Corporate Presentation

April 2024

disc medicine

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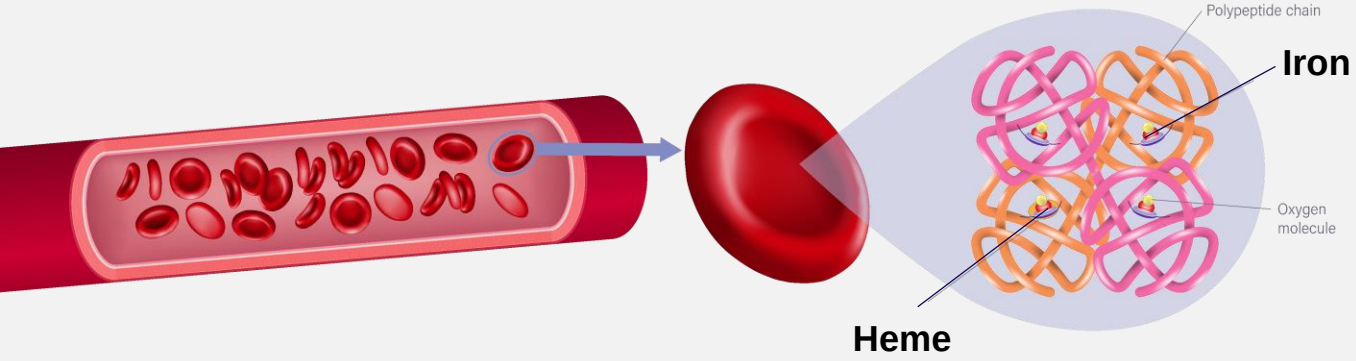
Bitopertin, DISC-0974, and DISC-3405 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide

Targeting Fundamental Pathways of Red Blood Cell Biology using Validated Mechanisms



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

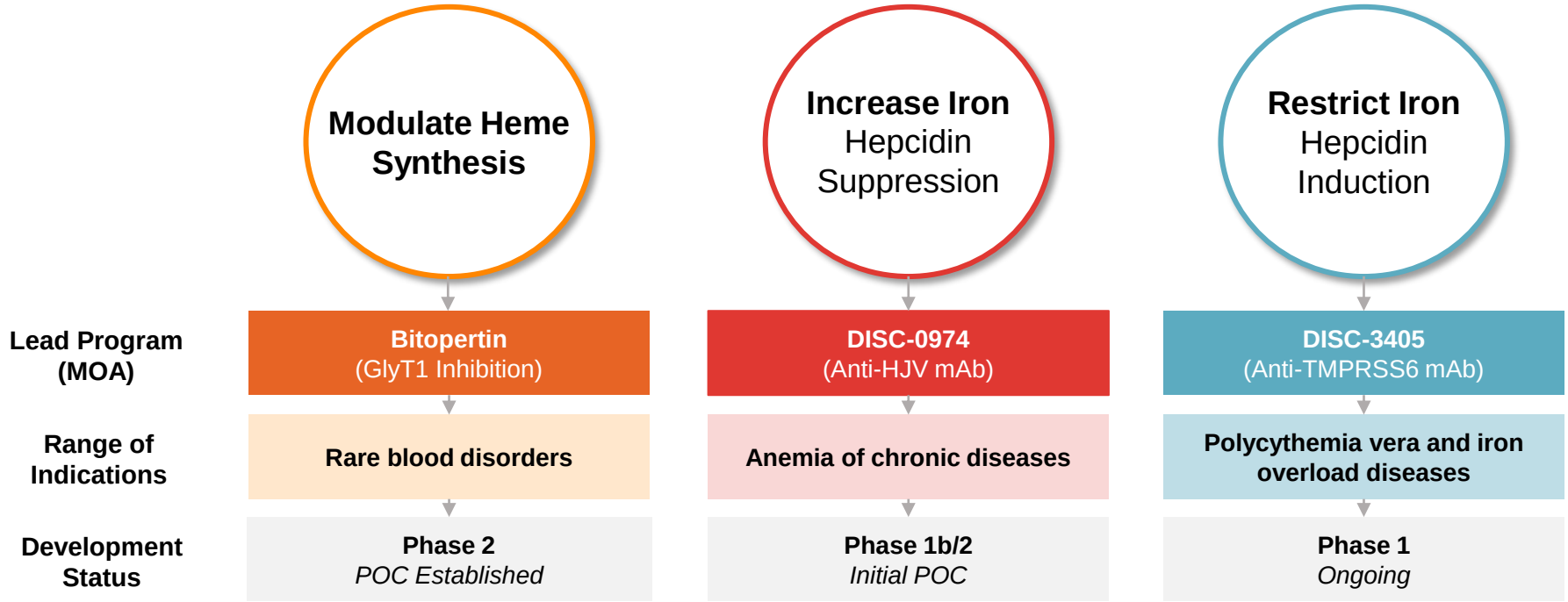
Key points of intervention across a wide range of diseases

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**

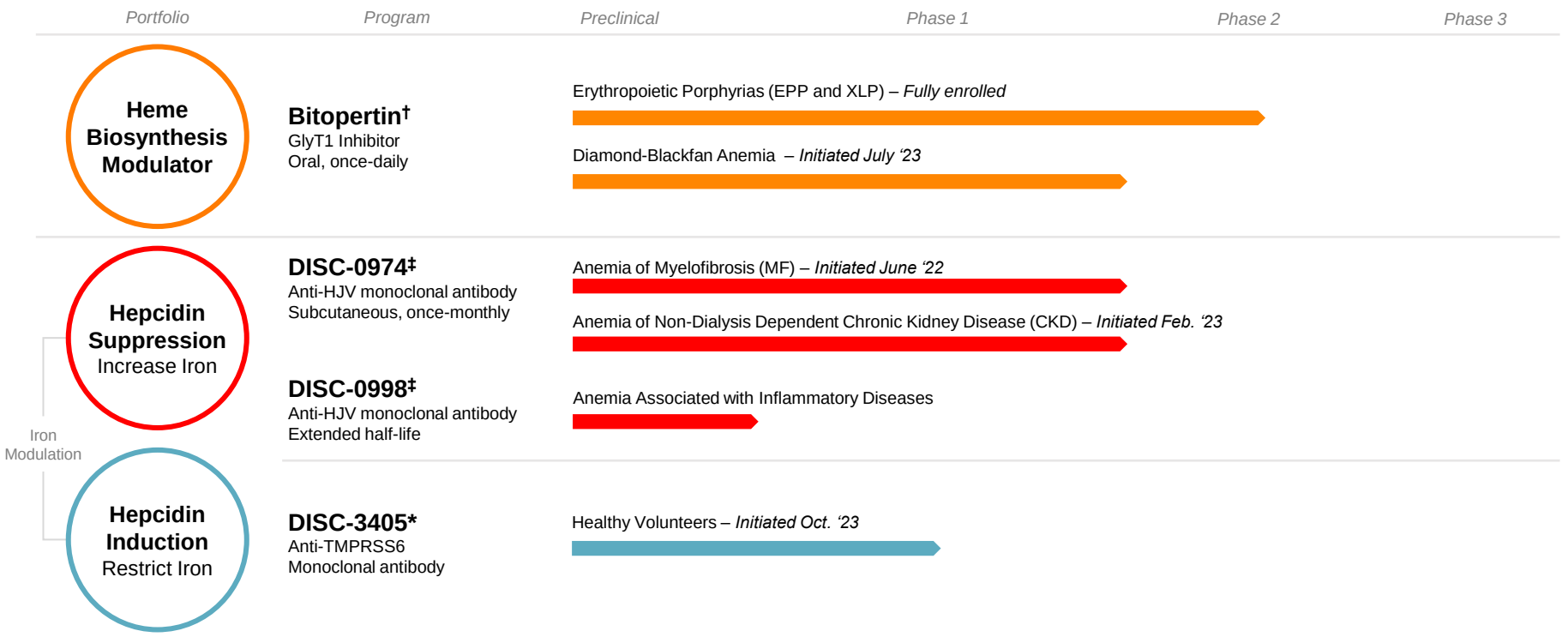
Bold = ongoing Disc trial

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; *in-licensed from Mabwell; formerly MWTX-003

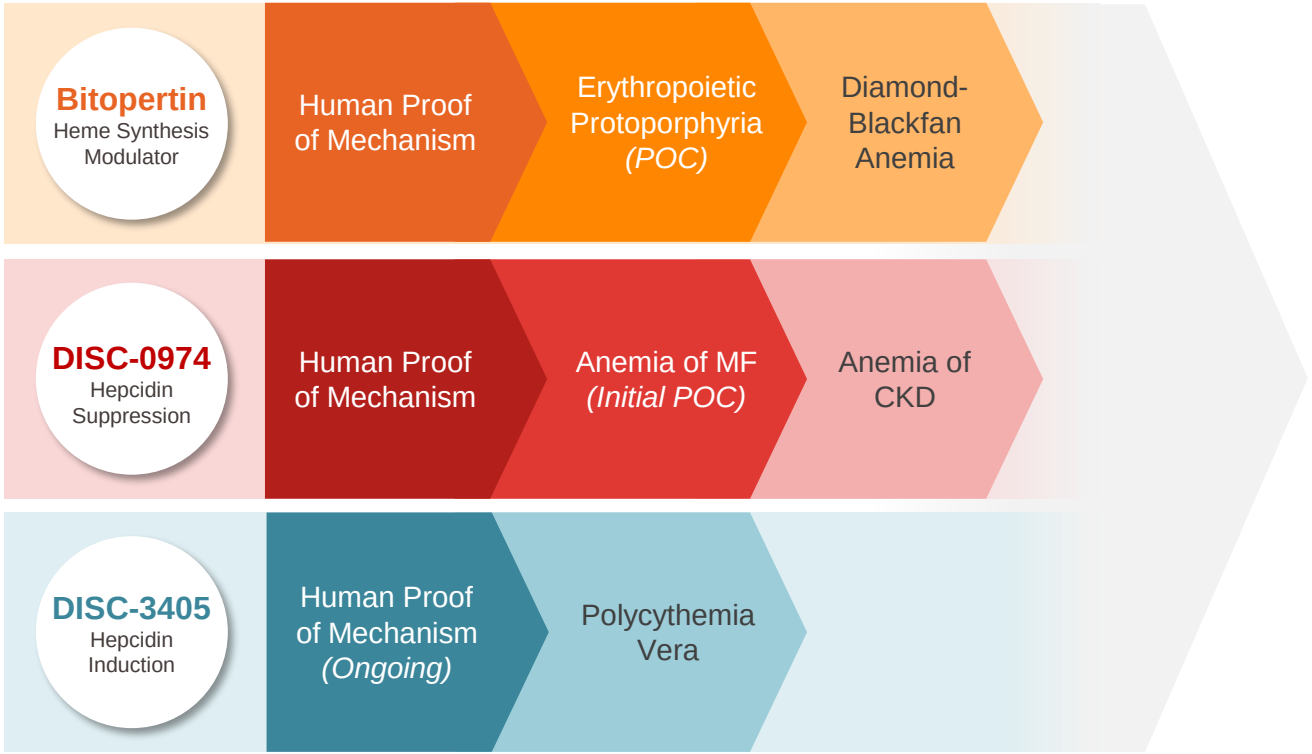
Projected Upcoming Milestones and Events

Multiple additional data catalysts anticipated in 2024 across portfolio

Program	Indication	H1 2024	H2 2024	2025
Bitopertin Heme Synthesis Modulator	**Erythropoietic Porphyrias (EPP and XLP)**	• Phase 2 AURORA Data (March-April)	• End of Ph 2 Meeting / Other Regulatory Interaction	• Development Activities Pending Regulatory Feedback
	Diamond-Blackfan Anemia (DBA)		• Initial Phase 2 Data	
DISC-0974 Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**	• Updated Phase 1b Data	• Final Phase 1b Data • Initiate Phase 2 Study	• Phase 2 Topline Data
	Anemia of Chronic Kidney Disease (CKD)		• Phase 1b Data (hemoglobin)	• Phase 2a Topline Data
DISC-3405 Hepcidin Induction	**Polycythemia Vera and Diseases of Iron Overload / Ineffective Erythropoiesis**	• Phase 1 SAD Data	• Phase 1 SAD/MAD Data	• Phase 2 in PV Initiation

SAD = single ascending dose; MAD = multiple ascending dose; PV = polycythemia vera

Disc Portfolio Provides Strong Foundation for Growth



Other Iron and Heme Disorders

- Beta Thalassemia
- Other Porphyrias
- Myelodysplastic Syndromes
- Sickle Cell Disease
- Hereditary Hemochromatosis
- Anemia of IBD
- Anemia of Cancer

Bitopertin

GlyT1 Inhibitor

Heme Biosynthesis Modulation

Bitopertin: Investigational Oral, Selective GlyT1 Inhibitor

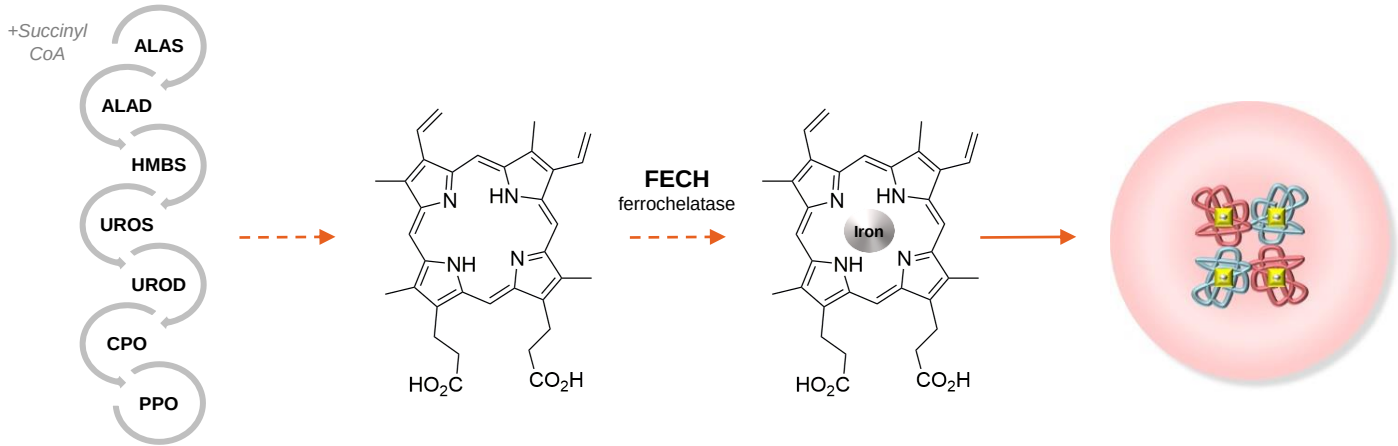
In multiple clinical trials by Roche, bitopertin was observed to modulate heme biosynthesis by blocking uptake of glycine in erythrocytes

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

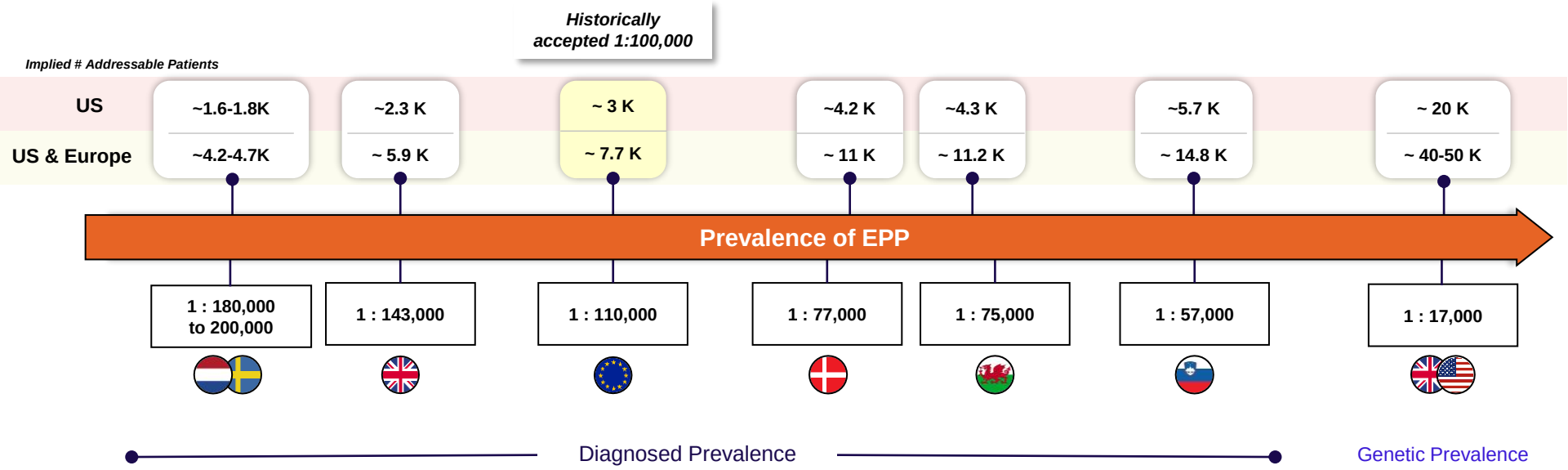
- Avoid sun / light, protective clothing, window tinting, Zn/Ti Oxide
- One FDA-approved agent, afamelanotide, a surgically-implanted tanning agent

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

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

Historical EPP estimates likely underrepresent prevalence

Based on methodology reported in literature and patient journey

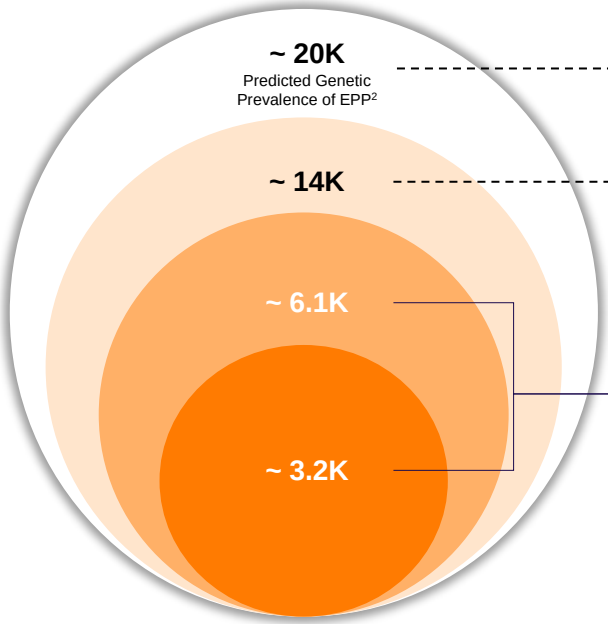


Clearview Healthcare Partners; Went et al (1984); Wahlin et al. (2011); Holme et al. (2006); Elder et al. (2013); Christiansen et al. (2016); Elder et al. (1990); Marko et al. (2007); Dickey et al. (2021)

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.

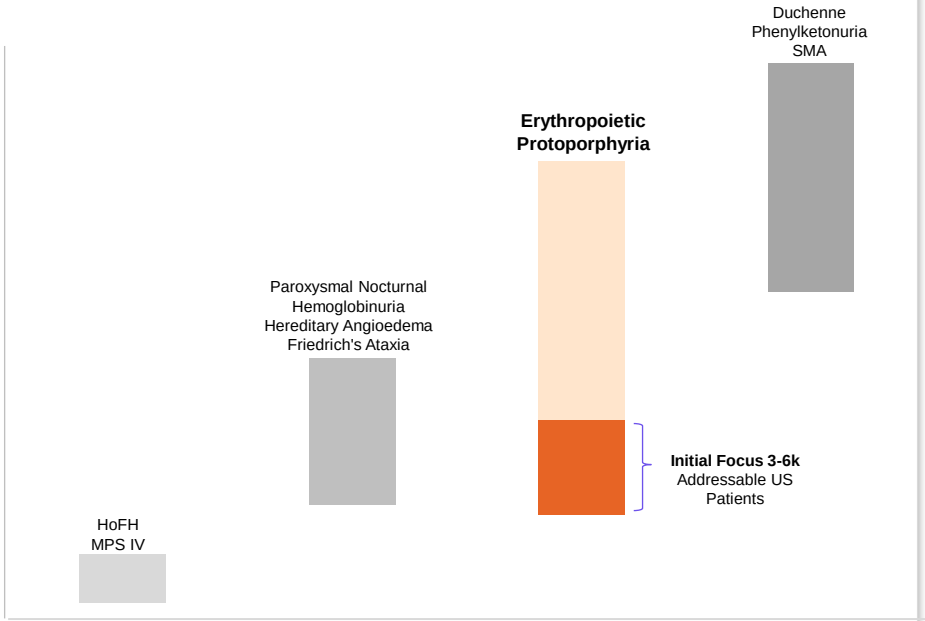


Expansion
Misdiagnosed or have not sought treatment for EPP

Growth
Patients with lower degree of engagement with HC system

Focus
Engaged EPP patients recent or recurring claims

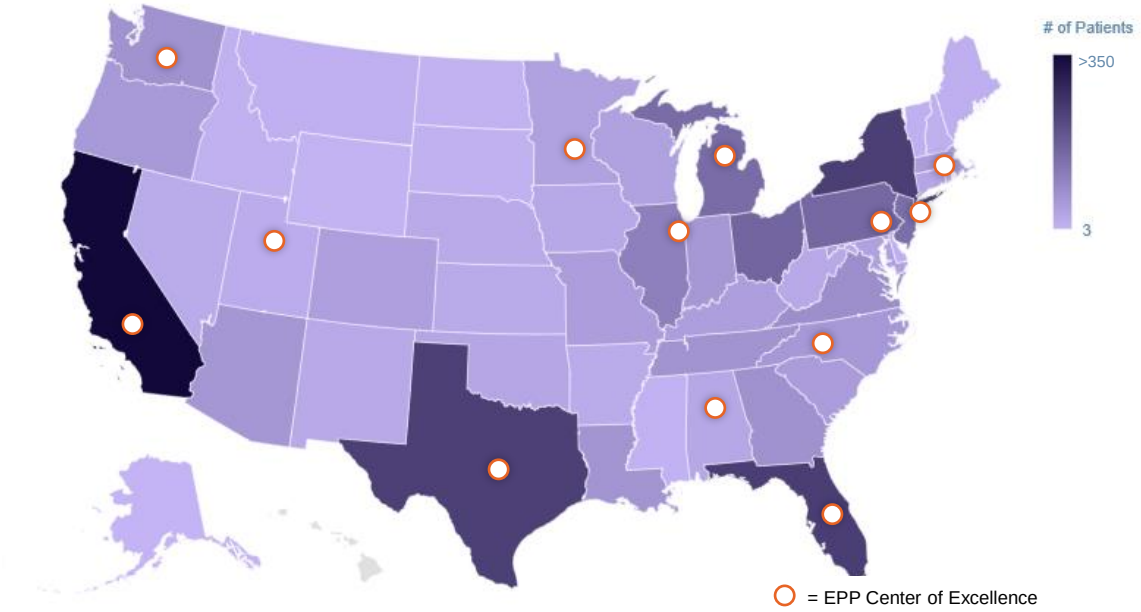
US EPP Prevalence Comparable to Major Rare Diseases



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

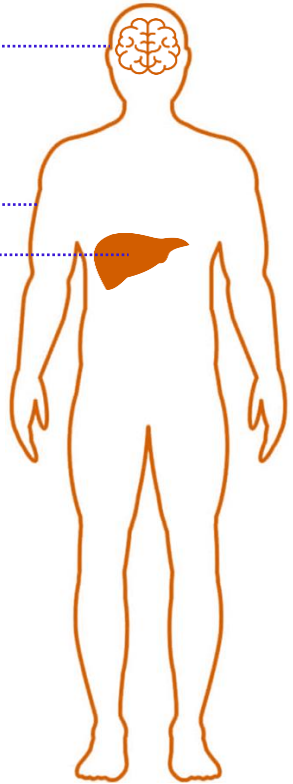
Real world data confirm EPP has a significant impact on patients' lives across multiple domains

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

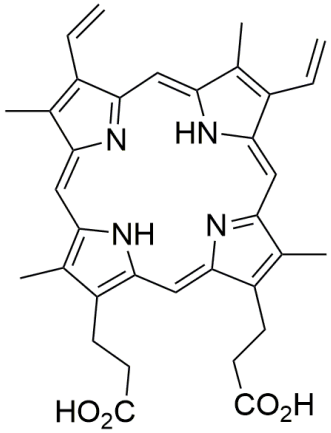
Toxic and photo-active metabolite accumulates in RBCs and is transported to skin and other organs, causing damage

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

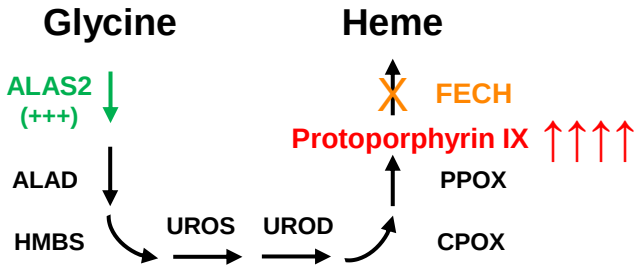
Other Complications

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

Bitopertin: Potential Disease-Modifying Treatment

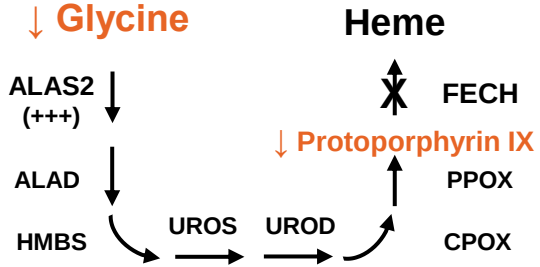
Designed to reduce disease-causing PPIX by limiting uptake of glycine into developing erythrocytes

EPP and XLP Patients
High PPIX Levels



Mutations result in reservoir of pathologically high levels of PPIX

Bitopertin Treatment
Designed to Reduce PPIX Levels



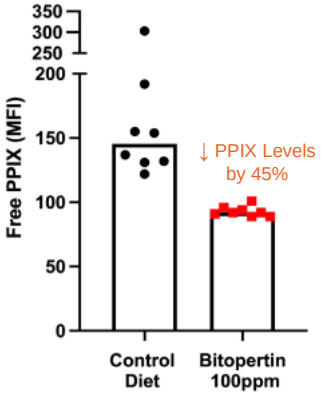
Potential first disease-modifying treatment for EPP and XLP

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

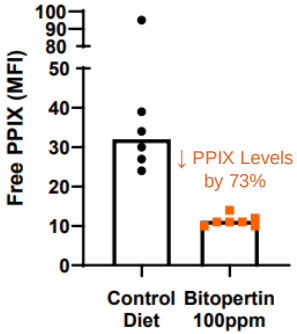
Bitopertin Reduced PPIX in Models of EPP / XLP

Effects on PPIX have the potential to be disease-modifying

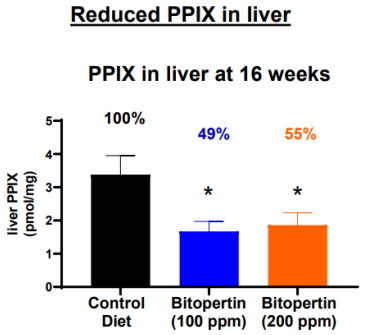
In vivo - EPP Model (Mouse)
FECH^{m1pas} Missense Mutation

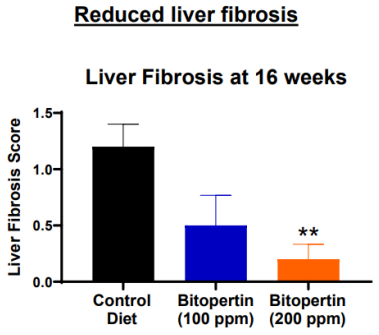


In vivo - XLP Model (Mouse)
ALAS2^{Q548X} Gain-of-Function Mutation



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





Bitopertin reduced PPIX, the driver of disease pathophysiology, and, based on the data, 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*

Bitopertin Robust Data Package

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

Non-Clinical	CMC	Clinical
✓ Genetic toxicity and Safety pharmacology	✓ Commercial-scale production	✓ Healthy volunteer studies
✓ Long-term GLP toxicology	✓ Optimized oral formulation (tablet and capsule)	✓ Drug-drug interaction studies
✓ Juvenile GLP toxicology studies supporting patients ≥2 y/o	✓ Highly stable molecule (at least 5 years)	✓ Hepatic impairment
✓ Carcinogenicity studies		✓ Renal impairment
✓ Full reproductive GLP toxicology		✓ TQT (heart rhythm) study
✓ Metabolites fully qualified		✓ 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

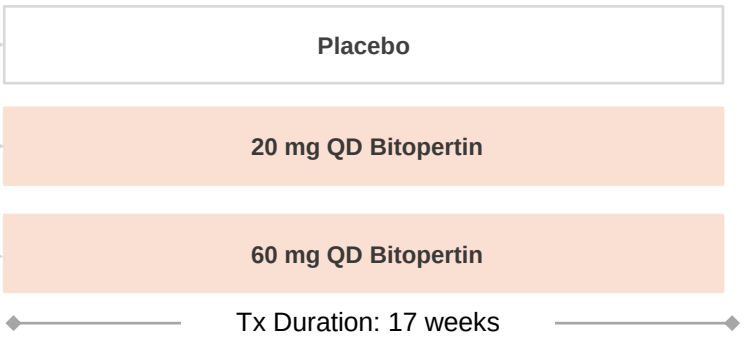
AURORA Trial: Ph 2 Trial in EPP

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

Trial Design

- Double-blind, placebo-controlled (1:1:1)
- EPP; 18 years +
- Stratified by light tolerance
- Not receiving afamelanotide
- US

Treatment Arms



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

Data availability: Fully enrolled; Topline data presented April 2024

Time to prodromal symptom = the time until a patient experiences an early warning signal of a phototoxic attack, measured through a weekly sunlight challenge; QD = daily, Tx = treatment; POC = proof of concept; QOL = quality of life

AURORA Disposition and Baseline Characteristics

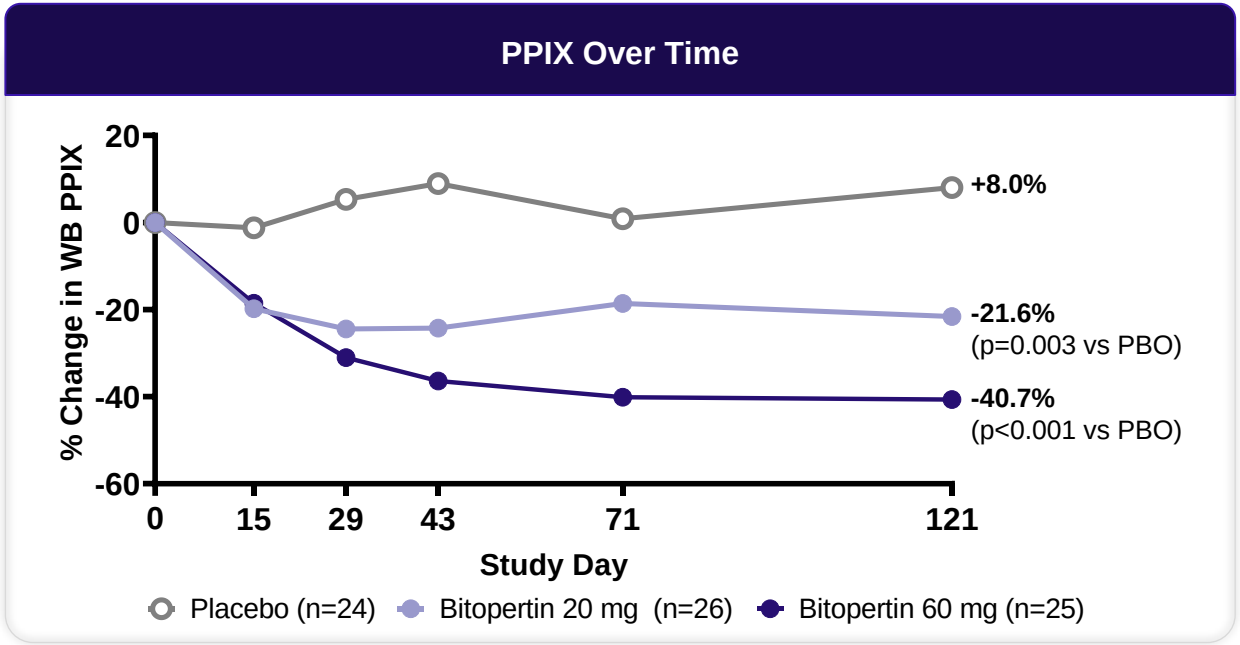
	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Randomized	24	26	25
Completed Study	24	26	22
Discontinued Prior to Day 121	0	0	3
Characteristic			
Mean Age, years	42.3	45.0	47.8
Female, n (%)	12 (50%)	14 (54%)	12 (48%)
White, n (%)	24 (100%)	24 (92%)	24 (96%)
Baseline PPIX, Mean ± SE (ng/mL)	8,691 ± 903	8,155 ± 1337	10,597 ± 983
Time to Prodrome, n (%)			
< 30 min	9 (38%)	9 (35%)	8 (32%)
≥ 30 min	15 (63%)	17 (65%)	17 (68%)
Geography, n (%)			
Midwest or Northeast	17 (71%)	15 (58%)	15 (60%)
South or West	7 (29%)	11 (42%)	10 (40%)
Seasonality, n (%)[a]			
Fall/Winter	10 (42%)	12 (46%)	11 (44%)
Spring/Summer	14 (58%)	14 (54%)	14 (56%)

[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
- Significant reductions observed in both 20 mg and 60 mg doses

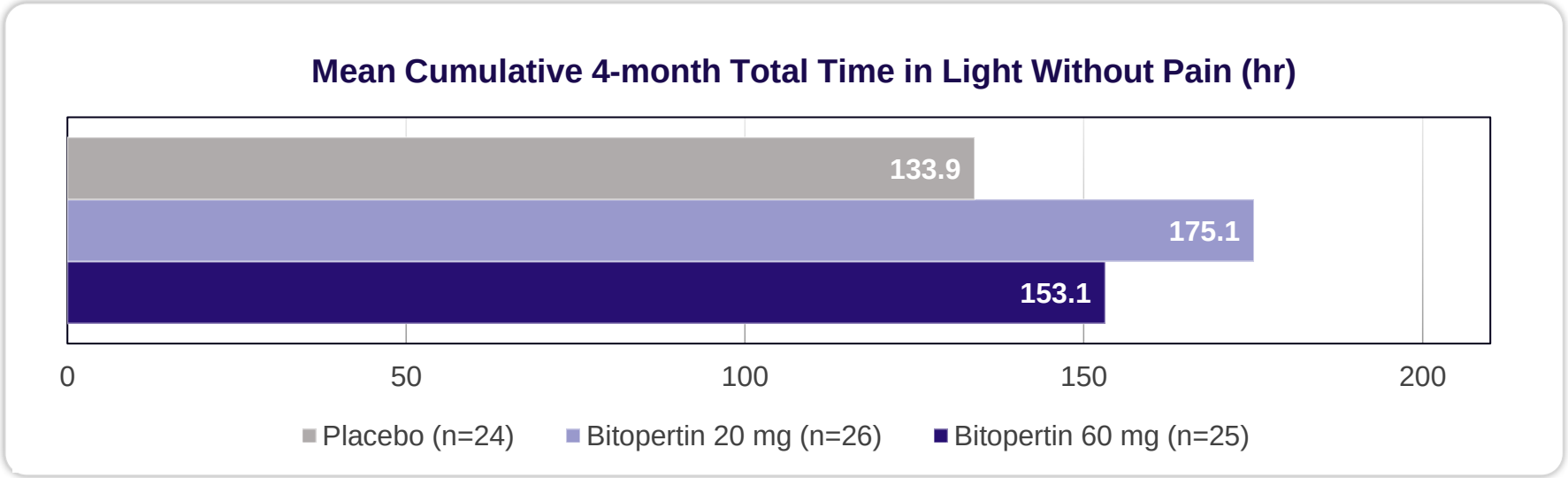


Least-squares means and p-values for percent changes in PPIX analyzed using a mixed model for repeated measures (MMRM) to compare 20 mg 60 mg bitopertin dose groups versus placebo.

AURORA Topline 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

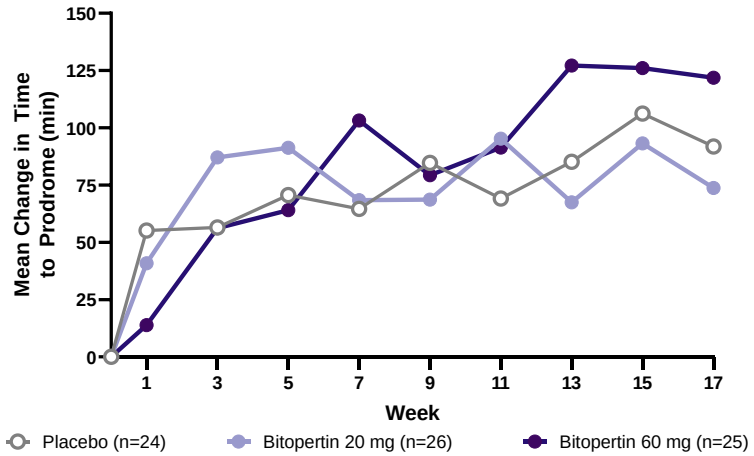


Least-squares means for cumulative time in light measured via daily diary, adding all time in light between the hours of 10:00 am and 6:00 pm on days without any pain, and analyzed using an analysis of variance model to compare 20 mg 60 mg bitopertin dose groups versus placebo.

AURORA Topline Data: Light Tolerance

- Large improvements in light tolerance in all treatment groups, as measured by the time to prodrome assessed in weekly sunlight challenges

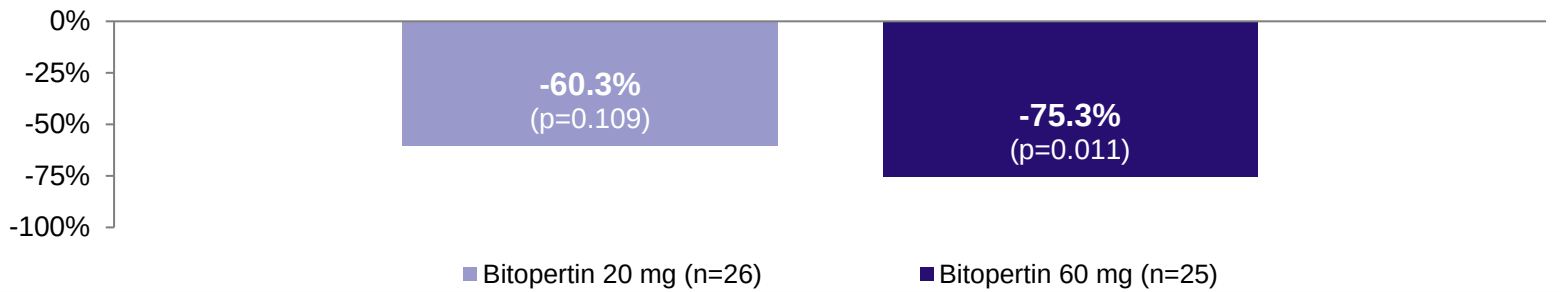
Time to Prodrome Averaged Over 2-Week Intervals



AURORA Topline Data: Phototoxic Reactions with Pain

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

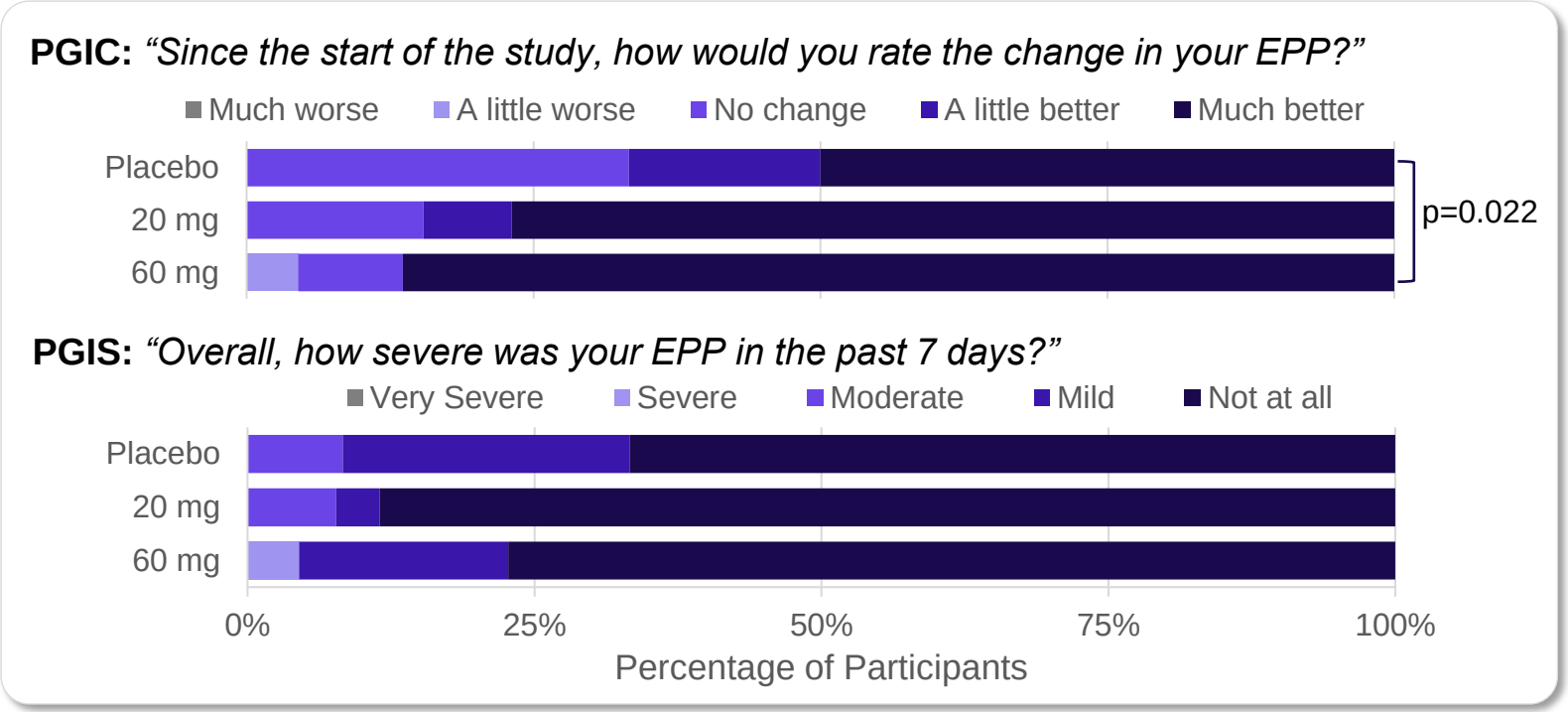
Incidence Rate Ratio of New Phototoxic Reactions with Pain vs. Placebo



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

AURORA Topline 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



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

AURORA Topline Data: Safety and Tolerability

- No serious adverse events with bitopertin
- Stable hemoglobin levels
- Favorable safety profile consistent with prior studies enrolling >4,000 participants

	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Subjects with any TEAE	18 (75%)	20 (77%)	22 (88%)
TEAEs leading to discontinuation	0	0	2 (8%)
SAEs	1 (4%)	0	0
Common TEAEs			
Dizziness	4 (17%)	4 (15%)	11 (44%)
Median Duration (days)	2.0	4.5	5.0
Nausea	2 (8%)	1 (4%)	4 (16%)
Alanine aminotransferase increased	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.
AE = adverse event; Hgb = hemoglobin; TEAE = treatment-emergent adverse event

AURORA Topline Data: Key Takeaways and Next Steps

- **Met primary endpoint, demonstrating dose-dependent, statistically significant reductions in protoporphyrin IX (PPIX) compared to placebo in both 20 mg and 60 mg dose groups**
- **Improved measures of light tolerance, including the key secondary endpoint, in both 20 mg and 60 mg dose groups, but did not meet statistical significance compared to placebo**
- **Dose-dependent reductions in the rate of phototoxic reactions with pain and improvements in PGIC, with statistical significance at the 60 mg dose group compared to placebo**
- **Generally well-tolerated with stable hemoglobin levels**

Next Steps for Bitopertin in EPP

- We plan to further evaluate the data internally and with KOLs, regulators, and patient advocacy groups to determine the optimal registrational endpoints moving forward

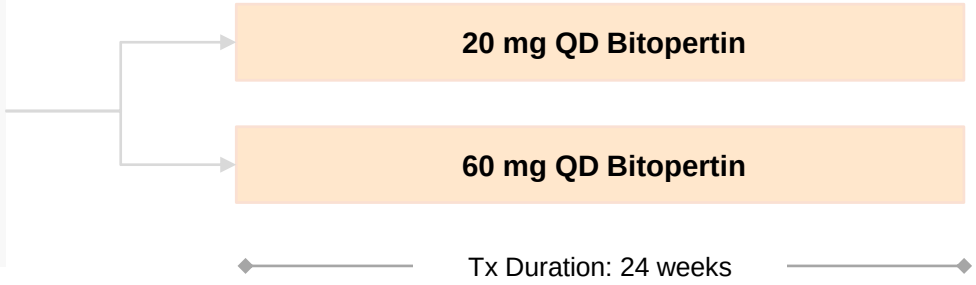
BEACON Trial: Open-Label Ph 2 Trial in EPP / XLP

Open-label, parallel-dose trial to establish POC and assess efficacy, safety in patients

Trial Design

- Open-label, randomized
- EPP and XLP
- Fully enrolled for adults and adolescents (ages 12-18)
- Two dose levels, parallel
- Not receiving afamelanotide
- Australia

Treatment Arms



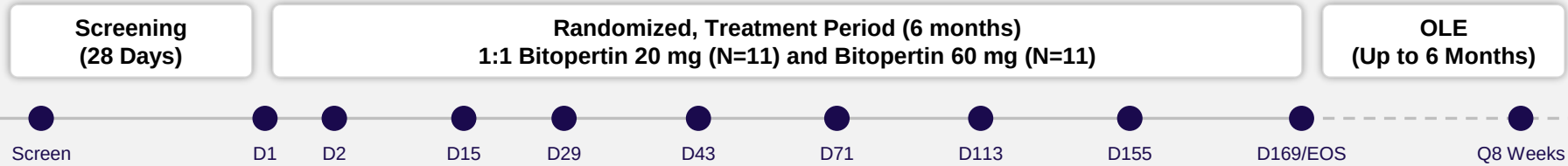
Trial endpoints: Changes in blood PPIX levels, light tolerance, time to prodromal symptom (TTPS), QOL, safety, tolerability, and PK

Data availability: Data on all patients presented at ASH 2023 (PPIX data, light tolerance, including the precedented pivotal endpoint, and safety)

Time to prodromal symptom = the time until a patient experiences an early warning signal of a phototoxic attack, measured through a weekly sunlight challenge; QD = daily, Tx = treatment; POC = proof of concept; QOL = quality of life

ASH 2023 BEACON Data: Trial Overview

Enrollment data as of 20 Oct 2023



	Bitopertin 20 mg (n=11)	Bitopertin 60 mg (n=11)	Total (n=22)
Enrolled	11	11	22
Completed Day 43	11	11	22
Completed Day 113	9	8	17
Completed Treatment Period (Day 169)	7	7	14

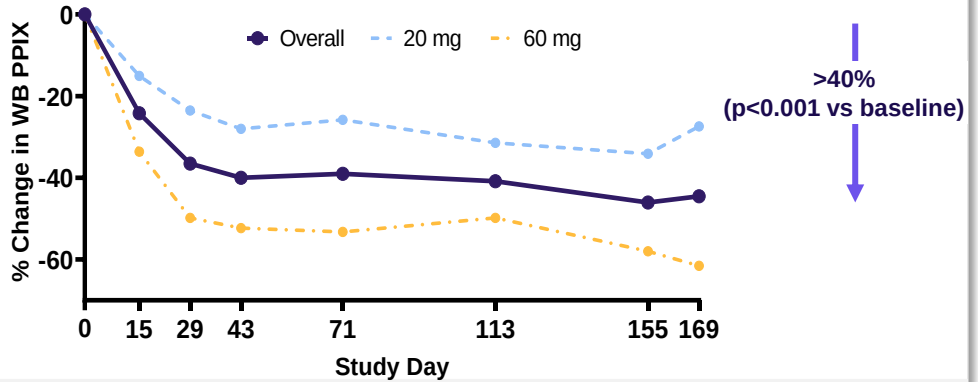
Study population is ~64% female with an average age of 44 years (range 20-73)

D = day; EOS = end of study; OLE = open-label extension

ASH 2023 BEACON Data: % Change in Whole-Blood PPIX

- Bitopertin significantly reduced whole-blood (WB) metal-free PPIX levels by >40%
- Dose-dependent reductions were observed across broad range of baseline whole-blood PPIX levels (144-3,410 µg/dL)

PPIX Changes Over Time

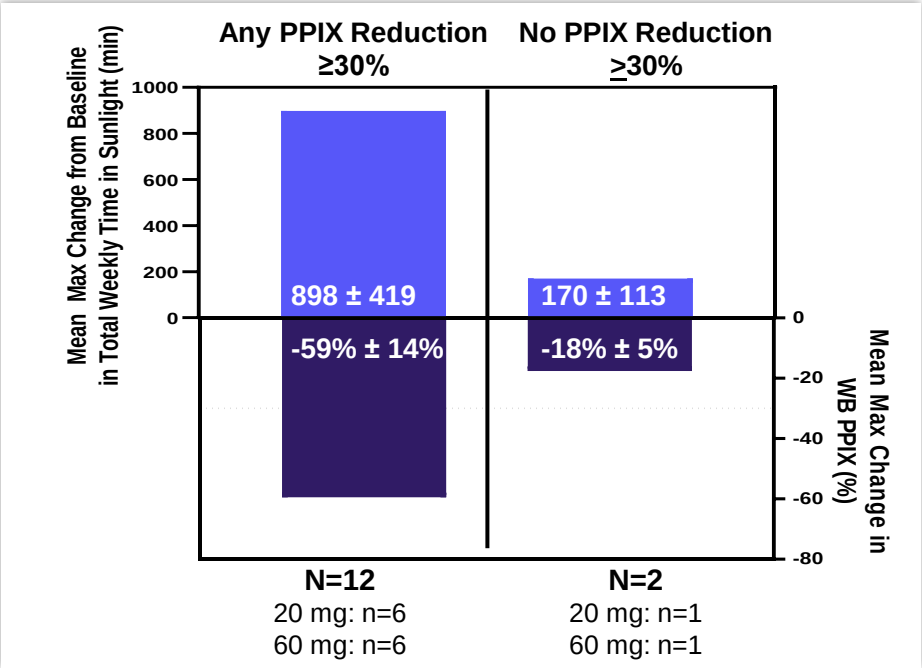


Overall N	22	22	20	22	16	16	13	8
20 mg	11	11	10	11	9	9	7	4
60 mg	11	11	10	11	7	7	6	4

PPIX data as of 18 September 2023. Least-squares means for percent changes in PPIX were analyzed using a mixed model for repeated measures; each dose group had a statistically significant reduction from baseline (20 mg p=0.0016, 60 mg p<0.0001).

ASH 2023 BEACON Data: PPIX and Light Tolerance

- Improvements in light tolerance were observed in every patients
- Greatest improvements in light tolerance seen in participants with any PPIX reduction ≥30%

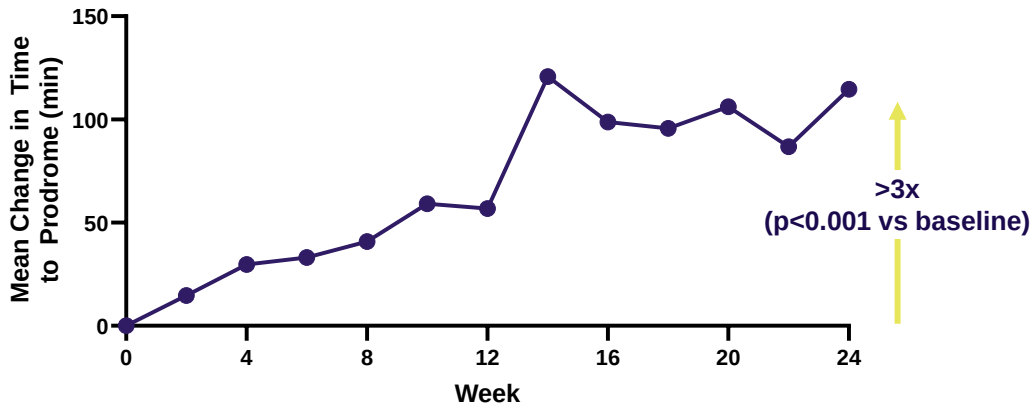


Data cutoff of October 20, 2023; Maximum changes from baseline in weekly total time in sunlight as assessed with a daily diary. Includes only participants who have completed through Day 169/EOS.

ASH 2023 BEACON Data: Time to Prodrome

- Improvements in light tolerance during sunlight-exposure challenges were significant (>3x) and increased with time

Time to Prodrome



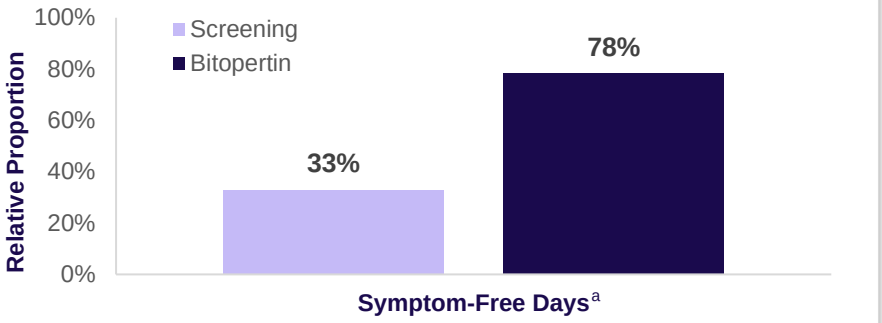
No. of Participants[a]	22	19	21	20	19	18	21	15	15	17	14	16	14
No. of Challenges	69	45	46	43	44	42	40	32	35	46	32	47	33

[a] The number of subjects with at least 1 sunlight-exposure challenge during a 2-week period. Time to prodrome data from weekly sunlight-exposure challenges were averaged over a 2-week period, including cumulative time in sunlight challenges where the participant did not report a prodrome, and were analyzed using MMRM for both 20 mg and 60 mg bitopertin dose groups combined.

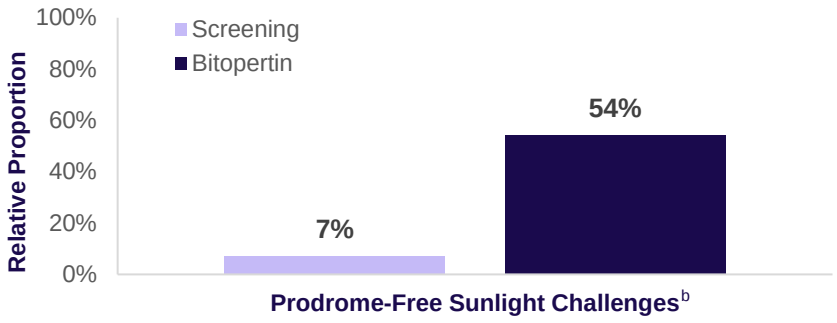
ASH 2023 BEACON Data: Light Tolerance

Days without Symptoms or Prodromes

- 92% reduction in patient-reported full phototoxic reactions[a]
- An increase in the proportion of total symptom-free days (no prodrome / early warning symptoms or full phototoxic reactions) with sunlight exposure was observed



	Days w/ Sunlight Exposure[c]
Screening	231
On-Treatment	2138

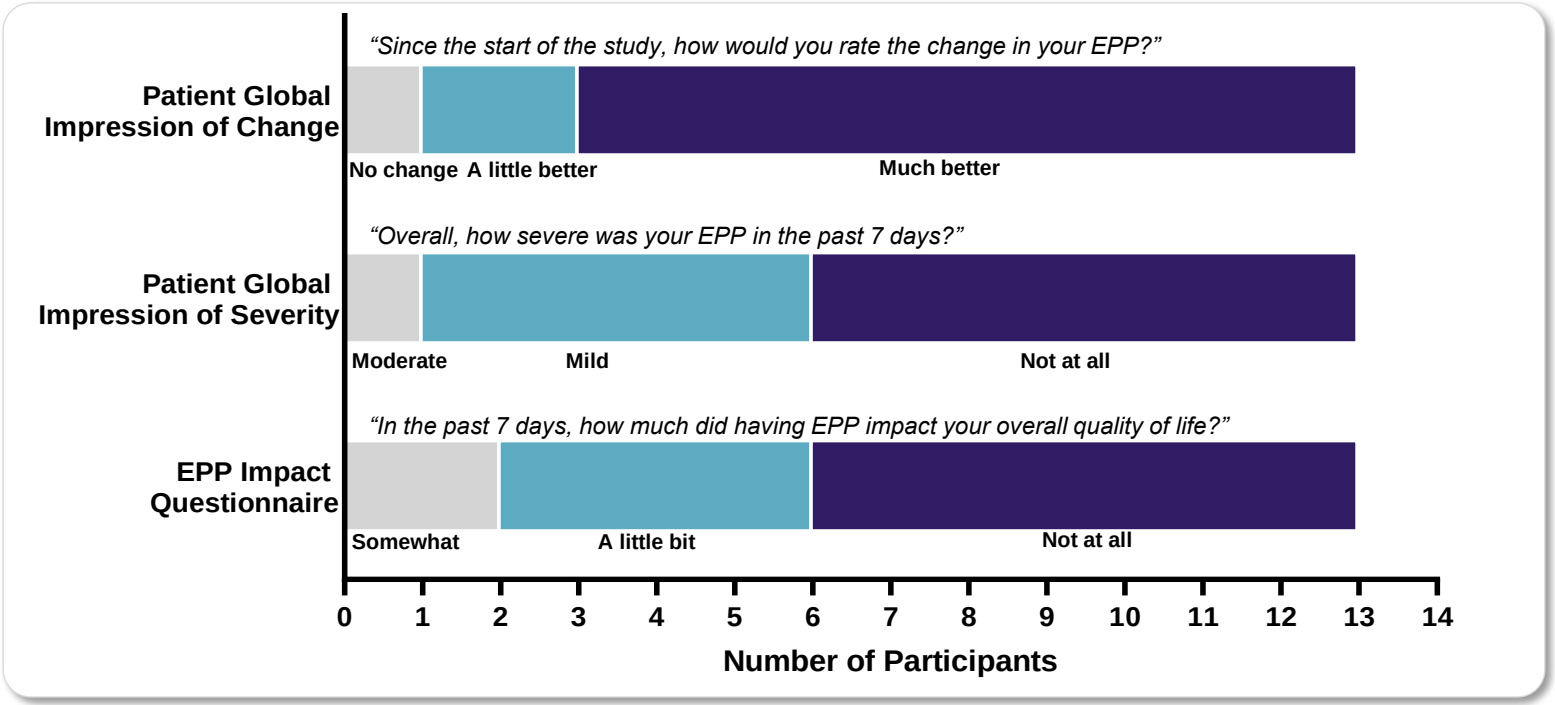


	Sunlight Challenges[c]
Screening	69
On-Treatment	623

[a] As assessed with a daily diary; [b] As assessed with a weekly sunlight challenge; [c] Summed across all participants. Percentages calculated relative to total number of days with sunlight exposure (left) or total number of weekly sunlight exposure challenges (right) from all study participants (n=22) during screening or while receiving bitopertin (20 mg and 60 mg dose groups combined).

ASH 2023 BEACON Data: Measures of Quality of Life

- Nearly all participants reported improvements in multiple quality-of-life measures at end of study

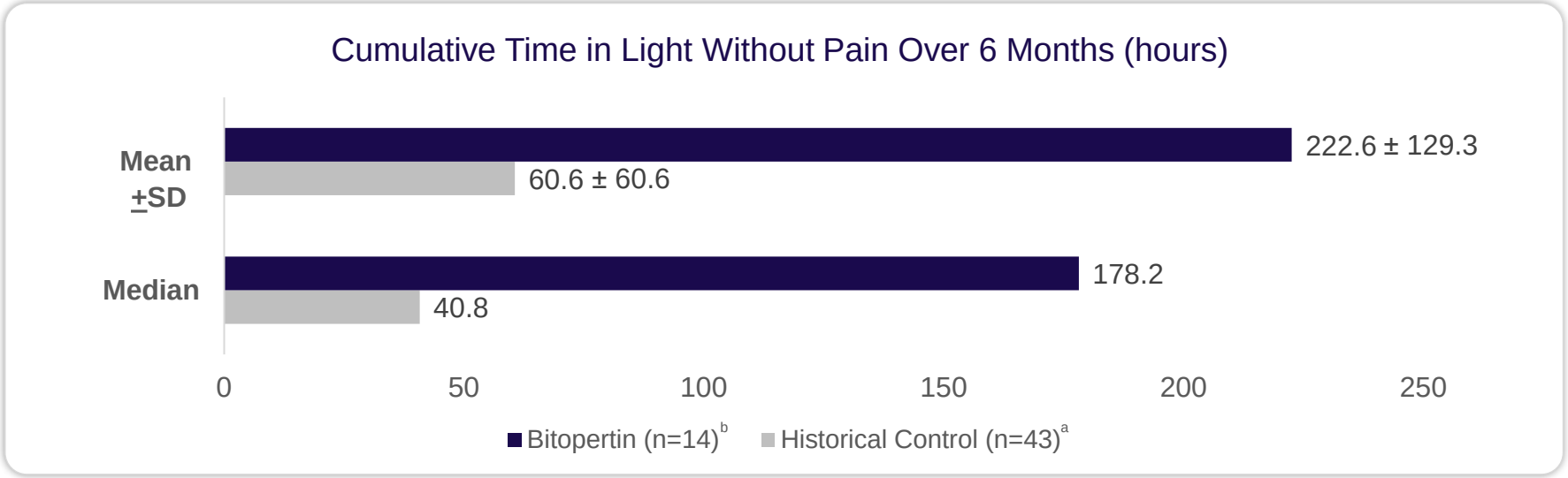


Only 13 participants who completed through Day 169/EOS with QOL responses.

ASH 2023 BEACON Data: Precedented Pivotal Endpoint

Cumulative Time in Light on Days without Pain

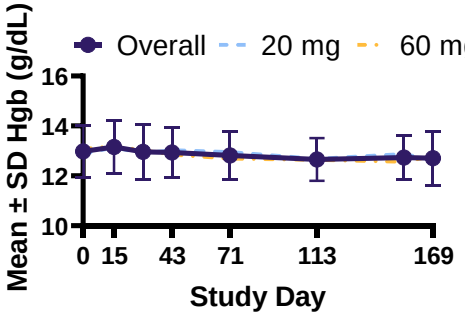
- Cumulative total time in light observed over 6-month treatment period with bitopertin represents >3x increase relative to historical control
- Improvements in average daily light tolerance with bitopertin increased with time



[a] Placebo arm from prior Phase 3 study in EPP (Langendonk et al. [2015] NEJM). [b] Includes data from participants who completed EOS visit (D169).
Cumulative time in light measured via daily diary, adding all time in light between the hours of 10 am and 6 pm on days without any pain; SD = standard deviation

ASH 2023 BEACON Data: Safety and Tolerability

- No serious adverse events
- Stable mean Hgb levels; no anemia AEs reported
- Favorable safety profile consistent with prior studies enrolling >4,000 participants
- Safety profile supports enrollment of adolescents



	Bitopertin 20 mg (n=11)	Bitopertin 60 mg (n=11)	Total (n=22)
Subjects with any TEAE	9 (82%)	9 (82%)	18 (82%)
TEAEs leading to discontinuation	1 (9%)[a]	0	1 (5%)
TEAEs reported in >1 subject			
Dizziness	3 (27%)	4 (36%)	7 (32%)
Lightheadedness	3 (27%)	2 (18%)	5 (23%)
Headache	3 (27%)	1 (9%)	4 (18%)
Nausea	1 (9%)	2 (18%)	3 (14%)

Includes all coded AE data as of 20 October 2023. [a] Grade 3 TEAE reported as "localized headache."
AE = adverse event; Hgb = hemoglobin; TEAE = treatment-emergent adverse event; SD = standard deviation

Key Takeaways from Updated BEACON Data at ASH

Proof of Concept

Significant reduction in PPIX at low and high doses

Functional Outcomes

Significant improvement in sunlight tolerance, including on precedented pivotal endpoint

Quality of Life Impact

Patients reported an improved quality of life

Safety

Generally well tolerated and no meaningful change in hemoglobin observed with bitopertin

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)

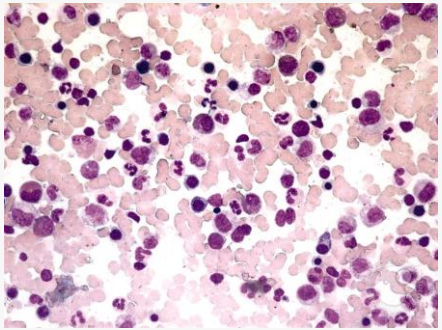
No approved treatments for DBA

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

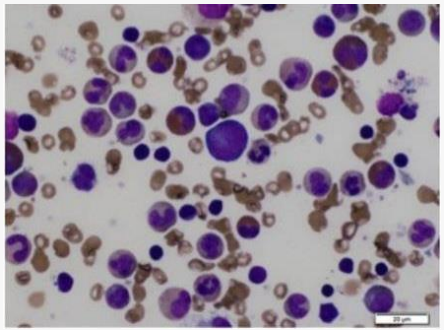
Rare disease with an incidence rate of 5-7 per 1 million live births

- Estimated worldwide prevalence of 5,000

Normal



DBA

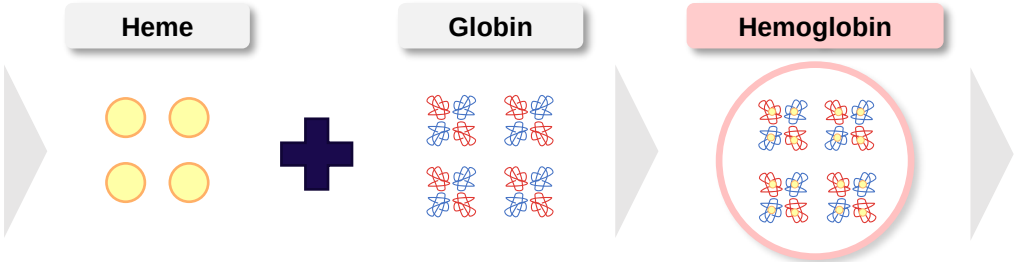


St. Jude's Children Hospital; Fatima et al, *Pediatric Hematology Oncology Journal*, March 2021;

Diamond Blackfan Anemia: Heme Toxicity

Normal Erythropoiesis

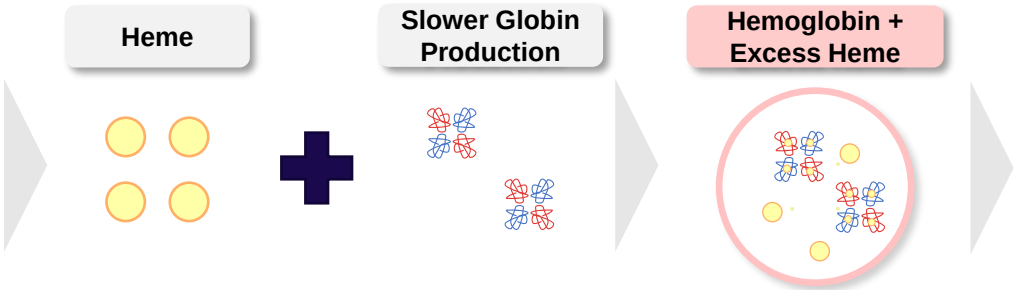
Glycine
Critical and initiating precursor for heme biosynthesis and is supplied by **GlyT1 transporter**



Complete Maturation

DBA Erythropoiesis

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



Heme toxicity and cell death

Yang et al, 2016 (Jan Abkowitz lab), Sci Transl Med. 8:338ra67, 2016

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**

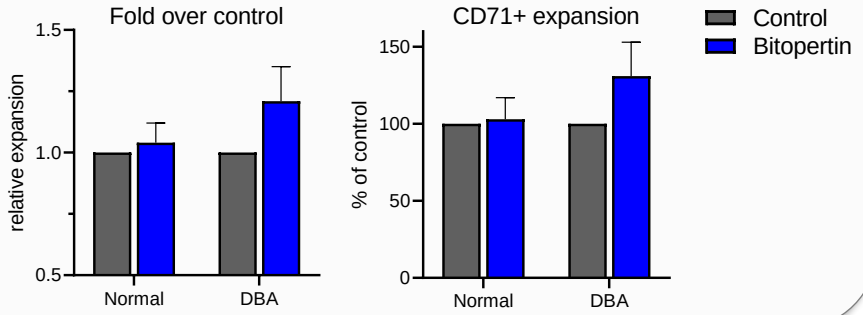
Less Heme

Slower Globin Production

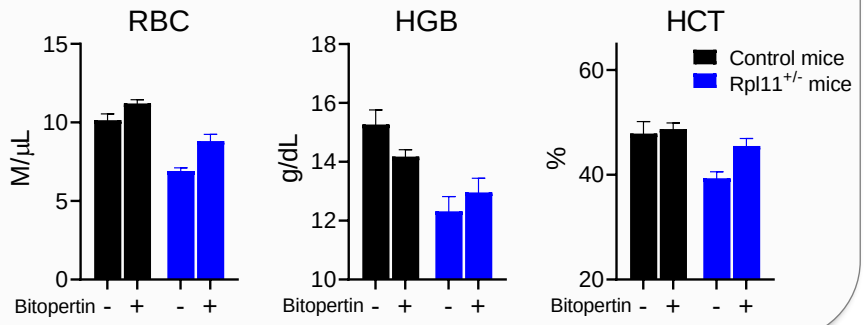
Hemoglobin

Complete Maturation

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



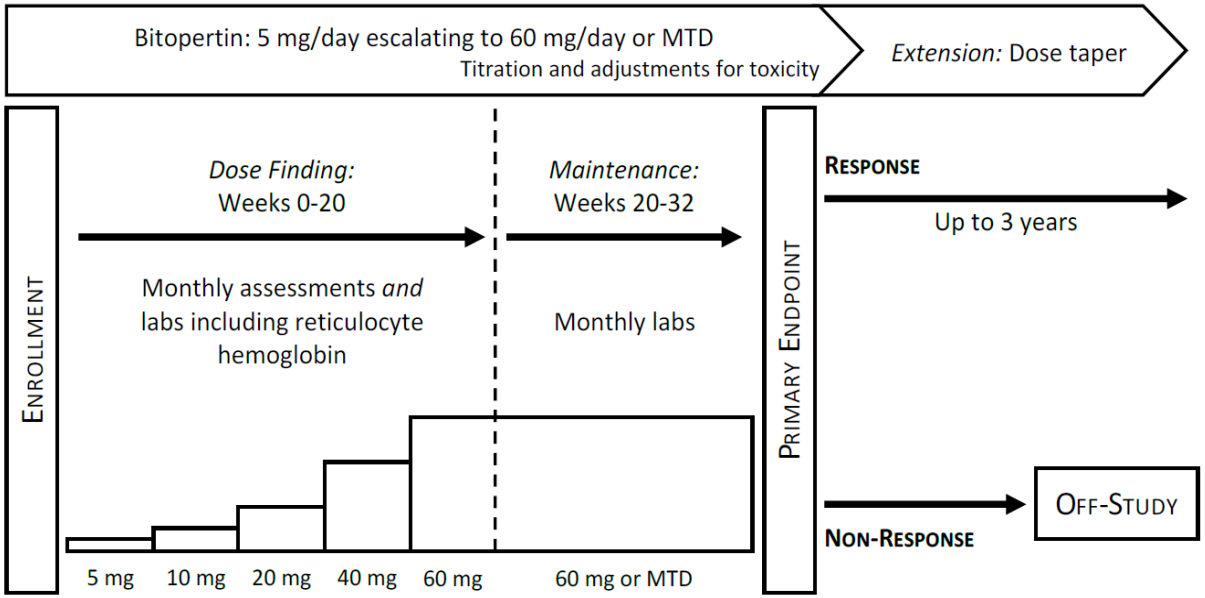
Rpl11 haploinsufficient mice were treated with 100 ppm bitopertin in chow (20 mg/kg/d) for 8 weeks



Diamond Blackfan Anemia Phase 2 Clinical Trial

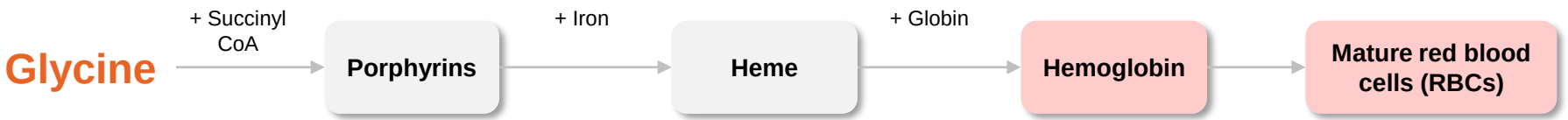
IIT conducted by the NIH under CRADA with Disc

- 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



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

Hepcidin Modulation

Iron Homeostasis

Iron is Fundamental to RBC Biology

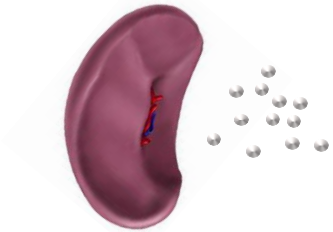
Hepcidin is a regulatory hormone that plays a central role in iron metabolism and homeostasis

Induced by Inflammation

Hepcidin

Gatekeeper Function: Blocks iron absorption and recycling

GI Tract
Iron Intake



Spleen
Iron Storage

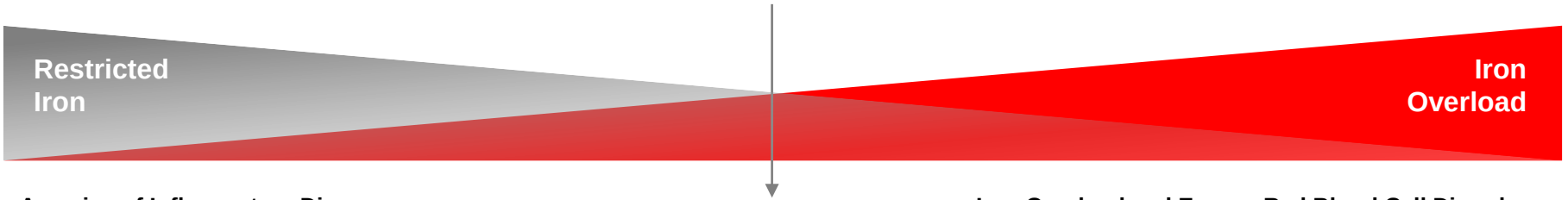
RBC Production in Bone Marrow

Hepcidin is a Therapeutic Target for Diseases

Dysregulated hepcidin drives a wide range of hematologic diseases

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

Regulated erythropoiesis



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

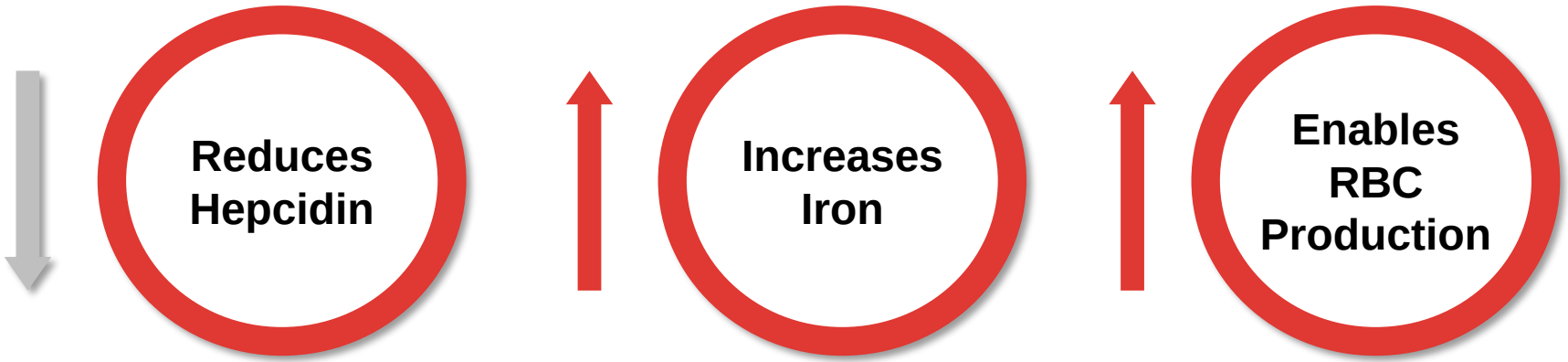
DISC-0974

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%

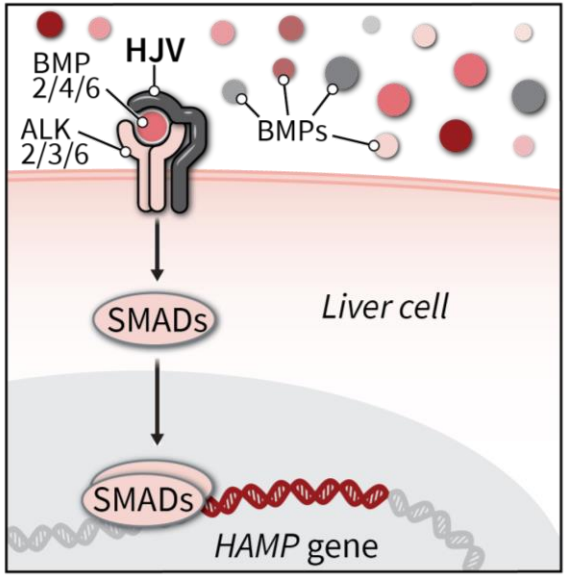
- **Anemia of inflammation** is the 2nd most common form of anemia
- **Estimated 40% of all anemias** are driven by or have an inflammatory component
- **Hepcidin is up-regulated** and correlates with anemia, driven by inflammation

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

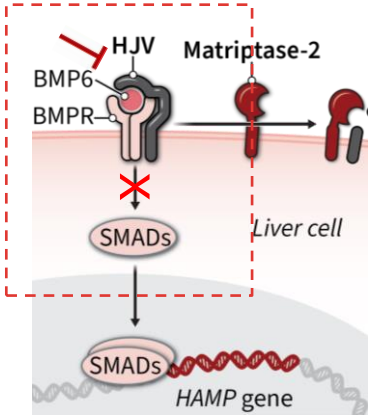
- **Genetic validation** in patients with Juvenile Hemochromatosis (lower hepcidin and elevated iron levels)
  - Loss-of-function mutations in HJV are phenotypically indistinguishable from mutations in *HAMP* (hepcidin) gene
- **Functionally specific** to hepcidin / iron
- **Tissue specific** expression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

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

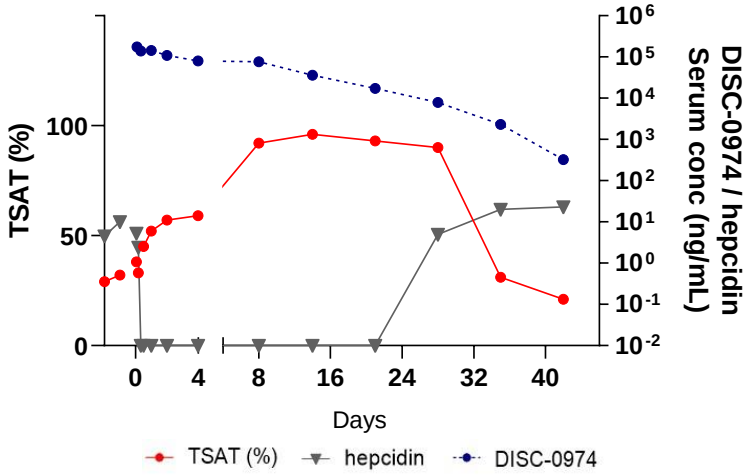
DISC-0974 Mechanism of Action

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)

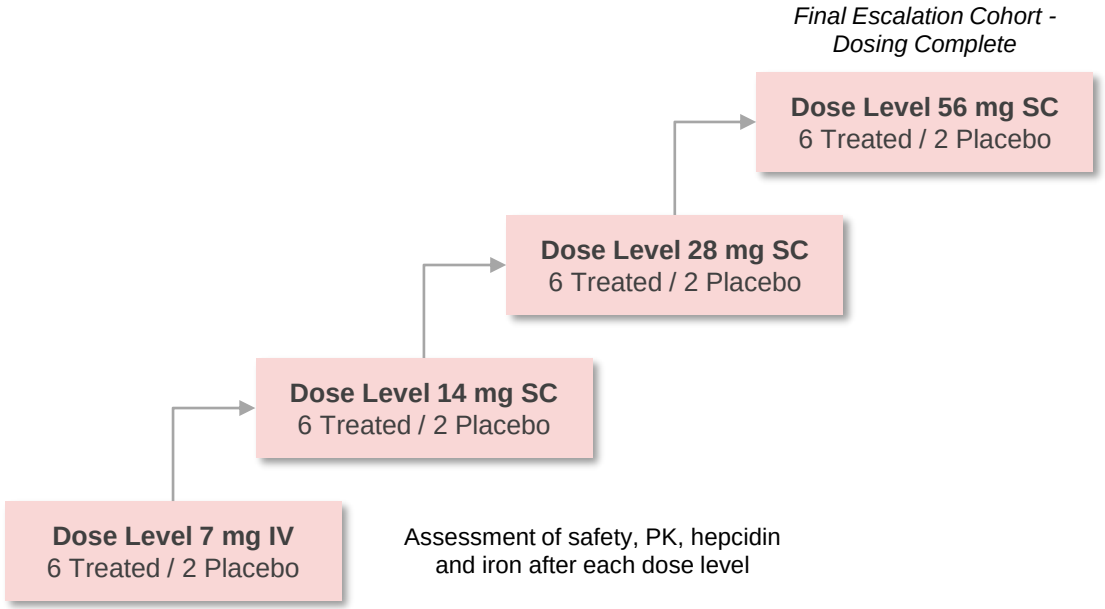


Phase 1 SAD Trial in Healthy Volunteers

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)

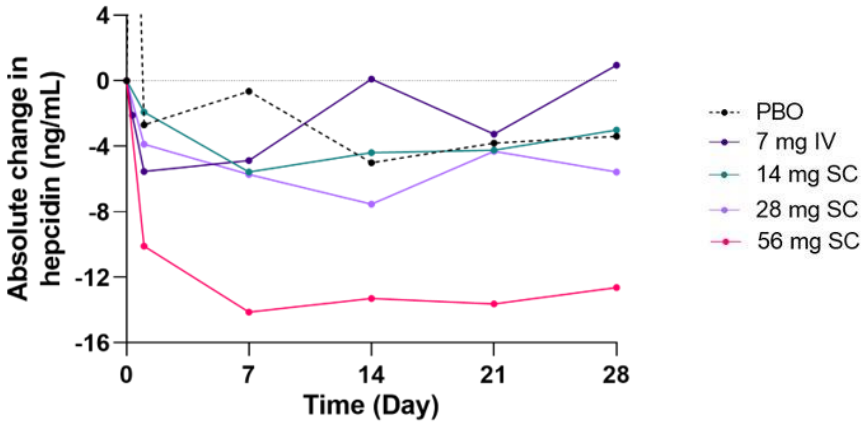


TSAT = transferrin saturation; IV = intravenous; SC = subcutaneous

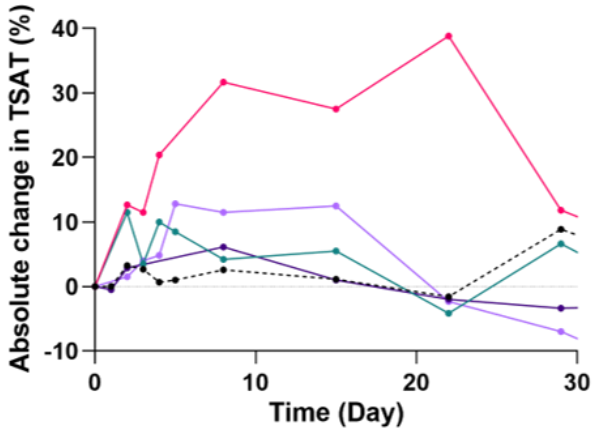
DISC-0974 Phase 1 SAD Data

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

DISC-0974 Reduced Hepcidin Production



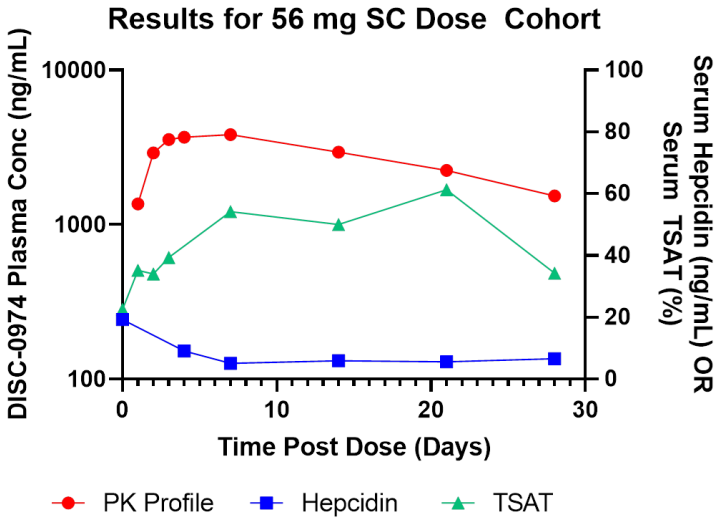
DISC-0974 Increased TSAT

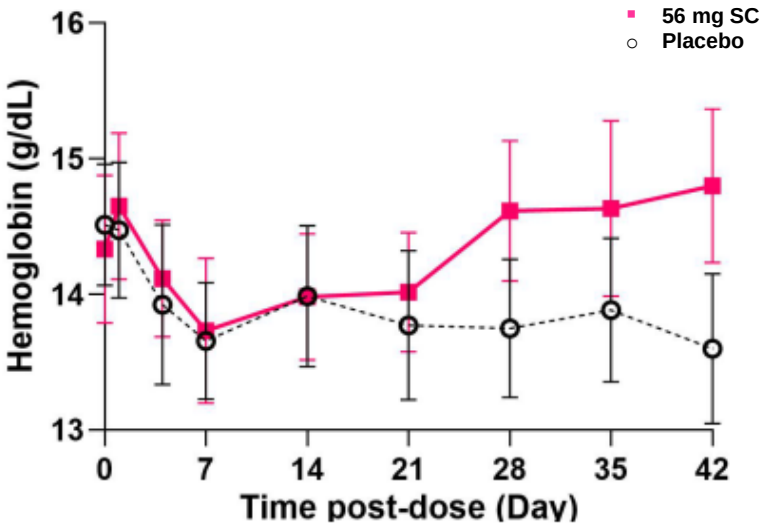


TSAT = transferrin saturation; SAD = single ascending dose

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

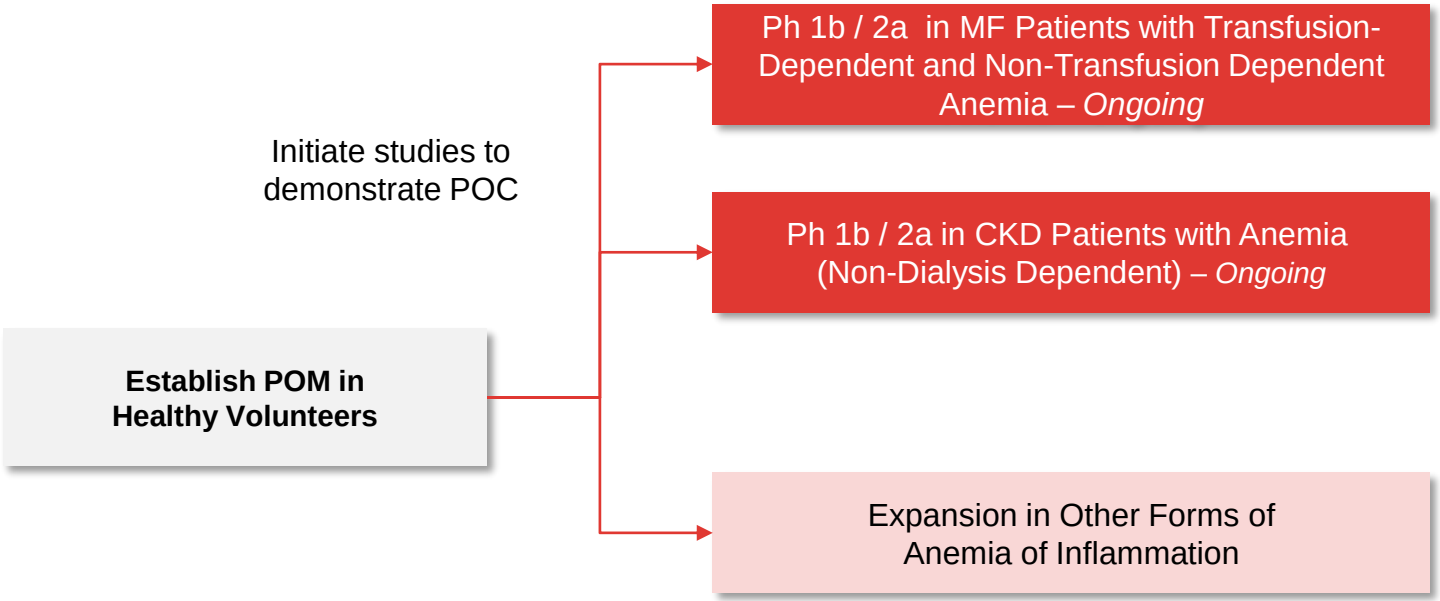
DISC-0974 Phase 1 SAD Safety

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

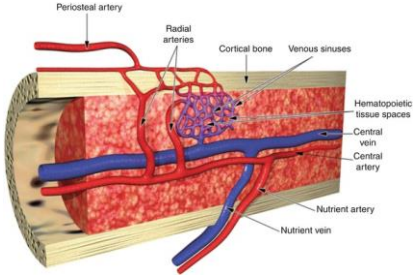
Aim to demonstrate POC in anemia of MF and CKD

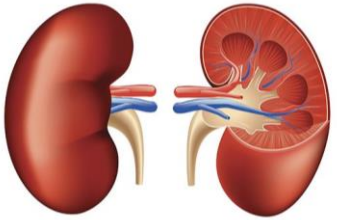


Plan to assess safety, PK, hepcidin, iron, hemoglobin and transfusion burden (MF) and others

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

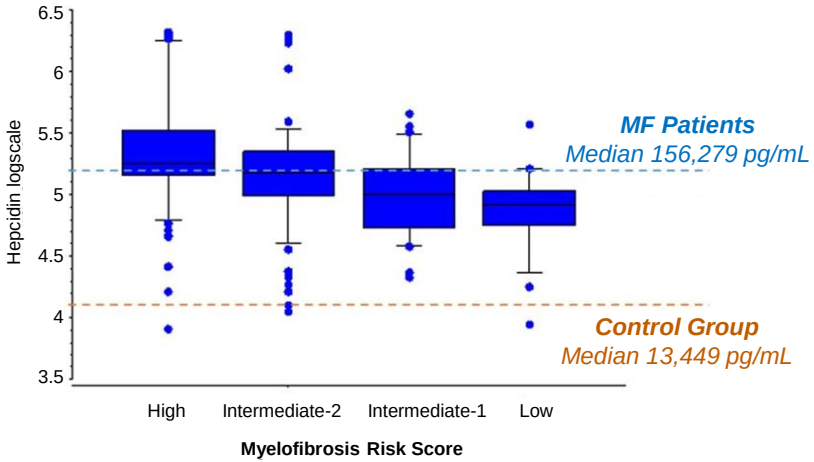
NDD: Non-Dialysis Dependent; DD: Dialysis Dependent

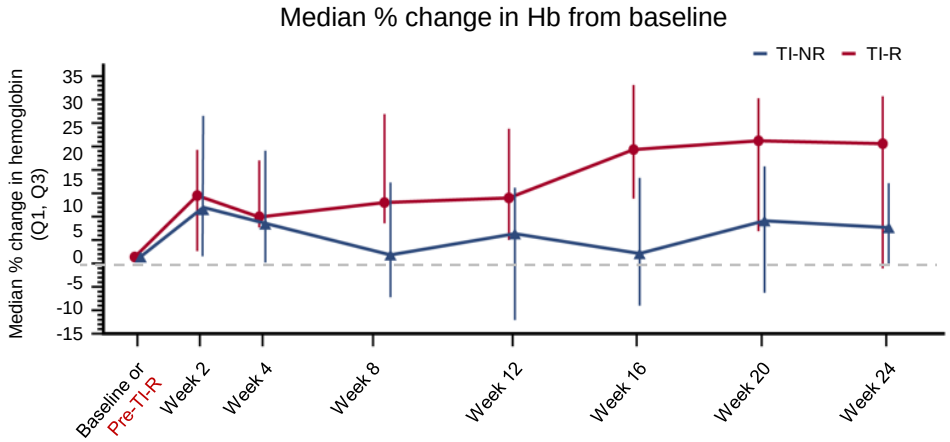
Hepcidin is a Key Driver of MF Anemia

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; *from third party

DISC-0974 MF Anemia Trial Overview

Data as of October 20, 2023

Phase 1b Dose Escalation

Design

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

Treatment Duration: 6 cycles (q28d)

Phase 2 Planned for Transfusion Dependent (TD) and Non-Transfusion Dependent (NTD)

Study Population

- N = 40-50
- Severity: DIPSS INT-2/High
- Planning transfusion-dependent and non-transfusion-dependent patients
- +/- JAK inhibitor permitted

Design

- Open-label
- Flexibility to add additional exploratory cohorts
- Key endpoints:
  - Transfusion independence (TI)
  - Hgb, iron, hepcidin, hematologic parameters

Treatment Duration: 6 cycles (q28d)

Data availability: Initial data presented at ASH 2023; updated Phase 1b data to be presented 1H 2024

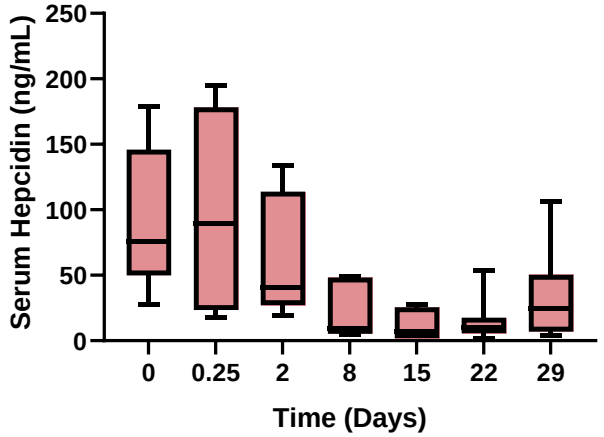
	DISC-0974 14 mg	DISC-0974 28 mg	DISC-0974 50 mg	Total
Enrolled	1	7	3	11
Concomitant JAK use	0	4 (57.1%)	0	4
Transfusion Dependent*	0	2 (28.6%)	0	2
Median Time Since Diagnosis (yrs)	1	6 (0-18)	2 (0-14)	-

*Defined as an RBC transfusion frequency of ≥6 units packed RBCs (PRBC) over the 84 days immediately prior to Screening. There must not be any consecutive 42-day period without an RBC transfusion in the 84-day period, and the last transfusion must be within 28 days prior to Screening; †Note: In Part 1, expect one patient per cohort until iron mechanism is engaged; BOIN = Bayesian Optimal Interval; DIPSS = Dynamic International Prognostic Scoring System; Hgb = hemoglobin; INT = intermediate; JAK = Janus kinase; q28d = every 28 days; SC = subcutaneous; DIPSS = Dynamic International Prognostic Scoring System

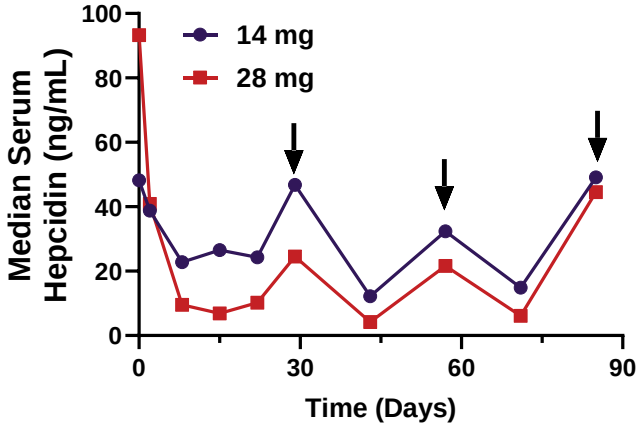
Initial DISC-0974 Anemia of MF Data: Hepcidin

- DISC-0974 decreased hepcidin in a dose-dependent manner
- Hepcidin decreases were consistent across all treated patients

Median and Range of Serum Hepcidin after 28 mg Dose



Median Serum Hepcidin

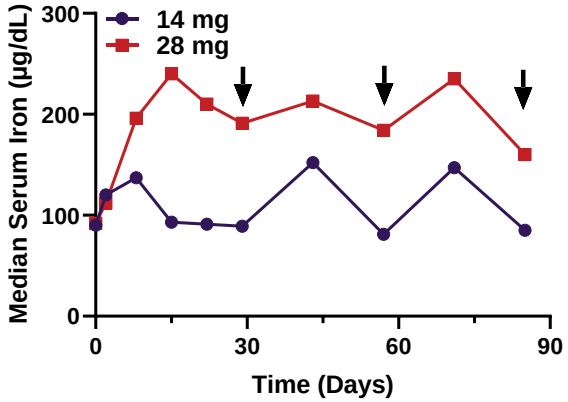


Arrows represent dosing days

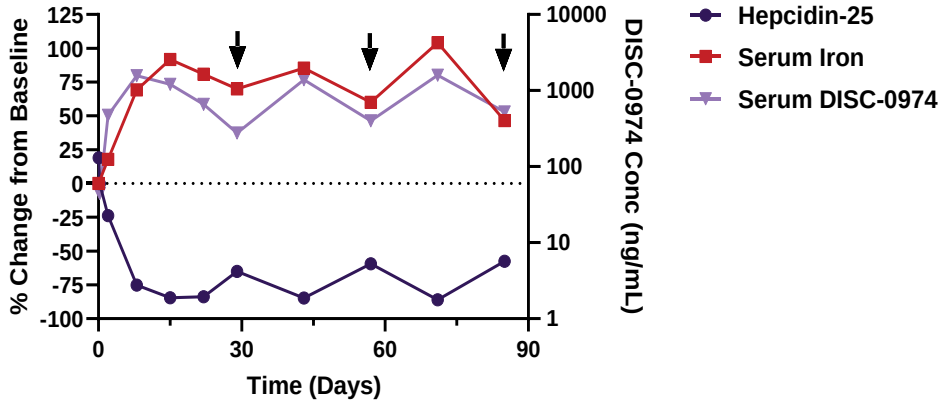
ASH 2023 DISC-0974 Anemia of MF Data: Serum Iron

- Serum iron increased in a dose-dependent manner
- Dosing at 28 mg led to a >75% decrease in serum hepcidin and a >75% increase in serum iron

Median Serum Iron



Hepcidin and Iron Change Relative to Baseline and DISC-0974 Concentration at 28 mg

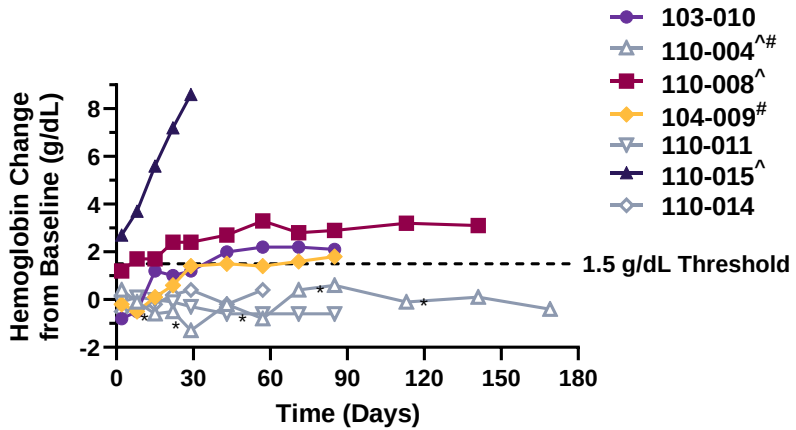


Arrows represent dosing days

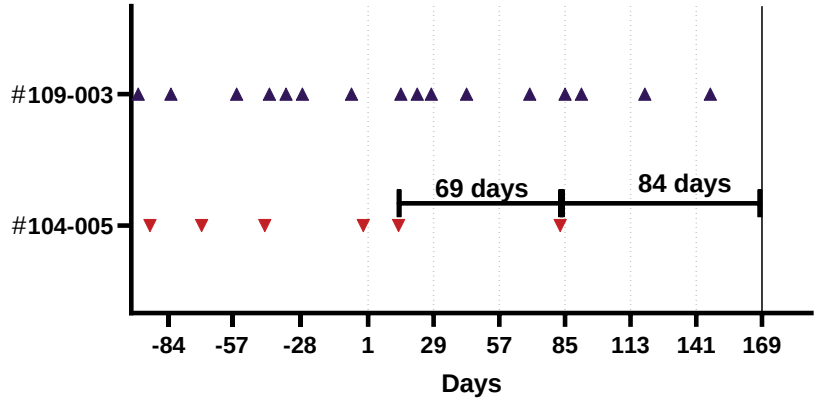
ASH 2023 DISC-0974 Anemia of MF Data: Hematologic Response

- Four of seven evaluable NTD subjects (57%) had ≥1.5 g/dL hemoglobin increase from baseline; effect was seen regardless of concomitant JAK inhibitor use
- One of the two transfusion-dependent subjects receiving 28 mg achieved transfusion independence[1]

Hemoglobin Increase from Baseline in NTD Patients



Transfusion Frequency in TD Patients



[1]Gale criteria *(Leukemia Research 35* (2011)*);* Five NTD subjects received 28 mg (103-010, 110-004, 110-008, 104-009, 110-011) and two subjects received 50 mg (110-014, 110-015) of DISC-0974 for more than 28 days as of the data cut; *Indicates transfusion. ^ Indicates transfusion during screening. # Indicates concomitant JAK inhibitor use.
NTD = non-transfusion dependent; TD = transfusion dependent

ASH 2023 DISC-0974 Anemia of MF Data: Safety

- Generally well tolerated at all evaluated dose levels
- Majority of AEs deemed not related to DISC-0974

AEs Occurring in ≥2 Subjects	14 mg DISC-0974 (N=1)		28 mg DISC-0974 (N=7)		50 mg DISC-0974 (N=3)	
	Any Grade	Grade 3	Any Grade	Grade 3	Any Grade	Grade 3
Subjects with event (n)	**0**	**0**	**6**	**3**	**2**	**1**
Fatigue	0	0	3	0	0	0
Anemia	0	0	4	2	1	1
Diarrhea	0	0	2	0	1	0
Nausea	0	0	2	0	0	0

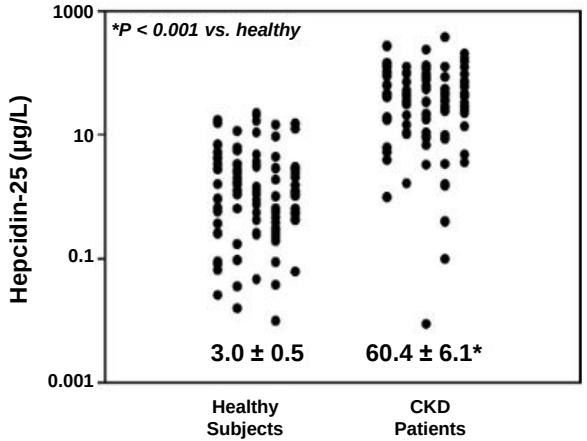
Related AEs: 1 subject with Grade 2 diarrhea treated at 50 mg. Grade 3 AE: headache was reported in 1 subject treated at 28 mg, unlikely related to DISC-0974. Serious AE: Grade 2 hip pain was reported in 1 subject treated at 28 mg, not related to DISC-0974. There were no ≥ Grade 4 AEs reported. AE = adverse event

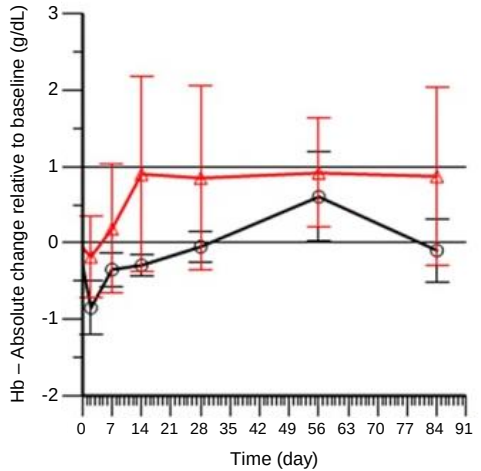
Hepcidin is a Key Driver of CKD Anemia

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



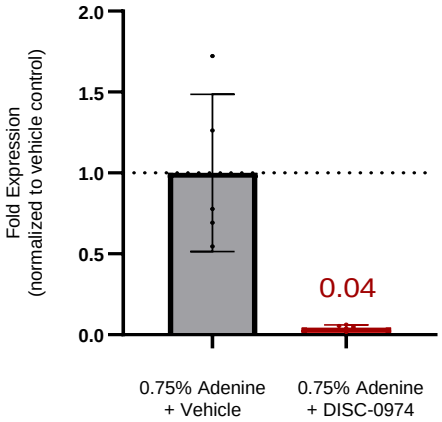


Sources: Troutt et al. (2013), *J Clin Lab Analy*; Sheetz et al. (2019) *Br J Clin Pharmacol.* (2019); *from third party

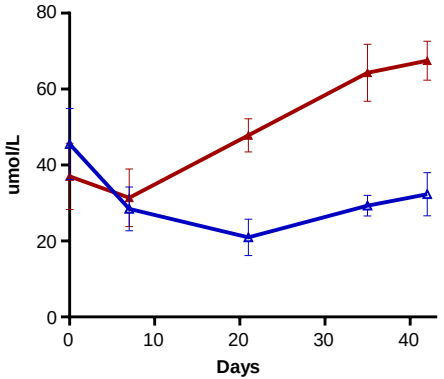
DISC-0974 Improved Anemia in Model of CKD

Rat Model of Adenine Diet-Induced CKD

DISC-0974 Reduced Hepcidin Expression

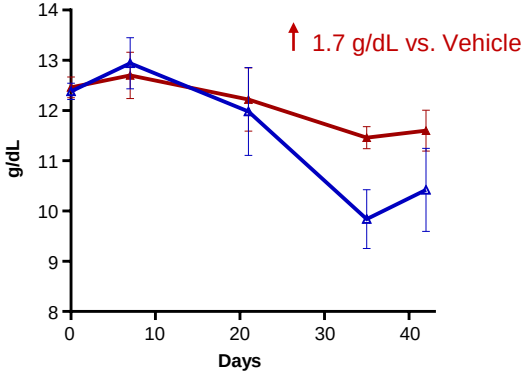


DISC-0974 Increased Serum Iron



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

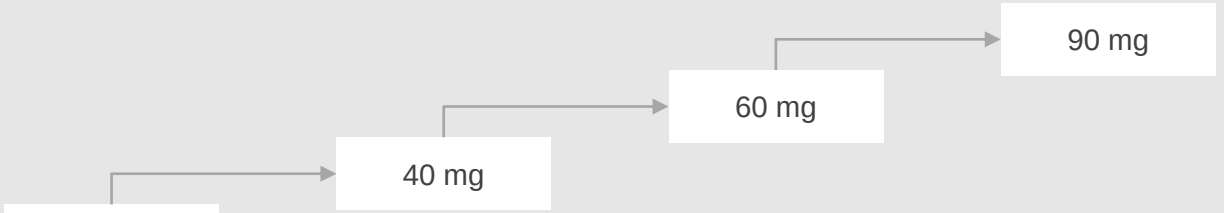
DISC-0974 NDD-CKD Anemia Trial Overview

Data as of October 20, 2023

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



N = 8 per Cohort (6 Active, 2 Placebo)
Assessment of safety, PK, hepcidin, and iron after each dose level

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

Data availability: Initial data presented at ASH 2023; updated Phase 1b data to be presented 2H 2024

	DISC-0974 28 mg	Placebo
Enrolled	6	2
Median Age (range), years	69.5 (55, 78)	74.5 (73, 76)
Median Baseline Hemoglobin (range), g/dL	9.7 (7.9, 10.5)	9.5 (9, 10)

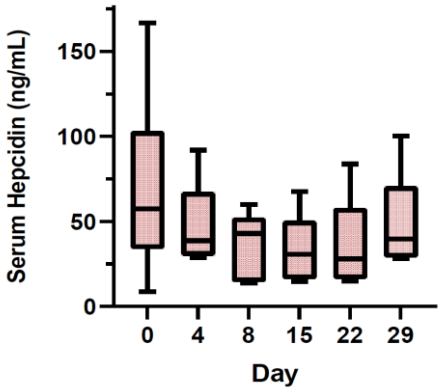
CKD = chronic kidney disease; Hgb = hemoglobin; NDD = non-dialysis dependent; PK = pharmacokinetics; TSAT = transferrin saturation

ASH 2023 DISC-0974 Anemia of CKD Data: Hepcidin and Iron

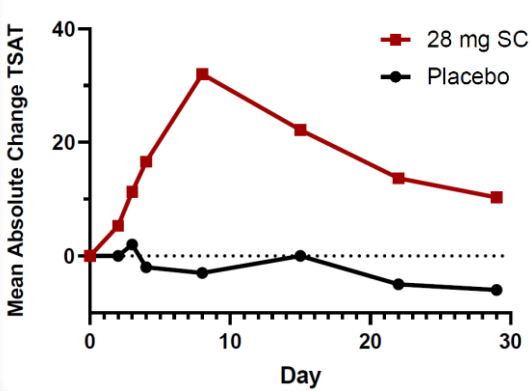
First Cohort: 28 mg SC

- Meaningful reduction in serum hepcidin with corresponding increase in serum iron
- Similar PK/PD relationship as seen in healthy volunteers

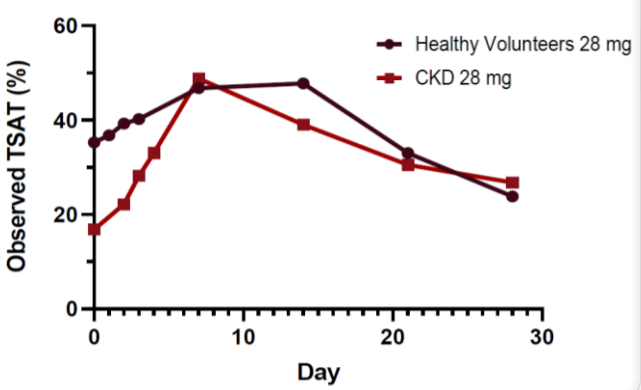
Hepcidin Changes Over Time



Iron Changes Over Time



Iron Changes Over Time vs. HV



Safety: DISC-0974 was generally well tolerated to date; 2 subjects treated with DISC-0974 28 mg had a TEAE (33%) vs. 2 on placebo (100%); 2 treated subjects had SAEs deemed not related to DISC-0974*

1 patient received IV iron during study week 4. For this patient, the iron and hepcidin data through week 3 only was included in this analysis; *1 "atrial fibrillation" and 1 "worsening of end stage renal disease; CKD = chronic kidney disease; HV = healthy volunteer; IV = intravenous; PK/PD = pharmacokinetic/pharmacodynamic; SAE = serious adverse event; SC = subcutaneous; TEAE = treatment-emergent adverse event

Key Takeaways from ASH 2023 DISC-0974 Data

Initial Proof of Concept

Dose-dependent, meaningful reductions in hepcidin and increases in iron

Signal of Hematologic Response

Improvements in hemoglobin and transfusion burden across broad range of MF patients

Safety

Generally well tolerated at all evaluated dose levels

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

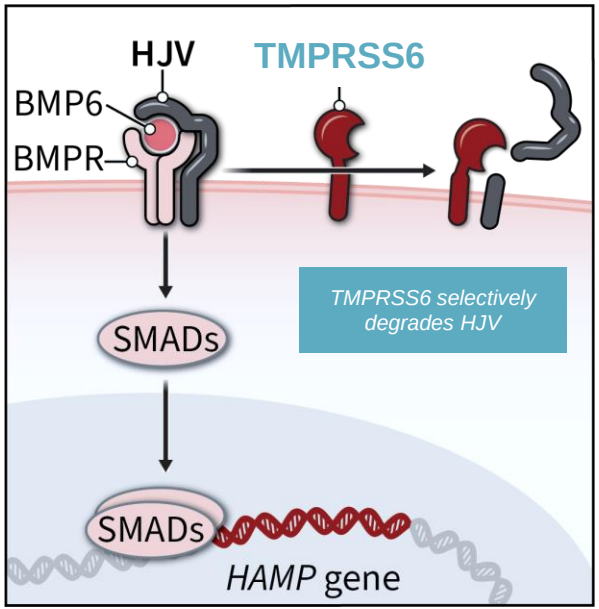
Enables Endogenous Production of Hepcidin

Promotes Iron Restriction
Decreases GI Absorption

Erythrocytosis (PV)
Ineffective Erythropoiesis
Iron Overload

Targeting TMPRSS6 to Increase Hepcidin

Potent, specific target controls endogenous hepcidin production



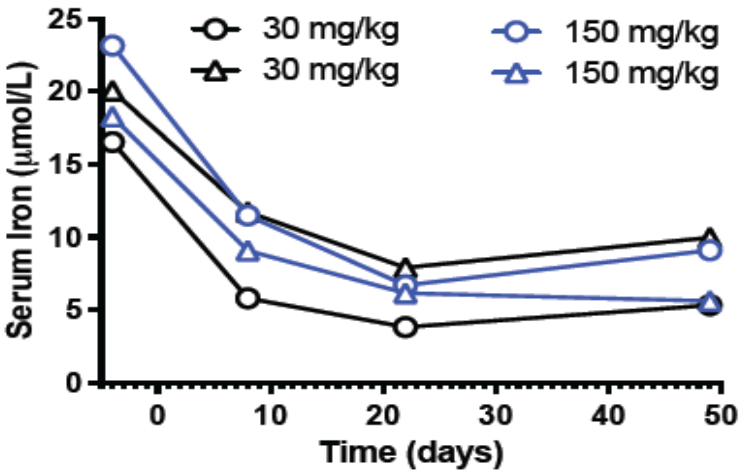
Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

- **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



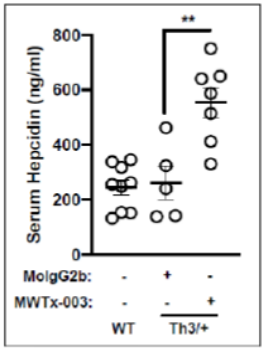
- Potent PD effects observed across multiple preclinical studies consistent with TMPRSS6 inhibition
  - Hepcidin: 3-4 fold induction
  - Serum iron: ~60-70% suppression
- DISC-3405 demonstrated excellent safety profile in non-clinical GLP safety studies

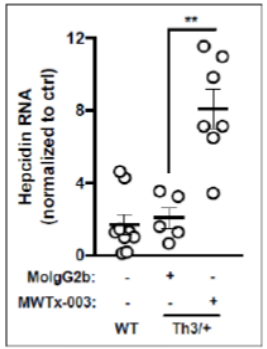
Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting

Effects in HbbTh3/+ Model of Beta-Thalassemia

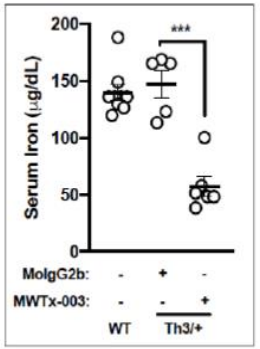
Significant effects on hallmarks of disease including iron overload, ineffective erythropoiesis and splenomegaly were observed

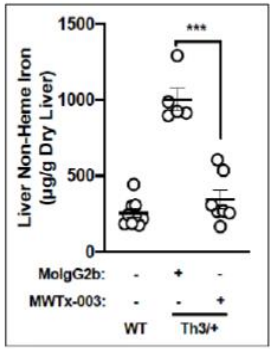
↑ Hepcidin Production
Up to 4-fold (mRNA)



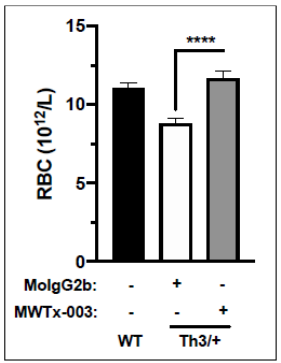


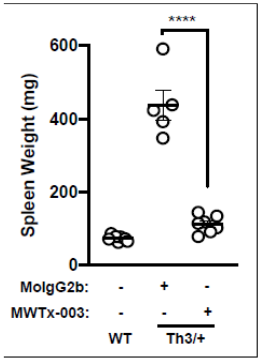
↓ Serum and Liver Iron
60-65% Reduction





↑ RBC Production
↓ Spleen Weight



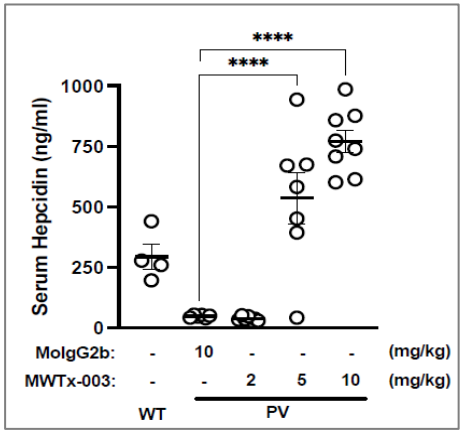


Chen B. et al Blood (2021) 138 (Supplement 1): 941, ASH 2021 Annual Meeting; HbbTh3/+ mice were treated with the lead anti-TMPRSS6 antibody at 10 mg/kg IP for 4 weeks

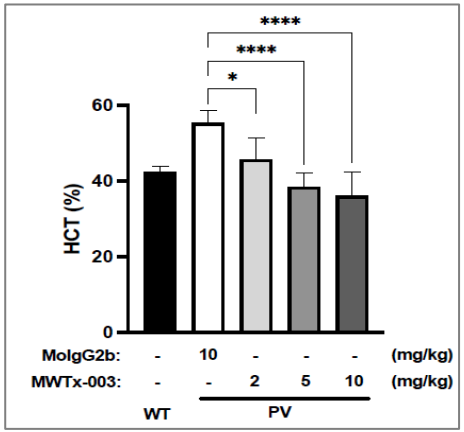
Effects in Jak2^{V617F} model of Polycythemia Vera

Significant effects on hallmarks of disease including hematocrit, hemoglobin, and RBC production

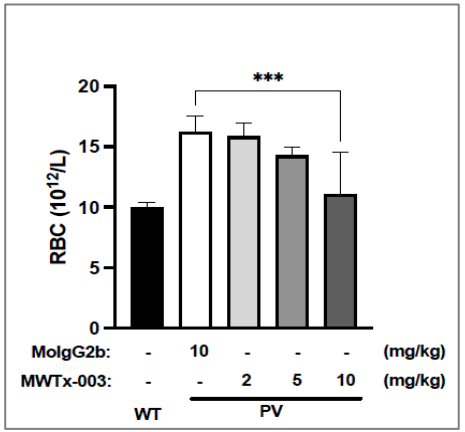
↑ Hepcidin Production



↓ Hematocrit



↓ RBC Production



Chen B. et al, ASH 2023 Annual Meeting; JAK2^{V617F} 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 Oct. ’23

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

Phase 2 Proof-of-Concept Trial 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

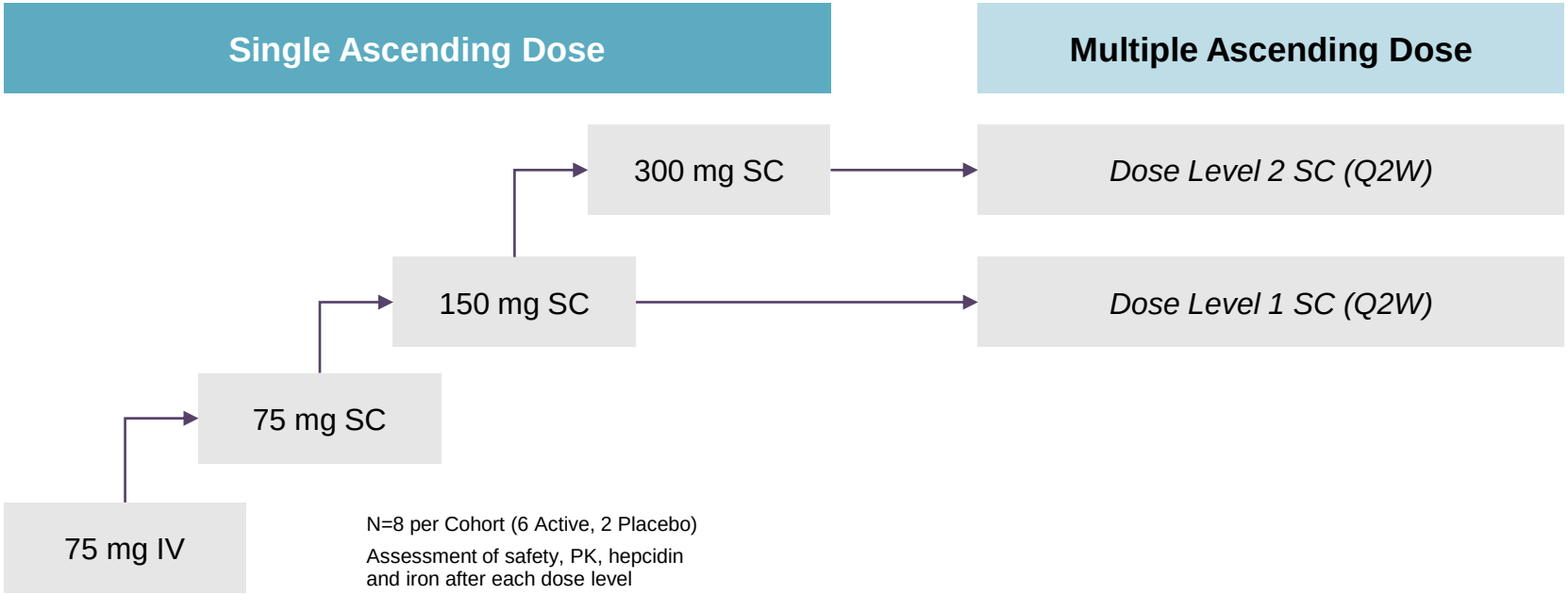
Additional POC Studies in a Range of Indications

- Hereditary Hemochromatosis
- Beta-thalassemia
- Myelodysplastic Syndromes

Hct = hematocrit; HV = healthy volunteers

DISC-3405 Phase 1 SAD / MAD Study

Phase 1 in healthy volunteers - ongoing



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

Data Availability: Initial SAD data to be presented 1H 2024

HV = healthy volunteers; IV = intravenous; SC = subcutaneous

Disc Continues Strong Growth Trajectory Towards Becoming a Leading Hematology Company

	Significant Accomplishments in 2023	*Strong Series of Catalysts in 2024*
Bitopertin	Positive initial Phase 2 data	• AURORA readout April 2024 • EPP development activities pending regulatory feedback • POC in DBA
DISC-0974	Initial POC in anemia of MF and CKD	• Additional POC data in MF and CKD anemia • Preclinical efforts on additional indications
DISC-3405	Initiation of Phase 1 study	• Initial healthy volunteer data in 2024 • Polycythemia vera as first indication

Supported by a strong cash position with runway well into 2026

Thank You

disc medicine