Monte Rosa Therapeutics Presents Preclinical Data at American Association for Cancer Research (AACR) Annual Meeting 2025 on the Potential of its CDK2-directed Molecular Glue Degrader to Treat HR-positive/HER2-negative Breast Cancer

4.28.2025

CDK2 molecular glue degrader (MGD) in combination with CDK4/6 inhibition and anti-estrogen therapy achieved superior tumor regression in vivo compared to standard of care CDK4/6 inhibition and anti-estrogen therapy

CDK2 MGD delayed resistance to CDK4/6 inhibition in vitro and displayed superior selectivity versus clinical-stage CDK2 inhibitors

BOSTON, April 28, 2025 (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 on the potential of its highly selective cyclin-dependent kinase 2 (CDK2)-directed molecular glue degrader, MRT-51443, to treat HR-positive/HER2-negative breast cancer at the American Association for Cancer Research (AACR) Annual Meeting 2025, being held April 25-30 in Chicago, IL.

"In preclinical models of HR-positive/HER2-negative breast cancer, the combination of MRT-51443 with a CDK4/6 inhibitor and anti-estrogen therapy drove robust tumor regressions, demonstrating notably deeper tumor responses than the standard of care combination alone," said Sharon Townson, Ph.D., Chief Scientific Officer of Monte Rosa Therapeutics. "These results suggest that our highly selective, oral CDK2 degrader MRT-51443 has the potential to improve on current standard of care therapy for HR-positive/HER2-negative breast cancer. In addition, we believe our MGD approach could avoid many of the toxicities associated with less selective CDK2 inhibitors, which is critically important for a potentially differentiated therapy in this patient population. The degree to which CDK2 degradation with MRT-51443 delayed resistance to CDK4/6 inhibition *in vitro* was also striking, as patients treated with CDK4/6 inhibitors often relapse because their tumors become reliant on the CDK2 pathway. We anticipate an IND submission for our cell cycle program in 2026."

The poster, entitled, "Selective Targeting of CDK2 Using Molecular Glue Degraders for the Treatment of HR-Positive/HER2-Negative Breast Cancer" (Poster Number LB422), will be displayed on April 30, 2025, from 9am to 12pm CST in Poster Section 51, Poster Board 4. The poster will be presented by Sofia Gkountela, Associate Director, Biology, and Nina Ilic-Widlund, Director, Biology, Monte Rosa Therapeutics.

Summary of findings:

- MRT-51443 exhibited potency, selectivity, and favorable drug-like properties.
- MRT-51443 demonstrated superior selectivity as compared to several clinical-stage small molecule CDK2 inhibitors.
- In cellular assays, MRT-51443 induced deep CDK2 degradation, resulting in CDK2-dependent cancer cell growth inhibition.
- Degradation of CDK2 with MRT-51443 delayed resistance to CDK4/6 inhibition *in vitro* and exhibited strong anti-tumor activity in combination with CDK4/6 inhibitors *in vivo.*
- MRT-51443 in combination with CDK4/6 inhibition and anti-estrogen therapy drove deep tumor regressions and achieved superior tumor regression compared to standard of care CDK4/6 inhibition and anti-estrogen therapy in HR+/HER2- breast cancer models.
- Specifically, in the MCF7 model, the combination of MRT-51443 + ribociclib + fulvestrant demonstrated median tumor growth of -77% versus -3% for ribociclib + fulvestrant. In the T47D model, MRT-51443 + ribociclib + fulvestrant demonstrated median tumor growth of -61% versus -10% for ribociclib + fulvestrant. The combination of MRT-51443 + ribociclib also resulted in robust tumor regression in both models.

About CDK2 MGDs and MRT-51443

Cyclin-dependent kinase 2 (CDK2) is a key driver of cell cycle progression in cancer, acting in coordination with CDK4 and CDK6 to drive cell proliferation. CDK4/6 inhibitors, in combination with endocrine therapy, are FDA-approved agents for the treatment of HR-positive/HER2-negative breast cancer; however, many patients become resistant because their tumors become reliant on CDK2. Targeting CDK2 in conjunction with CDK4/6 inhibition has the potential to provide more sustained clinical responses. In preclinical studies, Monte Rosa's next-generation CDK2-targeted MGD, MRT-51443, has demonstrated highly selective degradation of CDK2, with no detectable off-target activity. MRT-51443 induced robust downstream CDK2 pathway suppression and drove deep tumor regression, achieving greater anti-tumor activity than current standard of care therapeutics, in preclinical models of HR-positive/HER2-negative breast cancer when combined with either a CDK4/6 inhibitor or a CDK4/6 inhibitor plus an anti-estrogen therapy. Targeting CDK2 with MRT-51443 represents a potentially novel approach to treating HR-positive/HER2-

negative breast cancer in combination with current standard of care therapies.

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. Monte Rosa has a global license agreement with Novartis to advance VAV1-directed molecular glue degraders and 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 therapeutic potential of CDK2 degradation, including using the company's CDK2-directed MGDs, including MRT-51443, that degrading CDK2 in conjunction with CDK4/6 inhibition and hormone therapy has the potential to provide more sustained responses in patients with HR-positive/HER2-negative breast cancer than current standard of care therapy including CDK4/6 inhibition and hormone therapy, about preclinical data presented at the American Association for Cancer Research (AACR) Annual Meeting 2025 supporting the potential of its highly selective cyclin dependent kinase 2 (CDK2)-directed molecular glue degrader to treat HR-positive/HER2-negative breast cancer, and about the Potential of CDK2-directed MGDs, including MRT-51443, to provide more sustained responses in a difficult-to-treat patient population while avoiding toxicities typically associated with limited selectivity of CDK2 inhibitors, 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, 2024, filed with the U.S. Securities and Exchange Commission on March 20, 2025, 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