Soleno Therapeutics (SLNO)

Initiation Report

LifeSci Investment Abstract

Soleno Therapeutics (NasdaqCM: SLNO) is a biotechnology company focused on the development and commercialization of therapeutics for the treatment of rare diseases, and is currently assessing the potential of lead asset Diazoxide Choline Controlled-Release (DCCR) tablets for the treatment of patients with Prader-Willi Syndrome (PWS). Notably, the Company has transitioned to this point following a merger between Capnia and Essentialis, and was recently renamed Soleno Therapeutics. Soleno's DCCR has received Orphan Drug designation for PWS in the US, and may address several aspects of PWS. The Company plans to initiate a potentially registration-enabling Phase II/III trial in patients with this condition in 2017.

Key Points of Discussion

- **DCCR is a K_{ATP} Channel Activator in Development for PWS.** Soleno is developing DCCR tablets for the treatment of PWS, which is a genetic orphan disorder that causes excessive appetite, obesity, short stature, intellectual disability, and behavioral problems that begin in childhood and persist through adulthood. DCCR is a once-daily tablet formulation of diazoxide choline, a small molecule that activates adenosine triphosphate-sensitive potassium (K_{ATP}) channels. Soleno believes DCCR has potential in PWS as it may be able to help restore proper function of certain hypothalamic neurons to induce appetite-suppressing effects via the release of leptin and insulin, while also improving resistance to these hormones.
- **Prior Phase II Data Show Potential of DCCR to Modify Key Symptom of PWS.** Soleno conducted a Phase I/II study for DCCR in patients with PWS, which contained an open-label phase and a double-blind phase. Following 10 weeks of open-label treatment, patients receiving DCCR showed reductions in hyperphagia of 32% as compared to baseline ($p = 0.003$). During the double-blind portion of the study, which began directly after the open-label phase, patients receiving DCCR maintained median hyperphagia reductions of roughly 31%, whereas those that began receiving placebo rebounded to reductions of approximately 12% after 4 weeks ($p = 0.08$ with ANOVA analysis, and $p = 0.027$ with Mann-Whitney analysis). The Company planning to initiate a Phase II/III trial with DCCR for PWS in 2017.

Expected Upcoming Milestones

- 2017 – Secure orphan drug designation for DCCR in novel indications.
- 2017 – Explore licensing options for legacy products.
- H2 2017 – Initiate a Phase II/III study with DCCR for PWS.

Analysts

Patrick Dolezal, M.S. (AC)
(212) 915-2579
pdolezal@lifescicapital.com

Market Data

Price	$0.54
Market Cap (M)	$26
EV (M)	$15
Shares Outstanding (M)	47.6
Fully Diluted Shares (M)	69.3
Avg Daily Vol	15,386
52-week Range:	$0.47 - $0.75
Cash (M)	$10.5
Net Cash/Share	$0.22
Annualized Cash Burn (M)	$8.7
Years of Cash Left	1.2
Debt (M)	$0.0
Short Interest (M)	0.18
Short Interest (% of Float)	1.2%

Financials

FY Dec		2017A	2018A	2019A
EPS	Q1	(0.11)A	NA	NA
	Q2	NA	NA	NA
	Q3	NA	NA	NA
	Q4	NA	NA	NA
	FY	NA	NA	NA

For analyst certification and disclosures please see page 23

- **PWS Represents a Significant Unmet Need and Treatment Options are Limited.** Management of PWS primarily focuses on lifestyle modifications to prevent death related to obesity, as approximately half of deaths in PWS patients under the age of 18 are possibly related to food-seeking behavior, such as choking and accidents. We note that human growth hormone (HGH) supplementation is approved in the US and EU, which is due to the nearly ubiquitous deficiency of growth hormone (GH) in PWS patients. Approved therapies include Pfizer's (NYSE: PFE) *Genotropin* (somatropin) in the US and Novartis' (NYSE: NVS) biosimilar *Omnitrope* (somatropin) in the EU. Studies performed with somatropin have demonstrated positive effects in PWS patients such as increases in height, lean body mass, lean body mass to fat mass ratio, and decreases in fat mass.

  Importantly, treatment with somatropin is indicated in adjunct to dietary, environmental, and other lifestyle changes, as it does not address all symptoms occurring with the disease. The most critical aspects of PWS that remain untreatable include reducing food intake and curbing appetite, which are major contributors to the severe obesity that is responsible for disease morbidities and mortality. Somatropin use is also contraindicated in patients with severe obesity or severe respiratory impairment due to reports of sudden death, in addition to those with severe obstructive sleep apnea, cancer, or psychosis. We highlight the potential of Soleno's DCCR to address several core components of PWS, including hyperphagia and body composition.

- **Market Opportunity for PWS is Substantial.** While the lack of approved treatments for PWS alone make it difficult to assess the market, sales of Pfizer's (NYSE: PFE) *Genotropin* (somatropin) can provide some insight despite being indicate for PWS, in addition to, growth failure due to growth hormone deficiency (GHD), Turner syndrome, idiopathic short stature, and small for gestational age. This product achieved its highest revenue in 2008, with worldwide sales of approximately $900 million. While somatropin has been proven to improve growth and body composition, it does not affect the key disease component of hyperphagia and use is associated with substantial risk. Soleno is developing DCCR for the treatment of PWS, to help address the unmet need of this patient population. To assess the potential of DCCR for PWS, we performed a scenario analysis, which indicates that annual sales could be in the range of $1.1 billion given a moderate price point and 50% market penetrance.

- **Soleno has Potential to Pursue Hypothalamic Obesity or Smith-Magenis Syndrome in the Future.** Soleno is currently focused on the development of DCCR for the treatment of PWS, but has indicated the possibility of moving into related indications such as hypothalamic obesity or Smith-Magenis Syndrome (SMS). Hypothalamic obesity is characterized by hyperphagia and weight gain due to a compromised hypothalamus, while common features of SMS include mental retardation, obesity, short stature, and skeletal abnormalities. DCCR is a small molecule that activates K_{ATP} channel proteins, and has potential to treat patient populations similar to PWS, such as hypothalamic obesity and SMS due to its effects on hyperphagia, obesity, and body composition.

Financial Discussion

First Quarter 2017 Financial Results. In the first quarter ended on March 31, 2017, Soleno reported total revenue of $0.3 million, as compared to $0.4 million in the same period of 2016. Research and development expenses for the first quarter were $1.0 million, down from $1.8 million the prior year. In the first quarter of 2017, general and administrative expenses were $1.2 million, down from $1.9 million during the same period of 2016. Net loss for the first quarter was $2.9 million or $0.11 per share, as compared to $3.2 million or $0.22 per share for the first quarter of 2016. Cash and cash equivalents as of March 31, 2017 were $10.5 million, up from $2.7 million as of December 31, 2016.

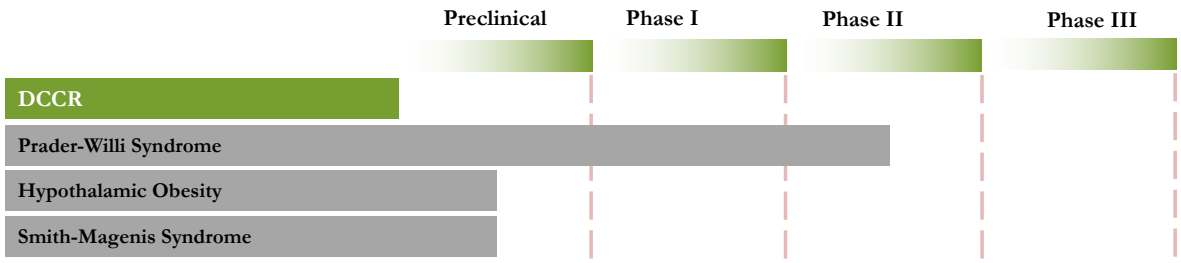
Merger with Essentialis. On March 8th, 2017, Soleno (then Capnia) announced the completion of a merger with Essentialis, a private company that was focused on the development of DCCR for the treatment of PWS. This marked the initiation of a transitional phase that has since produced Soleno, a Company focused on the development of therapeutics for the treatment of rare diseases. Concurrent with the transaction, Soleno also raised $10 million through a secondary issuance of common stock, in which prior Essentialis and novel investors participated.

Table of Contents

Company Description

Soleno is focused on the development and commercialization of therapeutics for the treatment of rare diseases, and is currently assessing the potential of lead asset Diazoxide Choline Controlled-Release (DCCR) tablets for the treatment of patients with Prader-Willi Syndrome (PWS). Notably, the Company has transitioned to this point following a merger between Capnia, which was previously focused on developing and commercializing an assortment of healthcare products, and Essentialis, a formerly private company that was developing DCCR. The combined entity was renamed Soleno Therapeutics and has refocused the Company's efforts on the development of DCCR for PWS. This is a genetic disorder characterized by excessive appetite, obesity, short stature, intellectual disability, and behavioral problems. Soleno's DCCR may address several aspects of PWS, and the Company plans to initiate a potentially registration-enabling Phase II/III trial in patients with this condition in 2017. The Company has also indicated an interest in evaluating DCCR in other related conditions in the future, such as hypothalamic obesity and Smith-Magenis syndrome. Soleno's full pipeline is presented in **Figure 1**.

Figure 1. Soleno's Development Pipeline



Source: LifeSci Capital

Diazoxide Choline Controlled-Release Tablet for Prader-Willi Syndrome

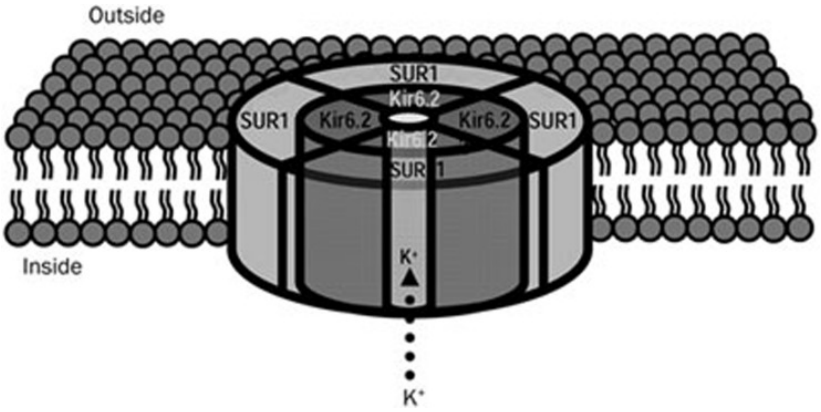
Soleno is developing lead asset Diazoxide Choline Controlled-Release (DCCR) tablets for the treatment of patients with Prader-Willi Syndrome (PWS). This condition is caused by the loss of gene expression on chromosome 15q11-q13, typically due to partial chromosomal deletion, and presents during infancy as hypotonia, difficulty feeding, and failure to thrive. Later in early childhood through adulthood, PWS also causes excessive appetite, obesity, short stature, intellectual disability, and behavioral problems. Management of PWS primarily focuses on lifestyle modifications to prevent life-threatening obesity and supplementation with human growth hormone (HGH). Common causes of death in patients with PWS are related to obesity, and include acute respiratory failure, cardiovascular disease, and/or high fever. Notably, approximately half of deaths in PWS patients under the age of 18 of deaths are possibly related to food-seeking behavior, such as choking and accidents. This disease is estimated to affect approximately 1 of every 15,000 people, which translates to 22,000 patients in the US. DCCR has received Orphan Drug designation for PWS in the US.

DCCR is a once-daily tablet formulation of diazoxide choline, a small molecule that activates adenosine triphosphate-sensitive potassium (K_{ATP}) channels. Soleno believes DCCR has potential in PWS as it may be able to help restore proper function of certain hypothalamic neurons to induce appetite-suppressing effects via the release of leptin and insulin, while also improving resistance to these hormones. Soleno has evaluated DCCR in the

treatment of PWS in a Phase I/II study, which had an open-label phase and a double-blind phase. After 10 weeks of open-label treatment, patients receiving DCCR showed 32% reductions in hyperphagia as compared to baseline ($p = 0.003$). In the double-blind part of the study, patients receiving DCCR maintained median hyperphagia reductions of roughly 31%, whereas those that began receiving placebo had reductions of approximately 12% after 4 weeks ($p = 0.08$ with ANOVA analysis, and $p = 0.027$ with Mann-Whitney analysis). The Company planning to initiate a Phase II/III trial with DCCR for PWS in 2017.

Mechanism of Action. Diazoxide Choline Controlled-Release (DCCR) is a once-daily tablet formulation of diazoxide choline, a small molecule that activates adenosine triphosphate-sensitive potassium (K_{ATP}) channel proteins. K_{ATP} channels are expressed in many cell types, including pancreatic β cells, skeletal and smooth muscles, and neurons.[1] They are composed of four Kir6 pore-forming subunits and four sulphonylurea receptor subunits, as shown in **Figure 2**.[2] These channel proteins respond to ratios of ATP to adenosine diphosphate (ADP), with increases in ATP/ADP leading to closed channels, and decreases in ATP/ADP causing open channels and repolarization or hyperpolarization. In this way, K_{ATP} channels are responsible for linking metabolism to membrane potential, which in turn drives certain cellular functions such as glucose homeostasis and hormone secretion.

Figure 2. Structure of K_{ATP} Channel Proteins



Source: Sun, et al., 2013.

In the case of PWS, it is important to consider the links between disease and hypothalamic dysfunction. Hypothalamus neurons that play critical roles in controlling feeding behavior reside in the arcuate nucleus of the hypothalamus (ARH) and include the proopiomelanocortin (POMC) and neuropeptide Y (NPY) or agouti-related peptide (AgRP) neurons. These types of neurons have complementary roles, as POMC neurons are anorexigenic, and reduce appetite, whereas NPY/AgRP neurons are orexigenic, and increase appetite.[3] The activity of both types of neurons are modulated by neurotransmitters and hormones, including serotonin, leptin, insulin and ghrelin. These effects are summarized in **Figure 3**.

[1] Yang, S. et al., 2004. Inhibition of ATP-sensitive potassium channels by haloperidol. *British Journal of Pharmacology, 143*(8), pp960-967.
[2] Sun, H. et al., 2014. Neuroprotective role of ATP-sensitive potassium channels in cerebral ischemia. *Acta Pharmacologica Sinica, 34*(1), pp24-32.
[3] Sohn, J. et al., 2015. Network of hypothalamic neurons that control appetite. *BMB Reports, 48*(4), pp229-233.

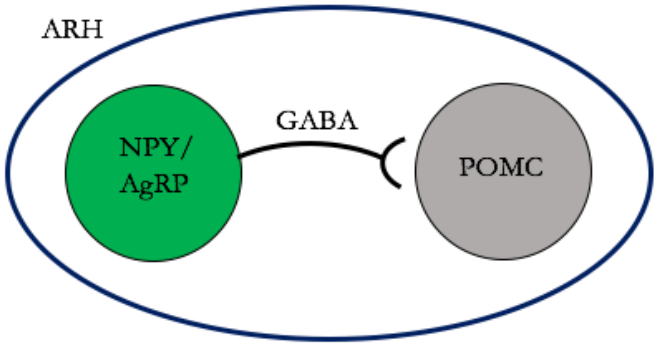
Figure 3. Effects of Various Neurotransmitters / Hormones on Hypothalamic Neurons

	POMC Neurons	NPY/AgRP Neurons	Effect
Serotonin	Excitation	Suppression	Anorexigenic
Leptin	Excitation	Suppression	Anorexigenic
Insulin	Excitation	Suppression	Anorexigenic
Ghrelin	Suppress	Excite	Orexigenic

Source: LifeSci Capital

POMC and NPY/AgRP neurons also form a local neural circuit in the ARH that contributes to appetite regulation. Specifically, NPY/AgRP neurons release GABA, an inhibitory neurotransmitter, which affects the POMC neurons and causes an orexigenic response and subsequently leads to greater food intake. The interaction between NPY/AgRP and POMC is presented in **Figure 4**. This circuit partially explains effects of leptin on POMC cells as well. Leptin increases the frequency of action potentials in these neurons through two distinct routes: depolarization of neuronal cation channels, and decreased GABAergic inhibition by NPY/AgRP neurons.[4]

Figure 4. Interaction Between NPY/AgRP and POMC in the ARH



Source: LifeSci Capital

PWS is characterized by excessive appetite and obesity, and individuals with this condition frequently suffer from insulin and leptin resistance. NPY/AgRP and POMC neurons are clear contributors to appetite regulation, where the excitation of NPY/AgRP neurons is associated with hunger and the excitation of POMC neurons is associated with fullness. NPY/AgRP neurons have been implicated as contributors to leptin resistance,[5] and treatment with DCCR has potential to act in a similar way as leptin and insulin to restore homeostasis to this neural circuit. DCCR has potential in PWS as it activates K_{ATP} channels of NPY/AgRP cells, which hyperpolarizes these neurons to reduce orexigenic signaling while also reducing the inhibition of anorexigenic POMC signaling. Soleno believes DCCR has potential to help restore proper function of the NPY/AgRP and POMC neuronal circuit to induce appetite-suppressing effects.

[4] Cowley, M.A. et al., 2001. Leptin activates anorexigenic POMC neurons through a neural network in the arcuate nucleus. *Nature, 411*(6836), pp480-4.

[5] Dhillon, S. et al., 2011. Cellular leptin resistance impairs the leptin-mediated suppression of neuropeptide Y secretion in hypothalamic neurons. *Endocrinology, 152*(11), pp4138-47.

Other relevant functions of K_{ATP} channel proteins include glucose uptake in skeletal muscle and glycemic control.[6] For example, diazoxide inhibits insulin release from pancreatic β cells and causes blood glucose to rise, and has been used in this context for the treatment of patients with hypoglycemia due to hyperinsulinism and insulinoma. This is relevant to individuals with PWS as they frequently suffer from insulin and leptin resistance, and DCCR has potential to improve these metabolic aspects of the disease.[7,8]

Safety. Diazoxide has a well-established safety profile since various formulations, including oral suspensions, capsules, and injectables, have been approved for indications such as hypoglycemia due to hyperinsulinism. The most frequently occurring AEs for an oral suspension of diazoxide include sodium and fluid retention, which could potentially lead to congestive heart failure in patients with compromised cardiac reserve. Other AEs include hirsutism affecting the forehead, back, and limbs, gastrointestinal issues, tachycardia, palpitations, thrombocytopenia, neutropenia, and skin rash. We also note the FDA has issued a warning for potential pulmonary hypertension in infants and newborns treated with diazoxide for hypoglycemia, requiring close monitoring and treatment cessation if necessary.

Soleno's DCCR is a tablet formulation of diazoxide that has been assessed in five Phase I and three Phase II studies for the treatment of people with obesity, dyslipidemia, and PWS. More than 210 patients have been enrolled to receive treatment with DCCR, and recent clinical findings have been consistent with previous data. In the open-label Phase I/II trial with DCCR for PWS, nearly all AEs were mild to moderate in severity and resolved with continued dosing. Furthermore, approximately 40% of AEs were expected disease complications of PWS such as respiratory infections, hypersomnia, peripheral edema, and constipation. Based on the long-standing body of safety data for diazoxide formulations and the observed AE profile for DCCR specifically, the safety and tolerability data are supportive of DCCRs continued development in PWS.

Prader-Willi Syndrome (PWS)

Prader-Willi Syndrome (PWS) is a genetic disorder that manifests during infancy as hypotonia, difficulty feeding, and failure to thrive. Later in early childhood through adulthood, PWS also causes excessive appetite, obesity, short stature, intellectual disability, and behavioral problems. This condition is caused by the loss of expression of genes located in the chromosome 15q11-q13 region. In PWS, this most commonly occurs from the paternal inheritance of a partial chromosomal 15 deletion combined with the effect of maternal imprinting, which is epigenetic silencing of the mothers' allele. Common causes of death in patients with PWS are related to obesity, and include acute respiratory failure, cardiovascular disease, and/or high fever. Notably, approximately half of deaths in PWS patients under the age of 18 of deaths are possibly related to food-seeking behavior, such as choking and accidents.[9] Management of PWS primarily focuses on lifestyle modifications to prevent life-threatening obesity and

[6] Miki, 2002. ATP-sensitive potassium channels participate in glucose uptake in skeletal muscle and adipose tissue. *Endocrinology and Metabolism, 283*(6), ppE1178-E1184.

[7] Huang, Q. et al., 2007. Diazoxide Prevents Diabetes through Inhibiting Pancreatic B-Cells from Apoptosis via Bcl-2/Bax Rate and P38-B Mitogen-Activated Protein Kinase. *Endocrinology, 148*(1), pp81-91.

[8] Standridge, M. et al., 2000. Diazoxide down-regulates leptin and lipid metabolizing enzymes in adipose tissue of Zucker rate. *The Federation of American Societies for Experimental Biology Journal, 14*(3), pp455-460.

[9] Butler, M. G. et al., 2017. Causes of Death in Prader-Willi Syndrome: Prader-Willi Syndrome Association (USA) 40-Year Mortality Survey. *Genetics in Medicine, 19*(6), pp635-642.

supplementation with human growth hormone (HGH). PWS patients receiving HGH therapy have demonstrated positive effects associated with treatment, including improvements in growth, fat mass, and lean body mass.

Causes and Pathogenesis

This condition is caused by the loss of expression of genes located on the chromosome 15q11-q13 region, which can occur due to various genetic issues. Genomic imprinting is typically responsible, which is a phenomenon of epigenetic silencing. Effectively this leads to one functional allele being inherited from one parent, and the other allele being silenced or imprinted. Certain sections of chromosome 15 are maternally imprinted, and a functional paternal allele is thus required for normal development. Approximately 70% of PWS cases are caused by a paternal deletion of the 15q11-q-13 region on chromosome 15, a location where the maternal alleles are imprinted.[10] Maternal disomy causes about 25% of cases, which is maternal inheritance of two imprinted chromosome 15 alleles without a paternal chromosome. The final 5% of PWS cases occur due to chromosomal translocations or other imprinting defects. The translation from genetics to the phenotype of PWS is not well understood, but there are classical features such as hyperphagia, hypogonadism, and growth hormone (GH) deficiency, which implicate hypothalamic dysfunction in disease pathogenesis.[11] Hypothalamic dysfunction is thought to be causative of many phenotypic PWS features, as it would explain deficiencies in GH, thyroid-stimulating hormone (TSH), adrenal insufficiency, and hypogonadism.[12]

Symptoms and Diagnosis

PWS is a genetic condition that affects the lives of those with the disease from birth through adulthood. One of the indicators of potential PWS is presentation of hypotonia during infancy, which is characterized by muscle weakness and is colloquially called floppy baby syndrome. Other symptoms presenting early on include failure to thrive and difficulties feeding, as infants with PWS are unable to coordinate the motor patterns necessary for sucking and swallowing. These symptoms are also consistent with hypotonia, as inadequate muscle development contributes to an inability to feed properly. Disease progression continues during late infancy or in early childhood with the emergence of excessive appetite, hyperphagia, obesity, short stature, intellectual disability, and behavioral problems.[13] Food craving and constant hunger are key features of PWS and begin in the first few years of life, which in turn leads to weight gain and subsequent obesity. Patients with the condition are known to eat large portions, horde or steal food, and consume unappealing items such as garbage or pet food.[14]

PWS can be diagnosed via genetic testing in individuals with the disease, or prenatally through both invasive and non-invasive techniques. The symptoms and characteristics that indicate possible PWS, are presented in **Figure 5**. Manifestation of these symptoms should be considered grounds to perform DNA testing for PWS, which is typically done via DNA methylation analysis. This method is capable of identifying more than 99% of all PWS types.

---

[10] Bittel, D.C. et al., 2005. Prader-Willi syndrome: clinical genetics, cytogenetics and molecular biology. *Expert Reviews in Molecular Medicine, 7*(14), pp1-20.

[11] Goldstone, A.P. et al., 2004. Prader-Willi syndrome: advances in genetics, pathophysiology and treatment. *TRENDS in Endocrinology and Metabolism, 15*(1), pp12-20.

[12] Aycan, Z. et al., Prader-Willi syndrome and growth hormone deficiency. *Journal of Clinical Research in Pediatric Endocrinology, 6*(2), pp62-7.

[13] Angulo, M.A. et al., 2015. Prader-Willi syndrome: a review of clinical, genetic, and endocrine findings. *Journal of endocrinological Investigation, 38*, pp1249-1263.

[14] Cassidy, S.B., 1997. Prader-Willi syndrome. *Journal of Medical Genetics, 34*, pp917-923.

Prenatal diagnosis is typically only performed when parents are at heightened risk to give birth to a child with PWS due to age (mother over 35) or genetics, such as the presence of a paternal imprinting defect or a familial translocation of chromosome 15.[15] This can be done in the first trimester through chorionic villi sampling (CVS), an invasive procedure that involves removing a sample of placenta, or amniocentesis, which is also invasive and requires an amniotic fluid sample. Ultrasound has also been useful to identify PWS, but can only be performed in the third trimester and is used more often to prepare for post-birth complications that may arise rather than initial diagnosis. Notably, approximately 95% of individuals with PWS have sporadic presentation with no apparent fetal malformations.

Figure 5. Criteria Warranting Genetic Testing for PWS

Relevant Age	Patient Features
Birth-2 years	• Hypotonia and difficulty feeding
2-6 years	• History of hypotonia and difficulty feeding • Global developmental delay • Short stature and/or low growth velocity • Hypogenitalism/hypogonadism
6-12 years	• History of hypotonia and difficulty feeding • Global developmental delay • Excessive eating and obesity • Hypogenitalism/hypogonadism
13 years or more	• Cognitive impairment, mild intellectual disability • Excessive eating, obesity • Hypogenitalism/hypogonadism • Short stature, small hands/feet • Behavioral issues, temper tantrums, obsessive-compulsive features

Source: Gunay-Aygun, M. et al., 2001.

Treatment

There is currently one approved therapy for PWS in the US and EU, though disease management primarily focuses on lifestyle modifications to prevent life-threatening obesity. Due to the nearly ubiquitous deficiency of growth hormone (GH) in PWS patients, human growth hormone (HGH) supplementation is available and patients receiving this therapy have demonstrated positive effects. Approved therapies include Pfizer's (NYSE: PFE) *Genotropin* (somatropin) in the US and Novartis' (NYSE: NVS) biosimilar *Omnitrope* (somatropin) in the EU. Other standard of care treatments include psychiatric consultation and lifestyle modifications such as environmental

[15] Butler, M.G. et al., 2017. Benefits and limitations of prenatal screening for Prader-Willi syndrome. *Prenatal Diagnosis, 37*, pp81-94.

control to minimize access to food, and a strict, well-balanced diet. Other symptoms are treated independently, such as daytime sleepiness, scoliosis, dental issues, and skin picking.[16]

Studies performed with somatropin have demonstrated positive effects in PWS patients such as increases in height, lean body mass, lean body mass to fat mass ratio, and decreases in fat mass. Two randomized, open-label, controlled studies were performed with somatropin in PWS patients. Participants were enrolled to receive either 0.24 or 0.36 mg/kg/week of somatropin or control. Data on linear growth are presented in **Figure 6**. These data indicate that patients receiving somatropin for 12 months showed significantly greater linear growth than those receiving no treatment ($p \leq 0.001$). Findings also show significant improvements in fat mass and lean body mass as compared to untreated control ($p < 0.005$). This translated to improvements in the fat mass to lean body mass ratio as well.

Figure 6. Effect of Somatropin on Linear Growth, Fat Mass, and Lean Body Mass

	Somatropin (0.24 mg/kg/week) n=15	Untreated control n=12	Somatropin (0.36 mg/kg/week) n=7	Untreated control n=9
Baseline height	112.7	109.5	120.3	120.5
Linear growth from 0-12 months	11.6**	5.0	10.7**	4.3
	Somatropin n=14		**Untreated control n=10**	
Fat mass at baseline	12.3		9.4	
Change in fat mass from 0-12 months	-0.9*		2.3	
Lean body mass at baseline	15.6		14.3	
Change from in lean body mass from 0-12 months	4.7*		0.7	

* denotes p-value < 0.005; **denotes p-value ≤ 0.001

Source: Genotropin Full Prescribing Information

Importantly, treatment with somatropin is used clinically in adjunct to dietary, environmental, and other lifestyle changes, as it does not address all symptoms occurring with the disease.[17] The most critical aspects of PWS that remain untreatable include reducing food intake and curbing appetite, which are major contributors to the severe obesity that is responsible for major disease morbidities and mortality. Somatropin use is also contraindicated in some common patient populations. For example, patients should not be treated if suffering from severe obesity or severe respiratory impairment, due to reports of sudden death in these populations. Treatment is also contraindicated for patients with severe obstructive sleep apnea, cancer, or psychosis. Soleno's DCCR could address several core components of PWS, including hyperphagia and body composition.

[16] Goldstone, A.P. et al., 2008. Recommendations for the Diagnosis and Management of Prader-Willi Syndrome. *The Journal of Clinical Endocrinology & Metabolism, 93*, pp4183-4197.

[17] Deal, C.L. et al., 2013. Growth Hormone Research Society Workshop Summary: Consensus Guidelines for Recombinant Human Growth Hormone Therapy in Prader-Willi Syndrome. *Journal of Clinical Endocrinology & Metabolism, 98*(6), ppE1072-E1087.

PWS Market Information

Epidemiology. The Prader-Willi Syndrome Association (PWSA) estimates that the prevalence of PWS is approximately 1 in 12-15,000 people in the US. Using the more conservative estimate, this translates into a target population of approximately 22,000 as determined by our analysis in **Figure 7**. The PWSA conducted a survey directed at parents and/or guardians of PWS patients that ran from 2004-2011, and 61% of respondents (393 of 643) indicated that their children, between 6 and 18 years of age, had been receiving human growth hormone therapy for PWS continuously or intermittently.[18]

Figure 7. PWS Patient Population in the US

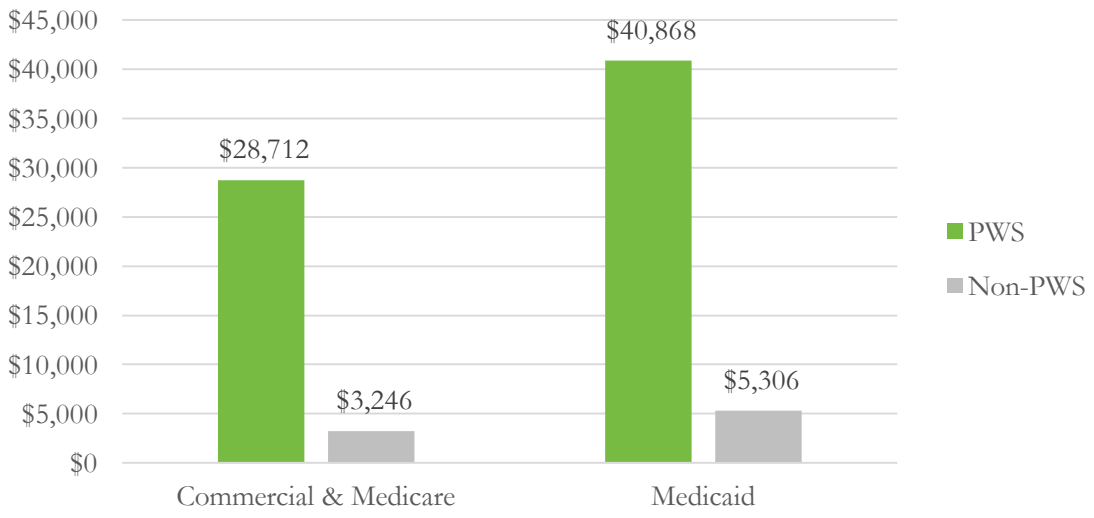
US Population	325 M
PWS Prevalence	1 out of 15,000
PWS Patients	22,000

Source: LifeSci Capital

PWS is also associated with a substantial economic burden, which was recently assessed by a retrospective study based on US administrative claims data from 2,030 patients collected during 2009-2014.[19] Key findings are presented in **Figure 8**, which shows that PWS patients with commercial insurance or Medicare had total care costs nearly 9-fold greater than non-PWS patients. PWS patients on Medicaid had total care costs almost 8-fold greater than non-PWS patients. The largest drivers of cost were outpatient care, inpatient care, and medication costs. Mean medication costs were $4,220 and $6,801 for patients with commercial insurance/Medicare and Medicaid, respectively. Investigators also noted that medication costs were largely driven by patient use of recombinant human growth hormone (rHGH) therapy. This indicates that insurers are willing to reimburse for a therapy that affects growth and body composition, despite associated risks and lack of effect on hyperphagia. We also note that only about one-half of patients in this study claimed to use a hormone therapy, meaning that cost per patient using these therapies is likely much higher than the reported means.

[18] Goranson, D.G. et al., 2011. Growth Hormone and Prader-Willi Syndrome. A Reference for Families and Care Providers.
[19] Shoffstall, A.J. et al., 2016. The high direct medical costs of Prader-Willi Syndrome. *The Journal of Pediatrics, 175,* pp137-43.

Figure 8. Mean Total Care Costs of Patients with PWS and Matched Controls



Source: Shoffstall, A.J. et al., 2016.

Market Size. The only approved therapy for PWS is rHGH, which has been proven to improve growth and body composition. However, rHGH does not affect the key disease component of hyperphagia and use is associated with substantial risk. Soleno is developing DCCR for the treatment of PWS in order to help address the unmet needs of this patient population. In order to assess the potential of DCCR in this indication, we performed a scenario analysis, which is presented in **Figure 9.** We found that for a drug such as DCCR, with 50% market penetrance and a moderate price point, annual sales could be in the range of $1.1 billion. This analysis is based on the following assumptions:

- **PWS Patient Population** – We assume that there are 22,000 patients with PWS in the US.
- **Drug Pricing** – We assume low, middle, and high price points for DCCR of $50,000, $100,000, and $150,000 per patient.

Figure 9. Scenario Analysis of US Sales Potential for DCCR

Penetrance	40%	50%	60%
Sales – Low	$440 M	$550 M	$660 M
Sales – Mid	$880 M	$1.1 B	$1.3 B
Sales – High	$1.3 B	$1.7 B	$2.0 B

Source: LifeSci Capital

The sales figures for Pfizer's (NYSE: PFE) *Genotropin* (somatropin) are presented in **Figure 10**. This product is a recombinant formulation of human growth hormone (rHGH), indicated for the treatment of patients with growth failure due to growth hormone deficiency (GHD), PWS, Turner syndrome, idiopathic short stature, and small for gestational age. *Genotropin* achieved its highest revenue in 2008, with worldwide sales of approximately $900 million.

This compound was initially approved for PWS in 2000, and we note the entrance of Sandoz' (NYSE: NVS) generic version in 2006. While sales numbers for Sandoz' *Omnitrope* (somatropin) are not available, current prescription trends indicate that this therapy and *Genotropin* split the market equally. Assuming similar price points, we estimate that the total addressable market for injectable rHGH products in the aforementioned indications is an opportunity of approximately $1.1 to $1.4 billion annually.

Figure 10. Worldwide Sales of *Genotropin*

	2014	2015	2016
***Genotropin* (somatropin)**	$723 M	$617 M	$579 M

Source: LifeSci Capital

It's important to note that while rHGH therapies are the only available treatments for PWS, they do not accurately reflect the opportunity for a few different reasons. First, PWS is one of several approved indications and it is difficult to parse apart which patient populations accounts for sales. Furthermore, slightly more than half of PWS patients utilize rHGH therapies, and labeling does not include effects on hyperphagia. For these reasons, we feel that pricing assumptions will likely vary greatly for a PWS-specific therapy.

Clinical Data Discussion

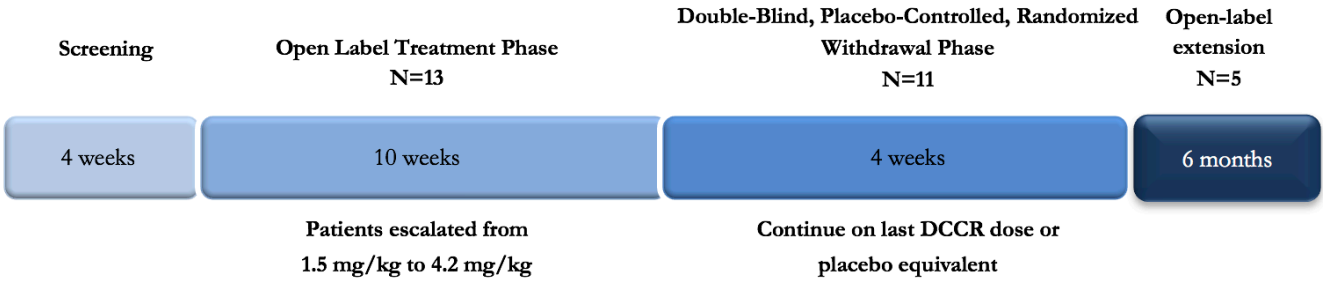
Soleno has evaluated DCCR in a Phase I/II study for the treatment PWS, which had an open-label phase and a double-blind phase. After 10 weeks of open-label treatment, patients receiving DCCR showed 32% reductions in hyperphagia as compared to baseline ($p = 0.003$). In the double-blind part of the study, patients receiving DCCR maintained median hyperphagia reductions of roughly 31%, whereas those that began receiving placebo had reductions of approximately 12% after 4 weeks ($p = 0.08$ with ANOVA analysis, and $p = 0.027$ with Mann-Whitney analysis). The Company is planning to initiate a Phase II/III trial with DCCR for PWS in 2017.

Phase I/II Trial with DCCR for PWS

Trial Design. This was a multi-part Phase I/II study with DCCR for the treatment of patients with PWS.[20] The trial had a 10 week open label treatment phase, followed by a 4 week randomized, double-blind, placebo controlled portion, and a 6 month open-label extension phase. The design of this study is in **Figure 11.**

[20] https://clinicaltrials.gov/show/NCT02034071

Figure 11. Trial Design of Phase I/II Study for DCCR

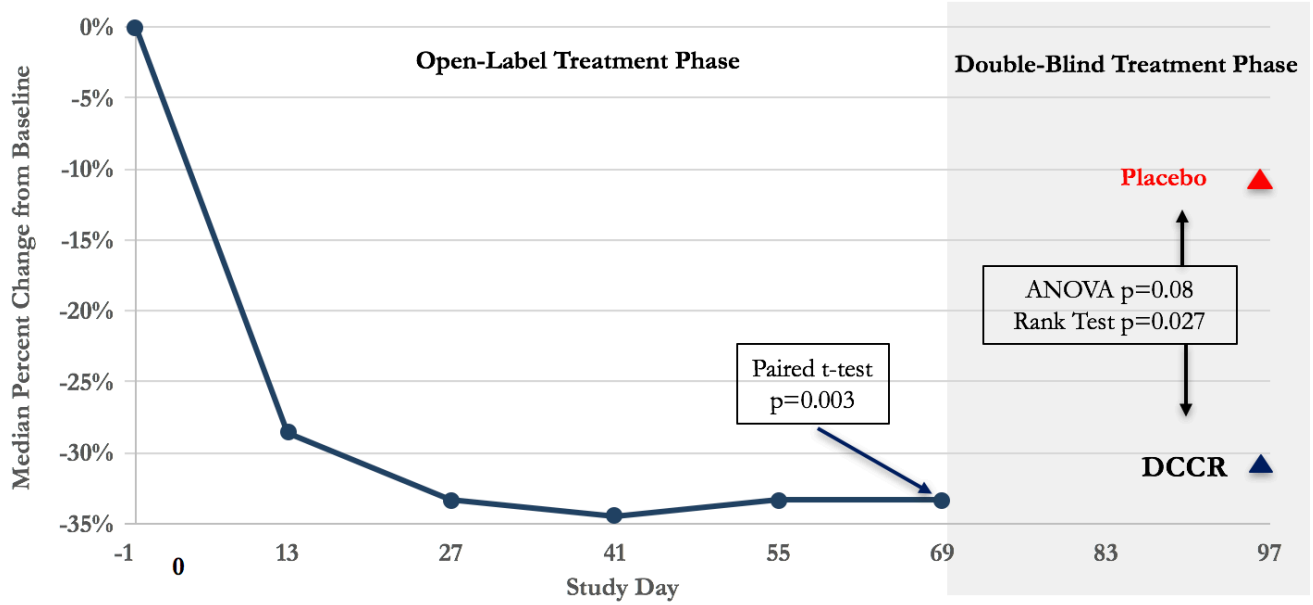


Source: Company Presentation

The open label portion enrolled 13 patients to receive doses of DCCR that escalated every 2 weeks, beginning at 1.5 mg/kg and progressing to 2.4, 3.3, and 4.2 mg/kg. After this portion of the study, 11 patients continued into the double-blind phase on the last dose of DCCR or began receiving placebo. This was followed by a 6 month open-label extension. Primary endpoints were the change in hyperphagia as assessed via modified Dykens hyperphagia questionnaire and resting energy expenditure, which were measured from the beginning to the end of the double-blind phase. Secondary endpoints included changes in weight, percent body fat, and levels of serum lipids such as triglycerides (TG), total cholesterol, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).

Trial Results. The Company reported that patients treated with all doses of DCCR showed a 32% median reduction in hyperphagia at the end of the open label treatment phase, a statistically significant decrease as compared to baseline ($p = 0.003$). Through the course of the double-blind treatment phase, participants receiving DCCR maintained median hyperphagia reductions of roughly 31%, whereas those that began receiving placebo ended this portion of the study with median hyperphagia reductions of approximately 12% ($p = 0.08$ with ANOVA analysis, and $p = 0.027$ with Mann-Whitney analysis). These results are presented in **Figure 12**. This is a positive preliminary finding, warranting further investigation with DCCR for the treatment of patients with PWS.

Figure 12. Median Change in Hyperphagia



Source: Company Presentation

Investigators also assessed the effects of DCCR on fat and lean body mass, which was measured with dual-energy x-ray absorptiometry (DEXA) scans. Results indicate that during the open-label phase of the study, patients receiving all doses of DCCR had significant reductions in fat mass as compared to baseline ($p = 0.011$), and significant increases in lean body mass ($p = 0.001$). The Company has also reported data on patients receiving the highest dose, 4.2 mg/kg DCCR, and these patients achieved numerically greater reductions in fat mass and gains in lean body mass than the cohort that included all patients. This hints at the potential of a dose-dependent response in these metrics with DCCR treatment. These data are presented in **Figure 13**. While these are significant results, the data come from a small number of patients during the open-label portion of the study. These open-label data make it unclear as to whether these findings are definitively a result of DCCR therapy or the placebo effect.

Figure 13. Changes in Fat Mass and Lean Body Mass at 10 Weeks

Source: Company Presentation

Other findings included reductions in aggressive behavior, which was determined by the behavioral assessment questionnaire from the PWS natural history study. Some of the noted changes include less object throwing, foul language, and destructive behavior. Biomarker data were also assessed, and indicate that treatment was associated with increases in HDL-C and reductions in TG, LDL-C, non-HDL-C, and total cholesterol. The Company has indicated that the safety profile of DCCR was consistent with prior studies, and nearly all AEs occurred with mild to moderate severity and resolved with continued dosing. Furthermore, approximately 40% of AEs were expected disease complications of PWS such as respiratory infections, hypersomnia, peripheral edema, and constipation.

Phase II Pharmacokinetic Study with DCCR in Healthy Subjects

Trial Design. This is an open-label Phase II pharmacokinetic trial with DCCR for the treatment of healthy subjects.[21] Approximately 32 patients will be enrolled into one of the five following treatment arms:

- Single dose of 75 mg DCCR following an overnight fast
- Single dose of 150 mg DCCR following an overnight fast
- Single dose of 300 mg DCCR following an overnight fast
- Single dose of 450 mg DCCR following an overnight fast
- Single dose of 300 mg DCCR following a standardized meal

The primary endpoints are pharmacokinetic measures over time, such as peak serum concentration (C_{max}) and the area under the plasma drug concentration curve from 0-24 hours (AUC_{0-24}). Secondary endpoints include other

[21] https://clinicaltrials.gov/show/NCT02893618

pharmacokinetic measures. Soleno has noted that this study is not currently ongoing, and will likely be conducted following the initiation of further studies in PWS.

Other Drugs in Development

There are just a handful of drugs in clinical stage development for the treatment of PWS, which are presented in **Figure 14**. These include Novo Nordisk's (NYSE: NVO) *Victoza*, an approved therapy to improve glycemic control in patients with type 2 diabetes, INSYS Therapeutics' (NasdaqGM: INSY) cannabidiol, and Rhythm Pharmaceuticals (private) setmelanotide, which is discussed in greater detail below. We note that every product has a distinct mechanism of action, and clinical data from these programs are somewhat limited at this point. To better appreciate these emerging candidates, it is also important to consider the aspect of PWS being targeted. Some products are primarily geared towards improving body composition, such as *Victoza*, which is being assessed for changes body mass index, and biosimilar somatropin, which is being tested for changes in height, lean body mass, and percent body fat. We note that secondary endpoints for *Victoza* include measures of hyperphagia and body weight as well, among others. Therapies primarily directed towards hyperphagia include Cannabidiol and Setmelanotide, and clinical trials also include endpoints on weight loss. Carbetocin is targeting hyperphagia as well, with obsessive compulsive behavior as a secondary endpoint. We note hyperphagia, behavioral control, and body composition are all important aspects of PWS, and a therapy such as DCCR, which has demonstrated potential to affect these components, may offer patients an appealing treatment option that addresses multiple concerns with a single pill.

Figure 14. Drugs in Development for Prader-Willi Syndrome

Drug	Company	Mechanism	Phase
Victoza (liraglutide)	Novo Nordisk A/S (NYSE: NVO)	Glucagon-like peptide-1 (GLP-1) receptor agonist	III[22]
Biosimilar somatropin	LG Life Sciences (KRX: 068870)	Recombinant human growth hormone (rHGH)	III[23]
DCCR	**Soleno (NasdaqCM: SLNO)**	**ATP-sensitive potassium channel activator**	**II[24]**
Cannabidiol	INSYS Therapeutics (NasdaqGM: INSY)	Synthetic cannabidiol	II[25]
Carbetocin	Levo Therapeutics (private)	Oxytocin receptor agonist	II[26]
Setmelanotide	Rhythm Pharmaceuticals (private)	Melanocortin-4 receptor (MC4R) agonist	II[27]

Source: LifeSci Capital

[22] https://clinicaltrials.gov/show/NCT02527200
[23] https://clinicaltrials.gov/show/NCT02204163
[24] https://clinicaltrials.gov/show/NCT02034071
[25] https://clinicaltrials.gov/show/NCT02844933
[26] https://clinicaltrials.gov/show/NCT01968187
[27] https://clinicaltrials.gov/show/NCT02311673

Setmelanotide – Rhythm Pharmaceuticals

Rhythm is a private biopharmaceutical company developing lead asset setmelanotide for the treatment of rare genetic disorders of obesity. Setmelanotide is an agonist of the melanocortin-4 receptor (MCR4), which is implicated in regulation of appetite and weight, and is being assessed in six disorders include PWS. The Company recently completed a randomized, double-blind, placebo controlled Phase II trial[28] with setmelanotide for the treatment of patients with PWS, although results have not yet been disclosed.

Competitive Landscape

Treatment Options for PWS are Limited. Management of PWS primarily focuses on lifestyle modifications to prevent life-threatening obesity, although there is one approved therapy in the US and EU. Due to the nearly ubiquitous deficiency of growth hormone (GH) in PWS patients, human growth hormone (HGH) supplementation is frequently utilized and confers several benefits. Approved therapies include Pfizer's (NYSE: PFE) *Genotropin* (somatropin) in the US and Novartis' (NYSE: NVS) biosimilar *Omnitrope* (somatropin) in the EU. Studies performed with somatropin have demonstrated positive effects in PWS patients such as increases in height, lean body mass, lean body mass to fat mass ratio, and decreases in fat mass.

Importantly, treatment with somatropin is indicated in adjunct to dietary, environmental, and other lifestyle changes, as it does not address all symptoms occurring with the disease. The most critical aspects of PWS that remain untreatable include reducing food intake and curbing appetite, which are major contributors to the severe obesity that is responsible for disease morbidities and mortality. Somatropin use is also contraindicated in some common patient populations. For example, patients with severe obesity or severe respiratory impairment should not be treated due to reports of sudden death, in addition to those with severe obstructive sleep apnea, cancer, or psychosis.[29] We highlight the potential of Soleno's DCCR to address several core components of PWS, including hyperphagia and body composition.

Market Opportunity for PWS is Substantial. The only approved therapy for PWS in the US is Pfizer's (NYSE: PFE) *Genotropin* (somatropin), which is a recombinant formulation of human growth hormone (rHGH). This product is indicated for the treatment of patients with growth failure due to growth hormone deficiency (GHD), PWS, Turner syndrome, idiopathic short stature, and small for gestational age. *Genotropin* achieved its highest revenue in 2008, with worldwide sales of approximately $900 million. This compound was initially approved for PWS in 2000, and we note the entrance of Sandoz' (NYSE: NVS) generic version in 2006. While sales numbers for Sandoz' *Omnitrope* (somatropin) are not available, current prescription trends indicate that this therapy and *Genotropin* split the market equally. Assuming similar price points, we estimate that the total addressable market for injectable rHGH products in the aforementioned indications is an opportunity of approximately $1.1 to $1.4 billion annually.

[28] https://clinicaltrials.gov/show/NCT02311673

[29] Deal, C.L. et al., 2013. Growth Hormone Research Society Workshop Summary: Consensus Guidelines for Recombinant Human Growth Hormone Therapy in Prader-Willi Syndrome. *Journal of Clinical Endocrinology & Metabolism, 98*(6), ppE1072-E1087.

It's important to note that while rHGH therapies are the only available treatments for PWS, they do not accurately reflect the opportunity for a few different reasons. First, PWS is one of several approved indications and it is difficult to parse apart which patient populations accounts for sales. Furthermore, slightly more than half of PWS patients utilize rHGH therapies, labeling does not include effects on hyperphagia, and pricing assumptions will likely vary for a PWS-specific therapy.

Late Stage Therapies in Development for PWS are Have Differentiated Mechanisms. There are just a handful of drugs in clinical stage development for the treatment of PWS, which include Novo Nordisk's *Victoza*, an approved therapy to improve glycemic control in patients with type 2 diabetes mellitus, INSYS Therapeutics' cannabidiol, and Rhythm Pharmaceuticals (private) setmelanotide. We note that every product in development has a distinct mechanism of action, making Soleno's DCCR the only ATP-sensitive potassium channel activator in the pipeline. We feel that this may be beneficial from a commercial perspective, as there will be no direct competitors and it seems possible that combination treatment with several of these agents could be used in the event of approval to address several aspects of PWS.

DCCR for the Treatment of Hypothalamic Obesity

Soleno is currently focused on the development of DCCR for the treatment of PWS, but has indicated the potential to pursue related indications such as hypothalamic obesity in the future. This condition is characterized by hyperphagia and weight gain due to a compromised hypothalamus, which is also implicated in the disease pathogenesis of PWS. One of the primary distinctions between these conditions is that hypothalamic obesity typically occurs after excision of a cranial tumor, trauma, or radiotherapy that causes structural damage to the hypothalamus. This leads to ineffective hormonal signal transduction from adipose tissue, which essentially sends the central nervous system into a state of starvation.[30] The sympathetic nervous system is also affected, which causes malaise, low energy, increased insulin secretion, and adipogenesis. People with hypothalamic obesity are unable to control weight gain with dieting or other lifestyle modifications, and pharmacologic treatment is limited to adrenergic drugs or octreotide to reduce insulin secretion. Surgical intervention of gastric bypass surgery has been demonstrated to be an effective treatment option as well, though complications can result and non-invasive options would likely be preferred. DCCR is a small molecule that activates adenosine triphosphate-sensitive potassium (K_{ATP}) channel proteins, and has potential to treat hypothalamic obesity due to its effects on hyperphagia and body composition in similar patient populations like PWS.

DCCR for the Treatment of Smith-Magenis Syndrome

Soleno may also assess the potential of DCCR for the treatment of Smith-Magenis Syndrome (SMS), another condition with numerous similarities to PWS. SMS is caused by a microdeletion of chromosome 17p11.2, which contains the retinoic acid-induced 1 (*RAI1*) gene and is characterized mental retardation, dysmorphism, sleep issues, and skeletal abnormalities.[31] Other common features include obesity, short stature, and hearing loss. Treatment of this condition is focused on management of symptoms, including melatonin or acebutolol for sleep disturbances, various educational training programs, and behavior management techniques. SMS has a prevalence of

[30] Lustig, R. H. et al., 2008. Hypothalamic obesity: causes, consequences, treatment. *Pediatric endocrinology reviews, 6*(2), pp220-227.
[31] Greydanus, D.E. et al., 2012. Smith-Magenis syndrome. *Handbook of clinical neurology, 111,* pp295-296.

approximately 1 in every 15-25,000 people.[32] The Company may assess DCCR for the treatment of SMS in the future, as this compound may improve obesity and body composition in this patient population.

Intellectual Property

Soleno has a robust intellectual property portfolio to protect lead asset DCCR, which includes the following issued or granted patients in each respective territory: 3 in the US, 3 in the EU, and 1 in Japan. The Company has indicated that these patents cover composition of matter, formulations, combinations, method of use, and method of manufacturing for DCCR. These patents are set to expire from 2026 to 2028. Soleno also has protections specific to PWS, and has indicated that these patents cover method of use for any K_{ATP} channel activator, diazoxide, and DDCR in this disease. The Company has made a new filing based on clinical data with DCCR in PWS patients, which could potentially extend patent protection to 2035.

Management Team

Anish Bhatnagar, M.D.
Chief Executive Officer

Dr. Bhatnagar was appointed Chief Executive Officer of Capnia in February 2014. He joined the Company in 2006, and has held positions of increasing responsibility since then, most recently as President and Chief Operating Officer. Dr. Bhatnagar is a physician with over 15 years of experience in the medical device and biopharmaceutical industries. His experience spans development of biologics, drugs, drug-device combinations and diagnostic, as well as therapeutic medical devices. His prior experience includes working at Coulter Pharmaceuticals, Inc. from 1998 to 2000, and Titan Pharmaceuticals, Inc. from 2000 to 2006. He is the author of several peer-reviewed publications, abstracts, and book chapters. He obtained his medical degree at SMS Medical College in Jaipur, India, and completed his Residency and Fellowship training in the U.S. at various institutions, including Georgetown University Hospital, and the University of Pennsylvania.

David O'Toole
Chief Financial Officer

Mr. O'Toole was appointed Chief Financial Officer of Capnia in July 2014. He has more than 30 years of experience in the accounting and finance sectors, and for the past 14 years has focused on the medical device, tools, and diagnostics industry. From September 2012 to June 2014, Mr. O'Toole was Senior Vice President and Chief Financial Officer at Codexis, Inc., a public company focused on developing biocatalysts. From May 2010 to August 2012, Mr. O'Toole was Vice President and Chief Financial Officer at Response Genetics, Inc., and served from May 2008 to August 2010 as Executive Vice President and Chief Financial Officer of Abraxis Bioscience, Inc. From 1992 to 2008, Mr. O'Toole worked at Deloitte & Touche LLP, where he served for 12 of those years as a partner. He worked at Arthur Anderson & Co. from 1984 to 1992 as an international tax manager. Mr. O'Toole received his Bachelor of Science degree in accounting from the University of Arizona, and is a certified public accountant.

[32] Elsea, S.H. et al., 2008. Smith-Magenis syndrome. *European Journal of Human Genetics, 16*(4), pp412-421.

Neil M. Cowen, Ph.D., MBA
Senior Vice President of Drug Development

Dr. Cowen joined Capnia as the Senior Vice President of Drug Development in March 2017, at the time of the Capnia and Essentialis merger. Previously, Dr. Cowen was part of the senior management team of Essentialis since its founding in May 2003, functioning first as founding CEO and most recently as President and CSO, directing the product development, finance and business development functions. From 2001 to 2003 Dr. Cowen served as VP for Strategic Development at Epicyte Pharmaceutical, directing the product development, regulatory, manufacturing, business development and HR functions of the company. From 1986 to 2001 Dr. Cowen functioned in various business development and research management roles in Dow Chemical and its subsidiaries, ending as Global Business Leader for biopharmaceuticals and animal health. Dr. Cowen has a PhD from Iowa State University an MBA from the University of Indianapolis, and BS and MS degrees from Michigan State University.

Risk to an Investment

We consider an investment in Soleno to be a high-risk investment. Soleno is currently focused on clinical-stage development and its marketed or approved products do not generate substantial revenues. Soleno has not entered Phase III clinical trials for its lead program. Failure to show convincing results in future pivotal clinical studies or failure to reach FDA or EMA approval could adversely affect Soleno's stock price. Regulatory approval to market and sell a drug does not guarantee that the drug will penetrate the market, and sales may not meet expectations. Soleno is not profitable and may need to seek additional financing from the public markets, which may result in dilution of existing shareholder value.

Analyst Certification

The research analyst denoted by an "AC" on the cover of this report certifies (or, where multiple research analysts are primarily responsible for this report, the research analyst denoted by an "AC" on the cover or within the document individually certifies), with respect to each security or subject company that the research analyst covers in this research, that: (1) all of the views expressed in this report accurately reflect his or her personal views about any and all of the subject securities or subject companies, and (2) no part of any of the research analyst's compensation was, is, or will be directly or indirectly related to the specific recommendations or views expressed by the research analyst(s) in this report.

DISCLOSURES

This research contains the views, opinions and recommendations of LifeSci Capital, LLC ("LSC") research analysts. LSC (or an affiliate) has received compensation from the subject company for producing this research report. Additionally, LSC expects to receive or intends to seek compensation for investment banking services from the subject company in the next three months. LSC (or an affiliate) has also provided non-investment banking securities-related services, non-securities services, and other products or services other than investment banking services to the subject company and received compensation for such services within the past 12 months. LSC does not make a market in the securities of the subject company.

Neither the research analyst(s), a member of the research analyst's household, nor any individual directly involved in the preparation of this report, has a financial interest in the securities of the subject company. Neither LSC nor any of its affiliates beneficially own 1% or more of any class of common equity securities of the subject company.

LSC is a member of FINRA and SIPC. Information has been obtained from sources believed to be reliable but LSC or its affiliates (LifeSci Advisors, LLC) do not warrant its completeness or accuracy except with respect to any disclosures relative to LSC and/or its affiliates and the analyst's involvement with the company that is the subject of the research. Any pricing is as of the close of market for the securities discussed, unless otherwise stated. Opinions and estimates constitute LSC's judgment as of the date of this report and are subject to change without notice. Past performance is not indicative of future results. This material is not intended as an offer or solicitation for the purchase or sale of any financial instrument. The opinions and recommendations herein do not take into account individual client circumstances, objectives, or needs and are not intended as recommendations of particular securities, companies, financial instruments or strategies to particular clients. The recipient of this report must make his/her/its own independent decisions regarding any securities or financial instruments mentioned herein. Periodic updates may be provided on companies/industries based on company specific developments or announcements, market conditions or any other publicly available information. Additional information is available upon request.