Corporate Presentation

March 2020 | Soleno Therapeutics

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SOLENO THERAPEUTICS

Soleno Therapeutics (NASDAQ: SLNO)

Orphan asset in Phase III Study for Prader-Willi syndrome

Phase III enrollment complete. Topline data 1H 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

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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

Financed through topline data in 1H2020

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

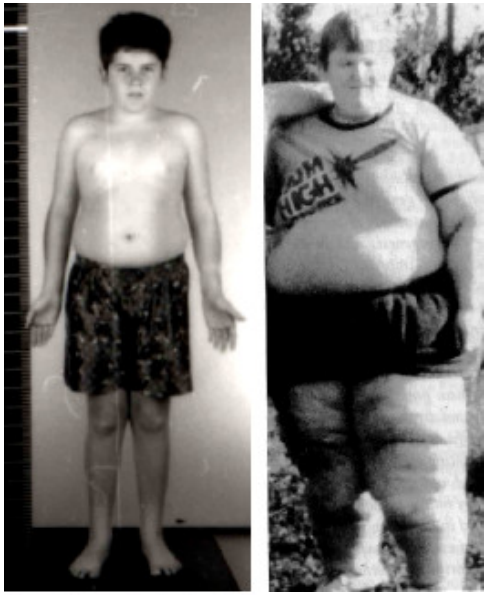
SOLENO THERAPEUTICS

Leadership Team

- Anish Bhatnagar, M.D.
  Chief Executive Officer
- Jim Mackaness
  Chief Financial Officer
- Neil M. Cowen, Ph.D.
  Senior VP, Drug Development
- Revati Shreeniwas, MD
  VP, Clinical 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
  - Aggressive behaviors
- PWS families have low QOL
  - Non-PWS siblings show high rates of post traumatic stress syndrome



SOLENO THERAPEUTICS

DCCR Once Daily Tablets

QD Dosing Critical to Facilitate Independence and Compliance

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

DCCR allows for slow release of diazoxide over 24 hours, and ensures stable levels of free diazoxide

Protected by multiple issued patents, including composition of matter

Characterized in 5 Phase I and 3 Phase II studies in healthy volunteers, obese, dyslipidemic or PWS subjects

More than 210 subjects dosed before Phase III in PWS

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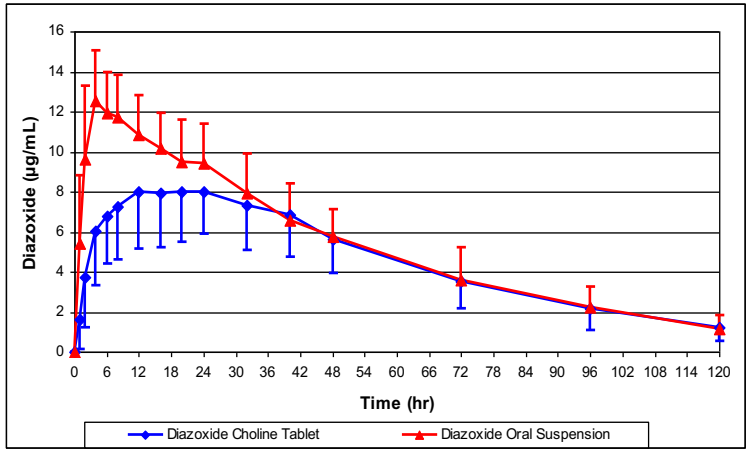
Diazoxide is Not Approved for Use in PWS

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 are C_{max}-associated

DCCR Proposed Mechanism of Action

Appetite controlled by 2 sets of neurons in the hypothalamus

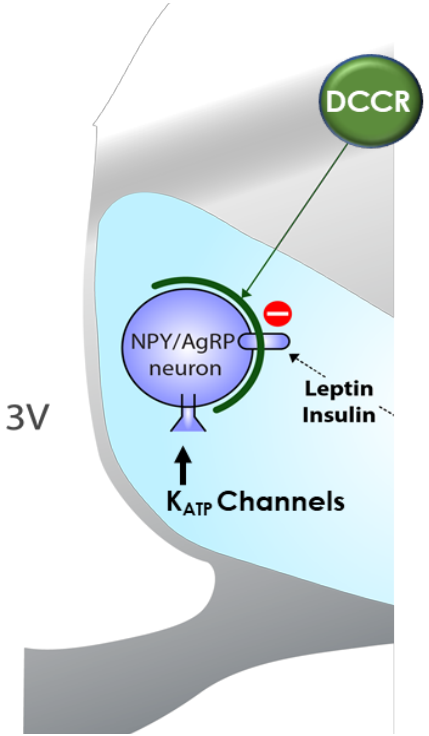
- NPY/AgRP: secrete NPY and AgRP, appetite stimulatory neuropeptides
- POMC: secretes POMC, an appetite suppressive neuropeptide

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



Snord116 Deletion

Increased activation of orexigenic pathways

Reduced activation of anorexic pathways

↓ 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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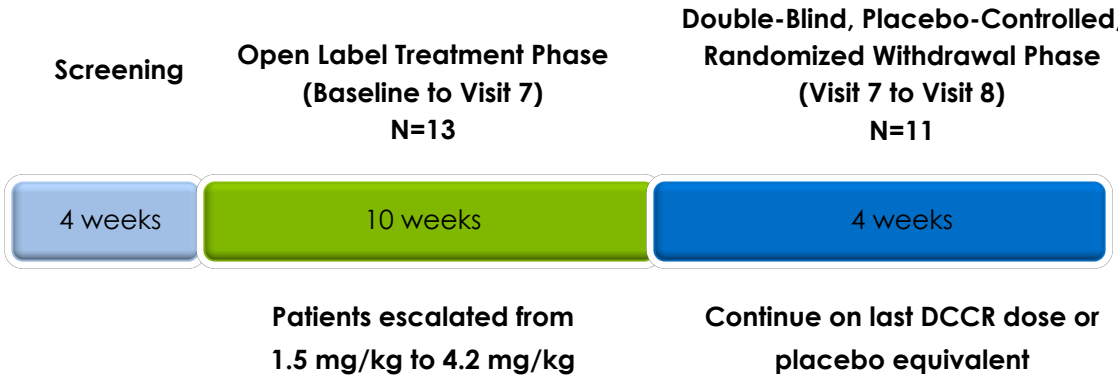
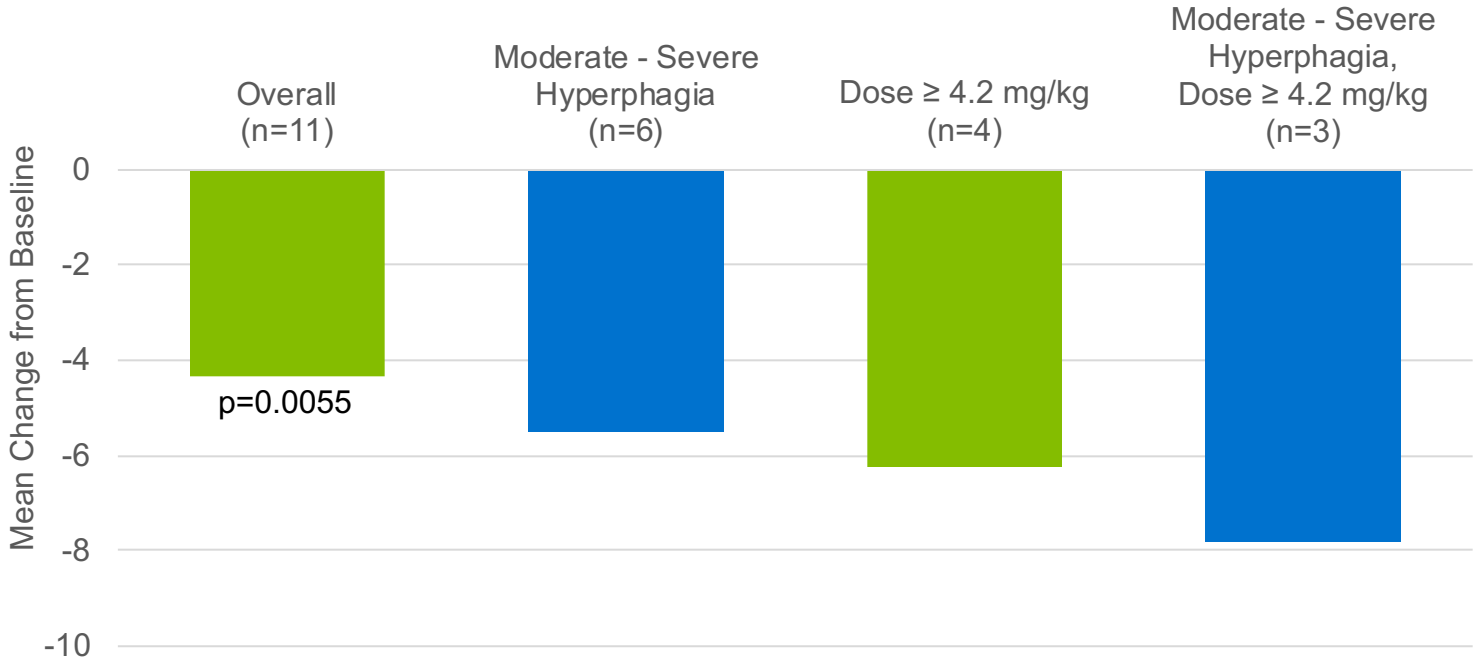
DCCR Pilot Study in PWS

- 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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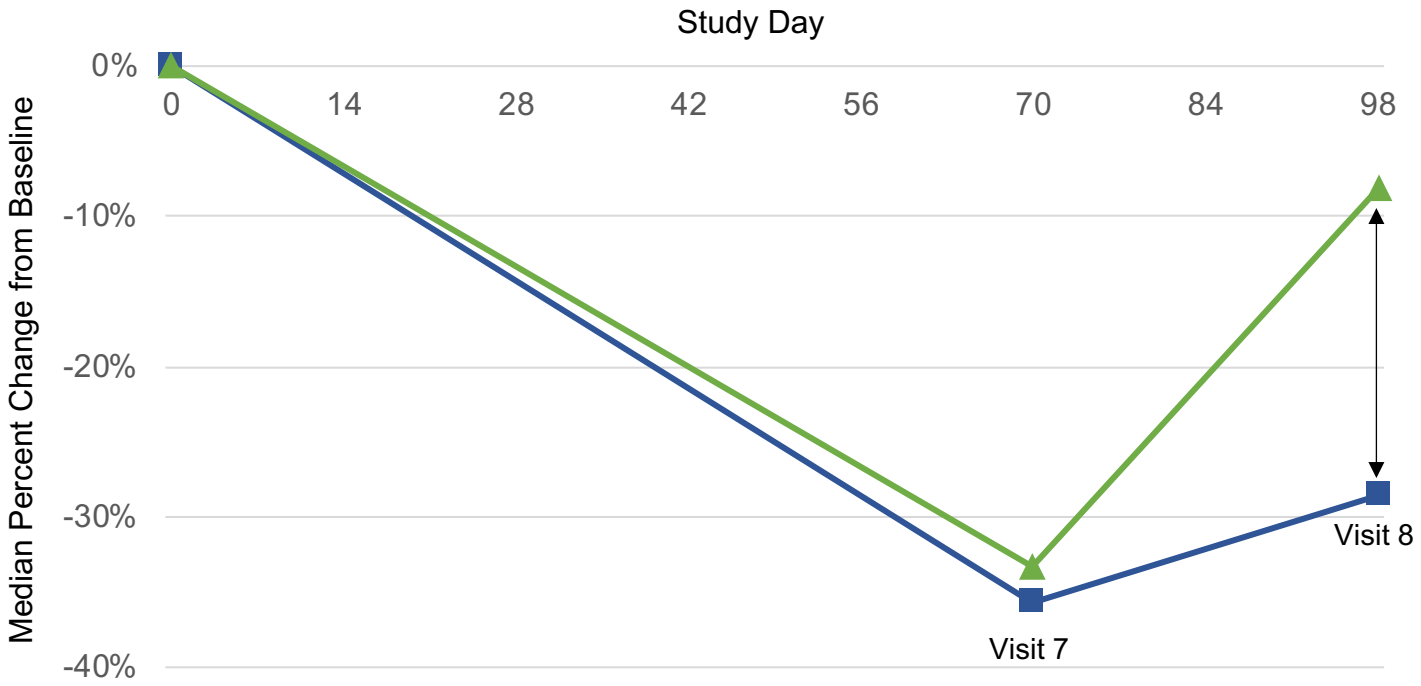
Placebo Reverses DCCR Treatment Effect

Patients with Moderate-Severe Hyperphagia



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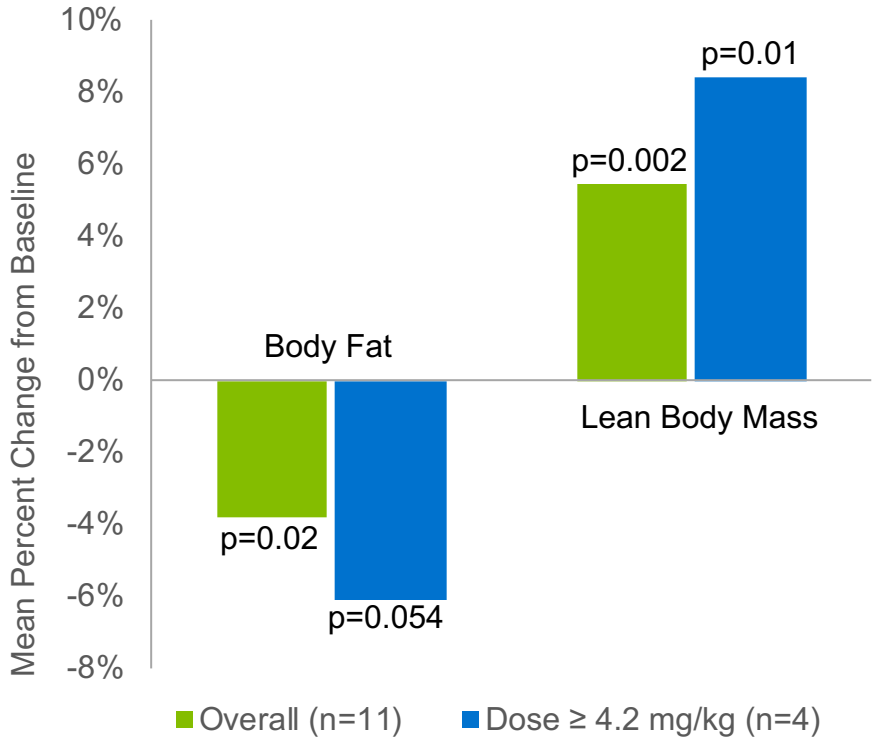
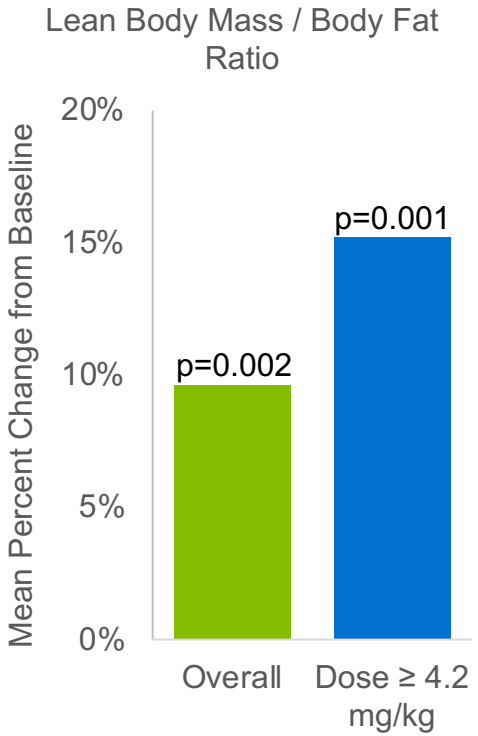
DCCR Impacts Body Fat and Lean Body Mass





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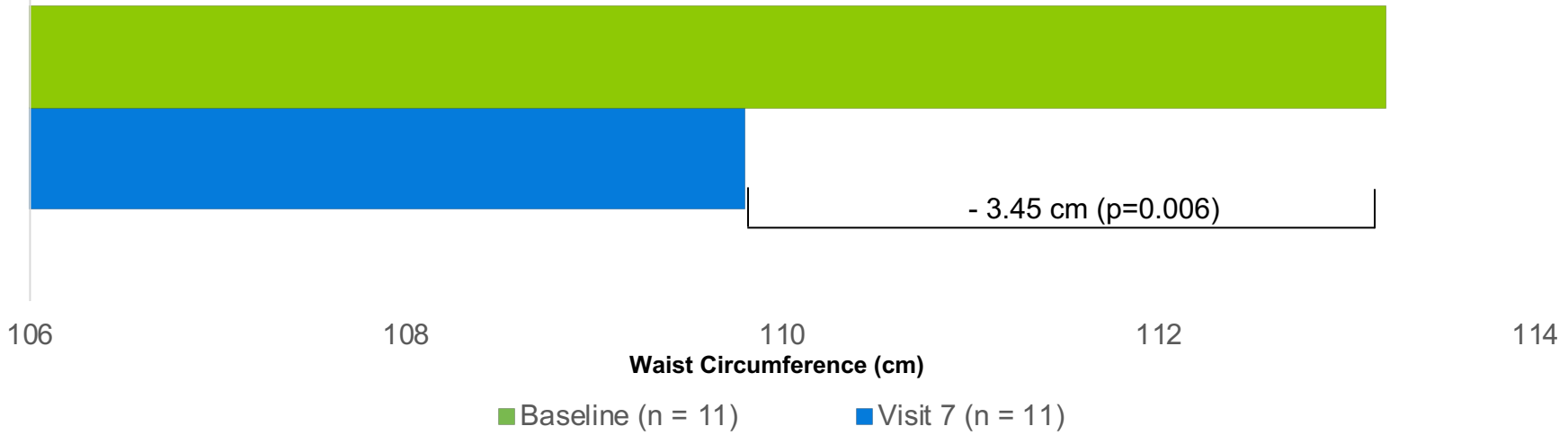
Waist Circumference

Significant Reduction from Baseline-V7

- Reduction consistent with a loss of visceral fat.



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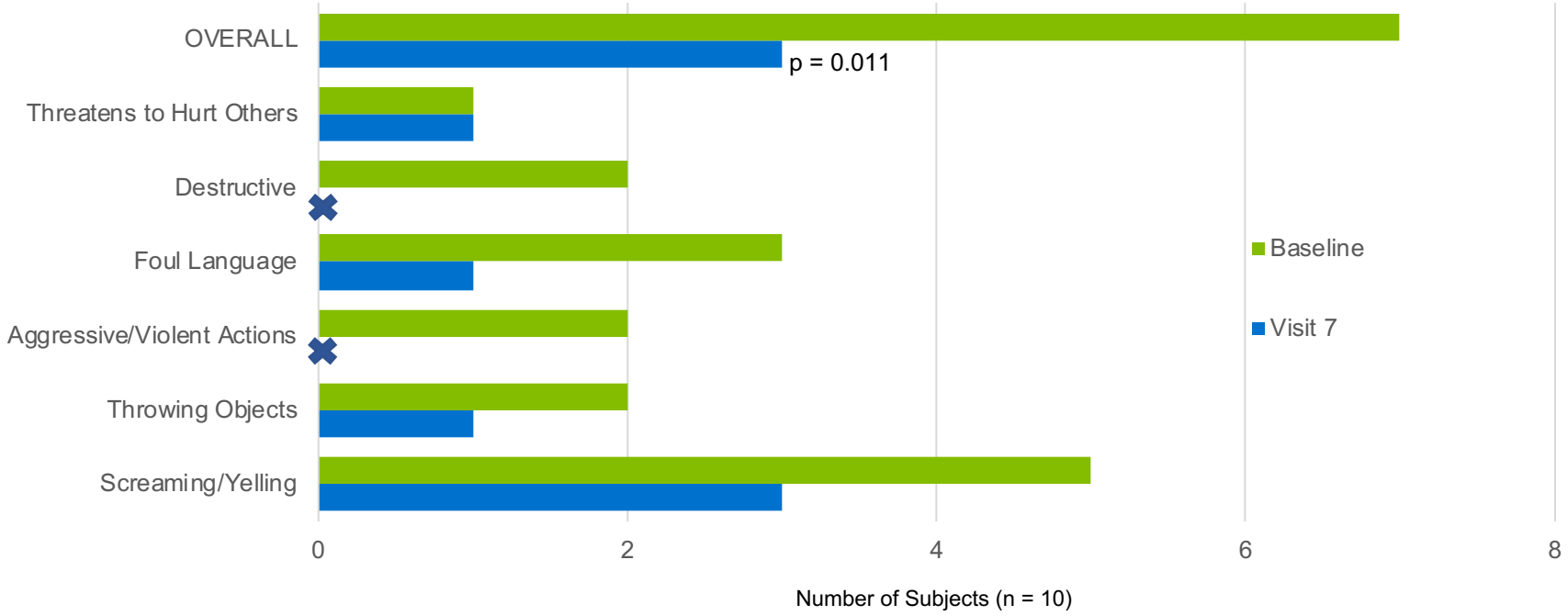
DCCR Reduces Aggressive Behaviors



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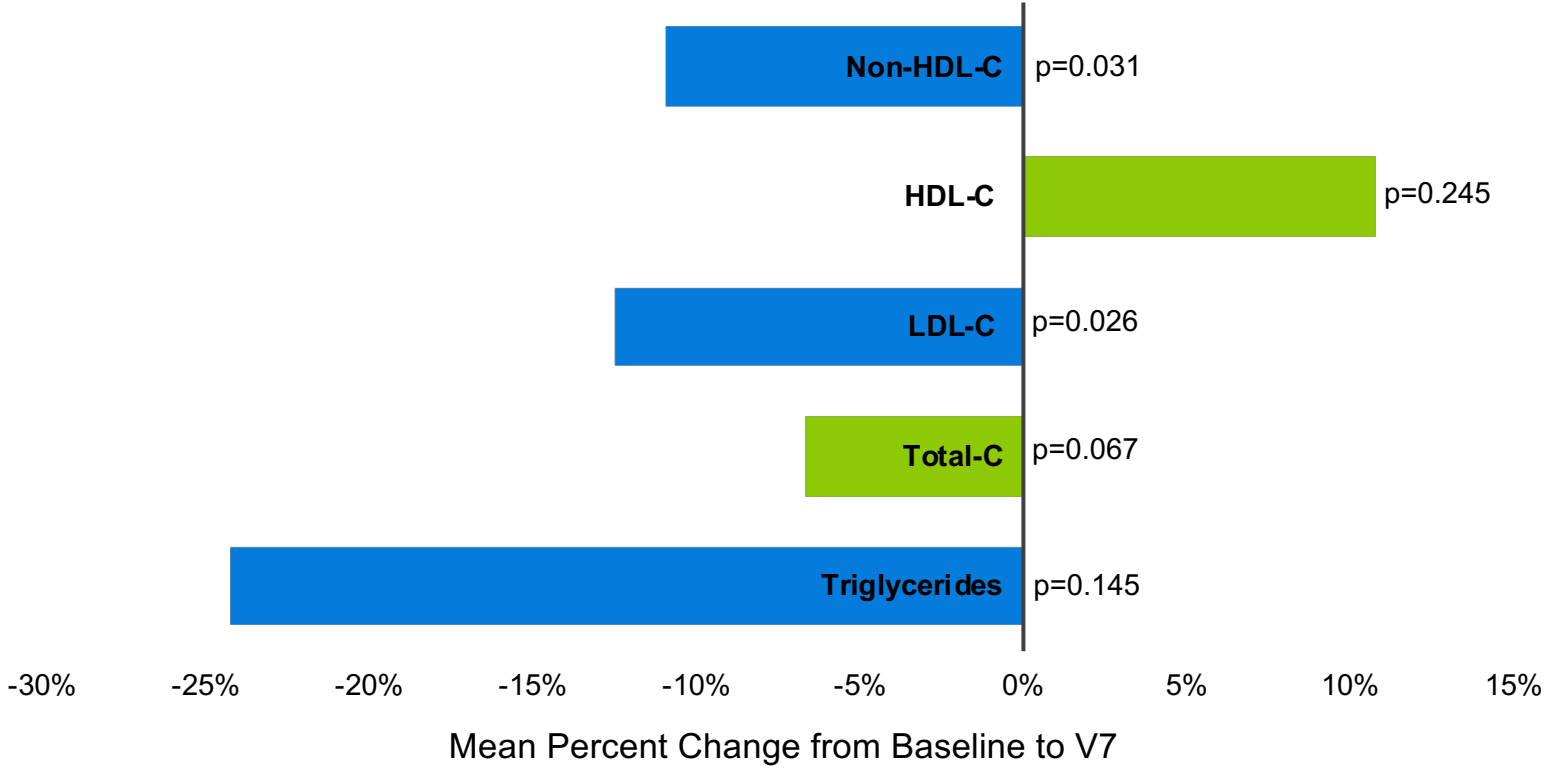
DCCR Impacts CV Risk Factors



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DCCR Safety

Consistent with Long History of Safe Use of Diazoxide

Safety profile of diazoxide in chronic use is well-known

Safety of DCCR consistent with that diazoxide

The most common adverse events with DCCR include hyperglycemia and peripheral edema

No serious, unexpected adverse events related to DCCR

Doses of DCCR used in the PWS studies are at the low end or below the equivalent labeled range for diazoxide

Estimated more than 120,000 patient-years of chronic use of diazoxide

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Regulatory Status

- FDA interactions in May 2017 (Type C) and Jan 2018 (EOP2) confirmed key aspects of Phase III development program in PWS
  - Hyperphagia as the primary endpoint
  - HQ-CT as the appropriate tool to assess hyperphagia
  - 3 months as appropriate randomized study duration (safety data in 9 month open-label study)
  - Patients as young as 4 years eligible
  - No BMI requirement for study entry
- US and EU Orphan Designation granted
- Fast Track designation granted for diazoxide choline development program in PWS

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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 randomized in a 2:1 ratio to DCCR or placebo
  - Genetically-confirmed PWS patients who are hyperphagic
- Study started May 2018, enrollment completed Jan 2020, topline data 1H 2020
- Primary endpoint – change in hyperphagia compared to placebo
- All patients completing C601 are eligible to enroll in C602

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Phase III Program Update*

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ACTIVE SITES

20 US

9 UK

Sites

C601

127

PATIENTS RANDOMIZED
POWERED TO DETECT A DIFFERENCE
OF 4 POINTS ON HQ-CT

C602

100%

PATIENTS COMPLETING 12
MONTHS CONTINUING ON
2-YEAR EXTENSION OF STUDY

DSMB has recommended continuation of
C601 study without any change at
two pre-defined times during the study

* As of March 4, 2020

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Collaboration with Casimir

The FDA's 21st Century Cures Act defines the importance of individual patient experience to the FDA's regulatory decision-making process

Soleno is collaborating with Casimir, a rare disease research organization, to collect individual patient outcome data from patients participating in C601/602

Outcome assessments will be based on interviews and/or videos before and during treatment with DCCR on C601/602

Casimir's past work has assisted with the approval of EXONDYS 51® for DMD

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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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Pipeline – Other Opportunities for DCCR

	Indication	US Population Estimate
Syndromic Obesity	Prader-Willi syndrome	21,000 – 28,000
	Potential Upside Opportunities for DCCR	
	Fragile X-PWS Phenotype	6,700 - 8,500
	Prader-Willi Like Syndrome	300 - 500
	Smith Magenis Syndrome	21,000 - 28,000
	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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Financial Highlights

Financed Through Topline Data

- Cash
  - Cash balance at end of Q4 2019 $20.7M
  - Potential additional cash post Topline Data* $12.0M
- No Debt
- Common shares outstanding at end of Q4 2019 44.6M
- Fully Diluted at end of Q4 2019 53.6M

*** Potential for additional ~$12 M in cash with exercise of ~6M warrants from Dec 2017 PIPE which terminate at the earlier of Dec 15, 2020 or 30 days following positive Phase III results for DCCR in PWS**

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