Cadrenal Therapeutics Announces Clinical Trial Initiation Plans for Tecarfarin in Patients with End-Stage Kidney Disease (ESKD) Transitioning to Dialysis

Advances knowledge about the use of tecarfarin in patients with severe kidney impairment, including dialysis

Pivotal step forward in pursuit of ESKD + Atrial Fibrillation (AFib) registration trial

Addresses a critical current treatment gap in patients with ESKD

PONTE VEDRA, Fla. – Cadrenal Therapeutics, Inc. (Nasdaq: CVKD), a biopharmaceutical company focused on developing transformative therapeutics that specifically address limitations of current anticoagulation therapy, today announced clinical trial initiation plans for its lead late-stage drug candidate, tecarfarin, in patients with ESKD who are transitioning to dialysis. Enrollment is planned to begin later this year and will include patients with and without atrial fibrillation (AFib).

Patients with severe kidney disease are already at high risk for thrombotic cardiovascular events such as myocardial infarction and stroke, along with a much greater risk of AFib and venous thromboembolism compared to subjects with normal kidney function. When ESKD patients require dialysis, their transition period comes with even greater risk of myocardial infarction, stroke, and a substantial increase in mortality.

“There is a critical need for safe, effective anticoagulants for use in ESKD patients,” said Quang X. Pham, Chairman and CEO of Cadrenal Therapeutics. “Tecarfarin’s orphan drug and fast-track designations in ESKD patients with AFib underscore this need, and we are excited to advance this program. This study will be an important step forward for the continued development of tecarfarin in ESKD and in other areas with real opportunities to improve patient outcomes with a potentially better vitamin K antagonist.”

Currently, there is limited evidence supporting the use of anticoagulant therapy in dialysis patients. Dialysis patients are often excluded from clinical trials due to their high underlying risk profile, and studies of direct oral anticoagulants (DOACs) in this patient population have not provided clear answers. Furthermore, a recent Phase 2 trial of chronic hemodialysis patients sponsored by a global company showed no benefit from the new class of Factor XI inhibitors in maintaining vascular access graft patency. To date, no prospective studies have examined the benefit of oral anticoagulation in preventing thrombotic events at the time of dialysis initiation.

“Initiating dialysis carries substantial excess risk of cardiovascular events and mortality, and to date, this risk has not been sufficiently addressed. Tecarfarin, a next-generation Vitamin K

antagonist with a unique metabolism pathway that is not significantly affected by kidney impairment, has potential promise in this area of unmet need," said Wolfgang Winkelmayer, Professor of Medicine and Chief of Nephrology at Baylor College of Medicine in Houston, Texas.

About Cadrenal Therapeutics, Inc.

Cadrenal Therapeutics, Inc. is a biopharmaceutical company developing transformative therapeutics to address limitations of current anticoagulation therapy specifically. Cadrenal's lead investigational product is tecarfarin, a novel oral vitamin K antagonist anticoagulant that is designed to address unmet needs in anticoagulation therapy. Tecarfarin is a reversible anticoagulant (blood thinner) designed to prevent heart attacks, strokes, and deaths due to blood clots in patients requiring chronic anticoagulation. Although warfarin is widely used off-label for several indications, extensive clinical and real-world data have shown it can have significant, serious side effects. With tecarfarin, Cadrenal is advancing an innovative solution to address the unmet needs in anticoagulation therapy, aiming to reduce the clinical complexities of managing Vitamin K antagonists and where DOACs remain inadequate or unproven.

Tecarfarin received Orphan Drug Designation (ODD) and fast-track status for the prevention of systemic thromboembolism (blood clots) of cardiac origin in patients with end-stage kidney disease and atrial fibrillation (ESKD+AFib). The company also received ODD for the prevention of thromboembolism and thrombosis in patients with implanted mechanical circulatory support devices, including Left Ventricular Assist Devices (LVADs). The company has submitted an Orphan Drug Designation Request to the US FDA for patients with chronic kidney disease who have an implanted mechanical heart valve (and consequently require lifelong anticoagulation with a VKA) who also have genetic predisposition to impaired CYP2C9 metabolism, and resulting associated challenges with achieving reliable degrees of anticoagulation with the long-term use of warfarin.

Cadrenal is opportunistically pursuing business development initiatives with a longer-term focus on creating a pipeline of cardiovascular therapeutics. For more information, visit https://www.cadrenal.com/and connect with us 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 statements regarding initiation of clinical trial for tecarfarin in

patients with ESKD transitioning to dialysis; initiation of registration trial in patients with ESKD and AFib, developing transformative therapeutics to specifically address limitations of current anticoagulation therapy; addressing a critical current treatment gap in patients with ESKD; enrollment in the planned clinical trial beginning later this year; the planned study being an important step forward for the continued development of tecarfarin in ESKD; improving patient outcomes with a potentially better vitamin K antagonist; tecarfarin offering potential promise in patients initiating dialysis; addressing the unmet needs in anticoagulation therapy; and Cadrenal's ability to pursue business development initiatives with a longer-term focus on creating a pipeline of cardiovascular therapeutics. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including the ability to develop transformative therapeutics to specifically address limitations of current anticoagulation therapy; the ability to address a critical current treatment gap in patients with ESKD; the ability to advance an innovative solution to address the unmet needs in anticoagulation therapy; the ability to initiate and successfully complete clinical trials on time and achieve desired results and benefits as expected; the ability of Cadrenal to build a pipeline of specialized cardiovascular therapeutics and other assets 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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