Monte Rosa Therapeutics Announces Fourth Quarter and Full Year 2023 Financial Results and Provides Corporate Update

March 14, 2024

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

MRT-6160, a VAV1-directed MGD designed to treat systemic and neurological autoimmune diseases, progressing toward expected IND submission in Q2 2024 and initiation of Phase 1 SAD/MAD study midyear

MRT-8102 nominated as first development candidate for NEK7 program, targeting diseases driven by IL-1b and the NLRP3 inflammasome; IND submission expected in Q1 2025

Entered into strategic discovery collaboration with Roche, further expanding potential applications of QuEEN™ discovery engine

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

BOSTON, March 14, 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 full year and fourth quarter ended December 31, 2023.

"We made excellent pipeline and corporate progress during 2023 and early 2024, highlighted by the encouraging initial clinical results reported from our MRT-2359 Phase 1/2 study in October. We also continued to advance our VAV1-directed MGD, MRT-6160, for autoimmune diseases toward the clinic, and we progressed MRT-8102, a NEK7-directed MGD targeting IL-1b and the NLRP3 inflammasome, into IND-enabling studies. We are excited about the broad potential of MRT-2359 in MYC-driven cancers, as well as the opportunity that exists with both the VAV1 and NEK7 programs to address pathways of emerging clinical significance in systemic and neurological autoimmune and inflammatory diseases," said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. "In addition, we entered into a strategic research collaboration with Roche to enable broader application of our technology. All combined, the terrific progress we made in the last 12 month highlights the uniqueness and differentiation of our approach and the strength of our ML/AI-driven QuEEN™ discovery engine. We look forward to building on that success with continued pipeline execution across multiple programs targeting substantial patient populations, and our anticipated cash runway into the first half of 2026 positions us well to do so."

2023 AND RECENT HIGHLIGHTS

- In October 2023, Monte Rosa announced interim clinical data from the Phase 1 dose escalation part of the ongoing Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors demonstrating tumor size reductions in heavily pretreated patients with biomarker-positive cancers and favorable pharmacokinetic (PK), pharmacodynamic (PD), and tolerability profiles. Enrollment is ongoing in backfill cohorts at clinically active doses using a 5-days-on-drug, 9-days-off-drug schedule and in dose escalation cohorts using a 21-days-on, 7-days-off-drug schedule. The Company anticipates determining the recommended Phase 2 dose in Q2 2024, reporting updated Phase 1 study results thereafter, and initiating the Phase 2 portion of the study before year-end.
- In December 2023, Monte Rosa received U.S. Food & Drug Administration (FDA) Fast Track designation for MRT-2359 for the treatment of patients with previously treated, metastatic small cell lung cancer (SCLC) with L-MYC or N-MYC expression. MRT-2359 previously received Fast Track designation from the FDA for the treatment of patients with previously treated, metastatic NSCLC with L-MYC or N-MYC expression.
- MRT-6160, a VAV1-targeting MGD designed to treat multiple systemic and neurological immunological and inflammatory diseases, is on track towards an anticipated Investigational New Drug (IND) application filing with the FDA in Q2 2024, and a Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) study initiation in healthy volunteers in midyear 2024. The Company recently completed preclinical GLP toxicology studies in rats and non-human primates, demonstrating a highly favorable profile with no significant changes in peripheral immunophenotyping assessments.
- Monte Rosa recently announced the nomination of MRT-8102 as the first development candidate for its NEK7 program, targeting diseases driven by IL-1b and the NLRP3 inflammasome. MRT-8102 is an orally bioavailable MGD that has shown potent, selective, and durable degradation of NEK7 and near-complete reduction of IL-1b in a non-human primate model following *ex vivo* stimulation of whole blood. IND-enabling studies are ongoing, and an IND submission is anticipated in Q1 2025. The Company is also advancing other differentiated NEK7-directed MGDs.
- In October 2023, Monte Rosa entered into a strategic collaboration and licensing agreement with global healthcare leader Roche to discover and develop MGDs against targets in cancer and neurological diseases. Under the terms of the agreement, Monte Rosa Therapeutics received an upfront payment of $50 million and is eligible to receive future preclinical, clinical, commercial, and sales milestone payments that could exceed $2 billion, as well as tiered royalties.

Roche has the option to expand the collaboration with an additional set of targets. If exercised, Monte Rosa would be eligible for an additional upfront payment of up to $28 million and potential preclinical, clinical, commercial, and sales milestones exceeding $1 billion, as well as tiered royalties.
- Edmund Dunn was recently promoted to Principal Accounting Officer. Edmund has more than 25 years of experience as a finance professional and has been with Monte Rosa since March of 2021. Andrew Funderburk was recently appointed as Senior Vice President, Head of Investor Relations and Strategic Finance. He was previously Managing Director at Kendall Investor Relations, LLC, and Managing Director and Partner at the healthcare and life sciences consulting firm Health Advances.

ANTICIPATED UPCOMING MILESTONES

- Announce the recommended Phase 2 dose for the MRT-2359 Phase 1/2 study in Q2 2024 and report updated Phase 1 clinical results thereafter. Initiate the Phase 2 portion of the study before year-end. The Company is exploring Phase 2 expansion cohorts in high-prevalence c-MYC-driven tumors such as hormone receptor-positive breast cancer and prostate cancer, as well as tumor types and patient populations driven by L- and N-MYC including NSCLC, 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. Monte Rosa expects to subsequently initiate proof-of-concept studies in autoimmune diseases spanning gastroenterology, 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 upcoming American Association for Cancer Research (AACR) Annual Meeting demonstrating that treatment with MRT-2359 resulted in marked tumor regressions in an AR-V7-expressing 22RV1 xenograft mouse model of c-MYC-driven prostate cancer associated with resistance to anti-androgen agents. The Company also plans to present at an educational session at AACR on molecular glue degraders.

FOURTH QUARTER AND FULL YEAR 2023 FINANCIAL RESULTS

Research and Development (R&D) Expenses: R&D expenses for the fourth quarter of 2023 were $27.1 million, compared to $24.9 million for the fourth quarter of 2022, and $111.3 million for the year ended December 31, 2023, compared to $85.1 million for the year ended December 31, 2022. These increases 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, and reflect increased personnel expense and external R&D costs including laboratory-related expenses to achieve these milestones. Non-cash stock-based compensation constituted $2.2 million of R&D expenses for Q4 2023, compared to $1.8 million in the same period in 2022, and $8.9 million and $5.6 million for the years ended December 31, 2023 and 2022, respectively.

General and Administrative (G&A) Expenses: G&A expenses for the fourth quarter of 2023 were $7.7 million compared to $7.6 million for the fourth quarter of 2022, and $32.0 million for the year ended December 31, 2023, compared to $27.3 million for the year ended December 31, 2022. The increase in G&A expenses was a result of increased headcount and expenses in support of the Company's growth and operations. G&A expenses included non-cash stock-based compensation of $1.8 million for the fourth quarter of 2023, compared to $1.6 million for the same period in 2022, and $7.7 million and $6.1 million for the years ended December 31, 2023 and 2022, respectively.

Net Loss: Net loss for the fourth quarter of 2023 was $33.3 million, compared to $30.8 million for the fourth quarter of 2022, and $135.4 million for the year ended December 31, 2023, compared to $108.5 million for the year ended December 31, 2022.

Cash Position and Financial Guidance: Cash, cash equivalents, restricted cash, and marketable securities as of December 31, 2023, were $237.0 million, compared to cash, cash equivalents, restricted cash, and marketable securities of $183.0 million as of September 30, 2023. The increase of $54 million was primarily related to the proceeds from the Roche collaboration and registered direct offering in Q4 2023.

The Company expects its cash and cash equivalents, including proceeds from the Roche collaboration, 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 demonstrate MRT-6160 inhibits 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-1b and the NLRP3 inflammasome. NEK7 has been shown to be required for NLRP3 inflammasome assembly, activation and IL-1b release both *in vitro* and *in vivo*. Aberrant NLRP3 inflammasome activation and the subsequent release of active IL-1b 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 potently, selectively, and durably degrades NEK7 and results in near-complete reductions of IL-1b 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 product development activities, our ability to grow our product pipeline, our ongoing clinical development of our GSPT1 degrader referred to as MRT-2359, including our expectations for the nature, significance, and timing for our disclosure of any initial data from our Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors, timing for our identification and any disclosure of a recommended phase 2 dose for MRT-2359, statements the Company's QuEEN ^{TM} discovery engine and the Company's view of its potential to identify degradable protein targets and rationally design MGDs with unprecedented selectivity, statements about our collaboration with Roche, statements about the advancement and timeline of our preclinical and clinical programs, pipeline and the various products therein, including the ongoing development of our VAV1-directed degrader, referred to as MRT-6160, the planned submission of an IND to the FDA for MRT-6160 in Q2 2024, and our expectations of timing for commencing any Phase 1 single ascending dose / multiple ascending dose (SAD/MAD) study initiation in healthy volunteers, our expectations regarding the potential clinical benefit for our programs and our expectations of timings for the program, the ongoing development of our NEK7-directed degrader, referred to as MRT-8102, the planned submission of an IND to the FDA for MRT-8102 in the first quarter of 2025, and our expectations of timing for clinical advancement for MRT-8102, statements around the identification and the timing of a development candidate for CDK2 and other programs, 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, 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)

	December 31,	
	2023	**2022**
Assets		
Current assets:		
Cash and cash equivalents	$ 128,101	$ 54,912

Marketable securities	104,312	207,914
Other receivables	505	7,656
Prepaid expenses and other current assets	3,294	4,444
Current restricted cash	—	960
Total current assets	236,212	275,886
Property and equipment, net	33,803	27,075
Operating lease right-of-use assets	28,808	34,832
Restricted cash, net of current	4,580	4,318
Other long-term assets	352	278
Total assets	$ 303,755	$ 342,389
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 11,152	$ 7,862
Accrued expenses and other current liabilities	14,600	14,580
Current deferred revenue	17,678	—
Current portion of operating lease liability	3,162	3,127
Total current liabilities	46,592	25,569
Deferred revenue, net of current	32,323	—
Defined benefit plan liability	2,713	1,533
Operating lease liability	42,877	43,874
Total liabilities	124,505	70,976
Commitments and contingencies		
Stockholders' equity		
Common stock, $0.0001 par value; 500,000,000 shares authorized, 50,154,929 shares issued and 50,140,233 shares outstanding as of December 31, 2023; and 500,000,000 shares authorized, 49,445,802 shares issued and 49,323,531 shares outstanding as of December 31, 2022	5	5
Additional paid-in capital	547,857	503,696
Accumulated other comprehensive loss	(2,724)	(1,752)
Accumulated deficit	(365,888)	(230,536)
Total stockholders' equity	179,250	271,413
Total liabilities and stockholders' equity	$ 303,755	$ 342,389

Consolidated Statements of Operations and Comprehensive Income (Loss)

(In thousands, except share and per share amounts)

	Three months ended December 31,		Year ended December 31,	
	2023	**2022**	**2023**	**2022**
Operating expenses:				
Research and development	$ 27,135	$ 24,868	$ 111,272	$ 85,061
General and administrative	7,728	7,621	32,039	27,323
Total operating expenses	34,863	32,489	143,311	112,384
Loss from operations	(34,863)	(32,489)	(143,311)	(112,384)
Other income (expense):				
Interest income, net	2,368	1,990	9,334	3,764
Foreign currency exchange gain (loss), net	(779)	(283)	(930)	10
Gain on disposal of fixed assets	—	—	24	109
Loss on sale of marketable securities	—	—	(131)	—
Total other income	1,589	1,707	8,297	3,883
Net loss before income taxes	$ (33,274)	$ (30,782)	$ (135,014)	$ (108,501)
Provision for income taxes	22	—	(338)	—
Net loss	$ (33,252)	$ (30,782)	$ (135,352)	$ (108,501)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.58)	$ (0.63)	$ (2.63)	$ (2.30)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	56,927,647	48,893,160	51,396,961	47,227,370
Comprehensive loss:				

Net loss	$ (33,252)	$ (30,782)	$ (135,352)	$ (108,501)
Provision for pension benefit obligation	(1,411)	619	(1,369)	718
Unrealized gain (loss) on available-for-sale securities	142	231	397	(449)
Comprehensive loss	$ (34,521)	$ (29,932)	$ (136,324)	$ (108,232)

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