Serdexmethylphenidate, a Prodrug of Dexmethylphenidate and Contained in Corium's ADHD Medication AZSTARYS® (serdexmethylphenidate and dexmethylphenidate), Has Low Relative Potential for Abuse

Three randomized, controlled clinical studies demonstrate long-acting serdexmethylphenidate yielded significantly lower abuse-related effects, fewer stimulant-like adverse events than dexmethylphenidate

***Results published in* Current Medical Research & Opinion**

Boston, MA, June 1, 2022 – Corium, Inc., a commercial-stage biopharmaceutical company leading the development and commercialization of novel central nervous system (CNS) therapies, announced that serdexmethylphenidate (SDX), the novel prodrug of dexmethylphenidate (d-MPH), has significantly lower potential for abuse and fewer stimulant-like adverse events compared to d-MPH. This peer-reviewed finding appears in the May 2022 publication of *Current Medical Research & Opinion*. AZSTARYS (serdexmethylphenidate and dexmethylphenidate) is the first and only medicine containing SDX and was approved by the U.S. FDA in March 2021 as a once-daily treatment for ADHD symptoms in patients aged 6 years and older.

"The studies demonstrate that SDX is associated with significantly lower abuse potential than d-MPH via oral, intranasal, and intravenous routes of administration. These results provide important information to enable patients, parents, caregivers, and healthcare professionals to consider the abuse potential of available ADHD therapies when making treatment decisions," said Charles Oh, MD, Chief Medical Officer of Corium.

As a prodrug, SDX is designed specifically to be pharmacologically inactive until reaching a patient's lower gastrointestinal tract, where, by design, SDX is gradually converted to d-MPH throughout the day. AZSTARYS, which is a Schedule II therapy, contains 70% SDX (a Schedule IV substance) and 30% d-MPH (a Schedule II substance). Consequently, AZSTARYS provides control of ADHD symptoms rapidly with the immediate-release d-MPH and for an extended duration with SDX while also providing a gradual offset of action. Once-daily AZSTARYS is available in the U.S. in three SDX/immediate-release d-MPH dose strengths of 26.1/5.2 mg, 39.2/7.8 mg, and 52.3/10.4 mg.

"The studies profiled the abuse potential of SDX relative to placebo and d-MPH via three administration routes using a rigorous experimental design in recreational stimulant users and analyses that used clinically meaningful assessments. The findings enhance our understanding of the relative abuse

potential of these drugs via oral and non-oral routes and demonstrate the reduced abuse potential of SDX, supporting its Schedule IV status," said Megan J. Shram, PhD, primary author, principal at Altreos Research Partners, Inc., Toronto, and Adjunct Professor of Pharmacology at the University of Toronto.

The three clinical studies documented that SDX via all three routes of administration tested—oral, intranasal, and intravenous (IV)—yielded statistically significantly lower abuse-related drug effects and stimulant-like adverse effects (AEs) than molar equivalent doses of d-MPH. These findings demonstrate that SDX has significantly lower abuse potential compared to d-MPH and support designating SDX as a Schedule IV controlled substance.

SDX, whether oral, intranasal, or intravenous, has lower potential for abuse

The three phase 1 randomized, double-blind, placebo- and active-controlled crossover studies evaluated the abuse-related effects of SDX chloride (Cl) compared to d-MPH hydrochloride (HCl) in healthy adults who are able to discriminate a stimulant from placebo. The primary endpoint was the maximum (Emax) Drug Liking (DL) score, rated on a bipolar 100-point scale. Scores higher than 50 (neutral midpoint) are associated with greater abuse potential. In each study, participants were required to discriminate a dose of d-MPH from placebo to continue in the treatment phase, during which they received a dose of SDX, an active comparator drug, and placebo in a randomized sequence, with washout periods between each treatment.

In the oral study, participants received 80 mg extended-release d-MPH HCl, 120 mg and 240 mg SDX Cl (molar equivalent to 60 and 120 mg d-MPH HCl, respectively), and placebo in a randomized, crossover design. The participants had significantly higher DL Emax scores following administration of 80 mg d-MPH HCl compared to 120 mg SDX Cl, (81.5 vs. 62.8, respectively, p=0.0011) or 240 mg SDX Cl (DL Emax=63.8, p=0.0058). Per FDA guidance, the oral study used two doses of SDX that were about two- to four-fold higher than the highest therapeutic dose contained in 52.3/10.4 mg strength of AZSTARYS.

In the intranasal study, participants received 40 mg d-MPH HCl, 80 mg SDX Cl (molar equivalent to 40 mg d-MPH HCl), and placebo in a randomized, crossover design. Drug Liking Emax scores were significantly higher following administration of d-MPH HCl compared to SDX Cl (93.2 vs. 71.0, respectively, p<0.0001).

In the intravenous study, participants received 15 mg d-MPH HCl, 30 mg SDX Cl (molar equivalent to 15 mg d-MPH HCl), and placebo in a randomized, crossover design. Drug Liking Emax scores were significantly higher following administration of d-MPH HCl compared to SDX Cl (84.3 vs. 56.6, respectively, p=0.001). Drug Liking Emax scores for IV SDX were also found to be non-inferior to placebo (56.6 vs. 53.8, respectively) using a prespecified non-inferiority margin. The IV study is the first to examine the abuse-related effects of IV d-MPH in a clinical laboratory

setting.

In addition to DL Emax, investigators employed visual analog scale assessments recommended for use in human abuse potential studies that included other “at-the-moment” effects, such as Feeling High, Good Effects, Bad Effects, Any Effects, and Drowsiness/Alertness, and retrospectively assessed endpoints that measured the overall balance of drug effects, such as Take Drug Again and Overall Drug Liking. In all three studies, secondary endpoints were generally consistent with the primary endpoint outcomes.

The article, Shram MJ, Setnik B, Webster L, Guenther S, Mickle TC, Braeckman R, Kanski J, Martin A, Kelsh D, Vince BD, Barrett AC. Oral, intranasal, and intravenous abuse potential of serdexmethylphenidate, a novel prodrug of d-methylphenidate. Curr Med Res Opin. 2022 May 16:1-40. doi: 10.1080/03007995.2022.2076474, is available via open access at https://www.tandfonline.com/doi/pdf/10.1080/03007995.2022.2076474.

About AZSTARYS

Approved by the FDA in 2021, AZSTARYS is first and only medicine with d-MPH and novel SDX prodrug technology for treatment of ADHD symptoms in patients aged 6 years and older. As a prodrug, SDX is specifically designed to be pharmacologically inactive until reaching the lower gastrointestinal tract, where SDX is gradually converted to d-MPH throughout the day. The result is a treatment that provides symptom control rapidly with the immediate-release d-MPH component and for an extended duration with the SDX component, with gradual offset of action.

AZSTARYS is available in the United States. In December 2021, Ark Biopharmaceutical and a Gurnet Point Capital affiliate signed an agreement providing exclusive rights to develop, manufacture, and commercialize AZSTARYS in Greater China. Corium and Gurnet Point Capital continue to explore opportunities in other geographies.

About ADHD

Attention-deficit hyperactivity disorder (ADHD) is a common neurodevelopment disorder marked by an ongoing pattern of inability to pay attention or hyperactivity with impulsive behaviors or both, which interferes with functioning or development. ADHD usually is diagnosed during childhood but often continues into adulthood. Children with ADHD may have trouble paying attention, controlling impulsive behaviors (may act without thinking about what the result will be), or be overly active. In the United States, an estimated 6.1 million children have received an ADHD diagnosis, including 2.4 million aged 6 to 11 years.

Indication and Important Safety Information for AZSTARYS (serdexmethylphenidate and dexmethylphenidate)

INDICATION
AZSTARYS is a central nervous system (CNS) stimulant indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in patients aged 6 years and older.

IMPORTANT SAFETY INFORMATION

WARNING: ABUSE AND DEPENDENCE

- **CNS stimulants, including AZSTARYS, other methylphenidate-containing products, and amphetamines, have a high potential for abuse and dependence. Assess the risk of abuse prior to prescribing, and monitor for signs of abuse and dependence while on therapy**

CONTRAINDICATIONS

- Known hypersensitivity to serdexmethylphenidate, methylphenidate, or other product components. Bronchospasm, rash, and pruritus have occurred with AZSTARYS. Hypersensitivity reactions such as angioedema and anaphylactic reactions have occurred with other methylphenidate products.
- Concomitant treatment with a monoamine oxidase inhibitor (MAOI) or use of an MAOI within the preceding 14 days, because of the risk of hypertensive crisis.

WARNINGS AND PRECAUTIONS

- Sudden death has been reported in association with CNS stimulant treatment at recommended doses in pediatric patients with structural cardiac abnormalities or other serious heart problems. In adults, sudden death, stroke, and myocardial infarction have been reported at recommended doses. Avoid use in patients with known structural cardiac abnormalities, cardiomyopathy, serious heart arrhythmias, coronary artery disease, or other serious heart problems.
- CNS stimulants cause an increase in blood pressure and heart rate. Monitor all patients for hypertension and tachycardia.
- *Exacerbation of Pre-existing Psychosis*: May exacerbate symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder. *Induction of a Manic Episode in Patients with Bipolar Disorder*: May induce a mixed/manic episode in patients with bipolar disorder. Prior to initiating treatment, screen for risk factors for developing a manic episode (e.g., comorbid or history of depressive symptoms, or a family history of suicide, bipolar disorder, or depression). *New Psychotic or Manic Symptoms*: At recommended doses, may cause psychotic or manic symptoms (e.g., hallucinations, delusional thinking, or mania) in patients without a history of psychotic illness or mania. Discontinue if symptoms occur.
- Cases of painful and prolonged penile erections and priapism have been reported with methylphenidate products. Immediate medical attention should be sought if signs or symptoms of prolonged penile erections or priapism are observed.
- CNS stimulants, including AZSTARYS, are associated with peripheral vasculopathy, including Raynaud's phenomenon. Signs and symptoms are usually intermittent and mild; very rare sequelae include digital ulceration and/or

soft tissue breakdown. Carefully observe patients during treatment for digital changes. Further evaluation may be required, including referral.
- CNS stimulants have been associated with weight loss and slowing of growth rate in pediatric patients. Monitor height and weight at appropriate intervals in pediatric patients. Treatment may need to be interrupted in children not growing or gaining weight as expected.

ADVERSE REACTIONS
- Based on accumulated data from other methylphenidate products, the most common (>5% and twice the rate of placebo) adverse reactions are appetite decreased, insomnia, nausea, vomiting, dyspepsia, abdominal pain, weight decreased, anxiety, dizziness, irritability, affect lability, tachycardia, and blood pressure increased.

DRUG INTERACTIONS
- Adjust dosage of antihypertensive drug as needed. Monitor blood pressure.
- Avoid use of AZSTARYS on the day of surgery if halogenated anesthetics will be used.

For additional safety information, click here for Prescribing Information and Medication Guide, including BOXED WARNING.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

About Corium
Corium, Inc., is a commercial-stage biopharmaceutical company that is leading the development and commercialization of CNS therapies that provide clinicians with important new treatment options for patients, their families, and their caregivers. Corium is commercializing two U.S. FDA approved products, ADLARITY®, approved in March 2022, and AZSTARYS. Corium has a robust development pipeline focused on addressing unmet needs in the treatment of patients with CNS conditions. In November 2018, all of Corium's outstanding stock was acquired by an affiliate of Gurnet Point Capital. For further information, please visit http://www.corium.com.

About Gurnet Point Capital
Gurnet Point Capital is a unique healthcare investment platform within the B-Flexion group and led by a team with deep expertise in an industry for which they share a passion, both as investors and senior executives. GPC invests long-term capital and supports entrepreneurs in building a new generation of companies that deliver outsized returns through active ownership. Based in Cambridge, MA, its remit encompasses life sciences and health care focused businesses, with a particular emphasis on businesses that have high growth potential in the product development and commercialization stages of their evolution. With its strategy of driving best in class operational transformation for these businesses, to create social impact while generating significant economic value, GPC is able to deliver differentiated results for

its investors and partners. For more, go to http://www.gurnetpointcapital.com.

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