Monte Rosa Therapeutics Presents Preclinical Data at ACR Convergence 2023 Demonstrating Potential of MRT-6160, a VAV1-targeted Molecular Glue Degrader, to Treat Immunological and Inflammatory Diseases

November 7, 2023

Data presented support broad potential therapeutic applications of MRT-6160 in a variety of autoimmune and inflammatory disorders driven by underlying dysregulation of T- and B-cells, including rheumatoid arthritis

Investigational New Drug filing for MRT-6160 expected in 1H 2024

Data will be presented during Poster Session A on Sunday, November 12, 2023 from 9:00-11:00 am PT

BOSTON, Nov. 07, 2023 (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 at the American College of Rheumatology (ACR) Convergence Annual Meeting held November 10-15 in San Diego, CA. The data demonstrate that MRT-6160, a novel, highly selective MGD targeting VAV1, attenuated disease progression in a murine collagen-induced arthritis (CIA) model.

In vitro, MRT-6160 induced selective degradation of VAV1, and attenuated TCR- and BCR-mediated activation and function of primary human T- and B-cells. In the CIA model, oral dosing of MRT-6160 elicited rapid VAV1 degradation across multiple tissues in a dose-dependent manner. Over the course of 20 days, MRT-6160 significantly decreased disease progression and endpoint functional scores compared to vehicle and showed a trend towards superior activity compared to an anti-TNF antibody.

"We are highly encouraged by these preclinical data, which we believe further establish the importance of VAV1 as a potential therapeutic target in T- and B-cell mediated autoimmunity, as well as MRT-6160's potential to broadly treat autoimmune and inflammatory diseases including rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease, psoriasis and other autoimmune diseases," said Owen Wallace, Ph.D., Chief Scientific Officer of Monte Rosa Therapeutics. "Together with extensive preclinical data in other models of autoimmunity, these promising results further support MRT-6160 as it advances to the clinic, and we look forward to our anticipated IND filing in the first half of next year."

Poster presentation details:

Poster Presentation: A VAV1-Directed Molecular Glue Degrader, MRT-6160, Reduces Joint Inflammation in the Collagen-Induced Arthritis Autoimmune Disease Model (abstract #0082)
Session: Poster Session A: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Date: Sunday, November 12, 2023
Time: 9:00-11:00 am PT
Presenter: Marisa Peluso, Director, Target and Discovery Biology
Location: Poster Hall

About VAV1 and MRT-6160
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 indications, such as multiple sclerosis, rheumatoid arthritis, and dermatological disorders.

MRT-6160 is a potent, highly selective, and orally bioavailable degrader of VAV1, which has shown deep degradation of its target with no detectable effects on other proteins. Preclinical studies demonstrate MRT-6160 inhibits disease progression in *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. Monta 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 in herein include, but are not limited to, statements about our product development activities, including our expectations around the potential of molecular glue degraders, the potential of our pipeline of molecular glue degraders, including our molecular glue degrader for VAV1, known as MRT-6160, , our expectation of the relevance of our pre-clinical data for VAV1 and/or MRT-6160 and the potential relevance of such with respect to potential therapeutic utility in immunological and/or inflammatory disorders, our expectations regarding the advancement and timing of ongoing pre-clinical and clinical development of MRT-6160, including our estimated timing for filing of an investigational new drug application therefor, our ability to initiate clinical studies for MRT-6160, our expectations regarding potential therapeutic opportunities for VAV1 as a target and specifically for MRT-6160, our expectations regarding medical needs and potential therapeutic opportunities 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 year ended December 31, 2022, 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.

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