

Degrading Proteins, Making Medicines

MRT-8102 GFORCE-1 Clinical Study Results

October 1, 2026



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 successfully research, develop and, if approved, commercialize our product candidates in current or future indications; statements regarding our progress in developing only-in-class and first-in-class MGD therapeutics; the timing, design, conduct, progress and results of our preclinical and clinical programs; statements regarding the significance, interpretation and potential implications of clinical data for MRT-8102, including safety, tolerability, target engagement, pharmacodynamic, biomarker, genetic and lipid data from GFORCE-1; the potential for MRT-8102 and NEK7 degradation to provide differentiated or clinically meaningful effects across ASCVD, coronary artery disease, gout, hidradenitis suppurativa and other NLRP3/IL-1-driven diseases; the potential relationship between observed biomarker effects and disease biology, clinical outcomes or therapeutic benefit; the potential use of biomarkers, imaging, genetics or pharmacogenomics to identify or enrich for patients who may benefit from treatment, inform dose selection or support more efficient clinical development; statements regarding our planned Phase 2 development program for MRT-8102, including the anticipated timing, design, conduct, endpoints, results and data disclosures for GFORCE-2, GEMINI-1 and GALAXY-1; the potential for such studies to demonstrate proof of concept, safety, efficacy, flare prevention, lesion response, cardiovascular benefit or other clinical outcomes and to inform potential future Phase 3 development; statements regarding the evaluation of additional proof-of-concept studies in further indications; the timing and outcome of regulatory interactions and submissions; statements regarding the potential clinical and commercial opportunities for MRT-8102, including estimates of patient populations, unmet need, market opportunity, competitive positioning and potential differentiation from other therapies, including comparisons to other anti-inflammatory modalities and lipid-modifying agents; statements regarding the effects of MRT-8102 on lipids and lipoproteins, including lipoprotein(a), and the potential clinical significance thereof; statements regarding the expected safety profile of MRT-8102 in patient populations with comorbidities, including chronic kidney disease; statements regarding MRT-9347 and other current or future product candidates, including MRT-2359 and preclinical and discovery-stage programs, their potential applications across immunology and inflammation, oncology, genetic and neurological diseases and other therapeutic areas, their differentiation, strategic value, the timing and results of anticipated clinical data updates, regulatory filings and other development milestones; statements regarding our expectations that our collaborator, Novartis, will advance MRT-6160 and other VAV1-directed MGDs in immune-mediated diseases, including the anticipated timing of additional Phase 2 study initiations; statements regarding our QuEEN™ discovery engine and the potential applications of our platform; the advancement and application of our partnered and wholly owned pipeline, including programs licensed or optioned to Roche and Novartis; our ability to optimize collaborations with industry partners; and our expectations regarding the timing and achievement of development, regulatory and commercial milestones and the success of our programs, among others. By their nature, these statements are subject to numerous risks and uncertainties, including those risks and uncertainties set forth in our 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, and any subsequent filings, that could cause actual results, performance or achievements to differ materially and adversely from those anticipated or implied in the statements, as well as the risks that preclinical results may not be predictive of clinical results; early, initial or interim clinical results may not be predictive of final results or the results of future trials; results observed in one study, population, dose group, analysis or indication may not be replicated in another; pharmacodynamic or biomarker effects may not translate into clinical or therapeutic benefit; and comparisons across separate studies or therapeutic modalities may not be reliable. Proposed clinical-trial designs and development plans remain subject to regulatory review and may change. You should not rely upon forward-looking statements as predictions of future events. Although our management believes that the expectations reflected in these statements are reasonable, we cannot guarantee that the future results, performance, events or 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 they are made and should not be construed as statements of fact. We undertake no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by applicable law. Certain information contained in these materials, and certain statements made orally during any presentation relating to these materials, are based on studies, publications, surveys and other data obtained from third-party sources and on our own internal estimates and research. While we believe these sources to be reliable as of the date of these materials, we have not independently verified, and make no representations regarding, the adequacy, fairness, accuracy or completeness of such information. No independent source has evaluated the reasonableness or accuracy of our internal estimates or research, and no reliance should be placed on information or statements based on such estimates or research.

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

MRT-8102, a selective first-in-class NEK7 MGD, demonstrated a favorable safety and tolerability profile, sustained NEK7 degradation, and broad normalization of elevated pathogenic drivers of ASCVD

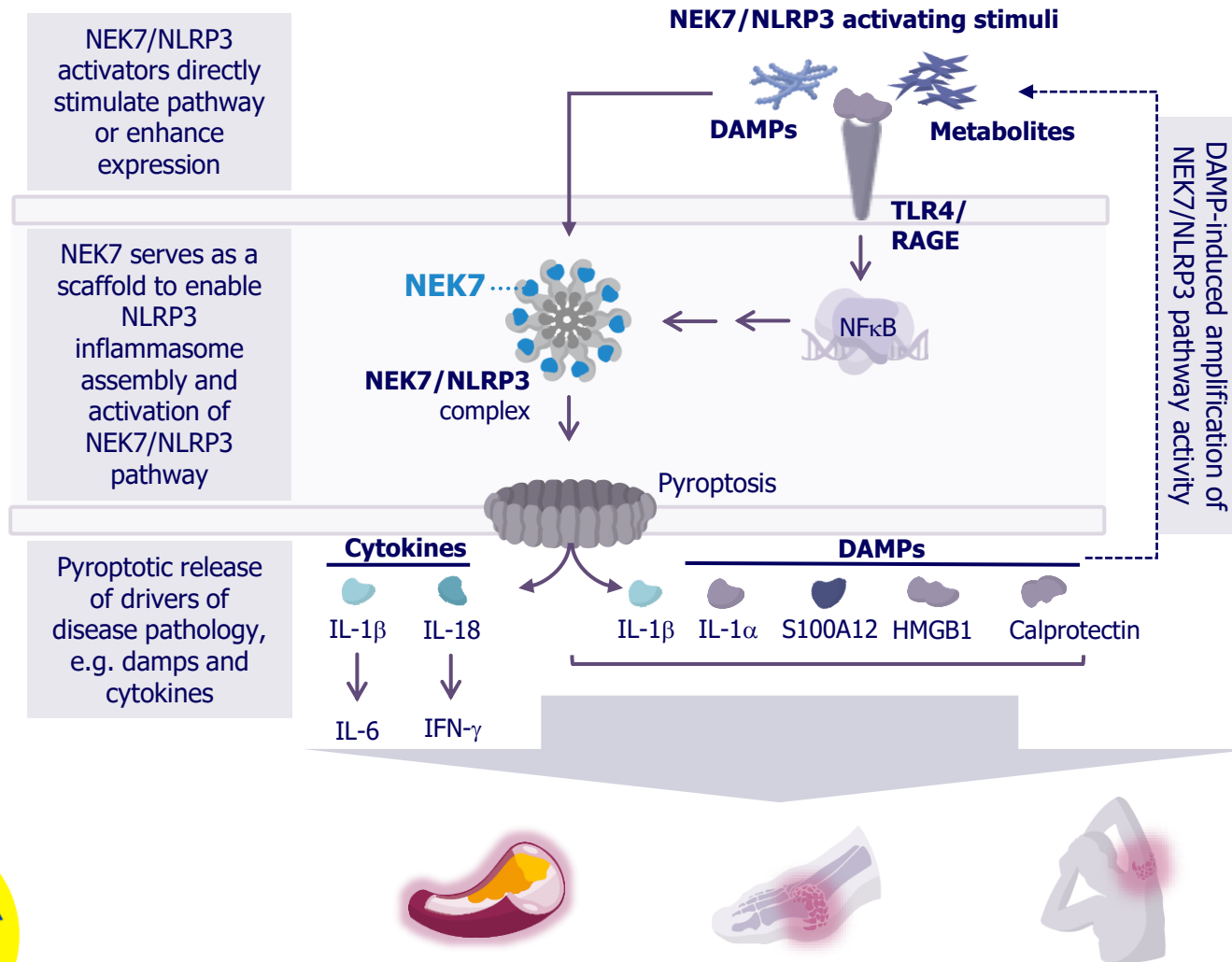
- **Study design:** 108 subjects with elevated CVD risk; 8-week study, randomized to MRT-8102 at 5, 20, and 40 mg QD, or placebo for 4 weeks dosing
- **Target engagement:** Robust, sustained, and equal NEK7 degradation across all three dose levels
- **Safety:** No SAEs; TEAE rate similar to placebo (33% 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:**
 - Pathogenic drivers of ASCVD, including IL-1 β , 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





Therapeutic Rationale for Degrading NEK7

NEK7 Enables Pathogenic NLRP3 Activation to Drive Disease Biology

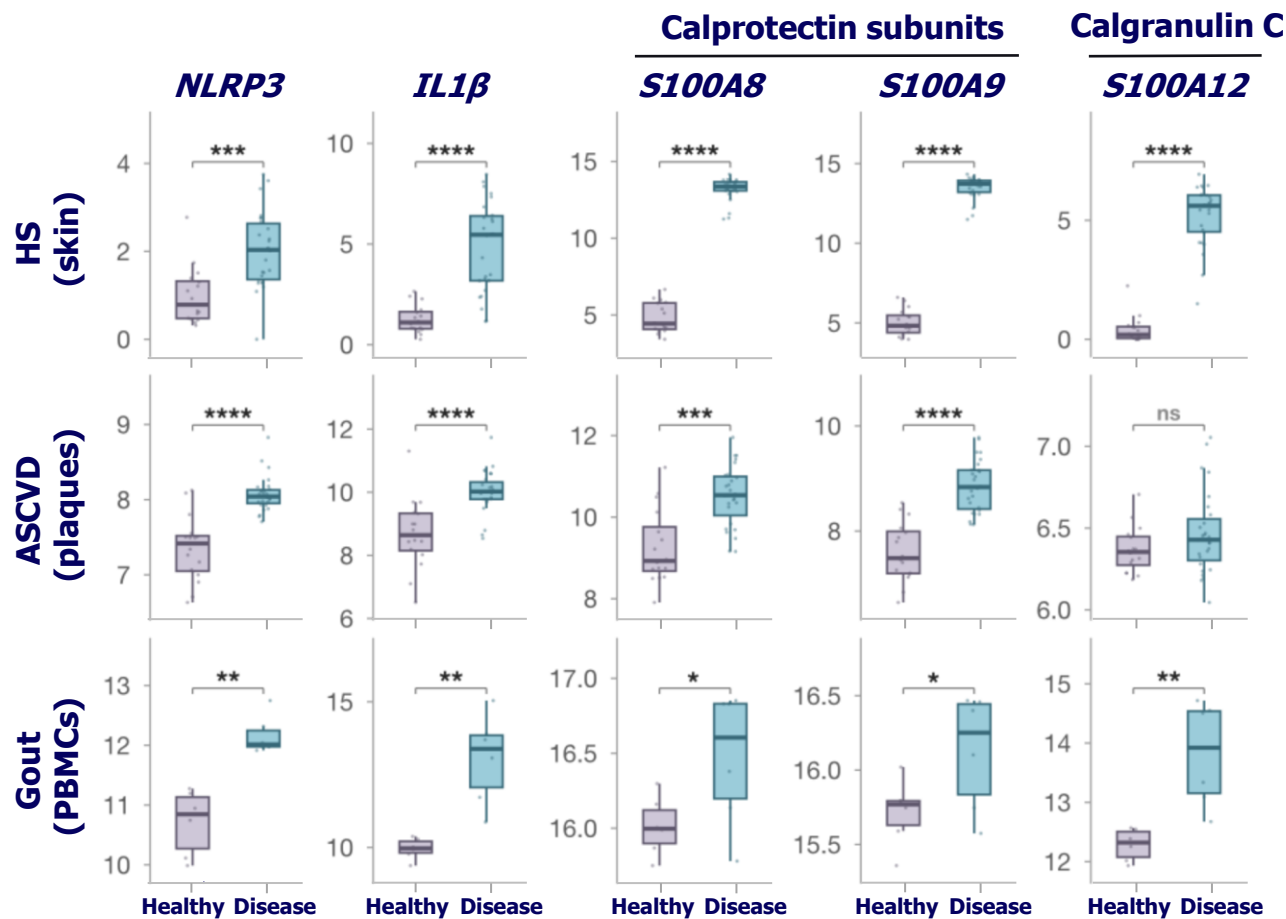
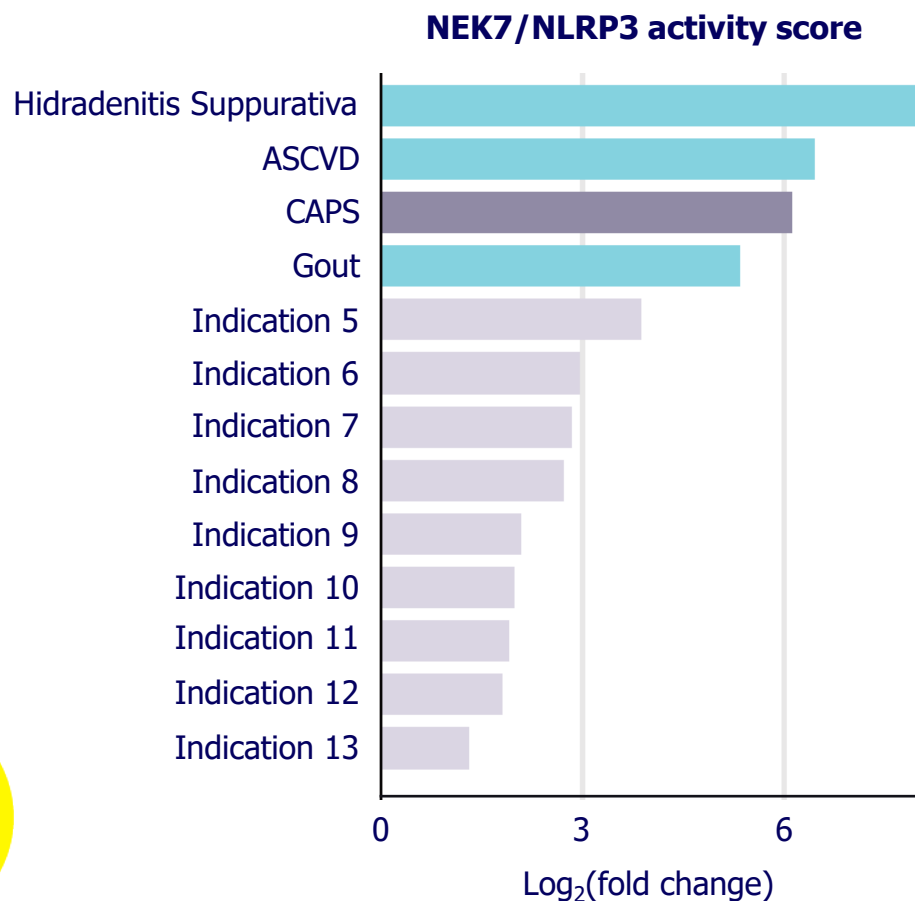


- Multiple metabolic and genetic factors can promote NEK7-mediated NLRP3 inflammasome complex assembly in a kinase-independent manner
- NEK7/NLRP3 pathway activation causes pyroptotic cell death, leading to release of **IL-1α/β, IL-18, and DAMPs (e.g., HMGB1, Calprotectin, S100A12)**
 - IL-1β and IL-18 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**

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

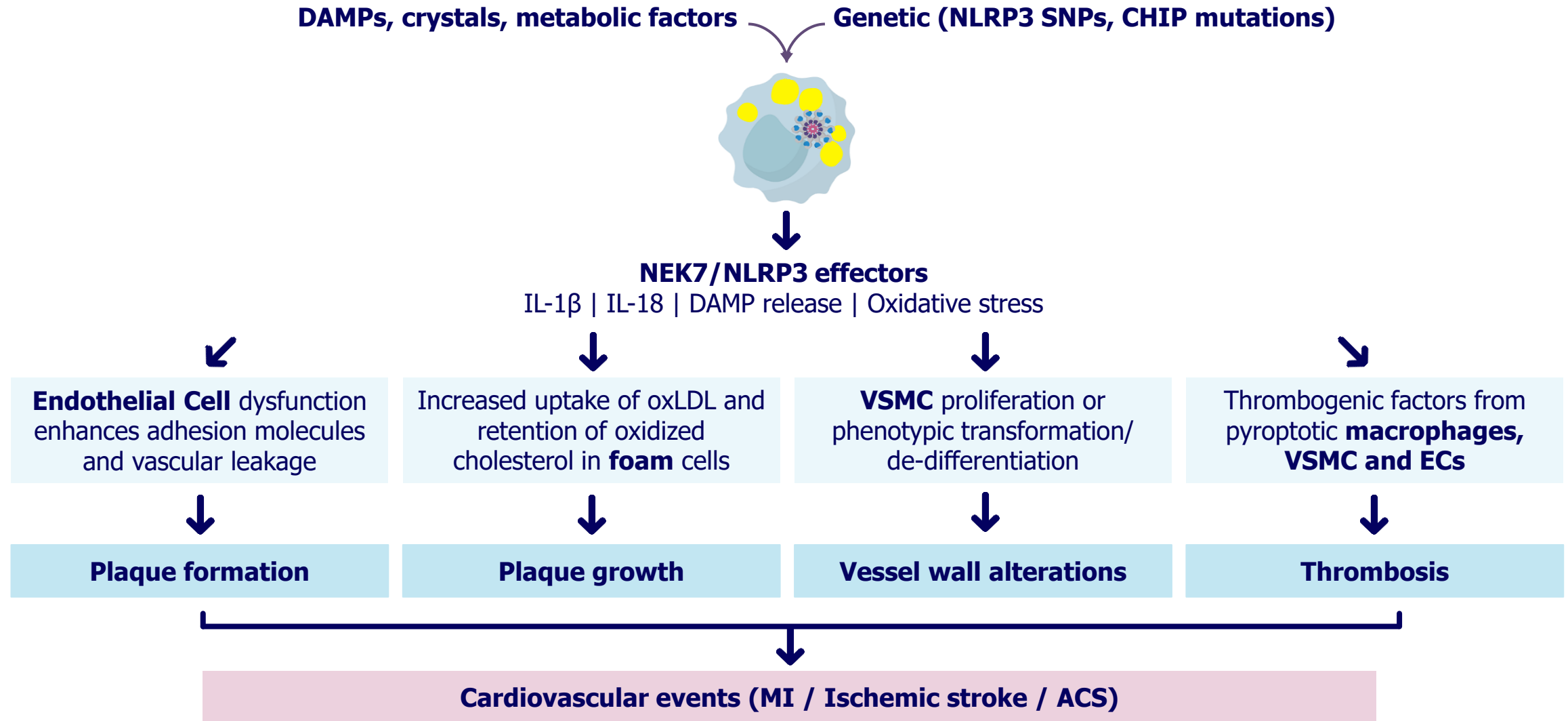
Upregulation of pathogenic cascade downstream of pyroptosis is conserved across the top NEK7/NLRP3-active indications



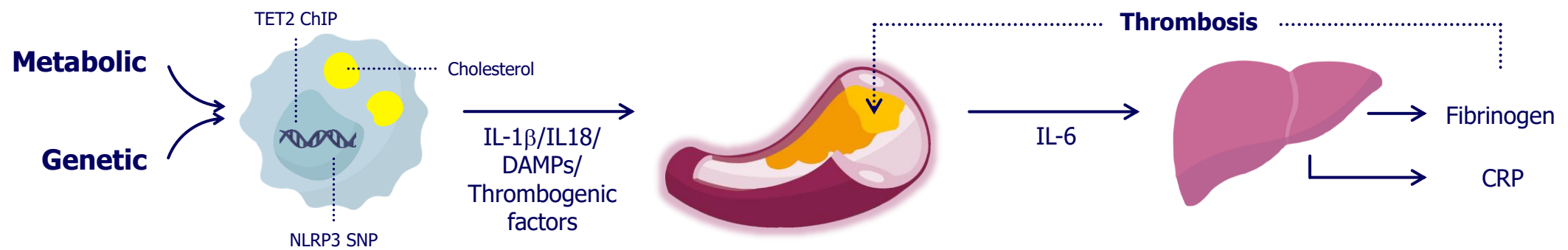


The Role of the NEK7/NLRP3 Pathway in ASCVD

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



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 - Baseline median CRP unknown - Colchicine reduced MACE by 31%; no risk of infection, significant GI AEs	4,745 pts $\leq$ 30 days post-MI randomized to colchicine or pbo - Baseline median CRP 4.28 mg/L - Colchicine reduced MACE by 23%; no risk of infection, significant GI AEs	10,061 pts $\geq$ 30 days post MI randomized to canakinumab (anti-IL-1β) or pbo - Mean time since MI 4.57 years - Baseline CRP $\geq$ 2mg/L (median 4.1 to 4.2) - 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 - Baseline CRP $\geq$ 2mg/L (median 4.5) No significant effect on MACE; risk of infection increased

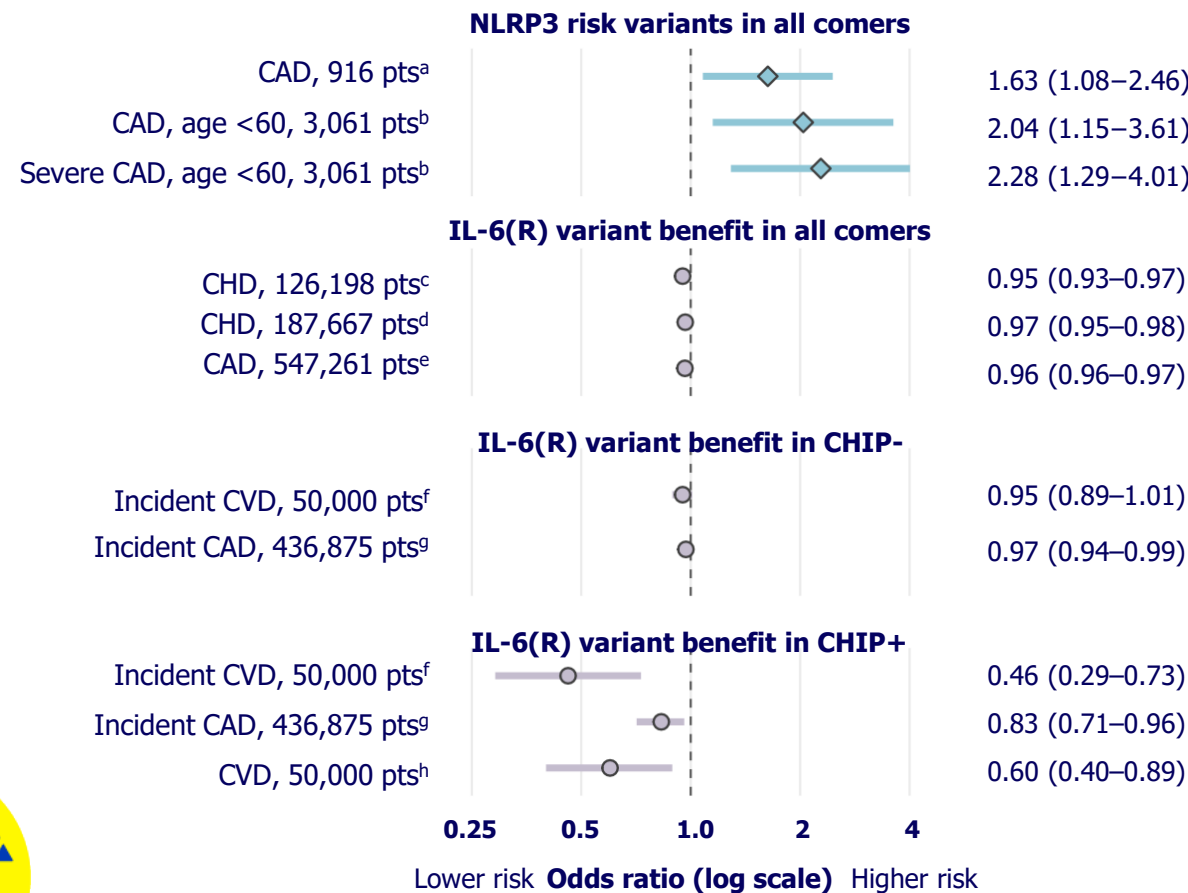
Clinical efficacy achieved

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

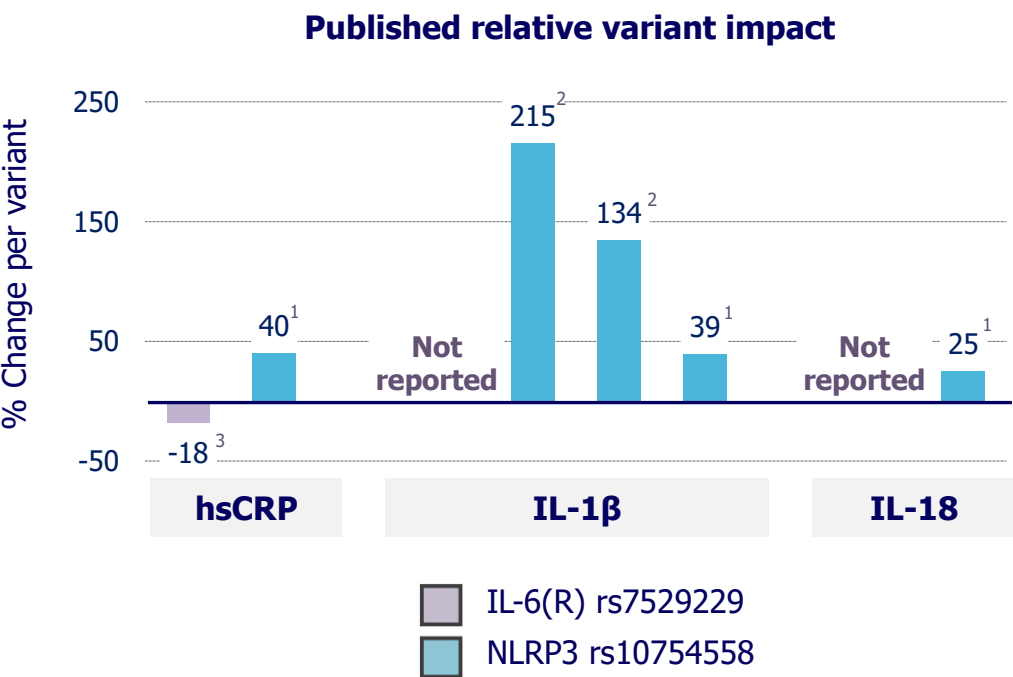


NLRP3 Activating Variants Increase Signaling and Cardiovascular Risk

**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**

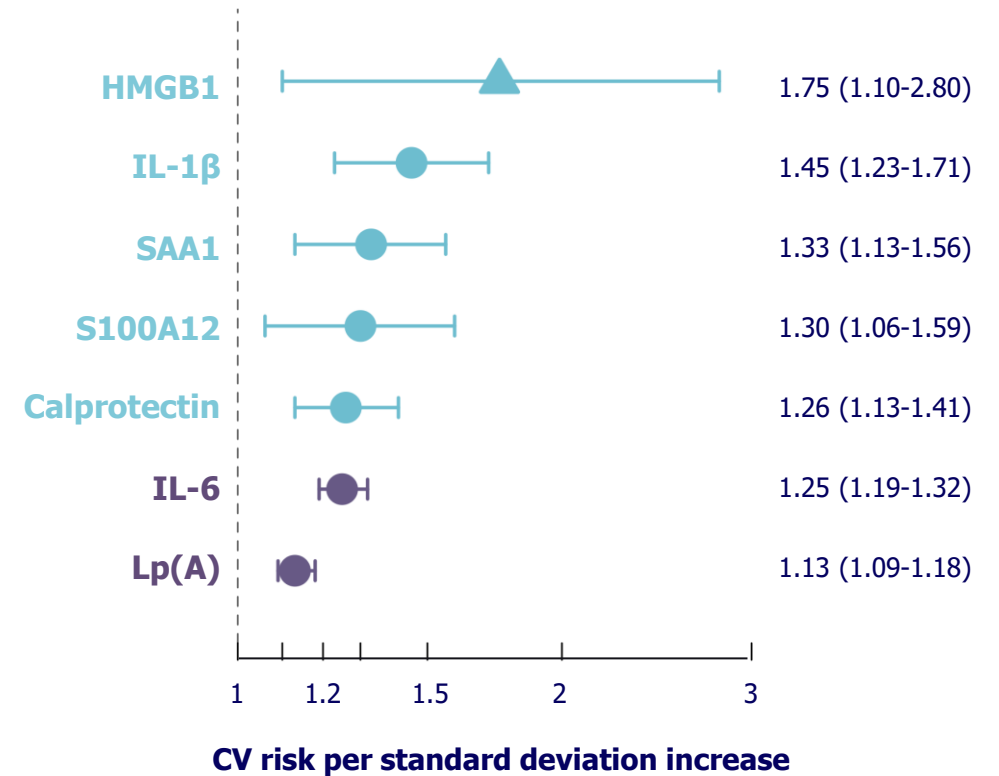
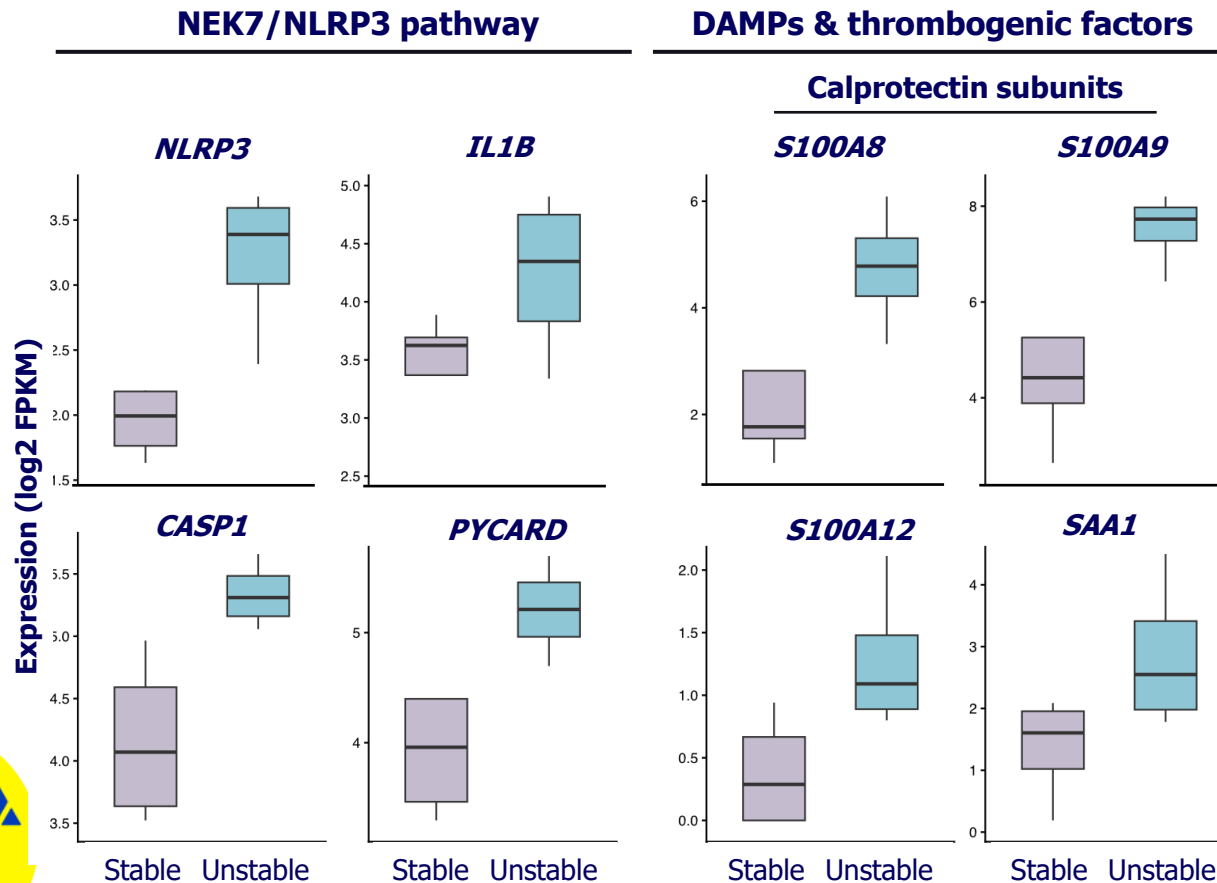


Left: ^aZhou et al. (2016); ^bSchunk et al. (2021); ^cSwerdlow et al. (2012); ^dSarwar et al. (2012); ^eRosa et al. (2019); ^fBick et al. (2019); ^gVlasschaert et al. (2023); ^hKessler et al. (2022); Right: ¹Wu et al. (2022); ²Zhou et al. (2016); ³Tchuisseu-Kwangoua et al. (2025). % differences: NLRP3 rs10754558 = (GG – CC)/CC; IL-6(R) rs7529229 (proxy rs2228145) = (CC – AA)/AA

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

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



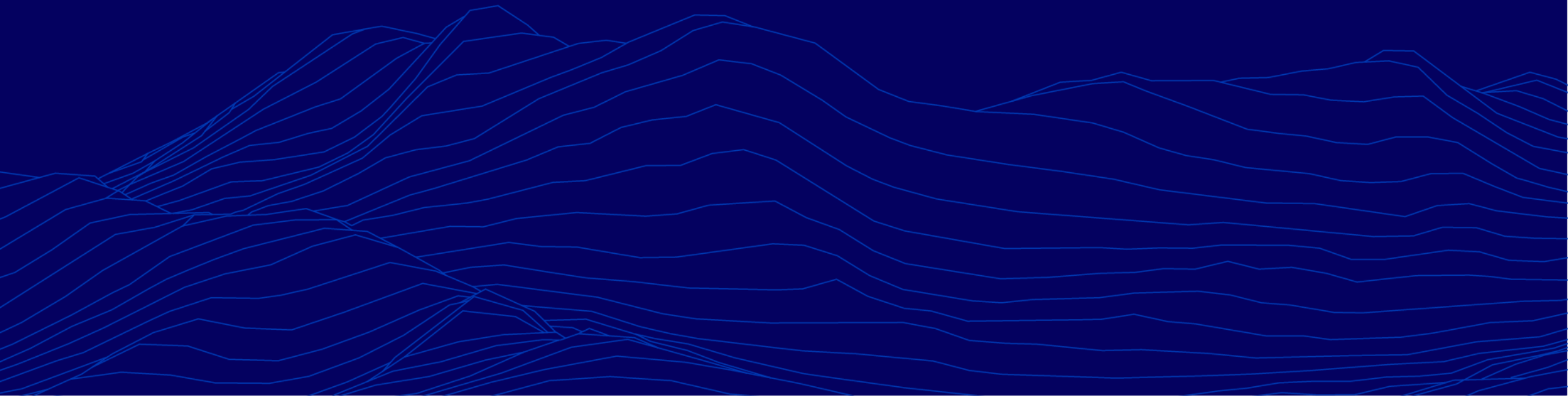
● Harmonized per-SD HR ▲ Non-harmonized (per-doubling, acute STEMI)

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

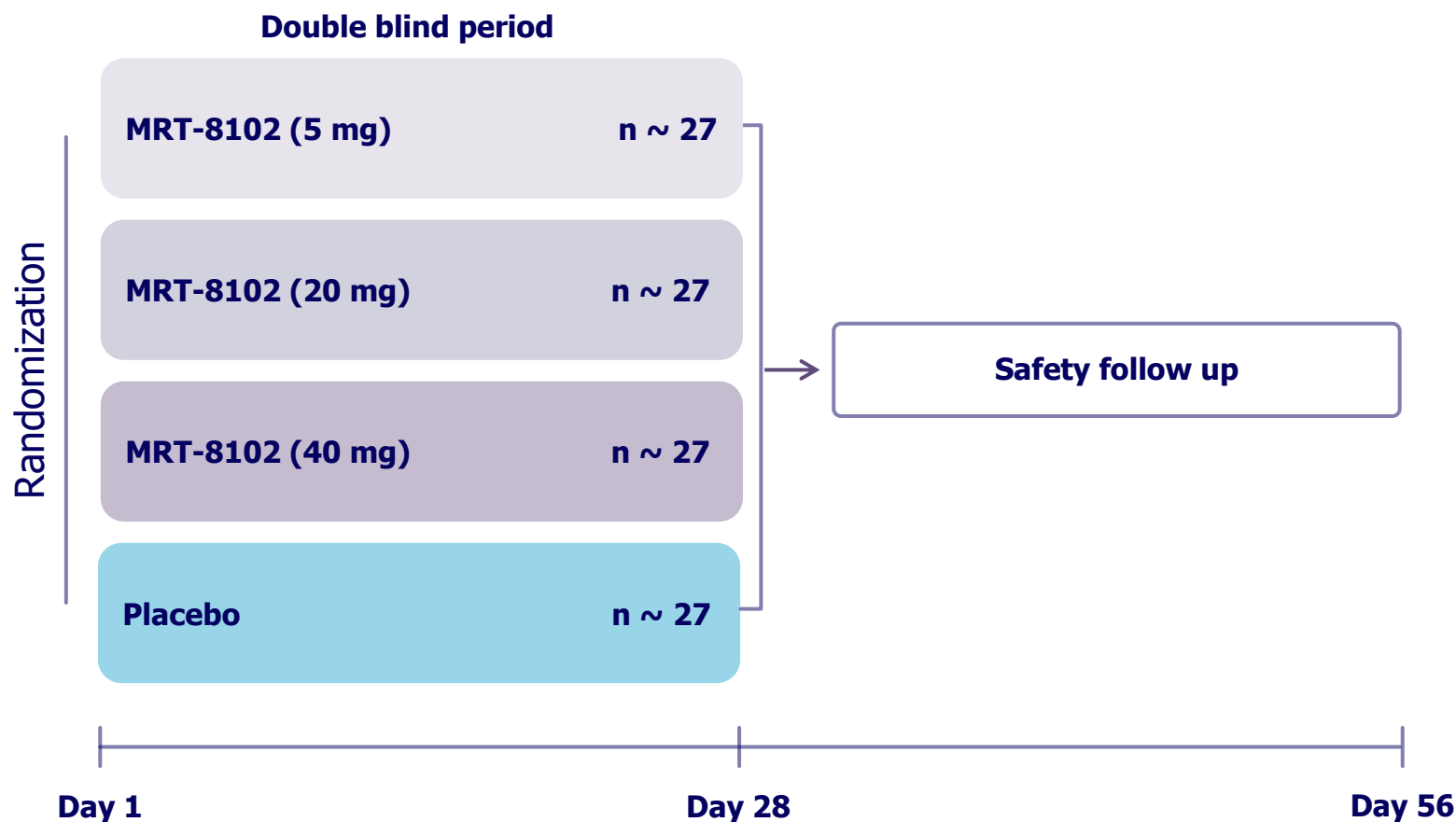
Data from PMIDs 24026779, 29957458, 21435605, 25341801, 39322770, 28845751, 28428221, 39178030, 30006491, 19622820, 23034020



Results of GFORCE-1 Study



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



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

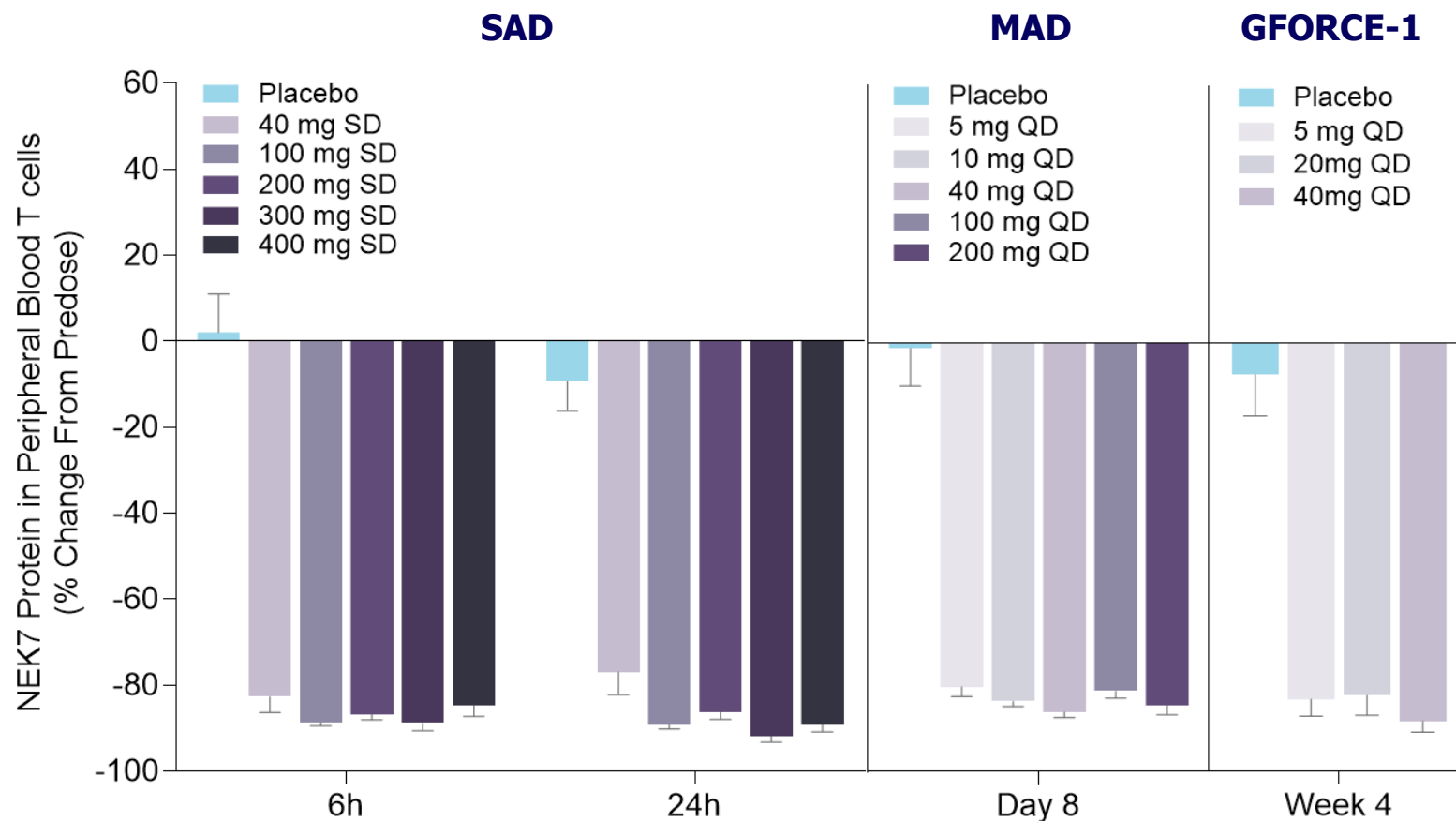
- NEK7 (target engagement)
- DAMPs and cytokines to inform ASCVD pathogenic drivers + systemic inflammation
- Thrombogenic factors
- Lipids, lipoproteins, and other markers of CV risk (Lp(a), LDL-C)

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

GFORCE-1 Participants Baseline Characteristics

Baseline Characteristics	Placebo (n=27)	MRT-8102 5 mg (n=27)	MRT-8102 20 mg (n=27)	MRT-8102 40 mg (n=27)	Total (n=108)
Median age, years (IQR)	45 (30 - 53)	38 (34 - 50)	40 (34 - 55)	41 (37 - 52)	41 (34 - 52)
Male, n (%)	12 (44.4)	8 (29.6)	11 (40.7)	13 (48.1)	44 (40.7)
Female, n (%)	15 (55.6)	19 (70.4)	16 (59.3)	14 (51.9)	64 (59.3)
Race, n (%)					
White	15 (55.6)	16 (59.3)	16 (59.3)	18 (66.7)	65 (60.2)
African American	11 (40.7)	9 (33.3)	10 (37.0)	8 (29.6)	38 (35.2)
American Indian/Alaska Native	0	1 (3.7)	0	1 (3.7)	2 (1.9)
Native Hawaiian/Pacific	1 (3.7)	0	0	0	1 (0.9)
Multiple	0	1 (3.7)	1 (3.7)	0	2 (1.9)
Median weight, kg (IQR)	96.0 (88.0 – 107.1)	99.8 (87.7 – 110.5)	94.2 (86.1 – 104.2)	92.8 (88.1 – 100.8)	94.5 (87.9 – 105.8)
Median BMI, kg/m² (IQR)	33.3 (32.3 – 36.1)	34.5 (32.7 – 38.3)	34.8 (32.3 – 37.0)	32.8 (31.0 – 35.5)	33.9 (32.2 – 36.6)
Median abdominal circumference, in (IQR)	43.0 (38.9 – 45.0)	43.0 (40.0 – 47.0)	42.0 (38.0 – 45.0)	41.0 (39.0 – 42.9)	42.3 (39.3 – 44.5)
Median hsCRP, mg/L (IQR)	4.8 (3.8 – 6.6)	6.4 (5.2 – 8.7)	5.6 (4.4 – 8.9)	6.3 (5.2 – 8.9)	5.7 (4.4 – 8.1)

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

GFORCE-1: Summary of Unblinded Safety Data

- 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*

MRT-8102 Demonstrated a Favorable Safety and Tolerability Profile Over the Period of 8 Weeks

Treatment-Emergent Adverse Events (AE)	Placebo (n=27)	MRT-8102 5 mg (n=27)	MRT-8102 20 mg (n=27)	MRT-8102 40 mg (n=27)
Participants with any AE, n (%)	8 (30)	7 (26)	8 (30)	12 (44)
Participants with any AE leading to treatment discontinuation, n (%)^a	0 (0)	0 (0)	3 (11)	5 (19)
Participants with any Grade 3 AE, n (%)^b	0 (0)	0 (0)	0 (0)	2 (7)
Participants with any Serious AE, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Infection or Infestation AE, n (%)	2 (7)	2 (7)	2 (7)	2 (7)
Serious Infection or Infestation AE, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Neutropenia AE, n (%)	0 (0)	0 (0)	0 (0)	0 (0)
Thrombocytopenia AE, n (%)	0 (0)	0 (0)	0 (0)	0 (0)

^aMRT-8102:

20 mg: grade 2 atopic skin reaction (n=1), grade 1 rash (n=2);

40 mg: asymptomatic, non-QTc related, grade 1 electrocardiogram change (n=3); grade 2 allergic reaction and pruritus (n=1); grade 3 elevation of liver enzymes (n=1) in a patient with incidental finding of asymptomatic hepatitis A

^bIn addition to the grade 3 liver enzyme elevation in the subject diagnosed with HepA, one episode of grade 3 shoulder pain in a patient with accidental shoulder dislocation was recorded



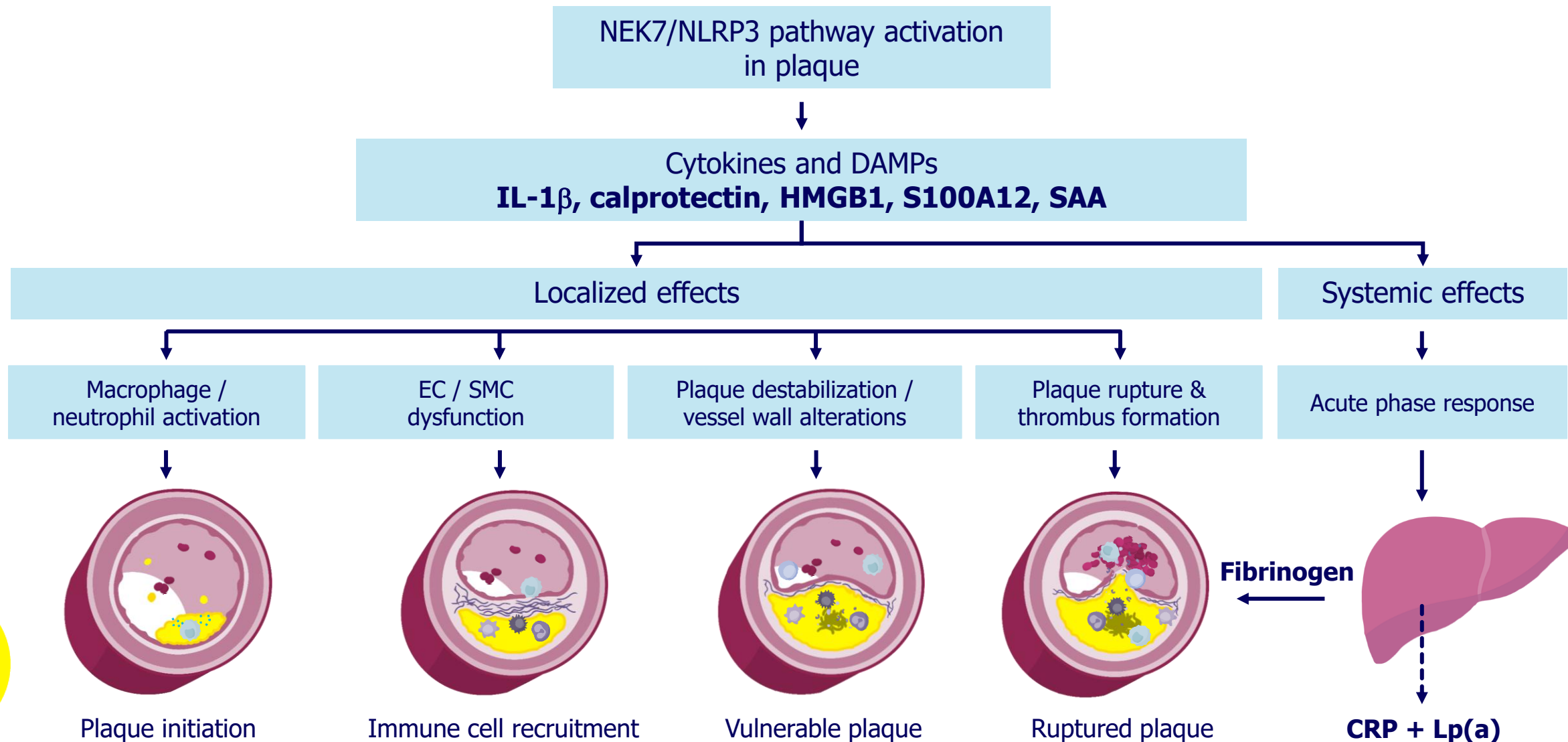
Clinical Activity of MRT-8102 on Key Pathogenic Drivers of ASCVD

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 CRP².
- **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

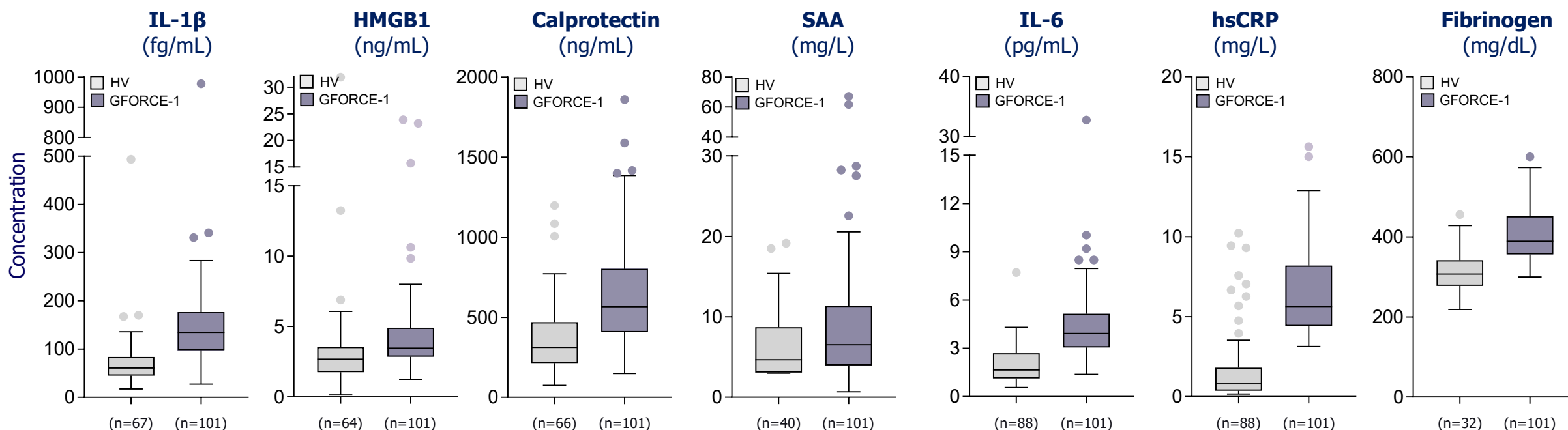
Key ASCVD Pathogenic Drivers and Markers of Systemic Inflammation Assessed in GFORCE-1



NEK7/NLRP3 Pathway Related Cytokines, DAMPs and Thrombotic Markers were Elevated at Baseline in GFORCE-1 Subjects

IL-1 β , DAMPs, and thrombogenic factors

Systemic acute phase response

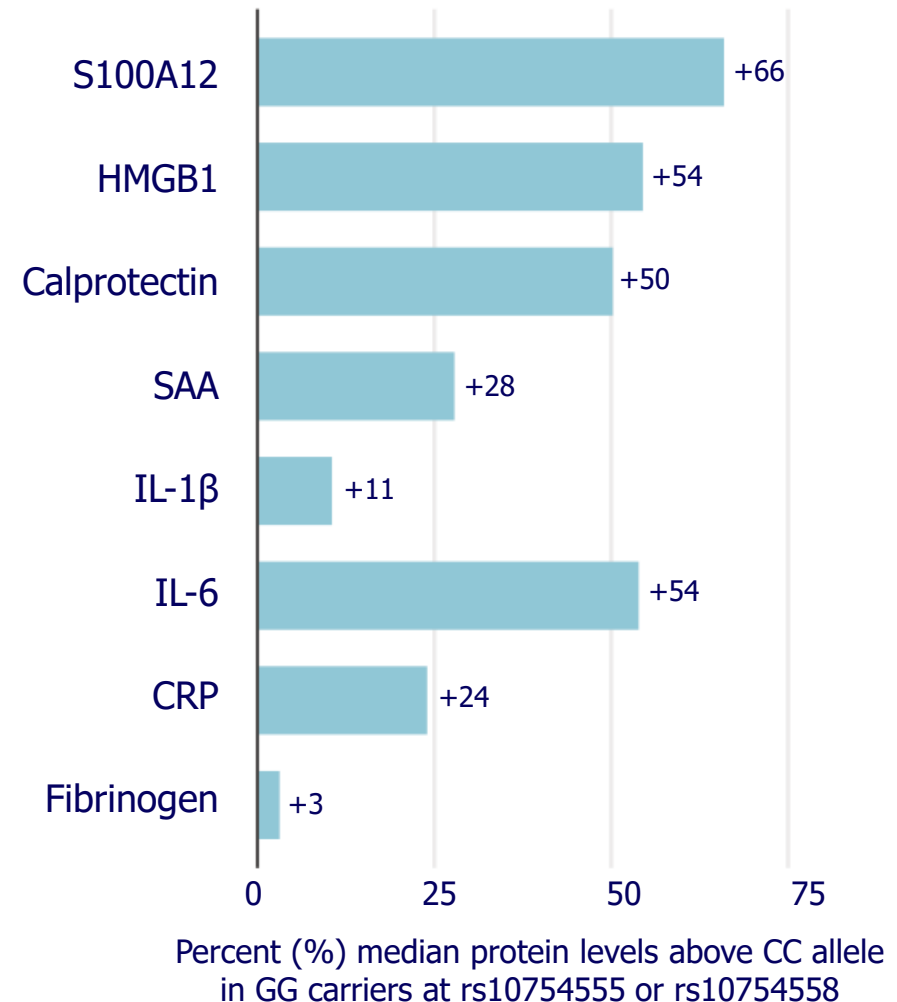


Baseline levels of key pathogenic drivers of ASCVD and systemic inflammatory biomarkers were elevated in GFORCE-1 relative to the levels observed in healthy volunteers

NLRP3 Risk Alleles Correlate to Baseline Increase of ASCVD Drivers

- Two high-priority NLRP3 risk SNPs, rs10754555 and rs10754558, have been linked to increased NLRP3 pathway activation and cardiovascular risk.
- In line with published data, **nearly 1 in 3 subjects (29%) carry a highest-risk genotype** (GG at either locus); over half of subjects (57%) carry moderate NLRP3 genetic risk.
- Significant increases in baseline levels of ASCVD drivers were identified, in particular for DAMPs and cytokines, in carriers of NLRP3 risk (GG) alleles, **suggesting elevated pathway activity and potential for faster and more severe atherosclerotic and thrombotic remodeling.**

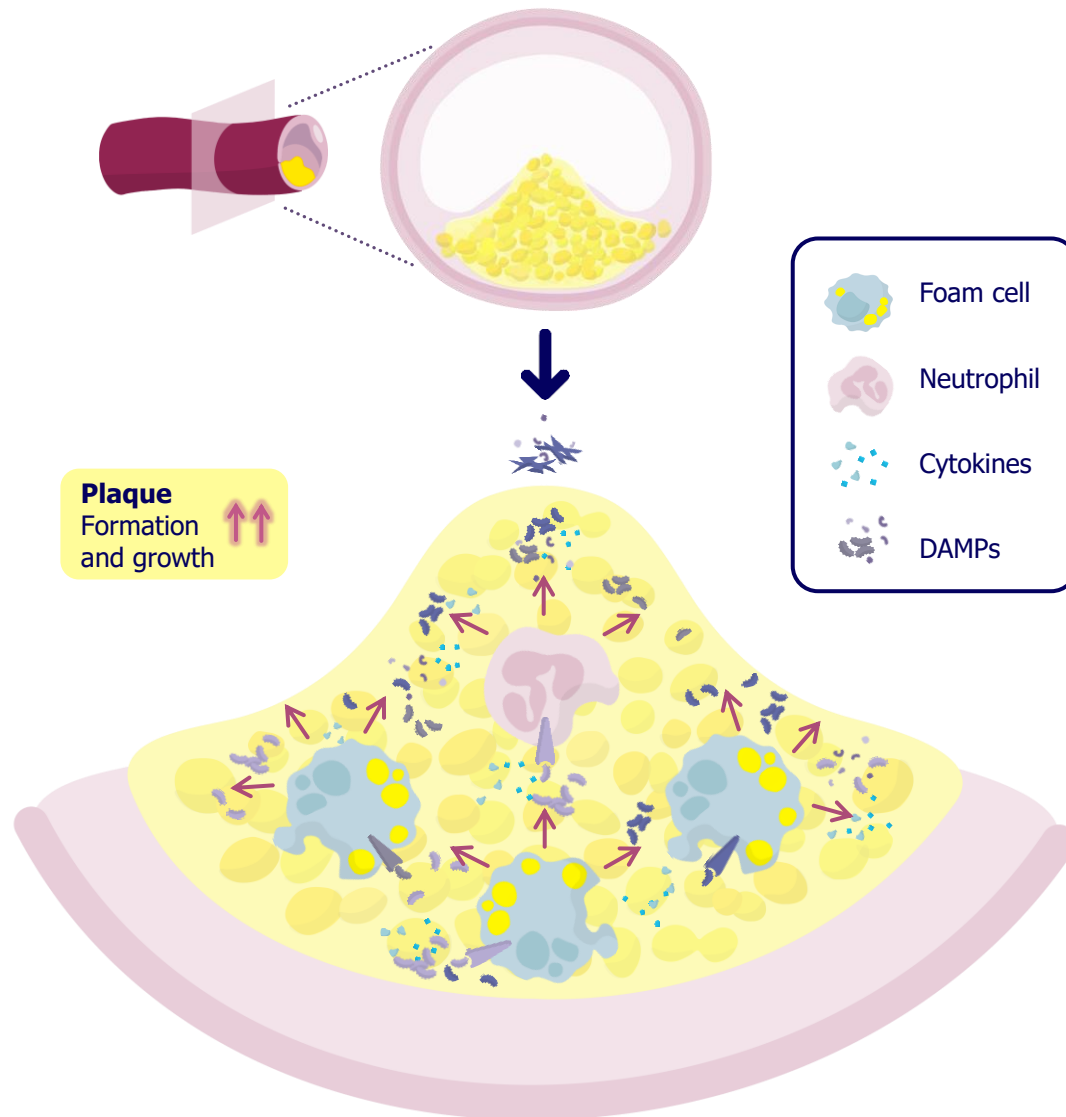
Elevated levels in NLRP3 risk allele carriers



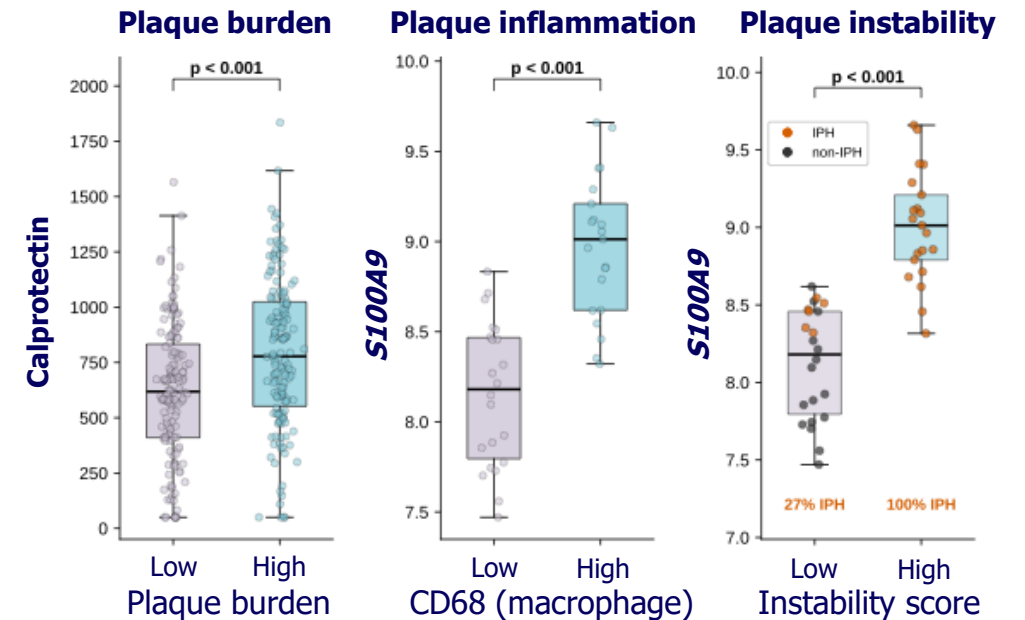


Modulation of Molecular Drivers of Plaque and Vascular Biology

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



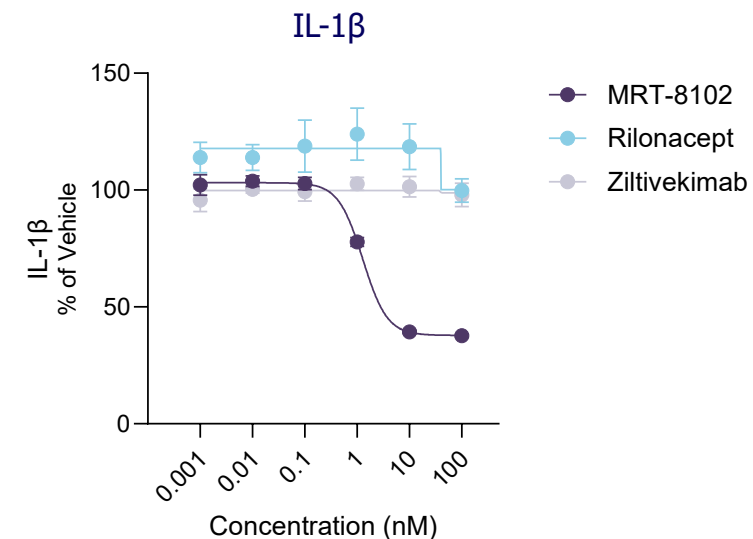
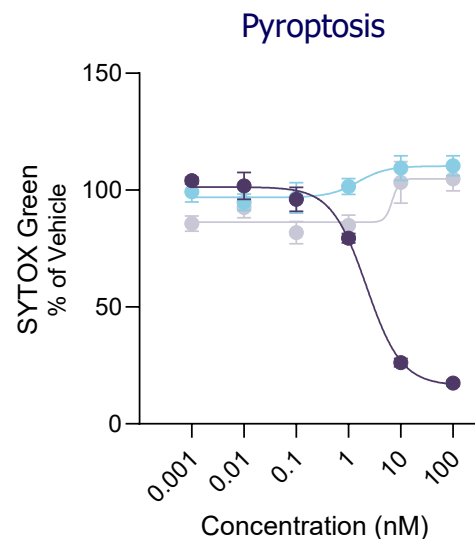
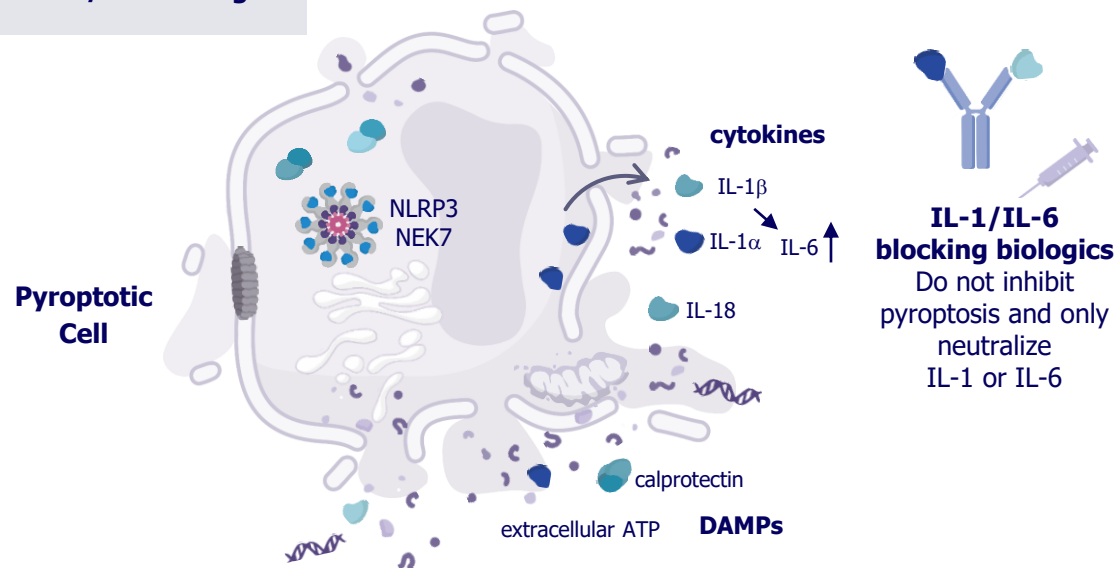
Calprotectin levels correlate with plaque burden, inflammation and instability



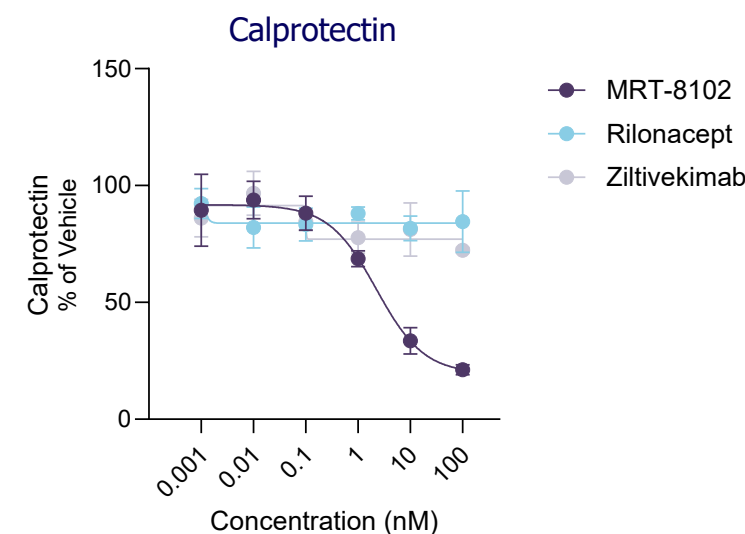
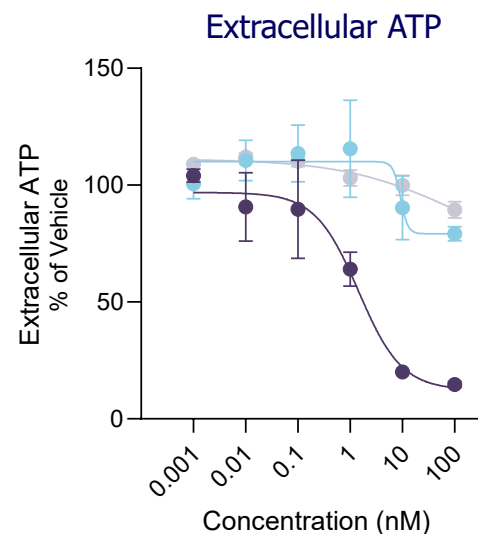
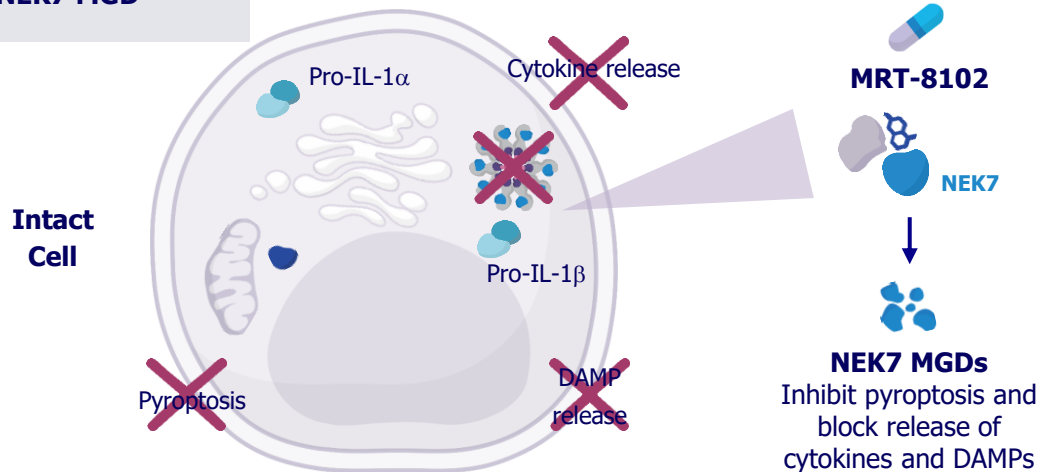
Circulating calprotectin levels significantly associate with increased plaque burden, enhanced plaque inflammation, and plaque instability

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

Anti-IL-1/IL-6 biologics

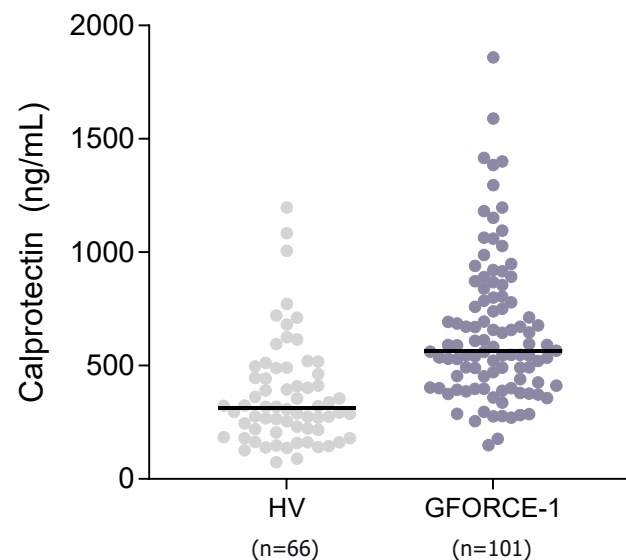


NEK7 MGD

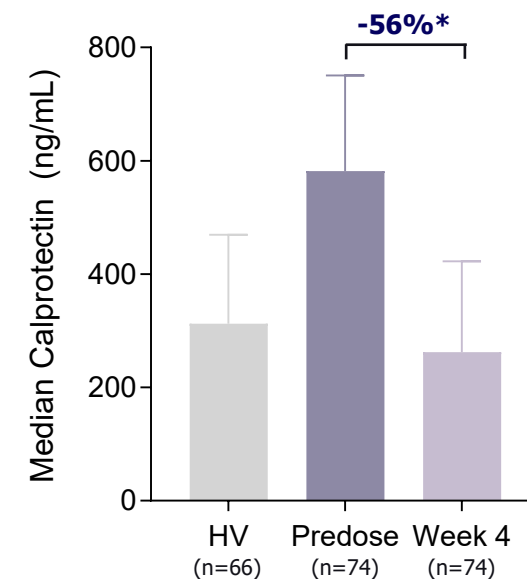
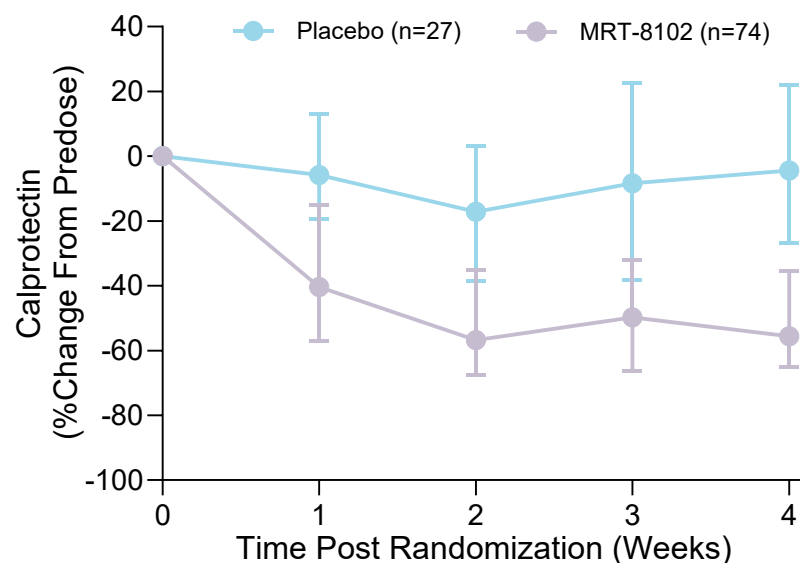


MRT-8102 Reduced Plasma Calprotectin to Healthy Volunteer Levels

Calprotectin is elevated in subjects with elevated CVD risk



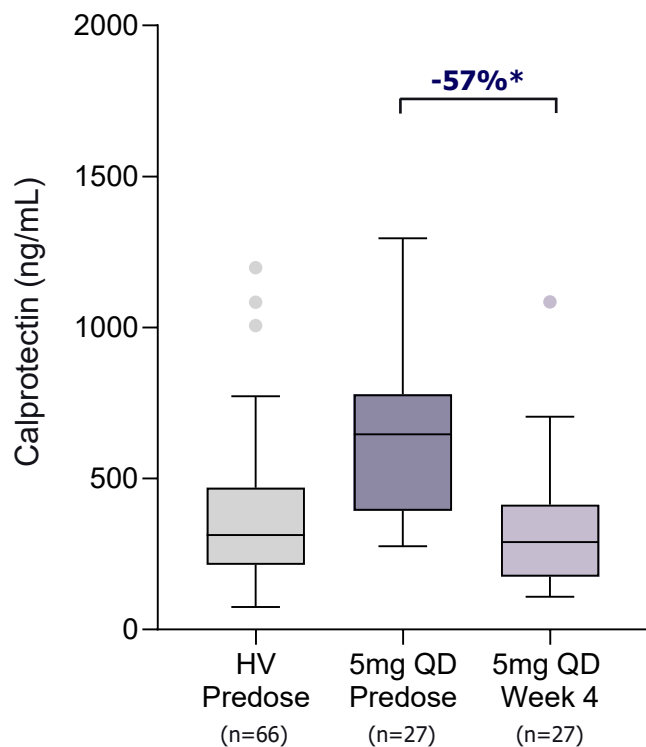
Treatment reduced Calprotectin to levels associated with low risk of future CV events (week 4)



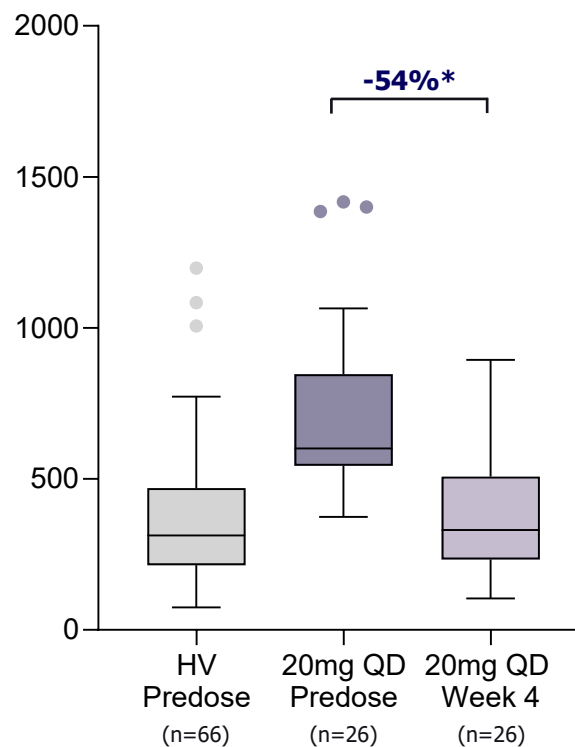
Median reduction of **56%** in plasma calprotectin to levels comparable to those observed in healthy volunteers after 4 weeks of dosing

Plasma Levels of Calprotectin were Equally Reduced Across all Dose Levels in Response to MRT-8102

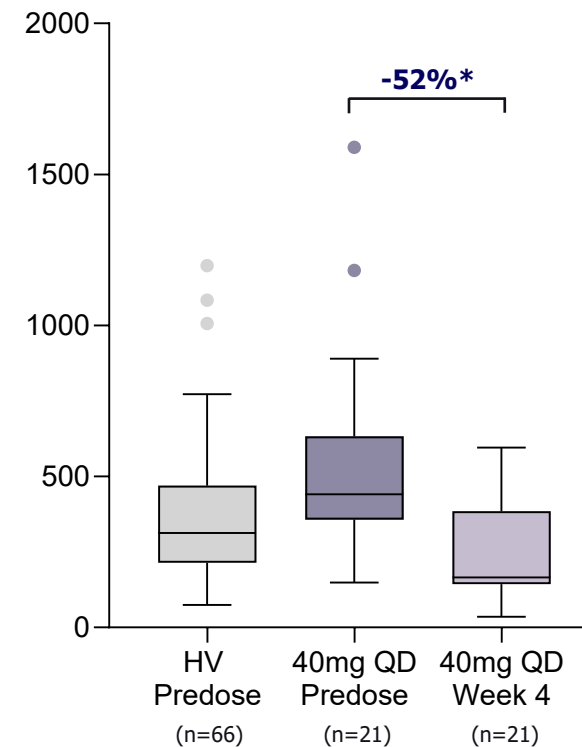
5mg QD
57% reduction



20mg QD
54% reduction

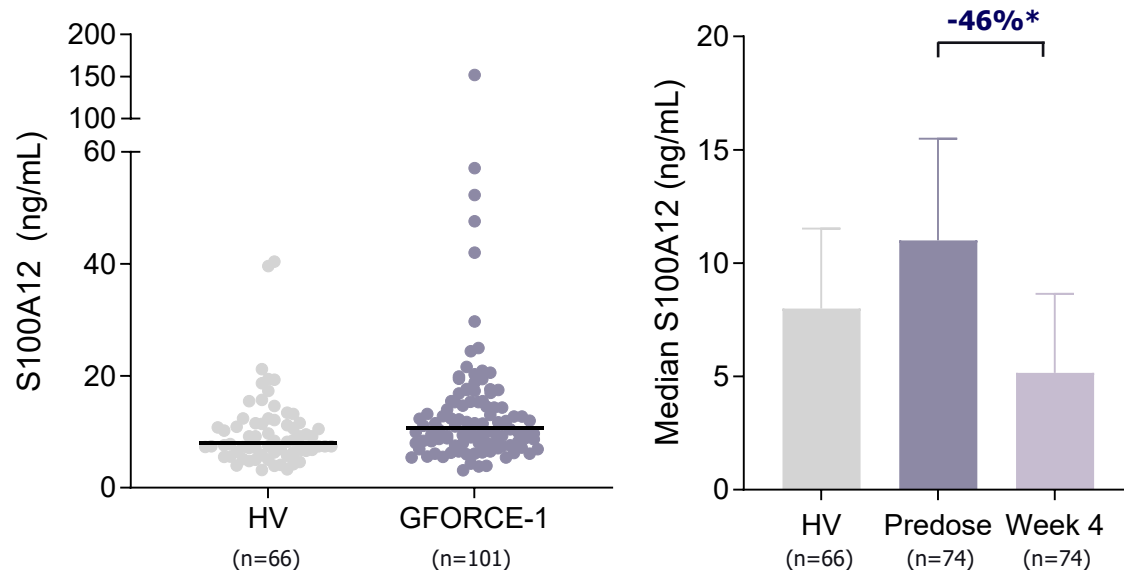


40mg QD
52% reduction

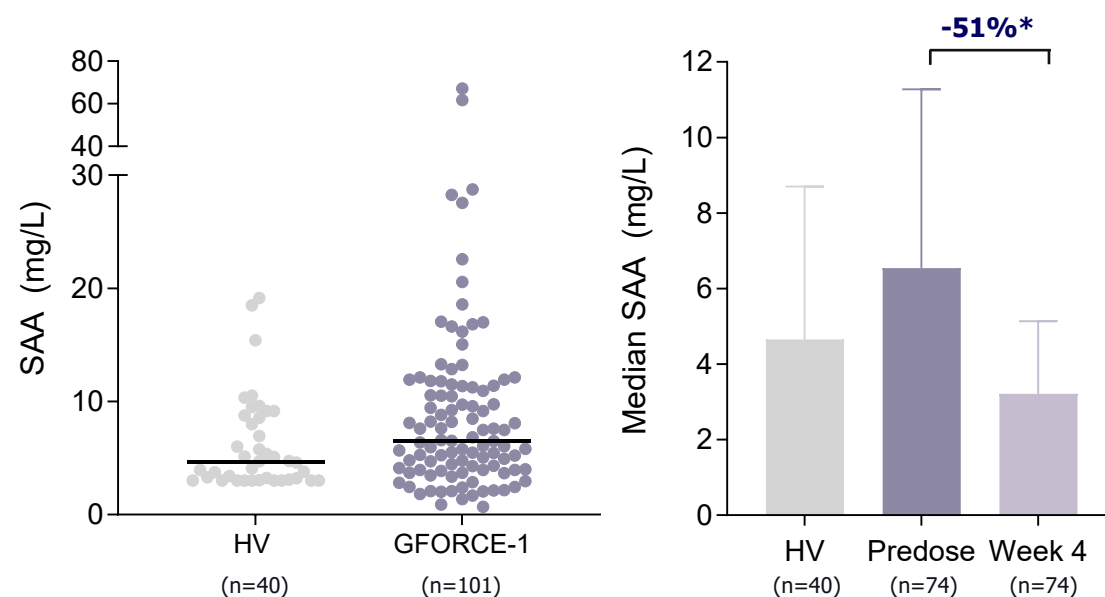


MRT-8102 Reduced Plasma S100A12 and Serum SAA to Healthy Volunteer Levels

MRT-8102 reduces S100A12 to levels in HVs



MRT-8102 reduces SAA to levels in HVs

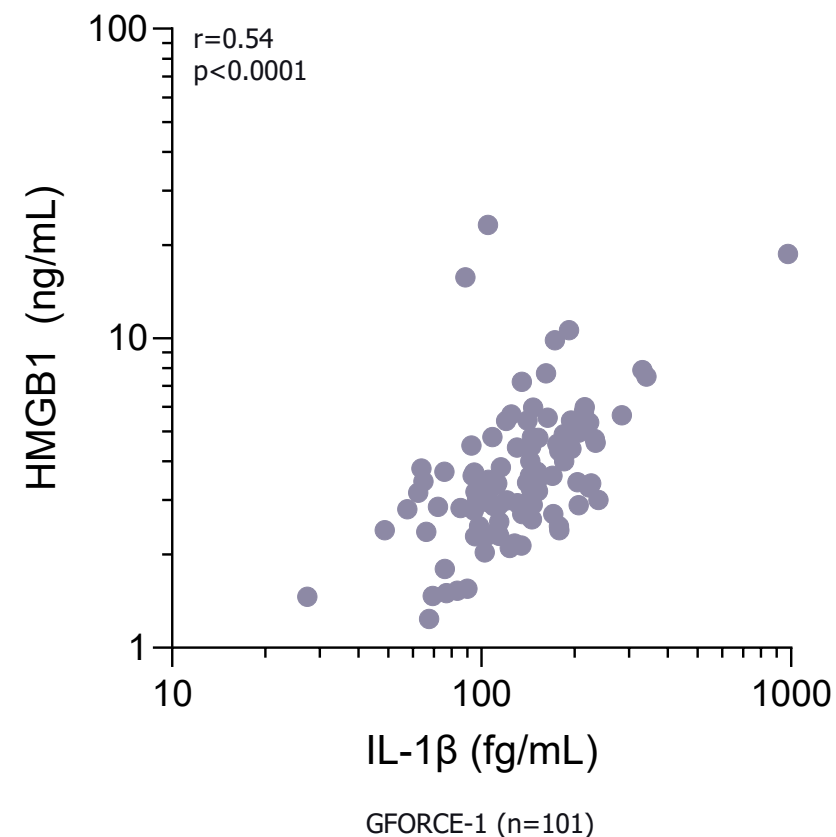
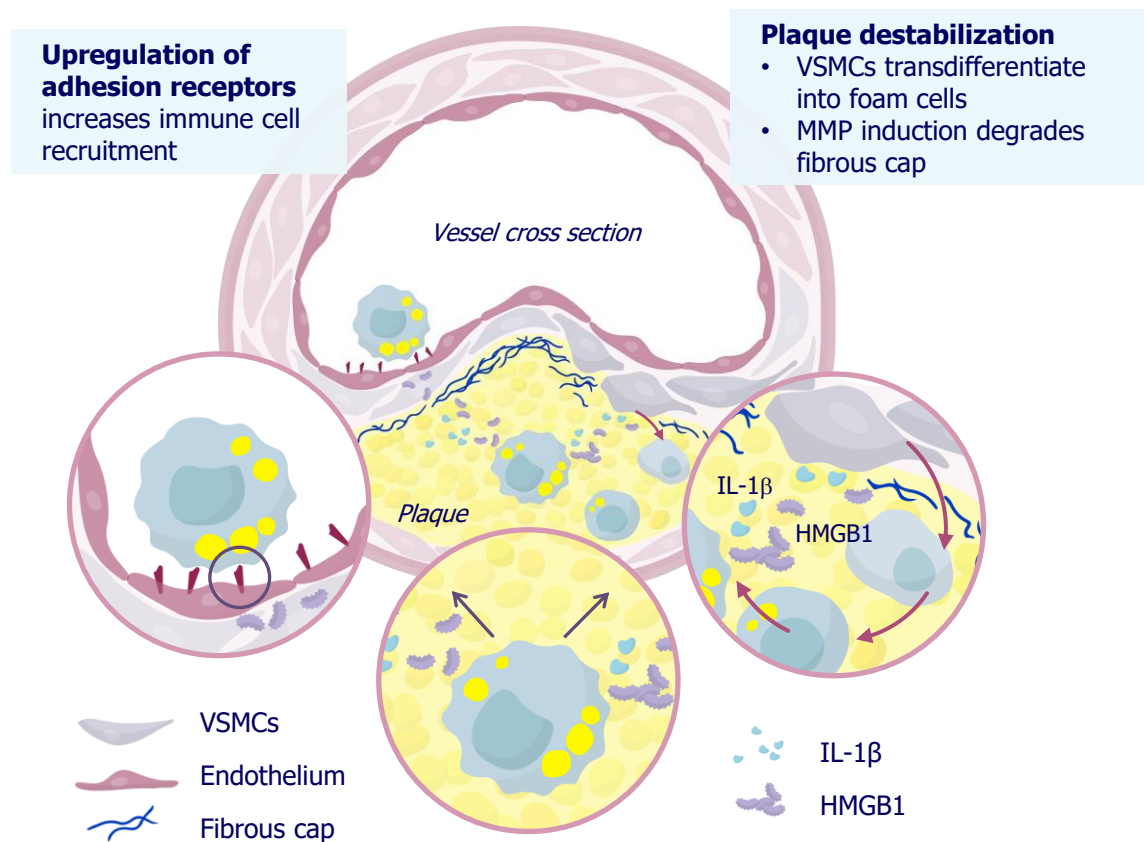


Median reduction of **46%** and **51%** in plasma S100A12 and serum SAA, respectively, to levels comparable to those observed in healthy volunteers after 4 weeks of dosing

Pathological Crosstalk between HMGB1 and IL-1 β Downstream of NEK7/NLRP3 Reinforces Plaque Progression and Instability in ASCVD

Biological crosstalk between HMGB1 and IL-1 β influences multiple aspects of vessel and plaque biology

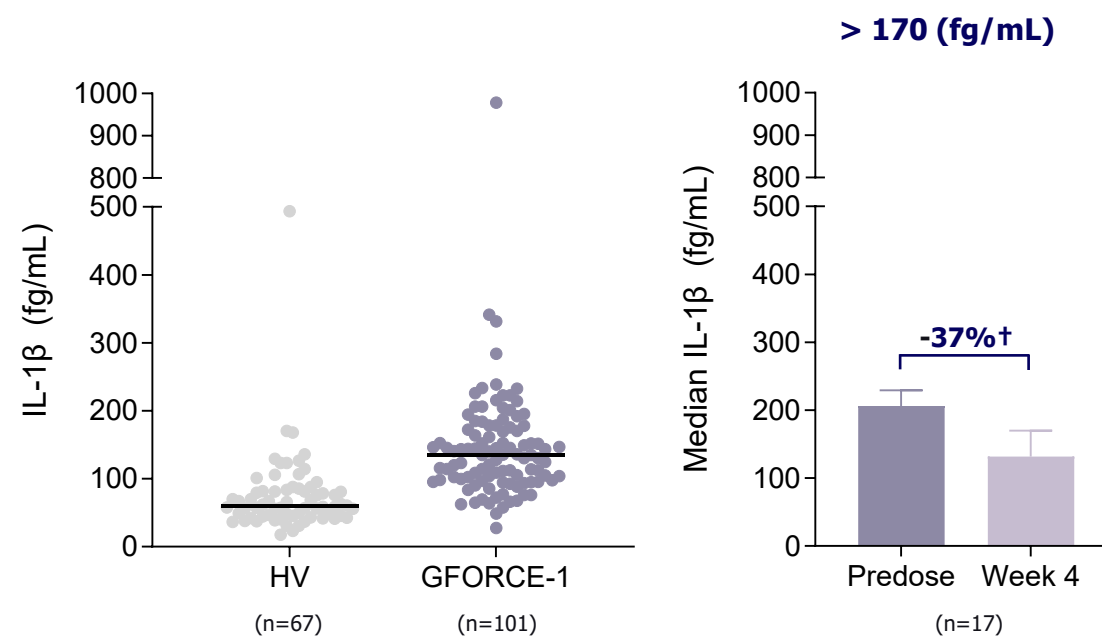
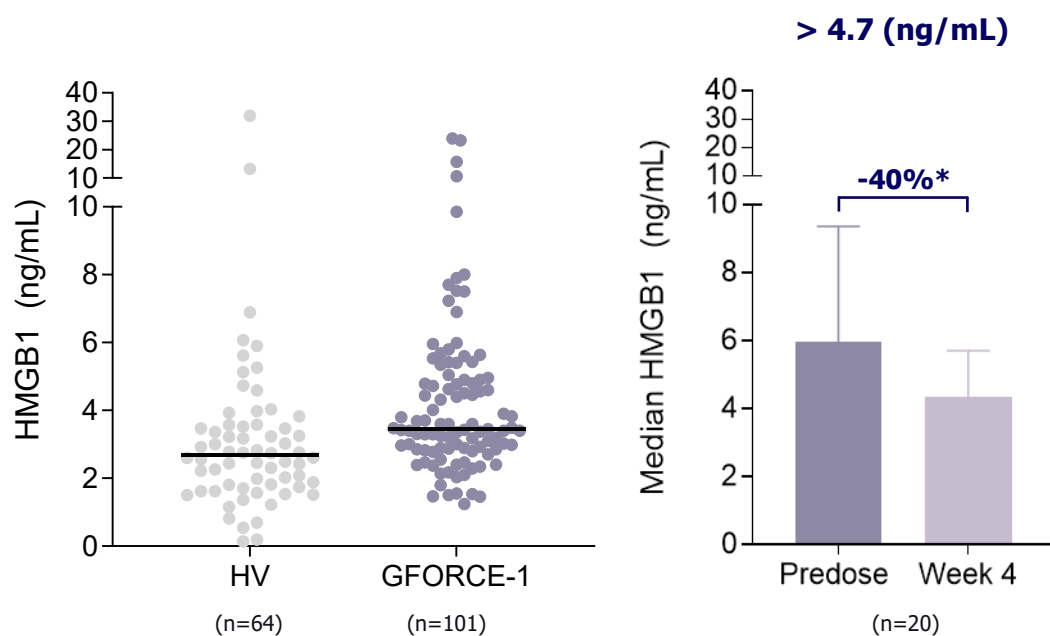
HMGB1 and IL-1 β baseline levels strongly correlate, reinforcing biological proximity



MRT-8102 Treatment Reduced HMGB1 and IL-1 β Levels

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

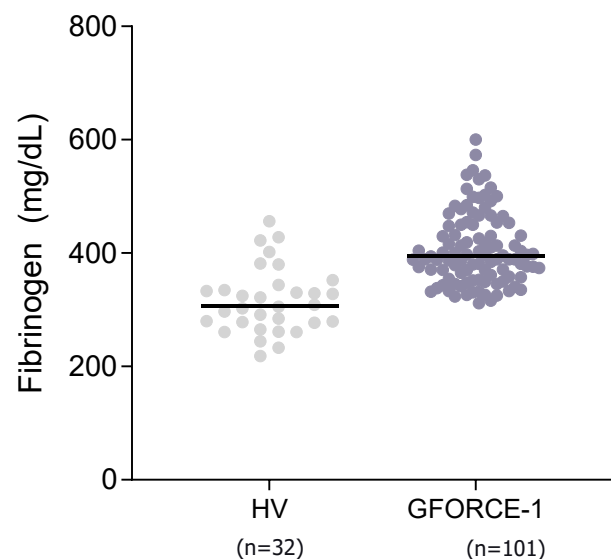
MRT-8102 treatment resulted in meaningful IL-1 β reduction in subjects with higher baseline levels



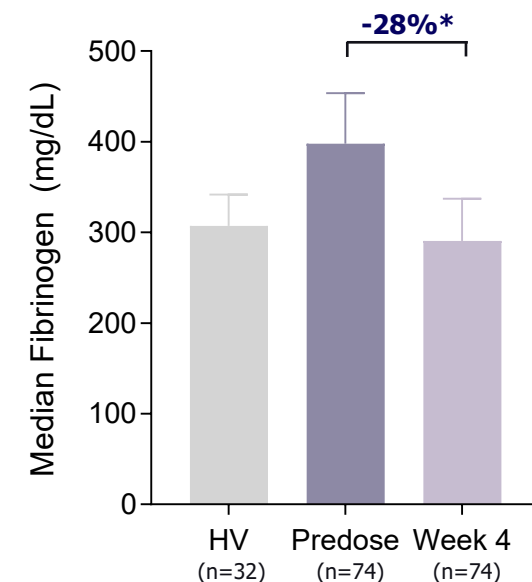
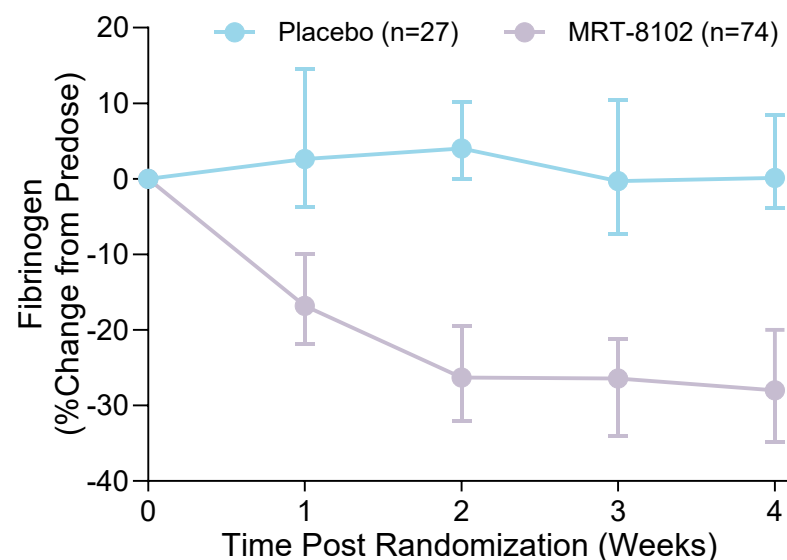
- HMGB1 and IL-1 β were elevated in GFORCE-1 population versus healthy volunteers (baseline)
- Treatment led to a median reduction of **40%** and **37%** in HMGB1 and IL-1 β levels, respectively, in subjects with elevated baseline levels; no statistically significant decrease in placebo

MRT-8102 Treatment Led to Reductions in Fibrinogen

Fibrinogen baseline is elevated in GFORCE-1 population



Treatment significantly reduced fibrinogen to normal physiological levels



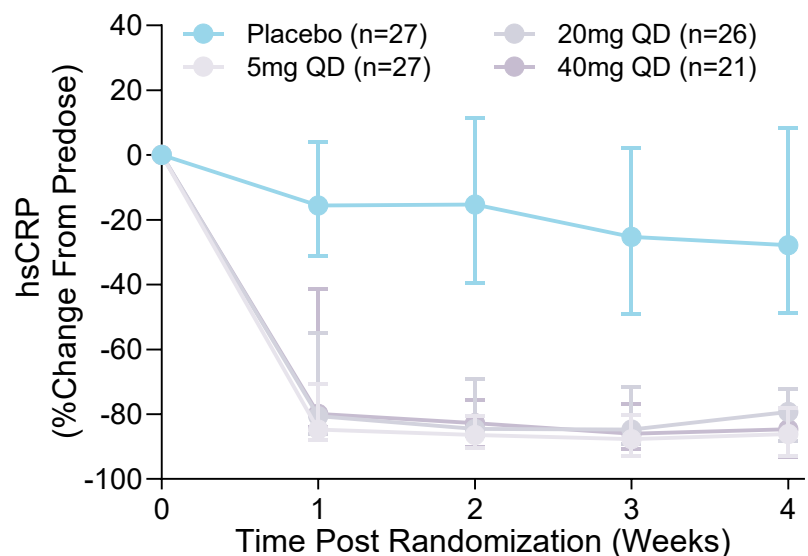
Median reduction of **28%** in fibrinogen to levels comparable to those observed in healthy volunteers after 4 weeks of dosing



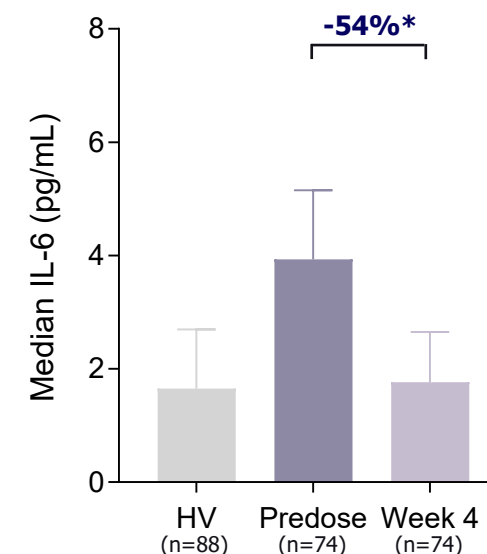
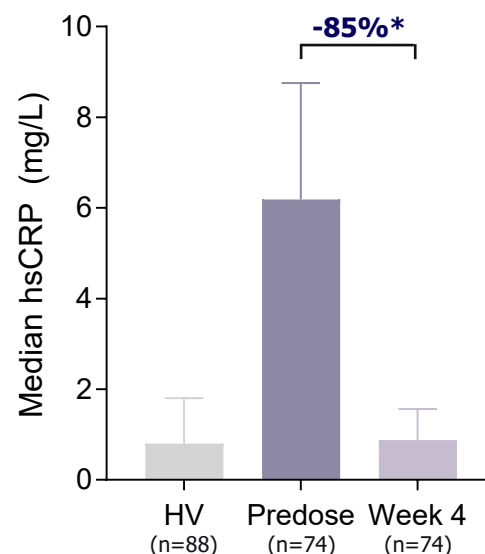
Markers of Systemic Inflammation

MRT-8102 Induced Rapid and Sustained Reductions in hsCRP and IL-6 Levels

Robust decrease of hsCRP after 4 weeks of dosing



hsCRP and IL-6 reduced to levels associated with low risk of future CV events



- Median reduction of **85%** in serum hsCRP to levels detected in healthy volunteers; **86%** of subjects showed suppression of hsCRP to <2 mg/L
- Median reduction of **54%** in plasma IL-6 to levels associated with low risk of future CV events



Update on Development Plans



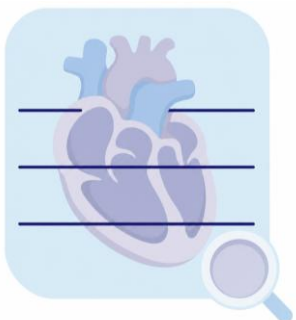
GFORCE-2: A Differentiated Phase 2 Approach

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

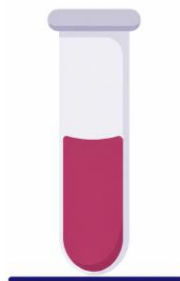
Imaging

Assess plaque inflammation using FAI (fat attenuation index) imaging for response and enrichment



ASCVD drivers and systemic biomarkers

DAMPs (calprotectin, S100A12, HMGB1), cytokines (IL-1 β , IL-18, IL-6) and thrombogenic factors (tissue factor, SAA, fibrinogen)



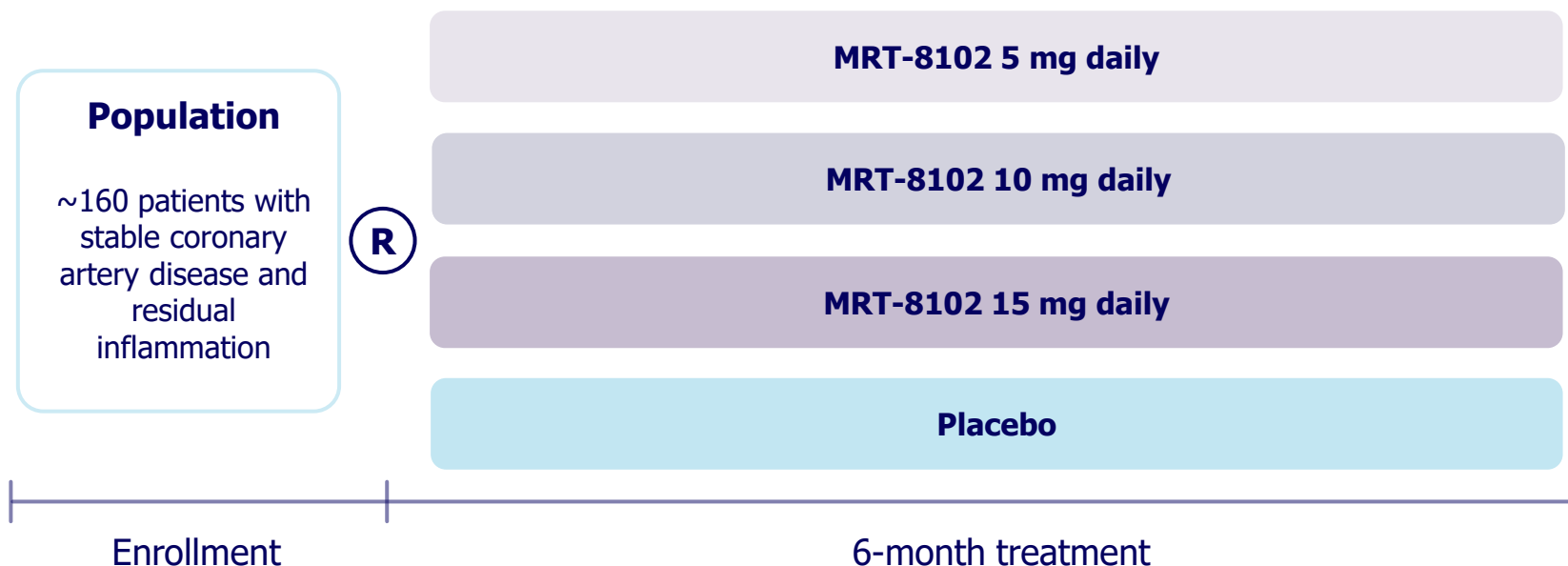
Genetics

Confirm genetic basis of NLRP3 activation (activating SNPs) and build correlation to baseline levels of molecular drivers of ASCVD, responses and FAI changes





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

Planned Phase 2 Studies for Gout and HS



Ph2 Study in Gout Flare Prevention
Following Acute Flare Management

**Initiation planned
Q4 2026 / Q1 2027**

Trial

- ~ 60 pts w/recurrent gout flares
- 12 weeks

Outcome

- Measures and PoC expectation
- Reduction in pain VAS by 72 hours
- Frequency of new flares



Ph2 Study in Moderate to Severe
Hidradenitis Suppurativa

**Initiation planned
H1 2027**

Trial

- ~ 160 pts w/moderate to severe HS
- 16 weeks

Outcome

- HiSCR75 after 16 weeks MRT-8102
relative to placebo





MRT-8102 Opportunities and Pipeline Update

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)

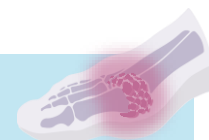
Large Market Opportunities Supported by Strong Biological Rationale

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-1 β 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-1 β , and DAMPs in lesional tissue
- **~400-450K** U.S. addressable population
- Significant unmet need with **~55%** patients poorly managed with SOC
- IL-1 antibodies **provide promising POC** for the NEK7/NLRP3 pathway
- Opportunity to target inflammasome assembly, **upstream of IL-1 and DAMP-driven pathogenesis in HS lesions**, unlike single-mediator TNF/IL-17 biologics

Summary and Next Steps

WHAT GFORCE-1 SHOWED

- **Favorable safety profile across all dose levels tested:** no SAEs, no infection signal
- **Robust, sustained target engagement:** ~80–90% NEK7 degradation at all dose levels
- **Broad normalization of ASCVD pathogenic drivers:** markers of local plaque progression, thrombosis, and systemic inflammation reduced to healthy-volunteer levels at all doses
- **A built-in precision-medicine hypothesis:** NLRP3 risk-alleles define a genetically enrichable population; plaque imaging could further define disease-modifiable population

WHAT'S NEXT

Program	Study	Milestone	Timing
Gout	GEMINI-1	Study initiation	Q4 2026/ Q1 2027
CAD	GFORCE-2	Study initiation	H1 2027
HS	GALAXY-1	Study initiation	H1 2027
Next-gen	MRT-9347	IND	Q4 2026

KEY CONSIDERATIONS

- GFORCE-2 design focused on imaging, levels of key molecular drivers of ASCVD and genetics to inform innovative and efficient Phase 3 study
- MRT-9347 (next-gen NEK7 degrader) provides strategic optionality across indications

MRT-8102's differentiated safety and translational activity profile de-risk a broad NEK7 franchise opportunity; heading into multiple Phase 2 starts through H1 2027



Monte Rosa Pipeline and Upcoming Milestones

	Target	Compound	Indication(s)	Preclinical	Phase 1	Phase 2	Phase 3	Next Anticipated Milestone
Immunology & Inflammation	VAV1 <i>Licensed to Novartis*</i>	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 2026
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 <i>Includes those licensed/optioned to Roche and Novartis</i>	Discovery	I&I, Oncology, Genetic and Neurological Diseases					Announce additional targets

* 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.

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



Q&A

Thank you

