



Novel Anti-TMPRSS6 Monoclonal Antibody Portfolio

Exclusive In-Licensing Agreement with
Mabwell Therapeutics

January 20, 2023



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Disc is Building a Leading Company Dedicated to Treating Hematologic Diseases

Focus on Hematologic Disorders

Immense medical need across a wide spectrum of disorders

Predictive, objective endpoints

Fundamental & Validated Pathways

Fundamental to red blood cell biology: iron and heme

Clinical and genetic evidence of target mechanism in humans

Multiple Clinical Programs with Broad Potential

Bitopertin in Phase 2

DISC-0974 in Phase 1b/2

New Program: MWTX-003 is Phase 1-Ready

Multiple Near-Term Catalysts

Data expected 2023:

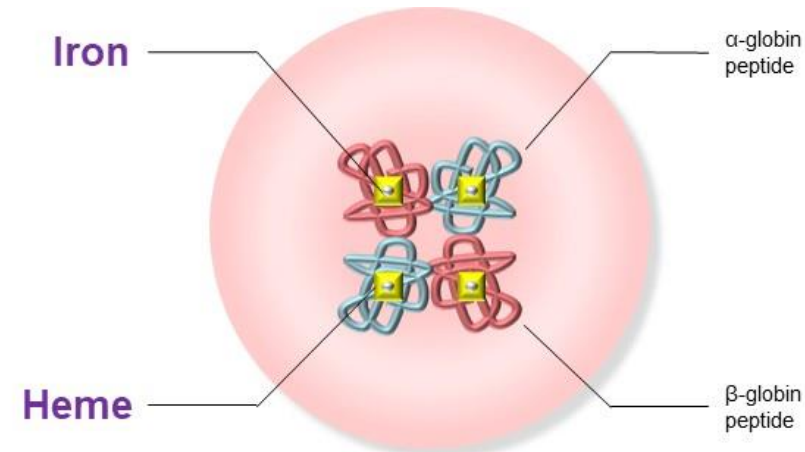
Bitopertin in EPP

DISC-0974 in MF and CKD

Initiate Ph 1 MWTX-003

Disc Targets Fundamental Pathways that Impact the Biology of Red Blood Cells

Iron and heme formation play a central role in erythropoiesis

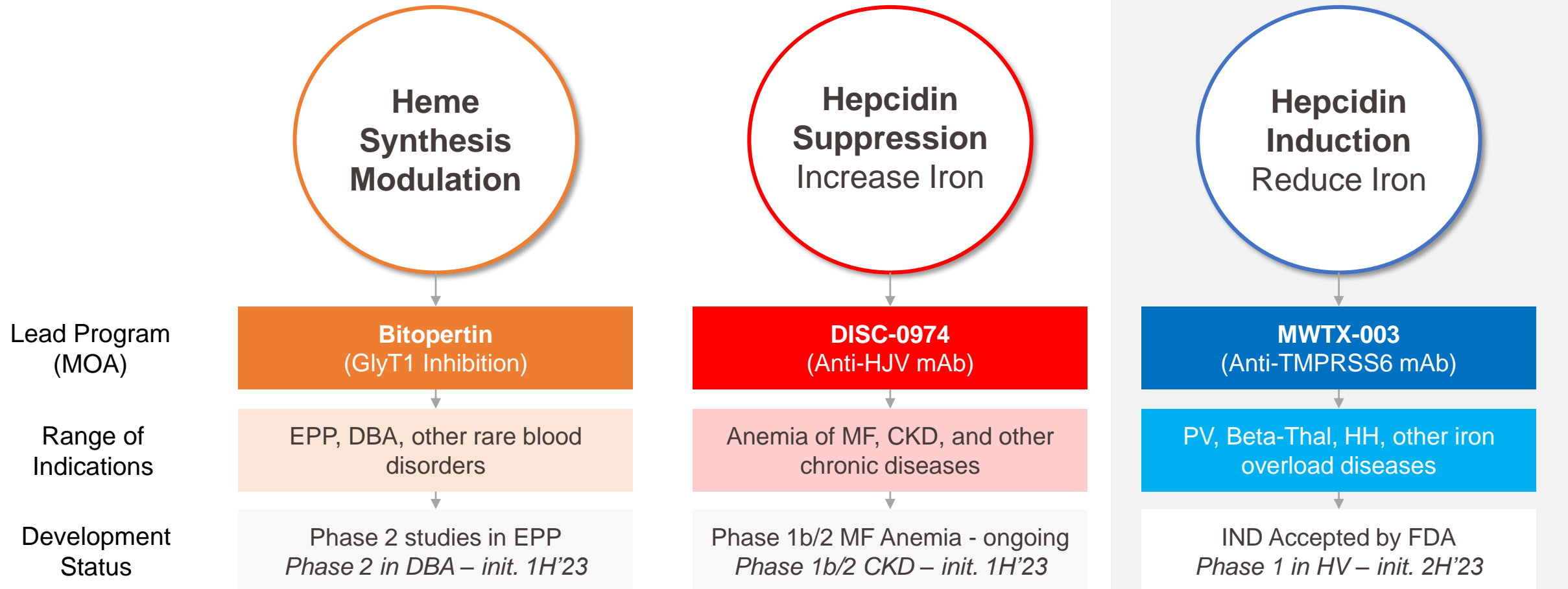


Critical points of intervention across multiple hematologic diseases

Wide Spectrum of Hematologic Diseases Addressable by Disc Portfolio






Severe Rare (000s)		Moderate Prevalence (100K+)				Widely Prevalent (MMs)			
Diamond-Blackfan Anemia	Erythropoietic Porphyrias	Beta-Thalassemia	Anemia of Myelofibrosis	Myelodysplastic Syndromes	Sickle Cell Disease	Polycythemia Vera	Hereditary Hemochromatosis	IBD Anemia	CKD Anemia

Disc's Portfolio Addresses Broad Spectrum of Hematologic Disorders



Disc's Hematology-Focused Pipeline

Multiple programs in development with pipeline-in-a-product potential

Portfolio	Program	Preclinical	Phase 1	Phase 2	Near-Term Milestones
Iron Modulation	Heme Biosynthesis Modulator Bitopertin† GlyT1 Inhibitor Oral, once-daily	Erythropoietic Porphyrias (EPP and XLP) – <i>Initiated July '22</i>  Diamond-Blackfan Anemia (planned) and other indications 			EPP / XLP <ul style="list-style-type: none"> Phase 2 BEACON Trial in EPP / XLP (open-label, initiated July '22) Phase 2 AURORA Trial in EPP (placebo-controlled, expected to initiate 2H '22) Interim open-label data expected by 1H'23
	Hepcidin Suppression Increase Iron DISC-0974‡ Anti-HJV monoclonal antibody Subcutaneous, once-monthly	Anemia of Myelofibrosis (MF) – <i>Initiated June '22</i>  Anemia of Chronic Kidney Disease (CKD) – <i>Initiation expected 1H'23</i> 			Proof-of-Mechanism <ul style="list-style-type: none"> Phase 1 SAD data presented June '22 Myelofibrosis Anemia <ul style="list-style-type: none"> Initiated Phase 1b / 2 trial in 1H'22 Interim open-label data expected in '23 CKD Anemia <ul style="list-style-type: none"> Expect to initiate Phase 1b / 2 trial 1H'23 Interim data expected in '23
	Hepcidin Induction Reduce Iron MWTX-003 Anti-TMPRSS6 Monoclonal antibody	Polycythemia Vera and Diseases of Iron Overload / Ineffective Erythropoiesis  New program in-licensed from Mabwell is phase 1-ready and strategically aligned with portfolio			Phase 1 Proof-of-Mechanism <ul style="list-style-type: none"> IND accepted by FDA Initiation of Phase 1 study 2H'23 Interim proof-of-mechanism data '24

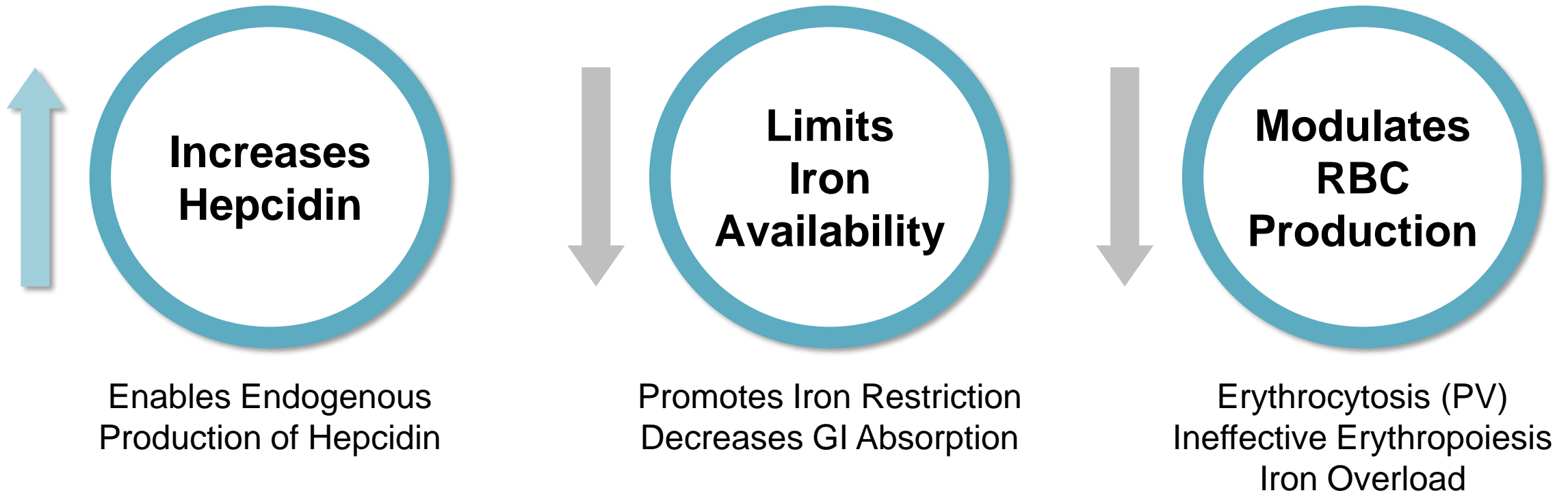
Expanding Disc's Portfolio in Benign Hematology

In-licensing anti-TMPRSS6 mAbs underscores Disc's leadership in hepcidin biology and iron homeostasis

Strategic Rationale	<ul style="list-style-type: none">• TMPRSS6 is an increasingly important target in benign hematology: there is burgeoning clinical and preclinical evidence validating TMPRSS6 and role of iron restriction in key diseases• Highly complementary mechanism and builds on Disc's expertise in hepcidin biology• Phase 1-ready MWTX-003 means capital-efficient path to clinical proof-of mechanism; Disc maintains guidance on operating runway into 2025
Mabwell Therapeutics	<ul style="list-style-type: none">• Based in San Diego; innovation center of fully-integrated biopharmaceutical company Mabwell (Shanghai) Bioscience; focused on discovery and development of antibody and protein-based drugs• Led by CEO Xin Du, PhD (formerly Scripps, UCSD, Silarus Therapeutics) and expert in TMPRSS6
Lead Antibody MWTX-003	<ul style="list-style-type: none">• Highly potent and durable effects in preclinical studies: ↑ hepcidin and ↓ iron; excellent non-clinical safety• Demonstrated efficacy in disease models of beta-thalassemia (presented ASH 2021) and polycythemia vera• IND accepted by U.S. FDA in November 2022 – expect to initiate phase 1 study 2H'23
Transaction Summary	<ul style="list-style-type: none">• Disc receives an exclusive license to Mabwell's portfolio of anti-TMPRSS6 antibodies• Financial terms \$10 million upfront and eligible milestone payments up to \$402.5 million; mid-to-high single digit tiered royalties on net sales• Disc territories: US, Europe and ROW excluding Greater China and Southeast Asia

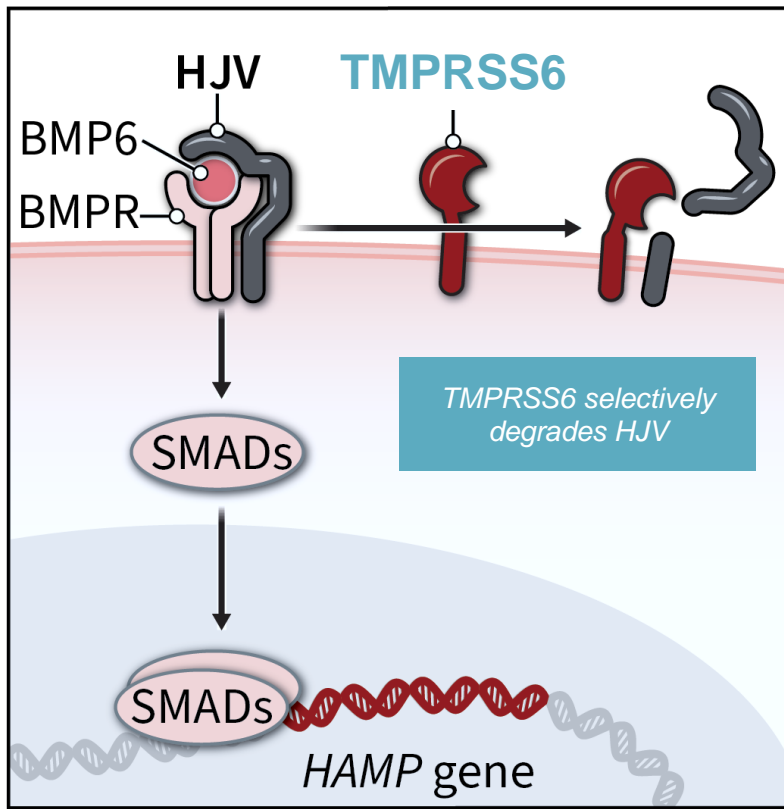
Anti-TMPRSS6 mAb Induces Hepcidin

Designed to limit iron levels with potential to address a wide range of hematologic disorders



Targeting TMPRSS6 to Increase Hepcidin

Potent, specific target controls endogenous hepcidin production



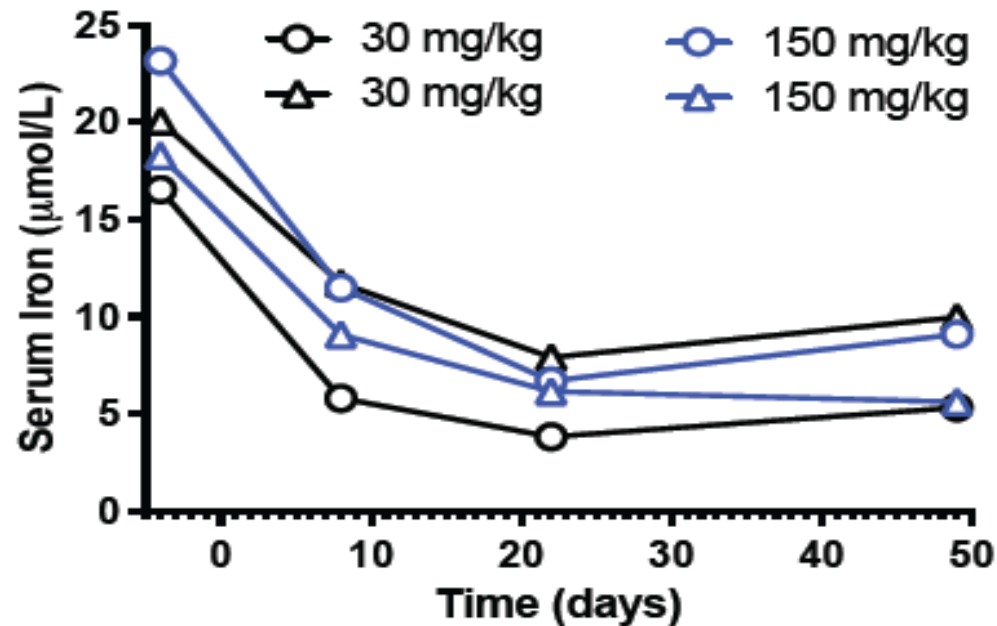
Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

- **Genetic validation** in patients with IRIDA (Iron-Refractory Iron Deficiency Anemia)
 - LOF TMPRSS6 mutation increases hepcidin and reduces iron availability
- **Functionally specific** to hepcidin / iron
- **Tissue specific** expression primarily in the liver

MWTX-003 Effects in Non-Human Primates

Results in deep and sustained suppression of serum iron levels

Single dose of MWTX-003 resulted in ~ 70% suppression of serum iron lasting 3 weeks



- Potent PD effects observed across multiple preclinical studies consistent with TMPRSS6 inhibition
 - Heparin: 3-4 fold induction
 - Serum iron: ~ 60-70% suppression
- MWTX-003 demonstrated excellent safety profile in non-clinical GLP safety studies

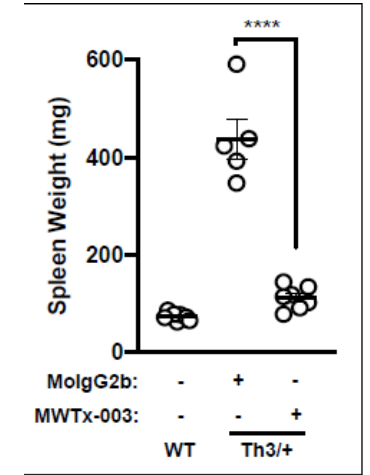
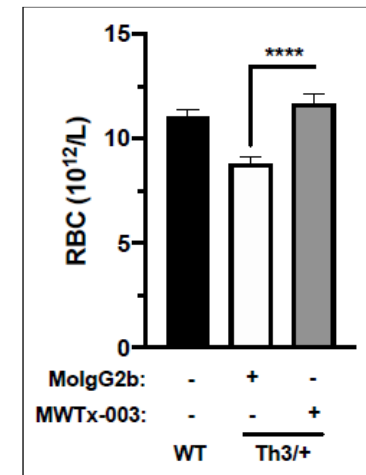
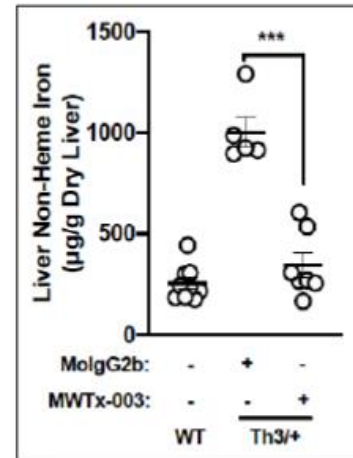
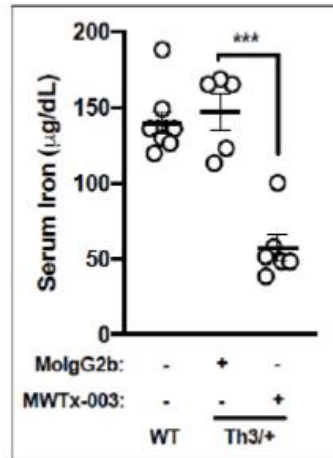
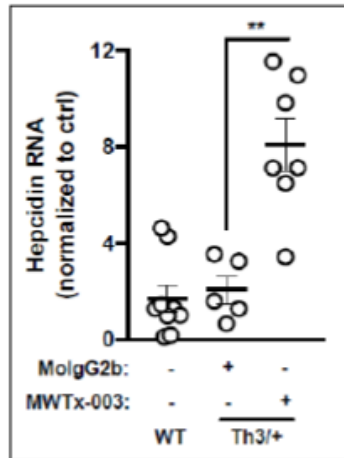
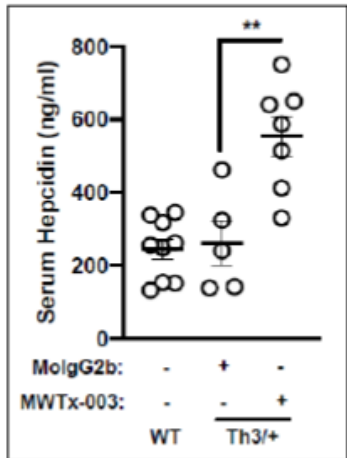
Effects in Hbb^{Th3/+} Model of Beta-Thalassemia

Significant effects on hallmarks of disease including iron overload, ineffective erythropoiesis and splenomegaly

↑ **Hepcidin Production**
Up to 4-fold (mRNA)

↓ **Serum and Liver Iron**
60-65% Reduction

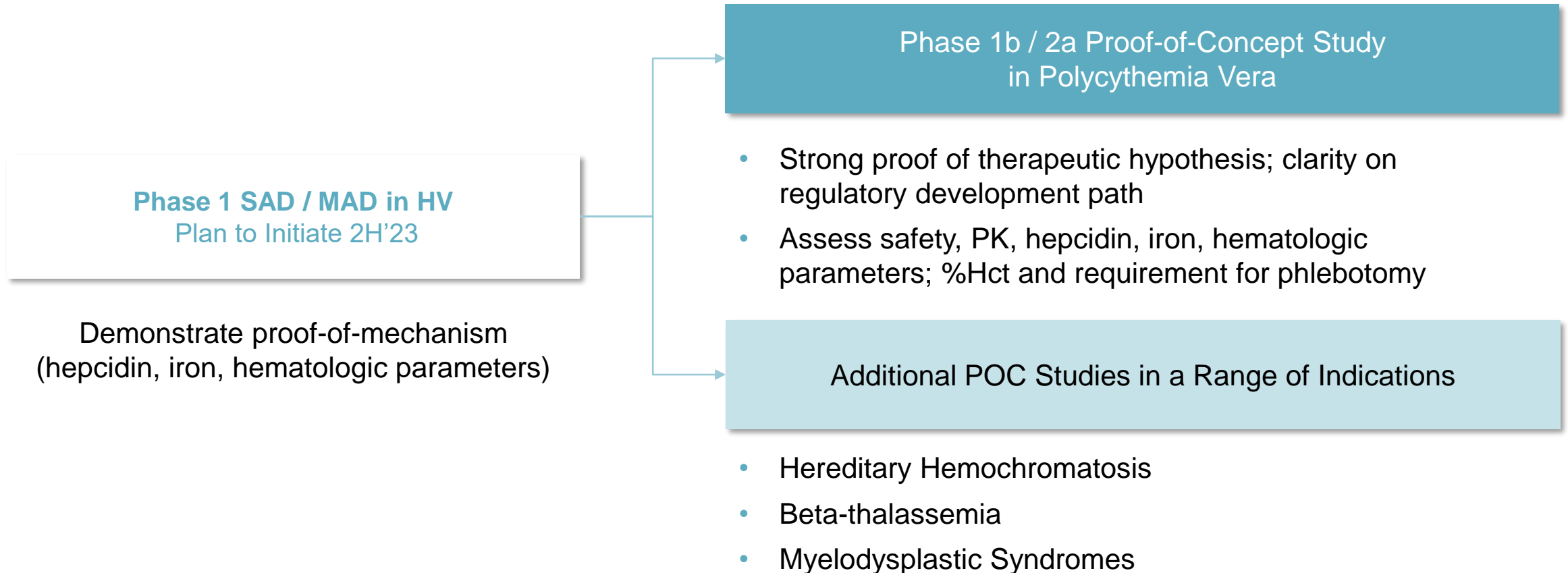
↑ **RBC Production**
↓ **Spleen Weight**



Hbb^{Th3/+} mice were treated with the lead anti-TMPRSS6 antibody at 10 mg/kg IP for 4 weeks

MTWX-003 Development Plans

Establish phase 1 proof-of-mechanism and advance program into POC studies with focus on Polycythemia Vera





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