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

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Executed global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed molecular glue degraders including MRT-6160 for immune-related conditions; $150M upfront payment, eligible for up to $2.1B milestones and U.S. P&L share

MRT-6160 Phase 1 SAD/MAD study ongoing with initial clinical data expected by Q1 2025

Phase 1/2 study of MRT-2359, in development for MYC-driven solid tumors, ongoing with updated clinical results anticipated by year-end

MRT-8102, a NEK7-directed molecular glue degrader targeting diseases driven by IL-1β and the NLRP3 inflammasome, on track for IND filing in H1 2025

Strengthened cash position, including anticipated $150 million upfront from Novartis, expected to fund operations into 2028 through multiple anticipated proof-of-concept clinical readouts

BOSTON, Nov. 07, 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 third quarter that ended September 30, 2024.

“We continue to make significant progress towards pioneering the discovery and development of highly selective molecular glue degraders against paradigm-shifting targets. The recently announced global license agreement with Novartis to advance VAV1-directed MGDs for immune-related conditions marks a transformative milestone towards that goal,” said Markus Warmuth, M.D., Chief Executive Officer of Monte Rosa Therapeutics. “We believe this agreement will accelerate and broaden the scope of clinical development of MRT-6160 across a spectrum of immune-mediated conditions while retaining substantial value for Monte Rosa. Moreover, the resources provided by this agreement are expected to meaningfully extend our cash runway and enable us to advance our pipeline to potential value-creating milestones and to further leverage our industry-leading QuEEN™ discovery engine to design and develop novel MGDs for previously undruggable targets across a variety of disease areas, including immunology and inflammation (I&I), cardiovascular, and metabolic diseases. We look forward to sharing initial clinical data from the ongoing Phase 1 study of MRT-6160 by Q1 2025.”

Dr. Warmuth continued, “We have made significant progress advancing our second I&I program, MRT-8102, toward an expected IND application in the first half of 2025. Turning towards our oncology pipeline, we look forward to sharing updated clinical results from the Phase 1 dose escalation portion of the MRT-2359 study by year-end, and we’re pleased with the progress of our cell cycle portfolio, including the CDK2 and cyclin E1 programs, with both advancing towards development candidate nominations.”

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. Monte Rosa continues to evaluate a higher 0.75 mg, 21 days on, 7 days off dose cohort.

MRT-6160, VAV1-directed MGD for immune-mediated conditions

- In October, the Company announced a global exclusive development and commercialization license agreement with Novartis to advance VAV1 MGDs including MRT-6160, currently in Phase 1 clinical development for various immune-related conditions. Under the terms of the agreement, Novartis will obtain exclusive worldwide rights to develop, manufacture and commercialize MRT-6160 and other VAV1 MGDs and will be responsible for all clinical development and commercialization, starting with Phase 2 clinical studies. Monte Rosa remains responsible for completion of the ongoing Phase 1 clinical study of MRT-6160. Novartis has agreed to pay Monte Rosa $150 million upfront. Monte Rosa is eligible to receive up to $2.1 billion in development, regulatory, and sales milestones, beginning upon initiation of Phase 2 studies, as well as tiered royalties on ex-U.S. net sales. Monte Rosa will co-fund any Phase 3 clinical development and will share any profits and losses associated with the manufacturing and commercialization of MRT-6160 in the U.S. The agreement is

subject to customary closing conditions including regulatory clearance.
- In August, Monte Rosa announced that the first participants had been dosed in an MRT-6160 Phase 1 single ascending dose/multiple ascending dose (SAD/MAD) study.

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

- In September, Monte Rosa presented preclinical data at the Inflammasome Summit demonstrating that its development candidate 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, is a potent, selective, and durable molecular glue degrader of NEK7. The data provide preclinical proof of concept that a NEK7 MGD leads to inhibition of the NLRP3 inflammasome and IL-1 release to reduce the effects of inflammation, supporting the potential to address central and peripheral inflammatory disorders.
- Monte Rosa expects to submit an IND application for MRT-8102 in H1 2025.

CDK2 and Cyclin E1-directed MGD programs

- In October, Monte Rosa presented preclinical data at the 36th EORTC-NCI-AACR Symposium on the potential of its cyclin E1 (CCNE1)-directed MGDs for the treatment of *CCNE1*-amplified solid tumors. The data demonstrated that Monte Rosa's MGD degrades cyclin E1 with a high level of selectivity, sparing other closely related proteins, including other cyclins, and cyclin-dependent kinases (CDKs). The data also showed that a cyclin E1-directed MGD led to downstream pathway inhibition and induced tumor growth suppression and regression preferentially in *CCNE1*-amplified and over-expressing tumor cell lines and xenograft models. Cyclin E1 MGDs may represent a potential novel therapeutic approach by directly and selectively targeting a frequently amplified non-enzymatic driver oncogene relevant in multiple solid tumors.
- Monte Rosa is progressing both its CDK2 and cyclin E1-directed MGD programs to development candidate nominations.

QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) discovery engine

- In October, Monte Rosa made a preprint available in BioRxiv entitled, "Mining the Cereblon Target Space Redefines Rules for Molecular Glue-induced Neosubstrate Recognition," which demonstrates a vast expansion of what had been considered druggable within the cereblon target space. Monte Rosa has identified more than 1,600 proteins predicted to be compatible with cereblon across diverse target classes that can potentially be targeted with molecular glue degraders.

ANTICIPATED MILESTONES

- Announce the recommended Phase 2 dose and data from the Phase 1 dose escalation portion of the MRT-2359 Phase 1/2 study including safety, biomarker data, and clinical activity before the end of 2024. The Company also expects to provide guidance on Phase 2 expansion cohorts before year-end.
- Report initial data from the Phase 1 SAD/MAD study of MRT-6160 in healthy volunteers by Q1 2025. The Phase 1 study of MRT-6160 is designed to provide early insights into safety, pharmacokinetics, VAV1 protein degradation, and key downstream pharmacodynamic markers including CD69, IL-2, IL-6, and IL-17.
- Submit an IND application for MRT-8102 in H1 2025.
- Nominate a CDK2 program development candidate before year-end 2024.

UPCOMING INVESTOR CONFERENCES

Monte Rosa management will participate in the following investor conferences:

- Guggenheim Securities Healthcare Innovation Conference (Boston, Mass.) – Markus Warmuth, M.D., Chief Executive Officer, to participate in a fireside chat, November 11, 2024, at 3:30 p.m. EST.
- Jefferies London Healthcare Conference (London, UK) – November 19, 2024.

A webcast of the fireside chat will be accessible via the "Events & Presentations" section of Monte Rosa's website at ir.monterosatx.com, and an archived version will be made available for 30 days following the presentation.

THIRD QUARTER 2024 FINANCIAL RESULTS

Collaboration revenue: Collaboration revenue for the third quarter of 2024 was $9.2 million. Collaboration revenue represents revenue recorded under the Roche license and collaboration agreement. No collaboration revenue was recognized during the same period in 2023.

Research and Development (R&D) expenses: R&D expenses for the third quarter of 2024 were $27.6 million, compared to $28.3 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 advancement 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 Q3 2024, compared to $2.3 million in the same period in 2023.

General and Administrative (G&A) expenses: G&A expenses for the third quarter of 2024 were $8.1 million compared to $8.7 million during the same period in 2023. G&A expenses included non-cash stock-based compensation of $1.6 million for the third

quarter of 2024, compared to $2.2 million for the same period in 2023.

Net loss: Net loss for the third quarter of 2024 was $23.9 million, compared to $30.3 million for the second quarter of 2024.

Cash position and financial guidance: Cash, cash equivalents, restricted cash, and marketable securities as of September 30, 2024, were $247.1 million, compared to cash, cash equivalents, restricted cash, and marketable securities of $267.1 million as of June 30, 2024. The end of Q3 cash position does not include the recently announced $150 million upfront payment due from Novartis, subject to customary closing conditions including regulatory clearance.

Based on current cash, cash equivalents, restricted cash, marketable securities, and the anticipated $150 million upfront payment due from Novartis, the Company expects its cash and cash equivalents to be sufficient to fund planned operations and capital expenditures into 2028.

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. MRT-6160 has shown promising activity in preclinical models of multiple immune-mediated conditions. Under the terms of an agreement announced in October 2024, Novartis will obtain exclusive worldwide rights to develop, manufacture and commercialize MRT-6160 and other VAV1 MGDs, subject to customary closing conditions including regulatory clearance.

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. Monte Rosa has a global license agreement with Novartis to advance VAV1-directed molecular glue degraders and 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 and to accelerate and broaden the scope of clinical development of MRT-6160 across a spectrum of immune-mediated conditions, 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 related to the Company's strategic agreements, goals of such agreements and any related milestone, royalty or other payments related thereto, statements related to the ability of the Company to advance its

pipeline to potential value-creating milestones, statements around the productivity of the QuEEN discovery engine and the potential of the Company's MGDs against a broad spectrum of targets, including undruggable targets across a variety of disease areas, such as I&I, cardiovascular, and metabolic diseases, 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 its ability to be selective, our expectations for the nature, significance, and timing for our disclosure of any data from our Phase 1 dose escalation portion of the MRT-2359 Phase 1/2 study, including safety, biomarker data and clinical activity, by the end of 2024, timing for our identification and any disclosure of a recommended Phase 2 dose for MRT-2359 by the end of 2024, and timing of our guidance on initiation of Phase 2 expansion cohorts by the end of 2024, (ii) the ongoing development of our VAV1-directed degrader, referred to as MRT-6160, and the timing of initial data from the Phase 1 SAD/MAD study by the first quarter of 2025 and our expectations regarding the potential clinical benefit for this program, including the contributions by Novartis, (iii) the ongoing development and progress of our NEK7-directed MGD, referred to as MRT-8102, and our expectations around its potential across neurologic indications amongst others, including our expectations to submit an IND to the FDA in the first half of 2025, and our statements around multiple anticipated preclinical and/or clinical readouts and their expected timing, including results from proof-of-concept patient studies, candidates and their applicability to various indications, progressing both our CDK2 and cyclin E1-directed MGD programs, the expected potential clinical benefit of any of our candidates, advancement and application of our pipeline, statements around the advancement and application of our platform, statements concerning our expectations regarding our ability to identify, nominate and the timing of our nominations of additional targets, product candidates, and development candidates, statements around our ability to capitalize on and potential benefits resulting from our research and translational insights, including announcements related to preclinical programs, as well as our the ability to optimize collaborations with industry partners on our development programs, statements about the closing of the transaction with Novartis, obligations under our collaboration agreements, expectations around the receipt of any payments under such agreements and the future development and commercialization of various products, 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 2028, inclusive of the anticipated upfront payment from Novartis, 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)

	September 30, 2024	December 31, 2023
Assets		
Current assets:		
Cash and cash equivalents	$ 125,575	$ 128,101
Marketable securities	116,611	104,312
Other receivables	595	505
Prepaid expenses and other current assets	8,426	3,294
Total current assets	251,207	236,212
Property and equipment, net	31,442	33,803
Operating lease right-of-use assets	27,364	28,808
Restricted cash	4,908	4,580
Other long-term assets	159	352
Total assets	$ 315,080	$ 303,755
Liabilities and stockholders' equity		

Current liabilities:		
Accounts payable	$ 3,978	$ 11,152
Accrued expenses and other current liabilities	15,099	14,600
Current deferred revenue	18,918	17,678
Current portion of operating lease liability	3,646	3,162
Total current liabilities	41,641	46,592
Deferred revenue, net of current	25,107	32,323
Defined benefit plan liability	2,823	2,713
Operating lease liability, net of current	40,052	42,877
Total liabilities	109,623	124,505
Commitments and contingencies		
Stockholders' equity		
Common stock, $0.0001 par value; 500,000,000 shares authorized, 61,378,108 shares issued and 61,377,484 shares outstanding as of September 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	659,798	547,857
Accumulated other comprehensive loss	(2,322)	(2,724)
Accumulated deficit	(452,025)	(365,888)
Total stockholders' equity	205,457	179,250
Total liabilities and stockholders' equity	$ 315,080	$ 303,755

Consolidated Statements of Operations and Comprehensive Income (Loss)
(In thousands, except share and per share amounts)

	Three months ended September 30,		Nine months ended September 30,	
	2024	**2023**	**2024**	**2023**
Collaboration revenue	$ 9,216	$ —	$ 14,975	$ —
Operating expenses:				
Research and development	27,616	28,306	82,697	84,137
General and administrative	8,127	8,662	26,394	24,311
Total operating expenses	35,743	36,968	109,091	108,448
Loss from operations	(26,527)	(36,968)	(94,116)	(108,448)
Other income (expense):				
Interest income	2,892	2,227	7,971	6,966
Foreign currency exchange gain (loss), net	(153)	27	414	(151)
Gain on disposal of fixed assets	—	—	—	24
Loss on sale of marketable securities	—	—	—	(131)
Total other income	2,739	2,254	8,385	6,708
Net loss before income taxes	$ (23,788)	$ (34,714)	$ (85,731)	$ (101,740)
Provision for income taxes	(71)	(170)	(406)	(360)
Net loss	$ (23,859)	$ (34,884)	$ (86,137)	$ (102,100)
Net loss per share—basic and diluted	$ (0.29)	$ (0.70)	$ (1.21)	$ (2.06)
Weighted-average number of shares outstanding used in computing net loss per common share—basic and diluted	82,011,670	49,814,903	71,173,647	49,533,143
Comprehensive loss:				
Net loss	$ (23,859)	$ (34,884)	$ (86,137)	$ (102,100)
Provision for pension benefit obligation	37	14	107	42
Unrealized gain on available-for-sale securities	311	171	295	255
Comprehensive loss	$ (23,511)	$ (34,699)	$ (85,735)	$ (101,803)

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