Monte Rosa Therapeutics Presents Updated Clinical Data from Phase 1/2 Study of MRT-2359 in Combination with Enzalutamide in Heavily Pretreated Metastatic Castration-Resistant Prostate Cancer Patients at ASCO Genitourinary Cancers Symposium (ASCO GU)

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In mCRPC patients with androgen receptor (AR) mutations, treatment with MRT-2359 in combination with enzalutamide led to a 100% PSA response rate (5 of 5 patients) and a 100% disease control rate, including 2 patients with RECIST partial responses and 3 with stable disease, all showing reduction in size of target lesions

Across all 15 evaluable patients, the overall RECIST disease control rate was 67%, and 10 of 15 patients showed tumor size reductions of target lesions

Combination of MRT-2359 and enzalutamide was generally well-tolerated with primarily Grade 1-2 adverse events (AEs); no treatment discontinuations due to AEs

Company plans to initiate a new, signal-confirming Phase 2 study of MRT-2359 targeting AR mutant patients in Q3 2026

Poster presentation on February 26 at 11:30 AM PST

BOSTON, Feb. 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 updated, positive clinical data from an ongoing Phase 1/2 clinical study evaluating MRT-2359 in combination with enzalutamide in heavily pretreated patients with metastatic castration-resistant prostate cancer (mCRPC). The data, being presented at the 2026 ASCO GU Symposium in San Francisco, CA, build on data released by the company in December 2025. MRT-2359 is an investigational, orally bioavailable, GSPT1-directed MGD discovered and developed by Monte Rosa.

“These data bolster the promising results we shared in December, continuing to reinforce MRT-2359's potential in mCRPC patients with AR mutations, a population with limited therapeutic options,” said Filip Janku, M.D., Ph.D., Chief Medical Officer of Monte Rosa Therapeutics. “Strikingly, in this updated dataset, 5 of 5 patients with AR mutations demonstrated a PSA response, including 2 PSA90 responses and 3 PSA50 responses. Based on the encouraging efficacy data and favorable safety profile observed to date, we plan to initiate a new Phase 2 study this year to evaluate MRT-2359 in combination with a second-generation AR-inhibitor in mCRPC patients with AR mutations. This Phase 2 study is designed to confirm MRT-2359’s clinical activity and position the program for advancement into registrational studies.”

The ongoing Phase 1/2 study evaluated 0.5 mg and 0.75 mg of MRT-2359 administered orally on a 21-days-on, 7-days-off drug schedule in combination with enzalutamide, an AR inhibitor. The study population as of the data cutoff date of January 30, 2026 included 23 individuals with advanced CRPC who were heavily pretreated, including 18 (78%) previously treated with a second-generation AR inhibitor, 19 (83%) previously treated with taxane chemotherapy, and 13 (57%) previously treated with Pluvicto®. For analysis of efficacy, all patients were required to be evaluable for RECIST (Response Evaluation Criteria in Solid Tumors) measurable disease and not known to have a neuroendocrine phenotype.

The poster, entitled, “MRT-2359 in Combination with Enzalutamide Suppresses Multiple Oncogenic Pathways to Drive Deep and Durable PSA and RECIST Responses in Heavily Pretreated, Metastatic Castration-Resistant Prostate Cancer Harboring AR Mutations” (Poster Board Number E16), will be displayed on Thursday, February 26, 2026, from 11:30 a.m. to 12:45 p.m. PST and from 5:45 p.m. to 6:45 p.m. PST in Poster Session A: Prostate Cancer.

Summary of Phase 1/2 Study Results in Metastatic CRPC Patients

- All 23 patients enrolled were evaluable for safety.
- The combination of MRT-2359 and enzalutamide was well-tolerated. Adverse events (AEs) were manageable, with the most common study drug-related AEs being fatigue, diarrhea, nausea and decreased appetite, which were classified as mild or moderate and not therapy-limiting. No patient discontinued therapy due to AEs.
- Of the 23 patients with mCRPC enrolled, 15 patients were evaluable for RECIST and were confirmed not to have neuroendocrine differentiation.
- Of the 15 efficacy-evaluable patients, all of whom were assessed for AR alteration status, 5 of 5 patients harboring AR mutations presented PSA responses, including 2 patients with PSA90 responses.
- Two RECIST partial responses (1 confirmed partial response and 1 unconfirmed partial response) were seen in the AR

mutant subset, and the RECIST disease control rate (DCR) in the AR-mutant setting was 100%. All 5 patients with AR mutations showed reduction in target lesion size.

- In addition, 5 patients with wild-type AR or positive for ARV7 transcripts had stable disease per RECIST, several of which were associated with tumor size reductions, resulting in a RECIST DCR of 67% (10 of 15) in the overall population of 15 evaluable patients. Ten of 15 patients showed tumor size reductions of target lesions.
- Consistent with reduction in target lesions, a significant decrease in total circulating tumor cell counts was noted in 4 of 5 patients with AR mutations; data are pending for the 5th patient.
- Data showed that treatment effects were durable, in particular in patients with AR mutations or naïve to AR inhibitors. Of patients with AR mutations, 2 of 5 remained on therapy for 10 cycles or longer, and 2 of 5 remained on drug as of the data cutoff.
- Clinical activity of the combination correlated to both MYC and AR pathway activity in baseline biopsies (as determined by RNAseq), and modulation of MYC, E2F, and AR pathways was seen by RNAseq in post-treatment tumor biopsies.

Monte Rosa plans to initiate a Phase 2 study of MRT-2359 in combination with a second-generation AR inhibitor. The study of up to 25 mCRPC patients, utilizing a two-stage design, is designed to efficiently assess the efficacy of MRT-2359 plus a second-generation AR inhibitor in mCRPC patients with AR mutations, with potential to expand the study into additional patient subsets, including patients naive to second-generation AR inhibitors. The study, anticipated to start in Q3 2026, will evaluate PSA response, RECIST response, duration of response, radiographic progression-free survival (rPFS), and safety.

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 in combination with the AR inhibitor enzalutamide is being investigated in an ongoing Phase 1/2 study (clinicaltrials.gov identifier NCT05546268) in patients with mCRPC. In heavily pretreated mCRPC patients, MRT-2359 plus enzalutamide demonstrated encouraging early signals of clinical response.

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 updated data from our Phase 1/2 clinical study evaluating MRT-2359 in combination with enzalutamide in heavily pretreated patients with metastatic CRPC, continuing to reinforce MRT-2359's potential in mCRPC patients with AR mutations, a population with limited therapeutic options, our expectations regarding the clinical activity observed with MRT-2359 in combination with enzalutamide in heavily pretreated mCRPC patients, our plans to initiate a new Phase 2 study in 2026 to evaluate MRT-2359 in combination with a next-generation AR inhibitor in mCRPC patients with AR mutations, our expectations that the planned design of the Phase 2 study will confirm MRT-2359's clinical activity and position the program for advancement into registrational studies, , the clinical significance of the clinical data read-out at upcoming scientific meetings and timing thereof, 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, 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