Soleno Therapeutics Announces Peer-Reviewed Publication of Results from Long-Term Open-Label Study of DCCR in Prader-Willi Syndrome

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One-Year Administration of DCCR in PWS Patients from DESTINY-PWS Demonstrates Significant Improvements in Hyperphagia and Other Behavioral Complications

REDWOOD CITY, Calif., Nov. 06, 2023 (GLOBE NEWSWIRE) -- Soleno Therapeutics, Inc. ("Soleno") (NASDAQ: SLNO), a clinical-stage biopharmaceutical company developing novel therapeutics for the treatment of rare diseases, today announced publication of one-year results from the Phase 3 DESTINY PWS study and the open-label extension period of Study C602 evaluating investigational, once-daily DCCR (Diazoxide Choline) Extended-Release tablets for patients with Prader-Willi syndrome (PWS). The paper, entitled "Diazoxide Choline Extended-Release Tablet in People with Prader-Willi Syndrome: Results from Long-Term Open-Label Study," was published in the peer-reviewed journal *Obesity* and can be found online here.

"We are pleased to publish results from the long-term study of DCCR demonstrating significant, sustained reductions in hyperphagia," said Anish Bhatnagar, M.D., Chief Executive Officer of Soleno Therapeutics. "Together with positive results from our recently completed randomized withdrawal period of Study C602, DCCR has shown significant and clinically meaningful benefits for the most burdensome symptoms of PWS. We believe it has the potential to be a safe and effective therapy for patients with PWS. We anticipate submitting an NDA to the FDA for DCCR in mid-2024."

The publication features results from 52-week administration of DCCR in participants with PWS enrolled in DESTINY PWS and/or Study C602, the long-term open-label extension study of participants who completed DESTINY PWS. The primary efficacy endpoint was change in hyperphagia total score from baseline, as measured using the Hyperphagia Questionnaire for Clinical Trials (HQ-CT). Other endpoints included behavioral assessments using the PWS Profile Questionnaire (PWSP), body composition, hormonal and metabolic measures, disease severity and safety.

Key Highlights from the Publication:

Primary Endpoint: Hyperphagia

- Statistically significant, clinically meaningful decreases in HQ-CT total score (mean [SE]) from baseline in overall population after receiving DCCR for 52 weeks (-9.9 [0.77]; p<0.0001).
- Highly significant, clinically meaningful decreases in HQ-CT total score from baseline were also observed after receiving DCCR for 13, 26, and 39 weeks (all p<0.0001).
- In participants with severe hyperphagia at baseline, 52-week DCCR treatment resulted in significantly greater reduction in HQ-CT score compared to the overall population (-15.2 [1.39]; p<0.0001).

Other Endpoints

- **PWS related behaviors:** Statistically significant improvements in all behavioral domains of the PWSP, which consist of aggressive behaviors, anxiety, compulsivity, depression, disordered thinking, and rigidity/irritability (all p<0.0001).
- **Body composition:** Significant improvements in lean body mass:fat mass ratio were seen (p=0.0005), consistent with increases in lean body mass (p<0.0001) and no significant changes in body fat mass.
- **Hormonal and metabolic measures:** Significant reductions in serum leptin (p<0.0001) and insulin (p=0.0004) and improvement in Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) (p=0.0033), consistent with the proposed mechanism of action of DCCR in PWS. In addition, a significant increase in adiponectin was observed (p<0.0001).
- **Disease severity:** Significant reduction in disease severity as assessed by both clinicians and caregivers using Clinical Global Impression of Severity and Caregiver Global Impression of Severity scores, respectively (both p<0.0001).
- **Safety:** DCCR was well-tolerated overall. Safety results are consistent with the safety profile of DCCR, with the most common drug-related treatment-emergent adverse events of hypertrichosis, peripheral edema, and hyperglycemia, the majority of which were grade 1 and infrequently resulting in study drug discontinuation.

DCCR has orphan designation for the treatment of PWS in the U.S. and EU and Fast Track designation from the U.S. FDA. Soleno recently announced positive topline results from its randomized withdrawal phase of Study C602. The U.S. Food and Drug Administration (FDA) previously acknowledged that data from this study has the potential to support an NDA submission for DCCR. Soleno anticipates submission of an NDA to the FDA in mid-2024.

About PWS
The Prader-Willi Syndrome Association USA estimates that PWS occurs in one in every 15,000 live births in the U.S. The hallmark symptom of this disorder is hyperphagia, a chronic feeling of insatiable hunger that severely diminishes the quality of life for PWS patients and their families. Additional characteristics of PWS include behavioral problems, cognitive disabilities, low muscle tone, short stature (when not treated with growth hormone), the accumulation of excess body fat, developmental delays, and incomplete sexual development. Hyperphagia can lead to significant morbidities (e.g., obesity, diabetes, cardiovascular disease) and mortality (e.g., stomach rupture, choking, accidental death due to food seeking behavior). In a global survey conducted by the Foundation for Prader-Willi Research, 96.5% of respondents (parent and caregivers) rated hyperphagia and 92.9% rated body composition as either the most important or a very important symptom to be relieved by a new medicine. There are currently no approved

therapies to treat the hyperphagia/appetite, metabolic, cognitive function, or behavioral aspects of the disorder. Diazoxide choline has received Orphan Drug Designation for the treatment of PWS in the U.S. and E.U., and Fast Track Designation in the U.S.

About DCCR (Diazoxide Choline) Extended-Release Tablets
DCCR is a novel, proprietary extended-release dosage form containing the crystalline salt of diazoxide and is administered once-daily. The parent molecule, diazoxide, has been used for decades in thousands of patients in a few rare diseases in neonates, infants, children and adults, but has not been approved for use in PWS. Soleno conceived of and established extensive patent protection on the therapeutic use of diazoxide and DCCR in patients with PWS. The DCCR development program is supported by data from five completed Phase 1 clinical studies in healthy volunteers and three completed Phase 2 clinical studies, one of which was in patients with PWS. In the Phase 3 DESTINY PWS study, DCCR showed promise in addressing hyperphagia, the hallmark symptom of PWS, as well as several other symptoms such as aggressive/destructive behaviors, fat mass and other metabolic parameters. After one-year of open-label DCCR, participants experienced significant, clinically meaningful reductions from baseline in hyperphagia and other common PWS behaviors. In a randomized withdrawal period of Study C602, participants who were randomized to placebo had highly statistically significant increases from baseline in HQ-CT total score compared to those randomized to continue on DCCR ($p = 0.0022$).

About Soleno Therapeutics, Inc.
Soleno is focused on the development and commercialization of novel therapeutics for the treatment of rare diseases. The company's lead candidate, DCCR extended-release tablets, a once-daily oral tablet for the treatment of Prader-Willi syndrome (PWS), is currently being evaluated in a Phase 3 clinical development program. For more information, please visit www.soleno.life.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical facts contained in this press release are forward-looking statements, including statements regarding the timing of any regulatory process or ultimate approvals and determining a path forward for DCCR for the treatment of PWS. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. These forward-looking statements speak only as of the date of this press release and are subject to a number of risks, uncertainties and assumptions, including the risks and uncertainties associated with market conditions, as well as risks and uncertainties inherent in Soleno's business, including those described in the company's prior press releases and in the periodic reports it files with the SEC. The events and circumstances reflected in the company's forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Except as required by applicable law, the company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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