Monte Rosa Therapeutics Announces First Participants Dosed in MRT-6160 Phase 1 Study

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MRT-6160, a potent and highly selective VAV1-directed molecular glue degrader, represents a potential novel therapeutic approach for systemic and neurological autoimmune and inflammatory diseases

Initial Phase 1 clinical results, including biomarker data to demonstrate pharmacodynamic effects, anticipated in Q1 2025

BOSTON, Aug. 19, 2024 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced that the first participants have been dosed in a Phase 1, single ascending dose / multiple ascending dose (SAD/MAD), healthy volunteer study evaluating MRT-6160, a VAV1-directed MGD being developed for systemic and neurological autoimmune diseases. The Company expects to obtain initial data from the Phase 1 study in Q1 2025.

“We are very pleased to initiate our Phase 1 clinical study of MRT-6160, a potent, highly selective, and orally bioavailable VAV1-directed MGD, which we believe is the first rationally designed MGD in clinical development for a non-oncology indication,” said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. “Our MGD-based therapeutic approach is well suited to degrade proteins that have been challenging to address with conventional modalities, and we believe we have opportunities to apply our technology to well-characterized targets like VAV1 that were previously considered undruggable. By degrading VAV1, a key regulator of T- and B-cell receptor activity, MRT-6160 could offer a differentiated approach to treat multiple autoimmune and inflammatory diseases. The Phase 1 study of MRT-6160 is designed to provide early insights into safety, pharmacokinetics, VAV1 protein degradation, and key downstream pharmacodynamic markers including CD69, IL-2, IL-6, and IL-17, helping to further inform our clinical strategy. We look forward to sharing initial clinical data from the study in Q1 2025, and subsequently initiating anticipated proof-of-concept studies in ulcerative colitis, rheumatoid arthritis, and potentially other indications.”

The development of MRT-6160 is supported by preclinical data in multiple models of autoimmune/inflammatory diseases and preclinical GLP toxicology data that suggest the potential for a differentiated therapeutic profile in T-cell, T/B-cell, and Th17-mediated systemic and neurologic autoimmune diseases. MRT-6160 has been shown to potently and selectively degrade VAV1 *in vitro* in human T and B cells and has demonstrated encouraging results in multiple preclinical studies of autoimmune disease, including in models of inflammatory bowel disease, rheumatoid arthritis, and multiple sclerosis.

About MRT-6160
MRT-6160 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader of VAV1, which in preclinical studies has shown deep degradation of its target with no detectable effects on other proteins. VAV1, a Rho-family guanine nucleotide exchange factor, is a key signaling protein downstream of both the T- and B-cell receptors. VAV1 expression is restricted to blood and immune cells, including T and B cells. Preclinical studies have shown that targeted degradation of VAV1 protein via an MGD modulates both T- and B-cell receptor-mediated activity. This modulation is evident both *in vitro* and *in vivo*, demonstrated by a significant decrease in cytokine secretion, proteins vital for maintaining autoimmune diseases. Moreover, VAV1-directed MGDs have shown promising activity in preclinical models of autoimmune diseases and thus have the potential to provide therapeutic benefits in multiple systemic and neurological autoimmune indications, such as inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, and dermatological disorders. Preclinical studies have demonstrated that MRT-6160 can inhibit disease progression in several *in vivo* autoimmunity models.

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 advancement and timeline of our MRT-6160 Phase 1 clinical study and our expectations for obtaining and disclosing data therefrom, our plans for our ongoing and future development of MRT-6160, our predictions concerning the relevance of our preclinical studies for the development of MRT-6160, and our predictions for the need and therapeutic relevance of a VAV1-directed MGD, including for MRT-6160. 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 fiscal year ended December 31, 2023, filed with the U.S. Securities and Exchange Commission on March 14, 2024, 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