Monte Rosa Therapeutics Provides Corporate Update and Key Anticipated Milestones for 2025

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Initial clinical data from Phase 1 SAD/MAD study of VAV1-directed molecular glue degrader (MGD) MRT-6160 expected in Q1 2025

Additional clinical results from Phase 1/2 study of MRT-2359 in MYC-driven solid tumors, including biomarker and activity data, anticipated in Q1 2025

MRT-8102, a NEK7-directed MGD targeting diseases driven by IL-1β and the NLRP3 inflammasome, on track for IND filing in H1 2025

Year-end cash and equivalents expected to be $377 million as of December 31, 2024 (unaudited) and anticipated to fund operations into 2028 through multiple anticipated proof-of-concept clinical readouts

Company to present at J.P. Morgan Healthcare Conference on Tuesday, January 14, at 5:15 p.m. PST

BOSTON, Jan. 10, 2025 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today outlined anticipated 2025 milestones ahead of its participation in the 43rd Annual J.P. Morgan Healthcare Conference. The company's presentation will focus on strategic priorities, goals, and milestones for 2025. These include anticipated Q1 2025 readouts from its ongoing Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors, the Phase 1 trial of MRT-6160, its VAV1-directed MGD for autoimmune diseases, for which it announced a global license agreement with Novartis in October 2024, and the continued advancement of the Company's earlier stage programs and QuEEN™ discovery engine.

"Last year was transformative for Monte Rosa, with significant validation of our capabilities to design and develop 'only-in-class' MGDs for previously undruggable targets across a broad range of disease areas, culminating in the successful licensing of MRT-6160 to Novartis for development across multiple immune-mediated conditions," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "We believe this agreement creates substantial value for Monte Rosa by accelerating and broadening the scope of clinical development for MRT-6160, but most of all we believe the deal validates our position as the leading MGD company."

Dr. Warmuth continued, "We enter 2025 in a very strong position with a cash runway that extends into 2028. This enables us to advance our pipeline programs to multiple anticipated clinical data readouts and to further leverage our industry-leading QuEEN™ discovery engine across areas including immunology and inflammation, cardiovascular, and metabolic diseases. Building on this tremendous momentum, we enter the new year excited to disclose additional Phase 1/2 clinical data for MRT-2359 in patients with MYC-driven solid tumors and initial data from our Phase 1 single and multiple ascending dose trial of MRT-6160, both of which are anticipated in the first quarter of 2025. In addition, Monte Rosa is positioned to advance its third clinical candidate, MRT-8102, into clinical development later this year, and we also expect to nominate development candidates for our CDK2 and second-generation NEK7 programs in the first and second half of the year, respectively."

Recent Program Achievements

MRT-2359, GSPT1-directed MGD for MYC-driven solid tumors

- In December, the Company provided a development progress update for the ongoing MRT-2359 Phase 1/2 study, demonstrating a favorable safety profile and targeted levels of GSPT1 degradation using a 21 days on, 7 days off drug dosing schedule in heavily pretreated solid tumor patients. The Company selected a recommended Phase 2 dose (RP2D) of 0.5 mg daily at a 21 days on, 7 days off drug dosing schedule.

MRT-6160, VAV1-directed MGD for immune-mediated conditions

- In October, the Company announced a global exclusive development and commercialization license agreement with Novartis to advance VAV1 MGDs, including MRT-6160, currently in Phase 1 clinical development for various immune-related conditions. Monte Rosa received a $150 million upfront payment for the agreement. Monte Rosa is eligible to receive up to $2.1 billion in development, regulatory, and sales milestones, beginning upon initiation of Phase 2 studies, as well as tiered royalties on ex-U.S. net sales. Monte Rosa will co-fund any Phase 3 clinical development and will share any profits and losses associated with the manufacturing and commercialization of MRT-6160 in the U.S.

MRT-8102, NEK7-directed MGD for inflammatory diseases driven by IL-1β and the NLRP3 inflammasome

- In September, Monte Rosa presented preclinical data at the Inflammasome Summit demonstrating that its development candidate MRT-8102, a first-in-class NEK7-directed MGD for the treatment of inflammatory diseases driven by interleukin-1β (IL-1β) and the NLRP3 inflammasome, is a potent, selective, and durable MGD of NEK7. The data provided preclinical proof of concept demonstrating that a NEK7 MGD leads to inhibition of the NLRP3 inflammasome and IL-1 release to reduce the effects of inflammation, supporting the potential to address central and peripheral inflammatory disorders.

CDK2 and Cyclin E1-directed MGD programs

- In December, at the 2024 San Antonio Breast Cancer Symposium, the Company presented preclinical data on the potential of its highly selective cyclin-dependent kinase 2 (CDK2)-directed molecular glue degrader to treat HR-positive/HER2-negative breast cancer. Data demonstrated deep tumor regression in preclinical models of HR-positive/HER2-negative breast cancer when combined with either a CDK4/6 inhibitor or a CDK4/6 inhibitor and endocrine therapy.
- In October, at the 36th EORTC-NCI-AACR Symposium, Monte Rosa presented preclinical data on the potential of its cyclin E1 (CCNE1)-directed MGDs for the treatment of *CCNE1*-amplified solid tumors. Cyclin E1 MGDs represent a potential novel therapeutic approach by directly and selectively targeting a frequently amplified non-enzymatic driver oncogene relevant in multiple solid tumors.

QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) discovery engine

- In October, Monte Rosa made a preprint available in BioRxiv entitled, “Mining the Cereblon Target Space Redefines Rules for Molecular Glue-induced Neosubstrate Recognition,” which demonstrates a vast expansion of what had been considered druggable within the cereblon target space. Monte Rosa has identified more than 1,600 proteins predicted to be compatible with cereblon across diverse target classes that can potentially be targeted with MGDs.

Key Anticipated Milestones for 2025

- Share updated data, including biomarker and activity data, from the MRT-2359 Phase 1/2 study in Q1 2025.
- Report initial data from the Phase 1 SAD/MAD study of MRT-6160 in healthy volunteers in Q1 2025, including data on safety, pharmacokinetics, VAV1 protein degradation, and key downstream pharmacodynamic markers.
- Submit an IND application for MRT-8102 in H1 2025.
- Nominate a development candidate for the second-generation NEK7 program with enhanced CNS penetration in H2 2025.
- Nominate a CDK2 program development candidate in H1 2025.

Cash Position and Financial Guidance
Unaudited cash, cash equivalents, restricted cash, and marketable securities are expected to be $377.0 million as of December 31, 2024, including the previously announced $150 million upfront payment from Novartis. Based on current cash, cash equivalents, restricted cash, and marketable securities, the Company expects its cash and cash equivalents to be sufficient to fund planned operations and capital expenditures into 2028.

J.P. Morgan Healthcare Conference Presentation
Dr. Warmuth will present Monte Rosa’s pipeline and business updates during a presentation at the 43rd Annual J.P. Morgan Healthcare Conference on Tuesday, January 14, 2025, at 5:15 p.m. PST. A webcast of the presentation will be accessible via the “Events & Presentations” section of Monte Rosa’s website at ir.monterosatx.com, and an archived version will be made available following the presentation.

About MRT-2359
MRT-2359 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader (MGD) that induces the interaction between the E3 ubiquitin ligase component cereblon and the translation termination factor GSPT1, leading to the targeted degradation of GSPT1 protein. The MYC transcription factors (c-MYC, L-MYC and N-MYC) are well-established drivers of human cancers that maintain high levels of protein translation, which is critical for uncontrolled cell proliferation and tumor growth. Preclinical studies have shown this addiction to MYC-induced protein translation creates a dependency on GSPT1. By inducing degradation of GSPT1, MRT-2359 is designed to exploit this vulnerability, disrupting the protein synthesis machinery, leading to anti-tumor activity in MYC-driven tumors.

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 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. MRT-6160 has shown promising activity in preclinical models of multiple immune-mediated conditions. Under the terms of an agreement announced in October 2024, Novartis has exclusive worldwide rights to develop, manufacture and commercialize MRT-6160 and other VAV1 MGDs.

About MRT-8102
MRT-8102 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader (MGD) that targets NEK7 for the treatment of inflammatory diseases driven by IL-1β and the NLRP3 inflammasome. NEK7 has been shown to be required for NLRP3 inflammasome assembly, activation and IL-1β release both in vitro and in vivo. Aberrant NLRP3 inflammasome activation and the subsequent release of active IL-1β and interleukin-18 (IL-18) has been implicated in multiple inflammatory disorders, including gout, cardiovascular disease, neurologic disorders including Parkinson's disease and Alzheimer's disease, ocular disease, diabetes, obesity, and liver disease. In a non-human primate model, MRT-8102 was shown to potently, selectively, and durably degrade NEK7, and resulted in near-complete reductions of IL-1β models following ex vivo stimulation of whole blood. MRT-8102 has shown a favorable profile in non-GLP toxicology studies.

About CDK2 MGDs
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 CDK2-targeted MGDs have demonstrated highly selective degradation of CDK2, with no detectable off-target activity, and induced robust downstream CDK2 pathway suppression and drove deep tumor regression 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 endocrine therapy. Targeting CDK2 with an MGD 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 sharing updated clinical data, including biomarker and activity data, from the MRT-2359 Phase 1/2 study in Q1 2025, reporting initial clinical data from the Phase 1 SAD/MAD study of MRT-6160 in healthy volunteers in Q1 2025, including data on safety, pharmacokinetics, VAV1 protein degradation, and key downstream pharmacodynamic markers, submitting an IND application for MRT-8102 in H1 2025, nominating a development candidate for the second-generation NEK7 program with enhanced CNS penetration in H2 2025, nominating a CDK2 program development candidate in H1 2025, among others, as well as statements concerning our pipeline of MGDs, including our ability to advance such throughout pre-clinical and clinical development and the therapeutic potentials thereof, statements concerning QuEEN, including our ability to use QuEEN to develop additional only-in-class MGDs for previously undruggable targets across a broad range of disease areas, including our ability to leverage and advance QuEEN across multiple therapeutic areas including immunology and inflammation, cardiovascular, and metabolic diseases, and statements, including estimates, concerning our available cash, cash equivalents, restricted cash, and marketable securities, our balance sheet and our expected ability to fund operations into 2028, 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

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