Corporate Presentation

January 2019 | Soleno Therapeutics

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SOLENO THERAPEUTICS

Investment Highlights

Orphan asset in Phase III Study

In Phase III for Prader-Willi Syndrome. Fast Track granted.

Significant commercial potential in PWS, an orphan indication with high unmet need. No approved treatments for hyperphagia, the key symptom of PWS

IP protection to 2035 and beyond

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 granted

Orphan designation in the US and EU

Significant upside potential in other indications

Compelling product profile

Addresses hallmark symptoms of PWS

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

Financed by leading healthcare investors

Closed on $16.5 million financing December 2018

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

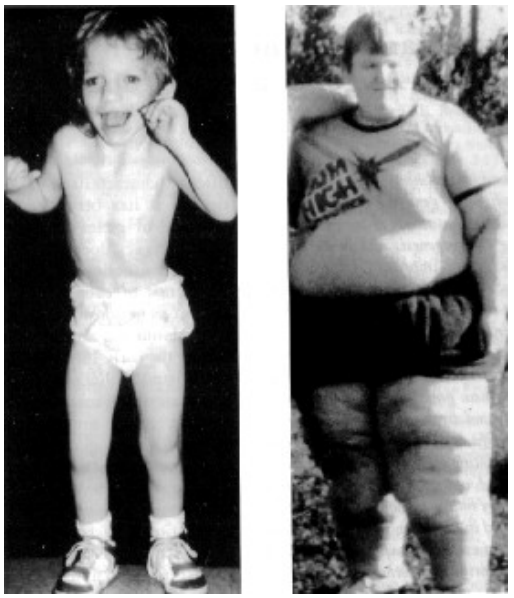
SOLENO THERAPEUTICS

Leadership Team

- Anish Bhatnagar, M.D.
  Chief Executive Officer
- Jonathan Wolter
  Chief Financial Officer
- Neil M. Cowen, Ph.D.
  Senior VP, Drug Development
- Kristen Yen, M.S.
  VP of Clinical Operations
- Patricia C. Hirano, M.P.H.
  VP of 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
- Incidence in the general population 1:12,000-1:15,000 individuals
- Elevated mortality rates
- Highest unmet needs
  - Hyperphagia
  - Aggressive behaviors
  - Increases in lean body mass/reductions in fat mass
- PWS families have low QOL
  - Normal siblings show high rates of post traumatic stress syndrome



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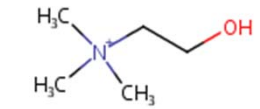
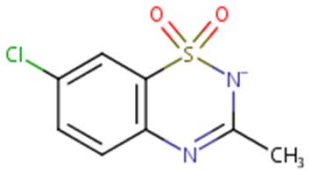
Diazoxide – Long History of Safe Use
DCCR – Extensive Pre-Clinical and Clinical Data

- Diazoxide I.V., Oral suspension and Capsule
  - K_{ATP} channel agonist approved in 1976
  - Previously used as IV treatment for malignant hypertension
  - BID/TID oral suspension for the treatment of hypoglycemia due to hyperinsulinism in infants, children and adults
- DCCR (diazoxide choline) Extended Release Tablets
  - QD tablet formulation of choline salt of diazoxide
  - Characterized in 5 Phase I and 3 Phase II studies in obese, dyslipidemic and PWS subjects
  - More than 210 treated subjects
  - Protected by multiple issued patents, including composition of matter

Diazoxide Choline





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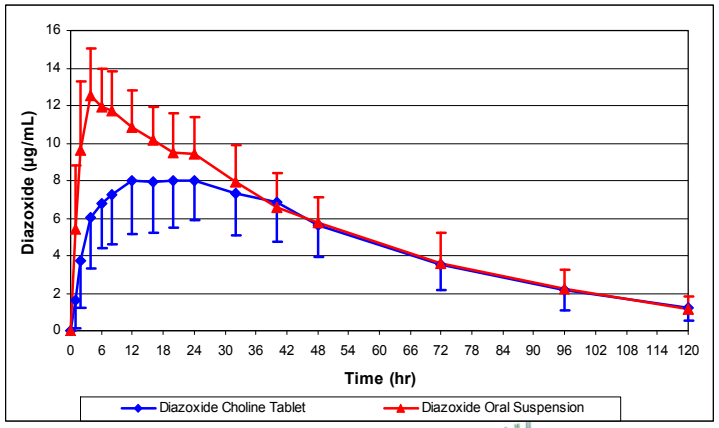
Proglycem

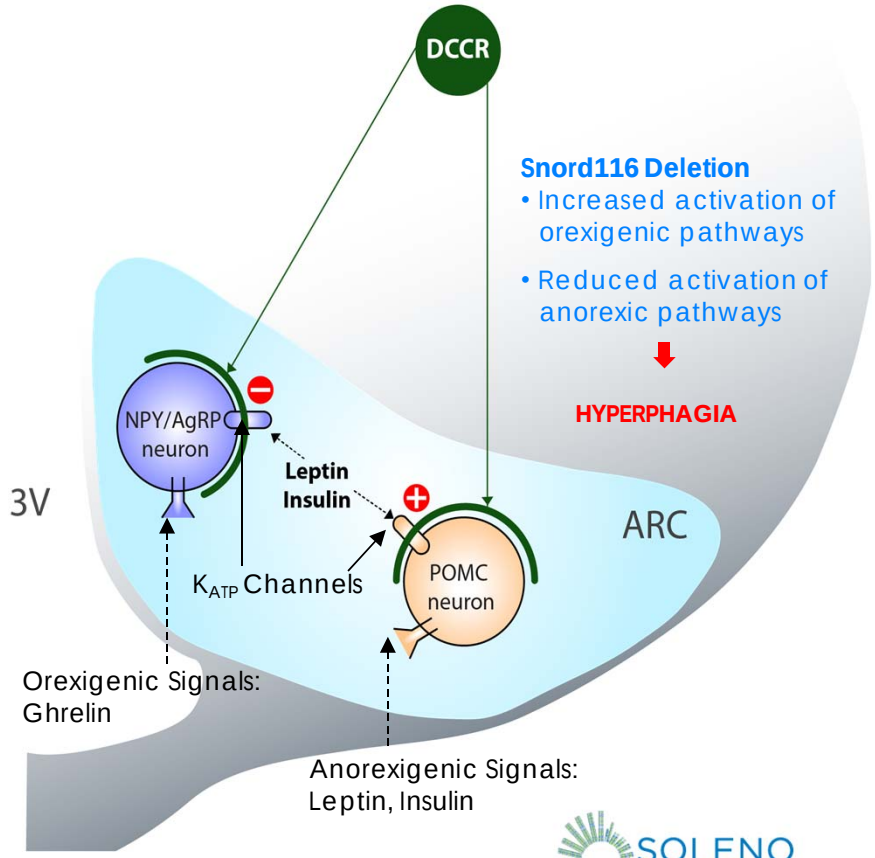
Challenges in the Treatment of PWS

- Proglycem has not been approved for use in PWS
  - Use in PWS blocked by issued Soleno patent claims
- Proglycem product is a TID/BID oral suspension with a long bitter aftertaste
  - There are challenges with the uniformity of dosing with the oral suspension
  - Rapid absorption leads to high Cmax
    - Rapid protein binding of diazoxide
    - Several of the most common adverse events are Cmax-associated
- DCCR allows for slow release of diazoxide over 24 hours, and ensures stable levels of free diazoxide
- DCCR will be more convenient, and potentially safer than Proglycem
  - To facilitate independence and better compliance, QD dosing is critical



DCCR Proposed Mechanism of Action

- Appetite controlled by 2 sets of neurons in the hypothalamus that express K_{ATP} channels
  - NPY/AgRP – secrete NPY and AgRP, appetite stimulatory neuropeptides
  - POMC – secretes POMC, an appetite suppressive neuropeptide
  - Elevations in NPY drive hyperphagia
- NPY expression is elevated in PWS
  - Loss of SNORD116 in the PWS critical region on chromosome 15 results in 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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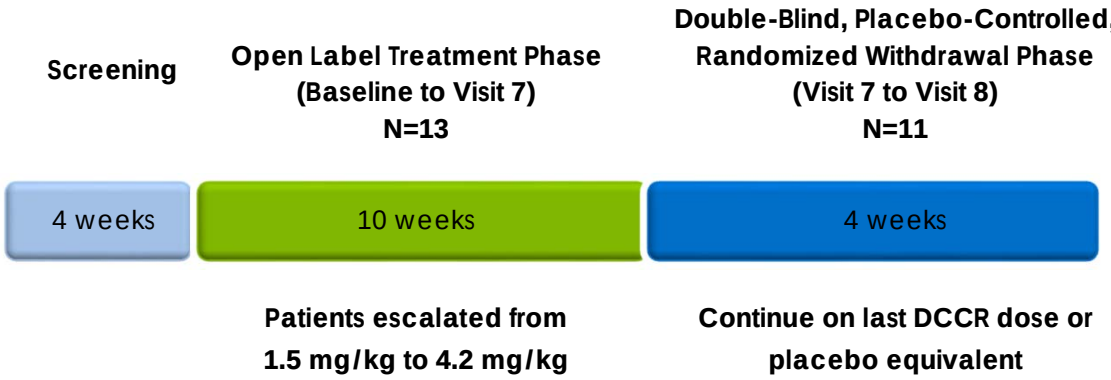
PC025 Pilot Study in PWS

- Randomized, Withdrawal, Single-Center Study of DCCR in overweight or 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

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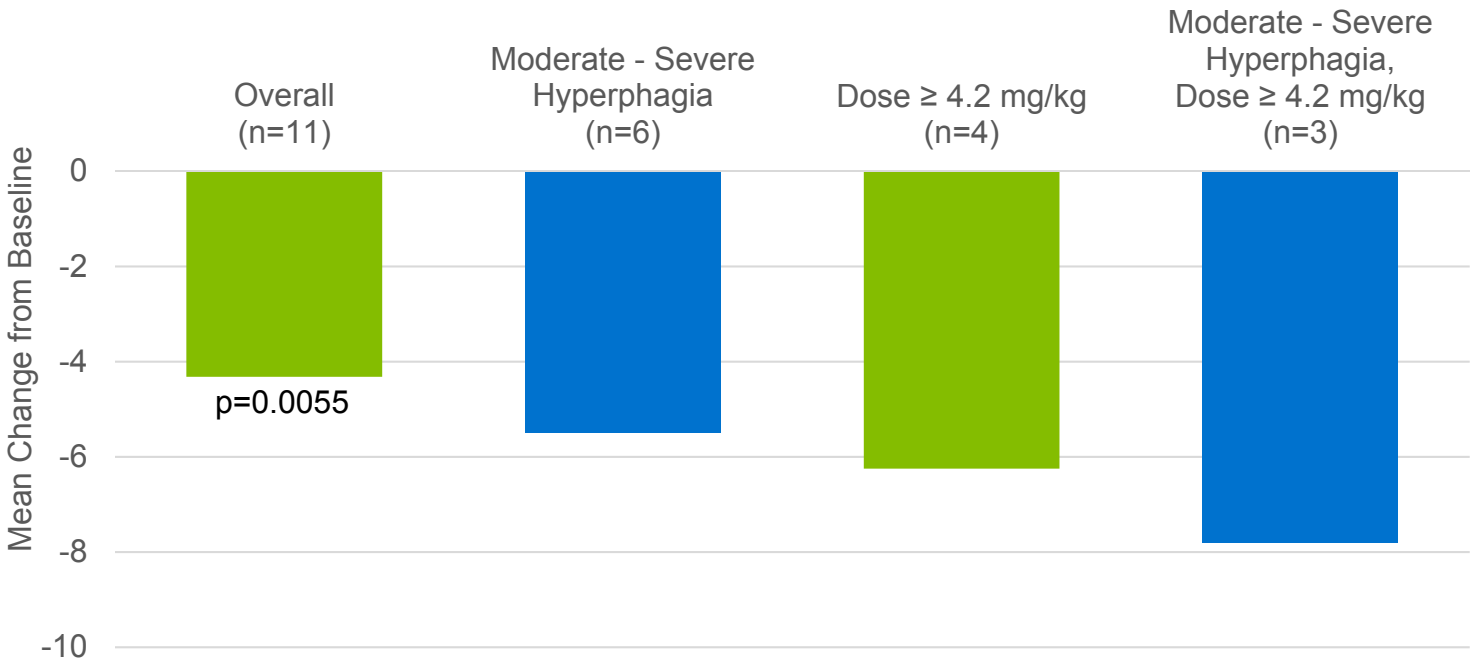
Hyperphagia Response During Open-Label Treatment

Greater at Highest Dose and Moderate-Severe Hyperphagia



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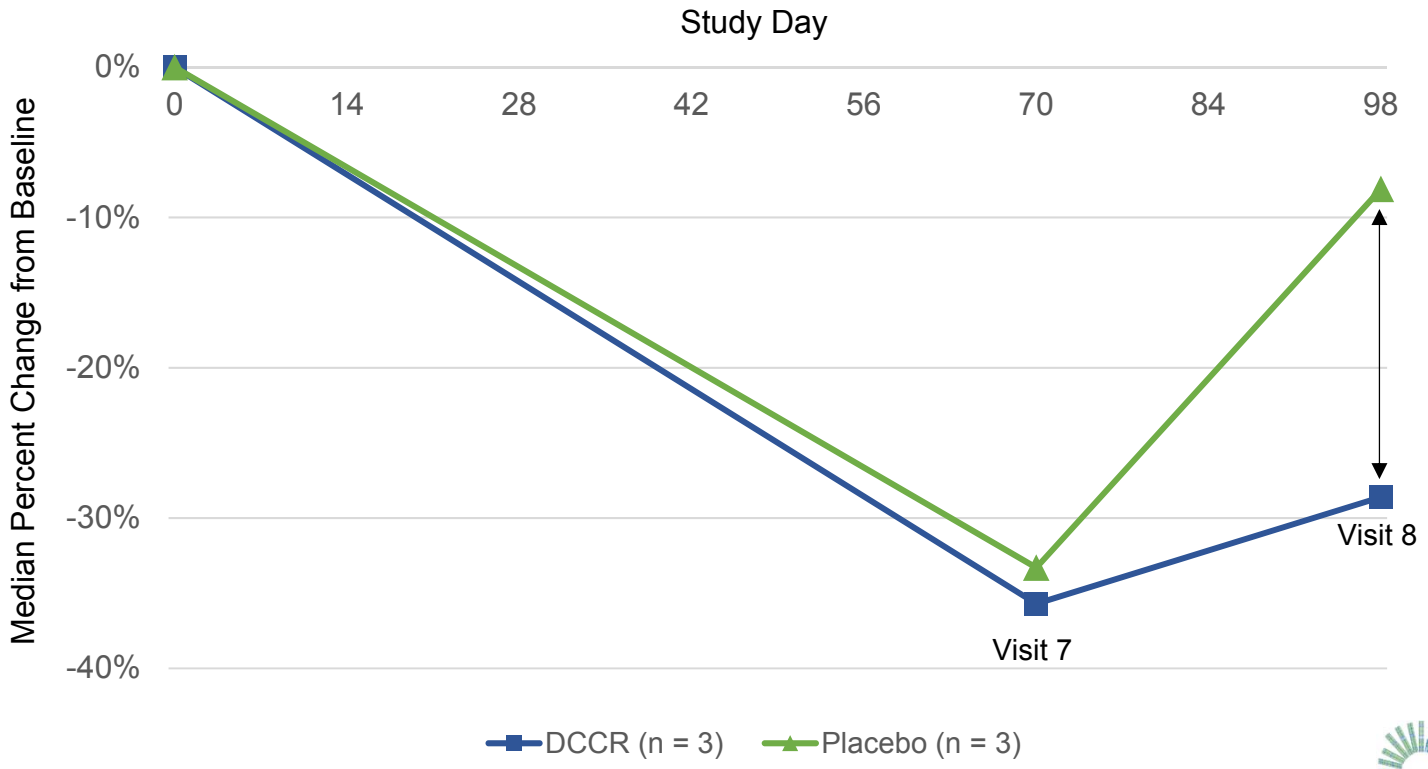
Placebo Reverses DCCR Treatment Effect

Patients with Moderate-Severe Hyperphagia



Hyperphagia Questionnaires

Comparison of HQ-CT to Modified Dykens Used in PC025

	Question
Both versions	How upset did the person generally become when denied a desired food?
	How often did the person try to bargain or manipulate to get more food at meals?
	How often did the person forage through trash for food?
	How often did the person get up at night to food seek?
	How persistent was the person in asking or looking for food after being told “no” or “no more”?
	How often did the person try to sneak or steal food (that you are aware of)?
HQ-CT	Outside of normal meal times, how much time did the person generally spend asking or talking about food?
	When others tried to stop the person from asking about food, how distressed did he or she generally appear?
	How often did food-related behavior interfere with the person’s normal daily activities, such as self-care, recreation, school, or work?
PC025	Once your child has food on their mind, how easy is it for you or others to re-direct your child away from food to other things?
	How clever or fast is your child in obtaining food?
	How variable is you child’s preoccupations or interests in food?

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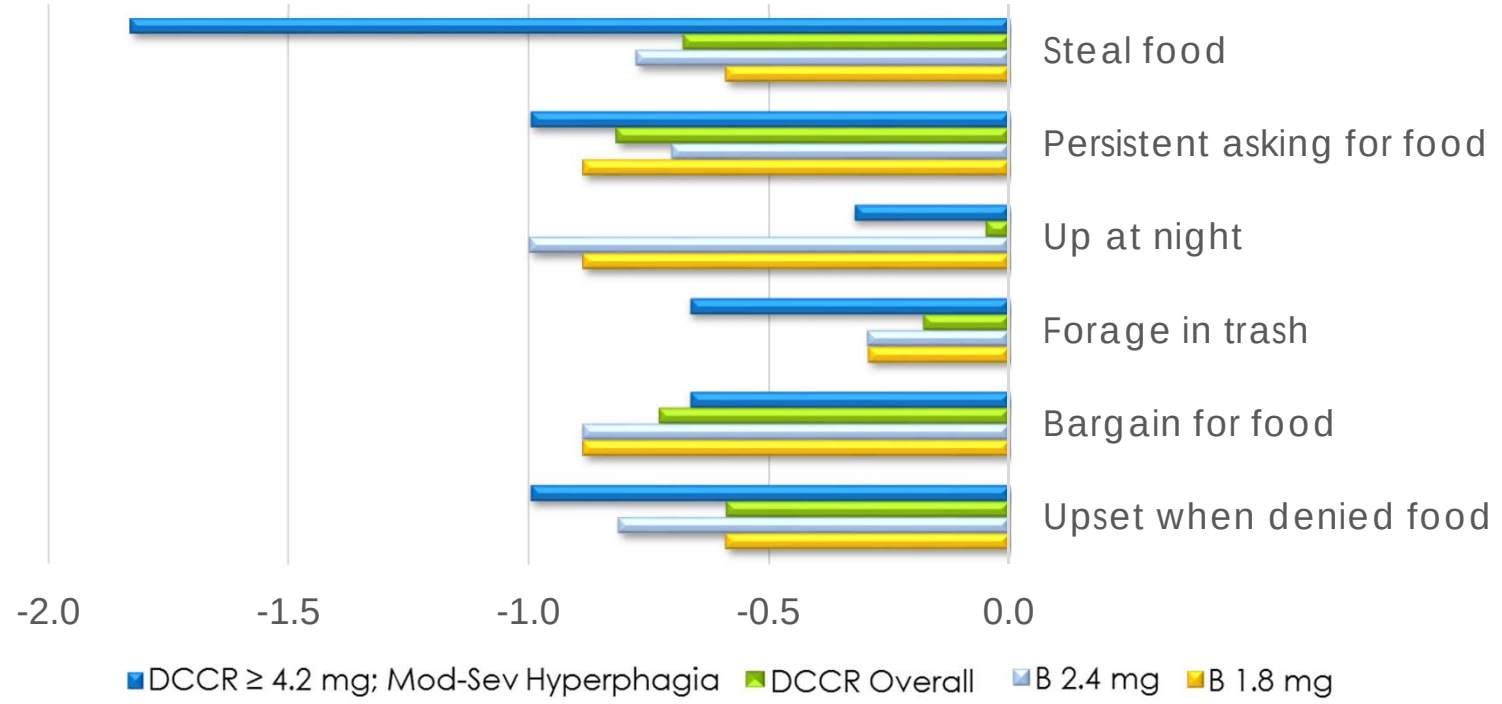
Response to 6 Common Hyperphagia Questions

2 Doses of Beloranib (ZAF-311) and DCCR (PC025)



Approximate comparison based on Figure 2a (Diabetes Obes Metab. 2017 May 29. doi: 10.1111/ dom.13021) for beloranib and actual DCCR data (PC025 mean change from baseline-Visit 7)

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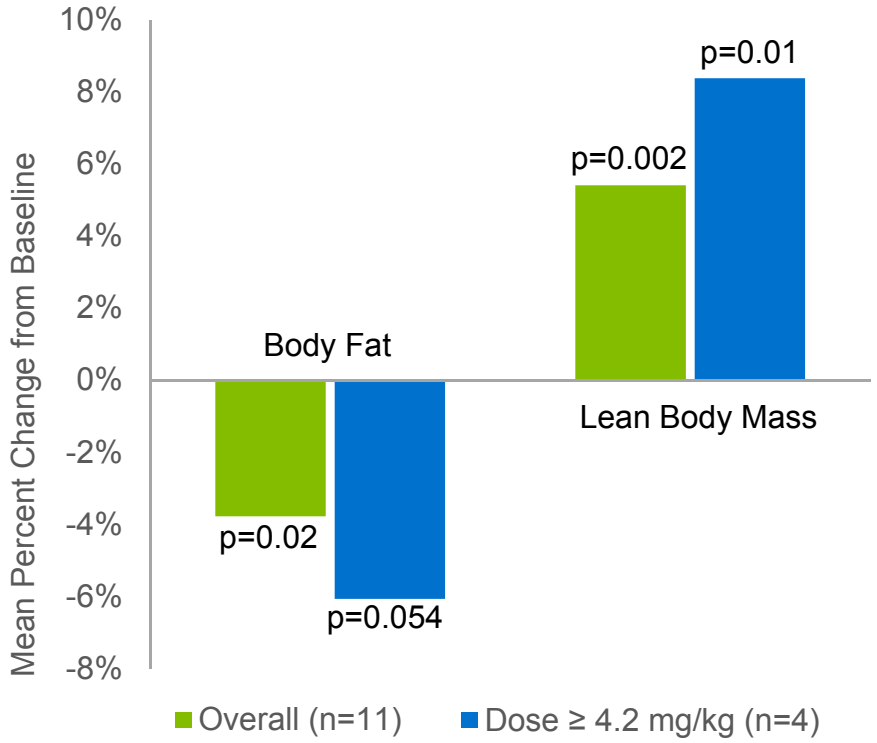
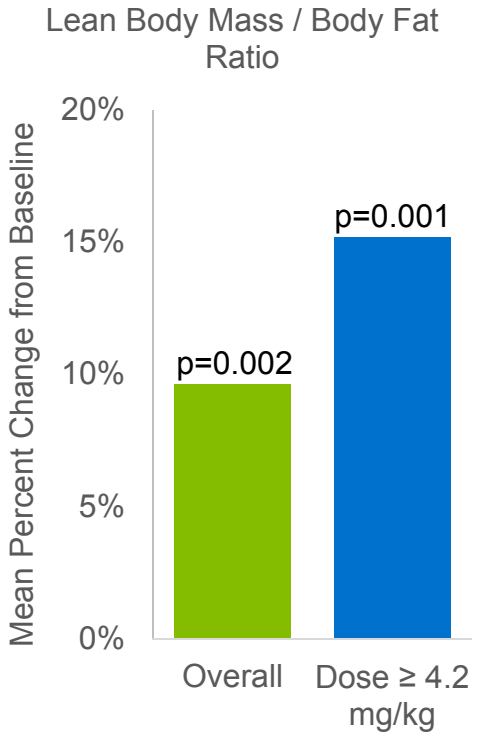
DCCR Impacts Body Fat and Lean Body Mass





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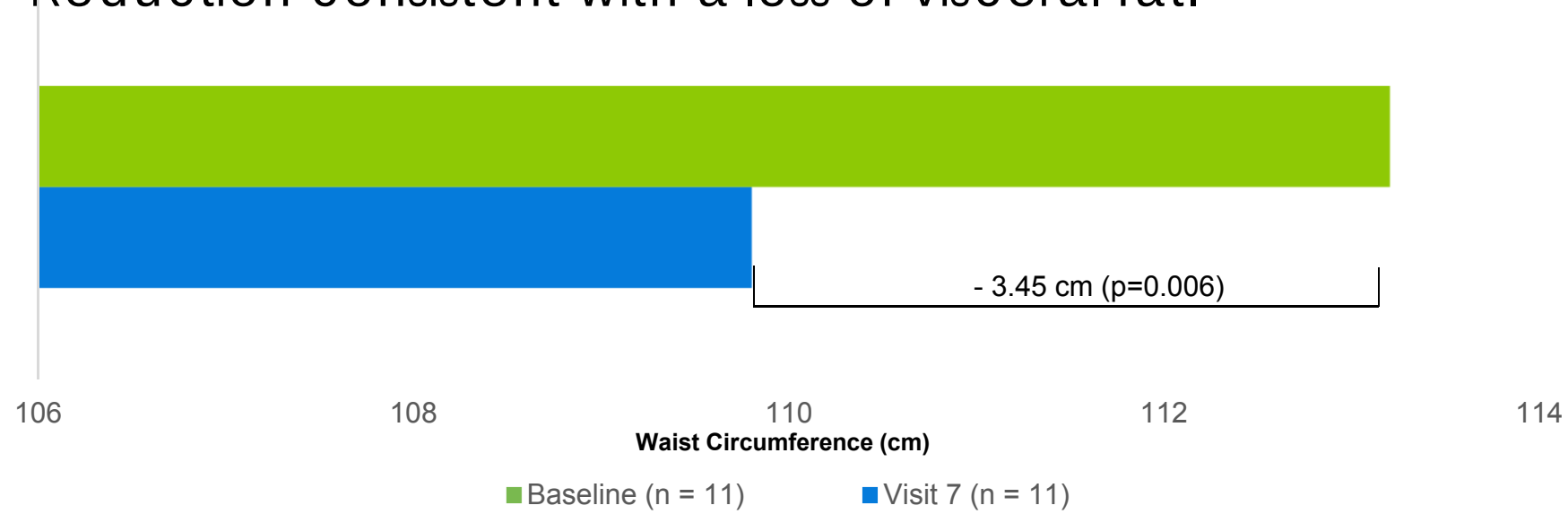
Waist Circumference

Significant Reduction from Baseline-V7

- Reduction consistent with a loss of visceral fat.



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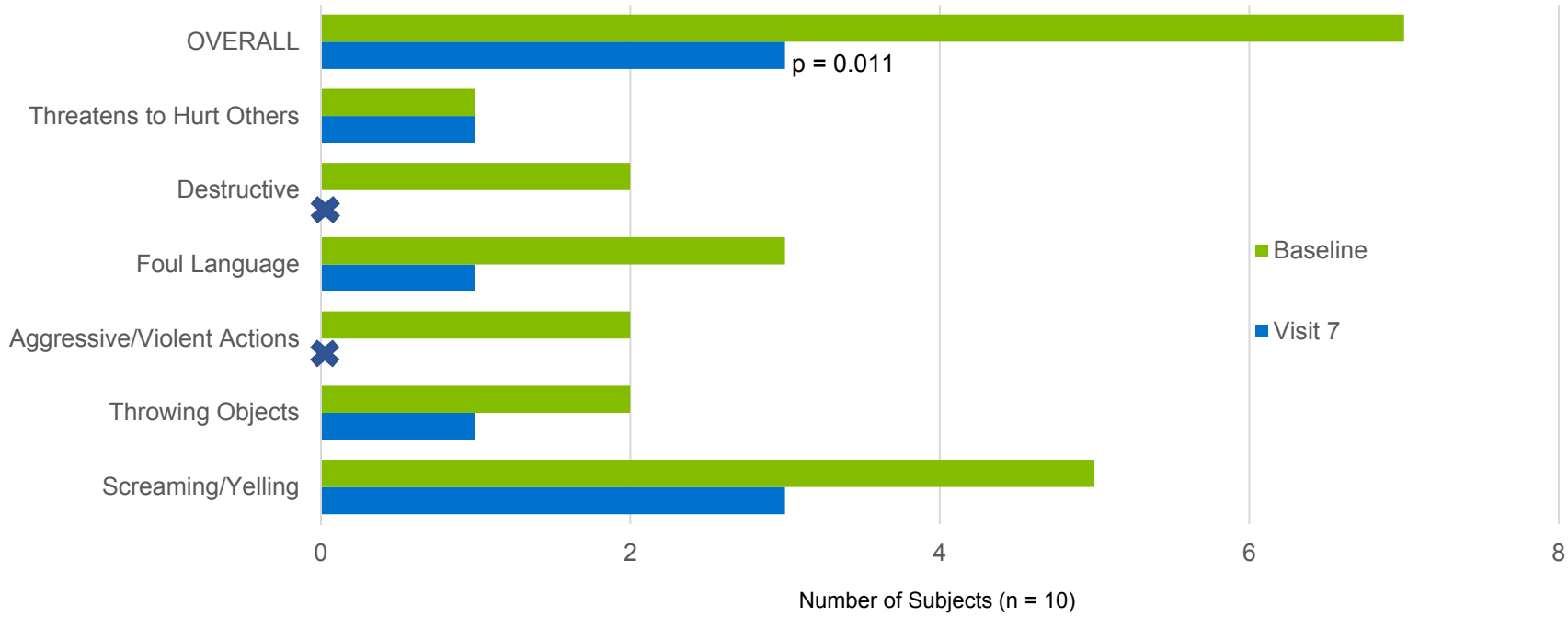
DCCR Reduces Aggressive Behaviors



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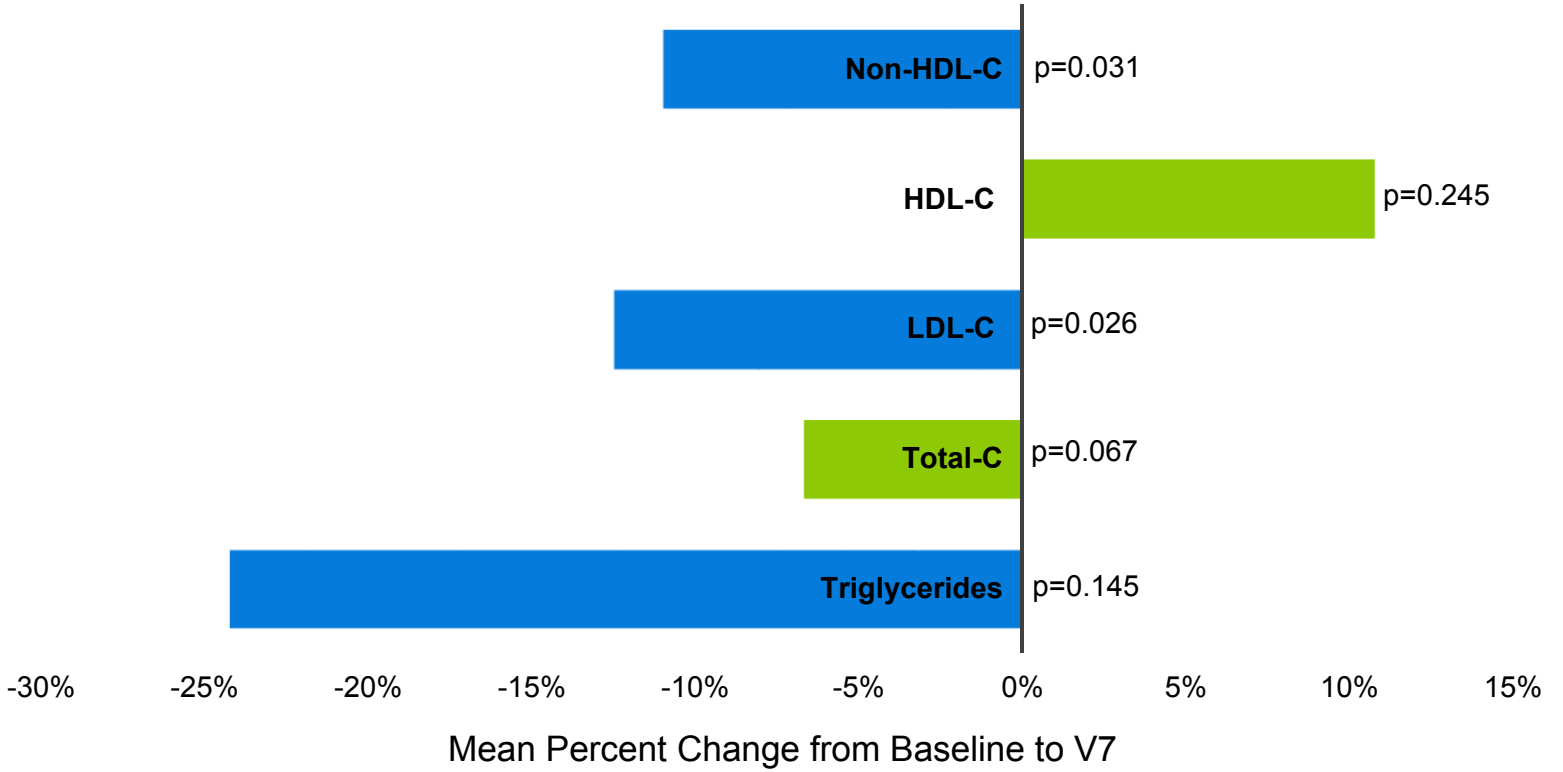
DCCR Impacts CV Risk Factors



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DCCR Safety

Consistent with Long History of Safe Use of Diazoxide

- Safety profile of Proglycem in chronic use is well-known
- In the development of DCCR, there have been no new safety findings
  - Most common adverse events include hyperglycemia and peripheral edema
- Doses of DCCR that will continue in development are at the low end or below the labeled range for Proglycem
- More than 120,000 patient-years of chronic use

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FDA Feedback

- FDA confirmed change in hyperphagia score (without a change in weight) compared to placebo as the primary endpoint for Phase III study
  - HQ-CT is the appropriate instrument to measure hyperphagia
- Dosing paradigm proposed for the Phase III study was acceptable.
- FDA proposed and Soleno agreed that the duration of the randomized double-blind placebo controlled study should be 3 months
- Safety information about DCCR could be obtained in a 9-month long-term, safety extension study
- Patients $\geq$ 4 years eligible to be enrolled regardless of BMI
- There was agreement on several other aspects of the study and the overall development program

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EMA Scientific Advice

- EMA supports change in hyperphagia score compared to placebo as the primary endpoint for the Phase III program
- Single Phase III efficacy study acceptable, with long-term safety data obtained from an extension study
- Treatment of children with hyperphagia acceptable without additional toxicology study(ies)
- Dosing paradigm proposed was acceptable
- There was agreement on several other aspects of the study and on the overall development program

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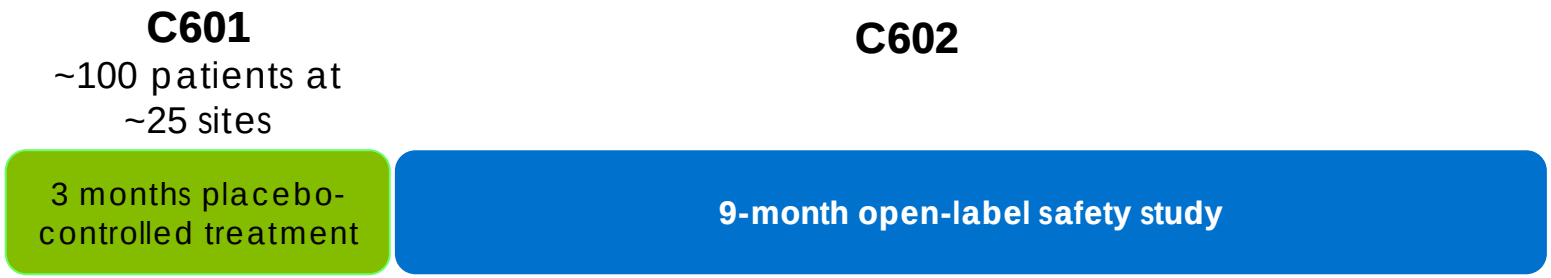
Phase III Program Design

- 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



- Patients will be randomized in a 2:1 ratio to DCCR or placebo
  - Genetically confirmed PWS patients with mod-severe hyperphagia
- Study started in May 2018
- Primary endpoint – change in hyperphagia compared to placebo
- All patients completing C601 are eligible to enroll in C602

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Extensive IP Protection

- Composition of matter protection (potential for extension to 2034 in US and to 2031 in EU)
- Issued/Granted Patents Primarily from 3 patent families
  - US: 6; EU: 3; JP: 1
  - Also granted patents in China, India, Canada and Australia
  - Expire in 2025 to 2035
  - US – up to 4 issued patents are orange book listable
- Several pending applications
- Covers composition of matter, formulations, combinations, method of use and method of manufacture

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Pipeline – Other Opportunities for DCCR

Indication	US Population Estimate
Prader-Willi syndrome	21,000 – 28,000[a]
Potential Upside Opportunities for DCCR	
Fragile X – PWS Phenotype	6,700 – 8,500[b]
Chronic Hyperinsulinism	820-1100[c]
Pediatric NASH	1.25m-3.0m[d]

Orphan drug designation was granted for PWS in the US and EU

[a] Prader-Willi Syndrome Association (USA), https://www.pwsausa.org/pws-statistics/
[b] Intractable & Rare Diseases Research 2016 5(4):255-261
[c] Orphanet J Rare Dis 2011 6:63
[D] Semin Pediatr Surg. 2009 18(3): 144–151

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2017-18 Accomplishments

- **1Q17** – Merger with Essentialis; completed concurrent $10M financing
- **May 2017** – Completed FDA guidance meeting for DCCR
- **August 2017** – Completed EMA Scientific Advice
- **2H17** – Completed $15M financing
- **2017** – Sale/JV of legacy marketed products and product candidates (Neoforce, Cosense etc)
- **October 2017** – Secured orphan drug designation for DCCR in the EU
- **January 2018** – Successfully completed EOP2 meeting with FDA
- **May 2018** – Started Phase III study
- **July 2018** – Received Fast Track designation from FDA for PWS
- **December 2018** – Completed $16.5M financing

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Financial Highlights

	9/30/18
Cash	**$10.2 (+$16.5M) ***
Debt	$ -
Shares outstanding:	
Common	**21.4M* (31.7M)**
Fully-Diluted	**30.4* (41.2M)**

*** Post private placement of $16.5M consisting of 10.3 million Common shares and .5 million warrants for Common shares, effective December 19, 2018, outstanding Common shares are 31.7 million and fully-diluted Common shares are 41.2 million**

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