# Degrading Proteins, Making Medicines

Innovating Beyond New Heights | November 2026



Monte Rosa Therapeutics

# Forward-Looking Statements

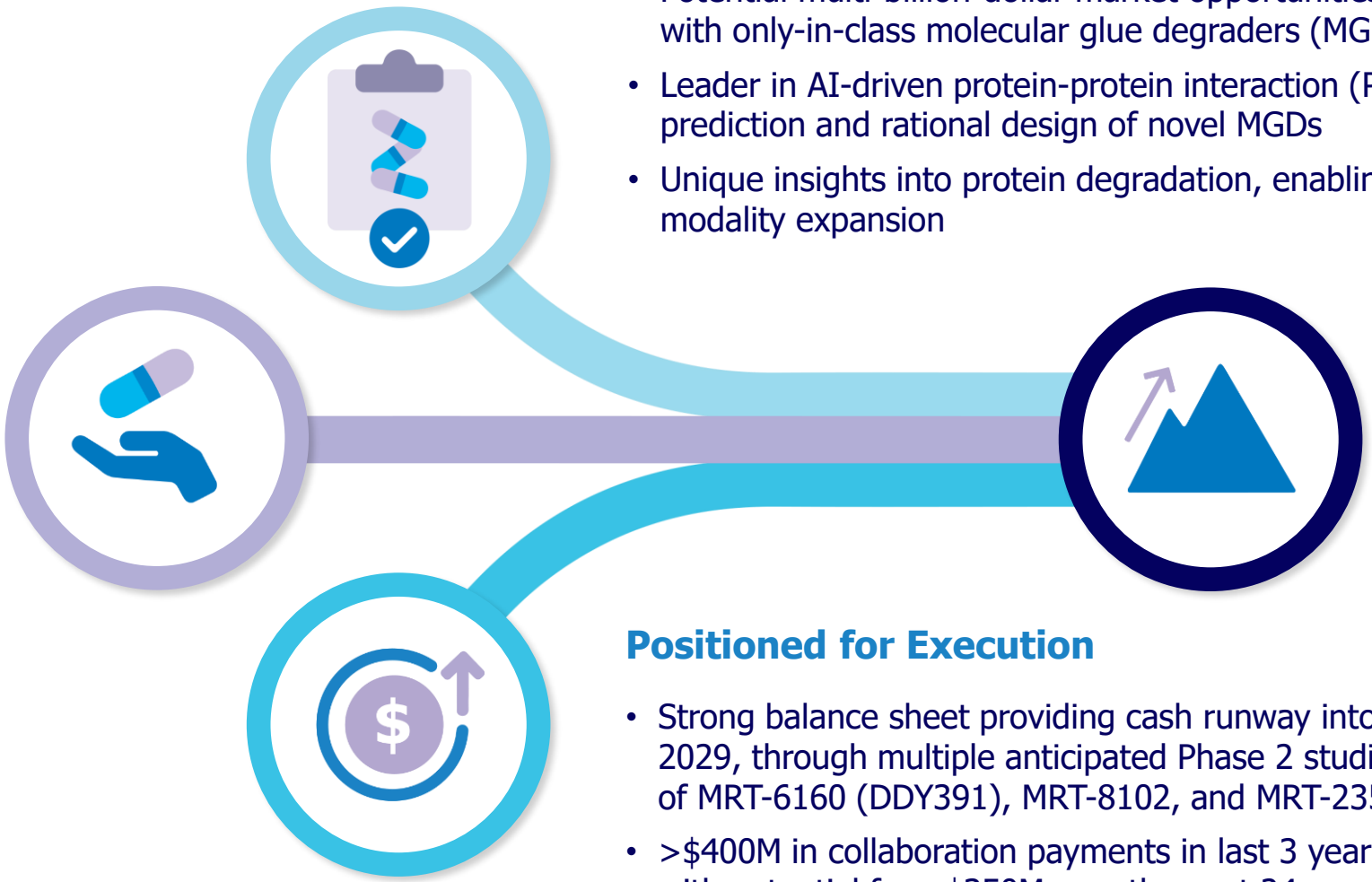
This communication includes express and implied "forward-looking statements," including forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include all statements that are not historical facts and, in some cases, can be identified 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 and to successfully complete research, development and commercialization of our drug candidates in current or future indications, including the timing and results of clinical trials; our progress in developing only-in-class and first-in-class molecular glue degrader ("MGD") therapeutics; the Company's QuEEN discovery engine, including its breadth, versatility and broad potential applications, and the Company's ability to create long-term value through focused pipeline execution and strategic collaborations, to expand the targetable protein space for MGD drug discovery, and to rationally design MGDs with unprecedented selectivity; the growing recognition of MGDs as a distinct and potentially transformative therapeutic modality and our ability to leverage unique insights into protein degradation to expand beyond current modalities, statements around potential multi-billion-dollar market opportunities and the potential for our product candidates to be only-in-class therapies, market size and patient population estimates, commercial opportunity projections and drug class sales projections (including projections incorporating assumptions about anticipated future product approvals), and third-party market data on which such estimates are based, statements about the advancement, timing, design and results of our preclinical and clinical programs, including: (i) the ongoing development of our VAV1-directed degrader MRT-6160 (DDY391), its ongoing Phase 2 studies in Sjögren's disease and psoriatic arthritis being conducted by Novartis, additional planned Phase 2 studies, and its potential broad application across immune-mediated diseases; (ii) the ongoing development of our NEK7-directed MGD MRT-8102, including expectations regarding planned studies in coronary artery disease, gout and hidradenitis suppurativa and their initiation, designs, endpoints, patient populations and data updates; the interpretation and potential clinical significance of results from GFORCE-1 and other clinical and preclinical studies; the potential use of imaging, biomarkers and genetics to inform further clinical development; the potential application of MRT-8102 in additional inflammatory and metabolic indications; and its potential to provide durable upstream pathway inhibition, a favorable safety profile and clinical benefit in these indications, including effects on cardiovascular inflammation and risk, gout flares and tophi, the potential to complement urate-lowering therapies, and disease activity in hidradenitis suppurativa, including the potential for upstream NEK7/NLRP3 pathway inhibition to provide advantages over downstream single-cytokine biologics; (iii) the ongoing development of a next-generation NEK7-directed MGD and expected IND submission timing; (iv) the ongoing Phase 1/2 clinical study evaluating MRT-2359 in combination with enzalutamide in heavily pretreated patients with metastatic CRPC, the interpretation and potential significance of results from that study, the potential clinical activity and opportunity for MRT-2359 in prostate cancer, the ongoing MODeFIRe-1 Phase 2 study evaluating MRT-2359 in combination with apalutamide in mCRPC patients with AR mutations, the potential to expand to other AR-driven populations, including patients without prior second-generation AR inhibitors, and potential expansion into earlier-line settings and combination regimens, and anticipated clinical data updates from the MRT-2359 program; and (v) our discovery programs, including CCNE1 and CDK2, the interpretation and potential clinical significance of preclinical data, including combination therapy data, anticipated IND submissions, plans to announce additional targets, the anticipated timing and significance of scientific presentations and clinical data readouts, the potential clinical benefit of our candidates and advancement and application of our platform; our ability to capitalize on research and translational insights, including the potential translational significance of preclinical data from NEK7-directed programs; our ability to optimize collaborations with industry partners; obligations under our collaboration agreements, including expectations regarding future milestone and other payments, actions taken by our collaborators, and the future development and commercialization of various products; regulatory filings for our development programs, including the planned timing of such regulatory filings, such as IND applications, and potential review by regulatory authorities; our use of capital, expenses and other financial results in the future, availability of funding for existing programs, our ability to fund planned operations into 2029 and anticipated cash runway; statements regarding the expected clinical benefit, efficacy, safety, tolerability, selectivity, differentiation, competitive positioning or other comparative performance of our product candidates relative to existing or investigational therapies, including statements based on cross-trial analyses, and 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, 2025 filed with the U.S. Securities and Exchange Commission on March 17, 2026, most recent Quarterly Reports on Form 10-Q 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, as well as the risk that outcomes of preclinical studies may not be predictive of clinical trial results and the risk that initial or interim results from a clinical trial may not be predictive of the final results of the trial or the results of future trials, and, with respect to comparisons between our product candidates and other therapies discussed in these materials, the risk that such comparisons are based on post-hoc analyses of publicly available information from different clinical trials conducted by different parties with different study designs and patient populations and that no head-to-head clinical trials have been conducted. 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. Market estimates and projections are not forecasts of revenue for our product candidates.

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# Monte Rosa Therapeutics – A Leader in Targeted Protein Degradation

## Delivering Value

- Uniquely differentiated pipeline with 3 clinical programs, addressing highly validated yet undruggable targets in indications with high unmet medical need
- Four Phase 2 initiations expected in 2026
- Multiple additional INDs for wholly owned pipeline anticipated over next 2 years
- Productive ongoing collaborations with industry-leading pharma partners



## Building the Future

- Potential multi-billion-dollar market opportunities with only-in-class molecular glue degraders (MGDs)
- Leader in AI-driven protein-protein interaction (PPI) prediction and rational design of novel MGDs
- Unique insights into protein degradation, enabling modality expansion

## Positioned for Execution

- Strong balance sheet providing cash runway into 2029, through multiple anticipated Phase 2 studies of MRT-6160 (DDY391), MRT-8102, and MRT-2359
- >$400M in collaboration payments in last 3 years with potential for >$350M over the next 24 months

# Most Disease-driving Biology Remains Inaccessible With Conventional Modalities

~15%
"druggable"



~85%

**of the human proteome is considered "undruggable" by conventional small-molecule or antibody approaches**

- **Many disease-driving proteins are not addressable with existing therapeutic modalities**, including small-molecule inhibitors, antibodies, and even other targeted protein degraders, because they lack enzymatic activity or suitable binding pockets.
- **Partial inhibition is often insufficient for validated oncogenic and immunologic targets**, leading to suboptimal efficacy, resistance, and dose-limiting toxicity. Most current drugs modulate protein function rather than eliminating the disease-causing protein.
- As a result, **a significant portion of validated disease biology remains beyond the reach of approved or investigational medicines**.

# Monte Rosa MGDs: Opportunity for Paradigm-Changing Medicines

- **MGDs are small molecules that remove the entire disease-causing protein** rather than partially suppressing its activity, eliminating both enzymatic and non-enzymatic functions
- **Protein elimination enables catalytic and durable pharmacology**, as a single MGD molecule can trigger thousands of repeated degradation events rather than requiring continuous target occupancy
- **MGD approach unlocks targets that are inaccessible to inhibitors or antibodies**, including intracellular proteins lacking well-defined binding pockets or enzymatic activity
- By degrading key signaling nodes, **MGDs can deliver more precise pathway-level modulation** with the potential for improved efficacy and selectivity versus traditional modalities
- AI/ML-powered **QuEEN™ product engine has delivered highly potent, exquisitely selective "only-in-class" MGDs**



# Next-Gen MGD-Based Therapeutics Delivering Meaningful Clinical Results

**MRT-6160/ DDY391 (VAV1)***

- VAV1 is an upstream T- and B-cell signaling node, enabling broad cytokine and autoantibody suppression with a single oral agent
- Phase 1 demonstrated **>90% VAV1 degradation** with **robust cytokine and CD69 suppression** and a favorable safety profile
- Phase 2a/b clinical trials (conducted by Novartis) ongoing in Sjögren's disease and psoriatic arthritis; Monte Rosa expects its collaborator Novartis to initiate additional Ph. 2 studies

**First-in-class VAV1 MGD for diverse immune-mediated diseases (e.g., Sjögren's disease, psoriatic arthritis, others)**

**MRT-8102 (NEK7)**

- NEK7 enables NLRP3 inflammasome assembly, providing upstream DAMPs/IL-1/IL-18 and pyroptosis blockade beyond current biologics
- GFORCE-1 study showed MRT-8102 **normalized multiple ASCVD pathogenic drivers** of local plaque inflammation, thrombosis, and systemic inflammation
- Phase 2 studies planned in patients with gout flares (Q4 2026 initiation), coronary artery disease (H1 2027), and hidradenitis suppurativa (H1 2027)

**First-in-class NEK7 MGD for NLRP3 inflammasome-driven diseases (e.g., coronary artery disease, gout, HS)**

**MRT-2359 (GSPT1)**

- GSPT1 degradation exploits a translation-termination vulnerability in MYC- and AR-driven tumors, particularly AR-mutant mCRPC
- Combination with AR inhibitor delivered compelling activity in heavily pretreated mCRPC, including **100% PSA response rate and RECIST PRs in AR-mutant patients**
- Signal-confirming Phase 2 (MODeFIRe-1) ongoing in AR-mutant mCRPC with a second-generation AR inhibitor

**First-in-class oral GSPT1 MGD for AR mutant metastatic CRPC**



* Novartis has exclusive worldwide rights to develop, manufacture and commercialize MRT-6160 (DDY391) and other VAV1 MGDs. Monte Rosa is eligible for up to $2.1B in development, regulatory, and sales milestones, beginning upon initiation of Phase 2 studies, and is also eligible for 30% US P&L share and ex-US tiered royalties.

# Monte Rosa Pipeline and Upcoming Milestones

| | Target | Compound | Indication(s) | Preclinical | Phase 1 | Phase 2 | Phase 3 | Next Anticipated Milestone |
|---|---|---|---|---|---|---|---|---|
| Immunology & Inflammation | **VAV1** *Licensed to Novartis** | MRT-6160 (DDY391) | Sjögren's Disease | | | | | Additional Ph 2 initiations |
| | | | Psoriatic Arthritis | | | | | |
| | **NEK7** | MRT-8102 | Coronary Artery Disease, Gout, Hidradenitis Suppurativa | | | | | Multiple Ph 2 initiations in 2026-27; gout data update in H2 2027 |
| | | Next Generation | NEK7/NLRP3-driven Diseases | | | | | IND submission in 2027 |
| Oncology | **GSPT1** | MRT-2359 | Castration-resistant Prostate Cancer | | | | | Ph 1/2 update in 2026; Ph 2 update in 2027 |
| | **CCNE1/ CDK2** | Discovery | CCNE1 Amplified Tumors ER+ Breast Cancer | | | | | IND submissions in 2027 |
| Various | **Multiple Targets** *Includes those licensed/optioned to Roche and Novartis* | Discovery | I&I, Oncology, Genetic and Neurological Diseases | | | | | Announce additional targets |



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Notes: IND = investigational new drug. ER = estrogen receptor. I&I = immunology and inflammation.

# Creating Value through Strategic Collaborations

| | NOVARTIS | | Roche |
|---|---|---|---|
| **Scope** | Global license for VAV1 molecular glue degraders, including MRT-6160 (DDY391) (Oct. 2024) | Collaboration for degraders to treat immune-mediated diseases (Sep. 2025) | Strategic collaboration to develop MGDs for cancer and neurological diseases (Oct. 2023) |
| **Financial Terms** | • **$150M upfront** payment<br>• Eligible for up to **$2.1B in development, regulatory, and sales milestones**, starting at Phase 2<br>• Novartis fully funds Phase 2<br>• Eligible for **30% US P&L share** and ex-US tiered royalties | • **$120M upfront** payment plus option maintenance payments<br>• Eligible for **option exercise** payments and development, regulatory, and sales **milestones**, and tiered royalties on global net sales<br>• Up to **$5.7B total deal value** | • **$50M upfront** payment<br>• Eligible for **>$2B preclinical, clinical, commercial and sales milestone payments** and tiered royalties |
| **Strategic Goal** | Accelerate and broaden scope of clinical development of MRT-6160 (DDY391) while retaining substantial value for Monte Rosa | Expedite additional I&I programs leveraging Monte Rosa QuEEN™ platform and Novartis capabilities in immune-mediated diseases | Expand platform to develop MGDs against previously undruggable targets in cancer and neurological diseases |



Notes: Under the terms of the Oct. 2024 Novartis agreement, Monte Rosa has a global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed MGDs, including MRT-6160 (DDY391). Novartis is responsible for conducting and funding Phase 2 studies. Monte Rosa will co-fund any Phase 3 clinical development and will share 30% of any profits and losses associated with the manufacturing and commercialization of MRT-6160 (DDY391) in the U.S., and is also eligible for tiered royalties on ex-U.S. net sales. Under the terms of the Sep. 2025 Novartis agreement, Monte Rosa granted Novartis an exclusive license to an undisclosed target and the exclusive option to obtain licenses to two programs from Monte Rosa's preclinical immunology portfolio. Under the terms of the Roche agreement, Monte Rosa Therapeutics will lead discovery and preclinical activities against multiple select cancer and neurological disease targets to a defined point. Roche gains the right to exclusively pursue further preclinical and clinical development of the compounds.

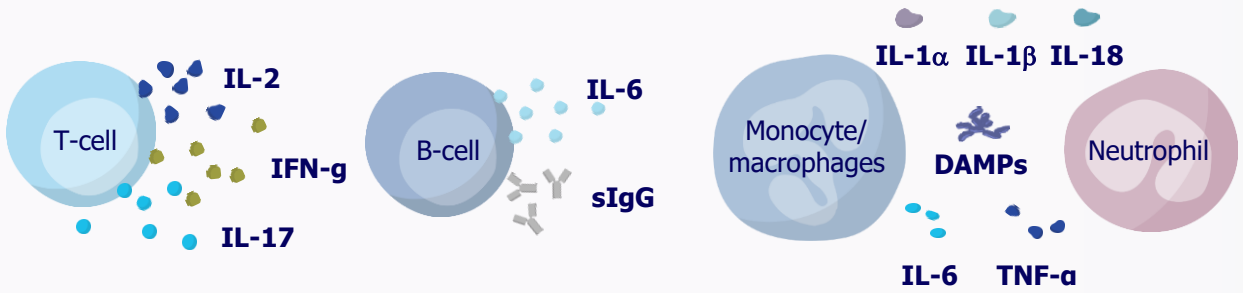
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# I&I Pipeline

# Beyond Biologics-in-a-Pill: Potential for Next-Generation I&I Drugs

## Degrading previously undruggable signaling nodes to modulate multiple cytokines

| | **VAV1 (Adaptive Immunity)** MRT-6160 (DDY391) | **NEK7 (Innate Immunity)** MRT-8102 |
|---|---|---|
| **Primary Cell Types** | T cells, B cells | Monocytes, macrophages, neutrophils |
| **Core Biology** | Antigen-driven activation | Inflammasome assembly |
| **Key Cytokines/ Immune Mediators** | IL-2, IL-17, IFN-γ, IL-6, sIgG | IL-1α/β, IL-18, DAMPs, IL-6, TNF-α |
| **Therapeutic Impact** | Targeted immune modulation | Control of inflammasome-driven inflammation |




- **Most current biologics inhibit single downstream cytokines**, often leaving parallel immune pathways active and limiting depth and durability of response
- **VAV1 and NEK7 sit at upstream control points in adaptive** (T- and B-cell) and innate (myeloid / neutrophil) immunity, respectively
- **Degrading these nodes suppresses entire cytokine programs**, not just individual mediators, across both arms of the immune system
- Upstream, multi-arm immune control **supports broader efficacy potential while using oral administration**, creating substantial differentiation versus injectable, single-target biologics therapies



*DAMPs = damage-associated molecular patterns*

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# VAV1 Program (MRT-6160/DDY391)

*Licensed to Novartis*

# MRT-6160 (DDY391) At a Glance

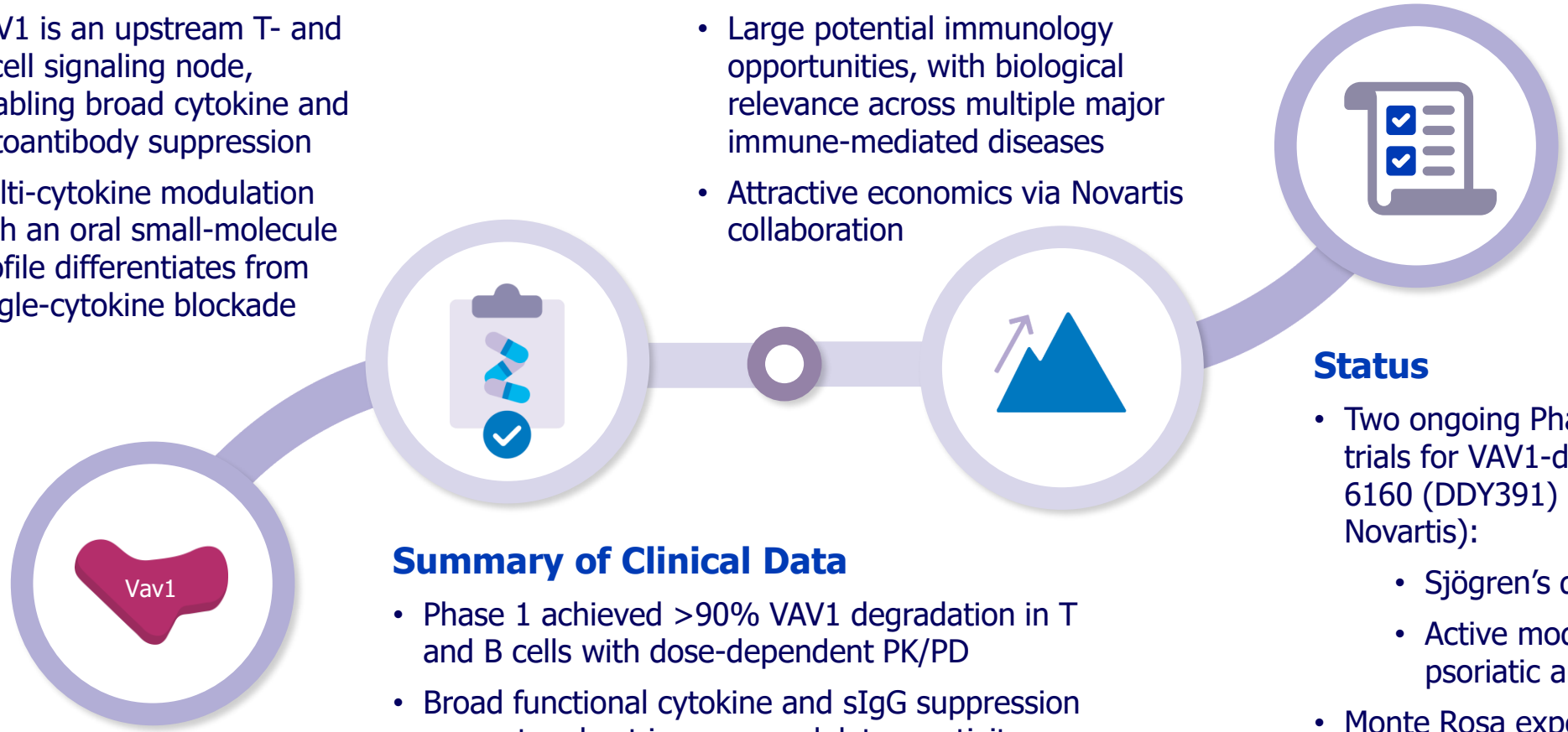
## First-in-class VAV1 MGD for diverse T and B-cell driven diseases

### VAV1 Rationale

- VAV1 is an upstream T- and B-cell signaling node, enabling broad cytokine and autoantibody suppression
- Multi-cytokine modulation with an oral small-molecule profile differentiates from single-cytokine blockade

### Opportunity

- Large potential immunology opportunities, with biological relevance across multiple major immune-mediated diseases
- Attractive economics via Novartis collaboration




### Summary of Clinical Data

- Phase 1 achieved >90% VAV1 degradation in T and B cells with dose-dependent PK/PD
- Broad functional cytokine and sIgG suppression supports robust immunomodulatory activity
- Favorable safety profile with no SAEs observed in Phase 1 study supports chronic use

### Status

- Two ongoing Phase 2a/b clinical trials for VAV1-directed MGD MRT-6160 (DDY391) (conducted by Novartis):
  - Sjögren's disease (SjD)*
  - Active moderate to severe psoriatic arthritis (PsA)**
- Monte Rosa expects its collaborator, Novartis, to initiate additional Phase 2 studies of MRT-6160 (DDY391) in immune-mediated diseases



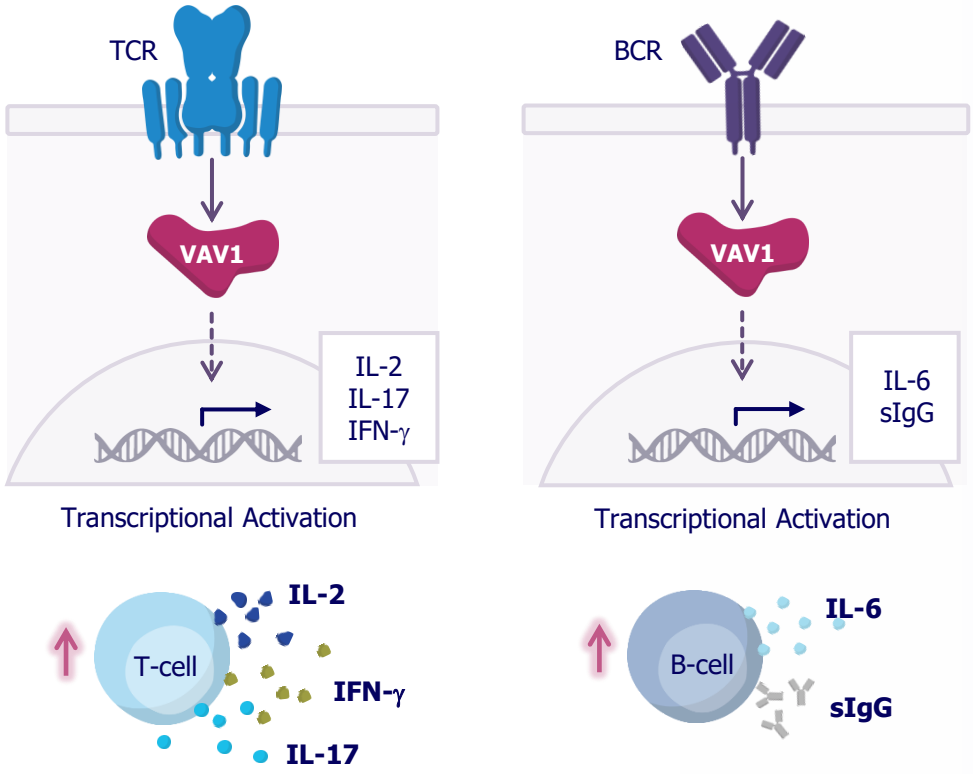
* NCT07737743. ** NCT07801495

Note: Monte Rosa has a global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed MGDs, including MRT-6160 (DDY391) . Novartis is responsible for conducting and funding Phase 2 studies. Monte Rosa will co-fund any Phase 3 clinical development and will share 30% of any profits and losses associated with the manufacturing and commercialization of MRT-6160 (DDY391) in the U.S., and is also eligible for tiered royalties on ex-U.S. net sales.

# MRT-6160: Upstream Immune Modulation via Targeted VAV1 Degradation

## Oral MGD delivering coordinated suppression of pathogenic T- and B-cell signaling

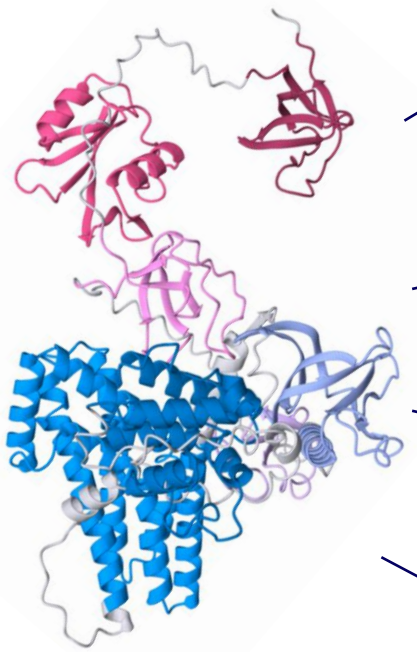
**MRT-6160 Reduces Multiple Pathogenic Cytokines (IL-2, IL-6, IL-17) and Secreted Antibodies (sIgG)**




- MRT-6160 is an oral molecular glue degrader that **selectively induces degradation of the VAV1 protein**
- Loss of VAV1 **disrupts T-cell and B-cell receptor signaling**, suppressing pathogenic activation and effector function
- VAV1 degradation **reduces multiple inflammatory cytokines and autoantibody production** rather than targeting a single mediator
- By acting on an upstream signaling node, MRT-6160 delivers **coordinated modulation of adaptive immune responses** through **clinically validated pathways**

# VAV1: Upstream Targeting Node Controlling Clinically Validated Pathways

| VAV1 signaling is associated with several T and B cell immunologic outcomes | Clinically validated pathway in autoimmune/inflammatory disease |
|---|---|



VAV1

T cell activation

ORENCIA® (abatacept)

RINVOQ® upadacitinib

B cell activation/Plasma cell differentiation (Antibody production)

Rituxan® Rituximab

VYVGART® Hytrulo

Th17 response

Cosentyx® (secukinumab)

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

Pro-inflammatory cytokine production

HUMIRA® adalimumab

ACTEMRA® tocilizumab

# MRT-6160 (DDY391) Ongoing Phase 2a/b Study in Sjögren's Disease (SjD)



## A serious, progressive, autoimmune disease

- Impacts multiple organs, causing a wide spectrum of symptoms such as dryness, fatigue, pain, and an increased risk of lymphoma
- Can carry a significant burden and impact on quality of life
- Estimated to affect up to 4M people in the U.S.
- Second most prevalent rheumatic autoimmune disease



| | |
|---|---|
| **Sponsor** | Novartis |
| **Purpose** | Evaluate efficacy, safety, and tolerability of MRT-6160 (DDY391) up to 52 weeks in participants with SjD and determine dose response relationship in participants to support dose selection for Phase 3 |
| **Phase** | 2a/b |
| **Design** | Randomized, double-blind, placebo-controlled, global multicenter |
| **Number of participants** | 344 estimated |
| **Primary endpoints** | Change from baseline in EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) at week 24 |
| **Identifier** | NCT07737743 |



*Sources: National Academies of Science, Engineering, and Medicine, Selected Immune Disorders and Disability (2022); Perella et al. Rheumatol Ther (2023); Negrini et al. Clin Exp Med. (2022); Mariette et al. N Engl J Med. (2018); Gairy et al. Rheumatology (2021); Narvaez et al. Sci Rep. (2020); clinicaltrials.gov. Note: Monte Rosa has a global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed MGDs, including MRT-6160 (DDY391). Novartis is responsible for conducting and funding Phase 2 studies. Monte Rosa will co-fund any Phase 3 clinical development and will share 30% of any profits and losses associated with the manufacturing and commercialization of MRT-6160 (DDY391) in the U.S. and is also eligible for tiered royalties on ex-U.S. net sales.*

# MRT-6160 (DDY391) Ongoing Phase 2a/b Study in Psoriatic Arthritis (PsA)



## A chronic, progressive, inflammatory disease

- Part of a family of life-long inflammatory diseases (spondyloarthritis) that target the joints
- Symptoms include joint pain and stiffness, skin and nail psoriasis, swollen toes and fingers, persistent painful swelling of the tendons, and irreversible joint damage
- Affects up to 2.4M people in the U.S. and up to 50M people worldwide
- Closely associated with psoriasis: up to 40% of patients with psoriasis may develop psoriatic arthritis



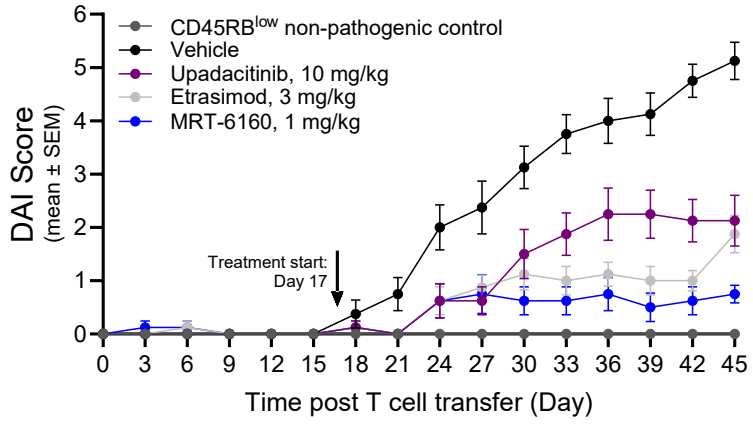
| | |
|---|---|
| **Sponsor** | Novartis |
| **Purpose** | Evaluate efficacy, safety, and tolerability of MRT-6160 (DDY391) in participants with psoriatic arthritis (PsA) and determine dose response relationship in participants to support dose selection for Phase 3 |
| **Phase** | 2a/b |
| **Design** | Randomized, double-blind, placebo-controlled, global multicenter |
| **Number of participants** | 220 estimated |
| **Primary endpoint** | Number of participants achieving American College of Rheumatology 50 (ACR50) response at Week 12 |
| **Identifier** | NCT07801495 |



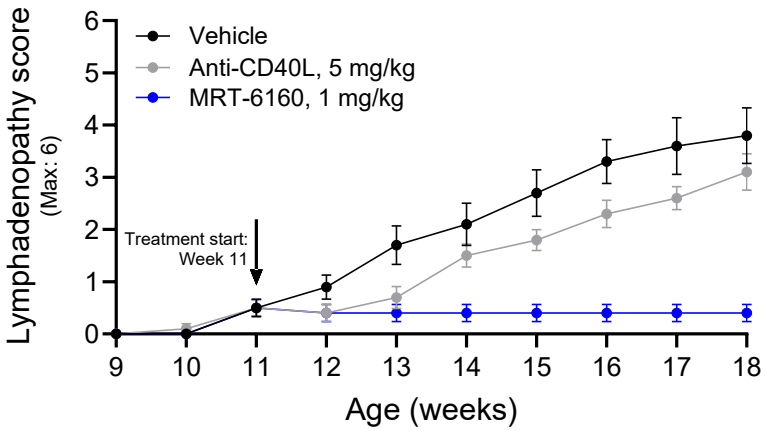
*Sources: National Psoriasis Foundation – Psoriasis statistics; Mease et al. Drugs (2014); clinicaltrials.gov.*
*Note: Monte Rosa has a global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed MGDs, including MRT-6160 (DDY391). Novartis is responsible for conducting and funding Phase 2 studies. Monte Rosa will co-fund any Phase 3 clinical development and will share 30% of any profits and losses associated with the manufacturing and commercialization of MRT-6160 (DDY391) in the U.S. and is also eligible for tiered royalties on ex-U.S. net sales.*

# Preclinical Data Support Broad Potential Application of MRT-6160

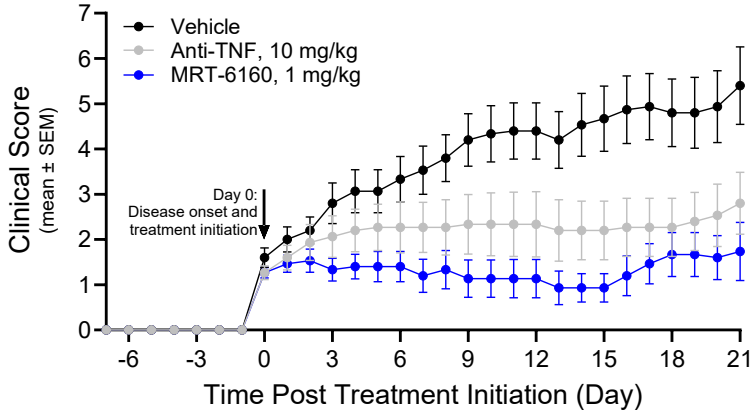
## T-cell transfer-induced colitis model of inflammatory bowel disease



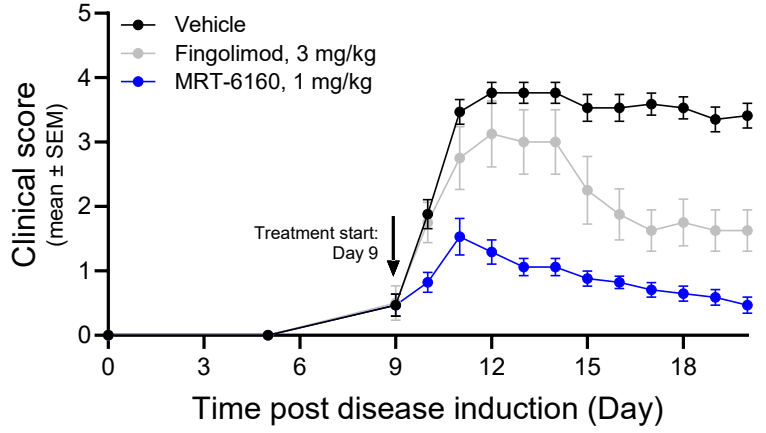

## MRL-Fas$^{lpr}$ spontaneous autoimmune disease model (e.g., SLE, Sjögren's)




## Collagen-induced arthritis model of autoimmune arthritis




## EAE model of neuroinflammatory disease (e.g., multiple sclerosis)



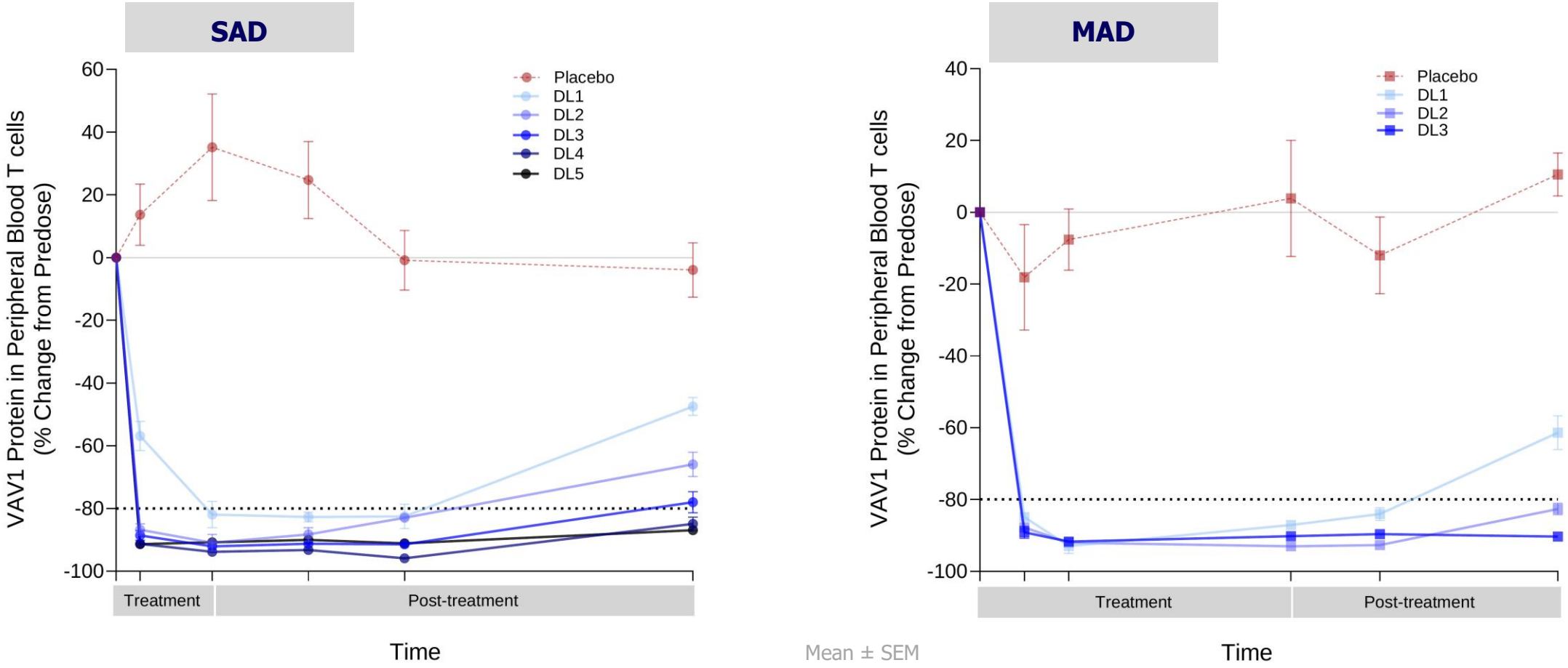

Sources: DDW 2024 poster_T-cell transfer colitis; ACR 2025 poster_MRL-FASlpr; EULAR 2024 poster_CIA; FOCIS_2025 poster_EAE model

EAE = experimental autoimmune encephalomyelitis; SLE = systemic lupus erythematosus

# Summary of Phase 1 Data

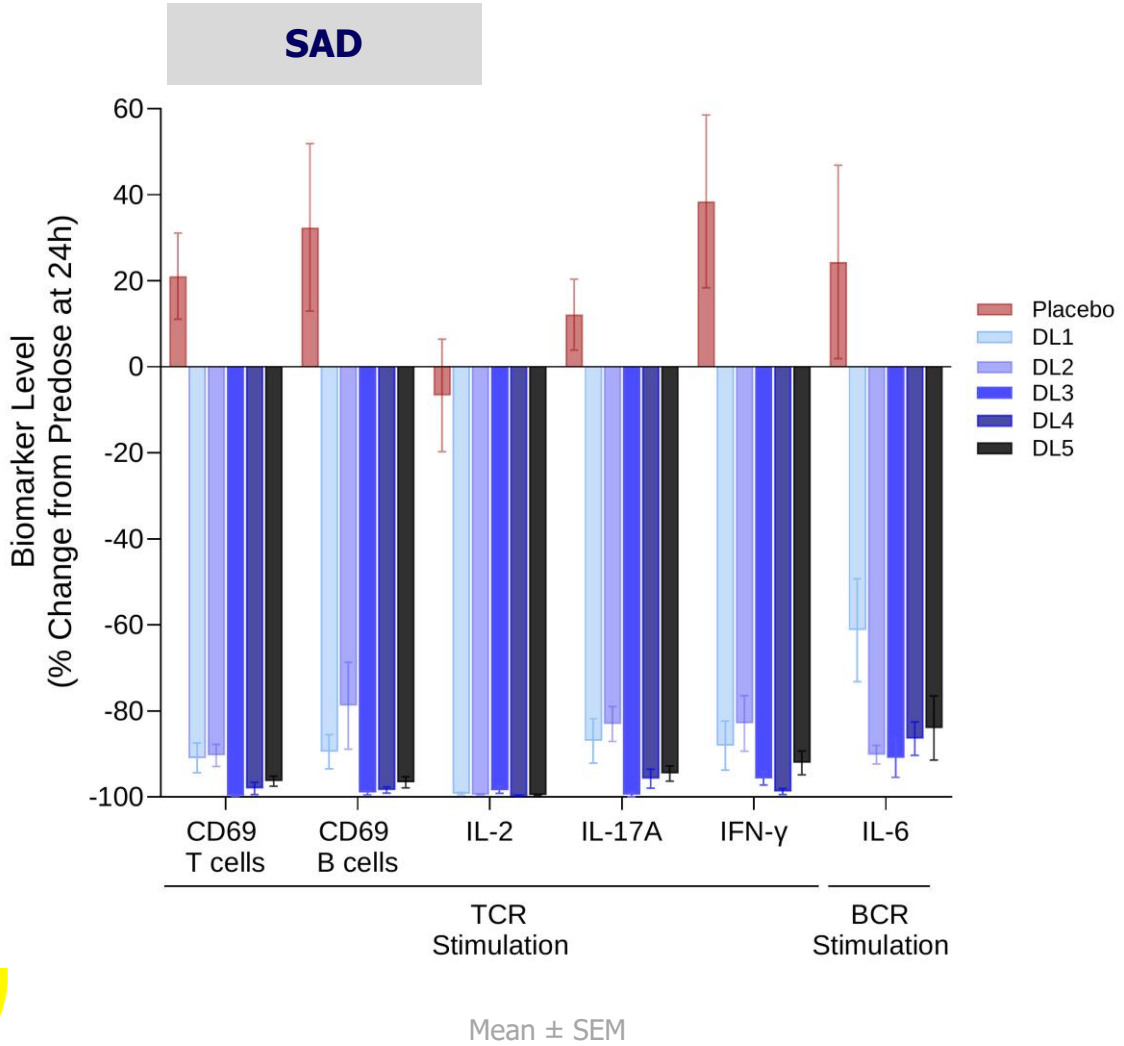
- Study design: Randomized, placebo-controlled study in >70 healthy volunteers of single-ascending (5 dose levels) and 7-day multiple-ascending (3 dose levels) oral doses
- Pharmacodynamic and functional *ex vivo* studies performed during Phase 1 suggest **significant effects on cytokine production** can be achieved **following** marked and sustained **degradation of VAV1** in humans
- 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 **broad potential applications in multiple immune-mediated diseases**

# 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

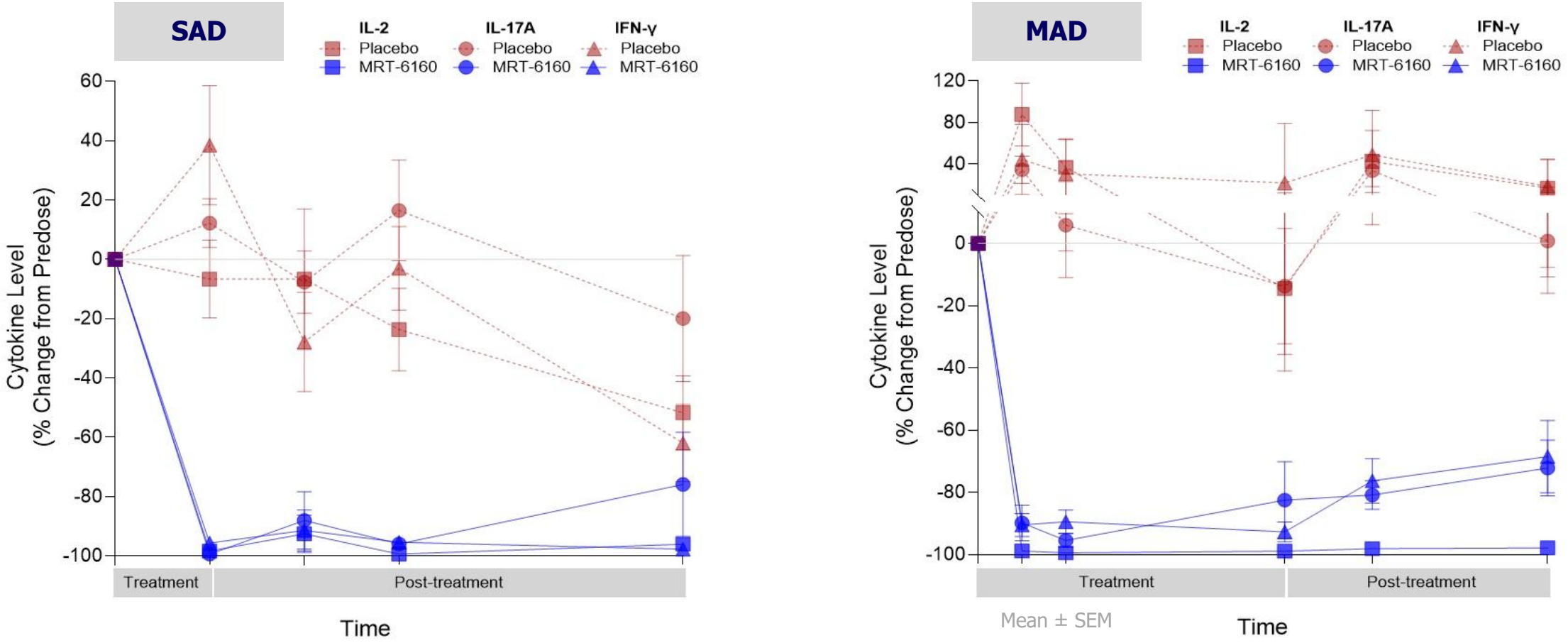



MRT-6160 treatment:

- 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 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)

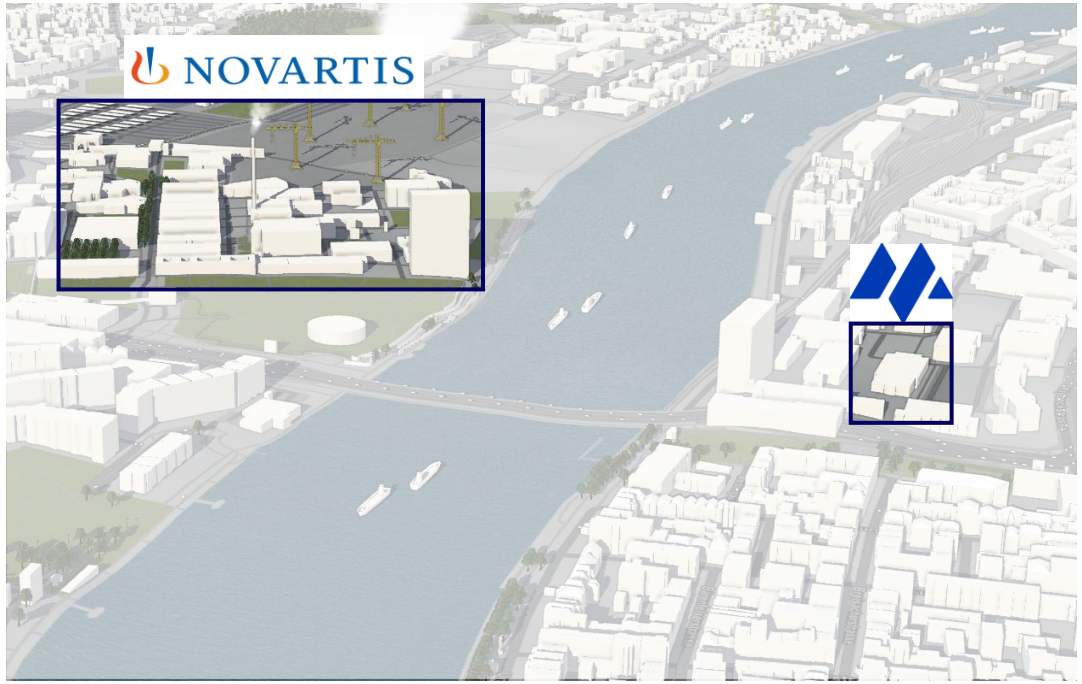
# Safety Summary

- 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)

# Strategic Agreement to Accelerate and Broaden MRT-6160 (DDY391) Development

NOVARTIS

| | |
|---|---|
| **Scope** | Global license agreement with Novartis to advance VAV1-directed molecular glue degraders including MRT-6160 (DDY391), in development for immune-mediated conditions (announced Oct. 2024) |
| **Financial Terms** | • $150M upfront payment<br>• Eligible for up to **$2.1B in development, regulatory, and sales milestones**, beginning upon initiation of Phase 2 studies<br>• Novartis fully funds Phase 2 studies<br>• Eligible for **30% US P&L share** and ex-US tiered royalties |
| **Strategic Goal** | **Accelerate and broaden scope of clinical development** of MRT-6160 (DDY391) while **retaining substantial value** for Monte Rosa |




**Basel**



Notes: Monte Rosa has a global exclusive development and commercialization license agreement with Novartis to advance VAV1-directed MGDs, including MRT-6160 (DDY391). Novartis is responsible for conducting and funding Phase 2 studies. Monte Rosa will co-fund any Phase 3 clinical development and will share 30% of any profits and losses associated with the manufacturing and commercialization of MRT-6160 (DDY391) in the U.S., and is also eligible for tiered royalties on ex-U.S. net sales.

Monte Rosa Therapeutics

# NEK7 Program (MRT-8102)

# MRT-8102 At a Glance

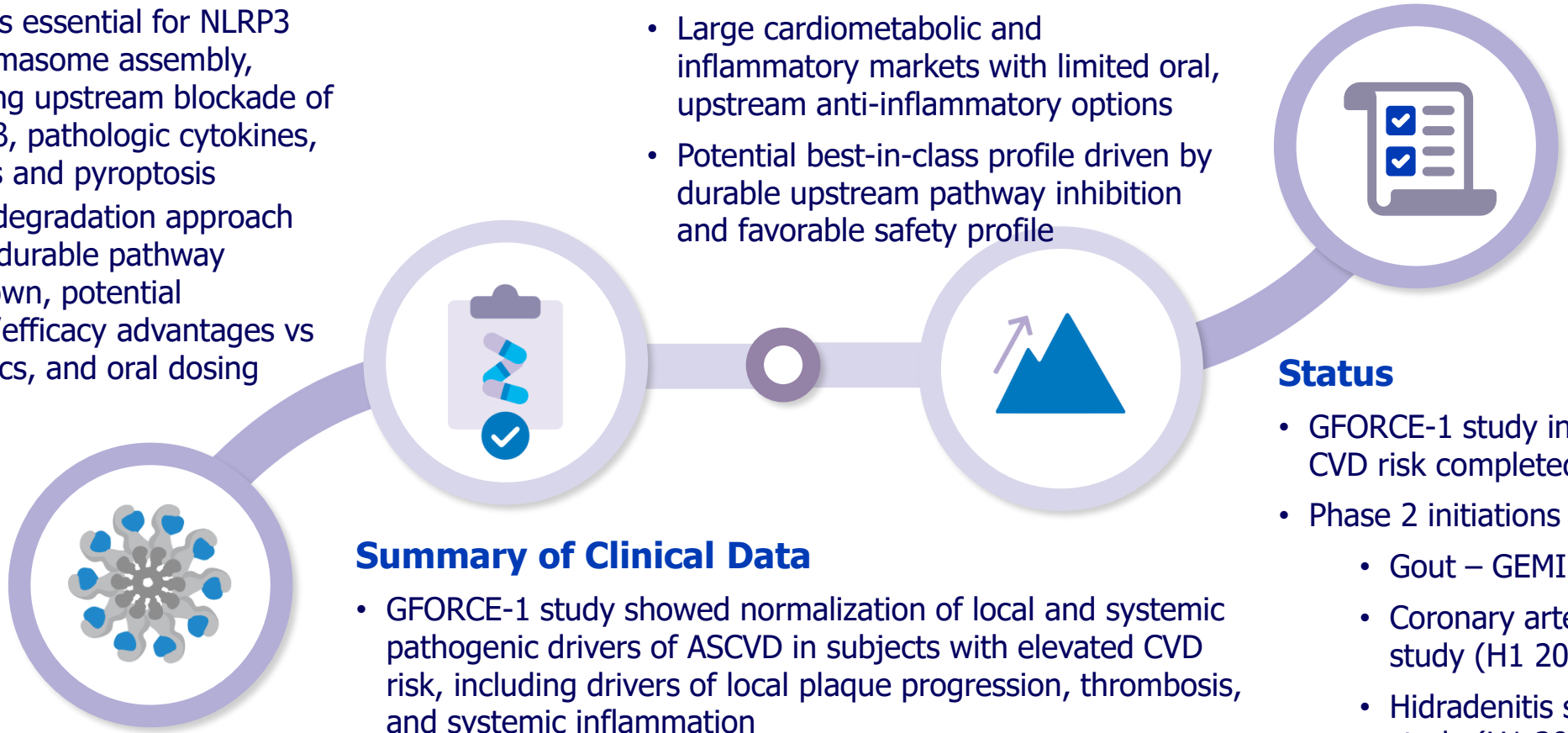
## First-in-class NEK7 MGD for NLRP3 inflammasome driven diseases

### NEK7 Rationale

- NEK7 is essential for NLRP3 inflammasome assembly, enabling upstream blockade of IL-1α/β, pathologic cytokines, DAMPs and pyroptosis
- NEK7 degradation approach offers durable pathway shutdown, potential safety/efficacy advantages vs biologics, and oral dosing

### Opportunity

- Large cardiometabolic and inflammatory markets with limited oral, upstream anti-inflammatory options
- Potential best-in-class profile driven by durable upstream pathway inhibition and favorable safety profile



### Summary of Clinical Data

- GFORCE-1 study showed normalization of local and systemic pathogenic drivers of ASCVD in subjects with elevated CVD risk, including drivers of local plaque progression, thrombosis, and systemic inflammation
- Data demonstrated favorable safety and tolerability profile for MRT-8102 over 4 weeks dosing + 4 weeks follow-up, with no SAEs; TEAE rates comparable to pbo; no evidence of increased infection risk*

### Status

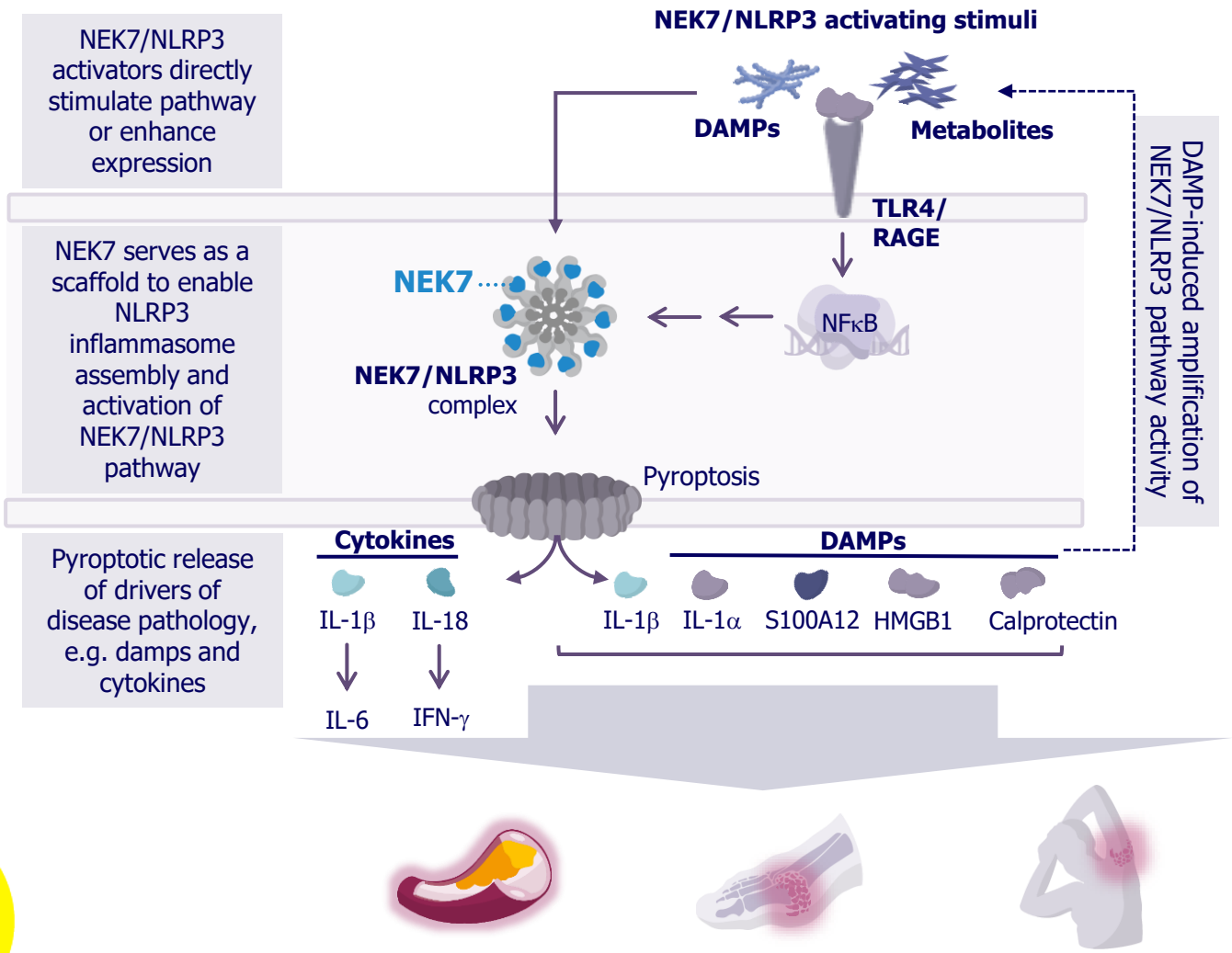
- GFORCE-1 study in subjects with elevated CVD risk completed
- Phase 2 initiations expected:
  - Gout – GEMINI-1 study (Q4 2026)
  - Coronary artery disease – GFORCE-2 study (H1 2027)
  - Hidradenitis suppurativa – GALAXY-1 study (H1 2027)



* As of Oct. 1, 2026 disclosure

**Note:** Comparisons between MRT-8102 and other therapies represented herein are based on post-hoc analyses comparing MRT-8102 clinical information with publicly available information for other therapies. Any comparisons use information from different clinical trials, conducted by different parties, at different points in time, with differences in trial designs and patient populations. No head-to-head clinical trials have been conducted, cross-trial comparisons should not be made, and this information is provided only for illustrative purposes.

# NEK7 Enables Pathogenic NLRP3 Activation to Drive Disease Biology



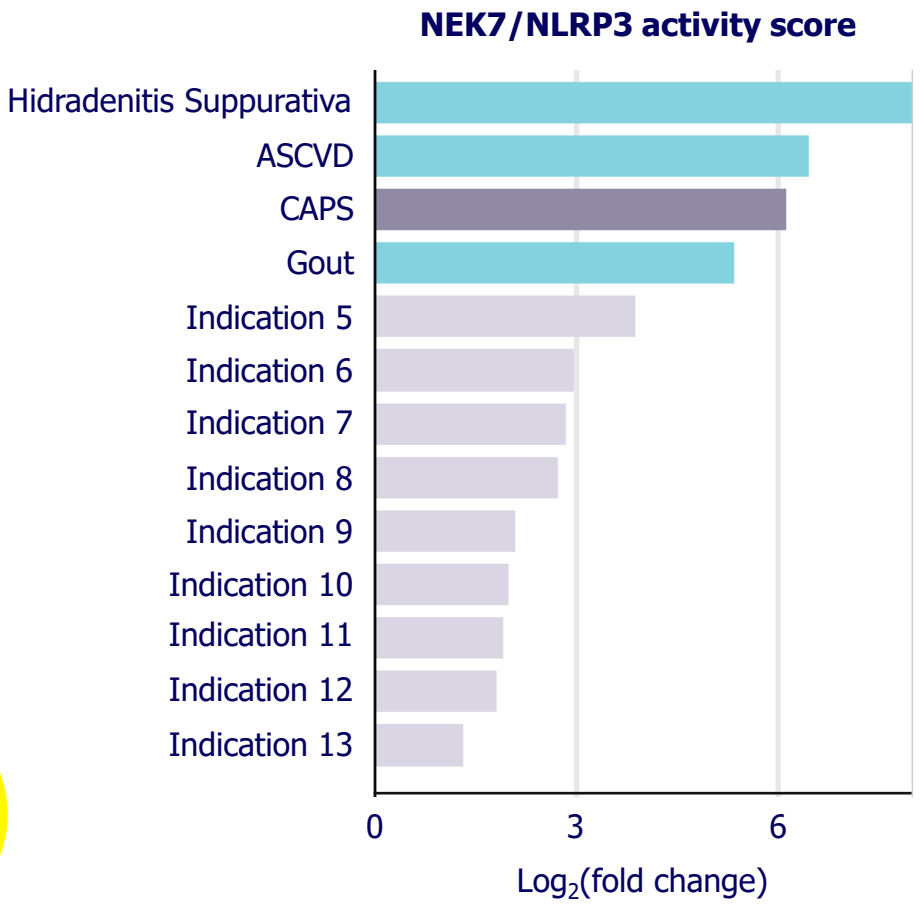

- Multiple metabolic and genetic factors can promote NEK7-mediated NLRP3 inflammasome complex assembly in a kinase-independent manner
- NEK7/NLRP3 pathway activation causes pyroptotic cell death, leading to release of **IL-1α/β, IL-18, and DAMPs (e.g., HMGB1, Calprotectin, S100A12)**
  - IL-1β and IL-18 are highly inflammatory cytokines
  - **DAMPs** further stimulate NEK7/NLRP3 activity and concomitantly promote NLRP3-independent cytokine/chemokine production in neighboring cells
  - DAMPs and IL-1β are responsible for the majority of local pathogenesis and tissue changes characteristic of ASCVD, gout, hidradenitis suppurativa (HS) and other indications
- **Interference with pathway at most upstream point, through NEK7 degradation, has potential to achieve most meaningful efficacy across NEK7/NLRP3 driven indications**, including ASCVD, gout and HS



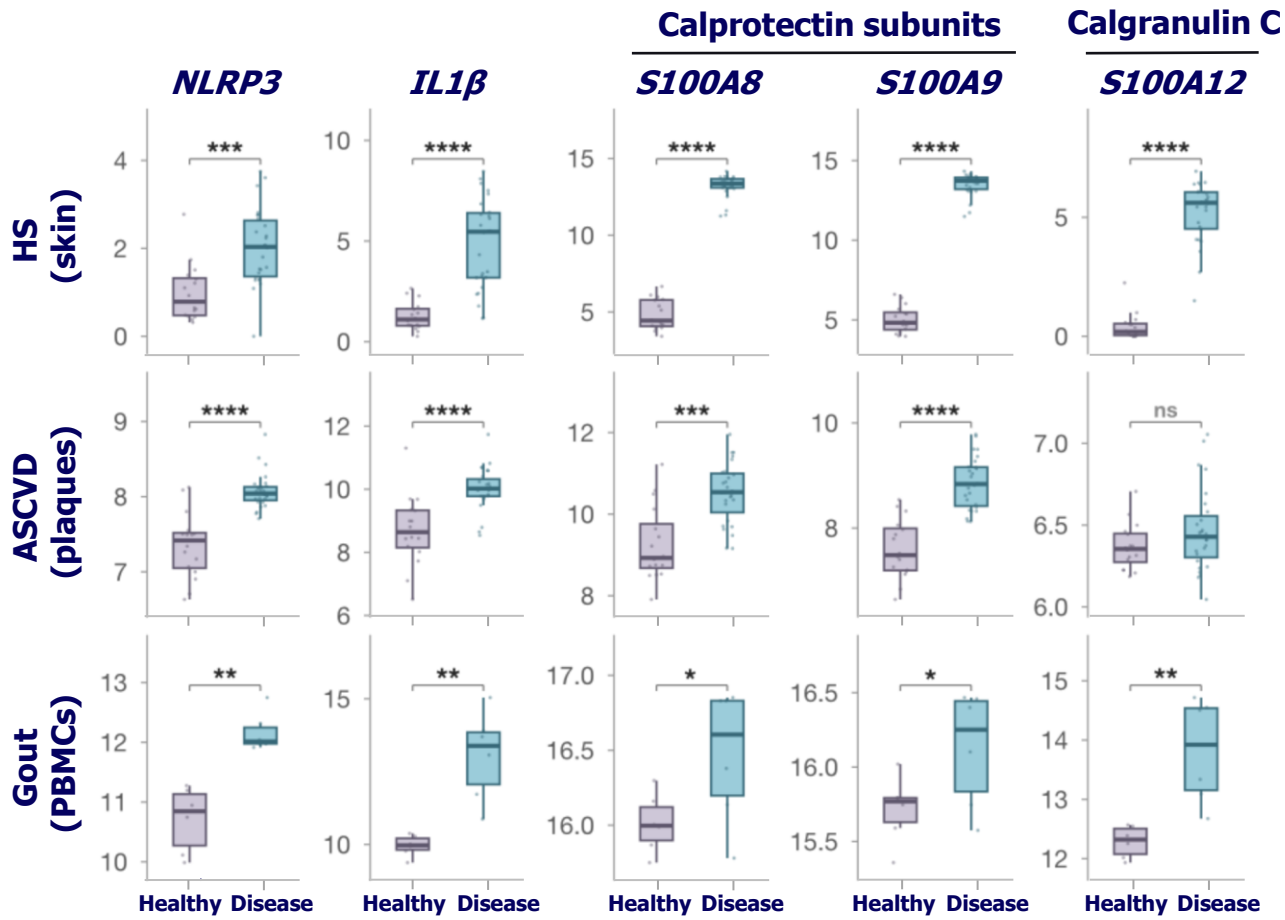
*DAMPs = damage-associated molecular patterns; HMGB1 = High-mobility group box 1; CRP = C-reactive protein*

# Members of the NEK7/NLRP3 Downstream Signaling Cascade are Elevated Across Multiple Indications with High Unmet Need

**ASCVD, HS and gout have highest pathological NEK7/NLRP3 activity scores**




**Upregulation of pathogenic cascade downstream of pyroptosis is conserved across the top NEK7/NLRP3-active indications**




*Data sources: accessions GSE155176, GSE163154, GSE160170*

# Large Market Opportunities Supported by Strong Biological Rationale

## Coronary artery disease



- **Central role of NEK7/NLRP3 in plaque biology** and atherogenic progression
- **~14M** U.S. patient population, with **45-50%** of patients having experienced at least one prior MI
- **>30%** of CAD patients suffer from **residual inflammatory risk** despite optimized lipid-lowering therapy
- **NEK7 degradation and NEK7/NLRP3 pathway inhibition** provide a novel, upstream approach **that goes beyond downstream single-cytokine depletion** to address residual CVD risk

## Gout



- **Canonical NEK7/NLRP3-pathway disease**: MSU crystals trigger NEK7-mediated NLRP3 assembly, driving IL-1β release and flare pathology
- **~10M** U.S. patient population, with **~30%** comorbid with renal disease
- SOC treatment often insufficient in preventing gout flares, resulting in **breakthrough flares**, a leading contributor to poor adherence
- High unmet need for long-term flare prophylaxis: **>55%** of gout-treating physicians surveyed are **not satisfied with current prophylaxis options** (**>65% for CKD co-morbid** patients)

## Hidradenitis suppurativa

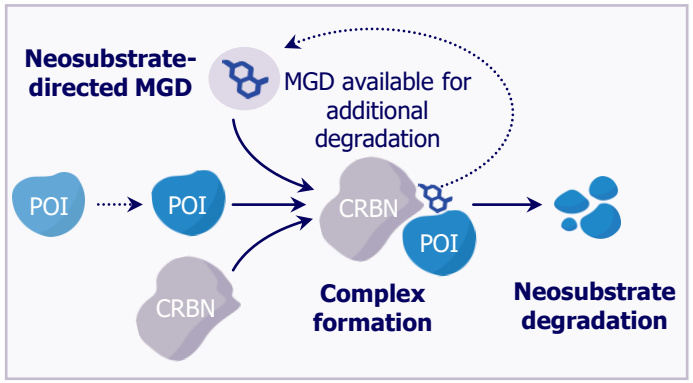


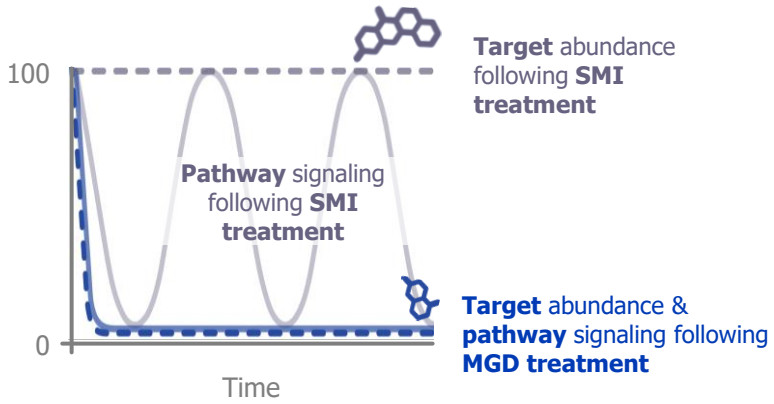
- **Highest NEK7/NLRP3-pathway activity score** of any indication studied, with consistent upregulation of NLRP3, IL-1β, and DAMPs in lesional tissue
- **~400-450K** U.S. addressable population; significant unmet need with **~55%** patients poorly managed with SOC
- Opportunity to target inflammasome assembly, **upstream of IL-1 and DAMP-driven pathogenesis in HS lesions**, unlike single-mediator TNF/IL-17 biologics
- IL-1 antibodies provide promising POC but NEK7/NLRP3 inhibition expected to impact broader array of pathological drivers than IL-1 biologics

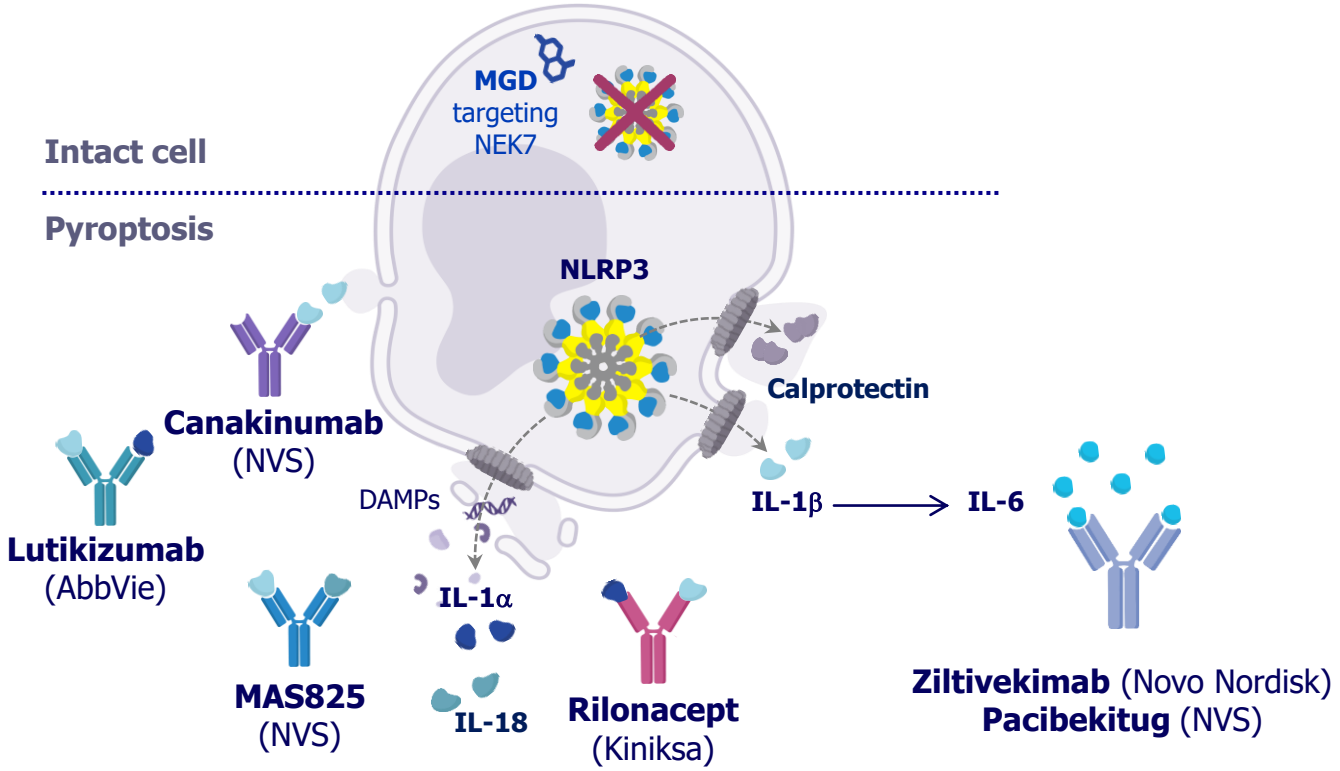


*Sources: Su et al. Journal of Vascular Surgery (2024); Alanaeme et al. Am Heart J Plus (2022); Peikert et al. Clin Res Cardiol. (2020); Martin et al. Circulation (2025); Virani et al. Circulation (2021); Tsao et al. Circulation (2023); Singh et al. Rheumatology (Oxford) (2019); Cowen Therapeutics Outlook (Oct 2024, Oct 2025); Monte Rosa survey of gout-treating physicians (Nov 2025)*

# NEK7-directed MGD MRT-8102 is Highly Differentiated Over Other NLRP3/IL-1/IL-6 Pathway Modalities




In contrast to small molecule inhibitors (SMIs), MRT-8102 induces **catalytic NEK7 degradation**, long-lasting inflammasome disassembly and inactivation, and sustained inhibition of cytokine release

Due to inhibition of NLRP3 assembly, MRT-8102 **prevents pyroptotic cell death-mediated release of inflammatory cytokines and DAMPs** known to drive disease pathology.

Mono- and bispecific biologics fail to inhibit pyroptosis, leading to incomplete blockage of the pathological drivers of disease

DAMP = damage-associated molecular pattern

# MRT-8102 for Coronary Artery Disease

# CAD: Large Opportunity to Address Atherosclerotic Risk with a Safe, Oral Treatment Targeting NEK7

## CAD Market Overview



**~14M**
Adults suffer from CAD in the U.S.

**45-50%**
Patients have experienced at least 1 prior MI

## High Unmet Medical Need in CAD

**>30%**
CAD patients suffer from residual inflammatory risk despite optimized lipid-lowering therapy

**~1 in 7**
CAD patients experience a subsequent MACE event within 5 years despite achieving target LDL-C level

**~30-fold**
Greater risk of cardiac mortality in patients* with high coronary plaque inflammation (determined by FAI score)

## MRT-8102 Opportunity

Potential to **complement existing lipid** and **metabolic therapies**

- Targeting NEK7/NLRP3 pathway could provide **broader suppression of atherogenic** and **thrombotic pathways**
- **Oral administration** aligns with SOC and facilitates potential combo approaches

Potential for **differentiated efficacy and safety profile vs. IL-1 and IL-6 antibodies**

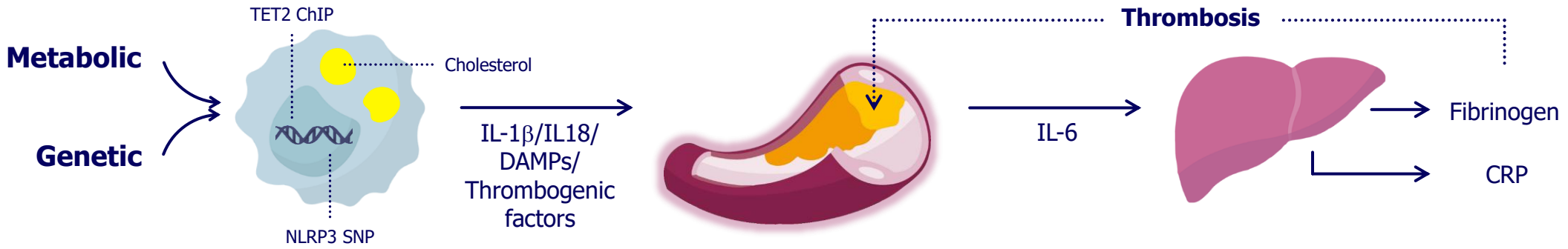
- Upstream mechanism addresses high-risk plaque biology **beyond** suppression of individual cytokines
- Ability to provide robust inflammation control **without increased infection risk**



**Risk of cardiac mortality captures all patients, with and without CAD, from ORFAN study undergoing diagnostic coronary CTA*

*Sources: Su et al. Journal of Vascular Surgery (2024); Alanaeme et al. Am Heart J Plus (2022); Martin et al. Circulation (2025); Chan et al. Lancet (2024); Hassan et al. Front Cardiovasc Med. (2026); Kim et al. Korean Circ J. (2026); Watanabe et al. J Am Heart Assoc. (2026); Virani et al. Circulation (2021); Tsao et al. Circulation (2023); Budoff et al. Eur Heart J. (2023); Peikert et al. Clin Res Cardiol. (2020); Wong et al. J Clin Lipidol. (2019); Sanchez-Bacaicoa et al. Eur J Clin Invest. (2021); Schwartz et al. J Am Coll Cardiol. (2021); O'Donoghue et al. Circulation (2022)*

# Clinical Experience Supports Upstream Targeting of NEK7/NLRP3 Pathway as a Superior Approach to Impact MACE




| LoDoCo2 | COLCOT | CANTOS | ZEUS |
|---|---|---|---|
| NEK7/NLRP3 pathway modulation | | IL-1β neutralization | IL-6 neutralization |
| • 5,522 pts with **chronic CAD (>6 months** post MI) randomized to ***colchicine*** or pbo<br>• Baseline median CRP unknown<br>• Colchicine **reduced MACE by 31%**; no risk of infection, significant GI AEs | • 4,745 pts ≤ 30 days **post-MI** randomized to ***colchicine*** or pbo<br>• Baseline median CRP 4.28 mg/L<br>• Colchicine **reduced MACE by 23%**; no risk of infection, significant GI AEs | • 10,061 pts **≥ 30 days post MI** randomized to ***canakinumab*** (anti-IL-1β) or pbo<br>• Mean time since MI **4.57 years**<br>• Baseline CRP≥2mg/L (median 4.1 to 4.2)<br>• Canakinumab **reduced MACE by 15%**; risk of infection increased | • 6,376 pts with **ASCVD and moderate-severe CKD** randomized to ***ziltivekimab*** (anti-IL-6) or pbo<br>• Baseline CRP≥2mg/L (median 4.5)<br>• No significant effect on MACE; risk of infection increased |

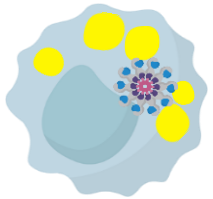
**Clinical efficacy achieved**



*Results are from separate clinical trials with different agents, populations and study designs and should not be interpreted as head-to-head comparisons*

# The Multifaceted Pathogenic Role of the NEK7/NLRP3 Pathway in Plaque Biology and Atherogenic Progression

**DAMPs, crystals, metabolic factors** | **Genetic (NLRP3 SNPs, CHIP mutations)**



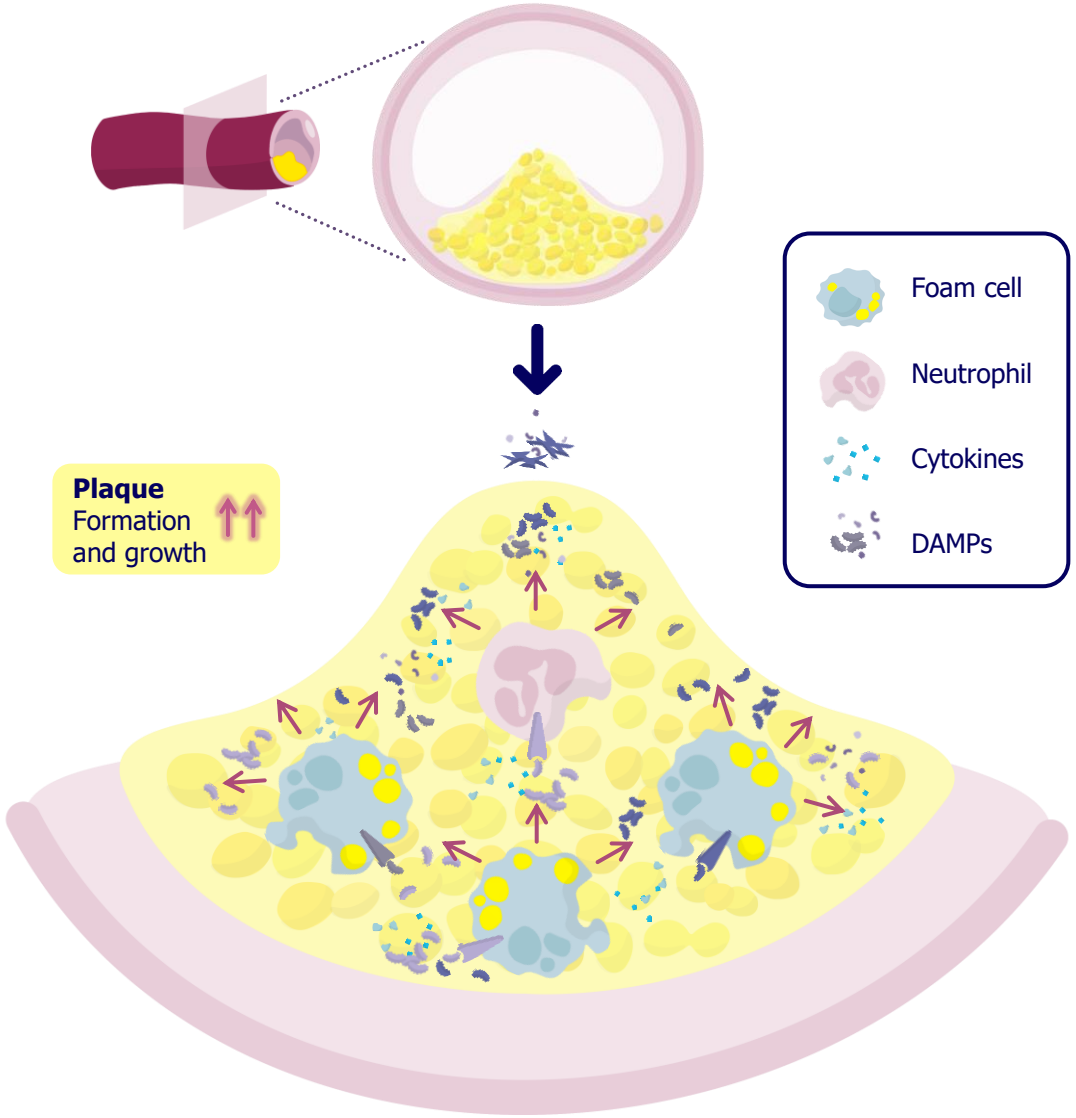
**NEK7/NLRP3 effectors**

IL-1β | IL-18 | DAMP release | Oxidative stress

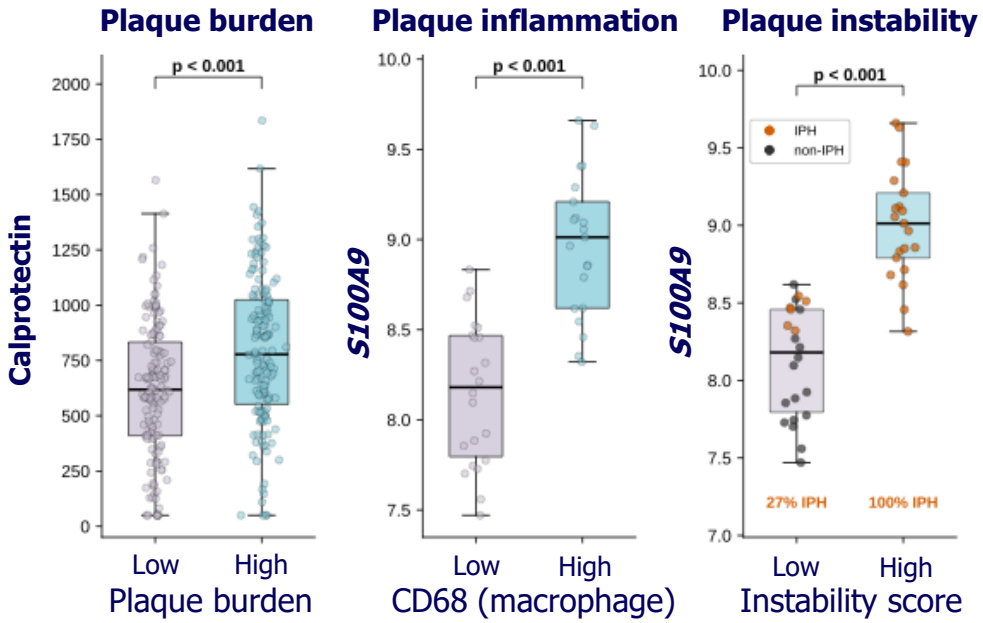
| | | | |
|---|---|---|---|
| **Endothelial Cell** dysfunction enhances adhesion molecules and vascular leakage | Increased uptake of oxLDL and retention of oxidized cholesterol in **foam** cells | **VSMC** proliferation or phenotypic transformation/ de-differentiation | Thrombogenic factors from pyroptotic **macrophages, VSMC and ECs** |
| **Plaque formation** | **Plaque growth** | **Vessel wall alterations** | **Thrombosis** |

**Cardiovascular events (MI / Ischemic stroke / ACS)**

# DAMPs, Including Calprotectin, Potently Activate NEK7/NLRP3 in Neighboring Cells to Amplify Plaque Burden and Instability




**Calprotectin levels correlate with plaque burden, inflammation and instability**

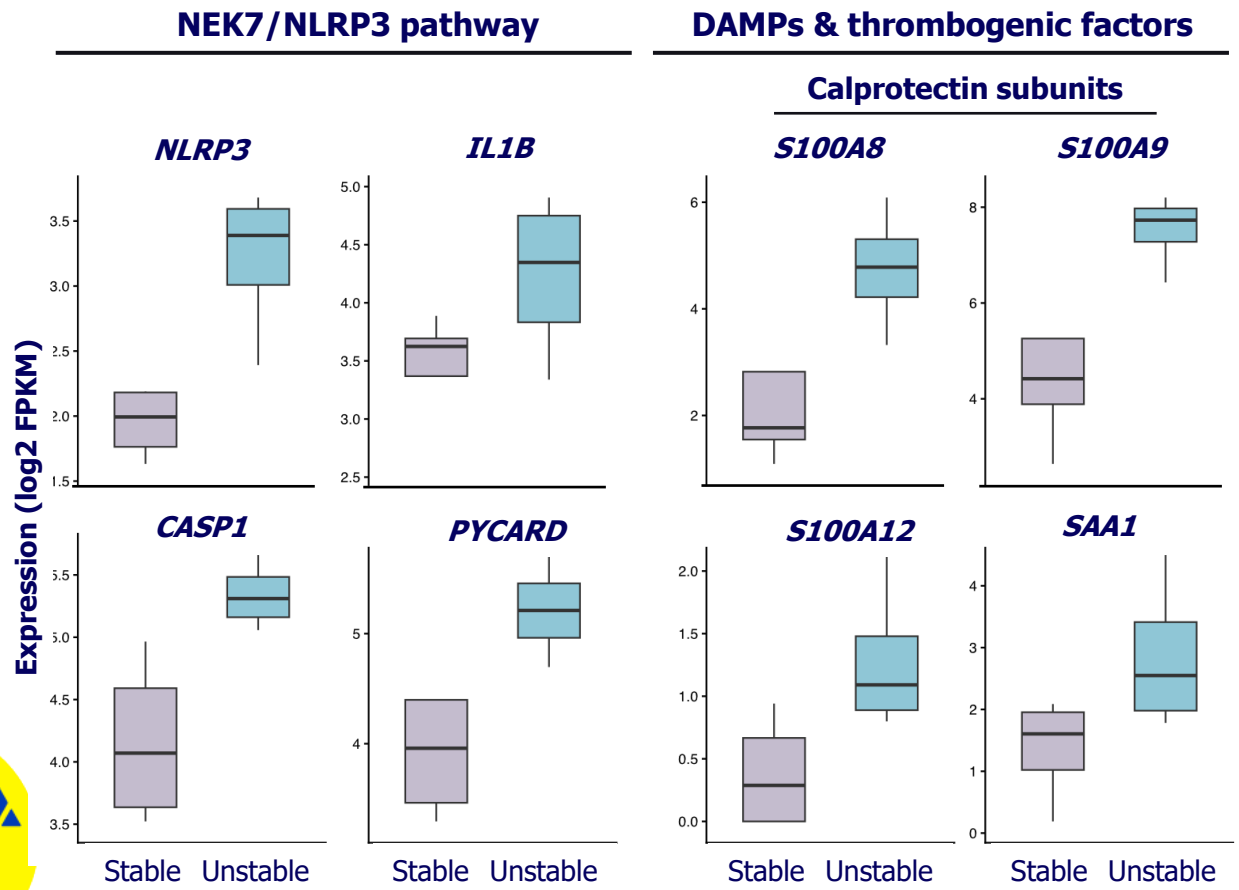



Circulating calprotectin levels significantly associate with increased plaque burden, enhanced plaque inflammation, and plaque instability

*Croce et al., Circulation, 2009. Data from Peng et al., Cardiovasc Diabetol, 2011, Cheng et al., Front Med, 2022, Cotoi et al. 2014, Demir et al., Medicina, 2026, and GSE163154. Simulated data (n = 300) calibrated to the meta-analytic pooled r = 0.290 (REML, 5 estimates, N = 1,133), median-split into burden groups, and compared by Mann–Whitney U test.*

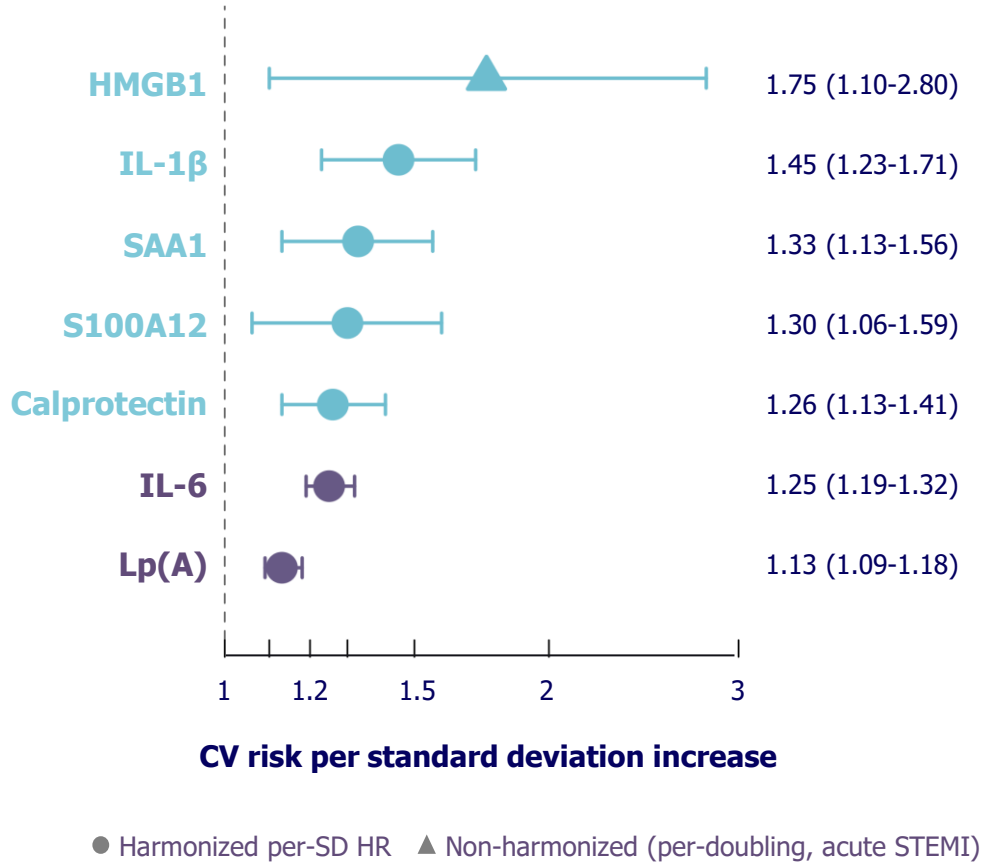
# Mediators of NLRP3 Pathway-Driven Atherosclerosis/-thrombosis are Established Cumulative Cardiovascular Risk Factors

## NLRP3, relevant cytokines, and DAMP levels are significantly increased in unstable plaques




*RNA-seq of stable and unstable section of human atherosclerotic plaques GEO GSE120521*

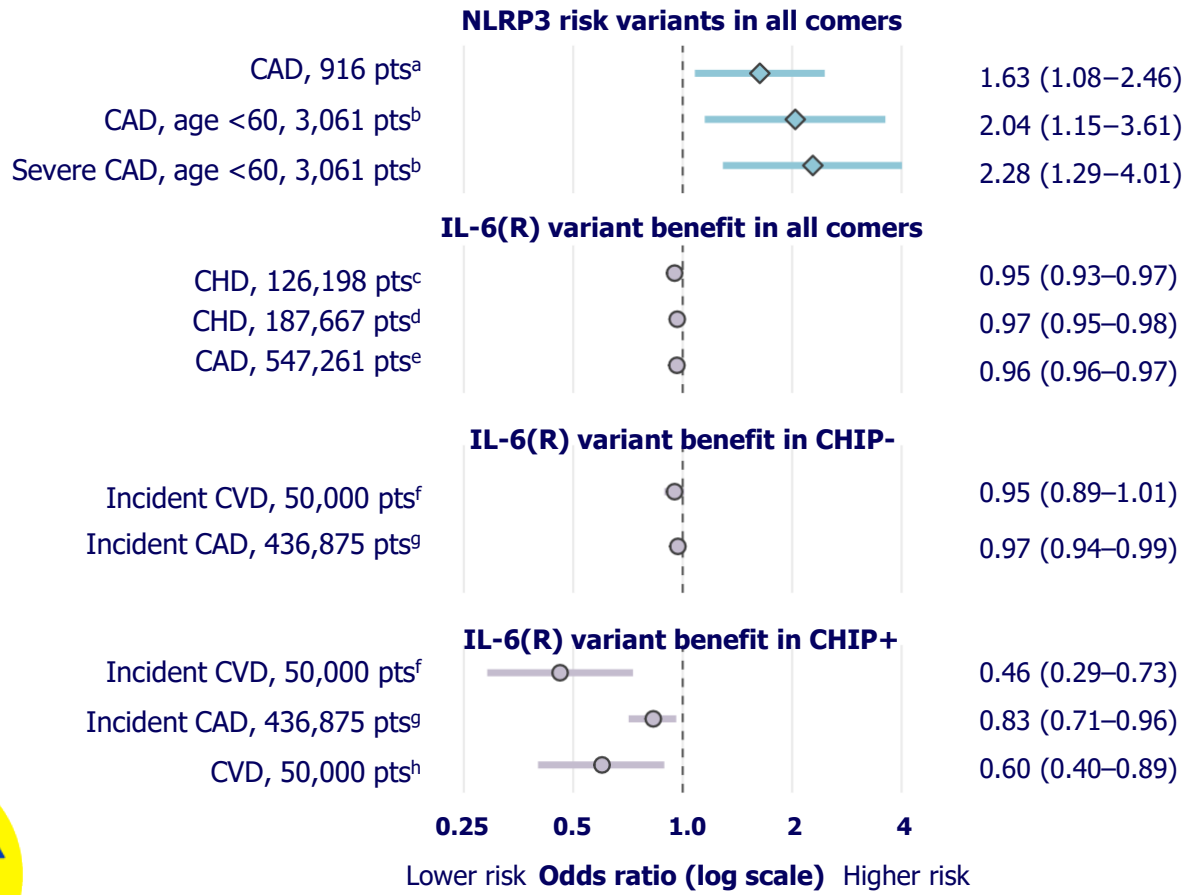
## Cumulative CV risk associated with NEK7/NLRP3-relevant cytokines, lipids, and DAMPs



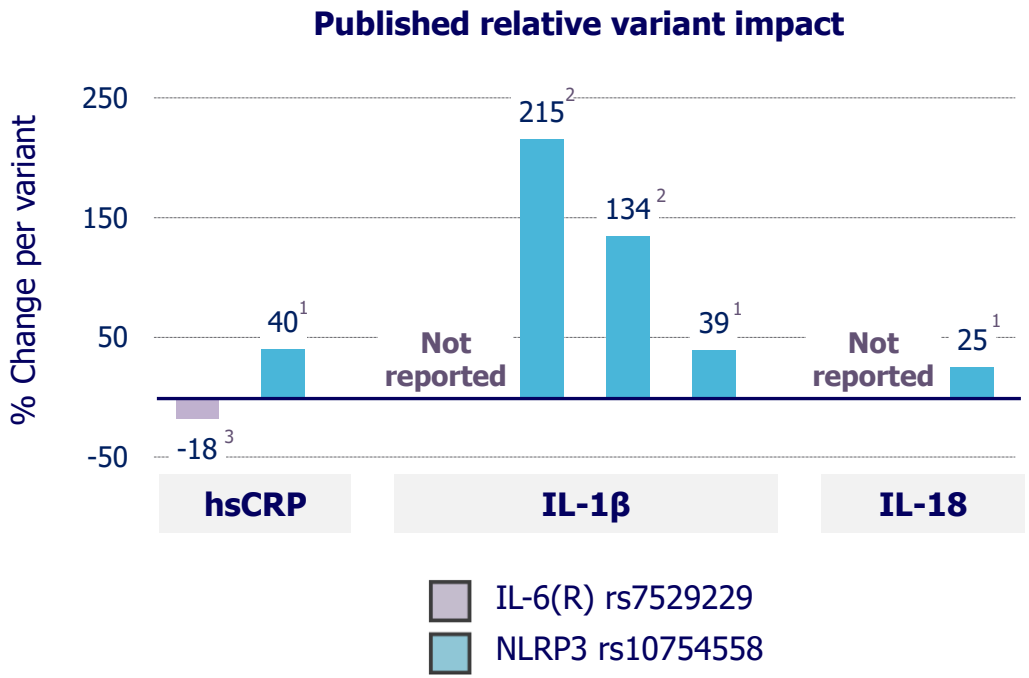

*Data from PMIDs 24026779, 29957458, 21435605, 25341801, 39322770, 28845751, 28428221, 39178030, 30006491, 19622820, 23034020*

# NLRP3 Activating Variants Increase Signaling and Cardiovascular Risk

## NLRP3 variant associated with strong risk of CVD; IL-6(R) benefit restricted to CHIP+ subgroup



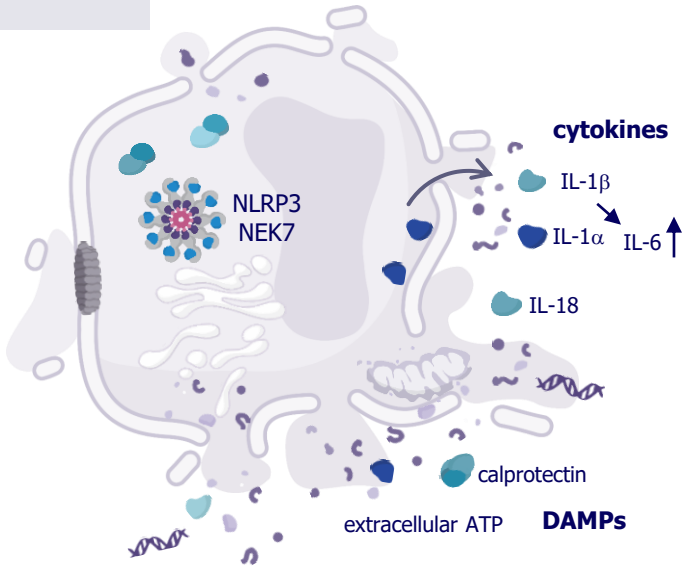

## NLRP3 risk variant shows larger effect on inflammatory cytokines and CRP compared to IL-6(R) variant

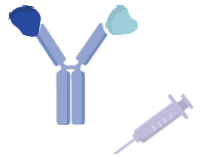



Left: [a]Zhou et al. (2016); [b]Schunk et al. (2021); [c]Swerdlow et al. (2012); [d]Sarwar et al. (2012); [e]Rosa et al. (2019); [f]Bick et al. (2019); [g]Vlasschaert et al. (2023); [h]Kessler et al. (2022); Right: [1]Wu et al. (2022); [2]Zhou et al. (2016); [3]Tchuisseu-Kwangoua et al. (2025). % differences: NLRP3 rs10754558 = (GG – CC)/CC; IL-6(R) rs7529229 (proxy rs2228145) = (CC – AA)/AA

# MRT-8102 Potently Inhibits Pyroptosis and Release of DAMPs and IL-1β

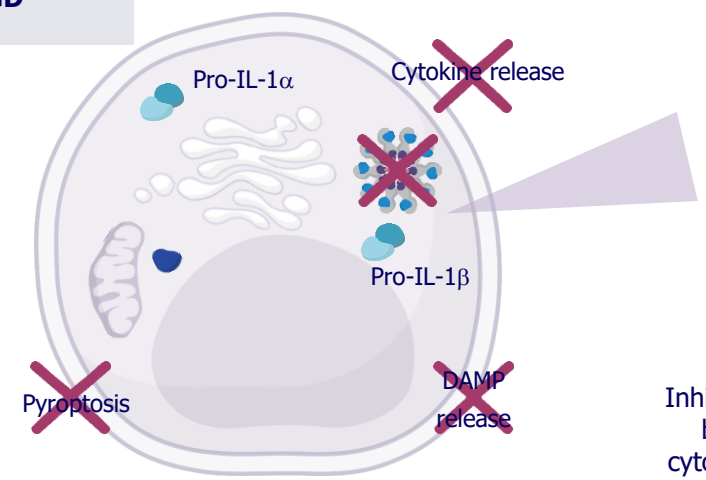
**Anti-IL-1/IL-6 biologics**

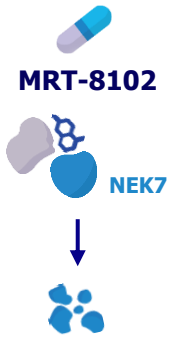


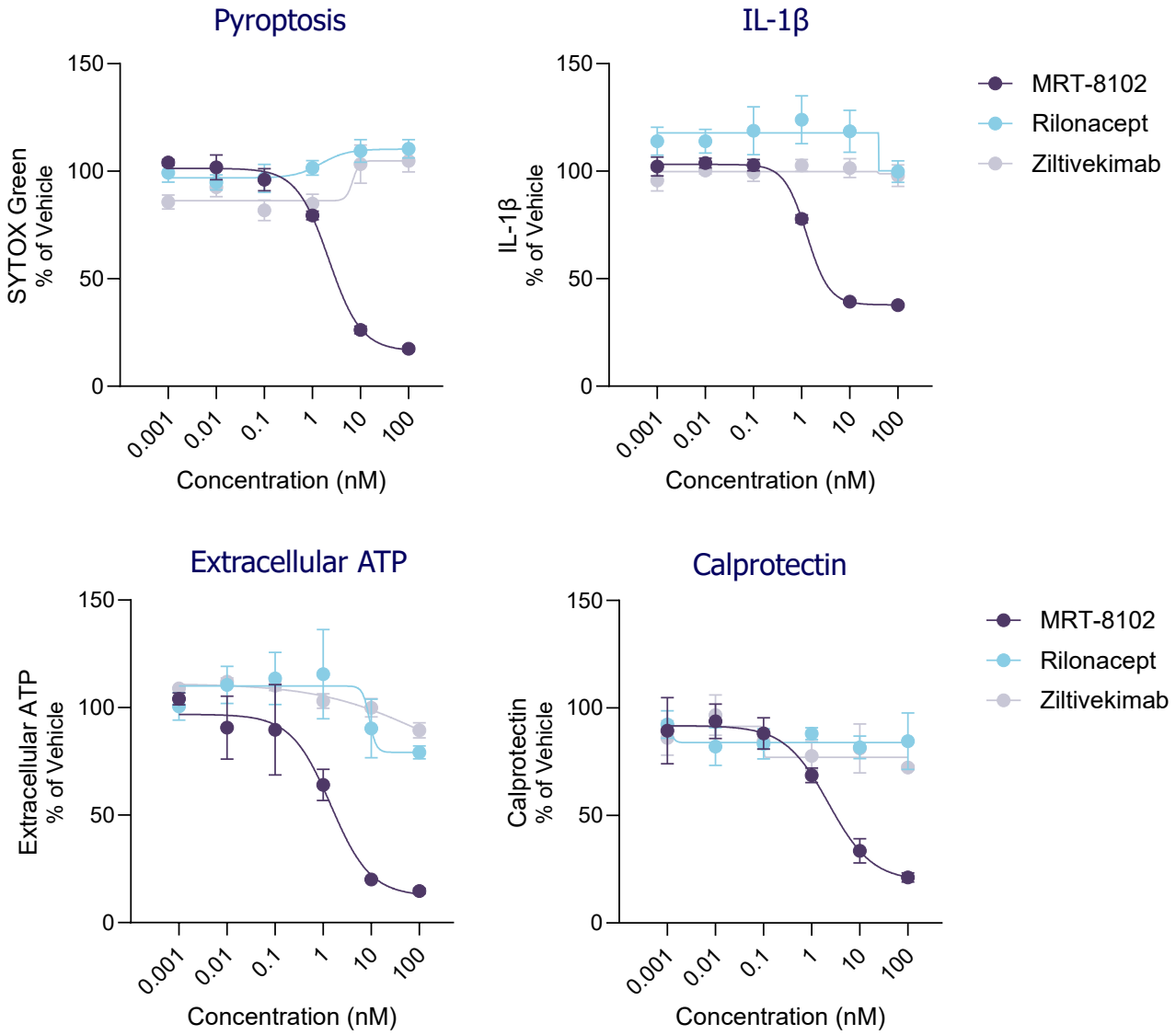
**IL-1/IL-6 blocking biologics**
Do not inhibit pyroptosis and only neutralize IL-1 or IL-6

**NEK7 MGD**




**NEK7 MGDs**
Inhibit pyroptosis and block release of cytokines and DAMPs




*DAMP = damage-associated molecular pattern; Data generated using LPS + Nigericin stimulation in human monocyte-derived macrophages (hMDM)*

# GFORCE-1 showed Broad Normalization of Elevated Pathogenic Drivers of ASCVD

**GFORCE-1: A Phase 1 Study of MRT-8102 in Subjects with Elevated CVD Risk**

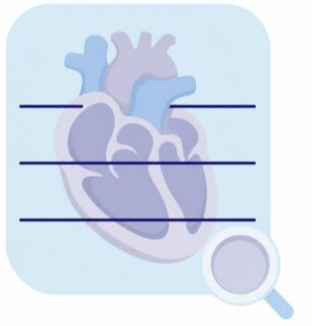
- **Study design**: 108 subjects with elevated CVD risk; 8-week study, randomized to MRT-8102 at 5, 20, and 40 mg QD, or placebo for 4 weeks dosing
- **Robust target engagement**: Sustained and equal NEK7 degradation across all three dose levels
- **Favorable safety and tolerability profile**: No SAEs; TEAE rate similar to placebo (33% vs. 30%); no increased infection risk
- **Activity on plaque and vessel wall biology and thrombogenic factors demonstrated**, supporting broad potential for MRT-8102 to impact ASCVD and other NEK7/NLRP3-driven disease:
  - **Pathogenic drivers** of ASCVD, including IL-1β, HMGB1, Calprotectin, S100A12, SAA, and Fibrinogen **reduced to healthy-volunteer levels** at all doses
- **Opportunity for precision medicine approach**: NLRP3 risk-allele carriers show higher baseline levels for DAMPs, suggestive of elevated pathway activity and potential for faster and more severe atherosclerotic remodeling, and identifying a genetically enrichable population for potential future development

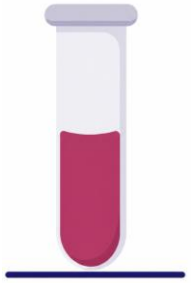
# GFORCE-2: A Differentiated Phase 2 Approach

**Inform an innovative & efficient Phase 3 study design focused on the patient population with the most modifiable disease**

- Focus on CAD, where NLRP3 and IL-1 targeting agents have shown success
- Continue dose exploration and establish long-term safety in a chronic disease setting
- Allow background medications; no CKD enrichment

| Imaging | ASCVD drivers and systemic biomarkers | Genetics |
|---|---|---|
| Assess plaque inflammation using FAI (fat attenuation index) imaging for response and enrichment | DAMPs (calprotectin, S100A12, HMGB1), cytokines (IL-1β, IL-18, IL-6) and thrombogenic factors (tissue factor, SAA, fibrinogen) | Confirm genetic basis of NLRP3 activation (activating SNPs) and build correlation to baseline levels of molecular drivers of ASCVD, responses and FAI changes |



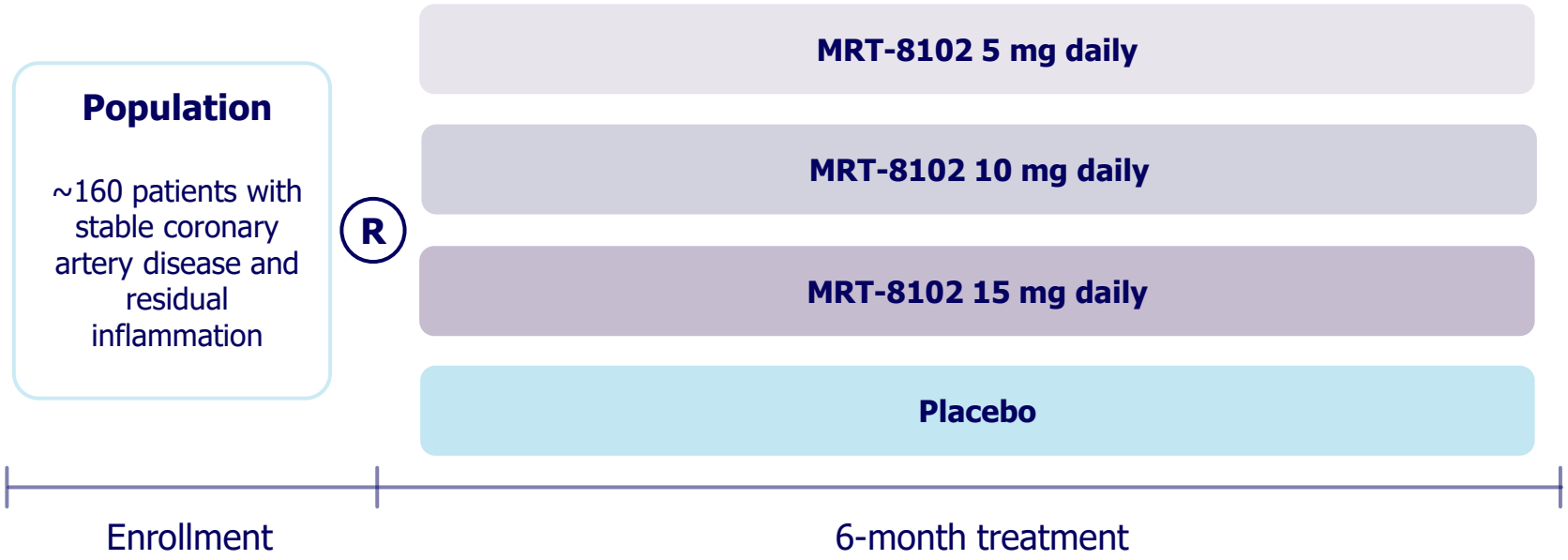






*Proposed trial design subject to review by FDA*

# GFORCE-2: A Phase 2b Study in Patients with Coronary Artery Disease




## Outcome measures

- Change in levels of key pathogenic ASCVD drivers including atherogenic, thrombogenic mediators and lipids
- Change in **local** cardiac imaging, from baseline to 6 months

## Exploratory endpoints

- Cardiac imaging
- Establish pharmacogenomic evidence base
- Liver fat/liver inflammation
- Anemia

**Study initiation planned for H1 2027**



*Proposed trial design subject to review by FDA*

# MRT-8102 for Treatment and Prevention of Gout Flares

# Gout: Large Market With High Unmet Need For New Prophylactic Therapies

## Gout Market Overview



**~10M**
Gout patients in the U.S.; present in ~15% of high-risk cardiovascular patients

**~30%**
Gout patients comorbid with stage 3-4 CKD

**30-40%**
Gout patients primarily managed by specialists*

## Significant unmet medical need in gout

**>55%**
Gout-treating physicians surveyed are **not satisfied** with current prophylaxis options

**>65%**
Gout-treating physicians **not satisfied** with prophylaxis treatment for gout patients comorbid with CKD

1L SOCs are either **contraindicated or lacking long-term safety data for CKD**, requiring dose titration and close monitoring

Low dose SOC treatment or fixed-dose strategies are often **insufficient** in preventing gout flares and result in **breakthrough flares**, a leading contributor to poor adherence to ULT (as low as 47%)

**IL-1 inhibitors** efficacious for flare treatment but are **cost/access-limited,** not indicated for flare prophylaxis due to safety concerns



## MRT-8102 Opportunity

**Strong efficacy potential** for flare management and long-term prophylaxis

**Favorable safety / tolerability** profile, providing sufficient inflammation reduction **without increased infection risk or GI side effects**

**Expected to be safe for use in CKD-comorbid patients** (no impact on kidney function)

Convenient **oral** regimen allowing for improved compliance



Note: * Includes rheumatologists and nephrologists

Source: Zhu et al. Am J Med. (2012); Mohammed et al. PLoS One (2019); Stern et al. Gout Urate Cryst. Depos. Dis. (2024); Schlesinger and Lipsky. Seminars in Arthritis and Rheumatism (2020); Yin et al. BMJ Open (2018); FitzGerald et al. Arthritis Care Res (2020); Maher et al. Arthritis Care Res (2020); Monte Rosa survey of gout-treating physicians (Nov 2025) and interviews

# Novel Urate-Lowering Gout Therapies Increase Need for Gout Flare Control

**US Gout Market = ~10M patients**

**Allopurinol**

**Febuxostat**
*(Boxed warning)*
*Increased CV death*

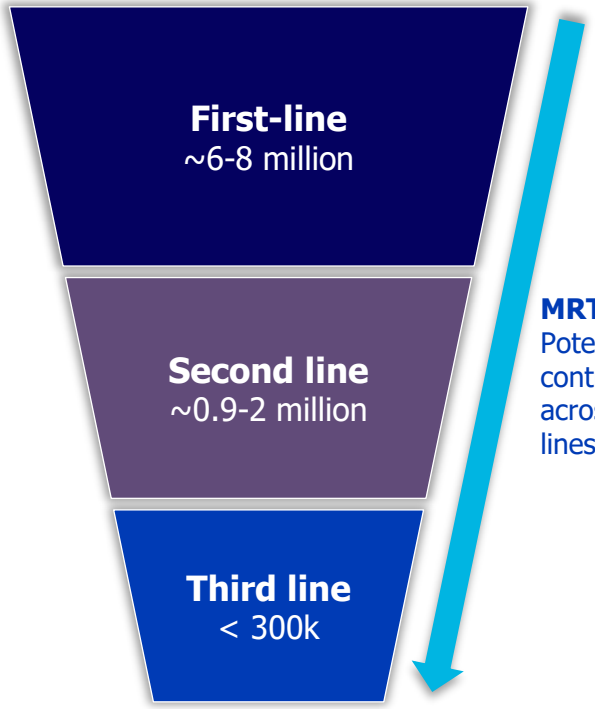
**Dotinurad**

**Pozdeutinurad**

**Lesinurad**
*Pulled due to acute renal failure*

**KRYSTEXXA**
*(Boxed warning)*

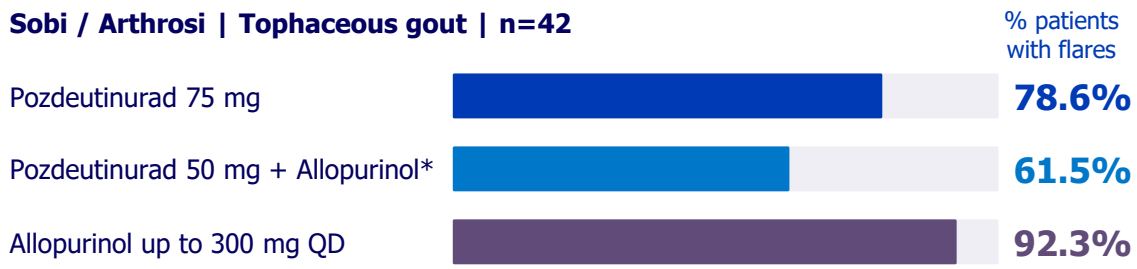
**NASP**
*Anaphylaxis & serious injection reaction*




**MRT-8102:**
Potential flare control therapy across multiple lines of therapy

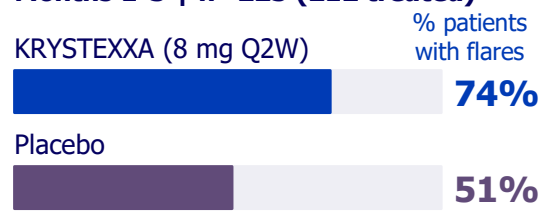
## Pozdeutinurad (URAT1i): AR882-203, Phase 2 | Months 0-6

**Sobi / Arthrosi | Tophaceous gout | n=42**



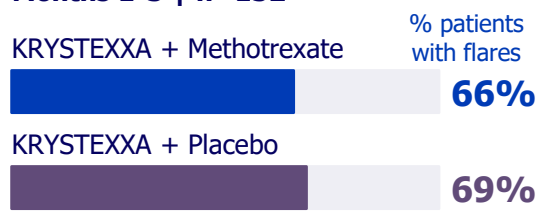

## KRYSTEXXA Pivotal Phase 3s

**Months 1-3 | n=225 (212 treated)**




## KRYSTEXXA MIRROR Phase 3

**Months 1-3 | n=152**




Flares rates increase following initiation of urate-lowering therapies (ULTs) across classes, including new URAT1 inhibitors (e.g., pozdeutinurad) and KRYSTEXXA



Note: Cross-trial context only: populations, prophylaxis, flare definitions and windows differ; MRT-8102 benefit remains to be demonstrated. REDUCE 2 (Pozdeutinurad Phase 3) topline reported urate responses, no flare rates. *Allopurinol dose in the combination arm not disclosed (up to 300 mg/day reported).
Sources: Khanna et al., Ann Rheum Dis (2025); Sobi REDUCE 2 release (May 2026); Krystexxa PI, Horizon (2022); Botson et al., Arthritis Rheumatol (2023)

# Gout Treatment Options Do Not Adequately Address Unmet Need

| Treatment Regimen | Mechanism of Action | Marketed Products | Key Pipeline Assets | Limitations / Restrictions |
|---|---|---|---|---|
| **Flare Control / Prophylaxis** | Broad anti-inflammatories | Colchicine | ABP-745 (Atom, Phase 2) | • Frequent **GI side effects**<br>• **Dose titration** and **close monitoring** needed in CKD comorbid population; breakthrough flares likely with lower doses |
| | | NSAIDs | - | • **Contraindicated** in CKD comorbid population; **CV risks** |
| | | Corticosteroids | - | • **Not suitable for long-term** prophylaxis use |
| | IL-1 inhibitors | ILARIS (Novartis)<br>KINERET (Sobi)*<br>ARCALYST (Regeneron)* | - | • **Increased infection risk** and **injectable ROA** greatly limit use |
| **Urate-lowering Therapies** | Reduce uric acid production (xanthine oxidase inhibitors) | Allopurinol | XRX-026 (XORTX, pre-registration) | • **Increase in flares** upon initiation of treatment<br>• **Dose titration** needed in CKD comorbid population |
| | | Febuxostat | - | • **CV boxed warning**<br>• **Increase in flares** upon initiation of treatment |
| | Increase uric acid excretion (uricosuric, URAT1 inhibitors) | Probenecid (generic uricosuric) | Dotinurad (Crystalys, Phase 3)**<br>Pozdeutinurad (Sobi, Phase 3)<br>Lingdolinurad (Atom, Phase 3) | • **Increase in flares** upon initiation of treatment, including new URAT1 agents<br>• Probenecid **contraindicated** in CKD comorbid population |
| | Breakdown uric acid (uricase, urinary alkalizer) | KRYSTEXXA (Amgen) | NASP (Sobi, pre-registration)<br>PRX-115 (Protalix, Phase 2)<br>DYV-700 (Dyve, Phase 2) | • **Increase in flares** upon initiation of treatment<br>• KRYSTEXXA requires **IV injections** every 2 weeks and **methotrexate** co-treatment; boxed warning for **anaphylaxis**<br>• NASP requires **IV injections**; reported incidence of **anaphylaxis** and **serious infusion reactions** |

**>$1.7B**

**KRYSTEXXA annual sales expected by 2029…**

**…despite a challenging regimen:**

- **IV infusion** every 2 weeks (8 mg)
- **With Methotrexate** co-dosed since 2022 label
- **Boxed Warning** anaphylaxis, infusion reactions
- **~70% flare** within 3 months of treatment initiation

**Patients, HCPs, and payers' acceptance of the treatment burden indicates significant unmet need in the gout market**



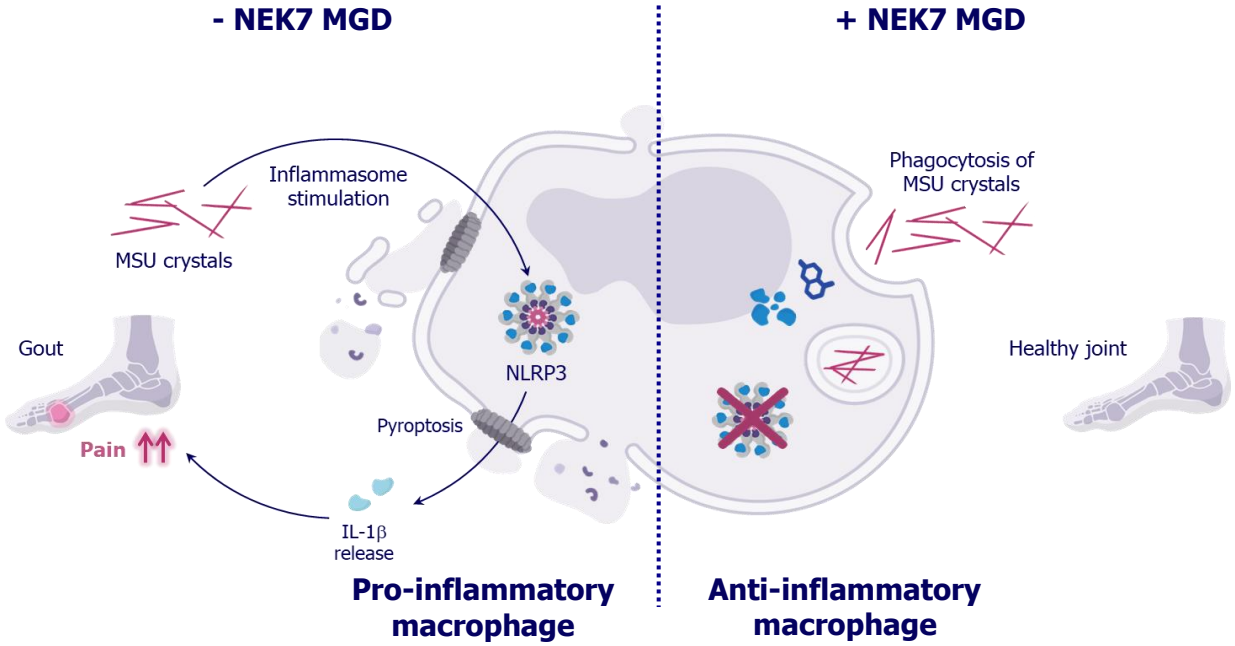
Note:* KINERET and ARCALYST are not FDA-approved for gout treatment and may be used off-label; ** Dotinurad is approved in Japan, China and other Asian markets but investigational in the U.S. and Europe

Sources: Drug labels, PharmaProjects, Evaluate, MRTx physician survey and interviews

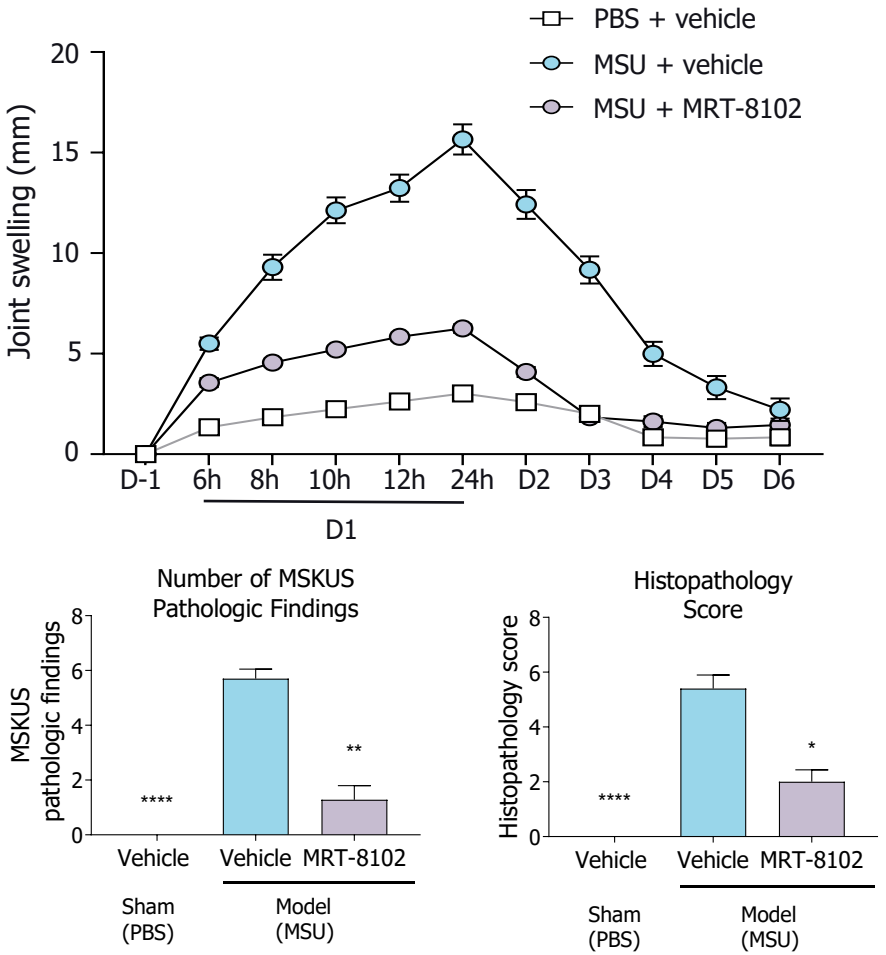
# MRT-8102 Has Potential to Resolve and Prevent Gout Flares

## MSU-driven activation of NLRP3/NEK7 pathway

## Resolution of inflammation and gout tophi via NEK7 MGD




## MRT-8102 reduces MSU-induced flare in a rabbit gout model



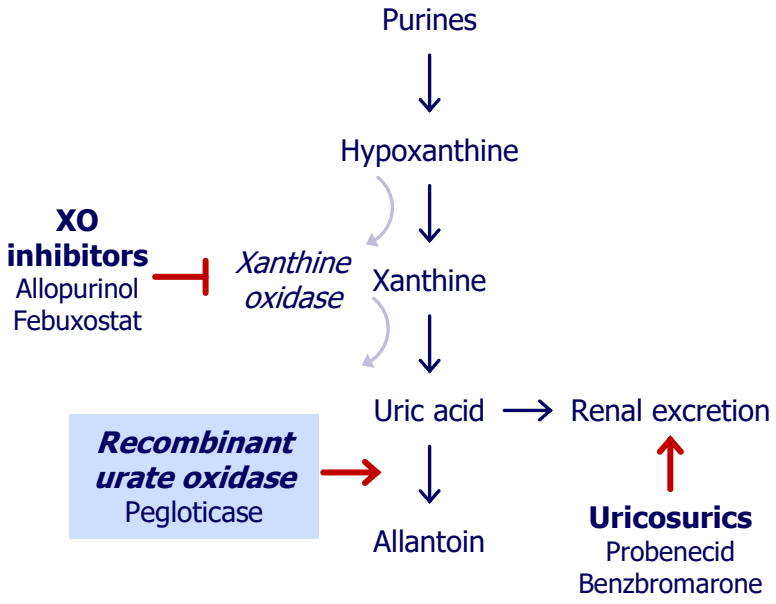

Preclinical data support that MRT-8102 treatment has potential to reduce tophi through enhanced phagocytic potential of macrophages without activation of NLRP3 and flares.

70% of patients experience flares within three months of Krystexxa treatment likely due to dissolution of tophi and resulting MSU-induced NLRP3 activation.

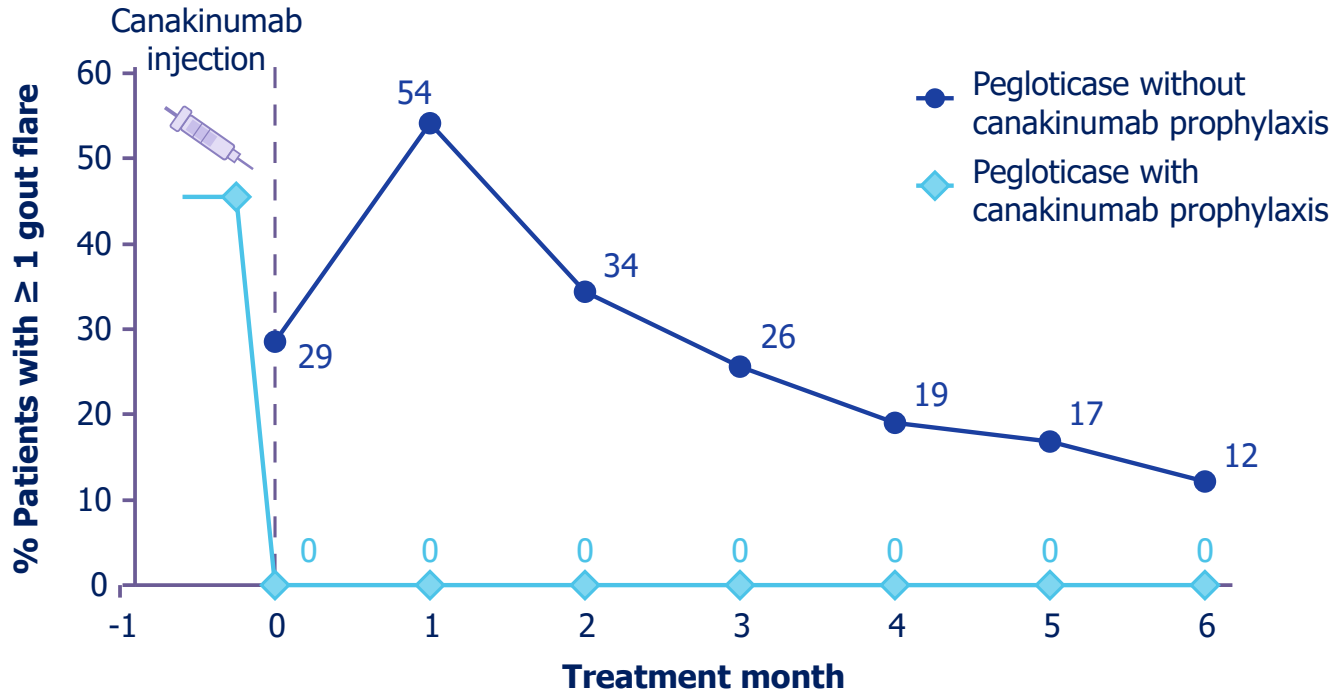
Rabbit gout model: intra-articular injection of MSU in rabbits on Day 0; daily dosing from Day -1, 50 mg/kg p.o.
Top: The degree of joint swelling was determined by measuring knee perimeter with a digital caliper, mean ± SEM.
Bottom: Musculoskeletal ultrasound (MSKUS) composite score at takedown, mean ± SEM; histopathology score obtained by semi-quantitative morphometry of H&E staining. Kruskal-Wallis test followed by Dunn's multiple-comparison test. *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

# Short-term Increase in Gout Flares Following ULT Treatment is Largely Driven by the NEK7/NLRP3-IL-1β Axis

**Urate lowering therapies can trigger a short-term increase in gout flares**




**Prophylaxis with canakinumab treatment prevents the short-term increase in gout flares following Pegloticase treatment**




**Rapid uric acid reduction can increase the likelihood of crystal mobilization and activate the NEK7/NLRP3 cascade, leading to a short-term induction of gout flares. Pathway modulation can prevent flares.**



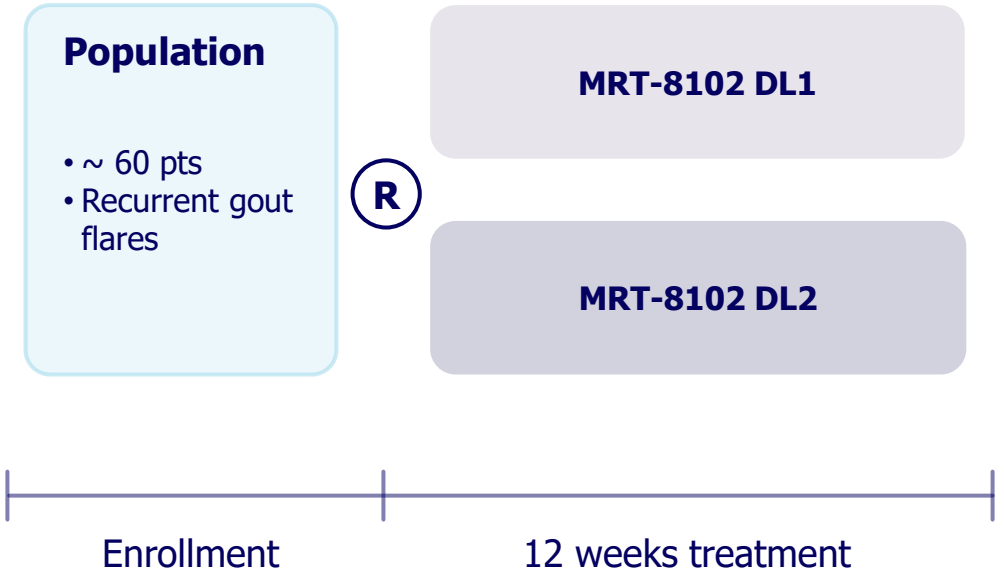
*Data with and without Canakinumab: Botson et al., 2022 (MIRROR), Botson and Peterson, 2024 (MIRROR RCT)*

# GEMINI-1 A Phase 2 Study in Gout Flare Prevention Following Acute Flare Management

## WHY MRT-8102 FOR GOUT

- Gout is a canonical NEK7/NLRP3 pathway disease: MSU crystals trigger NEK7-mediated NLRP3 complex assembly, driving release of IL-1β and DAMPs, and inducing flare pathology
- GFORCE-1 showed durable suppression of relevant NEK7/NLRP3 disease drivers, acting directly on gout's core mechanism; 40–60% of gout patients also carry elevated CV risk

## GEMINI-1 STUDY




**Goals**

- Dose exploration
- Safety and efficacy
- Establish PoC for flare prevention following acute flares

**Outcome measures and PoC expectation**

- Reduction in pain VAS by 72 hours
- Frequency of new flares

**Study initiation planned for Q4 2026; data update expected in H2 2027**



*GEMINI: Glue Elimination of Monosodium urate-Induced NEK7 Inflammation; proposed trial design subject to review by FDA*

# MRT-8102 for Hidradenitis Suppurativa

# HS: Significant Unmet Need for New Oral Therapies

## HS Market Overview



**2-3M**
Hidradenitis suppurativa patients in the U.S.

**400-450K**
Moderate-to-severe patients eligible for advanced therapies

## Large unmet medical need in HS

**55%**
Of HS patients are not well-managed with SOC, even with anti-TNF and anti-IL-17 biologic approvals

**<25%**
Of moderate-to-severe HS patients are treated with a biologic

## Promising IL-1 / inflammasome approach

Lutikizumab and abdakibart Phase 2/3 studies demonstrated the role of IL-1 in HS pathophysiology; however, NEK7/NLRP3 inhibition is expected to have a **broader impact on inflammatory and pathological drivers** including both IL-1 and DAMPs, potentially making NEK7 MGD **the next important MOA** in the HS treatment paradigm

## MRT-8102 Opportunity

Potential for **robust clinical activity** in both biologic-naïve and refractory patients

- Abdakibart and Lutikizumab provide promising POC for the IL-1 approach in HS
- NEK7/NLRP3 inhibition expected to impact broader array of pathological drivers than IL-1 biologics

Potential differentiation in **safety / tolerability** measures, including expected low risk of infection and neutropenia events

**Oral** regimen suitable for long-term maintenance treatment



Source: Jfri et al. JAMA Dermatology (2021); PharmaProjects; Piper Sandler (Apr 2026); HS Foundation; Cowen Therapeutics Outlook (Oct 2025); AlphaSense; TrialTrove; clinicaltrials.gov

# NEK7/NLRP3 and DAMPs Drive Feed-forward Loop in HS Progression

## 1 Follicular occlusion and rupture, DAMP release and sensing

- Follicular hyperkeratosis, occlusion and mechanical stress lead to follicular rupture and release of intracellular debris
- DAMP release due to tissue DAMAGE, recognition by PRRs on keratinocytes, myeloid cells

## 2 NFKb priming, NLRP3 activation and pyroptosis

- DAMP-PRR signaling activates NF-kB, promoting NLRP3 inflammasome
- Activated NLRP3 leads to release of IL1β & IL18 via GSDMD pores

**Key DAMPs in HS**:

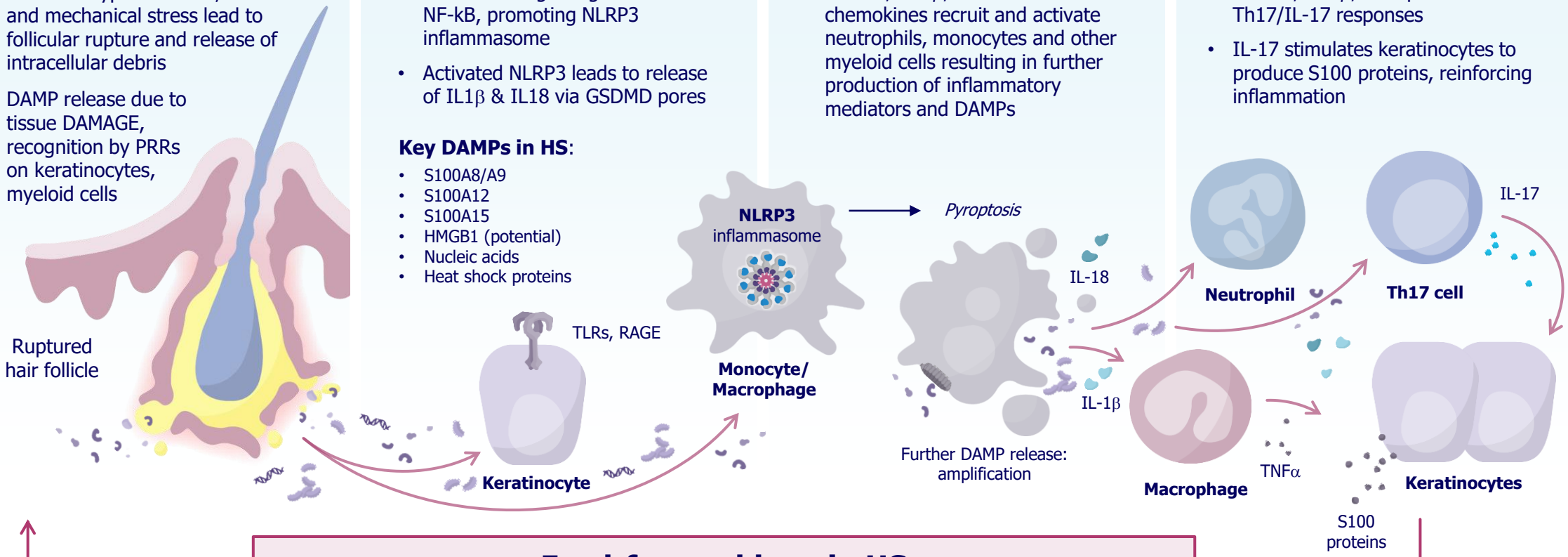
- S100A8/A9
- S100A12
- S100A15
- HMGB1 (potential)
- Nucleic acids
- Heat shock proteins

## 3 Innate immune cell recruitment and activation

- DAMPs, IL-1β, IL18 and chemokines recruit and activate neutrophils, monocytes and other myeloid cells resulting in further production of inflammatory mediators and DAMPs

## 4 IL-17 axis and keratinocyte amplification

- DAMPs, IL-1β, IL18 promote Th17/IL-17 responses
- IL-17 stimulates keratinocytes to produce S100 proteins, reinforcing inflammation




## Feed-forward loop in HS

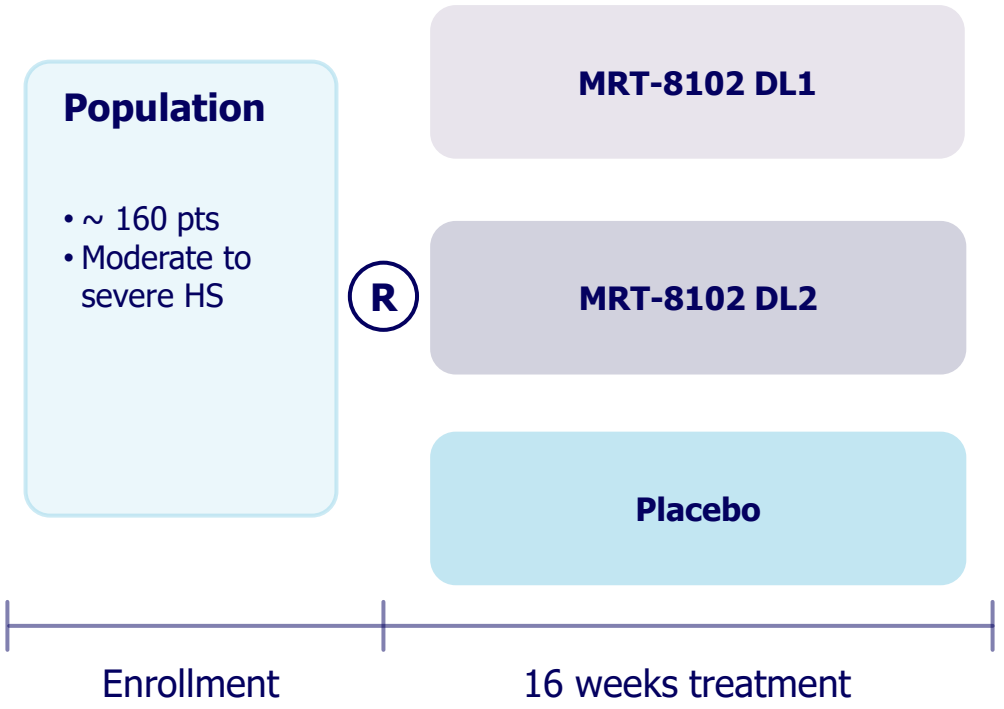
Tissue damage → DAMP release → innate immune activation → NLRP3/IL-1β/IL-18 → myeloid recruitment → tissue damage & pyroptosis → DAMP release → **sustained inflammation**

# GALAXY-1 A Phase 2 Randomized Study in Moderate to Severe Hidradenitis Suppurativa

## WHY MRT-8102 FOR HS

- HS ranks highest in NEK7/NLRP3 pathway score of any indication we studied, with consistent upregulation of NLRP3, IL-1β, and DAMPs in lesional tissue
- NEK7 degradation acts upstream of both the IL-1 and DAMP-driven pathology in HS lesions, unlike single-mediator TNF/IL-17 biologics
- IL-1 antibodies provide promising POC for the NEK7/NLRP3 pathway approach in HS

## GALAXY-1 STUDY




**Goals**
- Dose exploration
- Safety and efficacy

**Outcome measures and PoC expectation**
- HiSCR75 after 16 weeks MRT-8102 relative to placebo

**Study initiation planned for H1 2027**

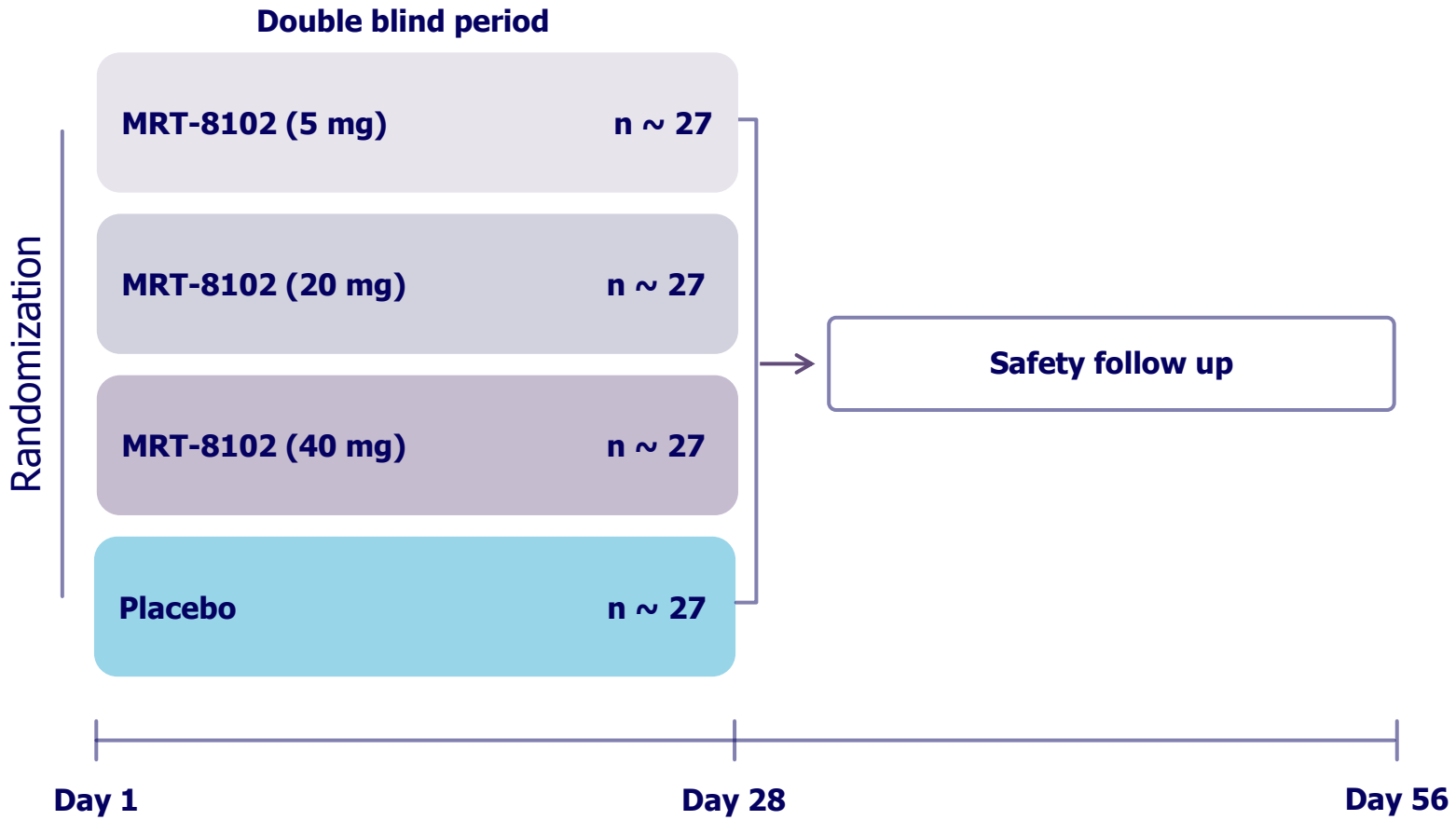


*GALAXY: Glue-mediated Attenuation of Lesions, Abscesses, and eXacerbations in HS therapY; proposed trial design subject to review by FDA*

# GFORCE-1 Clinical Study Results

As disclosed on October 1, 2026

# GFORCE-1 Study: Dose Exploration of MRT-8102 in Subjects with Elevated CVD Risk




CRP endpoint: absolute reduction and reduction to <2 mg/L
CRP measurements: pre-dose, D1, D7, D14, D21, D28, D35

**Study population**

- Obesity, elevated CRP ≥3 and <15 mg/L

**Primary endpoint**

- Safety and tolerability of 28 days dosing with 28 days follow up

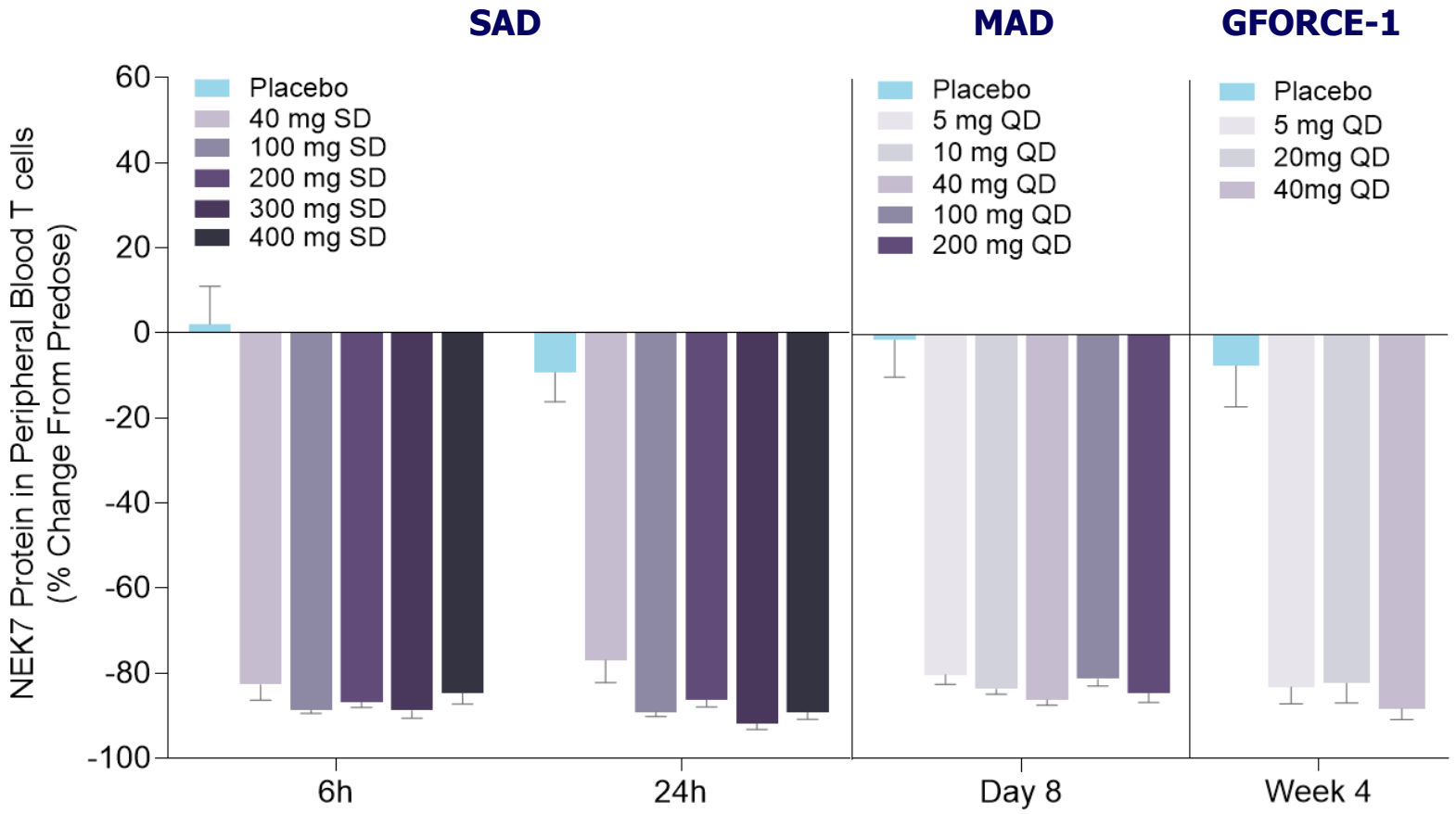
**Secondary endpoints**

- Change in CRP levels
- PK

**Additional exploratory PD endpoints**

- NEK7 (target engagement)
- DAMPs and cytokines to inform ASCVD pathogenic drivers + systemic inflammation
- Thrombogenic factors
- Lipids, lipoproteins, and other markers of CV risk (Lp(a), LDL-C)

# MRT-8102 Achieved Robust and Sustained NEK7 Degradation




Robust and sustained degradation of NEK7 noted in peripheral blood T cells (~80 - 90%) across all dose levels at week 4, consistent with preclinical findings



*Data are medians (IQR). SAD (n=48); MAD (n=40); GFORCE-1 (n=101)*

# MRT-8102 was Safe and Well Tolerated over 4 Weeks Dosing + 4 Weeks Follow-up, with no SAEs

- Safety data were collected over 8 weeks for 108 participants (MRT-8102, n=81; placebo, n=27)
- No SAEs were reported
- Frequency of treatment-emergent AEs (TEAEs) was similar between MRT-8102 (33% participants) and placebo (30% participants)
- Most (86%) of MRT-8102 TEAEs were grade 1*
- The most frequent TEAEs were
  - Headaches in 4% of participants on MRT-8102 and 11% of participants on placebo
  - Arthralgia in 5% of participants on MRT-8102 and 4% of participants on placebo
- There were no serious infections; frequency of minor infections was similar in participants on MRT-8102 (7% participants) and placebo (7% participants)



*There was one episode of grade 3 elevation of liver enzymes in a patient with incidental finding of asymptomatic hepatitis A, and one episode of grade 3 shoulder pain in a patient with accidental shoulder dislocation

# GFORCE-1 Population: Probing ASCVD Pathogenic Drivers in CVD Risk Subjects

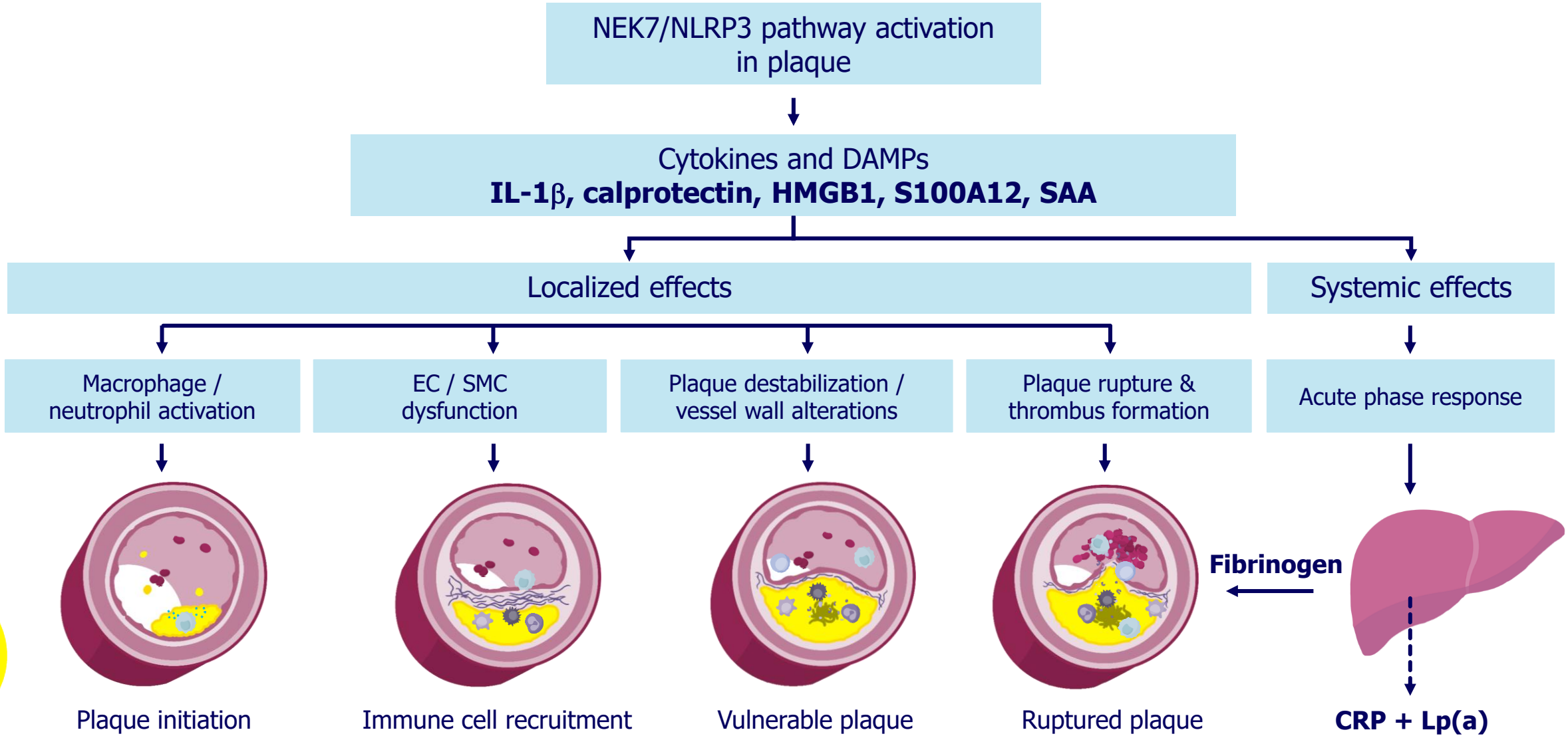
GFORCE-1 enrolled a population at risk of CVD and a biomarker profile that is informative of established ASCVD

- **Population**: Obese subjects at elevated CVD risk, reflecting a population with a high ratio of silent atherosclerosis; established ASCVD diagnosis not required
    - Based on REACT study, prevalence of silent atherosclerosis in general population ages 40-49 estimated to be up to 70%[1], presumably further enriched in GFORCE-1 by focus on obese subjects with high CRP[2].
- **Translational relevance**: Baseline levels of key local ASCVD drivers and systemic biomarkers were elevated and closely tracked patterns reported in diagnosed ASCVD patients; degree of elevation for some markers may not equal that in established ASCVD patients
- **Reference arm**: A separate healthy-volunteer cohort from the SAD/MAD arm of the trial (not risk-enriched) provided a real-world normal-range comparator for all analyses of key molecular drivers of ASCVD and systemic biomarkers
- **Genetic stratification**: NLRP3 SNP genotyping in a subset of participants enabled correlation of baseline elevation of key ASCVD drivers with validated NLRP3 risk alleles: risk-allele carriers show higher levels of key ASCVD pathogenic drivers



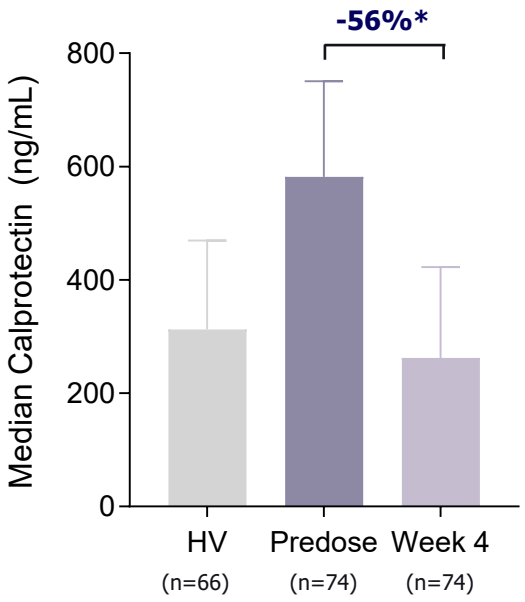
*[1]Bundgaard et al., 2026 NEJM "Prevalence of Silent Atherosclerosis Across Adult Life"; [2]Yang et al., 2013 International Journal of Cardiology .*

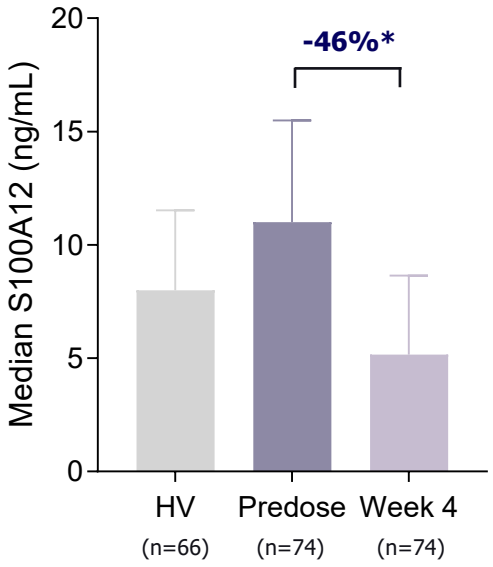
# Key ASCVD Pathogenic Drivers and Markers of Systemic Inflammation Assessed in GFORCE-1



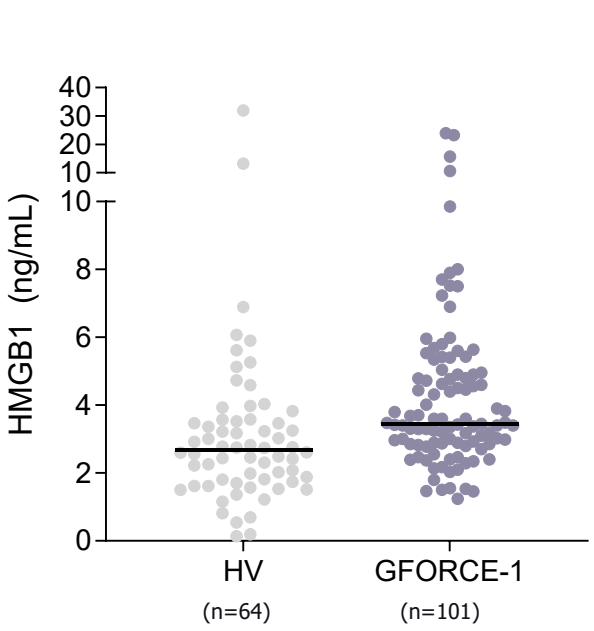
# MRT-8102 Reduced Plasma DAMPs to Healthy Volunteer Levels

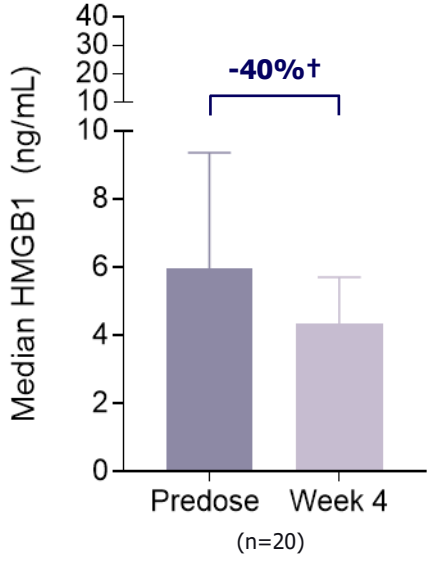
**MRT-8102 treatment reduced Calprotectin and S100A12 proteins to normal levels**




**MRT-8102 treatment resulted in meaningful HMGB1 reduction in subjects with higher baseline levels**




ASCVD-relevant DAMPs were normalized to levels observed in healthy volunteers after 4 weeks of dosing

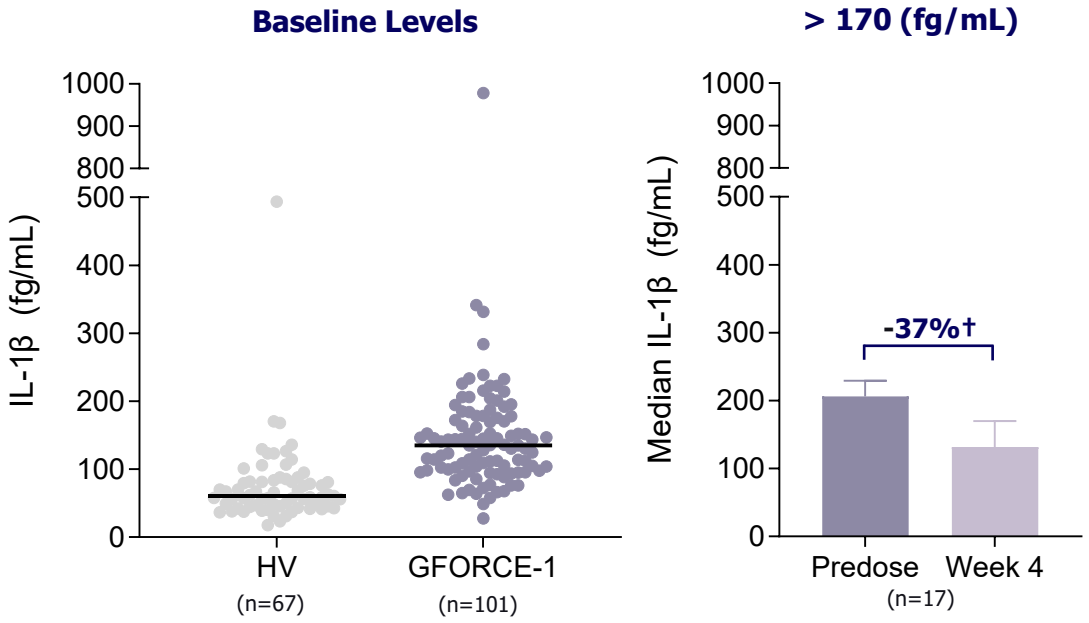


*Data are medians (IQR); GFORCE-1: placebo + MRT-8102 treated; HV: SAD and/or MAD part; † p=0.05, * p<0.0001 compared to predose (MRT-8102 treated); p-value from Wilcoxon test.*
*The 75th Percentile (Q3) of GFORCE-1 population (N=101, placebo and treatment) was used to define the cut-offs: 4.7 ng/mL for HMGB1. Analysis on median reduction based on MRT-8102 treated subjects (predose vs treatment at week 4).*

# NEK7 Degradation led to Rapid and Sustained IL-1β Suppression

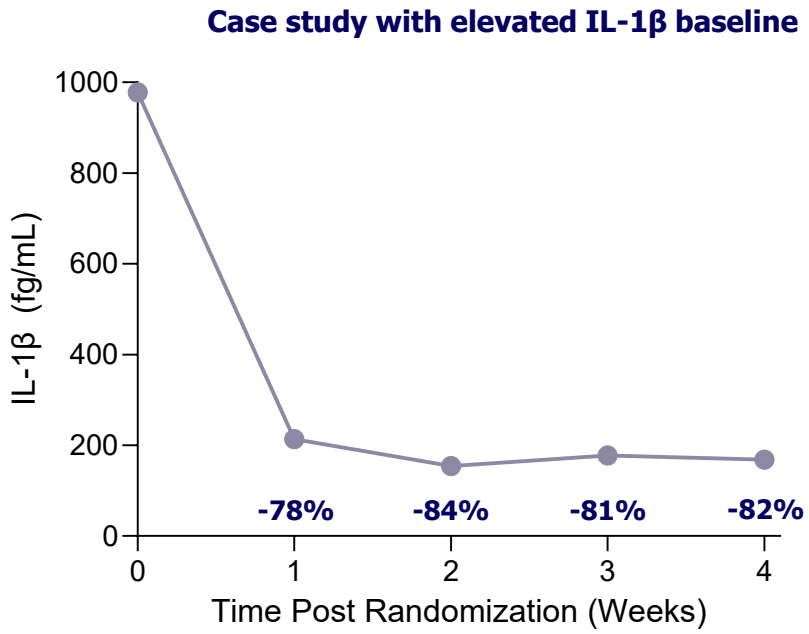
**MRT-8102 treatment resulted in meaningful plasma IL-1β reduction in subjects with higher baseline levels**

**Case Study: Rapid and sustained > 80% suppression of IL-1β in GFORCE-1 subject with elevated IL-1β baseline**









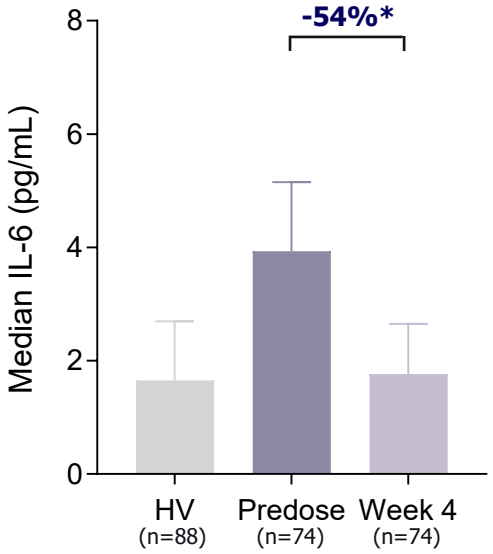

- Most subjects in GFORCE-1 cohort showed modest but consistent baseline elevation of IL-1β and downmodulation on treatment with MRT-8102
- In a subject with increase to levels consistent with autoimmune disease, a > 80% reduction of IL-1β was observed

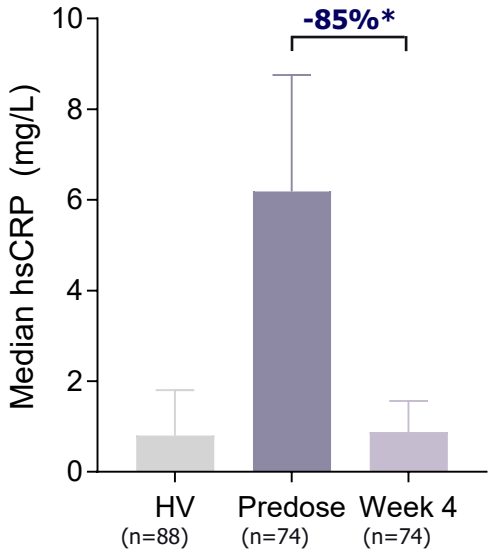


*Data are medians (IQR); GFORCE-1: placebo + MRT-8102 treated; HV: SAD and MAD part; † p=0.003 compared to predose (MRT-8102 treated); p-value from Wilcoxon test; % indicates Change from Predose; The 75th Percentile (Q3) of GFORCE-1 population (N=101, placebo and treatment) was used to define the cut-offs: 170 fg/mL for IL-1β. Analysis on median reduction based on MRT-8102 treated subjects (predose vs treatment at week 4).*

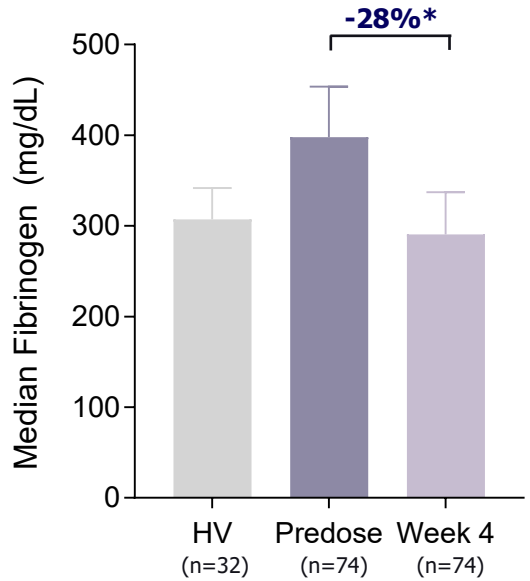
# NEK7 Degradation led to Normalization of IL-6, CRP, and Fibrinogen

**hsCRP and IL-6 reduced to levels observed in healthy volunteers**




**Treatment significantly reduced fibrinogen to normal physiological levels**




- MRT-8102-induced modulation of IL-1β/IL-6/CRP axis normalized plasma IL-6 and serum hsCRP to levels detected in healthy volunteers after 4 weeks of dosing
- Median reduction of 28% in fibrinogen to levels comparable to those observed in healthy volunteers after 4 weeks of dosing



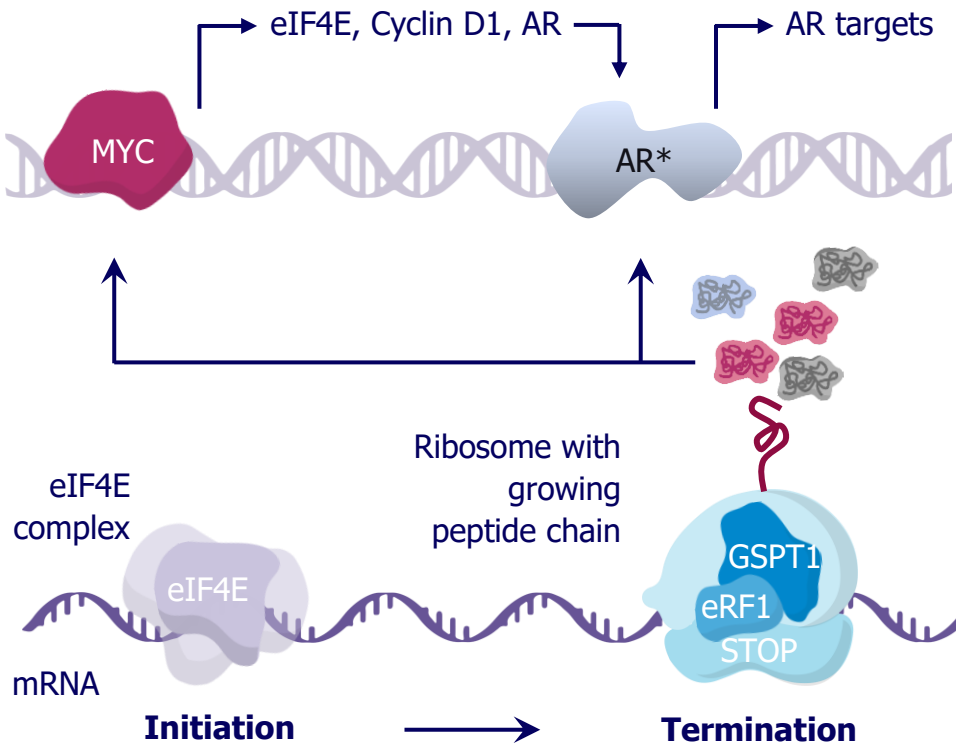
*Data are medians (IQR); GFORCE-1: placebo + MRT-8102 treated; HV: SAD and MAD part;* p<0.0001 compared to predose (MRT-8102 treated); p-value from Wilcoxon test ;% indicates Change from Predose; Analysis on median reduction based on MRT-8102 treated subjects (predose vs treatment at week 4).*

Monte Rosa Therapeutics

# Oncology Pipeline

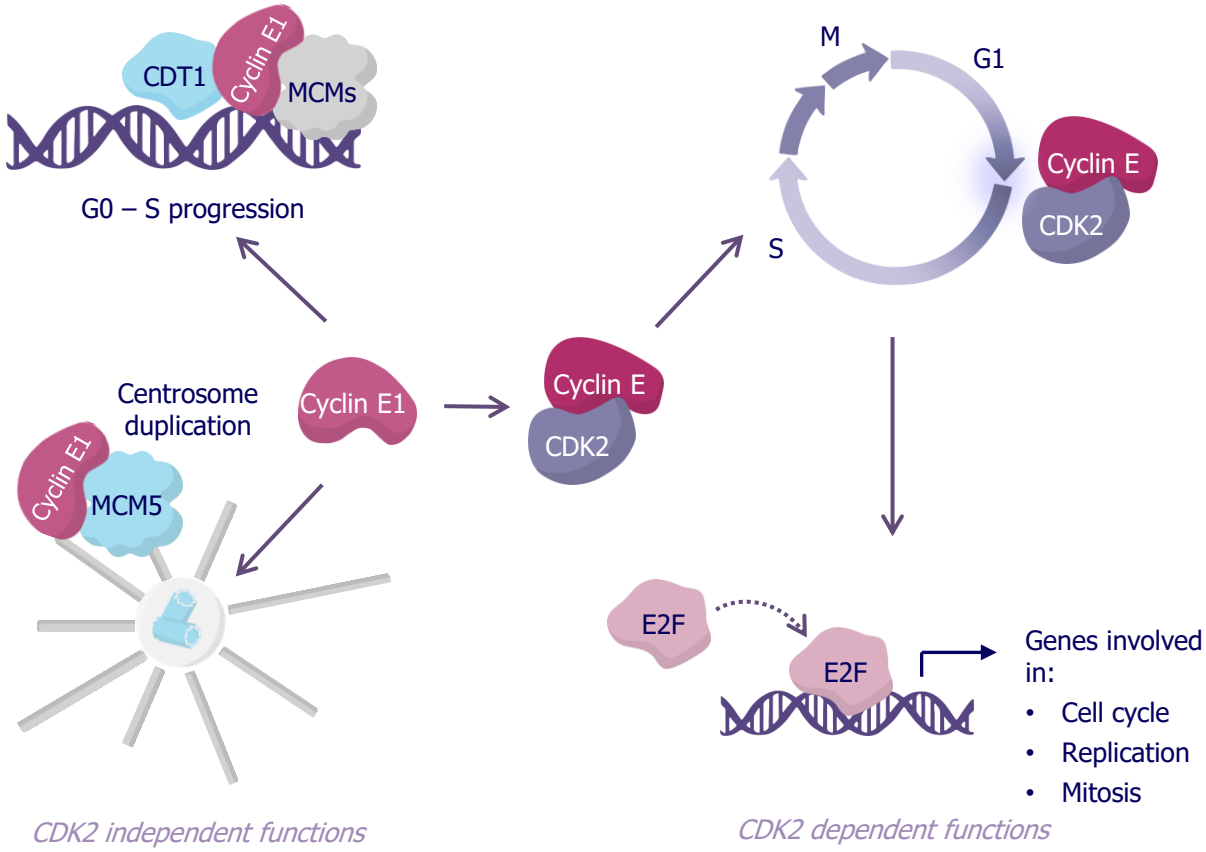
# Degrading Undruggable and Difficult-to-Drug Oncology Targets

**Therapy-resistant mCRPC is characterized by increased MYC, E2F, AR and other oncogenic pathway activity**




MRT-2359 + AR inhibitor suppressed multiple oncogenes including AR, MYC and Cyclin D1

**CCNE1 and CDK2 are highly validated targets for solid tumors that drive multiple hallmark cancer mechanisms**




CCNE1 and CDK2 are highly validated oncogenes in a variety of solid tumors, including breast, ovarian and endometrial cancer

Monte Rosa Therapeutics

# GSPT1 Program (MRT-2359)

# MRT-2359 At a Glance

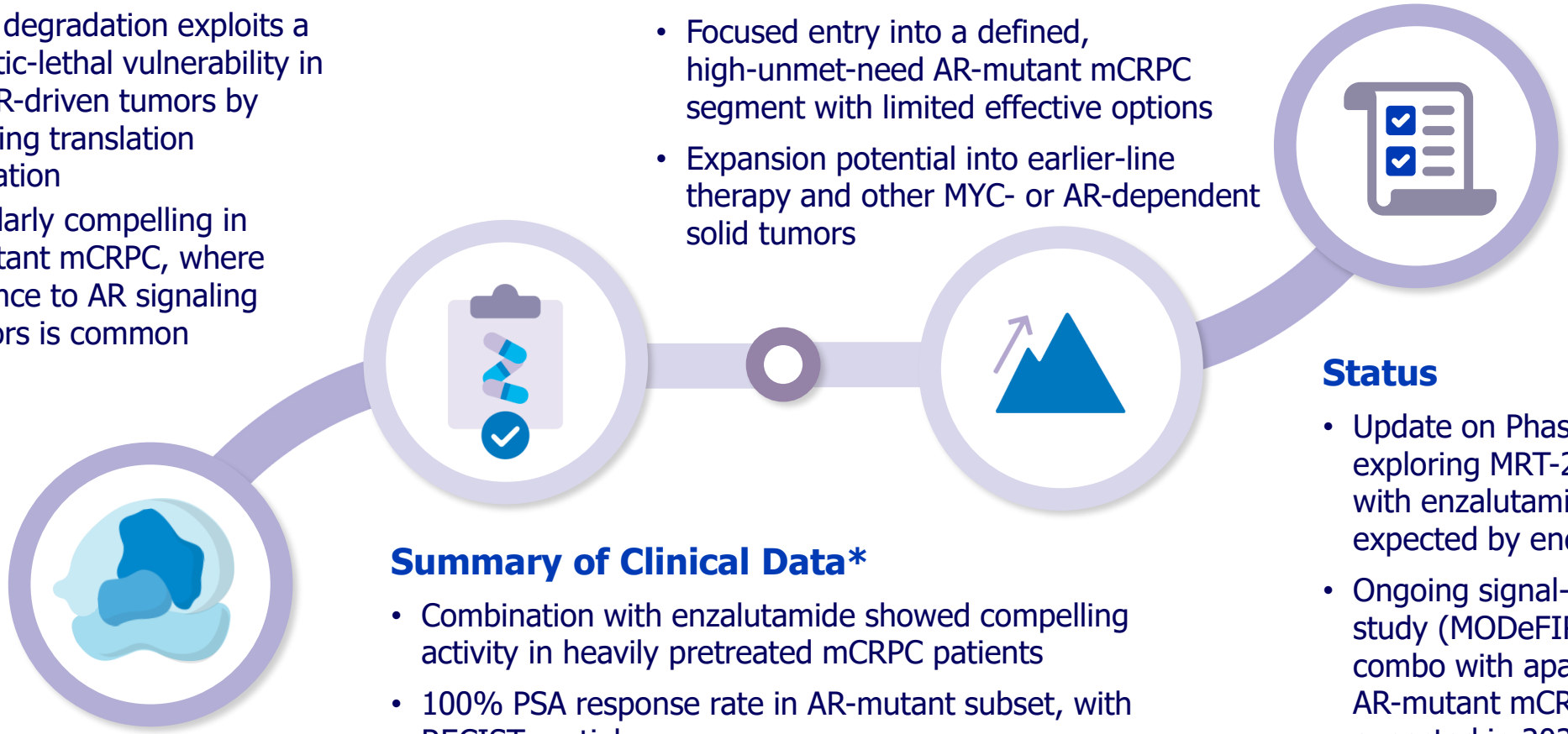
## First-in-class oral GSPT1 MGD for AR-mutant metastatic castration-resistant prostate cancer (mCRPC)

### GSPT1 Rationale

- GSPT1 degradation exploits a synthetic-lethal vulnerability in MYC/AR-driven tumors by disrupting translation termination
- Particularly compelling in AR-mutant mCRPC, where resistance to AR signaling inhibitors is common

### Opportunity

- Focused entry into a defined, high-unmet-need AR-mutant mCRPC segment with limited effective options
- Expansion potential into earlier-line therapy and other MYC- or AR-dependent solid tumors



### Summary of Clinical Data*

- Combination with enzalutamide showed compelling activity in heavily pretreated mCRPC patients
- 100% PSA response rate in AR-mutant subset, with RECIST partial responses
- Signals of durability and manageable safety profile support advancement into Phase 2 study

### Status

- Update on Phase 1/2 expansion arm exploring MRT-2359 in combination with enzalutamide in advanced CRPC expected by end of year
- Ongoing signal-confirming Phase 2 study (MODeFIRe-1) of MRT-2359 in combo with apalutamide in AR-mutant mCRPC; data update expected in 2027
- Potential expansion into earlier-line and additional AR-driven populations pending Phase 2 readout

* As of data cut-off of January 30, 2026, as disclosed Feb. 24, 2026

# Potential to Address Key Unmet Need for mCRPC Patients With AR Mutations

## mCRPC Market Overview



**~60K**
mCRPC annual incident population in the U.S.*

**~20-30%**
Patients carrying AR mutations post-ARPI treatment

## Unmet Need of mCRPC AR-mutant Population

| | |
|---|---|
| **Poor prognosis, easy to identify patient population** | • AR mutations in mCRPC patients have been reported to have **significantly shorter overall survival**<br>• AR mutations easily identified with **existing blood-based diagnostic tests** |
| **Limited treatment options** | • Currently, there is **no approved targeted therapy** for AR LBD-mutated patients<br>• Given AR LBD mutations are associated with **resistance** to 2nd generation ARPIs, therapy options for these patients are often limited to **chemo and radioligand therapies** |
| **Need for therapy with minimal QoL impact** | • Patients with AR LBD mutations often suffer from **significant side effects and poor quality of life** when taking chemo or radioligand therapies<br>• There is a strong desire among oncologists to have a **new non-chemo, non-radioligand treatment option** for AR LBD-mutated patients |

## MRT-2359 Opportunity in AR Mutant mCRPC

Potential for **high rates of durable responses** in AR-mutant patient population with high unmet need

Maintain patients on **all-oral regimen** well-suited for use in community urologist/ oncologist setting

**Well-tolerated** with minimal additive toxicity to standard-of-care AR inhibitors

Potential for indication expansion into earlier line in combination with 2nd generation AR inhibitors or radioligand therapy



Note: * U.S. drug-treatable mCRPC patient population (2026) from Clarivate
Source: Clarivate; Antonarakis et al. JCO Precision Oncology (2024); Stewart et al. J Clin Oncol (2024); MRTx interviews

# Clinical Data Summary

- MRT-2359 in combination with enzalutamide achieved compelling clinical activity in a subset of heavily pre-treated metastatic castration resistant prostate cancer (mCRPC) patients with androgen receptor (AR) mutations.
- Of the 5 patients with AR mutations:
  - 5 patients showed a PSA response, including 2 patients with PSA90 and 3 patients with PSA50 responses
  - 2 patients showed RECIST partial responses (1 confirmed, 1 unconfirmed)
  - 3 patients had stable disease (all with reduction in size of target lesions), leading to a 100% disease control rate in the AR mutant population
  - 2 patients remained on therapy for 10 cycles or longer and 2 patients remained on drug as of data cut off on January 30, 2026
- 5 additional patients without AR mutations had stable disease per RECIST, several of which associated with tumor size reductions of target lesions, resulting in an overall disease control rate (DCR) of 67% in a total of 15 evaluable patients
- Combination of MRT-2359 and enzalutamide was well tolerated with mild or moderate, manageable fatigue and GI adverse events (AEs) being the most frequent toxicities
- Data support potential of combination of MRT-2359 with 2$^{nd}$ generation androgen receptor inhibitors for mCRPC patients with AR mutations (up to 30% of 2$^{nd}$ line+ mCRPC), with additional potential in earlier line settings or in combination with other agents



*As disclosed Feb. 24, 2026; data cut-off January 30, 2026*

# MRT-2359 Phase 1/2 Clinical Study Design

## Phase 1: Dose Escalation

*Monotherapy of MRT-2359 in lung cancer, high-grade neuroendocrine tumors and solid tumors with N-/L-MYC amplification*

## Phase 2: Expansion Cohort

*Combination of MRT-2359 with enzalutamide in heavily-pretreated metastatic castration resistant prostate cancer (CRPC)*




As of January 30, 2026, enrolled 23 patients with heavily pretreated, RECIST measurable mCRPC



Well-tolerated dose level | 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, Clinical Characteristics and Prior Therapies: MRT-2359 Compared to Mevrometostat Phase I Trial

| Patient Characteristics | MRT-2359 + Enzalutamide Total (N=23) | Mevrometostat + Enzalutamide Phase I total (N=47)[1] |
|---|---|---|
| **Age, median (range), years** | 71 (54-83) | 70 (53 – 87) |
| **Race, N (%)** | | |
| White | 14 (61) | 40 (85) |
| Black | 7 (30) | 4 (9) |
| Asian | 0 (0) | 2 (4) |
| Other | 2 (9) | 1 (2) |
| **ECOG performance status, N (%)** | | |
| 0-2 | 23 (100) | 47 (100) |
| **Histology subtype, N (%)** | | |
| Adenocarcinoma | 20 (87) | 47 (100) |
| Adenocarcinoma with neuroendocrine differentiation[2] | 3 (13) | ND[3] |
| **Lesions at baseline, n (%)** | | |
| RECIST measurable disease | 23 (100) | 16 (34) |
| Soft tissue only | 1 (5) | 10 (21) |
| Liver metastases | 6 (27) | ND[3] |
| **Number of prior lines of therapy, median (range)** | 5 (1-18) | ND[3] |
| Prior abiraterone, second gen ARi naive N (%) | 5 (22) | 20 (43) |
| Prior second gen ARi +/- abiraterone N (%) | 18 (78) | 27 (57) |
| Prior docetaxel and/or cabazitaxel N (%) | 19 (83) | 23 (49) |
| Prior Pluvicto N (%) | 13 (57) | ND[3] |
| **Baseline PSA, ng/mL, median (range)** | 19.66 (0.66 – 4989) | 49.9 (0-9,650) |

*Data cut-off January 30, 2026*

Notes: [1] Mevrometostat + enzalutamide data from Schweizer et al. ASCO (2024). [2] Identified by RNAseq analysis of study tumor biopsies collected before dosing. [3] ND, not disclosed.
Comparisons between MRT-2359 and other therapies represented herein are based on post-hoc analyses comparing MRT-2359 clinical information with publicly available information for other therapies. Any comparisons use information from different clinical trials, conducted by different parties, at different points in time, with differences in trial designs and patient populations. No head-to-head clinical trials have been conducted, cross-trial comparisons should not be made, and this information is provided only for illustrative purposes.

# Combination of MRT-2359 and Enzalutamide was Well Tolerated and May be Favorable over EZH2 Inhibitors

**Treatment-Related AEs Occurring in ≥20% Patients**

| Dose Level | MRT-2359 0.5mg and Enzalutamide 160mg N=17 | | | | MRT-2359 0.75mg and Enzalutamide 160mg N=6 | | | | Total N=23 |
|---|---|---|---|---|---|---|---|---|---|
| **CTC AE V5 Grade** | **G1 (%)** | **G2 (%)** | **G3 (%)** | **G4 (%)** | **G1 (%)** | **G2 (%)** | **G3 (%)** | **G4 (%)** | **All grades** |
| **Fatigue** | 3 (18) | 4 (24) | 1 (6) | 0 | 2 (33) | 2 (33) | 0 | 0 | 12 (52) |
| **Diarrhea** | 5 (29) | 1 (6) | 1 (6) | 0 | 4 (67) | 0 | 0 | 0 | 11 (48) |
| **Nausea** | 1 (6) | 3 (18) | 1 (6) | 0 | 1 (17) | 2 (33) | 0 | 0 | 8 (35) |
| **Decreased appetite** | 1 (6) | 2 (12) | 0 | 0 | 2 (33) | 1 (17) | 1 (17) | 0 | 7 (30) |
| **Vomiting** | 1 (6) | 2 (12) | 0 | 0 | 1 (17) | 3 (50) | 0 | 0 | 7 (30) |
| **Anemia** | 3 (18) | 1 (6) | 0 | 0 | 0 | 0 | 2 (33) | 0 | 6 (26) |
| **Arthralgia** | 3 (18) | 1 (6) | 0 | 0 | 1 (17) | 1 (17) | 0 | 0 | 6 (26) |
| **Lymphopenia** | 1 (6) | 0 | 3 (18) | 0 | 0 | 0 | 1 (17) | 0 | 5 (22) |
| **Muscular Weakness** | 2 (12) | 2 (12) | 0 | 0 | 0 | 0 | 1 (17) | 0 | 5 (22) |
| **Neutropenia** | 2 (12) | 0 | 1 (6) | 0 | 0 | 0 | 2 (33) | 0 | 5 (22) |

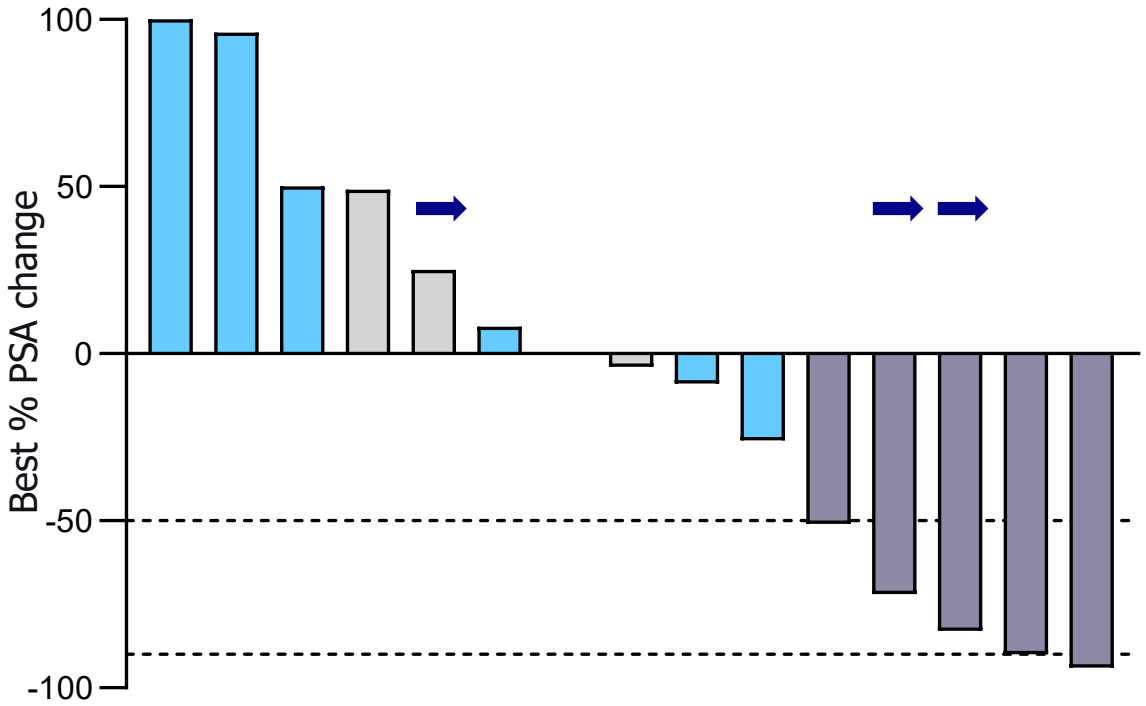
- Combination of MRT-2359 and enzalutamide was well tolerated
- Most frequent AEs were fatigue, diarrhea, and nausea which were classified as mild or moderate and were manageable and not therapy limiting



*Data cut-off January 30, 2026*

Note: Comparisons between MRT-2359 and other therapies represented herein are based on post-hoc analyses comparing MRT-2359 clinical information with publicly available information for other therapies. Any comparisons use information from different clinical trials, conducted by different parties, at different points in time, with differences in trial designs and patient populations. No head-to-head clinical trials have been conducted, cross-trial comparisons should not be made, and this information is provided only for illustrative purposes.

# MRT-2359 and Enzalutamide Achieved High PSA Response Rate in AR Mutant mCRPC



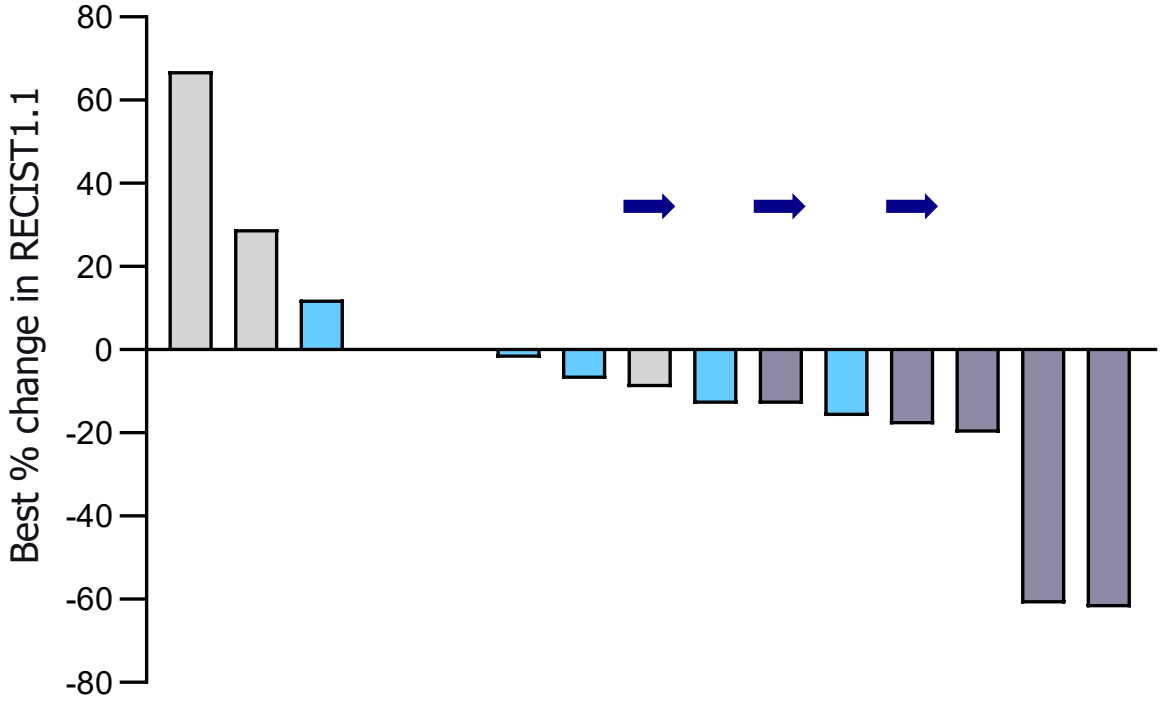

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **AR status** | V7 | V7 | V7 | WT | WT | V7 | V7 | WT | V7 | V7 | Mut | Mut | Mut | Mut | Mut |
| **RECIST Response** | PD | PD | SD | PD | SD | SD | SD | PD | SD | PD | SD | SD | SD | PR | PR |
| **RECIST %** | 0 | -13 | 0 | +29 | -9 | +12 | -2 | +67 | -16 | -7 | -20 | -18 | -13 | -62 | -61 |
| **Abiraterone** | + | - | + | - | + | + | + | - | + | - | + | + | + | + | + |
| **2nd gen ARi** | + | + | + | + | - | + | + | + | + | + | + | - | + | - | + |
| **Docetaxel** | + | + | + | + | - | + | - | + | + | + | + | + | + | + | + |
| **Pluvicto** | + | + | - | + | - | + | - | + | + | - | - | + | + | + | + |
| **Dose (mg)** | 0.75 | 0.75 | 0.5 | 0.5 | 0.5 | 0.75 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |

*Data cut-off January 30, 2026*

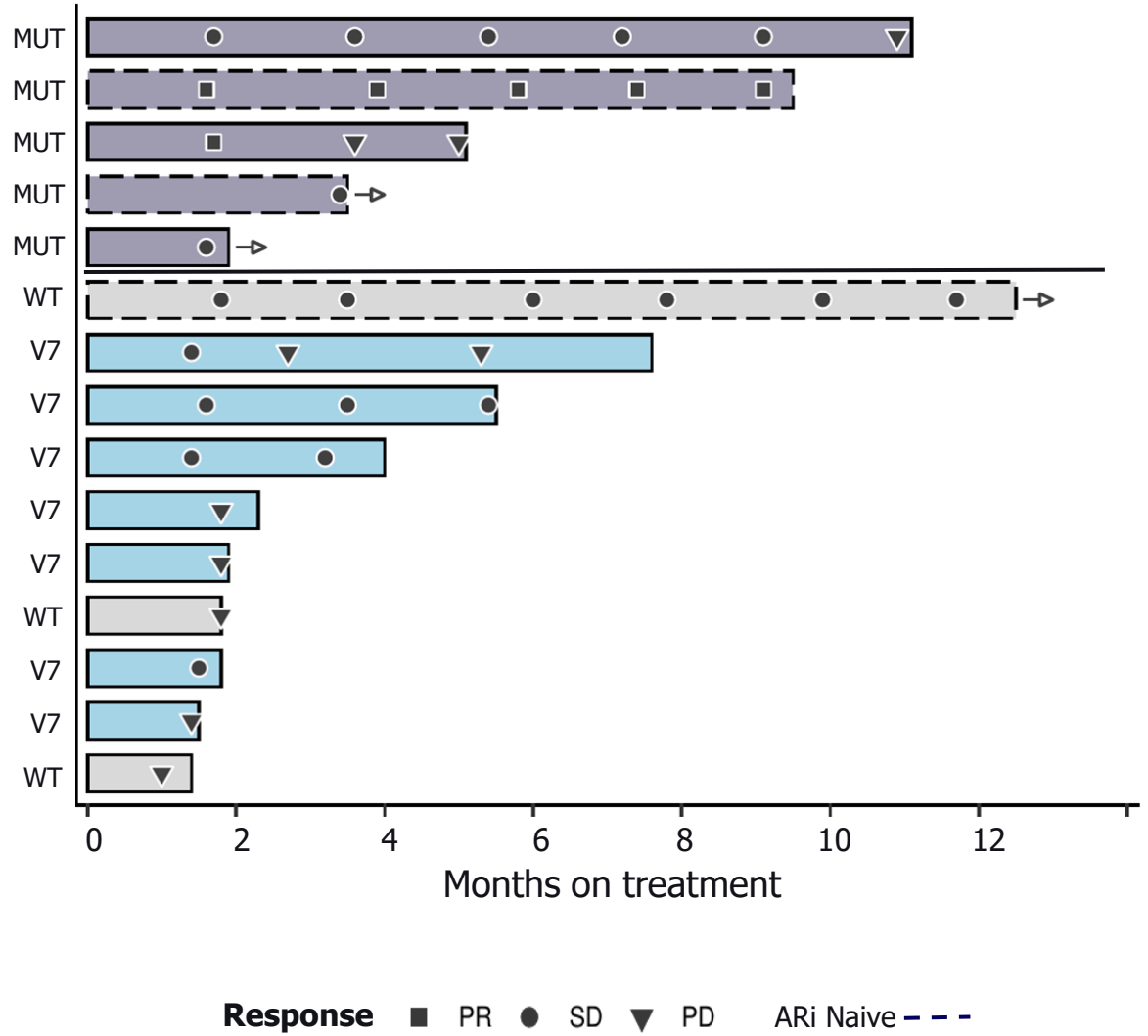
- MRT-2359 + enzalutamide achieved 100% PSA response rate; PSA response in 5 of 5 heavily pretreated patients with AR mutations
  - PSA50 (n=3)
  - PSA90 (n=2)
- PSA response rate in overall population suggests activity at least comparable to data shown in Phase 1 study of mevrometostat + enzalutamide

Note: Comparisons between MRT-2359 and other therapies represented herein are based on post-hoc analyses comparing MRT-2359 clinical information with publicly available information for other therapies. Any comparisons use information from different clinical trials, conducted by different parties, at different points in time, with differences in trial designs and patient populations. No head-to-head clinical trials have been conducted, cross-trial comparisons should not be made, and this information is provided only for illustrative purposes.

# MRT-2359 plus Enzalutamide Achieved Tumor Regressions in AR Mutant mCRPC



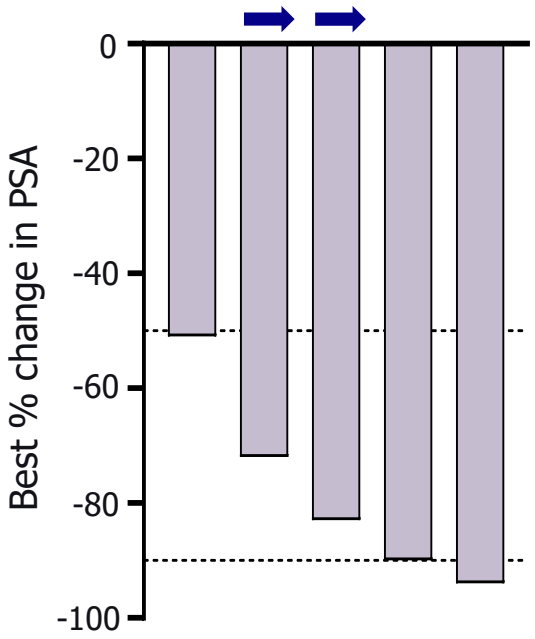

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **AR status** | WT | WT | V7 | V7 | V7 | V7 | V7 | WT | V7 | Mut | V7 | Mut | Mut | Mut | Mut |
| **RECIST Response** | PD | PD | SD | PD | SD | SD | PD | SD | PD | SD | SD | SD | SD | PR | PR |
| **RECIST %** | +67 | +29 | +12 | 0 | 0 | -2 | -7 | -9 | -13 | -13 | -16 | -18 | -20 | -61 | -62 |
| **Abiraterone** | - | - | + | + | + | + | - | + | - | + | + | + | + | + | + |
| **2nd gen ARi** | + | + | + | + | + | + | + | - | + | + | + | - | + | + | - |
| **Docetaxel** | + | + | + | + | + | - | + | - | + | + | + | + | + | + | + |
| **Pluvicto** | + | + | + | + | - | - | - | - | + | + | + | + | - | + | + |
| **Dose (mg)** | 0.5 | 0.5 | 0.75 | 0.75 | 0.5 | 0.5 | 0.5 | 0.5 | 0.75 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |




*Data cut-off January 30, 2026*

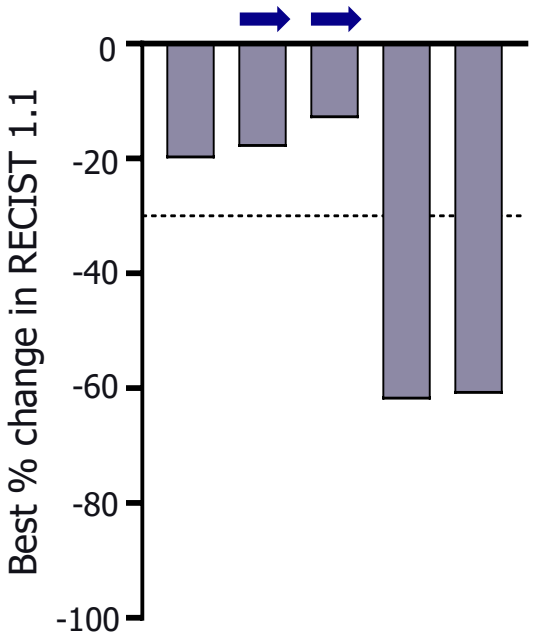
# Compelling Activity in Heavily Pretreated Patients with AR Mutations

## Best % change in PSA



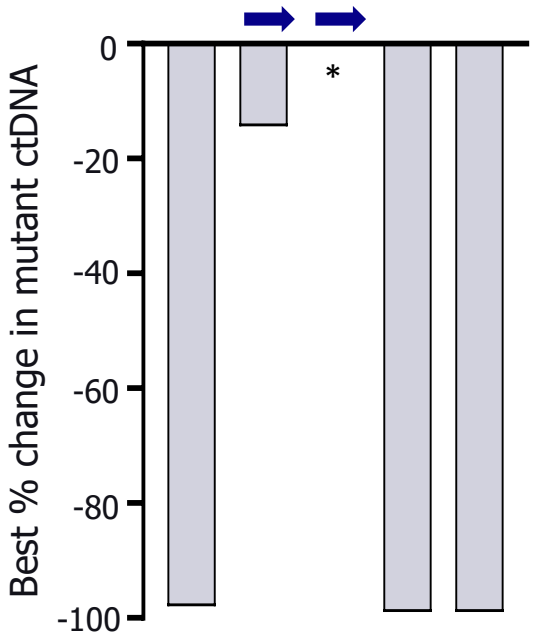

| Response | SD | SD | SD | PR | PR |
|---|---|---|---|---|---|
| RECIST % | -20 | -18 | -13 | -62 | -61 |
| Abiraterone | + | + | + | + | + |
| 2nd gen ARi | + | - | + | - | + |
| Docetaxel | + | + | + | + | + |
| Pluvicto | - | + | + | + | + |

## Best % change in RECIST



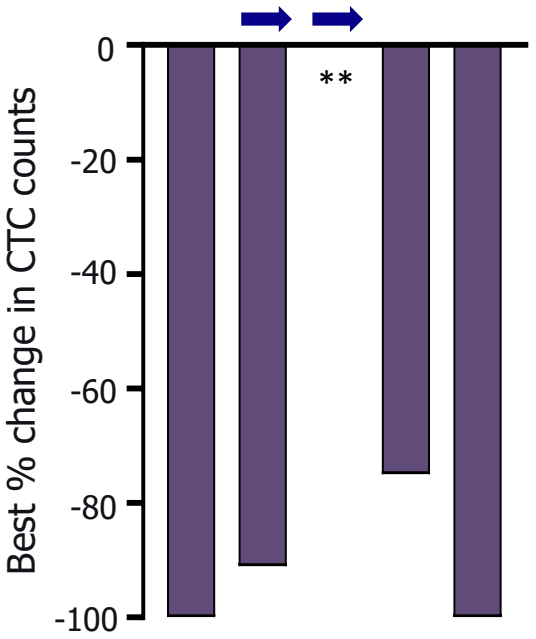

| SD | SD | SD | PR | PR |
|---|---|---|---|---|
| -20 | -18 | -13 | -62 | -61 |
| + | + | + | + | + |
| + | - | + | - | + |
| + | + | + | + | + |
| - | + | + | + | + |

## Best % change in ctDNA




| SD | SD | SD | PR | PR |
|---|---|---|---|---|
| -20 | -18 | -13 | -62 | -61 |
| + | + | + | + | + |
| + | - | + | - | + |
| + | + | + | + | + |
| - | + | + | + | + |

## Best % change in CTC counts




| SD | SD | SD | PR | PR |
|---|---|---|---|---|
| -20 | -18 | -13 | -62 | -61 |
| + | + | + | + | + |
| + | - | + | - | + |
| + | + | + | + | + |
| - | + | + | + | + |



*Data cut-off January 30, 2026*

**QC failed; **Data pending*

# MODeFIRe-1 MRT-2359 Phase 2 Study in CRPC (up to 25 pts)



**Study Population**

Simon's 2-Stage Design
(up to 25 pts)
mCRPC with AR mutations
PSA +/- RECIST measurable,
ARPI and chemo pretreated



**Treatment**

MRT-2359 0.5mg (21/7) +
2nd gen AR inhibitor apalutamide

28-day cycles

- Enrollment completion ~12 months after initiation
- Endpoints include PSA response, RECIST, DoR, rPFS, and safety

Potential to expand to other AR-driven populations, including patients without prior 2nd generation AR inhibitors, as well as into combinations with RL therapies independent of AR status

Study ongoing; clinical data update expected in 2027



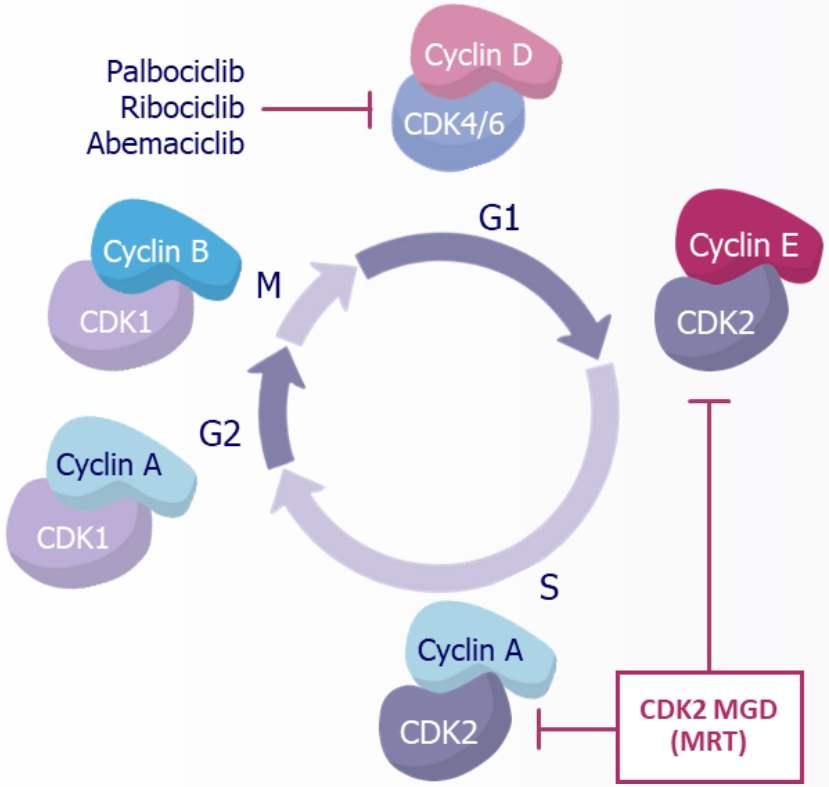
**MODeFIRe: Mo**lecular **De**grader **F**or **I**nhibitor **Re**sistance

Monte Rosa Therapeutics

# CDK2 Program

# CDK2 is a Key Driver of Cell Cycle Progression in Cancer

**CDK2: a key cell cycle regulator**




**Therapeutic hypothesis:**

- CDK2 is a key driver of cancers with cyclin dependent kinase pathway alterations
- MGDs will achieve greater selectivity against other CDKs and kinases in general, as well as more sustained pathway inhibition compared to inhibitors

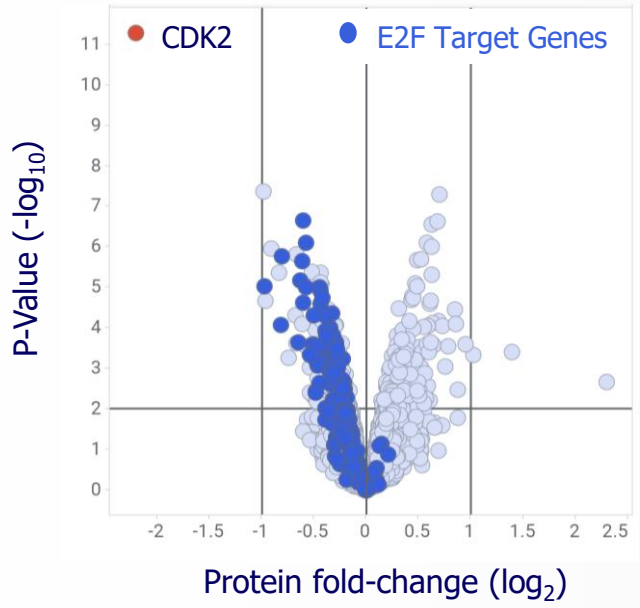
**Clinical Opportunity:**

- ER-positive breast cancer pre- and post-treatment with CDK4/6 inhibitors (~600K patients)

*Source: Clarivate (2026 drug-treated advanced/metastatic patient incident population in G7 countries)*

# Differentiated CDK2 Selectivity Supports Combination Strategies in ER+ BC

**Selective CDK2 degradation resulted in reduction of E2F pathway proteins**

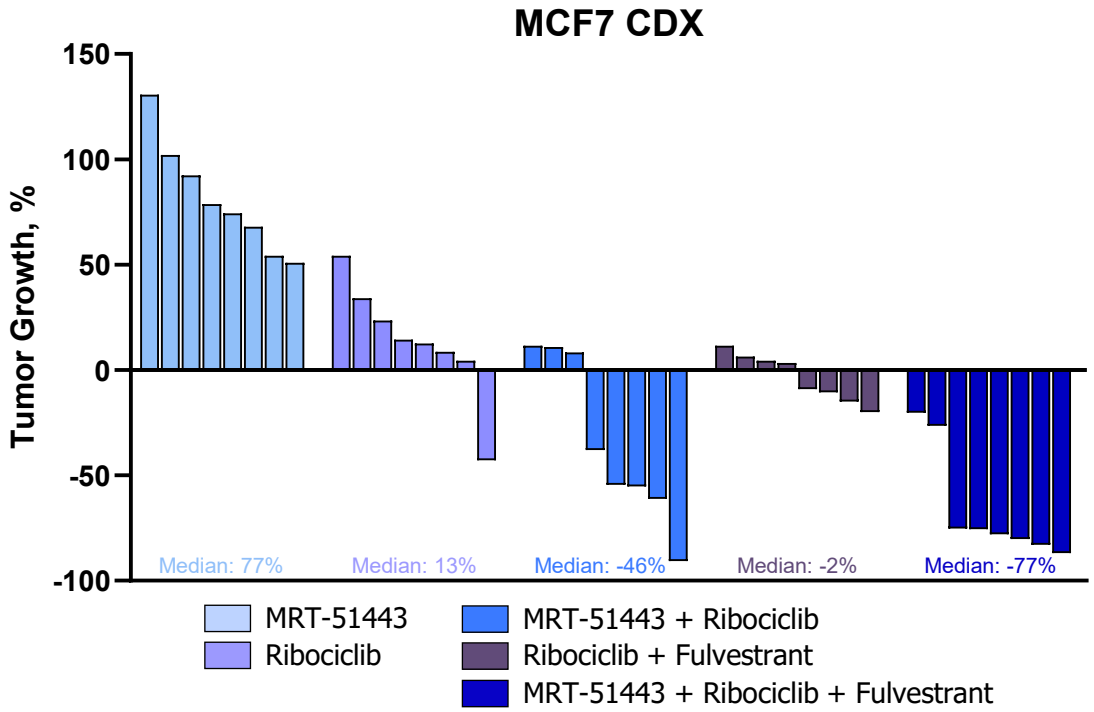



TMT Proteomics (24 hr/1μM)
MDA-MB-157

- MRT-51443 selectively degrades CDK2, leading to G1 arrest and inhibition of proliferation in CDK2-dependent cancer cells
- CDK2 degradation results in reduced expression of E2F target genes, confirming effective pathway shutdown at the transcriptional level
- Compared with clinical CDK2 inhibitors, MRT-51443 demonstrates superior selectivity with minimal off-target kinase activity, leading to less CDK2-independent growth inhibition and lack of impact on hematologic colony formation assays.
- Combination of a CDK2 MGD with CDK4/6 inhibition delays resistance onset in ER-positive breast cancer models in vitro
- Triple combination of MRT-51443 with ribociclib and fulvestrant drives robust tumor regression and meaningfully outperforms CDK4/6 inhibitor plus fulvestrant alone in ER-positive breast cancer xenografts

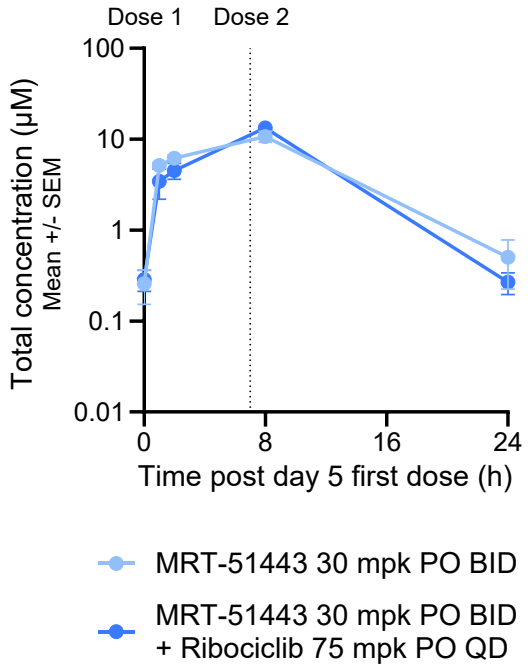
# CDK2 MGD Demonstrated Activity in Combination with Ribociclib (CDK4/6i) and Fulvestrant (SERD) in ER+ Breast Cancer Model MCF7

## MRT-51443 induces robust MCF7 CDX tumor regression in combination with ribociclib and fulvestrant

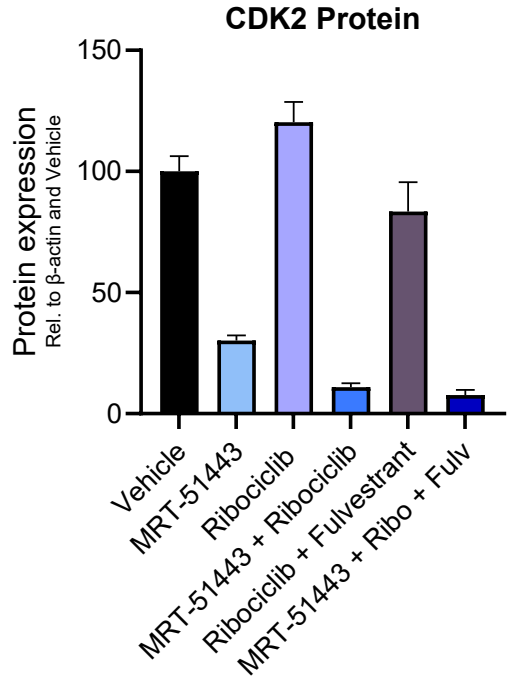



28-day efficacy in MCF7 CDX, % TGI listed; MRT-51443 30 mpk PO BID, ribociclib 75 mpk PO QD, fulvestrant 5 mg/mouse s.c. QW

## MRT-51443 exhibits favorable PK and PD properties in combination with ribociclib and fulvestrant



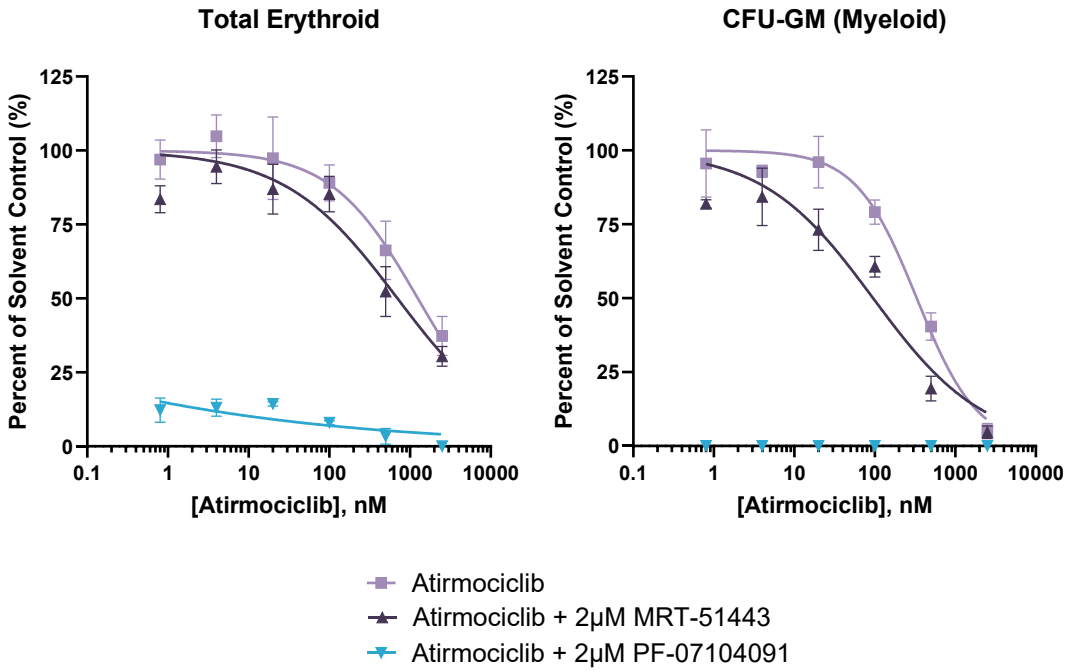

5-Day PK study in MCF7 CDX; Doses and concentrations as indicated



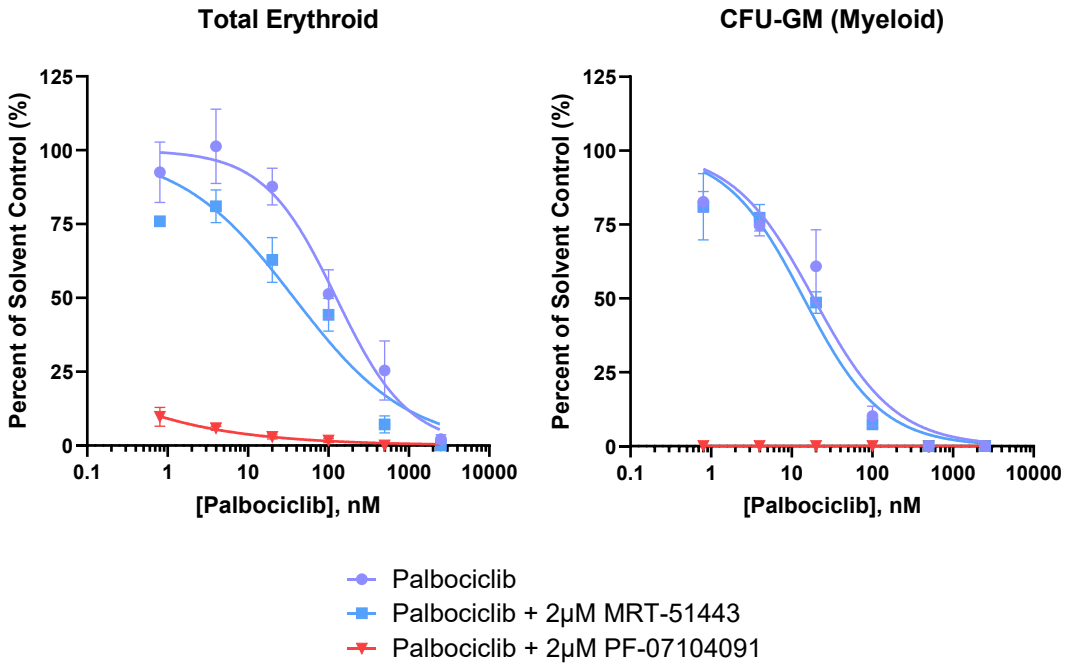

WB Quantification from MCF7 Efficacy; Harvested D28; analyzed by WB

# CDK2 MGD Exhibited Minimal Toxicity in Combination with CDK4 inhibitor or CDK4/6 inhibitor *in vitro*, compared to CDK2 Inhibition

**MRT-51443 has minimal impact on bone marrow progenitors in combination with CDK4 inhibition**




**MRT-51443 has minimal impact on bone marrow progenitors in combination with CDK4/6 inhibition**



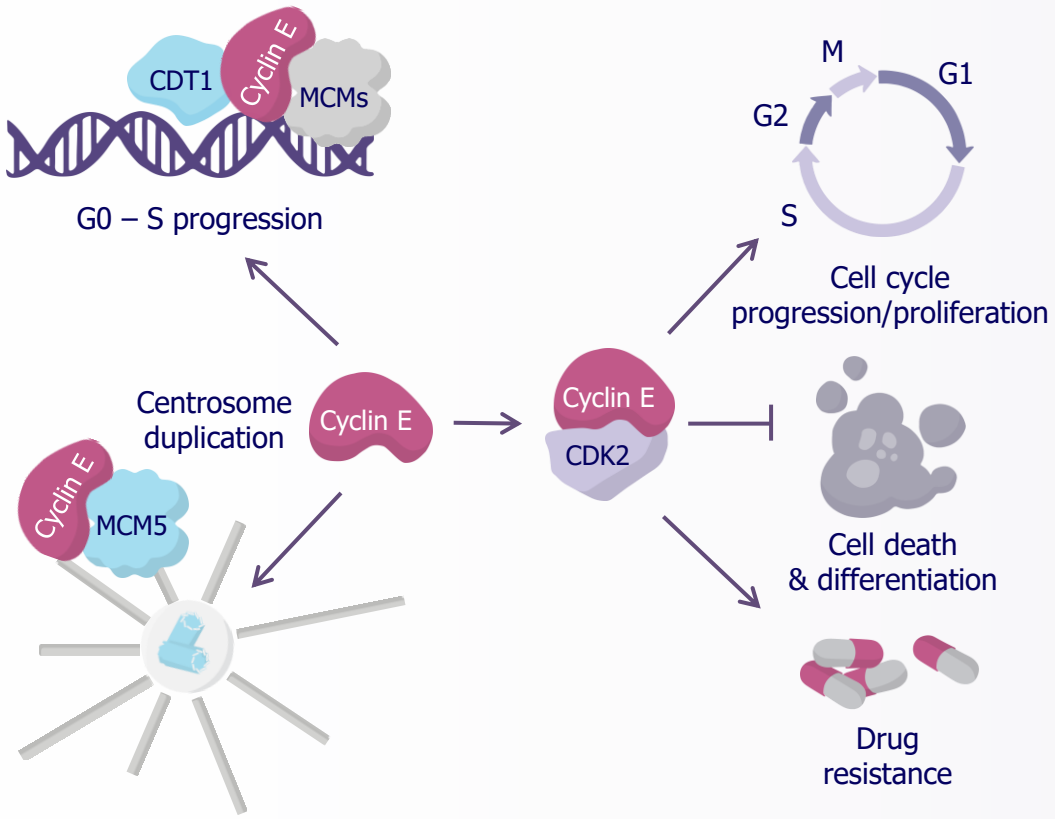

14-Day CFU assay, BFU-E and CFU-GM colonies
Drug concentrations as indicated

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# CCNE1 Program

# CCNE1 (Cyclin E1) is a Target for Solid Tumors with Deregulated Cyclin E1

**Cyclin E drives multiple hallmark cancer mechanisms**




**Therapeutic hypothesis:**

- CCNE1 (Cyclin E1) is a well-recognized human oncogene that drives multiple hallmarks of cancer, and has been considered undruggable
- Selective degradation of cyclin E1 can target tumors with deregulated cyclin E1 (amplification or overexpression)

**Clinical opportunity:**

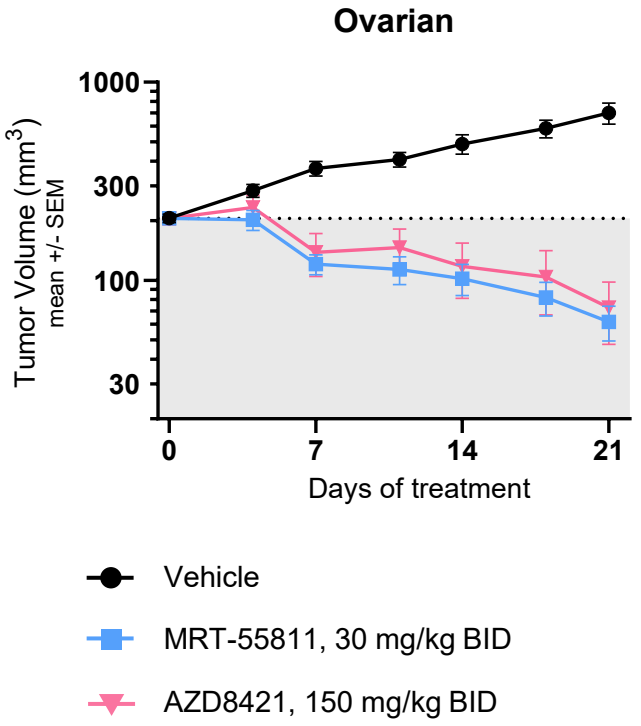
- First-in-class Cyclin E1 degraders for Cyclin E1 amplified cancers
  - Ovarian (~20% of ~80K patients), endometrial (~10% of ~50K patients), gastroesophageal cancer (~10% of ~200K patients), breast cancer and others



*Source: Clarivate (2026 drug-treated advanced/metastatic patient incident population in G7 countries)*

# Potent and Highly Selective CCNE1-directed MGDs

**MRT-55811 induced tumor regression in *CCNE1* amplified ovarian model**




21-day efficacy study in OVSAHO CDX

- MRT-55811 is a potent and highly selective CCNE1 molecular glue degrader that drives robust G1/S cell-cycle arrest in CCNE1-amplified cancer cells.
- CCNE1 degradation leads to downstream suppression of CDK2 activity and E2F pathway signaling, confirming on-mechanism cell-cycle inhibition
- MRT-55811 induces co-degradation and ubiquitination of the CCNE1–CDK2 holoenzyme, supporting a catalytic and durable mechanism of action
- The CCNE1 MGD shows superior selectivity and potency in high-CCNE1 tumors versus CDK2 and CDK4/6 inhibitors, particularly in ovarian, endometrial, gastric, and breast cancer models
- Treatment with MRT-55811 resulted in tumor regression across multiple CCNE1-amplified xenograft models, including gastric, ovarian, and breast cancers

Monte Rosa Therapeutics

# Team

# World-Class Leadership

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



**Markus Warmuth, M.D.**
Chief Executive Officer

H3 Biomedicine
Novartis



**Sharon Townson, Ph.D.**
Chief Scientific Officer

Kymera Therapeutics
Warp Drive Bio



**John Castle, Ph.D.**
Chief Data and Information Officer

agenus
BioNTech



**Magnus Walter, DPhil**
Chief Technology Officer

AbbVie
Lilly



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

The University of Texas MD Anderson Cancer Center



**Phil Nickson, Ph.D., J.D.**
Chief Business and Legal Officer

Momenta
FISH & RICHARDSON



**Jennifer Champoux**
Chief Operating Officer

H3 Biomedicine
Novartis



**Andrew Funderburk**
Chief Investor Relations and Strategy Officer

Kendall Investor Relations
Health Advances

# Thank you



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