Q4 and Full Year 2024 Earnings Call and Pipeline Update

Proteome Editing Through Molecular Glue Degraders

Innovating Beyond New Heights | March 2025

Monte Rosa Therapeutics

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 related to the Company's strategic agreements, goals of such agreements, including the ability to accelerate and broaden scope of clinical development of MRT-6160 while retaining substantial value for the Company, as well as to expand platform reach to discover and develop MGDs against previously undruggable targets, statements related to any milestone provided under the strategic agreements, royalty or other payments related thereto, statements around the productivity of the QuEEN discovery engine and the potential of the Company's MGDs against a broad spectrum of targets and potential applications thereof, statements about the advancement and timeline of its preclinical and clinical programs, including beliefs and/or statements related to next steps for specific programs and plans for such programs, statements about our ability to successfully complete research and further development and commercialization of our drug candidates in current or future indications, including the timing and results of our clinical trials and our ability to conduct and complete clinical trials, statements around multiple anticipated preclinical and/or clinical readouts and their expected timing, statements related to regulatory submissions, including timing thereof, and interactions with regulatory authorities, the applicability of candidates to various indications, the expected potential clinical benefit of any of our candidates, statements related to safety profiles and the implications thereof, statements around advancement and application of our pipeline 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 as well as our the ability to optimize collaborations with industry partners on our development programs, obligations under our collaboration agreements, expectations around the receipt of any payments under such agreements and the future development and commercialization of various products, our use of capital, expenses and other financial results in the future, availability of funding for existing programs, ability to fund operations into 2028, 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, 2024 filed with the U.S. Securities and Exchange Commission on March 20, 2025, 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.

Today's Update

Immunology & Inflammation

Oncology

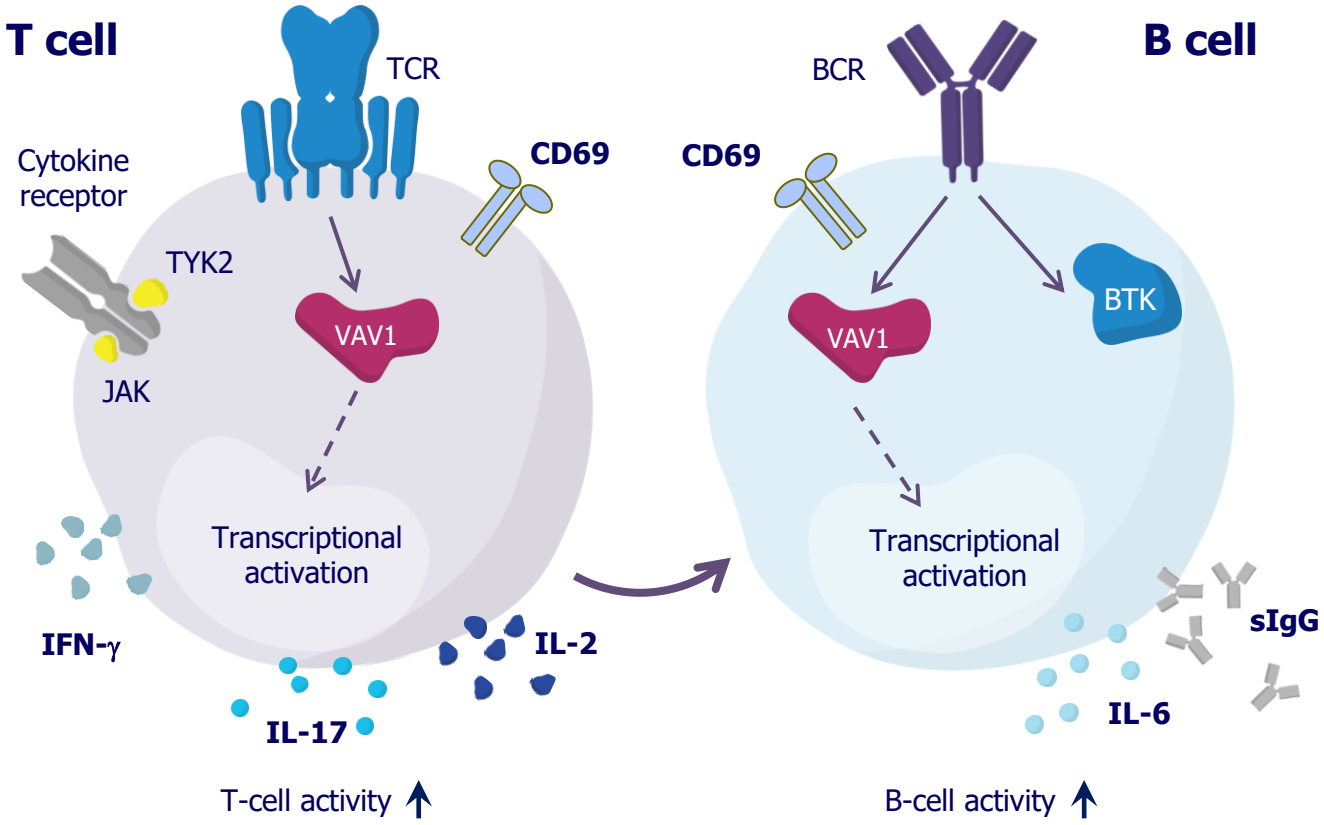
1. MRT-6160: Results from Phase 1 HV trial support clear path into broad Phase 2 development
2. NEK7: Progress towards IND filing, clinical development plan
3. QuEEN™: Building future "only-in-class" I&I opportunities
4. MRT-2359: Encouraging activity supports prioritizing further development in CRPC versus other expansion cohorts
5. CCNE1 and CDK2: Highly differentiated approaches, accelerated path to IND
6. Summary and concluding remarks

Monte Rosa Therapeutics

VAV1 Program (MRT-6160)

VAV1 is a Key Regulator of T- and B-cell Activity

VAV1 signaling is associated with several T and B cell immunologic outcomes and…



VAV1 signaling increases cytokine production, proliferation, and differentiation

TCR = T-cell receptor. BCR = B-cell receptor. IL-2, IFN-γ, IL-17 and IL-6 are cell signaling molecules (cytokines) that promote immune response. sIgG is the most common circulating antibody.

…plays a critical role across multiple clinically validated pathways in immune-mediated disease

ORENCIA® (abatacept)

RINVOQ® upadacitinib

Rituxan® Rituximab

VYVGART® Hytrulo

Cosentyx® (secukinumab)

omvoh™ (mirikizumab-mrkz) 300 mg/15 mL infusion | 100 mg/mL injection

HUMIRA® adalimumab

ACTEMRA® tocilizumab

Strategic Agreement to Accelerate and Broaden MRT-6160 Development

NOVARTIS

Scope

Global license agreement with Novartis to advance VAV1-directed molecular glue degraders including MRT-6160, in development for **immune-mediated conditions** (announced Oct. 2024)

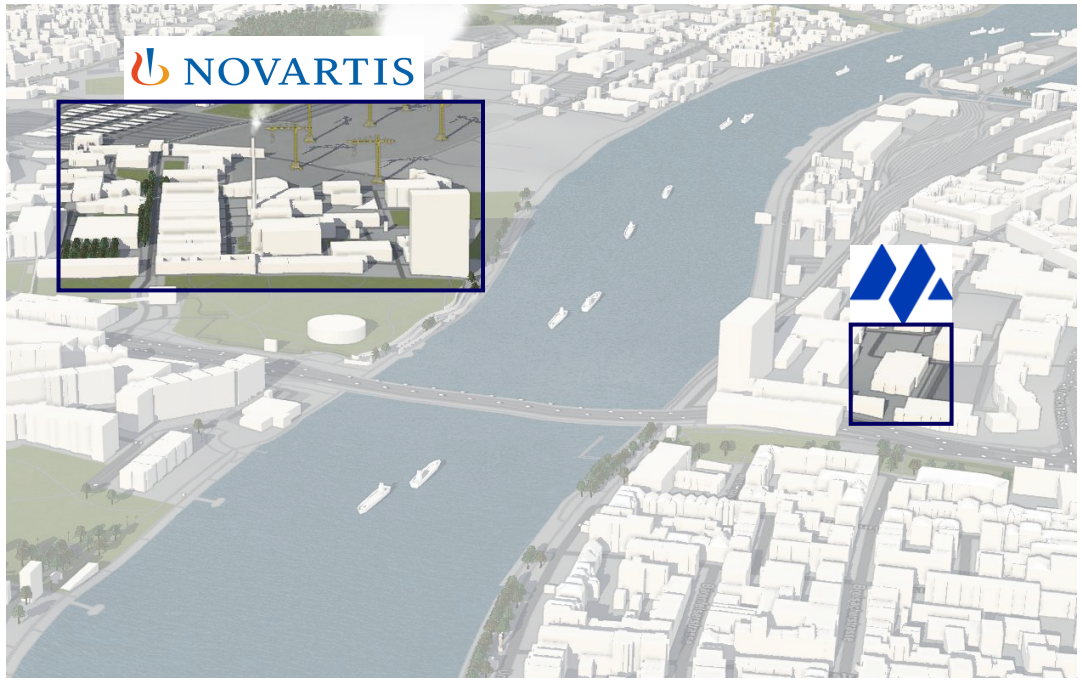
Financials

- $150M upfront payment
- Eligible for up to $2.1B in development, regulatory, and sales milestones, beginning upon initiation of Phase 2 studies
- Eligible for **US P&L share** and ex-US tiered royalties

Strategic Goal

Accelerate and broaden scope of clinical development of MRT-6160 while **retaining substantial value** for Monte Rosa

Basel



Notes: Under the terms of the Novartis 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. 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.

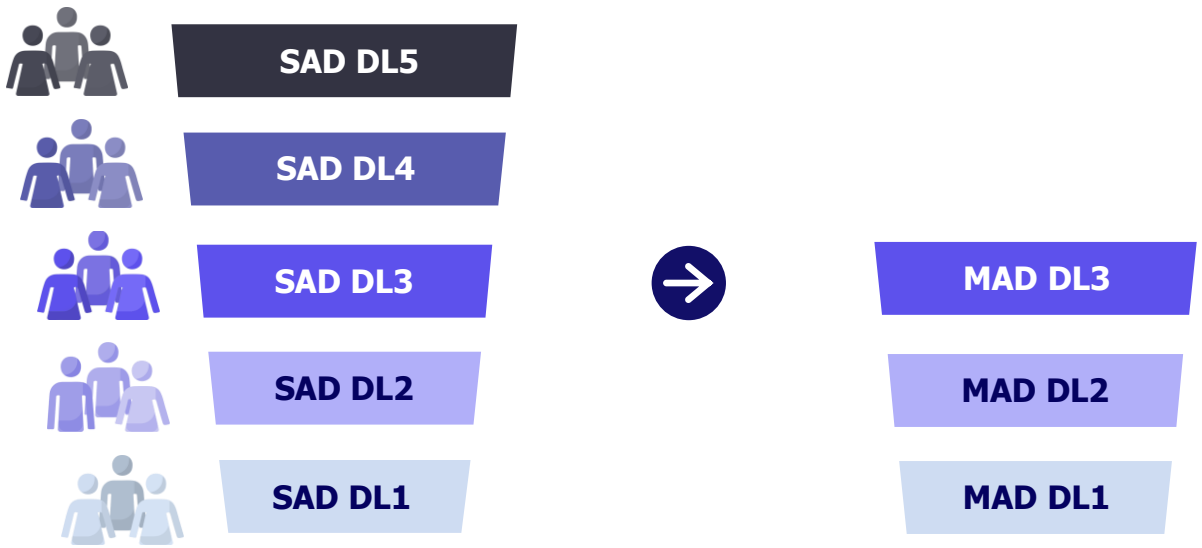
Safety, PK and PD Data from SAD and MAD Healthy Volunteers Phase 1 Trial of VAV1 MGD MRT-6160

MRT-6160 Phase 1 Healthy Volunteers Study: Design and Objectives

All cohorts randomized & placebo controlled

SAD cohorts
One oral dose

MAD cohorts
7 daily oral doses



Enrolled > 70 subjects

Study Endpoints

Primary

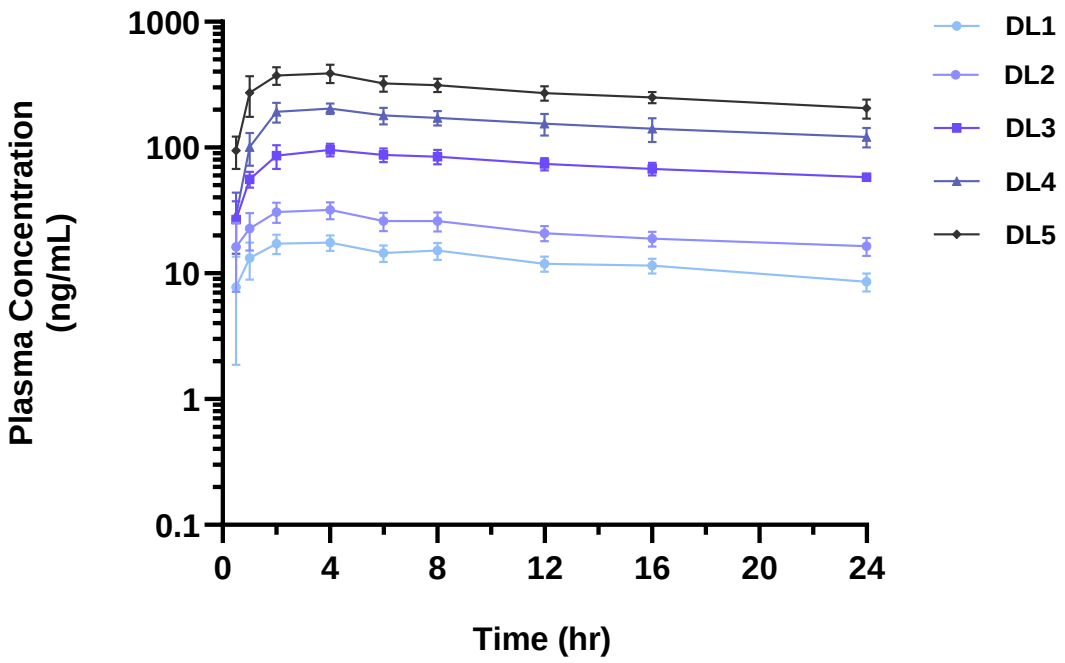
- Safety and tolerability

Secondary & exploratory

- Pharmacokinetics
- Pharmacodynamics
  - VAV1 degradation in T & B cells
  - Ex vivo response to TCR- and BCR-stimulation

MRT-6160 Displayed a Dose-Dependent Human Pharmacokinetic Profile

Plasma concentration vs time



Pharmacokinetic data (AVE ± SEM)

Dose Level	T1/2 (hr)	Cmax (ng/mL)	AUC0-24 (hr*ng/mL)
1	24.1± 2.6	18.3 ± 1.0	300.3 ± 16.4
2	26.8 ± 1.9	32.6 ± 2.2	527.0 ± 30.3
3	33.3 ± 2.9	100.9 ± 4.6	1736.3 ± 67.1
4	28.3 ± 1.6	216.2 ± 7.0	3615.2 ± 190.8
5	27.2± 1.7	399.0 ± 31.1	6593.7 ± 369.8

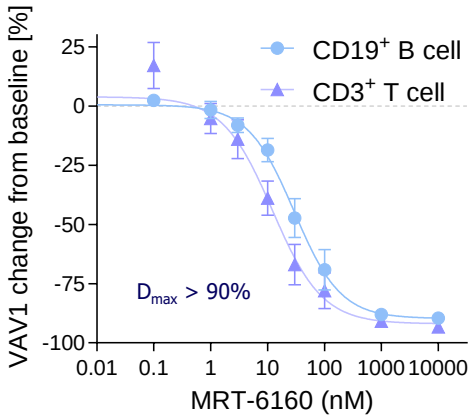
MAD ~2-fold increase in exposure at steady state
No food effect

In Vitro Assay Validation of PD and Immune Cell Functional Testing

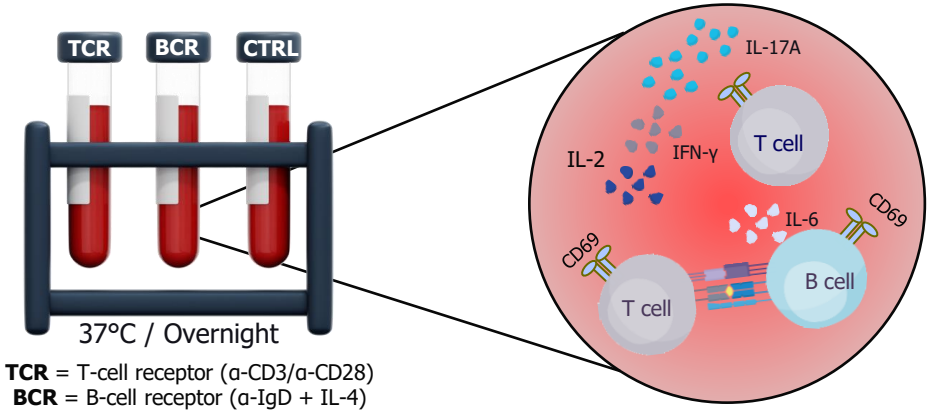
Degradation assessment

VAV1 protein expression by flow cytometry

In vitro data



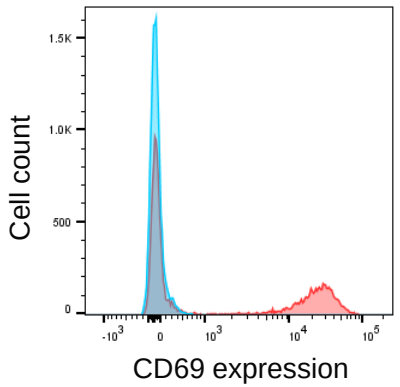
Ex vivo stimulation of whole blood to monitor T- & B-cell functions



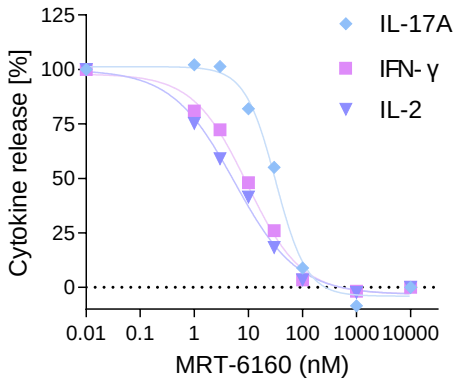
TCR = T-cell receptor (α-CD3/α-CD28)
BCR = B-cell receptor (α-IgD + IL-4)

CD69 upregulation on T & B cells by flow cytometry

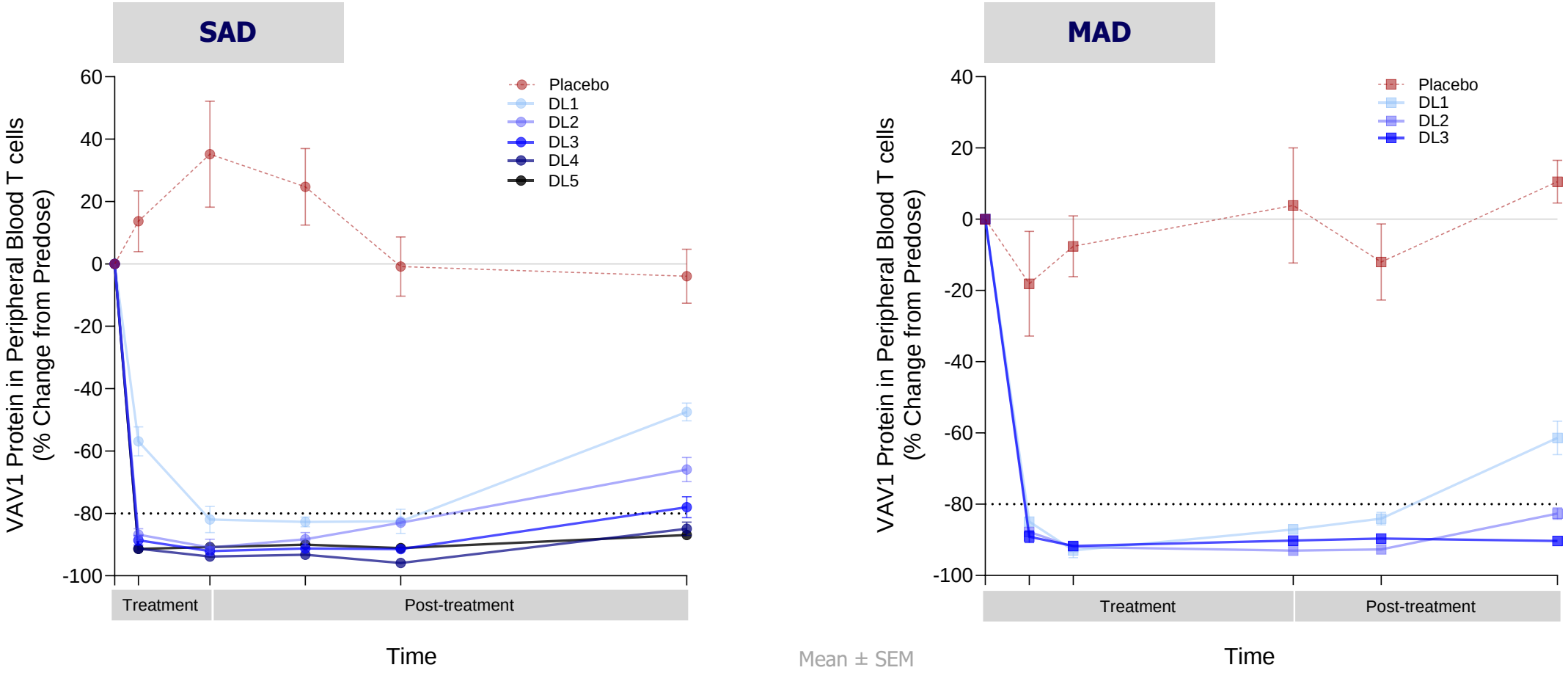
In vitro data



Cytokine secretion by immunoassay

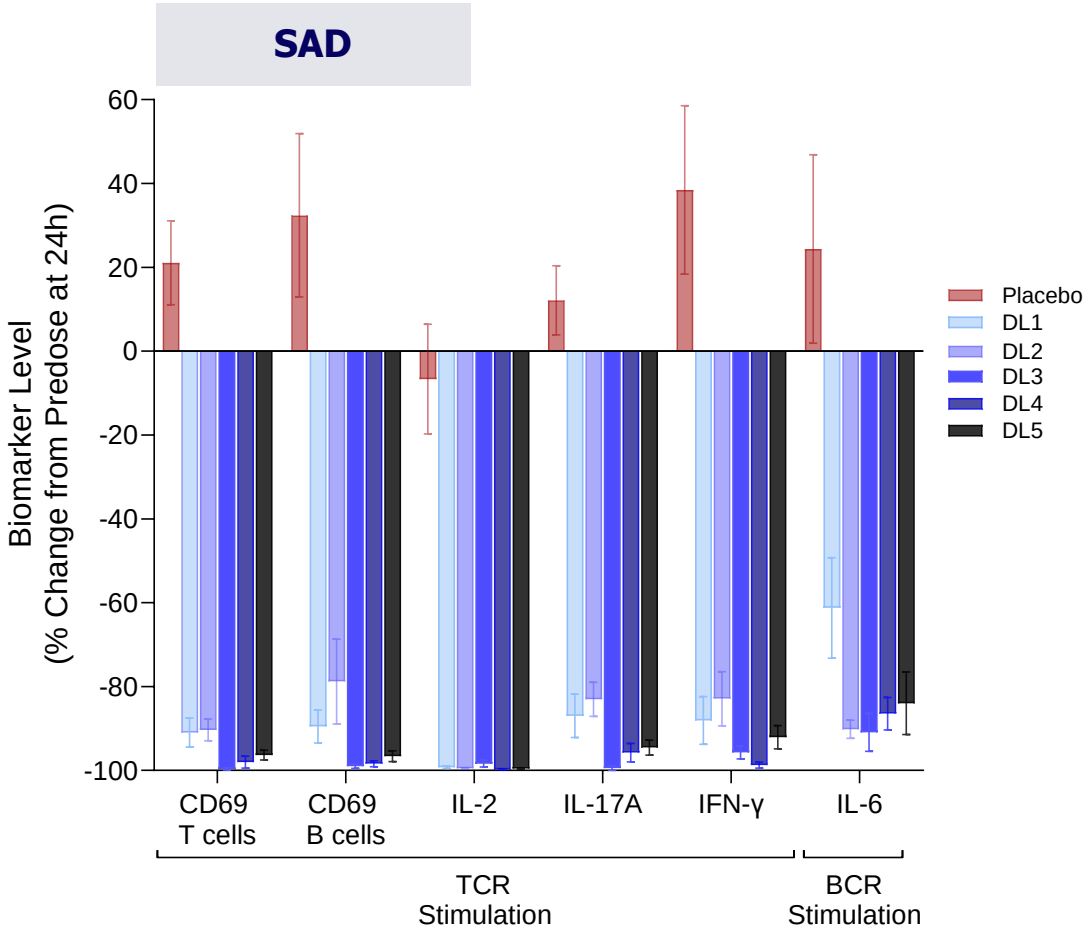


MRT-6160 Achieved Dose-Dependent VAV1 Degradation >90% in Peripheral Blood T Cells After Single and Multiple Dose Administration



- Dose-dependent, marked degradation of VAV1 in peripheral blood T cells (> 90%; except DL1)
- Similar results observed in peripheral blood B cells
- VAV1 protein reduction is sustained, with dose-dependent recovery post treatment

VAV1 Degradation by MRT-6160 Resulted in Significant Functional Inhibition of T and B Cells following a Single Dose Administration



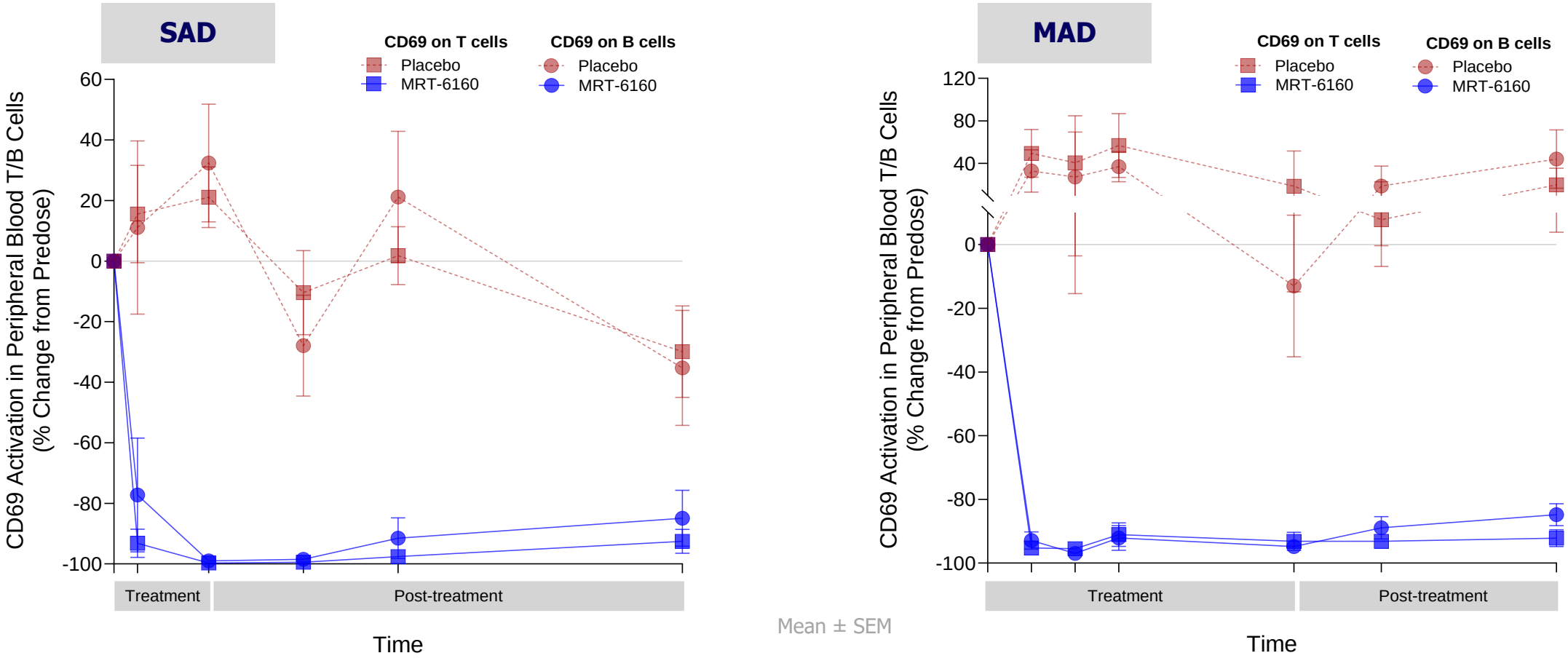
Mean ± SEM

MRT-6160 treatment:

- Significantly attenuated CD69 upregulation on T and B cells following TCR stimulation, reflecting functional inhibition
- Significantly (up to 99%) inhibited IL-2, IFN-γ and IL-17A secretion from whole blood derived T cells following ex vivo TCR stimulation
- Attenuated IL-6 production by 60-90% across dose levels following B-cell stimulation

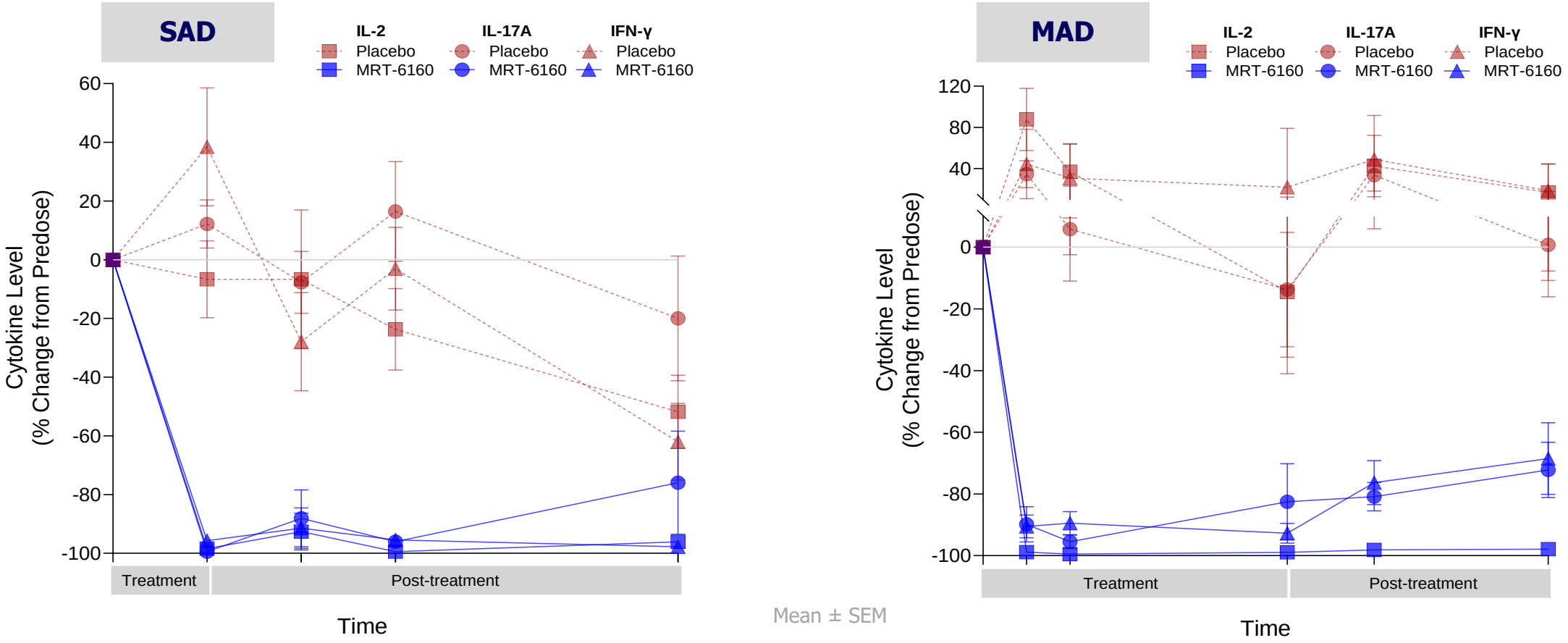
Pharmacodynamic studies suggest robust functional effects on cytokine production can be achieved with ≥80% degradation of VAV1

MRT-6160 Resulted in Sustained Suppression of TCR-mediated CD69 Activation following Single or Multiple Dose Administration



- Marked suppression of CD69 upregulation (>90%) in peripheral blood T and B cells following TCR stimulation (data for selected SAD and MAD dose shown as example)
- Similar results observed in peripheral blood B cells following BCR stimulation

MRT-6160 Resulted in Sustained Suppression of TCR-mediated Cytokine Production following Single or Multiple Dose Administration



- Significant and sustained suppression of IL-2, IL-17A and IFN-γ secretion from whole blood following ex vivo stimulation of TCR (data for selected SAD and MAD dose shown as example)

Safety Summary

- MRT-6160 was well tolerated with no serious adverse events (SAE)
- Observed treatment-emergent adverse events (TEAE) were mild (82%) or moderate (18%) and self-limiting
- Overall TEAE frequency was similar between MRT-6160 and placebo
- TEAE observed in 2 or more subjects treated with MRT-6160:
  - SAD: pain from vessel puncture (2)
  - MAD: cough (2), diarrhea (3), feeling hot (4), headache (5), nasal congestion (2), oropharyngeal pain (3) and pyrexia (2)

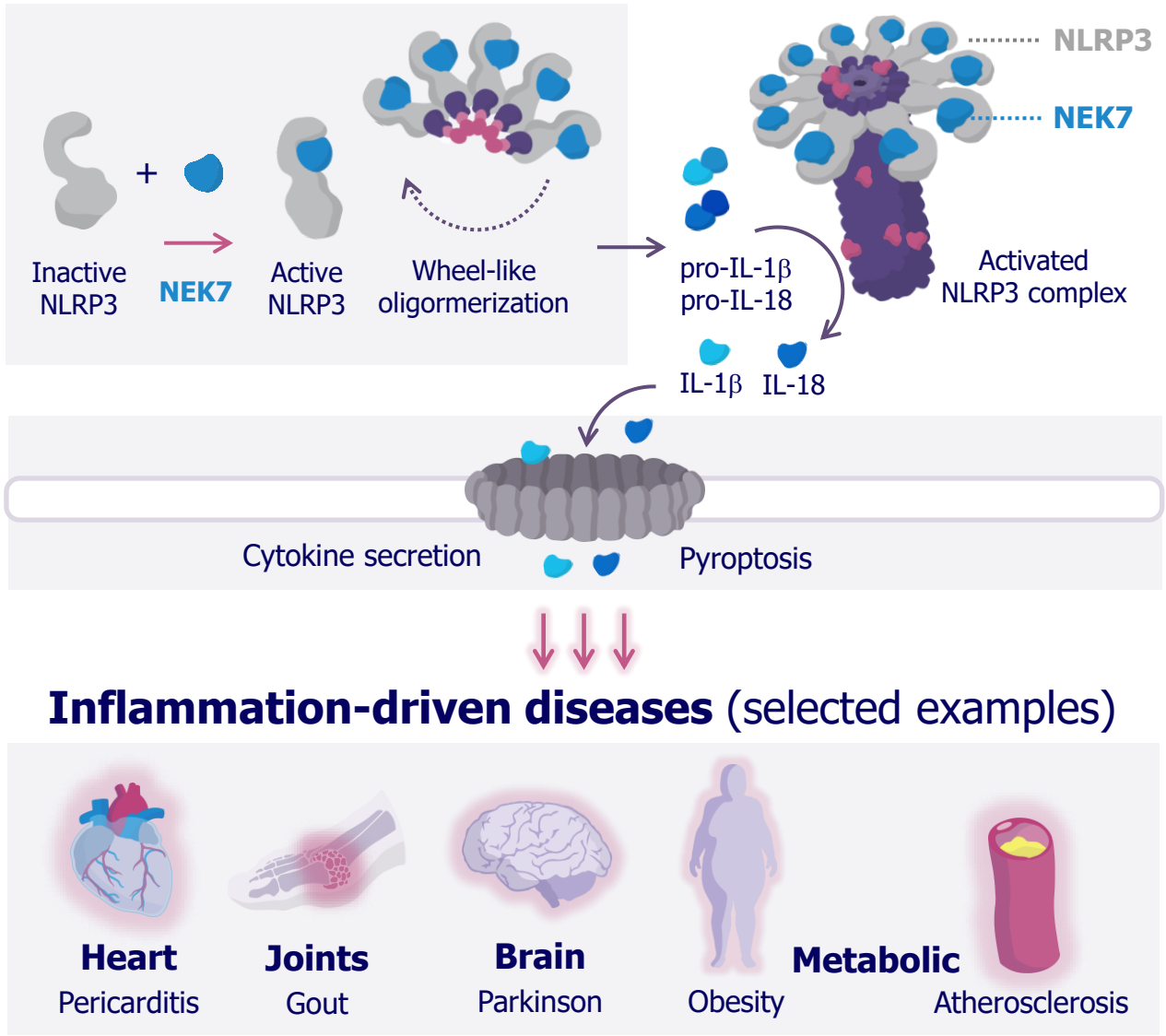
Conclusions

- Pharmacodynamic and functional ex vivo studies suggest significant effects on cytokine production can be achieved following marked and sustained degradation of VAV1
- Demonstrated levels of VAV1 degradation consistent with levels of degradation required to induce efficacy in preclinical models
- Functional impact on cytokine production consistent with levels predicted to be required to achieve efficacy in humans (based on benchmark clinical data)
- Highly favorable safety profile in humans
- **Presented Phase 1 data as well as chronic toxicology package support clear path into Phase 2 studies and broad potential applications in multiple immune-mediated diseases**

Monte Rosa Therapeutics

NEK7 Programs (MRT-8102 and CNS optimized)

NEK7 is a Key Regulator of NLRP3 Inflammasomes, IL-1 and IL-18



NEK7 enables NLRP3 assembly in a kinase-independent manner

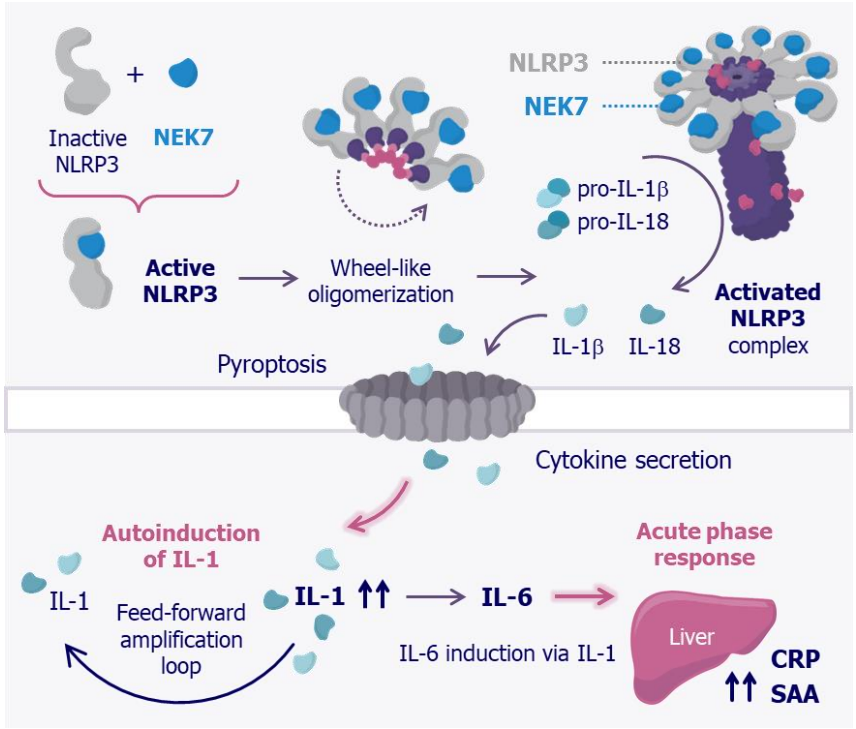
NEK7-deficient macrophages are severely impaired in **IL-1β and IL-18** secretion

NEK7 degradation has the potential to become an important treatment for **inflammation-driven diseases**

Lowering of CRP Levels Anticipated as a Result of NEK7 Degradation

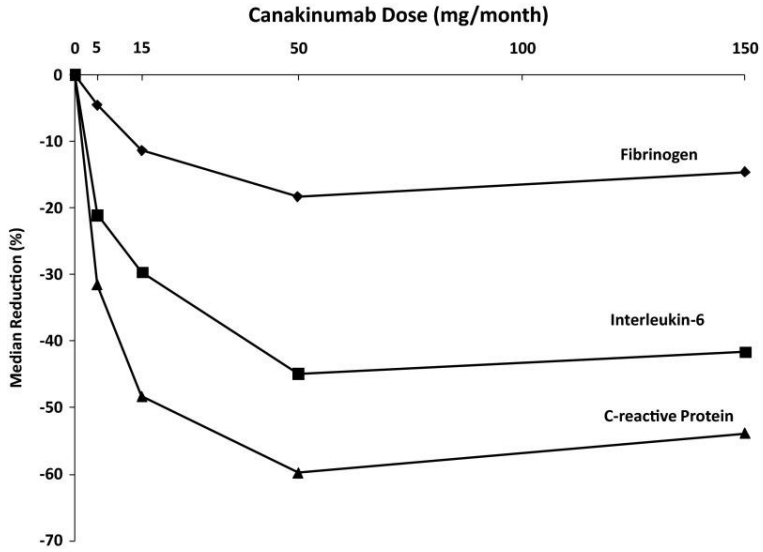
C-reactive protein (CRP) is an acute-phase protein downstream of NLRP3/NEK7 inflammasome

NLRP3/NEK7 activation in chronic inflammation



- IL-1α and IL-1β are highly inflammatory cytokines that induce high CRP concentration at sub-nanomolar concentrations in humans (Abbate, 2020)
- CRP is a long-term predictor of cardiovascular risk (Ridker, 1997)

Canakinumab (anti-IL-1β) leads to reductions in CRP



Ridker et al., 2012

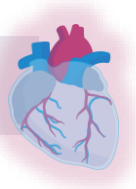
- In addition, several NLRP3 inhibitors have shown promising reductions in CRP in clinical trials
- Novartis NLRP3i, DFV890, is under investigation in a Ph2a trial of inflammatory marker (IL-6, IL-18) reduction in participants with coronary heart disease and elevated hsCRP (NCT06031844)

hsCRP = high sensitivity C-reactive protein
SAA = serum amyloid A

IL-1/NLRP3 Signaling is a Clinically Validated Pathway for Inflammatory Diseases

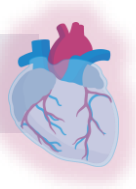
Cardio-immunology

Recurrent pericarditis



Rilonacept (IL-1α/β) – approved for recurrent pericarditis

Atherosclerotic cardiovascular disease



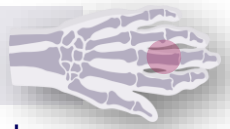
Canakinumab (IL-1β) – reduction in cardiac events

Rheumatology

Gout

Canakinumab (IL-1β) – approved for gout flares

Osteoarthritis



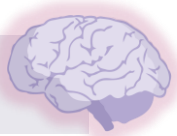
Canakinumab (IL-1β) – decreased rates of knee and hip replacement

Autoinflammation
CAPS

Anakinra (IL-1R), canakinumab (IL-1β), rilonacept (IL-1 α/β) – approved for CAPS

Neurology

Neuroinflammation
Epilepsy



Belnacasan (CASP1) – reduction in seizures

Metabolic
Weight loss

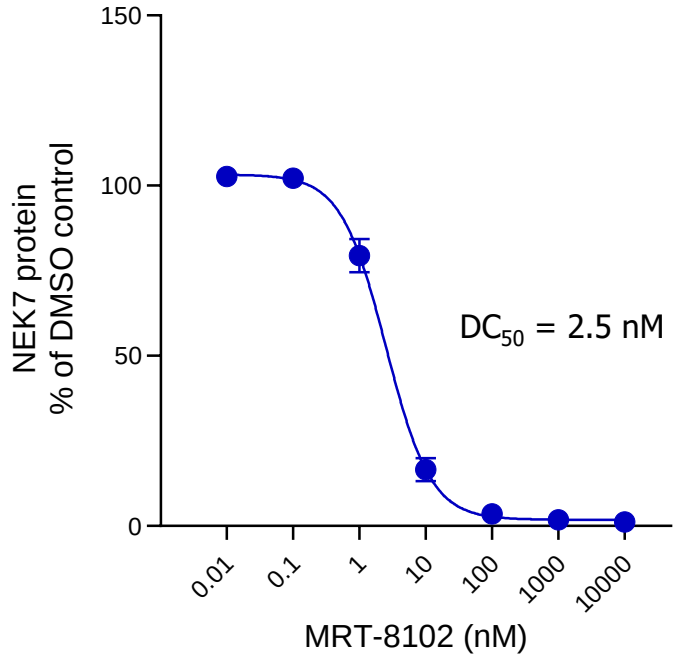
Multiple NLRP3 agents being studied for weight loss

MRT-8102: Efficient Development Path in Peripheral Inflammatory Diseases

Anticipated Studies	Goal/Objective
Phase 1 HV	• Safety, tolerability, and pharmacokinetics in healthy volunteers • NEK7 degradation in blood after single and multiple daily doses • Changes in levels of inflammatory cytokines
Planned Phase 1 (PoC) in High CRP, Cardio-immunology Indications	• Safety, and tolerability of 28-day dosing • Changes in CRP levels in subjects with high CRP • Generate data in cardio-immunology indications to support a path to registration
Further Development in Gout/Pseudogout, Osteoarthritis	• Changes in gout/pseudogout flare pain or osteoarthritic pain • Reduction in frequency of gout/pseudogout flares • Generate data to support registration studies

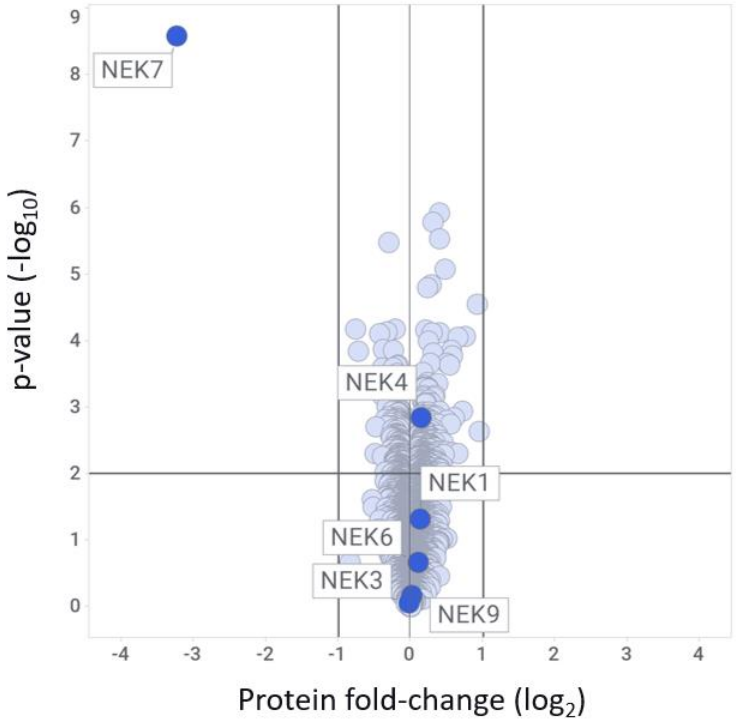
MRT-8102, a Potent and Highly Selective NEK7-directed MGD, Induced Durable Pharmacodynamic Modulation In Vivo

MRT-8102 potently degrades NEK7

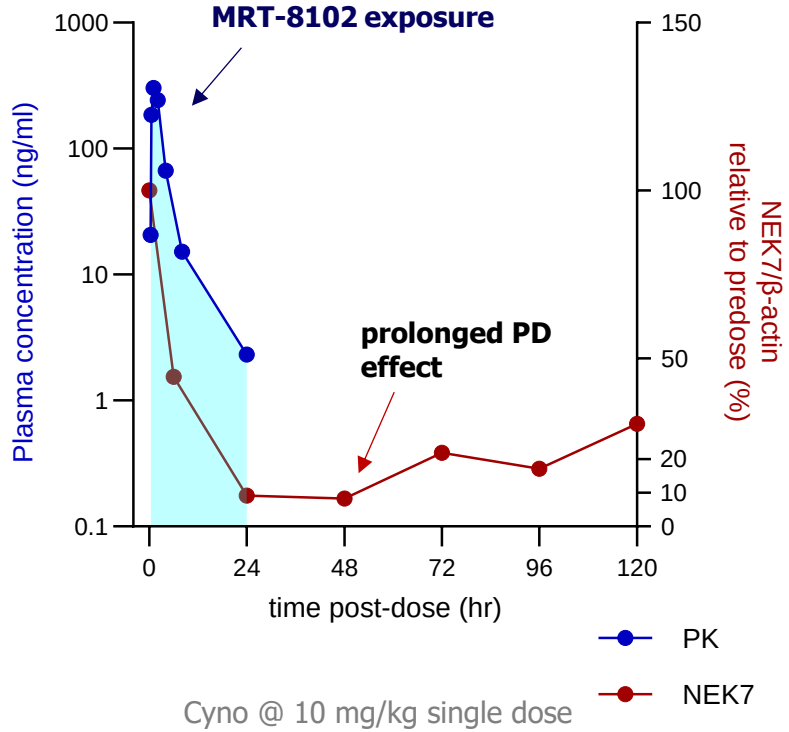


Human PBMC @ 24h treatment

MRT-8102 induces highly selective NEK7 degradation



MRT-8102 exposure results in prolonged PD effect

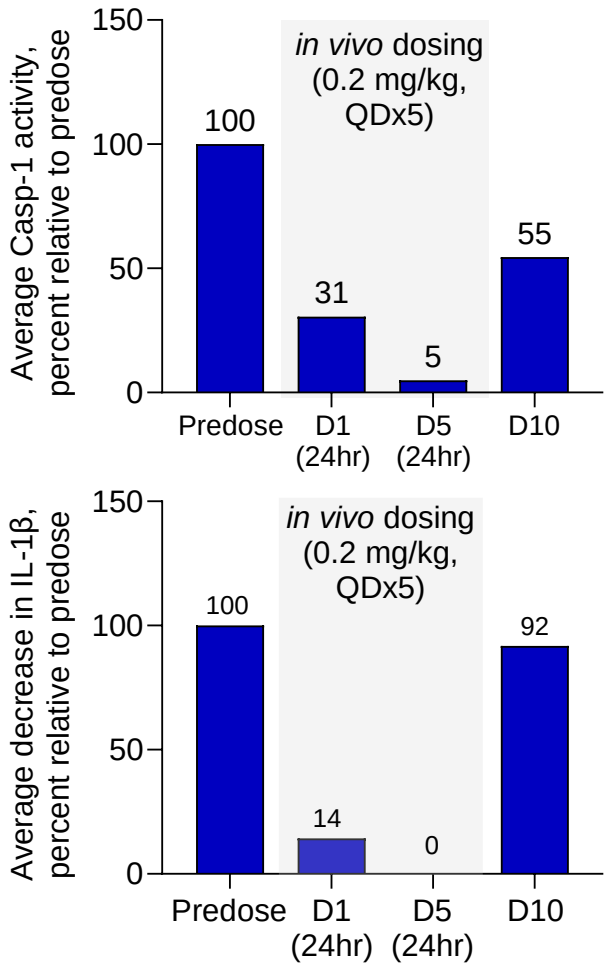


Cyno @ 10 mg/kg single dose

Potency, selectivity, and long-lasting pharmacodynamics create potential differentiation from competitive approaches

Preclinical GLP Tox Study Suggests Considerable Safety Margin

In vivo NEK7 degradation leads to inhibition of Caspase-1 activity and IL-1β release in ex vivo stimulation assay



IL-1β and Caspase-1 in plasma after ex vivo stimulation with LPS + nigericin in cynomolgus monkeys

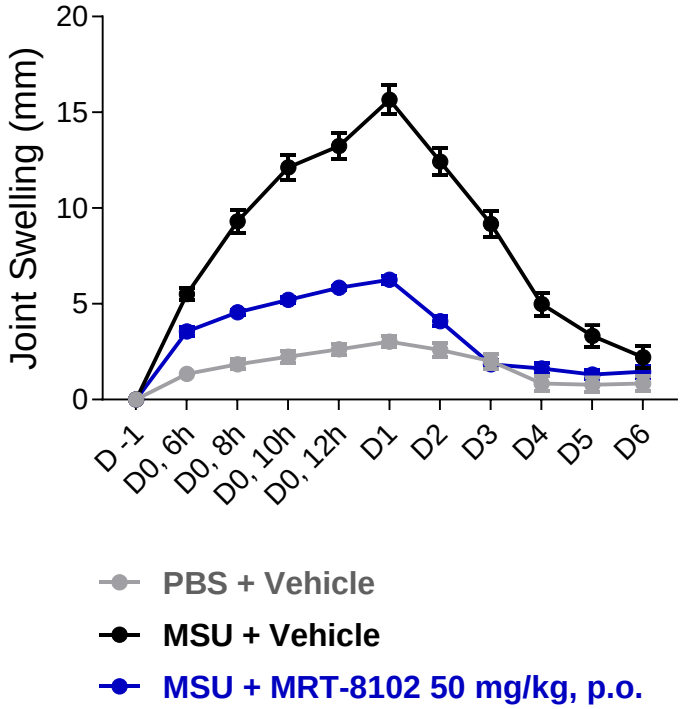
Toxicology summary in rats and cynos (28d GLP tox)

- No MRT-8102 related clinical signs, no changes in immunophenotyping, no gross or clinical pathology findings at any dose level
- The NOAEL was the highest dose tested, 150 mg/kg/day (rat) and 100 mg/kg/day (cyno)
- **>200-fold** exposure margin over projected human efficacious dose in both species
- No concerns related to in vitro off-targets, mutagenicity, phototoxicity, hERG or in vivo respiratory or CNS safety pharmacology (rat) or CV safety pharmacology (cyno)

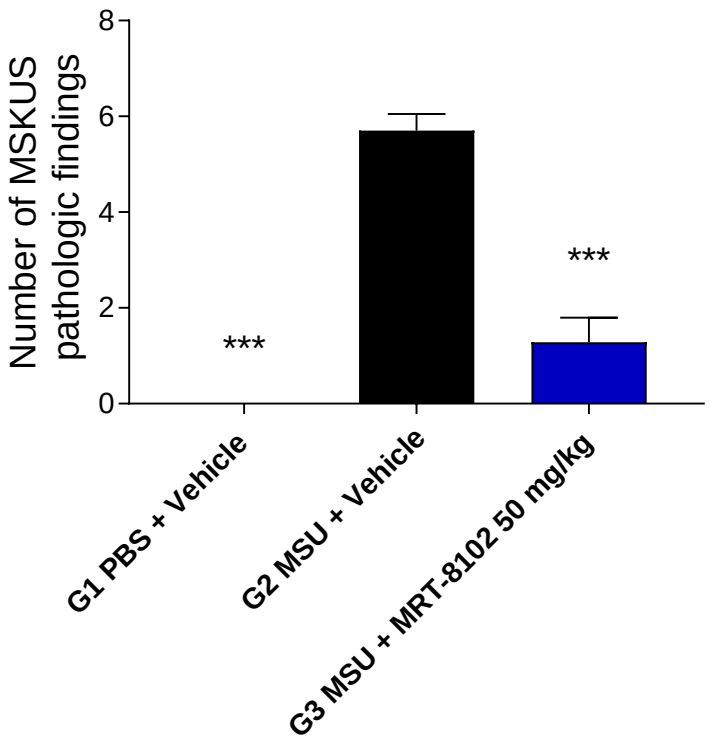
NOAEL = no observed adverse effect level

MRT-8102 Reduced MSU Crystal-driven Effects in Rabbit Gout Model

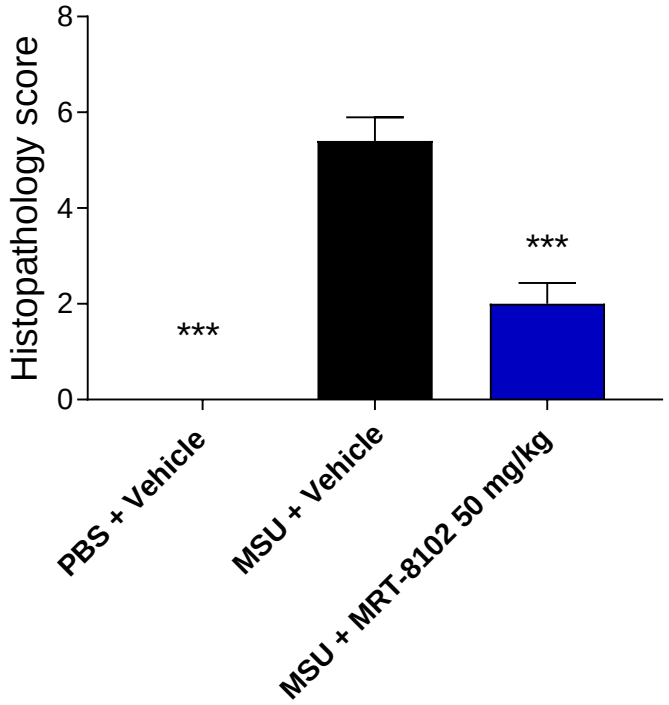
Joint swelling



MSKUS pathologic findings



Histopathology score

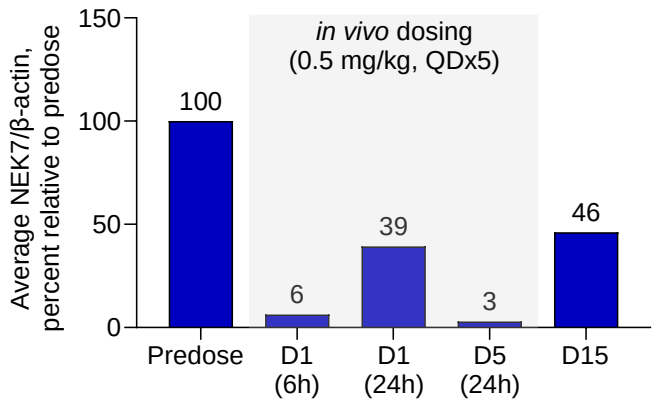


Daily dosing from day -1
Intra-articular injection of MSU on day 0
MSKUS = musculoskeletal ultrasound
*** denotes $p < 0.0005$ compared to MSU + Vehicle condition

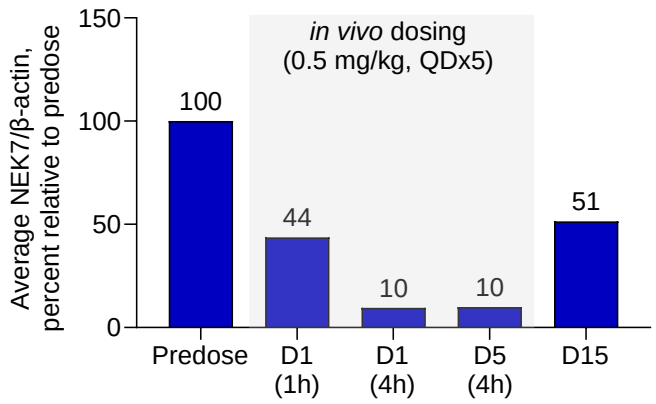
CNS-Optimized NEK7 Program

CNS-Optimized NEK7 MGD Demonstrated Profound NEK7 Degradation and Pathway Inhibition In Vivo Over Several Days in Cynomolgus Monkey

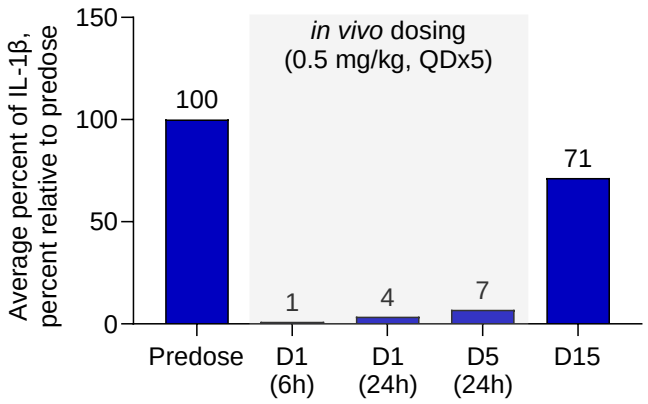
NEK7 in cyno PBMC



NEK7 in cyno CSF



IL-1β post-*ex vivo* stimulation



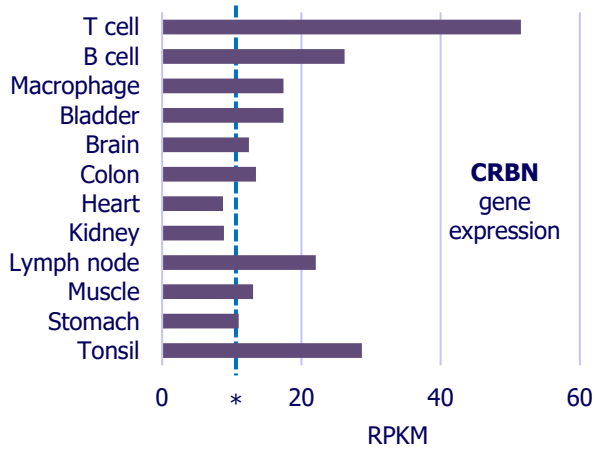
Excellent exposure in cyno blood and CSF, correlating with deep NEK7 degradation and functional inhibition of NLRP3 pathway following ex vivo stimulation

Monte Rosa Therapeutics

Building Future Opportunities in I&I

MGD Strengths Align with I&I Requirements

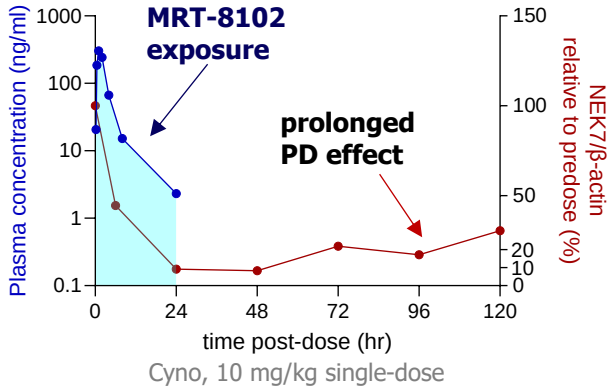
High degradation in immune and blood cells



CRBN is expressed highly in immune cells and immune relevant sites/organs

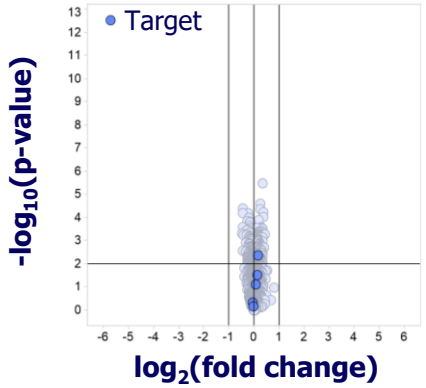
* Mean expression of all genes

Catalytic MOA drives sustained PD effect



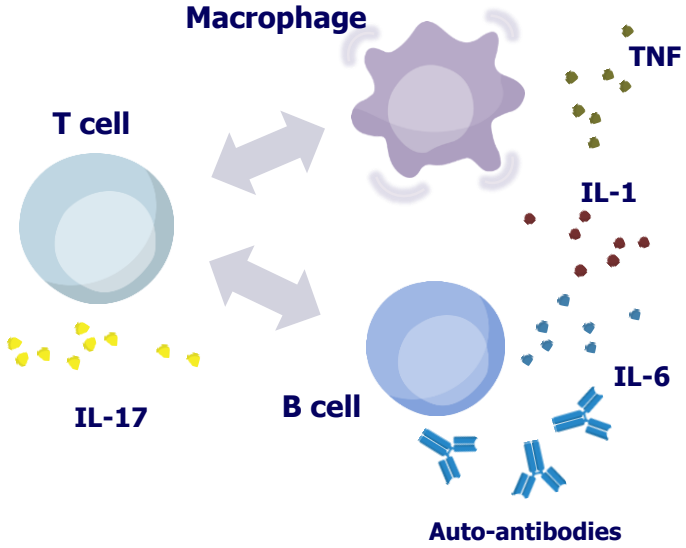
MGD catalytic action deletes the target protein, sustaining pathway modulation

Exquisite selectivity enables high therapeutic index



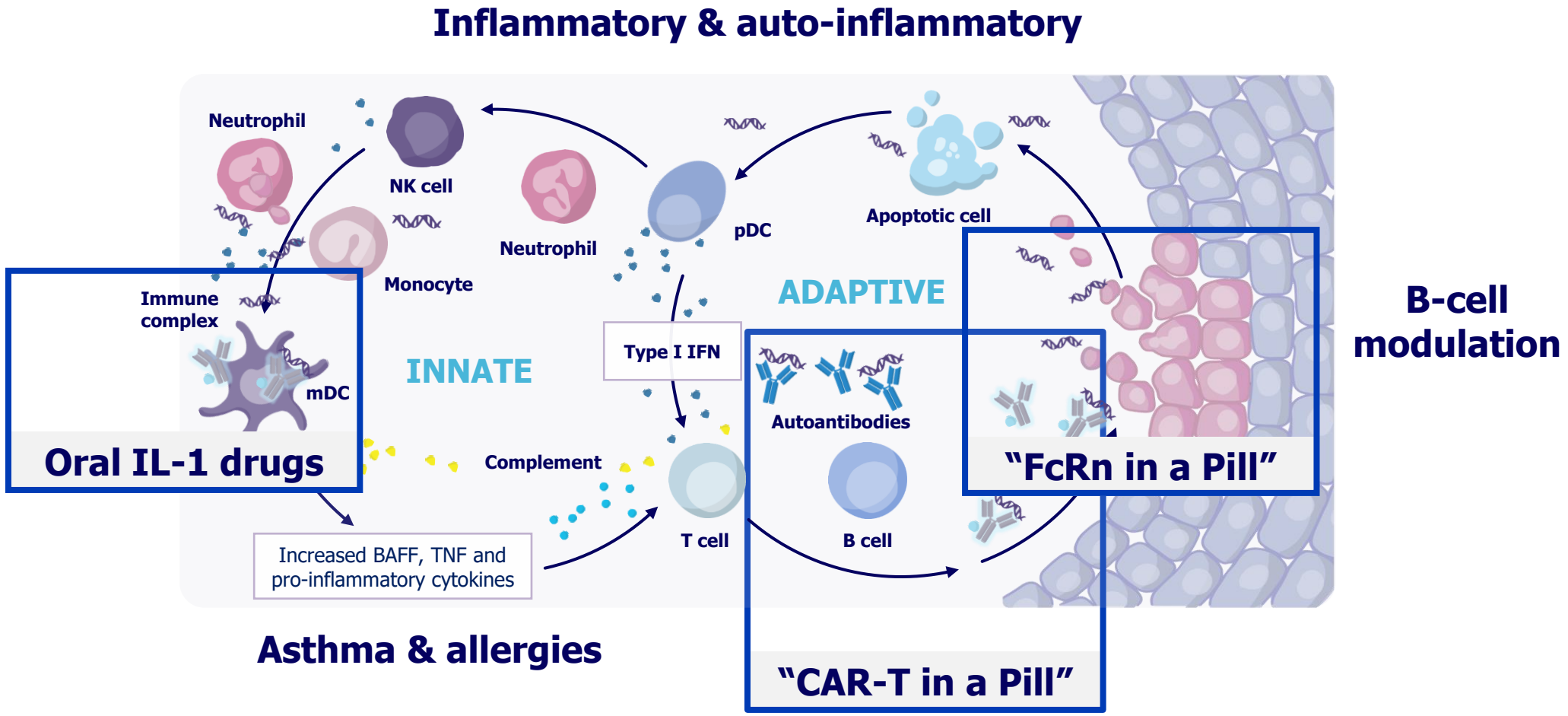
No MGD induced tox findings in 2 GLP tox studies (VAV1, NEK7)

Potential to deplete both membrane receptors and intracellular signaling nodes



Degrading upstream nodes modulates multiple cytokines

Degrading Undruggable Targets in Critical I&I Disease Pathways



Near term focus on building a portfolio of additional oral I&I drugs

Today's Update

Immunology & Inflammation

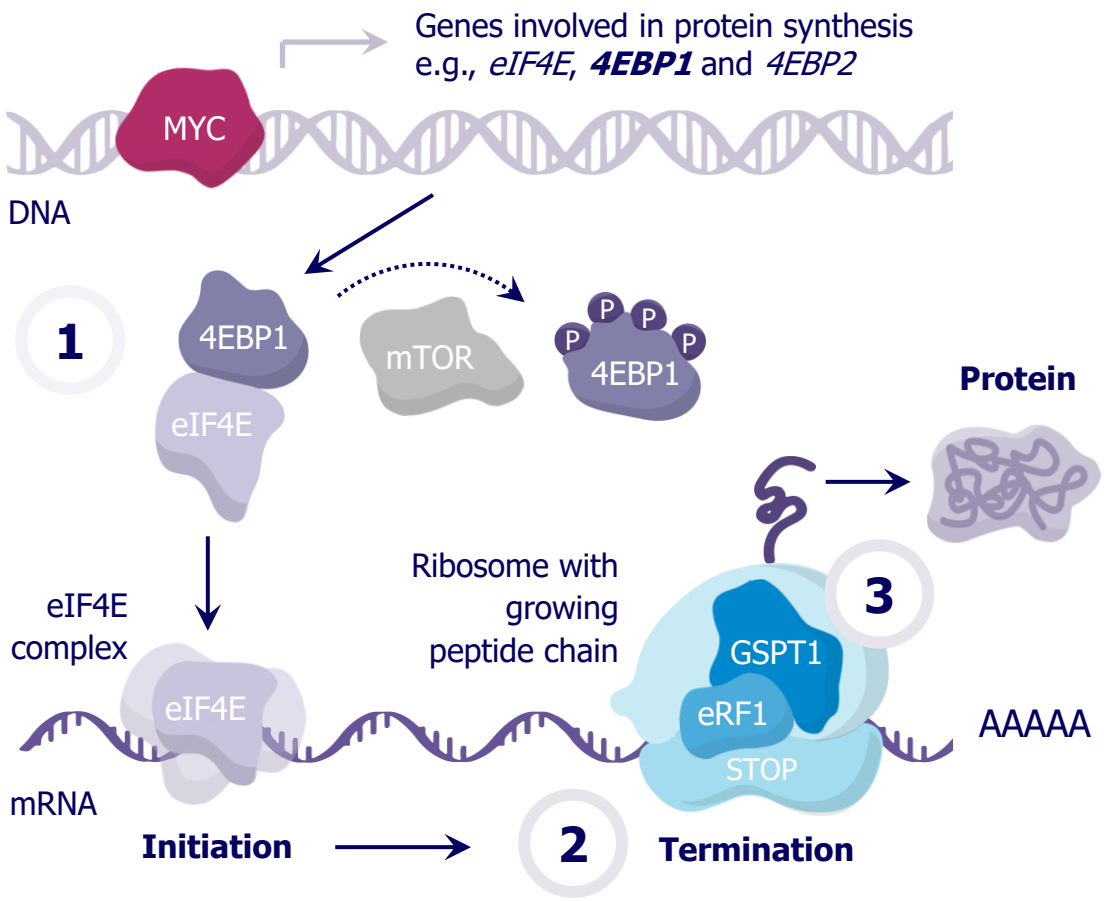
Oncology

1. MRT-6160: Results from Phase 1 HV trial support clear path into broad Phase 2 development
2. NEK7: Progress towards IND filing, clinical development plan
3. QuEEN™: Building future "only-in-class" I&I opportunities
4. MRT-2359: Encouraging activity supports prioritizing further development in CRPC versus other expansion cohorts
5. CCNE1 and CDK2: Highly differentiated approaches, accelerated path to IND
6. Summary and concluding remarks

Monte Rosa Therapeutics

GSPT1 program (MRT-2359)

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



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
leading to preferential activity of GSPT1 MGDs

MYC-Driven Pathologies Explored in MRT-2359 Phase 1/2 trial

Indication Size

N-MYC

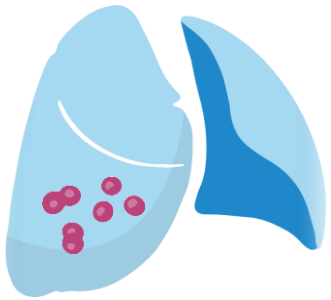
N-MYC High
and/or
L-MYC High

L-MYC

SCLC
L/N-MYC high

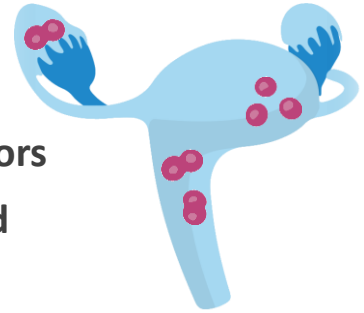
NSCLC
N-MYC high
SCLC/NE transformation

Neuroendocrine lung cancer



Neuroendocrine tumors

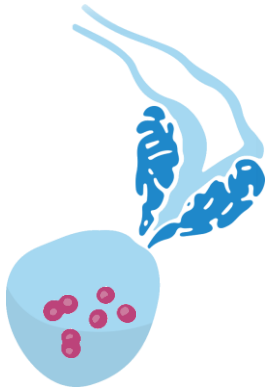
L-/N-MYC amplified tumors



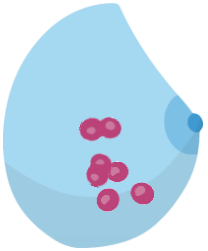
c-MYC High

c-MYC

Prostate cancer
AR positive including
AR-V7



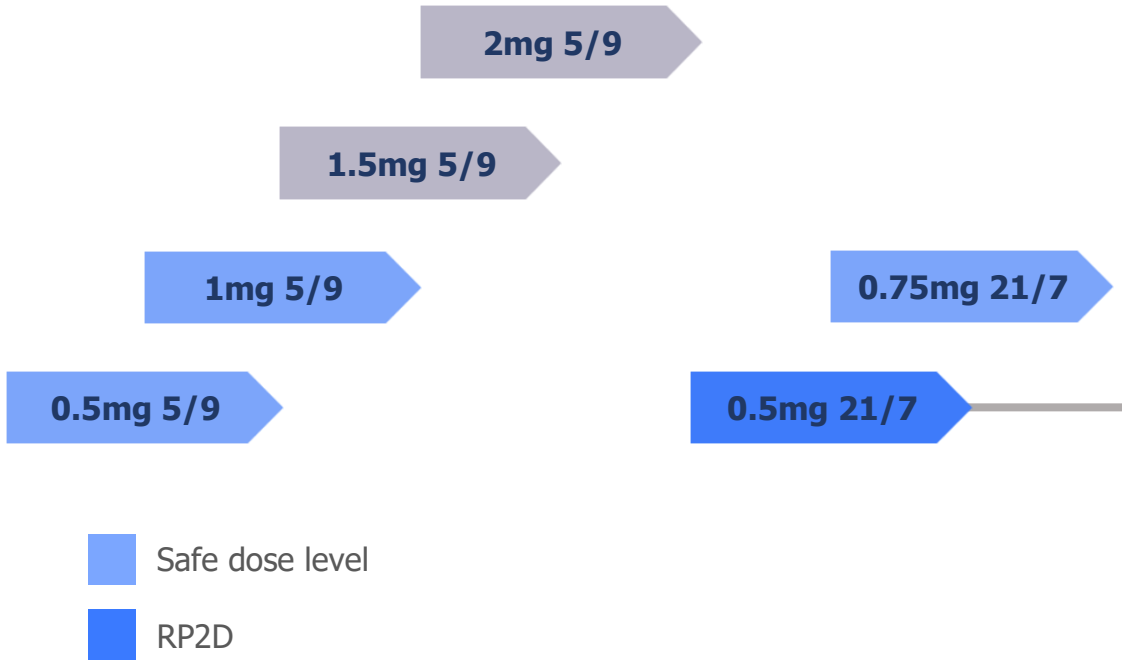
Breast cancer
ER positive metastatic



MRT-2359-001 Phase 1/2 Clinical Study Design

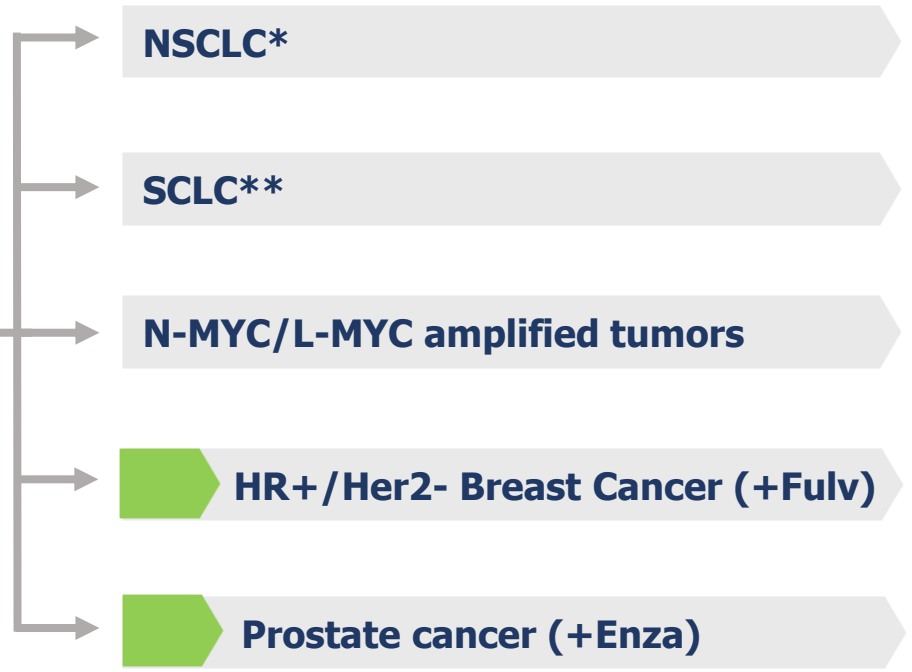
Phase 1: Dose Escalation

Lung cancer, high-grade neuroendocrine tumors and solid tumors with N-/L-MYC amplification



0.5mg 21/7 identified as RP2D

Phase 2: Possible Expansion Cohorts



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

Safety assessments initiated

5/9 = 5 days on drug, 9 days off drug; 21/7 = 21 days on drug, 7 days off drug; RP2D = recommended Phase 2 dose

Patient Demographics and Clinical Characteristics in Dose Escalation

Patient Characteristic	Total (N=59)*
Age, median (range), years	63 (30-80)
Female, N (%)	30 (51)
Race, N (%)	
White	48 (81)
Black	4 (7)
Asian	3 (5)
Other	4 (7)
ECOG performance status, N (%)	
0 or 1	58 (98)
2	1 (2)
Cancer type, N (%)	
Non-small cell lung cancer	23 (39)
Small cell lung cancer	13 (22)
High-grade neuroendocrine cancer	16 (27)
N-MYC or L-MYC amplified cancer	7 (12)
Number of prior lines of therapy, median (range)	3 (1-8)

** 32 patients treated on the 5/9 schedule and 27 patients on the 21/7 schedule*

Data cut off: 10 March 2025

MRT-2359 Treatment-Related AEs in ≥ 10% patients (N=59)

Dose Level	0.5 mg 5/9 (N=9)			1 mg 5/9 (N=13)			1.5 mg 5/9 (N=5)			2 mg 5/9 (N=5)			0.5 mg 21/7 (N=18)			0.75 mg 21/7 (N=9)		
CTC AE V5 Grade	G1-2 (%)	G3 (%)	G4 (%)	G1-2 (%)	G3 (%)	G4 (%)	G1-2 (%)	G3 (%)	G4 (%)	G1-2 (%)	G3 (%)	G4 (%)	G1-2 (%)	G3 (%)	G4 (%)	G1-2 (%)	G3 (%)	G4 (%)
Thrombocytopenia	0	0	0	0	0	1 (8)	2 (40)	1 (20)	1 (20)	2 (40)	1 (20)	2 (40)	2 (11)	0	1 (6)	3 (33)	0	1 (11)
Neutropenia	0	0	0	0	0	1 (8)	0	1 (20)	2 (40)	0	1 (20)	1 (20)	0	1 (6)	0	0	1 (11)	2 (22)
Leukopenia[#]	0	0	0	0	0	0	0	2 (40)	1 (20)	0	1 (20)	1 (20)	0	0	0	0	2 (22)	0
Anemia	0	0	0	0	1 (8)	0	1 (20)	1 (20)	0	1 (20)	1 (20)	0	1 (6)	1 (6)	0	1 (11)	1 (11)	0
Nausea	3 (33)	0	0	4 (31)	0	0	4 (80)	0	0	2 (40)	0	0	4 (22)	0	0	4 (44)	0	0
Vomiting	1 (11)	0	0	3 (23)	0	0	5 (100)	0	0	2 (40)	0	0	4 (22)	0	0	4 (44)	0	0
Diarrhea	1 (11)	0	0	3 (23)	0	0	1 (20)	1 (20)	0	1 (20)	0	0	1 (6)	0	0	3 (33)	0	0
Hypokalemia	0	0	0	2 (15)	0	0	0	0	0	1 (20)	0	0	3 (17)	0	0	1 (11)	0	0
Fatigue	0	0	0	3 (23)	0	0	0	0	0	0	0	0	2 (11)	0	0	4 (44)	0	0

Doses 0.5 mg, 1 mg 5/9 and 0.5 mg, 0.75 mg 21/7 were well tolerated with mostly low-grade AEs

Dose limiting toxicities were:

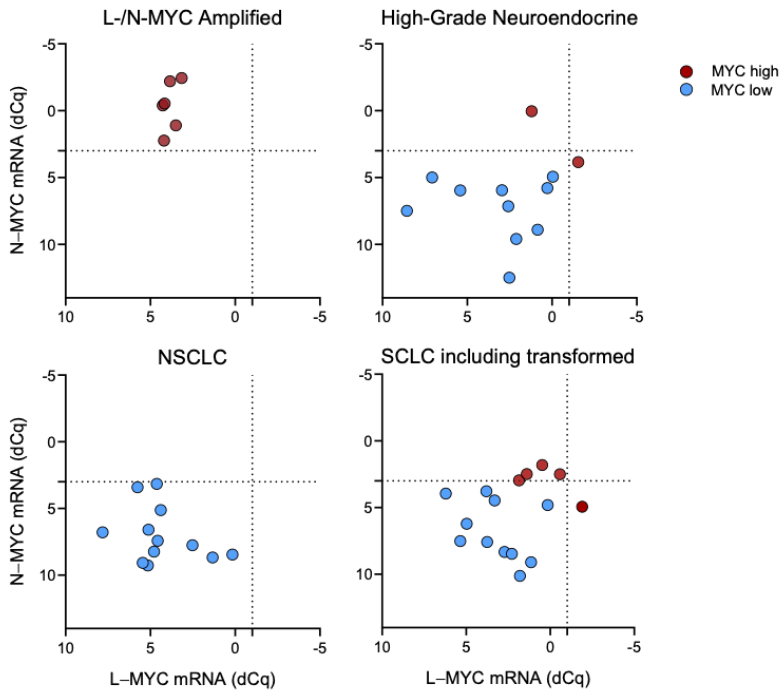
- thrombocytopenia (N=6), with or w/o neutropenia/leukopenia
- G3 ALT/AST (N=1)

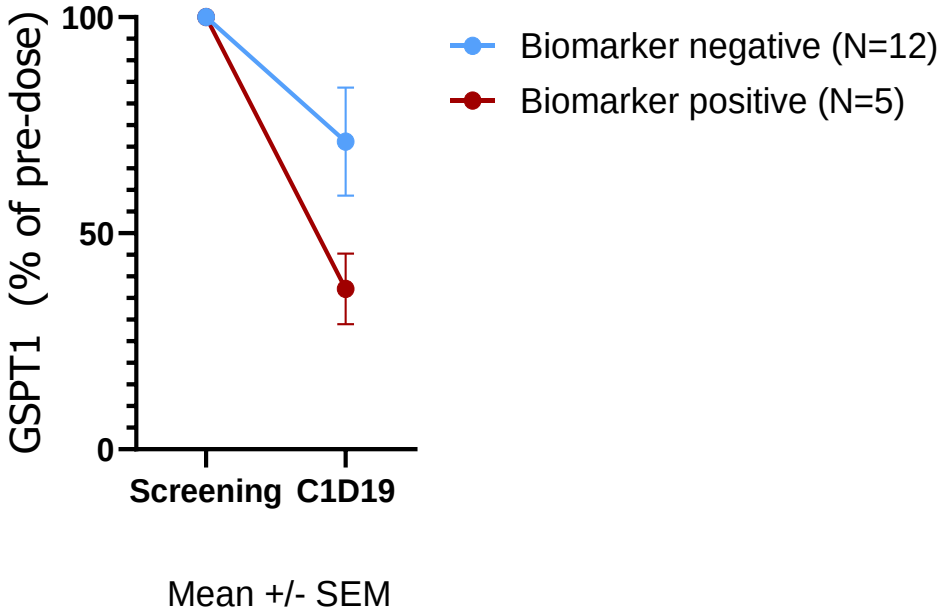
Importantly, dose-limiting toxicities reported with non-selective competitor GSPT1 degraders such as hypocalcemia, hypotension and cytokine release syndrome were not reported

[#] Data combined for 'leukopenia' and 'white blood cell count decreased'

Data cut off: 10 March 2025

Biomarker Status and PD modulation in L-/N-MYC Amplified Tumors, NSCLC, SCLC and High-Grade NE Tumors





- L-MYC and N-MYC expression in tumor tissue obtained at baseline was assessed in 46 patients
- Overall, as compared to preclinical data, lower than expected frequency of tumors with high L-MYC or N-MYC in NCSLC (0%), SCLC including transformed (31%) and HG NE tumors (17%)

Cut-off: N-MYC≤3; L-MYC≤-1

- Paired, tumor containing biopsies meeting QC criteria were obtained from 17 patients
- GSPT1 degradation assessed by targeted Mass Spec
- Optimal degradation of approximately 60% was achieved in biomarker high tumors, in line with preclinical data (see corporate deck)

Summary of Activity in SCLC, NSCLC, high-grade Neuroendocrine Tumors and L- and N-MYC Amplified tumors

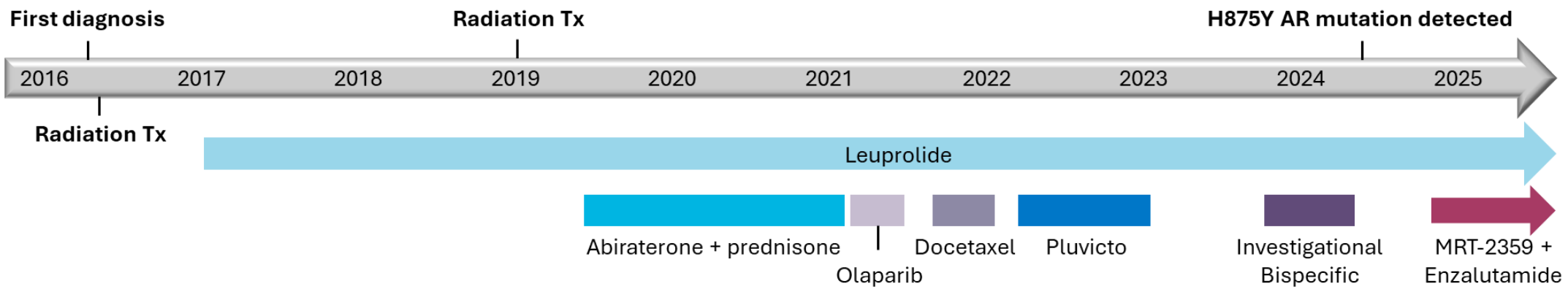
- L-MYC and N-MYC expression in tumor tissue obtained at baseline or known L-MYC or N-MYC amplification in the absence of tissue was available in 48 patients and 37 were evaluable for response assessment per RECIST 1.1

- <u>Activity in biomarker positive patients:</u>
  - High L-MYC or N-MYC expression (13 patients): 1 x PR, 4 x SD (DCR 38%)
  - Includes patients with L-MYC or N-MYC amplification without tumor tissue for expression analysis
- <u>Activity in biomarker negative patients:</u>
  - Low L-MYC and N-MYC expression (24 patients): 1 unconfirmed PR and 3 SD (DCR 17%),

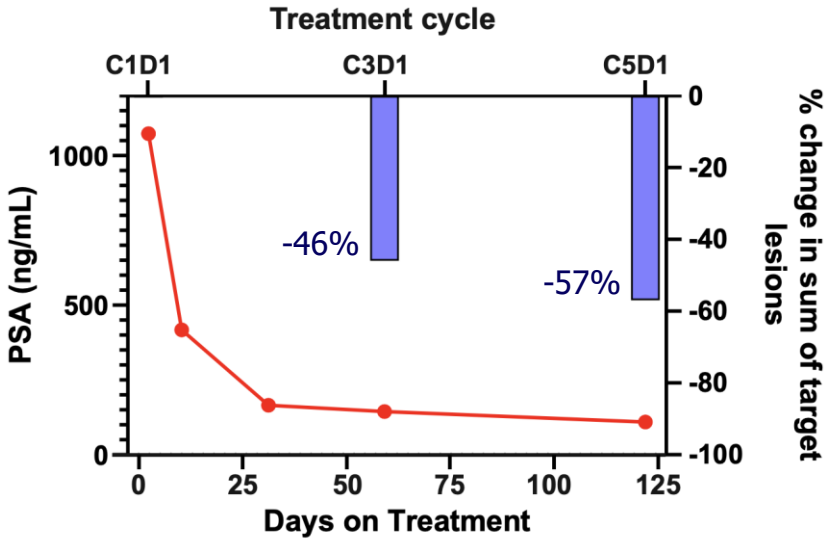
Current Data for MRT-2359 and Enzalutamide in Castrate-Resistant Prostate Cancer

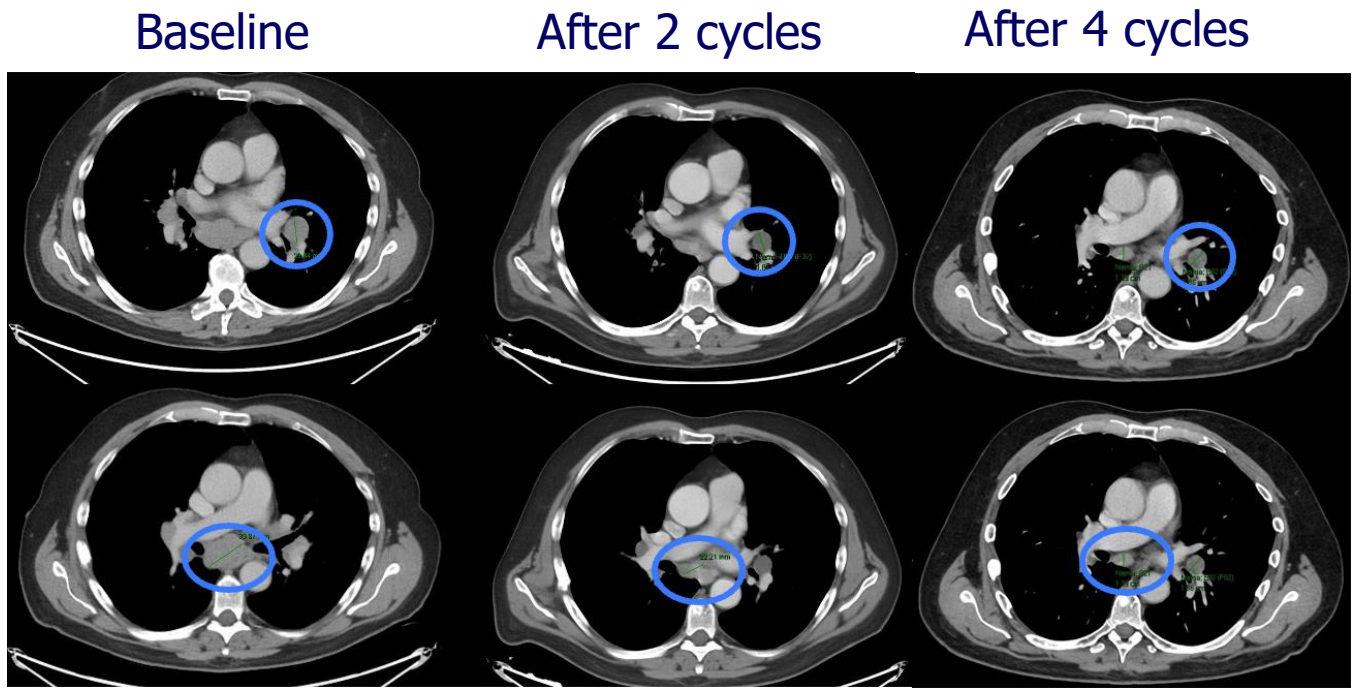
- As of 10 March 2025, RECIST 1.1 is available for 3 patients showing:
  - 1 PR (confirmed, -57%; heavily pretreated CRPC with AR LBD mutation H875Y)
  - 2 SDs (both CRPC with AR-V7 transcripts, multiple prior treatments including abiraterone and enzalutamide)
- PSA response is available for 2 patients showing 1 PSA response (-90%) in the patient with a confirmed PR per RECIST 1.1
- Safety profile has been favorable
- Safety and efficacy assessment continues following Simon 2-stage design
- Potential to expand to 20 - 30 patients if positive efficacy signal continues to be observed
- Further data from combination cohorts – including ER-positive breast patients – expected in H2 2025

Confirmed PR in Refractory CRPC with AR H875Y Mutation



Patient continues on study (C5)





Summary

- Encouraging early data in CRPC: 1 PR and 2 SD in first 3 evaluable, heavily pretreated patients with either AR mutations or AR-V7 expression
  - Opportunity to enroll 20 - 30 patients if positive efficacy signal continues to be observed
  - Large, high unmet need indication not requiring biomarker-based patient selection

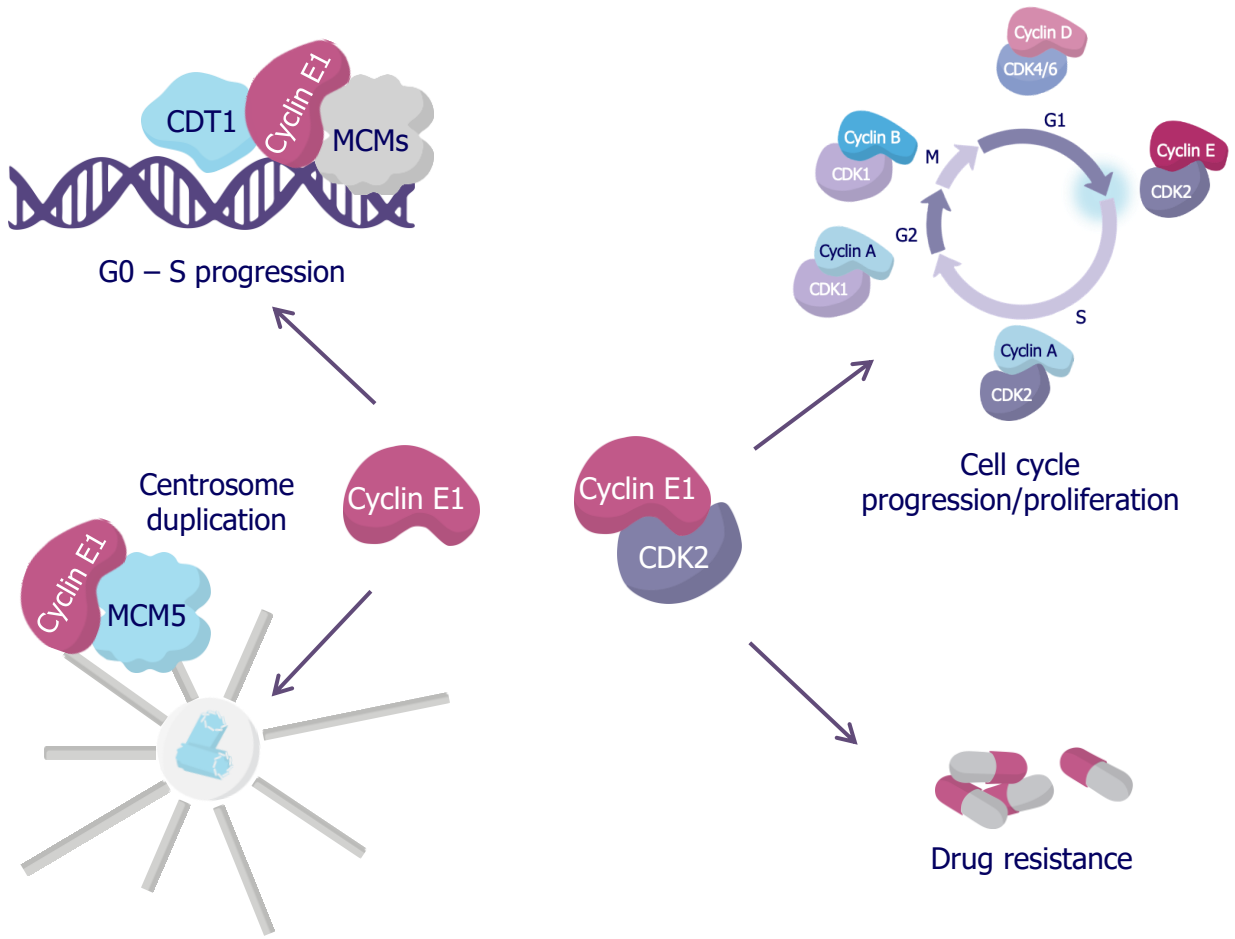
- Strategic decision made not to open expansion cohorts in lung cancer and NE tumors
  - Despite signals of clinical activity, low biomarker positivity in these indications does not support additional studies

Monte Rosa Therapeutics

CCNE1 (Cyclin E1) and CDK2 Programs

CCNE1 and CDK2 are Critical Drivers of Cancer Cell Cycle

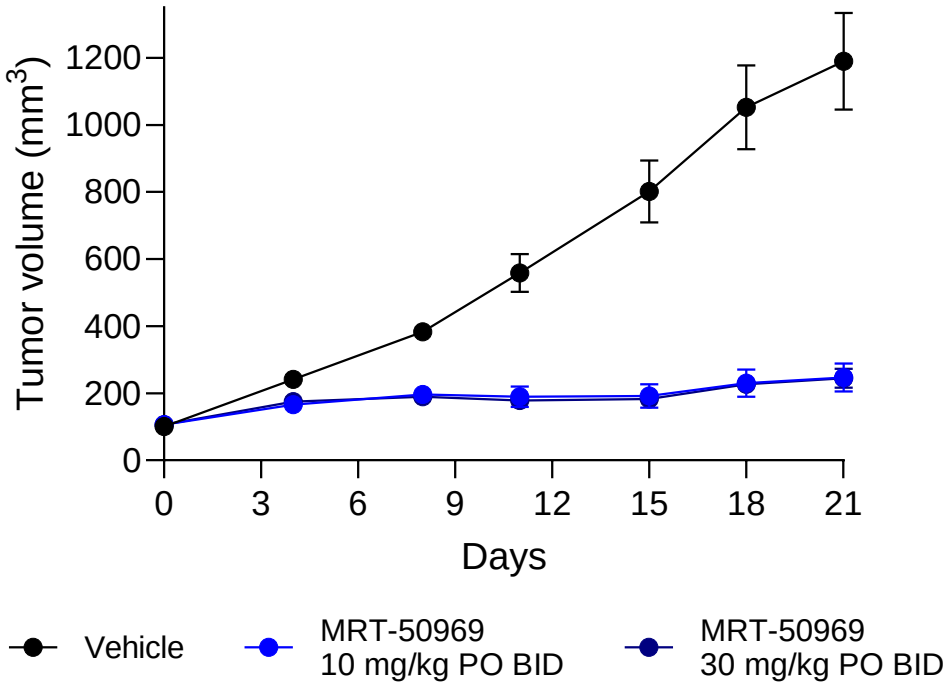
Cyclin E1 and CDK2 drive multiple hallmark cancer mechanisms



- CCNE1 and CDK2 are key drivers of cancers with cyclin dependent kinase pathway alterations
  - CCNE1 not druggable by conventional modalities
- CCNE1 and CDK2 MGDs are expected to ***achieve greater selectivity versus conventional CDK inhibitors***, as well as more sustained pathway inhibition compared to inhibitors
- CCNE1 dependent cancers include Ovarian and Endometrial cancer with CCNE1 amplifications as well as ER-positive breast cancer, amongst others

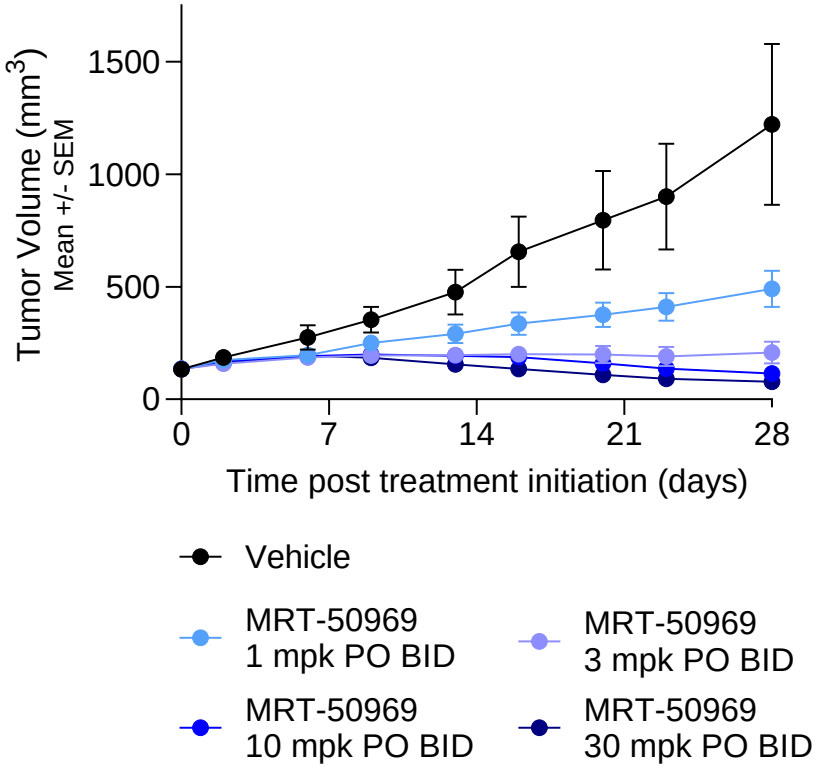
MRT-50969 Inhibits Tumor Growth in CCNE1 Amplified Gastric and Breast Cancer Models In Vivo

MRT-50969 inhibits tumor growth in CCNE1 amplified gastric cancer model



MKN1 CDX, 21-day efficacy study

MRT-50969 inhibits tumor growth in CCNE1 amplified breast cancer model



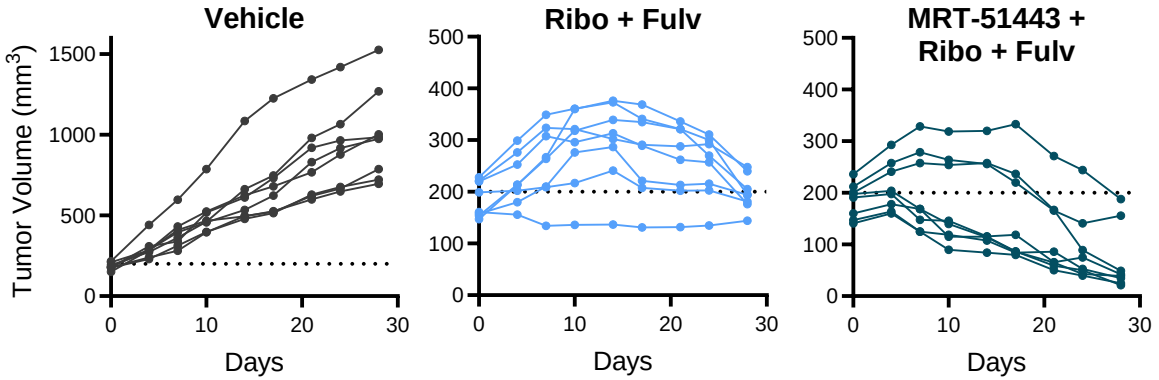
HCC1569 CDX, 28-day efficacy study

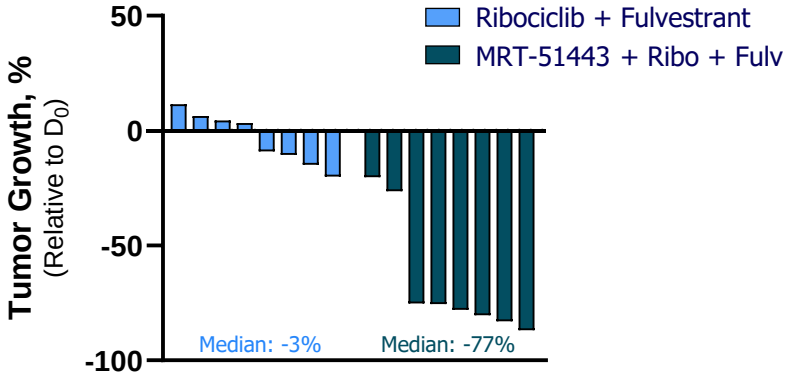
CDK2 MGD Demonstrates Activity in Combination with CDK4/6 Inhibitor and Fulvestrant in ER+ Breast Cancer Model

MRT-51443 induces robust tumor regression in combination with CDK4/6 inhibition and fulvestrant

MRT-51443 triple combination substantially reduces tumor growth vs. ribo + fulv

MCF7





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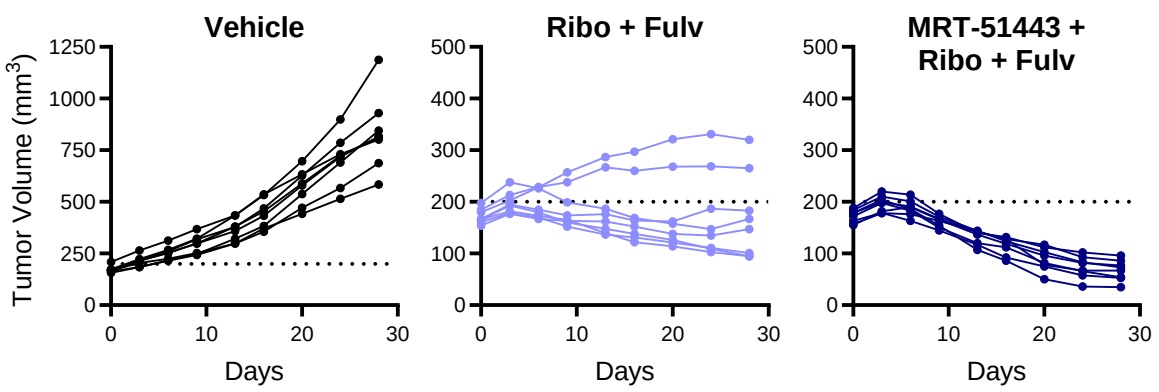

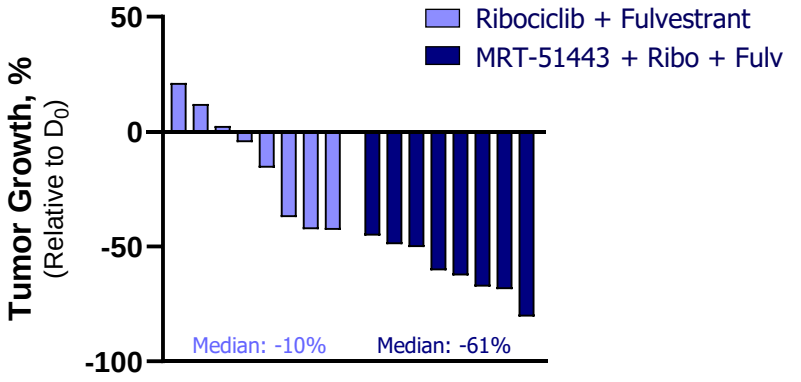

28-day efficacy; MRT-51443 30 mpk PO BID, ribociclib 75 mpk PO QD, fulvestrant 5 mg/mouse s.c. QW

Monte Rosa Therapeutics

Summary and Concluding Remarks

Monte Rosa Pipeline and Upcoming Milestones

	Target	Compound	Indication(s)	Discovery	IND-Enabling	Clinical	Next Anticipated Milestone	Ownership
Immunology & Inflammation	VAV1	MRT-6160	Immune-mediated Diseases				Phase 2 initiation	NOVARTIS *
	NEK7	MRT-8102	IL-1β/NLRP3-driven Inflammatory Diseases				IND submission in H1 2025	
		CNS Optimized					IND submission in 2026	
Oncology	GSPT1	MRT-2359	Castration-resistant Prostate Cancer				Additional CRPC data in H2 2025	
	CCNE1/CDK2	Discovery	CCNE1 Amplified Tumors, Breast Cancer				IND submission in 2026	
Various	Multiple Targets	Discovery	I&I, Genetic Diseases, Oncology				Lead optimization	
	Multiple Targets	Discovery	Oncology and Neurological Diseases				Undisclosed	Roche

Cash & equivalents of $377M as of December 31, 2024; cash runway anticipated into 2028

* Monte Rosa has an exclusive global license agreement with Novartis for this asset.


Q&A
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