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

FORM 8-K

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

Date of Report (Date of earliest event reported): January 9, 2023

MONTE ROSA THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

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

645 Summer Street, Suite 102
Boston, MA 02210
(Address of principal executive offices, including zip code)

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

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

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

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 7.01. Regulation FD Disclosure

On January 9, 2023, Monte Rosa Therapeutics, Inc. issued a press release titled "*Monte Rosa Therapeutics Outlines Progress Across Portfolio of Molecular Glue Degraders and Key Anticipated Milestones for 2023*" and provided a corporate update in conjunction with its participation at the 41st Annual J.P. Morgan Healthcare Conference in San Francisco, CA. The press release and presentation are furnished as Exhibit 99.1 and 99.2, respectively, to this Current Report on Form 8-K.

The information in this Form 8-K (including Exhibits 99.1 and 99.2) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

99.1	J.P. Morgan Healthcare Conference presentation furnished by Monte Rosa Therapeutics, Inc. on January 9, 2023.
99.2	Press release issued by Monte Rosa Therapeutics, Inc. on January 9, 2023, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

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

Monte Rosa Therapeutics, Inc.

Date: January 9, 2023

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


From Serendipity to Rational Design
Taking Molecular Glue Degraders to New Heights | January 2023
Monte Rosa
Therapeutics

Forward-Looking Statements

These materials include 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 in herein include, but are not limited to, statements about our product development activities, including our expectations around MRT-2359, such as for our ongoing clinical trial for MRT-2359 and the timing thereof and our expectations regarding the potential significance of obtaining Fast Track Designation from the FDA, the ongoing development of our QuEEN™ platform, the advancement, and timing thereof, of our pipeline and the various products therein, our ability to initiate and the timing of initiation of additional lead optimization programs, and our expectations regarding our ability to nominate and the timing of our nominations of additional development candidates, as well as our expectations of success for our programs and the strength of our financial position, among others. By their nature, these statements are subject to numerous risks and uncertainties, including the impact that the ongoing COVID-19 pandemic will have on our development activities and operations, as well as those risks and uncertainties set forth in our Annual Report on Form 10-K for the fourth quarter and full year ended December 31, 2021 filed, with the US Securities and Exchange Commission on March 29, 2022, and any subsequent filings, including our most recently filed Quarterly Report on Form 10-Q, 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.

Monte Rosa Therapeutics Highlights

Taking molecular glue degraders (MGDs) to new heights

Developing breakthrough drugs that **selectively degrade therapeutically-relevant proteins** previously considered undruggable

Five disclosed programs targeting high unmet medical needs in oncology, autoimmune disease, inflammation and other indications

PhI/II initiated for MRT-2359 with clinical development in MYC-driven tumors

AI-based degron prediction & rational design of highly selective MGDs enable a next-generation molecular glue-based targeted protein degradation platform

Strong financial position with $274M cash as of December 31, 2022, providing runway into 2025

World-Class Leadership

Deep expertise in molecular glue discovery, drug development and precision medicine

Markus Warmuth, M.D.
Chief Executive Officer

H3 Biomedicine
NOVARTIS

Ajim Tamboli, CFA
Chief Financial Officer

Columbia Threadneedle Investments
Lehman Brothers

Owen Wallace, Ph.D.
Chief Scientific Officer

Fulcrum Therapeutics
NOVARTIS

Sharon Townson, Ph.D.
Chief Technology Officer

KYMERA
Warp Drive Bio

John Castle, Ph.D.
Chief Data Scientist

agenus
BIONTECH

Filip Janku, M.D., Ph.D.
Chief Medical Officer

The University of Texas MD Anderson Cancer Center

Jullian Jones, Ph.D., J.D., MBA
Chief Business Officer

Lilly
Boehringer Ingelheim

Silvia Buonamici, Ph.D.
SVP, Drug Discovery Biology

H3 Biomedicine
NOVARTIS

Phil Nickson, Ph.D., J.D.
General Counsel

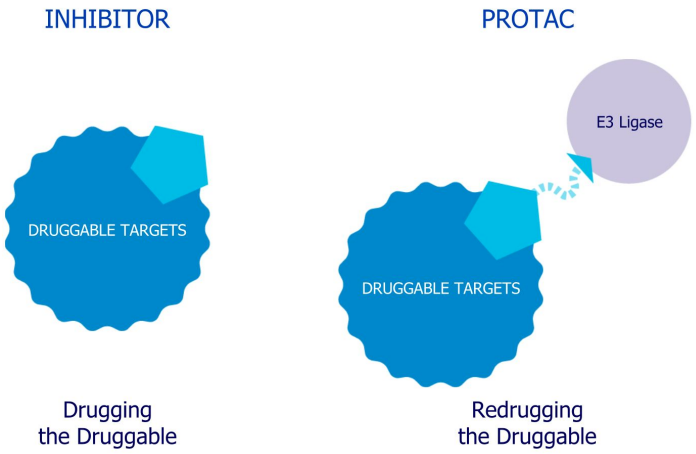
Momenta
FISH & RICHARDSON

Jennifer Champoux,
SVP, Operations

H3 Biomedicine
NOVARTIS

Molecular Glue Degraders (MGDs) – Drugging The Undruggable

Expanding target space, fostering a new generation of drugs



- Favorable drug-like properties
- Broad tissue distribution
- No hook effect

Drugging the Druggable

Redrugging the Druggable

Drugging the Undruggable

Expanding the Degradable Proteome

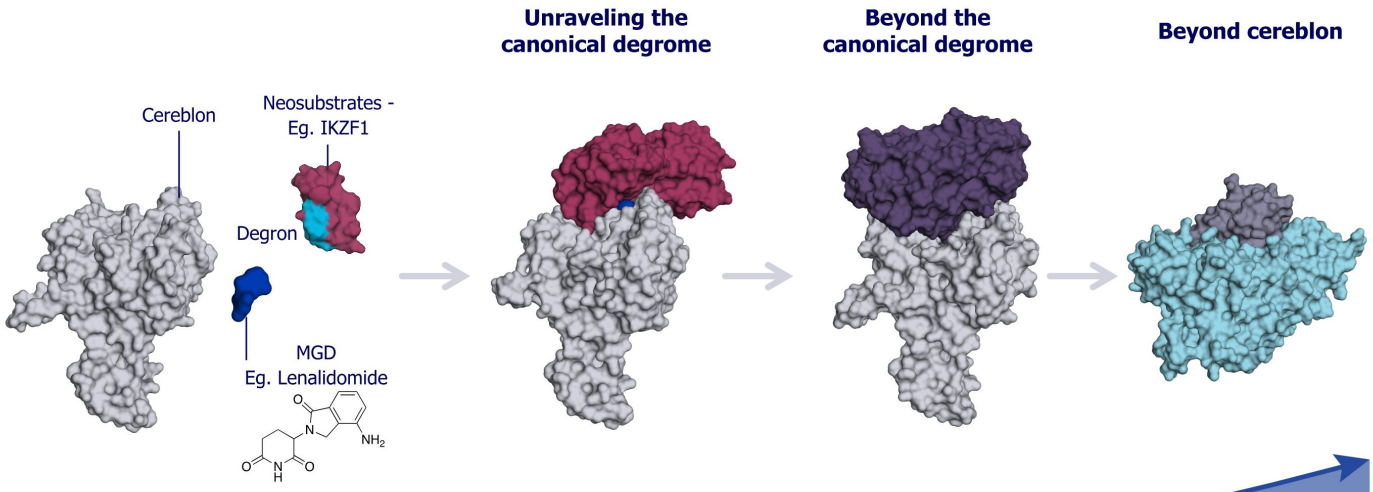
Target Space

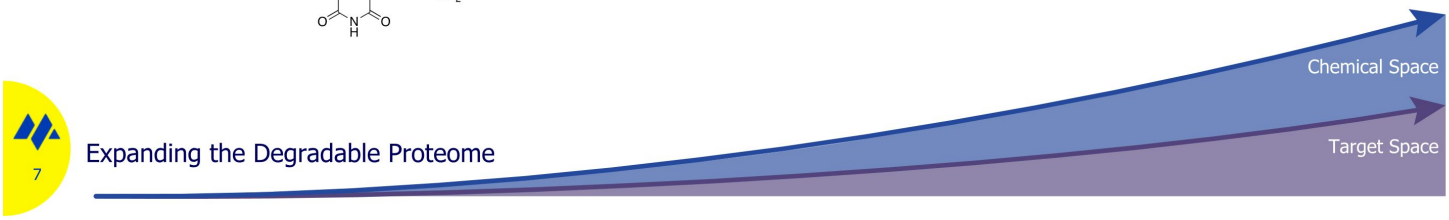
Monte Rosa Therapeutics

QuEEN™ Discovery Engine

Quantitative and Engineered Elimination of Neosubstrates

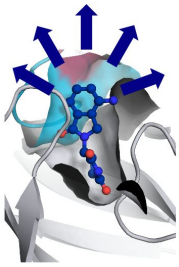
Our Rational Approach to Unleash the Full Potential of MGDs

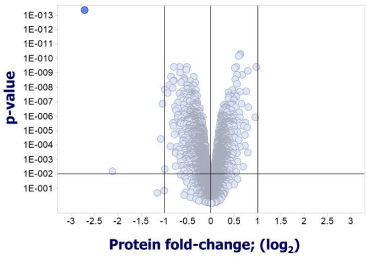


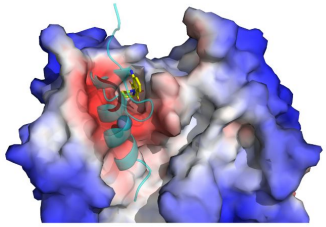


QuEEN™ Discovery Engine: Unique Capabilities Enable Our Rational and Target-Centric Approach to MGDs

Proprietary MGD library	Glueomics™ Engine	AI Engines OneVision™ and Rhapsody™
Diverse and growing library rationally designed using structural insights to engage a variety of degrons	Specialized suite of *in vitro* assays to globally assess proximity and degradation proteome-wide and in high throughput	*In silico* degron & ternary complex discovery using proprietary AI-powered algorithms

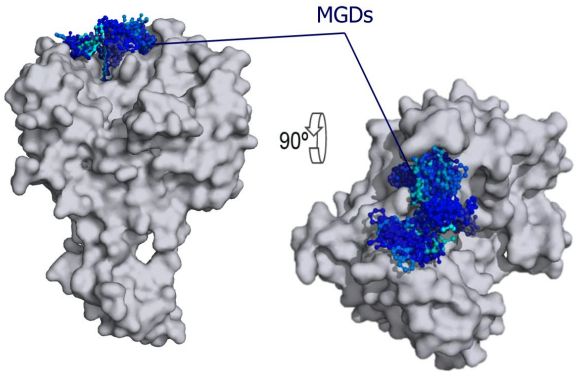






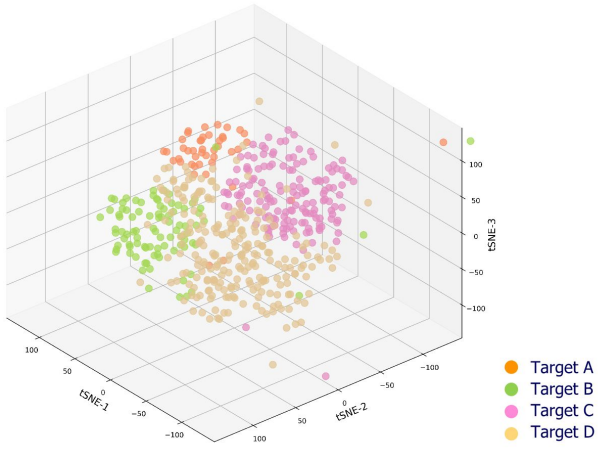
Integrated and iterative workflow leads to discovery of reprogrammable ligases, neosubstrates and MGDs

A CRBN-Centric Library Characterized by Novelty and Structural Diversity



Library characteristics

- Current library size 27K MGDs, continuing to expand
- High structural diversity and novelty
- Design focused on optimal drug-like properties



Chemical fingerprints of MGD hits

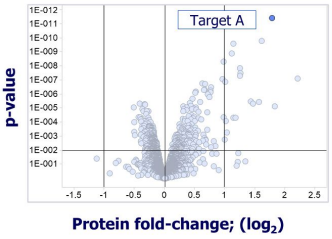
Leveraging different areas of the CRBN surface
to engage diverse degrons and targets

Omics Platforms Accelerate Degron and MGD Discovery and Validation

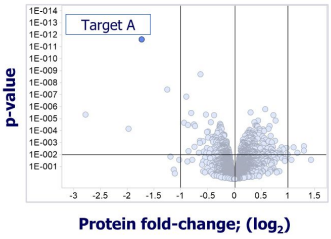
Chemo-proteomics

Proteome-wide profiling of up to 10K proteins to characterize MGD proximity, degradation and selectivity

Proximity (Turbo-ID)

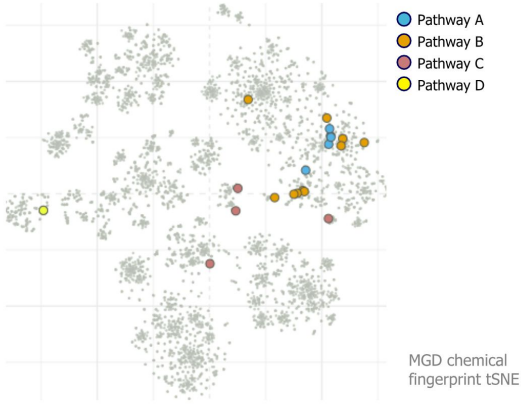


Degradation



Chemo-transcriptomics

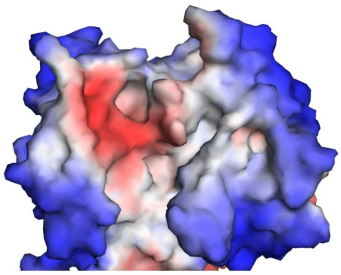
High-throughput transcriptomic profiling to characterize MGD pathway MOA, selectivity and structure-activity



Proprietary AI/ML Engines Allow for Discovery of Glueable Targets and Highly Selective MGDs

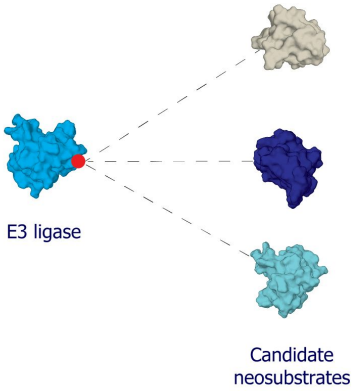
E3 ligase surface evaluation

PPI propensity & pocket identification for reprogrammability



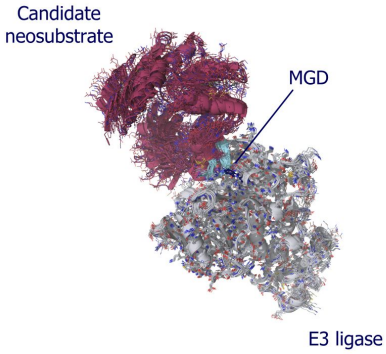
Proteome-wide glueability assessment

Surface complementarity connecting E3 ligases to neosubstrates

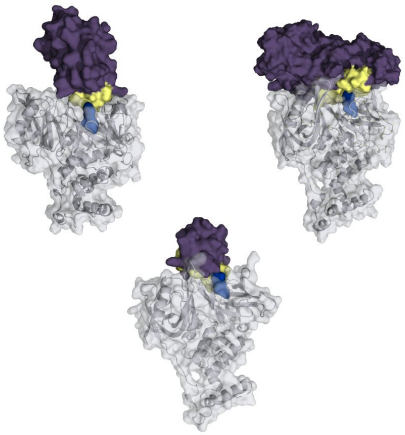


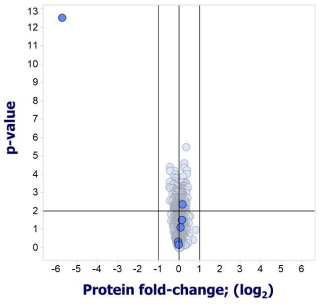
Ternary complex modelling and in-silico screening

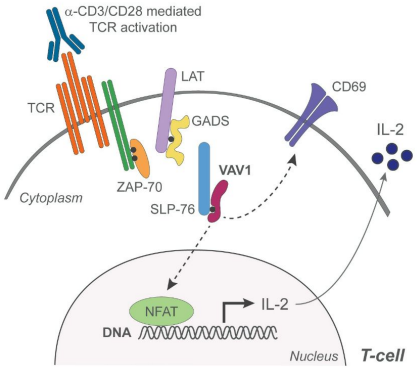
Fast algorithms leveraging ensembles, dynamics and quantum mechanics



A Rich, Differentiated Target Space Across Protein Domains and Diseases







Degrons

QuEEN has enabled the discovery of diverse degrons across various protein domains and classes

Selectivity

Degrons have unique sequences enabling design of MGDs with unprecedented level of selectivity

Targets

Our Degron Encyclopedia contains many highly credentialed, undruggable targets

Monte Rosa Therapeutics

Portfolio

Leveraging a Leading Drug Discovery Platform

Purpose-built to discover and develop a wide landscape of therapeutically-relevant MGDs

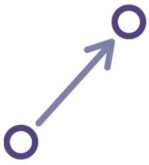
Monte Rosa's High-Value Proprietary Pipeline

Targets

Undruggable and inadequately drugged degron-containing proteins

Target non-catalytic and scaffolding functions

High level of target validation, preclinically and clinically



Clinical Path

Programs with a biomarker-based patient selection strategy and a clear path to the clinic

Opportunity for a rapid clinical PoC showing MOA and efficacy

Patient Benefit

Address high unmet needs

Drug a wide range of therapeutically-relevant proteins in oncology and beyond

Create synergies within therapeutic areas

Monte Rosa Pipeline

Rapidly advancing wholly owned MGD programs targeting undruggable proteins

Target (Degron)	Indication(s)	Discovery / IND-Enabling / Clinical	Next Anticipated Milestones	Ownership
GSPT1 (G-loop)	NSCLC, SCLC and other MYC-driven Malignancies		Initial clinical data disclosure in 2H 2023	
CDK2 (new)	Ovarian Cancer, Breast Cancer		Multiple development candidate nominations in 2H 2023	
NEK7 (G-loop)	Inflammatory Diseases			
VAV1 (new)	T and B Cell Malignancies, Autoimmune Disease			
Multiple SCD targets	SCD, β-Thalassemia		Lead optimization	
Undisclosed	Multiple			

Oncology · Autoinflammation · Oncology / immunology · Genetic diseases

Monte Rosa Therapeutics

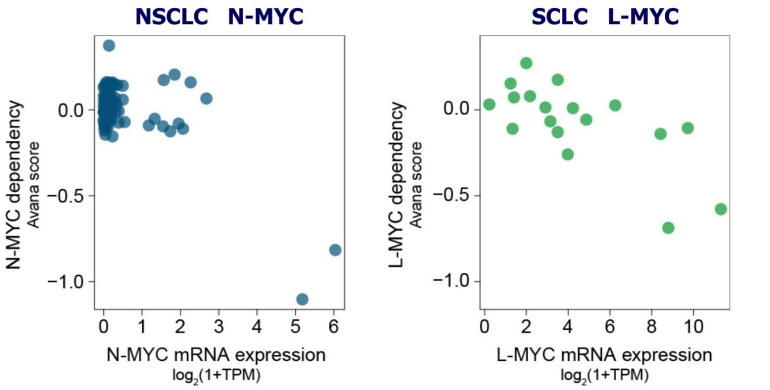
GSPT1 Program

MYC Family Transcription Factors are Key Cancer Dependence Genes

MYC family members are amongst the most dysregulated oncogenes in human cancer

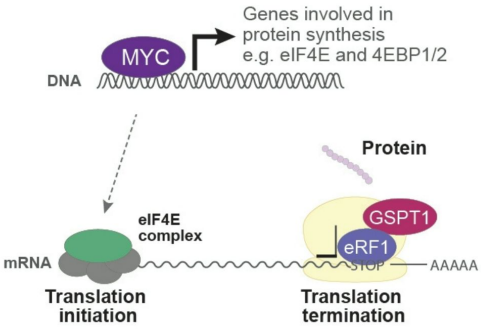
- **MYC up-regulation** dysregulates key cellular processes (e.g. ribosome biogenesis and **protein synthesis**)
- **MYC dysregulation** is frequently associated with **poor prognosis** and **unfavorable patient survival**
- **MYC family**: c-MYC, N-MYC, and L-MYC
- MYCs are **considered undruggable** by classic methods

Cells expressing high MYC are sensitive to MYC CRISPR KO

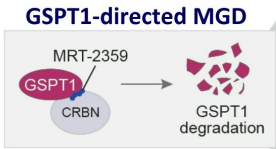


DepMap data, each dot represents a cell line

Targeting MYC-driven Tumors and Their Addiction to Protein Translation Through Degradation of GSPT1



- To sustain growth, MYC-driven tumors are **addicted to protein translation**
- This addiction creates a **dependency on** the translation termination factor **GSPT1**

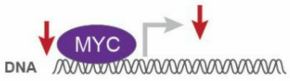


Synthetic lethality

MRT-2359 impairs protein synthesis in MYC high lines

Oncogene addiction

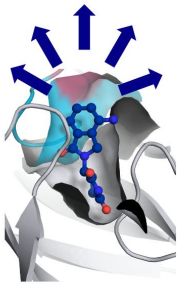
MRT-2359 affects MYC and targets in MYC high lines



QuEEN™ Discovery Engine Facilitates the Design of MRT-2359

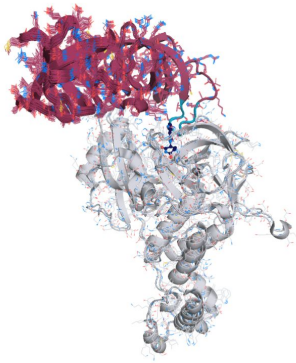
Proprietary MGD library

Diverse library, rationally designed, using structural insights to engage a variety of degrons

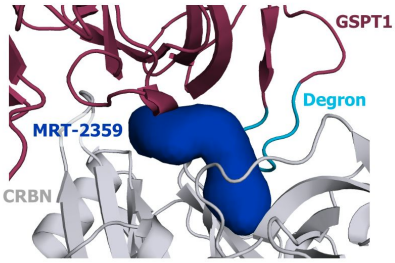


Rhapsody™

In silico ternary complex modelling using proprietary AI-powered algorithms



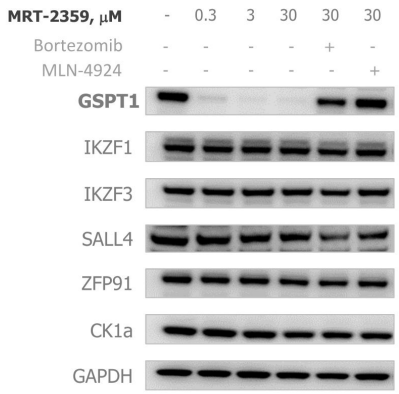
MRT-2359 is a potent GSPT1 degrader



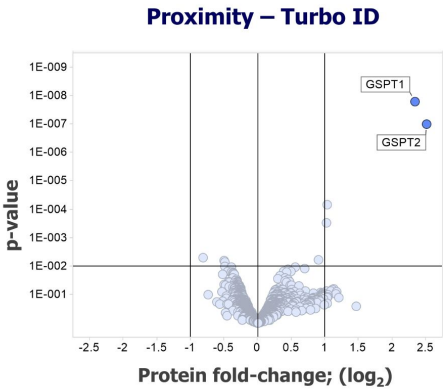
***in vitro* data**	
CRBN binding, K_i	113 nM
Ternary complex, EC_{50}	< 7 nM
Degradation, DC_{50}	80 nM

MRT-2359 is a GSPT1-directed MGD with Favorable Drug-like Properties

MRT-2359 is a selective GSPT1-directed MGD



6hr post treatment in MM1S and Kelly (SALL4)



1hr post treatment

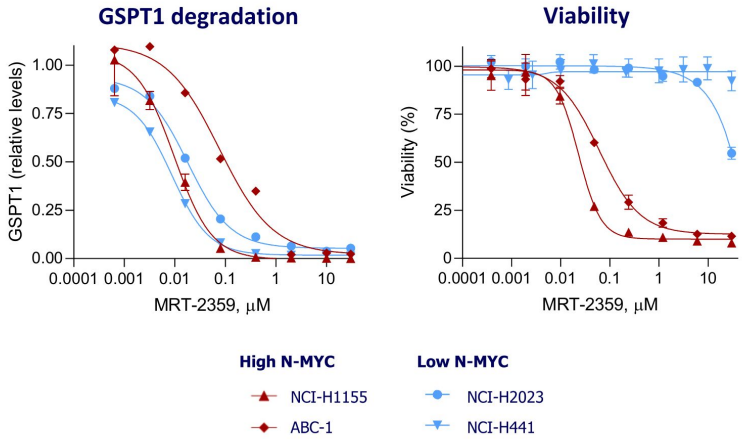
MRT-2359 is orally bioavailable and has favorable ADMET profile

ADMET profile	
CYP DDIs	> 30 µM
hERG inhibition patch clamp	EC_{50} > 30 µM
Oral bioavailability all species	~50%

- MRT-2359 does not inhibit or induce major CYPs
- MRT-2359 does not inhibit hERG
- MRT-2359 is orally bioavailable

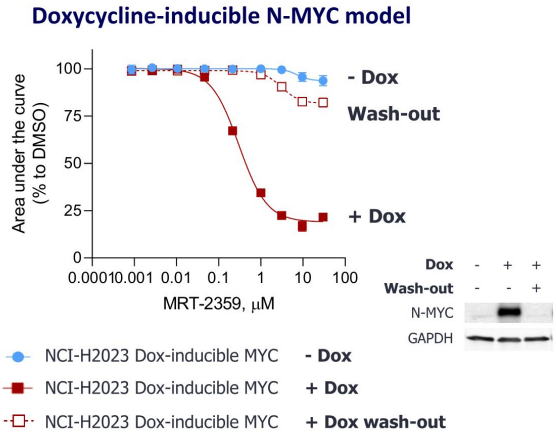
Preferential Activity of MRT-2359 in MYC-Driven NSCLC Lines

MRT-2359 induces GSPT1 degradation in all cell models, but show preferential antiproliferative activity in N-MYC high cell lines



GSPT1 western blot at 6 hr (N-Myc high) and 24 hr (low). 72 hr viability assay (CTG)

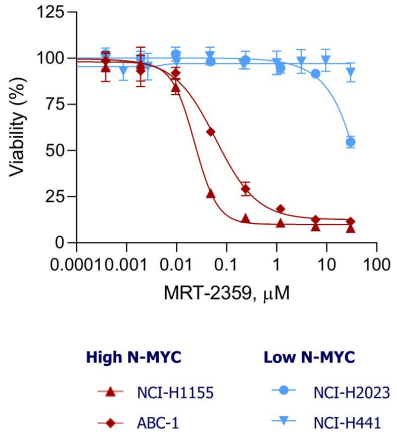
N-MYC overexpression sensitizes NCI-H2023 resistant cells to MRT-2359



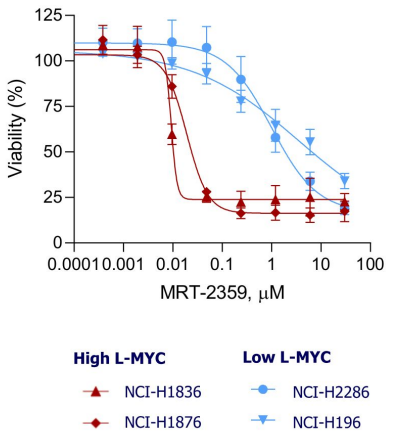
Incucyte, 96 hr post treatment

MRT-2359 Shows Preferential Activity in MYC High or Neuroendocrine (NE) Positive Cancer Lines

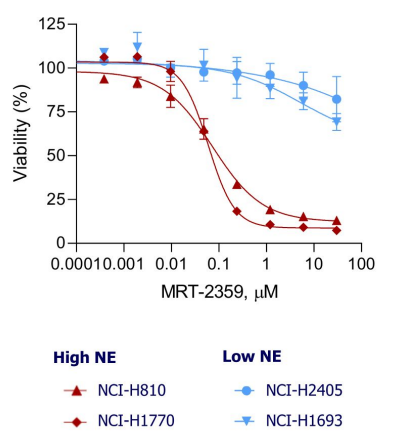
N-MYC high NSCLC lines



L-MYC high SCLC lines



NE positive lung lines



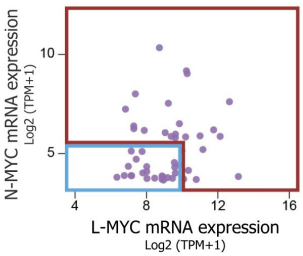
72 hr viability assay (CTG)

MRT-2359 Mouse-trial in NSCLC, SCLC and Lung NE Patient-derived Xenografts

Collection of PDX models

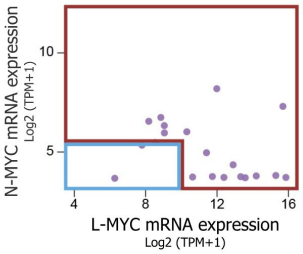
All models have been characterized by DNA and RNAseq

NSCLC



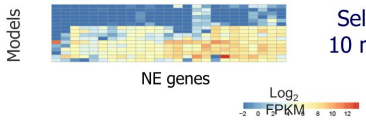
Selected 48 models

SCLC



Selected 20 models

Large cell NE carcinoma or NE lung cancer



Selected 10 models

L-MYC or N-MYC high

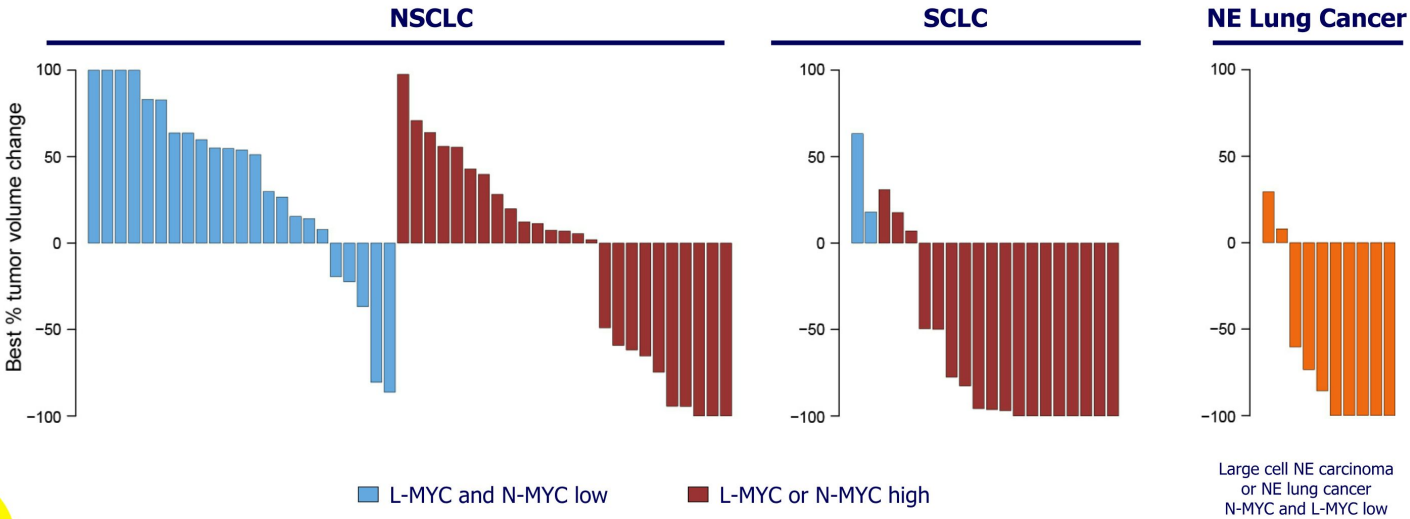
L-MYC and N-MYC low

Models selected across a range of N-MYC and L-MYC mRNA expression levels or NE status were treated with:

- Vehicle
- MRT-2359 10 mg/kg PO QD

3 mice for each treatment group

MRT-2359 Demonstrates Preferential Anti-tumor Activity in MYC High or Neuroendocrine (NE) Lung Cancer PDXs

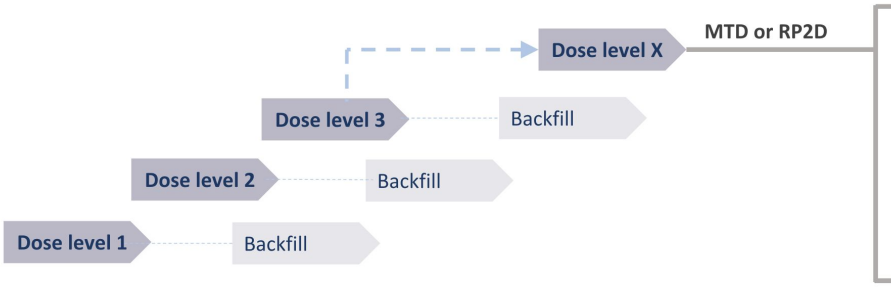


MRT-2359 10 mg/kg, PO, QD

MRT-2359-001 Clinical Study Design

Phase 1: Dose Escalation

Lung cancer (NSCLC & SCLC), DLBCL, high-grade neuroendocrine tumors, and N-/L-MYC amplified solid tumors



Backfill slots for additional patients for each dose level

Phase 2: Expansion Cohorts

NSCLC* – high N- or L-MYC expression
– low N- and L-MYC expression

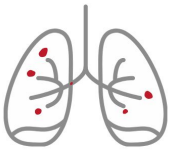
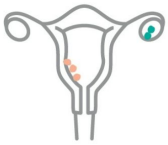
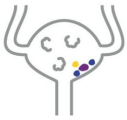
SCLC* – high N- or L-MYC expression
– low N- and L-MYC expression

Solid tumors – N- or L-MYC amplification

* Efficacy guided stratification per N-/L-MYC expression

Patient dosing initiated in October 2022

Targeting L-/N-MYC positive and Neuroendocrine Tumors with MRT-2359

Current focus		Future options	
	**Small cell lung cancer** **66K patients** – 70% MYC high		**Triple-negative breast cancer**
	Non-small cell lung cancer **352K patients** – 15% MYC high		**Ovarian cancer**
	Neuroendocrine lung cancer		**Endometrial cancer**
	**Neuroendocrine prostate cancer**		**Bladder cancer**

c-MYC driven indications being further explored in preclinical translational studies

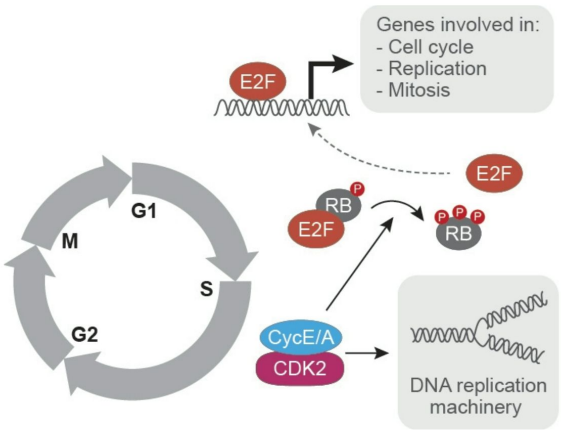
Patient diagnosed incidence #s, major markets (US, EU and JP): Decision Resources Group (DRG)
% population based on preliminary internal cut offs for high vs low expression applied to real world data provided by Tempus

Monte Rosa Therapeutics

CDK2 Program

CDK2 as a Target for Selected Solid Tumors

CDK2 is one of the key regulators of the cell cycle



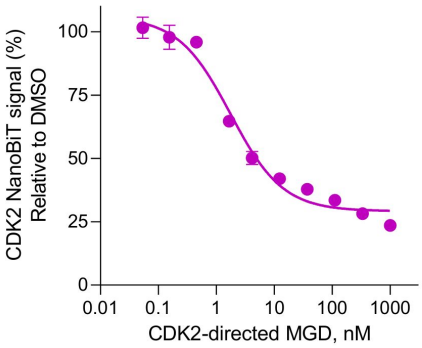
Therapeutic hypothesis: Tumors with CDK2 pathway activation by:

- High CyclinE1/E2 expression
- Loss of RB

Clinical Opportunity: CDK2 driven cancers: ER positive breast cancer pre and post treatment with CDK4/6 inhibitors (444K patients), ovarian cancer (63K patients), and endometrial cancer (118K patients)

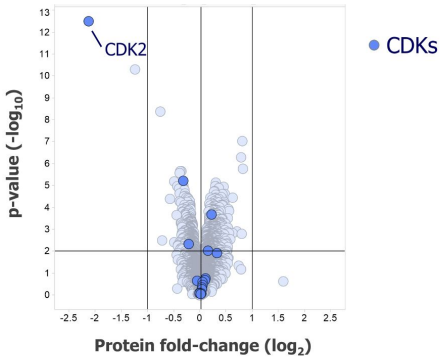
CDK2-directed MGD Shows Selective Degradation Over the Other CDKs

CDK2-directed MGD induces CDK2 degradation



NanoBiT assay (24hr) - HEK293

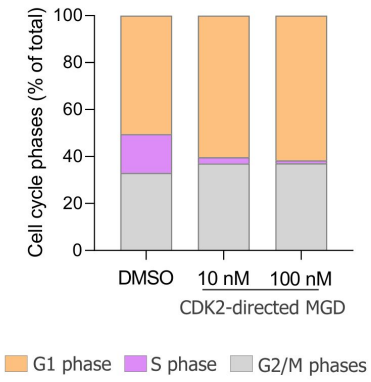
CDK2-directed MGDs are selective over other CDKs



TMT Proteomics (24hr) – HEK293

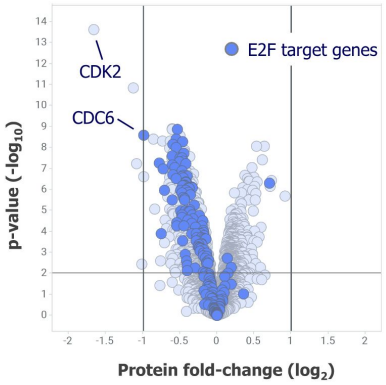
CDK2-directed MGD Shows Biological Activity in a CDK2-dependent Cell Line

CDK2 degradation arrests CDK2-dependent cells in G1 phase



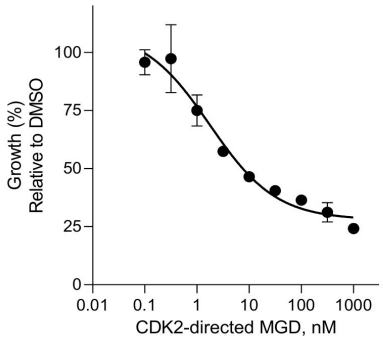
Cell cycle profile (48hr) – MDA-MB-157

CDK2 degradation results in reduction of E2F pathway proteins



TMT Proteomics (24 hr) – MDA-MB-157

CDK2-directed MGD inhibits proliferation of CDK2 dependent cells



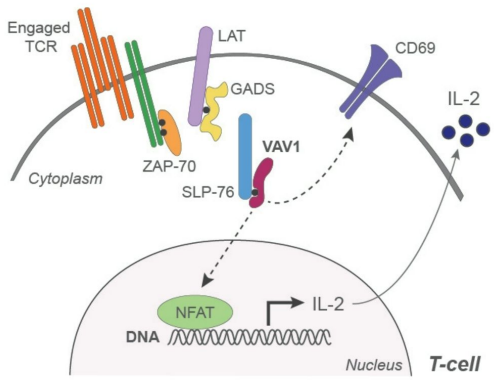
CyQuant assay (7d) – MDA-MB-157

Monte Rosa Therapeutics

VAV1 Program

VAV1 is a Highly Validated Target for Attenuating T-cell Activity

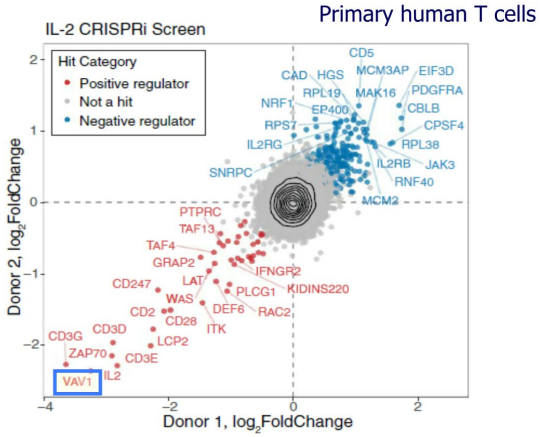
VAV1 controls several aspects of T-cell activity



TCR = T-cell receptor

Multiple CRISPR screens identified VAV1 as key player in T-cell function

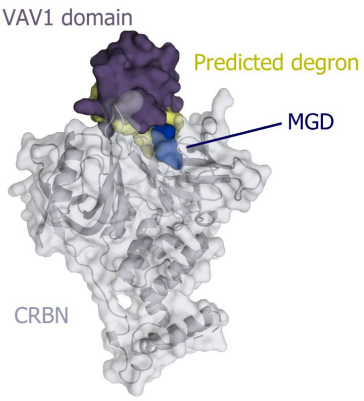
Primary human T cells



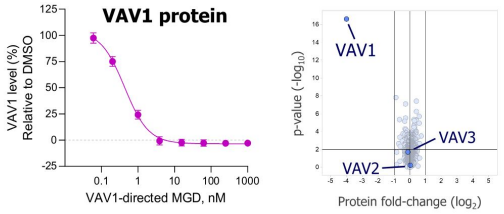
Schmidt et al., Science 2022

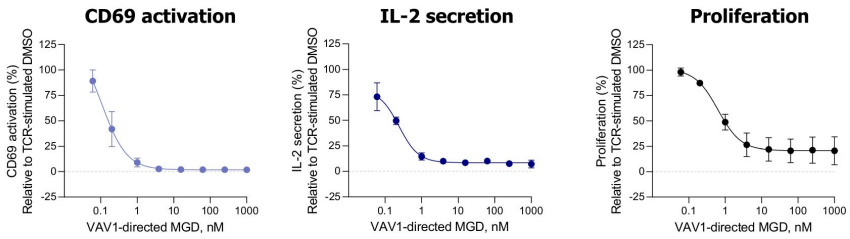
Discovery of Highly Selective VAV1-directed MGDs

Degron predicted and confirmed



MGD-induced degradation of VAV1 results in inhibition of TCR-mediated CD69 activation, IL-2 secretion, and proliferation

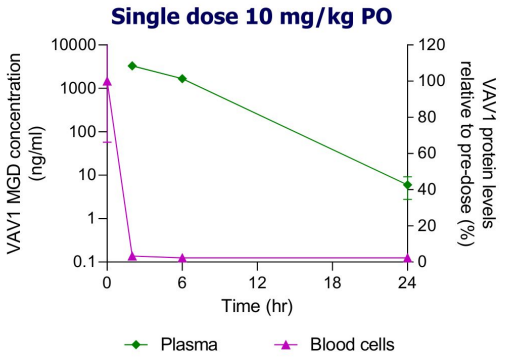




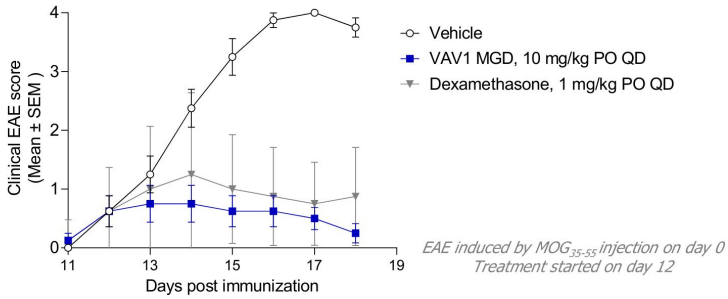
Human primary pan-T cells TCR stimulation = α-CD3/CD28

VAV1-directed MGD Inhibits Disease Progression in an EAE Mouse Model

MGD induces VAV1 degradation in PBMCs after a single oral dose in mice



MGD inhibits disease progression in experimental autoimmune encephalomyelitis (EAE) mouse model of multiple sclerosis



Additional autoimmune and immunology disease models are currently under evaluation

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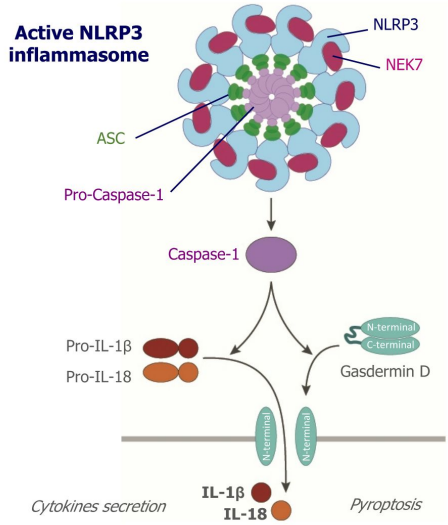
NEK7 Program

NEK7 (NIMA-Related Kinase 7) as a Target for Inflammatory Disease

NEK7 is an essential regulator of the inflammasome



Therapeutic hypothesis: Diseases with over-activated or mutated NLRP3 inflammasome

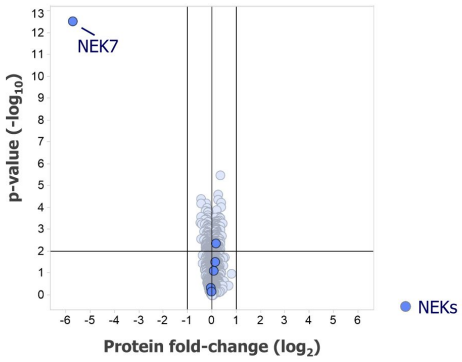
- NEK7 licenses NLRP3 assembly in a kinase independent manner
- NEK7-deficient macrophages are severely impaired in IL-1β and IL-18 secretion

Clinical opportunity: First-in-class NEK7 degraders for

- Over-activated NLRP3 inflammasome: metabolic pathologies, cardiovascular diseases, inflammatory issues and neurologic disorders
- NLRP3 activating mutations: Cryopyrin-associated periodic syndromes (CAPS)

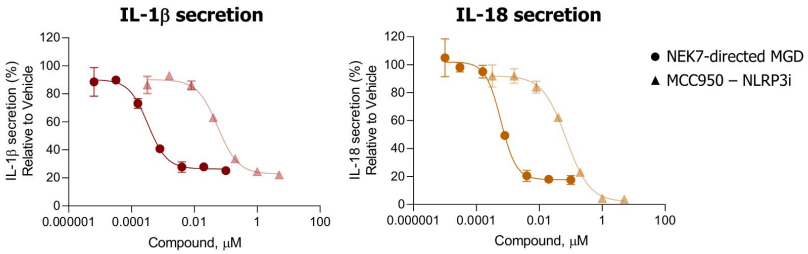
NEK7-directed MGDs modulate NLRP3 Pathway in human macrophages

NEK7-directed MGD shows high selectivity



TMT Proteomics (24hr) – U937

NEK7-directed MGD compared to NLRP3 inhibitor



IL-1β and IL-18 release (24hr) - human macrophages LPS/MSU stimulated

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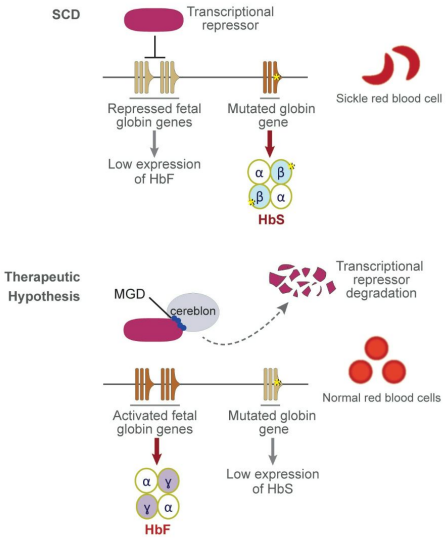
Sickle Cell Disease Program

Transcriptional Repressors as Targets for Hemoglobinopathies (SCD and β-Thalassemia)

Zinc finger domain-containing transcriptional repressors of the fetal globin genes



Therapeutic hypothesis: To reactivate expression of fetal hemoglobin (HbF) to compensate for mutated adult globin

Clinical Opportunity: First-in-class degraders for

- Sickle cell disease (SCD)
  - 155,000 patients (US and EU)
  - >6M patients (ROW)
- β-thalassemia
  - 17,000 patients (US and EU)

Patient diagnosed prevalence #s: DRG; www.notaloneinsicklecell.com

Monte Rosa Therapeutics

Summary

Monte Rosa Therapeutics

From serendipity to rational design of MGDs

Molecular glue-based targeted protein degradation platform developing breakthrough therapeutics that selectively degrade disease-causing proteins

Proprietary, **target-centric** drug discovery platform enabling **rational design**, and anticipated rapid development, of molecular glue-based degraders targeting the **undruggable proteome in oncology** and **non-oncology disease**

Initial platform focus on **cereblon-mediated protein degradation** with **hundreds of potential targets** to address; potential to reprogram other E3 ligases to access more of the undruggable proteome through other degrons

Extensive and compelling pre-clinical *in vivo* data for **GSPT1 program**, demonstrating **potent anti-tumor activity** in MYC-driven tumor models with development candidate MRT-2359

Phase 1/2 trial with MRT-2359 for the treatment of MYC-driven tumors including lung cancer patients ongoing

CDK2, NEK7, and VAV1 programs in lead optimization with **additional programs** at various stages of discovery


Thank You
Monte Rosa
Therapeutics

Monte Rosa Therapeutics Outlines Progress Across Portfolio of Molecular Glue Degraders and Key Anticipated Milestones for 2023

- MRT-2359 received Fast Track designation from the FDA for the treatment of patients with previously treated, metastatic non-small cell lung cancer (NSCLC) with L-MYC or N-MYC expression
- Disclosure of initial data from Phase 1 arm of ongoing Phase 1/2 clinical trial evaluating MRT-2359 expected in second half of 2023
- Nomination of multiple additional development candidates anticipated in 2023
- Company to present pipeline and corporate updates at 41st Annual J.P. Morgan Healthcare Conference on Wednesday, Jan. 11, 2023, at 11:15 a.m. PT

BOSTON, January 9, 2023 – Monte Rosa Therapeutics, Inc. (NASDAQ: GLUE), a biotechnology company developing novel molecular glue degrader (MGD)-based medicines, today outlined anticipated 2023 milestones ahead of its participation at the 41st Annual J.P. Morgan Healthcare Conference. The company's presentation will focus on strategic priorities for 2023, including its plans to report initial data from the Phase 1 arm of its ongoing Phase 1/2 clinical trial for MRT-2359, a highly selective and orally available GSPT1-directed MGD. Further, the company will present its development plan for its additional MGD candidates for patients with high unmet medical needs in oncology, autoimmune and inflammatory indications.

"In 2022, we made significant progress across our portfolio of highly selective molecular glue degraders, culminating in the initiation of our Phase 1/2 trial of MRT-2359 in MYC-driven tumors," said Markus Warmuth, M.D., CEO of Monte Rosa. "As we look ahead to 2023, with our lead program in the clinic, a rich pipeline of wholly owned preclinical programs, and backed by a strong cash position, we believe we are well positioned for success. We expect our programs to achieve important catalysts in 2023 that will bring us closer to fulfilling our vision of developing a new generation of MGD-based precision medicines for patients living with serious diseases."

2023 Key Milestones and Catalysts

- The U.S. Food and Drug Administration (FDA) has granted Fast Track designation to MRT-2359 for the treatment of patients with previously treated, metastatic NSCLC with L-MYC or N-MYC expression
- The company anticipates disclosing initial data from the Phase 1 arm of the ongoing Phase 1/2 clinical trial evaluating MRT-2359 in the second half of 2023
- The company anticipates the nomination of multiple development candidates in 2023 for its programs oncology, autoimmune and inflammatory diseases

J.P. Morgan Healthcare Conference

Dr. Warmuth will present Monte Rosa's pipeline and business updates during a presentation at the 41st Annual J.P. Morgan Healthcare Conference on Wednesday, January 11, 2023, at 11:15 a.m. PT. An archived webcast of the presentation will be made available via the "Events & Presentations" section of the company's investor site at https://ir.monterosatx.com/.

About MRT-2359
MRT-2359 is a potent, selective and orally bioavailable 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. Our preclinical studies have shown that this addiction to MYC-induced protein translation creates a dependency on GSPT1. By inducing degradation of GSPT1, MRT-2359 exploits this vulnerability, disrupting the protein synthesis machinery and leading to anti-tumor activity in MYC-driven tumors.

About the MRT-2359 Phase 1/2 study
Our ongoing Phase 1/2, open-label, multicenter study (Identifier: NCT05546268) will primarily assess the safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD), and preliminary clinical activity of MRT-2359 in patients with previously treated selected solid tumors, including non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), high-grade neuroendocrine cancer of any primary site, diffuse large B-cell lymphoma (DLBCL) and solid tumors with L-MYC or N-MYC amplification. In the Phase 1 portion of the study, patients will receive escalating doses of MRT-2359 to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D). Once the MTD and/or RP2D are determined, the anti-tumor activity of MRT-2359 will be assessed as part of the Phase 2 portion of the study, which includes L-MYC or N-MYC expression for stratification and selection.

About Monte Rosa
Monte Rosa Therapeutics is a biotechnology company developing novel molecular glue degrader (MGD) medicines for patients living with serious diseases such as oncology, autoimmune and inflammatory diseases. MGDs are small molecule protein degraders designed to employ the body's natural mechanisms to selectively eliminate therapeutically relevant proteins. The company's QuEEN™ (Quantitative and Engineered Elimination of Neosubstrates) platform enables it to rapidly identify protein targets and design highly selective degraders by combining diverse libraries of proprietary MGDs with in-house proteomics, structural biology, AI/machine learning, and computational chemistry capabilities. 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 in herein include, but are not limited to, statements about our product development activities, including our expectations around MRT-2359 and the potential significance of obtaining Fast Track Designation from the FDA, the ongoing development of our QuEEN™ platform and the advancement of our pipeline and the various products therein, our expectations regarding and the timing of our clinical trial for MRT-2359, our ability to initiate and the timing of initiation of additional lead optimization programs, and our expectations regarding our ability to nominate and the timing of our nominations of additional development candidates, as well as our

expectations of success for our programs and the strength of our financial position, among others. By their nature, these statements are subject to numerous risks and uncertainties, including the impact that the ongoing COVID-19 pandemic will have on our development activities and operations, as well as those risks and uncertainties set forth in our most recent Quarterly Report on Form 10-Q and Annual Report on Form 10-K for the year ended December 31, 2021 filed with the US Securities and Exchange Commission, and any subsequent filings, that could cause actual results, performance or achievement to differ materially and adversely from those anticipated or implied in the statements. You should not rely upon forward looking statements as predictions of future events. Although our management believes that the expectations reflected in our statements are reasonable, we cannot guarantee that the future results, performance or events and circumstances described in the forward-looking statements will be achieved or occur. Recipients are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made and should not be construed as statements of fact. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, any future presentations or otherwise, except as required by applicable law. Certain information contained in these materials and any statements made orally during any presentation of these materials that relate to the materials or are based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of these materials, we have not independently verified, and make no representations as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in these materials relating to or based on such internal estimates and research.

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