



A New Approach to Inflammatory Diseases

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on Autoimmunity

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Highlights

Advancing an Innovative Pipeline of NKT Cell Modulators for the Treatment of Inflammatory, Fibrotic and Autoimmune Diseases

NKT Science

Leveraging Natural Killer T (NKT) regulation to target earlier in the inflammatory cascade to interrupt disease progression

Innovative Small Molecules

Small molecule drugs that act like cell therapy
Provides favorable economics in manufacturing and dosing

High-Value Indications

~100K
People in the US¹
Idiopathic Pulmonary Fibrosis

~160K
People in the US²
Systemic Lupus Erythematosus

Encouraging Preclinical Data Observed to Date on Par with OFEV[®] (nintedanib), a Leading Tyrosine Kinase Inhibitor with 2025 Projected Sales of \$5 Billion³

1. Sharif, R. (2017). Overview of Idiopathic Pulmonary Fibrosis (IPF) and Evidence-Based Guidelines. Am J Manag Care, 23(11), 176–182
2. <https://www.cdc.gov/lupus/facts/detailed.html>
3. Projected sales per Evaluate Consensus

Pipeline Targeting High-Value Indications in Need of Innovation

Programs	Class	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Status
GRI-0621	Type 1 invariant NKT (iNKT) Antagonist	Idiopathic Pulmonary Fibrosis (IPF)			Phase 2a Biomarker Study		<p>Interim data Q3 2024</p> <p>Full topline data Q4 2024</p>
GRI-0803	Type 2 NKT Agonist	Initial Focus: Systemic Lupus Erythematosus (SLE)					<p>Topline data from Phase 1a/b expected H2 2024</p>
GRI-NKT	Type 2 NKT Agonists	Multiple Indications					<p>Multiple pipeline expansion opportunities</p>

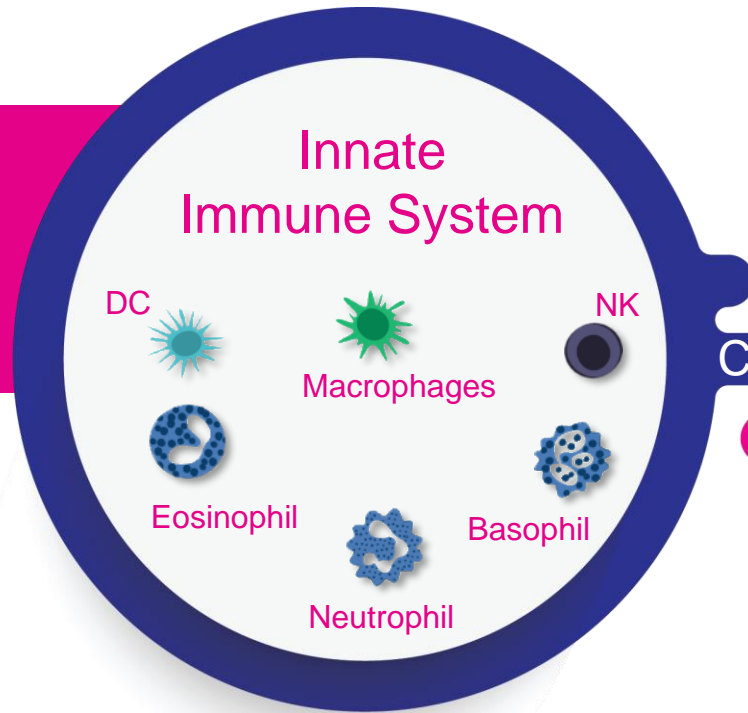
Library 500+ Proprietary Compounds to Fuel a Growing Pipeline

NKT Cells for Immune Regulation

Novel Immune Mechanism to Regulate the Adaptive-Innate Immune Axis & Reset Dysfunctional Immune Responses

Innate Immunity

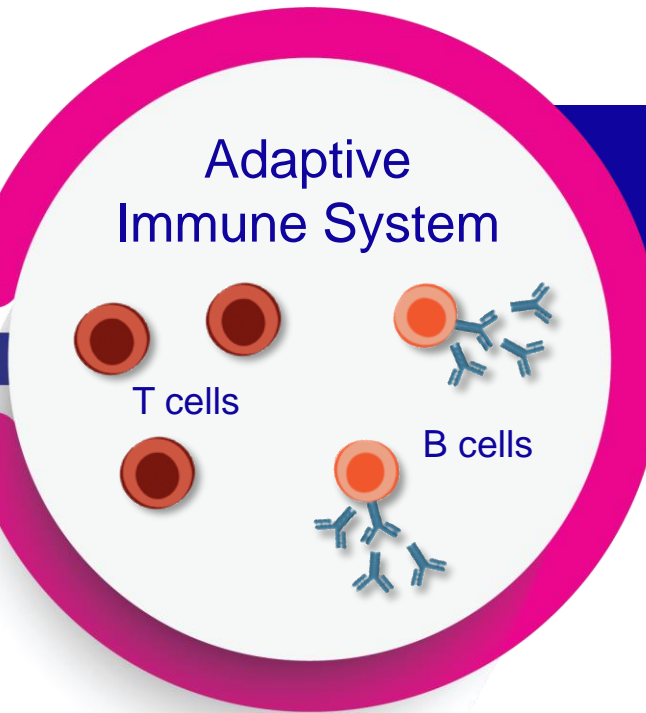
- Non-specific
- Fast to respond (hours)
- Activated by 'danger' signals
- First line of defense



Crosstalk

Adaptive Immunity

- Specific
- Slow to respond (days)
- Activated by specific pathogen recognition
- Generates immune memory



Regulating NKT Cells is a Selective Approach to Immunomodulation via Resetting the Immune Response

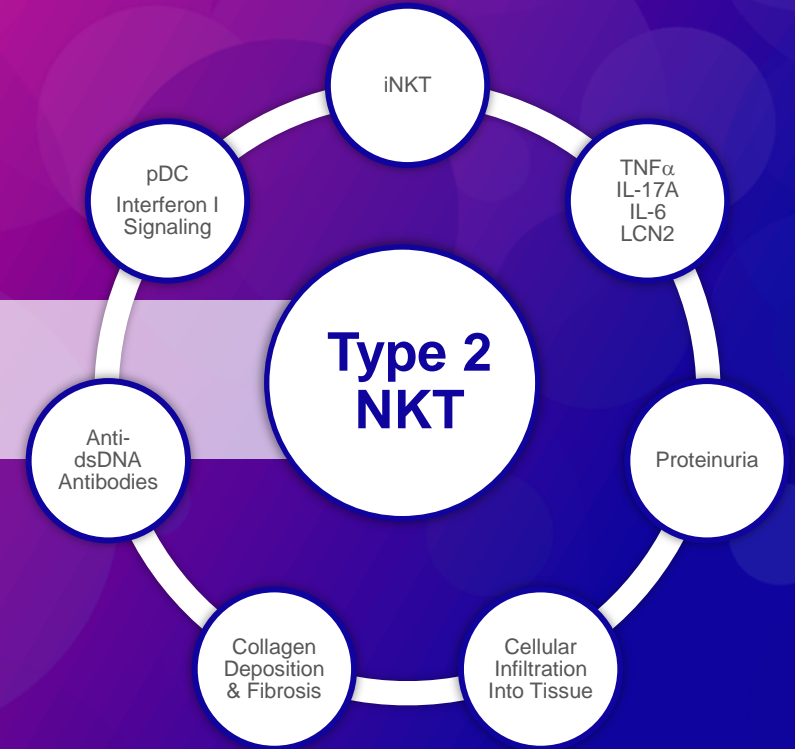


Natural Killer T Cells

Immune Cells that Bridge the Innate and Adaptive Immune Responses



Two Types:
iNKT
and
Type 2 NKT



Significantly Increased in Patients with Chronic Inflammatory Conditions

Regulate the Activity of Other Immune Cells and 'Reset' an Aberrantly Activated Immune Response

The Need in Systemic Lupus Erythematosus

The most common form of lupus, SLE, is an autoimmune disease in which the immune system attacks its own tissue and organs

~160K

PREVALENCE
Confirmed as definite SLE¹

70%

DIAGNOSIS
Number of all lupus cases²

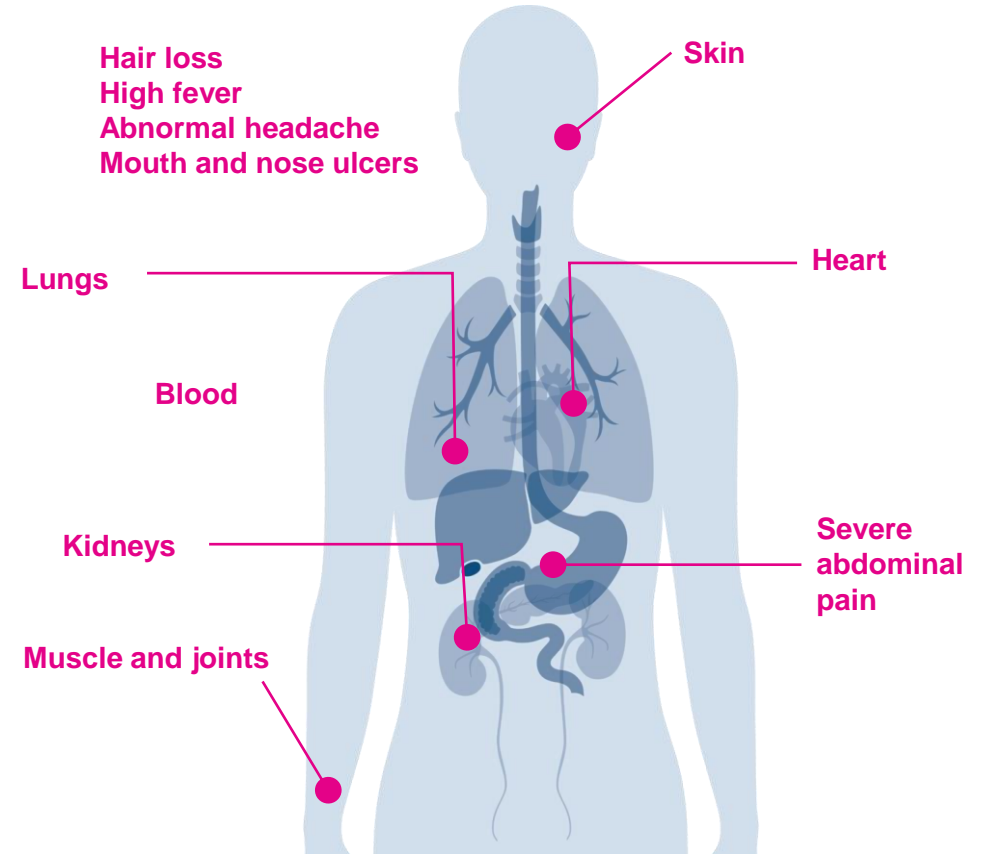
15 - 44

AGE RANGE
Commonly affects women of childbearing age¹

Current treatments are limited, consisting primarily of immunosuppressive therapies

Only 2 drugs approved for SLE in the past 50 years

Can Affect the Whole Body

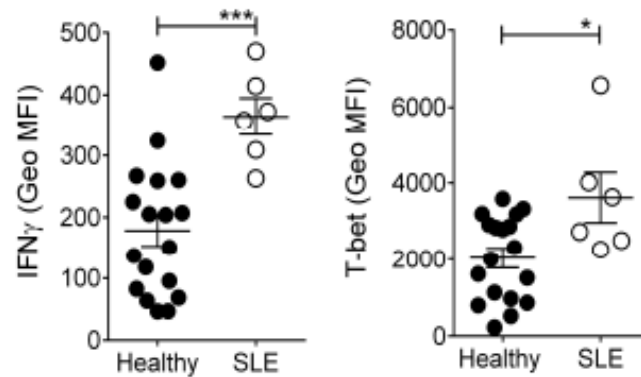


Kidney nephritis is a key driver of disease morbidity and represents potential target

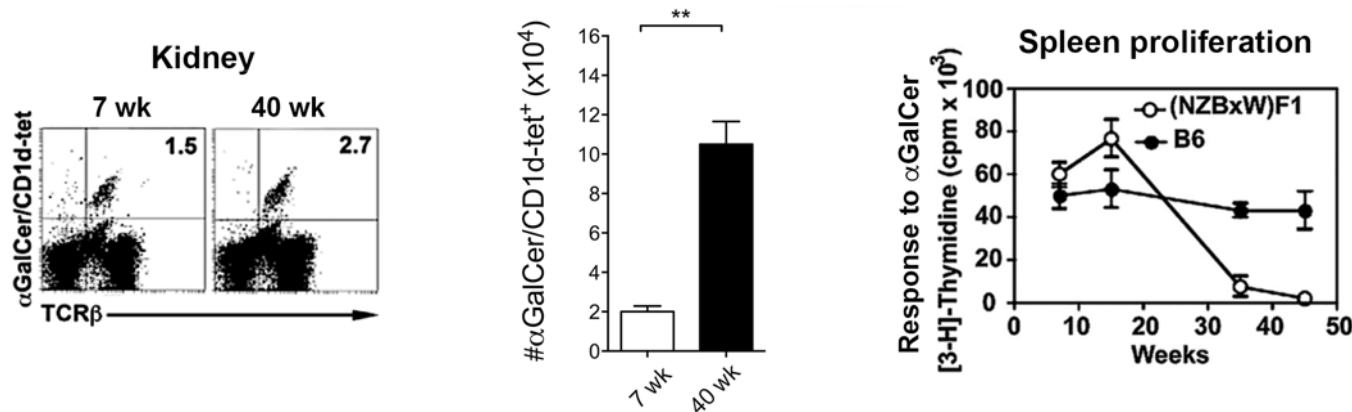
1. <https://www.cdc.gov/lupus/facts/detailed.html>
2. <https://www.lupus.org/resources/what-is-systemic-lupus-erythematosus-sle>

iNKT Accumulate & Activated in Lupus Patients and NZBWF1 Mice

Activation of iNKT in Lupus Patients



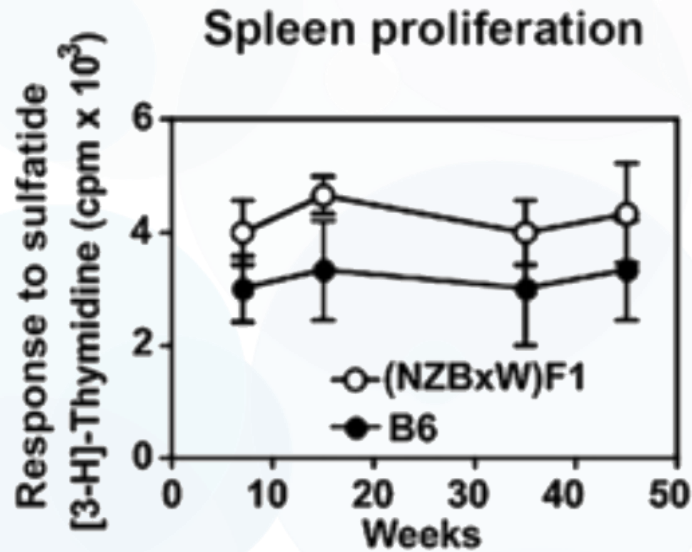
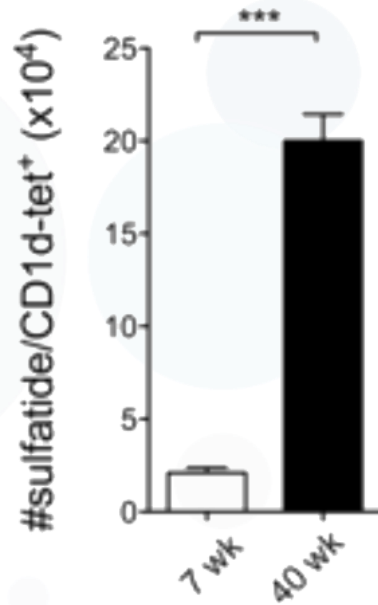
Chronic Activation of iNKT in NZBWF1 Kidney



Directly *ex vivo* iNKT cells from lupus patient PBMCs have an activated phenotype and express IFN γ and T-bet

Renal iNKT cells accumulate in NZBWF1 mice, and show progressive hyporesponsive to *in vitro* restimulation

Type 2 NKT cells Accumulate in Kidneys of NZBWF1 Mice with Disease Progression

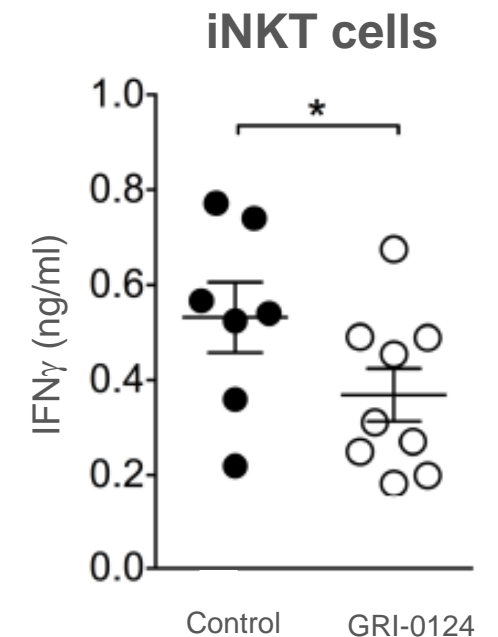
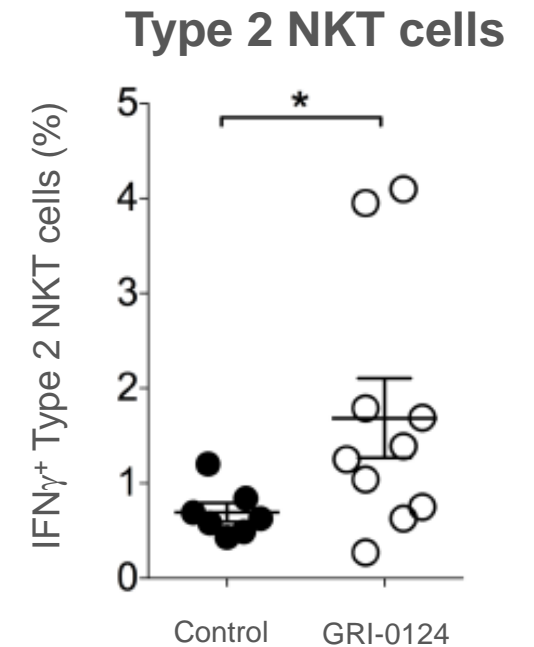


Type 2 NKT cells (sulfatide/CD1d tetramer⁺) accumulate in kidney, and remain responsive to in vitro stimulation

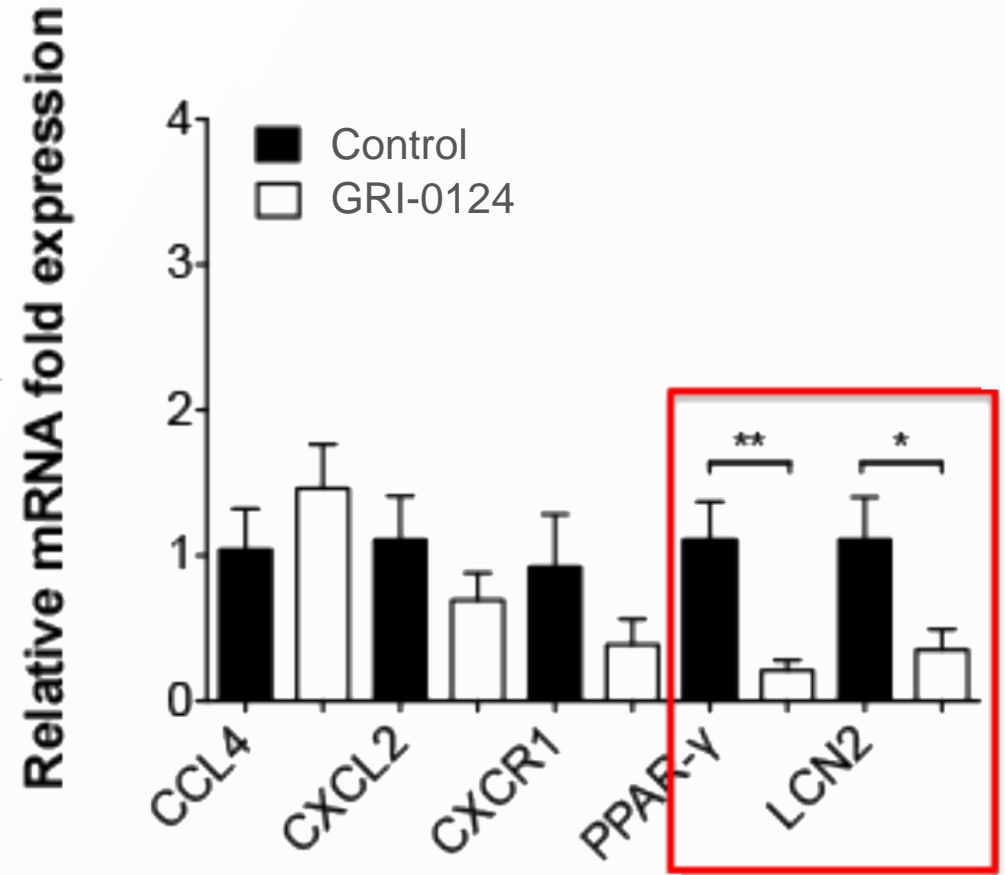
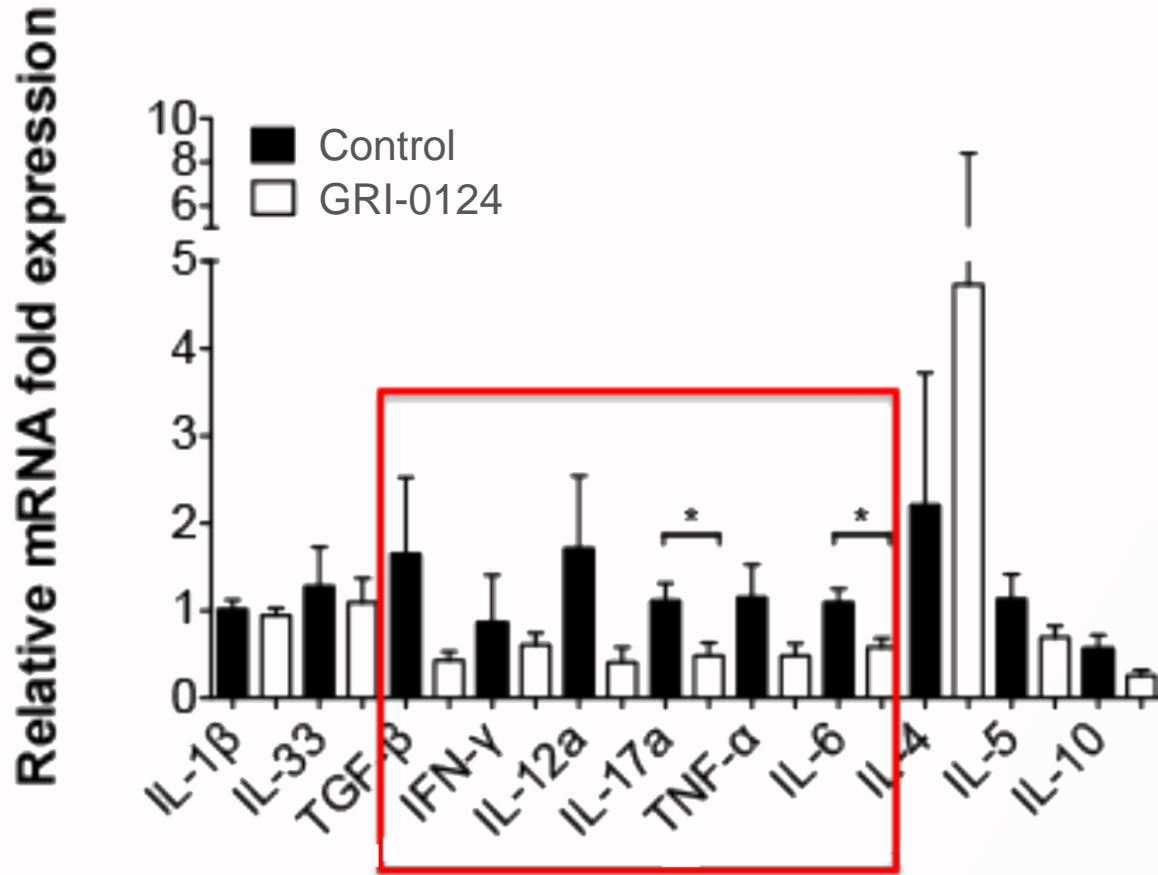
GRI-0124 Administration in NZBWF1 Mice Activates Type 2 NKT Cells and Leads to Inhibition of iNKT Cells

Type 2 NKT cells from GRI-0124 treated NZBWF1 mice (37 weeks) are activated ($\text{IFN}\gamma^+$) compared to Type 2 NKT cells from control-treated animals

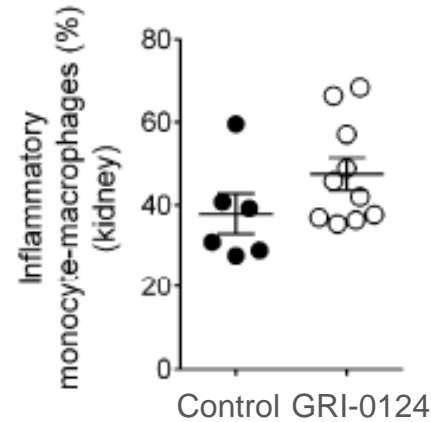
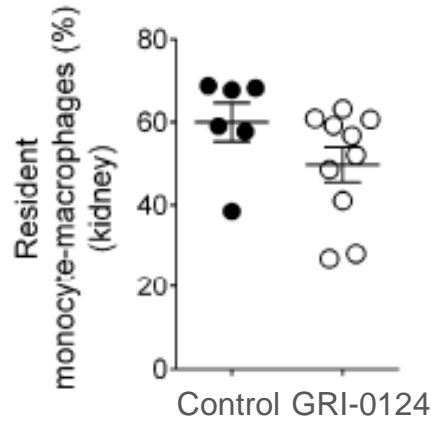
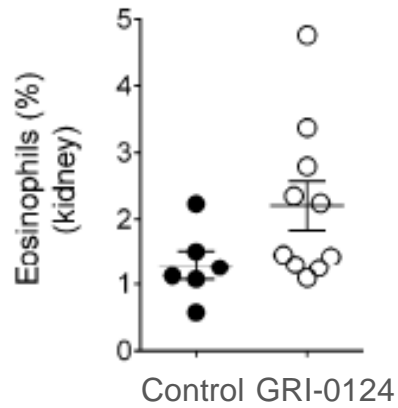
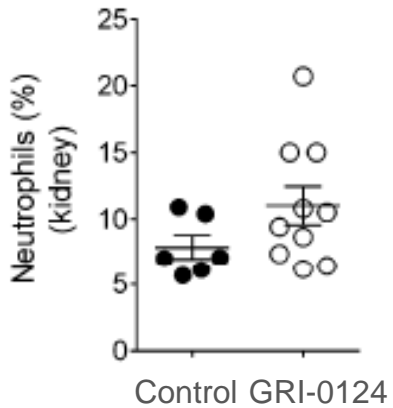
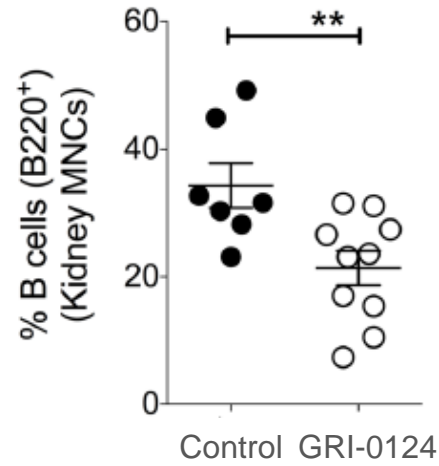
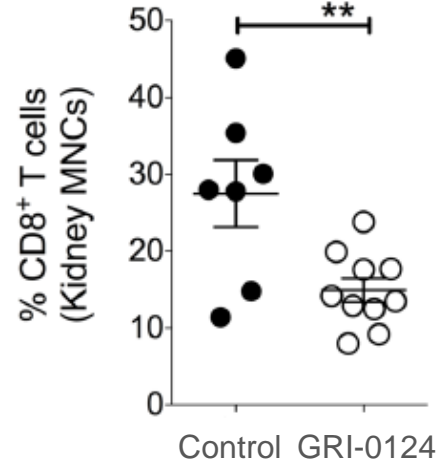
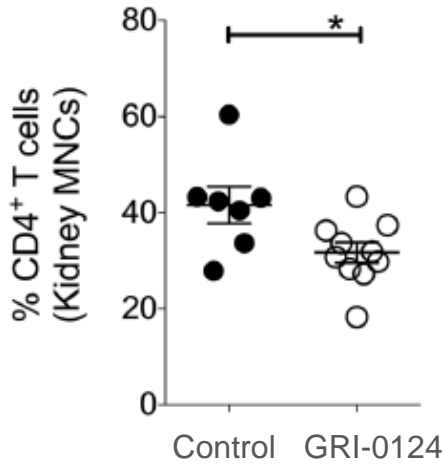
iNKT cells activation in NZBWF1 mice (37 weeks) is significantly inhibited in GRI-0124 treated mice



A Significant Inhibition of Pro-Inflammatory Cytokines as Well as Key Signaling Pathways in Kidneys of NZBWF1 Mice Treated with GRI-0124

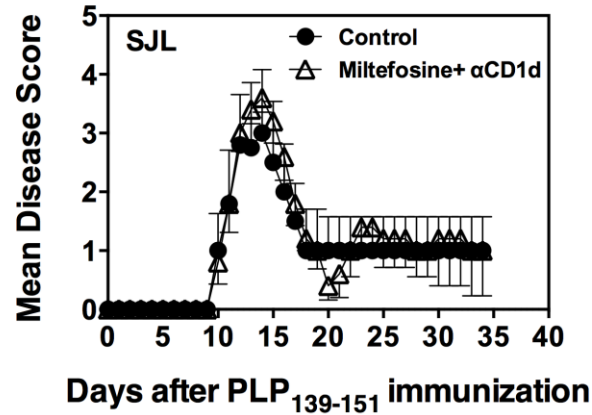
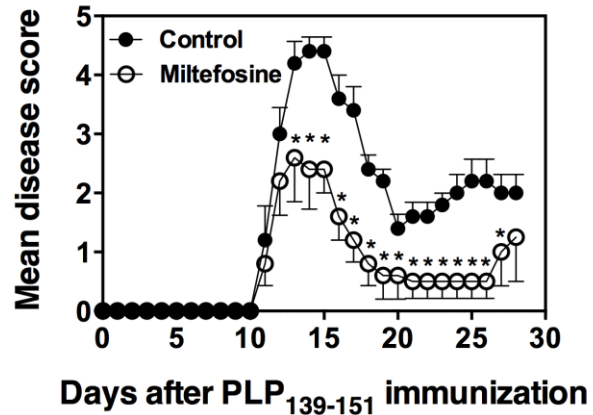
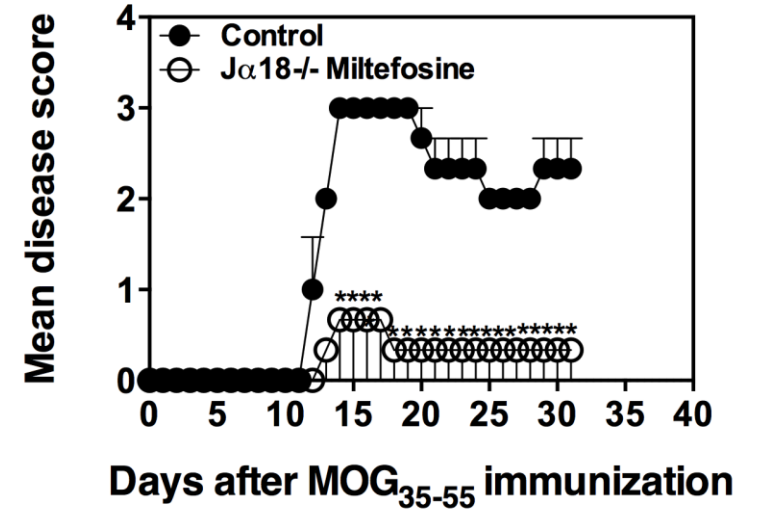
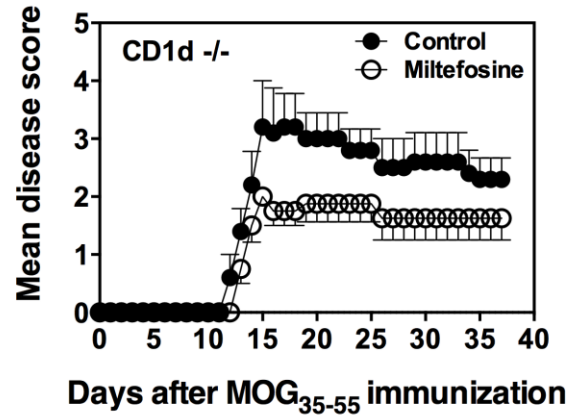
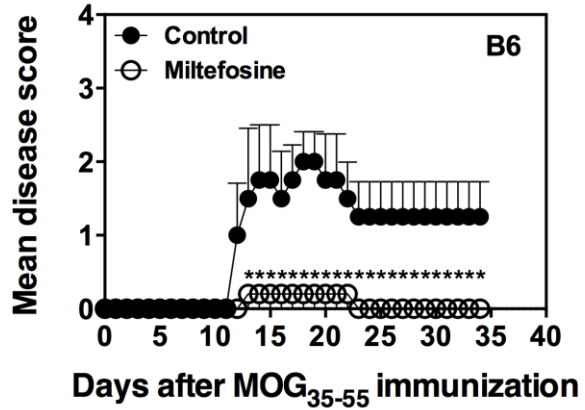


GRI-0124 administration significantly inhibits the infiltration of T & B cells into the kidney of NZBWF1 mice

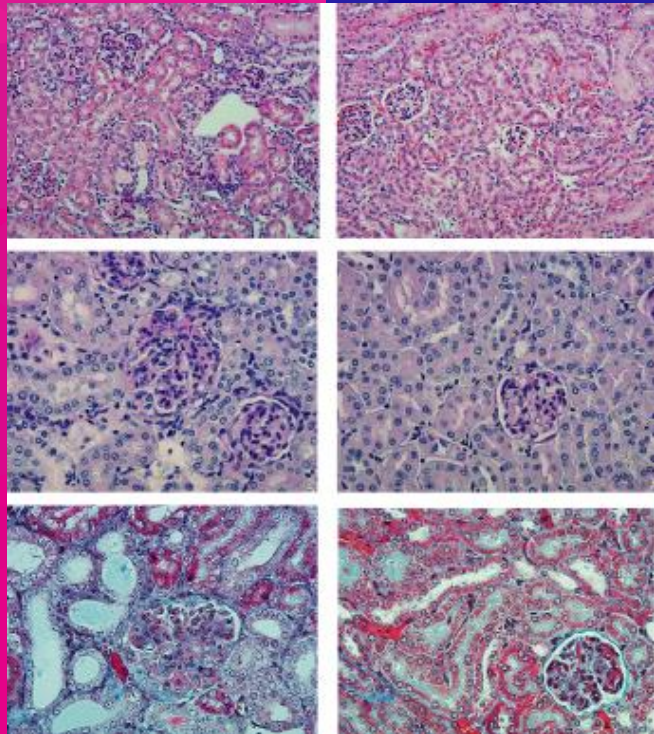


But GRI-0124 administration does not significantly change the infiltration of neutrophils, eosinophils, or macrophages into the kidneys of NZBWF1 mice

GRI-0124-mediated regulation is CD1d and iNKT-dependent



Oral administration of GRI-0124 Inhibits Lupus Nephritis in Model



Control

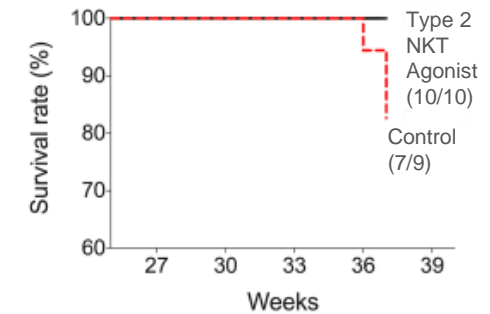
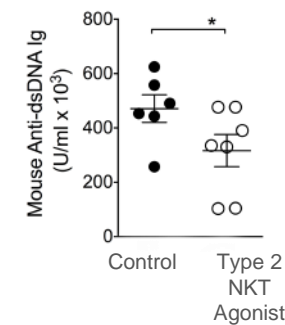
Type 2 NKT Agonist

✓ Inflammation Decreased

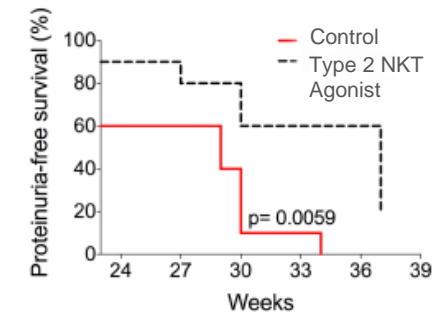
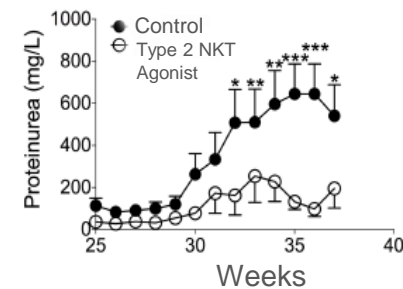
✓ Interstitial Anatomy Improved

✓ Collagen Deposition & Fibrosis Stopped

✓ Improvement in Auto-Antibodies & Overall Survival



✓ The Most Common Manifestation of Lupus Nephritis & Renal Damage, Proteinuria, Improved



GRI-0803

Initial Focus on Systemic
Lupus Erythematosus (SLE)

Extensive IP protection with issued
composition of matter and use patents
and market LOE through 2038

GRI-0803

2nd Generation Type 2 NKT Agonist

- ✓ Chemistry backbone based on type 2 GRI-0124
 - <400g/mol
 - <0.1% solubility in H₂O
 - Excellent bioavailability
- ✓ PK profile supporting q.d. administration orally
- ✓ No CV toxicology issues, no genotox and no activation or inhibition within CYP450 pathway
- ✓ No toxicology concerns to date

**Target IND Filing in Q3 2024 with
Topline Data Expected Q4 2024**

Steps Toward IND Filing

Validate bioanalytical methods
Complete cGMP manufacturing
Complete toxicology studies

Summary

iNKT cells accumulate in SLE patients and in NZBWF1 mice, have an activated phenotype and their hyporesponsiveness to *in vitro* stimulation suggests chronic activation

Type 2 NKT cells accumulate in NZBWF1 kidney, and remain responsive to *in vitro* restimulation

Type 2 NKT cell activation in NZBWF1 mice inhibit iNKT cell activity

Once-weekly GRI-0124

Inhibits pro-inflammatory cytokines and signaling pathways in NZBWF1 mice

Decreases pDC accumulation and MHC class II expression

Inhibits CD4+, CD8+ T cells, and B cells (↑ T1B and ↓ T2B cells)

Reduces renal cellular infiltration and fibrosis

Inhibits proteinuria, anti-dsDNA Ig, and improves overall survival and proteinuria-free survival



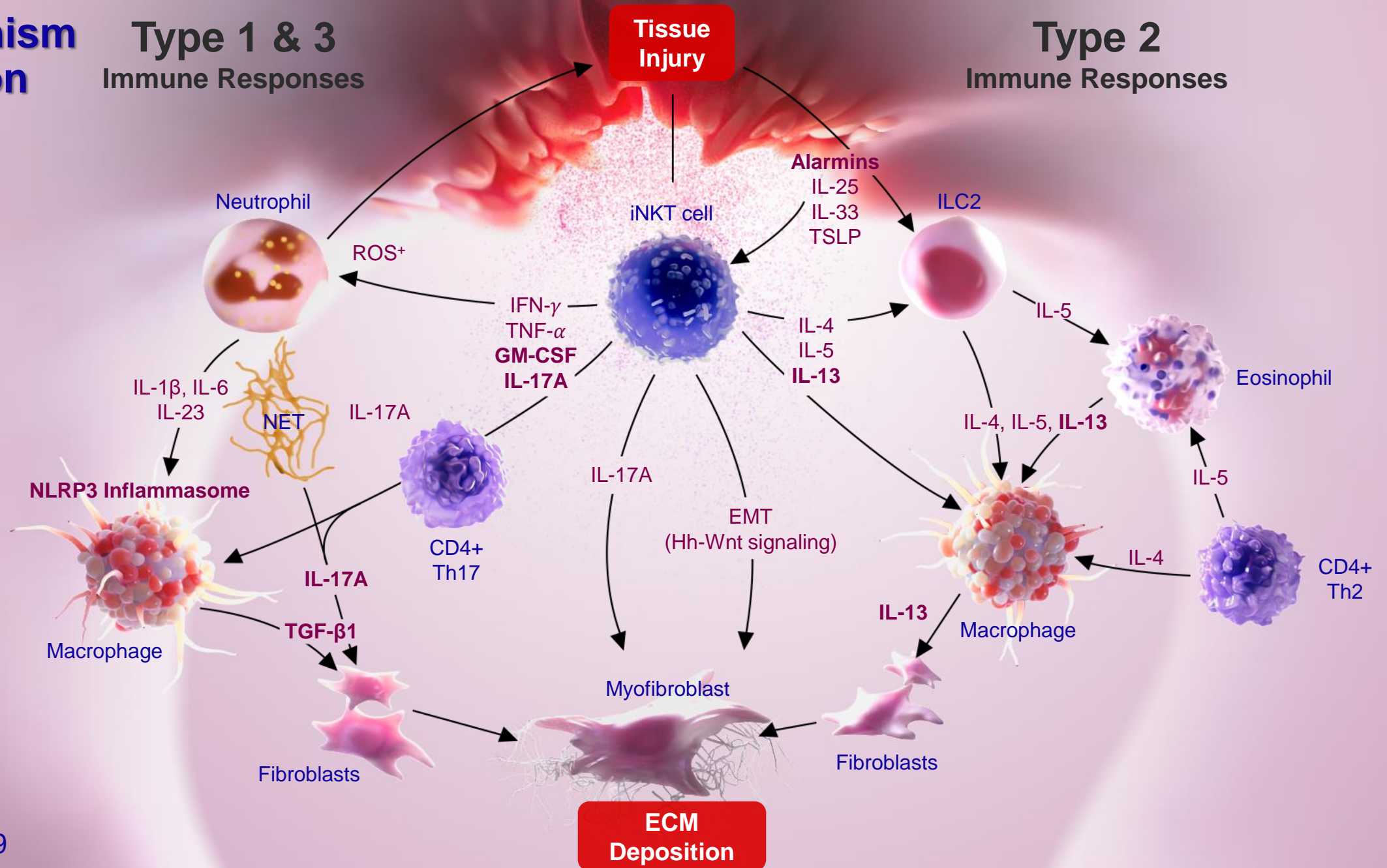
A New Approach to
Inflammatory Diseases

Thank You!

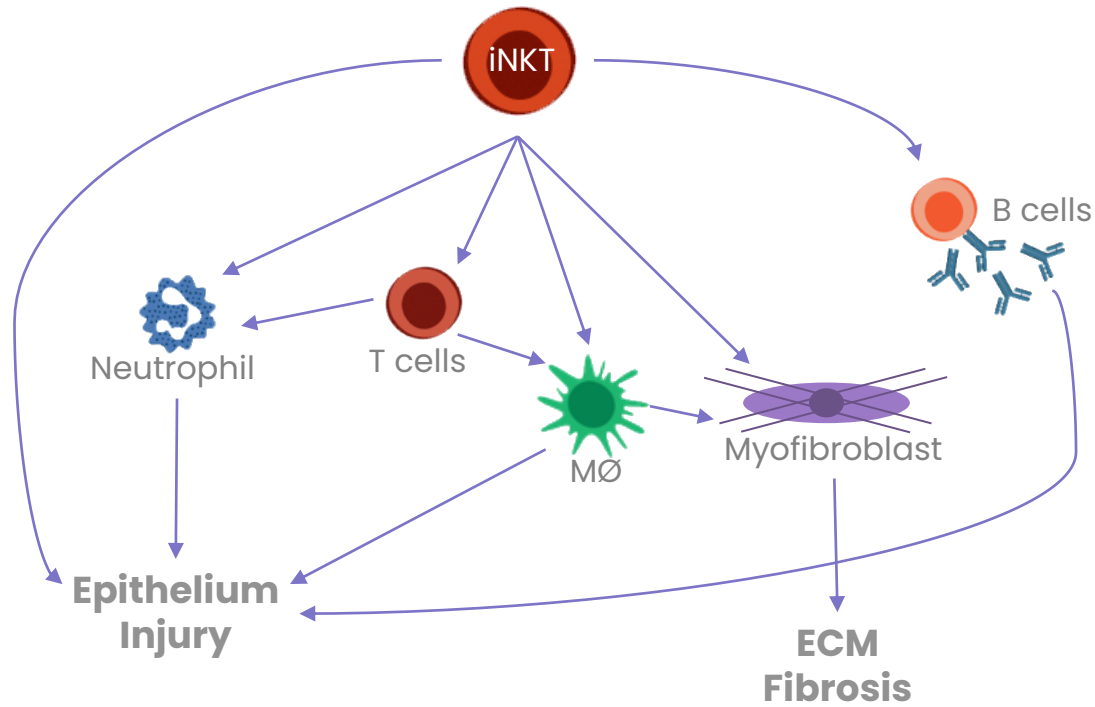
iNKT: Mechanism of Action

Type 1 & 3
Immune Responses

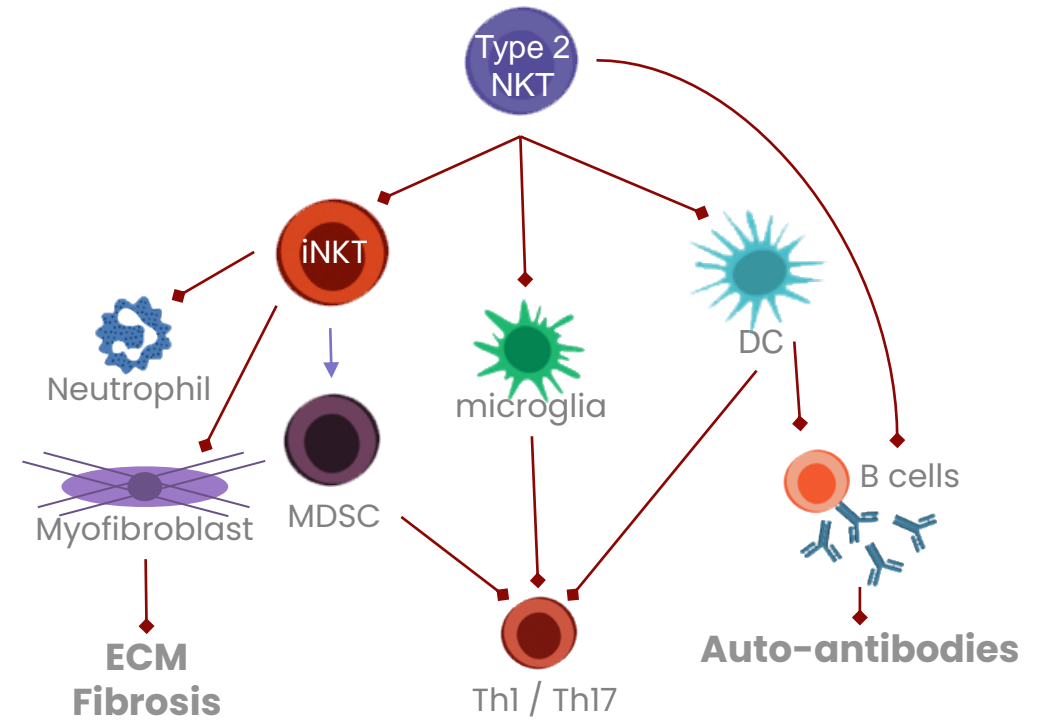
Type 2
Immune Responses



iNKT ARE EFFECTOR T CELLS & PROMOTE DYSREGULATED IMMUNITY



Type 2 NKT ARE REGULATORY T CELLS & RESET DYSREGULATED IMMUNITY



Rapidly Advancing into the Clinic

**Target IND Filing for GRI-0803 in H1 2024
with Topline Data Expected H2 2024**

Steps Toward IND Filing

- Validate bioanalytical methods
- Complete cGMP manufacturing
- Complete toxicology studies

Summary

Elevating Clinical Stage Biotechnology
Company Advancing Innovative Pipeline
Across Multiple Orphan and High-Value
Inflammatory, Fibrotic and Autoimmune
Diseases

**We Believe NKT Science is Compelling
to Fundamental Institutional Investors
and Big Pharma Partners**

NKT Science

Leading NKT regulation
technology targeting earlier in
the inflammatory cascade to
interrupt disease progression

High-Value Indications

Clinical pipeline in potential high-
value indications with multiple
pipeline expansion opportunities

Proven Team

Team with proven NKT,
immunology and drug
development experience