Kardigan Completes Enrollment in Phase 2b KATALYST-AV Trial and Announces New Evidence Supporting Patient Selection and Endpoints for the Evaluation of Ataciguat in Aortic Stenosis

November 6, 2026

Primary endpoint of aortic valve calcium in KATALYST-AV to be assessed at Week 48 alongside aortic valve area and measures of cardiac structure and function; topline data expected 2H 2027

Novel real-world data help identify key markers of risk, rate of progression of disease and worsening outcomes in aortic stenosis, informing patient selection criteria and potential endpoints for Phase 3 registrational trial

Company to host an investor webcast while at the American Heart Association Scientific Sessions on Saturday, November 7, 2026, at 8:00 AM ET

SOUTH SAN FRANCISCO, Calif. & PRINCETON, N.J.--(BUSINESS WIRE)--Nov. 6, 2026-- Kardigan®, Inc. (Nasdaq: KARD), a precision cardiovascular company, today announced enrollment completion in the Phase 2b KATALYST-AV trial of ataciguat in people with aortic stenosis (AS). The Company also shared insights from a pre-planned analysis of the trial's baseline data, as well as new evidence on disease progression from one of the largest real-world analyses conducted in approximately 45,000 people with AS. These analyses support the primary endpoint assessment of aortic valve calcium (AVC) at Week 48, alongside measures of cardiac structure and function, and an internal interim analysis at Week 24.

"Completing enrollment in KATALYST-AV is a foundational milestone for our program and an important one for people with aortic stenosis," said Tassos Gianakakos, co-founder, chief executive officer and board chair of Kardigan. "As with our other clinical programs, KATALYST-AV was specifically designed to enable us to learn and adapt as evidence accumulates. The real-world data give us a clearer picture of which AS patients progress more quickly to worsening outcomes and the markers associated with that progression, directly informing how we design our upcoming registrational trial. In addition, our analysis of aortic valve calcium in the KATALYST-AV baseline data is consistent with the variability observed in the real-world data, which indicates more time is needed to assess a robust reduction in calcium with ataciguat versus placebo. Together, these findings reinforce our development strategy addressing both valve calcification and ventricular dysfunction with ataciguat and strengthen our confidence in its potential to become the first therapy to slow the progression of aortic stenosis."

KATALYST-AV Baseline Data

A pre-planned analysis of the KATALYST-AV baseline characteristics showed that AVC varied widely across the enrolled population. Baseline data from the first 139 participants (out of 156 total enrolled) in the KATALYST-AV intent-to-treat population are consistent with the real-world findings (reported below) of markers and predictors of rapid progression, including 30% with left ventricular (LV) hypertrophy, 21% with elevated filling pressures, 14% with low flow and 26% with left atrial enlargement. Baseline AVC ranged from 320 to 1,983 Agatston units, with substantial overlap in participants with or without ventricular dysfunction.

Because calcium accrues at each patient's own rate across this wide range, the Company amended the KATALYST-AV protocol to allow more time to assess the change in AVC with the treatment of ataciguat versus placebo in people with aortic stenosis. An interim analysis at Week 24 will be reviewed internally to evaluate rates of progression and directional mechanistic trends of ataciguat on the valve and the ventricle to further inform the design of the Phase 3 registrational trial.

Real-World Analysis of Aortic Stenosis Progression[1]

The Company analyzed disease progression in a retrospective, de-identified dataset of approximately 45,000 people with mild-to-moderate AS from multiple U.S. academic medical centers. The real-world analysis showed that AS progresses through both the valve and the myocardium, two areas potentially targeted by the mechanism of ataciguat. Notably, AS patients with signs of cardiac damage on routine echocardiography were more likely to progress rapidly and experience worse outcomes. This analysis was designed to identify at-risk patients for the upcoming Phase 3 registrational trial for ataciguat.

In the analysis, baseline aortic valve area (AVA) was the strongest predictor of progression. Approximately 27% of patients progressed rapidly (defined as a decline in AVA of at least 0.1 cm^2/year), across both mild and moderate AS. Patients with signs of cardiac damage on routine echocardiography (LV hypertrophy, enlarged left atrium, low flow, or impaired relaxation) were more likely to progress rapidly, and rapid progression predicted higher rates of valve replacement, hospitalization and worsening heart failure.

AVC, an established predictor of adverse outcomes and a mechanistic marker of effect for ataciguat, varied widely in an exploratory analysis of the real-world data. Unlike AVA, AVC did not distinguish between rapid and normal progressors, indicating that a single baseline calcium measurement potentially reflects risk but not the pace of disease progression.

“These data add to the growing body of evidence that mild-to-moderate aortic stenosis is a continuum, with valvular disease and cardiac remodeling evolving at different rates across patients,” said Philippe Pibarot, DVM, PhD, FAHA, head of cardiology research, Université Laval. “Assessing changes in valve calcium over a longer period, alongside measures of disease progression, will provide a more complete picture of how changes in the valve relate to the course of the disease and outcomes that matter to patients.”

Additional details from the baseline data from KATALYST-AV and the real-world analysis will be presented during the Company’s webcast on Saturday, November 7.

KATALYST-AV Development Timeline

The primary endpoint in KATALYST-AV of AVC will now be assessed at Week 48, together with additional analyses evaluating change in AVA, LV mass index, stroke volume index, and E/e′. This allows for the effect of ataciguat on valve calcification to be read against the clinical course of disease. At Week 48, KATALYST-AV is powered to detect the same treatment effect assumed in the original design. At Week 24, the Company will conduct an internal interim analysis to assess the rates of progression and directional mechanistic trends of ataciguat on the valve and the ventricle. Together with the Week 48 results, these analyses will further inform the design and operational conduct of the upcoming Phase 3 registrational trial, including inclusion/exclusion criteria, endpoint selection, sample size, and follow-up duration.

The protocol amendment to the ongoing KATALYST-AV trial was made under blinded conditions without review of unblinded efficacy data and was not prompted by any safety finding. Kardigan expects to provide an update on its Phase 3 development plans in the first half of 2027 and to report Week 48 topline data in the second half of 2027.

Investor Webcast

The Company will host an investor webcast while at the American Heart Association Scientific Sessions on Saturday, November 7, 2026, at 8:00 AM ET, to provide more information on the real-world data of aortic stenosis disease progression and KATALYST-AV baseline data. Registration for the webcast is available on the Investors & Media section of the Kardigan website at https://ir.kardigan.bio/. Following the event, a replay of the presentations will be available on the website for a limited time.

About Ataciguat

Ataciguat is a once-daily, oral soluble guanylate cyclase activator being developed as a potential first-in-class treatment for AS and an alternative to the current “watchful waiting” approach and progression to valve replacement that is today’s standard of care. Ataciguat has the potential to revolutionize the management of AS as the first pharmacological therapy. Kardigan acquired rights to ataciguat, an investigational drug developed by, and in-licensed from, Sanofi and Mayo Clinic.

About Kardigan

Kardigan is a clinical-stage precision cardiovascular company developing medicines that target the root cause of specific cardiovascular diseases where no approved treatments exist. Led by a proven and experienced management team, Kardigan is reimagining cardiovascular drug discovery and development through an integrated approach that unites deep cardiovascular biology, real-world patient data, and advanced analytics to enable more precise, efficient, and informed development of novel therapies. Learn more about Kardigan and its mission at Kardigan.bio.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include express and implied statements regarding: Kardigan’s business, technology and strategy; the potential safety, efficacy and therapeutic benefits of its product candidates, including ataciguat’s potential effects on aortic valve calcification, the progression of aortic stenosis and myocardial structure and function; Kardigan’s plans and expectations concerning the design, conduct, timing, endpoints and results of its current and future clinical trials, including the ongoing KATALYST-AV Phase 2b clinical trial; the anticipated use of baseline, real-world and observational data to inform future research into aortic stenosis and future clinical development; and Kardigan’s expectations regarding its ability to advance product candidates into, and successfully complete, clinical trials and its commercialization efforts for any of its future approved products, if any.

The words “anticipate,” “believe,” “could,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “should,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are based on Kardigan’s current expectations and assumptions and are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. These risks and uncertainties include, among others: risks relating to Kardigan’s research and development activities; Kardigan’s ability to execute on its strategy, including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to preclinical and clinical development activities; Kardigan’s dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; Kardigan’s ability to attract, integrate and retain key personnel; risks related to Kardigan’s financial condition and need for substantial additional funds in order to complete development activities and commercialize a product candidate, if approved; risks related to regulatory

developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining Kardigan's intellectual property protections; and risks related to the competitive landscape for Kardigan's product candidates; as well as additional risks described under the heading "Risk Factors" in Kardigan's most recent Quarterly Report on Form 10-Q and in Kardigan's subsequent filings with the Securities and Exchange Commission.

Forward-looking statements are not guarantees of future performance, and undue reliance should not be placed on them. Forward-looking statements speak only as of the date made and should not be relied upon as representing Kardigan's views as of any subsequent date. Except as required by applicable law, Kardigan undertakes no obligation to update any forward-looking statement as a result of new information, future events or otherwise.

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[1] The real-world analysis was conducted using the nference nSights platform containing de-identified real-world data from the nference Federated Healthcare Network.

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