Monte Rosa Therapeutics Provides Corporate Update and Key Anticipated Milestones for 2024

1.8.2024

Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors on track; recommended Phase 2 dose (RP2D) expected in Q2 2024

Received US FDA Fast Track Designation for MRT-2359 for previously treated, metastatic small cell lung cancer with L- or N-MYC expression

MRT-6160, a VAV1-directed MGD, anticipated to initiate Phase 1 study in mid-2024, supporting potential future Phase 2 proof-of-concept studies in multiple autoimmune diseases

Strong cash position expected to fund operations into H1 2026 and enable advancement of pipeline programs through significant early clinical milestones

Company to present at J.P. Morgan Healthcare Conference on Wednesday, January 10, 2024, at 3:00 p.m. PT

BOSTON, Jan. 08, 2024 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today outlined anticipated 2024 milestones ahead of its participation in the 42nd Annual J.P. Morgan Healthcare Conference. The company's presentation, taking place on Wednesday, January 10, 2024, at 3:00 p.m. PT, will focus on strategic priorities for 2024, including anticipated progress with the ongoing Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors as well as future development plans for MRT-2359 and MRT-6160, its VAV1-directed MGD for autoimmune diseases.

"2023 was an exciting and highlight-filled year for Monte Rosa Therapeutics, including encouraging interim Phase 1/2 MRT-2359 clinical results, advancement of our VAV1-targeted MGD into IND enabling studies, and initiation of a strategic collaboration with Roche," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "Building on last year's successes, this year we look forward to announcing the RP2D for our MRT-2359 program and initiating multiple Phase 2 expansion cohorts in tumors characterized by high L- and N-MYC expression, with the potential to consider indication expansion into c-MYC-driven tumor types such as ER+ breast cancer and castration-resistant prostate cancer. Our highly selective VAV1-directed MGD MRT-6160 is anticipated to enter a Phase 1 healthy volunteer study this year with the aim to move efficiently into early proof-of-concept studies in patients across multiple autoimmune indications. Lastly, we also expect to nominate additional development candidates in 2024 for programs in both oncology and inflammation/immunology. Our strong balance sheet and cash runway into 1H 2026 positions us to advance our programs through important clinical milestones."

Recap of 2023 Achievements

- Presented interim data from the Phase 1/2 clinical trial of MRT-2359 demonstrating tumor reductions in patients with biomarker-positive cancers and favorable pharmacokinetic (PK), pharmacodynamic (PD), and tolerability profiles.
- Announced development candidate MRT-6160, a VAV1-directed MGD, for the treatment of autoimmune diseases, and presented preclinical data demonstrating that MRT-6160 attenuates autoimmune disease progression.
- Entered into a strategic collaboration and licensing agreement with Roche to discover and develop novel molecular glue degraders targeting cancer and neurological diseases, with a $50 million upfront payment and eligibility to receive future preclinical, clinical, commercial and sales milestone payments exceeding $2 billion, as well as tiered royalties.

Corporate Updates and Key Anticipated Milestones

- Monte Rosa announced today that it has received U.S. Food & Drug Administration Fast Track Designation for MRT-2359 for the treatment of patients with previously treated, metastatic small cell lung cancer (SCLC) with L-MYC or N-MYC expression.
- Monte Rosa expects to announce the RP2D for the MRT-2359 Phase 1/2 clinical trial in MYC-driven solid tumors in Q2 2024. Enrollment is ongoing in backfill cohorts at clinically active doses using a 5 days on drug, 9 days off drug schedule. The Company has simultaneously started dose escalation of higher dose density cohorts using a 21 days on, 7 days off schedule.
- The Company expects to submit an IND for MRT-6160, a VAV1-targeted MGD, in the first half of 2024 and to initiate a Phase 1 single ascending dose / multiple ascending dose study in healthy volunteers in mid-2024.
- The Company expects to nominate a development candidate for the NEK7 preclinical program in Q1 2024.
- The Company expects to nominate a development candidate for the CDK2 preclinical program in 2024.

J.P. Morgan Healthcare Conference Presentation

Dr. Warmuth will present Monte Rosa's pipeline and business updates during a presentation at the 42nd Annual J.P. Morgan Healthcare Conference on Wednesday, January 10, 2024, at 3:00 p.m. PT. 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 our *in vitro* 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 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 autoimmune indications, such as multiple sclerosis, rheumatoid arthritis, and dermatological disorders. 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. 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.

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 product development activities, our ongoing clinical development of our GSPT1 degrader referred to as MRT-2359, including our expectations for the nature, significance, and timing for our disclosure of any data from our Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors, timing for our identification and any disclosure of a recommended phase 2 dose for MRT-2359, statements about the advancement of our preclinical programs, pipeline and the various products therein, including the ongoing development of our VAV1-directed degrader, referred to as MRT-6160, and the planned submission of an IND to the FDA for MRT-6160 in the first half of 2024, and the timing of our planned phase 1 healthy volunteer study and early proof-of-concept studies in patients across multiple autoimmune indications, our expectations regarding the potential clinical benefit for this program and our expectations of timings for the program, statements around the advancement and application of our pipeline, including identification and the timing thereof of a development candidate for NEK7 and a development candidate for CDK2, statements around the advancement and application of our platform, and statements concerning our expectations regarding our ability to nominate and the timing of our nominations of additional targets, product candidates, and development candidates, as well as our expectations of success for our programs 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, 2023, 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. 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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