From Serendipity to Rational Design

Taking Molecular Glue Degraders to New Heights | October 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 the potential of molecular glue degraders ("MGDs"), the potential of our herein detailed pipeline of MGDs, our expectations for our collaboration with Roche, including the discovery and development of MGDs therefrom, and our expectations and estimates of potential future payments available under the collaboration, our ongoing pre-clinical and clinical development of our GSPT1 degrader referred to as MRT-2359, including our expectations regarding the potential relevance of certain interim clinical data, our expectations for the nature and timing of any additional clinical data releases for MRT-2359, including any full phase 1 clinical data release, and our expectations for the nature and timing of our ongoing and future clinical development of MRT-2359, including our plan to continue the Phase 1/2 study of MRT-2359 and its anticipated timing and progress, and our ability to enroll the requisite number of patients and dose each dosing cohort in the intended manner, the potential for MRT-2359 to benefit patients living with a variety of difficult-to-treat cancers, our expectations regarding the advancement, and timing thereof, of our pipeline and the various products therein, our ability to advance our development candidates, including MRT-6160 and our expectations for MRT-6160 to enter the clinic in 2024 and its potential applications across multiple autoimmune diseases, our expectations regarding potential therapeutic opportunities for our MGDs, and our clinical development expectations therefor, our expectations regarding patient populations and medical needs for any potential therapeutic opportunities for our MGDs, our expectations regarding our proprietary QuEEN™ platform and its potential to be highly productive and an industry-leading platform for designing MGDs to address hard-to-drug disease targets via degradation, combining experimentation with AI to push the boundaries of what is possible with MGDs, and the strength of our financial position, including our estimates of cash runway, among others. By their nature, these statements are subject to numerous risks and uncertainties, 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, 2022, filed, with the US Securities and Exchange Commission on March 16, 2023, 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. These materials remain the proprietary intellectual property of Monte Rosa Therapeutics and should not be distributed or reproduced in whole or in part without the prior written consent of Monte Rosa Therapeutics.

Monte Rosa Therapeutics – Call Highlights

Interim analysis of data from our Phase I dose escalation study of MRT-2359, providing evidence of optimal PD modulation, clinical activity and a favorable tolerability profile

Partnership with Roche to develop MGDs for oncology and neurological conditions – expands platform reach into neuroscience

Updated cash runway into Q3 2025

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Monte Rosa Therapeutics – Roche Partnership

Monte Rosa Tx – Roche Partnership: Summary

- Discovery partnership on targets in oncology and neurological disease
- Leverages synergies between Monte Rosa Tx – a leading molecular glue degrader company – and Roche – a leading global health care company
- Monte Rosa Tx performs preclinical drug discovery with Roche leading late preclinical discovery and clinical development
- Monte Rosa Tx to receive $50M upfront payment and potential preclinical, clinical, regulatory and sales milestones that could exceed $2B*
- Potential to expand collaboration to additional targets, which triggers potential additional payments including nomination, preclinical, clinical, regulatory and sales milestones
- Partnership provides additional validation of Monte Rosa Tx's QuEEN™ discovery engine and its opportunity to go beyond Oncology
- Monte Rosa Tx's publicly disclosed pipeline remains unencumbered*

* as disclosed in company 8K

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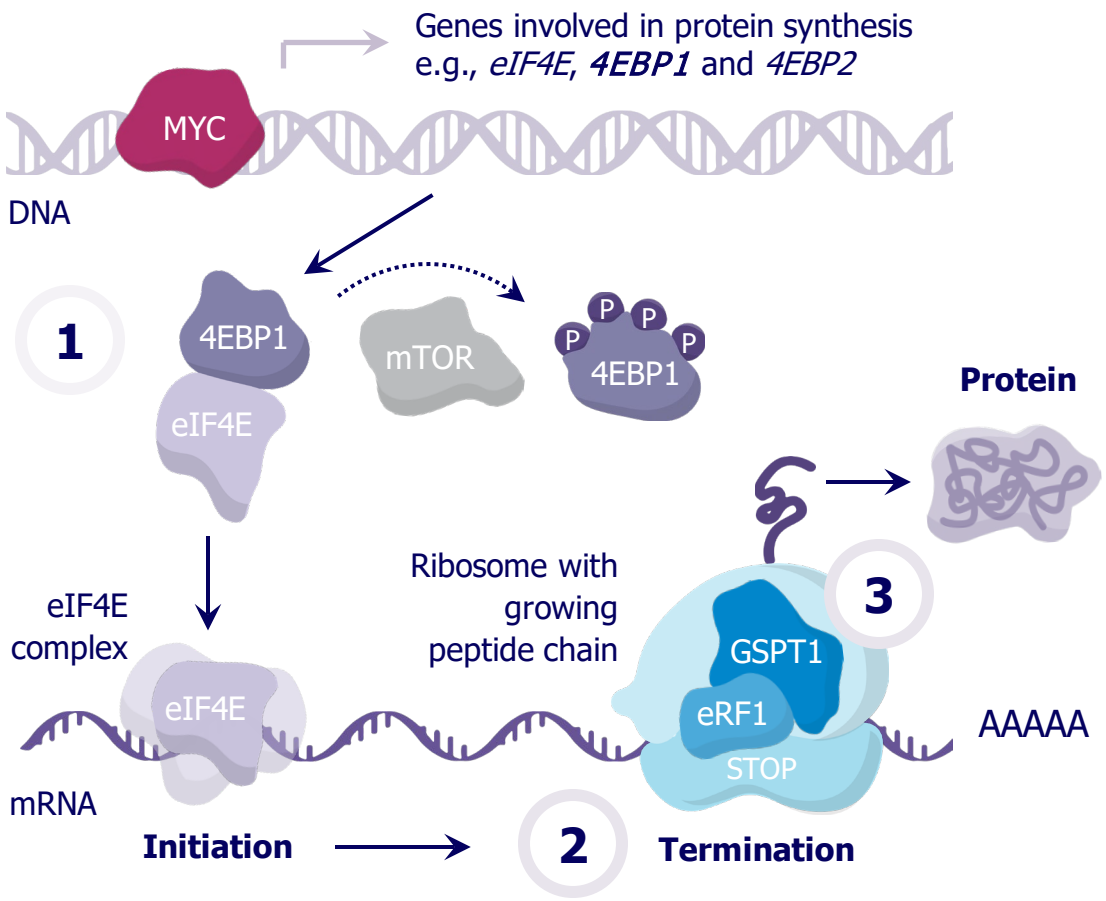
GSPT1 Program – Phase I Interim Update

Targeting MYC-driven Tumors and Their Addiction to Protein Translation



1

Addiction

To sustain growth, MYC-driven tumors are **addicted to protein translation**

2

Dependency

This addiction creates a dependency on the **translation termination factor GSPT1**

3

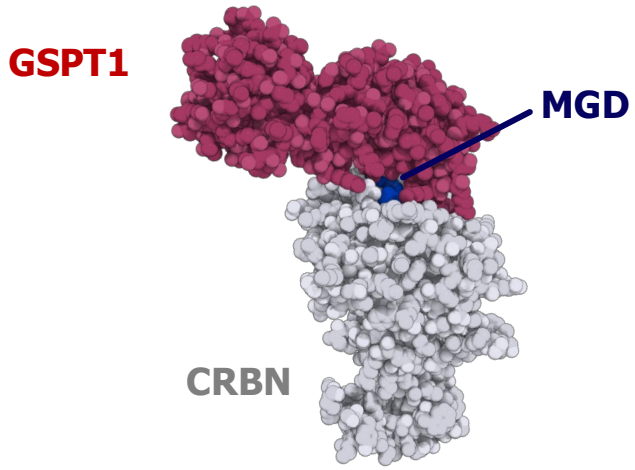
Therapeutic vulnerability

GSPT1 is a therapeutic vulnerability of MYC-driven tumors
which can be targeted using molecular glue degrader (MGD)

MRT-2359 is a Potent and Selective GSPT1 Degrader

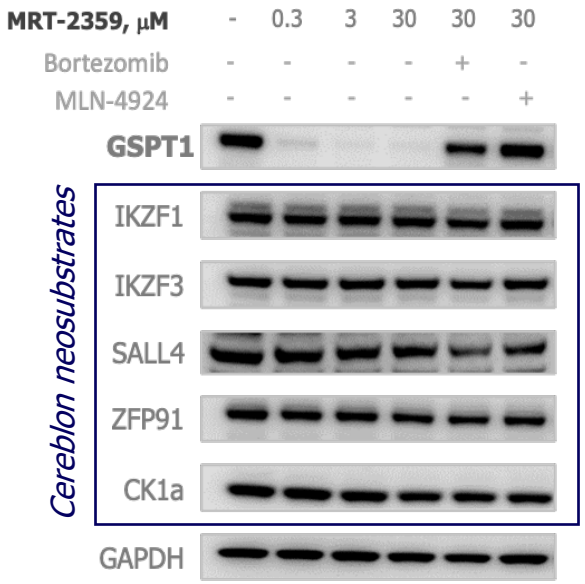
MRT-2359 is a potent GSPT1 degrader

Ternary complex modelling

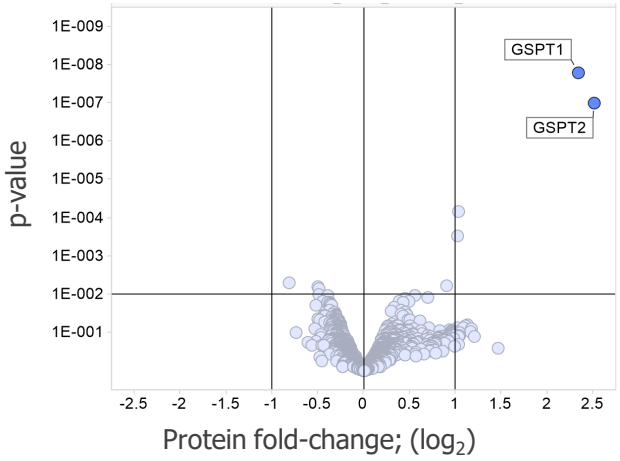


in vitro data	
CRBN binding, K_i	113 nM
Ternary complex, EC_{50}	< 7 nM
Degradation, DC_{50} (in disease relevant cell lines)	1 - 20 nM

MRT-2359 induced selective GSPT1 degradation and showed favorable ADME/DMPK profile



Proximity – Turbo ID

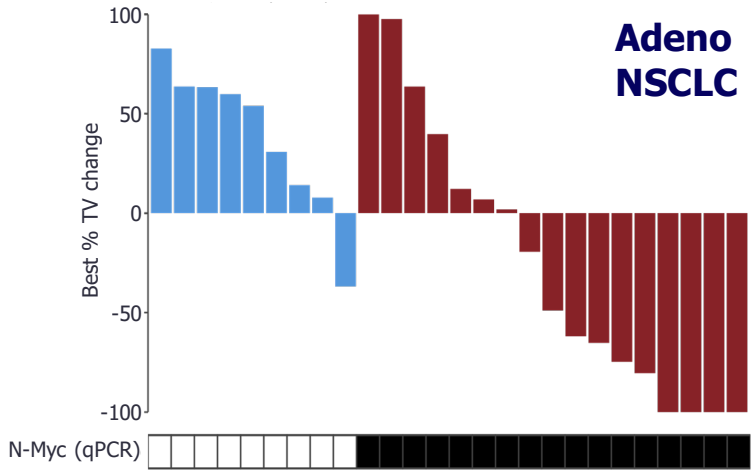


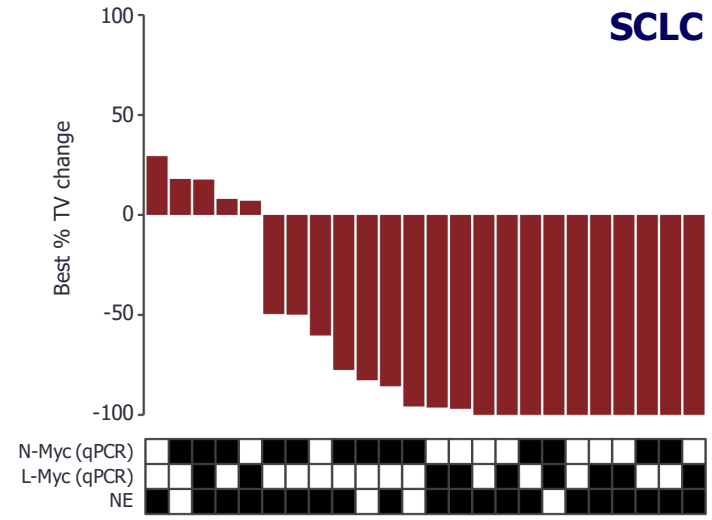
ADMET profile	
CYP DDIs	> 30 µM
hERG inhibition patch clamp	EC_{50} > 30 µM
Oral bioavailability all species	~50%

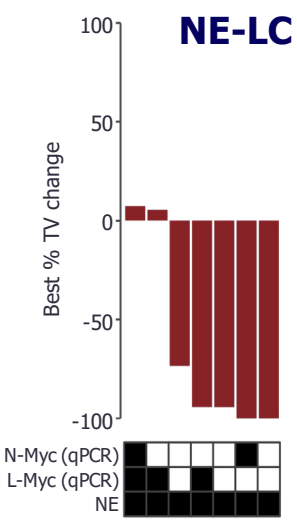
Activity of MRT-2359 in NSCLC, SCLC and Lung NE Patient-derived Xenograft Models

Collection of PDX models

MRT-2359
10 mg/kg QD

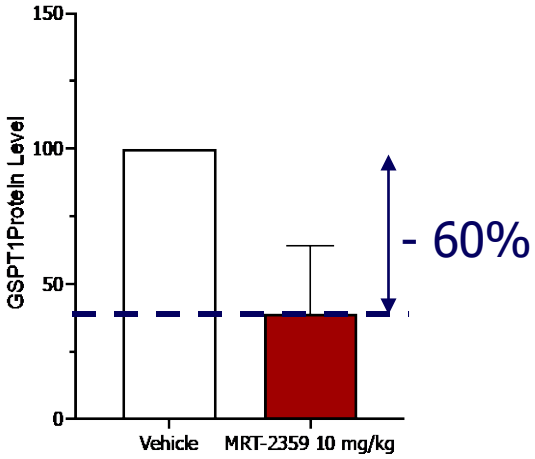






PD modulation

Targeted mass spectrometry
in 7 representative models

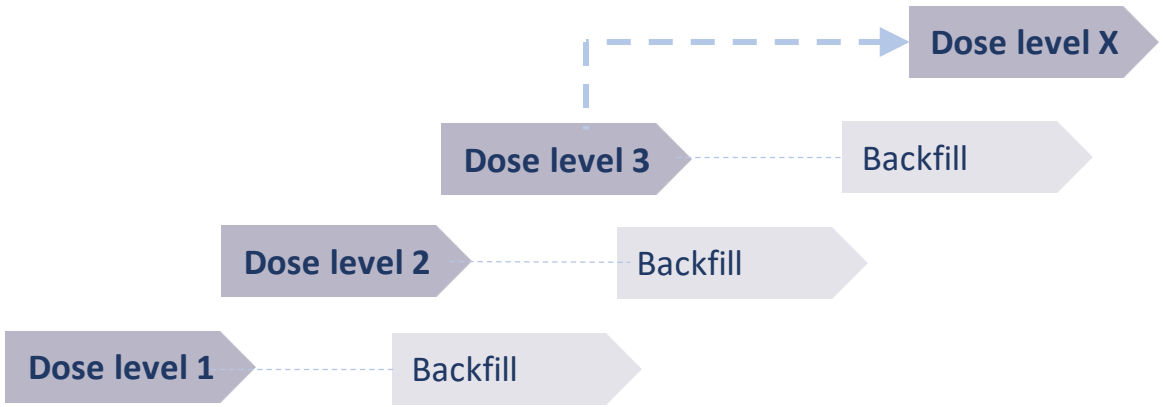


biomarker negative biomarker positive

MRT-2359-001 Phase 1/2 – Phase 1 Interim Update

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

Objectives of Phase I interim analysis

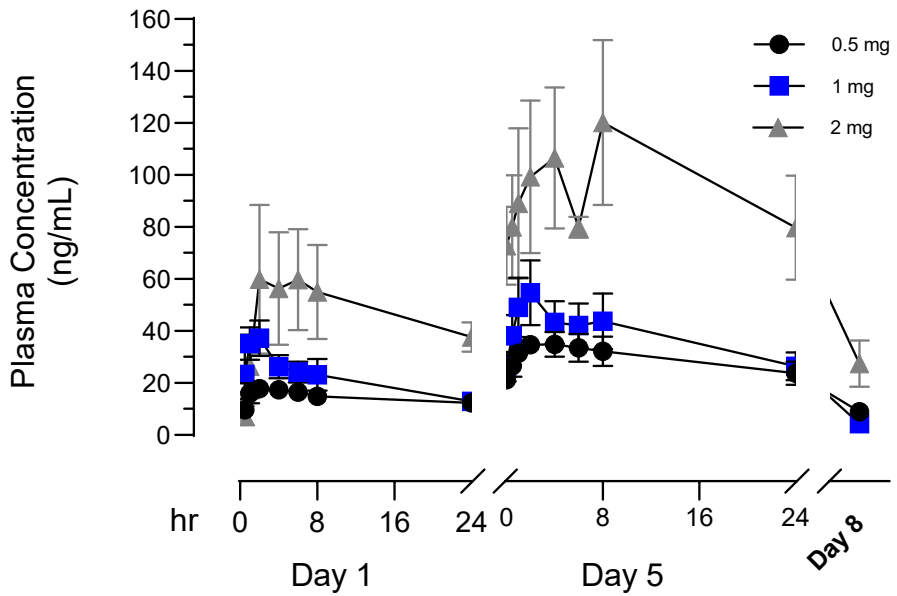
- ✓ Demonstrate dose dependent PK
- ✓ Demonstrate significant GSPT1 degradation at safe dose levels in PBMCs and tissue biopsies (60% based on preclinical data)
- ✓ Share potential preliminary efficacy signals in biomarker positive patients

Executive Summary

- As of September 7th, 2023, 3 dose levels (0.5 mg, 1 mg, 2 mg) have been completed with 21 patients enrolled (including backfill patients)
- Observed dose dependent PK after oral dosing
- Clinical data support that 0.5 mg starting dose was fully active based on pharmacodynamic (PD) assessment of peripheral blood mononuclear cells (PBMC) and tissue samples from patients, with optimal PD modulation across dose levels tested
- Encouraging initial clinical activity at all dose levels: 2 partial responses (PRs) (1 confirmed, 1 unconfirmed) and 1 stable disease (SD) in 6 evaluable, heavily pretreated patients identified with biomarker positive tumors; 1 SD in non-small cell lung cancer (NSCLC) with un-evaluable biomarker status
- Safety profile supports continued development:
  - Favorable adverse event (AE) profile at 0.5 and 1 mg
  - Grade 4 thrombocytopenia identified as dose limiting toxicity (DLT) at 2 mg
- Previously reported limitations of CC-90009 not observed:
  - No hypotension/cytokine release syndrome or clinically significant hypocalcemia observed at any dose level

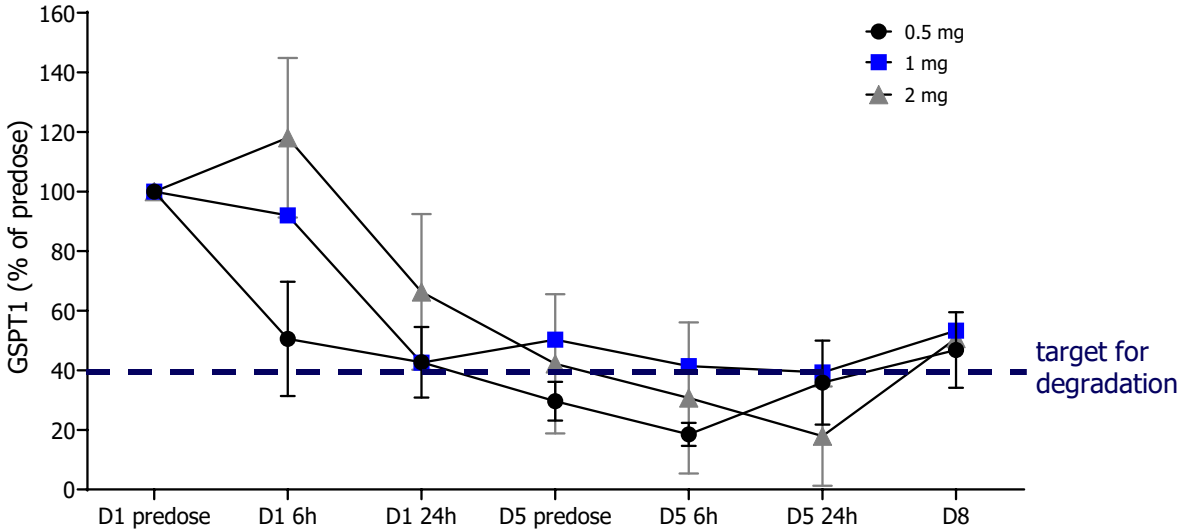
Summary of Pharmacokinetics and Pharmacodynamics

MRT-2359 displayed dose dependent plasma exposure



- Dose dependent exposure in line with preclinical PK models
- No food effect observed

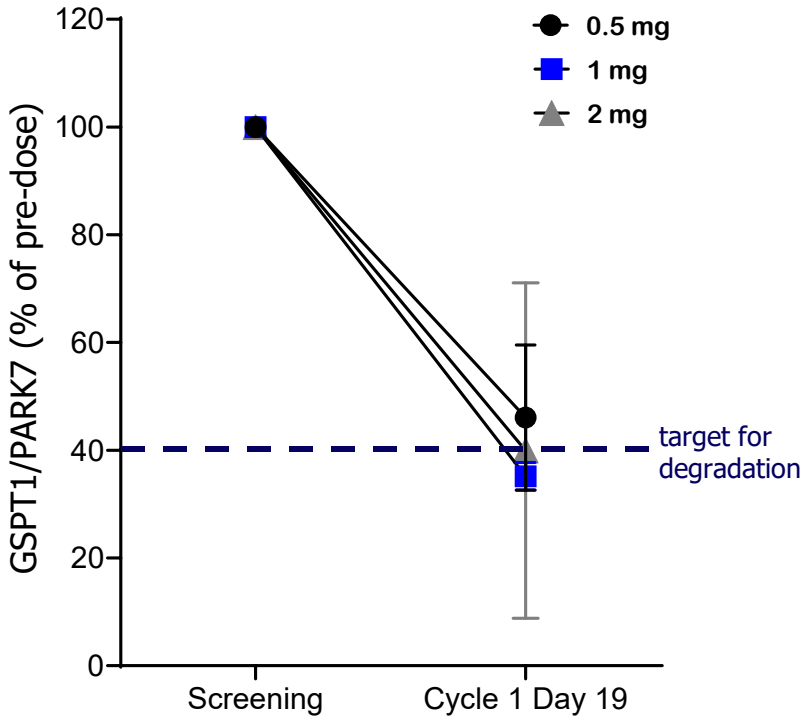
MRT-2359 displayed deep GSPT1 degradation in PBMCs at all dose levels



- GSPT1 expression assessed using targeted mass spectrometry
- PD modulation in PBMCs observed across all dose levels; level of degradation (~ 60%) in line with maximal degradation observed in preclinical studies using the same method
- Level of degradation equivalent across all dose levels, suggesting saturated PD response from 0.5 to 2 mg

GSPT1 Degradation by Targeted Mass Spectrometry in Tissue Biopsies

MRT-2359 reduced GSPT1 expression in human tissue biopsies



- GSPT1 degradation assessed from pre-treatment screening biopsies and biopsies taken at day 19
- Matched biopsies obtained from 11 patients across the 3 cohorts analyzed
- GSPT1 expression assessed using targeted mass spectrometry
- PD modulation seen in tissue biopsies in line with PD modulation seen preclinically at efficacious dose levels using same assay (targeted mass spectrometry)

MRT-2359: Treatment-Related AEs Occurring in ≥ 2 patients[#]

No observed clinically significant hypocalcemia or hypotension/cytokine release syndrome

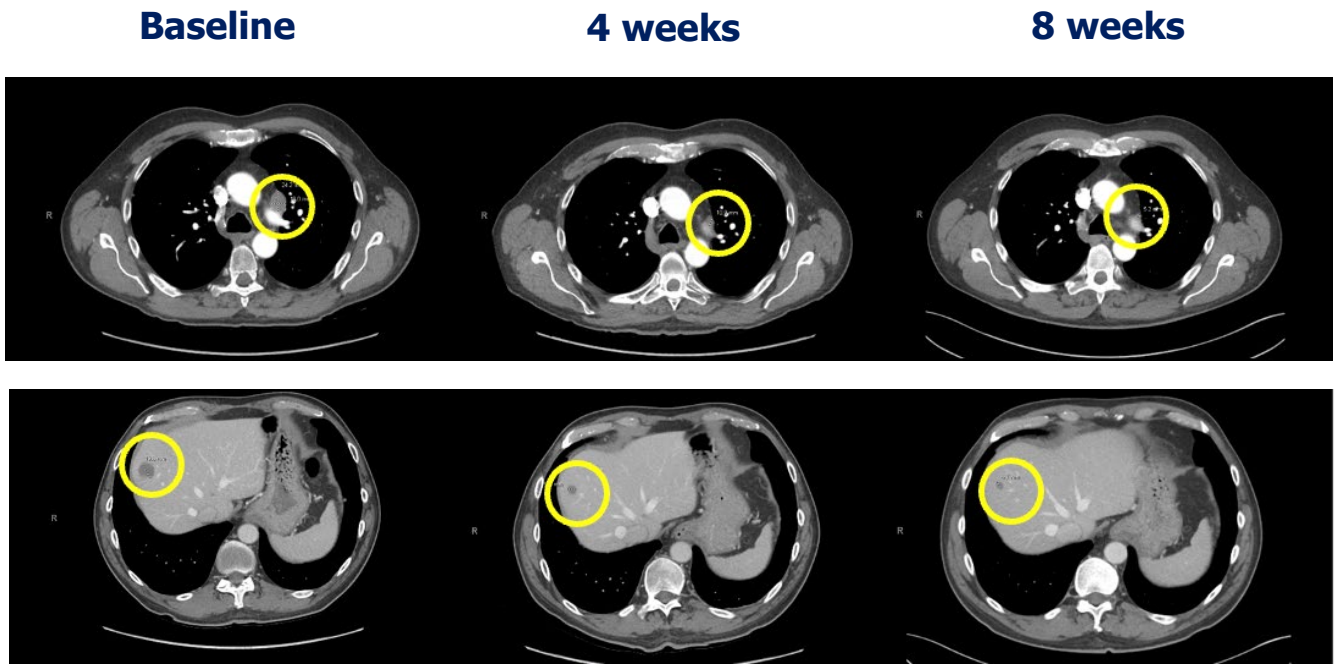
AE Preferred Term	0.5 mg (N=9)[##]		1 mg (N=7)[##]		2 mg (N=5) [##]		Overall (N=21)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Thrombocytopenia[###]	0	0	0	0	4 (80%)	3 (60%)[***]	4 (19%)	3 (14%)
Neutropenia[*]	0	0	0	0	2 (40%)	1 (20%)	2 (10%)	1 (5%)
Leukopenia	0	0	0	0	2 (40%)	2 (40%)	2 (10%)	2 (10%)
Nausea	3 (33%)	0	2 (29%)	0	1 (20%)	0	6 (33%)	0
Vomiting	1 (11%)	0	2 (29%)	0	1 (20%)	0	4 (19%)	0
Diarrhea[**]	1 (11%)	0	3 (43%)	0	1 (20%)	0	5 (24%)	0
Hypokalemia	0	0	1 (14%)	0	1 (20%)	0	2 (10%)	0
Fatigue	0	0	2 (29%)	0	0	0	2 (10%)	0
Decreased appetite	0	0	2 (29%)	0	0	0	2 (10%)	0
Rash	2 (22%)	0	0	0	0	0	2 (10%)	0

[#] Data cut-off: 7 SEP 2023
[##] MRT-2359 was given orally daily on the 5 days on and 9 days off schedule
[###] Data combined for 'thrombocytopenia' and 'platelet count decreased'

[*] Data combined for 'neutropenia' and 'neutrophil count decreased'
[**] Data combined for 'diarrhea' and 'feces soft'
[***] Dose limiting toxicity: Grade 4 thrombocytopenia in 2 patients

Confirmed PR in High Grade Neuroendocrine Bladder Cancer

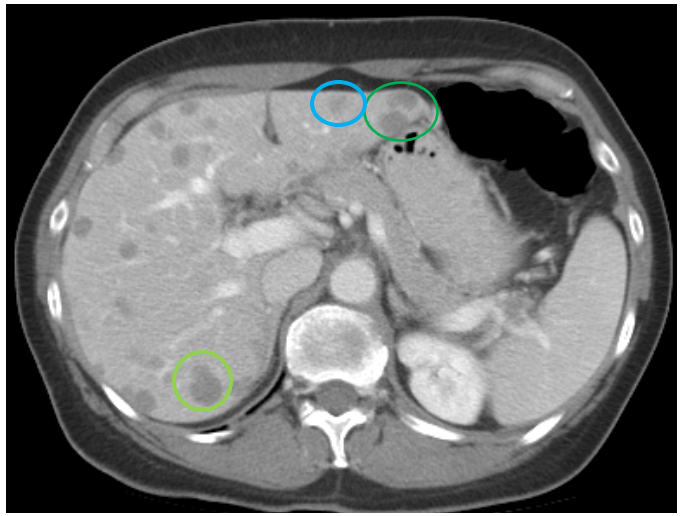
- High Grade (HG) neuroendocrine bladder cancer
- Baseline tumor biopsy demonstrated high N-MYC expression
- 4 prior lines of therapy including chemotherapy and pembrolizumab
- Patient initiated on 2 mg for first 5/9 regimen, then lowered to 1 mg and 0.5 mg and remains on therapy (> 3 month)
- CT scan after 4 weeks demonstrated PR (-34% per RECIST 1.1) that continued to improve at week 8 (-59% per RECIST 1.1)



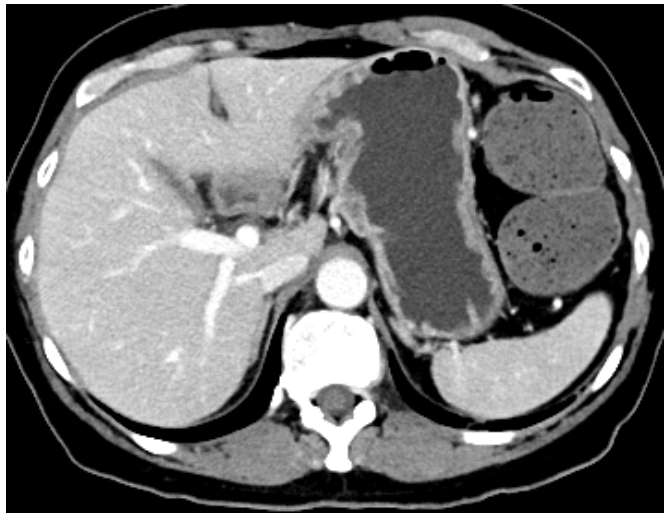
Unconfirmed PR in NSCLC with SCLC/NE Transformation

- NSCLC (adenocarcinoma)
- Baseline tumor biopsy demonstrated SCLC/NE transformation, low N- and L-MYC expression
- Multiple lines of prior therapy including chemotherapy, pembrolizumab and atezolizumab
- Patient initiated on 0.5 mg
- CT on C1D22 demonstrated resolution of liver metastases (-41% per RECIST 1.1)
- Patient experienced frequent dose interruptions due to bowel obstruction unrelated to MRT-2359

Baseline

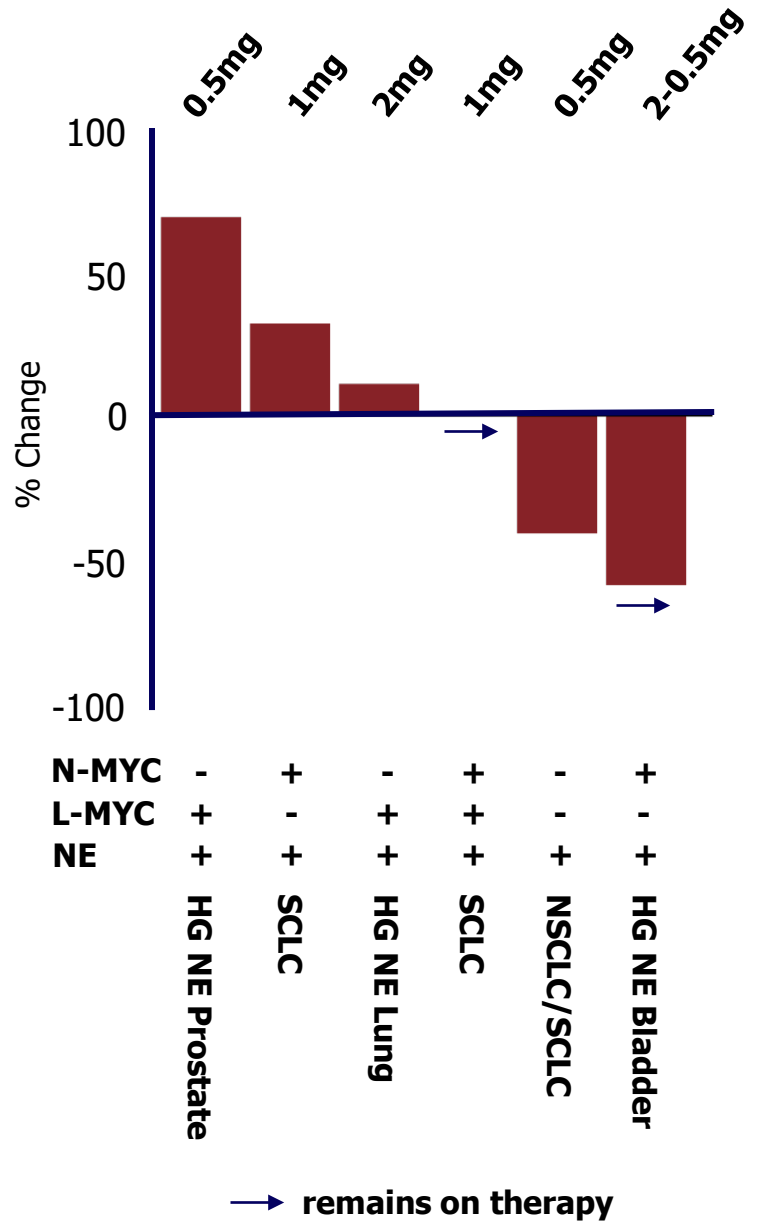


3 weeks



MRT-2359-001 – Preliminary Efficacy Data

- As of September 7th, 2023, 15/21 evaluable patients treated across 3 cohorts, 6/15 patients were identified as biomarker positive
- Of these 6 biomarker positive patients, 2 have experienced a PR (1 confirmed, 1 unconfirmed) and 1 patient has SD
  - PR (-59%) – HG NE bladder carcinoma
  - uPR (-41%) – NSCLC with SCLC/NE transformation
  - SD (0%) – SCLC (remains on therapy for > 4 months)
- In addition, one patient with NSCLC and unclear biomarker status remains on therapy for > 7 months with stable disease
- No clinical activity seen in biomarker negative patients



Summary and Next Steps

- Clinical data support that 0.5 mg starting dose was active based on PD assessment (PBMC and tissue), with optimal PD modulation across dose levels tested
- Encouraging initial clinical activity at all dose levels: 2 PRs (1 confirmed, 1 unconfirmed) and 1 SD in 6 evaluable, heavily pretreated patients identified with biomarker positive tumors; 1 SD in non-small cell lung cancer (NSCLC) with un-evaluable biomarker status
- Safety profile support further development:
    - Favorable AE profile at 0.5 and 1 mg
    - Grade 4 thrombocytopenia identified as dose limiting toxicity (DLT) at 2 mg
- Previously reported limitations of CC-90009 not observed:
    - No hypotension/cytokine release syndrome or clinically significant hypocalcemia observed at any dose level

Next Steps

- Currently dosing 1.5 mg, expected to complete DLT observation period by end of October
- Based on favorable tox profile, Company initiating intermittent dosing regimen of 21 days on and 7 days off drug (21/7)

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Portfolio

Monte Rosa Pipeline

Program/ Target	Indication(s)	Discovery / IND-Enabling / Clinical	Next Anticipated Milestones	Ownership
MRT-2359 (GSPT1)	NSCLC, SCLC and other MYC-driven Malignancies		Full Phase 1 data (update on timing in early 2024)	
MRT-6160 (VAV1)	Autoimmune Disease		IND expected in 1H 2024	
NEK7	Inflammatory Diseases		Additional development candidate nomination expected in 2023	
CDK2	Ovarian Cancer, Breast Cancer			
Multiple SCD targets	SCD, β-Thalassemia		Lead optimization	
Undisclosed	Multiple			
Discovery Targets	Oncology and Neurological Diseases		Undisclosed	Roche

Oncology Immunology Inflammation Genetic diseases

Monte Rosa Therapeutics - Highlights

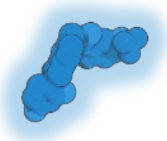
Taking molecular glue degraders (MGDs) to new heights

Rationally designed MGDs with potential to solve many of the limitations of other modalities by selectively degrading therapeutically relevant proteins considered undruggable or inadequately drugged

Highly productive, industry-leading platform for designing MGDs to address hard-to-drug disease targets via degradation, **combining experimentation with AI** to push the boundaries of what is possible with MGDs

Five promising, wholly-owned programs spanning oncology, autoimmune, inflammation and other TAs

Phase 1/2 clinical study ongoing with MRT-2359, with potential to treat difficult-to-drug MYC-driven cancers; optimal pharmacodynamic modulation and **early signs of clinical activity observed**



MRT-6160, highly selective VAV1-directed MGD, expected to enter clinic in mid-2024, with wide potential applications across autoimmune diseases

Partnership with Roche to develop MGDs for oncology and neurological conditions **– expands platform reach into neurology**

Strong financial position providing cash runway into Q3 2025


Thank You
Monte Rosa
Therapeutics