# Corporate Presentation

March 2024 | Soleno Therapeutics

# Certain Notices and Disclaimers

## Forward-Looking Statements

This presentation contains forward-looking statements that are subject to many risks and uncertainties. Forward-looking statements appear in a number of places throughout this presentation and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned product development and clinical trials; the timing of, and our ability to make, regulatory filings and obtain and maintain regulatory approvals for our product candidates; our intellectual property position; the degree of clinical utility of our products, particularly in specific patient populations; our ability to develop commercial functions; expectations regarding product launch and revenue; our results of operations, cash needs, and spending of the proceeds from this offering; financial condition, liquidity, prospects, growth and strategies; the industry in which we operate; and the trends that may affect the industry or us.

We may, in some cases, use terms such as "believes," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should," "approximately" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this presentation, we caution you that forward-looking statements are not guarantees of future performance and that our actual results of operations, financial condition and liquidity, and the development of the industry in which we operate may differ materially from the forward-looking statements contained in this presentation.

You should also read carefully the factors described in the "Risk Factors" sections and other parts of our Annual Reports on Form 10-K and Quarterly Reports on Form 10-Q, available at www.sec.gov, in order to better understand the risks and uncertainties inherent in our business and underlying any forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this presentation will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all. Any forward-looking statements that we make in this presentation speak only as of the date of such statement, and we undertake no obligation to update such statements to reflect events or circumstances after the date of this presentation or to reflect the occurrence of unanticipated events.

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



SOLENO THERAPEUTICS

# 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

**Orphan Drug and Fast Track Designations for PWS**

**Orphan designation in US and EU. 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**

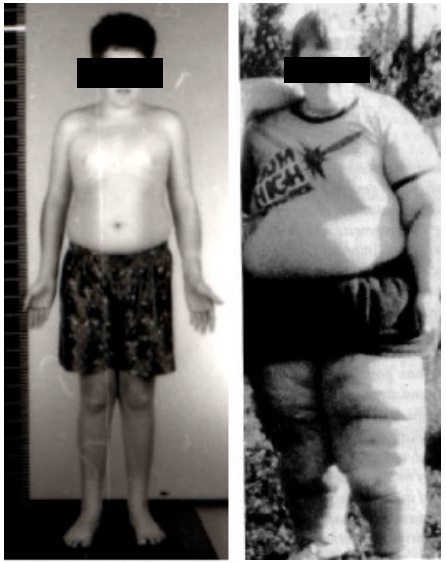
**Cash runway extends beyond potential launch of DCCR**

Oct 2023 ~$170M financing

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

# 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.*

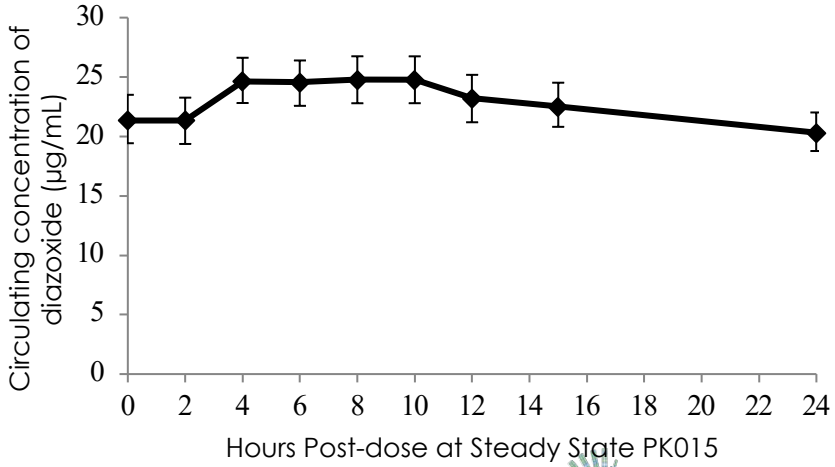
SOLENO THERAPEUTICS

# 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

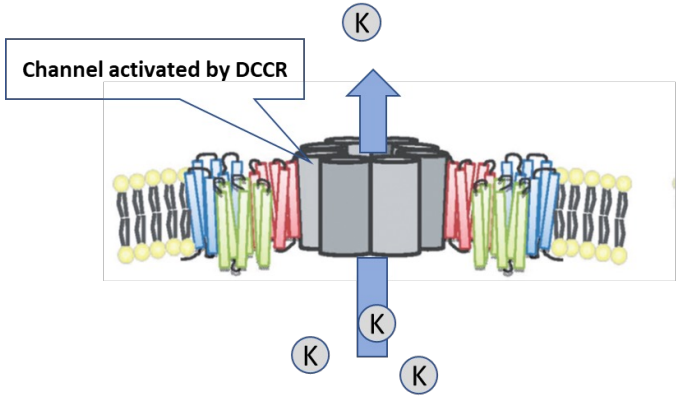
- Titration and dosing optimized to safely reach target dose and maintain therapeutic response

- 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

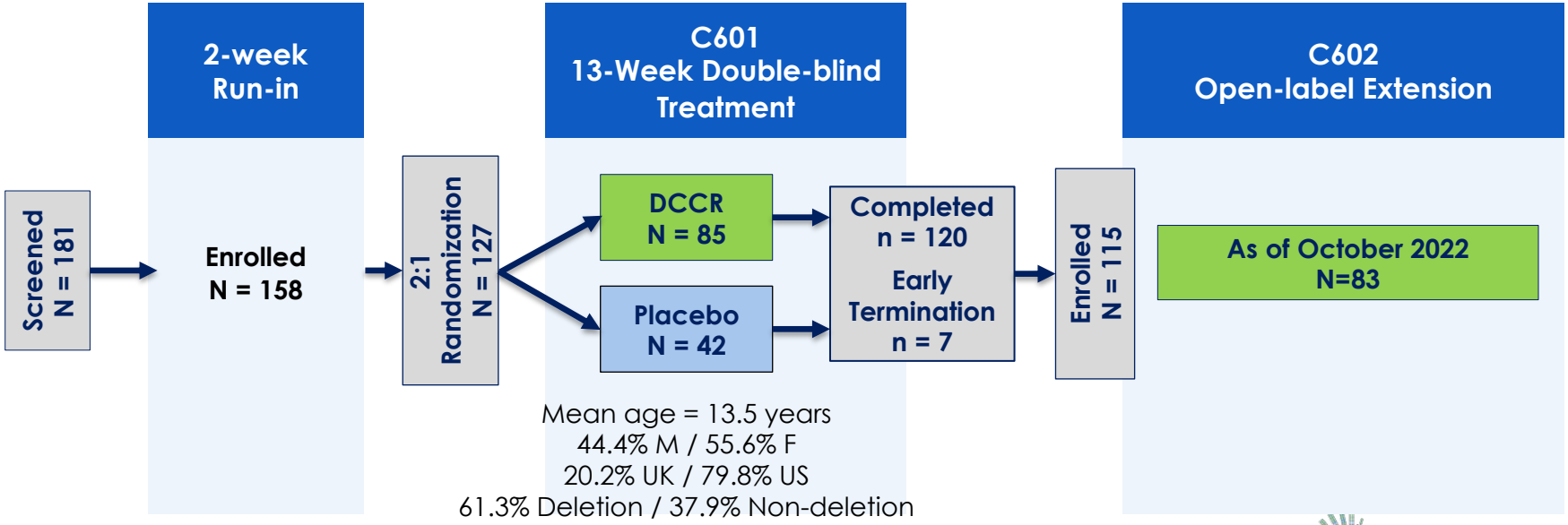
*Genes*, 11(4), 450. https://doi.org/10.3390/genes11040450.



SOLENO THERAPEUTICS

# 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** | |



SOLENO THERAPEUTICS

# C601 Behavioral Endpoints

| 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** |
| **DBC-2** | |
| Total Score | **0.009** |
| Communication Disturbance | **0.003** |
| Social Relating | **0.008** |

*Observed values through March 1, 2020*

SOLENO THERAPEUTICS

# C601 Key Hormonal and Metabolic Markers

| Change from Baseline at Week 13 | DCCR vs Placebo p-value |
|---|---|
| Decreased Acylated Ghrelin (active form) | **0.0182** |
| Decreased Leptin | **<0.0001** |
| Decreased Insulin | **0.0110** |
| Increased Adiponectin | **<0.0001** |

Long-term Data

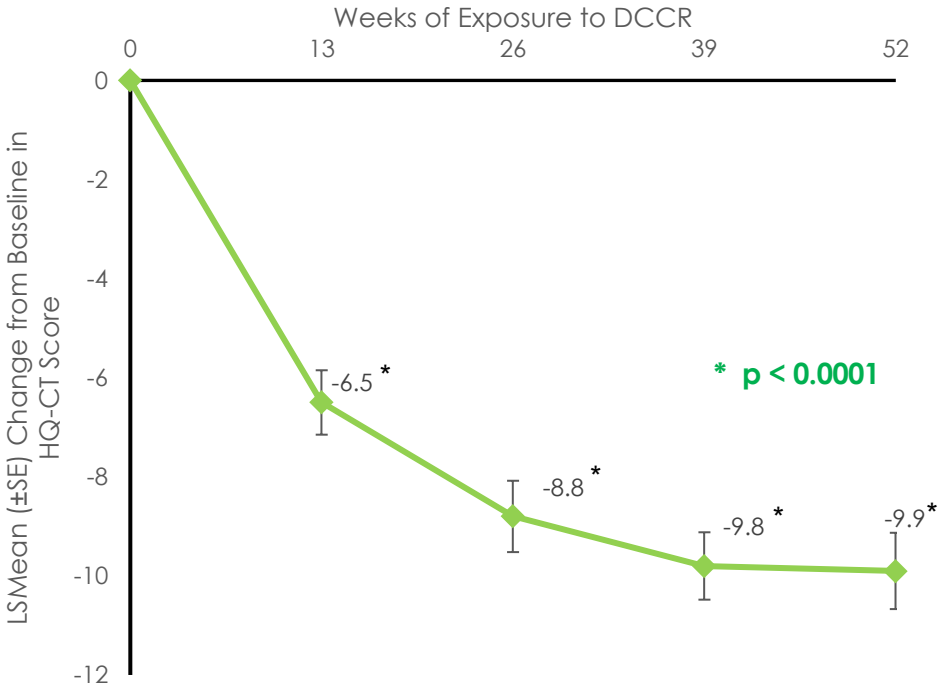
# DCCR 12 MONTHS INTERIM RESULTS AND COMPARISON TO PATH FOR PWS

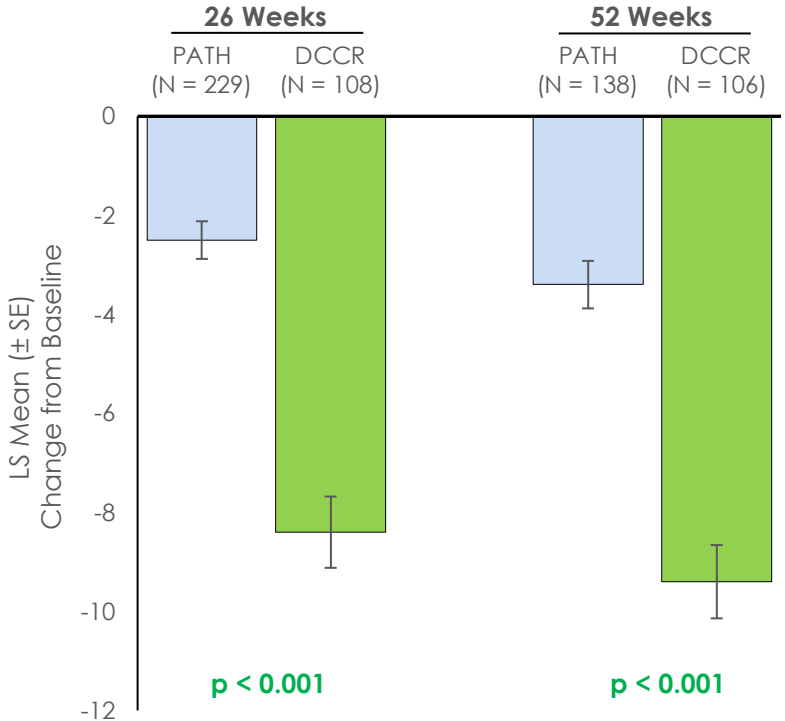
SOLENO THERAPEUTICS

# 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



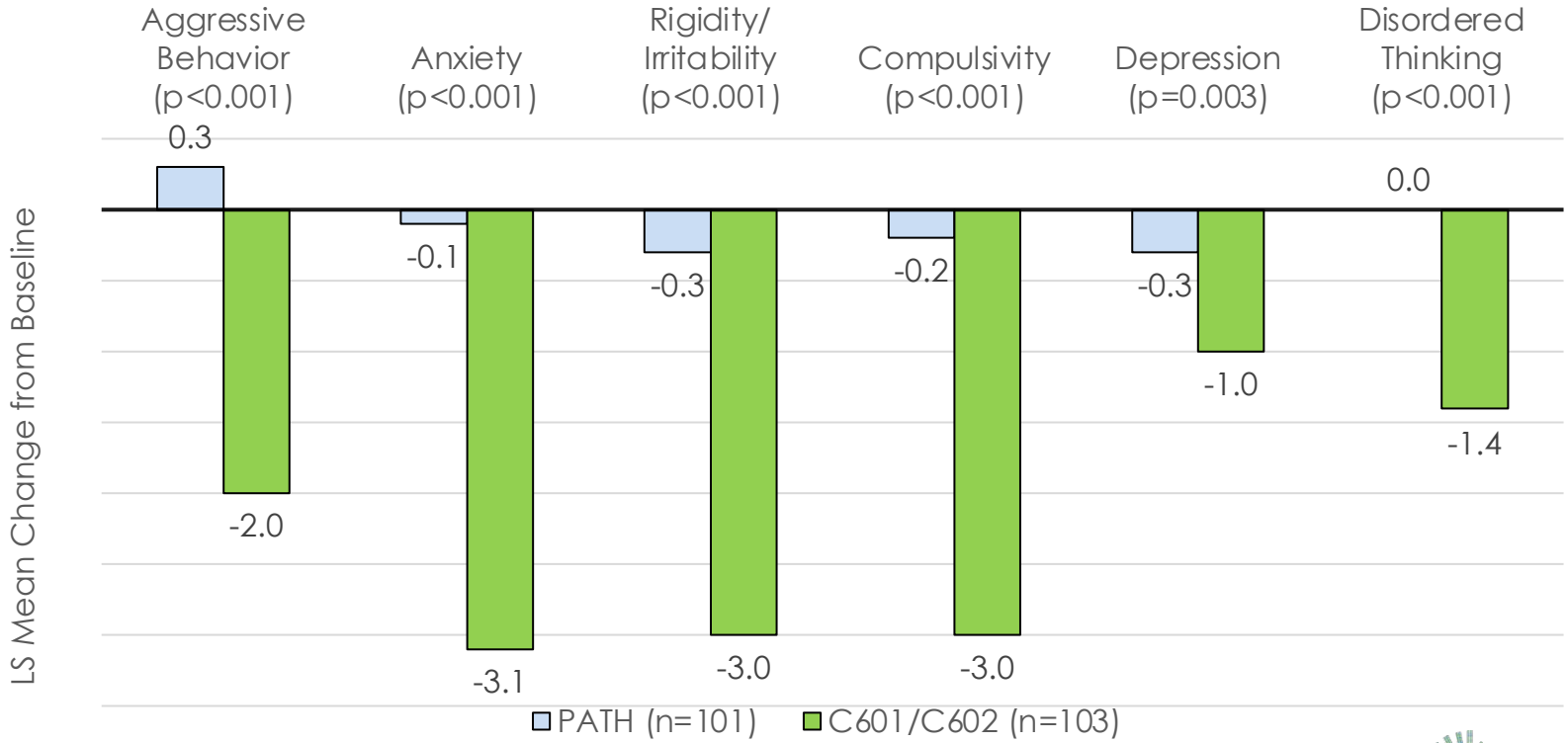
# C601/C602 PWS Profile Behavioral Change Results after One Year of DCCR

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



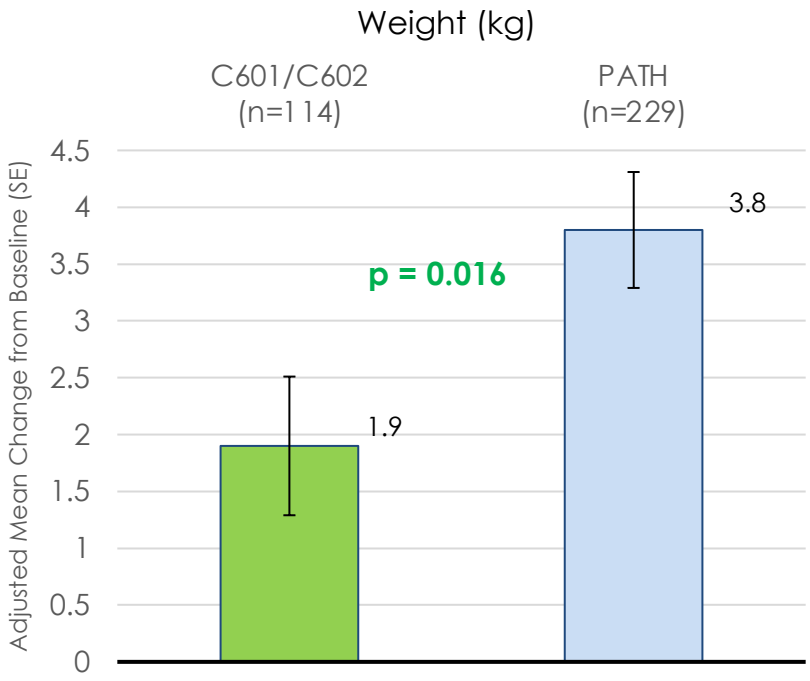
SOLENO THERAPEUTICS

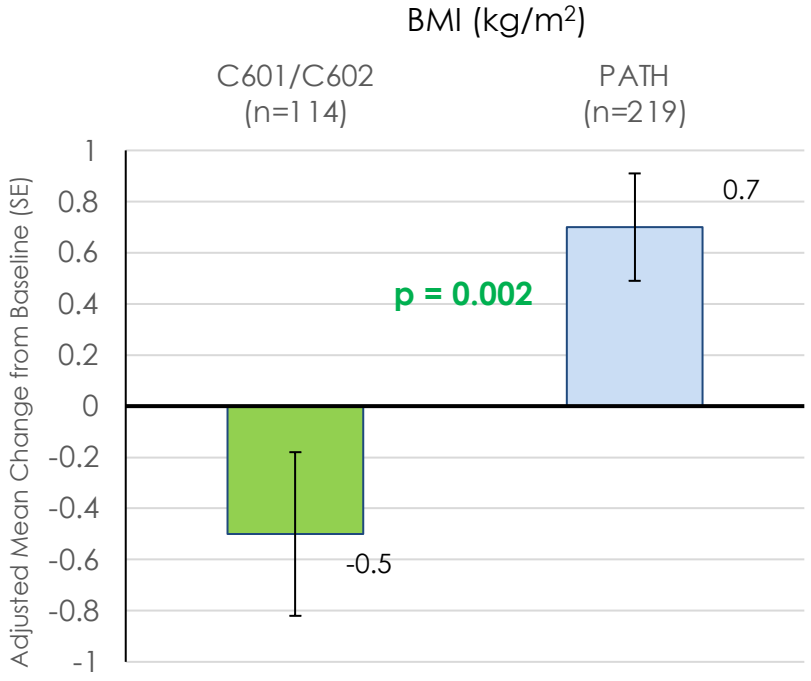
# C601/C602 Comparison to PATH – LS Mean Change in Behaviors from Baseline at Week 52



# 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** |



SOLENO THERAPEUTICS

# DCCR Safety Profile

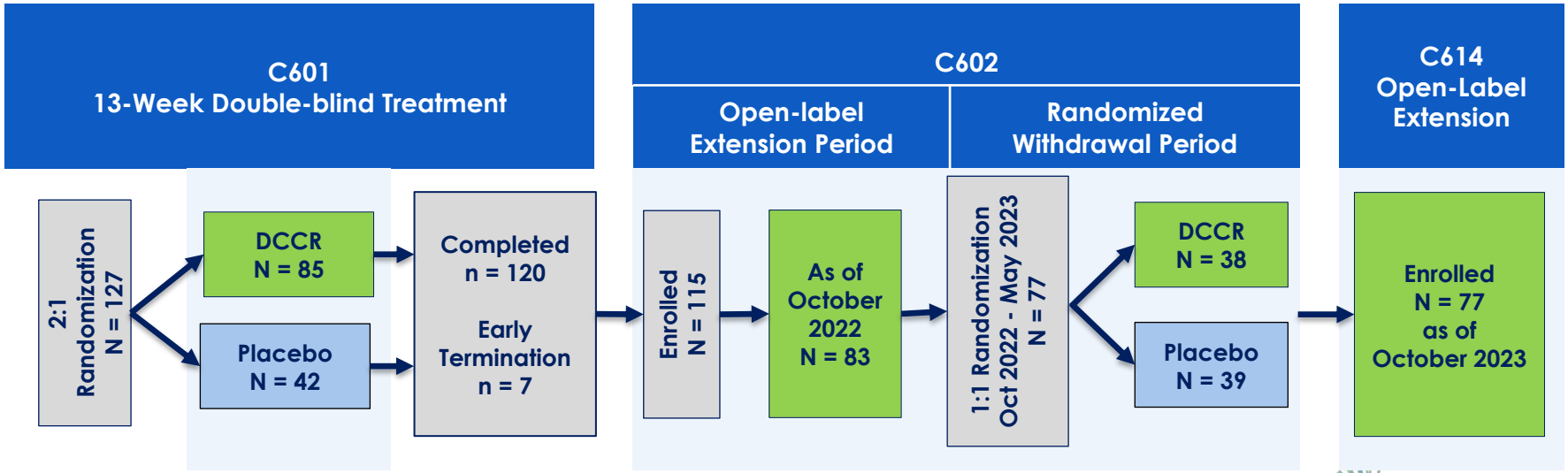
- ~100 patients treated for more than one year
- Safety profile generally consistent with prior experience with DCCR and the known profile of diazoxide
- The most common adverse events reported were hypertrichosis/hirsutism, peripheral edema and hyperglycemia
- Most events were Grade 1 or 2 in severity, 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



SOLENO THERAPEUTICS

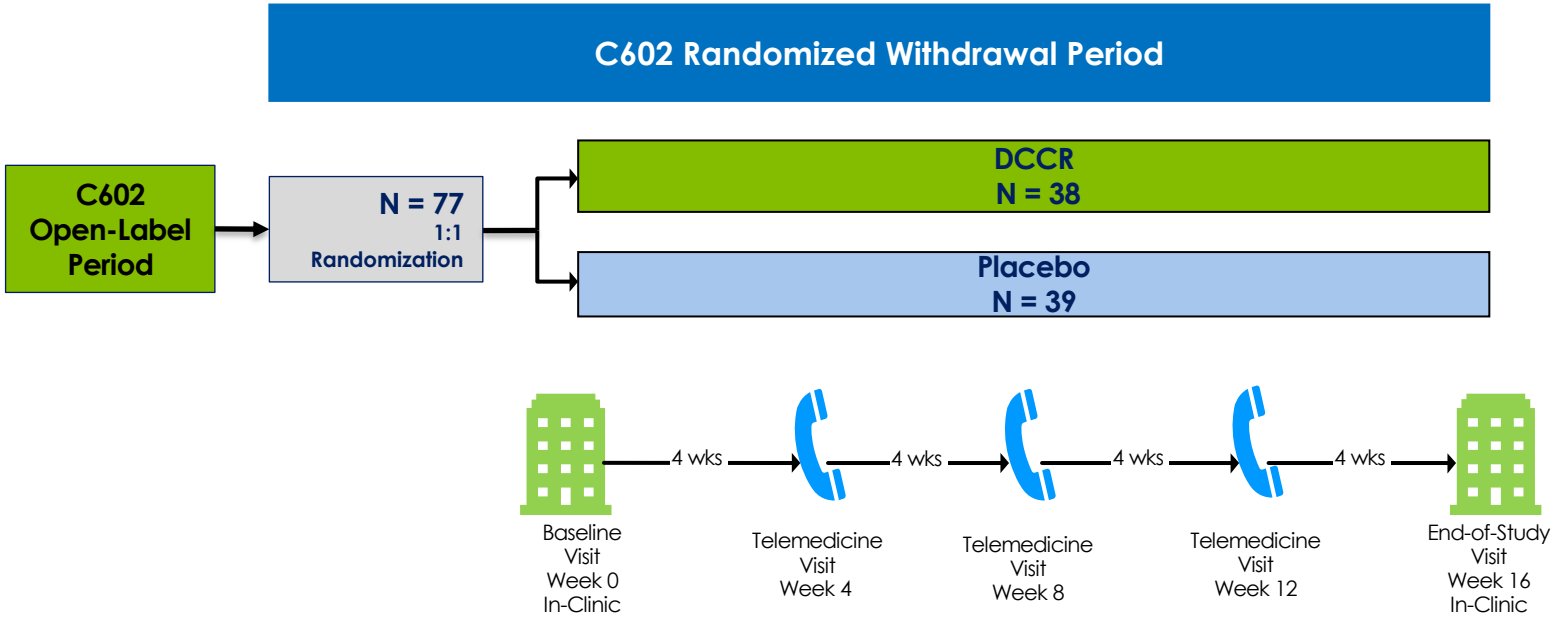
# DCCR Phase 3 Updated Clinical Program

- 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 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 |



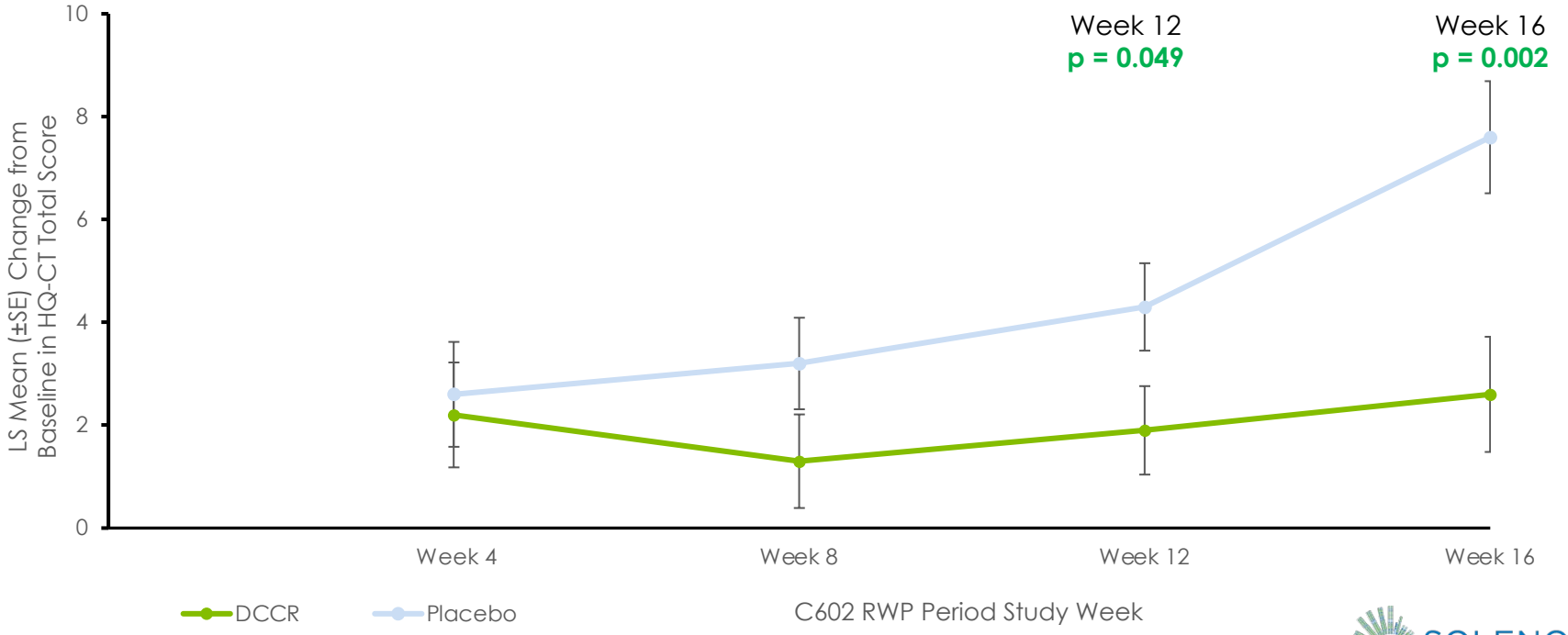
SOLENO THERAPEUTICS

# 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** |

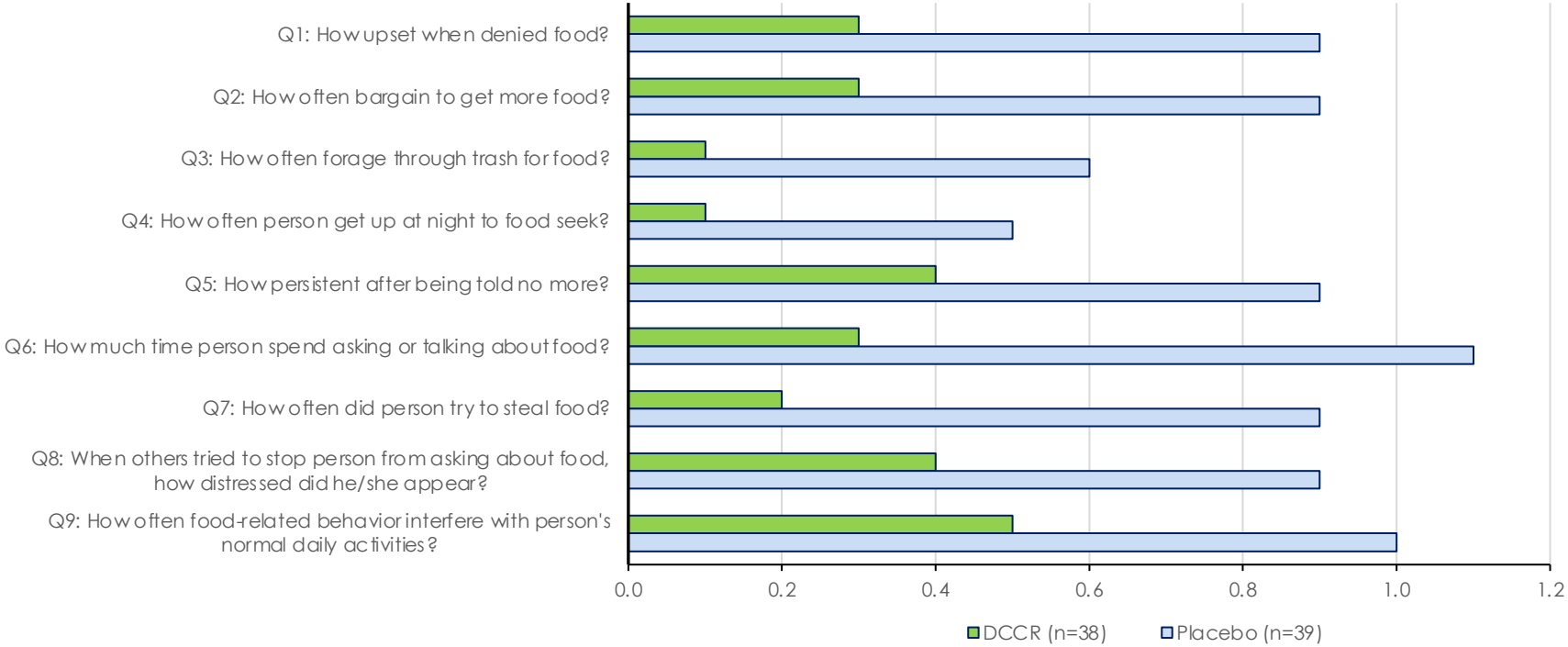
# C602 RWP HQ-CT Total Score at Week 16
## Change from Baseline for DCCR Compared to Placebo

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** |

SOLENO THERAPEUTICS

# 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 |

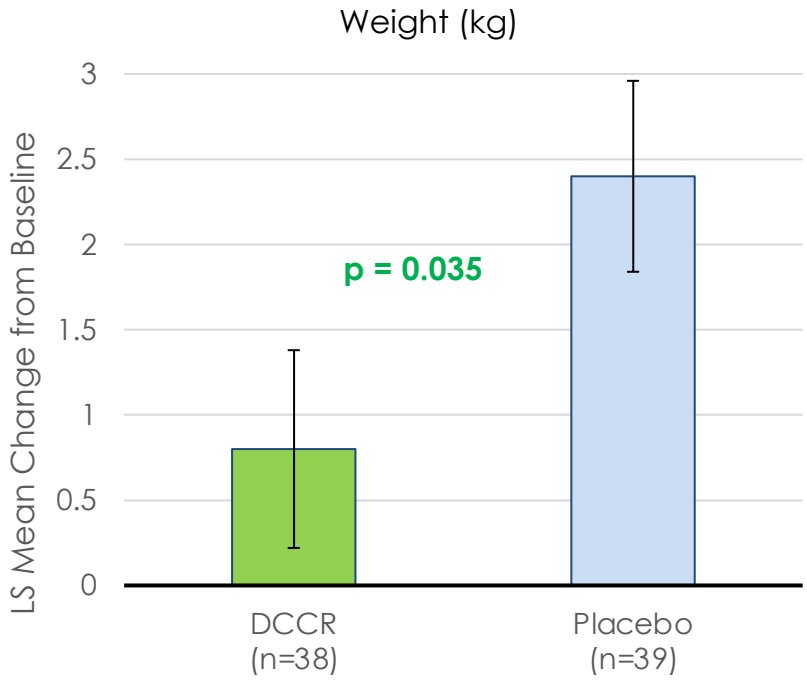
SOLENO THERAPEUTICS

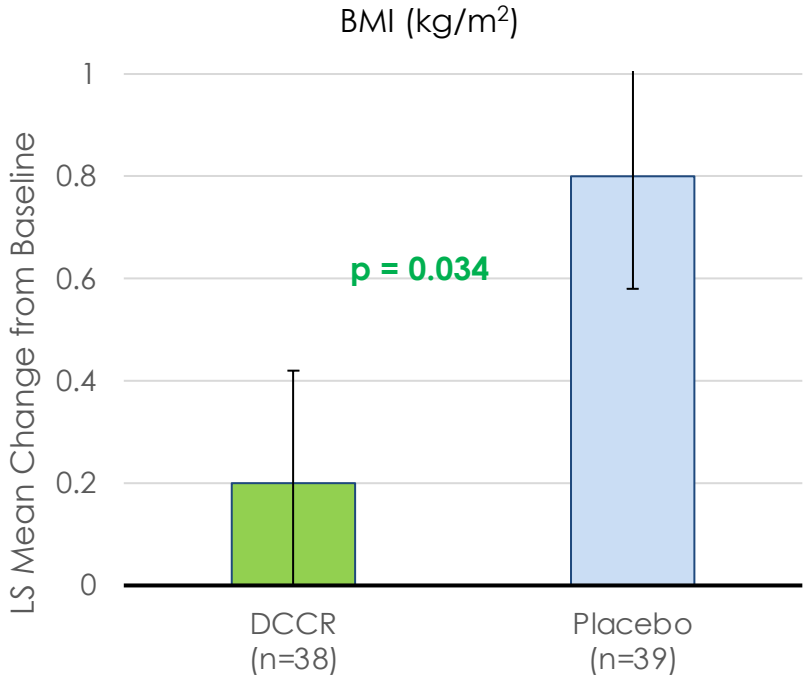
# C602 RWP Behavioral Endpoints at Week 16
## All PWSP Domains Trending in Favor of DCCR

| 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



# C602 RWP Safety Summary

## DCCR remains well-tolerated with no new safety signals upon randomized withdrawal

- **No SAEs** in DCCR arm (1 SAE in placebo arm)
- **No discontinuations** due to AEs
- Most AEs were **Grade 1 or 2**

## TEAEs – Most Frequent

| Preferred Term | DCCR N = 38 n (%) | Placebo N = 39 n (%) | All Subjects N = 77 n (%) |
|---|---|---|---|
| **Any TEAE** | **28 (73.7)** | **29 (74.4)** | **57 (74.0)** |
| 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) |



SOLENO THERAPEUTICS

# 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



SOLENO THERAPEUTICS

# 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



SOLENO THERAPEUTICS

# 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

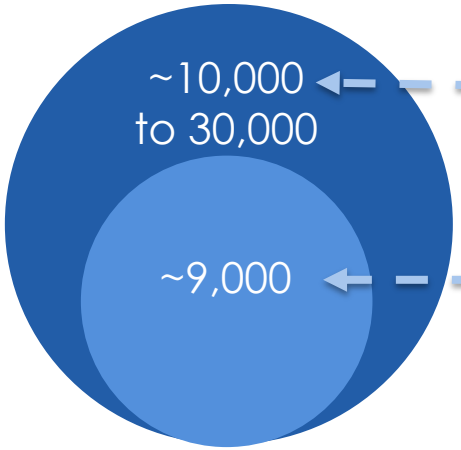
Potential expiration w/PTE 2038/2039



SOLENO THERAPEUTICS

# U.S. Market Opportunity and HCP Launch Landscape

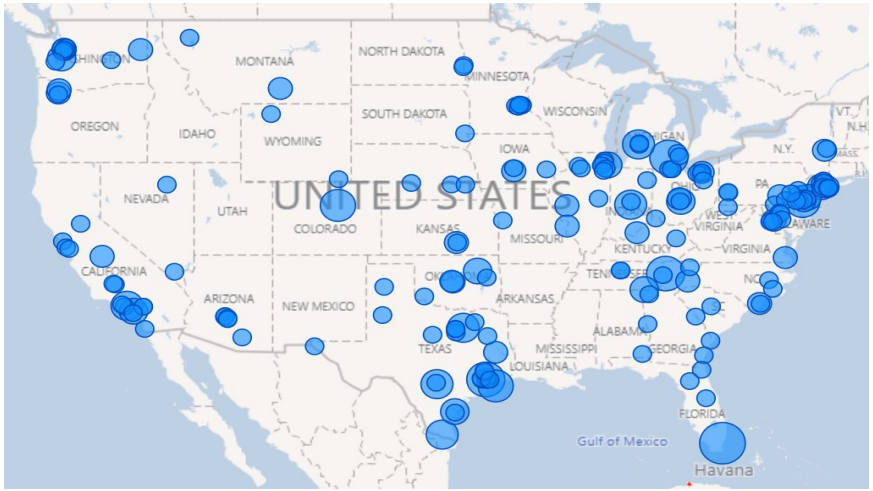
## PWS Patient Opportunity




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).



SOLENO THERAPEUTICS

# 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

# 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**

# Financial Highlights

## Cash

| Time | Cash |
|---|---|
| Dec 31, 2023 | $169.7m |
| FDA approval | + $16.9m |

Cash runway extends beyond potential launch of DCCR

## Fully Diluted Share Count

| December 31, 2023 | In Millions |
|---|---|
| Common stock | 31.7 |
| Pre-funded warrants | 4.3 |
| March 2022 – $4.50 | 1.9 |
| May 2024 Tranche B - $2.50 | 6.8 |
| Options and RSUs | 2.4 |
| Total | 47.1 |

# Next Steps

NDA preparations

- Regulatory Update expected 1Q2024
- NDA submission currently planned for mid-2024

Product manufacturing process validation underway

Continue commercialization planning and preparation

- Building commercial infrastructure
- Market Assessment, Claims Analysis, Payor Advisory Board underway

Continuing open-label DCCR in Study C614 for enrolled participants



SOLENO THERAPEUTICS

# 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*

SOLENO THERAPEUTICS

# Corporate Presentation

March 2024 | Soleno Therapeutics