disc medicine

Corporate Presentation

November 2026

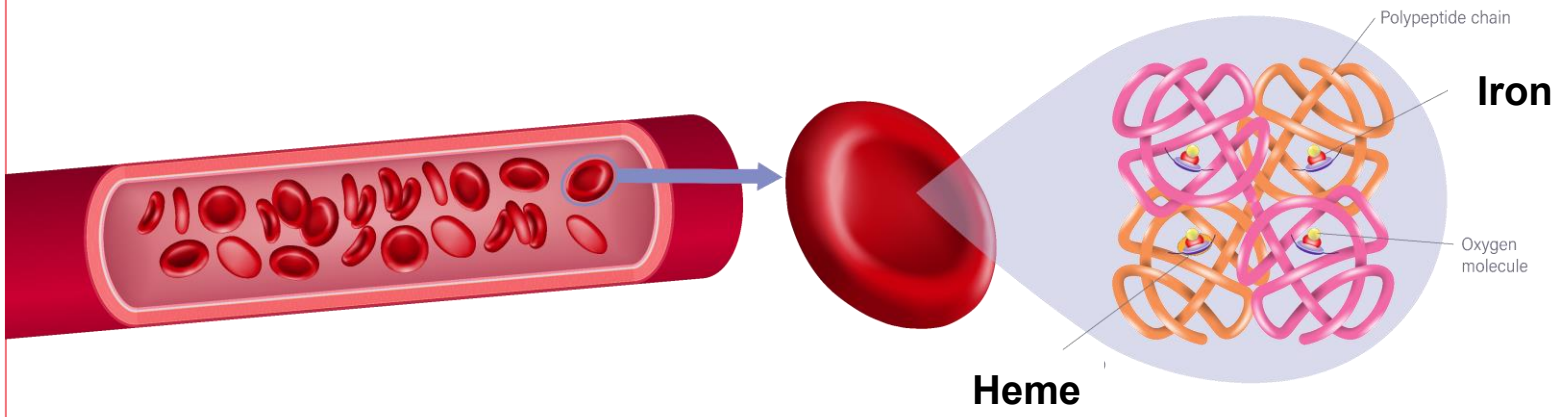
Disclaimer and FLS

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding Disc’s expectations with respect to its preclinical studies, clinical trials and research and development programs, in particular with respect to bitopertin, selcodebart (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 and commercial readiness activities; the registrational pathway for bitopertin, including the projected timeline for an NDA resubmission and the timing of an FDA decision; anticipated discussions with regulatory agencies; Disc’s expectations with respect to the potential launch and commercialization of bitopertin, if approved; the potential therapeutic benefits of bitopertin as a treatment for EPP, if approved; the market and potential opportunities for bitopertin, selcodebart 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.

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. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements as a result of a number of material risks and uncertainties including but 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 content and timing of decisions made by the FDA and other regulatory authorities; and the other risks and uncertainties described in Disc’s filings with the Securities and Exchange Commission, including in the “Risk Factors” section of Disc’s Annual Report on Form 10-K for the year ended December 31, 2025, and in subsequent Quarterly Reports on Form 10-Q. 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.

Bitopertin, selcodebart, 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

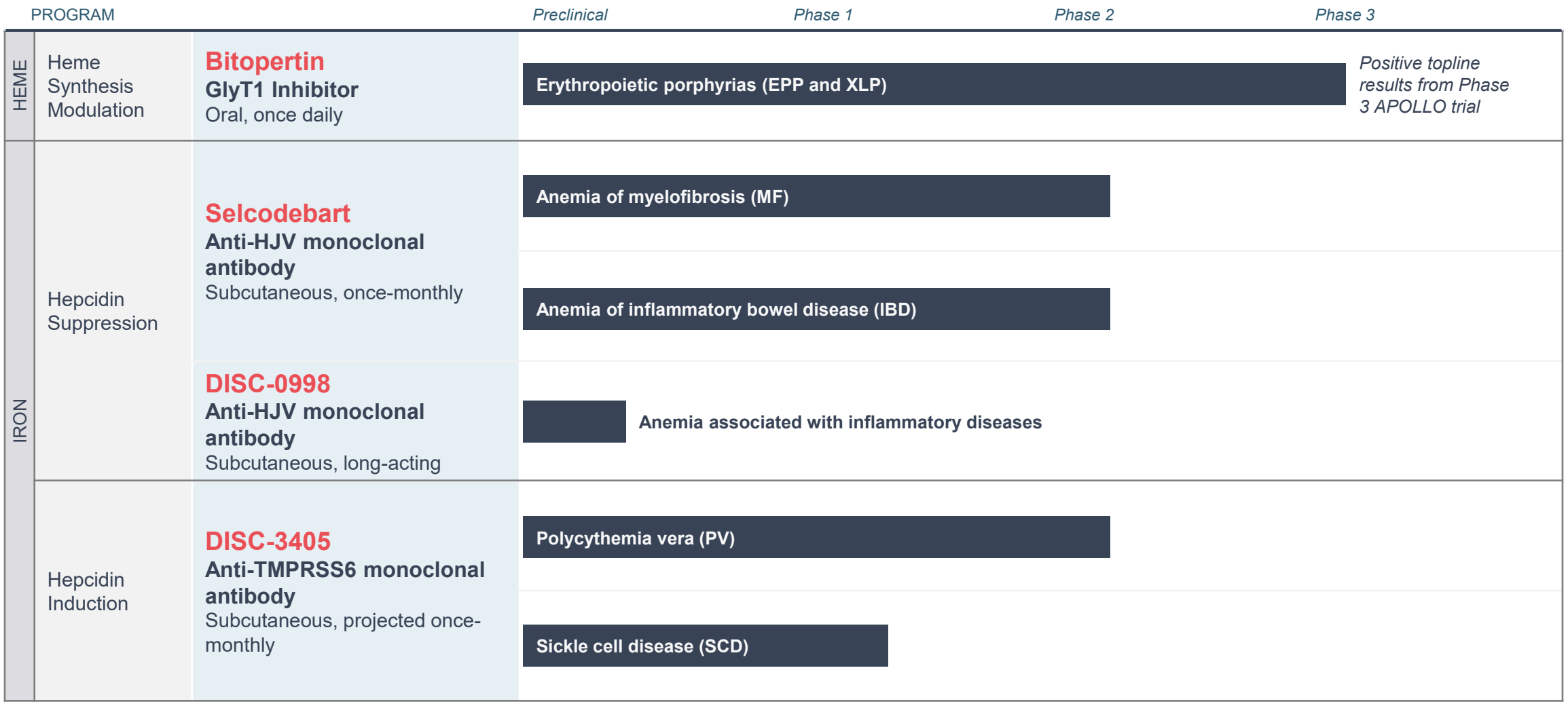
Trial in Progress or Completed

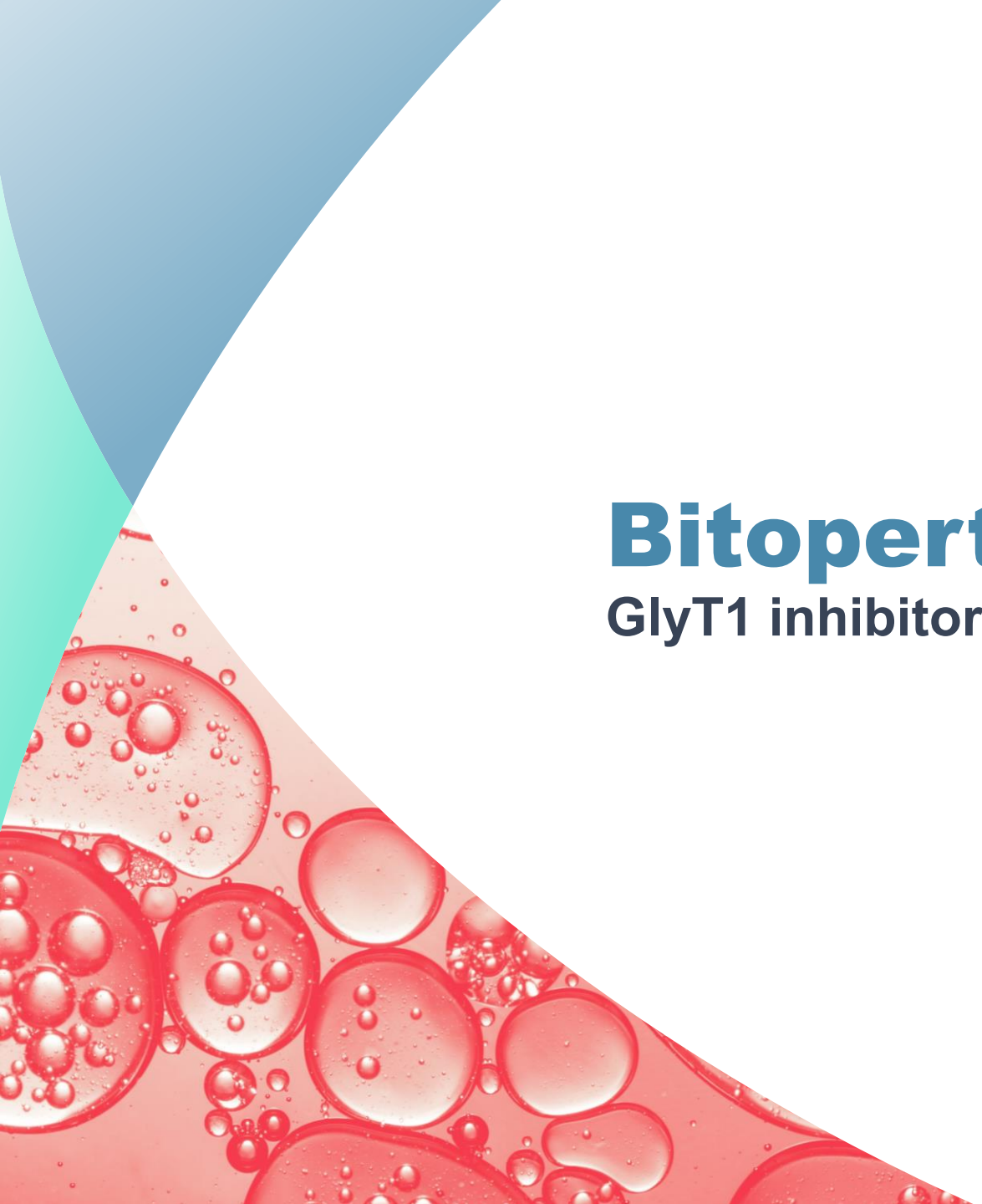
By targeting heme and iron, Disc's portfolio can address a wide range of hematologic disorders

	Modulate Heme Synthesis	**Increase Iron** Hepcidin Suppression	**Restrict Iron** Hepcidin Induction
Clinical Program (MOA)	**Bitopertin** (GlyT1 Inhibitor)	**Selcodebart (DISC-0974)** (Anti-HJV mAb)	**DISC-3405** (Anti-TMPRSS6 mAb)
Range of Indications	**Rare blood disorders**	**Anemia of MF, anemia of chronic diseases**	**Polycythemia vera and sickle cell disease**
Development Status	***Phase 3 Topline Results*** *Positive APOLLO Data*	**Phase 2** *POC Established*	**Phase 2** *Initial POC*

Disc's hematology-focused pipeline

Key programs driving upcoming catalysts





Bitopertin

GlyT1 inhibitor | Heme biosynthesis modulation

Bitopertin: Investigational oral, selective GlyT1 inhibitor

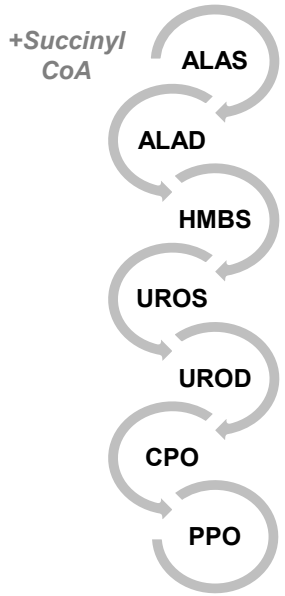
In multiple clinical trials by Roche, bitopertin was observed to modulate heme biosynthesis by blocking uptake of glycine in erythrocytes

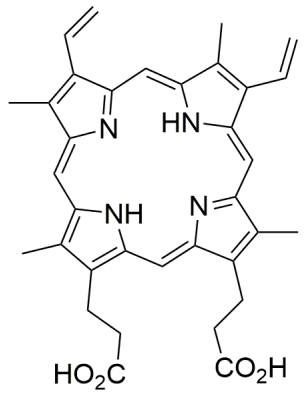
Glycine

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

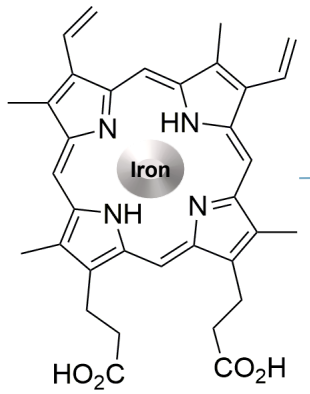
Bitopertin

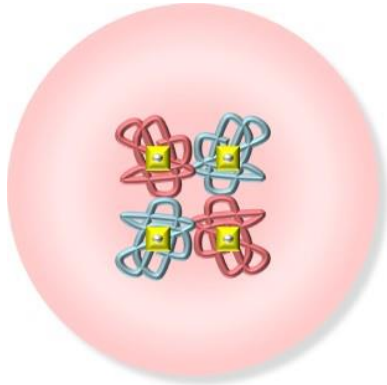
Designed to block glycine uptake in RBCs by inhibiting GlyT1





FECH
ferrochelatase





Porphyrin Synthesis → **Protoporphyrin IX (PPIX)** → **Heme** → **Hemoglobin**

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
- X-Linked Protoporphyria (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



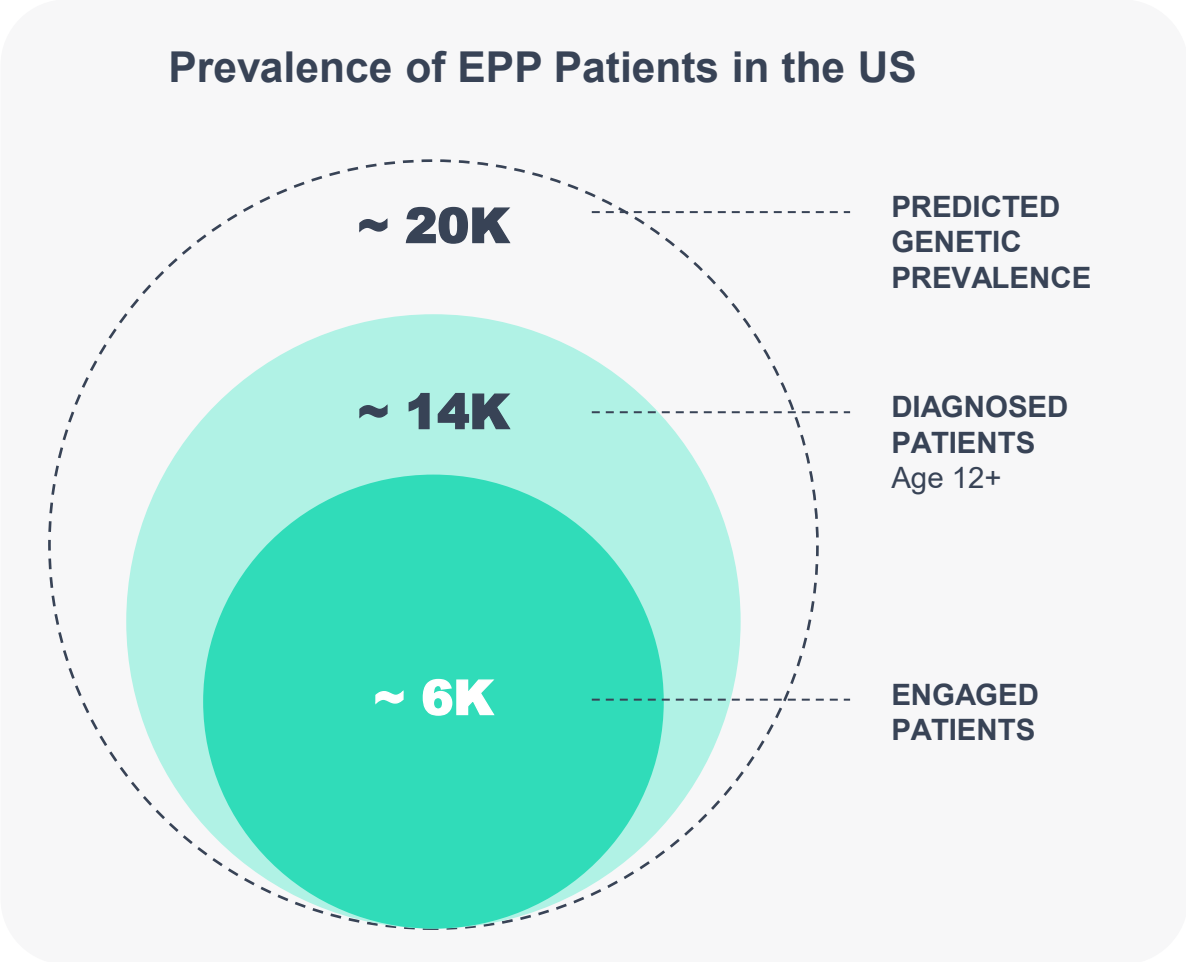
No cure or disease-modifying treatment

- 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 matches evidence of liver/biliary issues in claims population

Field Outreach

Through initial outreach, Disc field teams have validated 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

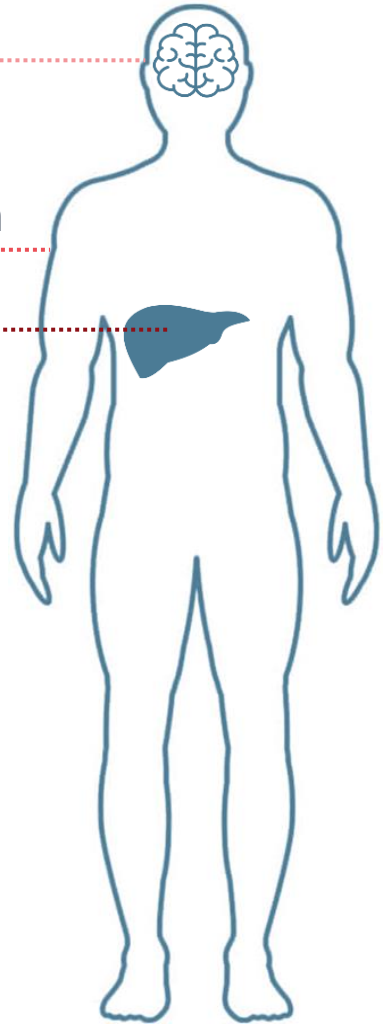
Psychosocial

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

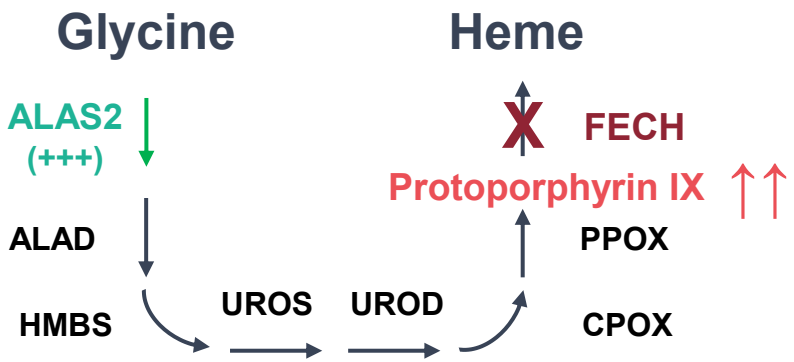
32% visit the ER each year

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

Bitopertin: Potential disease-modifying treatment

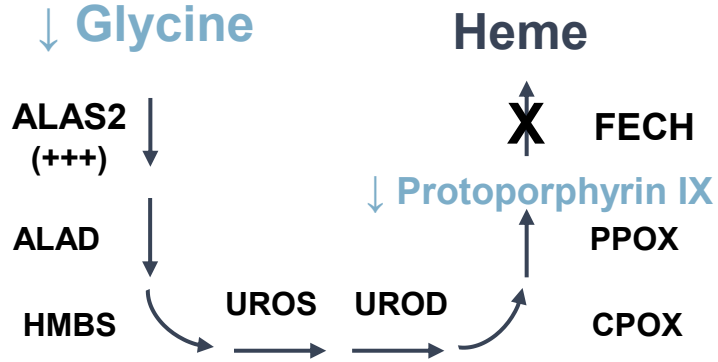
Designed to reduce disease-causing PPIX by limiting update of glycine into developing erythrocytes

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 – *Positive Topline Results*

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

Launched Expanded Access Program for eligible patients with EPP and XLP in the US and select other geographies in June 2026

APOLLO Topline Results: Key Takeaways

APOLLO met both prespecified co-primary endpoints and all secondary endpoints, demonstrating statistically significant reduction in PPIX, improvement in light tolerance, and other clinical benefits

Targets EPP pathophysiology:	*More time in light with improved light tolerance:*		*Fewer pain events:*	*Improvement in how patients felt:*
Reduction in whole blood **PPIX** vs. placebo	Increase in average monthly total **time in light** without pain during month 6 vs. placebo	Improvement in **cumulative total time in light** and average daily sunlight exposure **time to prodrome**	Reduction in incidence rate of **phototoxic reactions** vs. placebo	Improvement in **PGIC** and **PGIS** scores vs. placebo

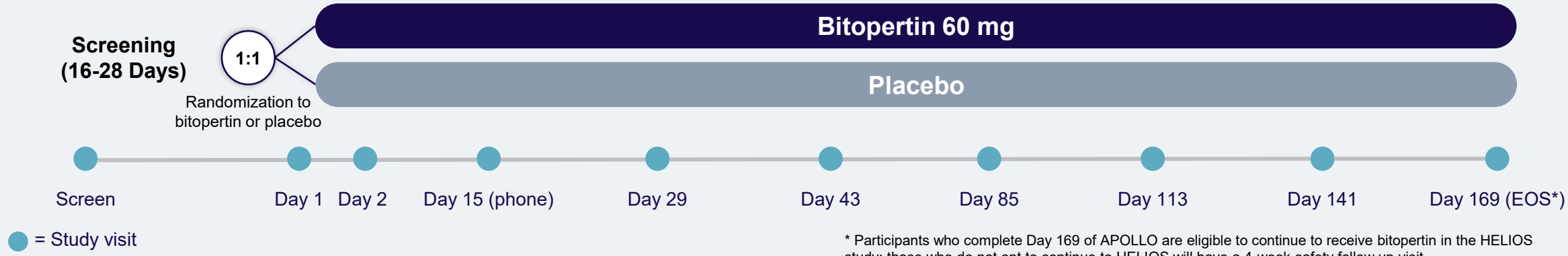
Co-Primary Efficacy Endpoints

- ✓ **Well-characterized safety and tolerability:** Previously studied in >4,000 clinical trial participants across development history with **no new safety signals** in APOLLO
- ✓ Patient friendly, **once daily oral** presentation
- ✓ **97%** rollover to HELIOS long-term extension trial

Based on these results, Disc plans to resubmit an NDA to the FDA by end of 2026

EPP=Erythropoietic Protoporphyria; PPIX=Protoporphyrin IX; PGIC=Patient Global Impression of Change; PGIS=Patient Global Impression of Severity; NDA=New Drug Application; FDA=Food and Drug Administration

APOLLO trial overview



Study Design

- Global, randomized**, double-blind, placebo-controlled Phase 3** study
- 6-month treatment period with once-daily bitopertin **60 mg or placebo**
- **183 participants** across US, UK, EU, Canada, and Australia

Trial Population

- Adults and adolescents aged ≥12 years with EPP or XLP
- Stratified by baseline light tolerance and geography

Study Efficacy Endpoints*

- **Co-Primary:** Average monthly total time in light without pain between 10:00am and 6:00pm during month 6 of treatment; percent change from baseline in whole blood metal-free PPIX after 6 months of treatment
- **Secondary:** Incidence rate of phototoxic reactions; cumulative total pain-free time in sunlight; change from baseline in average daily sunlight exposure time to prodrome

*Safety and tolerability was also a primary objective

Baseline Characteristics

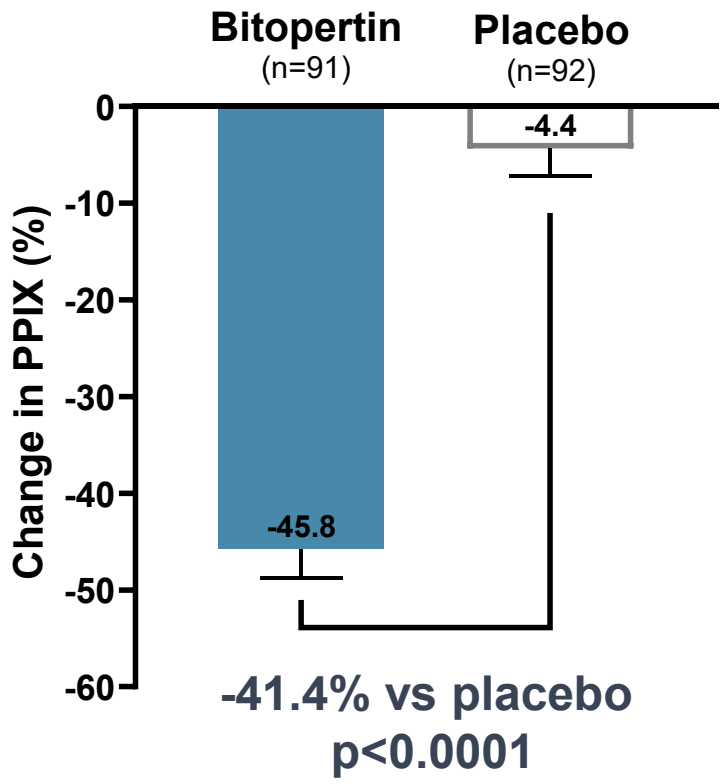
	Bitopertin (n=91)	Placebo (n=92)
Characteristic		
Mean Age, years	35.8	38.4
Age <18, n (%)	14 (15%)	20 (22%)
Female, n (%)	54 (59%)	53 (58%)
White, n (%)	81 (89%)	85 (92%)
EPP, n (%)	85 (93%)	86 (93%)
XLP, n (%)	6 (7%)	6 (7%)
Baseline PPIX, Mean ± SD (ng/mL)	9057 ± 5359	9660 ± 7068
Baseline Average Daily Light Exposure, Mean ± SD (hr)	0.9 ± 0.9	0.8 ± 1.1
Time to Prodrome, n (%)		
< 30 min	45 (49%)	46 (50%)
≥ 30 min	46 (51%)	46 (50%)
Geography, n (%)		
US	40 (44%)	42 (46%)
Ex-US	51 (56%)	50 (54%)
North	66 (73%)	66 (72%)
South	25 (28%)	26 (28%)
Seasonality, n (%)[a]		
Spring/Summer	47 (52%)	46 (50%)
Fall/Winter	44 (48%)	46 (50%)

[a] *Season corresponding to the last month on study with adjustments for northern and southern hemispheres*

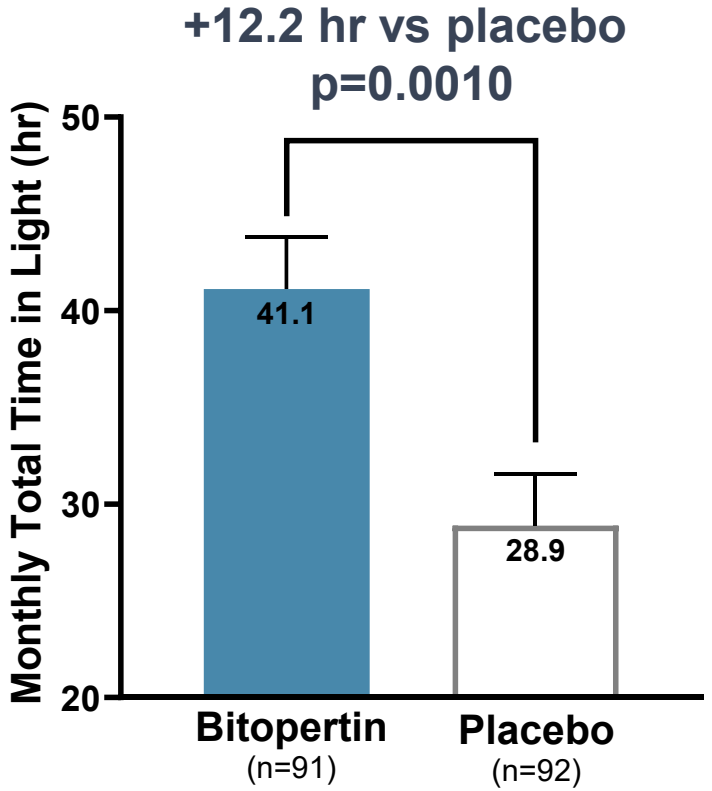
APOLLO Met Co-Primary Endpoints

Bitopertin significantly reduced whole blood metal-free PPIX (p<0.0001) and increased average total time in light without pain during month 6 of treatment (p=0.0010) relative to placebo

PPIX Reduction at Month 6



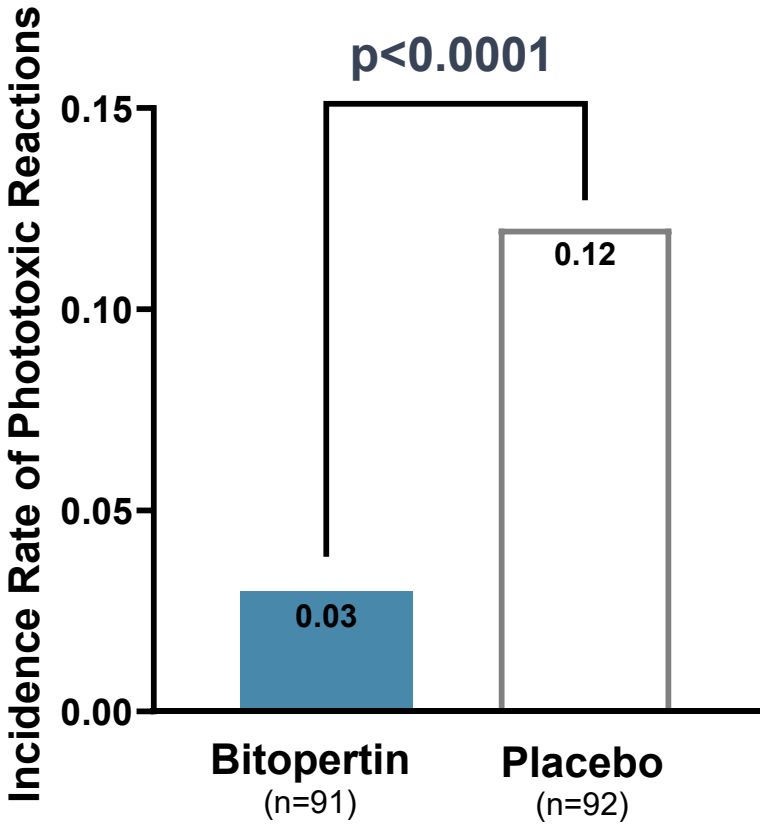
Average Total Time in Light During Month 6*

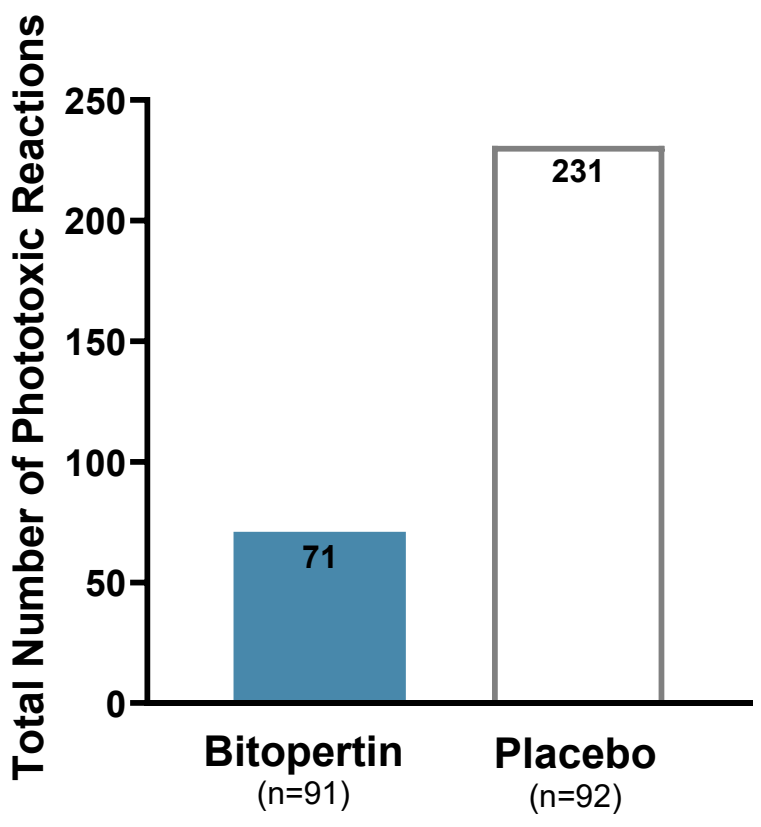


**Total daily sunlight exposure from 10:00am to 6:00pm on days without pain from a phototoxic reaction averaged over monthly (28-day) intervals and analyzed using MMRM to compare bitopertin vs placebo. Average baseline time in light over 14-day screening period: 11.4 hr for bitopertin and 10.7 hr for placebo.*

Secondary Endpoint: Phototoxic Reactions

Bitopertin significantly decreased the incidence rate of phototoxic reactions by 71% relative to placebo (IRR=0.29, p<0.0001)

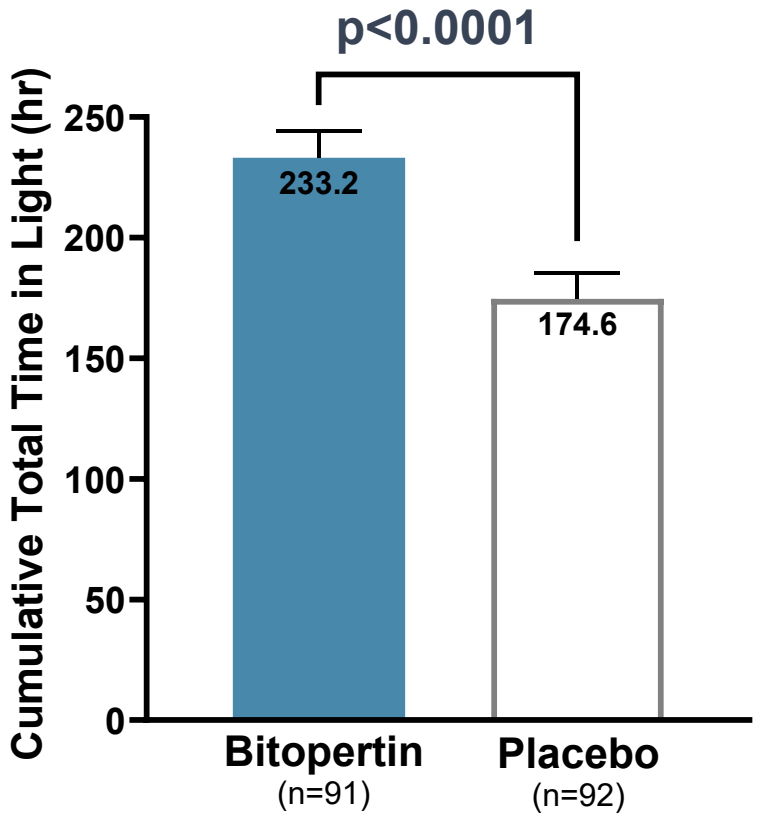




IRR: Incidence rate ratio for new phototoxic reactions over the 6 month treatment period analyzed using a negative binomial regression model with the natural logarithm of the exposure time (in weeks) as an offset.

Secondary Endpoint: Cumulative Time in Light

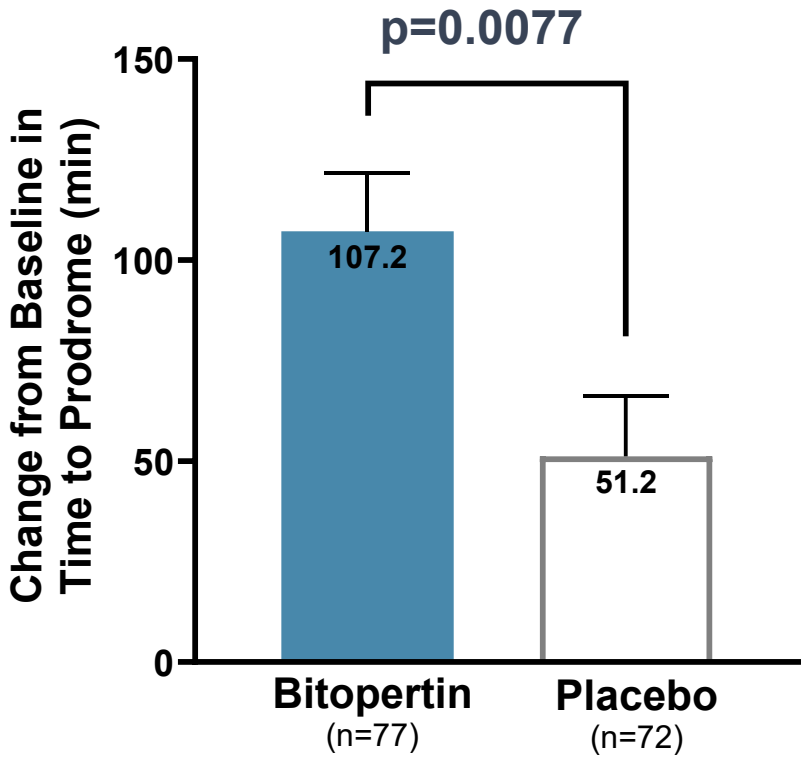
Bitopertin significantly increased cumulative total time in light without pain over the 6-month treatment period relative to placebo (p<0.0001)



Total daily sunlight exposure from 10:00am to 6:00pm on days without pain summed over the 6 month treatment period and analyzed using an analysis of covariance model to compare bitopertin vs placebo. Data plotted are LS Means ± standard error.

Secondary Endpoint: Time to Prodrome at 6 Months (Adults Only)

Bitopertin significantly increased change from baseline in the average daily sunlight exposure time to prodrome by 56 minutes relative to placebo (p=0.0077)



Time to prodrome data from weekly sunlight exposure challenges (adults only) were averaged over a 2-week period, including cumulative time in sunlight for challenges where the participant did not report a prodrome, and were analyzed using MMRM to compare bitopertin vs placebo.

Safety

Favorable safety and tolerability profile across adults and adolescents with no new safety signals identified

	Placebo (n=92)	Bitopertin (n=91)
Any TEAE	69 (75%)	77 (85%)
Grade 3 TEAE	3 (3%)	6 (7%)
Study discontinuation due to AE	0	0
SAE	2 (2%)	1 (1%)
Common TEAEs (reported in ≥10% all participants)		
Dizziness	10 (11%)	45 (50%)
Headache	19 (21%)	15 (17%)
Nausea	10 (11%)	18 (20%)
Fatigue	6 (7%)	15 (17%)

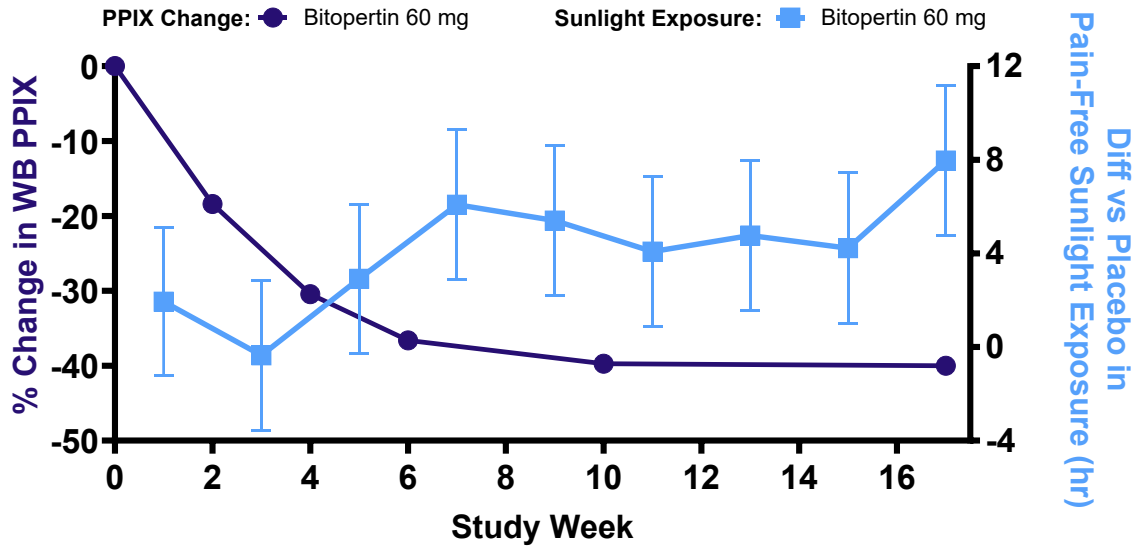
- No study discontinuations for any reason in the bitopertin group
- Dizziness was generally transient and generally occured upon initiation of treatment; all mild/moderate, as observed in AURORA

APOLLO reinforces a well-characterized safety and tolerability profile in >4,000 clinical trial participants across bitopertin's development history, with favorable long-term safety up to 2.5+ years exposure across the Disc EPP development program

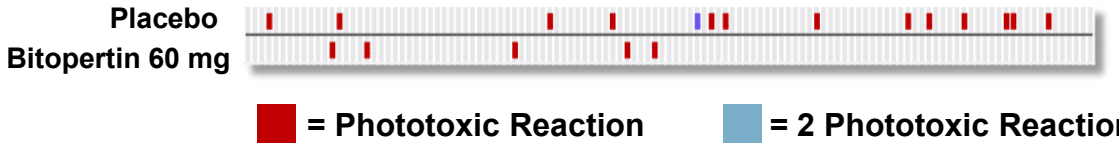
Summary of AURORA results

Bitopertin 60mg

AURORA



Phototoxic Reactions

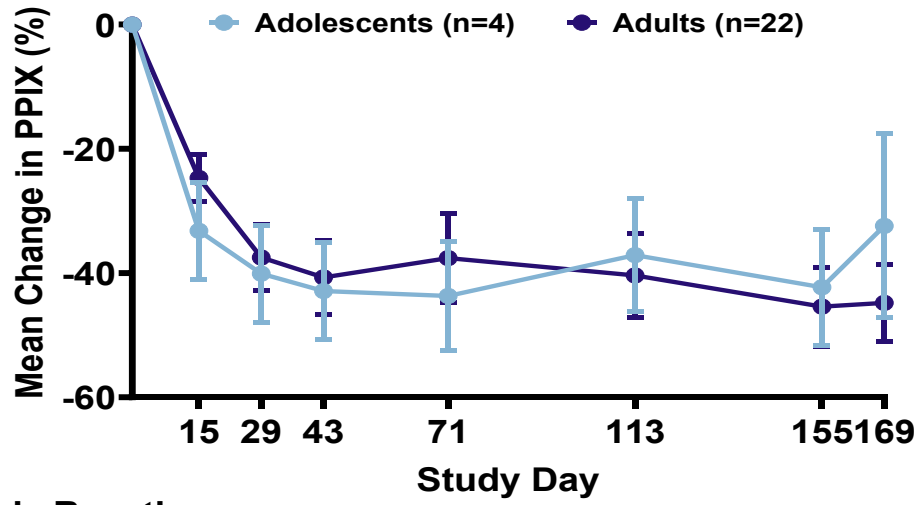


- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent, improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant 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**

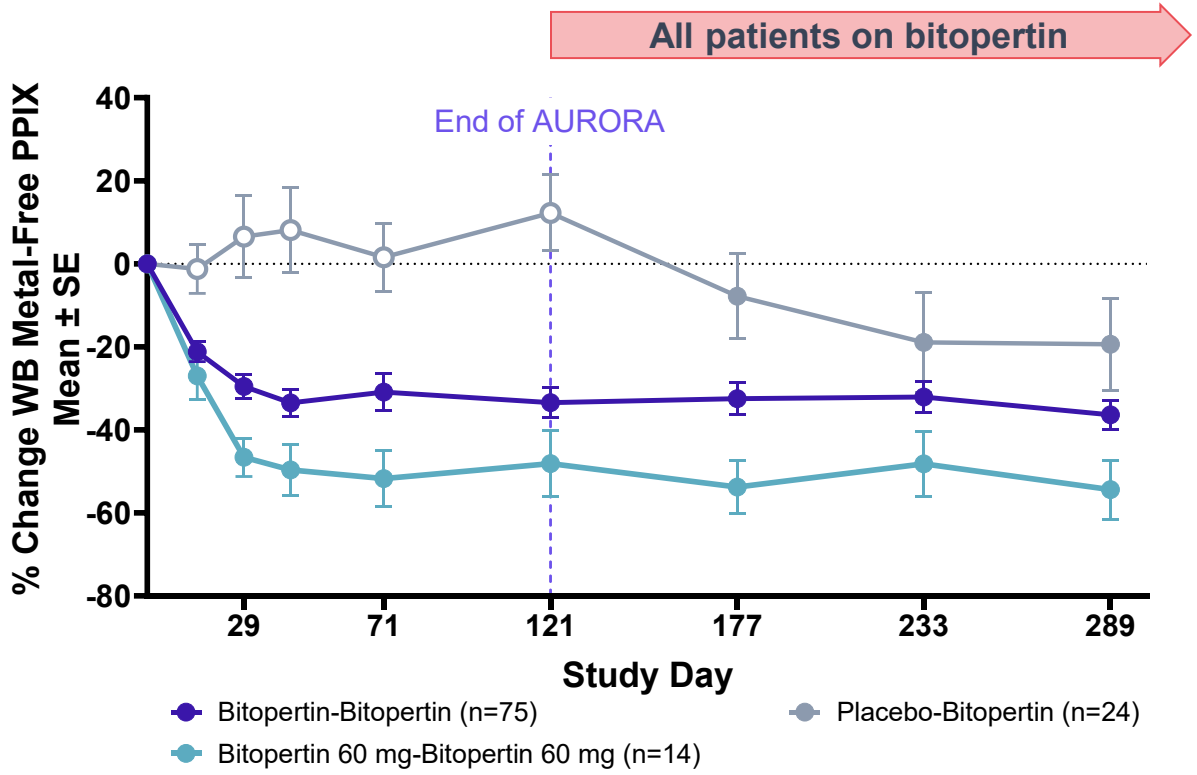
Light Tolerance Measure (Mean ± SD)	Tertile 3 (-43% to 25%)	Tertile 2 (-53% to -43%)	Tertile 1 (-98% to -53%)
Cumulative total time in sunlight without pain (hr)	145.6 ± 99.5	190.5 ± 111.6	262.1 ± 160.6
Average time in sunlight without pain (hr)	0.86 ± 0.6	1.1 ± 0.7	1.6 ± 1.0
Change from baseline in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

Bitopertin emerging therapeutic profile in EPP and XLP

Focused on the needs of patients

More time in the sun

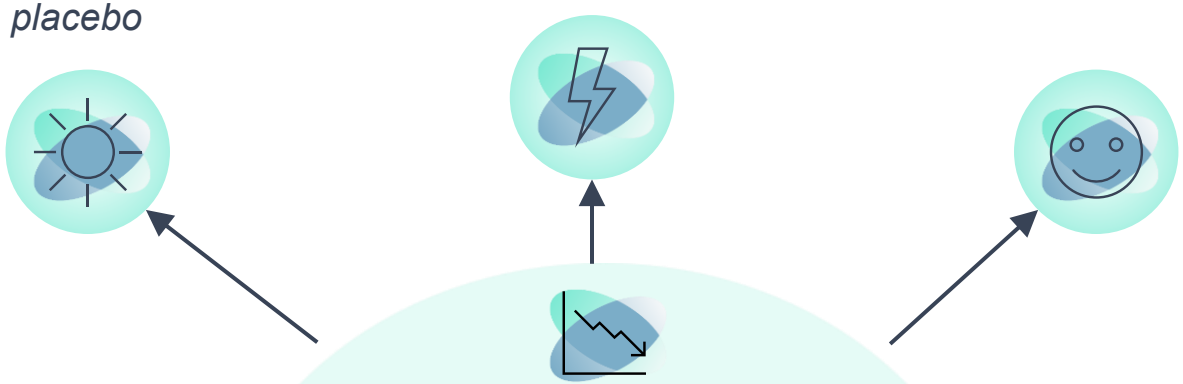
*Significant, **12.2 hr** increase in time in light during month 6 and **56 min** increase in time to prodrome vs. placebo*

Fewer phototoxic reactions

***71%** reduction in incidence rate of phototoxic reactions vs. placebo*

Patients felt better

Significant improvement in PGIC ($p<0.0001$) and PGIS* ($p<0.0001$) vs. placebo*



Targets underlying EPP & XLP pathophysiology

***>41%** reduction in PPIX vs. placebo*

Well-characterized safety and tolerability profile

>4,000 clinical trial participants across development history

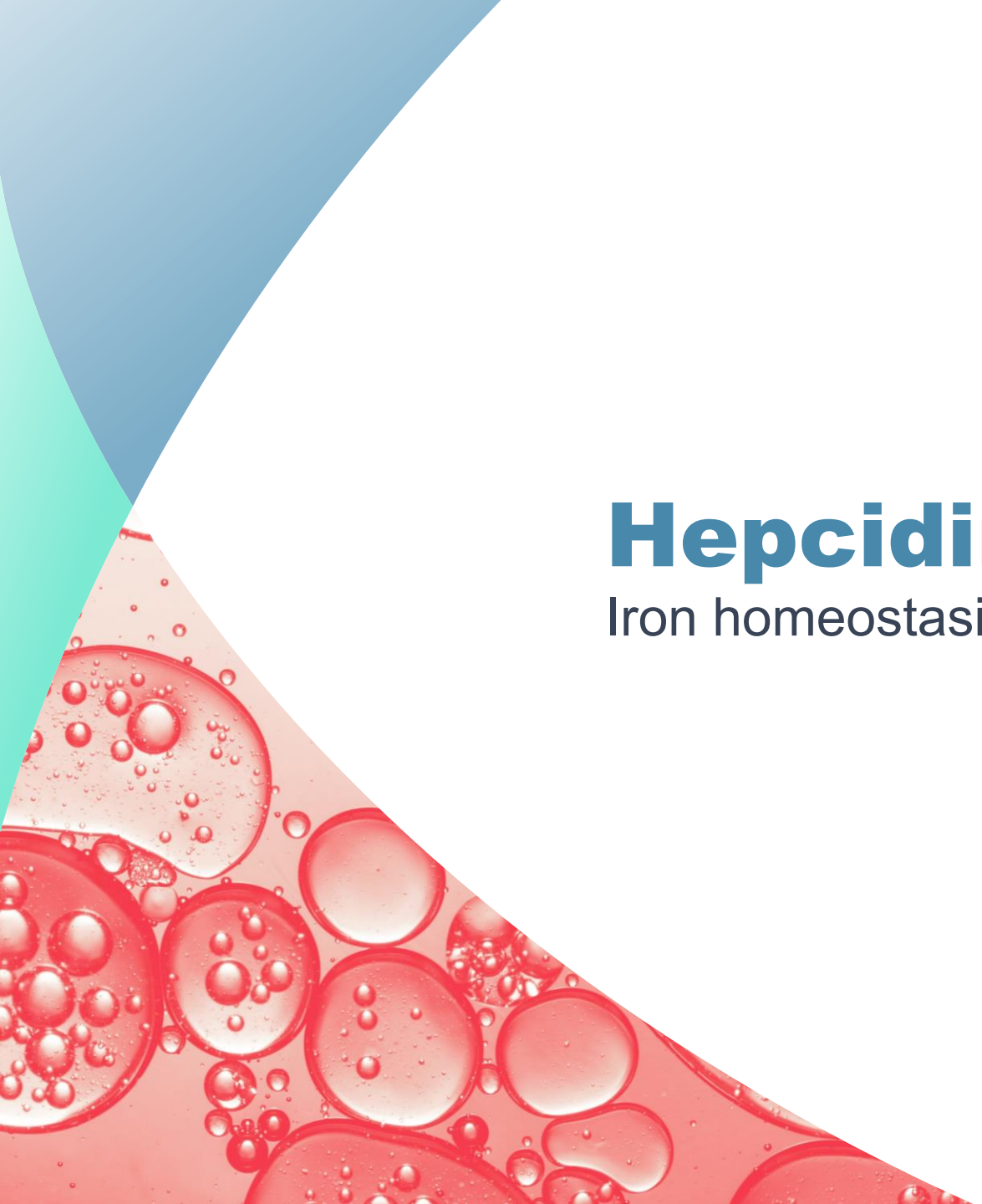
Daily oral

Patient-friendly presentation

*$p<0.0001$ at D169 by ordinal logistic regression of all Patient Global Impression of Change (PGIC) score / Patient Global Impression of Severity (PGIS) score data

Next steps for bitopertin in EPP

- **NDA resubmission planned by end of 2026 based on APOLLO data; FDA decision anticipated by mid 2027**
- Planning to present detailed data with additional insights from APOLLO during an upcoming medical conference
- HELIOS open-label extension study ongoing for patients rolled over from BEACON, AURORA, and APOLLO
- Continuing site activation and enrollment in the Expanded Access Program (EAP) for bitopertin for eligible patients with EPP and XLP in the US and other select countries
- Continuing commercial readiness efforts with focus on disease education, account profiling, and patient validation



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

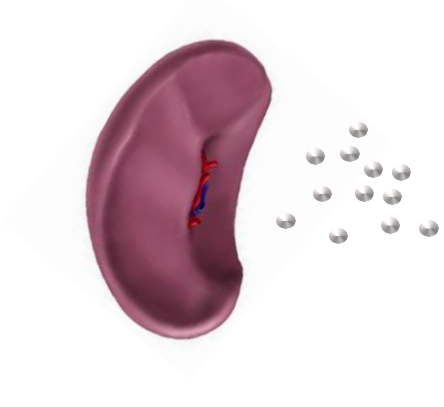


GI Tract
Iron Intake

Induced by Inflammation

Hepcidin

Gatekeeper Function: Blocks iron absorption and recycling



Spleen
Iron Storage



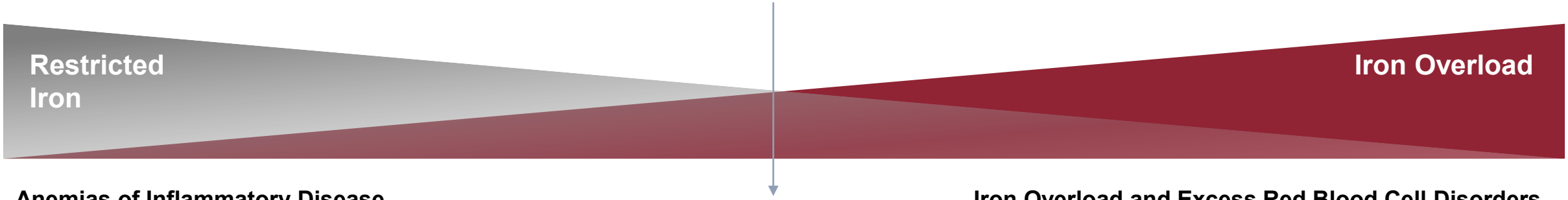
RBC Production in Bone Marrow

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

Selcodebart (anti-HJV mAb)
Reduce Hepcidin / Increase Iron

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

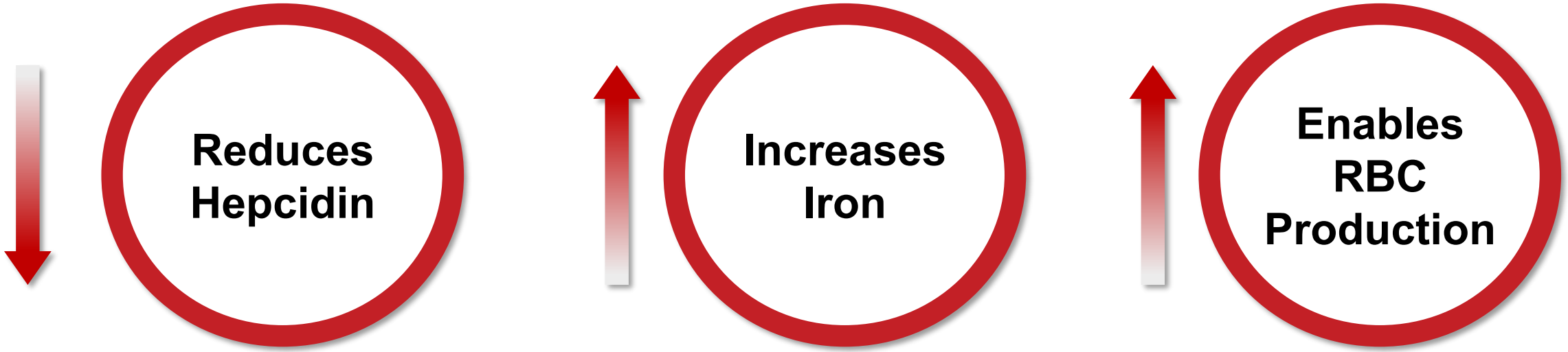


Selcodebart

Anti-HJV mAb | Hepcidin suppression

Selcodebart (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%

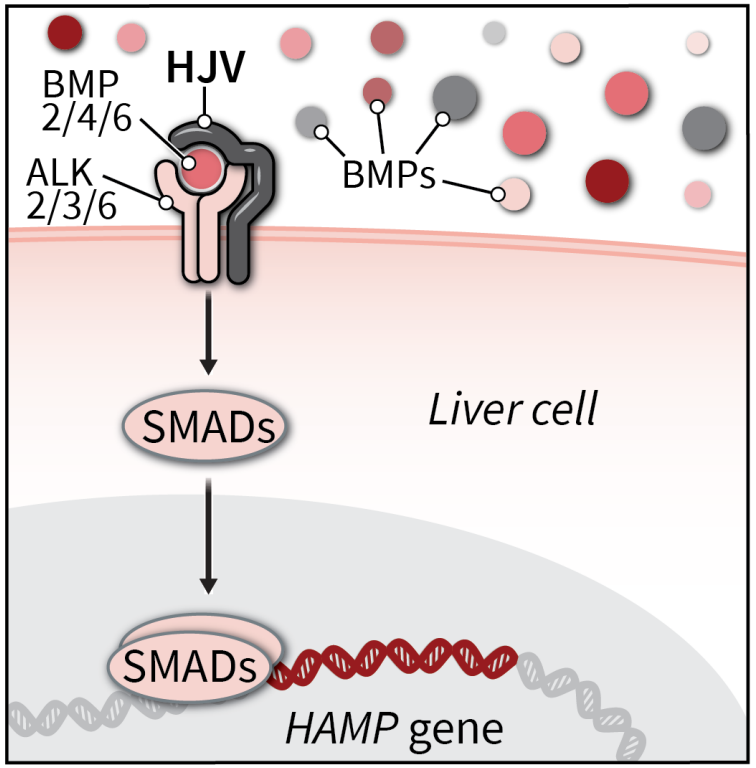
- Anemia of inflammation is the 2nd most common form of anemia
- Estimated 40% of all anemias are driven by or have an inflammatory component
- Hepcidin is up-regulated and correlates with anemia, driven by inflammation

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

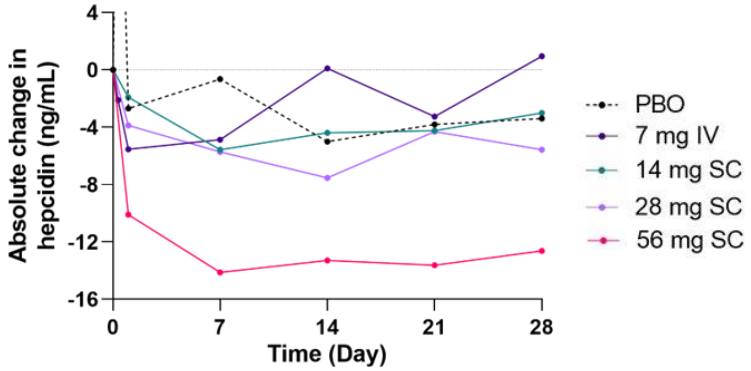
Established proof-of-mechanism based on hepcidin and iron parameters

Trial Design

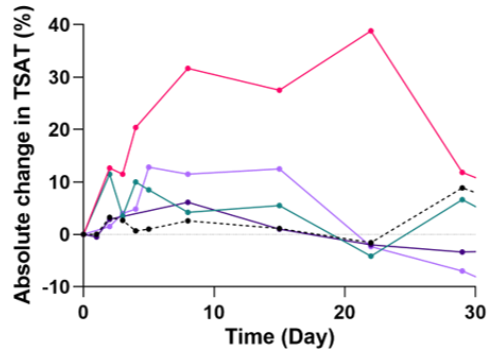
- Single-ascending dose in ≥32 healthy volunteers
- Key outcome measures:
  - Safety and PK
  - Hepcidin level, serum iron level, % TSAT
- Dose escalation until TSAT > 40% for at least 2 weeks
- Dose levels: 7 mg dose (IV); 14, 28 and 56 mg doses (SC)

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

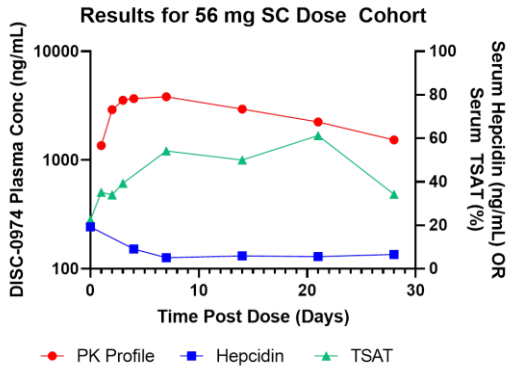
Selcodebart Reduced Hepcidin Production

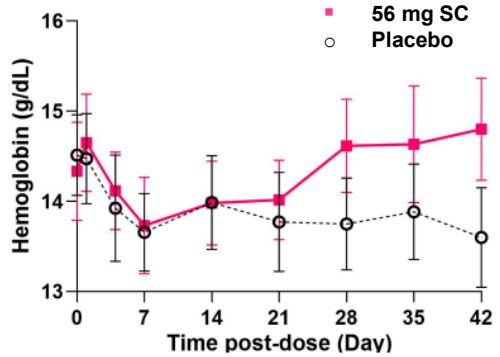


Selcodebart Increased TSAT



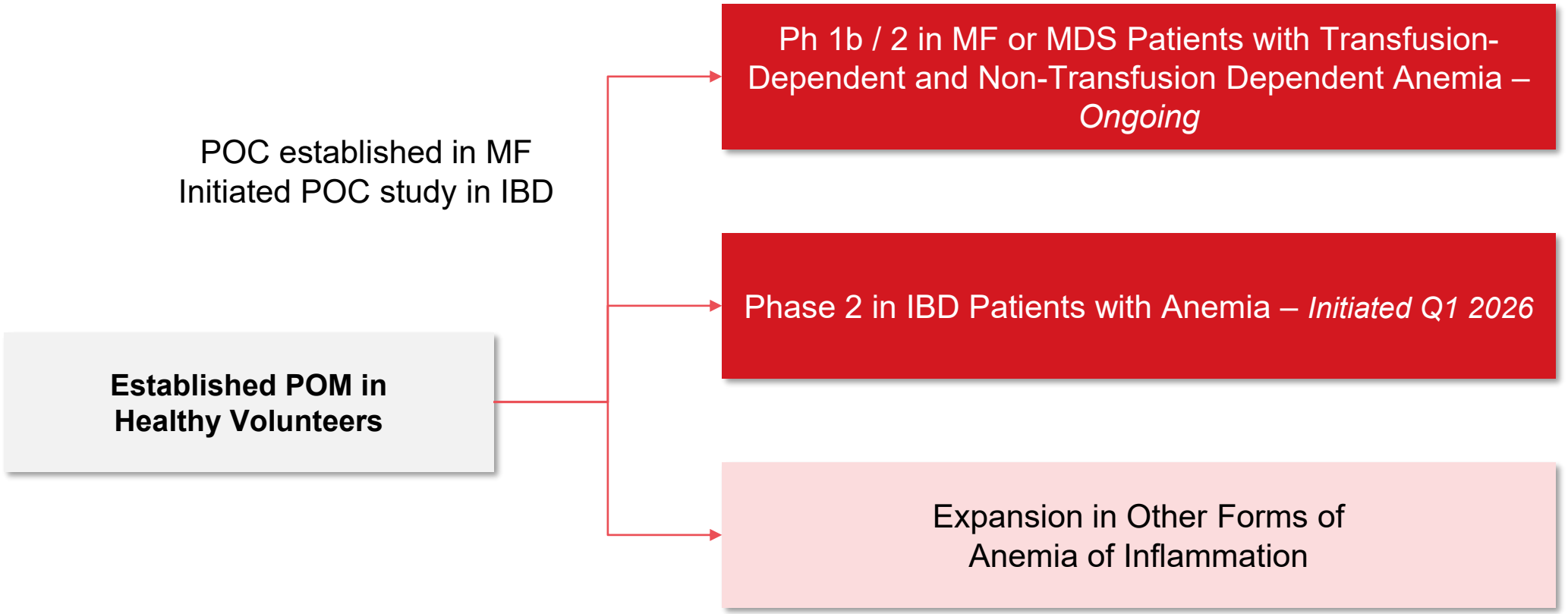
56 mg pharmacodynamic activity improved key clinical parameters (> 1g/dL Hgb)





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

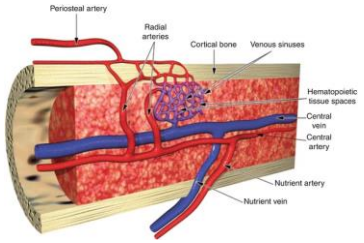
Selcodebart development strategy



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

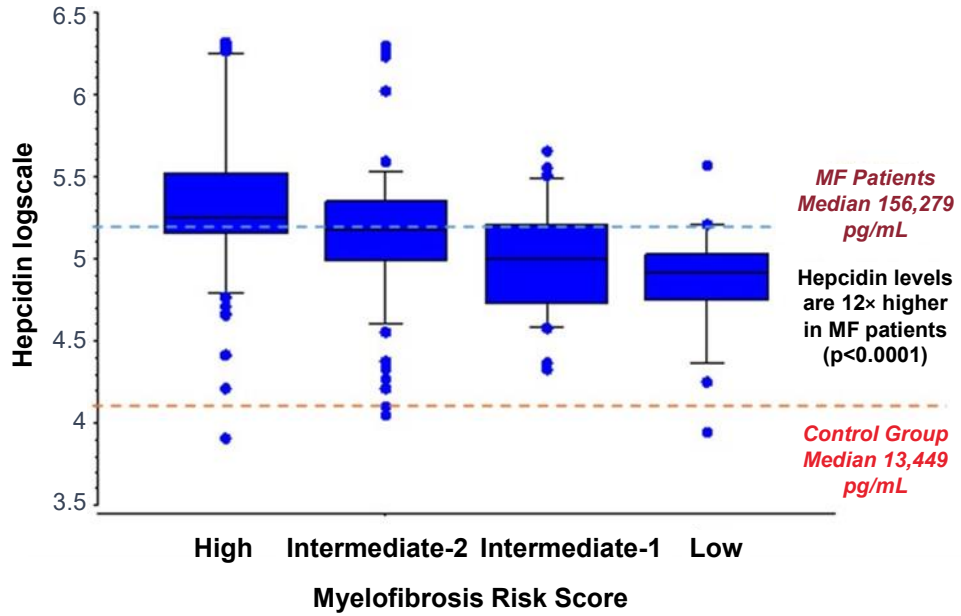
Etiology of Anemia

- 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 April 27, 2026

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

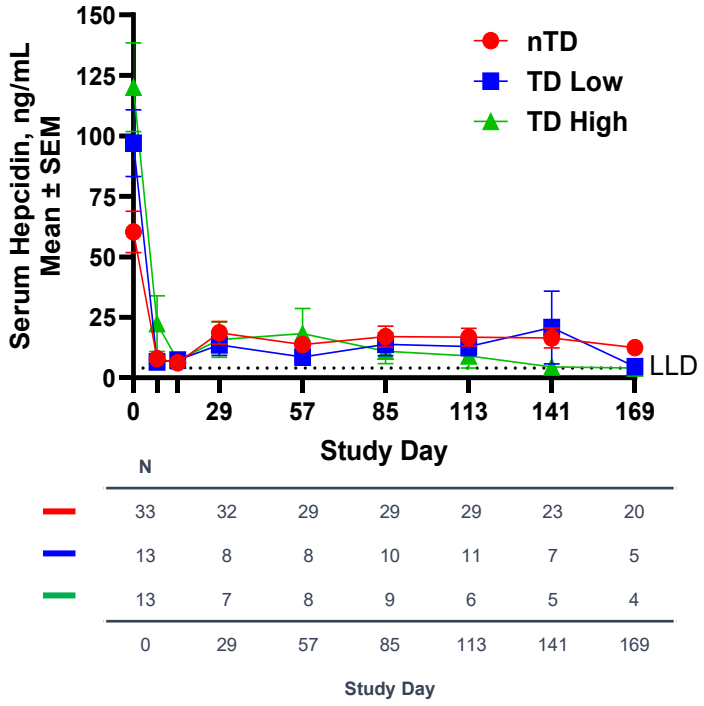
	nTD (n=35)	TD Low (n=13)	TD High (n=13)	Overall (n=61)
Age, median (range), years	70.0 (31, 83)	75.0 (60, 87)	73.0 (60, 87)	71.0 (31, 87)
Concomitant medication, n (%)	18 (51.4)	6 (46.2)	9 (69.2)	33 (54.1)
JAK inhibitor	17 (48.6)	6 (46.2)	9 (69.2)	32 (52.5)
Ruxolitinib	8 (22.9)	3 (23.1)	4 (30.8)	15 (24.6)
Momelotinib	8 (22.9)	3 (23.1)	4 (30.8)	15 (24.6)
Pacritinib	1 (2.9)	0	1 (7.7)	2 (3.3)
Hydroxyurea	1 (2.9)	0	0	1 (1.6)
Baseline hepcidin				
Median (range), ng/mL	39.1 (9.8, 174.1)	109.9 (37.4, 209.8)	108.0 (21.3, 227.3)	66.0 (9.8, 227.3)
Mean (SD), ng/mL	60.3 (49.0)	97.0 (49.9)	120.1 (66.3)	81.6 (58.2)
Baseline hemoglobin, median, g/dL	8.9	7.7	7.6	8.4

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

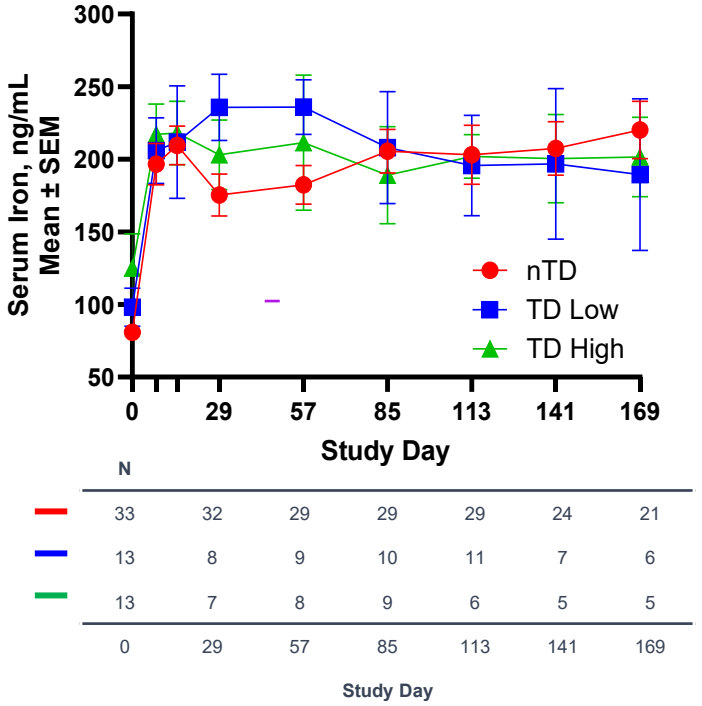
RALLY-MF phase 2 data

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

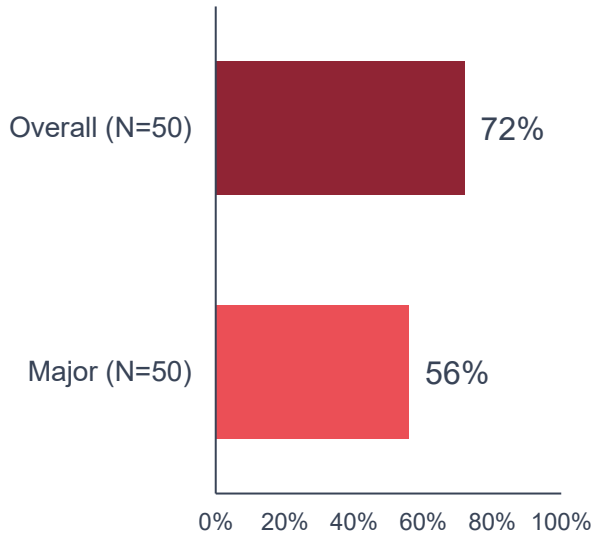
Hepcidin by Transfusion Cohort



Iron by Transfusion Cohort



Hematologic Response



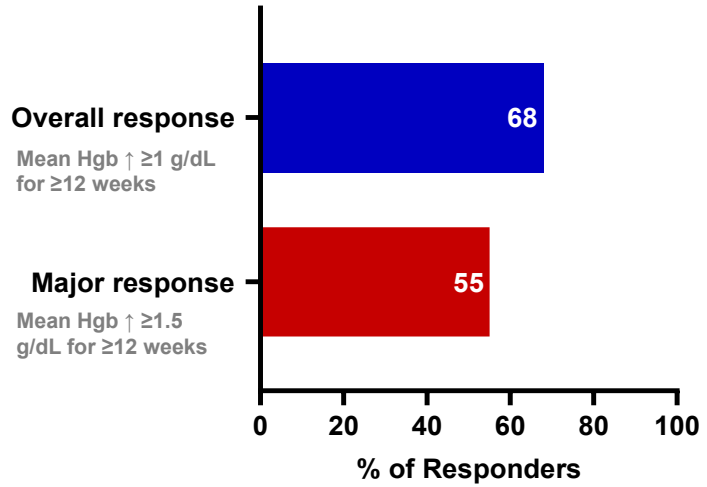
Data as of April 27, 2026

Abbreviations: LLD=lower limit of detection; TD=transfusion dependent; nTD=non-transfusion dependent; Analysis excludes values within 7 days of transfusion receipt. 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

RALLY-MF phase 2 data

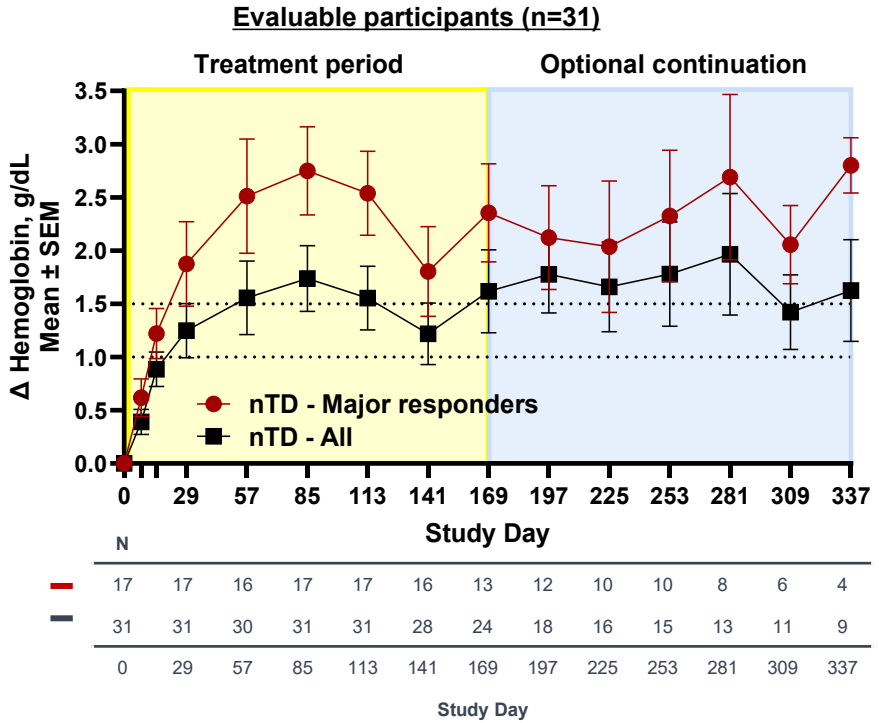
nTD (n=31): Early-acting, meaningful, and durable hemoglobin increases with 55% of patients achieving major response and 68% achieving overall response

nTD Hematologic Response



Response	Mean ± SD (days)
Time to major response during treatment period (n=17)	27 ± 30
Duration of longest major response through optional continuation phase (n=14)* with ongoing follow-up	318 ± 235

nTD Hemoglobin Increase from Baseline



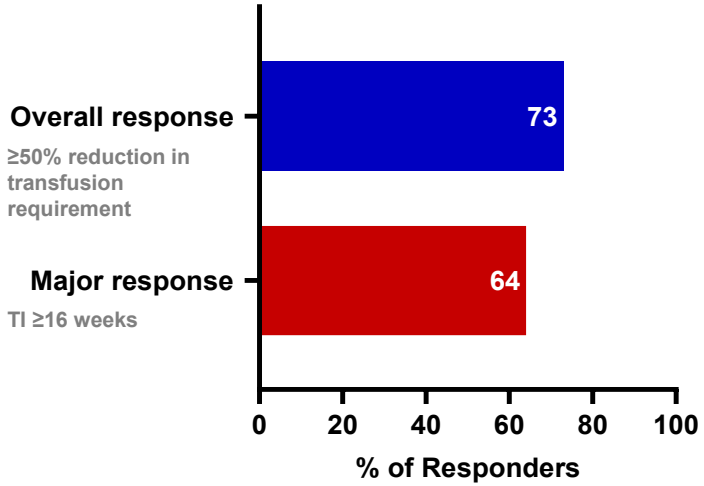
Data as of April 27, 2026

Analysis excludes values within 7 days of transfusion receipt. 9 nTD participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 8 nTD participants had a per protocol dose hold due to Hgb ≥12 g/dL. Abbreviations: EOS = end of study; Hgb = hemoglobin; TD = transfusion dependent.

RALLY-MF phase 2 data

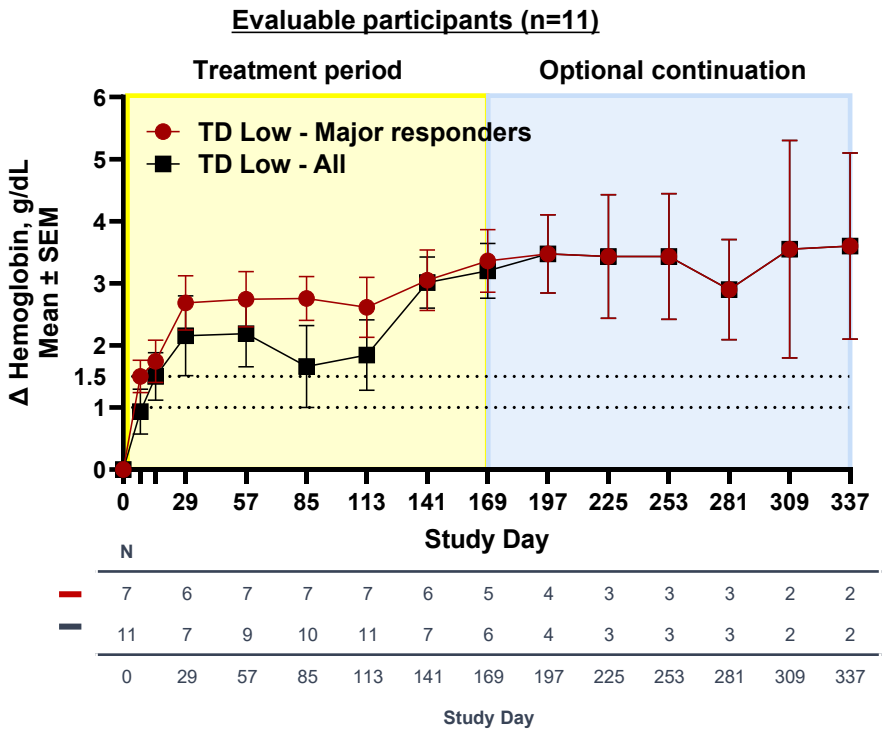
TD Low (n=11): Meaningful, and durable hemoglobin increases translating to transfusion reduction, with 64% of patients achieving major response and 73% achieving overall response

TD Low Hematologic Response



Response	Mean ± SD (days)
Time to major response (n=7)	4 ± 8
Duration of longest major response through optional continuation phase (n=6)** with ongoing follow-up	345 ± 243

TD Low Hemoglobin Increase from Baseline



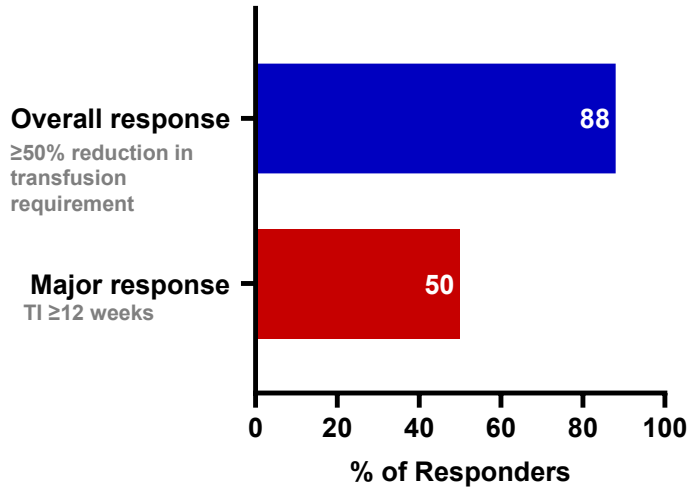
Data as of April 27, 2026

Analysis excludes values within 7 days of transfusion receipt. 5 TD Low participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 1 TD Low participant had a per protocol dose hold due to Hgb ≥12 g/dL. Abbreviations: Hgb = hemoglobin; TD = transfusion dependent.

RALLY-MF phase 2 data

TD High (n=8): Meaningful transfusion reduction, with 50% of patients achieving major response and 88% achieving overall response

TD High (n=8)



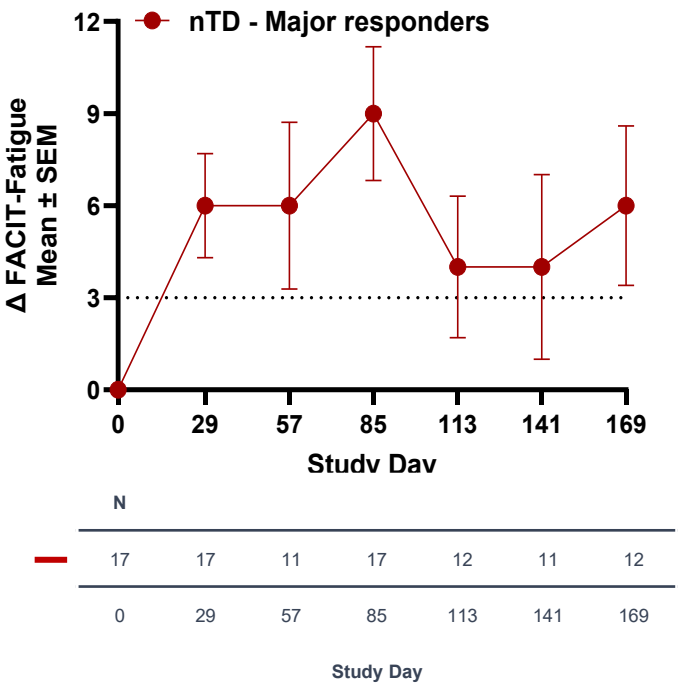
Response	Mean ± SD (days)
Time to major response (n=4)	2 ± 1
Duration of longest major response through optional continuation phase (n=2)** with ongoing follow-up	239 ± 18

Data as of April 27, 2026
Analysis excludes values within 7 days of transfusion receipt. 4 TD High participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. Abbreviation: TD = transfusion dependent.

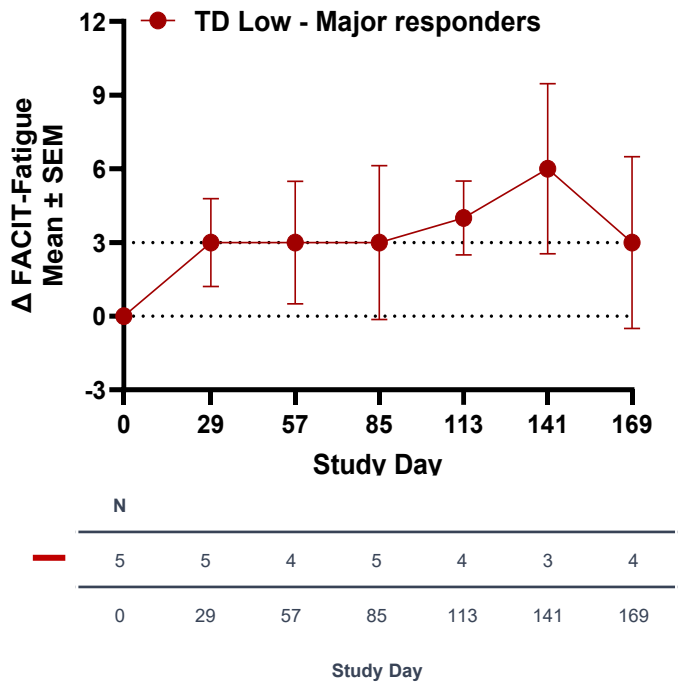
RALLY-MF phase 2 data

nTD and TD Low patients experienced clinically significant improvement in FACIT-Fatigue

FACIT-Fatigue (nTD patients)



FACIT Fatigue (TD Low patients)



- FACIT-Fatigue improvement and Hgb change were correlated 0.49 (p=0.0120) at EOS
- MPN-SAF TSS50 at EOS was achieved by 50% of nTD and TD low major responders
- PGIS improvement and Hgb change were correlated -0.76 (p=0.0004) at EOS

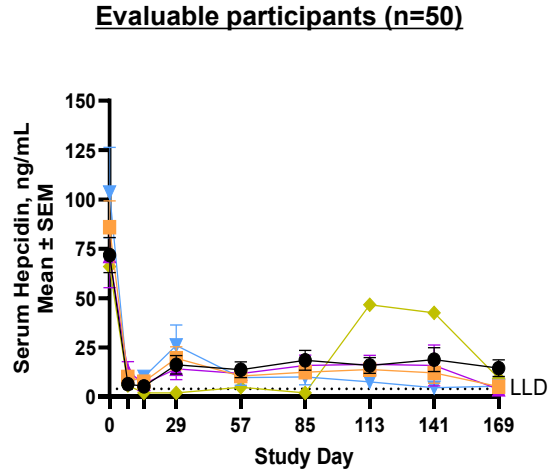
Data as of April 27, 2026

Abbreviations: EOS = end of study; Hgb = hemoglobin; MPN-SAF TSS50 = Myeloproliferative Neoplasm Assessment Total Symptom Score 50% reduction; PGIS = Patient Global Impression of Severity; TD = transfusion dependent. A 3-point change in the FACIT-Fatigue score is considered the threshold for clinical significance (Webster et al, Health Qual Life Outcomes. 2003;1:79).

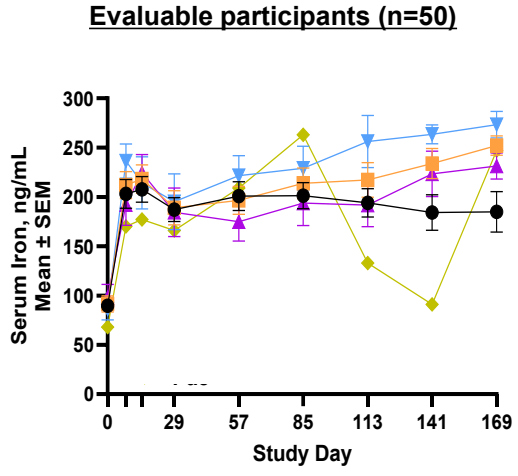
RALLY-MF phase 2 data

Selcodebart has demonstrated efficacy regardless of concomitant JAK inhibitor use, setting up for utilization across all anemic MF patients

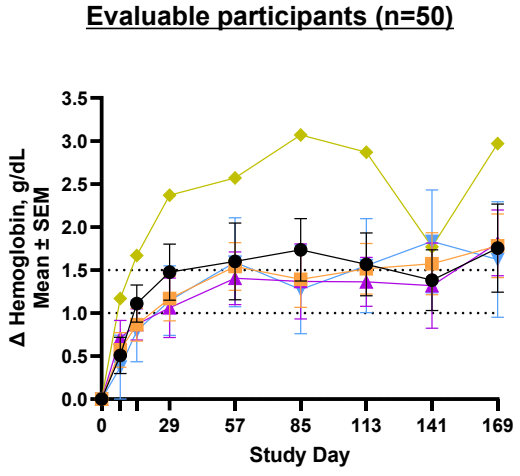
Hepcidin by JAKi Cohort



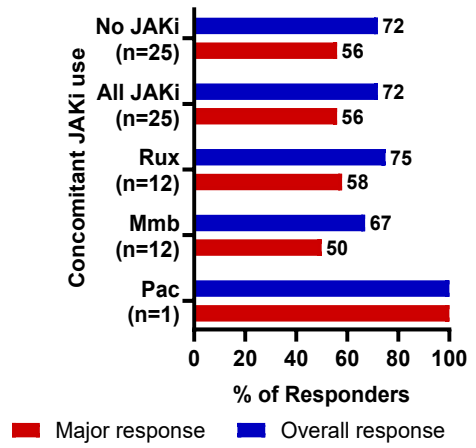
Iron by JAKi Cohort



Hemoglobin by JAKi Cohort



Response by JAKi Cohort





Data as of April 27, 2026

Abbreviations: JAKi = JAK inhibitor; LLD = lower limit of detection; mmb = momelotinib; pac = pacritinib; rux = ruxolitinib; Analyses exclude values within 7 days of transfusion receipt. Participant on concomitant pacritinib had study drug dose held on Days 85 and 113 due to Hgb >12 g/dL.

RALLY-MF phase 2 data

Safety

Preferred Term	nTD (n=35)	TD Low (n=13)	TD High (n=13)	Overall (n=61)
Any TEAE, n (%)	33 (94.3)	12 (92.3)	11 (84.6)	56 (91.8)
Related TEAE, n (%)	6 (17.1)	4 (30.8)	5 (38.5)	15 (24.6)
SAE, n (%)	8 (22.9)	1 (7.7)	3 (23.1)	12 (19.7)
AESIs, n (%)	2 (5.7)	0	0	2 (3.3)
≥ Grade 3 TEAEs, n (%)	13 (37.1)	6 (46.2)	6 (46.2)	25 (41.0)
Common TEAEs in >10% participants, n (%)				
Muscle spasms	10 (28.6)	1 (7.7)	2 (15.4)	13 (21.3)
Diarrhea	7 (20.0)	1 (7.7)	2 (15.4)	10 (16.4)
Fatigue	7 (20.0)	1 (7.7)	2 (15.4)	10 (16.4)
Anemia	2 (5.7)	4 (30.8)	3 (23.1)	9 (14.8)
Headache	6 (17.1)	2 (15.4)	1 (7.7)	9 (14.8)
Dizziness	6 (17.1)	1 (7.7)	1 (7.7)	8 (13.1)
Urinary tract infection	4 (11.4)	1 (7.7)	3 (23.1)	8 (13.1)
Fall	7 (20.0)	1 (7.7)	0	8 (13.1)
Hypertension	5 (14.3)	1 (7.7)	1 (7.7)	7 (11.5)
Back pain	5 (14.3)	2 (15.4)	0	7 (11.5)
Nausea	6 (17.1)	1 (7.7)	0	7 (11.5)
Abdominal pain	3 (8.6)	2 (15.4)	2 (15.4)	7 (11.5)
Constipation	4 (11.4)	0	3 (23.1)	7 (11.5)

Data as of April 27, 2026; AESI = AEs related to decrease in renal function, including creatinine increase Grade 2 or higher from baseline, per CTCAE criteria and acute kidney injury. AESIs: blood creatinine increased (n=2), chronic kidney disease (n=1), none of the AESIs were considered related to study drug. Related TEAEs occurring in ≥2 participants overall: diarrhea (n=5); none of the related TEAEs were considered serious. SAEs and Grade ≥3 AEs occurring in >1 participant: hypotension (n=2), cellulitis (n=2). SAEs and Grade <3 AEs: atrial fibrillation (n=1), upper gastrointestinal hemorrhage (n=1). Grade ≥3 AEs and Non-serious AEs occurring in >1 participant: anemia (n=7), lymphocyte count decreased (n=3), platelet count decreased (n=2). Abbreviations: AESI = adverse event of special interest; CTCAE = Common Terminology Criteria for Adverse Events; SAE = serious adverse event; TEAE = treatment-emergent adverse event.

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

Selcodebart 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 selcodebart to be the primary therapy to address MF anemia for all anemic patients

Selcodebart: Emerging product profile aiming to address key needs for MF anemia therapy

Key Needs for Anemia Therapy	Selcodebart Emerging Product Profile
1 Works across anemia severity levels	✓ Achieved POC in NTD, TD Low, and TD High patients
2 Works as a monotherapy 3 Works with any MF-directed therapy 4 Supports optimization MF-directed therapy regimen	✓ 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 selcodebart on optimization of underlying MF regimen in future studies
5 Superior response rates vs. current off-label anemia therapies	✓ 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

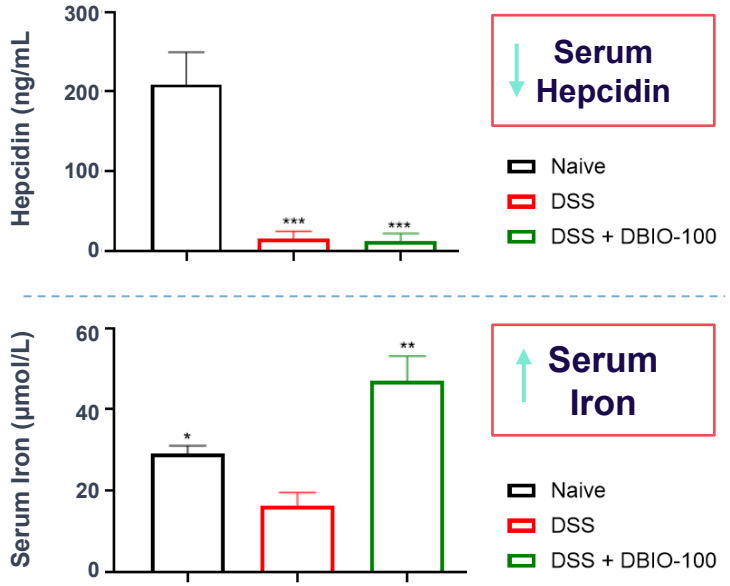
POC=Proof of concept; ORR=Overall Response Rate; MRR=Major Response Rate

Selcodebart in other anemias of inflammation

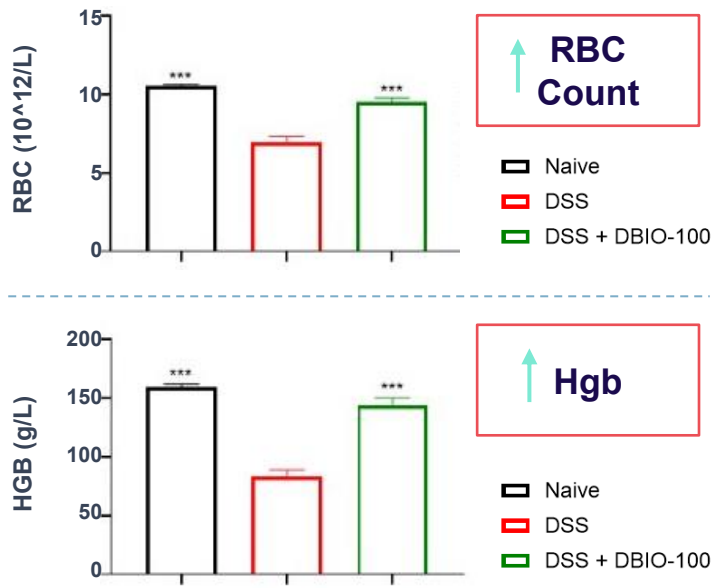
Inflammatory bowel disease mouse model

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

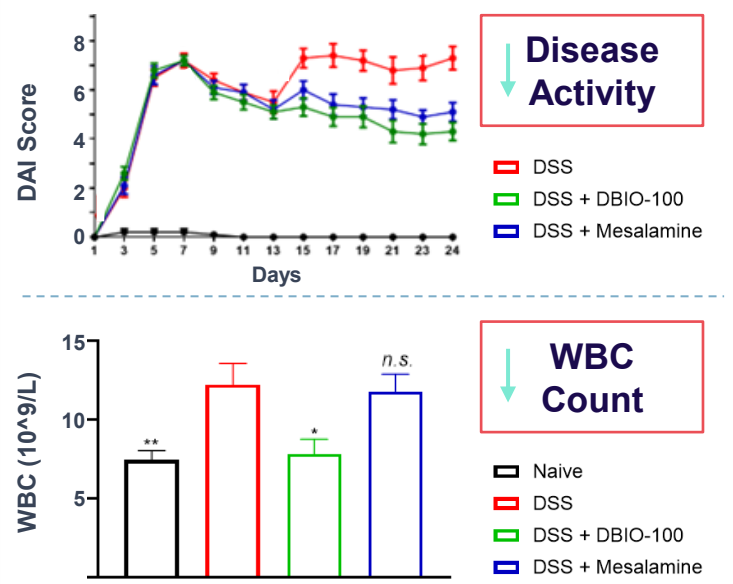
Target Engagement



Hematologic Improvement



IBD Disease Modification



DAI Score = Disease Activity Index

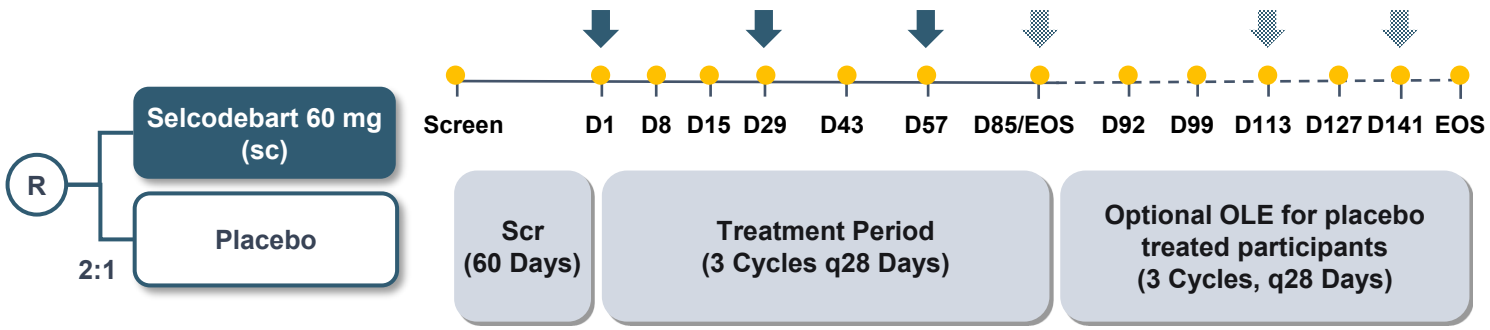
RALLY IBD: Phase 2 trial design

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 • Serum iron, TSAT, ferritin, serum hepcidin, reticulocyte count, CHr, and RBC count • Mean change in Hgb from baseline through Day 85 • Proportion of participants that achieve Hgb increase ≥1 g/dL and ≥ 2 g/dL through Day 85 • 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

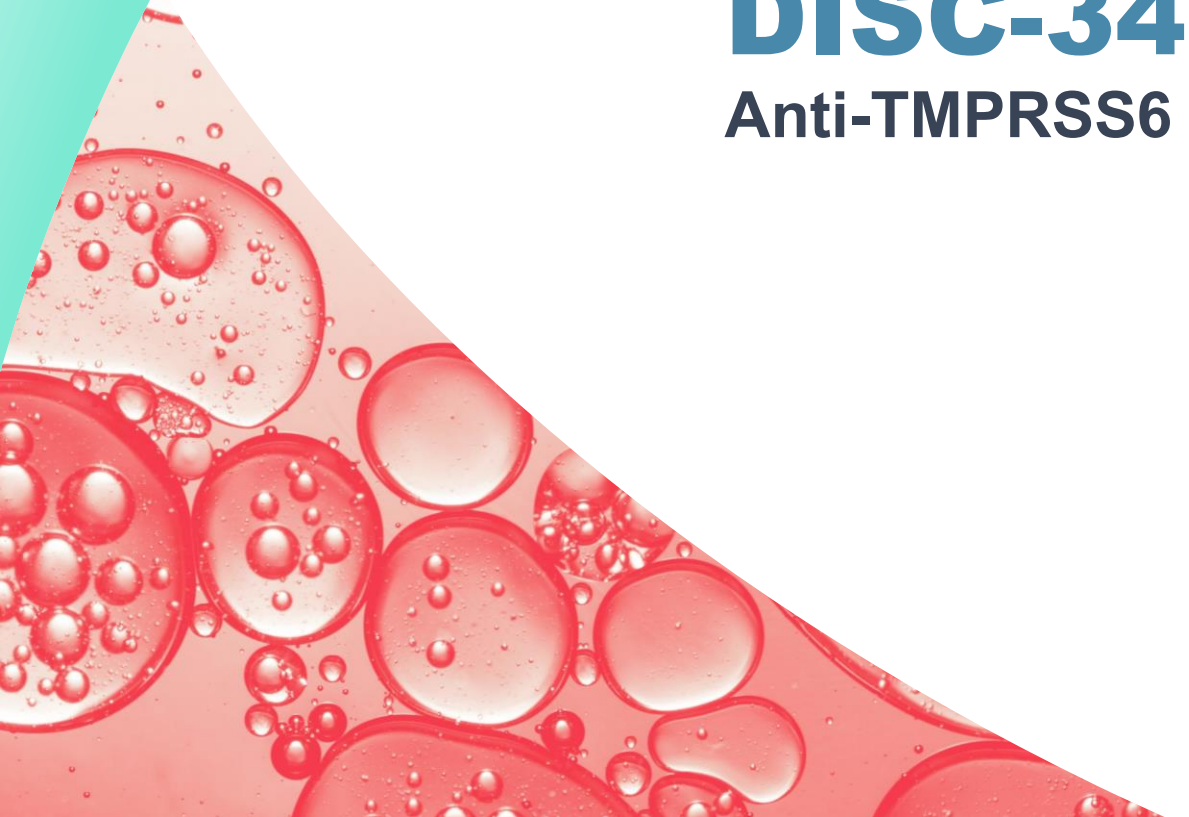
- Additional RALLY-MF data expected Q4 2026
- End of Phase 2 Meeting with FDA expected by end of year
- Phase 3 Pivotal trial initiation expected H1 2027

Other Anemias of Inflammation

- RALLY-IBD signal-seeking Phase 2 study in anemia of IBD with selcodebart 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 induction



Anti-TMPRSS6 mAb induces hepcidin

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



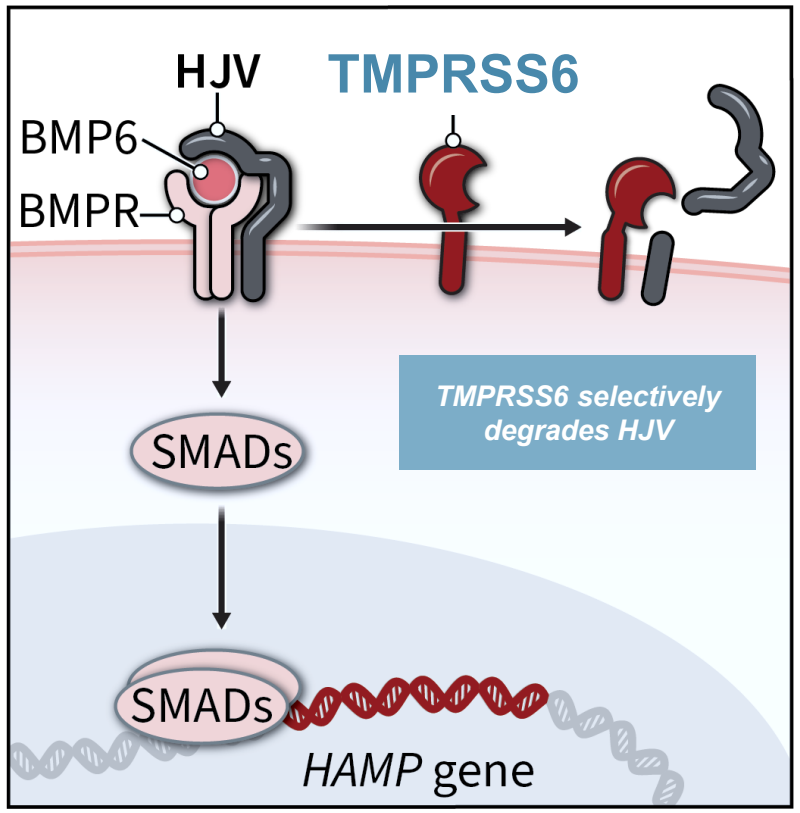
Enables Endogenous Production of Hepcidin

Promotes Iron Restriction Decreases GI Absorption

Erythrocytosis (PV)
Ineffective Erythropoiesis
Iron Overload

Targeting TMPRSS6 to increase hepcidin

Potent, specific target controls endogenous hepcidin production



Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

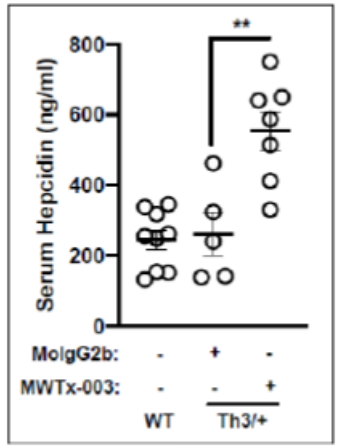
- Genetic validation in patients with IRIDA (Iron-Refractory Iron Deficiency Anemia)
- LOF TMPRSS6 mutation increases hepcidin and reduces iron availability
- Functionally specific to hepcidin / iron
- Tissue specific expression primarily in the liver

DISC-3405 in beta thalassemia and polycythemia vera

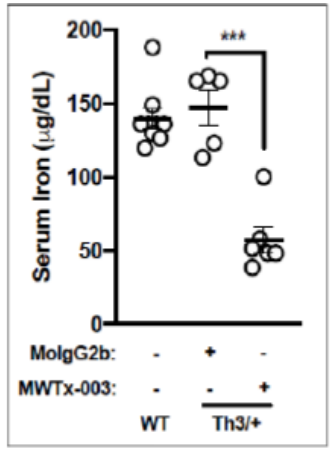
Significant effects on hallmarks of disease

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

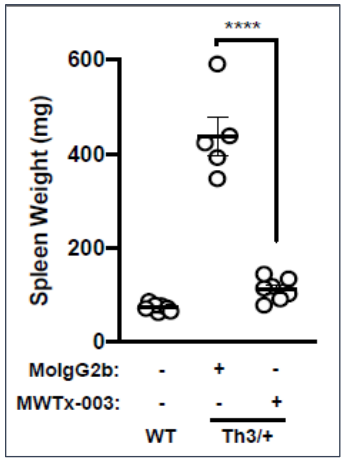
↑ Hepcidin Production



↓ Iron

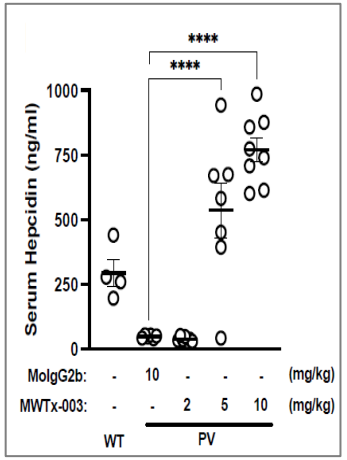


↓ Spleen Weight

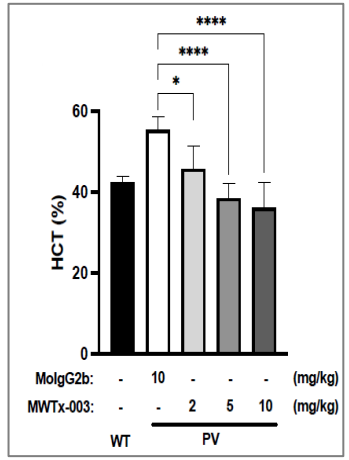


$Jak2^{V617F}$ model of Polycythemia Vera

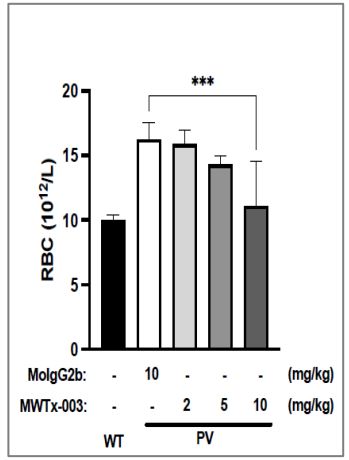
↑ Hepcidin Production



↓ 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 strategy

Phase 1 SAD/MAD in HV

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

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

- 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 – *Ongoing*

- 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 study in healthy volunteers

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

Single-Ascending Dose

75 mg IV → 75 mg SC → 150 mg SC → 300 mg SC

75 mg SC → 37.5 mg SC

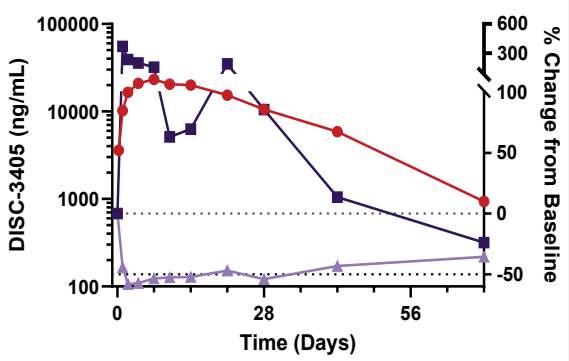
Multiple-Ascending Dose

150 mg SC (Q4W)

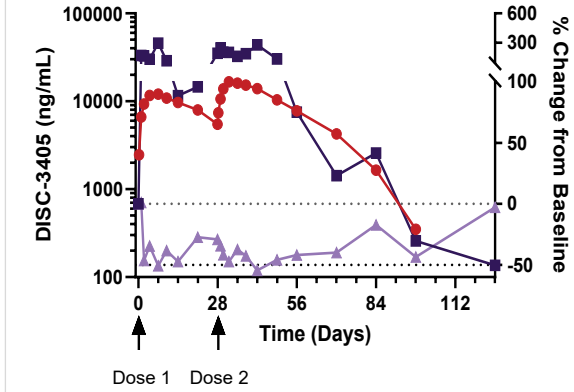
75 mg SC (Q4W)

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

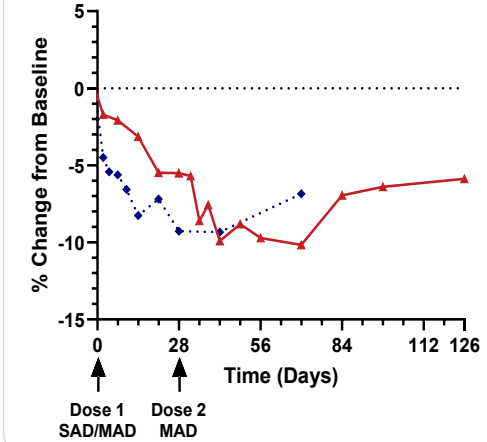
PK/PD: 300 mg SC SAD



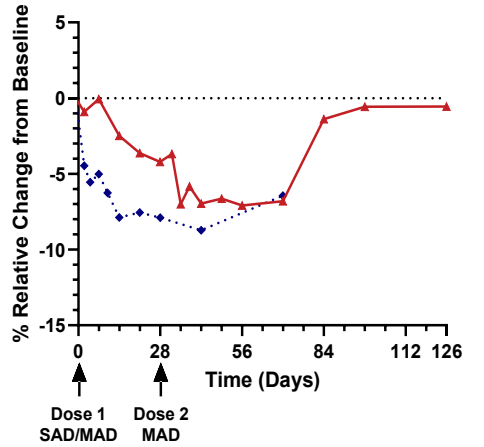
PK/PD: 150 mg SC MAD



Hemoglobin



Hematocrit



PK Hepcidin Serum Iron

150 SC, MAD 300 SC, SAD

DISC-3405: Iron pulse study in healthy volunteers

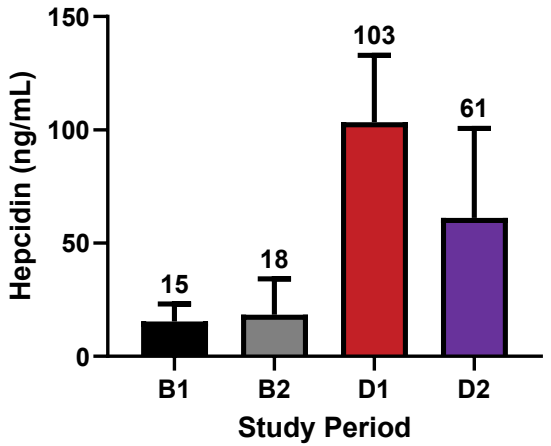
Strong inhibition of iron absorption with DISC-3405

Trial Design

- N=8 healthy volunteers received oral ferrous sulfate tablets
- Two sequential placebo occasions, 1 week apart, to assess intra-participant iron absorption variability:
  - **Baseline 1 (B1):** Placebo treatment on Day 1, followed by $FeSO_4$ (130 mg Fe) on Day 2
  - **Baseline 2 (B2):** Placebo treatment on Day 8, followed by $FeSO_4$ (130 mg Fe) on Day 9
- Healthy volunteers received 150 mg DISC-3405 (IV) on Day 15
- Iron absorption assessed using $AUC_{0\text{-}6h}$ 2 days (**Study Period D1**) and 15 days (**Study Period D2**) after drug treatment

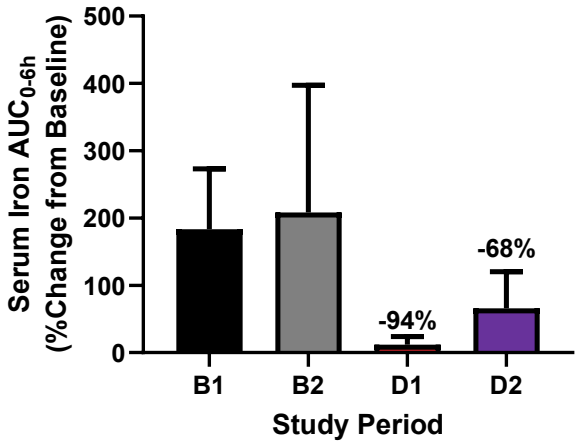
↑ DISC-3405 Increased Hepcidin Production

Average Hepcidin**



↓ **DISC-3405 Reduced Iron Absorption at D2 and D15**

Average Serum Iron**



Data confirms the mechanism of DISC-3405 and its ability to block dietary iron absorption, supporting the potential for treating iron overload conditions

**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

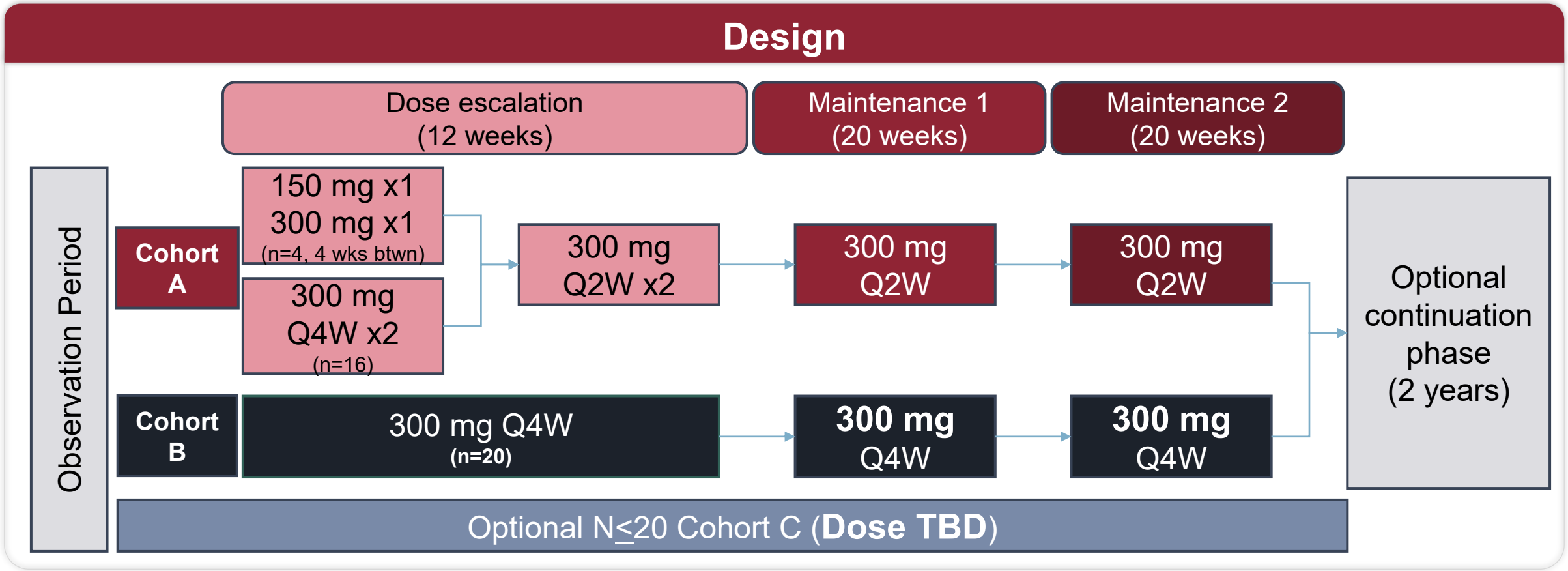
DISC-3405 is expected to be able to be used across the treatment landscape for PV

Current Treatment Options

- Phlebotomy
- Hydroxyurea
- Ruxolitinib
- Interferon
- Rusfertide

RESTORE-PV: Polycythemia vera phase 2 trial design

Data as of July 13, 2026: All 20 participants in Cohort A were dosed, with n=13 completing 26 weeks of the study, and 18 of 20 participants in Cohort B were dosed



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

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

RESTORE-PV: Baseline characteristics

Data as of July 13, 2026

	Cohort A (N=20)	Cohort B (N=20)
Age, years; mean (SD)	58.6 (13.3)	60.1 (11.4)
Sex, male; n (%)	16 (80.0)	8 (40.0)
Race	95% White 5% Black	95% White 5% Asian
Disease duration, years; mean (SD)	5.8 (5.7)	5.6 (3.7)
Risk		
High	65%	60%
Low	35%	40%
JAK2 mutation		
V617F	95%	100%
Exon 12	5%	0%
CRT use*		
None (PHL Only)	45%	50%
HU	40%	45%
IFN	15%	15%
Baseline PHL rate, 26 weeks prior to dosing; mean (SD)	3.7 (1.4), 0.14/week (0.05)	3.9 (2.1), 0.15/week (0.08) *N=18*
Baseline ferritin, ng/mL; mean (SD)	14.2 (7.9)	15.7 (9.3) *N=18*
Time on study since Day 1, days; mean (SD)	205.5 (62.2)	65.0 (30.3) *N=18*

Abbreviations: CRT= cytoreductive therapy; HU= hydroxyurea; IFN= interferon; PHL= phlebotomy

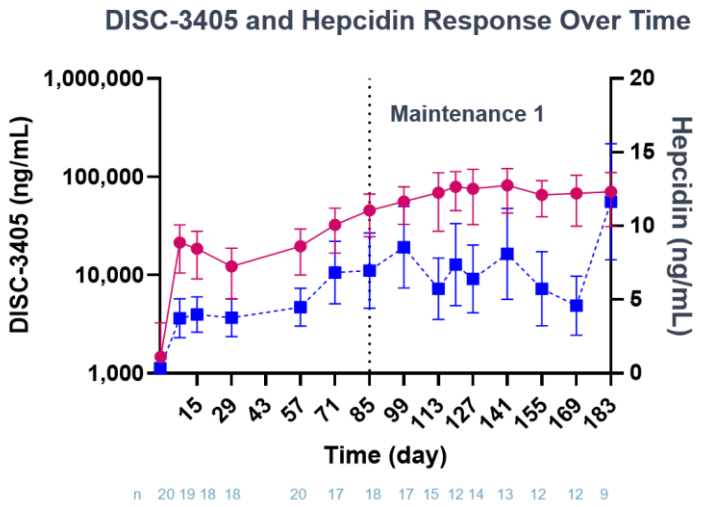
* IFN includes: Cohort A – n=3 for ropeginterferon-alfa-2b-njft; Cohort B – n=1 for ropeginterferon-alfa-2b-njft, n=2 peginterferon alfa-2a; n=2 patients in Cohort B on both HU and IFN

Only N=18 shown for baseline results in Cohort B as 2 participants in Cohort B were still in Observation Period at the time of data cut (July 13, 2026)

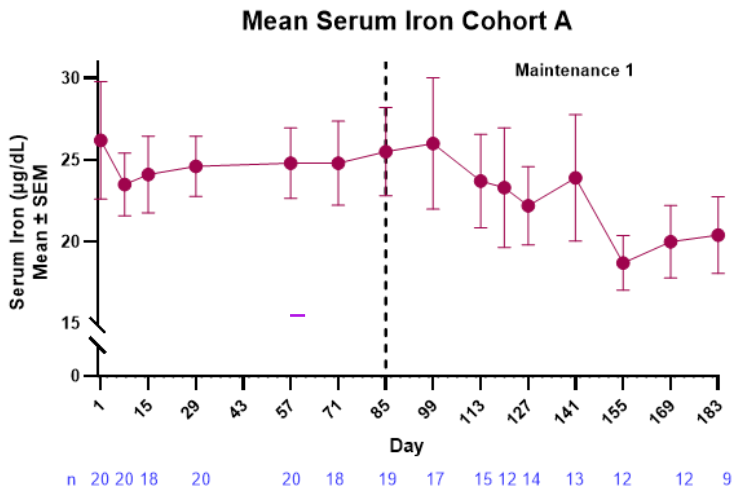
Initial RESTORE-PV phase 2 data

In participants from Cohort A, DISC-3405 administration increased hepcidin levels, leading to reduced serum iron and increased ferritin

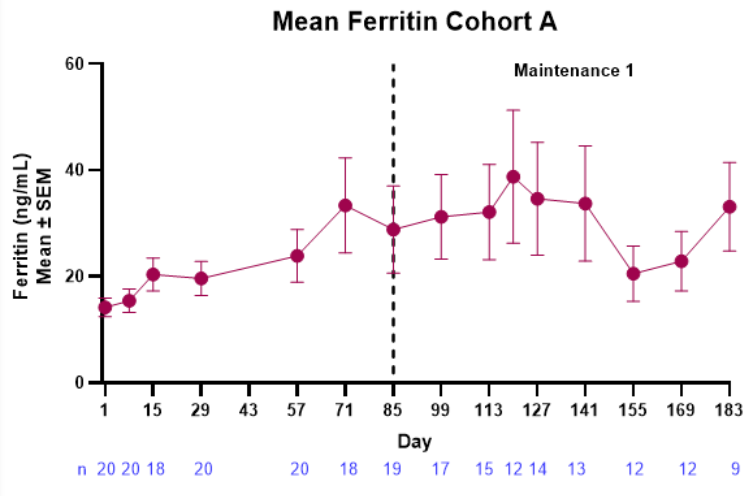
Hepcidin



Serum Iron



Ferritin

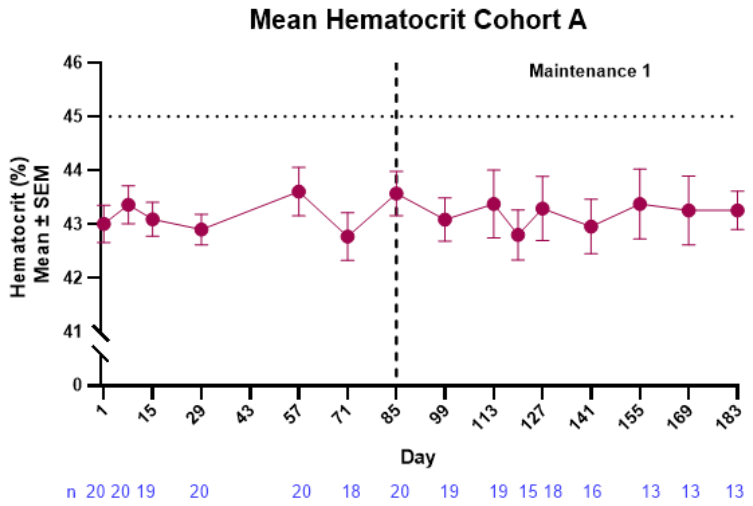


DISC-3405, ng/mL Hepcidin, ng/mL

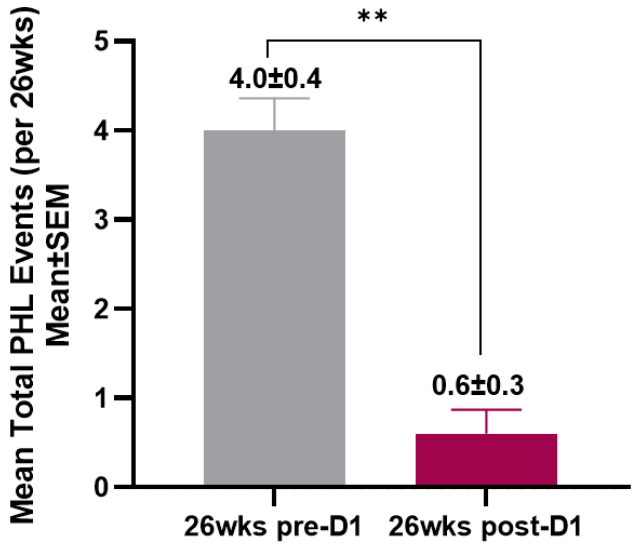
Initial RESTORE-PV phase 2 data

Restricting iron availability with DISC-3405 translated to controlled mean HCT <45%, reduced PHL burden, and improved symptoms in Cohort A participants who completed weeks 0-26 of therapy (n=13)

Hematocrit



Total PHL Events: 26 Weeks Pre- vs Post-Treatment Initiation (D1)



***p<0.0001*
Mean (SE) difference = -3.4 (0.5)
(95% CI: -4.5 to -2.3)

n=8/13 (61.5%) remained PHL-free

**Paired t-test
N=1 patient met PHL eligibility at 1 time point but did not receive PHL; Counting PHL+1 PHL eligibility event, the post-D1 26 weeks mean (SE) rate is 0.7 (0.3), with mean (SE) difference of -3.3 (0.6) and 95% CI -4.5 to -2.1; p<0.0001

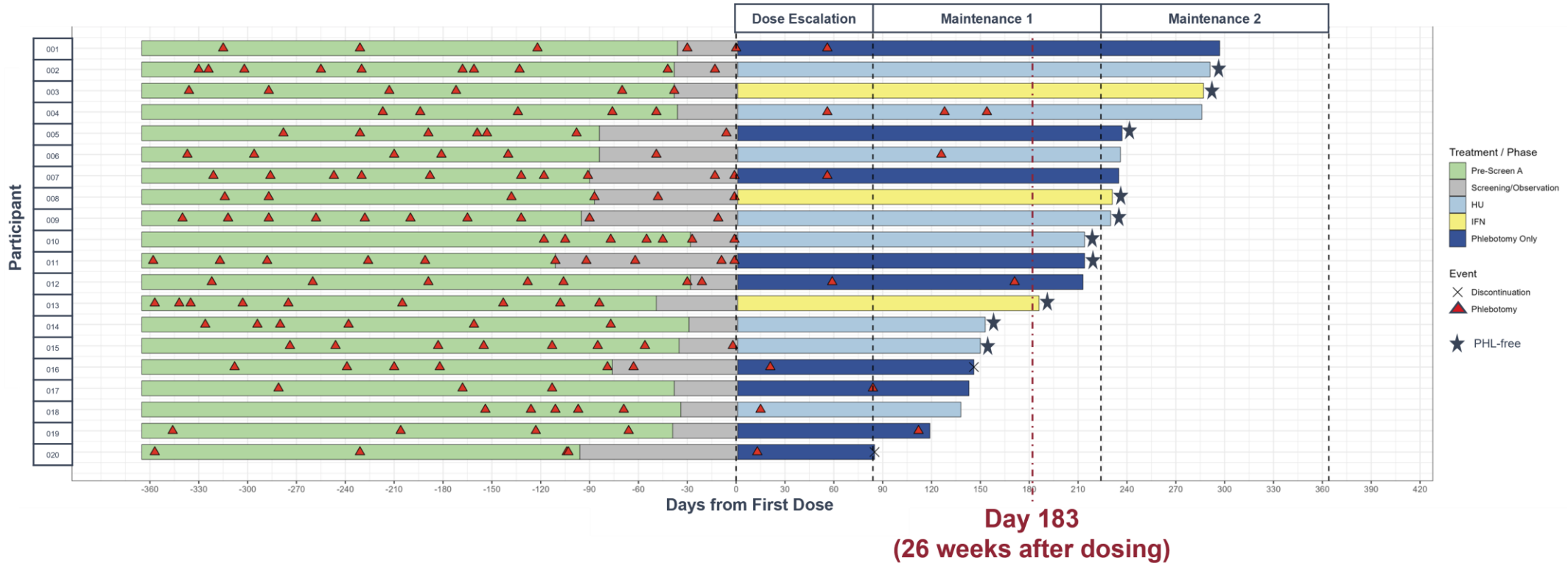
Participants had improved symptom scores on the MPN-SAF (n=11/13) and the PROMIS-F-SF 7a (n=12/13)

Abbreviations: HCT= hematocrit; PHL= phlebotomy

Initial RESTORE-PV phase 2 data

Of the n=9 participants who completed Maintenance 1, 77.8% (7/9) remained PHL-free during the Maintenance 1 period

DISC-3405 Reduced PHL Events in Cohort A Participants



N=2 patients voluntarily withdrew, not due to adverse events. N=2 patients met PHL eligibility at 1 time point each but did not receive PHL, and those episodes of PHL eligibility are not represented on the swim-lane plot. Data cutoff July 13, 2026. Abbreviations: PHL= Phlebotomy

Initial RESTORE-PV phase 2 data

Safety

Adverse Event	Cohort A (N=20)	Cohort B (N=18)	Total (N=38)
Any TEAE, n (%)*	16 (80.0)	11 (61.1)	27 (71.1)
Serious AE*	1 (5.0)	1 (5.6)	2 (5.3)
Related TEAE$^{\Delta}$	4 (20.0)	6 (33.3)	10 (26.3)
Abdominal pain	6 (30)	1 (5.6)	7 (18.4)
Injection site reaction†	3 (15.0)	2 (11.1)	5 (13.2)
Early satiety	4 (20.0)	0	4 (10.5)
Bone pain	3 (15.0)	0	3 (7.9)
Disturbance in attention	3 (15.0)	0	3 (7.9)
Dizziness	3 (15.0)	0	3 (7.9)
Contusion	2 (10.0)	1 (5.6)	3 (7.9)
Headache	1 (5.0)	2 (11.1)	3 (7.9)
Pyrexia	2 (10.0)	0	2 (5.3)
Hyperhidrosis	2 (10.0)	0	2 (5.3)
Decreased appetite	2 (10.0)	0	2 (5.3)
Muscular weakness	1 (5.0)	1 (5.6)	2 (5.3)
Constipation	1 (5.0)	1 (5.6)	2 (5.3)
Flank pain	1 (5.0)	1 (5.6)	2 (5.3)
Fatigue	1 (5.0)	1 (5.6)	2 (5.3)
Night sweats	0	2 (11.1)	2 (5.3)
Hot flush	0	2 (11.1)	2 (5.3)
Blurred vision	0	2 (11.1)	2 (5.3)

*Includes 1 unrelated Basal cell carcinoma diagnosed at Day 22 (Cohort A) in a participant who was symptomatic prior to study enrollment, 2 unrelated SAEs (headache, cholecystitis); ΔIncludes Possibly Related, Probably Related, Definitely Related AEs: Cohort A – Grade 1 Injection site reaction (n=3), Grade 2 Rash (n=1), Grade 1 Fatigue (n=1); Cohort B – Grade 1 Injection site reaction (n=2), Grade 1 Abdominal Pain (n=1), Grade 1 Headache (n=1), Grade 1 Stomatitis (n=1), Grade 2 Anemia (n=1), Grade 1 Sinus tachycardia (n=1), Grade 1 Peripheral sensory neuropathy (n=1); †Injection site reaction: includes injection site pain (n=3 Cohort A) and injection site reaction (n=2 Cohort B); only 1/5 was recurrent.

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

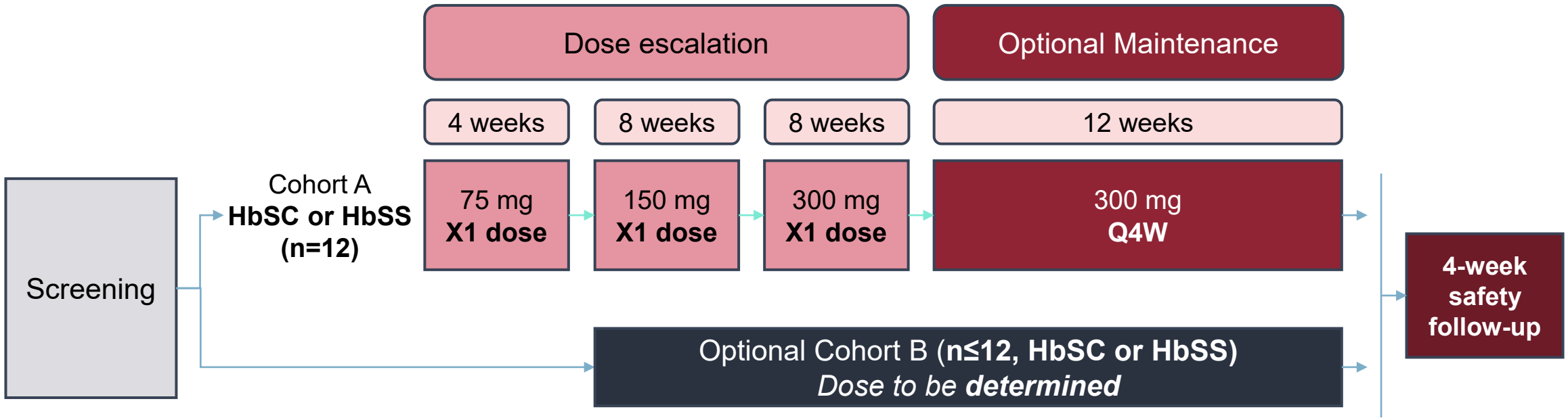
DISC-3405 in a Townes Model

- 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; initial data expected Q4 2026

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	2H 2026	2027
Bitopertin Heme Synthesis Modulation	**Erythropoietic Porphyrias (EPP & XLP)**	✓ APOLLO topline – Q4 2026 • Resubmit NDA by end of 2026	• FDA decision mid-2027 • Ex-US regulatory submissions
Selcodebart Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**	• Additional RALLY-MF Phase 2 data • End of Phase 2 Meeting	• Phase 3 initiation
	Anemia of Inflammatory Bowel Disease (IBD)		• RALLY-IBD Phase 2 Data
DISC-3405 Hepcidin Induction	**Polycythemia Vera (PV)**	• Additional RESTORE-PV Phase 2 data	• Topline RESTORE-PV Phase 2 Data • End of Phase 2 Meeting and Phase 3 initiation
	Sickle Cell Disease (SCD)	• Initial Phase 1b Data	• Topline Phase 1b data • Phase 2 initiation

Supported by a strong cash position with runway into 2030

Disc Medicine: Built for Sustainable Growth

Three programs addressing blockbuster markets with significant potential for expansion

Bitopertin
Positive APOLLO Topline

NDA resubmission to FDA expected by end of 2026

- EPP: Debilitating disease with high unmet need and defined patient population
- Data support differentiated profile for EPP

Selcodebart
POC Established

Additional MF data and Phase 3 plans expected by end of 2026

- 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
Initial POC Established

RESTORE-PV update and initial SCD data expected by end of 2026

- Potential for a differentiated profile within large addressable PV 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

MF=Myelofibrosis; IBD=Inflammatory bowel disease; PV=Polycythemia vera; SCD=Sickle cell disease

Thank you