Corporate Presentation

June 2024 | Soleno Therapeutics

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

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Soleno Therapeutics (NASDAQ: SLNO)

Strategic Highlights

NDA submission for DCCR[1] in PWS[2] planned mid-'24

Topline data from randomized withdrawal period reported in Sep 2023

Met primary endpoint with significant improvements 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 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

Mar 2024 cash ~$158m
Closed financing May 2024 for additional net ~$149m

[1]DCCR (Diazoxide Choline) Extended-Release tablets
[2]Prader-Willi syndrome

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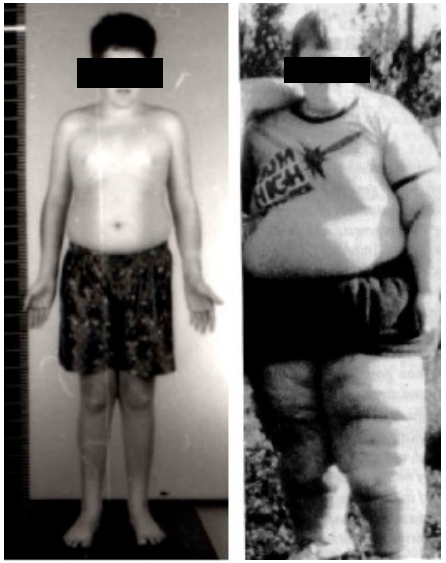
Prader-Willi Syndrome (PWS)

- 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 births
- Elevated mortality rates with mean age of death ~21 - 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
  - Caregiver burden higher for caregivers of people with PWS than those with Alzheimer's
  - Burden of care is highest after onset of hyperphagia
  - Require supervised care for life



Butler MG, et al., Genet Med. 2017 Jun;19(6):635-642.
Bellis SA, et al., The Eur J Med Genet. 2022 Jan;65(1):104379.
Kayadjanian N et al., PLoS One 2018 Mar 26; 12(3): e0194655.

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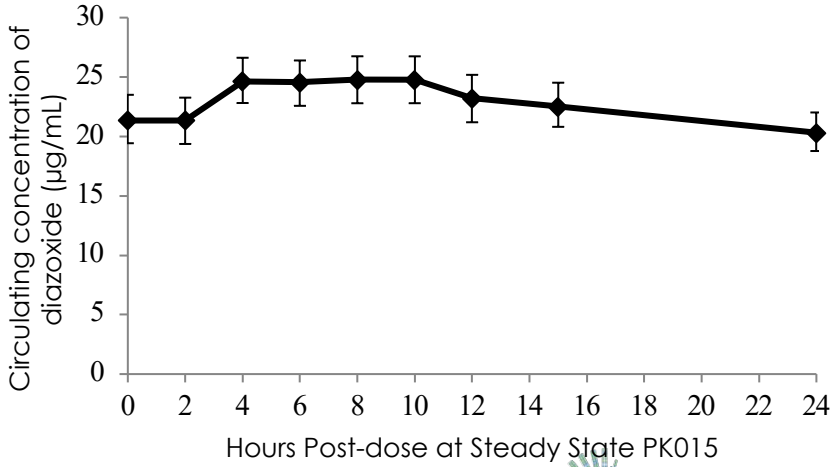
DCCR Was Developed to Facilitate Once Daily Dosing and Improve Response

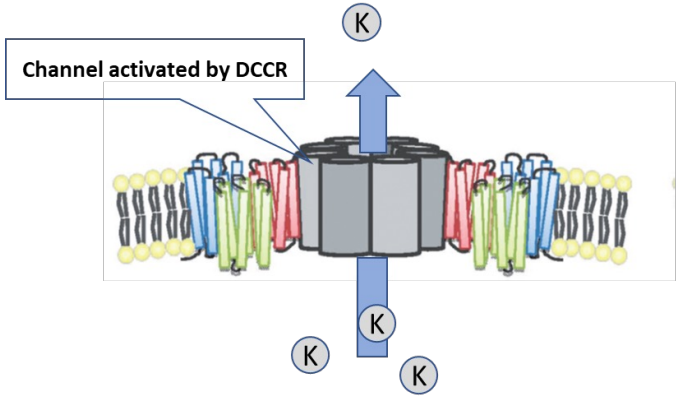
- Choline salt chosen to improve solubility
- Formulation developed to extend absorption throughout the GI tract

- 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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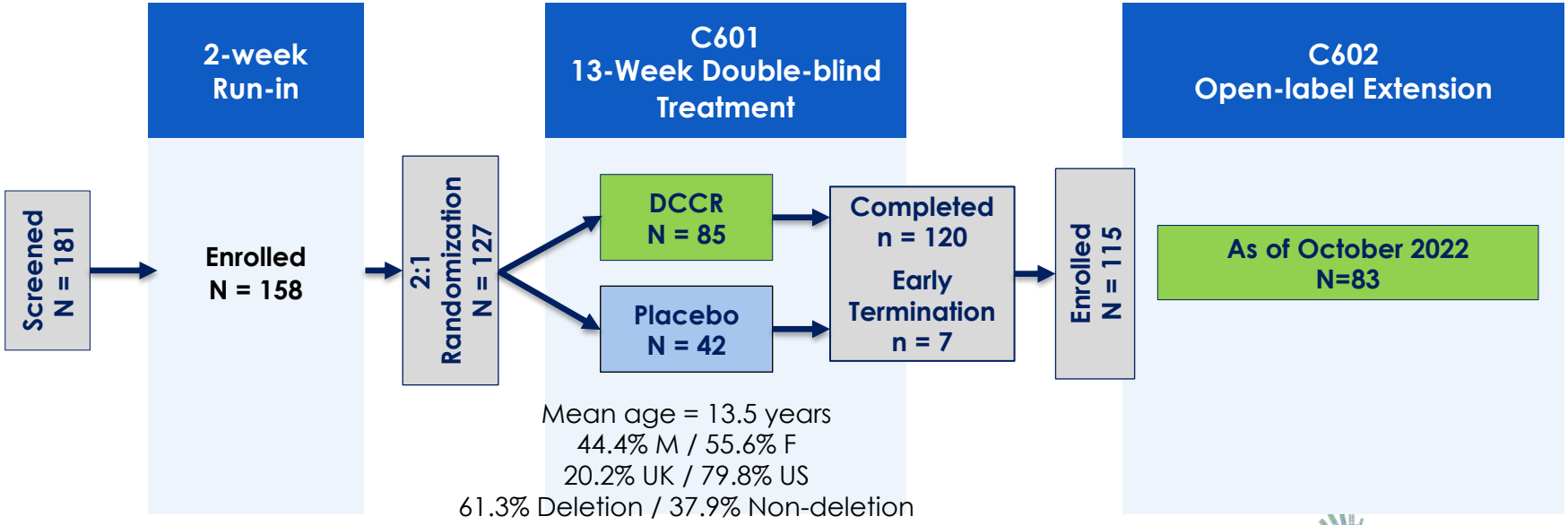
DCCR Phase 3 Clinical Program Design

- 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 Additional Endpoints

Change from Baseline at Week 13

PWSP Domain	DCCR vs Placebo p-value
Aggressive Behaviors	**0.048**
Anxiety	**0.018**
Rigidity, Irritability	**0.003**
Compulsivity	**0.008**
Depression	0.185
Disordered Thinking	**0.011**

Key Hormonal and Metabolic Markers	DCCR vs Placebo p-value
Decreased Acylated Ghrelin (active form)	**0.0182**
Decreased Leptin	**<0.0001**
Decreased Insulin	**0.0110**
Increased Adiponectin	**<0.0001**

Observed values through March 1, 2020

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Long-term Data

DCCR 12 MONTHS INTERIM RESULTS AND COMPARISON TO PATH FOR PWS

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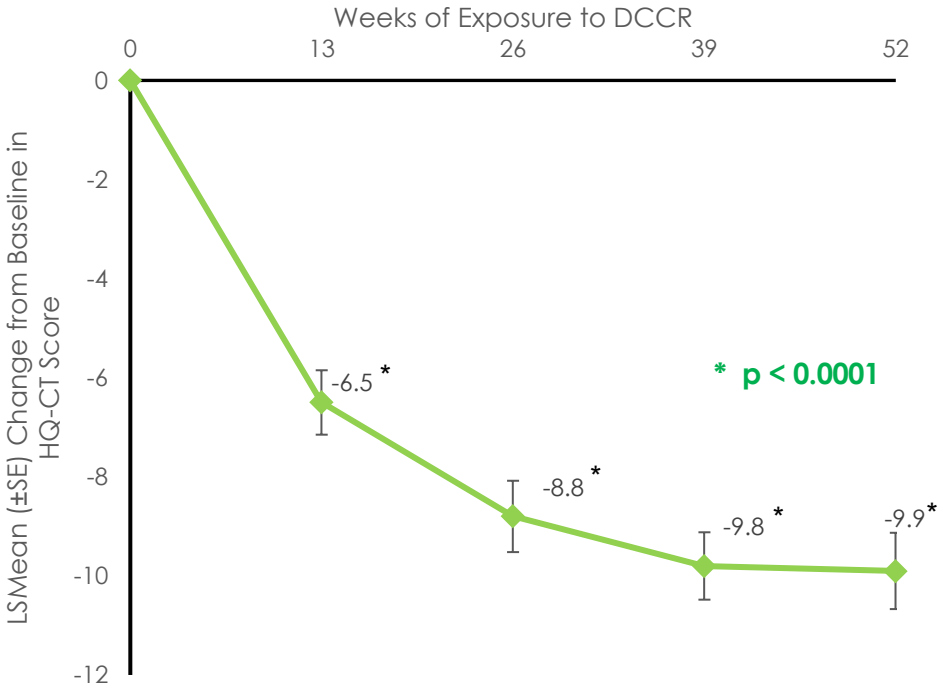
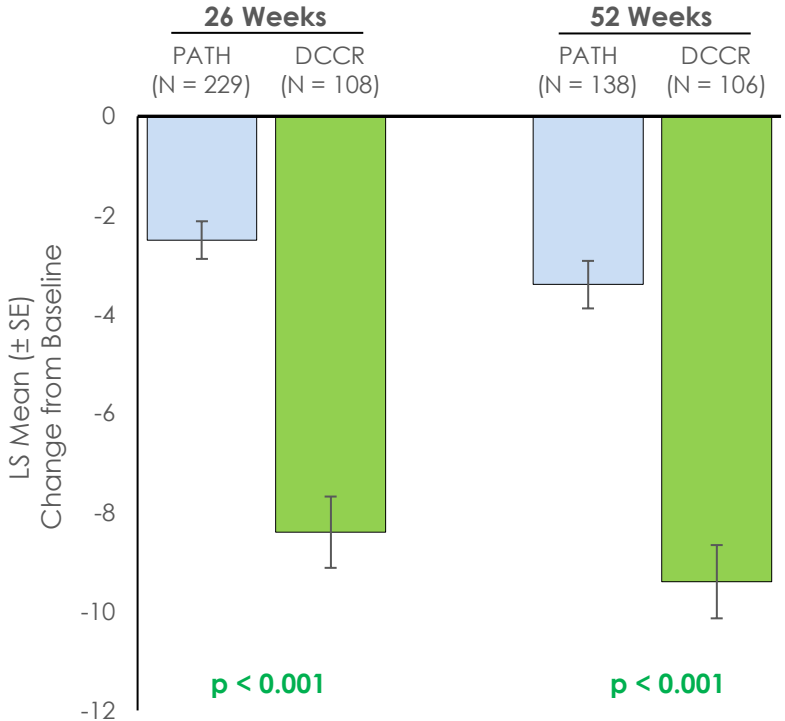
C601/C602 and PATH for PWS (PATH)

- 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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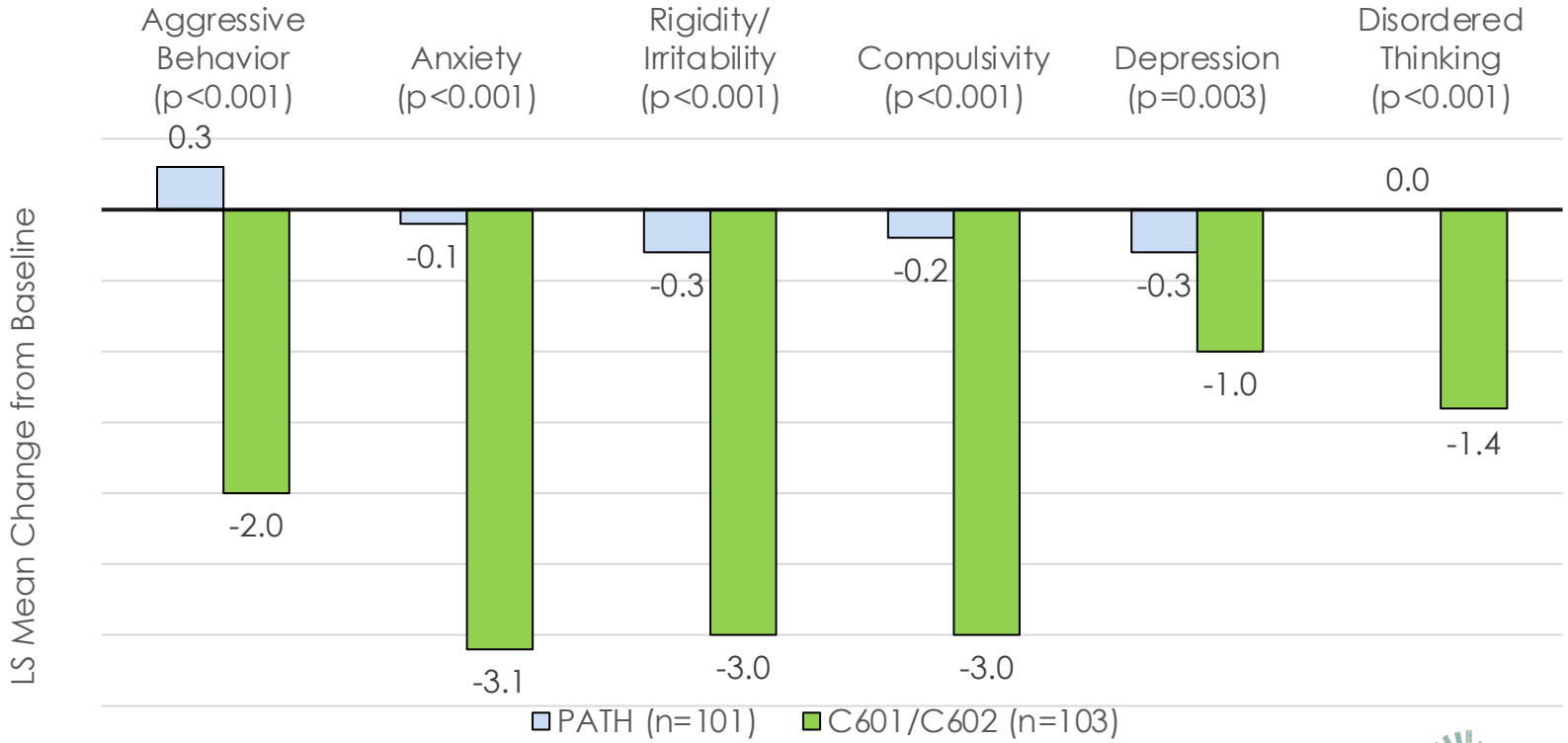
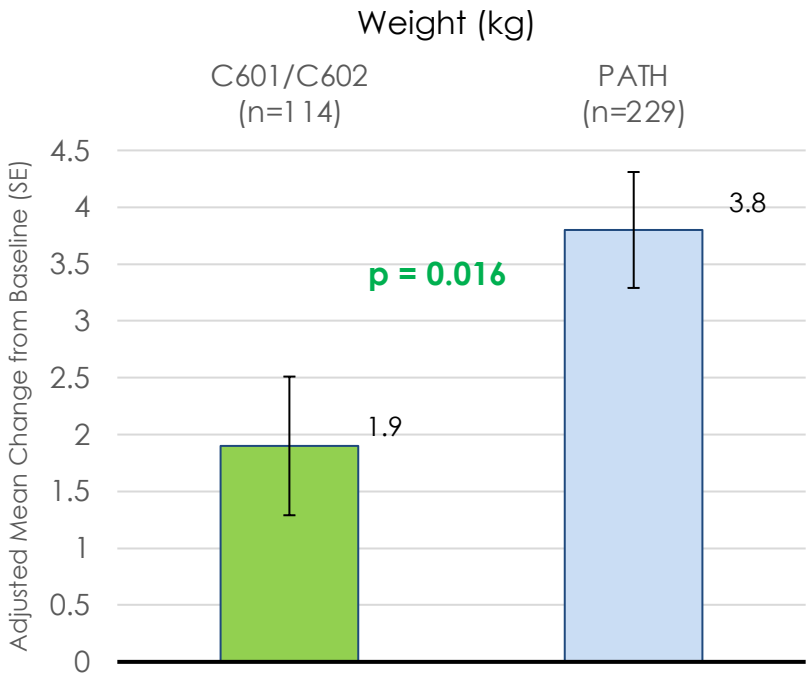
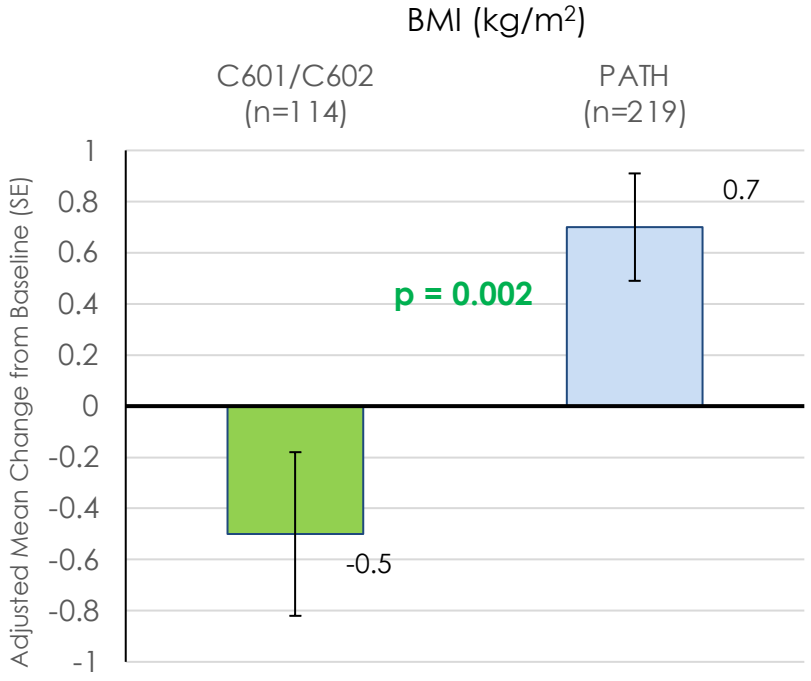
C601/C602 Comparison to PATH – LS Mean Change in Behaviors from Baseline at Week 52



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 patients treated for more than one year
- 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 events 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)
- Only 1 SUSAR (serious unexpected AE) - aggression in patient with known psychiatric history

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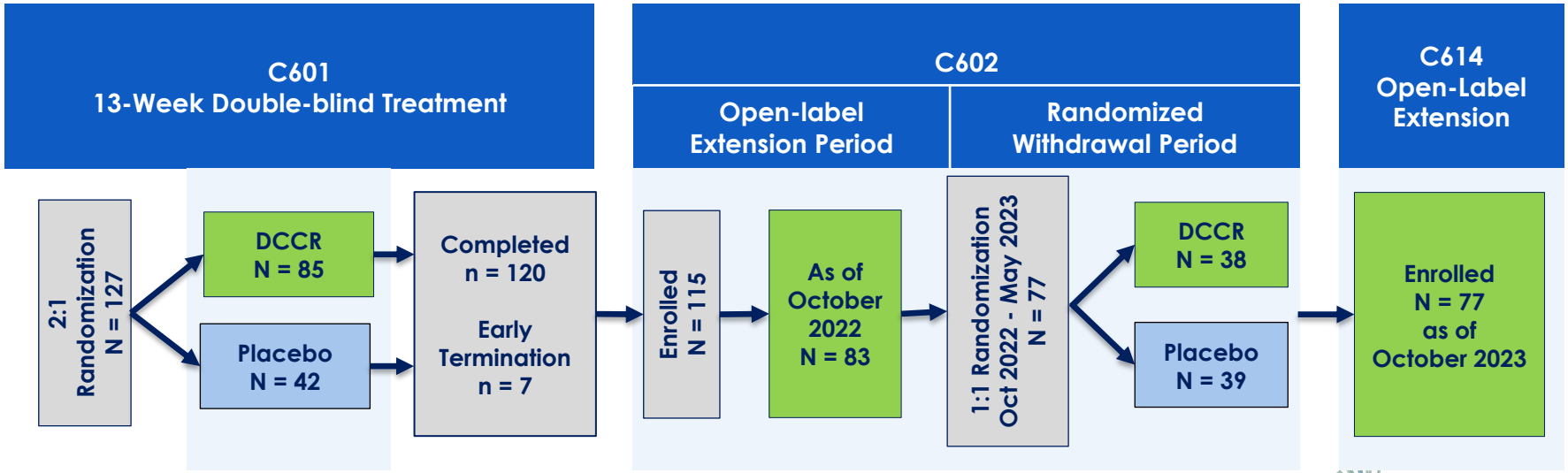
DCCR Phase 3 Updated Clinical Program

- 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 Participant Demographics and Baseline Characteristics Comparable Across Treatment Groups

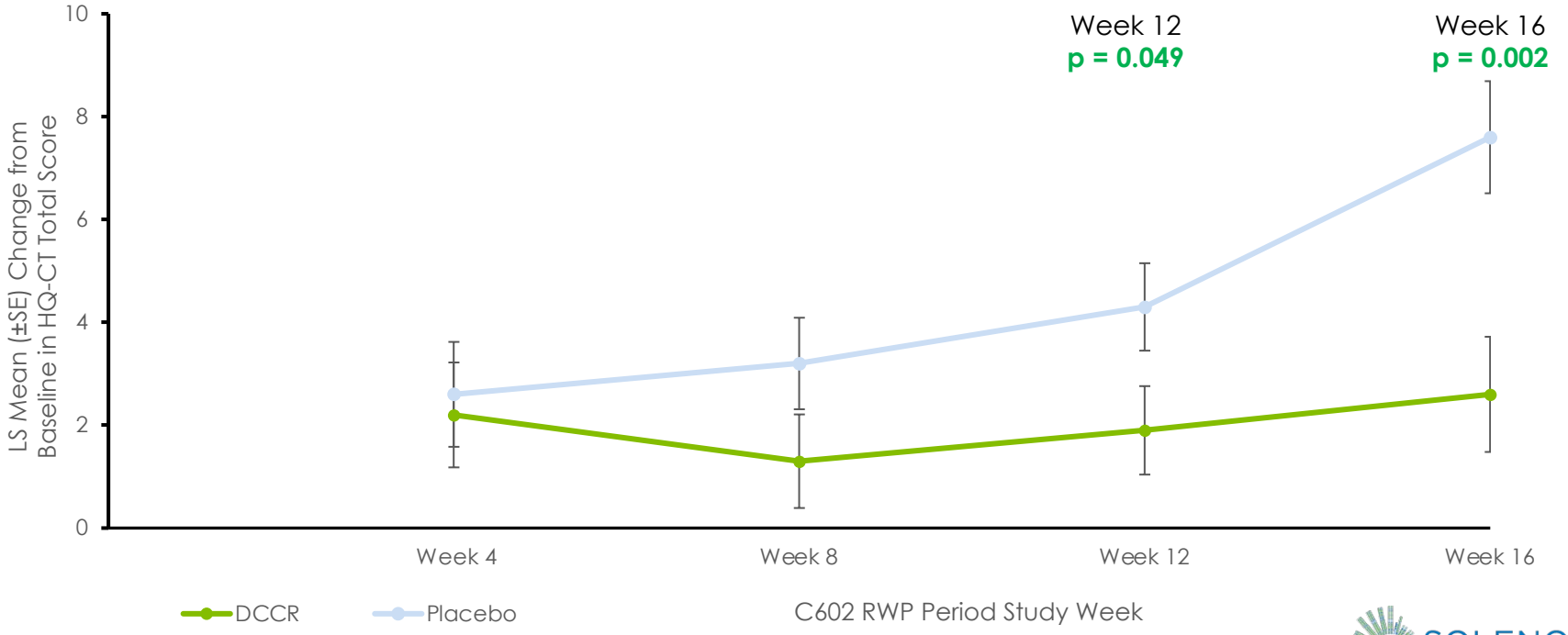
At RWP Randomization	DCCR N=38	Placebo N=39	All Subjects N=77
Age (Range) (yrs)	15.6 (7 – 29)	14.2 (9 – 23)	14.9 (7 – 29)
Female / Male (%)	47 / 53	64 / 36	56 / 44
Race (% White / % Black / % Multiple)	84 / 5 / 11	87 / 8 / 5	86 / 7/ 8
Weight (Range) (kg)	73.7 (29.7 – 143.2)	61.7 (33.3 – 92.4)	67.6 (29.7 – 143.2)
BMI (Range) (kg/m^2)	28.5 (15.6 – 49.0)	25.3 (16.1– 37.6)	26.9 (15.6 – 49.0)
Growth Hormone Use (n)	33	36	69
USA / UK (%)	84 / 16	77 / 23	81 / 20
HQ-CT Total Score	9.0 (0 – 26)	8.1 (0 – 19)	8.5 (0 – 26)
HQ-CT Category (<13 / 13-36 [%])	74 / 26	77 / 23	75 / 25

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

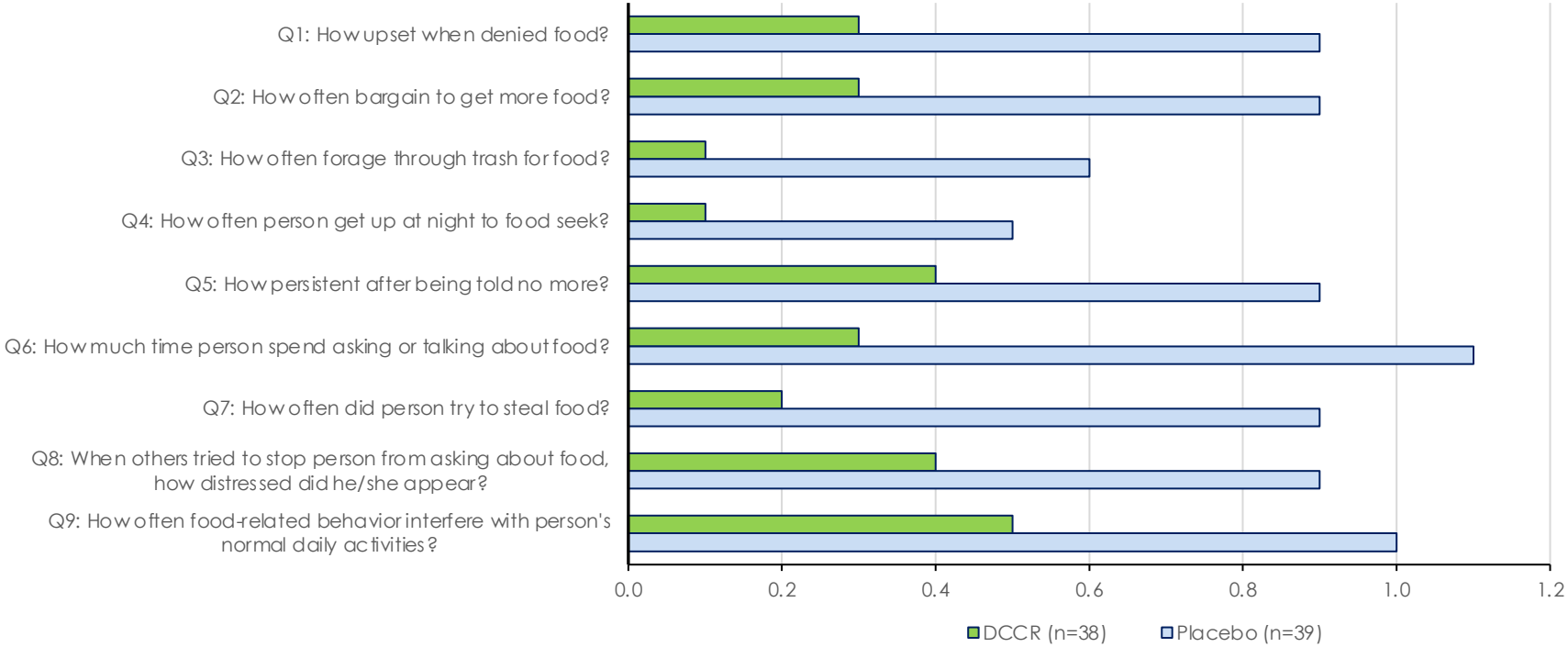
C602 RWP HQ-CT Total Score at Week 16
Change from Baseline for DCCR Compared to Placebo

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



C602 RWP HQ-CT Question by Question at Week 16

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



C602 RWP HQ-CT Total Score at Week 16
Statistically Significant Change from Baseline in Subgroups

Subgroup	LS Mean Difference (95% CI)	p-value
Overall	-5.0 (-8,1, -1.8)	**0.0022**
Sex		
Male	-6.0 (-11.0, -1.1)	**0.019**
Female	-4.7 (-9.0, -0.5)	**0.031**
Baseline HQ-CT Total Score		
< 13	-4.9 (-8.6, -1.1)	**0.012**
13 - 36	-6.5 (-12.4, -0.6)	**0.033**
Country		
USA	-4.5 (-8.3, -0.7)	**0.020**
UK	-7.9 (-12.3, -3.6)	**0.002**

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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

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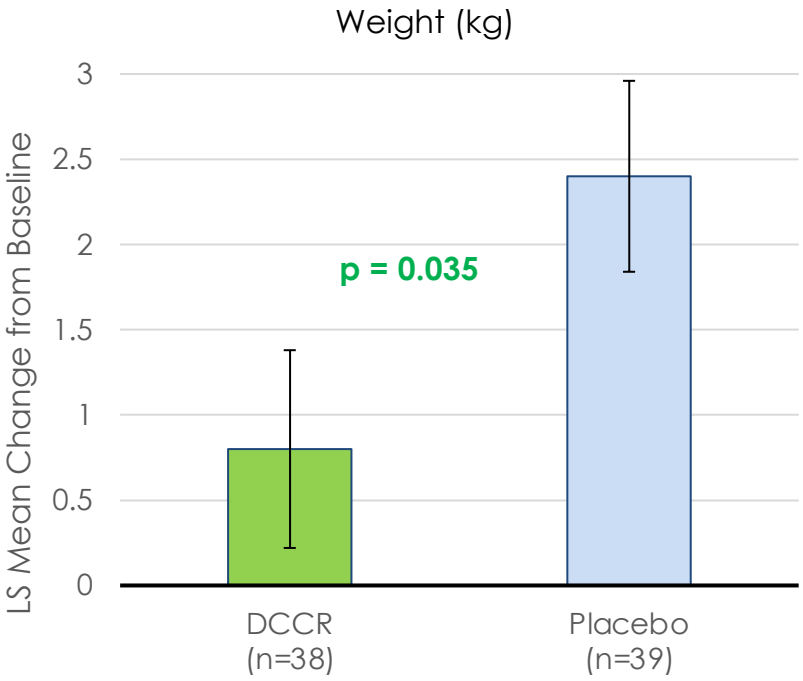
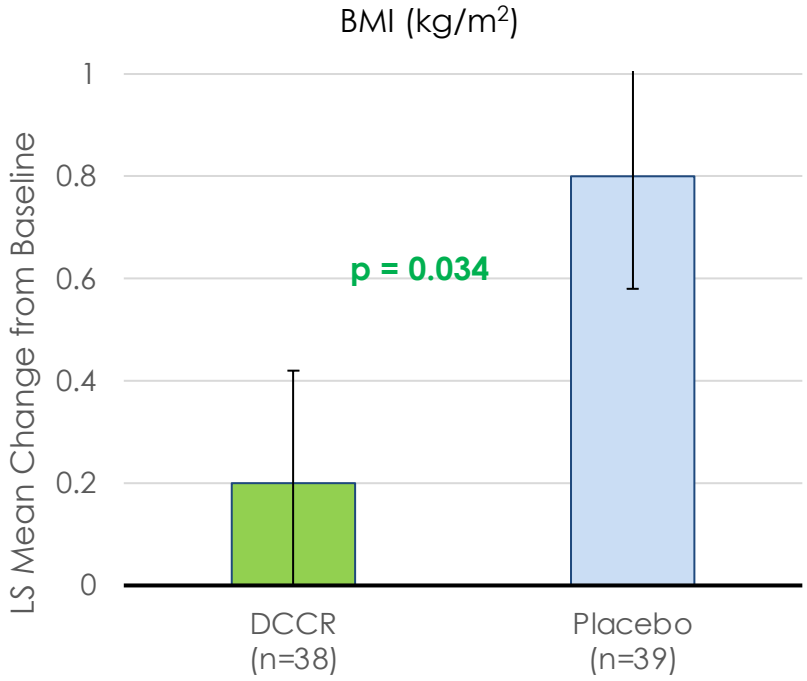
C602 RWP LSMean (SE) Changes from Baseline at Week 16 in Body Weight and BMI





C602 RWP Highly statistically significant change in primary endpoint supported by secondary and key objective endpoints

Primary Endpoint	Secondary Endpoints		Objective Endpoints	
HQ-CT Total Score	CGI-S	CGI-I	Body Weight (kg)	BMI (kg/m^2)
p = 0.0022	p = 0.079	p = 0.092	**p = 0.035**	**p = 0.034**

- Mean differences all PWS behavioral domains of the PWSP favored DCCR over placebo
- DCCR remained well tolerated with no new safety signals

CGI-S = Clinical Global Impression of Severity
CGI-I = Clinical Global Impression of Improvement

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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 FPWR and PWSA | USA-petition signed by 26,640 supporters requesting FDA regulatory flexibility for DCCR

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

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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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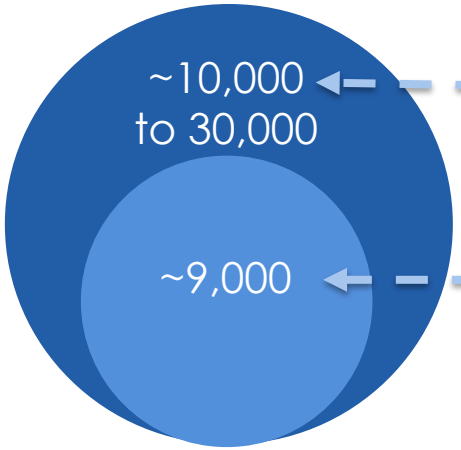
U.S. Market Opportunity and HCP Launch Landscape

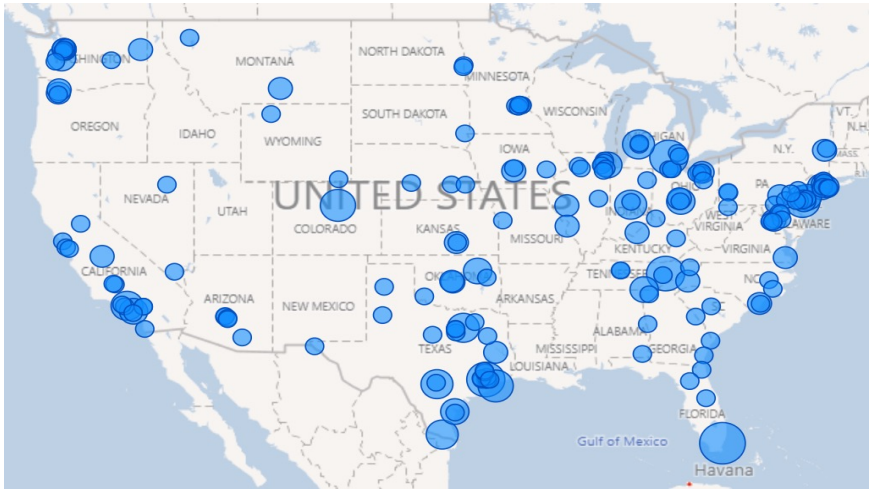
PWS Patient Opportunity



Based on estimate of 1 in 15,000 live births[1,2]

Est. U.S. Diagnosed[3]

Heatmap – Top 300 HCPs



[1] Driscoll DJ, et al., Prader-Willi Syndrome. 1998 Oct 6 [Updated 2023 Nov 2]. In: Adam MP, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1330/.

[2] Cassidy SB, et al., (2012). Prader-Willi syndrome. Genet. Med. 14(1): 10-26.

[3] McCandless SE, et al., (2020). SUN-604 U.S. Prevalence & Mortality of Prader-Willi Syndrome: A Population-Based Study of Medical Claims. Journal of the Endocrine Society 4(Supplement_1).

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Defining the PWS Market

	Pediatric Patients	Adult Patients
HCP Interactions	• The typical pediatric patient visits an HCP 6 times per year • Pediatric patients are most frequently seen by Ped and Adult Endos	• The typical adult patient visits an HCP 3 times per year • Adult patients are primarily seen by Adult Endocrinologists and Psychiatrists
Living Setting	• Pediatric patients primarily live with a caregiver at the caregivers home	• Adult patients live in Residential Homes, or with/near a caregiver

Source: Patient claims analysis conducted by ZS Associates.

Build commercial organization that will deliver at launch and in the future

1. **Build infrastructure to achieve efficient penetration at launch**
2. **Hire and deploy teams with rare disease experience**
3. **Design access strategy to secure rapid uptake of DCCR**
4. **Construct PWS centric patient support programs**

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Landmark Commercial Opportunity to Transform Lives of Patients with PWS

First-to-market treatment for hyperphagia in patients with PWS, if approved

Potential to significantly reduce hyperphagia and impact other PWS-related comorbidities

DCCR can become the foundational therapy for patients with PWS

Financial Highlights

Cash, cash equivalents and investments

Time	Cash
March 31, 2024	$158.4m
May 2023, 2024, Financing net proceeds	$148.8m
Total Pro Forma Cash	$307.2m

* Dec 2022 Tranche B warrants remaining to be exercised for a total of $16.5m

Fully Diluted Share Count

March 31, 2024	In Millions
Common stock	33.3
Pre-funded warrants	3.0
March 2022 – $4.50	1.8
May 2024 Tranche B - $2.50*	6.6
Options and RSUs	3.4
Total	**48.1**
May 2023	3.5
Pro Forma Total	**51.6**

Next Steps

NDA submission planned for mid-2024

Assessing regulatory path in the EU/UK

Continue commercialization planning and preparation

Continuing open-label DCCR in Study C614 for enrolled participants

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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June 2024 | Soleno Therapeutics