Monte Rosa Therapeutics Announces Initiation of IND Enabling Studies for MRT-8102, A First-in-Class NEK7 Directed Molecular Glue Degrader and NLRP3/IL-1β Pathway Inhibitor

March 11, 2024

MRT-8102 nominated as first NEK7-directed development candidate, targeting inflammatory diseases driven by IL-1β and the NLRP3 inflammasome

MRT-8102 and other NEK7 program MGDs are potentially applicable across a range of inflammatory disorders, metabolic disorders, as well as ocular and neurological diseases

IND-enabling studies ongoing; IND submission anticipated in Q1 2025

BOSTON, March 11, 2024 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced a novel development candidate, MRT-8102, a potent, highly selective and orally bioavailable NIMA related kinase 7 (NEK7)-directed MGD. MRT-8102 is expected to be developed for the treatment of inflammatory diseases driven by interleukin-1β (IL-1β) and the NLRP3 inflammasome, which are critical elements of the inflammatory process. This is the first development candidate to be declared from the Company's NEK7 development program.

"NEK7 is an essential component of the NLRP3 inflammasome pathway that has been implicated in many serious diseases, and we are excited to advance MRT-8102 toward clinical development," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "In preclinical non-human primate studies, MRT-8102 has demonstrated potent and selective degradation of NEK7, reducing downstream IL-1β. We believe MRT-8102 has the potential to be developed in multiple inflammatory diseases, including gout, pericarditis and other cardiovascular diseases. We are also evaluating opportunities for the program in CNS disorders such as Parkinson's disease as well as in obesity and other metabolic disorders in light of the ability of our NEK7-directed MGDs to penetrate the blood brain barrier. IND-enabling studies are underway, and we plan to file our first IND for the program in the first quarter of 2025. The advancement of MRT-8102, along with our VAV1-directed MGD MRT-6160, which is progressing toward an IND filing in the first half of this year, demonstrates the continued growth of our immunology and inflammation portfolio and the power and versatility of our QuEEN™ discovery engine."

The NLRP3 inflammasome is a multiprotein complex that regulates the innate immune system and inflammatory signaling. 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 gout, cardiovascular disease, neurological disorders including Parkinson's disease and Alzheimer's disease, ocular disease, diabetes, obesity, and liver disease. NEK7 has been shown to be required for NLRP3 inflammasome assembly, activation and IL-1β release both *in vitro* and *in vivo*, and Monte Rosa's own *in vitro* and *in vivo* work has shown that NEK7 degradation leads to blockade of the pathway leading to inhibition of the production of IL-1β.

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 driven by IL-1β and the NRLP3 inflammasome. 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 gout, cardiovascular disease, neurological disorders including Parkinson's disease and Alzheimer's disease, ocular disease, diabetes, obesity, and liver disease . In non-human primate models, MRT-8102 potently, selectively, and durably degrades NEK7 and results in near-complete reductions of IL-1β. MRT-8102 has shown a favorable safety profile in non-GLP toxicology studies.

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 in the areas of oncology, autoimmune and inflammatory diseases, and more. 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 identify degradable protein targets and rationally design MGDs with unprecedented selectivity. The QuEEN discovery engine enables access to a wide-ranging and differentiated target space of well-validated biology across multiple therapeutic areas. Monte Rosa has developed the industry's leading pipeline of MGDs, which spans oncology, autoimmune and inflammatory disease and beyond, and has a strategic collaboration with Roche to discover and develop MGDs against targets in cancer and neurological diseases previously considered impossible to drug. 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 the ongoing development of our NEK7 program, including our MGDs and product candidates therein, including our recently announced product candidate MRT-8102, our ability to generate additional product candidates for our NEK7 program, the therapeutic potential of NEK7 MGDs, including MRT-8102, including for the treatment of inflammatory diseases driven by IL-1β and the NRLP3 inflammasome, our expectations regarding the submission of any IND to the FDA for each of MRT-8102 and MRT-6160 and the timing thereof, our expectations of the nature and timing for clinical advancement for MRT-8102, and our expectations regarding the potential clinical benefit for this program. 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, 2023, filed with the U.S. Securities and Exchange Commission on March 16, 2023, 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.

Investors
Andrew Funderburk
ir@monterosatx.com

Media
Cory Tromblee, Scient PR
media@monterosatx.com