Corporate Presentation

February 2021 | Soleno Therapeutics

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You should also read carefully the factors described in the "Risk Factors" sections and other parts of our Annual Report on Form 10-K and Quarterly Report on Form 10-Q, available at www.sec.gov, in order to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation or to reflect the occurrence of unanticipated events.

SOLENO THERAPEUTICS

Soleno Therapeutics (NASDAQ: SLNO)

Strategic Highlights

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

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 designation in the US and EU. Fast Track granted

Significant upside potential in other indications

Addresses hallmark symptoms of PWS

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

Financed Phase III Program

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

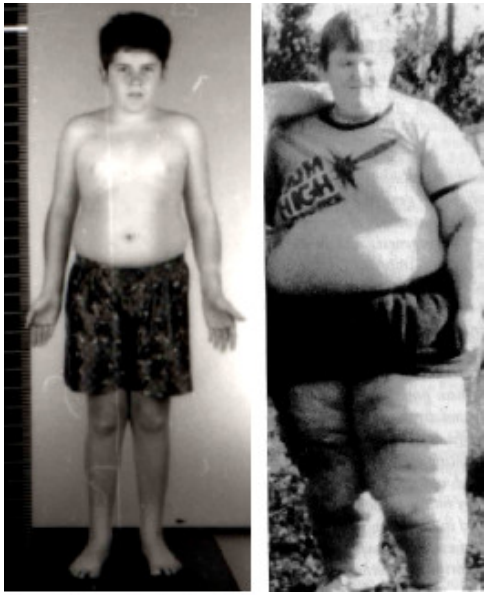
SOLENO THERAPEUTICS

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
  - Increases in lean body mass/reductions in fat mass
  - PWS-related behaviors
- PWS families have low QOL
  - 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 III program in PWS

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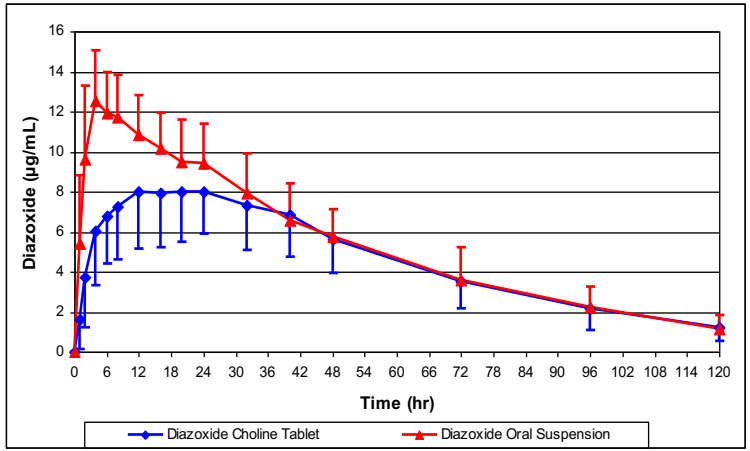
Diazoxide is Not Approved for Use in PWS

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

DCCR Proposed Mechanism of Action

Appetite controlled by 2 sets of neurons in the hypothalamus

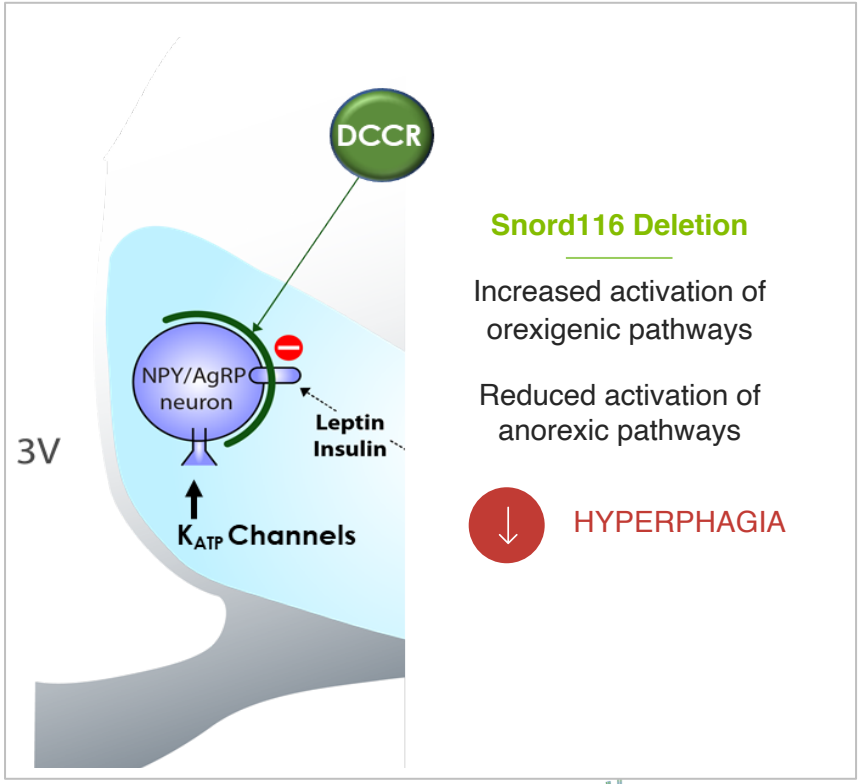
- NPY/AgRP: secrete NPY and AgRP, appetite stimulatory neuropeptides
- POMC: secretes POMC, an appetite suppressive neuropeptide

NPY expression is elevated in PWS

- Loss of SNORD116 in the PWS critical region on chromosome 15 leads to NPY overexpression
- Elevations in NPY drive hyperphagia

DCCR agonizes K_{ATP} channels in NPY/AgRP neurons

- Reduces secretion of NPY and AgRP, thereby reducing hyperphagia



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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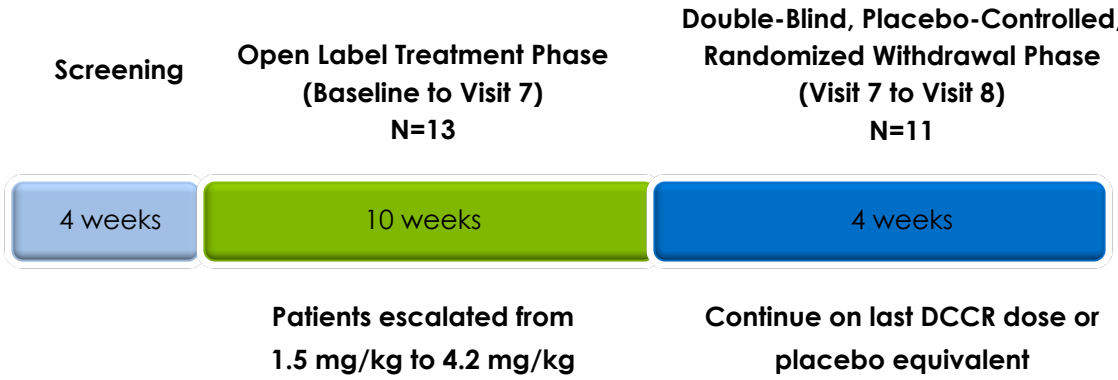
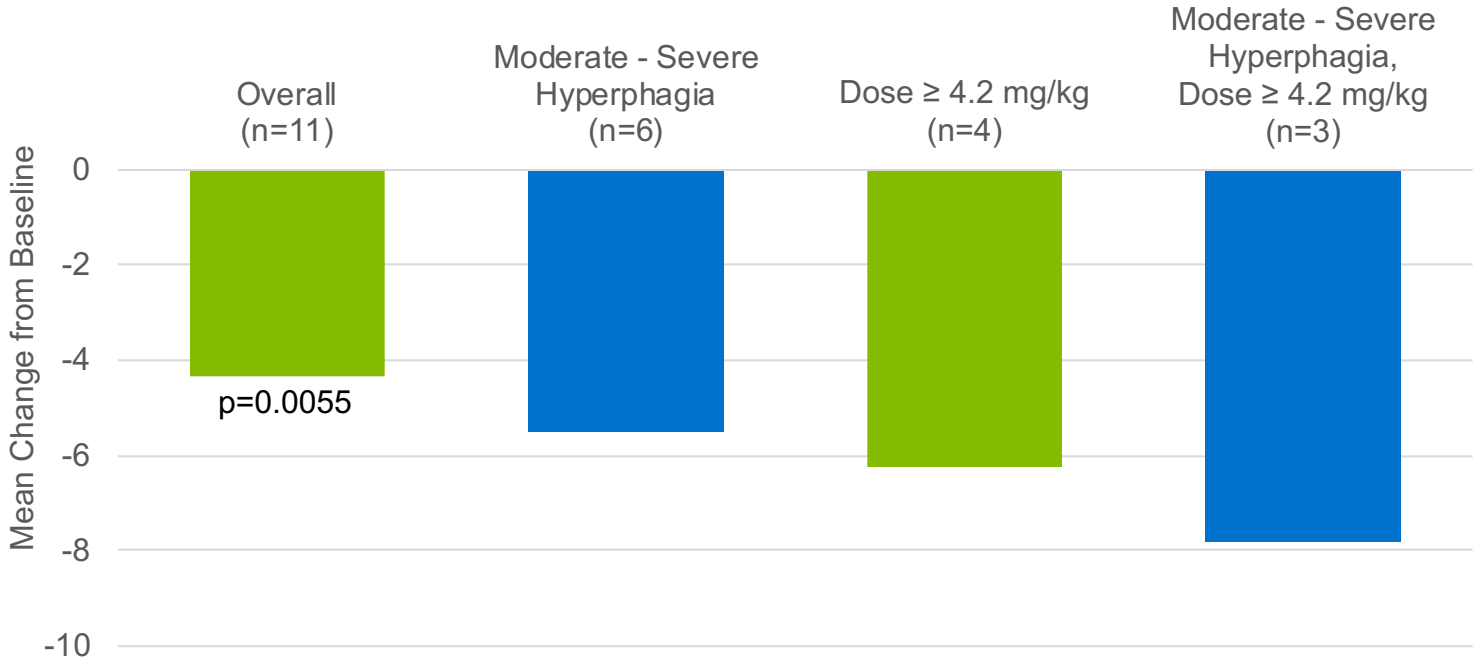
DCCR Pilot Study in PWS

- 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



Hyperphagia Response During Open-Label Treatment

Greater at Highest Dose and Moderate-Severe Hyperphagia



PLoS One. 2019 Sep 23;14(9):e0221615

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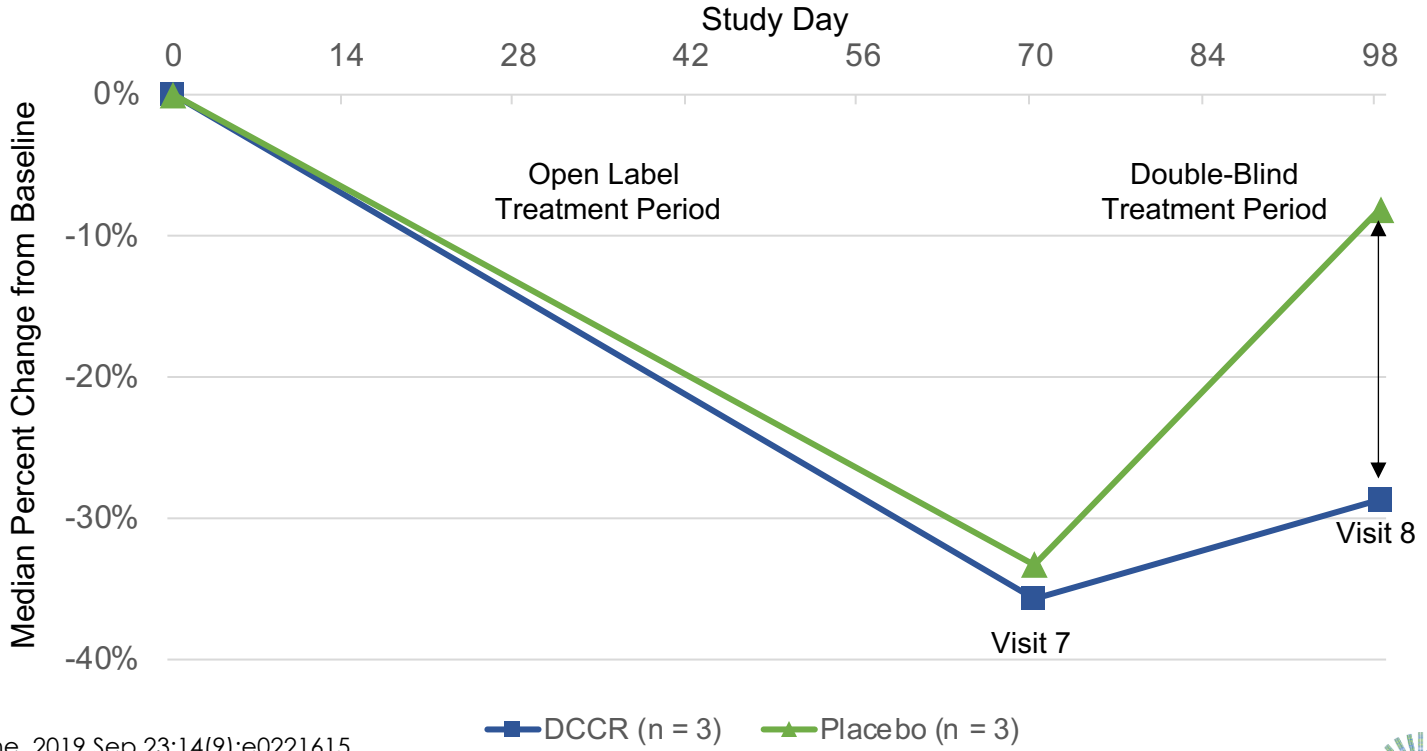
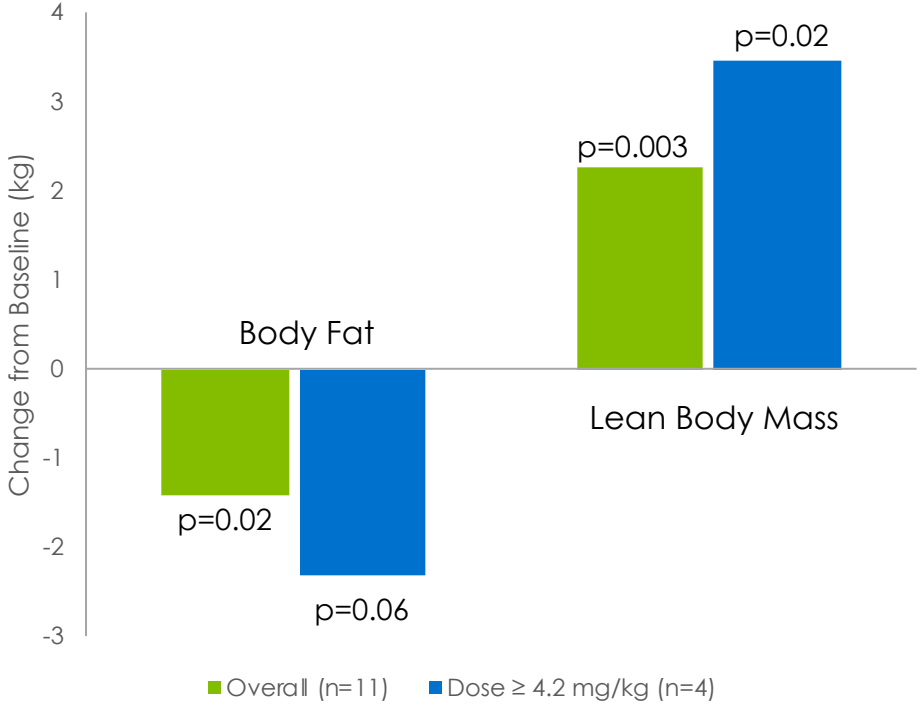
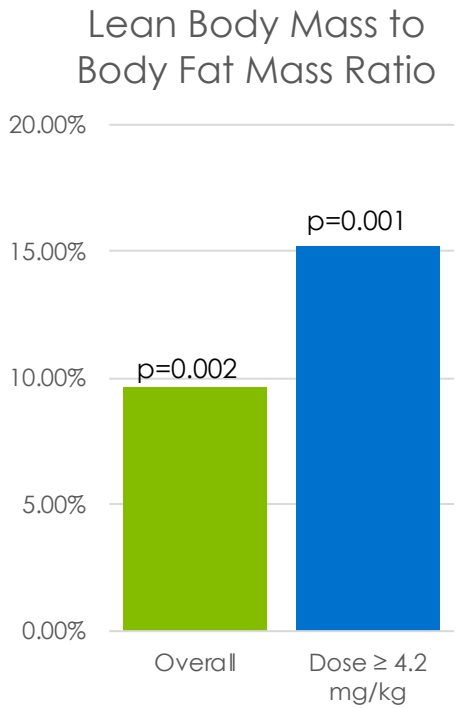
PC025: Changes in Hyperphagia in Subjects with Moderate to Severe Hyperphagia at Baseline



PLoS One. 2019 Sep 23;14(9):e0221615

PC025: DCCR Impact on Body Fat and Lean Body Mass

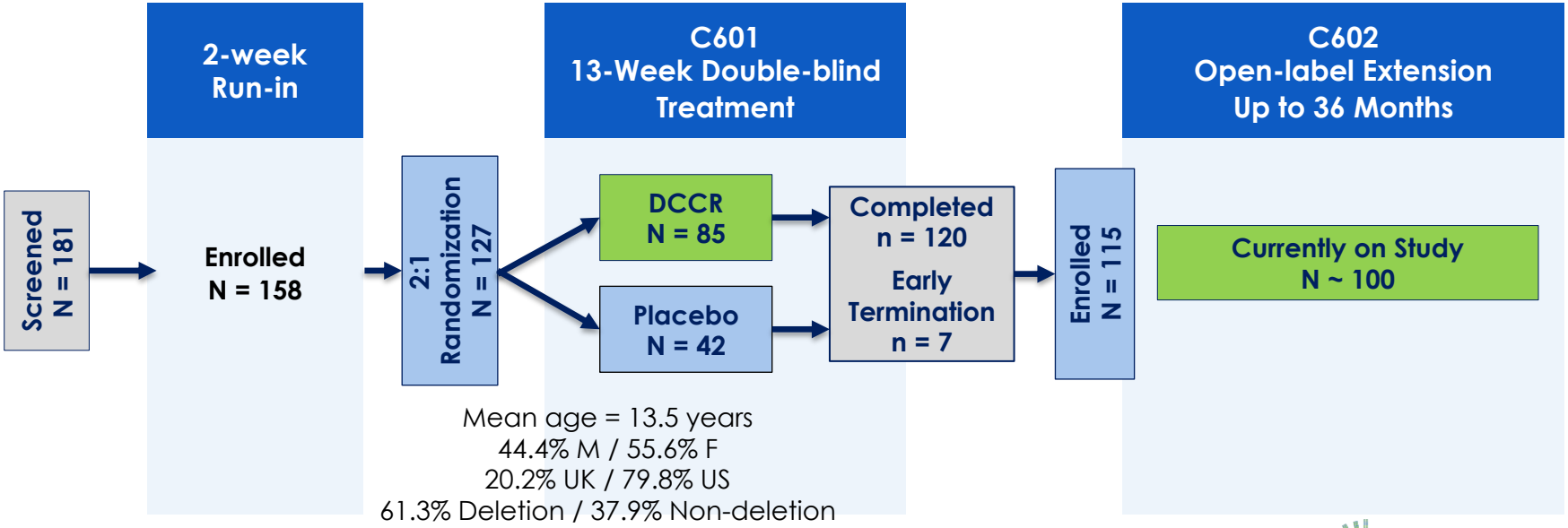




PLoS One. 2019 Sep 23;14(9):e0221615

Phase III Program Design

- C601 (DESTINY PWS): Multi-center, randomized, double-blind, placebo-controlled, parallel arm study in patients with PWS (Phase III)
- 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	

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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 conditions[3]
  - FPWR Global Registry COVID Pandemic Impact survey[4]
- 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, 2020(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.

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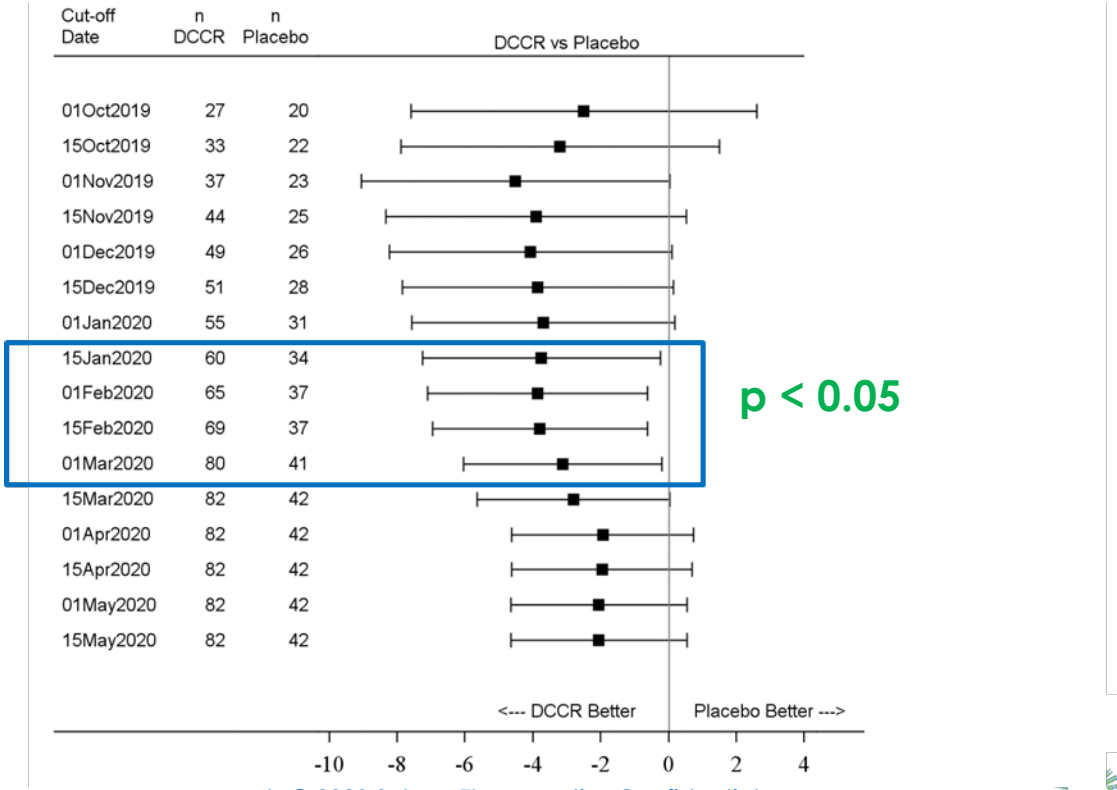
C601 HQ-CT Changes in HQ-CT by Cut-off Date



p < 0.05

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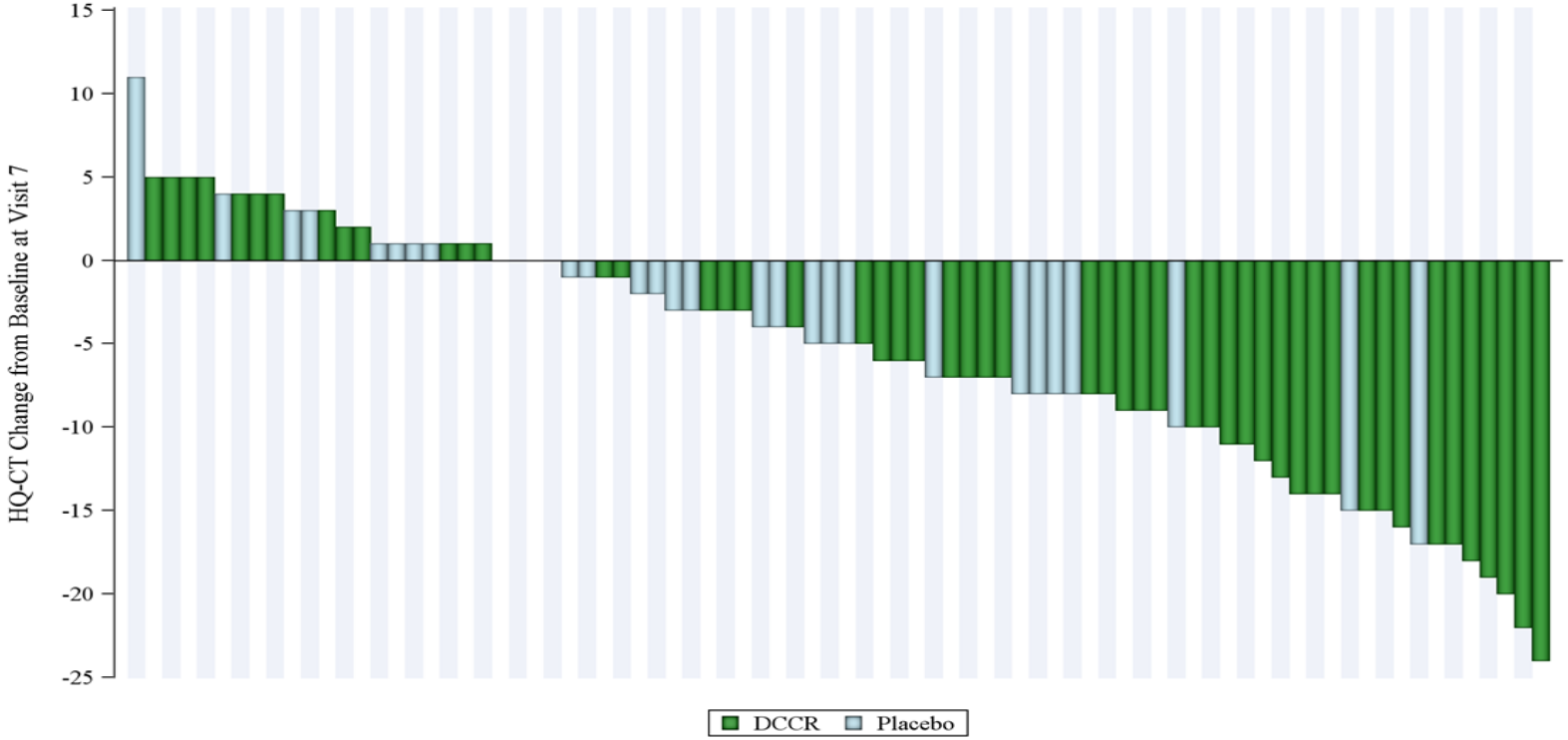
HQ-CT Changes from Baseline Waterfall Plot through March 1, 2020



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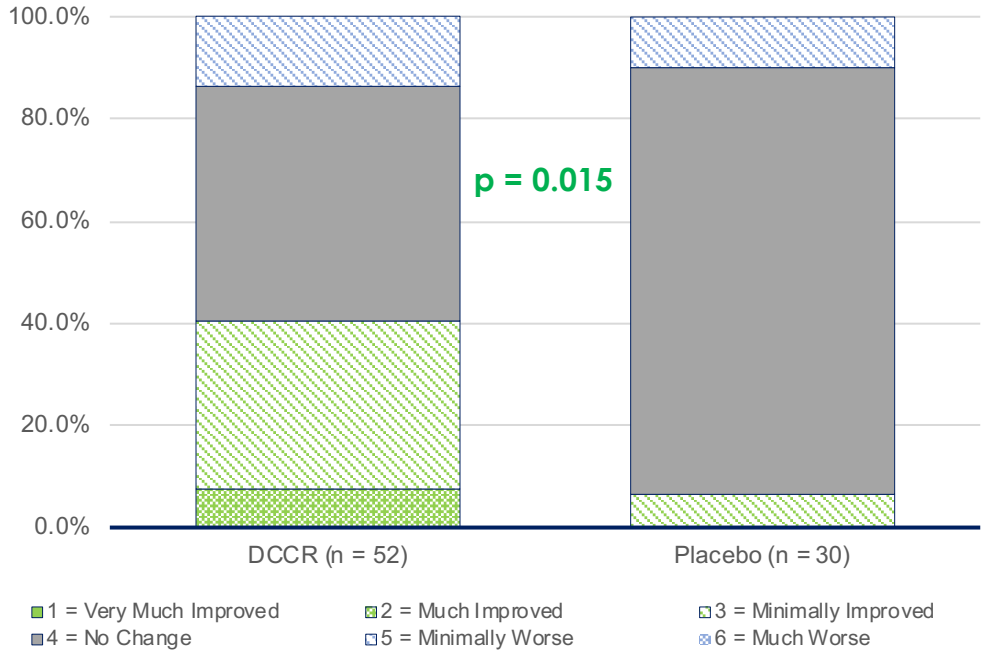
C601 Key Secondary Endpoint: CGI-I



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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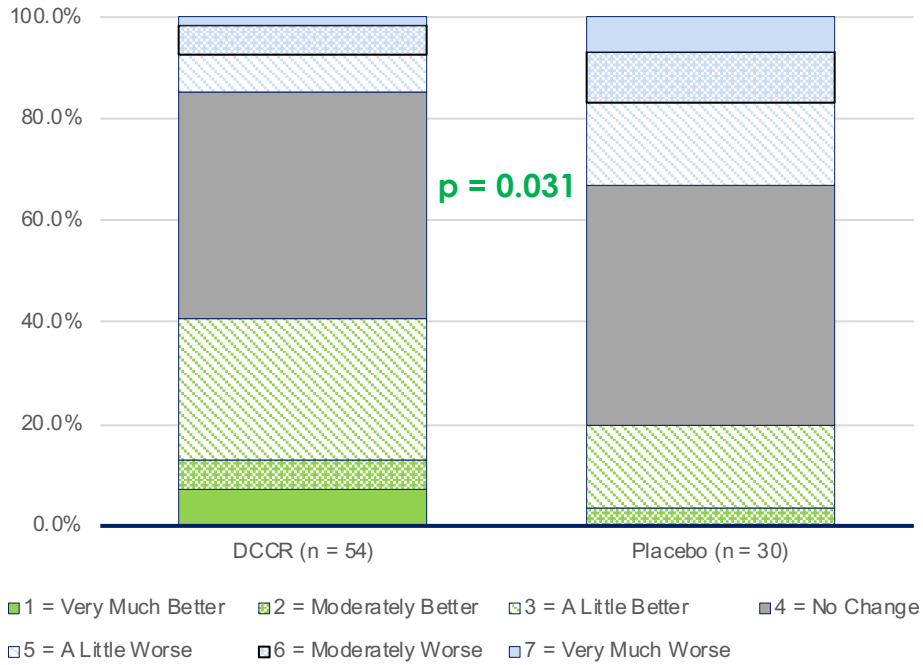
C601 Key Secondary Endpoint: Caregiver GI-C



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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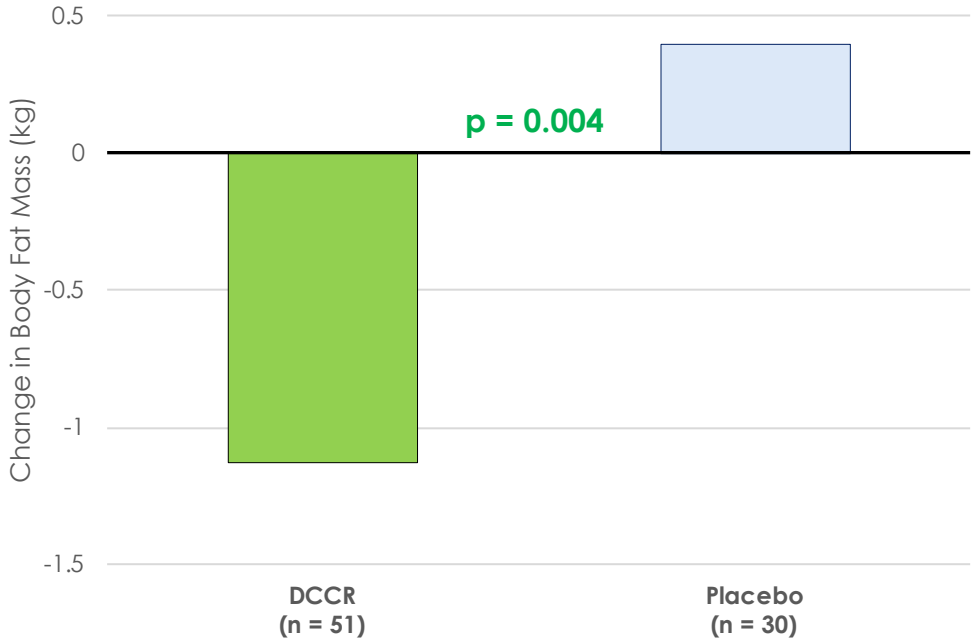
C601 Key Secondary Endpoint: Body Fat Mass



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

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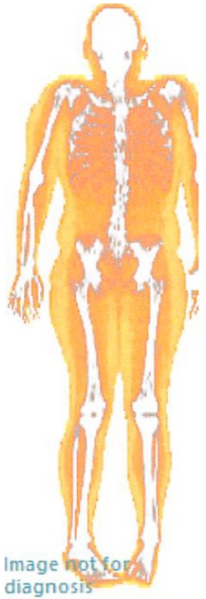
Body Composition Changes

C601 Baseline	Body Composition Parameter	After 12 months Open-label DCCR
121.28 kg	Total Mass (kg)	94.72
62.26 kg	Fat Mass (kg)	31.69
55.93 (kg)	Lean Mass (kg)	59.63
52.7% (kg)	Percent Body Fat	34.7%



Courtesy: Jennifer Miller, MD U Florida

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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**

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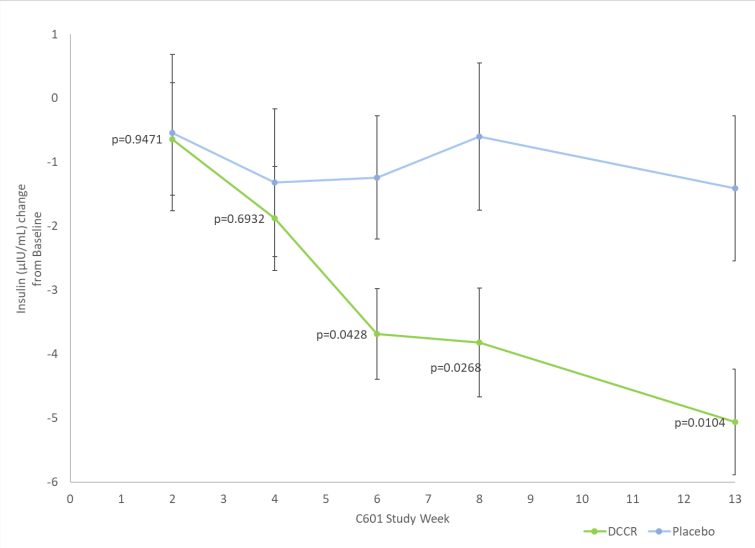
DCCR: Changes in Cardiometabolic Markers

Insulin
Change from Baseline



Change from Baseline to Visit 7 (through March 1, 2020)	DCCR vs Placebo p-value
Decreased Acylated Ghrelin (active form)	**0.009**
Decreased Leptin	**<0.0001**
Increased Adiponectin	**<0.0001**

Source: Soleno Therapeutics Preliminary Analysis

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Conclusions

- Clear impact of COVID pandemic on the caregivers and subjects in DESTINY PWS
- Primary, subjective key secondary, and several other efficacy variables 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

Courtesy: Jennifer Miller, MD U Florida

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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

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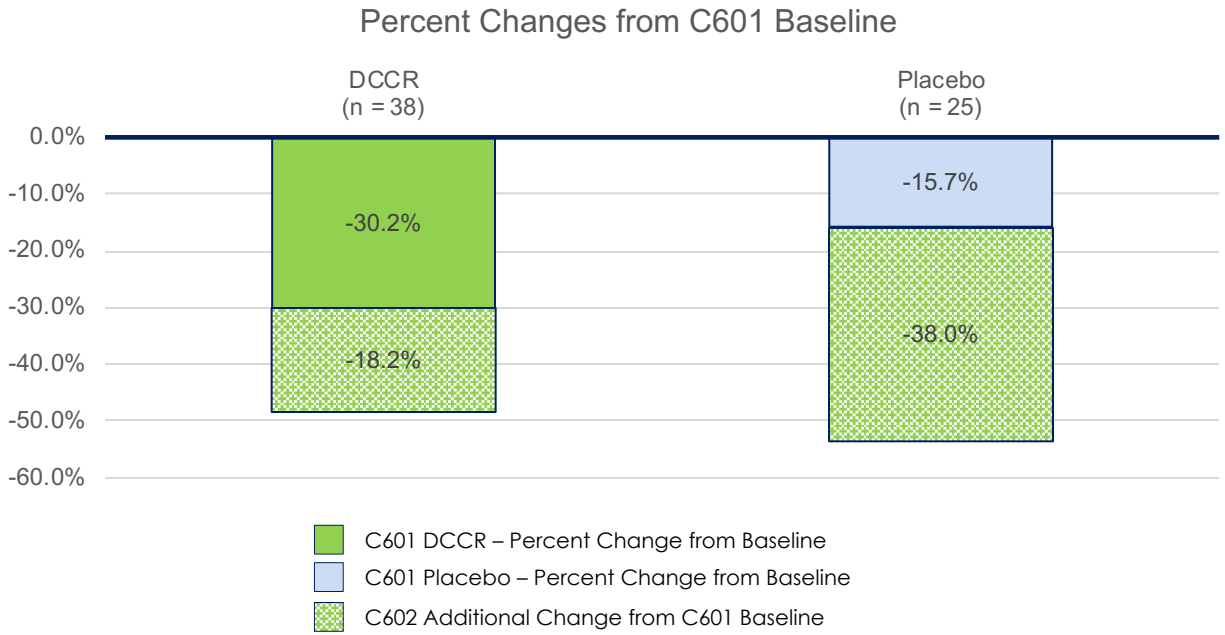
Changes in HQ-CT from C601 Baseline at Visit 7 and Further Changes in C602



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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 were reported in this study
- There were no serious unexpected adverse events (SUSARs) related to DCCR

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Next Steps

- Met with FDA Nov 2020, minutes issued Dec 2020
  - Discussed potential adequacy of data from completed and ongoing studies
  - Agreed to review plans for additional analyses, including comparisons 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
- Potential NDA submission in 2H 2021

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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

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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 DCCR drug active, drug product, method of manufacture in 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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Financial Highlights

- Cash balance at end of Q3 2020 $56.1M
- No Debt

- Closed Public Offering June 26th, 2020 $57.5M
- Common shares outstanding at end of Q3 2020 79.6M
- Fully Diluted shares at end of Q3 2020 89.9M

Spending remains consistent with previously discussed plans

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Key takeaways for creating shareholder value

- 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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Financed Phase III Program

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

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