Monte Rosa Therapeutics Announces First Patient Dosed in MODeFIRe-1, a Phase 2 Study of MRT-2359 in Combination with Apalutamide in Patients with AR Mutation-Positive Metastatic Castration-Resistant Prostate Cancer

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Study will evaluate PSA and RECIST response, duration of response, radiographic progression-free survival (rPFS), and safety

Updated data from the initial Phase 1/2 study of MRT-2359 plus enzalutamide in patients with advanced CRPC expected by end of year

BOSTON, Aug. 24, 2026 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced that the first patient has been dosed in MODeFIRe-1 (clinicaltrials.gov identifier NCT07745361), a Phase 2 study evaluating MRT-2359 in combination with apalutamide, a second-generation androgen receptor (AR) inhibitor, in patients with metastatic castration-resistant prostate cancer (mCRPC) with AR mutations. The study follows encouraging clinical data previously shared from the Company's Phase 1/2 study of MRT-2359 in combination with enzalutamide in heavily pretreated mCRPC patients. MRT-2359 is an investigational, orally bioavailable, GSPT1-directed MGD discovered and developed by Monte Rosa.

"Dosing the first patient in MODeFIRe-1 is an important step in advancing MRT-2359 as a potential therapy for patients with mCRPC with AR mutations, a population with limited therapeutic options," said Filip Janku, M.D., Ph.D., Chief Medical Officer of Monte Rosa Therapeutics. "This study builds on the encouraging results we observed in our Phase 1/2 study of MRT-2359 in combination with enzalutamide. As we disclosed previously, in that study of heavily pretreated, advanced CRPC patients – including those who had progressed on prior second-generation AR inhibitors, chemotherapy, and radioligand therapy – 5 of 5 patients with AR mutations demonstrated a PSA response, with a 100% disease control rate and two RECIST responses. MODeFIRe-1 pairs MRT-2359 with apalutamide using a design intended to efficiently further evaluate and potentially confirm clinical activity in this population. We believe this study can position MRT-2359 for advancement into registrational development if the data continue to support our earlier results, with the potential to also extend clinical benefit to additional AR-driven patient populations including patients without prior second-generation AR inhibitors, as well as into combinations with radioligand therapies independent of AR status."

MODeFIRe-1 will evaluate MRT-2359 at a dose of 0.5 mg administered orally on a 21 days on, 7 days off schedule over 28-day cycles, in combination with apalutamide. The study will enroll up to 25 patients with mCRPC with AR mutations, utilizing a Simon's two-stage design. Eligible patients must have AR mutations, PSA with or without RECIST-measurable disease, and prior treatment with a second-generation AR inhibitor. Study endpoints include PSA response, RECIST response, duration of response, radiographic progression-free survival (rPFS), PSA progression-free survival, and safety.

Enrollment in the initial Phase 1/2 study expansion arm in patients with advanced CRPC has been completed. A total of 6 patients with AR mutations were enrolled and treated with MRT-2359 in combination with enzalutamide. Monte Rosa plans to provide an update on this patient subset by the end of the year. Interim data were presented at the ASCO Genitourinary Cancers Symposium (ASCO GU) in February.

About MRT-2359
MRT-2359 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader (MGD) of GSPT1. MYC-driven cancers, including prostate cancer, depend on enhanced translation of oncoproteins to support rapid growth. MRT-2359 exploits this therapeutic vulnerability by disrupting translation through selective degradation of the translation termination factor GSPT1. MRT-2359 treatment reduced cellular abundance of many prostate cancer-relevant oncoproteins, including AR, MYC, and Cyclin D1-E2F, and demonstrated robust anti-tumor activity across multiple preclinical models of metastatic castration-resistant prostate cancer (mCRPC). MRT-2359 is being evaluated in combination with apalutamide in MODeFIRe-1, a Phase 2 study in mCRPC patients with AR mutations. In a Phase 1/2 study, the combination of MRT-2359 with the AR inhibitor enzalutamide demonstrated encouraging early signals of clinical response in mCRPC patients with AR mutations.

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. 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 rationally design MGDs with unprecedented selectivity. Monte Rosa has developed the industry's leading pipeline of first-in-class and only-in-class MGDs, spanning autoimmune and inflammatory diseases, oncology, and beyond, with three

programs in the clinic. Monte Rosa has ongoing collaborations with leading pharmaceutical companies in the areas of immunology, oncology, and neurology. 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 ability to grow our product pipeline, our ability to successfully complete research and further development and commercialization of our drug candidates in current or future indications, including the timing and results of our clinical trials and our ability to conduct and complete clinical trials, statements regarding the MODeFIRe-1 Phase 2 study evaluating MRT-2359 in combination with apalutamide in mCRPC patients with AR mutations, including the study design, planned enrollment of up to 25 patients, study endpoints, and the potential of the study to further evaluate clinical activity and position the program for advancement into registrational development, subject to discussions with regulatory authorities, our expectations regarding the potential to extend clinical benefit to additional AR-driven patient populations, including patients without prior second-generation AR inhibitors and combinations with radioligand therapies independent of AR status, our plans to provide updated data from the initial Phase 1/2 study expansion arm evaluating MRT-2359 in combination with enzalutamide in patients with advanced CRPC by the end of the year, statements regarding the clinical significance of the clinical data observed in the Phase 1/2 study and the potential of MRT-2359 to benefit patients with mCRPC with AR mutations, statements around our ability to capitalize on and potential benefits resulting from our research and translational insights, 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, 2025, filed with the U.S. Securities and Exchange Commission on March 17, 2026, 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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