Cadrenal Therapeutics Announces Phase 2 Results with Encouraging Reductions in Thrombotic Events for CAD-1005 in HIT, Supporting Clinical Advancement

Greater than 25% absolute reduction in thrombotic events with CAD-1005 versus placebo on a background of standard anticoagulant therapy, despite no difference in platelet count recovery

End-of-Phase 2 Meeting Scheduled for March 2026

PONTE VEDRA, Fla., Feb. 24, 2026 (GLOBE NEWSWIRE) — Cadrenal Therapeutics, Inc. (Nasdaq: CVKD), a late-stage biopharmaceutical company advancing novel therapies for life-threatening immune and thrombotic conditions, today announced encouraging results from a Phase 2 trial evaluating CAD-1005 (formerly VLX-1005) in patients with heparin-induced thrombocytopenia (HIT), a severe pro-thrombotic reaction to heparin, the most commonly used parenteral anticoagulant.

This randomized, blinded, placebo-controlled trial evaluated the safety and efficacy of CAD-1005, a selective inhibitor of 12-lipoxygenase (12-LOX), a critical immune signaling pathway implicated in HIT, in patients receiving standard anticoagulant therapy. To potentially validate a new surrogate endpoint, the previous investigational new drug sponsor, Veralox Therapeutics, selected platelet count recovery rate as the primary endpoint. Their trial did not meet this primary endpoint. The secondary endpoint was the incidence of new or worsening thrombotic events, including radiologic progression, which showed encouraging results. The study concluded in December 2025 following the transfer of program ownership from Veralox to Cadrenal. Although CAD-1005 did not significantly affect platelet recovery rate, CAD-1005-treated patients had fewer thrombotic events.

Highlights:

- **Primary Endpoint:** Thrombotic events continued to occur even after platelet count recovery in both groups. Platelet recovery rates were similar between the CAD-1005 and placebo arms. Platelet count recovery did not appear to be a surrogate marker for clinical efficacy.
- **Key Secondary Endpoint:** A high rate of thrombotic events (>75%) was observed in the placebo group, with fewer thrombotic events in the CAD-1005 group (50%), although the study was not powered to detect statistical significance. Adding an inhibitor of 12-LOX to standard anticoagulants to block the immunological mechanisms driving HIT may be more effective than anticoagulants alone in preventing thrombotic events.

Building on these secondary endpoint results, Cadrenal has been granted an End-of-Phase 2

(EOP2) meeting with the U.S. Food and Drug Administration (FDA) to align on a Phase 3 registration path. The Company considers this meeting a significant milestone in the development of CAD-1005, the only 12-LOX inhibitor in clinical development worldwide.

“The encouraging trend toward reduced thrombotic events in the CAD-1005 treatment arm is strong support for the company’s decision to acquire this asset and rapidly progress its development,” said Quang X. Pham, CEO of Cadrenal Therapeutics. “Inhibition of 12-LOX is an exciting therapeutic frontier, potentially targeting numerous inflammatory, thrombotic, and metabolic conditions.”

“We learned two very important things from this study, the only blinded placebo-controlled trial ever conducted in HIT,” said James Ferguson, MD, Chief Medical Officer of Cadrenal Therapeutics. “First, platelet count recovery was not an appropriate surrogate endpoint for clinical efficacy in a trial in which standard therapy event rates were strikingly high. Secondly, despite the relatively small number of patients, the reduction in thrombotic events with CAD-1005 is extremely encouraging. CAD-1005 could represent a major step forward as the only first-line therapy targeting the immune mechanisms responsible for HIT.”

“Our field (HIT) is full of anticoagulant use in the absence of randomized prospective trials,” said Steven E. McKenzie, MD, PhD, Professor of Medicine at Thomas Jefferson University and a member of the study steering committee. “We are enthusiastic about CAD-1005 in addressing both the underlying immune mechanism and the unmet medical need for this serious thrombotic disorder.”

Detailed trial results will be presented at a future scientific meeting.

About Heparin-Induced Thrombocytopenia (HIT)

Heparin is the most widely used in-hospital anticoagulant, with over 12 million patients receiving it in the United States each year. Heparin-induced thrombocytopenia (HIT) is a potentially life-threatening immune-mediated complication of heparin administration that occurs when antibodies to heparin activate platelets, leading to clots throughout the circulatory system, dramatically lowering platelet counts, and increasing the risk of bleeding. Complications of HIT include deep vein thrombosis, pulmonary embolism, stroke, myocardial infarction, amputation, and death, with mortality rates for HIT exceeding 20% in some studies. CAD-1005 is the only treatment in clinical development that targets the underlying immune drivers of HIT.

About CAD-1005

CAD-1005 is an investigational therapy being evaluated for the treatment of suspected HIT. CAD-1005 is designed to selectively inhibit 12-LOX, a pathway integral to the primary immune mechanisms driving HIT. Unlike existing therapies for HIT, which are only directed at

preventing thrombotic complications, this approach addresses the primary underlying cause of HIT. In preclinical models of HIT, CAD-1005 has been shown to prevent or treat HIT and halt the development of both thrombocytopenia and blood clots. The drug has not been associated with increased bleeding in animals or healthy human volunteers. CAD-1005 has received Orphan Drug Designation (ODD) and Fast Track designation from the U.S. Food and Drug Administration, as well as orphan drug status from the European Medicines Agency.

About the Study

The study was originally planned to enroll 60 patients, but was stopped in December 2025 after program ownership transferred to Cadrenal. Analysis of all existing trial data was recently completed. The final dataset includes 24 patients with a presumptive diagnosis of HIT, randomized to receive either CAD-1005 or a matching placebo; all patients received concomitant standard anticoagulant therapy, either argatroban or bivalirudin. The primary endpoint was the rate of platelet count recovery; a key secondary endpoint was the development of new or worsening thrombotic events, the composite of death, stroke, systemic embolism, myocardial infarction, deep venous thrombosis, superficial vein thrombosis, or skin necrosis. Primary analyses focused on 17 patients in whom HIT was confirmed by a central lab functional assay.

About Cadrenal Therapeutics, Inc.

Cadrenal Therapeutics, Inc. (Nasdaq: CVKD) is a late-stage biopharmaceutical company advancing novel therapies for life-threatening immune and thrombotic conditions. Its lead program, CAD-1005, is a first-in-class 12-LOX inhibitor for the treatment of heparin-induced thrombocytopenia (HIT), a deadly immune-mediated thrombotic disorder. CAD-1005 has received Orphan Drug and Fast Track designations from the U.S. Food and Drug Administration, as well as orphan drug status from the European Medicines Agency. Second-generation 12-LOX oral therapeutics are also under development.

The Company’s broader pipeline includes tecarfarin, a Phase 3-ready oral vitamin K antagonist for the treatment of patients with end-stage kidney disease and those with left ventricular assist devices, and frunexian, a parenteral, clinical-stage Factor XIa inhibitor designed for use in acute hospital settings. For more information, visit https://www.cadrenal.com/ and connect with the Company on LinkedIn.

Safe Harbor

Any statements 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.” The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “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. These statements include adding an inhibitor of 12-LOX to standard anticoagulants to block the immunological mechanisms driving HIT being more effective than anticoagulants alone in preventing thrombotic events; the encouraging trend toward reduced thrombotic events in the CAD-1005 treatment arm being strong support for the Cadrenal's decision to acquire this asset and rapidly progress its clinical development; full trial results being presented at a future scientific meeting; the reduction in thrombotic events with CAD-1005 being extremely encouraging, despite the relatively small number of patients; CAD-1005 representing a major step forward as the only first-line therapy targeting the immune mechanisms responsible for HIT; The EOP2 meeting being a significant milestone in the development of CAD-1005; CAD-1005 addressing both the underlying immune mechanism and the unmet medical need for this serious thrombotic disorder; the encouraging trend toward reduced thrombotic events in the CAD-1005 treatment arm being strong support for Cadrenal's decision to acquire this asset and rapidly progress its development; CAD -1005 addressing the underlying immune drivers of HIT; and presenting detailed trial results at a future scientific meeting. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including Cadrenal's ability to advance the clinical development of CAD-1005 for the treatment of HIT, including designing a pivotal Phase 3 registration study acceptable to the FDA; CAD-1005 having the ability to address the underlying immune mechanism and the unmet medical need for the serious thrombotic disorder; Cadrenal's ability to continue to advance novel therapeutics to treat or prevent thrombosis in high-risk patients; Cadrenal's ability to successfully complete clinical trials on time and achieve desired results and benefits as expected including support for CAD-1005's potential to be a treatment option for HIT, Cadrenal's ability to obtain regulatory approvals for commercialization of product candidates or to comply with ongoing regulatory requirements and the other risk factors described in the Company's Annual Report on Form 10-K for the year ended December 31, 2024, and the Company's subsequent filings with the Securities and Exchange Commission, 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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