UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 27, 2024

MONTE ROSA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-40522**	**84-3766197**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

321 Harrison Avenue, Suite 900
Boston, MA 02118
(Address of principal executive offices, including zip code)

(617) 949-2643
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	**GLUE**	**The Nasdaq Global Select Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure

On June 27, 2024, Monte Rosa Therapeutics, Inc. issued a press release titled “Monte Rosa Therapeutics Provides Development Progress Updates on MRT-2359 and MRT-6160”. The press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Form 8-K (including Exhibit 99.1) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

99.1	Press Release issued by Monte Rosa Therapeutics, Inc. dated June 27, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Monte Rosa Therapeutics, Inc.

Date: June 27, 2024

By: /s/ Markus Warmuth
Markus Warmuth
President and Chief Executive Officer

Monte Rosa Therapeutics Provides Development Progress Updates on MRT-2359 and MRT-6160

Ongoing Phase 1/2 Study of MRT-2359 for MYC-driven solid tumors demonstrates favorable safety and pharmacodynamic profile dosing 0.5 mg using a 21/7 schedule; currently assessing 0.75 mg dose level; final determination of recommended Phase 2 dose and updated clinical results anticipated in H2 2024

IND submission achieved for MRT-6160, a VAV1-directed MGD in development for systemic and neurological autoimmune diseases; initiation of Phase 1 SAD/MAD study expected this summer with Phase 1 clinical data anticipated in Q1 2025

BOSTON, Mass., June 27, 2024 – Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today announced progress updates for its two lead programs, MRT-2359, an MGD being developed for MYC-driven solid tumors, and MRT-6160, a VAV1-directed MGD in development for systemic and neurological autoimmune diseases.

“We are pleased with the progress of our two lead programs,” said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. “We continue to successfully recruit and advance our ongoing MRT-2359 Phase 1/2 study. We are encouraged by our initial safety and pharmacodynamic assessment of the 0.5 mg dose using the 21 days on, 7 days off regimen and, as such, we consider the 0.5mg dose with the 21 days on, 7 days off regimen a potential recommended Phase 2 dose. Importantly, this regimen allows for dosing of MRT-2359 twice as frequently per cycle compared to the 5 days on, 9 days off regimen previously explored in our study. Based on the favorable safety assessment for the 0.5 mg dose, we initiated a 0.75 mg, 21 days on, 7 days off dose cohort, which is currently ongoing. In the second half of the year, we expect to make a determination of our definitive recommended Phase 2 dose, share updated clinical efficacy and safety results from the dose escalation arm of the trial, and initiate enrollment of our Phase 2 expansion cohorts.”

Dr. Warmuth continued, “Moreover, today we are excited to announce the submission of our Investigational New Drug (IND) application to the U.S Food and Drug Administration (FDA) for MRT-6160, a highly selective and orally bioavailable MGD directed against VAV1. This milestone positions us to soon have our second highly promising program in the clinic, pending FDA clearance. We believe our IND is the first for a rationally designed MGD for a non-oncology indication, representing a significant step forward for Monte Rosa and the protein degradation field. MRT-6160 has been shown to potently and selectively degrade VAV1 in human T and B cells and has demonstrated encouraging results in multiple preclinical studies of autoimmune disease, including models of inflammatory bowel disease, rheumatoid arthritis, and multiple sclerosis. We expect to initiate a Phase 1 single ascending dose / multiple ascending dose (SAD/MAD) study later this summer and anticipate sharing initial clinical data for our MRT-6160 program in Q1 2025.”

Monte Rosa continues to evaluate MRT-2359 in a Phase 1/2 clinical trial in MYC-driven solid tumors (NCT05546268). The Company has completed enrollment of the 0.5 mg, 21 days on, 7 days off dose escalation cohort, and tolerability has been favorable with an AE profile similar to what has been observed using the 5 days on, 9 days off schedule at the same dose level. Enrollment is ongoing in the 0.75 mg, 21

days on, 7 days off dose escalation cohort. The Company is evaluating possible Phase 2 expansion cohorts, and anticipates utilizing a two-stage design to enroll patients to evaluate responses in each selected expansion cohort before proceeding with further enrollment.

MRT-6160 is on track for initiation of a Phase 1 SAD/MAD study this summer with Phase 1 clinical data expected in Q1 2025. Monte Rosa expects to subsequently initiate proof-of-concept (POC) studies in autoimmune/inflammatory diseases including ulcerative colitis and rheumatoid arthritis, with additional potential POC studies in dermatology, rheumatology, and neurology indications. Preclinical efficacy data in multiple models of autoimmune/inflammatory diseases and preclinical GLP toxicology data suggest the potential for a highly differentiated profile in T-cell, T/B-cell, and Th17-mediated systemic and neurologic autoimmune diseases.

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 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 systemic and neurological autoimmune indications, such as inflammatory bowel disease, rheumatoid arthritis, multiple sclerosis, and dermatological disorders. Preclinical studies have demonstrated that MRT-6160 can inhibit disease progression in several *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 the advancement and timeline of our clinical programs, including the ongoing clinical development of MRT-2359, our expectations for the determination of our recommended phase 2 dose and the timing thereof, including our identification of a potential and a definitive recommended phase 2 dose and there timings thereof, , the timing for our disclosure of any initial data from our Phase 1 clinical trial of MRT-2359 and our plans to initiate the enrollment of our Phase 2 expansion cohort portion of the study before year-end, our expectations about our ongoing development of MRT-6160, including around our filing of an IND for MRT-6160 with FDA and any statements predicting acceptance by FDA of our IND and the timing thereof, our expectations for our initiation of a Phase 1 SAD/MAD study later this summer and anticipate sharing initial clinical data for our MRT-6160 program in Q1 2025. 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 statements made in these materials relating to or based on such internal estimates and research.

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