Corporate Presentation

January 2025 | Soleno Therapeutics

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

Soleno Therapeutics (NASDAQ: SLNO)

Strategic Highlights

NDA for DCCR[1] in PWS[2] PDUFA date Mar -'25

Topline data from randomized withdrawal period reported in Sept 2023

Met primary endpoint with significant differences in hyperphagia

Decades-long safety profile of parent molecule

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

Potential for substantial patent term extension

Breakthrough, Orphan and Fast Track Designations

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

Significant upside potential in other indications

Orphan designation granted for GSD1a in US

>$2B US PWS market opportunity

Addresses the 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

Strong balance sheet

Cash runway extends beyond potential launch of DCCR

Dec 2024 cash, cash equivalents and short and long-term marketable securities ~$318m

Sufficient to fund Company well into commercial launch

1. *DCCR (Diazoxide Choline) Extended-Release tablets*
2. *Prader-Willi syndrome*

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Prader-Willi Syndrome: A Complex Rare, Genetic Neurobehavioral, Metabolic Disorder with Dire Unmet Needs

Disease Overview

- Due to loss or lack of expression of genes on chromosome 15
- Birth incidence ~1:15,000, diagnosed around birth in most cases
- Characteristics: Hyperphagia, significant behavioral problems, low IQ, low muscle mass, scoliosis
- High mortality rates with mean age of death ~30 years[2] but with many now living into the 50s or longer

Highest Unmet Needs

- Hyperphagia, an insatiable desire to eat, is present in virtually all patients with PWS[1,4]
- Disruptive PWS-related behaviors food and non-food related (e.g. significant aggression leading to ER visits)
- Abnormal body composition with low muscle mass and high fat mass[4]

Quality of Life

- People with PWS require supervised care for life[1] with children typically living with families and adults often in group homes
- Constant monitoring and creation of food secure zones greatly interfere with activities of daily life
- Caregiver burden is highest after onset of hyperphagia; higher than those measured in caregivers for persons with Alzheimer's[3]
- 92% of the siblings indicated moderate-to-severe PTSD[5]

1. *Soleno proprietary quant research*
2. *Butler MG, et al., Genet Med. 2017 Jun;19(6):635-642.*
3. *Kayadjanian N et al., PLoS One 2018 Mar 26; 12(3): e0194655*
4. *Global survey conducted by the Foundation for Prader-Willi Research*
5. *Mazaheri MM, et al., J Intellect Disabil Res. 2013 Sep;57(9):861-73.*

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Changing What it Means to Live with PWS

Potential to be the **first-to-market treatment** for hyperphagia in patients with PWS

Clinical program demonstrates ability to significantly reduce hyperphagia and impact other PWS-related comorbidities

DCCR can become the foundational therapy for patients with PWS

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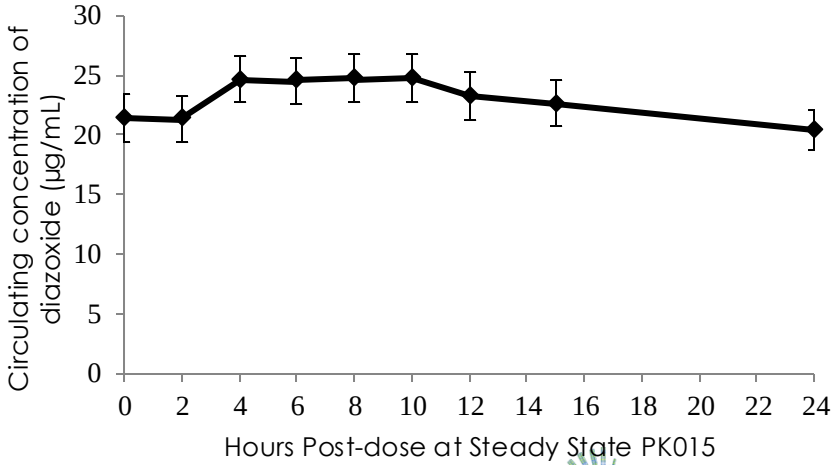
DCCR Was Developed to Facilitate Once Daily Dosing and Improve Response

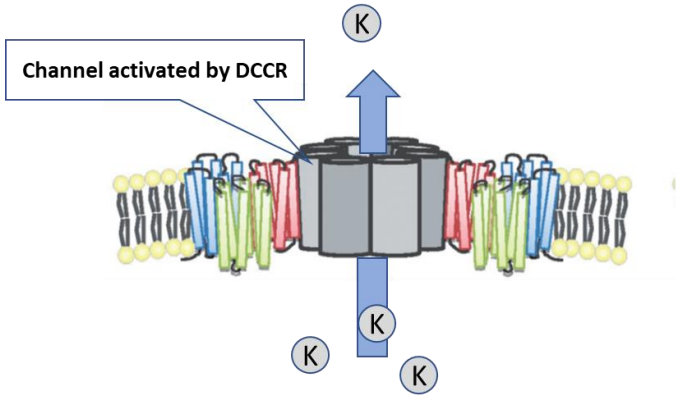
- Choline salt chosen to improve solubility
- Formulation developed to extend absorption throughout the GI tract

- Titration and dosing optimized to safely reach target dose and maintain therapeutic response

- DCCR dosed once daily to achieve stable intraday circulating drug levels
- Strong relationship between circulating drug levels with DCCR and therapeutic responses in PWS



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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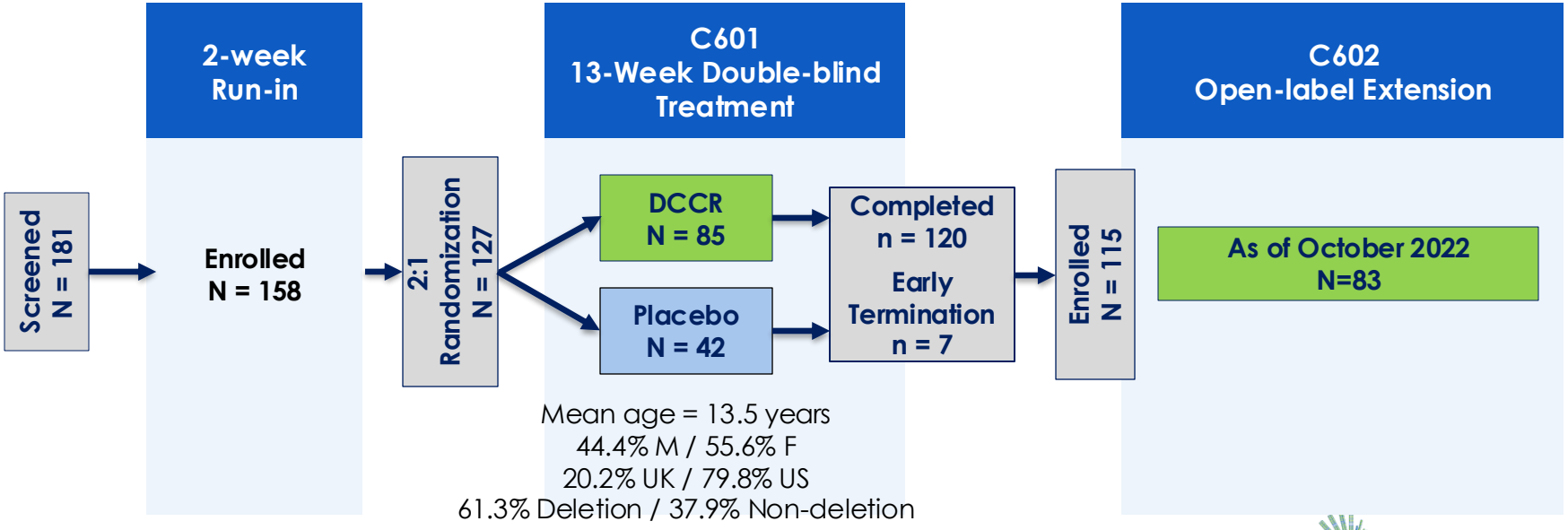
DCCR Phase 3 Clinical Program Design

- 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	All Data		Observed Data through March 1, 2020	
	DCCR (N = 82)	Placebo (N = 42)	DCCR (N = 82)	Placebo (N = 42)
Mean (SE) 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	**p-value**		**p-value**	
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	**0.023**		**0.003**	
Caregiver Global Impression of Change at Visit 7 (Caregiver GI-C)	0.41		**0.031**	

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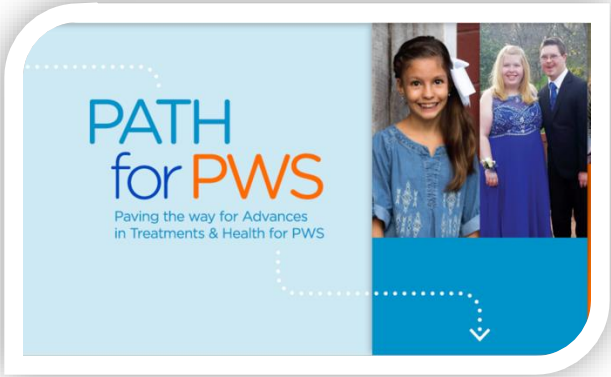
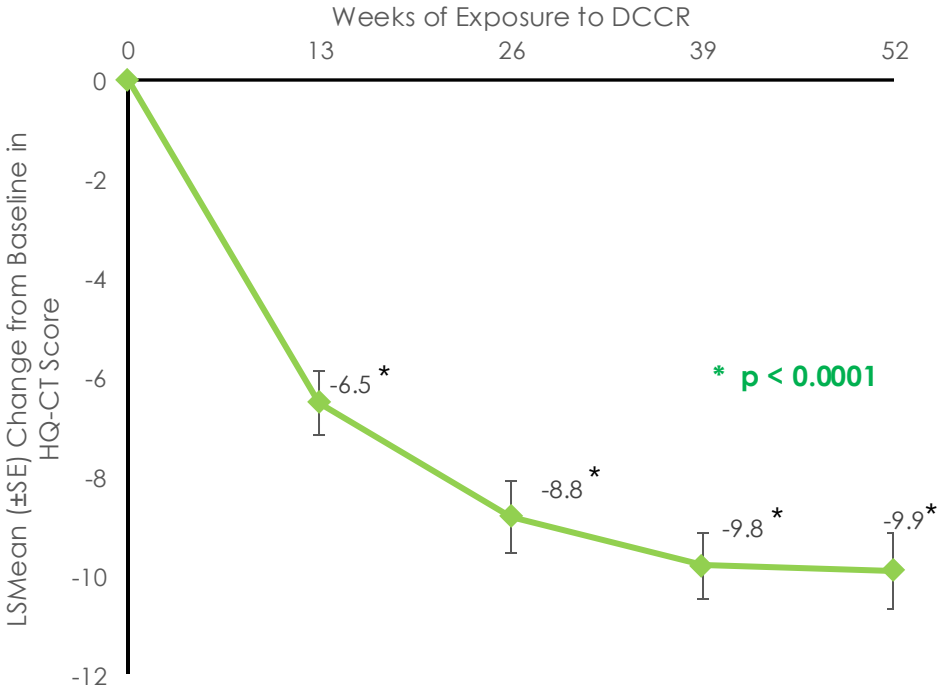
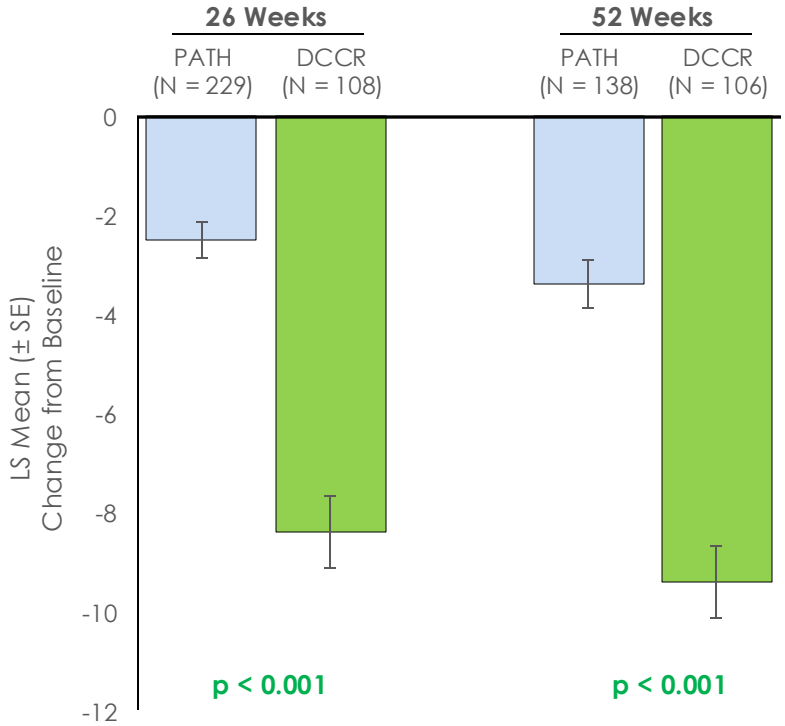
C601/C602 and PATH for PWS

- C602 was an ongoing, open-label extension study of DCCR in subjects who completed DESTINY PWS successfully
- PATH is an ongoing study evaluating the natural history of subjects with PWS
  - Sponsored by FPWR
  - ~ 650 active participants
  - 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 was conducted by an independent CRO



C601/C602 Hyperphagia Change from Baseline





C601/C602 PWS Profile Behavioral Change:
Results after One Year of DCCR

Domain	p-value
Aggressive Behaviors	<0.0001
Anxiety	<0.0001
Compulsivity	<0.0001
Depression	<0.0001
Disordered Thinking	<0.0001
Rigidity Irritability	<0.0001

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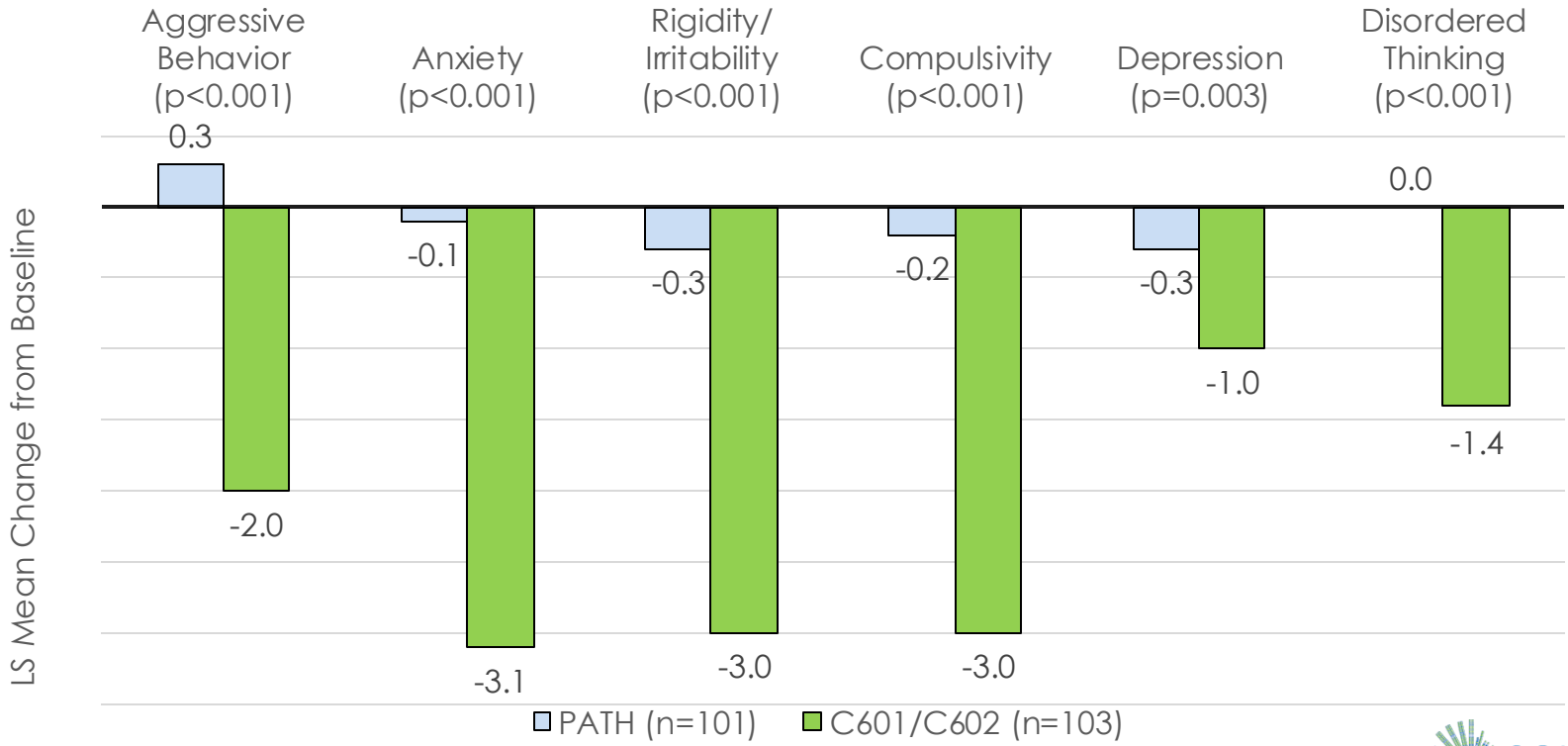
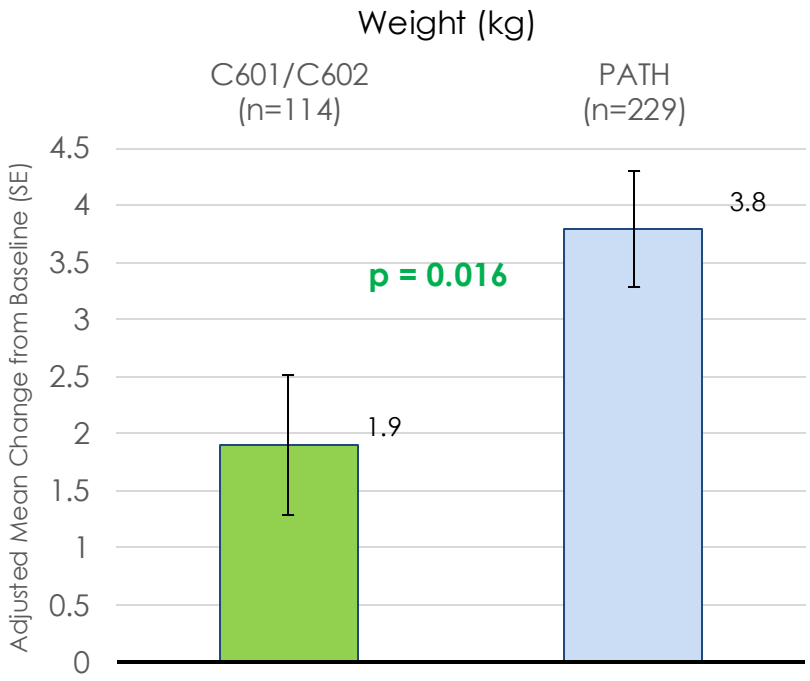
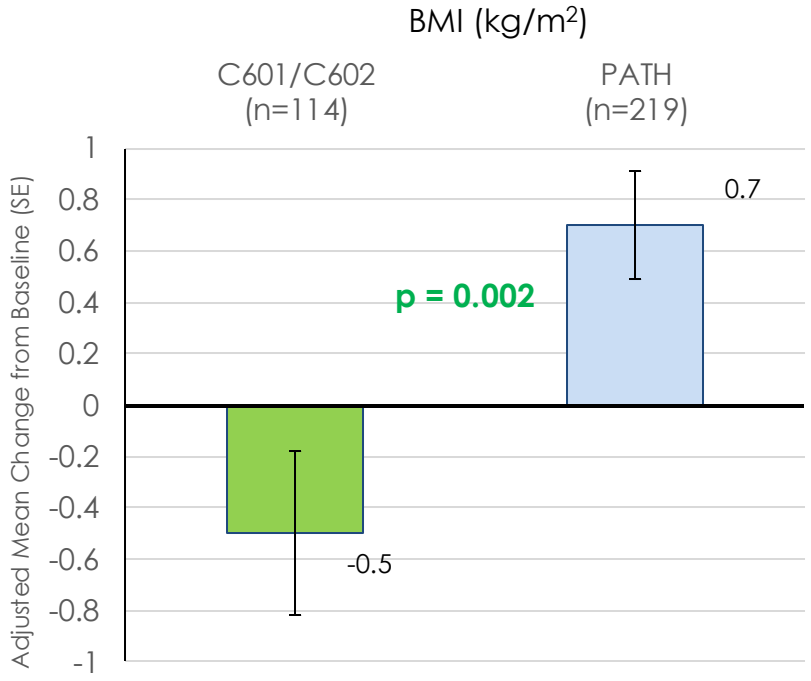
C601/C602 Comparison to PATH:

LS Mean Change in Behaviors from Baseline at Week 52



C601/C602 Comparison to PATH:
Mean Change in Body Composition from Baseline at Week 52





Endocrine and Hormonal Parameters After One-Year of DCCR

Mean change from Baseline at 1 Year	p-value
Decreased Leptin	**<0.0001**
Decreased Insulin	**0.0005**
Decreased HOMA-IR	**0.0236**
Increased Adiponectin	**<0.0001**

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DCCR Safety Profile

- >100 PWS patients treated >1 year
  - >400 total person-years of experience, including some patients with up to 6 years of continuous exposure
- Safety profile generally consistent with prior experience with DCCR and the known profile of diazoxide
- The most common adverse events reported were hypertrichosis/hirsutism, peripheral edema and hyperglycemia
- Most were Grade 1 or 2 in severity, no Grade 4 or higher events
- Typically self-limiting, some needing dose adjustment or treatment (e.g., with oral antidiabetics or short course diuretics)
- Two SUSARs (suspected unexpected serious AEs) – 1 event each of aggression and major depressive episode in patients with known psychiatric histories

Impact of DCCR

- *Photos provided with consent of the DCCR study participant's caregiver through University of Florida, USA*
- *Changes not representative of all participants*
- *Changes occurred over 12 or more months of DCCR once daily*

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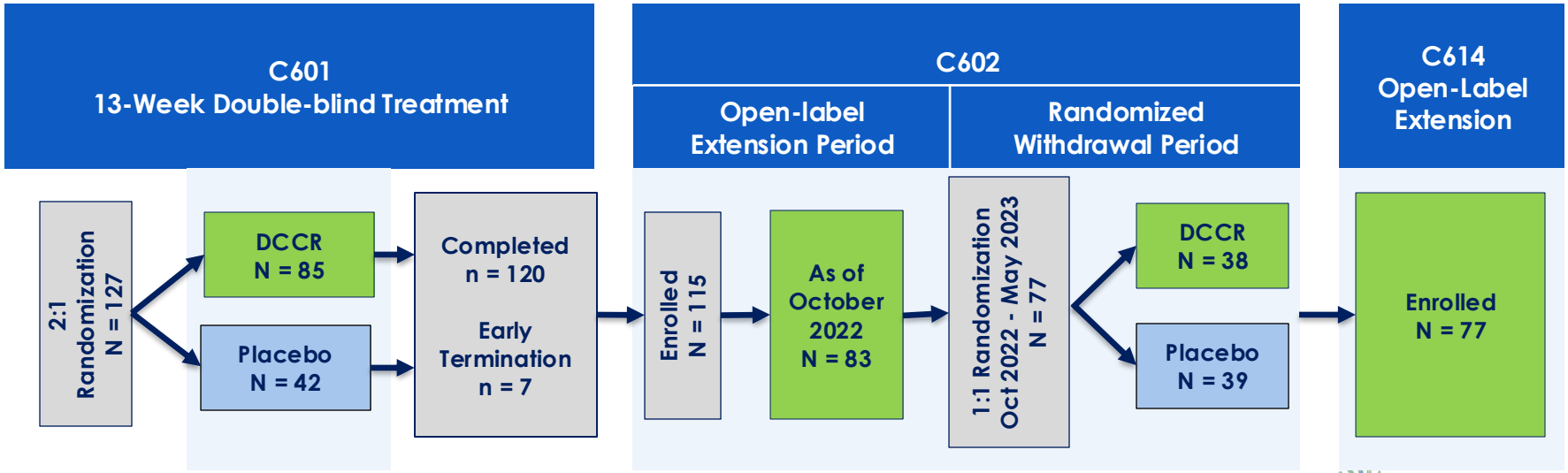
DCCR Phase 3 Updated Clinical Program

- FDA stated that additional controlled data are necessary to support an NDA submission
- In June 2022, the FDA acknowledged that data from a proposed randomized withdrawal period of C602 would potentially suffice
  - Randomized Withdrawal only included subjects who were currently enrolled in C602, no new subjects



C602 RWP Primary Endpoint:

HQ-CT Total Score at Week 16

Change from Baseline – Highly Statistically Significant

Week 16	DCCR N=38	Placebo N=39	DCCR vs Placebo
LSMean Change from Baseline in HQ-CT Total Score	2.6 (0.3, 4.8)	7.6 (5.4, 9.7)	-5.0 (-8.1, -1.8)
			p=0.0022

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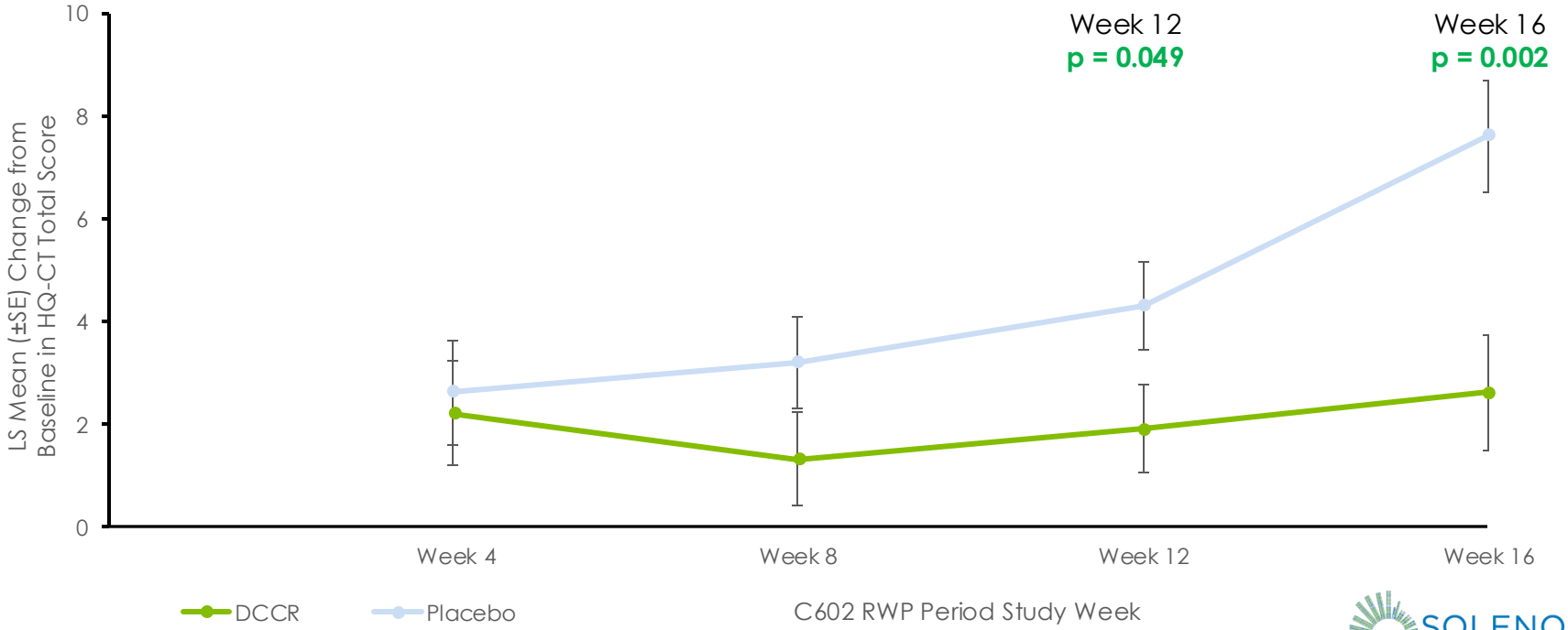
C602 RWP HQ-CT Total Score at Week 16

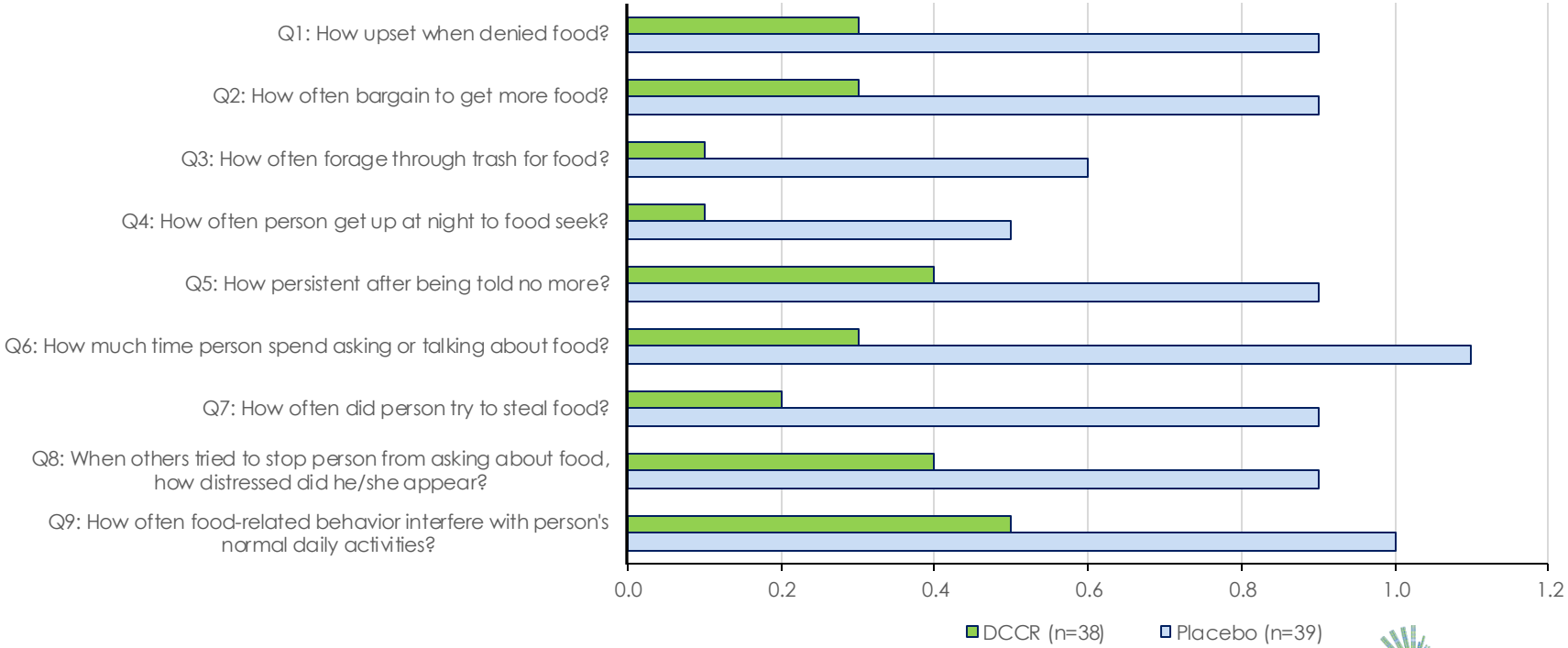
Change from Baseline for DCCR Compared to Placebo

LS Mean change from baseline highly statistically significant at Week 16; also statistically significant at Week 12



C602 RWP HQ-CT by Question at Week 16

Mean changes from baseline were worse (i.e., increased) for placebo than for DCCR on every question



C602 RWP Secondary and Behavioral Endpoints at Week 16

Strong trends showing worsening with Placebo

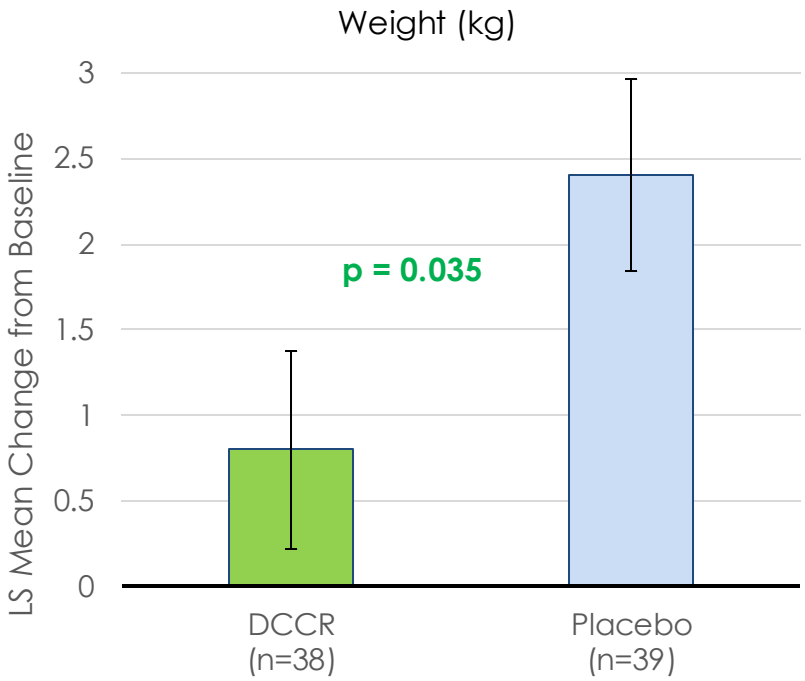
Secondary Endpoint	DCCR vs Placebo
Clinical Global Impression of Severity (CGI-S)	p = 0.079
Clinical Global Impression of Improvement (CGI-I)	p = 0.092

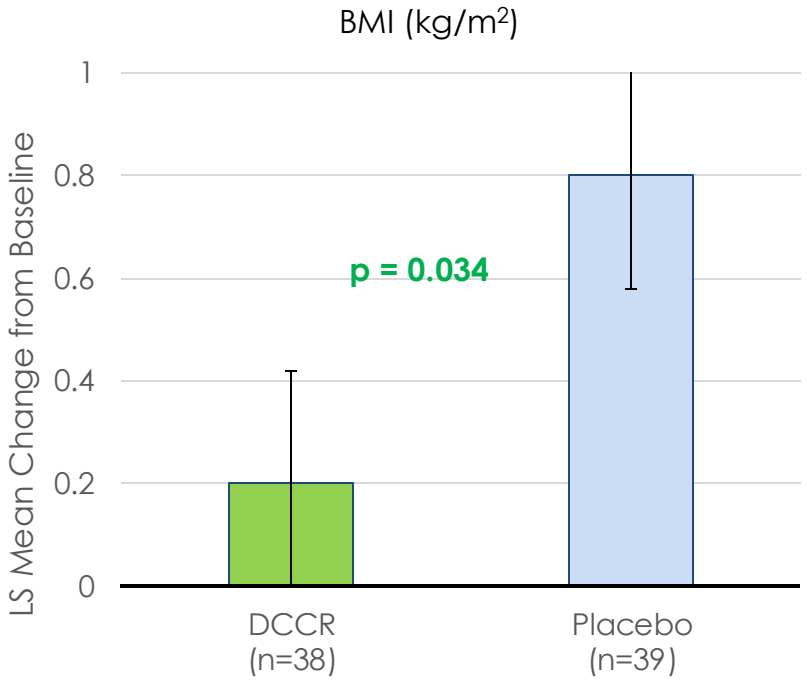
All PWSP Domains Trending in Favor of DCCR

PWSP Domain	DCCR worse than Placebo	Placebo worse than DCCR*
Aggressive Behaviors		✓
Anxiety		✓
Rigidity, Irritability		✓
Compulsivity		✓
Depression		✓
Disordered Thinking		✓

* p = not significant

C602 RWP LSMean (SE) Changes from Baseline at Week 16 in Body Weight and BMI





Regulatory Status in the US

- Breakthrough, Fast Track and Orphan designations
- NDA submitted June 2024
- NDA accepted August 2024
- Priority Review granted
- FDA currently does not plan to hold Advisory Committee
- Original PDUFA December 27, 2024, extended to March 27, 2025

Scientific Outreach & Community Engagement

Increasing levels of engagement with PWS community, physicians and advocacy groups

Growing body of clinical evidence presented at medical and scientific conferences by key opinion leaders and study physicians

Independent town hall meetings with study participants and caregivers sharing their testimony about DCCR

Independent FDA Externally-led Patient-Focused Drug Development (EL-PFDD) meeting on PWS, led by PWSA-USA

PWS Advocacy Coalition submitted a petition with 14,271 signatures requesting FDA filing and priority review of DCCR NDA

Extensive IP Protection

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

Uses of pharmaceutical formulations of K_{ATP} channel activators

PWS relevant claims: treatment of hyperphagia in PWS with diazoxide

20-Year Expiration 8/2025

Salts of K_{ATP} channel activators and uses thereof

PWS relevant claims: composition of matter (salt and polymorph), formulation, method of manufacture, methods to treat overweight, obese and obesity prone individuals

5 US patents
20-year expiration12/2026

Potential expiration w/PTA 3/2029

Potential expiration w/PTA & PTE 2034

Methods to treat PWS Patients

Specific claims to behavioral, body composition, and cardiometabolic marker changes in response to treatment with DCCR, diazoxide or K_{ATP} channel activators, dependent claims to treating hyperphagia

4 US patents + 1 application

20-Year expiration 11/2035

Potential expiration w/PTE 2038/2039

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PWS US Market is an Attractive Opportunity with a Clearly Defined Addressable Population

~85% of diagnoses are made with in the first year of life[1]

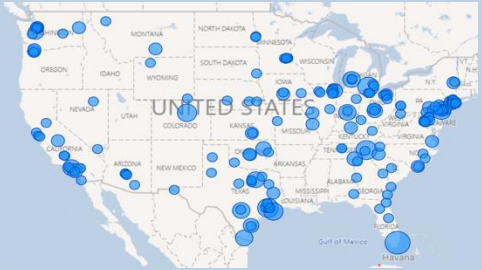
~10,000 patients identified in claims database

95% of HCPs state willingness to prescribe DCCR[2]

Primary driver for patients falling out of routine care is lack of available treatment for hyperphagia[2]

Majority of HCPs believe a product launch will encourage PWS patients re-engage[2]

~300 HCPs are primary treaters of **~2,100** PWS patients and influence treatment decisions for an additional **~2,000** patients[3]



1. *Wheeler, A.C., Gantz, M.G., Cope, H. et al. J Neurodevelop Disord 15, 37 (2023)*
2. *Soleno proprietary quant research*
3. *ICD10 claims data – Soleno purchased data*

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The PWS Market: Specific Considerations for Different Age Groups

Young patients (<25 years)

01

- Onset of hyperphagia and increasing disruptive PWS-related behaviors
- Caregivers and families are actively engaged in care (~4 visits/year)[1]
- Majority live with family, with support from schools
- Pediatric Endocrinologists are primary point of care, with support from multiple specialties

Adult patients (>25 years)

02

- Transition to adult care disrupts continuity of care, coincides with increased desire for independence
- Often isolated and reliant on food-security and 24/7 monitoring
- Majority of adults still live with family members, with ~20% individuals living in residential programs[2]
- Adult Endocrinologists are the primary treaters, mostly focused on mitigating health deterioration

1. *Soleno proprietary quant research*
2. *ICD10 claims data*

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Ideal Therapeutic Profile: Impact on the Hallmark Symptoms of PWS

Significant improvement in hyperphagia

Durable improvement in cardiometabolic markers & body composition

Reduction PWS-related behaviors, improving quality of life

Well-tolerated safety profile

Pathway to Successful US Launch of DCCR

Robust Clinical Program

- Differentiated Mechanism of Action
- Efficacy observed in multiple aspects of the disease in clinical trials
- ~5 years of response in clinical trial data
- Well characterized response profile

Rare Disease & Launch Capabilities

- Invested in analytics to map TAM
- Account profiling to define influence and catchment areas
- Hiring teams with deep rare disease and launch experience

Comprehensive Access Strategy

- Mapped payer mix to support rapid uptake
- Educating payers on value proposition
- Distribution partners with extensive rare disease experience

Stakeholder Engagement

- Deep community and advocacy engagement
- Launched digital property www.support4PWS.com
- Strong presence at medical congresses

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Building teams, infrastructure, and programs to commercialize DCCR

Supply Chain

- *3PL*
- *Specialty Pharmacy*

Market Access

- *Patient services program*
- *Payer engagement*

Medical Affairs

- *Med Info call center*
- *Standard response letters*
- *Medical Science Liaisons hired*

Marketing

- *Brand development*
- *Core field materials*
- *Disease State Education program*
- *Omnichannel programs*

Commercial Operations

- *Field CRM*
- *KPI dashboard*

Field Force

- *Field force senior leadership hired*
- *Field training*

Patient Advocacy

- *Community engagement*

Drug Safety

- *Pharmacovigilance reporting*
- *AE reporting policy*

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Significant Opportunity in Europe

- Confirmed high unmet need
- Strong thought leader support
- Concentrated market driven by centers of excellence
- Estimated ~9,500 diagnosed PWS patients in EU4 and UK[1]
- Planning to submit MAA in 1H2025

1. *Orpha Net Birth Prevalence of 1/22.5k*

Financial Highlights

Cash, cash equivalents and investments

Time	Cash
December 2024*	$318.4m
Outstanding warrants[1]	$5.2m
Pro Forma Total Cash	$323.6m

- *Includes short and long-term marketable securities
- [1]2.1m Dec 2022 Tranche B warrants remaining to be exercised for a total of $5.2m
- [2] Numbers from Q3 10Q

Fully Diluted Share Count

Dec 31, 2024	In Millions
Common stock	45.7
Pre-funded warrants	0.3
March 2022 warrants – $4.50	1.3
Dec 2022 Tranche B - $2.50[1]	2.1
Options and RSUs[2]	4.6
Pro Forma Total	**54.0**

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