disc medicine

# Corporate Presentation

May 2026

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This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding Disc’s expectations with respect to its preclinical studies, clinical trials and research and development programs, in particular with respect to bitopertin, DISC-0974 and DISC-3405, and any developments or results in connection therewith; projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; the registrational pathway for bitopertin, including the potential for traditional approval, the potential for the APOLLO clinical trial to serve as the basis for any such approval, and the timing of any such approval, if granted; anticipated discussions with regulatory agencies; Disc’s expectations with respect to the potential launch and commercialization of bitopertin, if approved; the market and potential opportunities for bitopertin, DISC-0974 and DISC-3405; the potential of Disc’s development programs in new indications; and the time period over which Disc’s capital resources will be sufficient to fund its anticipated operations. The use of words such as, but not limited to, “believe,” “expect,” “estimate,” “project,” “intend,” “future,” “potential,” “continue,” “may,” “might,” “plan,” “will,” “should,” “seek,” “anticipate,” or “could” or the negative of these terms and other similar words or expressions that are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Disc’s current beliefs, expectations and assumptions regarding the future of Disc’s business, future plans and strategies, clinical results and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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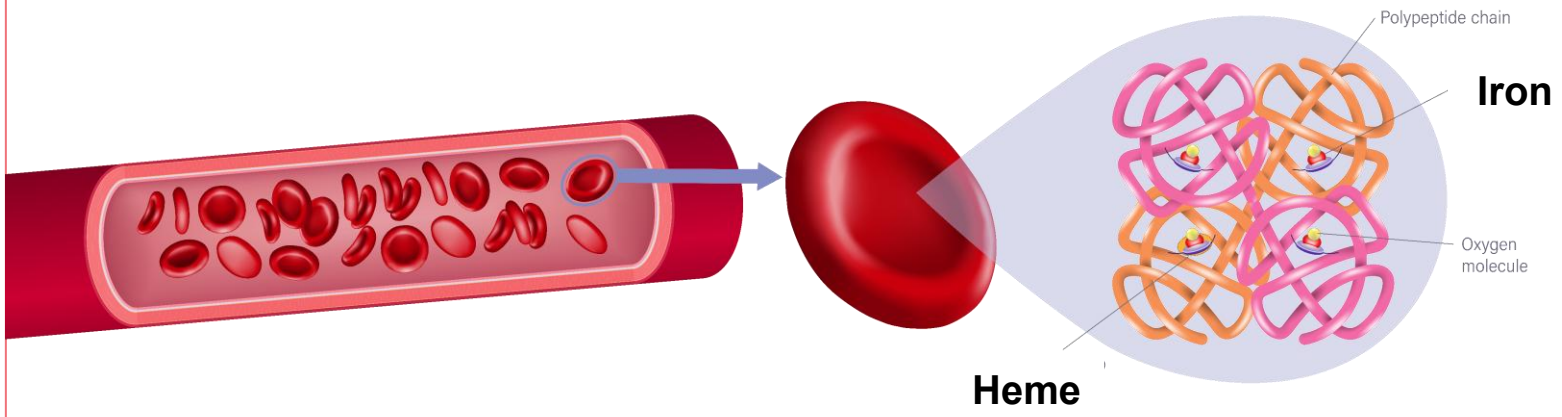
**Bitopertin, DISC-0974, and DISC-3405 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide**

# Targeting fundamental pathways of red blood cell biology using validated mechanisms




- Iron and heme metabolism are critical pathways with genetically validated targets
- Key points of intervention across a broad range of diseases

## Spectrum of Hematologic Diseases Addressable by Disc Portfolio

| Very Rare (thousands) | | | Moderate Prevalence (hundreds of thousands) | | | | | Widely Prevalent (millions) | |
|---|---|---|---|---|---|---|---|---|---|
| Diamond-Blackfan Anemia | Erythropoietic Porphyrias | Beta-Thalassemia | Anemia of Myelofibrosis | Myelodysplastic Syndromes | Sickle Cell Disease | Polycythemia Vera | Hereditary Hemochromatosis | IBD Anemia | CKD Anemia |

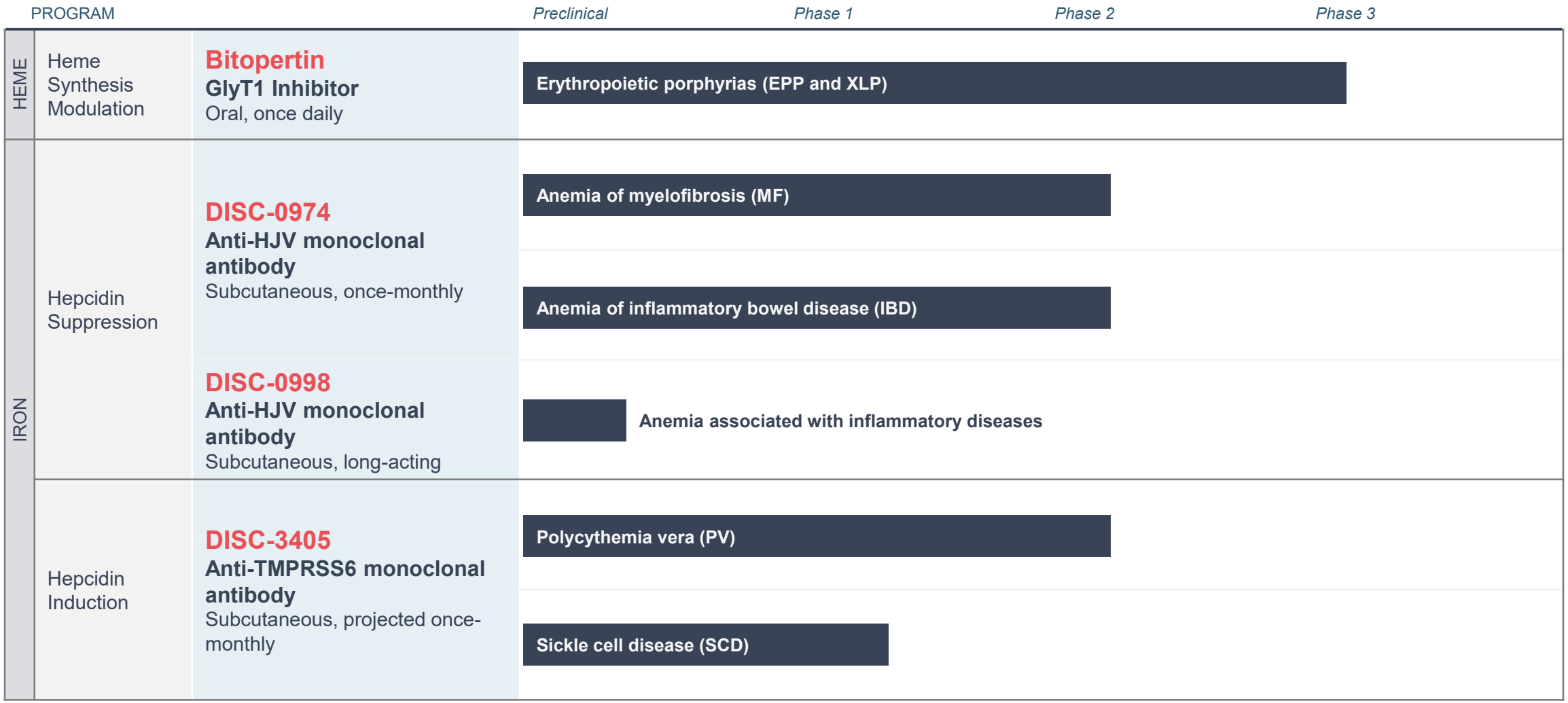
Trial in Progress or Completed

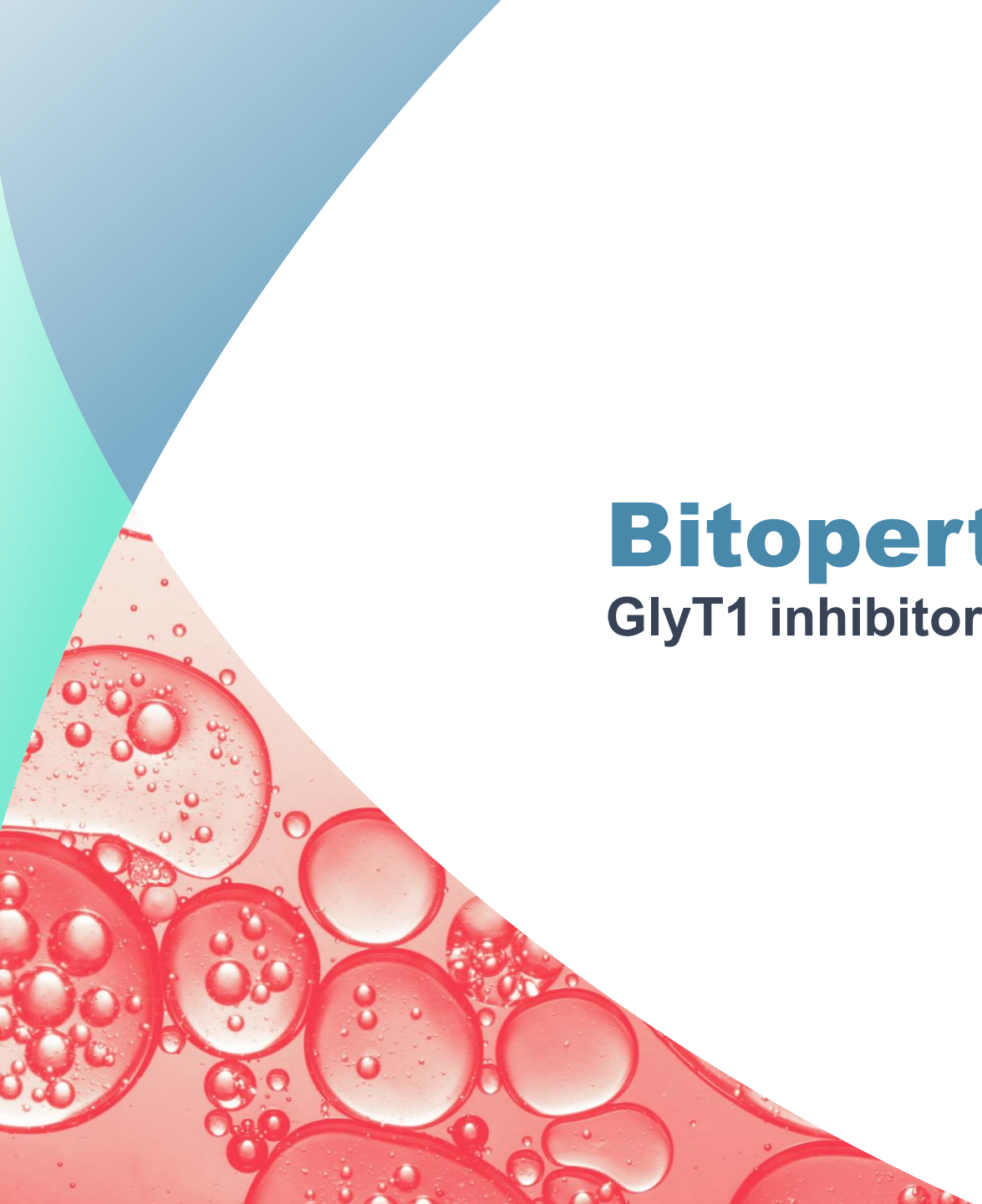
# By targeting heme and iron, Disc's portfolio can address a wide range of hematologic disorders

| | **Modulate Heme Synthesis** | **Increase Iron** Hepcidin Suppression | **Restrict Iron** Hepcidin Induction |
|---|---|---|---|
| **Clinical Program (MOA)** | **Bitopertin** (GlyT1 Inhibitor) | **DISC-0974** (Anti-HJV mAb) | **DISC-3405** (Anti-TMPRSS6 mAb) |
| **Range of Indications** | **Rare blood disorders** | **Anemia of chronic diseases** | **Polycythemia vera and iron overload diseases** |
| **Development Status** | **Phase 3** *POC Established* | **Phase 2** *Initial POC* | **Phase 2** *Ongoing* |

# Disc's hematology-focused pipeline

## Key programs driving upcoming catalysts





# Bitopertin

**GlyT1 inhibitor |** Heme biosynthesis modulation

# Bitopertin: Investigational oral, selective GlyT1 inhibitor

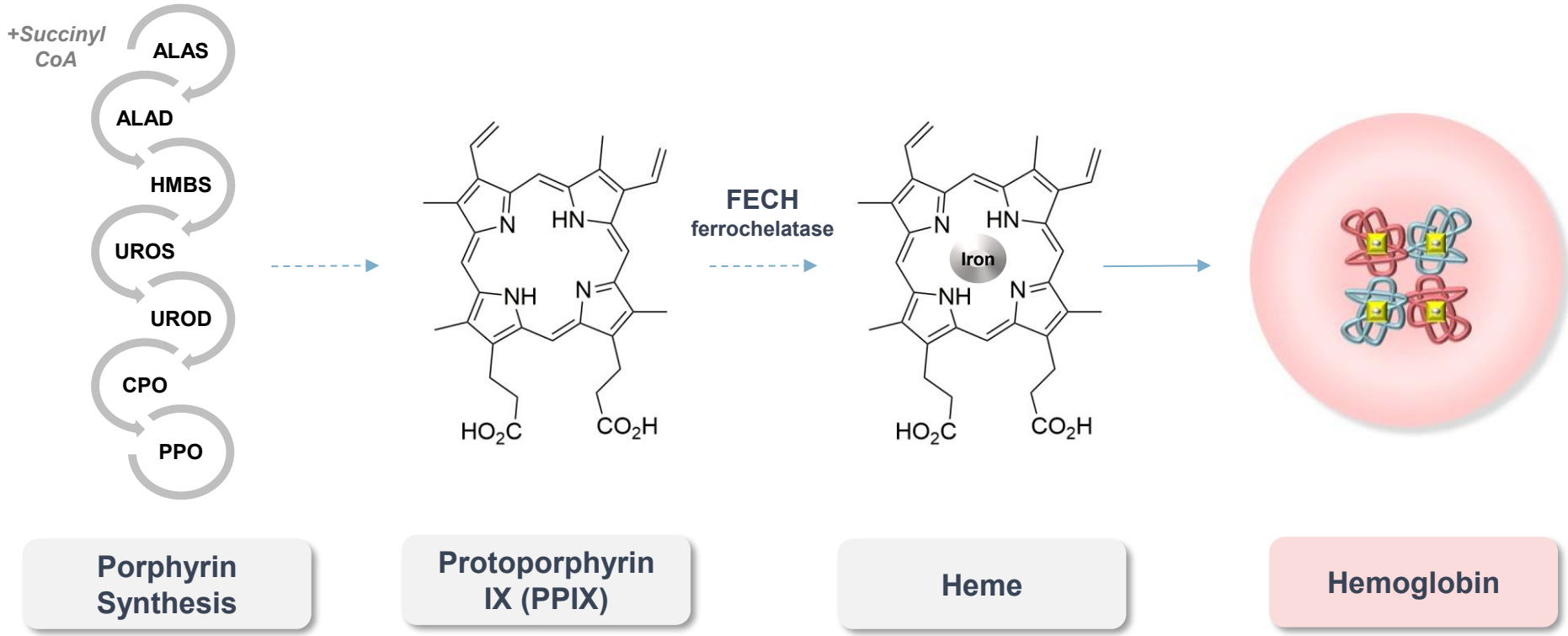
## In multiple clinical trials by Roche, bitopertin was observed to modulate heme biosynthesis by blocking uptake of glycine in erythrocytes

**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 the skin caused by light, as well as potential hepatobiliary complications and psychosocial impacts

### 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

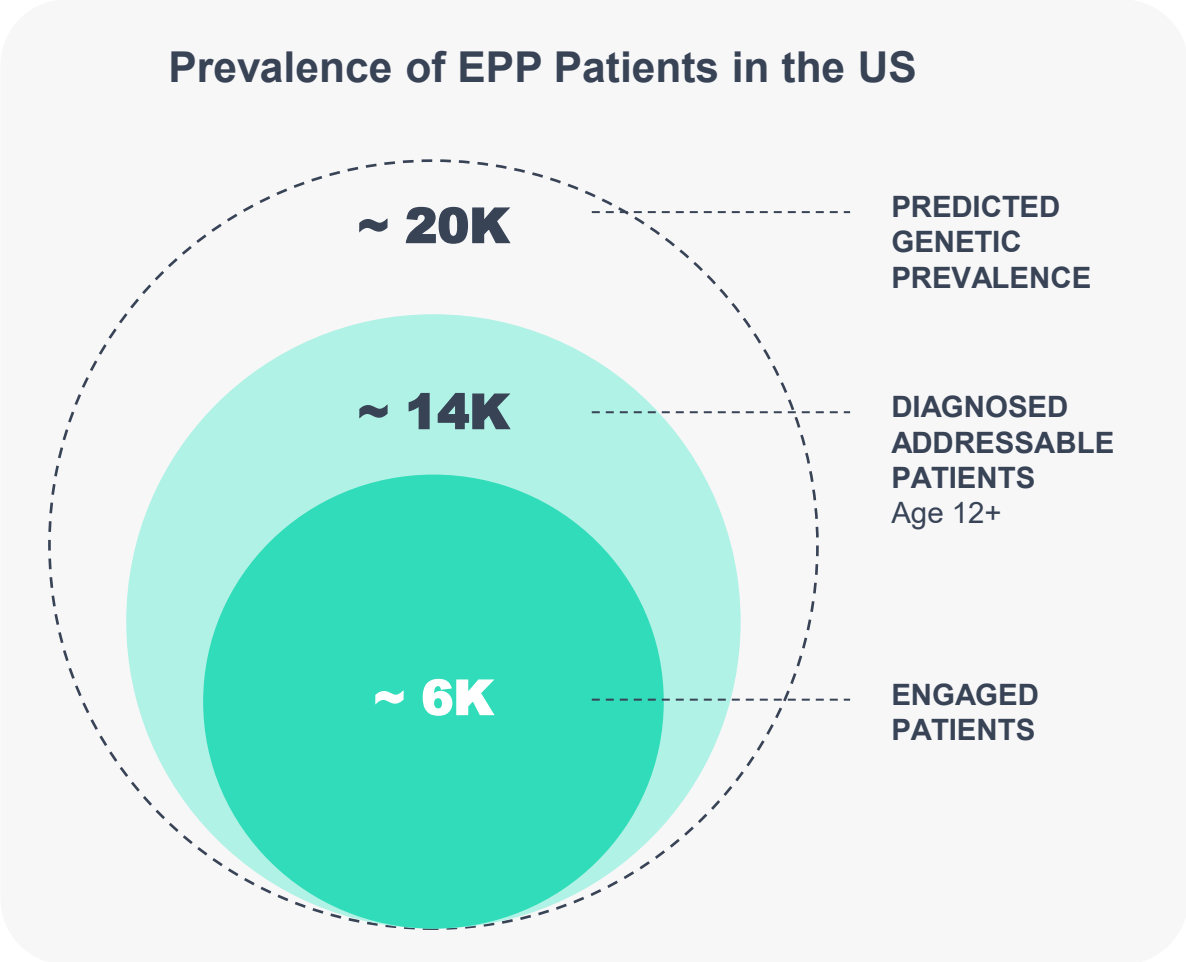
### No cure or disease-modifying treatment

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


Sources: Deybach et al (2009) Orphanet Journal of Rare Diseases; American Porphyria Foundation; Dickey et al (2021) Genet. Med.; Trinity Life Sciences; Komodo Claims Data (2016-2022); Balwani et al, JAMA Dermatology, 2017

# EPP: Well-defined rare disease population

## Patient population defined by claims analysis and validated by real-world evidence




### Epidemiology

Real world prevalence of hepatobiliary complications in EPP match evidence of liver/biliary issues in claims population

### In Person Outreach

Through initial outreach, Disc field team is validating patient numbers among top accounts

### Real-World Behaviors

Analysis of real-world / online activity on key topics related to EPP corroborates patient engagement levels predicted by claims analysis

Source: Trinity Life Sciences; Komodo Claims Data (2016-2022)

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

**56%** have anxiety and/or depression

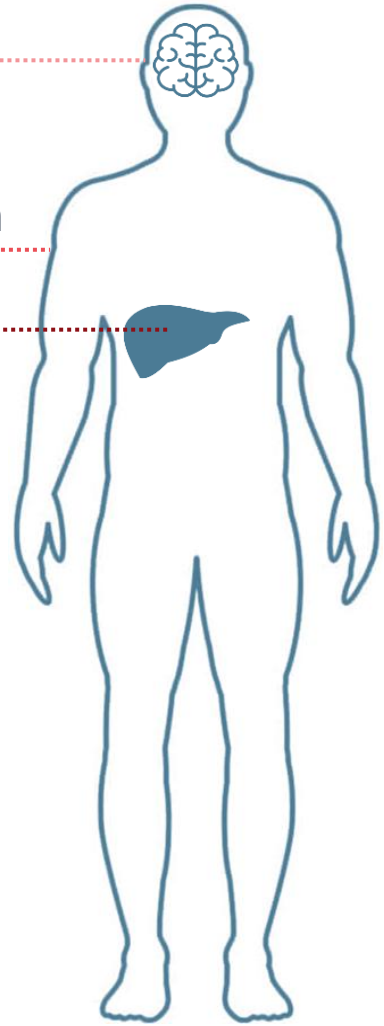
**Psychosocial**

**Skin**

**<30 min.** sun exposure before symptoms

**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

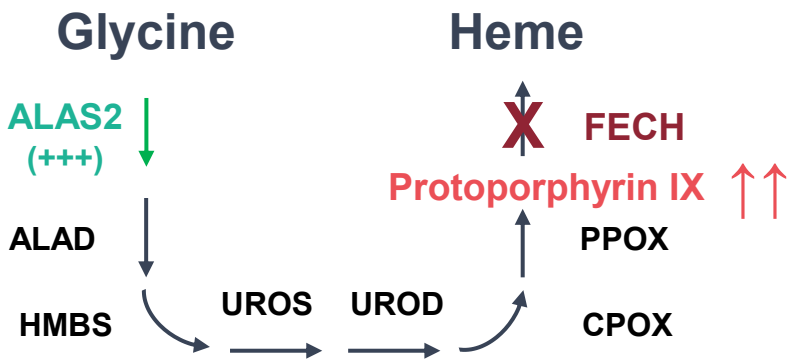
**32%** visit the ER each year

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

# Bitopertin: Potential disease-modifying treatment

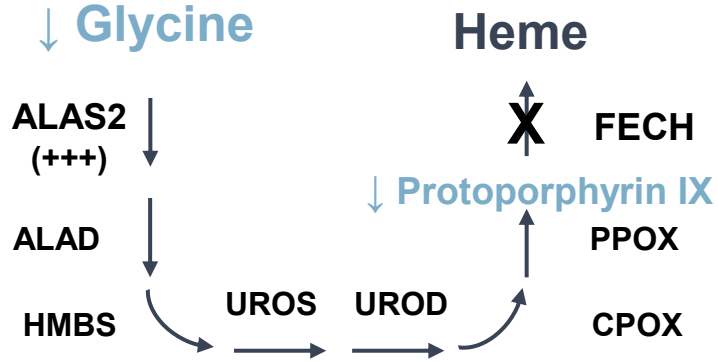
## Designed to reduce disease-causing PPIX by limiting update of glycine into developing erythrocytes

**EPP and XLP Patients**
High PPIX Levels




**Mutations result in reservoir of pathologically high levels of PPIX**

**Bitopertin Treatment**
Designed to Reduce PPIX Levels




**Potential first disease-modifying treatment for EPP and XLP**

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

# EPP development program

## BEACON, AURORA, HELIOS, and APOLLO studies

### Phase 2 – *Completed*

**BEACON**

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

**AURORA**

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

### Phase 3 – *Enrollment Complete*

**APOLLO**

- **EPP and XLP**; N=183 adults and adolescents
- **United States, Canada, Europe, Australia**
- **Double-blind, randomized, placebo-controlled**, 6-month study

### Open-label extension – *Ongoing*

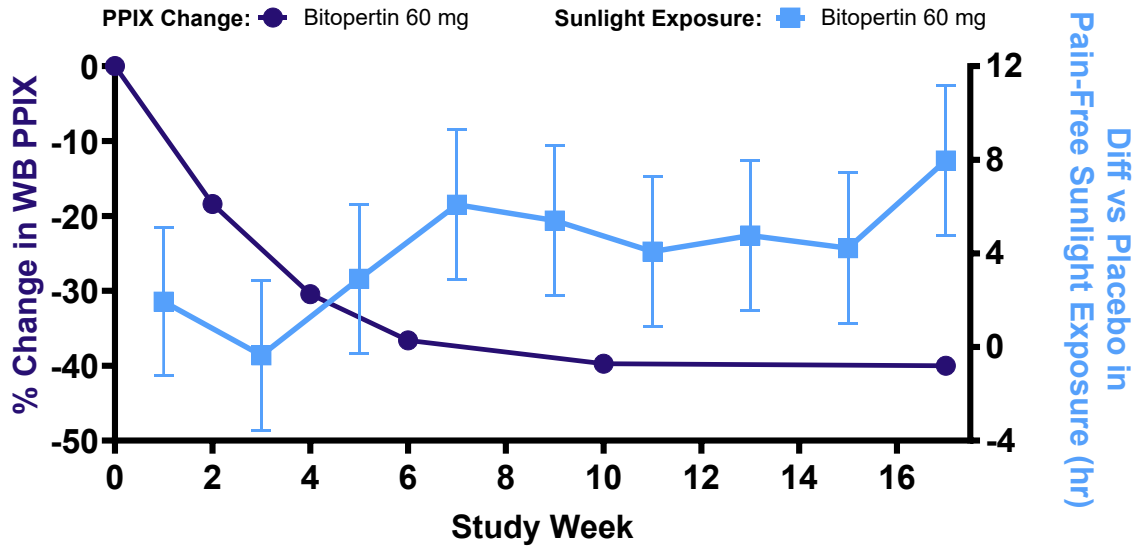
**HELIOS**

- **EPP and XLP**; adults and adolescents
- **Open-label long-term extension study** in US, Europe, and Australia

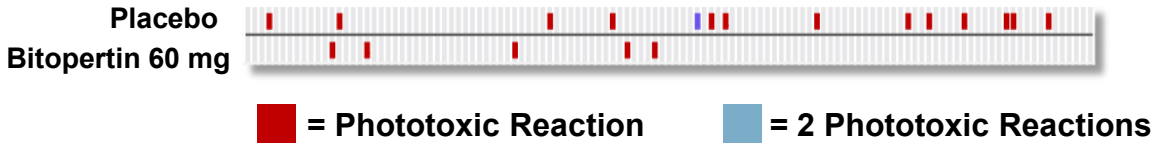
# Summary of AURORA results

## Bitopertin 60mg

AURORA




**Phototoxic Reactions**

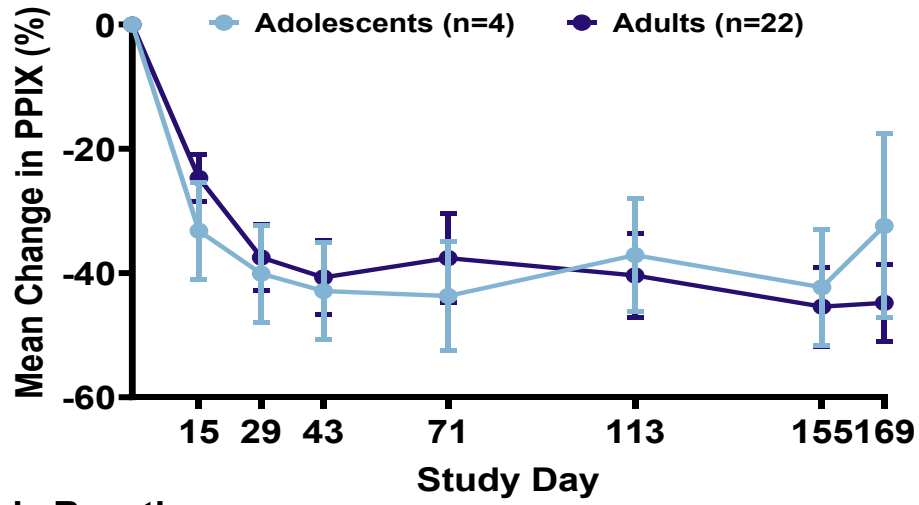



- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent, improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant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

# Summary of BEACON results

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

BEACON




**Phototoxic Reactions**

**Bitopertin 60 mg**

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

› PPIX reduction associated with **significant reduction in phototoxic reactions** from baseline

### Tertiles of PPIX Change

**PPIX Increased** ← → **PPIX Decreased**

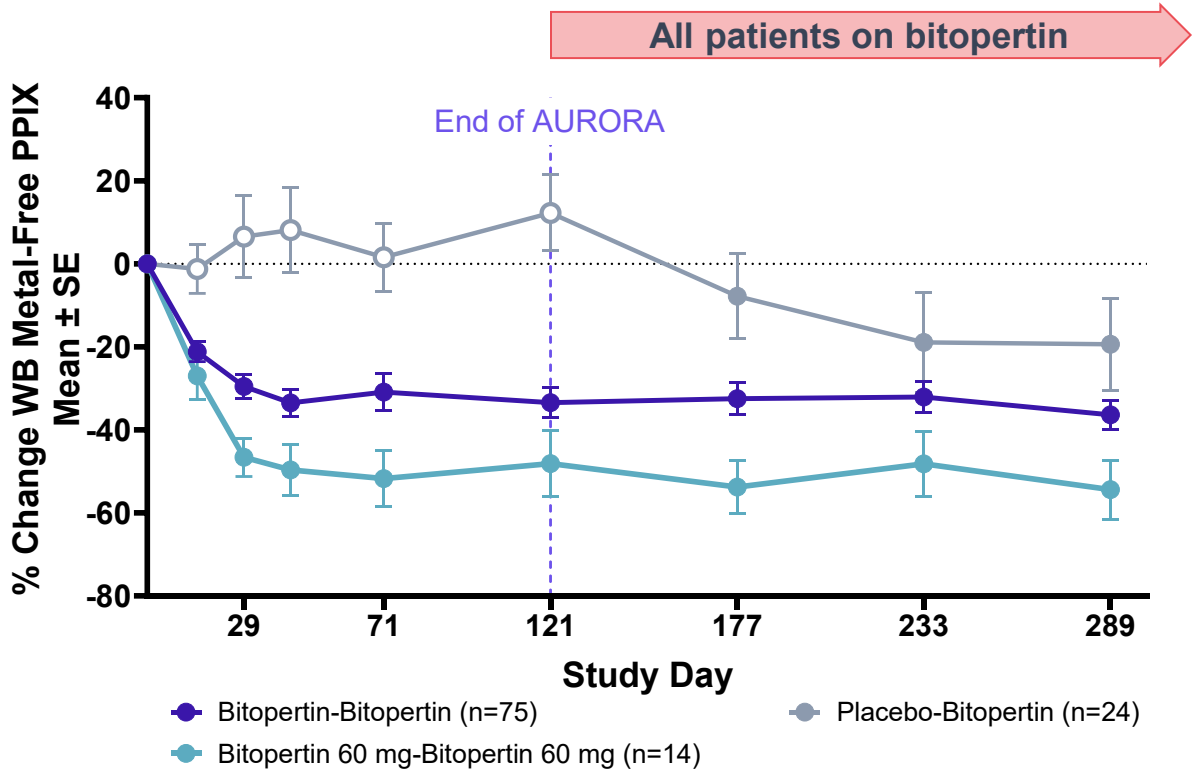
| Light Tolerance Measure (Mean ± SD) | Tertile 3 (-43% to 25%) | Tertile 2 (-53% to -43%) | Tertile 1 (-98% to -53%) |
|---|---|---|---|
| Cumulative total time in sunlight without pain (hr) | 145.6 ± 99.5 | 190.5 ± 111.6 | 262.1 ± 160.6 |
| Average time in sunlight without pain (hr) | 0.86 ± 0.6 |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

› PPIX reduction associated with **significant improvement in pain-free time in sunlight**

# Summary of HELIOS results

## Favorable long-term efficacy and safety

HELIOS




- Sustained reductions in PPIX with continued bitopertin treatment
- Greater PPIX decreases in participants who received 60 mg bitopertin continuously
- Continued treatment with 60 mg bitopertin reduced ALT, a marker of liver function
- Nearly all participants reported substantial improvements in QOL measures through week 24 of HELIOS
- Bitopertin exhibited favorable longer-term safety profile (up to 2+ years exposure)
- Safety profile similar across adults and adolescents with EPP or XLP

# APOLLO trial overview

## Enrollment completed in March 2026; topline data expected Q4 2026

| | |
|---|---|
| **N Size** | 183 patients across sites in the US, Canada, Europe, and Australia |
| **Trial Duration** | 6-month treatment period; Fully enrolled March 2026 |
| **Trial Design** | Randomized 1:1, double-blind, placebo-controlled |
| **Trial Population** | EPP and XLP patients ages 12+, stratified by baseline light tolerance and geography |
| **Dose** | 60 mg |
| **Co-primary Efficacy Endpoints** | • Average monthly total time in sunlight without pain between 10:00 and 18:00 during the last month of the 6-month treatment period<br>• Percent change from baseline in whole blood metal-free PPIX after 6 months of treatment |
| **Additional Endpoints** | • Occurrence of phototoxic reactions<br>• Cumulative total pain-free time in sunlight<br>• Change from baseline in time to prodrome<br>• Patient global impression of change (PGIC)<br>• Safety and tolerability |

### Robust Endpoint

- Longitudinal analysis leverages robust model that demonstrated significance in AURORA
- Accounts for time-dependent PPIX lowering effects with bitopertin and for waning of a placebo effect
- Focuses efficacy on month 6, after PPIX is fully reduced and potential placebo effect is expected to have waned

### Robust Study Design

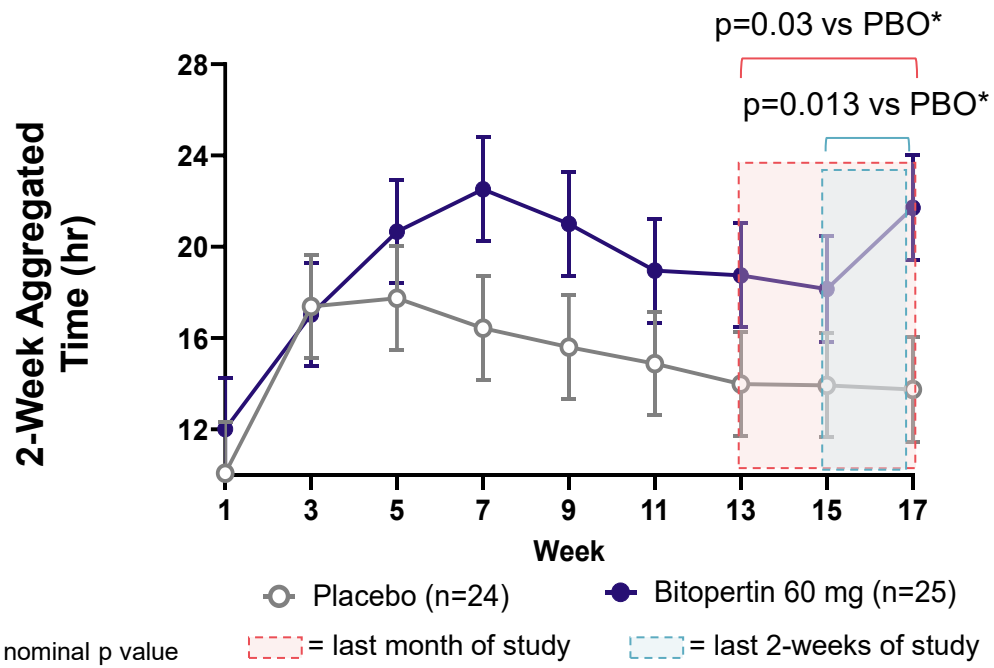
- Rigorous evaluation of baseline light tolerance required during screening and factored into analysis of the primary endpoint
- Stratification by geography to minimize confounding factors affecting light exposure across study arms
- The study design of n=75 per treatment group provided 80% power*; a study design with the same assumptions and n=183 would have >85% power

*Powered to detect a treatment effect of 11 hours for the monthly total time endpoint (representing an assumed ~20% reduction in the observed treatment effect in the last month of AURORA), with an assumed pooled standard deviation of 24 hours and an assumed 8% dropout rate

# Robust endpoints provide confidence in APOLLO

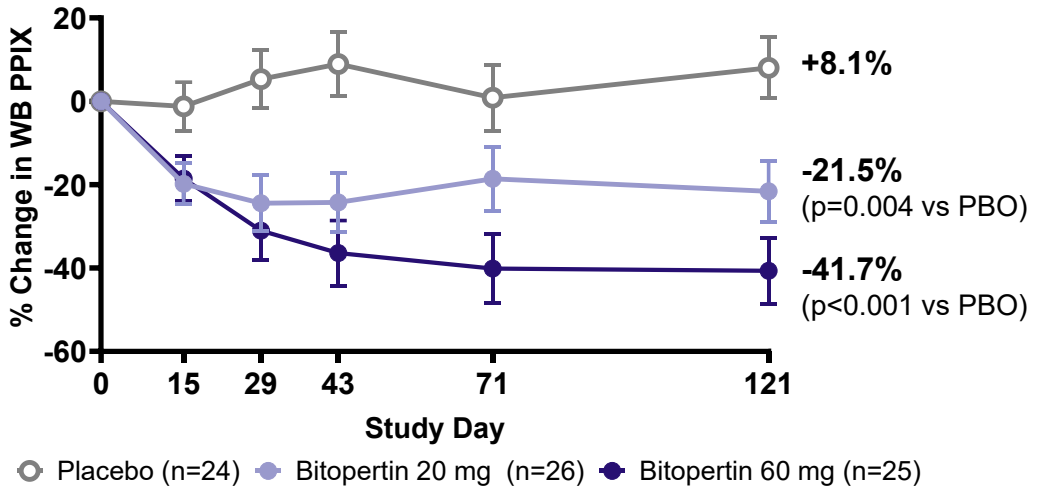
## Co-primary Endpoints: Average Monthly Time in Light without Pain and PPIX Change from Baseline

### AURORA: Sunlight Tolerance Over Time†




* nominal p value

### AURORA: PPIX Over Time




- Longitudinal analysis demonstrated significance and was robust in AURORA
- Accounts for time-dependent PPIX lowering effects with bitopertin and for waning of a placebo effect

- Prespecified primary endpoint with consistent, high statistical significance in BEACON and AURORA
- Recommended as co-primary by FDA, reflecting agency's acknowledgement of the importance of lowering PPIX in EPP

† Post-hoc longitudinal analysis adjusted for baseline

# Bitopertin: Potential to be the first approved medicine that targets the underlying cause of EPP

## Shown in clinical trials to reduce PPIX and improve multiple clinically meaningful measures of EPP

| | *Targets underlying pathophysiology of EPP* | *Meaningful improvement in sunlight tolerance* | *Functional benefit by reducing debilitating phototoxic reactions* | *Significantly improved how patients feel* |
|---|---|---|---|---|
| **AURORA*** | **50%** Reduction in PPIX vs. placebo | **2x** Improvement in pain-free time in sunlight vs. baseline | **75%** Reduction in phototoxic reactions vs. placebo | **Significant** Improvement in PGIC** vs. placebo |
| **BEACON*** | **60%** Reduction in PPIX vs. baseline at 60mg dose | **3x** Increase in time to prodrome vs. baseline | **92%** Reduction in phototoxic reactions vs. baseline | **95%** Patients reporting improvements in PGIC** vs. baseline |

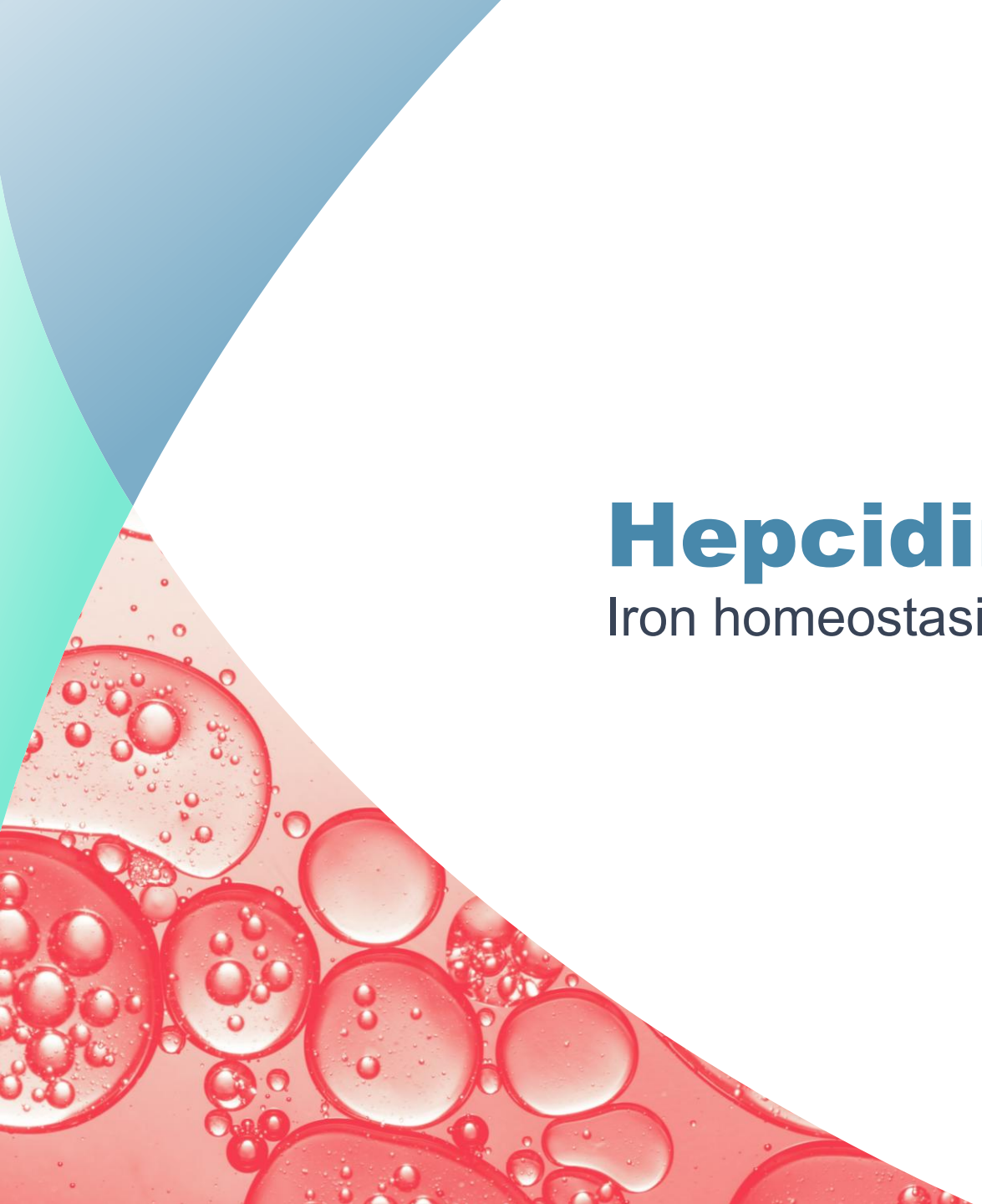
- ✓ **>80% rollover to HELIOS long term extension trial**
- ✓ **Long-term benefits on PPIX and PGIC up to 2+ years in HELIOS**
- ✓ **Well-characterized safety and tolerability profile in >4,000 clinical trial participants**
- ✓ **Patient friendly, once daily oral presentation**

*Based on 60mg dosing; **Patient Global Impression of Change

# Bitopertin next steps

**Planning submission for traditional FDA approval following accelerated approval CRL**

- Type A meeting with the US FDA to review approach for resubmission scheduled for Q2 2026
- Expect to present topline APOLLO data in Q4 2026 and, if positive, use this data to address the deficiency cited in the CRL
- Typical FDA goal date for review of CRL response is ~6 months, implying potential for an updated decision by mid-2027
- Focused efforts to validate accounts, further develop the market, and provide access to bitopertin for eligible patients



# Hepcidin Modulation

Iron homeostasis

# Iron is fundamental to RBC biology

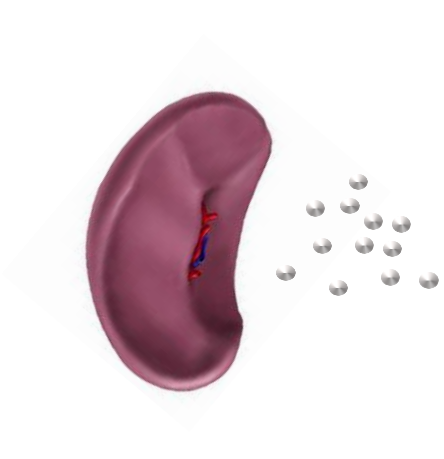
## Hepcidin is a regulatory hormone that plays a central role in iron metabolism and homeostasis

**GI Tract**
Iron Intake

**Induced by Inflammation**

**Hepcidin**

**Gatekeeper Function: Blocks iron absorption and recycling**



**Spleen**
Iron Storage

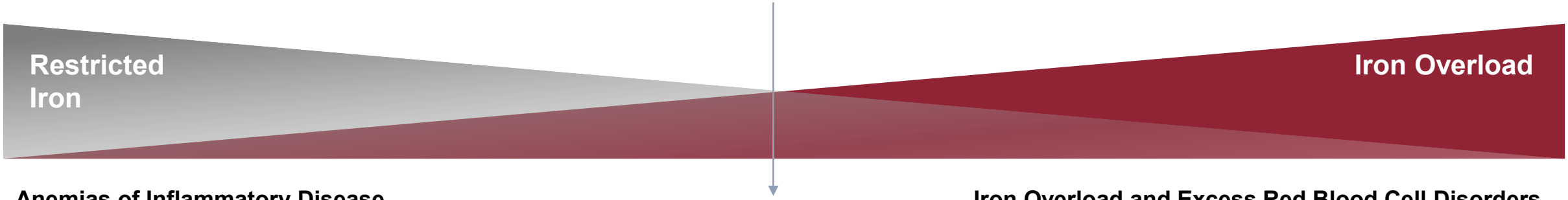
**RBC Production in Bone Marrow**

# Hepcidin is a therapeutic target for diseases

## Dysregulated hepcidin drives a wide range of hematologic diseases

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

Regulated erythropoiesis




Regulated iron

**Anemias of Inflammatory Disease**

- Myelofibrosis
- Autoimmune / Inflammatory Disorders

**Iron Overload and Excess Red Blood Cell Disorders**

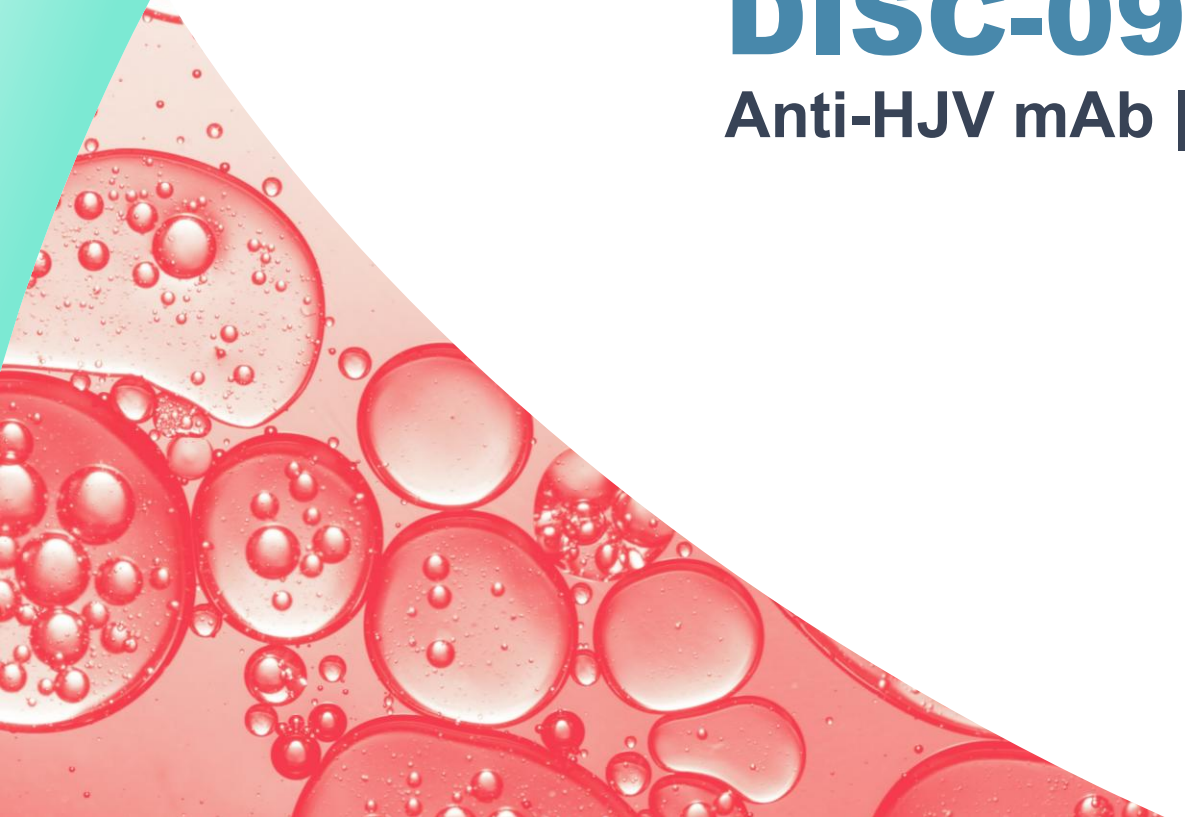
- Polycythemia Vera
- Sickle Cell Disease

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

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

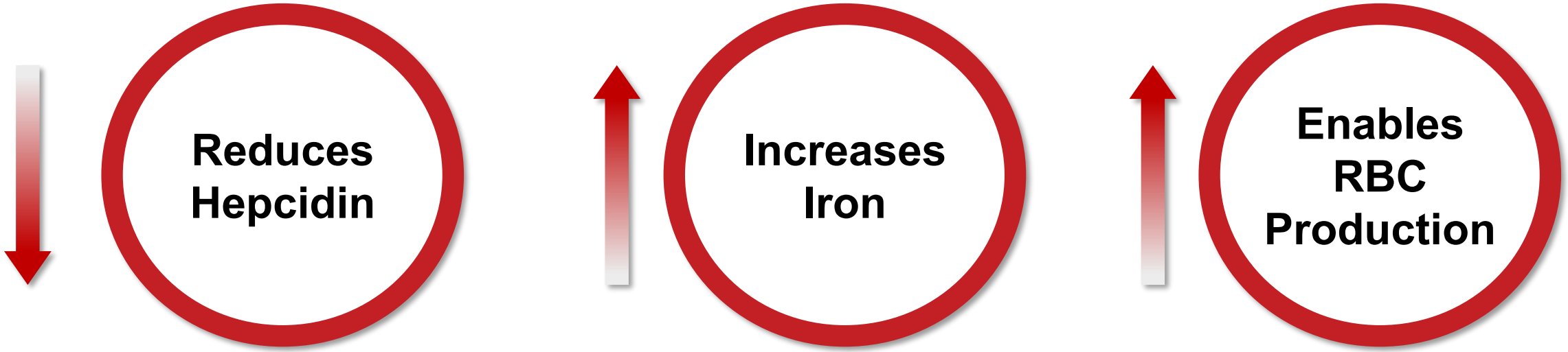
# DISC-0974

**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**

HJV = hemojuvelin

# Significant opportunity in anemia of inflammation

## Numerous chronic diseases associated with anemia from high hepcidin

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

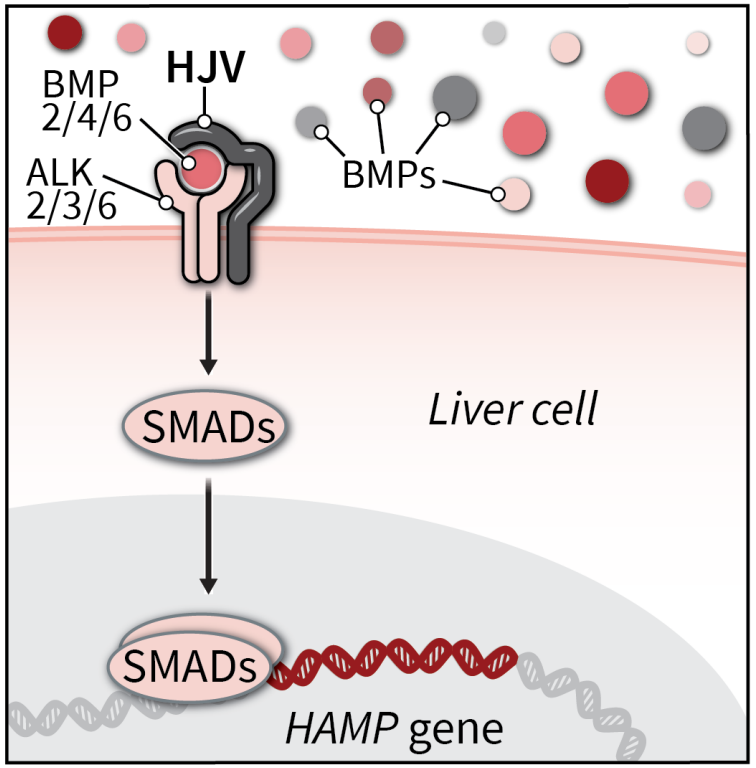
- Anemia of inflammation is the 2nd most common form of anemia
- Estimated 40% of all anemias are driven by or have an inflammatory component
- Hepcidin is up-regulated and correlates with anemia, driven by inflammation

**Bold = existing Disc trial**

Sources: Weiss (2019); Maccio (2014); Barraco (2016); 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

# Phase 1 SAD trial in healthy volunteers

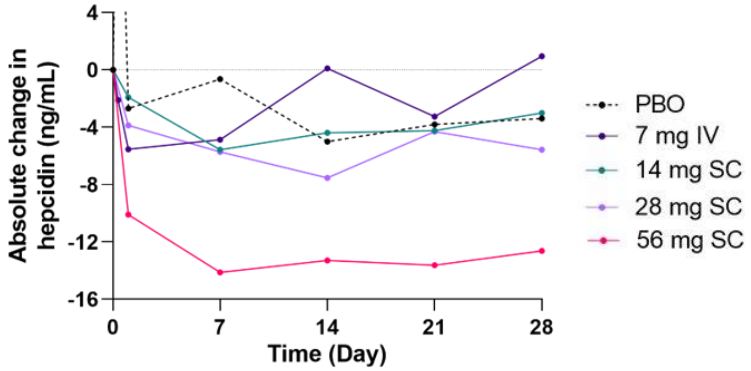
## Established proof-of-mechanism based on hepcidin and iron parameters

### Trial Design

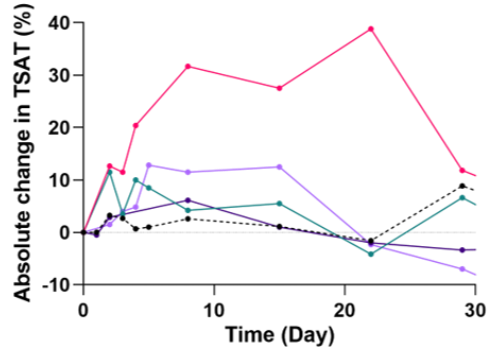
- Single-ascending dose in ≥32 healthy volunteers
- Key outcome measures:
  - Safety and PK
  - Hepcidin level, serum iron level, % TSAT
- Dose escalation until TSAT > 40% for at least 2 weeks
- Dose levels: 7 mg dose (IV); 14, 28 and 56 mg doses (SC)

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

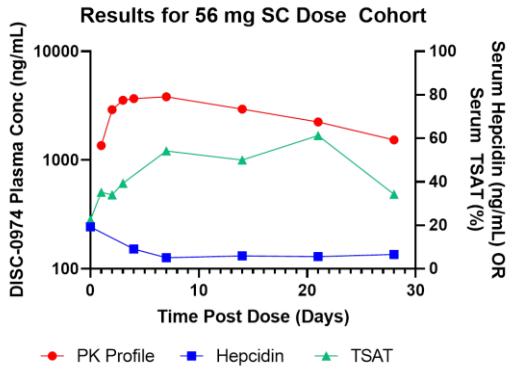
### DISC-0974 Reduced Hepcidin Production

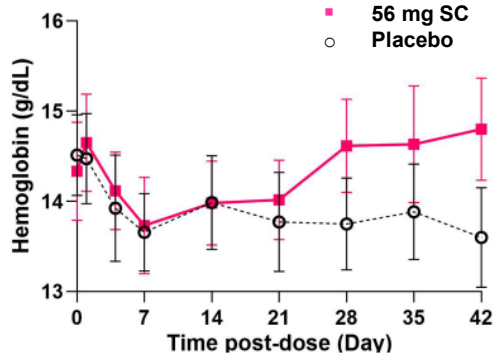



### DISC-0974 Increased TSAT



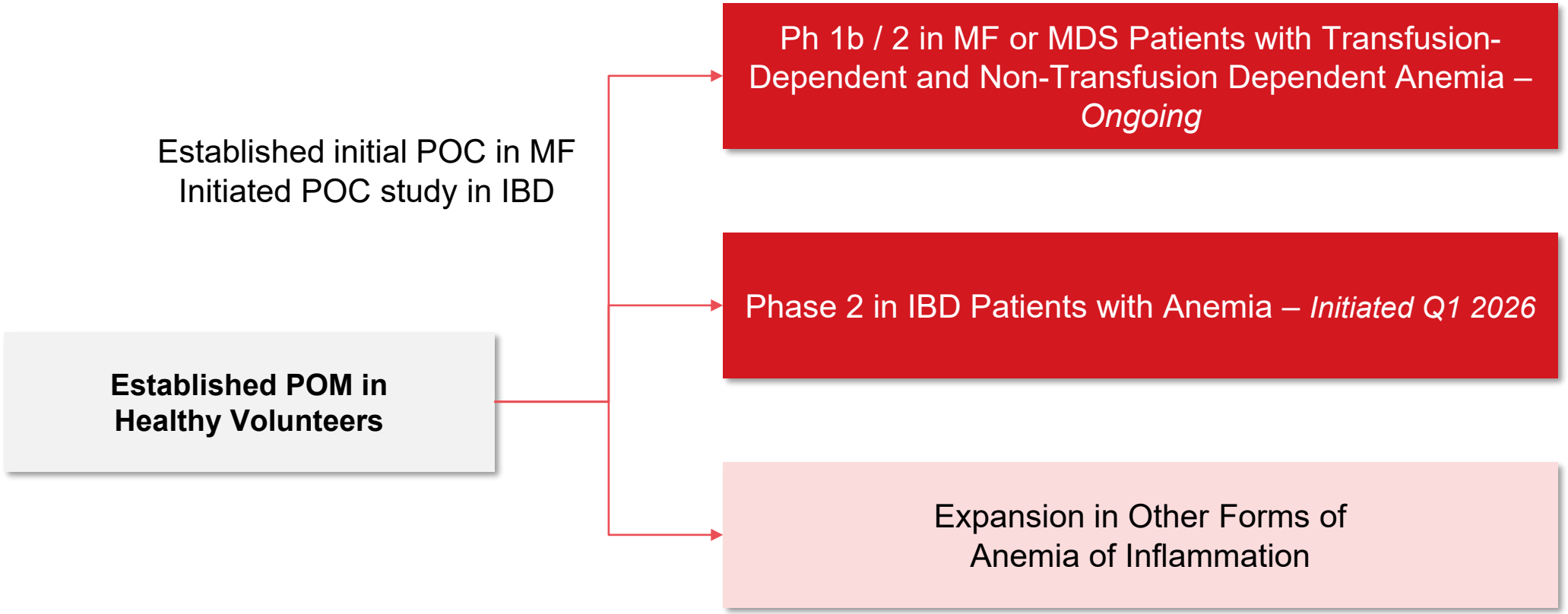

### 56 mg pharmacodynamic activity improved key clinical parameters (> 1g/dL Hgb)




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

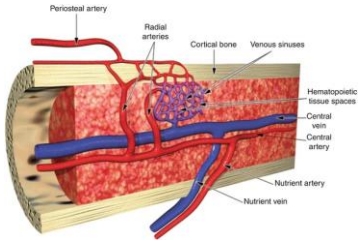
# DISC-0974 development strategy




CKD = chronic kidney disease; MDS = myelodysplastic syndrome; MF = myelofibrosis; POC = proof of concept; POM = proof of mechanism

# Hepcidin is a key driver of myelofibrosis (MF) anemia

## Anemia of MF




### Est. # Patients

- 25,000 patients (US)
- ~87% are anemic; severe and require transfusion

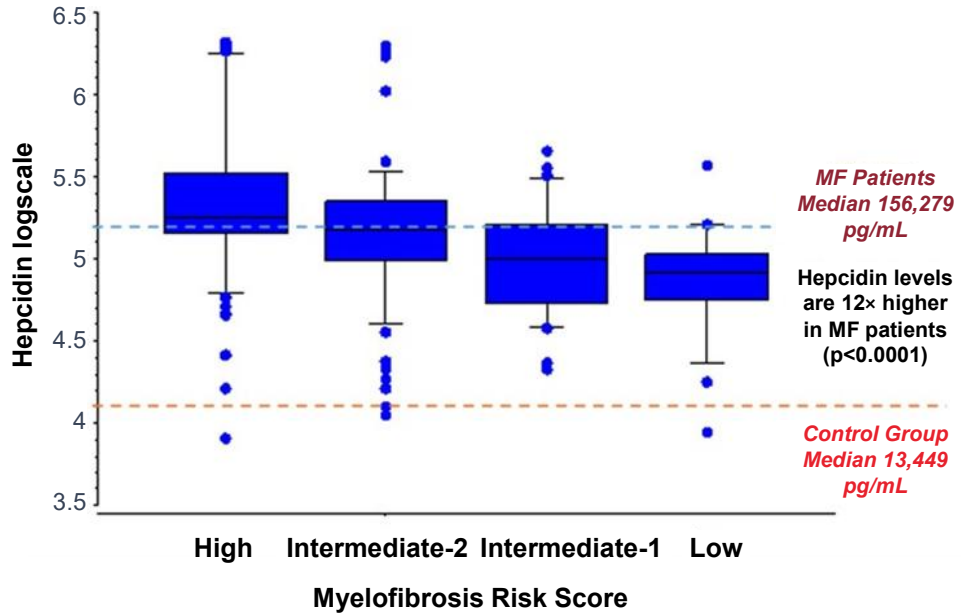
### Etiology of Anemia

- High hepcidin from inflammation
- JAK inhibitors worsen anemia; loss of marrow function

### Unmet Medical Needs

- Severe and difficult to treat; high transfusion burden
- No approved or effective anemia therapy
- Anemia limits optimal JAK inhibitor treatment

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




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

# RALLY-MF: Study overview and baseline characteristics

## Data as of October 16, 2025

| Screening (28 Days) | Treatment Period (6 cycles, q28 days) | Follow-Up (28 Days) | Optional Continuation (Up to 2 years) |
|---|---|---|---|

### Key Study Endpoints

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

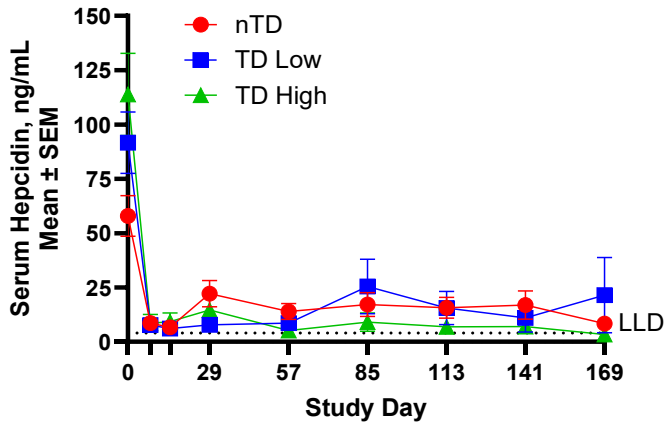
| | nTD (n=30) | TD Low (n=10) | TD High (n=7) | Overall (n=47) |
|---|---|---|---|---|
| **Age, median (range), years** | 69.5 (54, 83) | 74.5 (31, 87) | 72 (61, 87) | 70 (31, 87) |
| **Concomitant medication, n (%)** | | | | |
| **JAK inhibitor** | 15 (50) | 5 (50) | 5 (71) | 25 (53) |
| Ruxolitinib | 5 (17) | 2 (20) | 3 (43) | 10 (21) |
| Momelotinib | 8 (27) | 3 (30) | 2 (29) | 13 (28) |
| Pacritinib | 2 (7) | 0 | 0 | 2 (4) |
| **Hydroxyurea** | 1 (3) | 0 | 0 | 1 (2) |
| **Baseline hepcidin** | | | | |
| **Median (range), ng/mL** | 38.5 (14, 174) | 109.9 (47, 133) | 107.1 (57, 177) | 61.2 (14, 177) |
| **Mean (SD), ng/mL** | 57.9 (48) | 91.6 (37) | 113.9 (46) | 72.6 (50) |
| **Baseline hemoglobin, median (range), g/dL** | 8.9 (7.6, 10.1) | 7.4 (6.1, 11.4) | 7.6 (6.3, 8.8) | 8.5 (6.1, 11.4) |

nTD = non-transfusion dependent (Hgb <10 and 0 units transfused / 12 weeks); TD Low = 1-2 units transfused / 12 weeks; TD High = 3-12 units transfused / 12 weeks; TI = transfusion independence

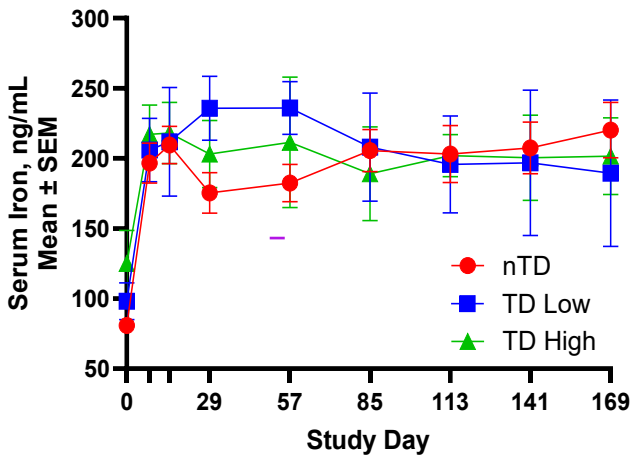
# Initial RALLY-MF phase 2 data

## Positive, durable benefits on hemoglobin and transfusion burden in anemia of MF across a broad range of patients

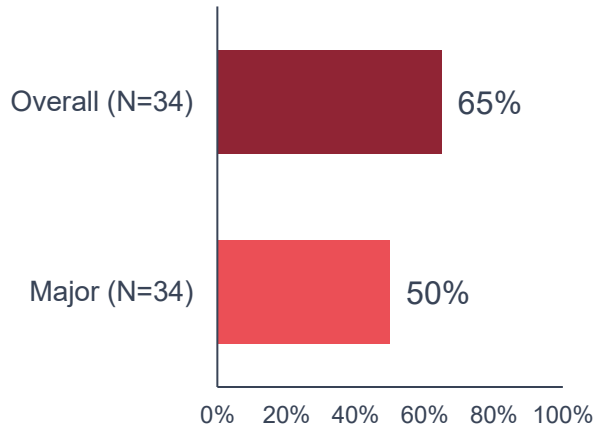
### Hepcidin by Transfusion Cohort

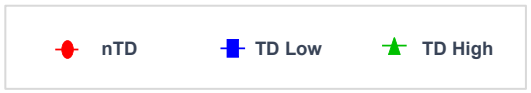



### Iron by Transfusion Cohort




### Hematologic Response




Abbreviations:. 6 nTD, 3 TD Low participants were considered non-evaluable due incomplete data entry at the time of data cut. 10 participants had a per protocol dose escalation at visit Day 57 due to insufficient response. 4 participants had a per protocol dose hold due to Hgb >12 g/dL. 68% of participants who completed study are participating in the optional continuation phase.; Overall response for NTD = Mean Hgb ↑ ≥1 g/dL for ≥12 weeks, for TD Low and TD High = ≥50% reduction in transfusion requirement; Major response for NTD = Mean Hgb ↑ ≥1.5 g/dL for ≥12 weeks, for TD Low = TI ≥16 weeks, and for TD High = TI ≥12 weeks

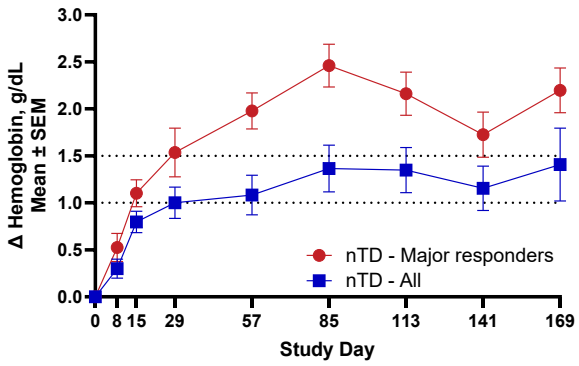
# Initial RALLY-MF phase 2 data

## nTD and TD Low patients had meaningful responses on hemoglobin and FACIT-Fatigue with greatest improvements seen in those achieving a major hematologic response

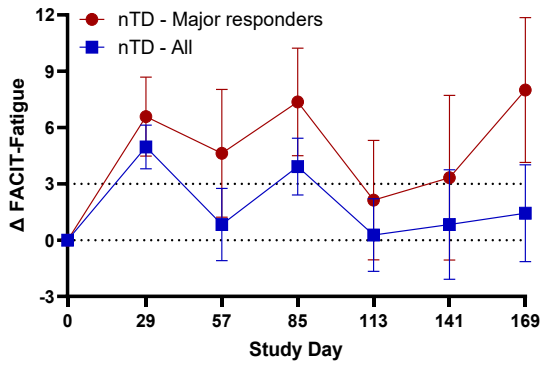
### Mean Change from Baseline Over Time

**nTD**

**Hemoglobin**

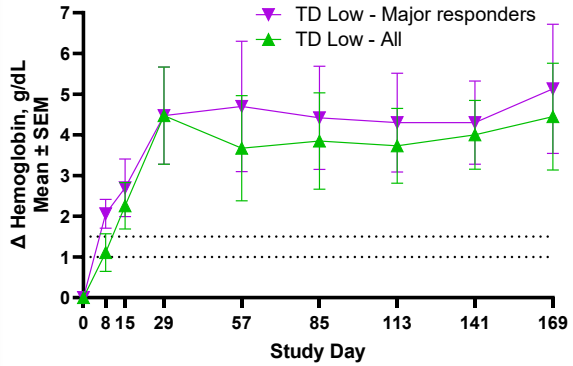



**FACIT-Fatigue**

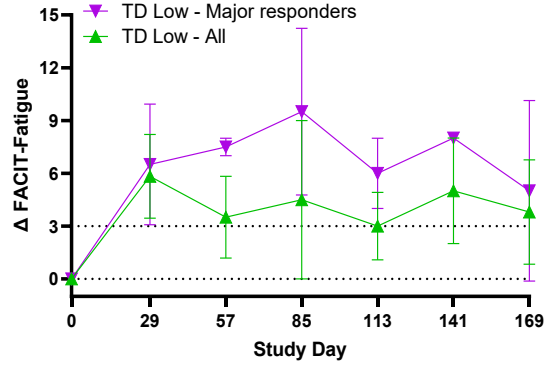



**TD Low**

**Hemoglobin**




**FACIT-Fatigue**

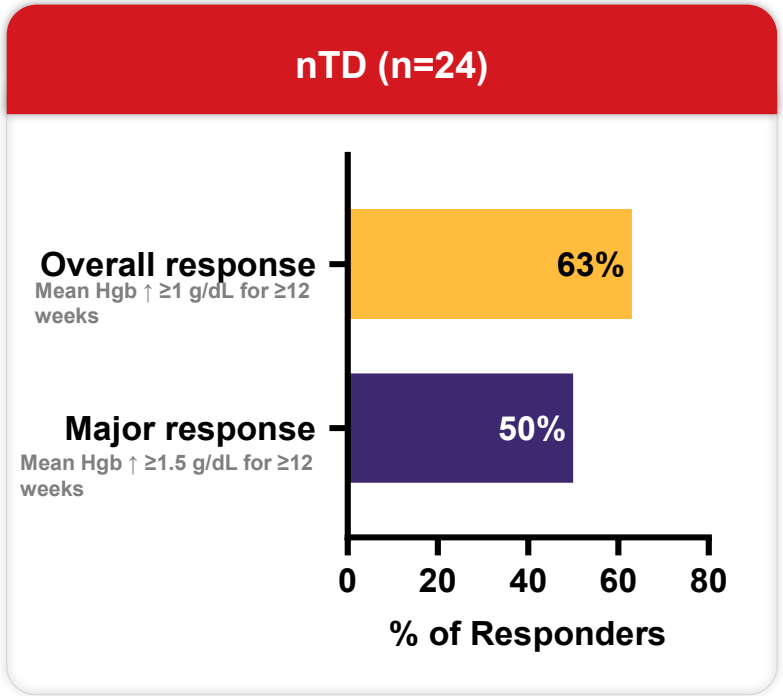


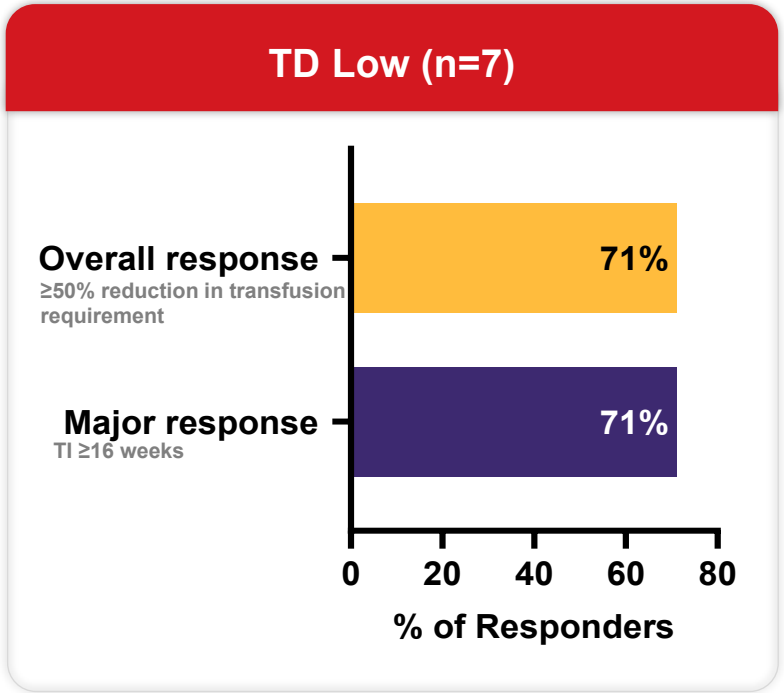

Hemoglobin analysis excludes values within 14 days from receipt of PRBC transfusion. * A 3-point change in the FACIT-Fatigue score was used as a threshold for clinical significance. Source: Webster et al, Health Qual Life Outcomes. 2003;1:79.

# Initial RALLY-MF phase 2 data

## Hematologic Response: nTD and TD Low Patients

- Hematologic response achieved across transfusion cohorts and regardless of concomitant JAKi use
- >60% overall response rate and ≥50% major response rate in both nTD and TD Low cohorts



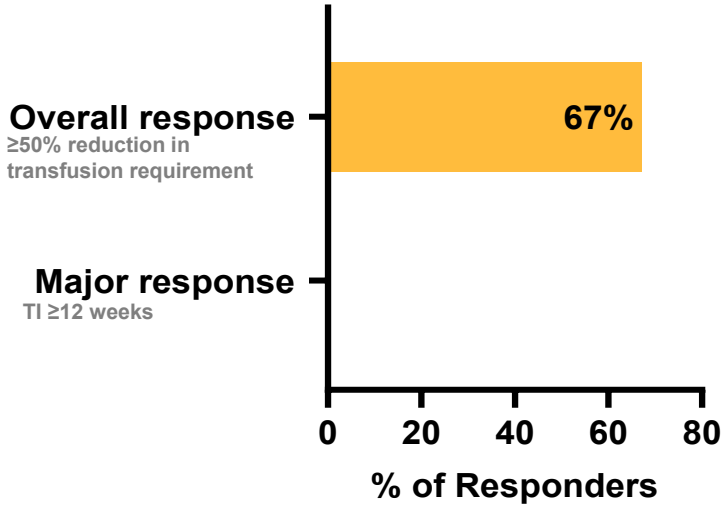

Abbreviations: Hgb = hemoglobin; TI = transfusion independence. 6 nTD, 3 TD Low participants were considered non-evaluable due incomplete data entry at the time of data cut. 10 participants had a per protocol dose escalation at visit Day 57 due to insufficient response. 4 participants had a per protocol dose hold due to Hgb >12 g/dL. 68% of participants who completed study are participating in the optional continuation phase.

# Initial RALLY-MF phase 2 data

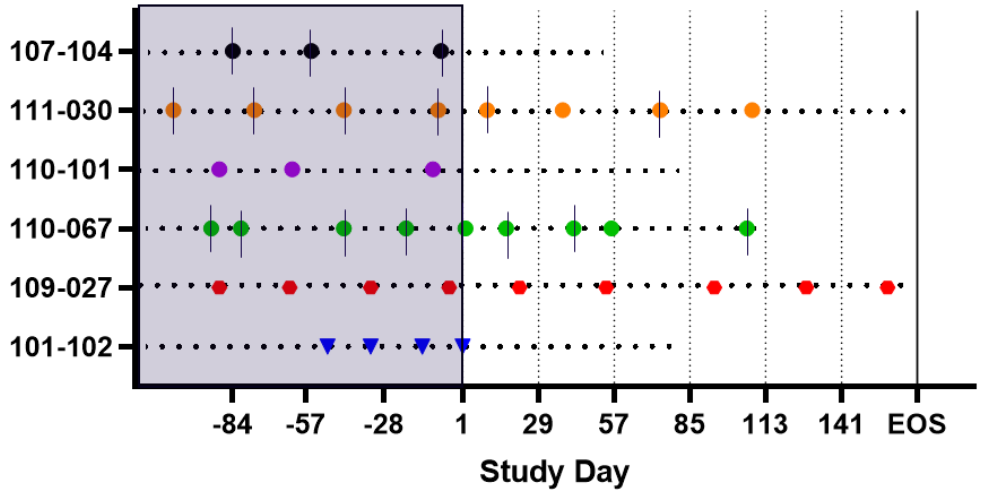
## Hematologic Response: TD High

- 67% of TD High patients with at least 85 days on study had ≥ 50% reduction in transfusion requirement
- Initial data for additional N=3 TD High patients trending towards major response of TI ≥12 weeks; Additional data to be presented midyear 2026

**TD High on Study ≥85 Days (n=3)**




**TD High with at Least One Dose of DISC-0974 (n=6)**

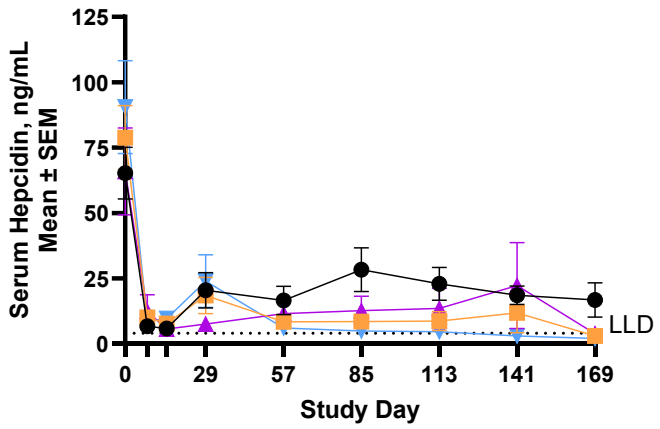



Abbreviations: Hgb = hemoglobin; TI = transfusion independence. 4 TD High participants were considered non-evaluable for hematologic response due incomplete data entry at the time of data cut. 10 participants had a per protocol dose escalation at visit Day 57 due to insufficient response. 4 participants had a per protocol dose hold due to Hgb >12 g/dL. 68% of participants who completed study are participating in the optional continuation phase.

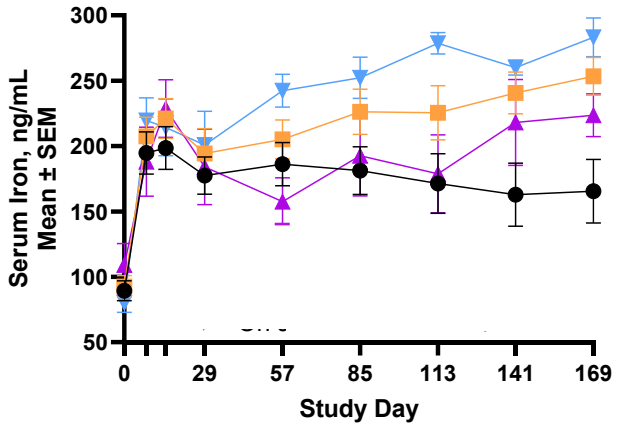
# Initial RALLY-MF phase 2 data

## DISC-0974 has demonstrated efficacy regardless of concomitant JAK inhibitor use, setting up for utilization across all anemic MF patients

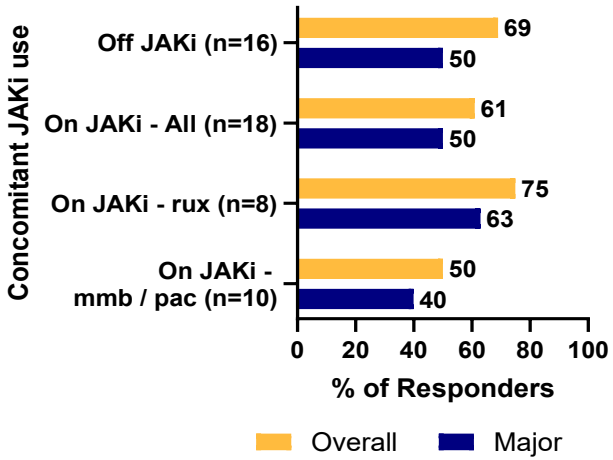
### Hepcidin by JAKi Cohort




### Iron by JAKi Cohort




### Response by JAKi Cohort





Abbreviations: Hgb = hemoglobin; JAKi = JAK inhibitor; mmb = momelotinib; pac = pacritinib; rux = ruxolitinib; TI = transfusion independence. 6 nTD, 3 TD Low, and 4 TD High participants were considered non-evaluable due incomplete data entry at the time of data cut. 10 participants had a per protocol dose escalation at visit Day 57 due to insufficient response. 4 participants had a per protocol dose hold due to Hgb >12 g/dL. 68% of participants who completed study are participating in the optional continuation phase.

# Initial RALLY-MF phase 2 data

## Safety

| Preferred Term | nTD (n=30) | TD Low (n=10) | TD High (n=7) | Overall (n=47) |
|---|---|---|---|---|
| **Any TEAE, n (%)** | 23 (76.7) | 7 (70.0) | 5 (71.4) | 35 (74.5) |
| **Related TEAE, n (%)** | 3 (10.0) | 4 (40.0) | 4 (57.1) | 11 (23.4) |
| **SAE, n (%)** | 7 (23.3) | 1 (10.0) | 1 (14.3) | 9 (19.1) |
| **AESIs, n (%)** | 2 (6.7) | 0 | 0 | 2 (4.3) |
| **≥ Grade 3 TEAEs, n (%)** | 11 (36.7) | 3 (30.0) | 2 (28.6) | 16 (34.0) |
| **Common TEAEs in >10% participants, n (%)** | | | | |
| Muscle spasms | 5 (16.7) | 2 (20.0) | 1 (14.3) | 8 (17.0) |
| Constipation | 4 (13.3) | 1 (10.0) | 2 (28.6) | 7 (14.9) |
| Diarrhea | 5 (16.7) | 1 (10.0) | 1 (14.3) | 7 (14.9) |
| Dizziness | 7 (23.3) | 0 | 0 | 7 (14.9) |
| Upper respiratory tract infection | 6 (20.0) | 1 (10.0) | 0 | 7 (14.9) |
| Fatigue | 5 (16.7) | 1 (10.0) | 1 (14.3) | 7 (14.9) |
| Anemia | 2 (6.7) | 3 (30.0) | 2 (28.6) | 7 (14.9) |
| Headache | 4 (13.3) | 0 | 1 (14.3) | 5 (10.6) |
| Hypertension | 3 (10.0) | 1 (10.0) | 1 (14.3) | 5 (10.6) |

Related TEAEs occurring in ≥2 participants overall: diarrhea (n=4), urinary tract infection (n=2), none of the related TEAEs were considered serious. SAEs and ≥Grade 3 AEs: sinus bradycardia (n=1), rib fracture (n=1), blood creatinine increased (n=1, AESI), chronic kidney disease (n=1, AESI), nephrolithiasis (n=1), cellulitis (n=2), diabetic foot infection (n=1), sepsis (n=1), gastric hemorrhage (n=1), anemia (n=1), vomiting (n=1). SAEs and <Grade 3 AEs: atrial fibrillation (n=1), upper gastrointestinal hemorrhage (n=1). ≥Grade 3 AEs and Non-serious AEs: anemia (n=6), lymphocyte count decreased (n=1), neuropathy peripheral (n=1), muscular weakness (n=1), hypocalcemia (n=1), dizziness (n=1), syncope (n=1) , blood creatinine phosphokinase increased (n=1), hypertension (3), prostate cancer (n=1). AESIs: blood creatinine increased (n=2), chronic kidney disease (n=1). 3 participants had early withdrawal from study due to patient or physician decision; there were no early withdrawals due to adverse events.

# Myelofibrosis opportunity

## Positioned for use across all anemia MF patients, regardless of background MF-directed therapy, setting up for a potential blockbuster opportunity

**~$2.0B**
Total Est. 2024 JAK Inhibitor US Sales (MF)

MF patients treated with JAK inhibitor

MF patients JAK-naïve or discontinued

**25K US MF patients**

**87% Anemic**

DISC-0974 target profile is designed to address the full MF anemia market:

**~22K Addressable Patients**

**Implies >$4B US Opportunity**

### Significant Unmet Need for Anemia-Focused Therapy

- Anemia is associated with worse disease prognosis and survival; impacts patient QOL and healthcare utilization
- Limits or contributes to failure of treatment with JAK inhibitors
- Current FDA-approved MF therapies focus on managing symptoms and spleen, not anemia
- Off-label anemia management tools are limited by efficacy, applicability, and tolerability

**Thinning of the competitive pipeline sets up the potential for DISC-0974 to be the primary therapy to address MF anemia for all anemic patients**

# DISC-0974: Emerging product profile aiming to address key needs for MF anemia therapy

## Key Needs for Anemia Therapy

1. **Works across anemia severity levels**
2. **Works as a monotherapy**
3. **Works with any MF-directed therapy**
4. **Supports optimization MF-directed therapy regimen**
5. **Superior response rates vs. current off-label anemia therapies**

## DISC-0974 Emerging Product Profile

- ✓ Achieved POC in NTD, TD Low, and TD High patients
- • Recruiting greater N for each cohort in ongoing Phase 2 trial

- ✓ Initial Phase 2 data showed encouraging efficacy as monotherapy and in combination with underlying MF therapies (ruxolitinib, momelotinib, and pacritinib)
- • Potential to explore impact of DISC-0974 on optimization of underlying MF regimen in future studies

- ✓ Initial ORR of 63-71% across all cohorts in Phase 2
- ✓ Initial MRR of 50-71% for NTD and TD low cohorts in Phase 2

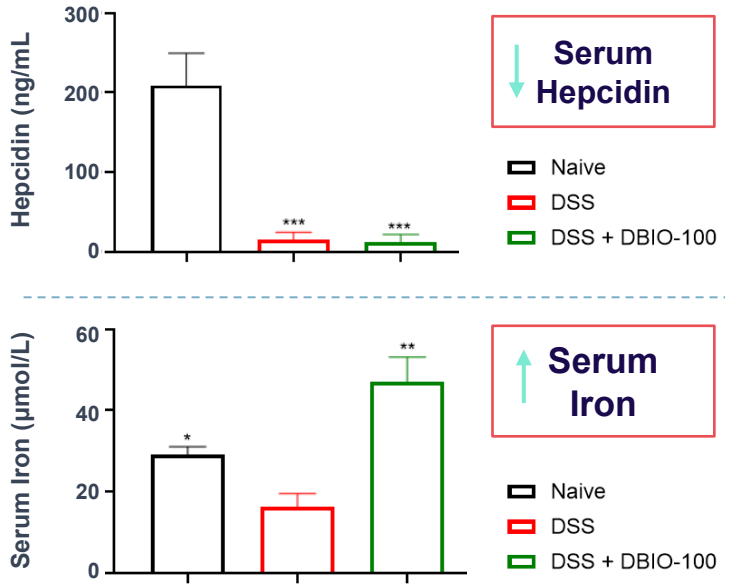
POC=Proof of concept; ORR=Overall Response Rate; MRR=Major Response Rate

# DISC-0974 in other anemias of inflammation

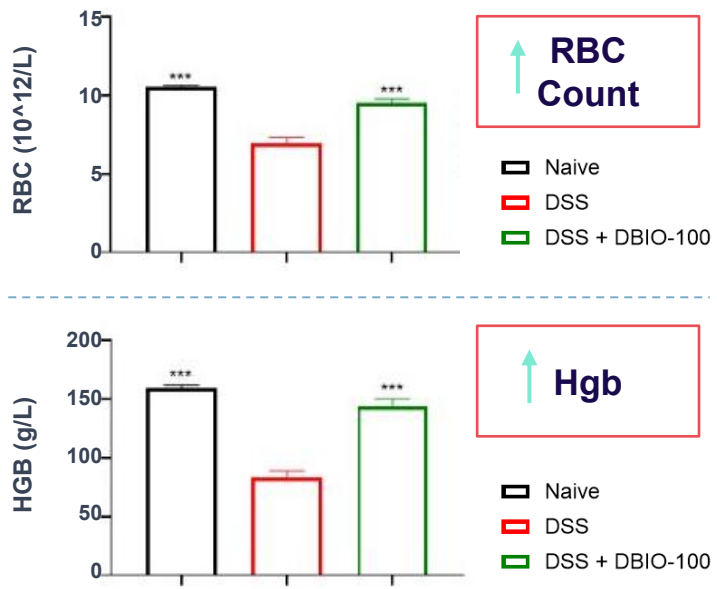
## Inflammatory bowel disease mouse model

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

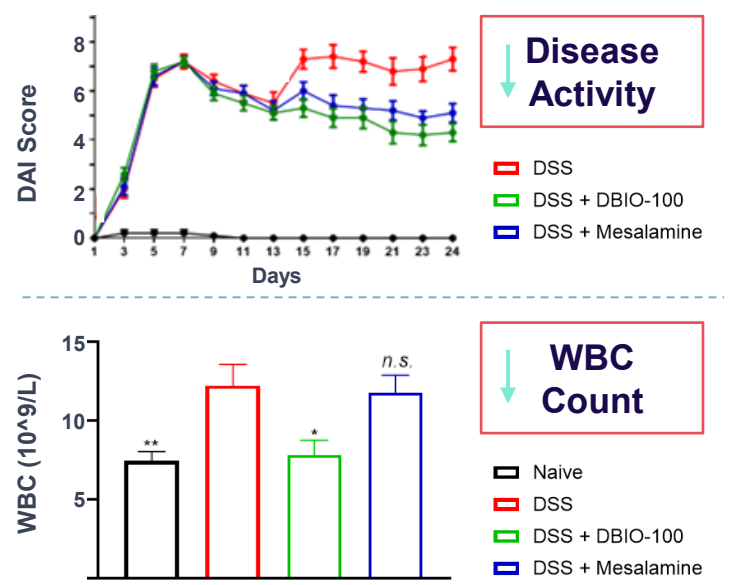
### Target Engagement




### Hematologic Improvement




### IBD Disease Modification




DAI Score = Disease Activity Index

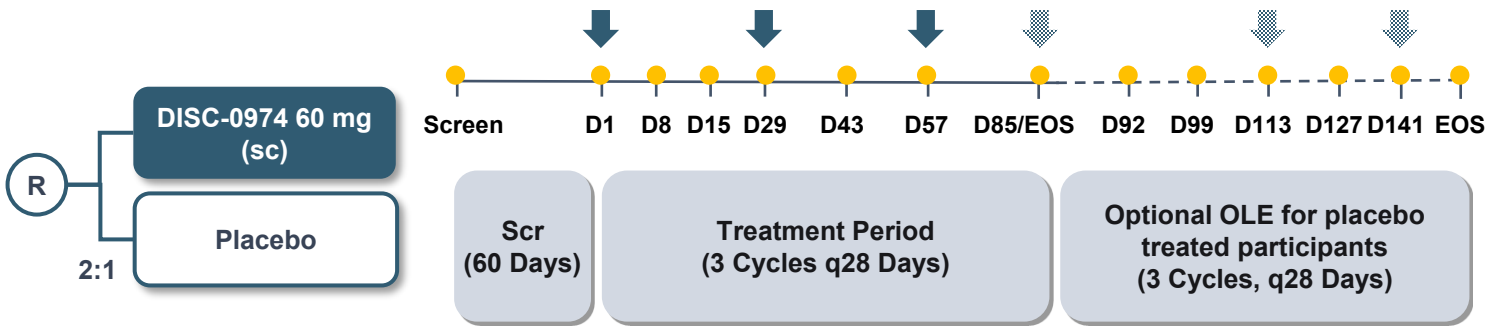
# RALLY IBD: Phase 2 trial design

## Initiated Q1 2026

### Study Population

- N=21
- ≥18 years of age with IBD
- Mild disease assessed by baseline endoscopy at screening
- Hgb ≥7 and <12 g/dL for females, and ≥7 and <13 g/dL for males
- Symptomatic anemia despite optimized, stable conventional IBD-directed therapy for 3 months
- Serum ferritin ≥75 µg/L
- Wash out of anemia directed therapies including PRBCs, ESAs, or IV iron required
- Concomitant use of JAKi disallowed

### Study Schema




### Key Study Endpoints

| | |
|---|---|
| **Primary** | • Maximal change from baseline in Hgb through Day 85 |
| **Secondary** | • TEAEs, vital signs, physical examination, ECGs, blood and urine testing<br>• Serum iron, TSAT, ferritin, serum hepcidin, reticulocyte count, CHr, and RBC count<br>• Mean change in Hgb from baseline through Day 85<br>• Proportion of participants that achieve Hgb increase ≥1 g/dL and ≥ 2 g/dL through Day 85<br>• Proportion of participants that hit dose holding criteria (Hgb increase of ≥2 g/dL from baseline or absolute Hgb of ≥15 g/dL) |

# Anti-HJV franchise: Next steps and future development

## Anemia of Myelofibrosis

- Updated data from RALLY-MF to be shared in an oral presentation at ASCO in June
- Topline RALLY-MF data expected Q4 2026
- End of Phase 2 Meeting with FDA expected by end of year
- Phase 3 Pivotal trial initiation expected H1 2027

## Other Anemias of Inflammation

- RALLY-IBD signal-seeking Phase 2 study in anemia of IBD with DISC-0974 initiated Q1 2026
- Exploratory work in additional anemia indications
- Continued IND-enabling activities for the long-acting anti-HJV (DISC-0998)

# DISC-3405

**Anti-TMPRSS6 mAb** | Hepcidin suppression

# Anti-TMPRSS6 mAb induces hepcidin

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

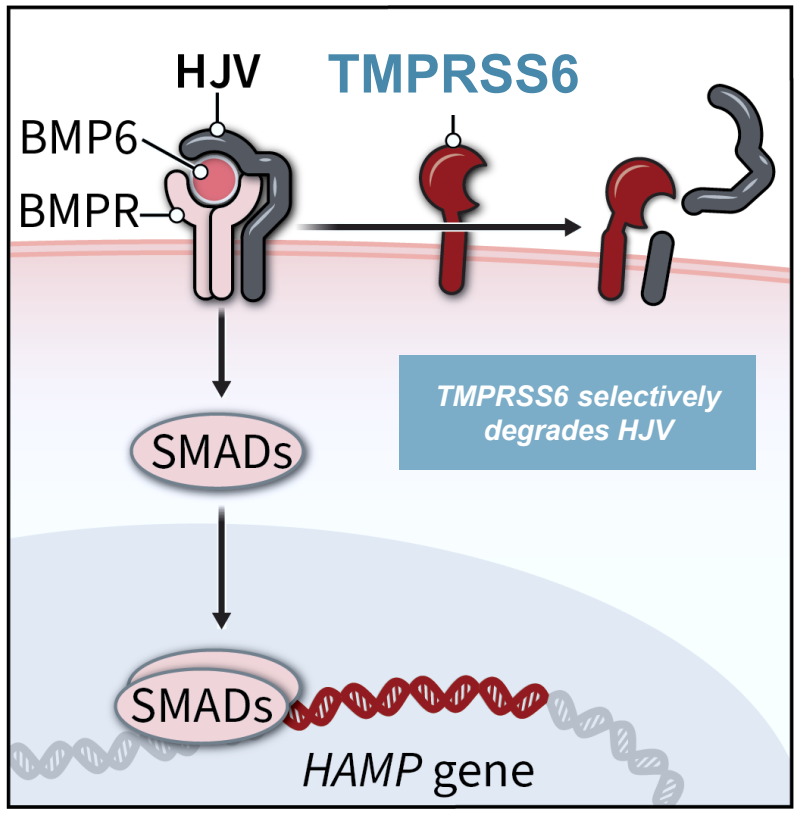

Enables Endogenous Production of Hepcidin

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**

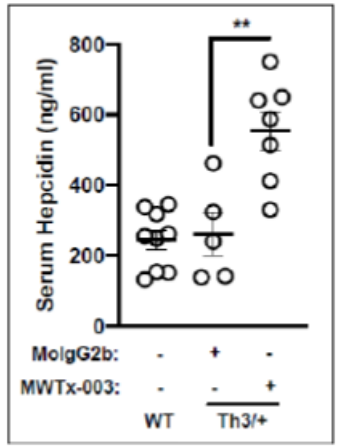
- Genetic validation in patients with IRIDA (Iron-Refractory Iron Deficiency Anemia)
- LOF TMPRSS6 mutation increases hepcidin and reduces iron availability
- Functionally specific to hepcidin / iron
- Tissue specific expression primarily in the liver

# DISC-3405 in beta thalassemia and polycythemia vera

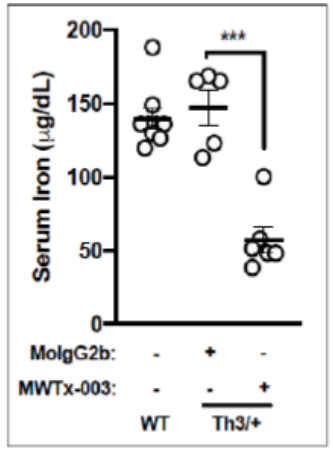
## Significant effects on hallmarks of disease

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

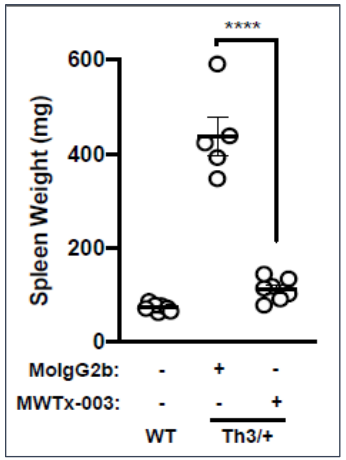
↑ Hepcidin Production




↓ Iron

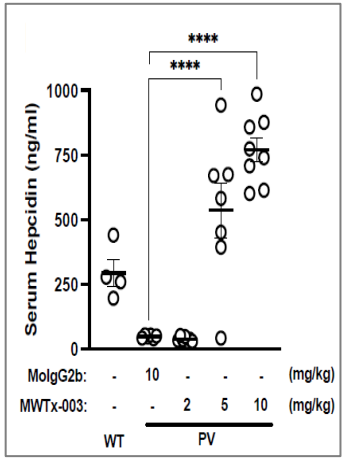



↓ Spleen Weight

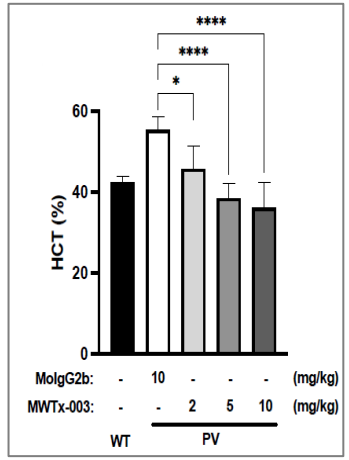



### $Jak2^{V617F}$ model of Polycythemia Vera

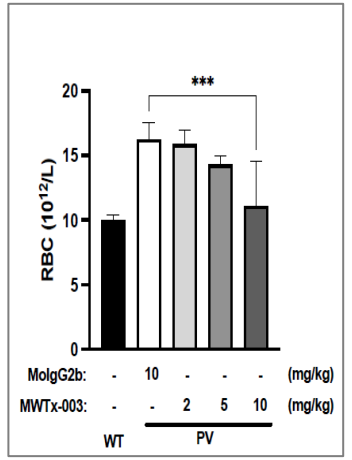
↑ Hepcidin Production




↓ Hematocrit




↓ RBC Production




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

# DISC-3405 development plans

## Advancing program into POC studies with Phase 2 polycythemia vera and planned Phase 1b sickle cell disease initiation anticipated by year end

**Phase 1 SAD/MAD in HV**

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

**Phase 2 Proof-of-Concept Study in Polycythemia Vera**

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

**Phase 1b in Sickle Cell Disease**

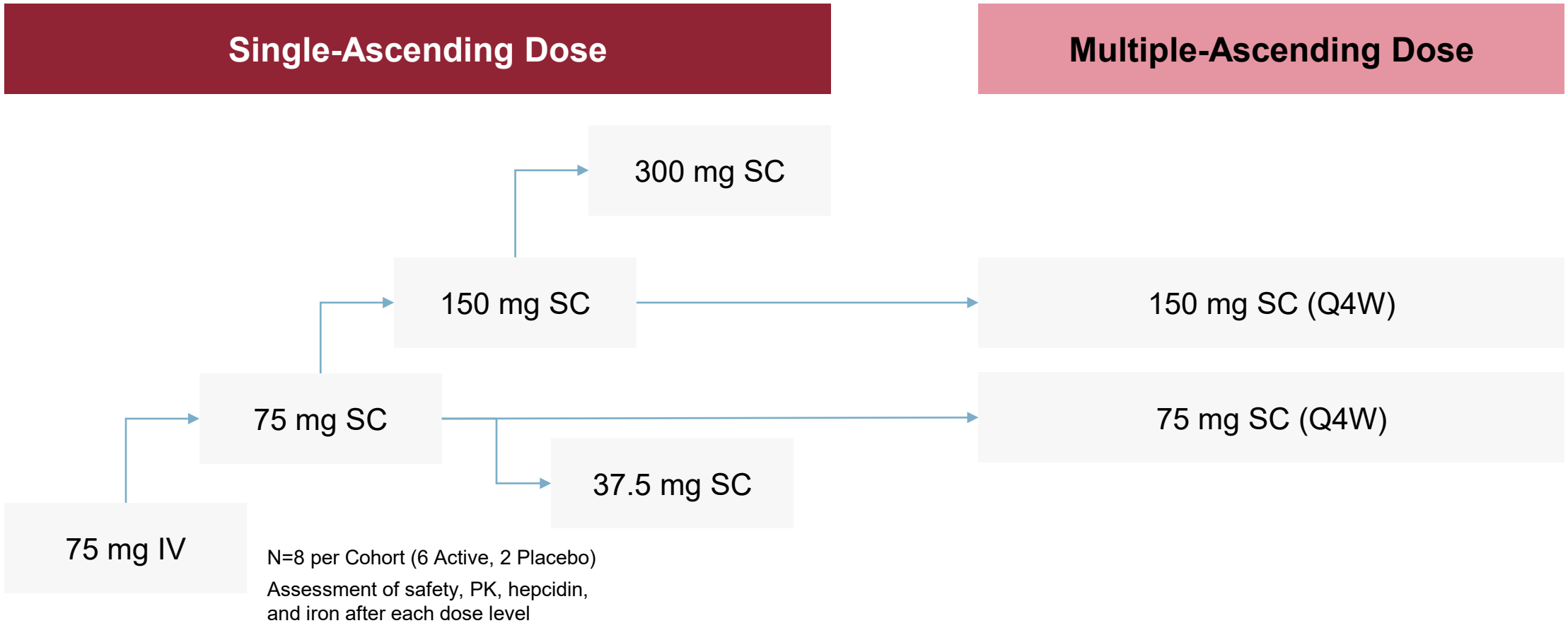
- Mechanistic rationale for iron restriction as a disease-modifying therapy for SCD
- Assess safety, PK, hepcidin, iron, hematologic parameters, hemolysis markers, and exploratory PROs

**Exploration of Other Indications**

*Hereditary Hemochromatosis, Beta-Thalassemia, Myelodysplastic Syndromes*

Hct = hematocrit; HV = healthy volunteers

# DISC-3405 Phase 1 healthy volunteer study overview

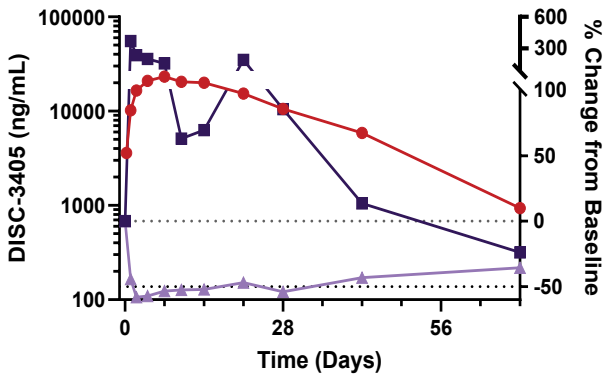



**Key Endpoints/Measures:** Iron, hepcidin, and other hematologic parameters, safety/tolerability

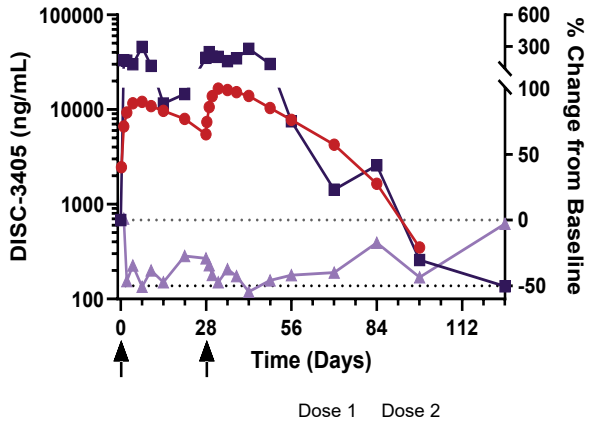
# DISC-3405 healthy volunteer data

## In healthy volunteers, DISC-3405 significantly increases hepcidin and decreases in iron, leading to reductions in hemoglobin and hematocrit that are expected to be beneficial in PV patients

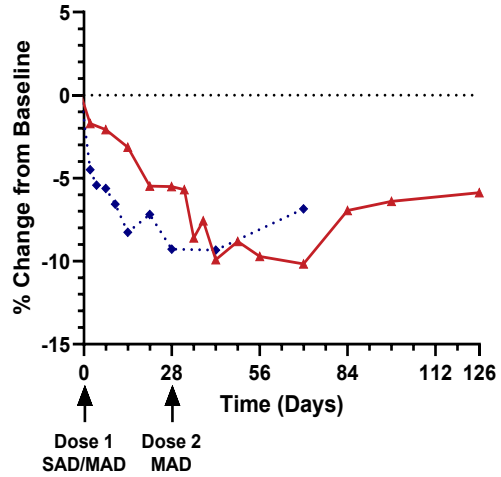
### PK/PD: 300 mg SC SAD



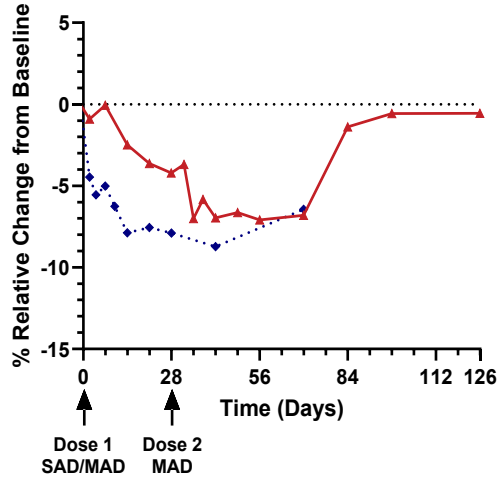

### PK/PD: 150 mg SC MAD




### Hemoglobin




### Hematocrit




PK  Hepcidin  Serum Iron

150 SC, MAD  300 SC, SAD

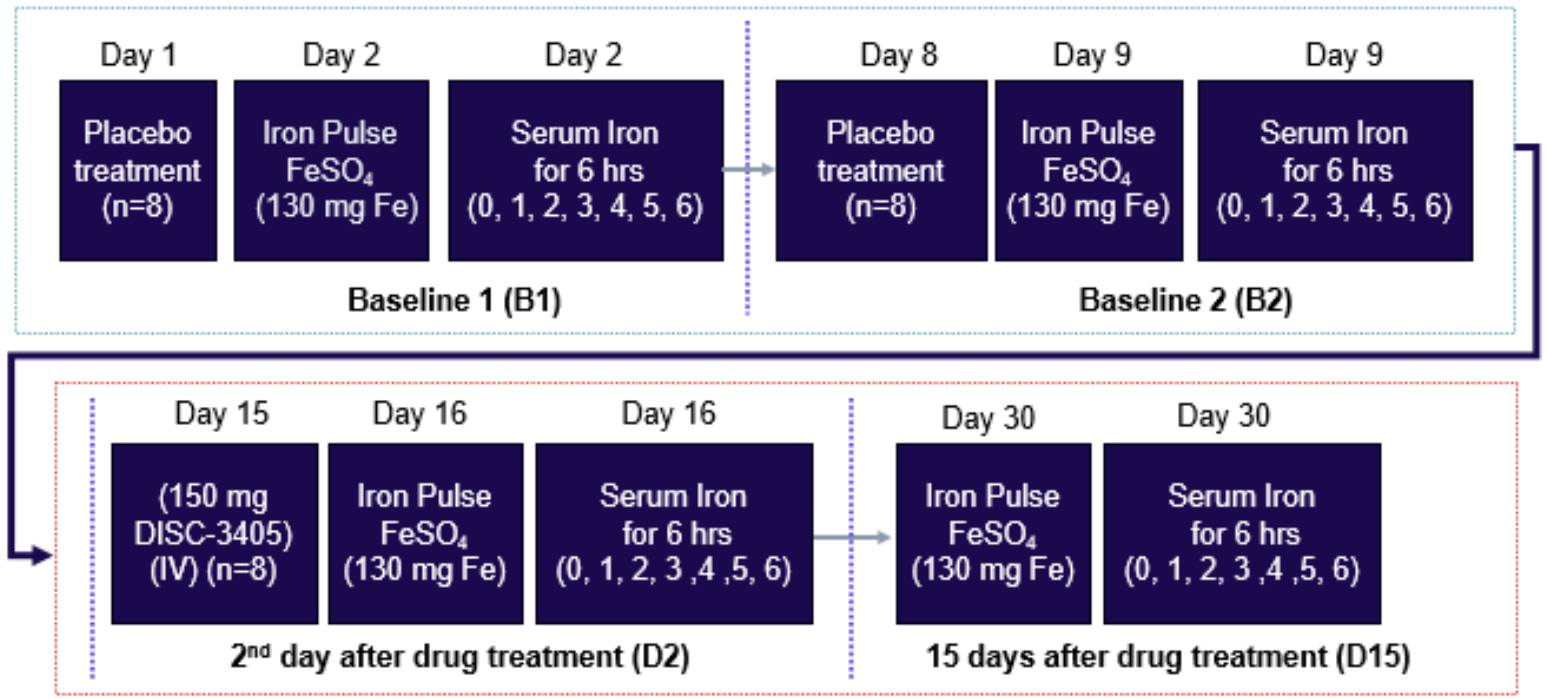
# DISC-3405: Iron pulse study in healthy volunteers

## Evaluating the effectiveness of DISC-3405 in inhibiting dietary iron uptake

**Conducted an iron pulse study to evaluate the effectiveness of DISC-3405 in inhibiting dietary iron uptake**:

- N=8 healthy volunteers received oral ferrous sulfate tablets
- Two sequential placebo occasions, 1 week apart, to assess intra-participant iron absorption variability
- Iron absorption assessed using $AUC_{0\text{-}6h}$

**Study Design**

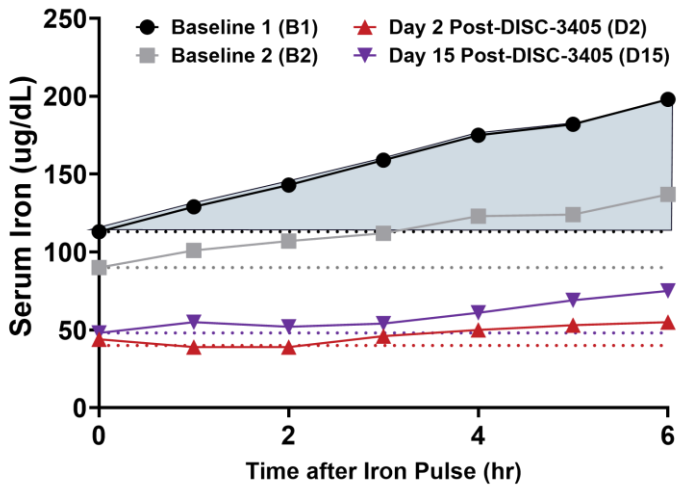


# DISC-3405: Iron pulse study in healthy volunteers

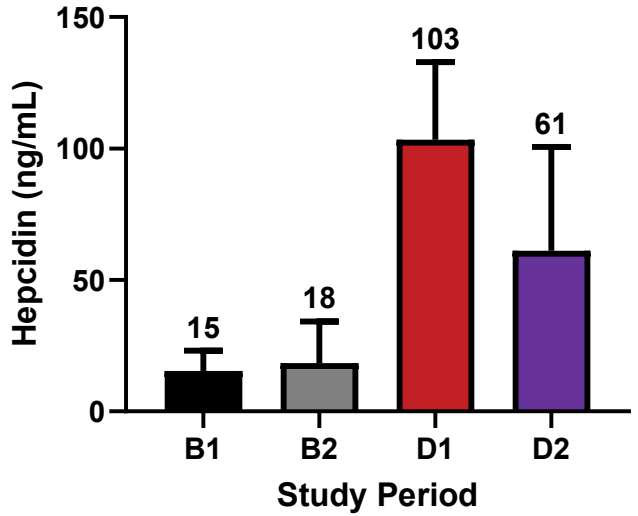
## Strong inhibition of iron absorption with DISC-3405

- DISC-3405 resulted in an average 94% reduction in iron absorption at Day 2 and 68% at Day 15
- Data confirms the mechanism of DISC-3405 and its ability to block dietary iron absorption, supporting the potential for treating iron overload conditions

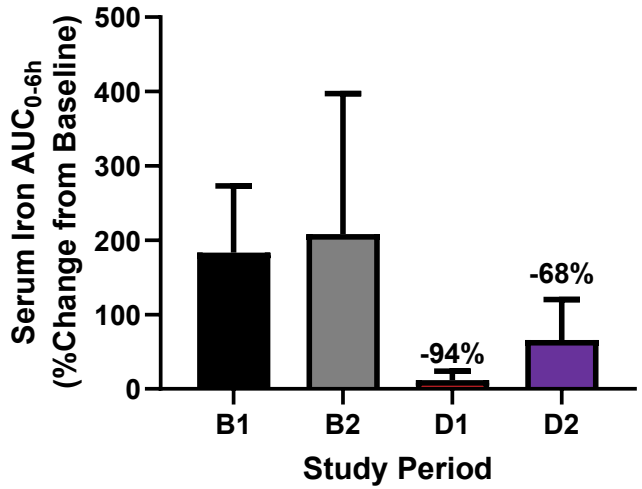
### Representative Serum Iron Profiles of One Participant*




### Average Hepcidin**




### Average Serum Iron**




*Each dotted line represents the baseline for each group. AUC0-6h was determined for each group using respective baselines. A shaded example is shown for the B1 group. **Data presented as mean ± SD. Value above bars are means/mean change from average baseline; Source: EHA 2025 Poster

# DISC-3405: Polycythemia vera opportunity

## Multi-billion-dollar market with significant unmet need for an effective, safe, and convenient treatment to maintain HCT <45%

### Polycythemia Vera
~150,000 US Patients

***Attractive Market***

~75k treated patients; significant room for market development; operational synergies with MF treaters

***Clear Unmet Need***

Treatments offer suboptimal HCT control, leading to increased risk of thrombotic events and other potential symptoms

***Validated Mechanism***

Targeting hepcidin has been shown to control HCT while reducing/eliminating phlebotomy and improving symptoms

***Favorable Presentation***

Target profile of monthly subcutaneous dosing with favorable safety / tolerability and no injection site reactions to-date

### DISC-3405 Positioning

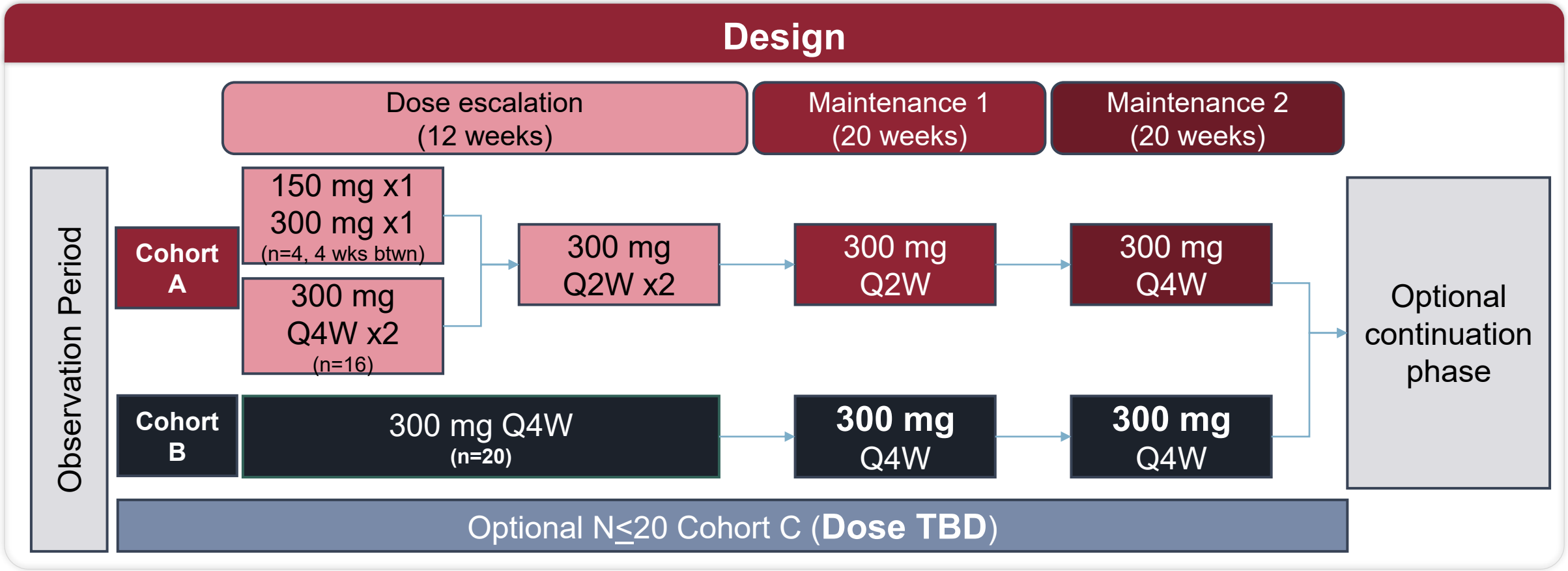
*DISC-3405 is expected to be able to be used across the treatment landscape for PV*

*Current Treatment Options*

- Phlebotomy
- Hydroxyurea
- Ruxolitinib
- Interferon

# RESTORE-PV: Polycythemia vera phase 2 trial design

**Initiated June 2025; significant interest in the study has led to a protocol amendment to increase the number of patients included**




**Endpoints:** Safety, PK, PD (hepcidin, iron, hematocrit), phlebotomy rate

**Initial Data Expected Q4 2026**

Optional cohort C (n<20) can be explored as an expansion of Cohorts A and B or to explore additional dose levels and dose regimens

# Iron restriction in sickle cell disease

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

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

113.Hemoglobinopathies, Excluding Thalassemia-Basic and Translational Science

Iron Restriction Improves Markers of Disease Severity in the Townes Mouse Model of Sickle Cell Anemia

Nermi Parrow PhD [1], Pierre-Christian Violet PhD * [2], Nisha George PhD * [3], Faris Ali * [1], Shivam Bhanvadia * [3], Mark Levine MD * [2], Robert E Fleming MD [4 5]

LETTER TO BLOOD | MARCH 18, 2021

**Dietary iron restriction improves markers of disease severity in murine sickle cell anemia**

**PB2505: THERAPEUTIC PHLEBOTOMY INSTANTLY AFFECTS BLOOD PARAMETERS AND VISCOCITY IN SICKLE CELL DISEASE PATIENTS**

**1112 Iron Deficiency in HbSC Disease Is Associated with Less Sickle Cell Disease-Related Complications – a Rationale for Repetitive Phlebotomy As Disease Modifying Therapy**

RED CELLS, IRON, AND ERYTHROPOIESIS | JANUARY 12, 2023

**Dietary iron restriction protects against vaso-occlusion and organ damage in murine sickle cell disease**

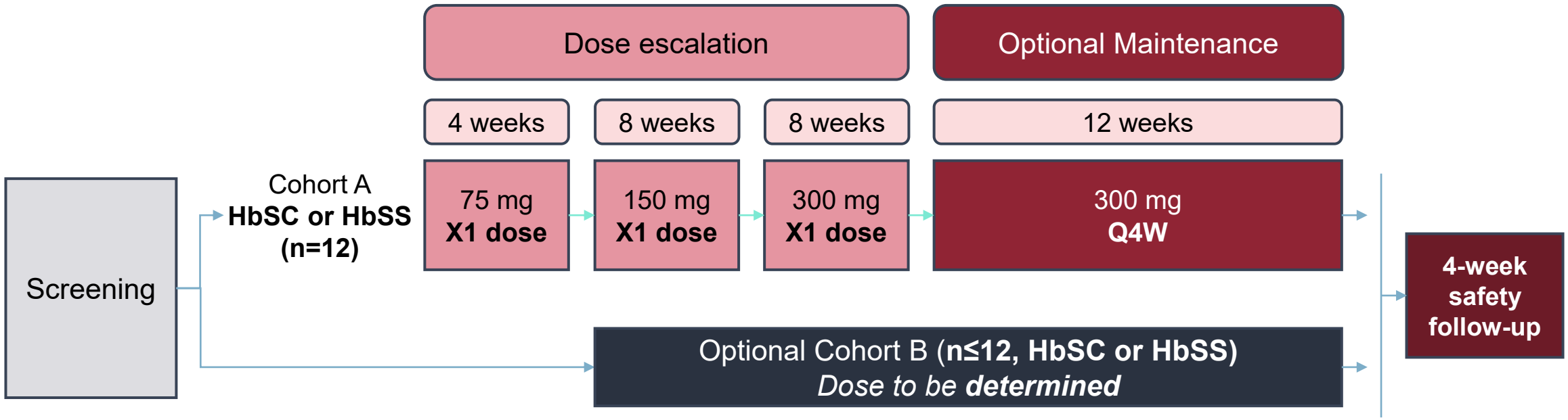
### DISC-3405 in a Townes Model

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

# Sickle cell disease phase 1b trial design

## Initiated October 2025

### Design




Sickle cell disease genotypes: HbSC = hemoglobin S and hemoglobin C; HbSS = homozygous hemoglobin S

**At least 1/3 participants must be HbSC and at least 1/3 participants must be HbSS**

**Endpoints:** Safety, PK, PD (hepcidin, iron, hematologic parameters, hemolysis markers)

**Exploratory endpoints:** PROs (pain, fatigue), changes in SCD complication rates

# Corporate Outlook

# Projected Upcoming Milestones and Events

## Multiple data catalysts anticipated through 2026-2027

| Program | Indication | 1H 2026 | 2H 2026 | 2027 |
|---|---|---|---|---|
| **Bitopertin**<br>Heme Synthesis Modulation | **Erythropoietic Porphyrias (EPP & XLP)** | • HELIOS Update | • APOLLO topline – Q4 2026<br>• Submit response to CRL – late 2026 | • FDA decision mid-2027<br>• Ex-US regulatory submissions |
| **DISC-0974**<br>Hepcidin Suppression | **Anemia of Myelofibrosis (MF)** | • Updated Interim RALLY-MF Phase 2 Data | • Topline RALLY-MF Phase 2 data<br>• End of Phase 2 Meeting | • Phase 3 initiation |
| | **Anemia of Inflammatory Bowel Disease (IBD)** | • RALLY-IBD Phase 2 initiation | | • RALLY-IBD Phase 2 Data |
| **DISC-3405**<br>Hepcidin Induction | **Polycythemia Vera (PV)** | | • Initial RESTORE-PV Phase 2 Data | • Topline RESTORE-PV Phase 2 Data<br>• End of Phase 2 Meeting and Phase 3 initiation |
| | **Sickle Cell Disease (SCD)** | | • Initial Phase 1b Data | • Topline Phase 1b data<br>• Phase 2 initiation |

**Supported by cash balance of $730M*, providing runway into 2029**

*as of March 31, 2026

# Disc Medicine: Built for Sustainable Growth

## Three programs addressing blockbuster markets with significant potential for expansion

### Bitopertin
### Phase 3 Ongoing

**CRL response expected to be submitted in Q4 2026**

- EPP: Debilitating disease with high unmet need and defined patient population
- Strong product profile and robust Phase 3 trial design to support resubmission

### DISC-0974
### POC Established

**Additional MF data and Phase 3 plans expected by EOY**

- Potential to be the primary therapy to address anemia across all MF patient types
- Significant opportunity in anemias of inflammation, beginning with IBD

### DISC-3405
### POC Study Initiated

**Data for PV and SCD expected by EOY**

- Strong therapeutic hypothesis in PV with large addressable market
- Additional indications like SCD have potential to be additive blockbuster opportunities

**$2B+** EPP US Addressable Market | **$4B+** MF Anemia US Addressable Market | **$7B+** PV US Addressable Market