Corium's New Once-Weekly Transdermal Alzheimer's Dementia Therapy ADLARITY® (donepezil transdermal system) Provides Drug Delivery Equivalent to Oral Donepezil With Favorable GI Side Effect Profile

Trial results reported at Alzheimer's Association International Conference

Boston, MA, August 1, 2022 – Corium, Inc., a commercial-stage biopharmaceutical company leading the development and commercialization of novel central nervous system (CNS) therapies, announced today that both strengths of its new once-weekly ADLARITY (donepezil transdermal system) maintain equivalent daily exposure of donepezil when compared to oral formulations of donepezil, along with a favorable overall gastrointestinal (GI) side effect profile, according to trial results reported in a poster (68981) at the Alzheimer's Association International Conference 2022 in San Diego.

ADLARITY, which uses Corium's proprietary CORPLEX™ technology, is the first and only once-weekly transdermal formulation of donepezil approved by the U.S. Food and Drug Administration. It is indicated for patients with mild, moderate, or severe dementia of the Alzheimer's type in 5 milligram per day (mg/day) or 10 mg/day once-weekly formulations.

"The study results demonstrated that convenient once-weekly ADLARITY, which applies Corium's proprietary CORPLEX™ technology, offers significant potential benefit to patients and caregivers because it is equivalent to an oral pill taken daily but offers a lower risk of troublesome GI side effects," said Charles Oh, Chief Medical Officer of Corium. "This evidence underscores why Adlarity is an important advance in the treatment options for adults with dementia due to Alzheimer's disease."

"The doses of the once-weekly donepezil transdermal system were equivalent to oral donepezil on a milligram-per-day basis, and the safety profile of the transdermal system formulation, including the lower overall incidence of GI side effects, support its use in treating patients with dementia of the Alzheimer's type," said Pierre N. Tariot, MD, lead author of the AAIC 2022 poster and director of the Banner Alzheimer's Institute in Phoenix, Ariz.

Donepezil is the most prescribed medication in a class of Alzheimer's drugs known as acetylcholinesterase inhibitors and is the active ingredient in the oral medication Aricept®. ADLARITY delivers seven days of a consistent dose of donepezil through a patient's skin, maintaining the level of medicine needed for effective treatment. The transdermal delivery directly through a patient's skin bypasses the digestive system, resulting in a low possibility of GI side effects and making it easier for patients living with Alzheimer's disease and their caregivers to administer the treatment reliably. In contrast, oral donepezil is absorbed through a patient's digestive system, a route associated with significant GI side effects and fluctuations in the concentration of drug in circulation.

Patients may be switched from 5 mg/day or 10 mg/day oral donepezil directly to the once-weekly ADLARITY by their prescriber. ADLARITY is conveniently placed by a patient or caregiver on a patient's back, upper-outer thigh, or upper buttocks.

ADLARITY Transdermal System Equivalent in Donepezil Release Activity to Donepezil Pills With Fewer GI Adverse Events Overall

Investigators compared the extent of donepezil exposure from the once-weekly ADLARITY vs. a once-daily oral formulation in 60 healthy adults in the phase 1 trial (NCT04617782). They examined the amount of donepezil in the participants' blood, including the maximum plasma concentration (C_{max}) and the total amount of drug exposure (area under the curve or AUC).

The trial included three treatment periods of 5 weeks each. In the first period, all the participants received 5 mg/day ADLARITY. 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. Per FDA guidance, two pharmaceutical products are bioequivalent if the 90% confidence interval of the geometric mean ratio (GMR) for AUC and C_{max} is within 80–125%. The phase 1 study concluded that the GMR for AUC and C_{max} were within the bioequivalence range when comparing the 10 mg/day ADLARITY transdermal system to 10 mg/day oral donepezil.

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.

Fewer nervous system disorders overall were reported as well: 14.5% for 10 mg/day ADLARITY compared to 30.4% for 10 mg/day oral donepezil. Respectively, the incident rates were 14.5% vs. 12.5% for headache, 3.6% vs. 19.6% for dizziness, and zero vs. 10.7% for somnolence.

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.

The trial investigators plan to submit the complete trial data for publication in a peer-review journal.

ADLARITY Launch

Corium will begin its initial launch of ADLARITY in early fall 2022, when it will be available for prescription and use. In 2023, Corium will begin the national phase of the launch and further build out its commercial team in conjunction with ADLARITY becoming covered by Medicare Part D. In the interim, Corium will continue to expand coverage for and access to

ADLARITY with other health insurers and engage in medical education activities.

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 6.5 million Americans are living with Alzheimer's disease in 2022, 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 2021, more than 11 million Americans provided an estimated 16 billion hours of unpaid care for patients with Alzheimer's disease.

About CORPLEX

Corium has deep expertise in transdermal technology and an industry-leading track record of developing and manufacturing transdermal products. ADLARITY's approval represents an important milestone for Corium's proprietary and proven CORPLEX transdermal technology. CORPLEX was developed with the goal of optimizing clinical benefits for patients by delivering continuous, controlled, and sustained release of a drug over a defined time. Corium is developing other CNS therapies applying its CORPLEX technology and maintains a robust patent portfolio covering CORPLEX and ADLARITY.

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 FDA-approved CNS products in the U.S., including an ADHD medicine. 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.

Corium's President and CEO is Perry J. Sternberg, a biotechnology and pharmaceutical industry leader with more than 25 years of commercial experience across a wide range of therapeutic areas, including ADHD in diverse markets. Prior to joining Corium, Mr. Sternberg served a dual role at Shire Plc (Shire) as the Head of U.S. Commercial for seven therapeutic area business units, as well as the Chief Commercial Officer/Head of the Neuroscience Division, before the acquisition of Shire by Takeda Pharmaceutical Corporation Limited in early 2019.

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.

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:** ADLARITY may cause skin application-site reactions. 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 is likely to exaggerate succinylcholine-type muscle relaxation during anesthesia.
- **Cardiovascular conditions:** 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:** ADLARITY may cause diarrhea, nausea, and vomiting. Although in most cases these effects have been transient, some cases lasted 1 to 3 weeks. Patients should be monitored closely during initiation and titration of ADLARITY.
- **Peptic ulcer disease and gastrointestinal bleeding:** ADLARITY may increase gastric acid secretion. Patients should be monitored closely for active or occult gastrointestinal bleeding, especially those with a history of ulcer disease or those receiving concurrent nonsteroidal anti-inflammatory drugs (NSAIDs).
- **Genitourinary conditions:** Although not observed in clinical trials of ADLARITY, bladder outflow obstruction may occur.
- **Seizures:** ADLARITY is believed to have some potential to cause generalized convulsions; however, seizure activity may also be a manifestation of Alzheimer's

disease.

- **Pulmonary conditions:** ADLARITY should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.

ADVERSE REACTIONS

The most common side effects of ADLARITY (>3%) 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 donepezil, 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.

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Contact:
Corium, Inc.
Heather Gartman
Gartman PR
Gartmanpr@gmail.com
202-413-4226