PRESS RELEASE

Kardigan Announces Positive Phase 2 Data for Tonlamarsen in Patients with Uncontrolled Hypertension Presented as Late-Breaker at ACC.26 and Simultaneously Published in JACC

Patients treated with tonlamarsen experienced statistically significant reductions in plasma angiotensinogen levels and clinically meaningful changes in systolic blood pressure

Results support initiation of Phase 2b clinical trial of tonlamarsen in patients with acute severe hypertension

SOUTH SAN FRANCISCO, Calif., and PRINCETON, N.J., March 28, 2026 — Kardigan™, a clinical-stage precision therapeutics company developing medicines that target the root cause of specific cardiovascular diseases where no approved treatments exist, today announced results from KARDINAL, a Phase 2 clinical trial evaluating the effects of tonlamarsen in patients with uncontrolled hypertension despite treatment with two or more antihypertensive medications. Data were presented at the American College of Cardiology's Annual Scientific Session & Expo (ACC.26) and simultaneously published in The Journal of the American College of Cardiology (JACC). In the clinical trial, tonlamarsen, an investigational antisense oligonucleotide (ASO) targeting angiotensinogen (AGT), demonstrated a statistically significant reduction in plasma AGT levels and a clinically meaningful reduction in in-office systolic blood pressure (oSBP) from baseline to Week 20. These results highlight the intended biological effect of tonlamarsen and support

evaluation in Kardigan's planned Phase 2b clinical trial in patients with acute severe hypertension (ASH) post-hospitalization.

After a four-week placebo run-in period, all eligible subjects received a single 90 mg tonlamarsen injection for a four-week active run-in period and were then randomized to continued monthly dosing of tonlamarsen or placebo for 16 weeks. The results of the clinical trial demonstrated a dose-dependent, statistically significant reduction in AGT levels, with patients receiving five monthly doses of 90 mg tonlamarsen achieving a 67% mean reduction from baseline to Week 20 compared with a 23% mean reduction in patients receiving a single dose ($p<0.0001$, co-primary endpoint). Reduction in oSBP from baseline to Week 20 did not differ significantly between treatment groups due to an unexpected, prolonged reduction in blood pressure in the single-dose arm ($p=0.97$, co-primary endpoint).

In additional analyses, both treatment groups demonstrated a clinically meaningful reduction in oSBP of -6.7 mmHg when compared within group from baseline to Week 20 (single-dose tonlamarsen group: 95% CI, -9.8 to -3.5 mmHg; five-dose tonlamarsen group: 95% CI, -9.8 to -3.6 mmHg). Notably, in a post hoc analysis, participants with the highest hypertensive burden (oSBP >150 mmHg at baseline) in the five-dose tonlamarsen group experienced the greatest reductions in oSBP (-8.9 mmHg at Week 20), supporting the clinical rationale for evaluating tonlamarsen in patients with ASH. An additional post hoc analysis showed that participants who received five doses of tonlamarsen experienced a decline in surges of at-home systolic blood pressure (hSBP) above 150 mmHg over the course of the study relative to baseline at Week 0. Furthermore, an absolute 28% reduction in such surges was observed for the five-dose tonlamarsen arm at Week 20 compared to those who received a single dose (50%; 95% CI: 34.9-65.1 versus 78%; 95% CI: 64.0 to 88.5).

Tonlamarsen was generally well-tolerated, with a safety profile comparable to prior studies. Worsening renal function was uncommon and there were no meaningful signs of treatment-related hypotension or hyperkalemia.

"The KARDINAL clinical trial supported tonlamarsen's hypothesized mechanism of action by demonstrating sufficient modulation of angiotensinogen, resulting in clinically meaningful blood pressure lowering, and potential for a favorable safety profile, particularly in patients with higher hypertensive burden," said Jay Edelberg, M.D., Ph.D., co-founder and chief medical officer at Kardigan. "Together, these findings strengthen our therapeutic hypothesis for tonlamarsen in patients with acute severe hypertension and will inform the

KARDINAL-ASH Phase 2b clinical trial in this high-risk population with an urgent unmet medical need."

KARDINAL was a randomized, double-blind, placebo-controlled, parallel group, Phase 2 clinical trial for the management of chronic hypertension in 198 patients with uncontrolled hypertension (systolic blood pressure greater than 135 mmHg and less than or equal to 170 mmHg) on a background of two to five therapies for the chronic management of hypertension, including greater than 80% on angiotensin-converting enzyme (ACE) or angiotensin receptor blocker (ARB) therapy. The clinical trial was designed to assess the safety and efficacy of tonlamarsen, including the use of the Prolaio™ technology platform for home-based, high-density blood pressure and ECG data collection to support the objective assessment of blood pressure management and heart failure parameters. The baseline mean oSBP of participants was 147.6 mmHg and 145.9 mmHg for the single dose and five-dose tonlamarsen arms respectively.

"While continued dosing with tonlamarsen reduced angiotensinogen more than a one-time treatment, both treatment strategies reduced blood pressure to a similar extent," said Luke Laffin, M.D., principal investigator and co-director of the Center for Blood Pressure Disorders in the Heart, Vascular & Thoracic Institute at Cleveland Clinic. "It's important to continue to study tonlamarsen in patients who really need it, including those with acute severe hypertension, since so many struggle to take daily medications."

Tonlamarsen is one of three late-stage investigational candidates that Kardigan is developing in parallel, as part of its portfolio of targeted product candidates designed to modify the underlying cause of various cardiovascular diseases. The company intends to start the tonlamarsen randomized Phase 2b clinical trial in ASH later this year. The company is also developing danicamtiv[i], an investigational cardiac myosin activator targeting familial and genetic dilated cardiomyopathy (DCM) driven by sarcomeric mutations to restore cardiac function through direct activation in both the left atrium and left ventricle, and ataciguat[ii], a once-daily, investigational oral soluble guanylate cyclase (sGC) activator, as a potential first-in-class treatment for moderate calcific aortic valve stenosis and an alternative to "watchful waiting."

About Acute Severe Hypertension (ASH)
Acute severe hypertension (ASH) is a sudden elevation in blood pressure greater than or equal to 180/110 mmHg. Approximately six million patients present in emergency rooms with ASH and about two million cases lead to hospitalization each year in the United States. Following hospital discharge, patients with ASH are in a high-risk, vulnerable

period, and often experience ongoing health challenges in the weeks and months after hospitalization, with persistent hypertension and continued risk of acute end-organ damage. ASH, often triggered by stress-hormones, is associated with dysregulation of angiotensinogen (AGT), a key upstream precursor in the Renin-Angiotensin-Aldosterone System (RAAS), the main pathway in blood pressure regulation. While many people who develop ASH have underlying chronic resistant or uncontrolled hypertension, the near-term risk associated with this acute event is underappreciated and has rarely been studied as a separate condition. There are currently no treatments indicated for the post-hospitalization management of blood pressure in patients with ASH.

About Tonlamarsen

Tonlamarsen is an investigational, subcutaneous, once-monthly, liver-directed antisense oligonucleotide (ASO) designed for the management of blood pressure in patients with acute severe hypertension (ASH) post-hospitalization. Tonlamarsen targets hepatic angiotensinogen (AGT), the sole precursor of the Renin-Angiotensin-Aldosterone System (RAAS), which regulates blood pressure, vascular tone, and blood volume. By directly down-modulating AGT at its source in the liver, tonlamarsen is designed to modulate the RAAS pathway upstream as an alternative approach to improving blood pressure management. Kardigan in-licensed exclusive worldwide development and commercialization rights to tonlamarsen, an investigational drug discovered and developed by Ionis Pharmaceuticals.

About Kardigan

Kardigan is a clinical-stage precision therapeutics 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. The company is based in South San Francisco, California and Princeton, New Jersey. To learn more, visit Kardigan.bio.

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[i] Kardigan in-licensed exclusive worldwide development and commercialization rights to danicamtiv, an investigational drug discovered at MyoKardia and further developed by Bristol Myers Squibb.
[ii] Kardigan acquired rights to ataciguat, an investigational drug developed by, and in-licensed from, Sanofi and Mayo Clinic.