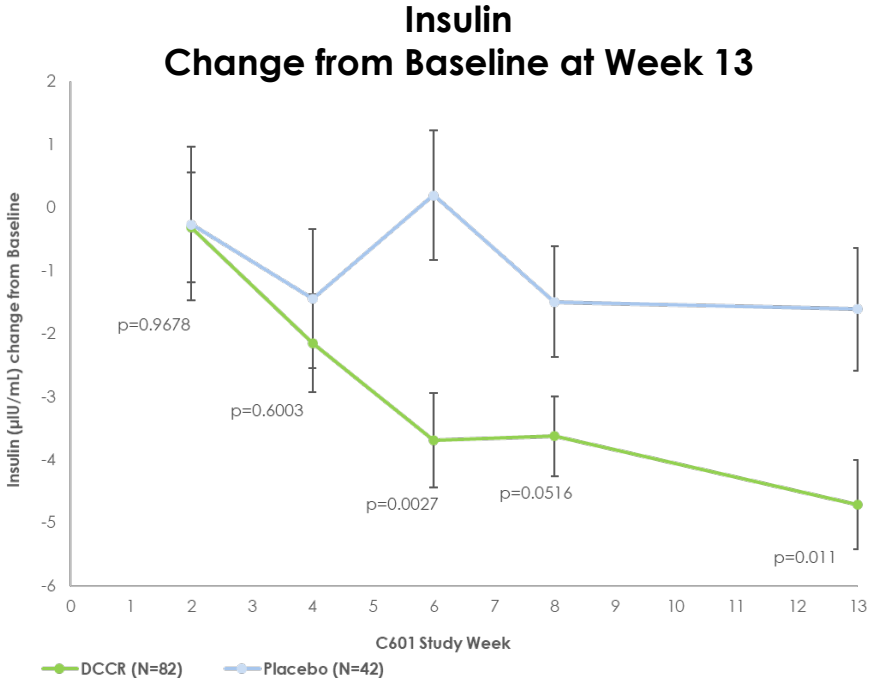
C601 Mean Changes from Baseline in Key Endocrine and Hormonal Parameters



Change from Baseline at Week 13	DCCR vs Placebo p-value
Decreased Acylated Ghrelin (active form)	0.018
Decreased Leptin	<0.0001
Increased Adiponectin	<0.0001

ITT Population

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Long-term data:

12 MONTHS INTERIM RESULTS FROM STUDY C602 AND COMPARISON TO PATH FOR PWS

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C602 and PATH for PWS

- C602 is an ongoing, open label extension study of DCCR in subjects who completed DESTINY PWS successfully
- PATH for PWS is an ongoing study evaluating the natural history of subjects with PWS
  - Sponsored by FPWR
  - More than 700 families enrolled
  - Completion of several questionnaires online every 6 months, including HQ-CT and PWSP by caregivers of people with PWS
  - PATH for PWS analysis set included subjects who met C601/602 inclusion criteria of age, baseline hyperphagia, weight and caregiver
- The statistical comparison of DCCR data to PATH for PWS was independent of Soleno, conducted by an independent CRO

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C602 Demographics and Baseline Characteristics

Parameter	C601 / C602 N=124	PATH for PWS N=229
Age (years)		
Mean ± SD (N)	13.6 ± 6.94 (124)	17.9 ± 9.49 (229)
Sex		
Female	55.6% (69/124)	52.0% (119/229)
Male	44.4% (55/124)	48.0% (110/229)
Weight (kg)		
Mean ± SD (N)	62.3 ± 30.18 (124)	66.7 ± 26.72 (229)
BMI (kg/m^2)		
Mean ± SD (N)	27.6 ± 9.65 (124)	28.9 ± 9.76 (212)
HQ-CT (Baseline)		
Mean ± SD (N)	21.6 ± 6.67 (123)	18.2 ± 4.99 (229)

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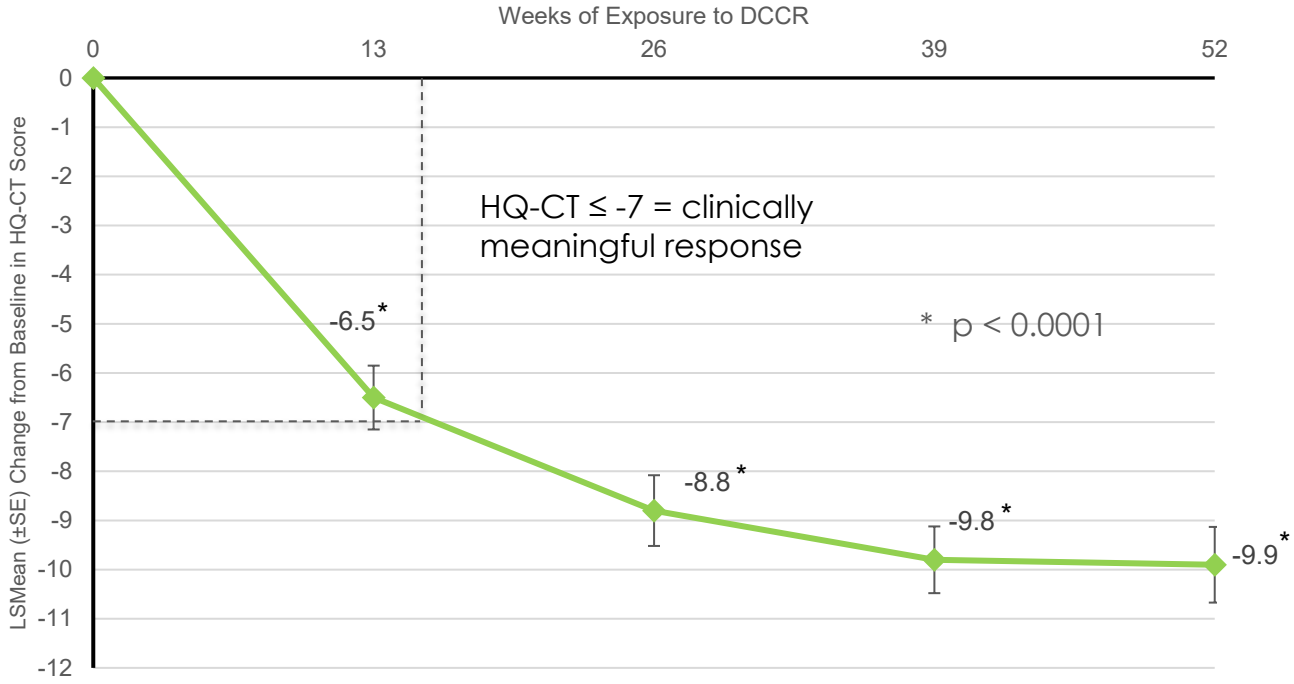
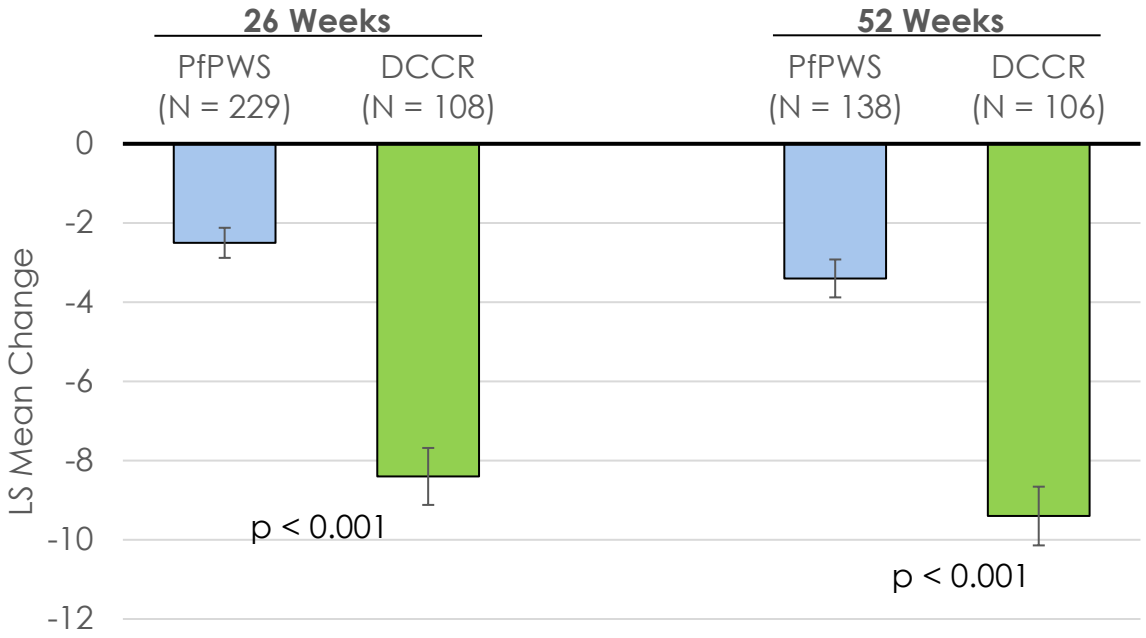
DCCR Hyperphagia Change from Baseline



Change in Hyperhagia with DCCR Compared to PfPWS



PWS Profile Behavioral Change Results after One Year of DCCR

Domain	P-value
Aggressive Behaviors	<0.0001
Aggressive Destructive subfactor	< 0.0001
Anxiety	<0.0001
Compulsivity	<0.0001
Depression	<0.0001
Disordered Thinking	<0.0001
Rigidity Irritability	<0.0001

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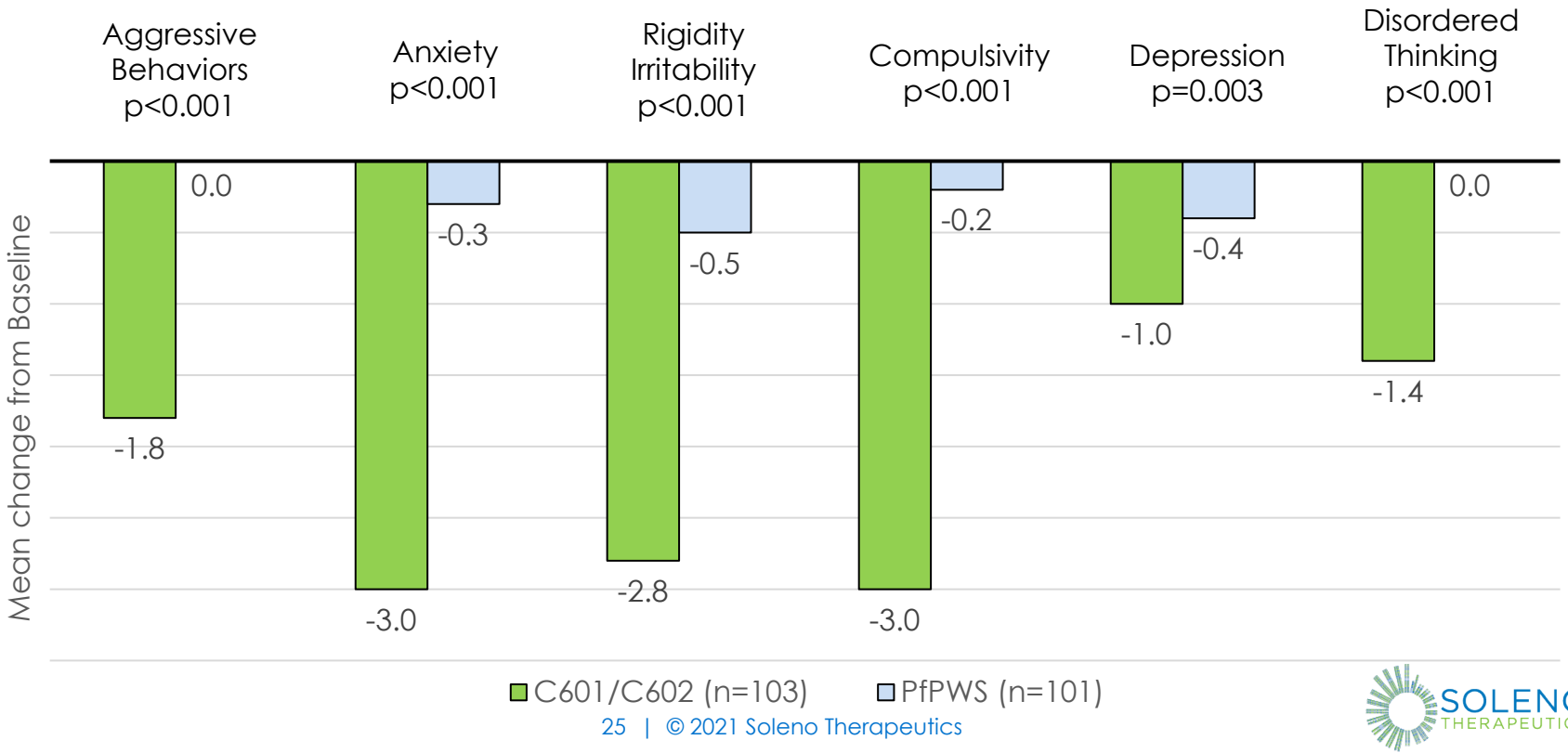
Comparison to PfPWS – Change from Baseline at Week 52



Endocrine and Hormonal Parameters After One-Year of DCCR

Parameter	p-value
Decreased Leptin (pg/mL)	**<0.0001**
Increased Adiponectin (ng/mL)	**<0.0001**
Decreased Fasting Insulin (µIU/mL)	**0.0004**
Decreased HOMA-IR	**0.0033**

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DCCR Safety Profile

- ~100 patients treated for more than one year
- 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

Highlights of Data Through C602 One-Year of DCCR

- Consistent results with highly statistically significant improvement across all behavioral and key endocrine and hormonal measures after receiving DCCR for one year
  - Hyperphagia and PWS behaviors significantly improved compared with Path for PWS
- Safety profile remains as expected and consistent with prior experience with DCCR and diazoxide

DCCR Status

- As a result of DESTNY PWS (C601) not meeting its primary endpoint in the overall analysis, FDA has stated that additional controlled data are necessary to support an NDA submission

- As a result of ongoing dialogue with the FDA they agreed to review 1-year C602 data and comparison to natural history to assess if the data may suffice for 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 and PWSA USA jointly initiated and submitted a petition to FDA Leadership requesting regulatory flexibility and review of an NDA for DCCR when submitted
    - Signed by 26,640 supporters
- "Town Halls" organized by families to discuss personal experiences with DCCR during studies C601 and C602

Financial Highlights

- Cash balance at end of Q2 2021 $33.6M
- No Debt

- Common shares outstanding at end of Q2 2021 79.8M
- Fully Diluted shares at end of Q2 2021 87.1M

➢ Company has continued to invest in CMC and other programs necessary for potential submission of an NDA

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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)

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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

* Orphan designation granted for diazoxide choline in 2021

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Key Takeaways

- PWS is a rare disease, US estimated prevalence of 10,000 – 20,000 people
- DCCR is focused on treating the highest unmet needs of PWS for which no approved treatments exist
- Phase 3 program through 1 year of receiving DCCR supports the long-term efficacy and safety of DCCR
- Once a day tablet formulation with strong potential for 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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