Cadrenal Therapeutics Highlights Research Supporting 12-LOX Inhibition in Reducing Inflammation in Obesity and Type 2 Diabetes

PONTE VEDRA, Fla., March 12, 2026 (GLOBE NEWSWIRE) — Cadrenal Therapeutics, Inc. (Nasdaq: CVKD), a biopharmaceutical company developing innovative treatments for life-threatening immune and thrombotic conditions, today highlighted recent scientific findings demonstrating the potential of its first-in-class 12-lipoxygenase (12-LOX) inhibitor, CAD-1005, to target inflammatory consequences of obesity and Type 2 diabetes.

The study builds on prior animal research showing that inhibiting 12-LOX with CAD-1005 delays the onset of autoimmune diabetes in non-obese diabetic mice. The findings highlight 12-LOX as a key factor in obesity-associated inflammation and suggest that 12-LOX inhibition could be a therapeutic strategy to improve glucose homeostasis and peripheral inflammation in the setting of obesity and type 2 diabetes.

In the setting of obesity, 12-LOX overexpression leads to:

- Adipocyte dysfunction following recruitment of pro-inflammatory macrophages into adipose tissue triggering an inflammatory reaction that impairs tissue insulin sensitivity.
- Elevated 12-LOX activity in the pancreas causes oxidative stress and -cell dedifferentiation, hallmarks of Type 2 Diabetes progression.

In preclinical models, oral administration of CAD-1005 (formerly VLX-1005) demonstrated significant therapeutic benefits, including improved glycemic control, reduced pancreatic β-cell loss, reduced numbers of inflammatory cells in adipose (fat) and pancreatic tissues, and lower levels of pro-inflammatory cytokines in adipose tissues. Inhibiting 12-LOX acts as a selective “switch” to deactivate these pathways and interrupts a cycle of chronic inflammation, providing a dual benefit of restoring healthy metabolic signaling and protecting tissues from inflammatory damage.

Link to publication:
https://link.edgepilot.com/s/ca8ee2a3/c_cA13QyP0eg7_nCqlb4HQ?u=https://pubmed.ncbi.nlm.nih.gov/40186458/

Selective 12-LOX inhibition specifically targets important inflammatory signaling pathways that were previously difficult to reach, with potential applications across multiple areas. Unlike other treatments for obesity and diabetes, Cadrenal’s 12-LOX inhibitor is designed to block inflammatory signals in adipose tissues and the pancreas – key drivers of the metabolic derangements that accompany adiposity and diabetes. Cadrenal believes that CAD-1005 is the only product in clinical development that uses this mechanism to inhibit adipo-inflammatory signaling and potentially add to the benefits of existing GLP-1 obesity medications.

Cadrenal acquired the 12-LOX portfolio in December 2025. CAD-1005 is also being evaluated for suspected Heparin-Induced Thrombocytopenia (HIT), a severe pro-thrombotic reaction to heparin. The results of a recent Phase 2 trial demonstrated a reduction in thrombotic events in patients with HIT. Next-generation development includes CAD-2000, an orally bioavailable 12-LOX inhibitor.

“While our near-term priority remains the clinical development of CAD-1005 for HIT, these findings highlight the broader potential of 12-LOX inhibition in other inflammatory conditions,” said Quang X. Pham, CEO of Cadrenal Therapeutics. “We look forward to sharing our findings about 12-LOX in other disease areas with interested partners.”

About 12-LOX

Lipoxygenases are a family of enzymes involved in lipid metabolism that facilitate the incorporation of oxygen into polyunsaturated fatty acids. The enzymatic activity of 12-LOX ultimately produces 12-HETE, a lipid molecule that easily crosses cell membranes. Inside cells, 12-HETE promotes oxidative stress, while outside cells, it modulates various signaling pathways to regulate inflammation and provoke pro-inflammatory effects. In human blood, 12-LOX is primarily found in platelets and leukocytes; it is also overexpressed in the pancreas of patients with diabetes and in certain cancer cells. In HIT, 12-LOX plays a key role in platelet activation via the IgG receptor. Early efforts to develop 12-LOX inhibitors struggled because they lacked specificity for 12-LOX.

About CAD-1005

CAD-1005, an investigational therapy being evaluated for suspected HIT, is a potent, highly selective small molecule inhibitor of human 12-LOX. It is currently the only selective 12-LOX inhibitor in clinical development. CAD-1005 is designed to target 12-LOX specifically, a pathway crucial to the primary immune mechanisms that cause HIT. Unlike existing therapies for HIT, which mainly focus on preventing blood clots, this approach addresses the root cause of HIT. In preclinical models, CAD-1005 has been shown to prevent or treat HIT and stop the development of thrombocytopenia and blood clots. The drug has not been linked to 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 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 and orphan drug status from the European Medicines Agency. Second-generation 12-LOX oral therapeutics are also under development for chronic indications.

The Company's broader pipeline features tecarfarin, a late-stage oral vitamin K antagonist designed to prevent heart attacks, strokes, and deaths due to blood clots in patients requiring chronic anticoagulation, including for patients with end-stage kidney disease and left ventricular assist devices, and frunexian, a parenteral Factor XIa inhibitor intended 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 Cadrenal developing innovative treatments for life-threatening immune and thrombotic conditions; CAD-1005 targeting inflammatory consequences of obesity and Type 2 diabetes; 12-LOX inhibition improving glucose homeostasis and peripheral inflammation in the setting of obesity and type 2 diabetes; 12-LOX inhibition having potential applications across multiple areas; Cadrenal's 12-LOX inhibitor blocking inflammatory signals in adipose tissues and the pancreas – key drivers of the metabolic derangements that accompany adiposity and diabetes; CAD-1005 inhibiting adipo-inflammatory signaling and potentially add to the benefits of existing GLP-1 obesity medications; advancing the clinical development of CAD-1005 for the treatment of HIT; the development of CAD-2000, an orally bioavailable 12-LOX inhibitor; the broader potential of 12-LOX inhibition in other inflammatory conditions; sharing findings about 12-LOX in other disease areas with interested partners; CAD-1005 targeting 12-LOX specifically, a pathway crucial to the primary immune mechanisms that cause HIT, and addressing the root cause of HIT; CAD-1005 successfully preventing or treating HIT and stopping the development of thrombocytopenia and blood clots; Cadrenal advancing novel therapies for life-threatening immune and thrombotic conditions; Cadrenal developing second-generation 12-LOX oral therapeutics for chronic indications; tecarfarin preventing heart attacks, strokes, and deaths due to blood clots in patients requiring chronic anticoagulation, including for patients with end-stage kidney disease and left ventricular assist devices; and frunexian being used in acute hospital settings. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including Cadrenal developing innovative treatments for life-threatening immune and thrombotic conditions; advancing the clinical

development of CAD-1005 for the treatment of HIT; Cadrenal advancing novel therapies for life-threatening immune and thrombotic conditions; Cadrenal developing second-generation 12-LOX oral therapeutics for chronic indications; tecarfarin preventing heart attacks, strokes, and deaths due to blood clots in patients requiring chronic anticoagulation, including for patients with end-stage kidney disease and left ventricular assist devices; frunexian being used in acute hospital settings; 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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