Monte Rosa Therapeutics Advances Second Development Candidate, MRT-6160, a Novel, Highly Selective Molecular Glue Degrader Targeting VAV1 for the Treatment of Autoimmune Diseases

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- Preclinical data establish MRT-6160's ability to potently and selectively degrade VAV1 and inhibit disease progression in autoimmunity models, supporting potential applications across multiple autoimmune diseases
- Planned IND filing in the first half of 2024

BOSTON, May 23, 2023 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced its second development candidate, MRT-6160, a novel, potent, and selective molecular glue degrader (MGD) of VAV1. The Company plans to file an Investigational New Drug (IND) application for MRT-6160 in the first half of 2024 and to develop the molecule as a potential treatment for autoimmune diseases.

"MRT-6160 is a potent, orally bioavailable MGD designed to degrade VAV1, an important protein involved in the signaling pathways of T and B cells. Our *in vitro* studies have shown that MRT-6160 selectively degrades VAV1 without detectable effects on other proteins. By targeting VAV1, MRT-6160 attenuates multiple aspects of T- and B-cell function and inhibits disease progression in established *in vivo* models of autoimmunity," said Owen Wallace, Ph.D., Chief Scientific Officer of Monte Rosa. "The underlying biology and our preclinical data both demonstrate that MRT-6160 acts as an immune modulator, which has the potential to avoid the broad immune suppression seen with other approaches. We look forward to progressing our clinical plan developed with the goal of providing early insights into safety, PK and PD, and proof of concept regarding differentiated effects on key immunomodulatory signaling pathways."

"Our goal centers on pioneering therapeutically meaningful new drugs for patients with serious diseases. By addressing VAV1, a validated but previously undruggable target, we believe we've created a potentially groundbreaking therapy for patients suffering from a range of serious autoimmune conditions, particularly those involving both T- and B cell-mediated autoimmunity," said Markus Warmuth, M.D., CEO of Monte Rosa. "MRT-6160 is expected to be our second MGD to enter clinical trials, showcasing the continued productivity of our QuEEN™ platform. We anticipate significant progress and milestones in our portfolio in the upcoming year, including initial clinical data from our GSPT1 MGD, MRT-2359, in the second half of this year and filing of an IND application for MRT-6160 in the first half of next year."

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 we believe have the potential to provide therapeutic benefits in multiple autoimmune 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 biotechnology company developing novel molecular glue degrader (MGD) medicines for patients with serious diseases such as oncology, autoimmune and inflammatory diseases. MGDs are small molecule protein degraders that employ the body's natural mechanisms to selectively eliminate therapeutically relevant proteins. The Company's QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) platform enables it to rapidly identify protein targets and design highly selective degraders by combining diverse libraries of proprietary MGDs with in-house proteomics, structural biology, AI/machine learning, and computational chemistry capabilities. 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, GSPT1, known as MRT-2159, NEK7, and CDK2, and our earlier stage, undisclosed molecular glue degraders, our expectations regarding the advancement, and timing thereof, of our pipeline and the various products therein, our ability to advance our development candidates, including MRT-6160, toward IND, our ability to initiate and the timing of initiation of additional lead optimization programs, and our expectations regarding our ability to nominate and the timing of our nominations of additional development candidates, our expectations regarding potential therapeutic opportunities for our molecular glue degraders, and our clinical development expectations therefor, our expectations regarding patient populations and medical needs for any potential therapeutic opportunities for our molecular glue degraders, our expectations for our ongoing clinical trial for MRT-2359 and the timing thereof, our expectations regarding our proprietary QuEEN™ platform and its potential for the discovery of product candidates, and the strength of our financial position, 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, 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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