Monte Rosa Therapeutics Announces Compelling Clinical Activity of MRT-2359 in Combination with Enzalutamide in Heavily Pretreated Metastatic Castration-Resistant Prostate Cancer Patients with Androgen Receptor Mutations

12.16.2025

In mCRPC patients with androgen receptor (AR) mutations, treatment with MRT-2359 in combination with enzalutamide led to a 100% PSA response rate (4 of 4 patients) and a 100% disease control rate, including 2 patients with RECIST responses and 2 with stable disease

Combination of MRT-2359 and enzalutamide was generally well-tolerated with primarily Grade 1-2 adverse events

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

Updated MRT-2359 data expected to be presented at ASCO Genitourinary Cancers Symposium in February 2026

Conference call and webcast planned for today at 8 a.m. ET

BOSTON, Dec. 16, 2025 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced positive interim 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). MRT-2359 is an investigational, orally bioavailable, GSPT1-directed MGD discovered and developed by Monte Rosa.

“We continue to be highly encouraged by the clinical activity observed with MRT-2359 in combination with enzalutamide in heavily pretreated mCRPC patients, a population with limited therapeutic options, with an overall disease control rate (DCR) of 64%. The responses seen in the subset of patients harboring AR mutations were particularly compelling, with 4 of 4 patients demonstrating a PSA response, including 2 PSA90 responses and 2 PSA50 responses. Two of the 4 patients with AR mutations showed a RECIST response, and the DCR in the AR mutant population was 100%. We believe these results are especially promising given that most of the patients with AR mutations, even more so than in the overall mCRPC trial population, received prior chemotherapy as well as radioligand therapy, or even experimental bispecific antibodies,” said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. “We were also pleased to see through our biomarker work that MRT-2359 significantly impacted both the MYC and the E2F signaling pathways, suggesting a mechanism of action that is at least in part independent of inhibiting AR signaling, and confirming our preclinical studies. Given these findings and the favorable safety profile observed to date, we believe there is a significant opportunity for MRT-2359 in the rapidly evolving treatment landscape of prostate cancer.”

“While the data from the ongoing trial continue to mature, we plan to initiate a new, signal-confirming Phase 2 study, evaluating MRT-2359 in combination with a second-generation AR inhibitor in mCRPC patients with AR mutations,” said Filip Janku, M.D., Ph.D., Chief Medical Officer of Monte Rosa Therapeutics. “Data from this study have the potential to confirm MRT-2359’s clinical activity and may position the program for advancement into registrational studies. We also look forward to presenting updated data from the ongoing Phase 1/2 study at the ASCO Genitourinary Cancers Symposium conference in February.”

The 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 December 3, 2025, included 20 individuals with advanced CRPC who were heavily pretreated, including 15 (75%) previously treated with a second-generation AR inhibitor, 16 (80%) previously treated with taxane chemotherapy, and 11 (55%) previously treated with Pluvicto®. For analysis of efficacy, all patients were required to be evaluable for measurable disease and not have acquired neuroendocrine differentiation, as determined by RNAseq from screening biopsies.

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

- All 20 patients enrolled were evaluable for safety.
- The combination of MRT-2359 and enzalutamide maintained a favorable safety profile, with manageable, primarily gastrointestinal adverse events that were classified as mild or moderate (Grade 1 or Grade 2).
- Of the 20 patients enrolled, 14 patients were evaluable for RECIST (Response Evaluation Criteria in Solid Tumors) and were confirmed to have non-neuroendocrine mCRPC.
- Of the 14 evaluable patients, all of whom were assessed for AR alteration status using post hoc ctDNA analysis, 4 were

confirmed to have AR mutations, and all 4 of those had 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 DCR in the AR-mutant setting was 100%.
- 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 DCR of 64% (9 of 14) in the overall population of 14 evaluable patients.
- Data showed that treatment effects were durable, in particular in patients with AR mutations or naïve to AR inhibitors.
- 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 paired tumor biopsies.

Monte Rosa plans to present updated data from the Phase 1/2 study of MRT-2359 at the ASCO Genitourinary Cancers Symposium in February.

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 an AR inhibitor in mCRPC patients with AR mutations, with potential to expand the study into additional patient subsets, including patients naïve to 2nd generation AR inhibitors, should the activity in the AR mutant patient population confirm. The study will evaluate PSA response, RECIST response, duration of response, progression-free survival (PFS), radiographic progression-free survival (rPFS), and safety. The study is anticipated to start in 2026.

The Phase 1/2 study also included six patients with hormone receptor (HR)+ breast cancer. Data from this population demonstrated a favorable safety profile. However, results did not present sufficient evidence of activity to support further development in this population.

Updated Guidance for MRT-8102
Monte Rosa announced today that it plans to present interim Phase 1 data on MRT-8102 in early 2026. MRT-8102 is a first-in-class, NEK7-directed MGD for inflammatory diseases driven by the NLRP3 inflammasome, IL-1β, and IL-6. The ongoing Phase 1 study includes single-ascending dose/multiple-ascending dose (SAD/MAD) cohorts in healthy volunteers, as well as a Part 3 cohort designed to evaluate potential early proof of concept in subjects at increased CVD risk. The Company has initiated dosing in Part 3 of the study.

Investor Conference Call
Monte Rosa will host a conference call and webcast presentation today, Dec. 16, 2025, at 8:00 a.m. ET. A webcast of the presentation will be accessible via the “Events & Presentations” section of Monte Rosa’s website at ir.monterosatx.com. Registration for the conference call is available at the following link. An archived version of the webcast will be made available for 30 days following the presentation.

About MRT-2359
MRT-2359 is a potent, highly selective, and orally bioavailable investigational molecular glue degrader (MGD) of GSPT1. 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. MRT-2359 is being investigated in an ongoing Phase 1/2 study (clinicaltrials.gov identifier NCT05546268) in solid tumors, including castration-resistant prostate cancer (CRPC). In heavily pretreated CRPC patients, a patient group characterized by widespread expression of c-MYC, MRT-2359 demonstrated encouraging early signals of clinical response.

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 linked to NLRP3, IL-1β, and IL-6 dysregulation. 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 cardiovascular disease, gout, osteoarthritis, neurologic disorders including Parkinson’s disease and Alzheimer’s disease, and metabolic disorders. 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 and caspase-1 following *ex vivo* stimulation of whole blood. MRT-8102 has demonstrated a considerable safety margin (>200-fold exposure margin over projected human efficacious dose) in GLP toxicology studies. MRT-8102 is currently being investigated in a Phase 1 study (clinicaltrials.gov identifier NCT07119125) in healthy participants and participants at elevated cardiovascular disease risk.

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 promising interim results from our ongoing Phase 1/2 clinical study evaluating MRT-2359 in combination with enzalutamide in heavily pretreated patients with metastatic CRPC, our expectations regarding the clinical activity observed with MRT-2359 in combination with enzalutamide in heavily pretreated mCRPC patients and the significant opportunity for MRT-2359 in the rapidly evolving treatment landscape of prostate cancer, our plans to initiate a signal-confirming Phase 2 study evaluating MRT-2359 in combination with a second generation AR inhibitor in mCRPC patients with AR mutations and timing thereof, with potential to expand into additional patient subsets, the potential for the data from this study to 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, our plans to present interim Phase 1 data on MRT-8102 in early 2026, 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.

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