Monte Rosa Therapeutics Announces First Quarter 2024 Financial Results and Provides Corporate Update

May 9, 2024

MRT-2359, a molecular glue degrader (MGD) being developed for MYC-driven solid tumors, advancing in ongoing Phase 1/2 clinical trial; determination of recommended Phase 2 dose expected in Q2 2024; Phase 1 clinical data anticipated in H2 2024

MRT-6160, a VAV1-directed MGD in development for systemic and neurological autoimmune diseases, on track toward expected IND submission in Q2 2024 and initiation of Phase 1 SAD/MAD study mid-year; Phase 1 clinical data expected in Q1 2025

MRT-8102, a first-in-class NEK7-directed MGD and NLRP3/IL-1β pathway inhibitor, demonstrated efficient blood-brain barrier penetration and CNS activity in non-human primates (NHPs); IND submission on track for Q1 2025

New discovery program unveiled for CCNE1-directed MGDs; first to directly drug important, previously undruggable solid tumor oncology target

Strong cash position expected to fund operations into H1 2026, enabling advancement of MRT-2359, MRT-6160, and MRT-8102 programs through clinical milestones

BOSTON, May 09, 2024 (GLOBE NEWSWIRE) -- Monte Rosa Therapeutics, Inc. (Nasdaq: GLUE), a clinical-stage biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today reported business highlights and financial results for the first quarter ending March 31, 2024.

"We're excited by the significant advances made across our entire portfolio, including both our oncology and immunology/inflammation programs," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "Our Phase 1/2 clinical trial evaluating MRT-2359 for MYC-driven solid tumors is on track and we plan to announce the recommended Phase 2 dose later this quarter and to report clinical data from this program in the second half of the year. We eagerly anticipate the initiation of a Phase 1 study of MRT-6160, the first of our MGD drug candidates for immune-related diseases, in mid-2024, with results from the study expected in Q1 2025. Preclinical GLP toxicology data we've announced today, along with data in multiple disease models, suggest the potential for a highly differentiated profile across multiple autoimmune diseases. Additionally, MRT-8102, our NEK7-directed MGD targeting diseases driven by IL-1β and the NLRP3 inflammasome, is rapidly progressing toward clinical studies. We've recently demonstrated strong CNS exposure and NEK7 degradation in non-human primates, supporting the potential development of MRT-8102 in neurologic indications and obesity amongst others, in addition to its potential use in gout, pericarditis, and other peripheral inflammatory conditions. We're also very pleased to announce our discovery program for CCNE1 (Cyclin E1), a well-validated oncology target generally considered undruggable by conventional modalities. We believe our ability to degrade CCNE1 potently and selectively and to elicit anti-tumor activity in *in vivo* models provides further validation for the differentiation of our QuEEN™ discovery engine and the potential of our MGDs against a broad spectrum of targets."

Dr. Warmuth concluded, "The rapid and efficient progression of our pipeline clearly illustrates the power of our AI/ML-driven QuEEN™ discovery engine. Through our ongoing internal efforts as well as our research collaboration with Roche, we look forward to continuing this strong progress."

RECENT HIGHLIGHTS

MRT-2359, GSPT1-directed MGD for MYC-driven solid tumors

- Monte Rosa continues to evaluate MRT-2359 in a Phase 1/2 clinical trial in MYC-driven solid tumors (NCT05546268). Enrollment is ongoing in backfill cohorts at clinically active doses using a 5-days-on, 9-days-off drug schedule and in dose escalation cohorts using a 21-days-on, 7-days-off drug schedule. The Company is on track to determine the recommended Phase 2 dose (RP2D) in Q2 2024 and report Phase 1 study results in H2 2024. Monte Rosa expects to initiate the Phase 2 portion of the study before year-end.
- The Company presented preclinical data at the American Association for Cancer Research (AACR) Annual Meeting demonstrating that treatment with MRT-2359 resulted in marked tumor regressions in the AR-V7- and c-MYC-expressing 22RV1 xenograft mouse model of prostate cancer associated with resistance to anti-androgen agents.

MRT-6160, VAV1-directed MGD for systemic and neurological autoimmune/inflammatory diseases

- The MRT-6160 program is on track for an anticipated Investigational New Drug (IND) submission to the U.S. Food and Drug Administration (FDA) in Q2 2024, and initiation of a Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) study in mid-2024. Phase 1 results are anticipated in Q1 2025.
- The Company today announced additional results from completed preclinical GLP toxicology studies of MRT-6160 in rats and non-human primates (NHPs). The data demonstrate a highly favorable safety profile with no significant changes in peripheral immune cell compartments.
- Monte Rosa expects to present additional preclinical data for MRT-6160 in models of autoimmune and inflammatory diseases at the upcoming Digestive Disease Week (DDW) and European Alliance of Associations for Rheumatology (EULAR) medical meetings.

MRT-8102, NEK7-directed MGD for inflammatory diseases driven by IL-1β and the NLRP3 inflammasome

- In March 2024, Monte Rosa announced the initiation of IND-enabling studies for MRT-8102, a first-in-class NEK7-directed MGD for the treatment of inflammatory diseases driven by interleukin-1β (IL-1β) and the NLRP3 inflammasome, critical elements of the inflammatory process. This is the first development candidate to be declared from the Company's NEK7 development program.
- Monte Rosa today announced that MRT-8102 has demonstrated highly favorable CNS exposure and degradation in a study in cynomolgus monkeys. The data support the potential for development of MRT-8102 in diseases including Parkinson's disease, Alzheimer's disease, and obesity. The Company is evaluating applications across multiple inflammatory disorders.
- Monte Rosa expects to submit an IND application for MRT-8102 in Q1 2025.

CCNE1-directed MGD program for CCNE1-amplified tumors

- Monte Rosa today announced a new discovery program for CCNE1 (Cyclin E1)-directed MGDs for the treatment of CCNE1-amplified tumors. CCNE1, a key component of the cell cycle and a known driver of many cancers, is generally considered an undruggable target by conventional modalities.

Additional corporate updates

- In October 2023, Monte Rosa entered into a strategic collaboration and licensing agreement with Roche, a global healthcare leader, to discover and develop MGDs against targets in cancer and neurological diseases. The collaboration continues to advance research activities according to plan.

ANTICIPATED MILESTONES

- Announce the recommended Phase 2 dose for the MRT-2359 Phase 1/2 study in Q2 2024 and report Phase 1 clinical results in H2 2024. Initiate the Phase 2 portion of the study before year-end. The Company is evaluating Phase 2 expansion cohorts in high-prevalence c-MYC-driven tumors including hormone receptor-positive breast cancer and prostate cancer, as well as tumor types and patient populations driven by L- and N-MYC including non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), and solid tumors with amplifications of L- and N-MYC.
- Submit an IND application for MRT-6160 in Q2 2024 and initiate a Phase 1 SAD/MAD study in healthy volunteers in mid-2024; report results from the Phase 1 study 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.
- Submit an IND application for MRT-8102 in Q1 2025.
- Nominate a development candidate for the CDK2 preclinical program in 2024.

UPCOMING PRESENTATIONS

- Monte Rosa plans to present a poster at the Digestive Disease Week (DDW) Conference on May 21, 2024, in Washington, DC, titled, "MRT-6160, a VAV1-Directed Molecular Glue Degrader, Inhibits Disease Progression in a T-cell Transfer Mediated Murine Colitis Model Concomitant with Reduced Calprotectin Expression."
- Monte Rosa plans to present a poster at the European Alliance of Associations for Rheumatology (EULAR) Conference on June 14, 2024, in Vienna, Austria, titled, "MRT-6160, a VAV1-Directed Molecular Glue Degrader, Reduces Joint Inflammation, Cytokine Production, and Autoantibody Levels in a Collagen-Induced Arthritis Disease Model."

FIRST QUARTER 2024 FINANCIAL RESULTS

Collaboration Revenue: Collaboration revenue for the first quarter of 2024 was $1.1 million, compared with $0 during the same period in 2023. Collaboration revenue represents revenue recorded under the Roche License and Collaboration agreement.

Research and Development (R&D) Expenses: R&D expenses for the first quarter of 2024 were $27.0 million, compared to $26.8 million during the same period in 2023. R&D expenses were driven by the successful achievement of key milestones in our R&D organization, including the continuation of the MRT-2359 clinical study, the progression and growth of our preclinical pipeline, the preparation of MRT-6160 to enter the clinic, and the continued development of the Company's QuEEN™ discovery engine. Non-cash stock-based compensation constituted $2.7 million of R&D expenses for Q1 2024, compared to $2.1 million in the same period in 2023.

General and Administrative (G&A) Expenses: G&A expenses for the first quarter of 2024 were $9.0 million compared to $7.5 million during the same period in 2023. The increase in G&A expenses was a result of increased headcount, stock-based compensation expense, and fees paid to consultants in order to support our growth and operations. G&A expenses included non-cash stock-based compensation of $2.2 million for the first quarter of 2024, compared to $1.8 million for the same period in 2022.

Net Loss: Net loss for the first quarter of 2024 was $32.0 million, compared to $33.3 million for the fourth quarter of 2023.

Cash Position and Financial Guidance: Cash, cash equivalents, restricted cash, and marketable securities as of March 31, 2024, were $197.8 million, compared to cash, cash equivalents, restricted cash, and marketable securities of $237.0 million as of December 31, 2023. The decrease of

$39.2 million was primarily due to operational use of cash.

The Company expects its cash and cash equivalents to be sufficient to fund planned operations and capital expenditures into the first half of 2026.

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 systemic and neurological autoimmune indications, such as multiple sclerosis, rheumatoid arthritis, inflammatory bowel disease, and dermatological disorders. Preclinical studies have demonstrated that MRT-6160 can inhibit disease progression in *in vivo* autoimmunity models.

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 driven by IL-1β and the NLRP3 inflammasome. 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 gout, cardiovascular disease, neurologic disorders including Parkinson's disease and Alzheimer's disease, ocular disease, diabetes, obesity, and liver disease. 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 models following *ex vivo* stimulation of whole blood. MRT-8102 has shown a favorable profile in non-GLP toxicology studies.

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 ability to grow our product pipeline, statements around the Company's QuEEN™ discovery engine and the Company's view of its potential to identify degradable protein targets and rationally design MGDs with unprecedented selectivity, statements around the power and differentiation of the QuEEN discovery engine and the potential of the Company's MGDs against a broad spectrum of targets, statements about the advancement and timeline of our preclinical and clinical programs, pipeline and the various products therein, including (i) our product development activities, our ongoing clinical development of MRT-2359, our expectations to announce the recommended Phase 2 dose later in the second quarter of 2024, the timing for our disclosure of any initial data from our Phase 1 clinical trial of MRT-2359 in the second half of 2024, and our plans to initiate the Phase 2 portion of the study before year-end, (ii) the ongoing development of MRT-6160, and the planned submission of an IND to the FDA for MRT-6160 in the second quarter of 2024, our expectations of timing for initiation of a Phase 1 SAD/MAD study mid-2024 and the timing for our disclosure of Phase 1 clinical data of MRT-6160 in the first quarter of 2025, as well as our expectation to present additional preclinical data in models of autoimmune and inflammatory diseases at the upcoming DDW and EULAR medical meetings and our expectation to initiate POC studies for MRT-6160 in autoimmune/inflammatory diseases including ulcerative colitis and rheumatoid arthritis, with additional potential POC studies, dermatology, rheumatology, and neurology indications in mid-2024, (iii) our ongoing development of MRT-8102 and our expectations around its potential across neurologic indications and obesity amongst others, as well as potential use in gout, pericarditis, and other peripheral inflammatory conditions, including our expectations to submit an IND to the FDA in the first quarter of 2025, and (iv) our expectations to nominate a development candidate for the CDK2 preclinical program in 2024, 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, statements regarding regulatory filings for our development programs, including the planned timing of such regulatory filings, such as IND applications, and potential review by regulatory authorities as well as our expectations of success for our programs and the strength of our financial position, our use of capital, expenses and other financial results in the future, availability of funding for existing programs, ability to fund operations into the first half of 2026, 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 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.

Consolidated Balance Sheets
(in thousands, except share amounts)
(Unaudited)

	March 31, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 99,752	$ 128,101
Marketable securities	93,140	104,312
Other receivables	601	505
Prepaid expenses and other current assets	5,543	3,294
Total current assets	199,036	236,212
Property and equipment, net	34,036	33,803
Operating lease right-of-use assets	28,422	28,808
Restricted cash	4,863	4,580
Other long-term assets	389	352
Total assets	$ 266,746	$ 303,755
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,828	$ 11,152
Accrued expenses and other current liabilities	10,713	14,600
Current deferred revenue	20,407	17,678
Current portion of operating lease liability	3,345	3,162
Total current liabilities	41,293	46,592
Deferred revenue, net of current	28,529	32,323
Defined benefit plan liability	2,568	2,713
Operating lease liability	41,837	42,877
Total liabilities	114,227	124,505
Commitments and contingencies		
Stockholders' equity		
Common stock, $0.0001 par value; 500,000,000 shares authorized, 50,210,309 shares issued and 50,200,304 shares outstanding as of March 31, 2024; and 50,154,929 shares issued and 50,140,233 shares outstanding as of December 31, 2023	5	5
Additional paid-in capital	553,063	547,857
Accumulated other comprehensive loss	(2,693)	(2,724)
Accumulated deficit	(397,856)	(365,888)
Total stockholders' equity	152,519	179,250
Total liabilities and stockholders' equity	$ 266,746	$ 303,755

Consolidated Statement of Operations and Comprehensive Loss
(in thousands, except share and per share amounts)
(unaudited)

	Three months ended March 31,	
	2024	2023
Collaboration revenue	$ 1,064	$ —
Operating expenses:		
Research and development	27,026	26,755
General and administrative	8,985	7,504
Total operating expenses	36,011	34,259

Loss from operations	(34,947)	(34,259)
Other income (expense):		
Interest income, net	2,442	2,437
Foreign currency exchange (loss) gain, net	620	(85)
Loss on sale of marketable securities	—	(131)
Total other income	3,062	2,221
Net loss before income taxes	(31,885)	(32,038)
Provision for income taxes	(83)	—
Net loss	$ (31,968)	$ (32,038)
Net loss per share—basic and diluted	$ (0.53)	$ (0.65)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	60,156,187	49,347,473
Comprehensive loss:		
Net loss	$ (31,968)	$ (32,038)
Other comprehensive loss:		
Provision for pension benefit obligation	35	14
Unrealized gain (loss) on available-for-sale securities	(4)	345
Comprehensive loss	$ (31,937)	$ (31,679)

Investors
Andrew Funderburk
ir@monterosatx.com

Media
Cory Tromblee, Scient PR
media@monterosatx.com