Cadrenal Therapeutics Highlights Additional Need for a New Vitamin K Antagonist (Tecarfarin) Following Updates from the Recent European Society of Cardiology Congress

Tecarfarin is the only known Novel Vitamin K Antagonist in Development

PONTE VEDRA, Fla., Sept. 5, 2023 — **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 certain rare medical conditions, today cited recent data that underscores additional need for an improved Vitamin K Antagonist (VKA). The Company believes tecarfarin is the solution for this unmet need.

At the recent European Society of Cardiology Congress (ESC) in Amsterdam, The Netherlands, the open-label "FRAIL-AF" trial was presented, revealing that switching International Normalized Ratio (INR)-guided VKA treatment to direct oral anticoagulants (DOACs aka NOACs) in frail older patients with Atrial Fibrillation (AFib) was associated with more bleeding complications compared to continuing VKA treatment, without an associated reduction in thromboembolic complications. Reports indicate that this unique trial was stopped early for futility in seeking superiority for the direct oral anticoagulant (DOAC) strategy. FRAIL-AF was deemed the most important study from ESC, according to Medscape.

In the report, study author Geert-Jan Geersing, MD, PhD, of the University Medical Center Utrecht in the Netherlands, at the ESC Congress concluded that "Switching from a VKA to a NOAC should not be considered without a clear indication in frail older patients with AFib."

Cadrenal is developing tecarfarin, a novel Vitamin K Antagonist, targeted for indications where existing VKAs fail to achieve sufficiently stable anticoagulation and DOACs (Eliquis-class drugs) are not widely prescribed.

"The findings of the FRAIL-AF study highlight the benefits of VKAs compared to DOACs in an additional unique patient population," commented Quang Pham, CEO of Cadrenal Therapeutics. "Tecarfarin, an enhanced VKA, avoids the existing metabolism problems of currently available VKAs by using an alternate metabolic pathway. We believe tecarfarin will provide improved outcomes for patients with certain rare medical conditions. Cadrenal has identified three such rare medical conditions: End-Stage Kidney Disease (ESKD) with Atrial

Fibrillation (AFib); Left Ventricular Assist Devices (LVADs); and Antiphospholipid Syndrome (APS)."

Currently, tecarfarin has orphan drug and Fast Track designations for the prevention of systemic thromboembolism (blood clots) of cardiac origin in patients with ESKD and AFib, providing for 7-year marketing exclusivity.

Based on management's market analysis studies and expected adoption rates, these three rare medical conditions present a U.S. market opportunity in excess of $2 billion per year.

ABOUT CADRENAL THERAPEUTICS, INC.

Cadrenal Therapeutics is developing tecarfarin, a late-stage novel oral and reversible anticoagulant (blood thinner), to prevent heart attacks, strokes, and deaths due to blood clots in patients with certain rare medical conditions. Tecarfarin has orphan drug and Fast Track designations for the prevention of systemic thromboembolism (blood clots) of cardiac origin in patients with ESKD and AFib. Tecarfarin is specifically designed to leverage a different metabolism pathway than the oldest and most commonly prescribed Vitamin K Antagonist (warfarin) used in the prevention of thrombosis. 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 being the solution for an improved Vitamin K Antagonist, tecarfarin providing improved outcomes for patients with certain rare medical conditions and End-Stage Kidney Disease with Atrial Fibrillation; Left Ventricular Assist Devices; and Antiphospholipid Syndrome presenting a U.S. market opportunity in excess of $2 billion per year.

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 be an improved Vitamin K Antagonist, the ability to advance tecarfarin within patients with rare medical conditions, the ability to penetrate the U.S. market for patients with End-Stage Kidney Disease with Atrial Fibrillation; Left Ventricular Assist Devices; and Antiphospholipid Syndrome and the other risk factors

described in the Company's Annual Report on Form 10-K for the year ended December 31, 2022, 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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