Corporate Presentation

April 2023

disc medicine

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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

MWTX-003 is Phase 1-Ready

Multiple Near-Term Catalysts

Data expected 2023:

Bitopertin in EPP

DISC-0974 in MF and NDD-CKD

Initiate Ph 1 MWTX-003

EPP (Erythropoietic Protoporphyria); XLP (X-linked Protoporphyria); MF (myelofibrosis); NDD (non-dialysis dependent) CKD (chronic kidney disease)

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Our Executive Team

Deep experience building companies and bringing therapies to patients

John Quisel, JD, PhD | CEO & President

Former EVP & Chief Business Officer at Acceleron Pharma; 14 years through transformative Celgene partnerships, IPO and launch of Reblozyl®; led re-acquisition and positioning of sotatercept for PAH

Brian MacDonald, MB, ChB, PhD | Chief Innovation Officer

Founder and former Board Member of Disc Medicine; founder and CEO of Merganser Biotech; Previously at Zelos Therapeutics, 3-Dimensional Pharmaceuticals, GlaxoSmithKline

Jonathan Yu, MBA | Chief Business Officer

Qpex Biopharma (Co-founder), The Medicines Company, Acceleron Pharma, and Johnson & Johnson. Leadership roles in corporate strategy, finance and operations licensing, M&A, and commercial planning

Srikanth Venkatraman, PhD | SVP Chemistry

Merck and Schering-Plough, leadership roles in discovery, manufacturing and formulation, including for Victrelis® (boceprevir), first approved HCV protease inhibitor

Hua Yang, PhD | SVP Nonclinical R&D

Agios, Millennium / Takeda, BMS. Leadership positions in DMPK and Clinical Pharmacology, including for approved therapies IDHIFA® (enasidinib), TIBSOVO® (ivosidenib) and PYRUKIND® (mitapivat)

Joanne Bryce, CPA | Chief Financial Officer

Former CFO of Arkuda Therapeutics, Dyne Therapeutics, and Quartet Medicine; previously at WiTricity, Speedy Packets, Narrative Communications; Arthur Andersen

Will Savage, MD, PhD | Chief Medical Officer

Magenta Therapeutics and Shire / Takeda; Trained in Pediatric Hematology & Transfusion Medicine; Faculty at Harvard Medical School, Johns Hopkins University School of Medicine

Rahul Khara, PharmD, JD | General Counsel

Former VP Legal and Chief Compliance Officer at Acceleron Pharma, supported commercial launch of Reblozyl® and eventual acquisition by Merck; Arnold & Porter, LLP; Sidley Austin LLP

Min Wu, PhD | VP Biology

Proteostasis, FORMA, Agios, AVEO Oncology. Discovery and development across range of therapeutic areas including oncology and orphan disease including AATD, CF, lysosomal storage disease and others

Jeremy Brinkerhoff, CPA | VP Finance

Former Partner at CFGI, a portfolio company of The Carlyle Group and largest non-audit accounting advisory firm in US and focused on life science companies; Covidien; PwC

Our Investors & Advisors

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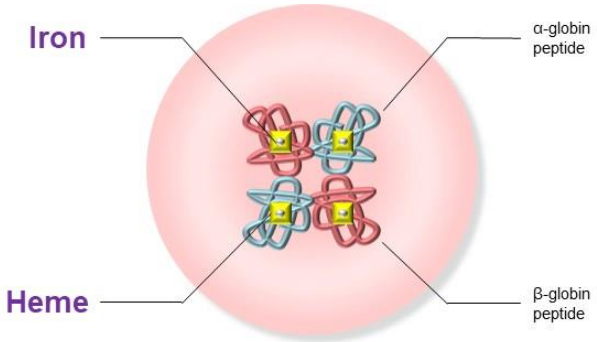
Targeting Fundamental Pathways that Impact the Biology of Red Blood Cells

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 (US and Europe)

Severe Rare (000s)			Moderate Prevalence (100K+)				Widely Prevalent (MMs)		
Diamond-Blackfan Anemia ~ 5,000 (WW)	Erythropoietic Porphyrias ~7,500	Beta-Thalassemia 20,000+	Anemia of Myelofibrosis 30,000	Myelodysplastic Syndromes 200,000	Sickle Cell Disease 200,000	Polycythemia Vera 200,000+	Hereditary Hemochromatosis 1 Million (US)	IBD Anemia 1 Million+ (US)	CKD Anemia 6 Million+ (US)

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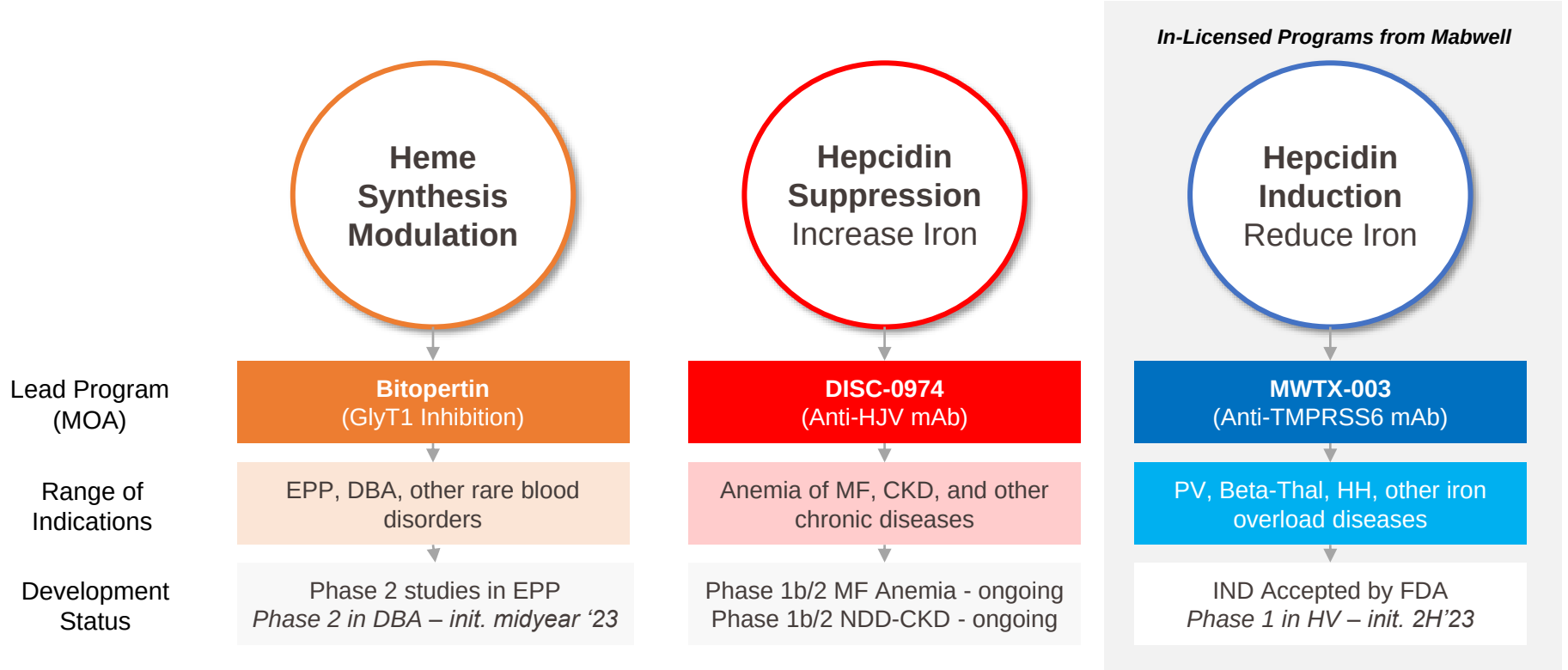
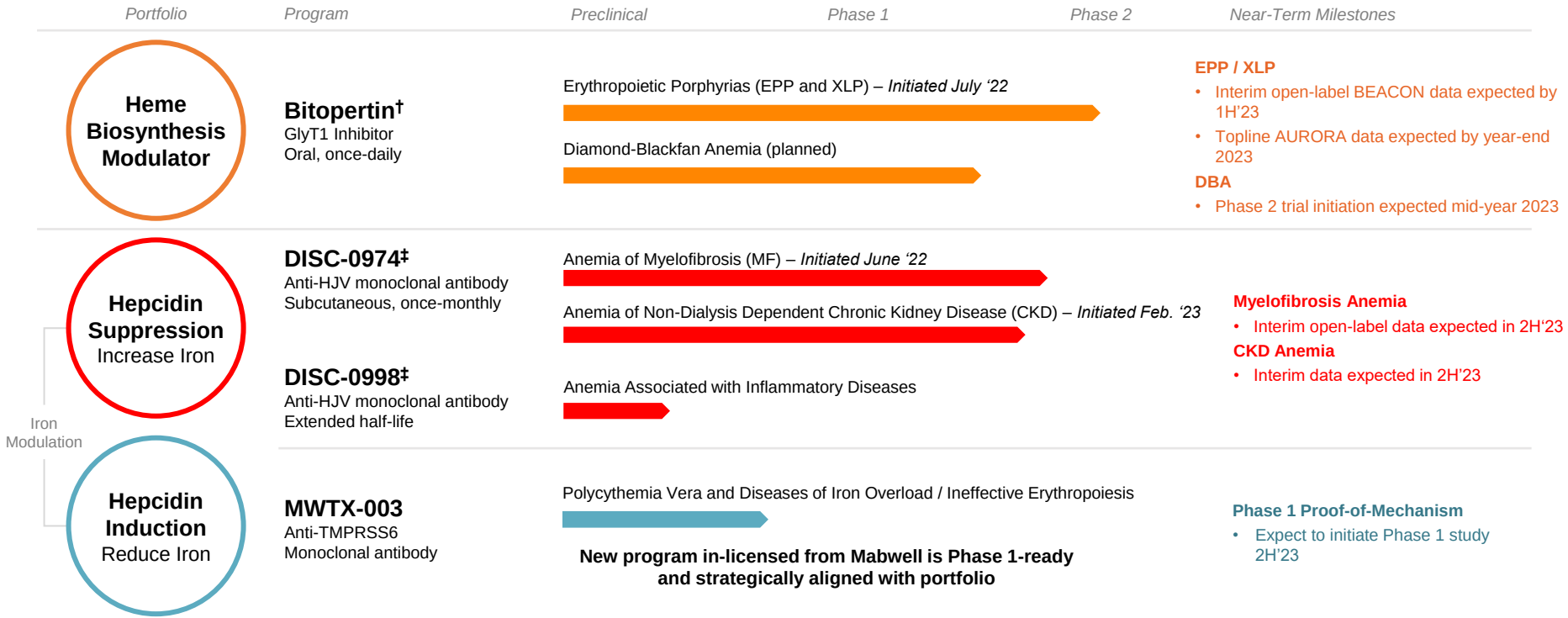
Disc's Portfolio Addresses Broad Spectrum of Hematologic Disorders



Disc's Hematology-Focused Pipeline

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



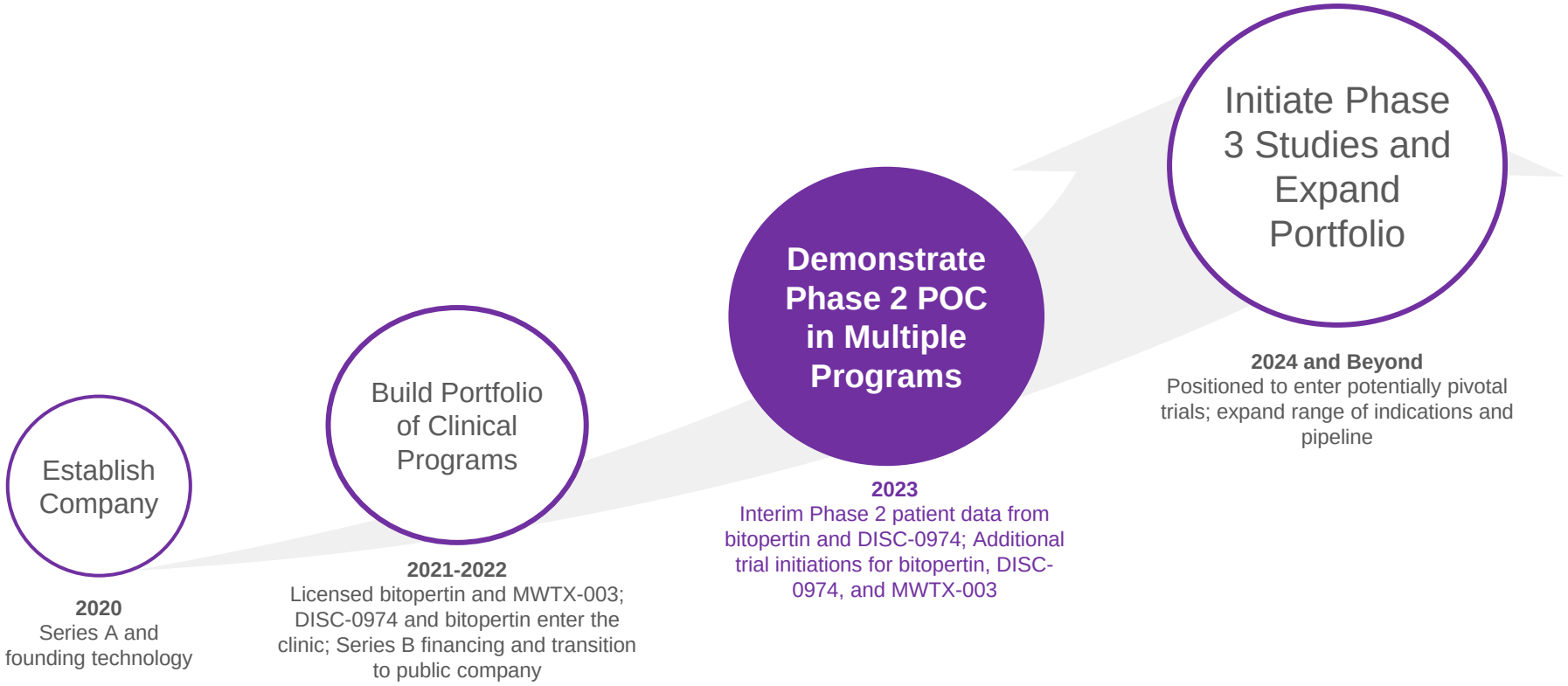
† Bitopertin in-licensed from Roche; ‡ DISC-0974 and DISC-0998 in-licensed from Abbvie

Upcoming Milestones and Events

Multiple catalysts expected beginning mid-year and through 2024

Program	Indication	H1 2023	H2 2023	2024
Bitopertin Heme Synthesis Modulator	Erythropoietic Porphyrias (EPP and XLP)	• Interim Ph 2 BEACON (open-label)	• Ph 2 BEACON data • Ph 2 AURORA data	• End of Ph 2 Meeting • *Next steps tbd*
	Diamond-Blackfan Anemia (DBA)	• Initiate Ph 2 DBA study (mid-year)		• Interim Ph 2 DBA data
DISC-0974 Hepcidin Suppression	Anemia of Myelofibrosis (MF)		• Interim Ph 1b/2 MF data	• Ph 2 MF data
	Anemia of Chronic Kidney Disease (CKD)	• Initiate Ph 1b/2 CKD Study	• Interim Ph 1b/2 CKD data	• Ph 2 CKD data
MWTX-003 Hepcidin Induction	Polycythemia Vera and Diseases of Iron Overload / Ineffective Erythropoiesis		• Initiate Ph 1 SAD / MAD study	• Phase 1 SAD / MAD data

Strong Growth Trajectory Towards Building a Leading Hematology Company



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Bitopertin

GlyT1 Inhibitor

Heme Biosynthesis Modulation

Bitopertin: Oral, Selective GlyT1 Inhibitor

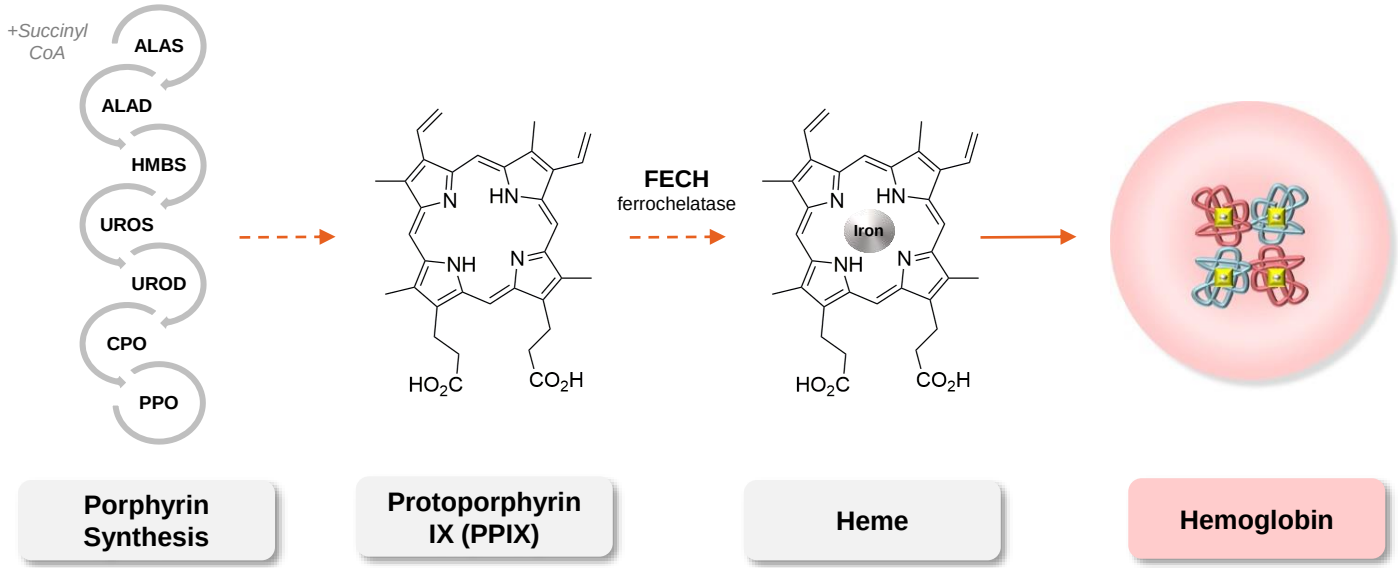
In multiple clinical trials by Roche, bitopertin was observed to modulate heme biosynthesis by blocking uptake of glycine in erythrocytes

Glycine

Critical and initiating precursor for heme biosynthesis and is supplied by **GlyT1 transporter**

Bitopertin

Blocks glycine uptake in RBCs by inhibiting GlyT1



Heme Biosynthesis Pathway

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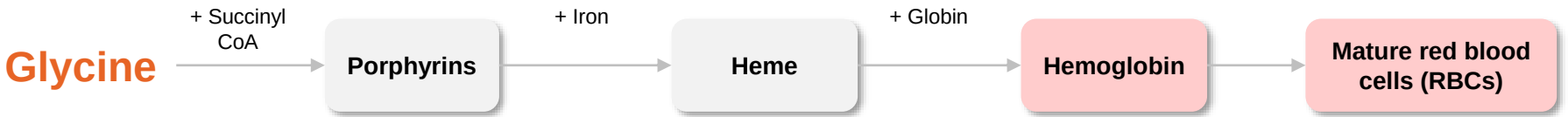
Dysregulated Hemoglobin Synthesis Drives Disease

Inhibiting heme synthesis with bitopertin has potential to address a wide range of hematologic diseases



Porphyrin Toxicity

Erythropoietic Protoporphyria
X-Linked Protoporphyria
Congenital Erythropoietic Porphyria
Hepatic Porphyrias

Heme Toxicity

Diamond-Blackfan Anemia
Myelodysplastic Syndromes

Globin Toxicity

Beta-Thalassemia
Sickle Cell Disease

Excess RBCs

Polycythemia Vera

bold (trial ongoing) / **bold (trial planned)**

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Erythropoietic Protoporphyria (EPP)

Rare, debilitating and lifelong condition characterized by extreme pain and damage to skin caused by light

Genetic condition caused by defective heme biosynthesis – deficient enzyme ferrochelatase

- Lifelong and presents in early childhood
- Caused by accumulation of toxic metabolite PPIX
- XLP, mechanistically similar disease, also PPIX-related

Debilitating and potentially life-threatening

- Skin: severe, disabling pain attacks (days), edema, burning
- Hepatobiliary disease: gallstones, liver dysfunction or failure
- Psychosocial well-being (fear, anxiety) and development

No cure or disease-modifying treatment

- Avoid sun / light, protective clothing, window tinting, Zn/Ti Oxide
- One FDA-approved agent, afamelanotide, a surgically-implanted tanning agent

EPP and XLP Prevalence:

Approximately 7-8k+ addressable patients in US and Europe; recent genetic studies suggest number may be higher

Image sources: *Daily Mail Australia* (2019); FDA Scientific Workshop on EPP (2016); Buonuomo et al. (2014) *Arch Dis Child*

Sources: Deybach et al (2009) *Orphanet Journal of Rare Diseases; American Porphyria Foundation;* Dickey et al (2021) *Genet. Med.*

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EPP Impacts Multiple Aspects of Patients' Lives

Attacks are easily triggered and result in excruciating pain that has neuropathic qualities and can last for days

Madelyn
11-Year Old Patient

"I can only tolerate about 10 minutes of direct sunlight before I get a reaction.

These reactions can last up to five days. When I have a reaction, I can't sleep because the pain is so strong. It hurts so much."

Darlene & Nanelle
Adult Patients

"It's like a chemical burn. It's like a burn from the inside out as opposed to the surface."

"If you've ever worked with jalapenos or habanero peppers, you know. That burning gets on your hands, and there's nothing you can do. It takes about five to seven days for it to wear off."

Kristin
Mother of boy with EPP

"I'm deeply concerned about what this is doing to his mind. I see his personality changing before my eyes.

The anxiety, the isolation, the loneliness, how people treat him, how he's treating the world around him, it's changing. I can see it - that's really hard to manage as a parent."

Meghan
16-Year Old Patient

"My life and that of my family's is completely different than it would if I were able to be in the sun.

The curtains in our home are always closed. There are no outside activities during the day -- no beach, no picnics, no washing the car or cutting the lawn, no camping, no theme parks."

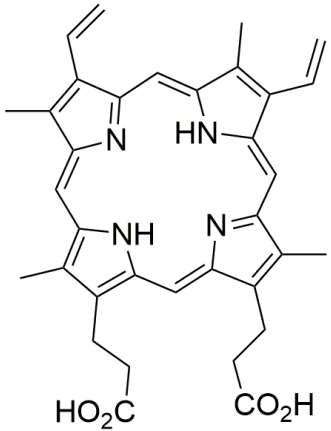
Sources: FDA Scientific Workshop on EPP

PPIX is a Driver of Disease in EPP / XLP Patients

Toxic and photo-active metabolite accumulates in RBCs and is transported to skin and other organs, causing damage

Skin

- Porphyrin ring absorbs light and **emits energy and heat**
- Oxidative damage to endothelial capillaries and surrounding tissue, perivascular edema, complement activation
- Pain, burning sensation, swelling, inflammation, chronic skin lesions



Protoporphyrin IX

Hepatobiliary

- PPIX accumulation in bile canaliculae, causing oxidative damage
- Cholelithiasis requiring surgery or impaired liver function (~25%) and end-stage liver disease requiring transplant (2-5%)
- Clinical and biochemical surveillance

Psychosocial

- Issues with focus and concentration
- Lack of sleep, physical and social isolation
- Significant lifestyle modification, fear and anxiety

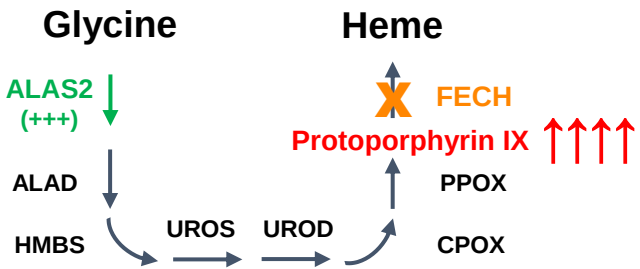
Other Complications

- Nutritional deficiency resulting in osteoporosis and propensity for fractures, chronic alterations to skin (e.g. fragile), mild anemia

Bitopertin: Potential Disease-Modifying Treatment

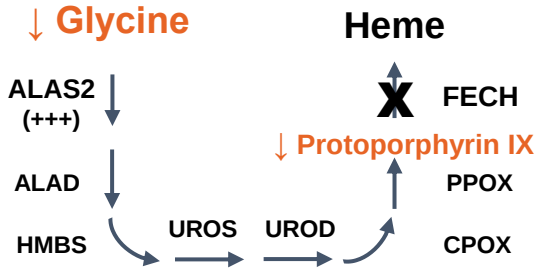
Designed to reduce disease-causing PPIX by limiting uptake of glycine into developing erythrocytes

EPP and XLP Patients
High PPIX Levels



Mutations result in reservoir of supra-physiological levels of PPIX

Bitopertin Treatment
Designed to Reduce PPIX Levels



Potential first disease-modifying treatment for EPP and XLP

Figures adapted from Halloy et al. (2021) *Cell Chem Biol*

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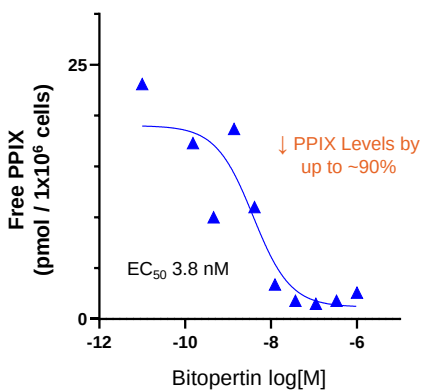
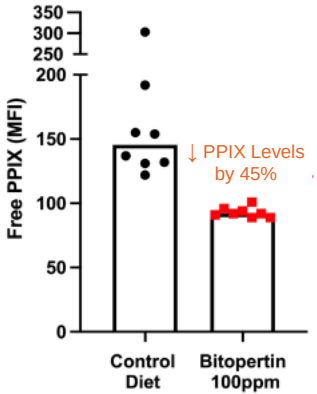
Bitopertin Reduced PPIX in Models of EPP / XLP

Effects on PPIX have the potential to be disease-modifying

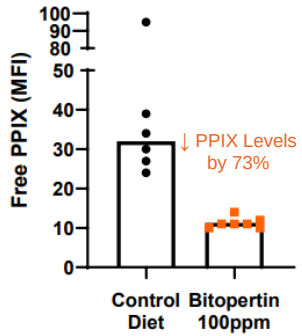
In vitro – EPP Model (K562 Cell)
FECH$^{IVS3\text{-}48C/KO}$ Mutation



In vivo - EPP Model (Mouse)
FECH^{m1pas} Missense Mutation



In vivo - XLP Model (Mouse)
ALAS2^{Q548X} Gain-of-Function Mutation



Bitopertin reduces PPIX, the driver of disease pathophysiology, and is expected to be disease-modifying

- Reductions in PPIX levels of ≥30% reported in literature to have a major impact on photosensitivity in patients[†];
- Bitopertin has been shown in an animal model of EPP (data presented at ASH 2022) to reduce liver fibrosis

Data presented at the 63rd ASH Annual Meeting (December 2021); Studies performed in collaboration with Boston Children's Hospital (PI: Paul Schmidt, Advisor: Mark Fleming)
Sources: [†] Heerfordt et al. (2016) *Br J. Dermatol.;* Wulf et al. (2019) *Photodiagn and Photodyn Ther;* Poh-Fitzpatrick (1997) *J Am Acad Derm*

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Bitopertin Robust Data Package

Extensive non-clinical, CMC and clinical development has already been completed

Non-Clinical

- ✓ Genetic toxicity and Safety pharmacology
- ✓ Long-term GLP toxicology
- ✓ Juvenile GLP toxicology studies supporting patients ≥2 y/o
- ✓ Carcinogenicity studies
- ✓ Full reproductive GLP toxicology
- ✓ Metabolites fully qualified

CMC

- ✓ Commercial-scale production
- ✓ Optimized oral formulation (tablet and capsule)
- ✓ Highly stable molecule (at least 5 years)
- ✓ Available commercial-grade drug substance (metric tons)

Clinical

- ✓ Healthy volunteer studies
- ✓ Drug-drug interaction studies
- ✓ Hepatic impairment
- ✓ Renal impairment
- ✓ TQT (heart rhythm) study
- ✓ Pharmacokinetics in patients of Asian descent
- ✓ 30+ Other clinical trials

Note: Total clinical experience of bitopertin is extensive and includes 700+ HV and 4,000 patients in over 30 clinical trials; all trials referenced conducted by Roche

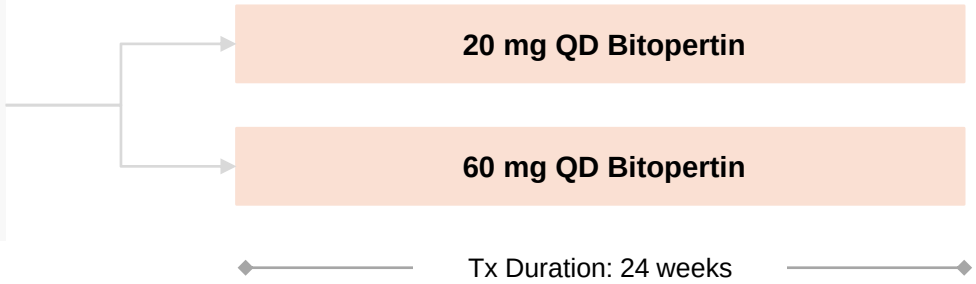
BEACON Trial: Open-Label Ph 2 Trial in EPP / XLP

Open-label, parallel-dose trial to establish POC and assess efficacy, safety in patients (N~20)

Study Design

- Open-label, randomized
- EPP and XLP; 18 years +
- Two dose levels, parallel
- Not receiving afamelanotide
- Australia (study open July ‘22)

Treatment Arms



Study measures: Changes in blood PPIX levels, light tolerance, time to prodromal symptom (TTPS), hepatobiliary markers, QOL, safety / PK

Data availability: Interim, open-label, PPIX data expected by 1H 2023

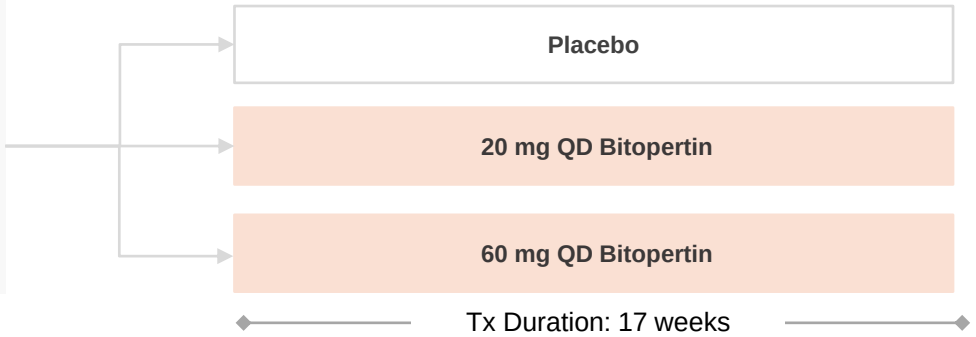
AURORA Trial: Ph 2 Trial in EPP

Randomized, Double-Blind, Placebo Controlled trial to assess efficacy, safety in patients (N~75)

Study Design

- Double-blind, placebo-controlled (1:1:1)
- EPP; 18 years +
- Stratified by light tolerance
- Not receiving afamelanotide
- US (IND cleared, start 2H 2022)

Treatment Arms



Study measures: Changes in blood PPIX levels, time in daylight without pain, light tolerance, time to prodromal symptom (TTPS), hepatobiliary markers, QOL, safety / PK

Data availability: Data expected by 2H 2023

Development Status and Upcoming Milestones

Phase 2 BEACON and AURORA trials initiated, BEACON data expected by 1H’23

Operational activities to enable initiation of patient studies completed

- Roche license signed May 2021
- GMP clinical supply completed June 2022
- BEACON trial - Open-label, parallel-dose trial in EPP and XLP patients in AU – *initiated July 2022*
- AURORA trial – Randomized, placebo-controlled trial in EPP patients in US – *initiated October 2022*

Next milestones

- Interim open label data from the BEACON trial – *expected by 1H 2023*
- Phase 2 IIT in Diamond-Blackfan Anemia – *site contracting in process, startup expected midyear 2023*
- AURORA trial data – *expected 2H 2023*
- Planning underway for studies in additional indications

Hepcidin Modulation

Iron Homeostasis

Iron is Fundamental to RBC Biology

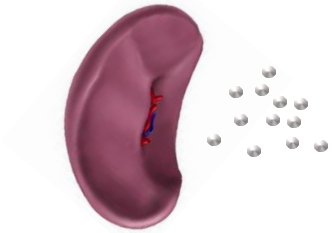
Hepcidin is a regulatory hormone that plays a central role in iron metabolism and homeostasis

Induced by Inflammation

Hepcidin

Gatekeeper Function: Blocks iron absorption and recycling

GI Tract
Iron Intake



Spleen
Iron Storage

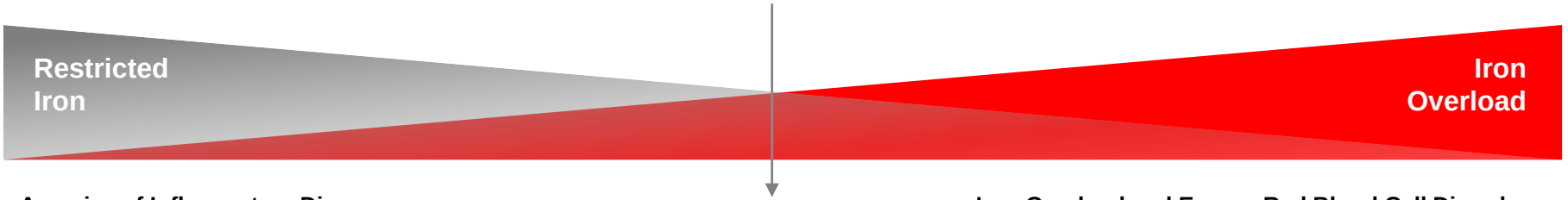
RBC Production in Bone Marrow

Hepcidin is a Therapeutic Target for Diseases

Dysregulated hepcidin drives a wide range of hematologic diseases

High Hepcidin ← **Normal Hepcidin** → **Low Hepcidin**

Regulated erythropoiesis



Regulated iron

Anemias of Inflammatory Disease

- Myelofibrosis
- Chronic Kidney Disease
- Autoimmune / Inflammatory Disorders

Iron Overload and Excess Red Blood Cell Disorders

- Polycythemia Vera
- Hereditary Hemochromatosis
- Myelodysplastic Syndromes

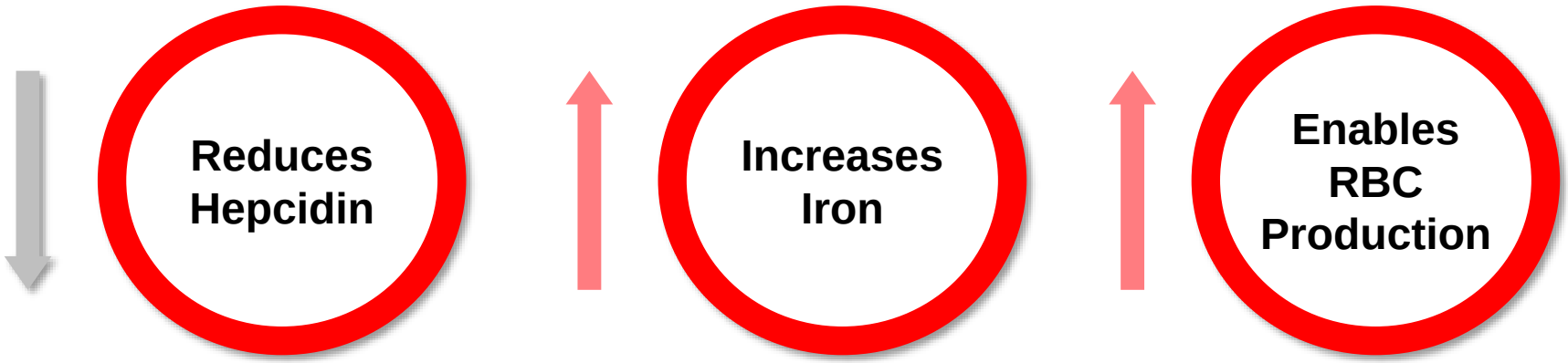
DISC-0974

Anti-HJV mAb

Hepcidin Suppression

DISC-0974: Novel Anti-HJV mAb to Suppress Hepcidin

Designed to enhance iron availability to address a wide range of hematologic disorders



Inhibits endogenous production of hepcidin

Releases iron stores
Enables GI absorption

Potential to treat wide range of anemias

Anemia of Inflammation or Chronic Disease

Inflammation caused by a wide range of conditions results in anemia due to elevated hepcidin

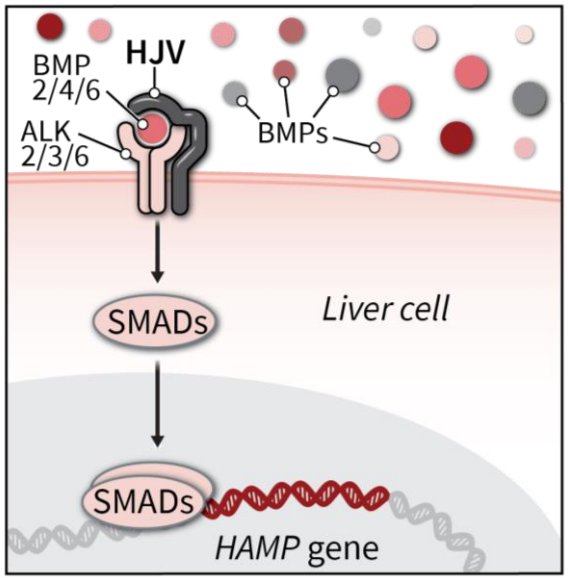
Anemia Types	US Prev.	Est. % Anemic
Myelofibrosis (MF)	17-18.5K	87%
Chronic Kidney Disease (CKD)	37 MM	17-50%
Inflammatory Bowel Disease	1.6 MM	25-35%
Anemia of Cancer	17 MM	35-80%
Systemic Lupus Erythematosus	210K	50%

- **Anemia of inflammation (also called Anemia of Chronic Disease or ACD)** is the 2nd most common form of anemia
- **Estimated 40% of all anemias** are driven by or have an inflammatory component
- **Hepcidin is up-regulated** and correlates with anemia, driven by inflammation

Sources: Weiss (2019); Maccio (2014); Tefferi (2012); *Lupus Foundation;* Stauffer (2014); Filmann (2014); Koutroubakis (2015); *Crohn's and Colitis Foundation*

Targeting Hemojuvelin (HJV) to Suppress Hepcidin

Critical and specific target for hepcidin expression



Inhibiting Hemojuvelin (HJV) Prevents Hepcidin Expression and Increases Iron

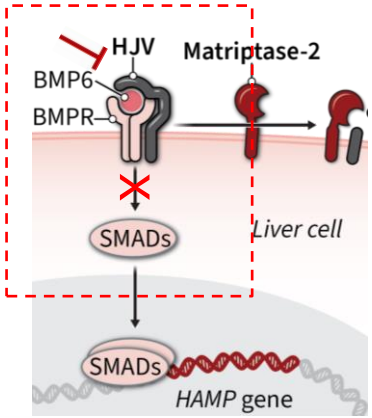
- **Genetic validation** in patients with Juvenile Hemochromatosis (lower hepcidin and elevated iron levels)
  - Loss-of-function mutations in HJV are phenotypically indistinguishable from mutations in *HAMP* (hepcidin) gene
- **Functionally specific** to hepcidin / iron
- **Tissue specific** expression primarily in the liver

Sources: Finberg et al, (2010) *Blood;* Zhang et al, (2010) *J Biol Chem*

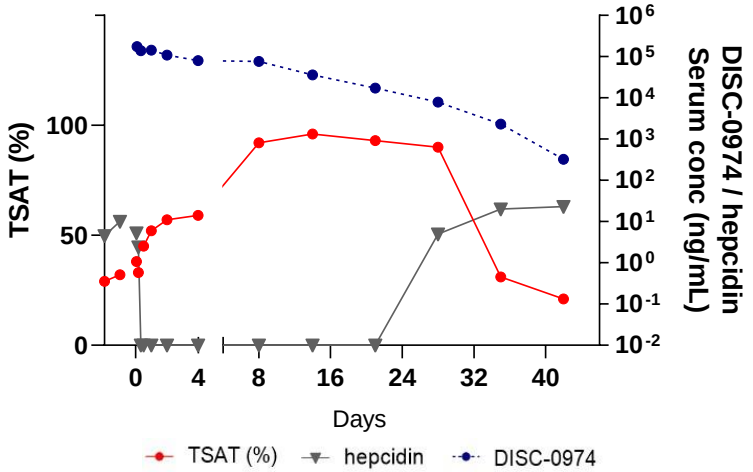
DISC-0974 Mechanism of Action

Designed to reduce hepcidin and increase serum iron levels

DISC-0974 mAb binds to and prevents signaling through hemojuvelin (HJV) co-receptor



Potent and rapid effects on hepcidin and iron with single 5 mg / kg dose (NHP)



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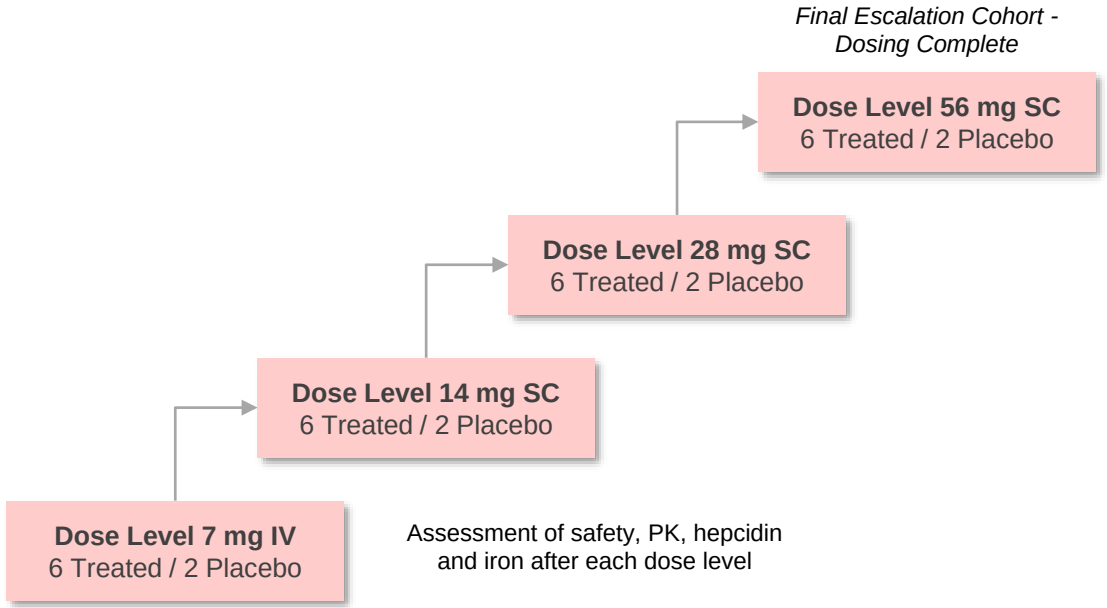
Phase 1 SAD Trial in Healthy Volunteers

Establish proof-of-mechanism based on hepcidin and iron parameters (dosing completed)

Study Design

- Single-ascending dose in ≥32 healthy volunteers
- Key outcome measures:
  - Safety and PK
  - Hepcidin level, serum iron level, % TSAT
- Dose escalation until TSAT > 40% for at least 2 weeks
- Dose levels: 7 mg dose (IV); 14, 28 and 56 mg doses (SC)

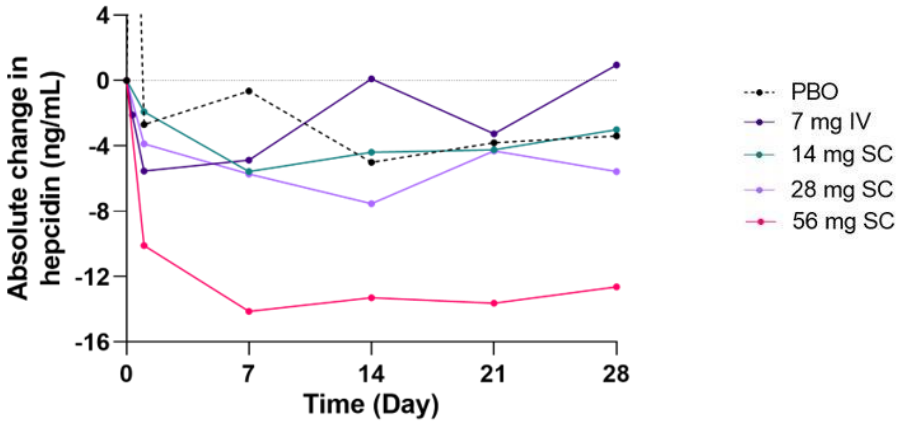


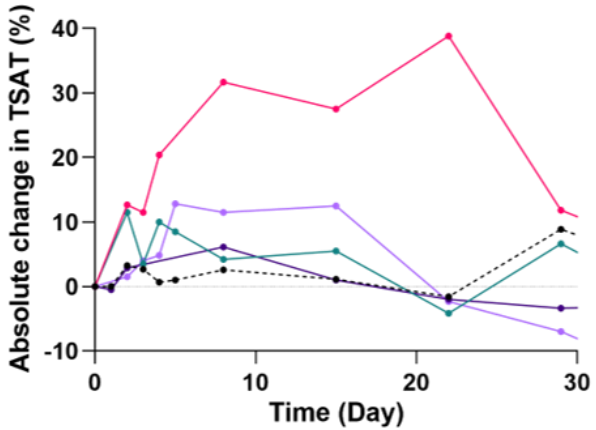
DISC-0974 Phase 1 SAD Preliminary Data

Dosing of DISC-0974 resulted in reduction of hepcidin and iron mobilization

↓ DISC-0974 Reduced Hepcidin Production

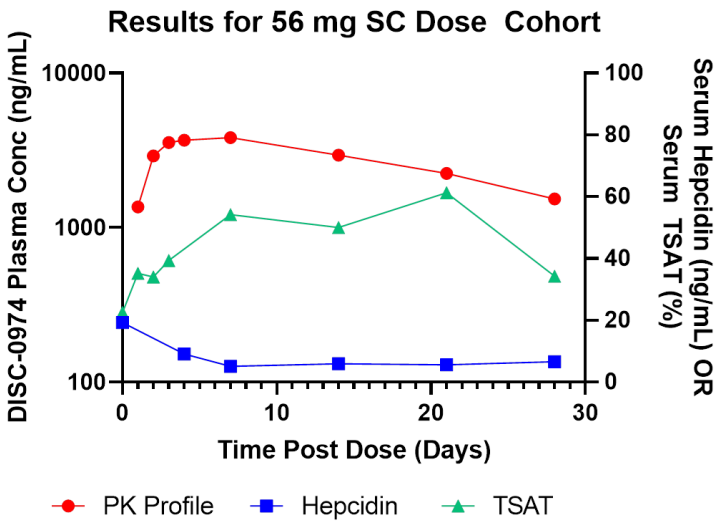
↑ **DISC-0974 Increased TSAT**

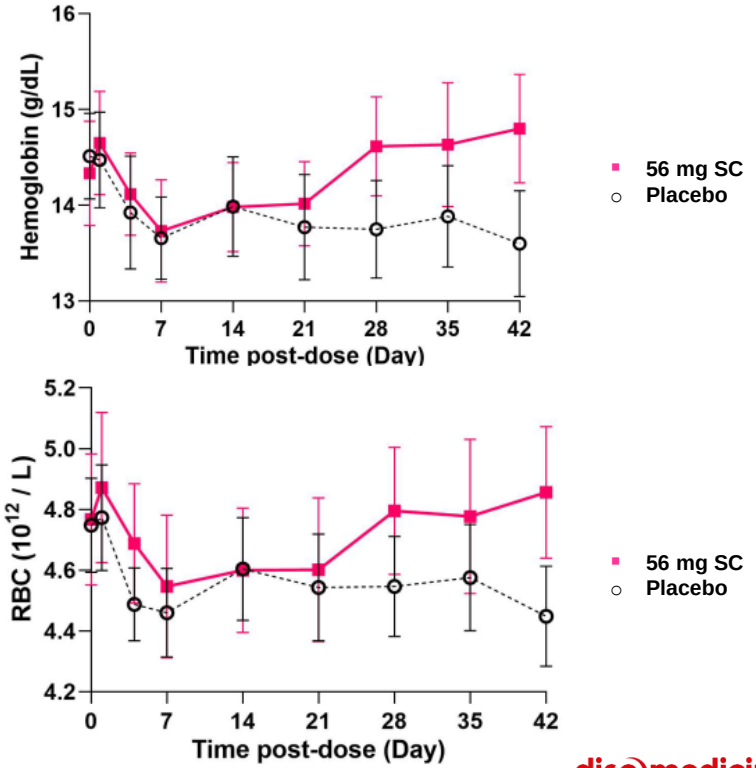




DISC-0974 Phase 1 SAD Preliminary Data (cont.)

Top dose (56 mg) pharmacodynamic activity improves key clinical parameters (> 1g/dL Hgb)





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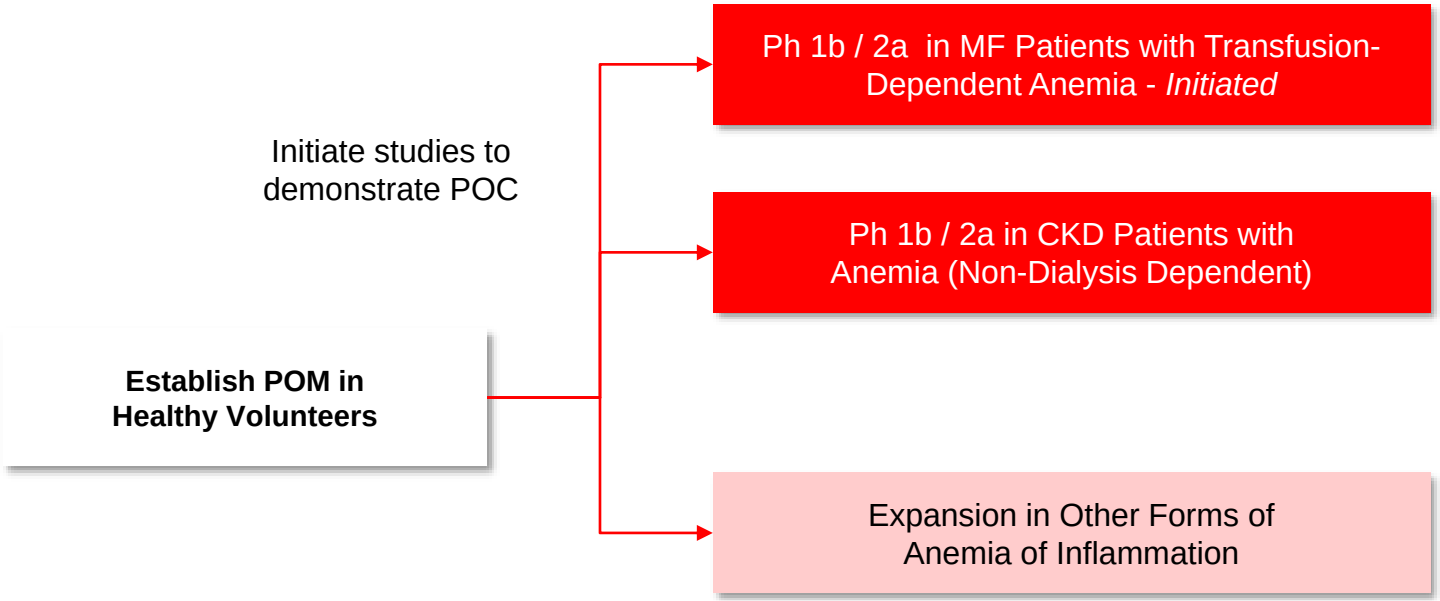
DISC-0974 Phase 1 SAD Preliminary Safety

Safety profile is consistent with selective target biology and preclinical studies; no serious or AEs > Grade 1

	Total n=42	Pooled Placebo n=10	7 mg IV n=8	14 mg SC n=6	28 mg SC n=6	28 mg IV n=6	56 mg SC n=6
Diarrhea	1 (2.4)	1 (10.0)	0	0	0	0	0
Dizziness	2 (4.8)	0	0	0	0	1 (16.7)	1 (16.7)
Dyspepsia	1 (2.4)	0	0	0	0	0	1 (16.7)
Eye pruritis	1 (2.4)	0	0	0	1 (16.7)	0	0
Hand swelling	1 (2.4)	0	0	0	0	1 (16.7)	0
Headache	1 (2.4)	0	0	0	1 (16.7)	0	0
Myalgia	1 (2.4)	0	0	0	0	0	1 (16.7)
Nasal congestion	1 (2.4)	0	0	0	0	0	1 (16.7)
Pain in extremity	1 (2.4)	1 (10.0)	0	0	0	0	0
Seasonal allergy	1 (2.4)	0	0	0	1 (16.7)	0	0
Vessel puncture site bruise	1 (2.4)	1 (10.0)	0	0	0	0	0
Vomiting	1 (2.4)	1 (10.0)	0	0	0	0	0

DISC-0974 Development Strategy

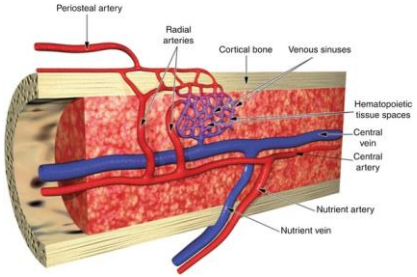
Demonstrate POC in anemia of MF and CKD

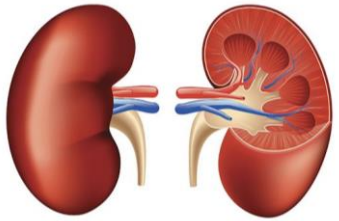


Plan to assess safety, PK, hepcidin, iron, hemoglobin and transfusion burden (MF) and others

DISC-0974: Anemia of Inflammation

Initiate development in parallel in anemias of MF and NDD-CKD





	Anemia of Myelofibrosis (MF)	Anemia of CKD (NDD and DD)
Est. # Patients	16,000 to 18,500 patients (US alone)	5 to 6 million patients (US alone)
Etiology of Anemia	High hepcidin from inflammation JAKi's worsen anemia; Loss of marrow function	High hepcidin from inflammation & poor renal clearance Compromised erythropoietin production
Unmet Medical Needs	Severe and difficult to treat; high transfusion burden No approved or effective anemia therapy Anemia limits optimal JAKi treatment	Majority patients untreated or under-treated ESAs restricted due to safety and black box Mean Hb 9.3 g/dL in patients initiating dialysis

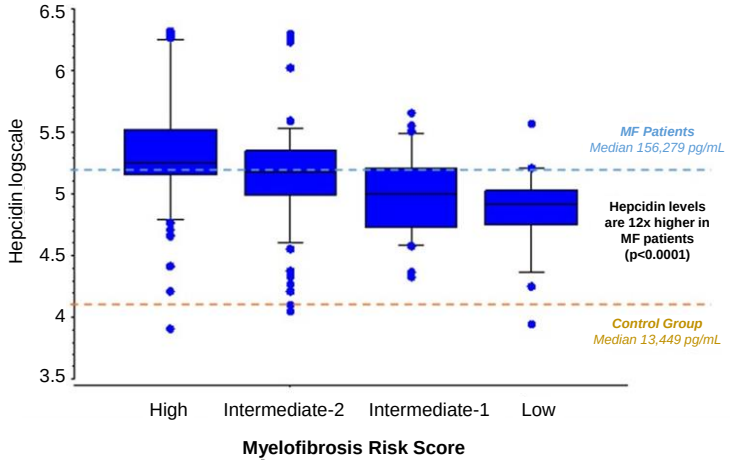
NDD: Non-Dialysis Dependent; DD: Dialysis Dependent

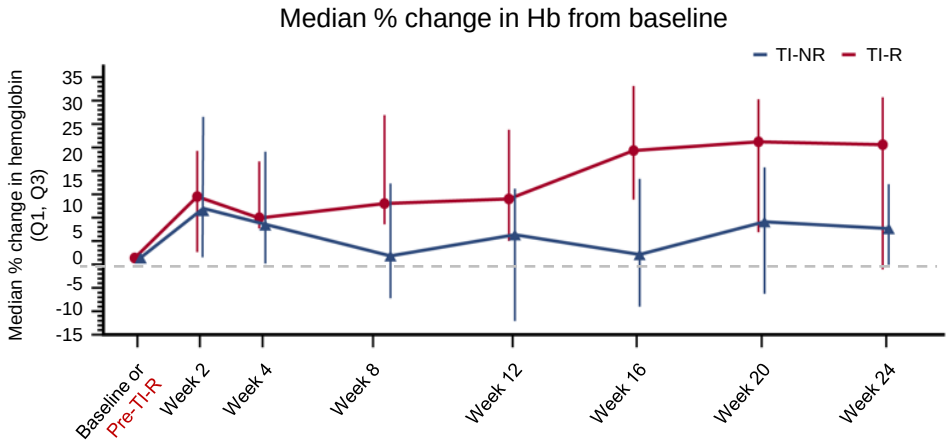
Hepcidin is a Key Driver of MF Anemia

Clinical POC that inhibiting hepcidin axis can impact Hb Levels

Hepcidin Levels are Elevated in MF
~ 12x higher than control and associated with severity of anemia and transfusion burden

Clinical Proof-of-Principle
Hepcidin suppression increased Hb and reduced transfusion burden (41% TI and 85% transfusion reduction)





Source: Pardanani et al (2013) *Am. J. Hematol;* Oh et al., (2020) *Blood Adv:* TI-R: Transfusion-Independent for > 12 weeks by week 24; TI-NR: Transfusion Independent Non-Response

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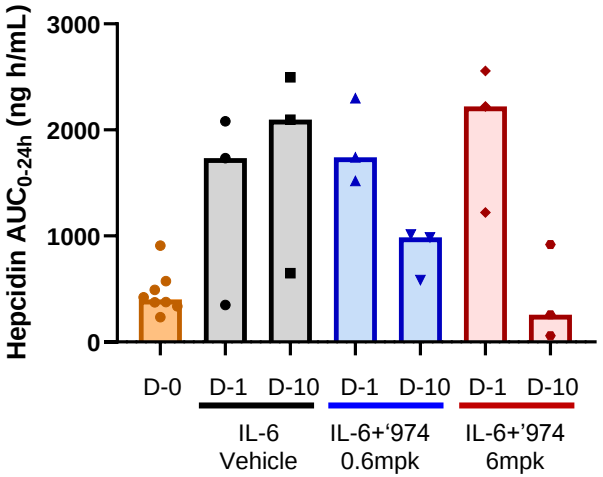
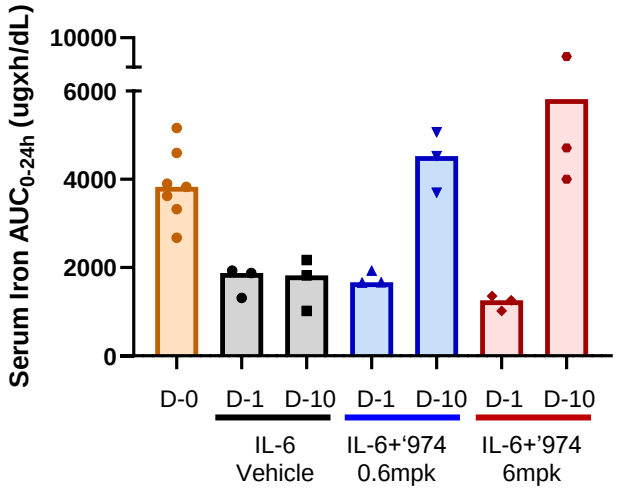
DISC-0974 Lowered Hepcidin in Inflammation Model

NHP: IL6-induced hepcidin and hypoferremia

↓ DISC-0974 Reduced Hepcidin Production



↑ DISC-0974 Increased Serum Iron Levels



Similar effects in animal models of infection-induced hypoferremia, IRIDA and anemia of inflammation

Phase 1b / 2 Study in MF Anemia

Evaluate efficacy and safety and position program for pivotal study; Ph 1b data expected 2023

Phase 1b Dose Escalation in Pts

Design

- N =1-9 per cohort†, initial dose: 14 mg SC
- Open-label, adaptive design (BOIN), accelerated titration
- Receiving transfusions or Hb < 10 g/dL
- Key endpoints: Hemoglobin, Iron, Hepcidin

Treatment Duration: 6 cycles (q28d)

Phase 2 Study Focused on Transfusion-Dependent (TD) Patients

Patient Population

- N ~ 26
- Severity: DIPSS INT-2/High
- Transfusion Dependent
- +/- JAK inhibitor permitted

Design

- Open-label
- Flexibility to add additional exploratory cohorts
- Key endpoints:
  - Transfusion-independence (TI)
  - Hb, Iron, Hepcidin, hematologic parameters

Study Arms

DISC-0974 in TD MF

Treatment Duration: 6 months (q28d)

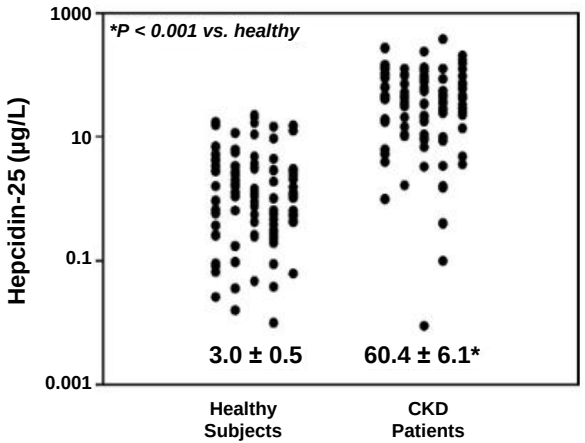
†Note: In Part 1, expect one patient per cohort until iron mechanism is engaged

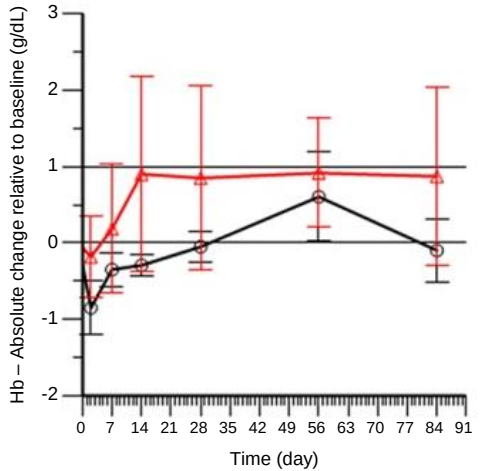
Hepcidin is a Key Driver of CKD Anemia

Clinical POC that inhibiting hepcidin axis can impact Hb Levels

Hepcidin Levels Elevated in CKD Patients
~ 20x higher than healthy subjects and increases with disease severity

Clinical Proof-of-Principle
Hepcidin inhibition via single dose of mechanistically similar BMP-6 mAb increases Hb in dialysis patients





Sources: Troutt et al. (2013), *J Clin Lab Analy*; Sheetz et al. (2019) *Br J Clin Pharmacol.* (2019)

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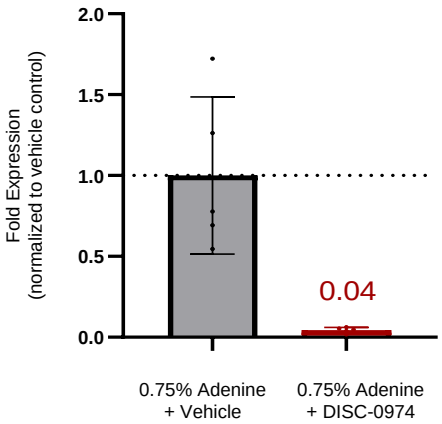
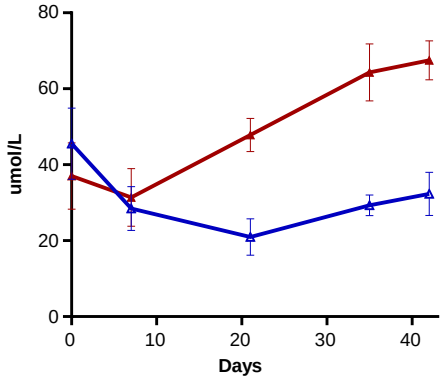
DISC-0974 Improved Anemia in Model of CKD

Rat Model of Adenine Diet-Induced CKD

↓ DISC-0974 Reduced Hepcidin Expression

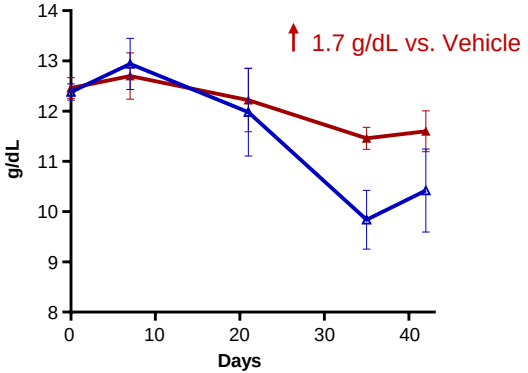


↑ DISC-0974 Increased Serum Iron



Red: 0.75% Adenine + DISC-0974 (20 mg/kg)
Blue: 0.75% Adenine + Vehicle

↑ DISC-0974 Increased Hemoglobin Levels



Red: 0.75% Adenine + DISC-0974 (20 mg/kg)
Blue: 0.75% Adenine + Vehicle

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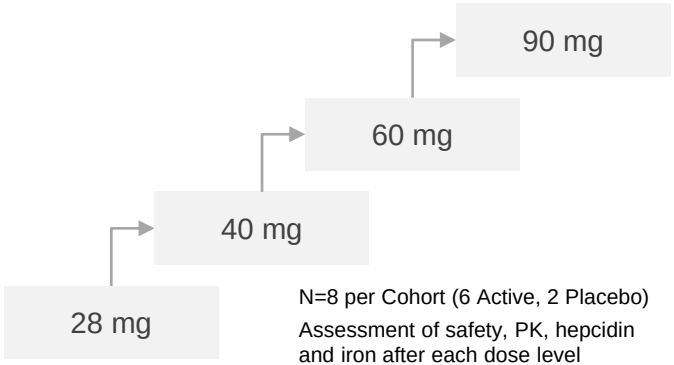
Phase 1b / 2a POC Study in NDD-CKD Anemia

Evaluate efficacy and safety in non-dialysis dependent patients

Study Population

- Stage II-V CKD; Adult
- Not receiving dialysis
- Hb (g/dL) < 10.5 (F), 11 (M)
- Exclude iron-deficient anemia by ferritin, TSAT, and hepcidin (hepcidin > median of healthy controls)

Phase 1b Single-Ascending Dose



N=8 per Cohort (6 Active, 2 Placebo)

Assessment of safety, PK, hepcidin and iron after each dose level

Phase 2a Open-Label, Multiple-Dose

Dose TBD x 3 (Once-monthly)

DISC-0974 (n=12); Placebo (n=4)

Treatment Duration: 3 months (q28d)

Key Endpoints / Measures: Change in hemoglobin; iron, hepcidin, and other hematologic parameters, safety / PK

Data availability: Interim data expected in 2H'2023

Development Status and Upcoming Milestones

Ongoing phase 1b/2 study in MF and plans to initiate phase 1b/2 study in NDD-CKD 1H’23

Operational activities to enable initiation of patient studies completed

- Ph 1 SAD study – completed; excellent safety profile and proof of mechanism for hepcidin and iron modulation; data presented at EHA, June 2022
- Obtained pre-IND feedback from hematology division of FDA for next studies in MF and CKD
- GMP clinical supply completed
- Initiated Ph 1b/2 study in MF anemia – *study active and recruiting (NCT05320198)*
- Ph 1b/2 study in NDD-CKD anemia – *study active and recruiting (NCT05745883)*

Next milestones

- Interim open label data from Ph 1b/2 study in MF anemia – ***expected 2H’23***
- Interim data from Ph 1b cohorts NDD-CKD anemia – ***expected 2H’23***
- Planning underway for studies in additional indications

MWTX-003

Anti-TMPRSS6 mAb

Hepcidin Induction

Anti-TMPRSS6 mAb Induces Hepcidin

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

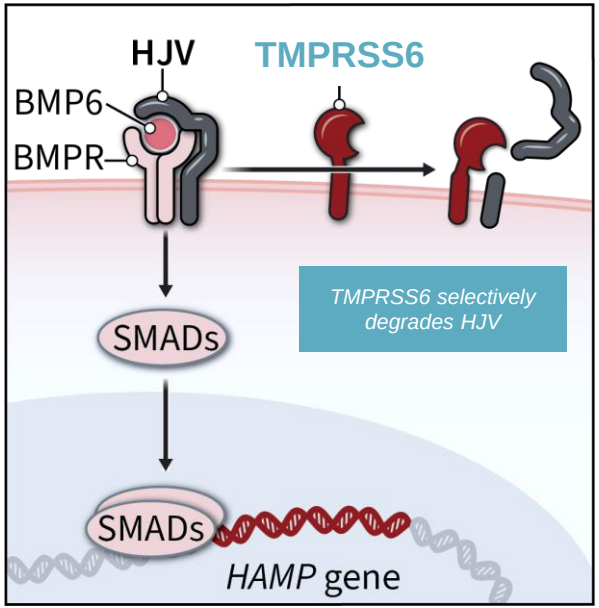
Enables Endogenous Production of Hepcidin

Promotes Iron Restriction
Decreases GI Absorption

Erythrocytosis (PV)
Ineffective Erythropoiesis
Iron Overload

Targeting TMPRSS6 to Increase Hepcidin

Potent, specific target controls endogenous hepcidin production



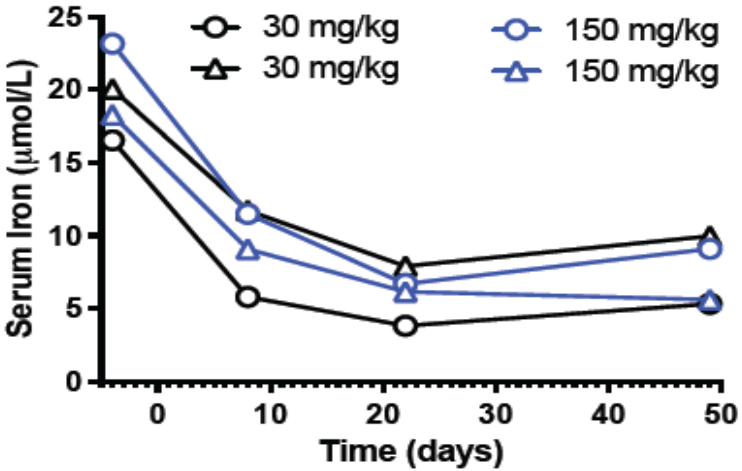
Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

- **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
  - Hepcidin: 3-4 fold induction
  - Serum iron: ~ 60-70% suppression
- MWTX-003 demonstrated excellent safety profile in non-clinical GLP safety studies

Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting

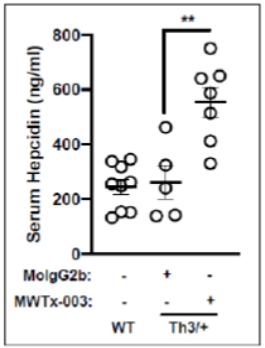
Effects in HbbTh3/+ Model of Beta-Thalassemia

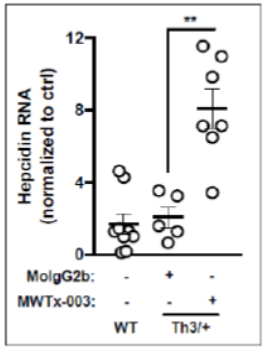
Significant effects on hallmarks of disease including iron overload, ineffective erythropoiesis and splenomegaly

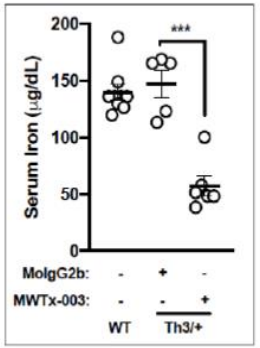
↑ Hepcidin Production
Up to 4-fold (mRNA)

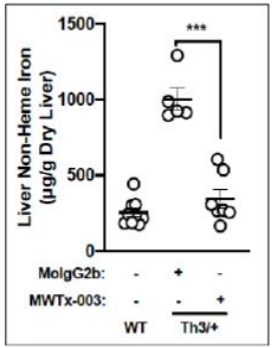
↓ Serum and Liver Iron
60-65% Reduction

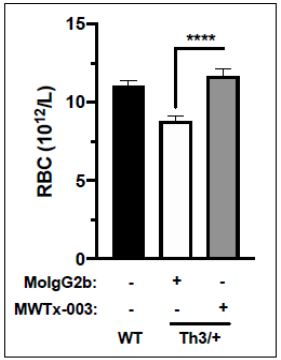
↑ RBC Production
↓ Spleen Weight

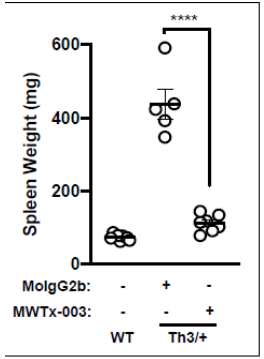












HbbTh$^{3/+}$ mice were treated with the lead anti-TMPRSS6 antibody at 10 mg/kg IP for 4 weeks

Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting

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MTWX-003 Development Plans

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

Phase 1 SAD / MAD in HV
Plan to Initiate 2H'23

Demonstrate proof-of-mechanism (hepcidin, iron, hematologic parameters)

Phase 1b / 2a Proof-of-Concept Study in Polycythemia Vera

- Strong proof of therapeutic hypothesis; clarity on regulatory development path
- Assess safety, PK, hepcidin, iron, hematologic parameters; %Hct and requirement for phlebotomy

Additional POC Studies in a Range of Indications

- Hereditary Hemochromatosis
- Beta-thalassemia
- Myelodysplastic Syndromes

Disc is Building a Leading Company Dedicated to Treating Hematologic Diseases

- **Clinical-stage biopharmaceutical company developing therapies for hematologic diseases**
  - Focused on fundamental and well-validated pathways that affect heme biosynthesis and iron homeostasis
- **Portfolio of 3 distinct “pipeline-in-a-product” programs with broad applications and opportunity for growth**
  - Bitopertin (Phase 2): Potential 1st disease-modifying treatment for debilitating, orphan diseases EPP / XLP
  - DISC-0974 (Phase 1b/2): Targeting anemia of inflammation opportunity with non-ESA mechanism
  - MWTX-003 (IND accepted): Targeting polycythemia vera and disease of iron overload
- **Entering catalyst-rich period with multiple data read-outs anticipated across portfolio in next 6-12 months**
  - Interim data DISC-0974 Phase 1b/2 trials in anemias of NDD-CKD and MF; interim data bitopertin Phase 2 trial in EPP / XLP
- **Strong foundation positions us to build Disc into a leading hematology company**
  - Leadership with deep experience developing and commercializing therapies; strong balance sheet with support from top-tier healthcare investors

Thank You

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