

Cadrenal Therapeutics Advances Multi-Indication Strategy for CAD-1005; Launches Phase 2a Acute Kidney Injury (CSA-AKI) Clinical Plan to Accelerate Pharma Partnering at Upcoming BIO 2026

- **New high-value indication for** Phase 3-ready asset with data intended to support clinical development and strategic partnering discussions
- **Additional billion-dollar target-** Cardiac Surgery-Associated Acute Kidney Injury (CSA-AKI), a serious complication affecting 35,000 U.S. patients annually, with no approved FDA-approved targeted therapies
- **Dual-Purpose Synergy** – Planned Phase 2a proof-of-concept trial expected to generate safety, renal injury signals, and 12-LOX pathway biology in high-risk cardiac surgery patients, while generating high-value data potentially relevant to the Company’s lead HIT indication
- **Capital-Efficient Development:** Leverages shared in-hospital ICU infrastructure and an intravenous (IV) formulation to offer a turnkey critical care franchise for a global pharmaceutical partner
- **Maximizes 12-LOX Platform Valuation** – Strongly positioned for upcoming strategic collaboration and licensing meetings at BIO 2026

PONTE VEDRA, Fla., June 15, 2026 (GLOBE NEWSWIRE) — Cadrenal Therapeutics, Inc. (Nasdaq: CVKD), a biopharmaceutical company advancing novel therapies for life-threatening immune and thrombotic conditions, today announced that it plans to initiate a Phase 2a proof-of-concept clinical trial of its lead drug candidate, CAD-1005, being studied to prevent Acute Kidney Injury (AKI) in high-risk patients undergoing cardiac surgery. The trial is expected to begin later this year.

“The addition of a CSA-AKI indication further expands CAD-1005’s potential as a multi-billion-dollar critical care platform,” said Quang X. Pham, Chief Executive Officer of Cadrenal Therapeutics. “CAD-1005’s potent, selective 12-LOX inhibition interrupts inflammatory and cell-death cascades frequently associated with cardiac surgery – a mechanism built for success in this population. This dual-indication program offers a turnkey franchise opportunity for pharmaceutical companies seeking to dominate hospital critical care applications and we believe creates a high-value inflection point for Cadrenal to secure a well-capitalized strategic partner and fund our pipeline expansion through non-dilutive collaborations.”

The planned study is intended to expand the clinical evaluation of CAD-1005 into a high-unmet-need acute-care setting while generating data that may be relevant to Cadrenal’s lead Phase 3-ready program in heparin-induced thrombocytopenia (HIT). HIT is a condition caused by an immune response to the widely used hospital blood thinner, heparin, resulting in blood clots that can cause death, amputation, stroke, and significantly increase healthcare costs. The Company expects to discuss the CSA-AKI clinical plan, its implications for CAD-1005’s

broader development strategy, and potential non-dilutive collaboration opportunities at the BIO International Convention.

Cardiac surgery remains a cornerstone of cardiovascular care, but it is often complicated by CSA-AKI, which affects roughly 35,000 U.S. patients each year. CSA-AKI represents a potential treatment market estimated at \$1 billion annually, a subset of the broader AKI market. CSA-AKI is associated with an approximately 8-fold increase in hospital mortality and significantly increases the risk of progressive, permanent kidney failure. There are currently no FDA-approved targeted pharmacologic therapies to prevent CSA-AKI. Cardiac surgery patients are also at risk for the potentially catastrophic complication of HIT. The planned Phase 2a trial builds on encouraging preclinical data in multiple animal models for CAD-1005 in AKI, as well as existing Phase 1 safety data. Moreover, it leverages the clinical overlap between AKI and HIT in cardiac surgery, enabling Cadrenal to efficiently collect dual-purpose validation data. Thus, in addition to potentially establishing proof of concept in the multi-billion-dollar AKI market, the trial will also generate key safety and mechanistic data that could help to de-risk the pivotal Phase 3 registration path for HIT.

About Cadrenal Therapeutics, Inc.

Cadrenal Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing a first-in-class 12-LOX therapeutic platform focused on thrombosis, inflammation, and the prevention of ischemia-reperfusion-related organ and tissue damage. The Company's lead asset, CAD-1005, is a selective 12-LOX inhibitor designed to address diseases driven by immune-mediated platelet activation, oxidative stress, and inflammatory tissue injury. CAD-1005 is being developed for heparin-induced thrombocytopenia (HIT), with additional development opportunities in acute kidney injury (AKI) and other critical-care indications characterized by ischemia-reperfusion injury and inflammatory organ damage.

Cadrenal is advancing its 12-LOX platform because this target is suspected to represent a central biological pathway across a broad range of acute and chronic diseases, creating the potential for a differentiated therapeutic pipeline targeting a common disease mechanism. The Company's plans include developing next-generation oral 12-LOX inhibitors for larger chronic disease opportunities.

Cadrenal's broader pipeline includes tecarfarin, a late-stage anticoagulant for patients requiring chronic anticoagulation, and frunexian, a Factor XIa inhibitor for acute hospital use.

For more information, visit <https://www.cadrenal.com/> and connect with the Company on LinkedIn.

About CAD-1005

CAD-1005 is an investigational therapy under evaluation for the treatment of suspected HIT.

CAD-1005 is designed to selectively inhibit 12-LOX, a pathway integral to the primary immune mechanisms that drive HIT. Unlike existing therapies for HIT, which are directed only at preventing thrombotic complications, this approach targets the primary underlying cause of HIT. 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 Acute Kidney Injury (AKI)

AKI is one of the most common and serious complications of cardiac surgery, affecting 20-30% of patients after cardiopulmonary bypass (CPB) and requiring renal replacement therapy (RRT) in approximately 1-5% of cases. It significantly increases morbidity, mortality, ICU length of stay, and the long-term risk of chronic kidney disease. There are currently no drugs approved for the prevention of AKI.

About 12-LOX

Lipoxygenases are lipid-metabolizing enzymes that catalyze the conversion of fatty acids into key components of cellular signaling pathways. One of these, 12-Lipoxygenase (12-LOX), plays a key role in the pathogenesis of AKI, immune-mediated platelet activation, and HIT. CAD-1005 is a selective inhibitor of 12-LOX and the only one in clinical-stage development. It has promising preclinical data in AKI and more recent preliminary Phase 2 data in HIT. Genetic depletion or pharmacological inhibition of 12-LOX has been shown to be protective against disease development and/or progression in animal models of diabetes, pulmonary, cardiovascular, and metabolic diseases.

About Heparin-Induced Thrombocytopenia (HIT)

Heparin is the most widely used in-hospital anticoagulant, with more than 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, markedly 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.

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 plans for a Phase 2a proof-of-concept clinical trial of CAD-1005 being studied to prevent Acute Kidney Injury (AKI) in high-risk patients undergoing cardiac surgery; enrollment to begin later this year; data intended to support clinical development and strategic partnership discussions; CAD-1005’s potential as a multi-billion-dollar critical care platform; the dual-indication program creating a high-value inflection point for Cadrenal to secure a well-capitalized strategic partner and fund its pipeline expansion through non-dilutive collaborations; being strongly positioned for upcoming strategic collaboration and licensing meetings at BIO 2026; potential to establish proof-of-concept in the multi-billion-dollar AKI market and the trial generating key safety and mechanistic data that could help to de-risk the pivotal Phase 3 registration path. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the ability to raise sufficient capital to continue progress of CAD-1005; the ability to advance to Phase 3 study evaluating CAD-1005 in patients with HIT; the ability to successfully design and complete the Phase 2a study and derive the results needed for further clinical development; 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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