

Cadrenal Therapeutics Announces Positive Outcome from FDA Type D Meeting for Phase 3 Registration Study of CAD-1005 in Heparin-Induced Thrombocytopenia

FDA Alignment on Primary Endpoint and Path Forward for Phase 3 Registration Study

CAD-1005 Targets a Significant Unmet Need, with Approximately 50,000 Confirmed Acute HIT Diagnoses Annually in the U.S. and an Estimated \$2 Billion in Peak Annual Revenue Opportunity

PONTE VEDRA, Fla., Aug. 31, 2026 (GLOBE NEWSWIRE) — Cadrenal Therapeutics, Inc. (Nasdaq: CVKD), a late-stage biopharmaceutical company advancing specialized therapies for critical care cardiology and orphan cardiovascular conditions, today announced positive feedback from a Type D Meeting with the U.S. Food and Drug Administration (FDA) held on July 28, 2026. During the meeting, Cadrenal and the FDA aligned on key aspects of the protocol and Statistical Analysis Plan (SAP) for the Phase 3 registrational study of CAD-1005, the Company's first-in-class 12-lipoxygenase (12-LOX) inhibitor in development to treat heparin-induced thrombocytopenia (HIT). HIT is a potentially life-threatening immune reaction to heparin, a widely used blood thinner, and can lead to dangerous blood clots.

In the U.S., heparin-induced thrombocytopenia (HIT) is a high-stakes emergency that affects approximately 50,000 patients with acute HIT each year. Current therapeutic options rely on standard anticoagulants to reduce thrombotic risk; however, they do not target the underlying immune mechanisms that drive this destructive cardiovascular cascade. CAD-1005 is a novel 12-LOX inhibitor designed to halt the core immune signaling pathway that drives platelet activation and vascular thrombosis. Developed as an essential add-on to standard anticoagulation, CAD-1005 targets a critical population and is projected to generate \$2 billion in peak annual revenue.

During the Type D meeting, the FDA agreed on an optimized definition of worsening HIT for the primary endpoint, based on progression of thrombotic events through Day 14 of treatment or hospital discharge. To ensure high-quality, reliable endpoint evaluation across clinical sites, the worsening component of the primary endpoint will also include extension of an existing thrombus into a new vascular segment or bed, avoiding potential site-to-site variability from manual size measurements. The updated composite primary endpoint will measure the proportion of Serotonin Release Assay-positive (SRA+) participants with adjudicated new or worsening composite thromboembolic events (CTEs) through Day 14 or hospital discharge. Additionally, the FDA agreed to use placebo control in the Phase 3 trial, with standard anticoagulation therapeutics for both the CAD-1005 and placebo control arms.

"We are very pleased with the collaborative, constructive feedback from the FDA during this Type D meeting," said Quang X. Pham, Chief Executive Officer of Cadrenal Therapeutics.

“Securing agreement on the primary endpoint definition and the blinding protocols for our saline control provides greater clarity on the regulatory path forward for CAD-1005. We have incorporated the Agency’s recommendations into our Phase 3 protocol and Statistical Analysis Plan, strengthening the design of a registration study intended to evaluate whether CAD-1005 can reduce dangerous thrombotic events that persist in patients with HIT despite current anticoagulant therapies.”

The Phase 3 trial design will also assess bleeding as a major safety endpoint using standard International Society on Thrombosis and Haemostasis (ISTH) criteria. All safety analyses will be conducted in the safety population of patients who receive at least one dose of the study drug.

About Cadrenal Therapeutics, Inc.

Cadrenal Therapeutics, Inc. is a late-stage biopharmaceutical company advancing specialized therapies for critical care cardiology and orphan cardiovascular conditions. The Company’s pipeline includes CAD-1005, tecarfarin, and frunexian. CAD-1005 is a novel investigational therapeutic in development for the treatment of heparin-induced thrombocytopenia (HIT) and Cardiac Surgery-Associated Acute Kidney Injury (CSA-AKI). CAD-1005 is designed to selectively inhibit 12-lipoxygenase (12-LOX), an enzyme central to platelet immune activation and thrombo-inflammatory signaling in HIT. CAD-1005 is intended to be used alongside existing standards of care and is being developed to address the underlying biological mechanisms that drive disease progression. CAD-1005 has an Orphan Drug Designation (“ODD”) from the U.S. Food and Drug Administration (“FDA”) for prophylaxis of thrombosis in patients with HIT, FDA Fast Track designation for the treatment and prevention of HIT, and an orphan designation from the European Medicines Agency for the treatment of platelet-activating factor 4 disorders. Second-generation 12-LOX oral therapeutics (CAD-2000) are also in development for chronic indications.

The Company’s broader pipeline includes tecarfarin, a late-stage oral vitamin K antagonist designed to prevent heart attacks, strokes, and deaths from blood clots in patients requiring chronic anticoagulation, including those with end-stage kidney disease and atrial fibrillation, those with left ventricular assist devices, and potentially those with Kawasaki disease (KD), an acute, self-limited, febrile illness that primarily affects children under 5 years old and is the leading cause of acquired heart disease in developed countries. The Company recently submitted a request to the FDA for Rare Pediatric Disease Designation (RPDD) for tecarfarin for “Prevention of the Formation of Life-Threatening Blood Clots Inside Coronary Artery Aneurysms in Children with Kawasaki Disease”. Tecarfarin has also received Orphan Drug and Fast Track designations from the FDA.

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, without limitation, statements regarding the planned Phase 3 registration study of CAD-1005, the development of CAD-1005 to treat HIT; CAD-1005 potentially halting the core immune signaling pathway that drives platelet activation and vascular thrombosis; CAD-1005 being an essential add-on to standard anticoagulation; CAD-1005 unlocking a projected \$2 billion in peak annual revenue; the worsening component of the primary endpoint of optimized definition of worsening HIT assessing extension of an existing thrombus into a new vascular segment or bed, avoiding potential site-to-site variability from manual size measurements; the updated composite primary endpoint measuring the proportion of Serotonin Release Assay-positive (SRA+) participants with adjudicated new or worsening composite thromboembolic events (CTEs) through Day 14 or hospital discharge; the regulatory path forward for CAD-1005; the registration study evaluating whether CAD-1005 can reduce dangerous thrombotic events that continue to occur in patients with HIT despite current anticoagulant therapies; the Phase 3 trial design evaluating bleeding as a major safety endpoint using standard International Society on Thrombosis and Haemostasis (ISTH) criteria; all safety analyses in the Phase 3 trial being conducted in the true safety population of patients who receive at least one dose of the study drug; the Company advancing specialized therapies for critical care cardiology and orphan cardiovascular conditions; CAD-1005 being successfully developed to treat HIT and CSA-AKI; CAD-1005 selectively inhibiting 12-LOX, an enzyme central to platelet immune activation and thrombo-inflammatory signaling in HIT; CAD-1005 being intended to be used alongside existing standards of care and being developed to address the underlying biological mechanisms that drive disease progression; second-generation 12-LOX oral therapeutics (CAD-2000) being developed for chronic indications; tecarfarin, a late-stage oral vitamin K antagonist, potentially preventing heart attacks, strokes, and deaths from blood clots in patients requiring chronic anticoagulation, including those with end-stage kidney disease and atrial fibrillation, those with left ventricular assist devices, and potentially those with Kawasaki disease; and the FDA's ultimate decision regarding the Company's request for RPDD for tecarfarin for the prevention of life-threatening blood clots inside coronary artery aneurysms in children with Kawasaki Disease; Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the Company's ability to advance its programs to clinical trial readiness; the Company's ability to enter into development, licensing, and commercialization transactions for CAD-1005, frunexian, and tecarfarin; the Company's ability to secure nondilutive grants to

advance its programs; and the other risk factors described in the Company's Annual Report on Form 10-K for the year ended December 31, 2025, 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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