Corporate Presentation

December 2024

disc medicine

Disclaimer and FLS

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding Disc’s expectations with respect to its AURORA Phase 2 and BEACON Phase 2 clinical trials of bitopertin and the results thereof, its Phase 1b/2 clinical trial of DISC-0974 in patients with MF and NDD-CKD patients with anemia, its initial SAD data in its Phase 1 clinical trial of DISC-3405 in healthy volunteers; projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; and Disc’s belief about operating expenses and that it will have capital to fund Disc well into 2027. The use of words such as, but not limited to, “believe,” “expect,” “estimate,” “project,” “intend,” “future,” “potential,” “continue,” “may,” “might,” “plan,” “will,” “should,” “seek,” “anticipate,” or “could” or the negative of these terms and other similar words or expressions that are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Disc’s current beliefs, expectations and assumptions regarding the future of Disc’s business, future plans and strategies, clinical results and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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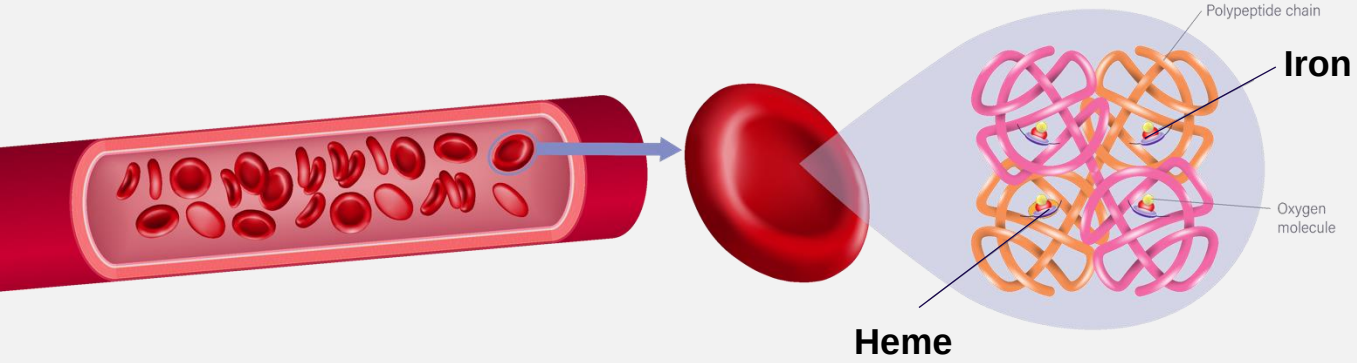
Bitopertin, DISC-0974, and DISC-3405 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide

Targeting Fundamental Pathways of Red Blood Cell Biology using Validated Mechanisms



Iron and heme metabolism are critical pathways in hematology with genetically-validated targets

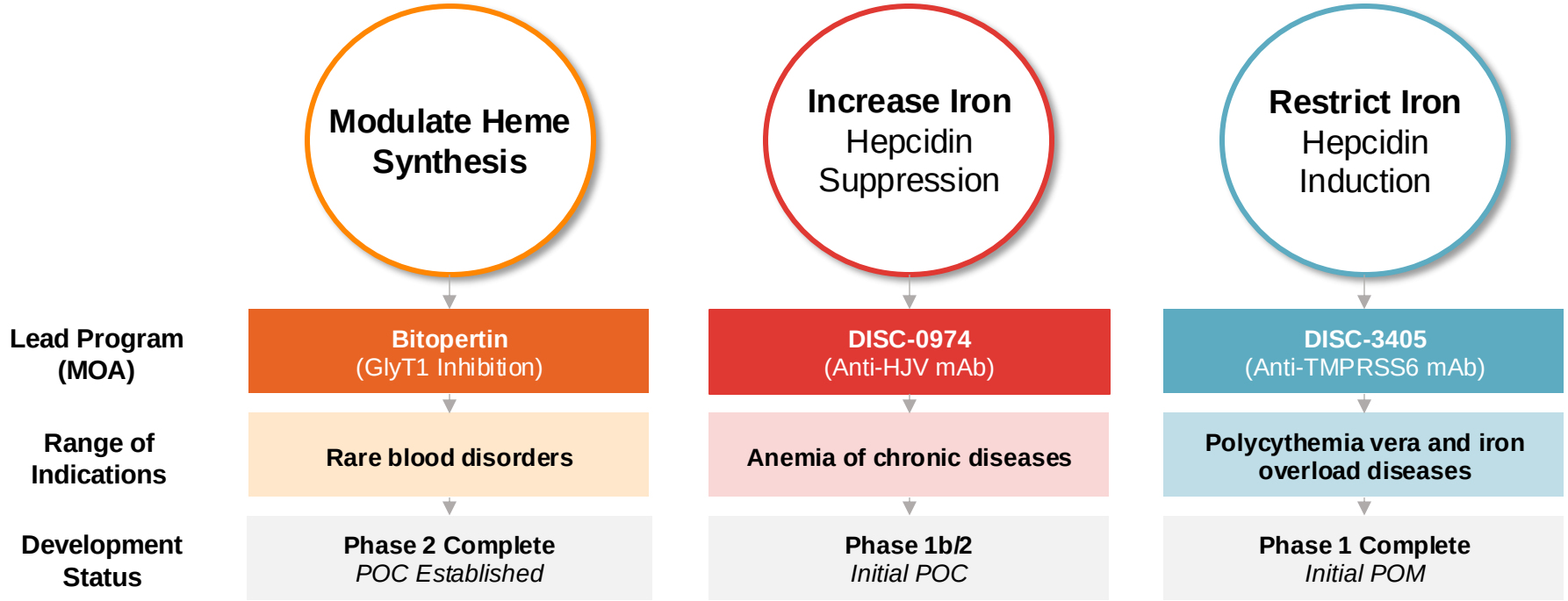
Key points of intervention across a wide range of diseases

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**

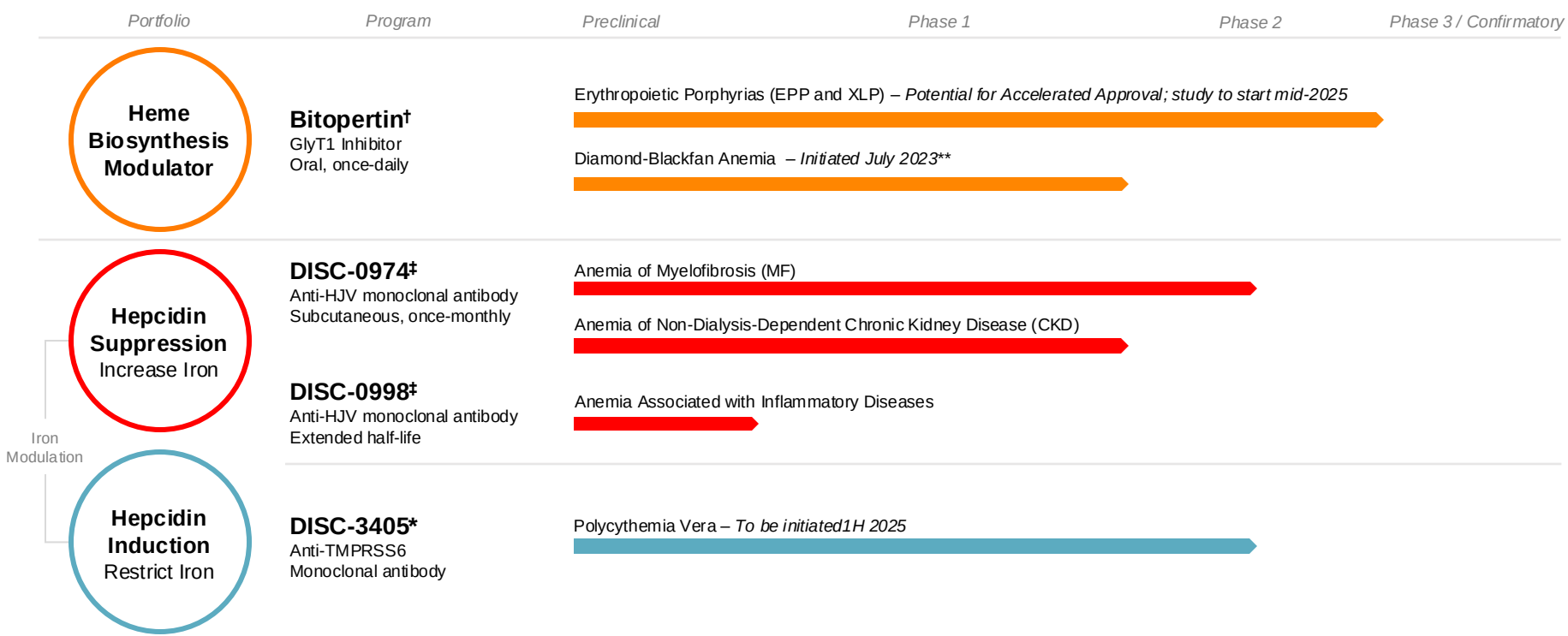
Bold = ongoing Disc trial

By Targeting Heme and Iron, Disc's Portfolio Can Address a Wide Range 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; *DISC-3405 in-licensed from Mabwell (formerly MWTX-003); **IIT with the NIH

Projected Upcoming Milestones and Events

Multiple additional data catalysts anticipated in the next 18 months

Program	Indication	H1 2025	H2 2025	2026
Bitopertin Heme Synthesis Modulator	**Erythropoietic Porphyrias (EPP and XLP)**	• Feedback from Type C Meeting with FDA • APOLLO Study Initiation	*Guidance on NDA timing to be provided in Q1 2025*	
	Diamond-Blackfan Anemia (DBA)	• IIT ongoing →		
DISC-0974 Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**		• Initial Phase 2 Data	• Final Phase 2 Data
	Anemia of Chronic Kidney Disease (CKD)		• Phase 1b Multiple-Dose Data	• Phase 2a Initiation • Initial Phase 2a Data
DISC-3405 Hepcidin Induction	**Polycythemia Vera**	• Phase 2a Study Initiation		• Phase 2a Data

Supported by a strong cash position with runway well into 2027

Bitopertin

GlyT1 Inhibitor

Heme Biosynthesis Modulation

Bitopertin: Investigational Oral, Selective GlyT1 Inhibitor

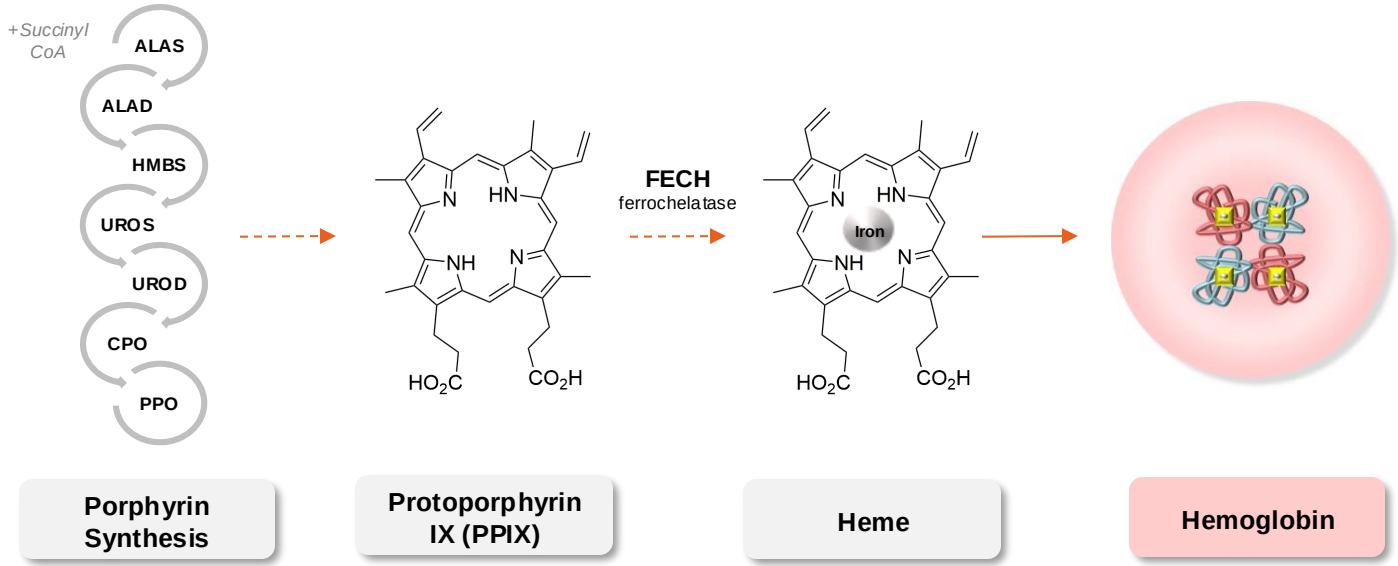
In multiple clinical trials by Roche, bitopertin was observed to modulate heme biosynthesis by blocking uptake of glycine in erythrocytes

Glycine

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

Bitopertin

Designed to block glycine uptake in RBCs by inhibiting GlyT1



Heme Biosynthesis Pathway

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

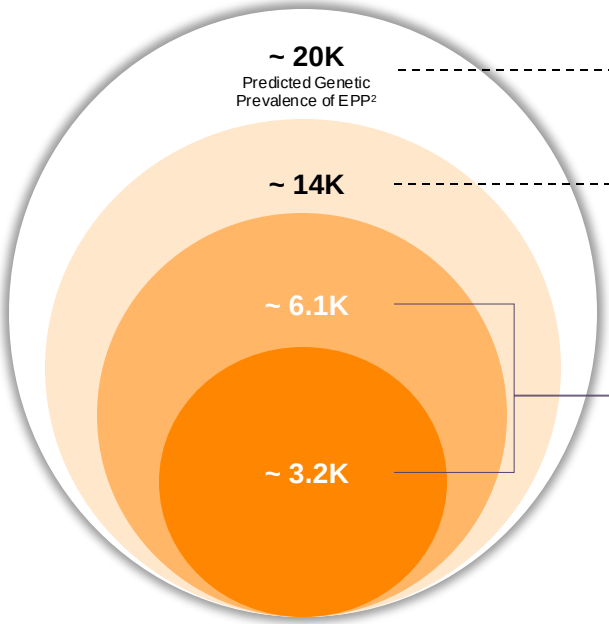
- Avoid sun / light, protective clothing, window tinting, Zn/Ti Oxide
- One FDA-approved agent, afamelanotide, a surgically-implanted tanning agent

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

EPP Prevalence: Est. 3-6K addressable patients in the US

Based on analysis of ICD-10 codes in claims data

Prevalence of EPP Patients in the U.S.

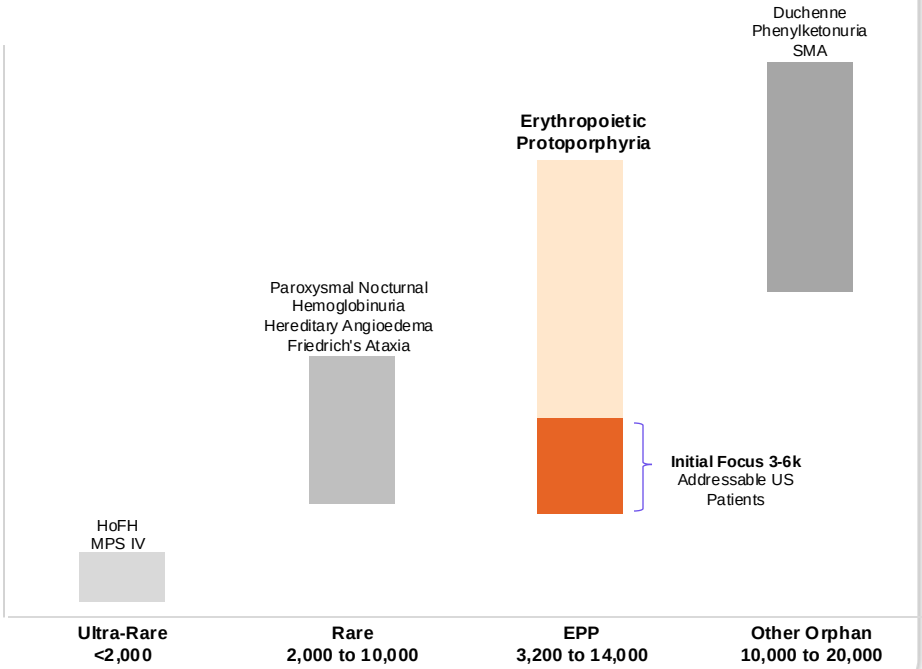


Expansion
Misdiagnosed or have not sought treatment for EPP

Growth
Patients with lower degree of engagement with HC system

Focus
Engaged EPP patients recent or recurring claims

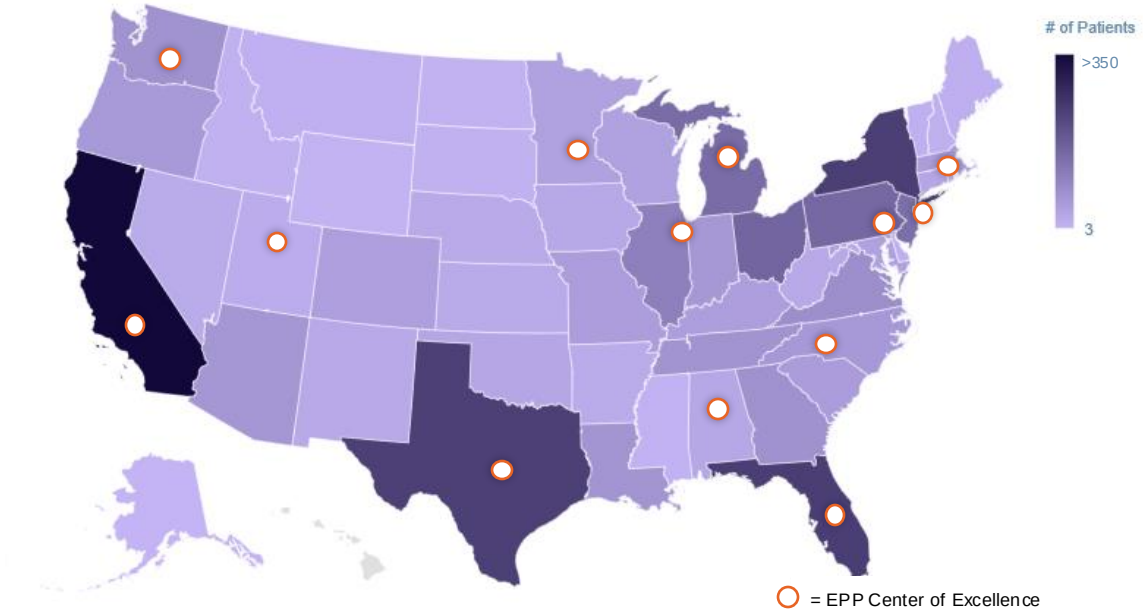
US EPP Prevalence Comparable to Major Rare Diseases



Source: Trinity Life Sciences; Komodo Claims Data (2016-2022); *Dickey et al, Genetic Medicine, 2021; HC = healthcare

EPP patients are identifiable and can be addressed through a highly efficient operating model

Distribution of EPP Patients



Concentration of patients in key accounts enables a targeted and efficient field force

Source: Trinity Life Sciences; Komodo Claims Data (2016-2022); United Porphyria Association; American Porphyria Foundation

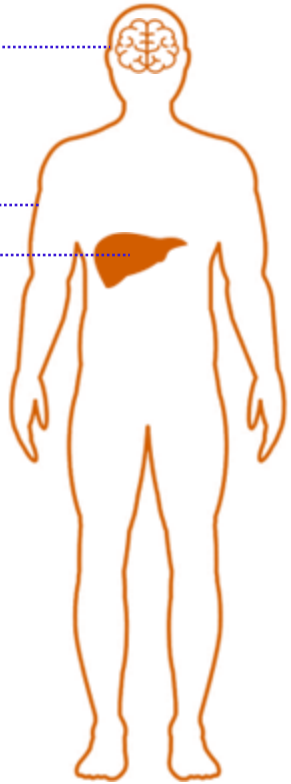
Real world data confirm EPP has a significant impact on patients' lives across multiple domains

56%
have anxiety and/or depression

Psychosocial

<30 min.
sun exposure before symptoms

Skin



34%
have liver and/or biliary issues

Hepatobiliary Complications

Concomitant Medication

57%
receive steroid treatment

30%
treated with narcotics

19%
get prescription Vitamin D

Healthcare Utilization

38%
inpatient stay in past 3 years

32%
visit the ER each year

Source: Trinity Life Sciences; Komodo Claims Data (2016-2022); Balwani et al, JAMA Dermatology, 2017

PPIX is a Driver of Disease in EPP / XLP Patients

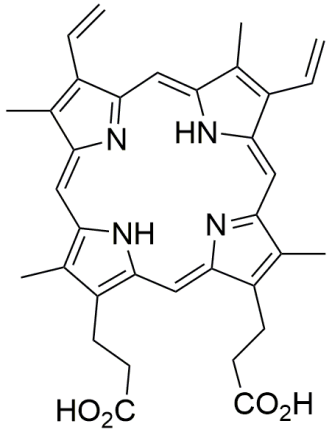
Toxic and photo-active metabolite accumulates in RBCs and is transported to skin and other organs, causing damage

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

Psychosocial

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



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

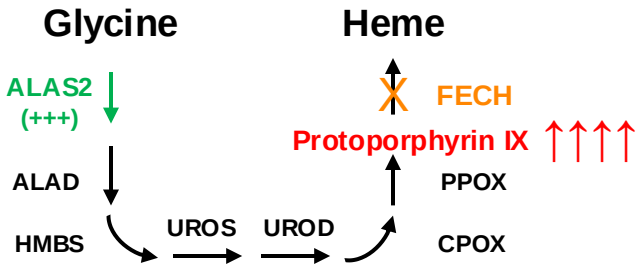
Other Complications

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

Bitopertin: Potential Disease-Modifying Treatment

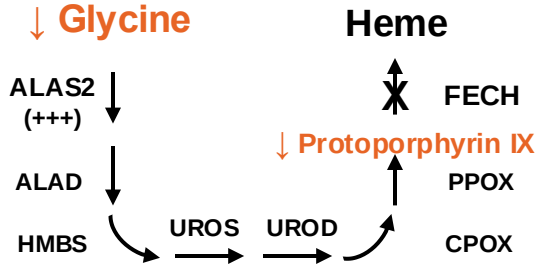
Designed to reduce disease-causing PPIX by limiting uptake of glycine into developing erythrocytes

EPP and XLP Patients
High PPIX Levels



Mutations result in reservoir of pathologically high 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

EPP Development Program

BEACON, AURORA, and HELIOS Studies

BEACON

- **EPP and XLP**; N = 26 (22 adults, 4 adolescents)
- **Australia**
- **Open-label, randomized, 24-week study**

AURORA

- **EPP**; N = 75 adults
- **United States**
- **Double-blind, randomized, placebo-controlled, 17-week study**

HELIOS

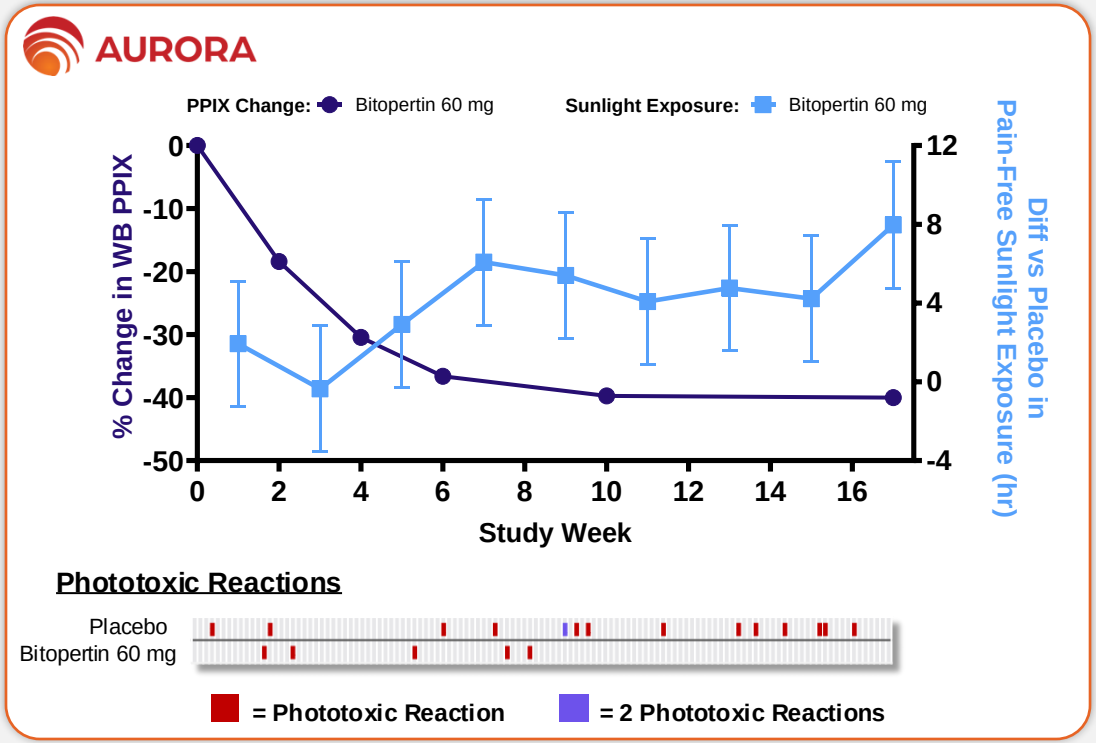
- **EPP and XLP**; adults and adolescents
- **US and Australia**
- **Open-label extension study** (>80% rollover from BEACON and AURORA)

Trial endpoints: Changes in blood PPIX levels, time in daylight without pain, light tolerance, time to prodromal symptom (TTPS), QOL, safety / tolerability

Data availability: Received positive feedback from EOP2 meeting with the FDA opening up a potential pathway to accelerated approval; Update on FDA Type C meeting on confirmatory trial design to be provided in Q1 2025; APOLLO study to begin by mid-2025

Summary of AURORA Results

Bitopertin 60 mg

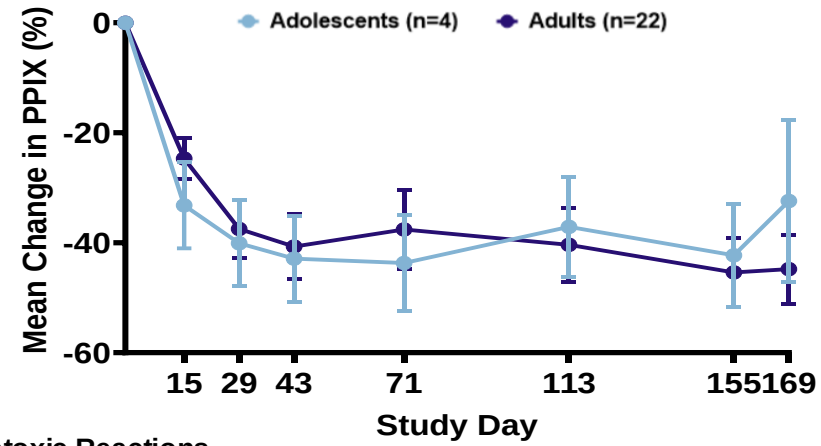


- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent, improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant improvement in PGIC vs placebo**
  86% reported EPP was ‘much better’
- **Clear association between PPIX reduction and clinical endpoints**

Summary of BEACON Results

Consistent with AURORA data, with similar results in adults and adolescents

BEACON



Phototoxic Reactions

Bitopertin 60 mg

Compared to 16 reactions in the 4-week baseline period (92% reduction)

Tertiles of PPIX Change

PPIX Increased **PPIX Decreased**

Light Tolerance Measure (Mean ± SD)	Tertile 3 (-43% to 25%)	Tertile 2 (-53% to -43%)	Tertile 1 (-98% to -53%)
Cumulative total time in sunlight without pain (hr)	145.6 ± 99.5	190.5 ± 111.6	262.1 ± 160.6
Average time in sunlight without pain (hr)	0.86 ± 0.6	1.1 ± 0.7	1.6 ± 1.0
Change from baseline in time to prodrome (min)	85.3 ± 78.8	96.0 ± 109.0	165.5 ± 128.8

Significant reductions in PPIX, improvements in pain-free time in sunlight, reductions in rate of phototoxic reactions, and improvement in QoL with clear association between PPIX reduction and clinical endpoints

Key Takeaways from Positive End of Phase 2 Meeting

- Alignment with the FDA on all proposed study parameters
- FDA acknowledged that EPP is a serious and potentially life-threatening disease with significant unmet medical need
- FDA agreed that average monthly time in sunlight without pain at the end of a 6-month treatment period can be used as a primary endpoint
- PPIX reduction may be sufficient as a surrogate endpoint supportive of accelerated approval
- Proceeding to APOLLO, a 6-month study with a 60 mg dose of bitopertin in EPP and XLP patients ages 12+, by mid-2025

Diamond Blackfan Anemia

Genetic condition caused by defective erythropoiesis

- Mutations in ribosomal protein genes (classically RPS19)
- Heme/globin imbalance: excess heme accumulation leading to toxicity as globin synthesis is delayed

Characterized by severe anemia that presents in infancy

- Anemia, fatigue, delayed growth, cardiac or renal defects, risk of malignancy
- Patients may also have distinct physical features / congenital abnormalities (i.e., cleft palate, thumb and upper limb abnormalities, short stature, microcephaly)

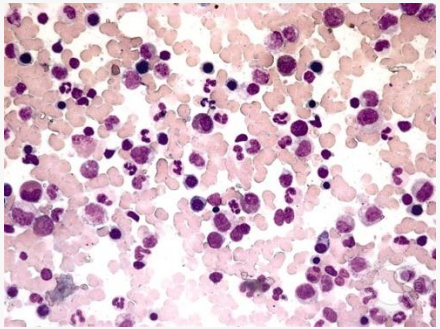
No approved treatments for DBA

- Patients receive steroids and blood transfusions to manage their condition
- Median life expectancy is 38 years, with 25% mortality by age 50

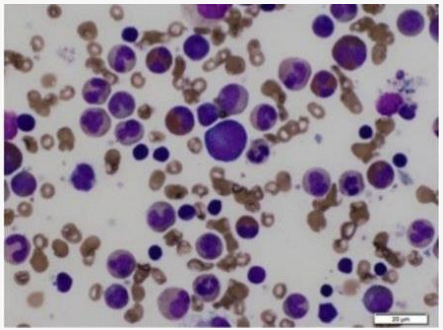
Rare disease with an incidence rate of 5-7 per 1 million live births

- Estimated worldwide prevalence of 5,000

Normal



DBA



St. Jude's Children Hospital; Fatima et al, Pediatric Hematology Oncology Journal, March 2021

Bitopertin in Diamond Blackfan Anemia

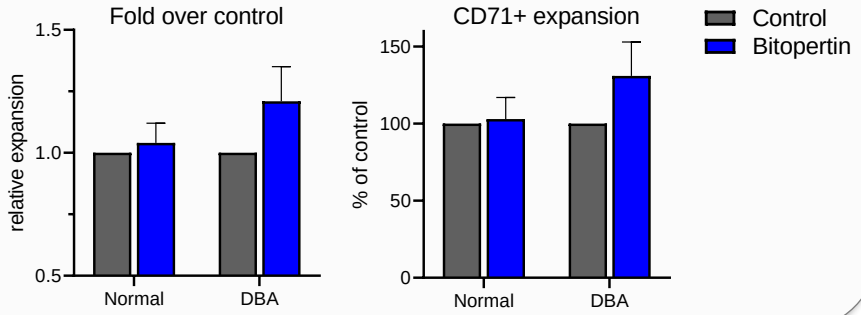
By slowing the influx of glycine, bitopertin lowers heme production, reducing the amount of excess heme and preventing cell death

Glycine

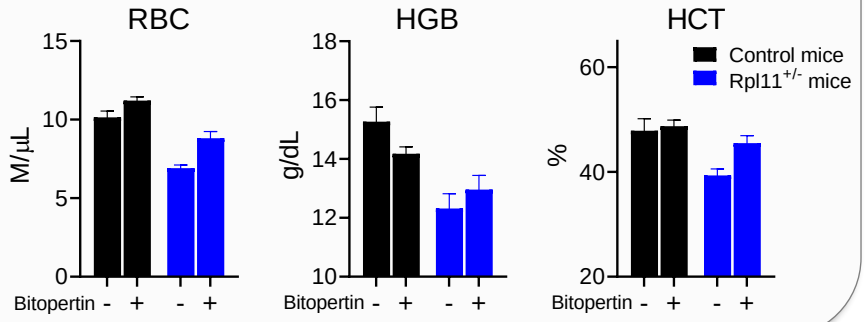
Critical and initiating precursor for heme biosynthesis and is supplied by **GlyT1 transporter**

Less Heme + **Slower Globin Production** → **Hemoglobin** → ***Complete Maturation***

Primary human marrow in erythroid differentiation cultures treated with 10 ng/ml bitopertin for 7 days



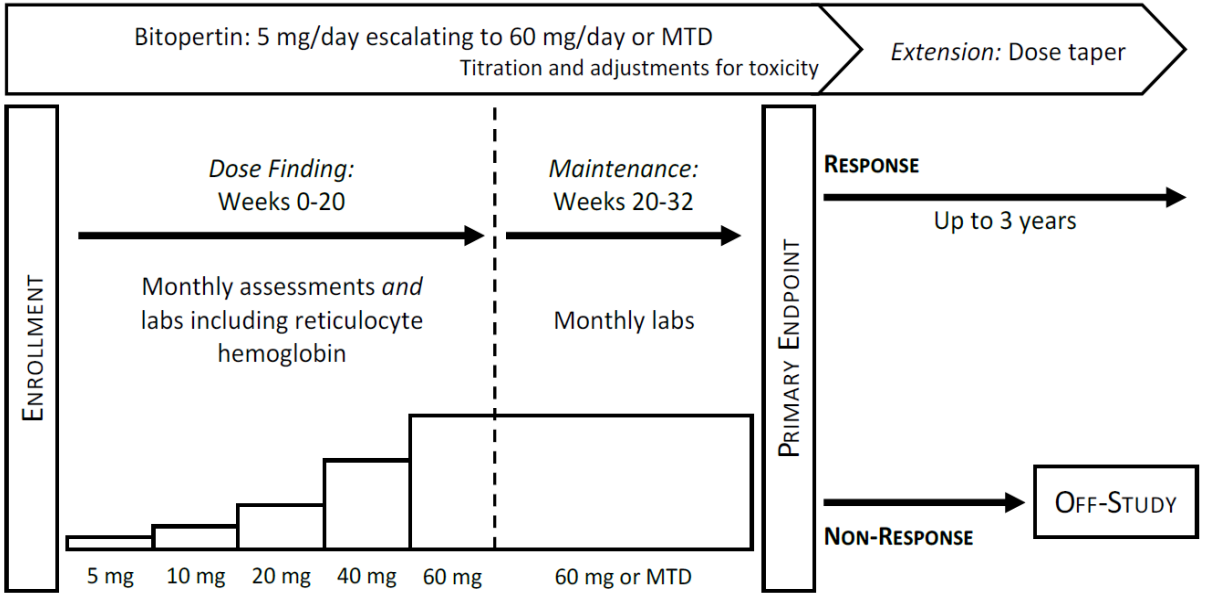
Rpl11 haploinsufficient mice were treated with 100 ppm bitopertin in chow (20 mg/kg/d) for 8 weeks



Diamond Blackfan Anemia Phase 2 Clinical Trial

IIT conducted by the NIH under CRADA with Disc

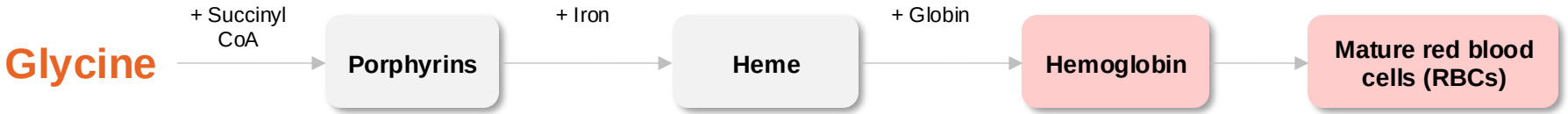
- Single-arm, dose-escalation study with extension
- N=15-25 patients with steroid-refractory and/or relapsed disease, or steroid intolerant
- Response defined as >50% reduction in RBC transfusions over 8-week period or an increase in pre-transfusion hemoglobin of >1.5 g/dL



14 patients have been enrolled; bitopertin has been well-tolerated with safety consistent with prior studies; efficacy evaluation is ongoing

Multiple Additional Potential Applications of Bitopertin

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)

Hepcidin Modulation

Iron Homeostasis

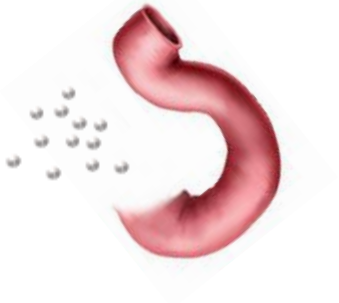
Iron is Fundamental to RBC Biology

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

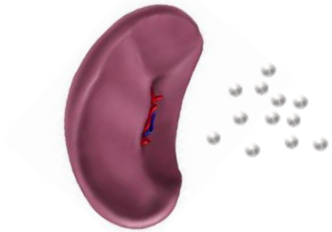
Induced by Inflammation

Hepcidin

Gatekeeper Function: Blocks iron absorption and recycling



GI Tract
Iron Intake



Spleen
Iron Storage

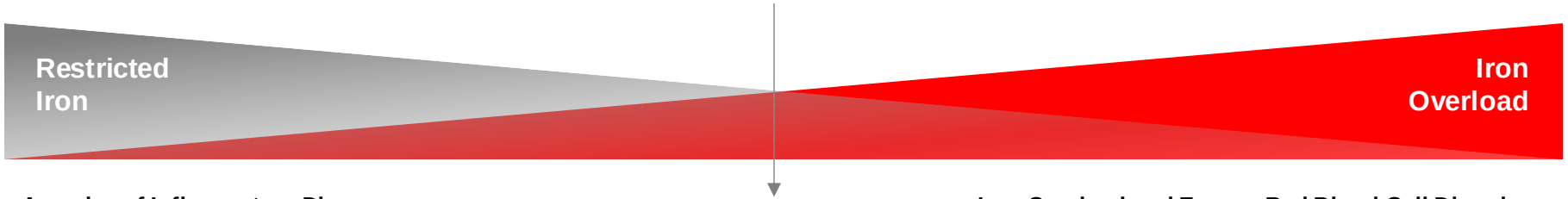
RBC Production in Bone Marrow

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

DISC-0974 (anti-HJV mAb)
Reduce Hepcidin / Increase Iron

Iron Overload and Excess Red Blood Cell Disorders

- Polycythemia Vera
- Hereditary Hemochromatosis
- Myelodysplastic Syndromes

DISC-3405 (anti-TMPRSS6 mAb)
Induce Hepcidin / Restrict Iron

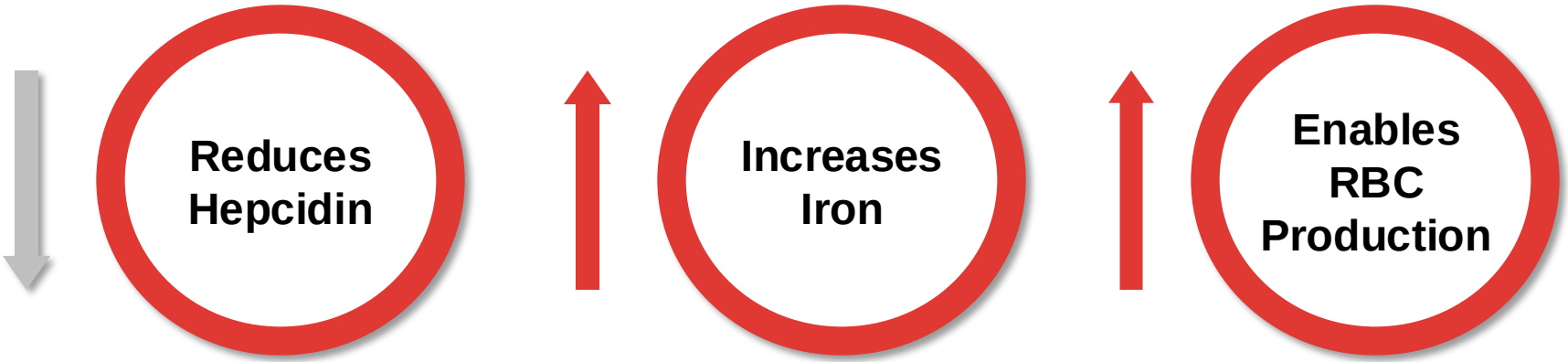
DISC-0974

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

Significant Opportunity in Anemia of Inflammation

Numerous chronic diseases associated with anemia from high hepcidin

Anemia Types	US Prev.	Est. % Anemic
Myelofibrosis (MF)	16-18.5K	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%

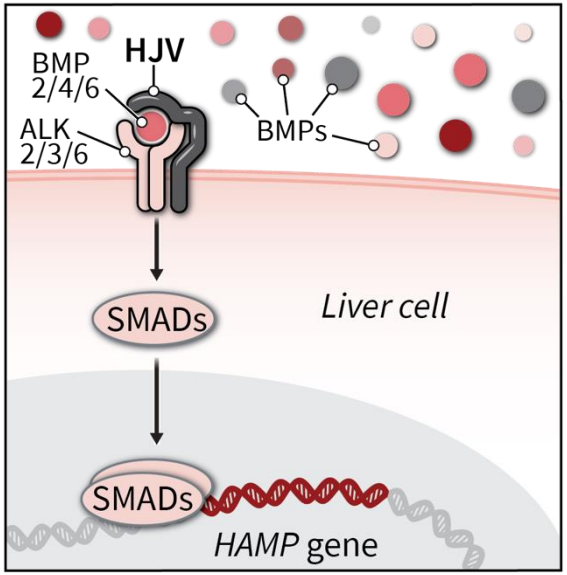
- **Anemia of inflammation** is the 2nd most common form of anemia
- **Estimated 40% of all anemias** are driven by or have an inflammatory component
- **Hepcidin is up-regulated** and correlates with anemia, driven by inflammation

Bold = ongoing Disc trial

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

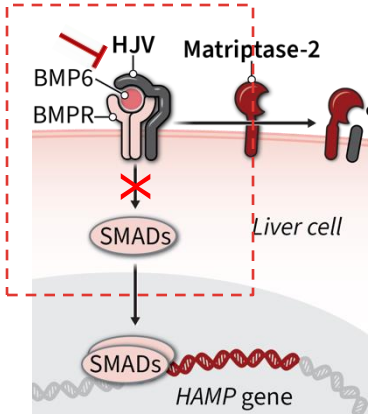
- **Genetic validation** in patients with Juvenile Hemochromatosis (lower hepcidin and elevated iron levels)
  - Loss-of-function mutations in HJV are phenotypically indistinguishable from mutations in *HAMP* (hepcidin) gene
- **Functionally specific** to hepcidin / iron
- **Tissue specific** expression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

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

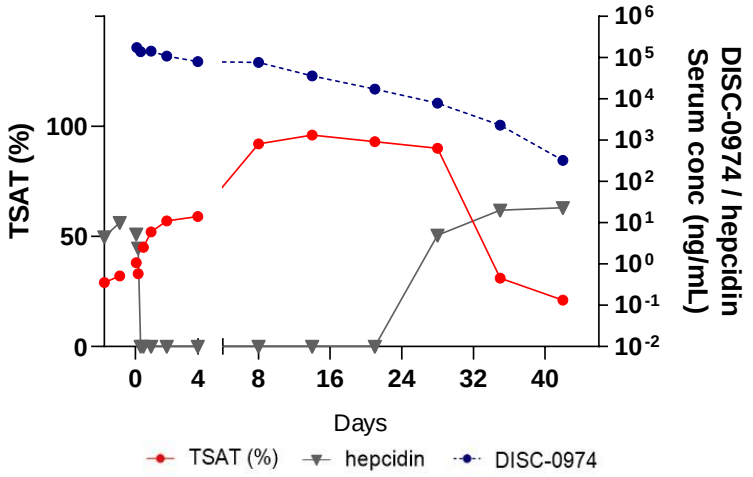
DISC-0974 Mechanism of Action

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)

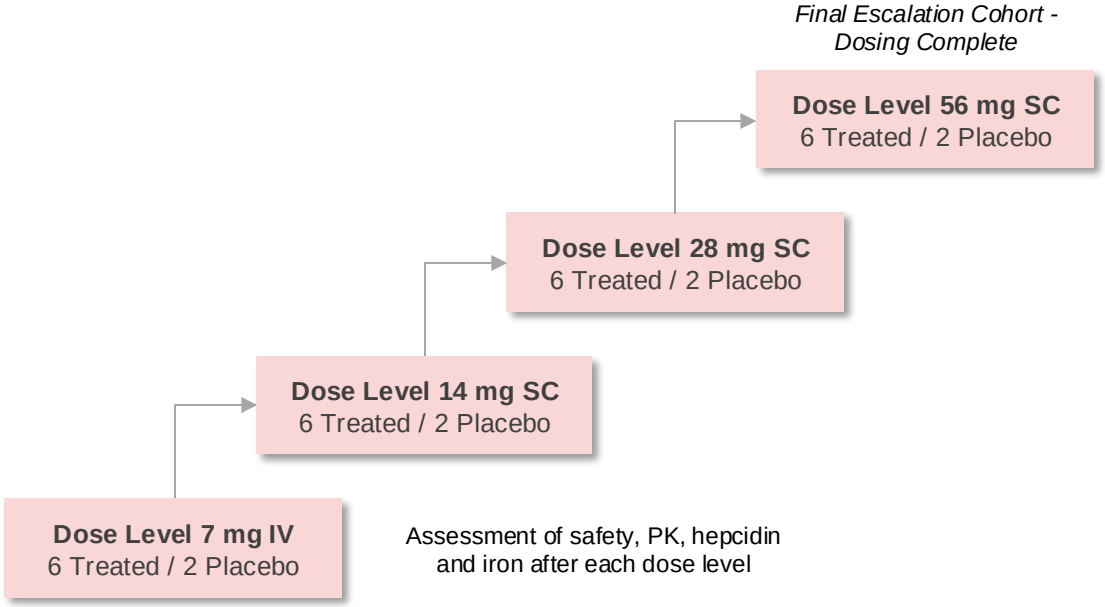


Phase 1 SAD Trial in Healthy Volunteers

Established proof-of-mechanism based on hepcidin and iron parameters

Trial 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)

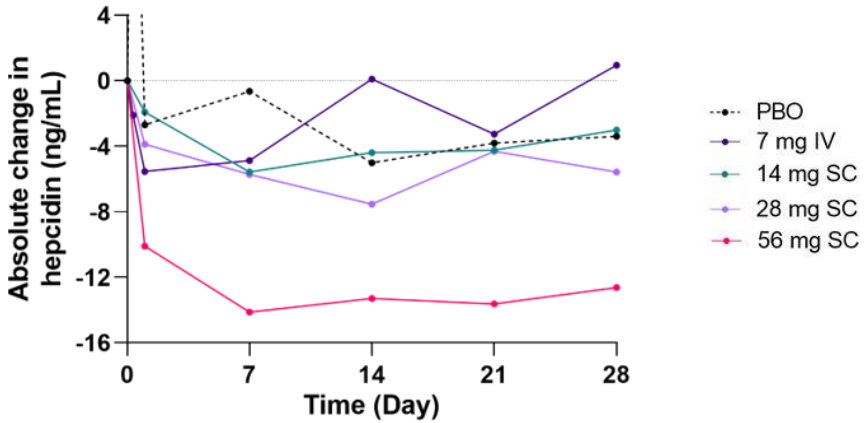


TSAT = transferrin saturation; IV = intravenous; SC = subcutaneous

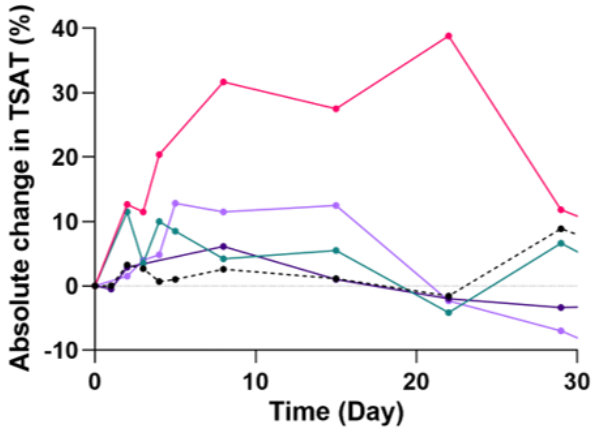
DISC-0974 Phase 1 SAD Data

Dosing of DISC-0974 demonstrated a reduction of hepcidin and iron mobilization

DISC-0974 Reduced Hepcidin Production



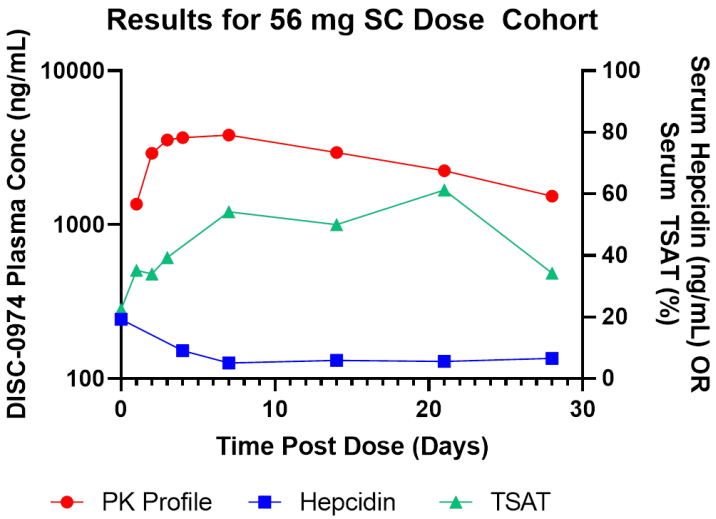
DISC-0974 Increased TSAT

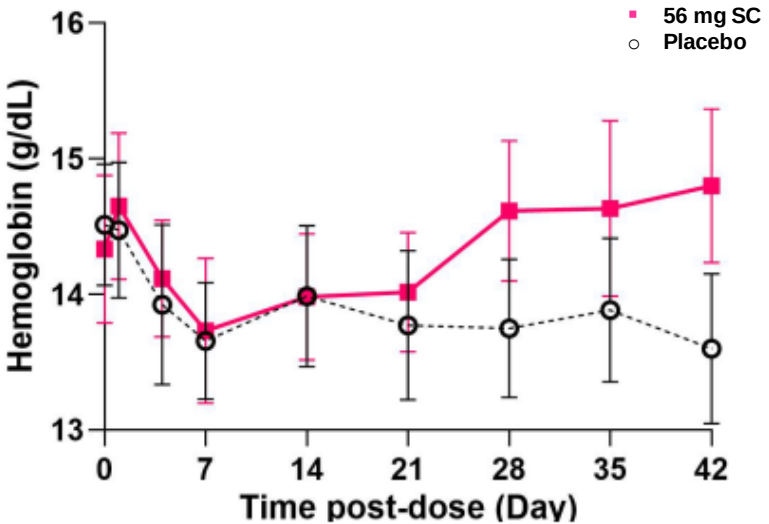


TSAT = transferrin saturation; SAD = single ascending dose

DISC-0974 Phase 1 SAD Data (cont.)

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





Hgb = hemoglobin; SAD = single ascending dose

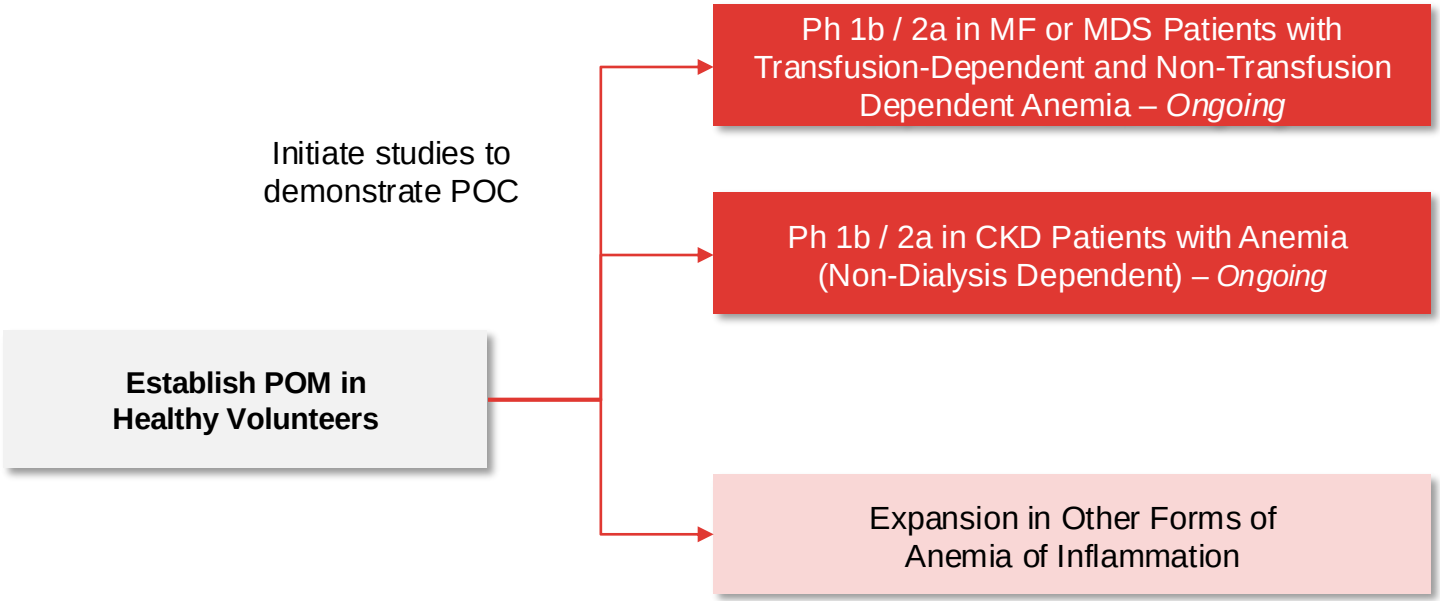
DISC-0974 Phase 1 SAD Safety

Safety profile was 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
Peripheral 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

Aim to demonstrate POC in anemia of MF and CKD

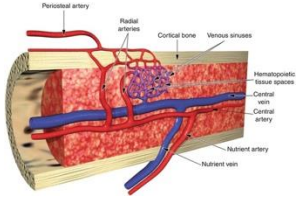


Plan to assess safety, PK, hepcidin, iron, hemoglobin and transfusion burden (MF and MDS) and others

Hepcidin is a Key Driver of Myelofibrosis (MF) Anemia

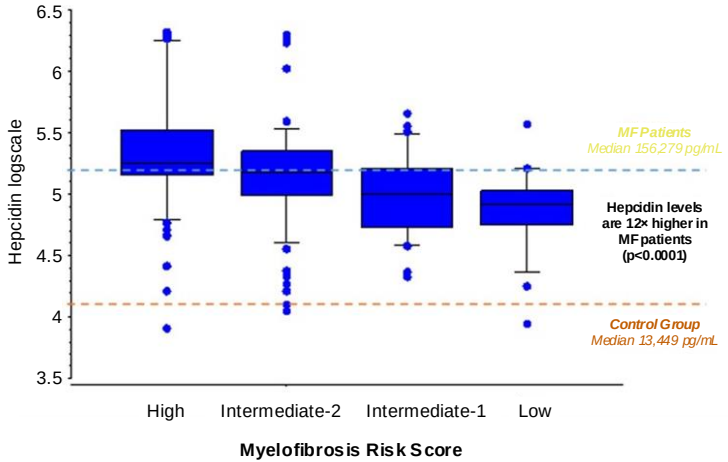
Anemia is severe and prevalent in MF and can limit treatment

Anemia of MF



- **Est. # Patients**
  - 25,000 patients (US)
  - ~87% are anemic; severe and require transfusion
- **Etiology of Anemia**
  - High hepcidin from inflammation
  - JAK inhibitors worsen anemia; loss of marrow function
- **Unmet Medical Needs**
  - Severe and difficult to treat; high transfusion burden
  - No approved or effective anemia therapy
  - Anemia limits optimal JAK inhibitor treatment

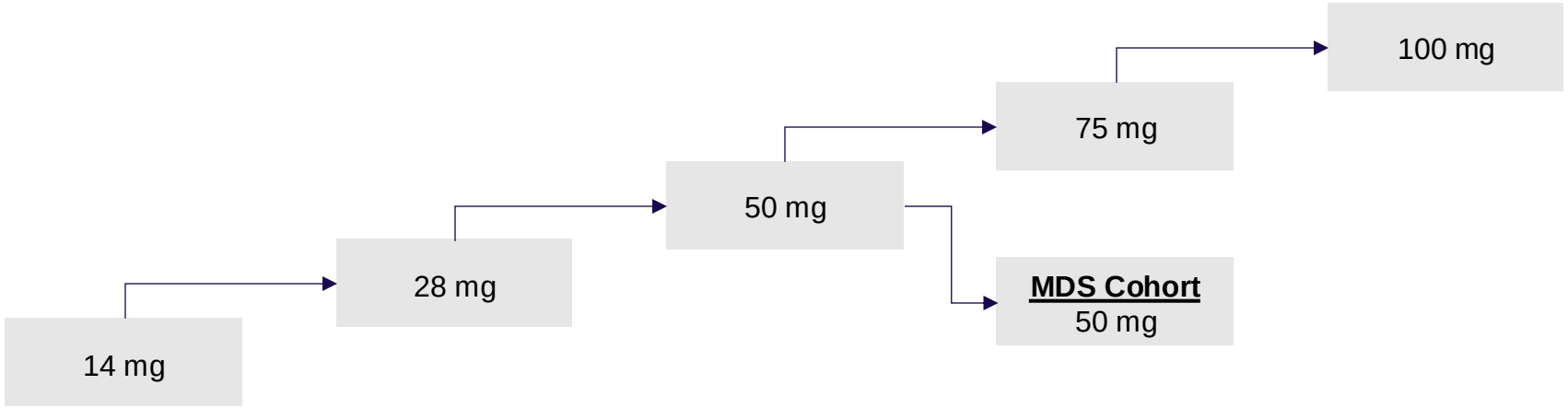
Hepcidin Levels are Elevated in MF
~ 12× higher than control and associated with severity of anemia and transfusion burden



Source: Pardanani et al (2013) Am. J. Hematol

DISC-0974 Phase 1b Anemia of MF Study Overview

Subcutaneous dosing once monthly for 6 months



Key Endpoints/Measures: Iron, hepcidin, and other hematologic parameters, safety/tolerability

Data Availability: Final data presented at ASH 2024; Phase 2 study initiated

DISC-0974 Anemia of MF Phase 1b

Study overview – enrollment data as of October 17, 2024

Screening (28 Days)	Treatment Period (6 months)	Optional Continuation (Up to 2 years)

	14 mg	28 mg	50 mg	75 mg	100 mg	Overall
Treated, N	1	7	12	9	6	35
Completed study, N (%)	1 (100)	6 (86)	12 (100)	8 (89)	5 (83)	32 (91)
Subjects with early withdrawal (N)*	0	1	0	0	1	2
Participating in continuation, N (%)	0	2 (29)	10 (83)	8 (89)	4 (67)	24 (69)
Concomitant JAK inhibitor, N (%)	0	4 (57)	6 (50)	2 (22)	1 (17)	13 (37)
Baseline hepcidin, median (min, max), ng/mL	48	93 (21, 171)	90 (9, 156)	47 (23, 188)	64 (12, 375)	69 (9, 375)
Baseline hemoglobin, median (min, max), g/dL	8.2	8.4 (6.7, 9.3)	8.4 (5.5, 10)	8.8 (6.7, 9.9)	8.3 (5.5, 9)	8.4 (5.5, 10)

Study Endpoints

Primary: Safety and tolerability; **Secondary:** Hematologic response, pharmacodynamic markers of mechanism engagement

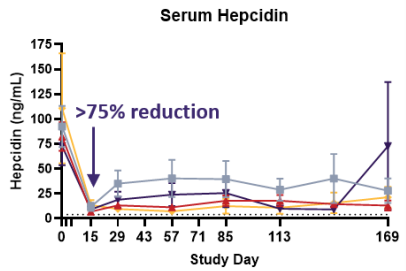
*Reason for early withdrawal: Physician decision due to inadequate response (n=2)

DISC-0974 Anemia of MF Phase 1b Results

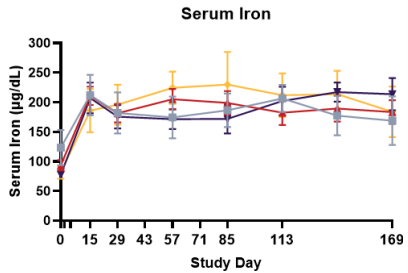
Pharmacodynamics

- DISC-0974 demonstrated consistent decreases in hepcidin and increases in serum iron across patients
- Iron mobilization translated to increased reticulocyte hemoglobin and hemoglobin from baseline

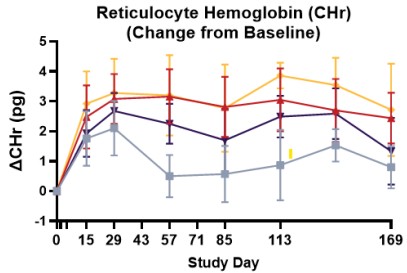
↓ Serum Hepcidin



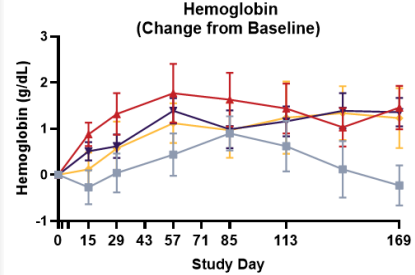
↑ Serum Iron



↑ Reticulocyte Hemoglobin



↑ Hemoglobin

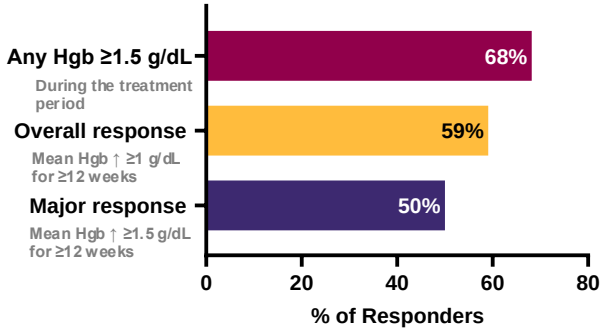


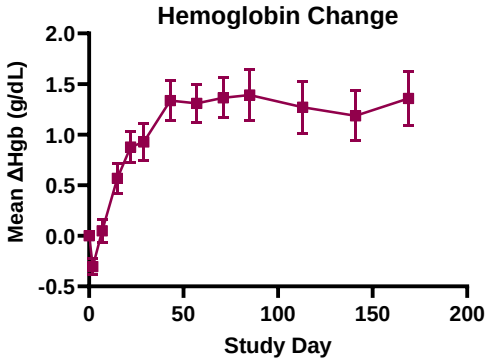
28 mg 50 mg 75 mg 100 mg

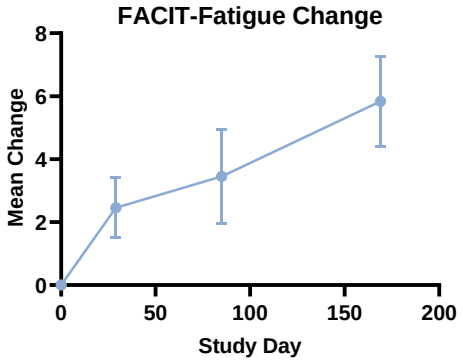
DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: nTD participants* (n=22)

68% of nTD[1] participants achieved a Hgb Increase of ≥1.5 g/dL during study period; 50% achieved a sustained Hgb response for ≥12 weeks







67% of participants (n=9) receiving concomitant JAKi therapy achieved durable response

Response	Mean ± SD (days)
Time to first Hgb increase for major response	36 ± 18
Duration of response during treatment period	150 ± 27

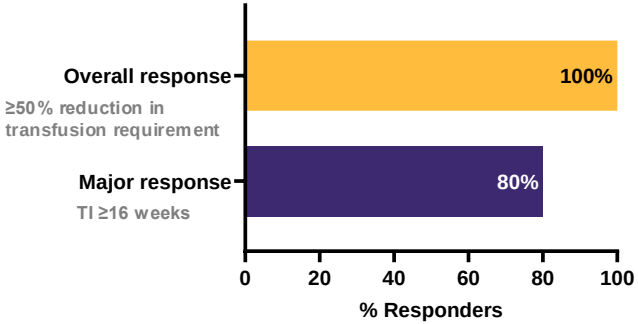
17 of 22 nTD participants have received continuation treatment with median response not reached. Follow-up ongoing (maximum 14.7 months).

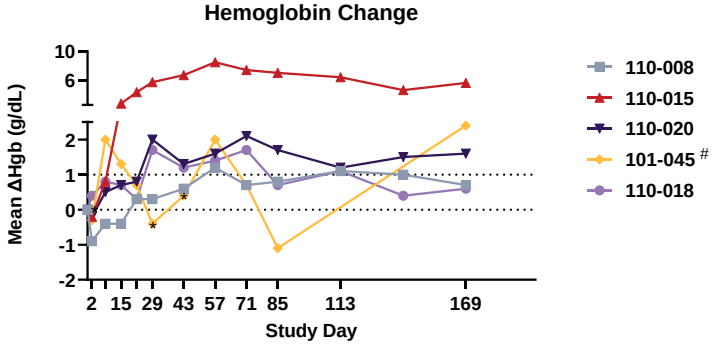
[1]nTD participants: Baseline Hgb <10 with 0 units PRBC in the 84 days prior to screening. * Participants dosed at 28-100 mg dose levels.

DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: TD Low participants (n=5)

100% of TD Low[1] participants achieved a ≥50% reduction in transfusion requirement; 80% of participants achieved TI-16 weeks^





No TD Low participants were receiving concomitant JAKi therapy

*Indicates transfusion; #Indicates patient receiving transfusion during treatment period.

Response	Mean ± SD (days)
TD Low duration of major response during treatment period	171 ± 4

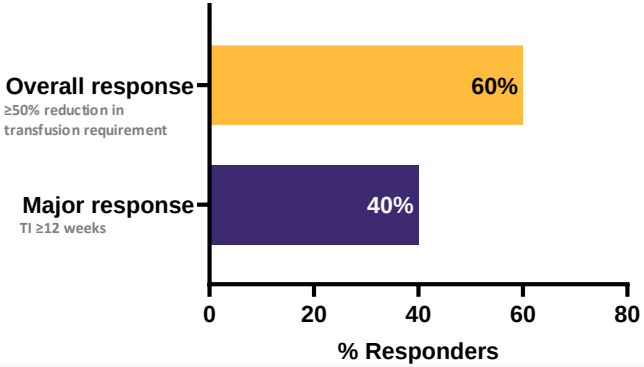
5 of 5 TD Low participants have received continuation treatment with median response not reached. Follow-up ongoing (maximum 16.6 months).

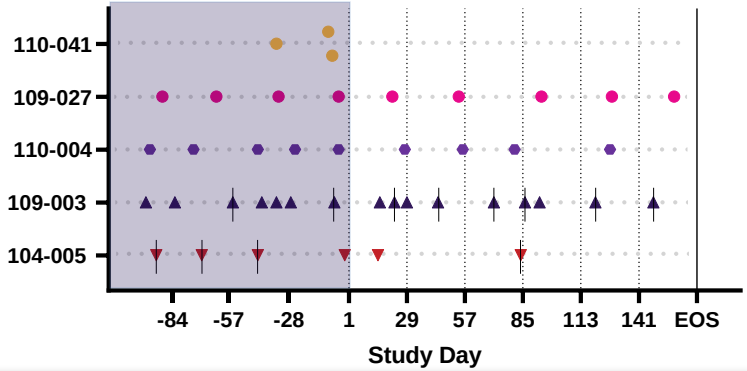
[1]TD Low: Participants receiving 1-2 units PRBC in the 84 days prior to screening. ^ with a minimum Hgb of 7 g/dL.

DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: TD High participants (n=5)

60% of TD High[1] participants achieved a ≥50% reduction in transfusion requirement; 40% of participants achieved TI-12 weeks^





50% of participants (n=4) receiving concomitant JAKi therapy achieved ≥50% transfusion reduction; 25% achieved TI-12

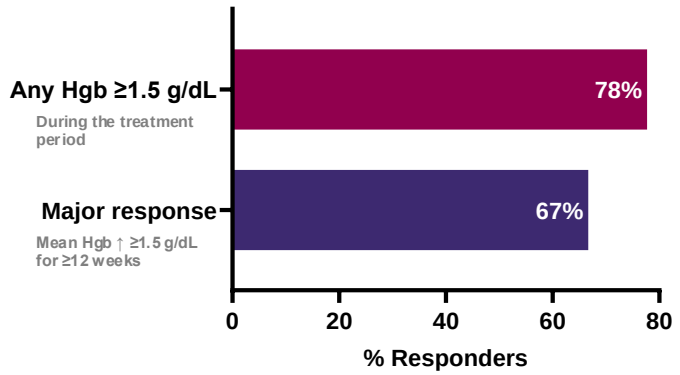
Response	Mean ± SD (days)
TD High duration of major response during treatment period	127 ± 60

[1]TD High: Participants receiving 3-12 units PRBC in the 84 days prior to screening. ^ with a minimum Hgb of 7 g/dL; 2 TD-high participants were considered not evaluable due to incomplete data entry at time of data cut.

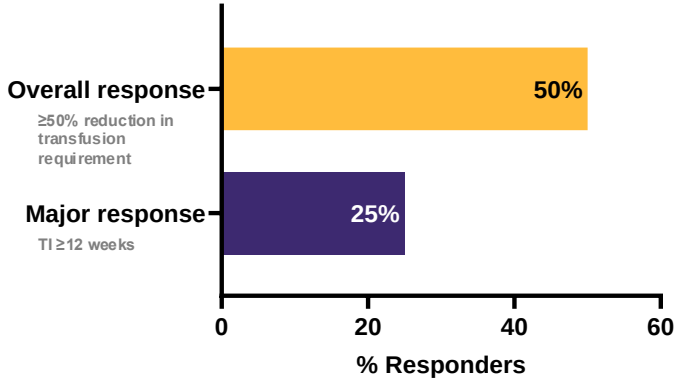
DISC-0974 Anemia of MF Phase 1b Results

Hematologic response with concomitant JAKi therapy (n=13)

nTD Response (n=9)



TD High Response (n=4)



Overall, 54% of participants receiving concomitant JAKi therapy achieved a major hematologic response

DISC-0974 Anemia of MF Phase 1b Results

Safety

Preferred Term	28 mg (n=7)	50 mg (n=12)	75 mg (n=9)	100 mg (n=6)	Overall (n=35)
Any TEAE	6 (85.7)	12 (100)	8 (88.9)	6 (100)	32 (94.1)
Related AE	4 (57.1)	6 (50)	5 (55.6)	1 (16.7)	16 (47.1)
SAE	1 (14.3)	2 (16.7)	0	1 (16.7)	4 (11.8)
Common TEAEs in ≥5 participants					
Diarrhea	3 (42.9)	5 (41.7)	5 (55.6)	1 (16.7)	14 (41.2)
Nausea	2 (28.6)	2 (16.7)	2 (22.2)	2 (33.3)	8 (23.5)
Vomiting	1 (14.3)	2 (16.7)	0	3 (50.0)	6 (17.6)
Constipation	0	4 (33.3)	1 (11.1)	0	5 (14.7)
Fatigue	3 (42.9)	3 (25.0)	1 (11.1)	3 (50.0)	10 (29.4)
Lymphocyte count decreased	1 (14.3)	2 (16.7)	2 (22.2)	1 (16.7)	6 (17.6)
Dizziness	0	2 (16.7)	2 (22.2)	3 (50.0)	7 (20.6)
Headache	1 (14.3)	1 (8.3)	1 (11.1)	2 (33.3)	5 (14.7)
Dyspnea	0	1 (8.3)	2 (22.2)	2 (33.3)	5 (14.7)
Hyperhidrosis	1 (14.3)	1 (8.3)	1 (11.1)	2 (33.3)	5 (14.7)
Anemia	5 (71.4)	4 (33.3)	0	0	9 (26.5)
Hypertension	0	3 (25.0)	3 (33.3)	0	6 (17.6)

No TEAEs were reported at the 14 mg dose level. Related AEs occurring in ≥2 participants: diarrhea (n=6); SAEs: arthralgia, cellulitis related to cat scratch, cellulitis related to cat bite, and kidney infection; ≥Grade 3 AEs: anemia, lymphocyte count decreased, platelets decreased, cellulitis, kidney infection (same as SAE), muscular weakness, and headache.

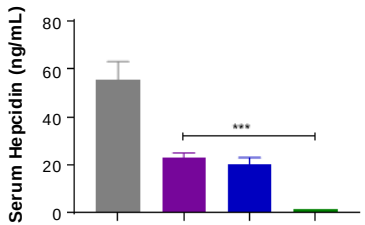
DISC-0974 Alleviated Ruxolitinib-Induced Anemia in Mice

Wild-type mouse model

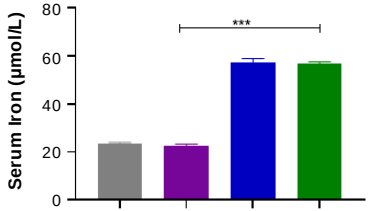
- Treating wild-type mice with ruxolitinib reduced hemoglobin and induced anemia
- Adding a mouse analog of DISC-0974 reversed these effects, further decreasing hepcidin, increasing serum iron, and increasing hemoglobin

Target Engagement

↓ Serum Hepcidin



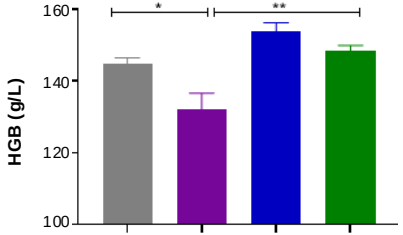
↑ Serum Iron



Vehicle | Ruxolitinib (90 mg/kg)-BID | DBIO-100 (20 mg/kg)-QW | Ruxolitinib (90 mg/kg)-BID +DBIO-100 (20 mg/kg)-QW

Hematologic Improvement

↑ Hemoglobin



- Ruxolitinib alone reduced Hgb by **~1.1 g/dL**
- Adding DISC-0974 analog increased Hgb by **~0.9 g/dL**

Vehicle | Ruxolitinib (90 mg/kg)-BID | DBIO-100 (20 mg/kg)-QW | Ruxolitinib (90 mg/kg)-BID +DBIO-100 (20 mg/kg)-QW

Phase 2 MF Anemia Study Overview

Study Population

- N= ~90 (30 per cohort)
  - 12 patients carried over from Phase 1b*
- Adult patients with MF and anemia
  - Hgb <10 g/dL on ≥3 assessments over 12 weeks, or
  - 1 or more PRBC units transfused in 12 weeks
- Severity: DIPSS INT-1/High
- +/- JAK inhibitor permitted

Design

Screening (28 Days) → **Treatment Period** (6 Cycles q28 Days) → **Follow-Up** (28 Days) → **Continuation Treatment** (q28 Days – optional)

Open-Label, 3 cohorts

- nTD: N=30*
- TD Low: N=30*
- TD High: N=30*

Exploratory cohort

momelotinib / pacritinib
nTD, TD Low, or TD High; N=10

Flexibility to add exploratory cohorts

Key endpoints:

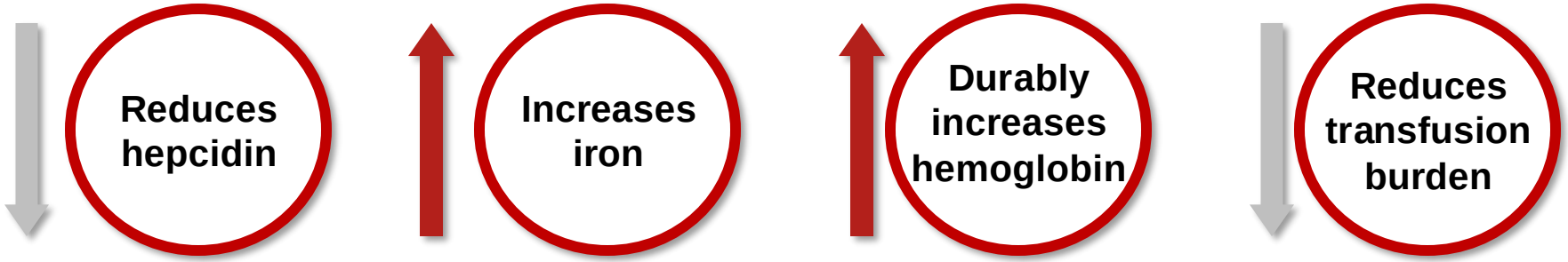
- Anemia response defined by cohort (TI, transfusion burden reduction, Hgb change)
- Iron, hepcidin, hematologic parameters
- FACIT fatigue score

Phase 2 Dosing: 50 mg, SC, q28 days

*Patients carried over from Phase 1b: nTD n=8, TD (Low + High) n=4

Summary of DISC-0974 in MF Anemia

DISC-0974 demonstrated improved hemoglobin response and transfusion burden in MF



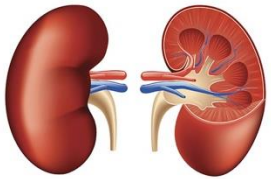
➢ **Next Steps**

- Phase 2 study initiated
- Initial data readout expected H2 2025

Hepcidin is a Key Driver of CKD Anemia

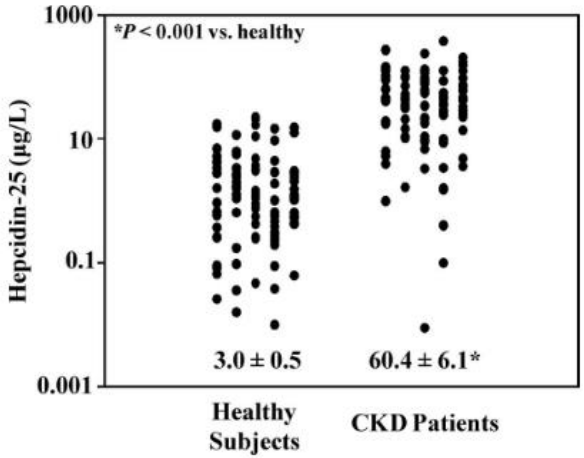
Pervasive issue that is currently highly under-treated

Anemia of CKD



- **Est. # Patients**
  - 5 to 6 million anemic NDD-CKD patients in the US alone
- **Etiology of Anemia**
  - High hepcidin from inflammation & poor renal clearance
  - Compromised erythropoietin production
- **Unmet Medical Needs**
  - Majority patients untreated or under-treated
  - ESAs restricted due to safety and black box
  - Mean Hb 9.3 g/dL in patients initiating dialysis

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

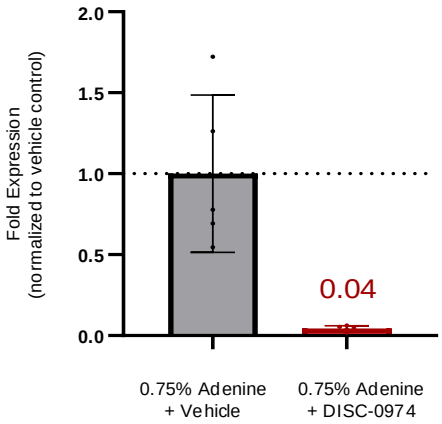


Sources: Troutt et al. (2013), J Clin Lab Analy; Sheetz et al. (2019) Br J Clin Pharmacol. (2019); *from third party; NDD: Non-Dialysis Dependent; DD: Dialysis Dependent

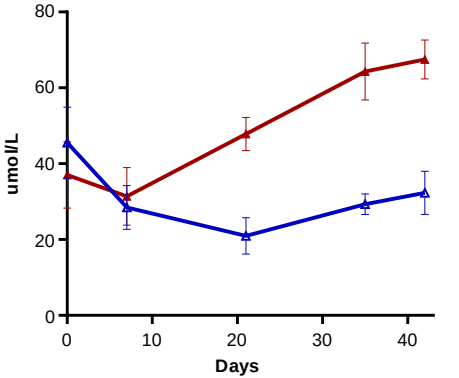
DISC-0974 Improved Anemia in Model of CKD

Rat Model of Adenine Diet-Induced CKD

DISC-0974 Reduced Hepcidin Expression

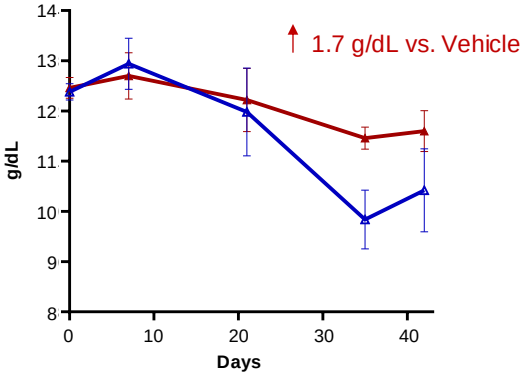


DISC-0974 Increased Serum Iron



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

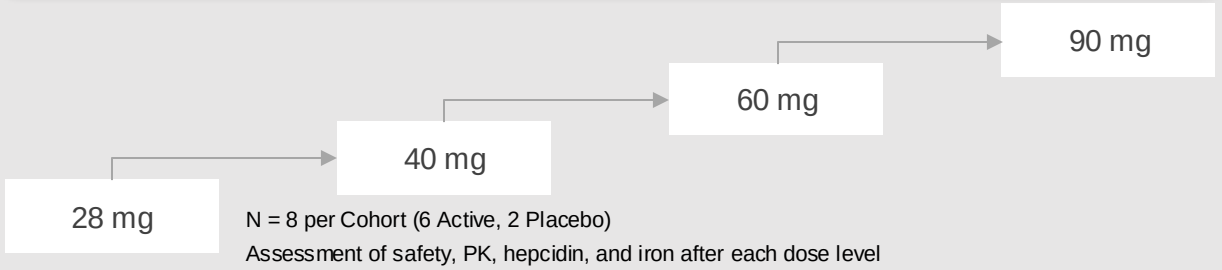
DISC-0974 NDD-CKD Anemia Trial Overview

Data as of September 16, 2024

Trial Population

- Stage II-V CKD; Adult
- Not receiving dialysis
- Hgb (g/dL) <10.5 (F), 11 (M)
- Exclude iron-deficient anemia by ferritin and TSAT

Phase 1b | Single-Ascending Dose



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

Data availability: Updated Phase 1b data presented in October 2024; Phase 1b multiple-dose data expected by end of 2025

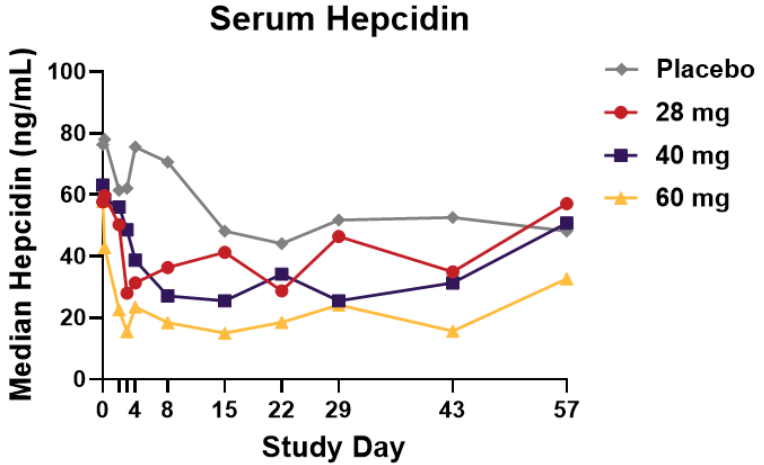
	28 mg DISC-0974 (n=9)	40 mg DISC-0974 (n=6)	60 mg DISC-0974 (n=6)	Pooled Placebo (n=7)
CKD Stage, n (%)				
Stage 2	0	1 (16.7)	1 (16.7)	0
Stage 3	2 (22.2)	0	2 (33.3)	2 (28.6)
Stage 4	5 (55.6)	5 (83.3)	3 (50.0)	5 (71.4)
Stage 5	2 (22.2)	0	0	0
Baseline hepcidin, median (range), ng/mL	57.7 (24.0, 170.6)	63.2 (50.0, 109.6)	57.8 (29.2, 156.9)	76.3 (36.8, 122.3)
Baseline hemoglobin, median (range), g/dL	9.8 (8.6, 10.6)	10.6 (10.0, 11.2)	10.8 (10.1, 11.0)	9.6 (9.0, 10.9)

CKD = chronic kidney disease; Hgb = hemoglobin; NDD = non-dialysis dependent; PK = pharmacokinetics; TSAT = transferrin saturation

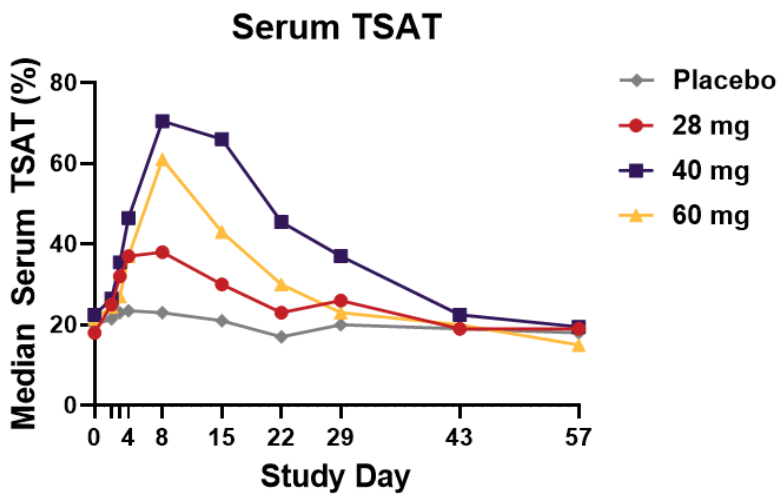
ASN 2024 DISC-0974 Anemia of CKD Data: Hepcidin and Iron

- Meaningful reduction in serum hepcidin with corresponding increase in serum TSAT

Hepcidin Changes Over Time



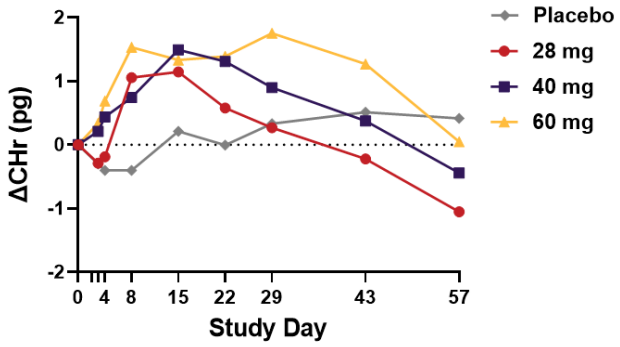
Iron Changes Over Time



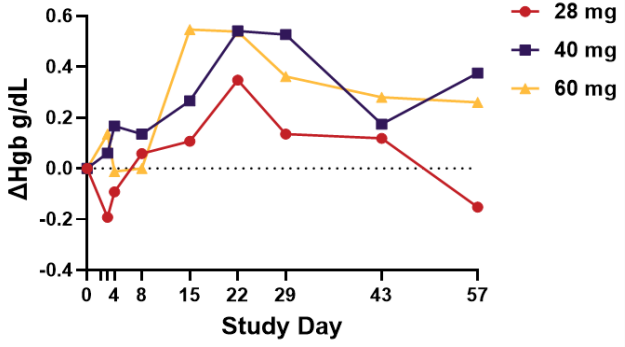
ASN 2024 DISC-0974 Anemia of CKD Data: Hematologic Parameters

- Early and sustained increase in mean reticulocyte hemoglobin across all dose groups
- Increase in mean hemoglobin from baseline across dose groups, with maximal observed individual increases in hemoglobin up to +0.95 g/dL at 28 mg, +1.5 g/dL at 40 mg, and +1.8 g/dL at 60 mg

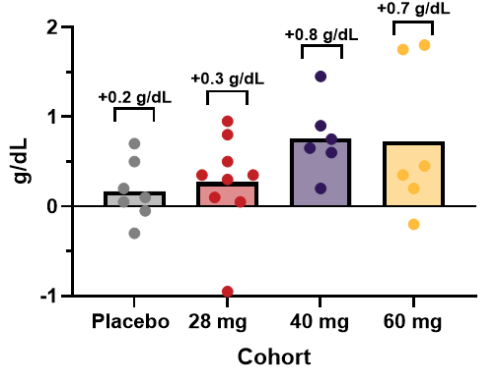
Reticulocyte Hemoglobin Content (CHr)



PBO-Corrected Hgb Change from Baseline



Maximal Change in Hemoglobin



Placebo-corrected hemoglobin change from baseline after administration of 28 mg DISC-0974 (red), 40 mg DISC-0974 (blue), or 60 mg DISC-0974 (yellow) using the difference of the least-squares means. Mean maximal change in hemoglobin from baseline after treatment through Day 29 of study with dots representing individual values.

ASN 2024 DISC-0974 Anemia of CKD Data: Safety

- Generally well tolerated at all evaluated dose levels

Adverse occurring in ≥2 participants at any dose level	28 mg DISC-0974 (n=9)	40 mg DISC-0974 (n=6)	60 mg DISC-0974 (n=6)	Pooled Placebo (n=7)
Metabolic Acidosis	1 (11.1)	1 (16.7)	1 (16.7)	1 (14.3)
Hyperkalemia	0	1 (16.7)	2 (33.3)	0
Anemia	2 (22.2)	0	0	2 (28.6)
Atrial fibrillation	1 (11.1)	0	1 (16.7)	0
Hypertension	0	0	0	2 (28.6)

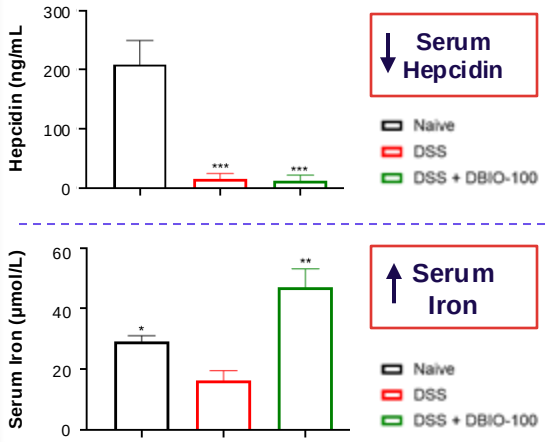
Related AEs: 1 participant with Grade 1 hyperkalemia treated at 60 mg; 1 participant with Grade 1 dizziness treated at 60 mg; 1 participant with Grade 2 Eosinophilia and Grade 2 Renal failure (Creatinine 1.2X baseline at day 29 with resolution by day 57). ≥ Grade 3 AEs: 1 participant treated at 28 mg with Grade 4 ESRD (dialysis eligible prior to enrollment), Grade 4 anemia and Grade 3 fluid retention; 1 participant treated at 40 mg with Grade 3 hypervolemia. Serious adverse events: 3 participants including 1 participant treated at 28 mg with Grade 4 ESRD (same as "≥ Grade 3 AE" participant with ESRD); 1 participant treated at 28 mg with Grade 2 atrial fibrillation (medical history of atrial fibrillation); 1 participant treated at 60 mg with Grade 1 atrial fibrillation (medical history of atrial fibrillation).

DISC-0974 in Other Anemias of Inflammation

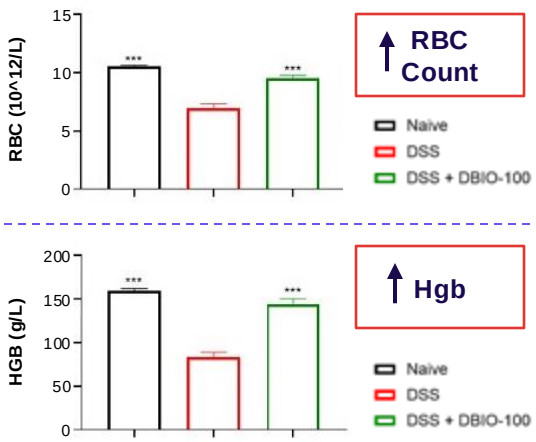
Inflammatory bowel disease mouse model

- Mouse analog of DISC-0974 supressed hepcidin, increased serum iron, and increased hemoglobin in anemic IBD mice
- Treatment also demonstrated disease-modifying and anti-inflammatory effects

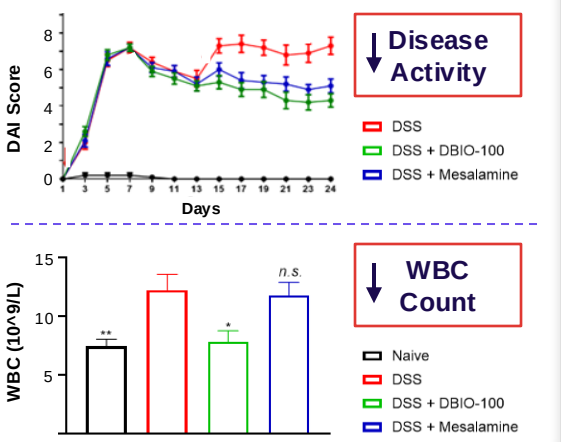
Target Engagement



Hematologic Improvement



IBD Disease Modification



DAI Score = Disease Activity Index

DISC-3405

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

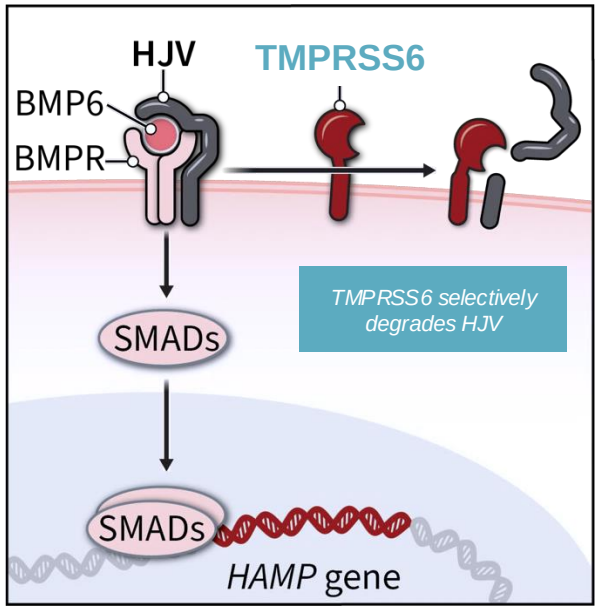
Enables Endogenous Production of Hepcidin

Promotes Iron Restriction Decreases GI Absorption

Erythrocytosis (PV) Ineffective Erythropoiesis Iron Overload

Targeting TMPRSS6 to Increase Hepcidin

Potent, specific target controls endogenous hepcidin production



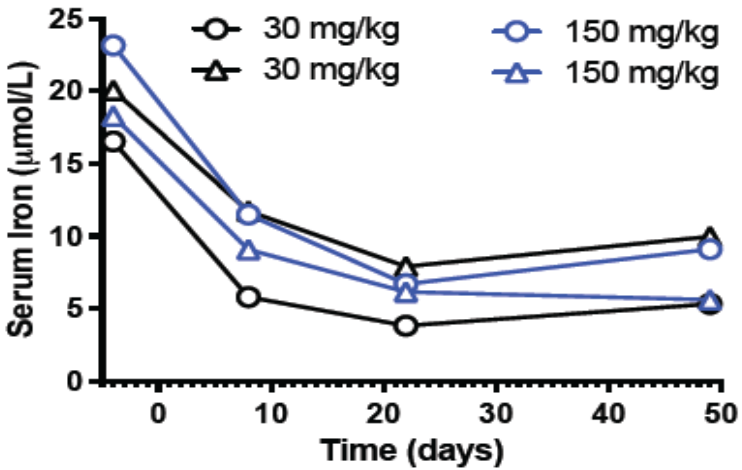
Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

- **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

DISC-3405 Effects in Non-Human Primates

Resulted in deep and sustained suppression of serum iron levels

Single dose of DISC-3405 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
- DISC-3405 demonstrated excellent safety profile in non-clinical GLP safety studies

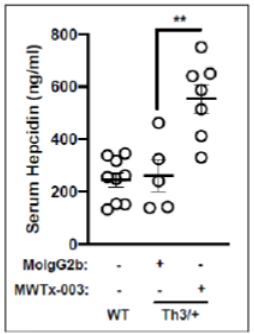
Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting

DISC-3405 in Beta Thalassemia and Polycythemia Vera

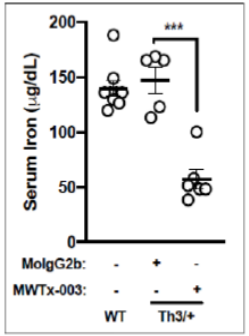
Significant effects on hallmarks of disease

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

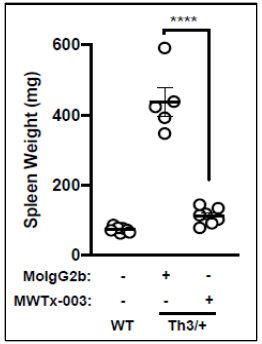
↑ Hepcidin Production



↓ Iron

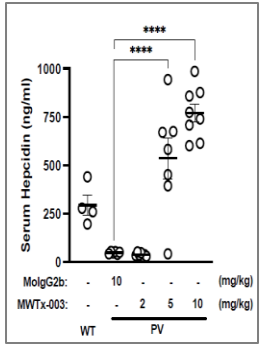


↓ Spleen Weight

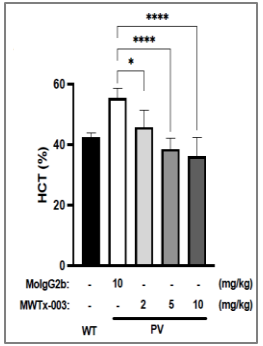


$Jak2^{V617F}$ model of Polycythemia Vera

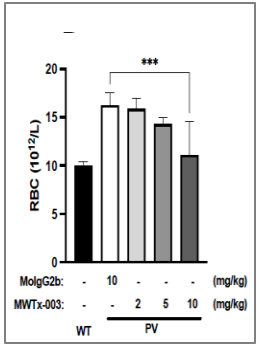
↑ Hepcidin Production



↓ Hematocrit



↓ RBC Production



Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting; HbbTh3/+ mice were treated with the lead anti-TMPRSS6 antibody at 10 mg/kg IP for 4 weeks; Chen B. et al, ASH 2023 Annual Meeting; JAK2V617F mice were treated with anti-TMPRSS6 mAb MWTx-003 at 2, 5, or 10 mg/kg IP every 4 days for 3 weeks

DISC-3405 Development Plans

Phase 1 in healthy volunteers ongoing; aim to advance program into POC studies with focus on polycythemia vera

Phase 1 SAD/MAD in HV
Initiated October 2023

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

Phase 2 Proof-of-Concept Study in Polycythemia Vera

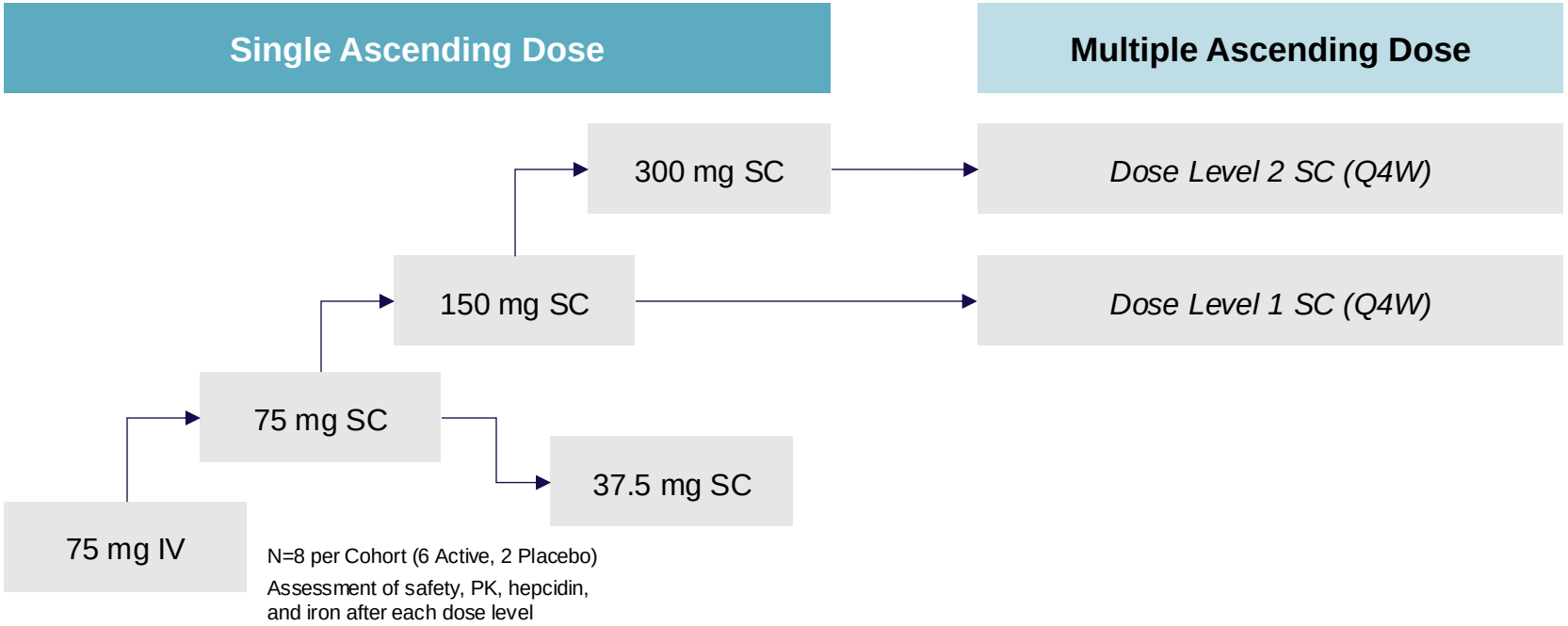
- Strong proof of therapeutic hypothesis; clarity on regulatory development path
- Assess safety, PK, hepcidin, iron, hematologic parameters; % Hct and requirement for phlebotomy

Additional POC Studies in a Range of Indications

- Hereditary Hemochromatosis
- Beta-Thalassemia
- Myelodysplastic Syndromes
- Sickle Cell Disease

Hct = hematocrit; HV = healthy volunteers

DISC-3405 Phase 1 Healthy Volunteers Study Overview



Key Endpoints/Measures: Iron, hepcidin, and other hematologic parameters, safety/tolerability

DISC-3405 Phase 1 Healthy Volunteer Study: Baseline and Demographics

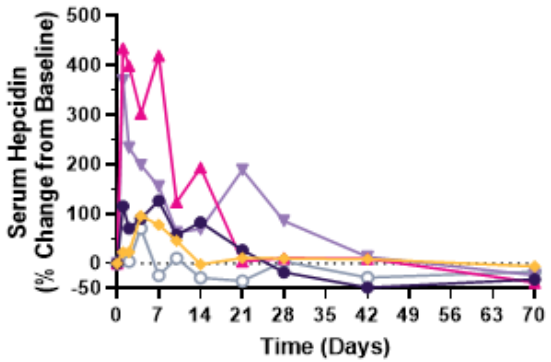
Characteristic	Placebo n=14	37.5 mg SC n=6	75 mg IV n=6	75 mg SC* n=12	150 mg SC* n=12	300 mg SC n=6
Age, years Median (range)	45 (39, 62)	53.5 (42, 64)	39.5 (23, 49)	52.5 (30, 61)	40 (25, 64)	36.5 (22, 38)
Gender, Female, n (%)	4 (28.6)	5 (83.3)	3 (50.0)	6 (50)	5 (41.7)	0 (0)
Hepcidin, ng/mL	15.0 (5.2, 50.1)	26.2 (6.1, 84.2)	19.4 (2.0, 36.6)	23.2 (4.4, 69.8)	12.8 (4.6, 27.6)	18.7 (8.6, 45.0)
Serum Iron, ug/dL	91.6 (41, 180)	88.7 (43, 127)	99.2 (74, 127)	92.9 (33, 154)	85.3 (43, 138)	106.2 (54, 135)
Hemoglobin, g/dL	14.5 (12.2, 16.0)	13.2 (10.7, 17.7)	13.8 (12.1, 15.6)	14.2 (12.7, 16.0)	14.3 (13.0, 17.7)	15.4 (14.4, 16.7)
Hematocrit, %	42.7 (38.3, 47.1)	39.7 (34.3, 50.2)	41.5 (37.1, 45.5)	41.7 (38.7, 45.0)	42.2 (39.4, 50.5)	45.2 (42.3, 48.2)
RBC, 10^{12}/L	4.8 (4.1, 5.8)	4.5 (4.0, 5.7)	4.6 (3.8, 5.2)	4.6 (4.2, 5.2)	4.7 (4.0, 5.8)	5.1 (4.8, 5.8)

IV = intravenous; RBC = red blood cell; SC = subcutaneous; Baseline is defined as Study Day -1, prior to receiving study drug.
*75 and 150 mg SC include both SAD and MAD cohorts

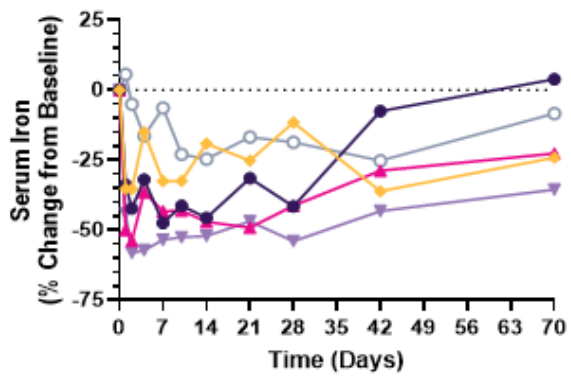
Updated DISC-3405 HV Data: Hepcidin, Iron, and Ferritin

- DISC-3405 produced dose-related increases in serum hepcidin, with corresponding reductions in serum iron across all dose levels
- DISC-3405 resulted in deep reductions in serum iron (ranging from 50-80% from baseline) that were sustained and support a once-monthly SC dosing regimen

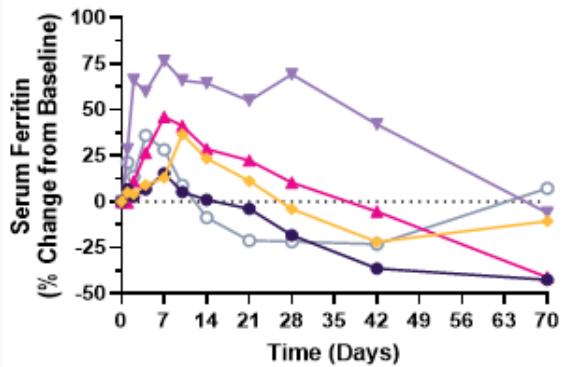
% Change from Baseline: Hepcidin



% Change from Baseline: Iron



% Change from Baseline: Ferritin



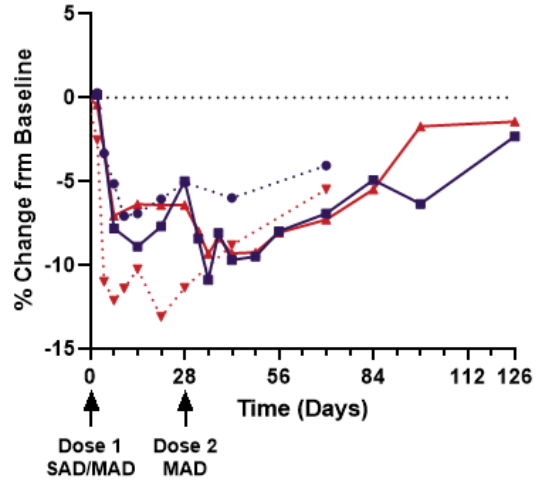
Placebo SC | 37.5 mg SC | 75 mg SC | 150 mg SC* | 300 mg SC

*One participant randomized to 150 mg SC was excluded from PD analysis due to history of anemia and recent hemorrhoidal bleeding, not disclosed prior to enrollment, deeming the participant ineligible

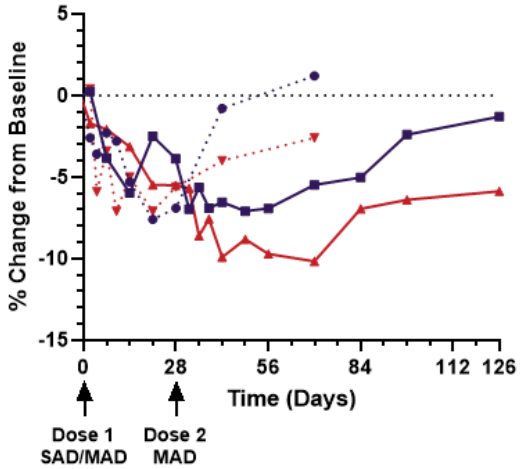
Updated DISC-3405 HV Data: Hematologic Response

- Single and repeat dosing of DISC-3405 demonstrated meaningful reductions in hematologic parameters (reticulocyte hemoglobin, hemoglobin, and hematocrit)

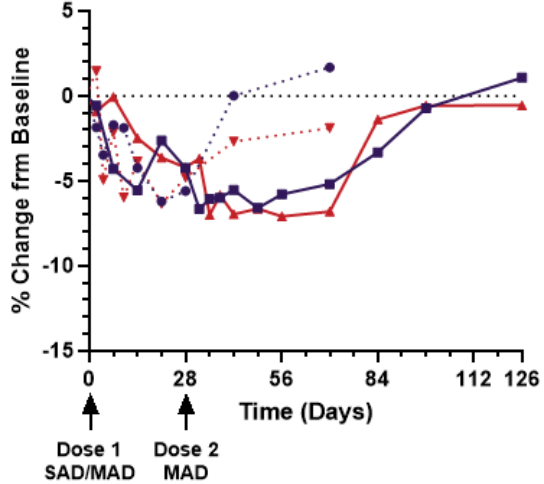
Reticulocyte Hemoglobin



Hemoglobin



Hematocrit



75 SC, SAD | 75 SC MAD | 150 SC SAD* | 150 SC MAD

SC = subcutaneous; *One participant randomized to 150 mg SC (SAD) was excluded from PD analysis due to history of anemia and recent hemorrhoidal bleeding not disclosed prior to enrollment, deeming the subject ineligible.

Updated DISC-3405 HV Data: Safety

- Generally well tolerated at all evaluated dose levels; no serious AEs, > Grade 2 AEs, or AEs leading to study withdrawal were reported

Adverse Event	Placebo n=14	37.5 mg SC SAD n=6	75 mg IV SAD n=6	75 mg SC SAD n=6	150 mg SC SAD n=6	300 mg SC SAD n=6	75 mg SC MAD n=6	150 mg SC MAD n=6
Sore Throat	0	0	1	0	0	0	0	0
Nausea	0	1	0	1	0	0	1	0
Headache	1	1*	0	0	0	0	1	1
Cough	0	0	0	0	1	0	0	0
Rhinorrhea	0	0	0	0	1	0	0	0
Lightheadedness	0	0	0	1	0	0	0	0
Increased ALT	0	0	0	0	1*	0	0	0
Increased AST	0	0	0	0	1*	0	0	0
Fatigue	0	0	0	0	0	0	0	2

* Grade 2 AEs; 1 participant reported a self-limited headache; 1 participant was observed to have isolated, self-limited elevations of AST and ALT.

DISC-3405 Phase 1 Healthy Volunteer Study Summary

- Dose-dependent increases in hepcidin and corresponding reductions in serum iron levels across all dose levels
- Deep and sustained reductions in serum iron (50-80% from baseline)
- Meaningful reductions in reticulocyte hemoglobin, hemoglobin, and hematocrit in both SAD and MAD cohorts
- Data set supportive of a once-monthly subcutaneous dosing regimen in polycythemia vera and iron-overload conditions
- DISC-3405 was well tolerated with no injection-site reactions

Iron Restriction in Sickle Cell Disease

Potential for iron restriction through inhibition of TMPRSS6 to benefit SCD by reducing HbS concentration

Growing Body of Evidence for Iron Restriction for Disease Modification in Sickle Cell Disease

DISC-3405 in a Townes Model

- 3 and 10 mg/kg IP weekly for 8 weeks
- Reduced HbS concentration
- Improved markers of inflammation
- Improved markers of hemolysis

Disc Continues Strong Growth Trajectory Towards Becoming a Leading Hematology Company

	Significant Accomplishments in 2024	*Important Catalysts in 2025*
Bitopertin	• Positive data across two Phase 2 studies • Encouraging EOP2 Meeting with path to accelerated approval	• Guidance on Type C meeting with FDA • Initiation of APOLLO study
DISC-0974	• Updated positive data in anemia of MF • Phase 2 initiation in anemia of MF • Positive SAD data in anemia of CKD	• Initial Phase 2 data in anemia of MF • Phase 1b multiple-dose in anemia of CKD • Preclinical efforts on additional indications
DISC-3405	• Positive healthy volunteer data • Preclinical data in sickle cell disease	• Polycythemia vera as first indication • Preclinical efforts on additional indications

Supported by a strong cash position with runway well into 2027

Thank You

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EHA 2024

AURORA Data

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AURORA Study: Disposition and Baseline Characteristics

	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Randomized	24	26	25
Completed Study	24	26	22
Discontinued Prior to Day 121	0	0	3
Characteristic			
Mean Age, years	42.3	45.0	47.8
Female, n (%)	12 (50%)	14 (54%)	12 (48%)
White, n (%)	24 (100%)	24 (92%)	24 (96%)
Baseline PPIX, Mean ± SE (ng/mL)	8,691 ± 903	8,155 ± 1,337	10,597 ± 983
Daily Sunlight Exposure (hr), Mean (range)	1.29 (0.18, 3.31)	1.17 (0.26, 4.03)	1.07 (0.04, 2.78)
Time to Prodrome, n (%)			
< 30 min	9 (38%)	9 (35%)	8 (32%)
≥ 30 min	15 (63%)	17 (65%)	17 (68%)

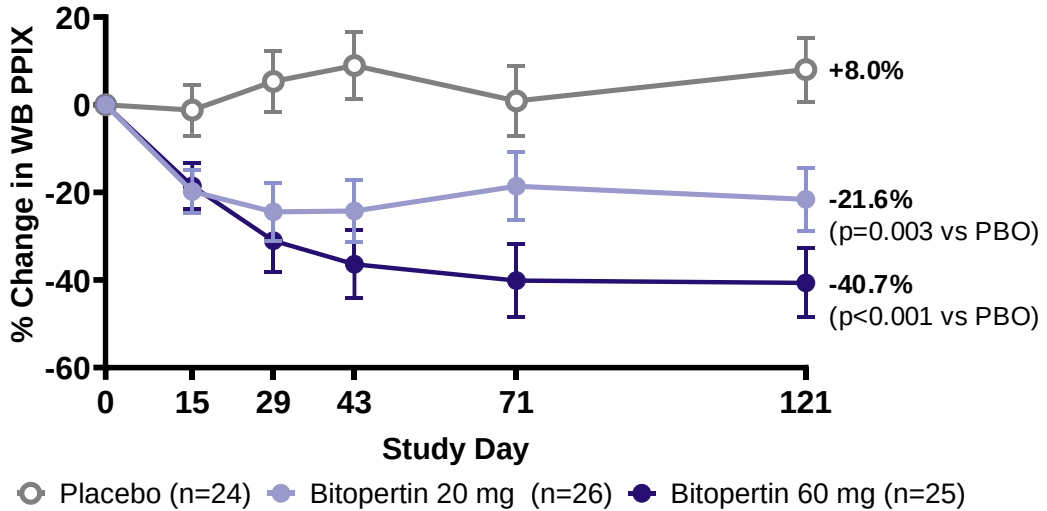
[a] Season that encompasses majority of participant's double-blind treatment period

AURORA Met Primary Endpoint

Statistically significant reductions in whole-blood (WB) metal-free PPIX

- Bitopertin reduced PPIX levels consistent with BEACON, taking ~6-8 weeks to reach max reduction
- Significant reductions observed in both 20 mg and 60 mg doses

PPIX Over Time

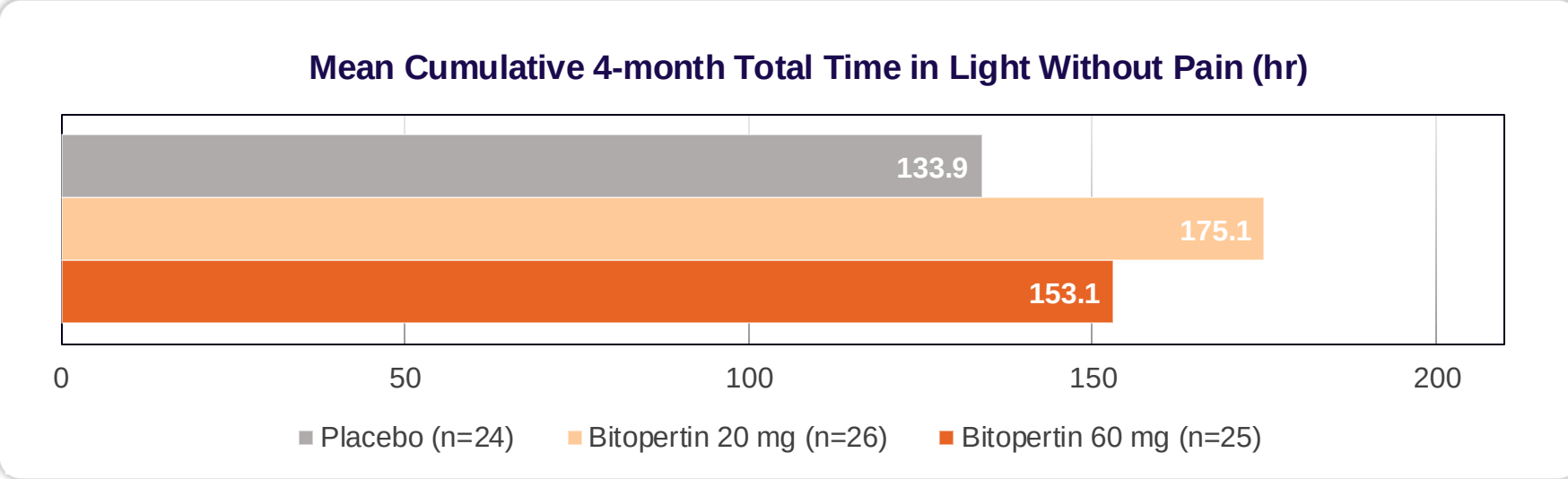


Least-squares means and p-values for percent changes in PPIX analyzed using a mixed model repeated measures (MMRM) to compare 20 mg and 60 mg bitopertin dose groups versus placebo.

Updated AURORA Data: Key Secondary Endpoint

Cumulative time in light without pain

- Bitopertin treatment effect similar to BEACON results
- Did not meet statistical significance due to strong performance of placebo arm

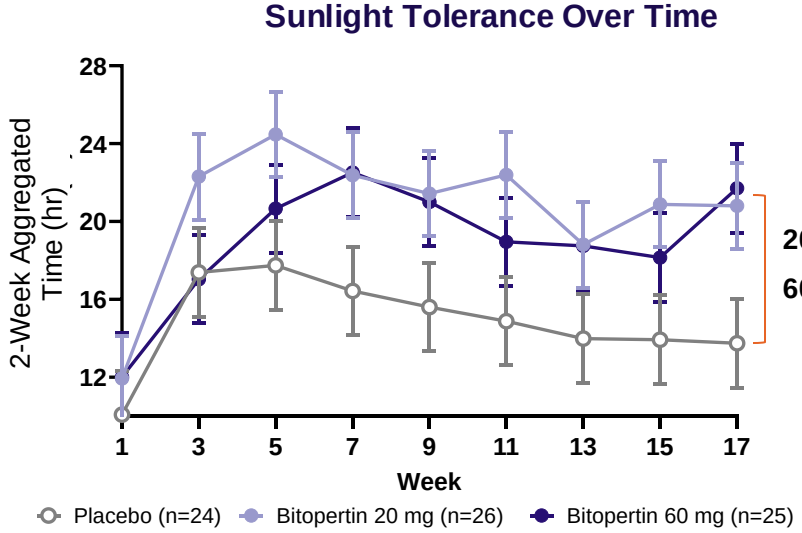


Least-squares means for cumulative time in light measured via daily diary, adding all time in light between the hours of 10:00 am and 6:00 pm on days without any pain, and analyzed using an analysis of variance model to compare 20 mg , 60 mg bitopertin dose groups versus placebo.

Updated AURORA Data: Time in Light Without Pain

Post-hoc longitudinal analysis adjusted for baseline

- Statistically significant improvements in daily time in light compared to placebo
- Meaningful changes in daily time in light relative to baseline



20 mg: p=0.026 vs PBO

60 mg: p=0.013 vs PBO

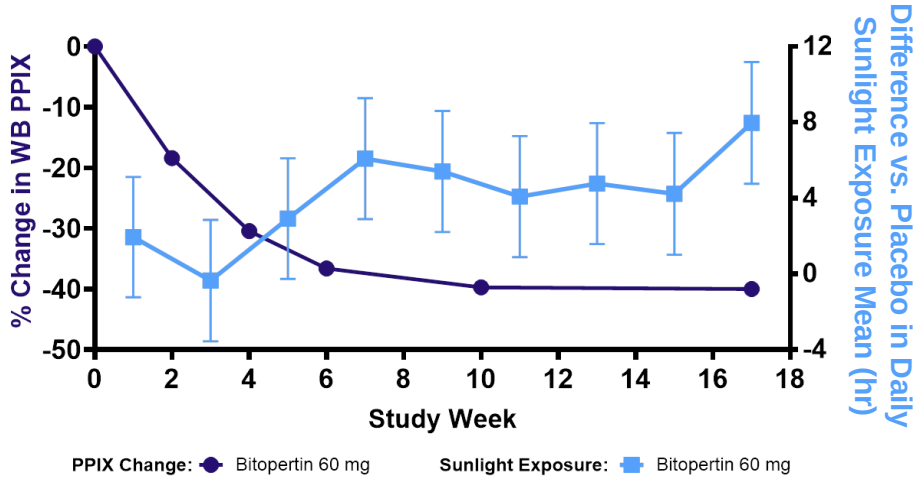
Change from Baseline	
Bitopertin 60 mg (n=25)	2.0x
Bitopertin 20 mg (n=26)	1.9x
Placebo (n=24)	1.1x

Total daily sunlight exposure from 10:00am to 6:00pm on days without pain aggregated over 2-week periods and analyzed using MMRM to compare 20 mg and 60 mg bitopertin dose groups vs placebo. Mean ± SE baseline daily sunlight exposure (hr) during 14-day screening period: 11.1 ± 1.9 for 20 mg, 10.7 ± 1.7 for 60 mg, 12.2 ± 2.1 for placebo.

Updated AURORA Data: Light Tolerance

- Timing of PPIX reduction aligns with the time course of increases in sunlight tolerance

Change in PPIX and Placebo-Corrected Sunlight Exposure for 60 mg Group



Updated AURORA Data: Phototoxic Reactions with Pain

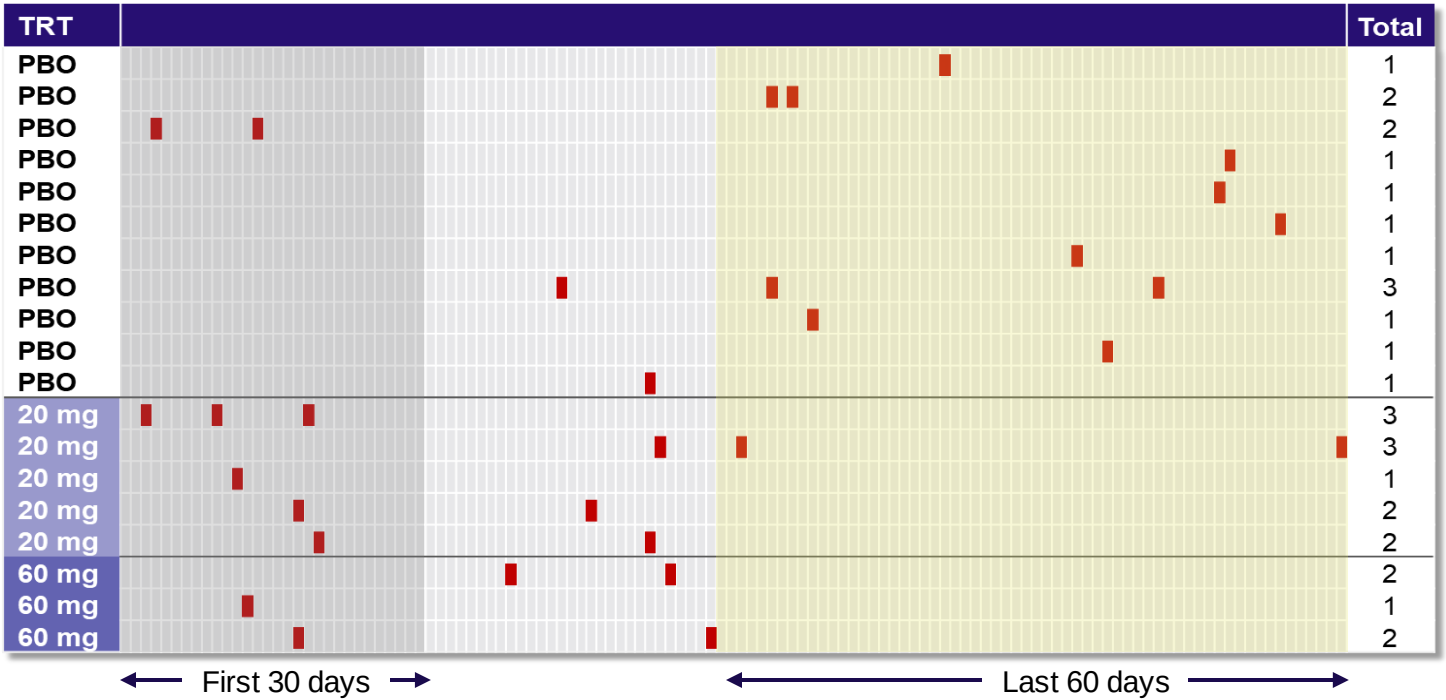
- Dose-dependent reduction in rate of phototoxic reactions with pain, reaching statistical significance in the 60 mg dose group
- Max pain score reduced with bitopertin

Incidence Rate Ratio of New Phototoxic Reactions with Pain vs. Placebo

	Screening (2-4 weeks)		Double-Blind Period (17 weeks)		
	# of New Reactions	# of Participants	# of New Reactions	# of Participants	Median Max Pain Score
Placebo (n=24)	4	2 (8%)	15	11 (46%)	5.0
Bitopertin 20 mg (n=26)	11	8 (31%)	11	5 (19%)	4.0
Bitopertin 60 mg (n=25)	8	6 (24%)	5	3 (12%)	3.5

Updated AURORA Data: Phototoxic Reactions with Pain

- Consistent with profile for PPIX reductions reaching a nadir, time course of phototoxic reactions showed greater bitopertin treatment effect during the last 60 days of study



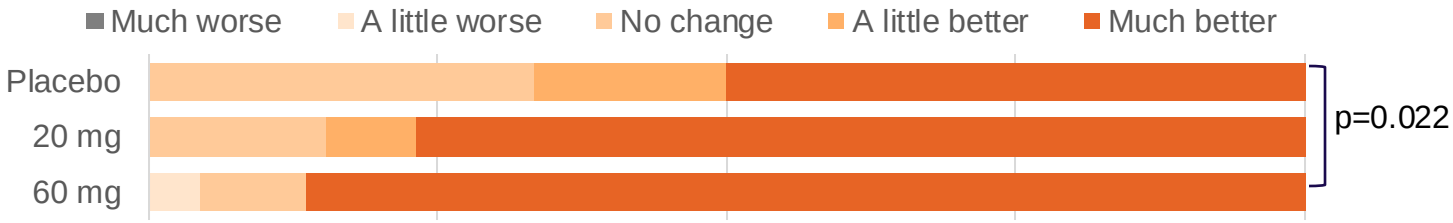
Participants reporting new phototoxic reactions during double-blind period and corresponding study day for new reaction (shown in red)

= New Phototoxic Reaction

Updated AURORA Data: Patient-Reported Outcomes

- Dose-dependent improvements in Patient Global Impression of Change (PGIC), reaching statistical significance in the 60 mg dose group at end of study
- Improved PGIC responses are associated with greater reductions in PPIX

PGIC: *"Since the start of the study, how would you rate the change in your EPP?"*



% PPIX Change	PGIC Response				
	Much worse	A little worse	No change	A little better	Much better
N	0	1	14	6	48
Mean (SD)	-	43.8	6.7 (64.9)	-0.4 (15.2)	-25.9 (31.7)

Percentages calculated using data for PGIC from participants who completed the study (D121): n=26 for 20 mg bitopertin, n=22 for 60 mg bitopertin; n=24 for placebo

Updated AURORA Data: PPIX Change and Light Tolerance

- Greater PPIX reductions in bitopertin participants reporting no phototoxic reactions (-36.5%) vs phototoxic reactions (-4.0%)
- PPIX reductions associated with improvements in multiple measures of light tolerance

Tertiles of PPIX Change

PPIX Increased ← → **PPIX Decreased**

Light Tolerance Measure (Mean ± SD)	Tertile 3 (-7% to 190%)	Tertile 2 (-38% to -7%)	Tertile 1 (-88% to -38%)
Cumulative total time in sunlight without pain (hr)	117.5 ± 83.2	124.5 ± 68.3	161.1 ± 142.6
Average time in sunlight without pain (hr)	1.16 ± 0.83	1.20 ± 0.72	1.61 ± 1.32
Change from baseline in time to prodrome (min)	64.1 ± 123.8	109.4 ± 121.1	117.4 ± 148.6

Tertile 1 = 6 participants at 20 mg, 16 at 60 mg, and 2 on placebo; Tertile 2 = 13 participants at 20 mg, 6 at 60 mg, and 5 on placebo; Tertile 3 = 7 participants at 20 mg, 1 at 60 mg, and 17 at placebo

Safety and Tolerability

- No serious adverse events reported with bitopertin
- Stable hemoglobin levels
- Favorable safety profile consistent with prior studies enrolling >4000 participants

	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Participants with any TEAE, n (%)	18 (75%)	20 (77%)	22 (88%)
TEAEs leading to discontinuation, n (%)	0	0	2 (8%)
SAEs, n (%)	1 (4%)	0	0
Common TEAEs			
Dizziness, n (%)	4 (17%)	4 (15%)	11 (44%)
Median Duration (days)	2.0	4.5	5.0
Nausea, n (%)	2 (8%)	1 (4%)	4 (16%)
Alanine aminotransferase increased, n (%)	3 (13%)	1 (4%)	2 (8%)

TEAEs leading to discontinuation: rash and dizziness; common TEAEs include those reported in >5 participants during study regardless of treatment assignment.
SAE = serious adverse event; TEAE = treatment-emergent adverse event

Summary of EPP Bitopertin Data

BEACON and AURORA Studies

AURORA

- Significant reductions in PPIX 40% vs placebo
- Time-dependent, 2x improvements in pain-free time in sunlight
- Significant 75% reduction in rate of phototoxic reactions vs placebo
- Significant improvement in PGIC vs placebo

Targets underlying pathophysiology of EPP	
Significant improvement in sunlight tolerance	
Functional benefit by reducing debilitating phototoxic reactions	
Significantly improved how patients feel	

BEACON

- Significant reductions in PPIX >40% vs baseline
- Significant 3x increase in sunlight tolerance (time to prodrome)
- 92% reduction in number of phototoxic reactions vs baseline
- Nearly all (95%) participants reported improvements in PGIC