Corium Announces Publication of ADLARITY® (donepezil transdermal system) Clinical Trial Data: Drug Exposure Equivalent to Oral Donepezil With Favorable GI Side Effect Profile

ADLARITY is the only once-weekly transdermal system delivering the most widely-prescribed medication for patients with Alzheimer's dementia

Uses Corium's well-established proprietary CORPLEX™ technology

BOSTON, September 19, 2022 /PRNewswire/ -- Corium, Inc., a fully-integrated biopharmaceutical company leading the development and commercialization of novel central nervous system (CNS) therapies, announced publication of its phase 1 healthy volunteer study results for ADLARITY (donepezil transdermal system) in the peer-reviewed *Journal of Alzheimer's Disease*. The article, "Comparison of Steady-State Pharmacokinetics of Donepezil Transdermal Delivery System with Oral Donepezil," reports that Corium's novel once-weekly Alzheimer's dementia treatment delivered drug exposure equivalent to oral donepezil while presenting lower gastrointestinal (GI) adverse events overall compared to oral donepezil. The article is currently available online and expected to be published in the hardcopy of the *Journal of Alzheimer's Disease*, Volume 90, Issue 1, on October 25, 2022.

"Transdermal delivery offers meaningful potential benefits over oral administration, including ease of use, maintenance of steady concentrations of drugs, reduced gastrointestinal adverse effects, and better treatment compliance. The availability of a transdermal formulation of donepezil gives clinicians, patients, and their caregivers an important new option to consider when treating dementia of the Alzheimer's type," said study co-author Pierre N. Tariot, M.D., director of the Banner Alzheimer's Institute in Phoenix, AZ.

The FDA approved ADLARITY in 5 or 10 milligram per day (mg/day) formulations in March 2022. ADLARITY is the first and only once-weekly patch to continuously deliver consistent doses of donepezil through the skin. Donepezil is the most prescribed medication in a class of Alzheimer's drugs known as acetylcholinesterase inhibitors. ADLARITY also is the first approved prescription drug product using Corium's proprietary CORPLEX transdermal technology, which has been used for years in consumer products.

"The study demonstrated the equivalent exposure of Adlarity to oral donepezil and supports the use of ADLARITY as a compliant and safe once-weekly dosing regimen for treatment of patients with dementia of the Alzheimer type," said Charles Oh, M.D., Chief Medical Officer of Corium. "The trial also shows Corium's commitment to addressing the unmet needs of patients with CNS disorders."

ADLARITY Transdermal System: Equivalent to Oral Donepezil Exposure, Fewer GI Adverse Events Overall

In the trial, investigators compared the extent of donepezil exposure from the once-weekly ADLARITY to a once-daily oral donepezil formulation in 60 healthy adults (NCT04617782). The trial included three treatment periods of 5 weeks each. In the first period, all the participants received ADLARITY weekly, which provided 5 mg/day of donepezil. In the second period, participants were randomized to receive either 10 mg/day once-weekly ADLARITY or 10 mg/day daily oral donepezil, followed by switching to the alternative treatment, ADLARITY or oral donepezil, in the third period. All the participants knew which treatment they received in this open-label trial. Investigators examined the amount of donepezil in the participants' blood, including the maximum plasma concentration (Cmax) and the total amount of drug exposure (area under the curve or AUC).

Per FDA guidance, two pharmaceutical products are bioequivalent if the 90% confidence interval of the geometric mean ratio (GMR) for AUC and Cmax is within 80–125%. The study concluded that the GMR for AUC and Cmax were within the bioequivalence range when comparing the 10 mg/day ADLARITY transdermal system to 10 mg/day oral donepezil.

Investigators recorded similar incidences of total adverse events (AEs) across treatments, including 53.3% of participants receiving 5-mg/day ADLARITY, 54.5% for 10-mg/day ADLARITY, and 57.1% for oral donepezil. Investigators noted no serious AEs, AEs leading to treatment discontinuation, or deaths during the study.

In the study, fewer overall gastrointestinal AEs occurred with administration of 10-mg/day ADLARITY than 10 mg/day oral donepezil: 14.5% vs. 53.6%, respectively. The respective incidence rates were 5.5% vs. 17.9% for constipation, 1.8% vs. 30.4% for nausea, 3.6% vs. 12.5% for diarrhea, 5.5% vs. 1.8% for abdominal pain, and zero vs. 5.4% for vomiting.

ADLARITY Availability

Corium is taking a phased approach to launching ADLARITY, with initial product launch this fall. Initially, a dedicated team of field sales representatives and an established virtual sales team will educate physicians about ADLARITY and provide educational materials and resources for their patients. As Medicare and Medicaid coverage becomes available, Corium will broaden launch efforts, with a nationwide launch planned for 2023.

Physicians interested in receiving more information or resources can request field representative support via Adlarity.com. Corium also is supporting patient access to ADLARITY under CoriumCares™, a patient access and support program offering information about copay assistance for eligible commercially-insured patients, product trial, and reimbursement. More information is available at www.Adlarity.com or by calling (800) 910-8432.

About Alzheimer’s Disease

Alzheimer’s disease is a progressive and irreversible brain disorder. It involves changes in brain tissue including abnormal buildup of proteins as well as loss of neuron function. The resulting damage leads to the loss of remembering, reasoning, and thinking abilities. The related behavioral changes include the loss of independence in activities of daily living and self-care. Dementia ranges in severity from mild, when it is just beginning to affect a person’s functioning, to moderate, to severe, when the person must depend on others for the basic activities of day-to-day life. Patients with advanced Alzheimer’s disease may be unable to chew and swallow easily.

An estimated 6.2 million Americans were living with Alzheimer’s disease in 2021, with a possible rise to 13.8 million by 2060. Globally, more than 55 million people have dementia, and Alzheimer's disease may account for 60 to 70 percent of patients, according to the World Health Organization. The U.S. Centers for Disease Control and Prevention estimates that in 2020, more than 11 million Americans provided an estimated 15.3 billion hours of unpaid care for patients with Alzheimer’s disease.

Indication and Important Safety Information for ADLARITY (donepezil transdermal system)

INDICATION
ADLARITY is indicated for the treatment of mild, moderate, and severe dementia of the Alzheimer’s type.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
ADLARITY is contraindicated in patients with known hypersensitivity to donepezil or to piperidine derivatives or with a history of allergic contact dermatitis with use of ADLARITY.

WARNINGS AND PRECAUTIONS
• Application site skin reactions: Skin application-site reactions have occurred with ADLARITY. These reactions are not necessarily indicative of sensitization; however, allergic contact dermatitis may occur and should be suspected if application-site reactions spread beyond the size of the transdermal system, there is evidence of a more intense local reaction, and symptoms do not significantly improve within 48 hours of transdermal system removal.
• Anesthesia: ADLARITY, as a cholinesterase inhibitor, is likely to exaggerate succinylcholine-type muscle relaxation during anesthesia.
• Cardiovascular conditions: Cholinesterase inhibitors, including ADLARITY, may have vagotonic effects on the sinoatrial and atrioventricular nodes. These effects may manifest as bradycardia or heart block in patients both with and without known underlying cardiac conduction abnormalities. Syncopal episodes have been reported in association with the use of donepezil.
• Nausea and vomiting: Donepezil has been shown to produce diarrhea, nausea, and vomiting.

Although in most cases these effects have been transient, some cases lasted 1 to 3 weeks. Patients should be observed closely during initiation and titration of ADLARITY.
• Peptic ulcer disease and gastrointestinal bleeding: Cholinesterase inhibitors, including ADLARITY, may increase gastric acid secretion. Patients should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those with a history of ulcer disease or those receiving concurrent nonsteroidal anti-inflammatory drugs (NSAIDs). Clinical studies of donepezil tablets in a dose of 5 mg/day to 10 mg/day have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding.
• Genitourinary conditions: Although not observed in clinical trials of ADLARITY, cholinomimetics, including ADLARITY, may cause bladder outflow obstruction.
• Seizures: Cholinomimetics, including ADLARITY, are believed to have some potential to cause generalized convulsions; however, seizure activity may also be a manifestation of Alzheimer's disease.
• Pulmonary conditions: Cholinesterase inhibitors, including ADLARITY, should be prescribed with caution to patients with a history of asthma or obstructive pulmonary disease.

ADVERSE REACTIONS
The most common side effects (>3%) of ADLARITY 10 mg/day TDS were headache (15%), application- site pruritus (9%), muscle spasms (9%), insomnia (7%), abdominal pain (6%), application- site dermatitis (6%), constipation (6%), diarrhea (4%), application site pain (4%), dizziness (4%), abnormal dreams (4%) and skin laceration (4%).

DRUG INTERACTIONS
Cholinesterase inhibitors, including ADLARITY, have the potential to interfere with the activity of anticholinergic medications. A synergistic effect may be expected when cholinesterase inhibitors are given concurrently with succinylcholine, similar neuromuscular blocking agents, or cholinergic agonists such as bethanechol.

For additional safety information, click here for the Prescribing Information and Patient Information.

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 fully-integrated biopharmaceutical company that is leading the development and commercialization of CNS therapies that provide physicians with innovative treatment options for patients, their families, and their caregivers. Corium is commercializing two U.S. FDA approved products, ADLARITY and AZSTARYS. 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.

About the Journal of Alzheimer's Disease

Now in its 25th year of publication, the *Journal of Alzheimer's Disease* (JAD) is an international multidisciplinary journal to facilitate progress in understanding the etiology, pathogenesis, epidemiology, genetics, behavior, treatment, and psychology of Alzheimer's disease. The journal publishes research reports, reviews, short communications, book reviews, and letters-to-the-editor. Groundbreaking research that has appeared in the journal includes novel therapeutic targets, mechanisms of disease, and clinical trial outcomes. JAD has a Journal Impact Factor of 4.160 according to Journal Citation Reports (Clarivate, 2022). The journal is published by IOS Press. https://www.j-alz.com/.

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