



Monte Rosa Therapeutics Announces Positive Results for MRT-8102 in GFORCE-1 Phase 1 Study Showing Normalization of Key Pathogenic Drivers of ASCVD in Subjects with Elevated CVD Risk

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In obese subjects at elevated cardiovascular disease (CVD) risk, MRT-8102, a NEK7-directed molecular glue degrader in development for the treatment of NLRP3/IL-1-driven inflammatory diseases, normalized multiple atherosclerotic cardiovascular disease (ASCVD) pathogenic drivers of local plaque inflammation, thrombosis, and systemic inflammation

Robust and sustained NEK7 degradation observed across 5 mg, 20 mg, and 40 mg once-daily dose levels, with similar biomarker reductions at all three doses

HMGB1, calprotectin, S100A12, and SAA, damage-associated molecular patterns (DAMPs) linked to atherosclerotic plaque progression and instability, and IL-1 β , all established key pathogenic drivers of ASCVD, were reduced to levels comparable to normal physiological levels seen in the healthy volunteer population of Phase 1 study

MRT-8102 was safe and well tolerated over four weeks of dosing and four weeks of follow-up, with no serious adverse events, treatment-emergent adverse event rates comparable to placebo, and no evidence of increased infection risk

Phase 2 trials planned across coronary artery disease (GFORCE-2), gout (GEMINI-1), and moderate to severe hidradenitis suppurativa (GALAXY-1)

Company to host conference call and webcast today, Oct. 1, at 8:00 a.m. ET

BOSTON, Oct. 01, 2026 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced positive data from GFORCE-1, a Phase 1 study evaluating MRT-8102, a NEK7-directed MGD being developed for the treatment of inflammatory conditions driven by the NEK7/NLRP3 pathway.

"The GFORCE-1 data are highly encouraging and show that MRT-8102 does precisely what we designed it to do: potently and selectively degrade NEK7 and reduce levels of upstream and downstream drivers of residual plaque inflammation and thrombotic risk, and it does so with a differentiated and favorable safety profile," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "We are particularly excited about our translational approach, including our unique and broad analysis of the NEK7/NLRP3 upstream pathway, that has allowed us to gain unprecedented insights into how inhibition of the pathway through NEK7 degradation leads to normalization of many of the most important drivers of atherosclerotic plaque formation, progression, and rupture. To that end, we observed compelling reductions of HMGB1, calprotectin, S100A12, SAA, and IL-1 β . These DAMPs and cytokines are linked to pathogenic biology within atherosclerotic plaques and vessel walls, and they have been identified as independent risk factors of much greater significance than some of the systemic inflammatory markers evaluated in other studies. We have also seen intriguing correlation of these markers with NLRP3 risk alleles, opening up opportunities for a precision medicine approach. The GFORCE-1 study results, alongside a body of genetic, biological, and clinical data, reinforce our rationale for degrading NEK7 to simultaneously dampen multiple key ASCVD disease drivers that can lead to atherosclerosis, plaque progression, and thrombogenesis. We believe targeting NEK7 at the top of the NLRP3 signaling cascade has the potential to provide a degree of clinical impact across NEK7/NLRP3-driven diseases not achievable by targeting individual downstream cytokines."

Filip Janku, M.D., Ph.D., Chief Medical Officer of Monte Rosa Therapeutics, commented, "We believe our results represent the most comprehensive translational data set reported to date for the NEK7/NLRP3 pathway. GFORCE-1 was designed to provide a broad view of the pharmacodynamic activity and safety of MRT-8102, and the profile we observed further bolsters our enthusiasm for continued development in cardiovascular disease and other indications. With dose selection now informed by these data, we plan to initiate GFORCE-2, a focused Phase 2b study in patients with coronary artery disease, in the first half of 2027. In GFORCE-2, our goal is to connect imaging-based coronary artery plaque assessment, such as fat attenuation index (FAI), with NLRP3 genetics and molecular drivers of local disease pathogenesis and systemic inflammation to inform the design of an innovative and efficient Phase 3 study focused on the most disease-modifiable patient population. We also expect to initiate GEMINI-1, a Phase 2 study in gout, in Q4 2026 or Q1 2027, and GALAXY-1, a Phase 2 study in moderate to severe hidradenitis suppurativa, in the first half of 2027, representing additional substantial opportunities associated with this pathway."

GFORCE-1 (clinicaltrials.gov identifier NCT07119125) enrolled 108 obese subjects with elevated CVD risk, randomized to MRT-8102 at once-daily doses of 5 mg, 20 mg, or 40 mg, or to placebo. The GFORCE-1 study followed best-in-class data from

the single ascending dose (SAD) and multiple ascending dose (MAD) cohorts in healthy volunteers, and those data were [previously reported](#). The GFORCE-1 study evaluated safety and tolerability, along with multiple pharmacodynamic markers, over a four-week treatment regimen, followed by four weeks of safety follow-up. Multiple dose levels were explored to support dose selection for further development across various NLRP3-driven diseases, including ASCVD, gout, and hidradenitis suppurativa.

Summary of GFORCE-1 Results

- GFORCE-1 enrolled 108 obese subjects with elevated CVD risk, randomized to MRT-8102 at 5 mg, 20 mg, or 40 mg once daily, or to placebo, for 4 weeks of dosing and 4 weeks of follow-up safety evaluation.
- MRT-8102 achieved robust and sustained NEK7 degradation, with a median reduction of approximately 80 to 90% observed across all three dose levels.
- Both local drivers of plaque growth and progression and systemic inflammatory biomarkers were substantially reduced following MRT-8102 administration at all three dose levels to levels comparable with baseline values from Phase 1 healthy volunteers.
- Median values of calprotectin, S100A12, and SAA, which are critical drivers of ASCVD progression, were lowered by 56%, 46%, and 51%, respectively.
- Median values of HMGB1 and IL-1 β were elevated at baseline and decreased toward healthy volunteer levels following treatment among subjects with elevated levels. Median reductions were 40% and 37%, respectively, in subjects with levels in the top quartile.
- The thrombogenic factor fibrinogen was reduced by a median of 28% to levels consistent with those in healthy volunteers.
- IL-6 and hsCRP, biomarkers of systemic inflammation, were reduced by a median of 54% and 85%, respectively. All three doses of MRT-8102 resulted in rapid and sustained reductions in hsCRP to levels comparable to baseline in healthy volunteers from the healthy volunteer cohorts.
- MRT-8102 administration reduced median lipoprotein(a) by 24%, comparable to PCSK9 inhibitors. Unlike IL-6(R) blockade, MRT-8102 treatment did not increase LDL-C or triglyceride levels.
- Significant increases in baseline biomarker levels were identified in carriers of NLRP3 risk alleles (approximately 30% of the GFORCE-1 population), particularly for DAMPs and IL-1 β , suggesting a higher-risk, genetically enrichable population for potential future development.
- MRT-8102 was well tolerated over four weeks of dosing and four weeks of follow-up. No serious adverse events (SAEs) were reported. Rates of treatment-emergent adverse events (TEAEs) were similar between MRT-8102 and placebo, occurring in 33% of MRT-8102 participants and 30% of placebo participants, with no evidence of increased infection risk.

Phase 2 Program for MRT-8102

Monte Rosa expects to initiate multiple Phase 2 studies of MRT-8102 in indications with high unmet need and strong biologic rationale for targeting the NEK7/NLRP3 pathway:

- GFORCE-2, a focused Phase 2b study of MRT-8102 in patients with stable coronary artery disease and residual inflammation, is expected to initiate in H1 2027. The study design, pending regulatory feedback, will evaluate changes in local pathogenic drivers of ASCVD, systemic biomarkers, and cardiovascular imaging over a six-month dosing period to specifically observe modulation of plaque biology, as well as changes in inflammatory, thrombogenic, and lipid mediators of disease. The Company is working to complete long-term preclinical toxicology studies to support this 6-month study.
- GEMINI-1, a Phase 2 study of MRT-8102 in patients with gout, is expected to initiate in Q4 2026 or Q1 2027. The study will investigate prevention of flare recurrence following management of acute flares with MRT-8102. Initial data are expected in H2 2027.
- GALAXY-1, a Phase 2 study of MRT-8102 in patients with moderate to severe hidradenitis suppurativa, is expected to initiate in H1 2027.

Investor Conference Call

Monte Rosa will host a conference call and webcast presentation today, October 1, 2026, at 8:00 a.m. ET. A webcast of the presentation will be accessible via the “Events & Presentations” section of Monte Rosa’s website at ir.monterosatx.com. Registration for the conference call is available at the following [link](#). An archived version of the webcast will be made available for 30 days following the presentation.

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 and IL-1 dysregulation. NEK7 has been shown to be required for NLRP3 inflammasome assembly, activation, and IL-1 β release both *in vitro* and *in vivo*. NLRP3 inflammasome activation causes pyroptotic cell death, leading to the release of IL-1 α/β , IL-18, and DAMPs such as HMGB1, calprotectin, S100A12, and SAA. IL-1 β

and IL-18 are highly inflammatory cytokines, and DAMPs further stimulate NLRP3 activity while promoting NLRP3-independent cytokine and chemokine production in neighboring cells. Together, DAMPs and IL-1 are responsible for the majority of the local inflammation and tissue changes characteristic of ASCVD, gout, hidradenitis suppurativa, and other indications. The NEK7/NLRP3 inflammasome plays a multifaceted role in plaque biology, contributing to plaque formation, plaque growth, vessel wall alterations, and thrombosis.

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 about our ability to grow our product pipeline, our ability to successfully complete research and further development and commercialization of our drug candidates in current or future indications, including the timing and results of our clinical trials and our ability to conduct and complete clinical trials, statements regarding our progress and speed of development of only-in-class and first-in-class molecular glue degrader therapeutics, statements around the Company's QuEEN™ discovery engine and the broad potential applications of the platform and the Company's ability to create long-term value through focused pipeline execution and strategic collaborations, statements about the advancement and timeline of our preclinical and clinical programs, pipeline and the various products therein, statements regarding the positive Phase 1 data of MRT-8102 from the GFORCE-1 study, including the safety, tolerability, target engagement, and other results observed, statements regarding the potential of MRT-8102 to normalize local and systemic pathologic drivers of ASCVD and to address NLRP3/IL-1-driven inflammatory diseases, our expectations regarding the potential of targeting NEK7 at the top of the NLRP3 inflammasome signaling cascade to provide differentiated clinical impact across NLRP3-driven diseases, including compared with targeting individual downstream cytokines, statements regarding the planned initiation of GFORCE-2, a Phase 2b study of MRT-8102 in patients with stable coronary artery disease and residual inflammation, including the expected timing, study design, regulatory feedback regarding the study design, use of coronary artery imaging, NLRP3 genetics and biomarkers to identify a disease-modifiable patient population and inform the design of a potential Phase 3 study, and the completion of long-term preclinical toxicology studies to support GFORCE-2, statements regarding the planned initiation of GEMINI-1, a Phase 2 study of MRT-8102 in patients with gout, including the expected timing, study design and objective of evaluating prevention of flare recurrence, and the expected timing of initial data, statements regarding the planned initiation of GALAXY-1, a Phase 2 study of MRT-8102 in patients with moderate to severe hidradenitis suppurativa, including the expected timing, statements regarding dose selection informed by GFORCE-1 data for further development across various NLRP3-driven diseases, statements regarding a genetically enrichable higher-risk population identified through NLRP3 risk alleles for potential future development, statements regarding opportunities for MRT-8102 in inflammatory diseases and statements around our expectations of success for our programs, 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, 2025, filed with the U.S. Securities and Exchange Commission on March 17, 2026, 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, as well as the risk that outcomes of preclinical studies may not be predictive of clinical trial results and the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials. 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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