



## Monte Rosa Therapeutics Presents Preclinical Data at Digestive Disease Week 2024 Highlighting Therapeutic Potential of MRT-6160 in Inflammatory Bowel Disease

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*MRT-6160, a VAV1-directed molecular glue degrader (MGD), inhibits colitis disease progression and colon inflammation, lowers inflammatory mucosal cytokines, and reduces expression of IBD-associated genes in a colitis model*

*Initiation of MRT-6160 Phase 1 SAD/MAD study anticipated in mid-year 2024 with Phase 1 clinical data expected in Q1 2025*

*Poster presentation today at 12:30 pm ET*

BOSTON, May 21, 2024 (GLOBE NEWSWIRE) -- [Monte Rosa Therapeutics, Inc.](https://www.monte-rosa.com) (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced the company will present preclinical data at Digestive Disease Week (DDW) 2024, being held May 18-21 in Washington, D.C. The data showed that MRT-6160-mediated degradation of VAV1 inhibited disease progression in a T-cell transfer murine model of colitis. VAV1 is a key signaling protein downstream of both the T- and B-cell receptors and its degradation has potential to treat multiple T-cell and/or Th17 mediated autoimmune and inflammatory diseases, including ulcerative colitis (UC).

"VAV1 is a well-validated target with significant therapeutic potential in autoimmune and inflammatory diseases but is generally considered undruggable via conventional modalities. These promising preclinical data support our hypothesis that VAV1 is an important target in inflammatory bowel disease (IBD) and also demonstrate MRT-6160's ability to potentially address the underlying disease biology and provide therapeutic benefit," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "We're particularly encouraged to see significant reductions in colitis disease activity and progression as well as corroborating data demonstrating the reduction of pro-inflammatory cytokines and decreased expression of multiple IBD-associated genes. MRT-6160 is on track for an IND submission this quarter with initiation of a Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) study mid-year. We look forward to sharing clinical data from this program in Q1 2025."

The poster, entitled "MRT-6160, a VAV1-Directed Molecular Glue Degradator, Inhibits Disease Progression in a T-cell Transfer Mediated Murine Colitis Model Concomitant with Reduced Calprotectin Expression" (Poster Number Tu1727), will be presented today by Marisa Peluso, Director, Target and Discovery Biology for Monte Rosa Therapeutics, during the Session, "Animal Models of IBD: Pre-Clinical Treatment of Intestinal Inflammation," at 12:30 pm ET.

### Summary of findings:

- MRT-6160 was shown to inhibit disease progression, prevent colon inflammation, and reduce pro-inflammatory cytokine production in a murine T-cell transfer model of colitis.
- MRT-6160-mediated murine (m)VAV1 degradation prevented disease progression by 85% compared to vehicle ( $P < 0.0001$ ), and also reduced the disease activity index (DAI) score compared to a standard of care control.
- Transcriptional analysis of colon tissue showed reduced expression of inflammatory-disease associated T-cell activation, Th17 differentiation, chemokine, and calprotectin subunit genes.
- MRT-6160 reduced CD4<sup>+</sup> T-cell expression of TNF and IL-17A, demonstrating a highly favorable profile compared to active control of anti-TNF antibodies.
- Additionally, *in vitro* treatment of human PBMCs with MRT-6160 led to concentration-dependent degradation of human (h)VAV1 in immune cells and inhibited T-cell receptor (TCR)-mediated expression of pro-inflammatory cytokines and proliferation.

### 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 systemic and neurological autoimmune indications, such as multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, 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 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](http://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, statements around the Company's QuEEN™ discovery engine and the Company's view of its potential to identify degradable protein targets and rationally design MGDs with unprecedented selectivity, statements around the power and differentiation of the QuEEN discovery engine and the potential of the Company's MGDs against a broad spectrum of targets, statements about the advancement and timeline of our preclinical and clinical programs, pipeline and the various products therein, including the ongoing development of MRT-6160, and the planned submission of an IND to the FDA for MRT-6160 in the second quarter of 2024, our expectations of timing for initiation of a Phase 1 SAD/MAD study mid-2024 and the timing for our disclosure of Phase 1 clinical data of MRT-6160 in the first quarter of 2025, as well as our expectation to present additional preclinical data in models of autoimmune and inflammatory diseases at the upcoming medical meetings and our expectation to initiate POC studies for MRT-6160 in autoimmune/inflammatory diseases including ulcerative colitis and rheumatoid arthritis, with additional potential POC studies, dermatology, rheumatology, and neurology indications in mid-2025, our expectations of success for our programs and the strength of our financial position, our use of capital, expenses and other financial results in the future, availability of funding for existing programs, ability to fund operations into the first half of 2027, 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, 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.

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