2023 ASH Management Call

Clinical Data Updates:
Bitopertin and DISC-0974

December 11, 2023

disc medicine

Disclaimer and FLS

This presentation includes “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements include express or implied statements relating to Disc's management team's expectations, hopes, beliefs, intentions or strategies regarding Disc’s expectations with respect to its AURORA Phase 2 and BEACON Phase 2 clinical studies of bitopertin and the results thereof, its Phase 1b/2 clinical studies of DISC-0974 in patients with MF and NDD-CKD patients with anemia, its Phase 1 clinical study 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; Disc’s business plans and objectives; Disc's analysis of market potential for patients with EPP; and Disc’s beliefs about operating expenses and that it will have capital to fund Disc well into 2026. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intends,” “may,” “might,” “plan,” “possible,” “potential,” “predict,” “project,” “should,” “suggest,” “will,” “would” and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. 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. Disc may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and investors should not place undue reliance on these forward-looking statements. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond Disc's control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to: the adequacy of Disc's capital to support its future operations and its ability to successfully initiate and complete clinical trials; the nature, strategy and focus of Disc; the difficulty in predicting the time and cost of development of Disc's product candidates; Disc's plans to research, develop and commercialize its current and future product candidates; the timing of initiation of Disc's planned preclinical studies and clinical trials; the timing of the availability of data from Disc's clinical trials; Disc's ability to identify additional product candidates with significant commercial potential and to expand its pipeline in hematological diseases; the timing and anticipated results of Disc's preclinical studies and clinical trials and the risk that the results of Disc's preclinical studies and clinical trials may not be predictive of future results in connection with future studies or clinical trials and may not support further development and marketing approval; the other risks and uncertainties described in our Annual Report on Form 10-K for the year ended December 31, 2022, Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023 and September 30, 2023, and other documents filed by Disc from time to time with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. None of Disc, nor its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law.

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

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

Agenda

01 **Introduction and Data Summary**
John Quisel, JD, PhD, Chief Executive Officer

02 **Bitopertin in EPP**
- **Updated BEACON Data**
  Bruce Wang, MD, Professor of Gastroenterology, University of California San Francisco
  Will Savage, MD, PhD, Chief Medical Officer
- **EPP Commercial Opportunity**
  Jonathan Yu, Chief Business Officer

03 **DISC-0974**
- **Initial Data in Anemia of Myelofibrosis**
  Will Savage, MD, PhD, Chief Medical Officer
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04 **Closing Remarks**
John Quisel, JD, PhD, Chief Executive Officer

05 **Q&A Session**

Bitopertin: Summary of Phase 2 BEACON Data Update

Data presented at ASH established proof of concept and demonstrated functional benefit for EPP patients. Key findings:

Significant, dose-dependent **reductions in PPIX levels**

Significant increases in **sunlight tolerance**

Improved patients' reported **quality of life**

Generally well tolerated with stable mean hemoglobin levels

DISC-0974: Summary of Initial Data from Phase 1b Studies in MF and CKD

Initial data from both Phase 1b studies in MF and CKD demonstrated proof of concept and improvement in anemia. Key findings:

Substantial **reductions in hepcidin levels**

Corresponding **increases in iron levels**

Positive impact on **hematologic parameters** across a broad range of MF patients

Generally well tolerated at all evaluated dose levels

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Bruce Wang, MD

Professor at UCSF

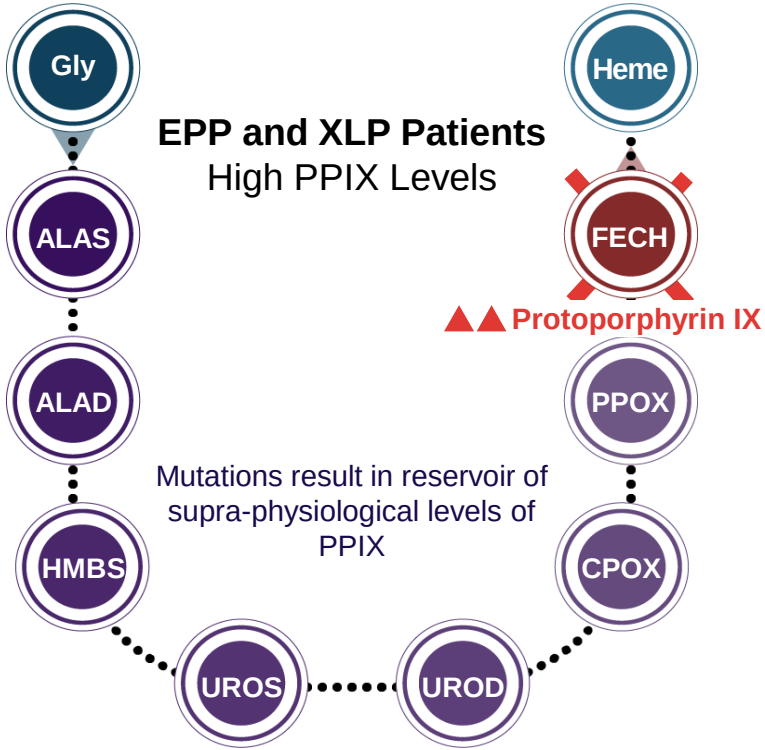
Principal Investigator in US Porphyrias Consortium

Disclosures

- Alnylam (consultant, investigator in clinical trial, grant funding)
- Disc Medicine (consultant, investigator in clinical trial)
- Mitsubishi-Tanabe (consultant, investigator in clinical trial, grant funding)
- Recordati Rare Diseases (consultant)

In EPP, a genetic mutation leads to the buildup of protoporphyrin IX (PPIX)

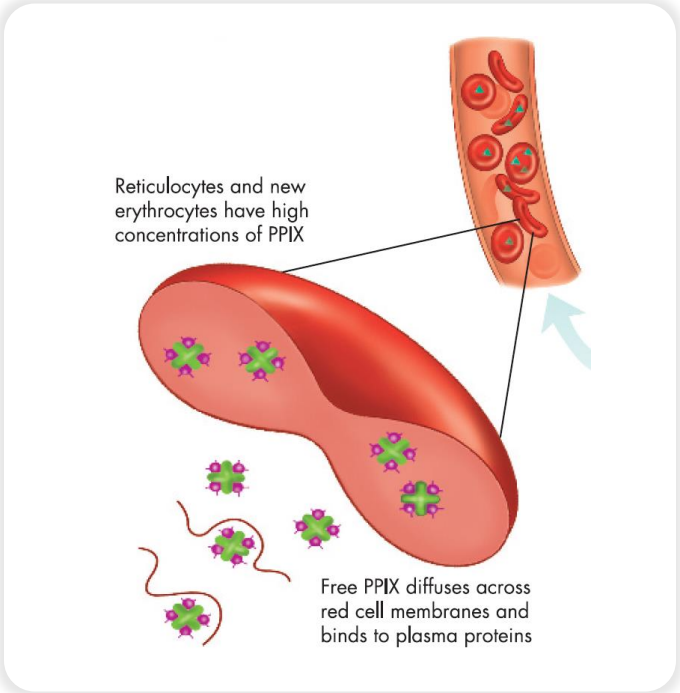
- In most patients, EPP is caused by deficient ferrochelatase activity due to mutations of the FECH gene
- The deficiency causes a failure to convert protoporphyrin IX (PPIX) into heme in the terminal step of heme synthesis
- PPIX substantially accumulates in erythrocytes, plasma, skin, and liver



Elder et al. Cell Mol Biol (Noisy-le-grand). 2009;55(2):118-126.

PPIX is a highly toxic and photoreactive metabolite

- PPIX molecule absorbs light radiation
- Absorption increases energy content and enables excess energy to be transferred to oxygen, resulting in reactive oxygen species (ROS)
- These oxygen species can injure tissue by membrane lipid peroxidation, complement activation, and mast cell degranulation
- PPIX is also highly toxic independent of the photosensitizing reactions, particularly impacting the liver



Sachar et al, *J Pharmacol Exp Ther.* 2016; Phillips et al, *Mol Genet Metab*, 2019;

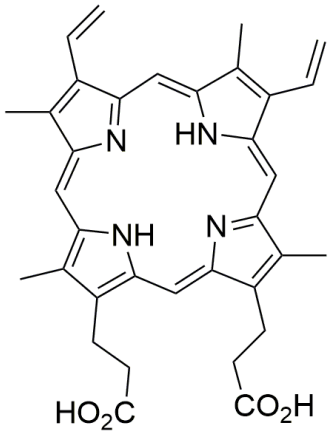
Accumulation of this toxic metabolite can cause a variety of symptoms

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

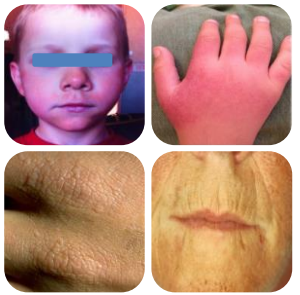
Other Complications

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

Naik et al. (2019) *JIMD Rep*; Levy (2023) *Gastroenterol Hepatol*; Obi et al. (2022) *Front Cell Dev Bio*; Di Pierro et al. (2022) *Diagnostics*.

Of these symptoms, the primary manifestation is photosensitivity that can result in debilitating pain

- Upon exposure to the sun, EPP patients experience **disabling pain attacks** that can last for days
- These attacks cause burning sensations, swelling, itching, and erythema, and can lead to **chronic skin lesions and scarring**



As a result, EPP patients take extreme measures to avoid sunlight

- EPP patients **spend most of their time indoors**, avoiding the light, causing them to miss many daily activities
- When patients do have to go outside, they may **completely cover their skin** to avoid sun exposure, wearing long sleeves, hats, and gloves even in summer

Bitopertin: Investigational Oral, Selective GlyT1 Inhibitor

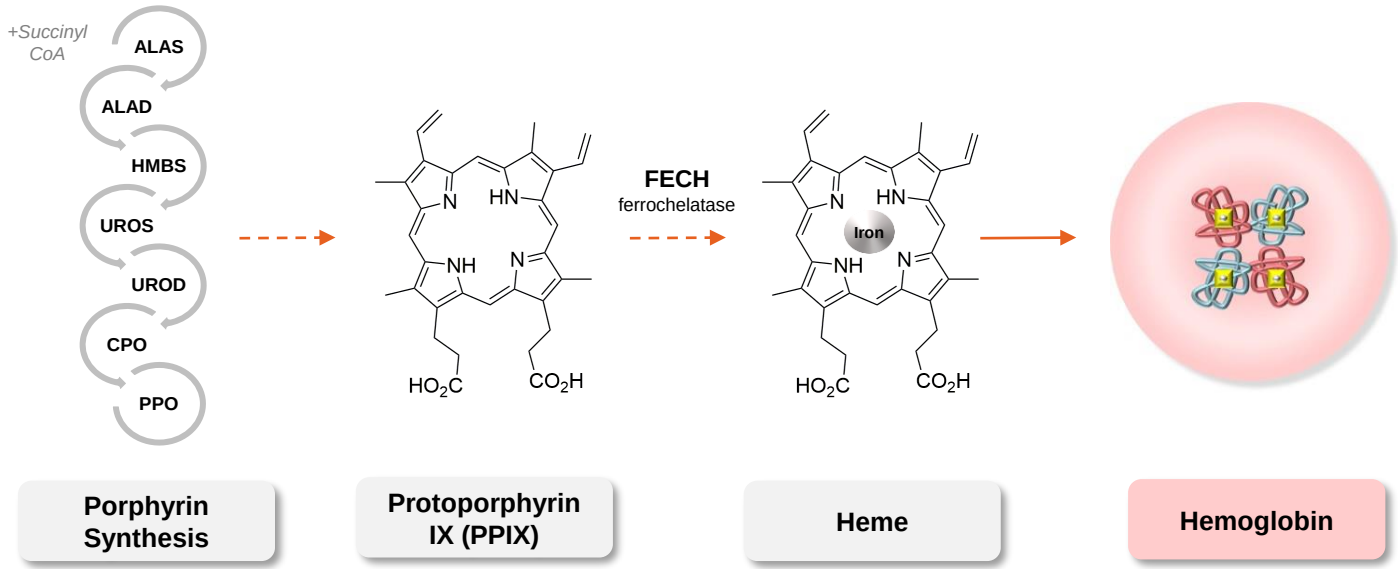
Bitopertin modulates heme biosynthesis by blocking uptake of glycine in erythrocytes

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

GlyT1 = glycine transporter 1; RBC = red blood cell

EPP Phase 2 Development Program

Ongoing BEACON and AURORA Trials—Enrollment Complete

Today's Focus

BEACON

- **EPP and XLP**; N = >22 (fully enrolled for adults, now enrolling adolescents)
- **Australia** (study opened July '22)
- **Open-Label, randomized, 24-week study**

Data Early 2024

AURORA

- **EPP**; N = 75 (fully enrolled)
- **US** (study opened October '22)
- **Double-blind, placebo-controlled, 17-week study**

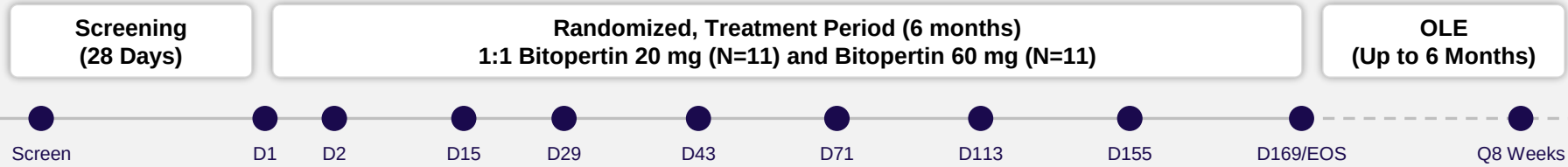
Trial Endpoints:

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

*Time to prodromal symptom = the time until a participant experiences an early warning signal of a phototoxic attack measured through a weekly sunlight challenge. If a participant is unable to elicit a prodrome during a sunlight challenge, the amount of time the participant chose to remain in light is recorded.
D = day; EOS = end of study; OLE = open-label extension; PK = pharmacokinetics

BEACON 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

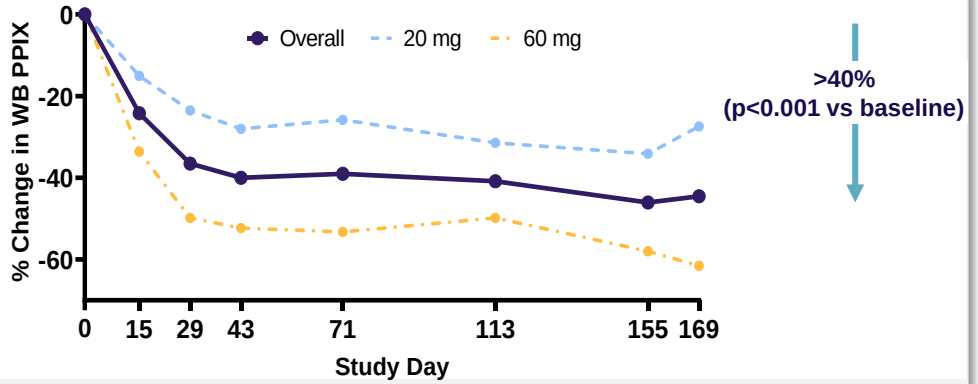
Study population is ~64% female with an average age of 44 years (range 20-73)

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

Updated 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

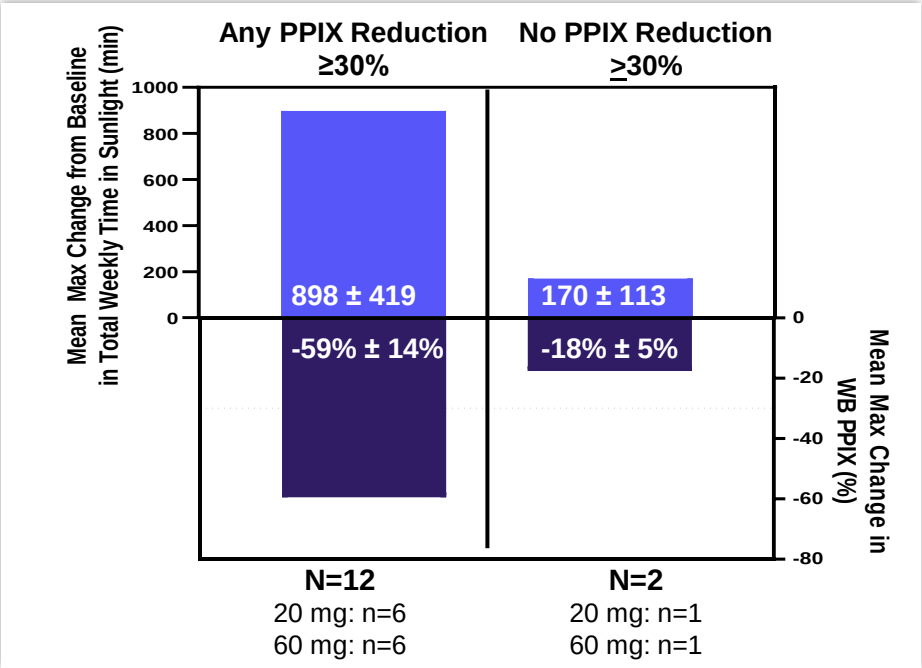


Overall N	22	22	20	22	16	16	13	8
20 mg	11	11	10	11	9	9	7	4
60 mg	11	11	10	11	7	7	6	4

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).

Updated 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%

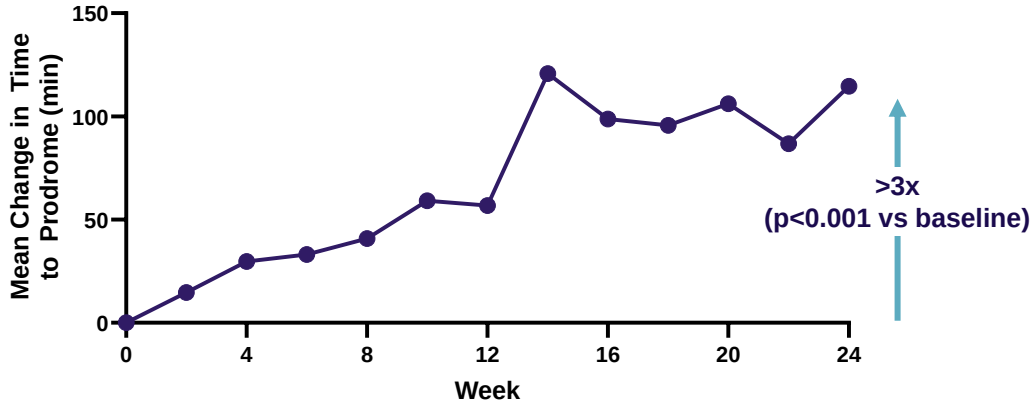


Data cutoff of October 20, 2023; Maximum changes from baseline in weekly total time in sunlight as assessed with a daily diary. Includes only participants who have completed through Day 169/EOS.

Updated BEACON Data: Time to Prodrome

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

Time to Prodrome



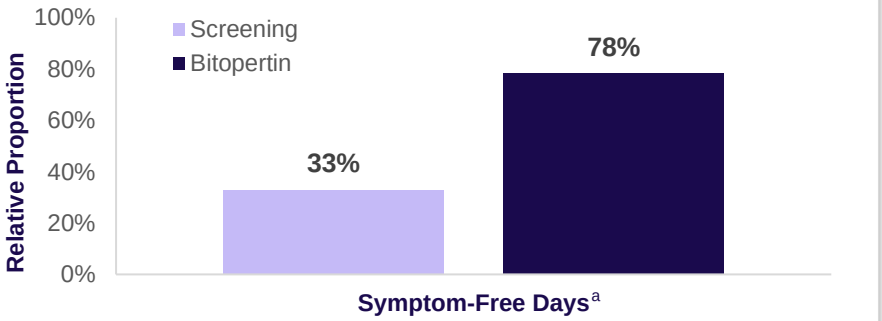
No. of Participants[a]	22	19	21	20	19	18	21	15	15	17	14	16	14
No. of Challenges	69	45	46	43	44	42	40	32	35	46	32	47	33

[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.

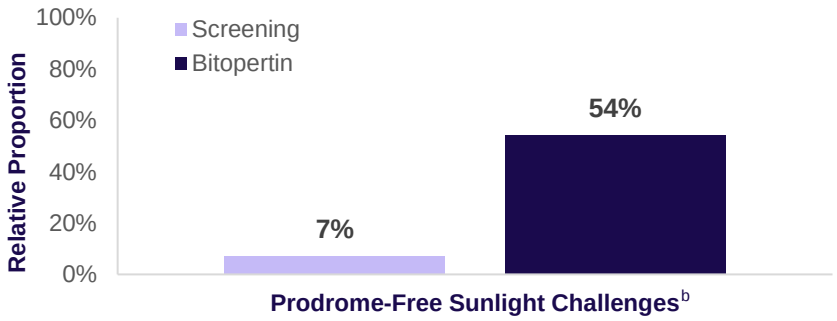
Updated BEACON Data: Light Tolerance

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

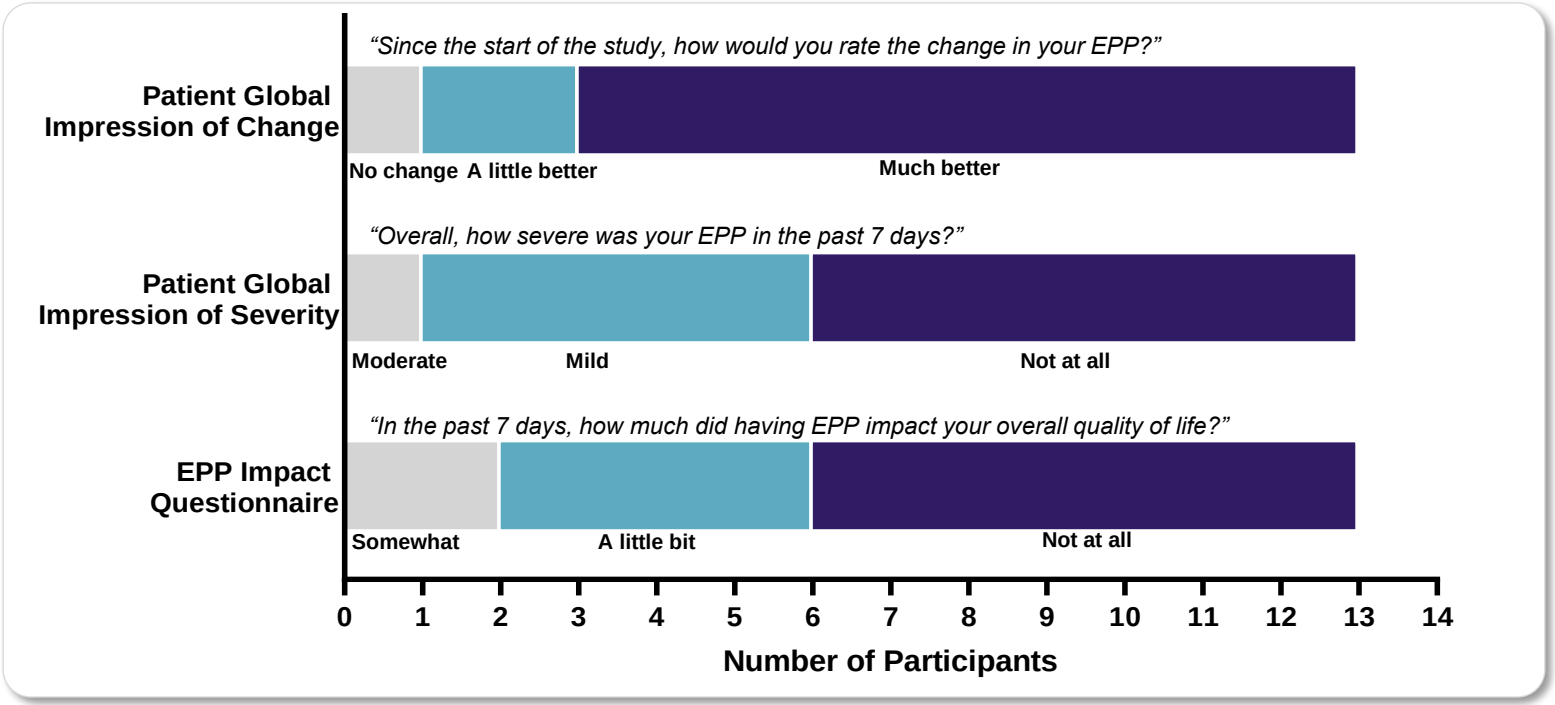


	Sunlight Challenges[c]
Screening	69
On-Treatment	623

[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).

Updated BEACON Data: Measures of Quality of Life

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

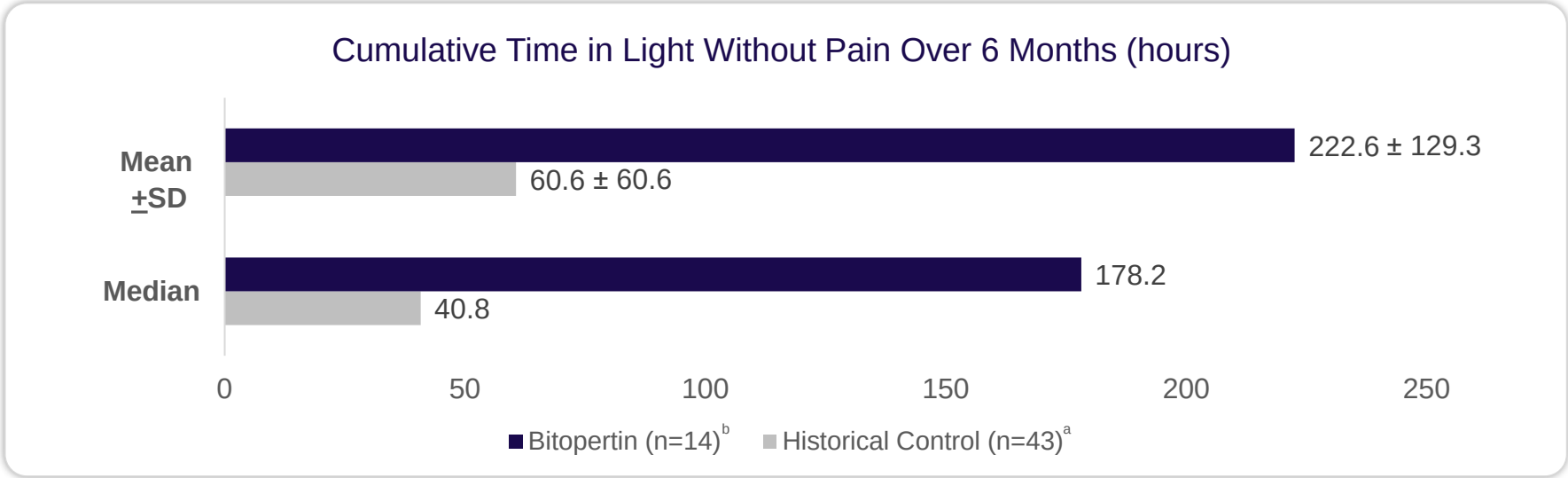


Only 13 participants who completed through Day 169/EOS with QOL responses.

Updated BEACON Data: Precedented Pivotal Endpoint

Cumulative Time in Light on Days without Pain

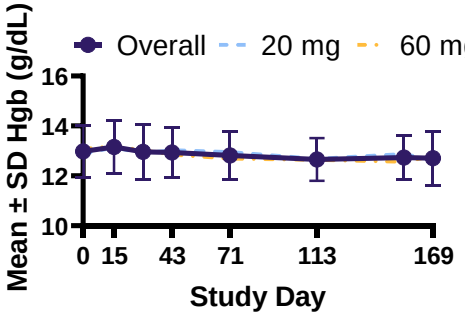
- Cumulative total time in light observed over 6-month treatment period with bitopertin represents >3x increase relative to historical control
- Improvements in average daily light tolerance with bitopertin increased with time



[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 or prodrome; SD = standard deviation

Updated 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

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

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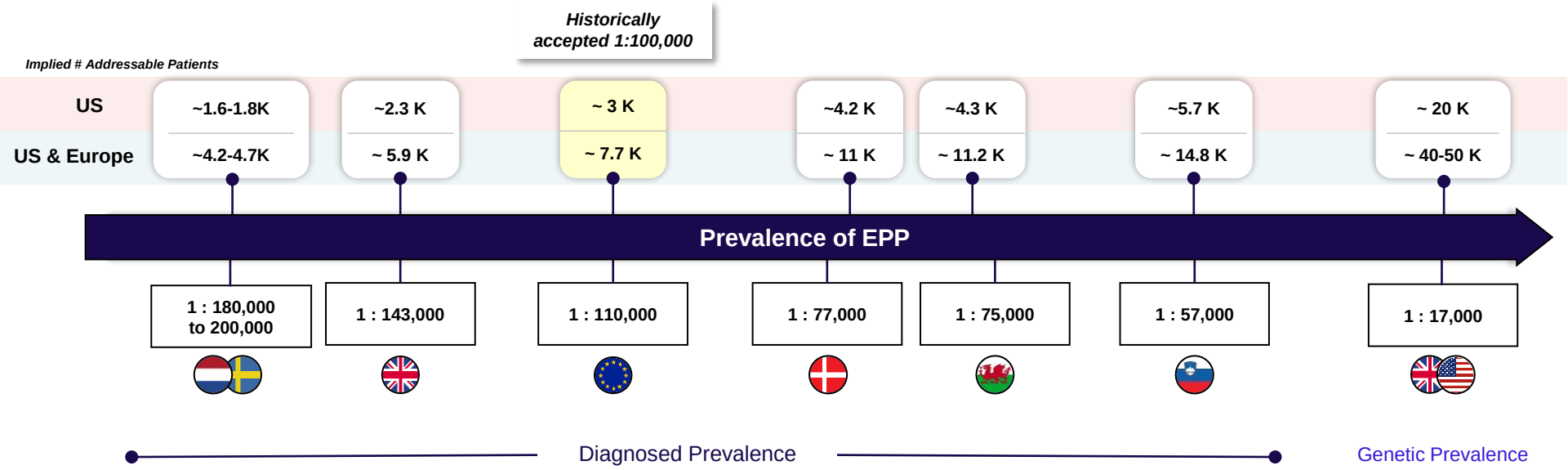
Historical EPP estimates likely underrepresent prevalence

Based on methodology reported in literature and patient journey

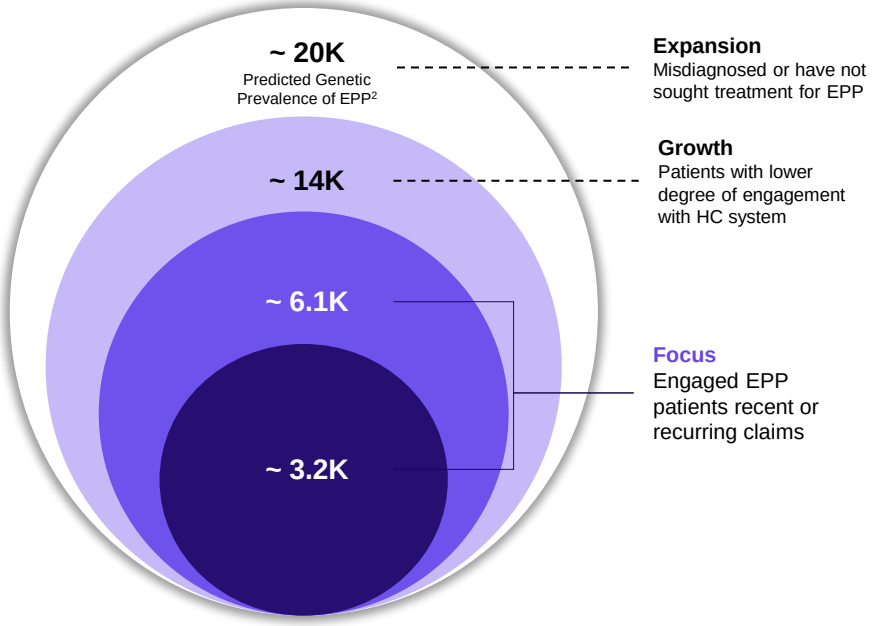


Clearview Healthcare Partners; Went et al (1984); Wahlin et al. (2011); Holme et al. (2006); Elder et al. (2013); Christiansen et al. (2016); Elder et al. (1990); Marko et al. (2007); Dickey et al. (2021)

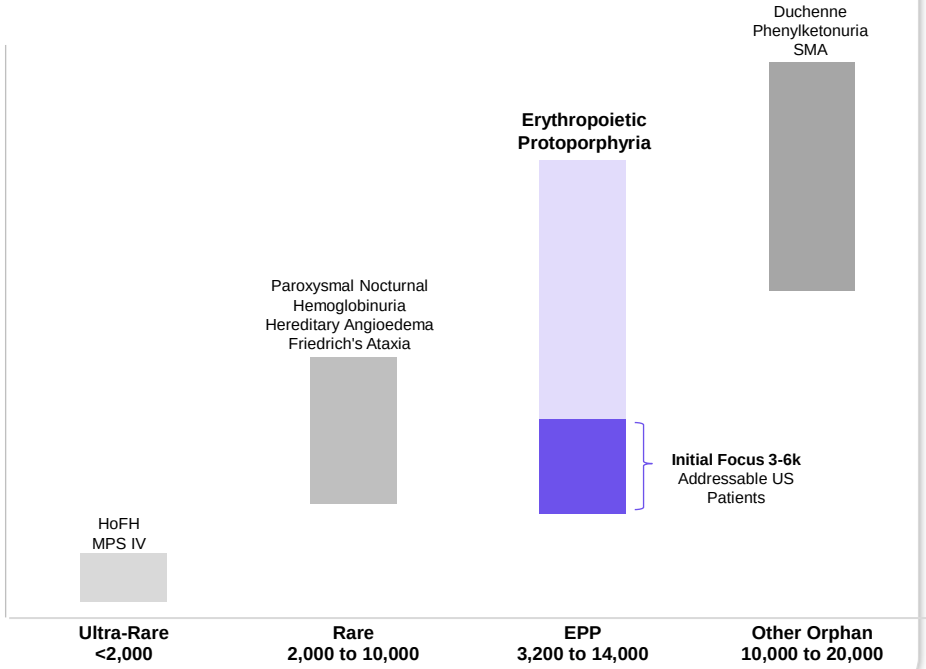
EPP Prevalence: Est. 3-6K addressable patients in the US

Based on analysis of ICD-10 codes in claims data

Prevalence of EPP Patients in the U.S.



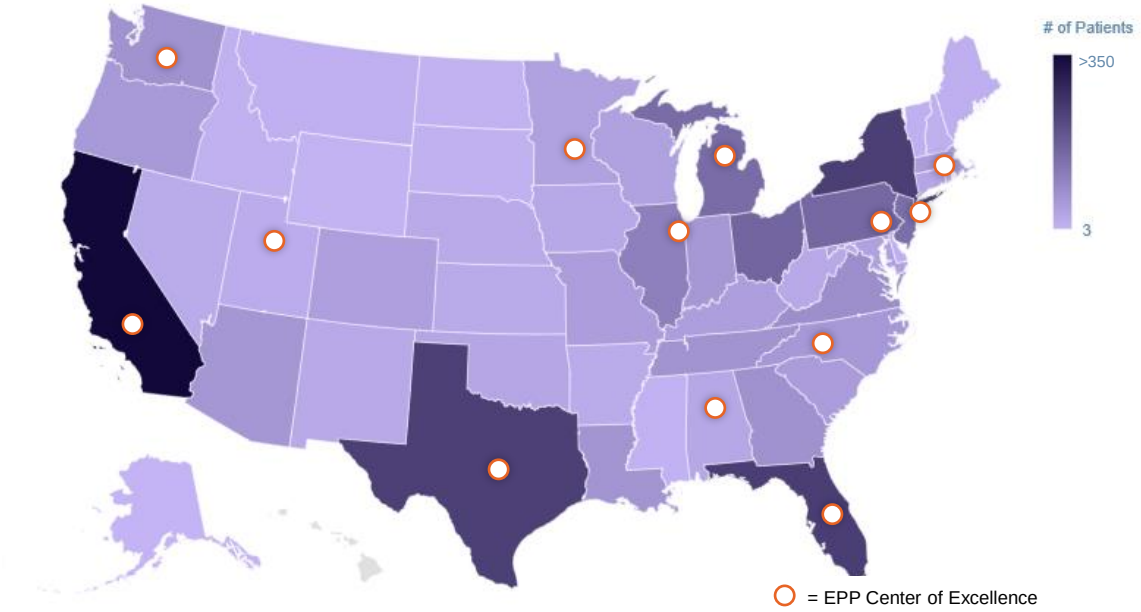
US EPP Prevalence Comparable to Major Rare Diseases



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

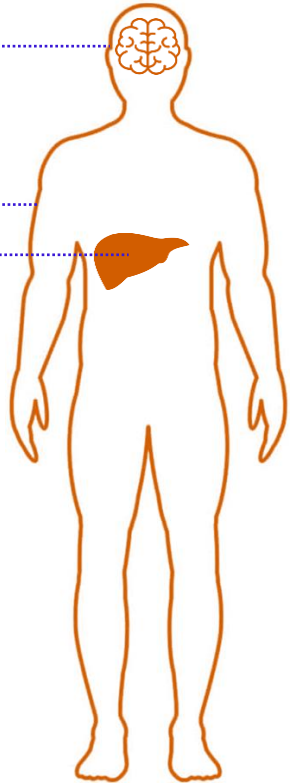
Real world data confirm EPP has a significant impact on patients' lives across multiple domains

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

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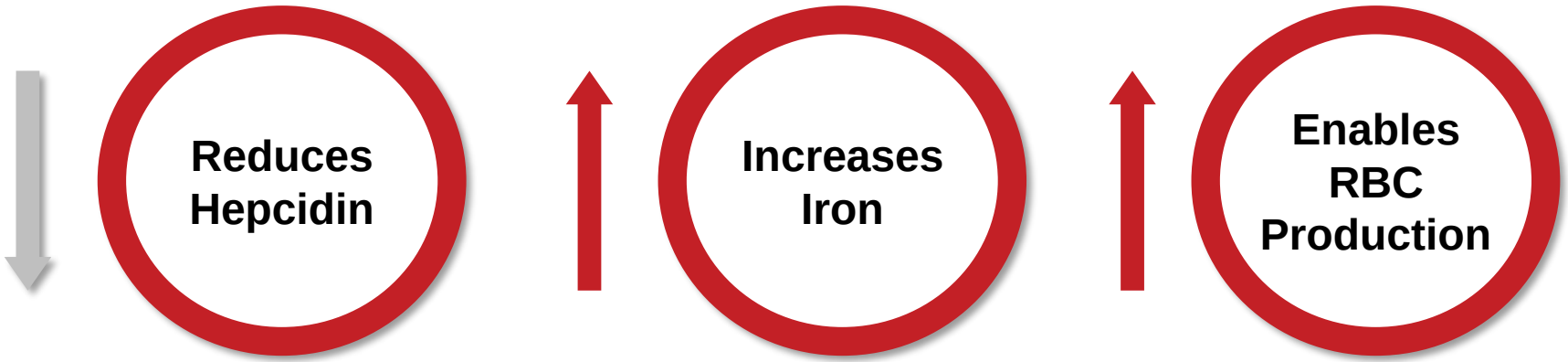
DISC-0974: Novel Anti-HJV mAb to Suppress Hepcidin

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



Inhibits endogenous production of hepcidin

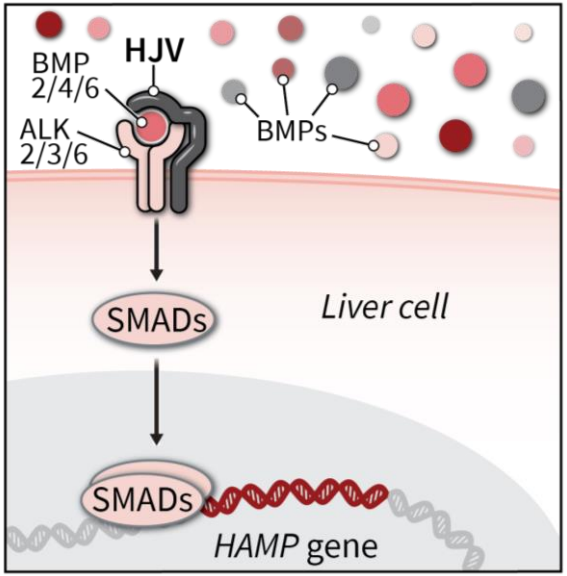
Releases iron stores
Enables GI absorption

Potential to treat wide range of anemias

HJV = hemojuvelin

Targeting HJV to Suppress Hepcidin

Critical and specific target for hepcidin expression



Inhibiting Hemojuvelin (HJV) Prevents Hepcidin Expression and Increases Iron

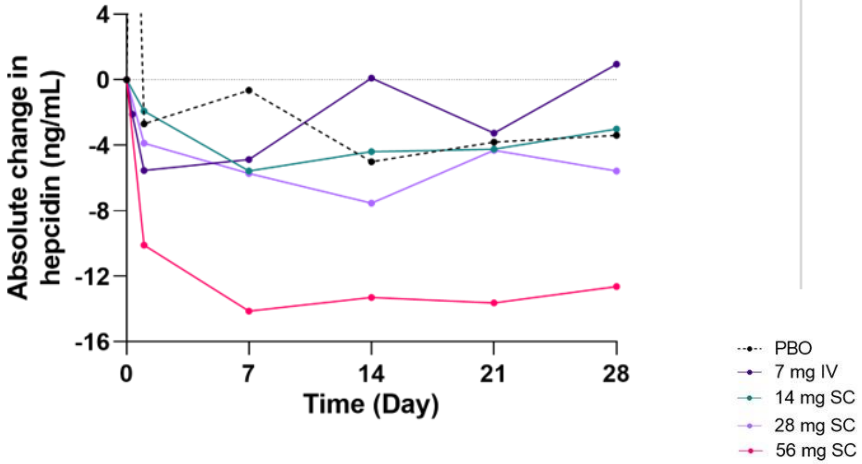
- **Genetic validation** in patients with Juvenile Hemochromatosis (lower hepcidin and elevated iron levels)
  - Loss-of-function mutations in HJV are phenotypically indistinguishable from mutations in *HAMP* (hepcidin) gene
- **Functionally specific** to hepcidin/iron
- **Tissue-specific** expression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

Sources: Finberg et al, (2010) Blood; Zhang et al, (2010) J Biol Chem; ALK = Activin receptor-like kinase; BMP = Bone morphogenetic protein; HAMP = hepcidin antimicrobial peptide; HJV = hemojuvelin

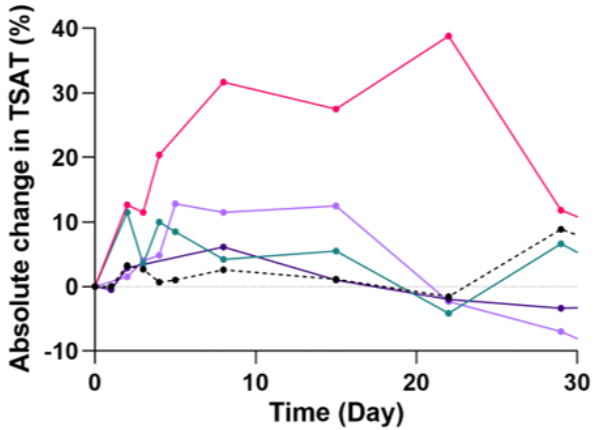
DISC-0974 Phase 1 SAD Healthy Volunteer Data

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

DISC-0974 Reduced Hepcidin Production



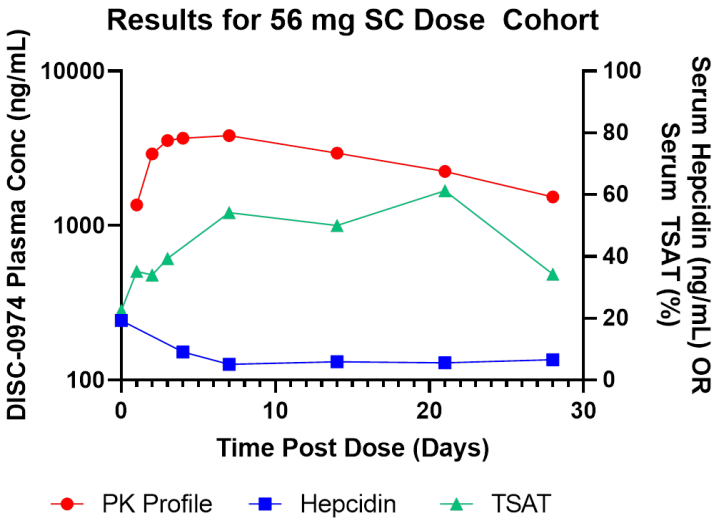
DISC-0974 Increased TSAT

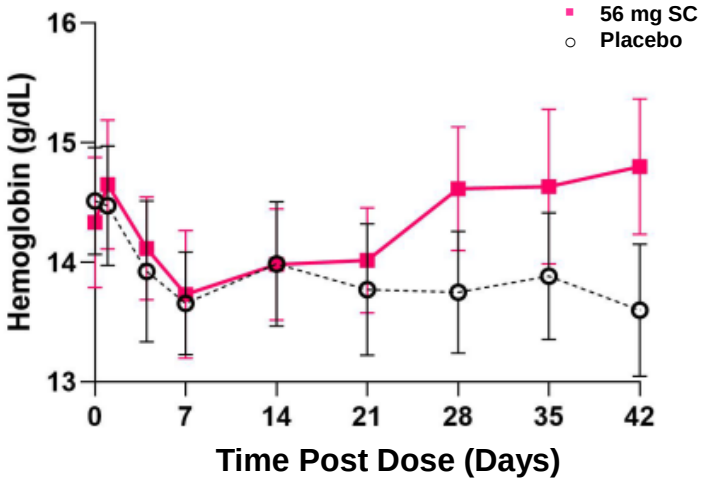


IV = intravenous; PBO = placebo; SAD = single ascending dose; SC = subcutaneous; TSAT = transferrin saturation

DISC-0974 Phase 1 Healthy Volunteer SAD Data (cont.)

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



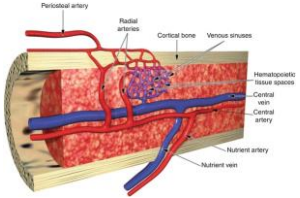


Conc = concentration; Hgb = hemoglobin; PK = pharmacokinetic; SAD = single ascending dose; SC = subcutaneous; TSAT = transferrin saturation

Hepcidin is a Key Driver of Myelofibrosis (MF) Anemia

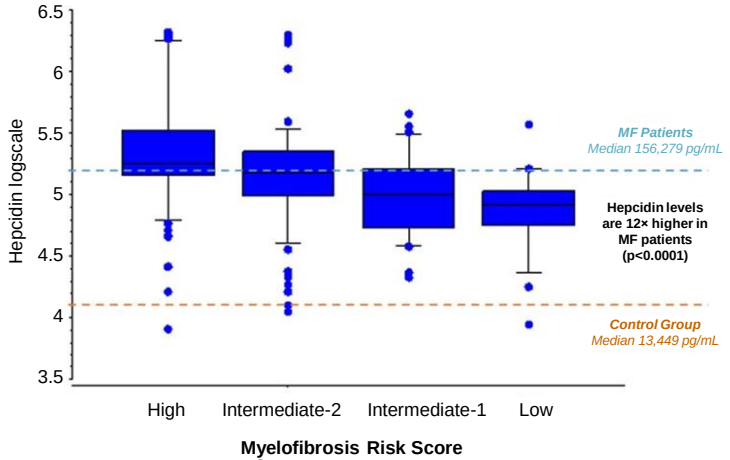
Anemia is severe and prevalent in MF and can limit treatment

Anemia of MF



- **Est. # Patients**
  - 16,000 to 18,500 patients (US)
  - ~87% are anemic; severe and requires 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; Teferri (2017) Blood Cancer Journal

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)

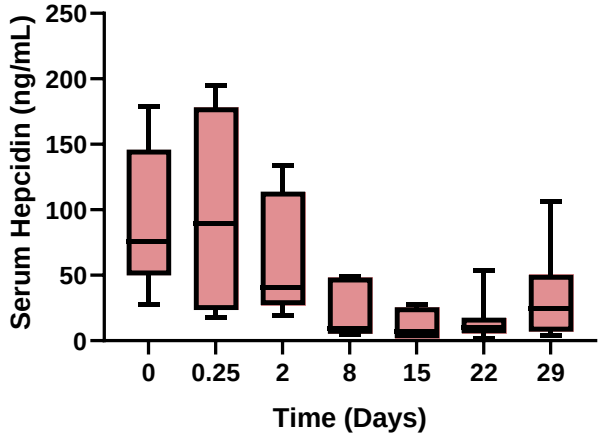
	DISC-0974 14 mg	DISC-0974 28 mg	DISC-0974 50 mg	Total
Enrolled	1	7	3	11
Concomitant JAK use	0	4 (57.1%)	0	4
Transfusion Dependent*	0	2 (28.6%)	0	2
Median Time Since Diagnosis (yrs)	1	6 (0-18)	2 (0-14)	-

*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

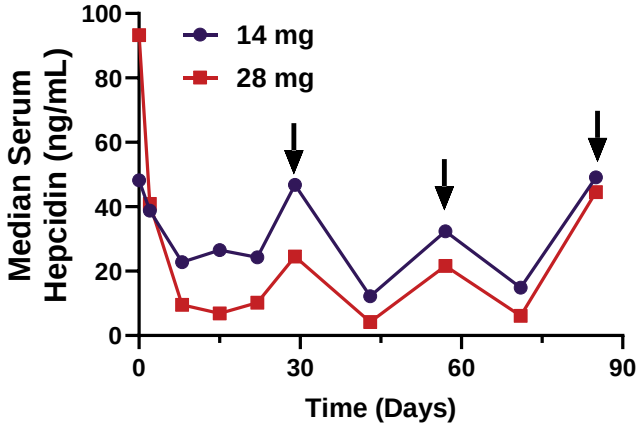
Initial DISC-0974 Anemia of MF Data: Hepcidin

- 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

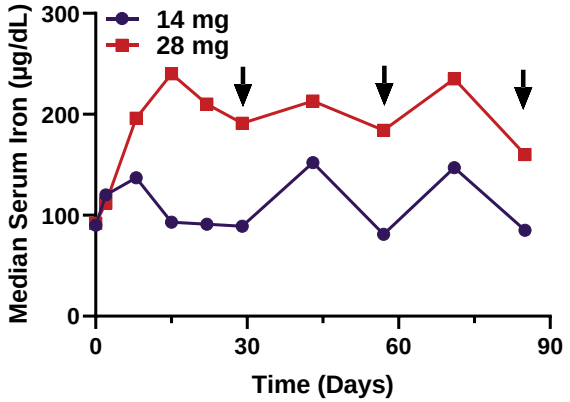


Arrows represent dosing days

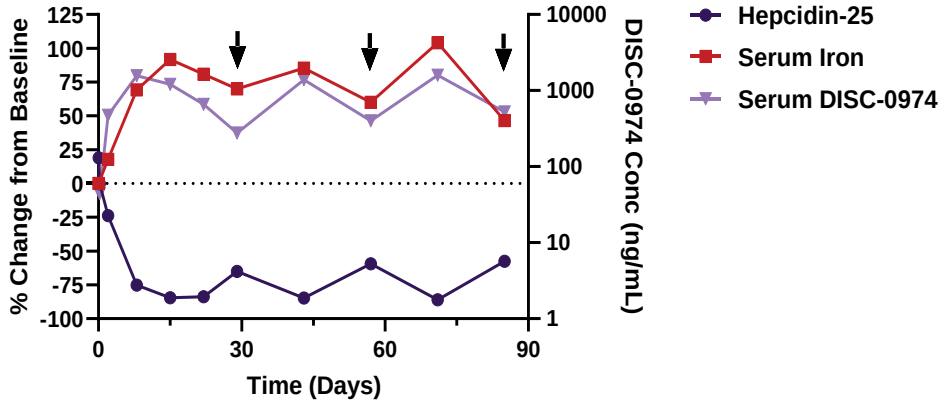
Initial DISC-0974 Anemia of MF Data: Serum Iron

- 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

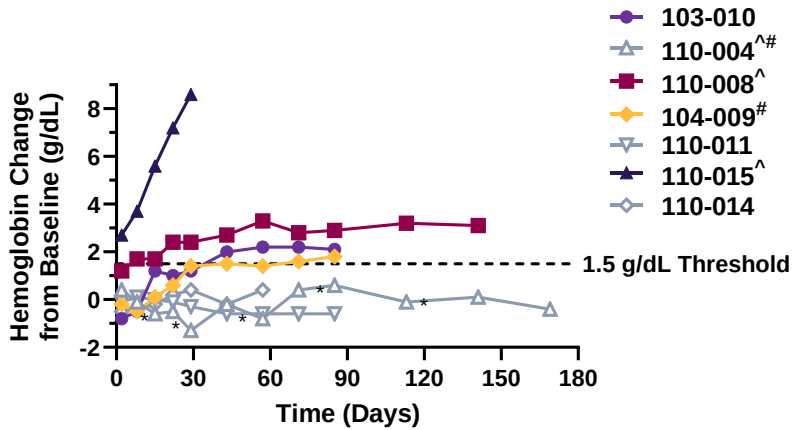


Arrows represent dosing days

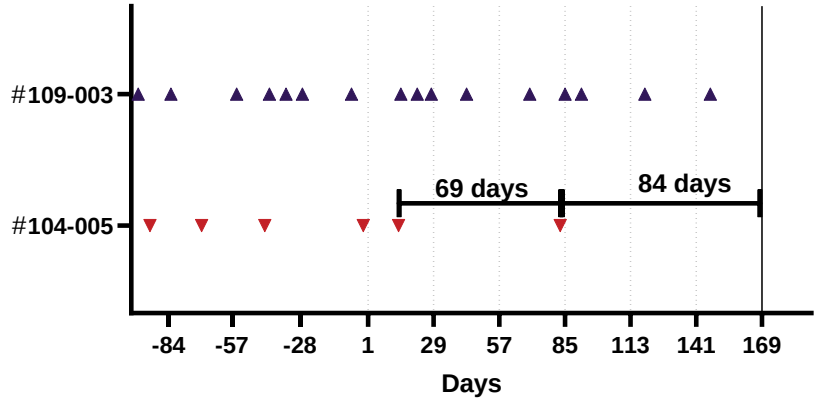
Initial DISC-0974 Anemia of MF Data: Hematologic Response

- 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

Initial 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

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05 **Q&A Session**

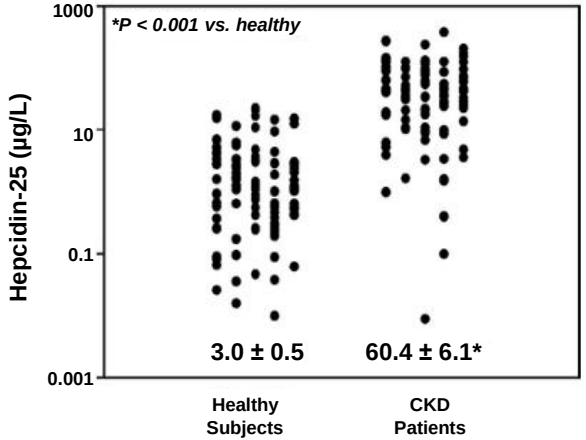
Hepcidin is a Key Driver of CKD Anemia

Anemia is a significant issue in CKD, with most patients currently untreated

Anemia of CKD (NDD and DD)

- **5-6M CKD Patients with Anemia (US Only)**
  - ~17 to 50% of CKD patients are anemic; increases w/ stage
  - Nearly all anemic patients are non-dialysis dependent (NDD)
- **Hepcidin is a Driver of CKD Anemia**
  - High hepcidin from inflammation
  - Poor renal clearance leads to accumulation of hepcidin
- **Unmet Medical Needs**
  - Majority patients untreated or under-treated
  - ESAs restricted due to safety and black box
  - Mean Hgb 9.3 g/dL in patients initiating dialysis

Hepcidin Levels Elevated in CKD Patients
~20× 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)
CKD = chronic kidney disease; DD = dialysis dependent; ESA = erythropoietin-stimulating agent; Hgb = hemoglobin; NDD = non-dialysis dependent

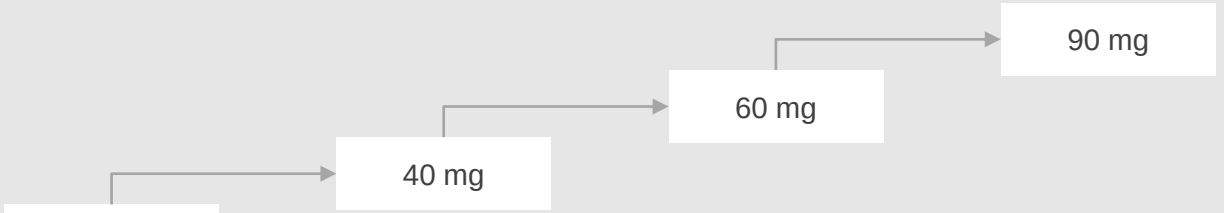
DISC-0974 NDD-CKD Anemia Trial Overview

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

	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)

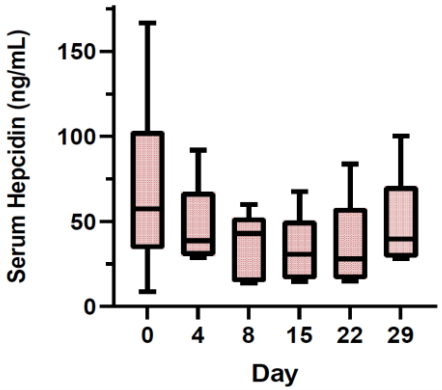
CKD = chronic kidney disease; Hgb = hemoglobin; NDD = non-dialysis dependent; PK = pharmacokinetics; TSAT = transferrin saturation

Initial DISC-0974 Anemia of CKD Data: Hepcidin and Iron

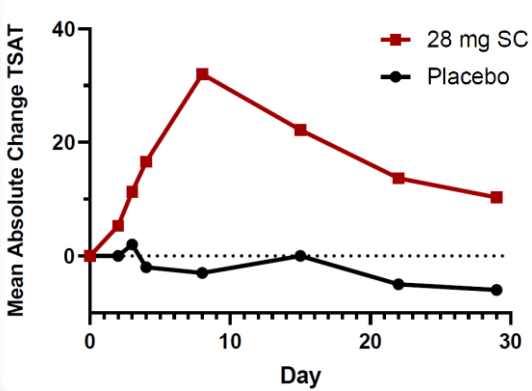
First Cohort: 28 mg SC

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

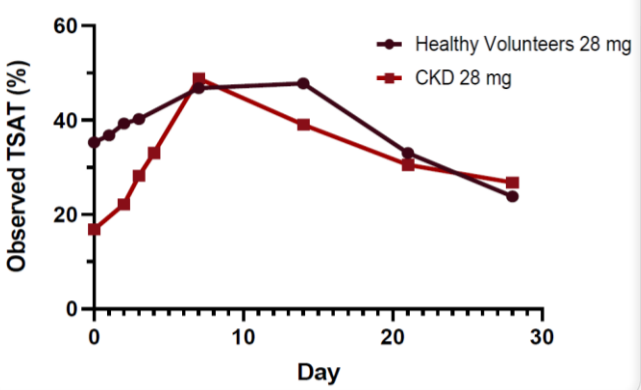
Hepcidin Changes Over Time



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 Initial 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

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Summary of Data

Bitopertin
Heme Synthesis Modulator

- Consistent, significant reductions in PPIX; >40% on average
- Significant improvement in sunlight tolerance across multiple measures:
  - >3x increase in time to prodrome
  - >3x increase in cumulative time in light vs. historical controls
  - Increase in symptom-free days
- Improvements in quality of life
- Generally well tolerated

DISC-0974
Hepcidin Suppression

Phase 1b/2 in Myelofibrosis and Anemia

- Initial data demonstrated:
  - Consistent decrease in serum hepcidin (>75%) and increase in iron
  - Hematologic responses in a broad range of pts

Phase 1b/2 in NDD-CKD and Anemia

- Initial data from the 28 mg cohort demonstrated:
  - Meaningful reductions in hepcidin and increase in iron, similar PK/PD as HVOL
- Generally well tolerated

AE = adverse event; HVOL = healthy volunteers; PD = pharmacodynamics; PK = pharmacokinetics; PPIX = protoporphyrin IX; NTD = non-transfusion dependent; TD = transfusion dependent

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 early 2024 • Regulatory interactions & Phase 3 prep • 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

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