# Corporate Presentation

November 2023 | Soleno Therapeutics

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



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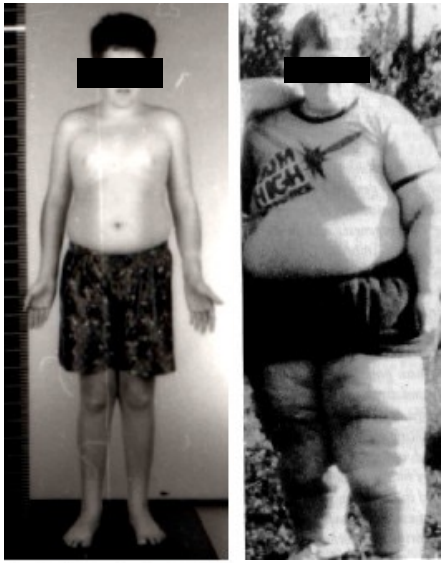
# Prader-Willi Syndrome (PWS)

- 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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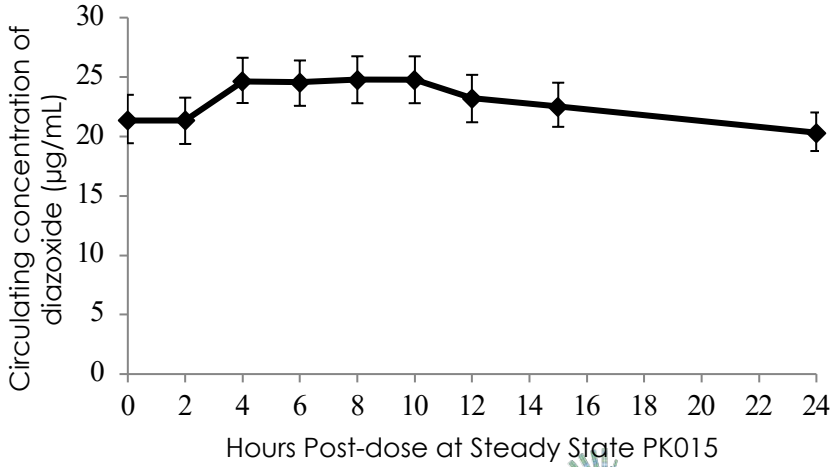
# DCCR Was Developed to Facilitate Once Daily Dosing and Improve Response

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

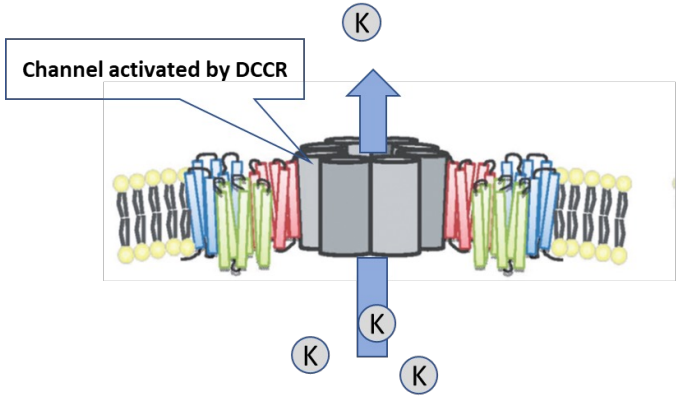
- Titration and dosing optimized to safely reach target dose and maintain therapeutic response

- 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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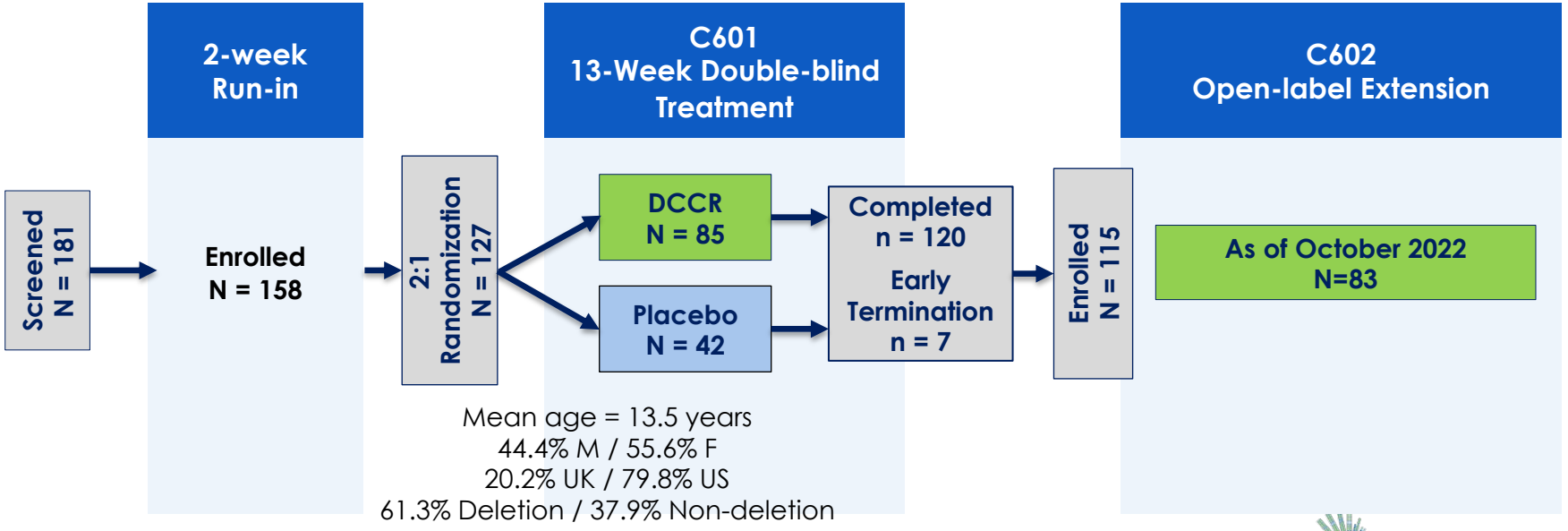
# DCCR Phase 3 Clinical Program Design

- 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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Long-term Data

# DCCR 12 MONTHS INTERIM RESULTS AND COMPARISON TO PATH FOR PWS

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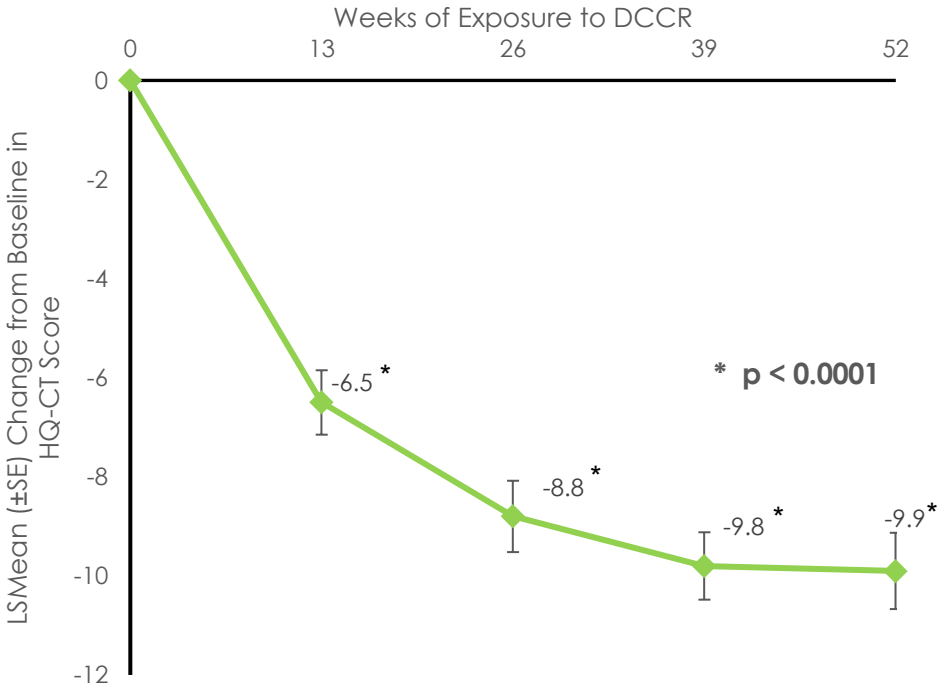
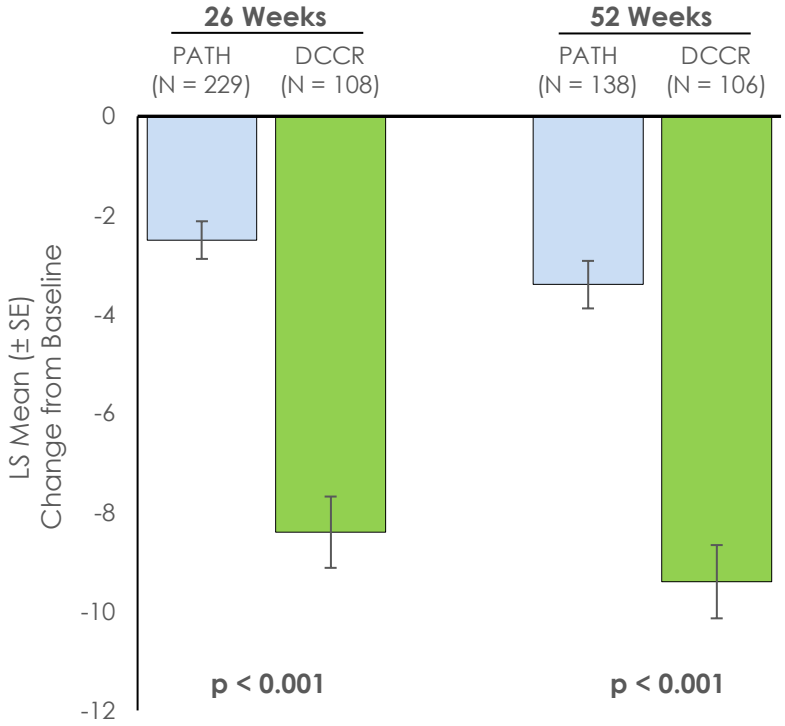
# C601/C602 Hyperphagia Change from Baseline



# 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, 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)
- No DCCR-related serious unexpected adverse events (SUSARs)



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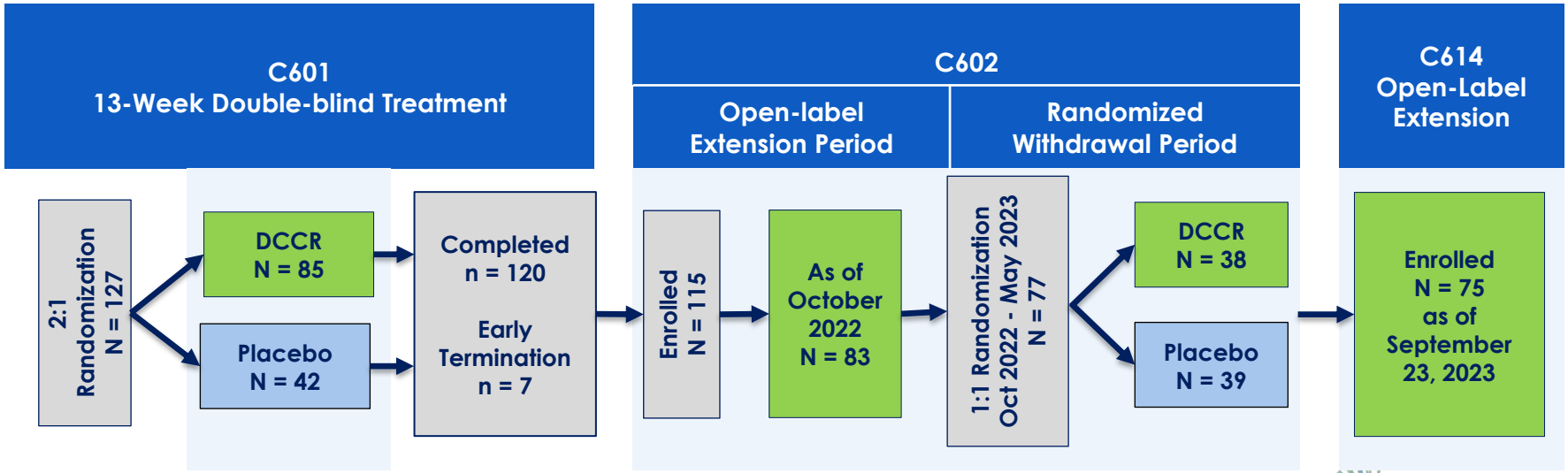
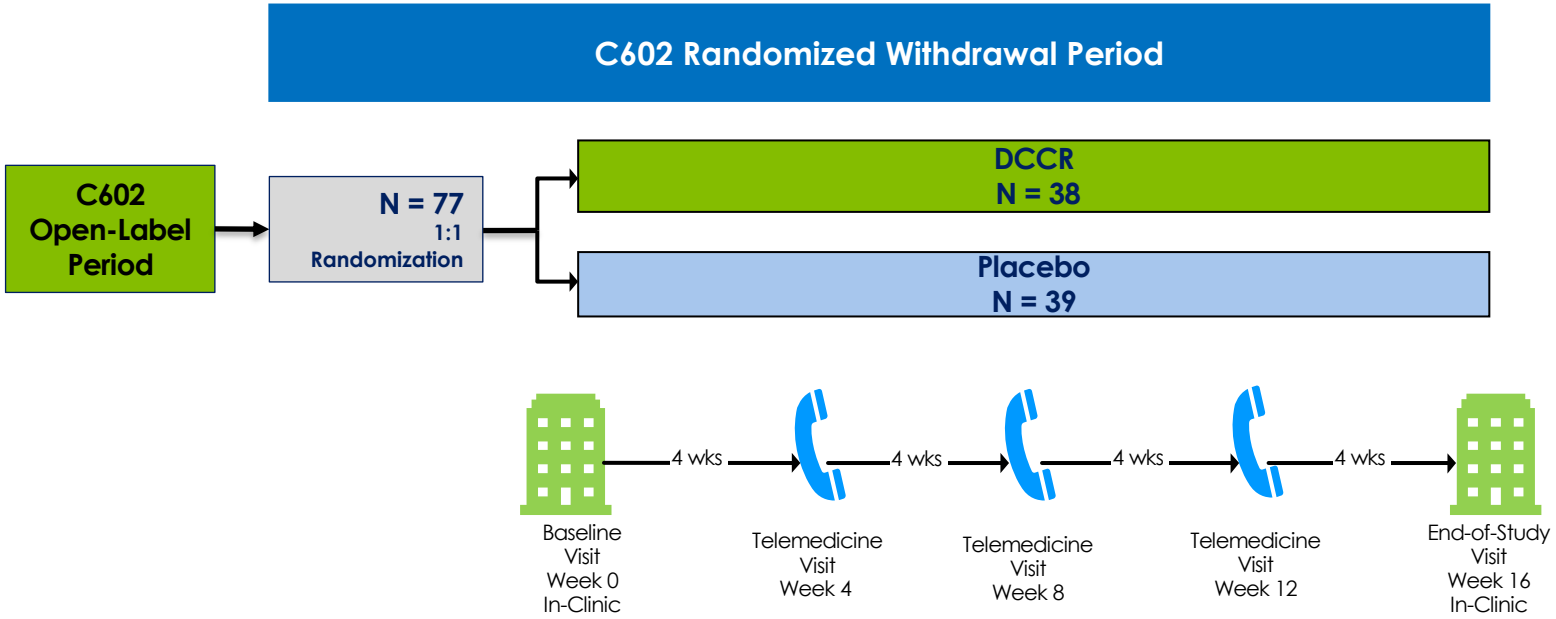
# DCCR Phase 3 Updated Clinical Program

- 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
  - Subjects currently enrolled in C602, no new subjects



# C602 Randomized Withdrawal Study Design



# 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 |



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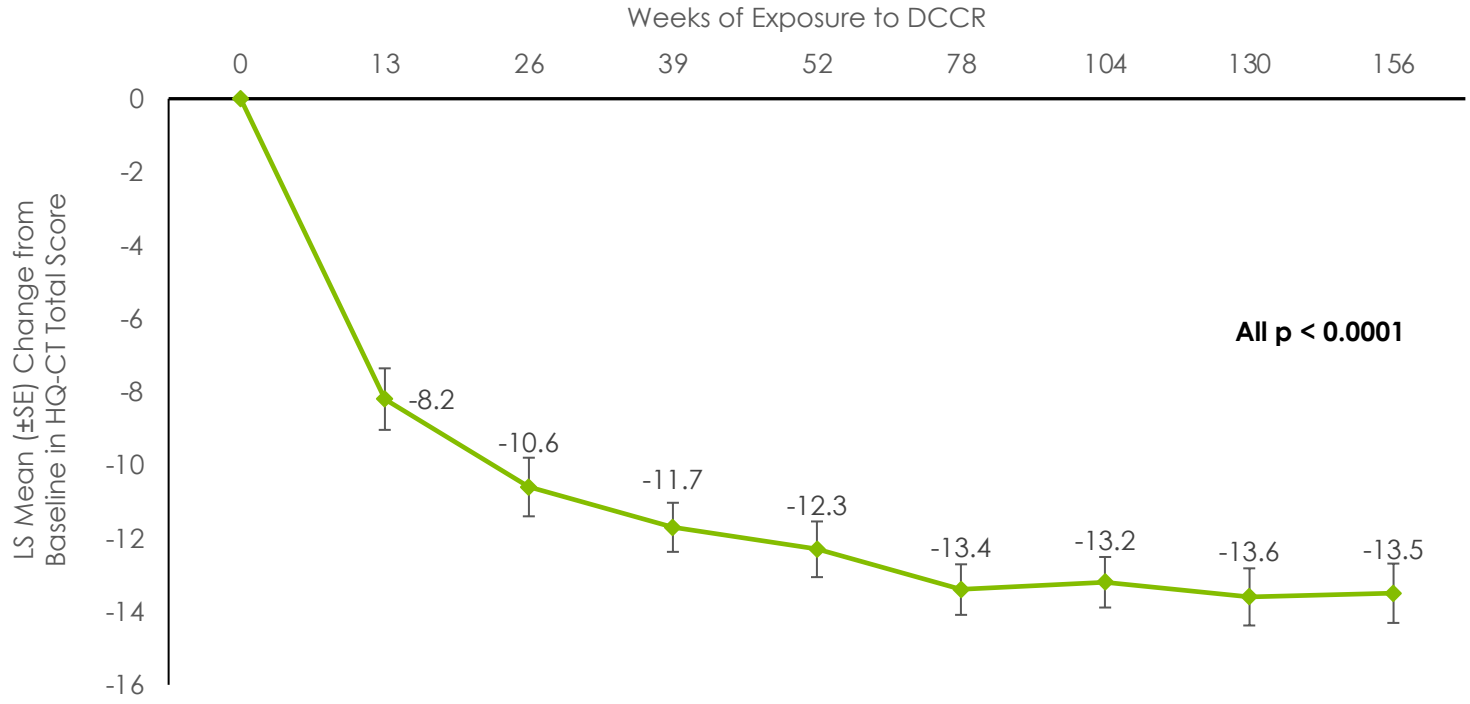
# C602 Long-term HQ-CT Change from Baseline Durable Response Over >2 years



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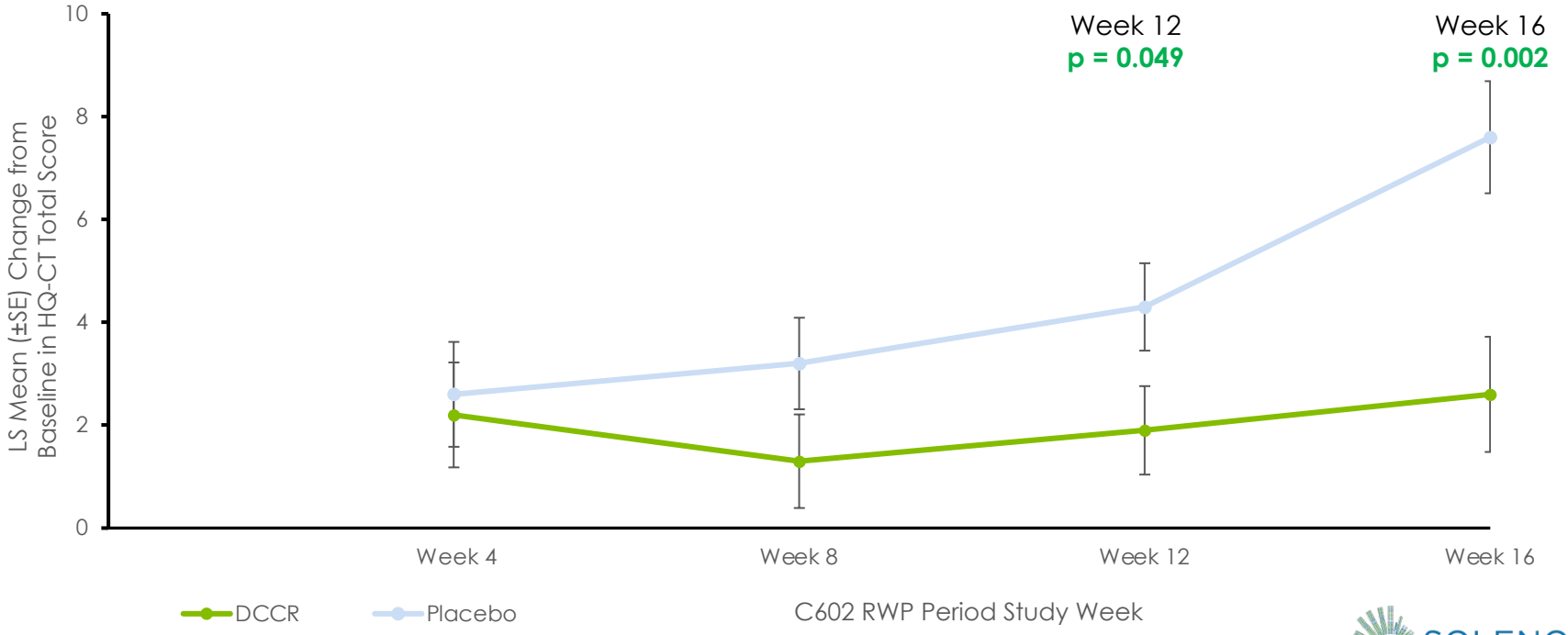
# C602 RWP HQ-CT Total Score at Week 16
## Change from Baseline for DCCR Compared to Placebo

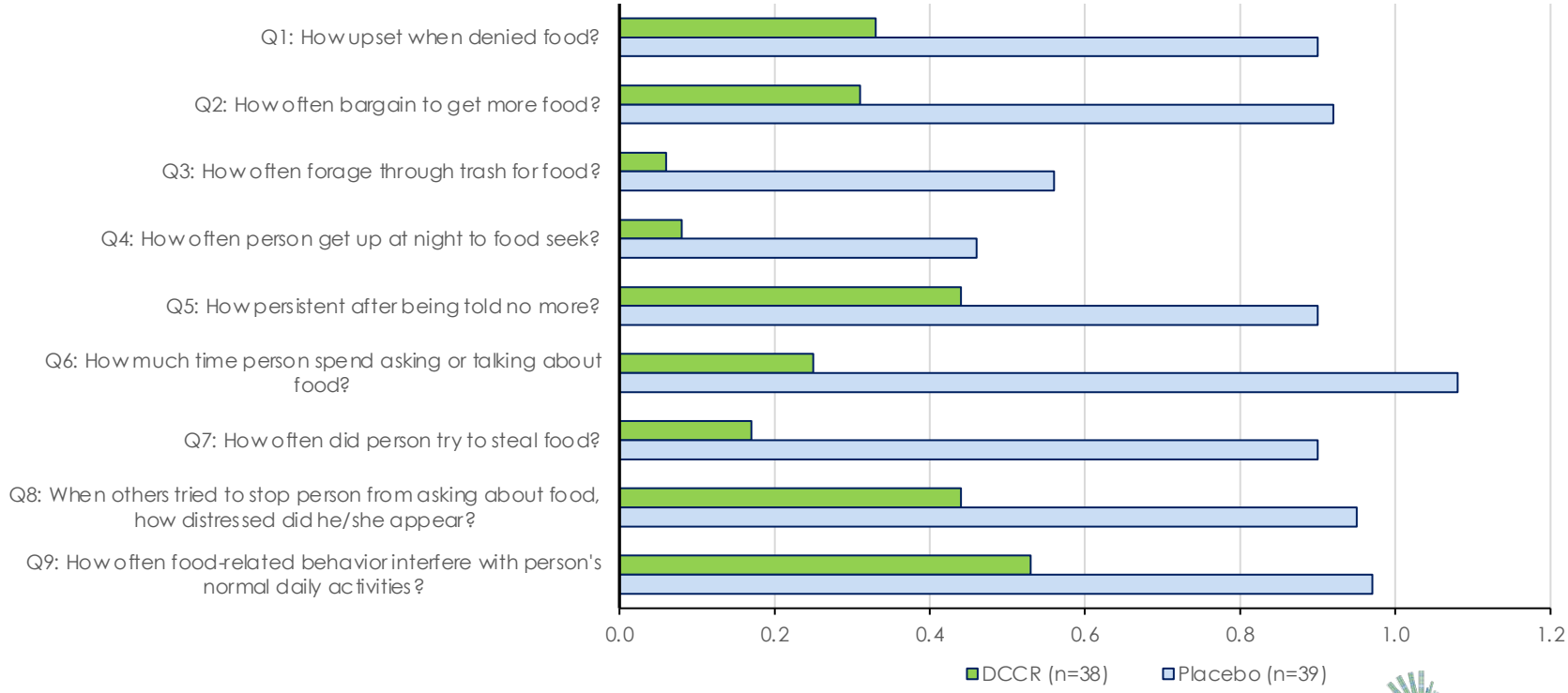
LS Mean change from baseline highly statistically significant at Week 16; also statistically significant at Week 12



# C602 RWP HQ-CT 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 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 |

# C602 RWP Behavioral Endpoints at Week 16
## 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

| Parameter | DCCR (N = 38) | Placebo (N = 39) | Difference (95% CI) | p-value |
|---|---|---|---|---|
| Body Weight (kg) | 0.8 (0.58) | 2.4 (0.56) | -1.6 (-3.1, -0.1) | **0.035** |
| BMI ($kg/m^2$) | 0.2 (0.22) | 0.8 (0.22) | -0.6 (-1.2, -0.1) | **0.034** |

# C602 RWP Safety Summary

No DCCR-related Serious TEAEs

No New Safety Signals

## Adverse Event Overview

| No. of subjects who experienced at least one: | DCCR N = 38 n (%) | Placebo N = 39 n (%) | All Subjects N = 77 n (%) |
|---|---|---|---|
| TEAE | 28 (73.7) | 29 (74.4) | 57 (74.0) |
| TEAE related to study drug | 7 (18.4) | 11 (28.2) | 18 (23.4) |
| TEAE leading to premature discontinuation of study drug | 0 | 0 | 0 |
| Serious TEAE (SAE) | 0 | 1 (2.6) | 1 (1.3) |
| SAE related to study drug or leading to death | 0 | 0 | 0 |

## TEAEs – Most Frequent

| Preferred Term | DCCR N = 38 n (%) | Placebo N = 39 n (%) | All Subjects N = 77 n (%) |
|---|---|---|---|
| Dermatillomania | 5 (13.2) | 6 (15.4) | 11 (14.3) |
| Abnormal behavior | 5 (13.2) | 5 (12.8) | 10 (13.0) |
| Aggression | 3 (7.9) | 5 (12.8) | 8 (10.4) |
| Hypertrichosis | 2 (5.3) | 5 (12.8) | 7 (9.1) |
| Food craving | 3 (7.9) | 4 (10.3) | 7 (9.1) |



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# 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 (i.e., aggressive behaviors, anxiety, rigidity/ irritability, compulsivity, depression, and disordered thinking) favored DCCR over placebo

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 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 to treat PWS

Specific claims to behavioral and body composition changes in response to DCCR treatment

- Extensive protection of diazoxide choline, DCCR formulation and use, method of manufacture, treatment of PWS and more generally, in syndromic obesity expiring 2025 - 2035



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# Financial Highlights

## Pro Forma Cash

| Time | Cash |
|---|---|
| Sept 30, 2023* | $52.4m |
| Pro forma Sept 30, 2023** | $173.9m |
| FDA approval*** | + $17.5m |

* As per Q3 10Q
** Includes additional net proceeds from Closing of Oct 2023 financing and Dec 2022 financing
*** Additional $17.5m due upon FDA approval

## Oct 2023 Financing

- $69.0m gross proceeds from public offering and $60.0m concurrent private offering
- $16m included in Sept 30, 2023, cash balance

## Dec 2022 Financing

- $60m commitment – Tranche A and B warrants
- $42.5m received to date
- $17.5m after FDA approval - Tranche B 7m shares remaining at $2.50

# Next Steps

- Continue open-label DCCR in Study C614 for eligible participants
- Continue NDA preparations
  - Likely timing for submission ~mid-2024 (TBD)
- Product manufacturing process validation
- Continue commercialization planning and preparation

 

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# 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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November 2023 | Soleno Therapeutics