# Monte Rosa Therapeutics Presents Preclinical Data at AHA Scientific Sessions 2025 on the Potential of MRT-8102, a NEK7-directed Molecular Glue Degrader, to Treat Cardiovascular and Cardiometabolic Diseases

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*Data support NEK7 as a potential novel and differentiated therapeutic approach to modulate the NLRP3 inflammasome in multiple cardiovascular and cardiometabolic diseases, including pericarditis and atherosclerosis*

*Initial data from a Phase 1 study of MRT-8102 in healthy volunteers and elevated CVD-risk subjects on track for first half of 2026*

*Poster presentation on November 8 at 10:30 a.m. CST*

BOSTON, Nov. 08, 2025 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced the company will present preclinical data on the potential of MRT-8102, a first-in-class, NEK7-directed MGD for inflammatory diseases driven by the NLRP3 inflammasome, at the American Heart Association's Scientific Sessions 2025, held November 7-10 in New Orleans, LA.

"These promising findings reinforce our belief in the highly differentiated profile of MRT-8102, the only clinical-stage degrader targeting NEK7, as a potential treatment for cardiovascular and cardiometabolic diseases such as pericarditis, atherosclerosis, and others," said Sharon Townson, Ph.D., Chief Scientific Officer of Monte Rosa Therapeutics. "By modulating the NLRP3/IL-1/IL-6 pathway upstream of other approaches, MRT-8102 potently inhibited pyroptotic cell death and inhibited the release of multiple inflammatory cytokines. Furthermore, MRT-8102 has the potential to block cholesterol crystal-induced cardiovascular inflammation characterized by pyroptosis and cytokine release that leads to atherosclerotic plaque pathogenesis. We are encouraged by the growing interest in targeting the NLRP3/NEK7 inflammasome to treat cardiovascular disease, and we believe we have a unique approach to achieve this. We continue to enroll our Phase 1 study of MRT-8102 and look forward to presenting initial data in healthy volunteers and elevated CVD-risk subjects in the first half of 2026."

The poster, entitled, "Selective Degradation of NIMA-related kinase 7 (NEK7) via a Molecular Glue Degrader Inhibits IL-1 Downstream of NLRP3 Inflammasome Activation: A Novel Therapeutic Approach for Cardiovascular Inflammation" (Poster Number #Sa4063), will be displayed on Saturday, November 8, 2025 from 10:30 to 11:30 a.m. CST in a poster session entitled, "Novel Cellular Stress Sensors in Cardiovascular Pathology: Metabolic, Mechanical, and Immune Interactions." The poster will be presented by Daric Wible, Ph.D., Senior Scientist II, Biology, Monte Rosa Therapeutics.

**Summary of key findings:**

- MRT-8102 is a selective, potent, and durable NEK7 degrader. Activation of the NLRP3 inflammasome critically depends on NEK7.
- Administration of MRT-8102 led to inhibition of NLRP3 inflammasome *in vitro* and *in vivo* and subsequently inhibited production of multiple inflammatory cytokines.
- In *in vitro* assays, MRT-8102 inhibited pyroptotic membrane permeabilization in stimulated human monocyte-derived macrophages (hMDM), unlike anti-IL-1 and anti-IL-6 therapies. Additionally, only MRT-8102 inhibited release of multiple cytokines from stimulated hMDM.
- *In vitro,* NEK7 degradation inhibited cholesterol crystal-induced NLRP3 inflammasome activation, a key driver of atherosclerotic plaque pathogenesis, more potently than selnoflast, an NLRP3 inhibitor currently in development.
- In a mouse peritonitis model, MRT-8102 led to potent inhibition of the cytokines IL-1β, IL-1α, IL-6, and TNF in peritoneal lavage.
- MRT-8102 demonstrated near-complete suppression of IL-1β and Caspase-1 activity in *ex vivo*-stimulated whole blood from orally dosed cynomolgus monkeys.
- Degrading NEK7 to modulate the inflammasome represents a novel and differentiated approach with potential therapeutic application in multiple cardiovascular and cardiometabolic diseases, including pericarditis and atherosclerosis.

**About MRT-8102**
MRT-8102 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader (MGD) that targets NEK7 for the treatment of inflammatory diseases linked to NLRP3, IL-1β, and IL-6 dysregulation. NEK7 has been shown to be required for NLRP3 inflammasome assembly, activation and IL-1β release both *in vitro* and *in vivo*. Aberrant NLRP3 inflammasome activation and the subsequent release of active IL-1β and interleukin-18 (IL-18) has been implicated in multiple inflammatory disorders, including cardiovascular disease, gout, osteoarthritis, neurologic disorders including Parkinson's disease and Alzheimer's disease, and metabolic disorders. In a non-human primate model, MRT-8102 was shown to potently, selectively, and

durably degrade NEK7, and resulted in near-complete reductions of IL-1β and caspase-1 following *ex vivo* stimulation of whole blood. MRT-8102 has demonstrated a considerable safety margin (>200-fold exposure margin over projected human efficacious dose) in GLP toxicology studies. MRT-8102 is currently being investigated in a Phase 1 study (clinicaltrials.gov identifier NCT07119125) in healthy participants and participants at elevated cardiovascular disease risk.

**About Monte Rosa**
Monte Rosa Therapeutics is a clinical-stage biotechnology company developing highly selective molecular glue degrader (MGD) medicines for patients living with serious diseases. MGDs are small molecule protein degraders that have the potential to treat many diseases that other modalities, including other degraders, cannot. Monte Rosa's QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) discovery engine combines AI-guided chemistry, diverse chemical libraries, structural biology, and proteomics to rationally design MGDs with unprecedented selectivity. Monte Rosa has developed the industry's leading pipeline of first-in-class and only-in-class MGDs, spanning autoimmune and inflammatory diseases, oncology, and beyond, with three programs in the clinic. Monte Rosa has ongoing collaborations with leading pharmaceutical companies in the areas of immunology, oncology and neurology. For more information, visit www.monterosatx.com.

**Forward-Looking Statements**
This communication includes express and implied "forward-looking statements," including forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include all statements that are not historical facts and in some cases, can be identified by terms such as "may," "might," "will," "could," "would," "should," "expect," "intend," "plan," "objective," "anticipate," "believe," "estimate," "predict," "potential," "continue," "ongoing," or the negative of these terms, or other comparable terminology intended to identify statements about the future. Forward-looking statements contained herein include, but are not limited to, statements around the potential of the Company's NEK7-directed MGD, referred to as MRT-8102, to address inflammatory diseases driven by the NLRP3 inflammasome, including cardiovascular disease and cardiometabolic disease, including pericarditis and atherosclerosis, the Company's belief that MRT-8102 could offer a differentiated approach to treating multiple inflammatory diseases based on the potency, selectivity, and durable pharmacodynamics seen in its preclinical studies, the Company's belief in the potential for MRT-8102 to treat cardiovascular disease by blocking cholesterol crystal-induced cardiovascular inflammation characterized by pyroptosis and cytokine release that leads to atherosclerotic plaque pathogenesis, our expectations for the continuing advancement of our Phase 1 study and the timing thereof, including updates related to status, safety data, pharmacokinetics, NEK7 protein degradation, and key downstream pharmacodynamic markers and the timing of any clinical data read-outs, including the potential readout of initial data in healthy volunteers and elevated CVD-risk subjects expected in the first half of 2026, as well as our expectations of success for our programs, including for MRT-8102, among others. By their nature, these statements are subject to numerous risks and uncertainties, including those risks and uncertainties set forth in our most recent Annual Report on Form 10-K for the year ended December 31, 2024, filed with the U.S. Securities and Exchange Commission on March 20, 2025, and any subsequent filings, that could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the statements. You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, performance, or events and circumstances described in the forward-looking statements will be achieved or occur. Recipients are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, any future presentations, or otherwise, except as required by applicable law. Certain information contained in these materials and any statements made orally during any presentation of these materials that relate to the materials or are based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of these materials, we have not independently verified, and make no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in these materials relating to or based on such internal estimates and research.

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