# Cadrenal Therapeutics Highlights Presentation of New Trial Data at ISHLT Conference Demonstrating the Importance of Anticoagulation Quality in LVAD Patients

***Tecarfarin, which recently received Orphan Drug Designation from the FDA for the prevention of thromboembolism and thrombosis in patients with an implanted mechanical circulatory support device, has the potential to improve the time in therapeutic range a factor correlated in the ARIES-HM3 trial with better patient outcomes***

PONTE VEDRA, Fla., June 3, 2024 — **Cadrenal Therapeutics, Inc.**, (Nasdaq: CVKD), a biopharmaceutical company developing tecarfarin, a late-stage novel oral and reversible anticoagulant (blood thinner) designed to prevent heart attacks, strokes, and deaths due to blood clots in patients with rare cardiovascular conditions, today highlighted a groundbreaking presentation at the International Society for Heart & Lung Transplantation (ISHLT) 44th Annual Meeting & Scientific Sessions.

These new findings from secondary analyses of the ARIES-HM3 trial were released in a presentation titled, “Impact of Vitamin K Antagonist (VKA) Therapy On Outcomes In a Randomized Controlled Trial of Aspirin Removal In Left Ventricular Assist Device (LVAD) Patients – A Pre-Specified Analysis From the Aspirin and Hemocompatibility Events With a Left Ventricular Assist Device in Advanced Heart Failure, or the ARIES-HM3, Randomized Clinical Trial.”

The ARIES-HM3 trial data demonstrated that lower time in therapeutic range, or TTR, translated directly to excessive bleeding events. The “average” patient in the ARIES-HM3 study had a 30% rate of serious bleeding events even after aspirin was eliminated as part of the antithrombotic regimen, and persistent bleeding was inversely correlated with TTR.

The ARIES-HM3 clinical study was sponsored by Abbott (NYSE: ABT), which evaluated a new clinical approach to patient management that included removal of aspirin as part of the antithrombotic regimen warfarin. The data is currently under review by the FDA. Labeling changes related to the antithrombotic regimen have not been approved by the FDA at this time.

Dr. Mandeep Mehra, who chaired the ARIES-HM3 study, holds the William Harvey

Distinguished Chair in Advanced Cardiovascular Medicine and is Executive Director of the Center for Advanced Heart Disease at Brigham and Women's Hospital, commented, "This comprehensive analysis identifies adequacy of VKA use (as measured by TTR) as a significant risk marker for bleeding events and provides new clinical direction for further mitigation of bleeding to enhance hemocompatibility with the HeartMate 3 LVAD." Mehra continued, "Each incremental improvement of 10% above the median of 56% TTR trends in a significant further reduction in bleeding rate. Tecarfarin could potentially be an important therapy for patients with LVADs who all require chronic anti-coagulation since it does not get affected by drug-drug interactions or changes in kidney function like warfarin and deserves further study."

"The ARIES-HM3 trial data underscores the deficiencies of warfarin and the need for a new VKA therapy for patients with LVADs. We believe our drug candidate, the next-generation VKA tecarfarin, with its unique retrometabolic design that provides for more stable anticoagulation than warfarin, is the much-needed replacement therapy. We intend to pursue a pivotal trial evaluating tecarfarin effectiveness for LVAD patients," said Quang Pham, Founder, Chairman and Chief Executive Officer of Cadrenal Therapeutics. "Cadrenal commends Abbott's commitment to LVAD patients in sponsoring this important trial and analyses."

On April 9, 2024, Cardenal Therapeutics announced that the United States Food and Drug Administration (FDA) had granted tecarfarin Orphan Drug Designation for the prevention of thromboembolism and thrombosis in patients with an implanted mechanical circulatory support device, which includes the left ventricular assist device (LVAD).

The current market-leading direct oral anticoagulants (DOACs), such as Eliquis, are not indicated for patients with LVADs due to a lack of evidence of benefit, while the level of anticoagulation achieved with warfarin was achieved in the target range only 56% of the time in the ARIES-HM3 trial. Patients whose level of anticoagulation was in the therapeutic range > 56% had better outcomes than those with lower levels. This highlights the potential role for investigating new VKA agents in improving clinical outcomes in LVAD patients.

VKA anticoagulation is prescribed for the prevention of LVAD-related clotting. However, the only available VKA is warfarin, which was approved for human use in 1954. Tecarfarin has been shown to improve TTR, particularly in patients taking multiple medications, and be more stable in patients with renal dysfunction which is common in LVAD patients.

**ABOUT CADRENAL THERAPEUTICS, INC.**

Cadrenal Therapeutics is developing tecarfarin for unmet needs in anticoagulation therapy. Tecarfarin is a late-stage novel oral and reversible anticoagulant (blood thinner) to prevent heart attacks, strokes, and deaths due to blood clots in patients with rare cardiovascular conditions. Tecarfarin has orphan drug and fast-track designations from the FDA for the prevention of systemic thromboembolism (blood clots) of cardiac origin in patients with end-

stage kidney disease (ESKD) and atrial fibrillation (AFib) and just received orphan drug designation for the prevention of thrombosis and thromboembolism in patients with ventricular assist devices (VADs). Cadrenal is also pursuing additional regulatory strategies for unmet needs in anticoagulation therapy for patients with thrombotic antiphospholipid syndrome (APS). Tecarfarin is a next-generation Vitamin K Antagonist (VKA) specifically designed to use a different metabolism pathway than the oldest and most commonly prescribed VKA warfarin. Tecarfarin has been evaluated in eleven (11) human clinical trials and more than 1,000 individuals. In Phase 1, Phase 2, and Phase 2/3 clinical trials, tecarfarin has generally been well-tolerated in both healthy adult subjects and patients with chronic kidney disease. For more information, please visit: www.cadrenal.com.

**Safe Harbor Statement**

Any statements contained in this press release about future expectations, plans, and prospects, as well as any other statements regarding matters that are not historical facts, may constitute “forward-looking statements.” These statements include statements regarding tecarfarin having the potential to improve the time in therapeutic range which analysis of the ARIES-HM3 trial reveals is associated with better patient outcomes. TTRs as predicting increased risk for bleeding events, the VKA tecarfarin, filling the market void for a next-generation VKA, the Company pursuing a pivotal trial evaluating tecarfarin effectiveness for LVAD patients. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the ability of tecarfarin to improve the time in therapeutic range, the ability of the Company to advance tecarfarin with patients with left ventricular assist devices (LVADs), thrombotic APS, and those with AFib and ESKD and the other risk factors described in the Company’s Annual Report on Form 10-K for the year ended December 31, 2023, and the Company’s subsequent filings with the SEC, including subsequent periodic reports on Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. Any forward-looking statements contained in this press release speak only as of the date hereof and, except as required by federal securities laws, the Company specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events, or otherwise.

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