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

8.8.2024

IND clearance achieved for MRT-6160, a VAV1-directed MGD in development for systemic and neurological autoimmune diseases; on track to initiate Phase 1 SAD/MAD study this summer with initial clinical data expected in Q1 2025

Ongoing Phase 1/2 Study of MRT-2359 for MYC-driven solid tumors demonstrated a favorable safety and pharmacodynamic profile at 0.5 mg with a 21 days on/7 days off schedule; dosing ongoing at 0.75 mg using a 21/7 schedule; final determination of recommended Phase 2 dose and updated clinical results anticipated in H2 2024

Achieved first program and financial milestones from strategic research collaboration with Roche

Strong cash position expected to fund operations into H1 2027 and through multiple anticipated clinical readouts including from proof-of-concept patient studies for MRT-2359, MRT-6160, and MRT-8102

BOSTON, Aug. 08, 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 second quarter that ended June 30, 2024.

“The IND clearance of our VAV1-directed MGD MRT-6160 represents a major corporate milestone for Monte Rosa, signifying what we believe to be the first clinical-stage, rationally designed MGD for a non-oncology indication,” said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. “Our MRT-2359 program for MYC-driven solid tumors is in an ongoing Phase 1/2 study and we look forward to announcing the recommended Phase 2 dose, sharing updated clinical efficacy and safety results from the dose escalation arm of the trial, and initiating enrollment of our Phase 2 expansion cohorts in the second half of the year. Our second immunology/inflammation program, MRT-8102, a NEK7-directed MGD targeting diseases driven by IL-1β and the NLRP3 inflammasome, continues to advance and we expect to submit an IND application in the first half of next year. Our strategic collaboration with Roche has been progressing rapidly, and we are very pleased to announce today that we have reached our first set of research milestones, which we believe further validates the productivity of our QuEEN Discovery Engine. Our strong balance sheet, augmented by our recent financing, is expected to provide cash runway into H1 2027, funding the Company through multiple anticipated milestones including proof-of-concept readouts for our three lead programs.”

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). In June 2024, the Company announced that it had obtained encouraging initial safety and pharmacodynamic data from the 0.5 mg dose using the 21 days on, 7 days off regimen. This regimen represents dosing of MRT-2359 twice as frequently per cycle compared to the 5 days on, 9 days off regimen previously evaluated in this study. Based on the favorable safety assessment for the 0.5 mg dose, the Company continues to evaluate a higher 0.75 mg, 21 days on, 7 days off dose cohort. In the second half of the year, Monte Rosa expects to make a final determination of the MRT-2359 recommended Phase 2 dose, share updated clinical activity and safety results from the dose escalation arm of the trial, and initiate enrollment of MRT-2359 Phase 2 expansion cohorts.

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

- Monte Rosa today announced that its Investigational New Drug (IND) submission for MRT-6160 has been accepted by the U.S. Food and Drug Administration (FDA). Initiation of a Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) study is expected this summer and initial clinical results are anticipated in Q1 2025.
- In July, Monte Rosa reported the publication of a review article titled, *VAV1 as a putative therapeutic target in autoimmune and chronic inflammatory diseases*, co-authored by Prof. Dr. Markus F. Neurath, Friedrich-Alexander-University Erlangen-Nürnberg, and Prof. Leslie J. Berg, University of Colorado School of Medicine, in the peer-reviewed journal *Trends in Immunology*, a Cell Press journal. The publication highlights how novel approaches targeting VAV1 have therapeutic potential in T and B-cell-mediated autoimmune and chronic inflammatory diseases.
- In June, Monte Rosa presented preclinical data at the EULAR 2024 conference demonstrating that MRT-6160 inhibited disease progression, pro-inflammatory cytokines, and autoantibody production in the collagen-induced arthritis murine model of rheumatoid arthritis.

- In May, Monte Rosa presented preclinical data at Digestive Disease Week 2024 demonstrating that MRT-6160 inhibited colitis disease progression and colon inflammation, lowered inflammatory mucosal cytokines, and reduced expression of IBD-associated genes in a T-cell transfer murine model of colitis.

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

- In March, 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. MRT-8102 has demonstrated highly favorable central nervous system (CNS) exposure and degradation in a study in non-human primates, supporting its potential development in neurologic indications and obesity, in addition to potential use in gout, pericarditis, and other peripheral inflammatory conditions. The Company is evaluating applications across multiple inflammatory disorders.
- Monte Rosa expects to submit an IND application for MRT-8102 in H1 2025.

CDK2 and Cyclin E1-directed MGD programs

- In May, Monte Rosa 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.
- Monte Rosa is progressing both programs to development candidate nominations and expects to nominate a development candidate for the CDK2-directed MGD program by year-end.

Additional Corporate Updates

- Monte Rosa announced today that it achieved pre-specified research milestones and earned milestone payments under its strategic collaboration and licensing agreement with Roche. In October 2023, Monte Rosa entered into a strategic collaboration and licensing agreement with Roche to discover and develop MGDs against targets in cancer and neurological diseases. Under the terms of the agreement, Monte Rosa 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.
- In May, the Company announced an underwritten public offering providing gross proceeds of approximately $100 million.
- In May, Monte Rosa announced three leadership team promotions: Sharon Townson, Ph.D., to Chief Scientific Officer; Phil Nickson, Ph.D., J.D., to Chief Business and Legal Officer; and Jennifer Champoux to Chief Operating Officer.

ANTICIPATED MILESTONES

- Announce the recommended Phase 2 dose for the MRT-2359 Phase 1/2 study and report Phase 1 clinical activity and safety results in H2 2024. The Company also plans to 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.
- Initiate a Phase 1 SAD/MAD study with MRT-6160 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 H1 2025.
- Nominate a development candidate for the CDK2 preclinical program in 2024.

SECOND QUARTER 2024 FINANCIAL RESULTS

Collaboration Revenue: Collaboration revenue for the second quarter of 2024 was $4.7 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 second quarter of 2024 were $28.1 million, compared to $29.1 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 $2.6 million of R&D expenses for Q2 2024, compared to $2.3 million in the same period in 2023.

General and Administrative (G&A) Expenses: G&A expenses for the second quarter of 2024 were $9.3 million compared to $8.1 million during the same period in 2023. The increase in G&A expenses resulted from increased headcount, stock-based compensation expense, and fees paid to consultants to support growth and operations. G&A expenses included non-cash stock-based compensation of $1.9 million for the second quarter of 2024, compared to $1.9 million for the same period in 2023.

Net Loss: Net loss for the second quarter of 2024 was $30.3 million, compared to $32.0 million for the first quarter of 2024.

Cash Position and Financial Guidance: Cash, cash equivalents, restricted cash, and marketable securities as of June 30, 2024, were $267.1 million, compared to cash, cash equivalents, restricted cash, and marketable securities of $197.8 million as of March 31, 2024.

The Company expects its cash and cash equivalents to be sufficient to fund planned operations and capital expenditures into the first half of 2027.

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 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 productivity 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 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 updated data from our Phase 1/2 clinical trial of MRT-2359 in MYC-driven solid tumors in the second half of 2024, timing for our identification and any disclosure of a recommended Phase 2 dose for MRT-2359 in the second half of 2024, and timing of enrollment of Phase 2 expansion cohorts in the second half of 2024, (ii) the ongoing development of our VAV1-directed degrader, referred to as MRT-6160, and the planned Phase 1 SAD/MAD study in the summer of 2024 with initial clinical data expected in the first quarter of 2025 and our expectations regarding the potential clinical benefit for this program, (iii) the ongoing development of our

NEK7-directed MGD, referred to as MRT-8102, and our expectations around its potential across neurologic indications 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 our statements around multiple anticipated clinical readouts, including results from proof-of-concept patient studies for MRT-2359, MRT-6160, and MRT-8102, advancement and application of our pipeline, including identification and the timing thereof of a development candidate for CDK2 until the end of 2024, statements around the advancement and application of our platform, 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, 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 2027, as well as our expectations of success for our programs, strength of collaboration relationships and the strength of our financial position, 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)

	June 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 108,847	$ 128,101
Marketable securities	153,358	104,312
Accounts receivable	9,000	—
Other receivables	842	505
Prepaid expenses and other current assets	5,849	3,294
Total current assets	277,896	236,212
Property and equipment, net	33,250	33,803
Operating lease right-of-use assets	27,893	28,808
Restricted cash, net of current	4,866	4,580
Other long-term assets	209	352
Total assets	$ 344,114	$ 303,755
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 6,473	$ 11,152
Accrued expenses and other current liabilities	12,759	14,600
Current deferred revenue	19,645	17,678
Current portion of operating lease liability	3,471	3,162
Total current liabilities	42,348	46,592
Deferred revenue, net of current	33,596	32,323
Defined benefit plan liability	2,614	2,713
Operating lease liability	40,885	42,877
Total liabilities	119,443	124,505
Commitments and contingencies		
Stockholders' equity		

Common stock, $0.0001 par value; 500,000,000 shares authorized, 61,333,597 shares issued and 61,328,282 shares outstanding as of June 30, 2024; and 50,154,929 shares issued and 50,140,233 shares outstanding as of December 31, 2023	6	5
Additional paid-in capital	655,501	547,857
Accumulated other comprehensive loss	(2,670)	(2,724)
Accumulated deficit	(428,166)	(365,888)
Total stockholders' equity	224,671	179,250
Total liabilities and stockholders' equity	$ 344,114	$ 303,755

Consolidated Statements of Operations and Comprehensive Income (Loss)

(In thousands, except share and per share amounts)

	Three months ended June 30,		Six months ended June 30,	
	2024	**2023**	**2024**	**2023**
Collaboration revenue	$ 4,695	$ —	$ 5,759	$ —
Operating expenses:				
Research and development	28,055	29,076	55,081	55,831
General and administrative	9,282	8,145	18,267	15,649
Total operating expenses	37,337	37,221	73,348	71,480
Loss from operations	(32,642)	(37,221)	(67,589)	(71,480)
Other income (expense):				
Interest income, net	2,637	2,302	5,079	4,739
Foreign currency exchange gain (loss), net	(53)	(93)	567	(178)
Gain on disposal of fixed assets	—	24	—	24
Loss on sale of marketable securities	—	—	—	(131)
Total other income	2,584	2,233	5,646	4,454
Net loss before income taxes	$ (30,058)	$ (34,988)	$ (61,943)	$ (67,026)
Provision for income taxes	(252)	(190)	(335)	(190)
Net loss	$ (30,310)	$ (35,178)	$ (62,278)	$ (67,216)
Net loss per share attributable to common stockholders—basic and diluted	$ (0.43)	$ (0.71)	$ (0.95)	$ (1.36)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	71,233,992	49,431,922	65,695,095	49,389,931
Comprehensive loss:				
Net loss	$ (30,310)	$ (35,178)	$ (62,278)	$ (67,216)
Provision for pension benefit obligation	35	14	70	28
Unrealized gain (loss) on available-for-sale securities	(12)	(261)	(16)	84
Comprehensive loss	$ (30,287)	$ (35,425)	$ (62,224)	$ (67,104)

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