disc medicine

Corporate Presentation

June 15, 2026

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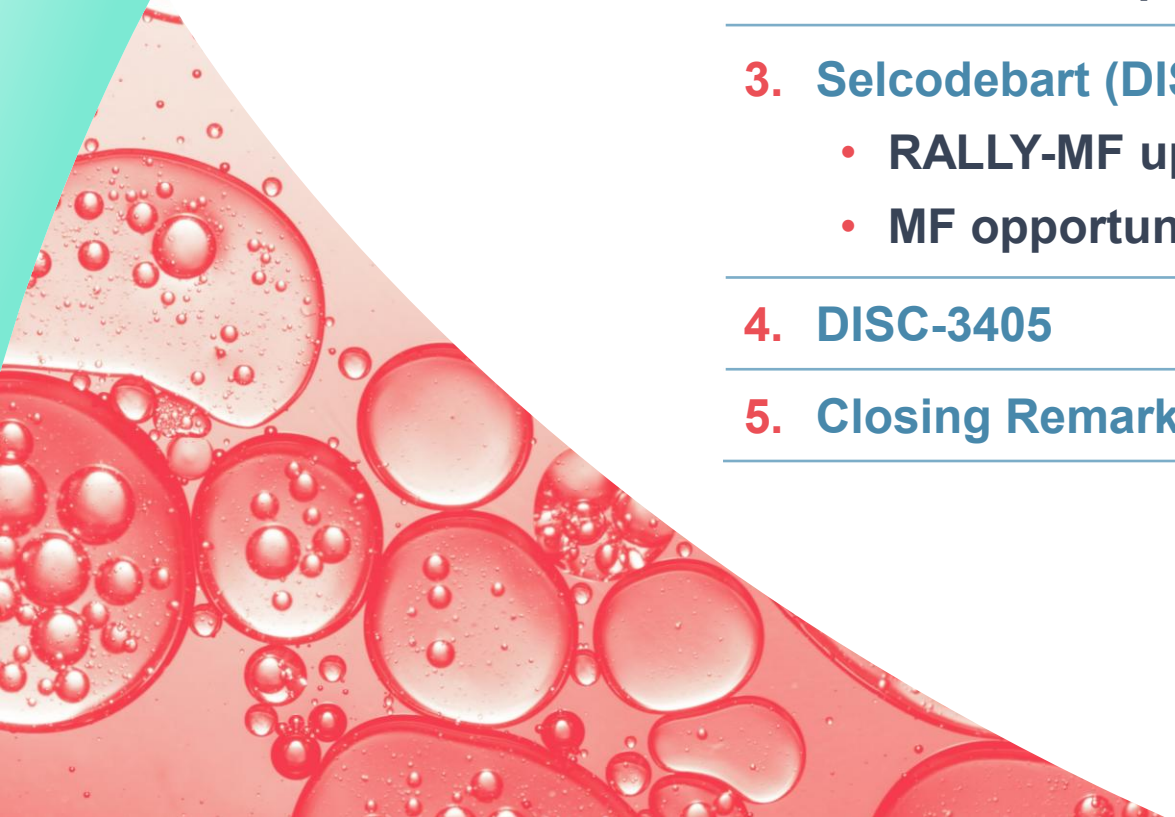
Bitopertin, DISC-0974, and DISC-3405 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide

Agenda

1. Introduction
2. Bitopertin in EPP
   - Type A meeting summary and next steps
   - EPP data update: HELIOS open label extension
3. Selcodebart (DISC-0974)
   - RALLY-MF update
   - MF opportunity and HJV franchise next steps
4. DISC-3405
5. Closing Remarks and Q&A Session



Disc's hematology-focused pipeline

Key programs driving upcoming catalysts

	PROGRAM		Preclinical	Phase 1	Phase 2	Phase 3
HEME	Heme Synthesis Modulation	**Bitopertin** **GlyT1 Inhibitor** Oral, once daily			Erythropoietic porphyrias (EPP and XLP)	
IRON	Hepcidin Suppression	**Selcodebart (DISC-0974)** **Anti-HJV monoclonal antibody** Subcutaneous, once-monthly			Anemia of myelofibrosis (MF)	
					Anemia of inflammatory bowel disease (IBD)	
		DISC-0998 **Anti-HJV monoclonal antibody** Subcutaneous, long-acting			Anemia associated with inflammatory diseases	
	Hepcidin Induction	**DISC-3405** **Anti-TMPRSS6 monoclonal antibody** Subcutaneous, projected once-monthly			Polycythemia vera (PV)	
					Sickle cell disease (SCD)	

Summary of Updates

Bitopertin

- **Update on Type A Meeting with FDA:**
  - Aligned with the FDA that the Phase 3 APOLLO study can serve as the basis for CRL response
  - On track for CRL response submission by EOY
- **Updated data from HELIOS open label extension study in EPP:**
  - Sustained reductions in PPIX for >1 year with continued bitopertin treatment
  - Sustained, significant improvements in average light tolerance and time to prodrome
  - Favorable longer-term safety profile with up to 2.5+ years of exposure

Selcodebart (DISC-0974)

- **Updated data from RALLY-MF Phase 2 trial in anemia of MF:**
  - Meaningful, durable benefits on hemoglobin and transfusion burden for a broad range of patients
  - 72% overall response rate and 56% major response rate across subpopulations (NTD, TD Low, TD High)
  - Similar response rates regardless of background therapy
  - Robust symptom benefit by FACIT-Fatigue and MPN-SAF Total Symptom Score
- **Reinforces positioning as potential standard of care for ~22K US anemic MF patients**

DISC-3405 RESTORE-PV Phase 2 trial in PV and Phase 1b trial in SCD ongoing with initial data expected in Q4

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Bitopertin in EPP: Progressing toward CRL response by end of 2026

- In Type A meeting, aligned with the FDA that the Phase 3 APOLLO study can serve as the basis for CRL response and, if successful, support a traditional approval
- APOLLO trial fully enrolled in March 2026 and topline data expected in Q4 2026
- On track for expected CRL response submission by end of 2026
- Launched Expanded Access Program (EAP) for bitopertin for eligible patients with EPP and XLP in the US and other select countries
- Continuing commercial preparation efforts with focus on disease education, account validation, and patient identification

HELIOS: EPP Open-Label Extension

Study overview – data as of November 1, 2025

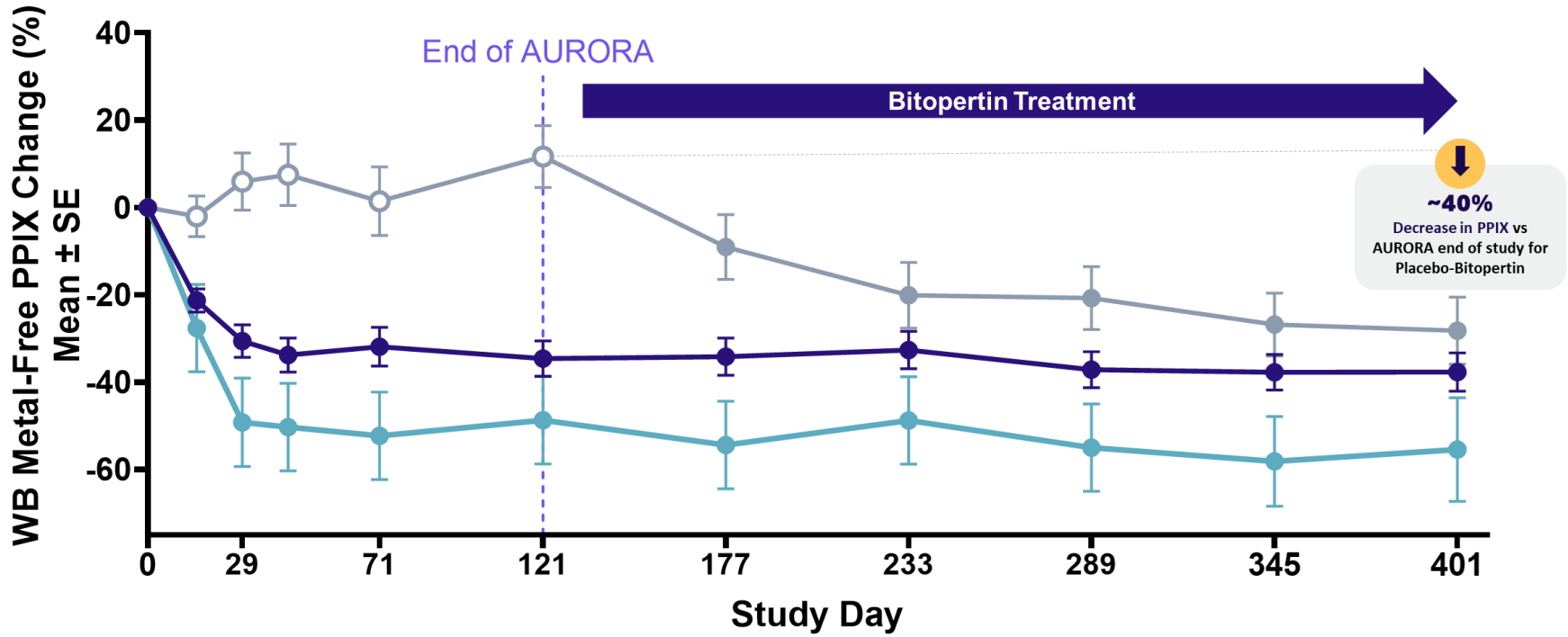
	PBO → Bitopertin (n=21)	Bitopertin → Bitopertin (n=65)	Total (n=86)
Enrolled	21	65	86
Discontinued treatment	1 (5%)	3 (5%)	4 (5%)
Completed Week 24	20 (95%)	62 (95%)	82 (95%)
Mean ± SD age, years	41.9 ± 11.1	46.2 ± 15.1	45.2 ± 14.3
Age <18 years	0	3 (5%)	3 (3%)
EPP, n (%)	21 (100%)	64 (98%)	85 (99%)
XLP, n (%)	0	1 (2%)	1 (1%)
Mean ± SD baseline PPIX (ng/mL)	8546 ± 6335	5990 ± 4185	6606 ± 4873

Baseline defined as Day 1 of HELIOS. ALT = alanine aminotransferase; PBO = placebo; PPIX = protoporphyrin IX SD = standard deviation; W = week; XLP = X-linked protoporphyria

HELIOS Update: PPIX

Sustained reductions in PPIX for >1 year with continued bitopertin treatment, with greater reductions in participants who received continuous treatment with 60 mg of bitopertin

PPIX Change from Baseline



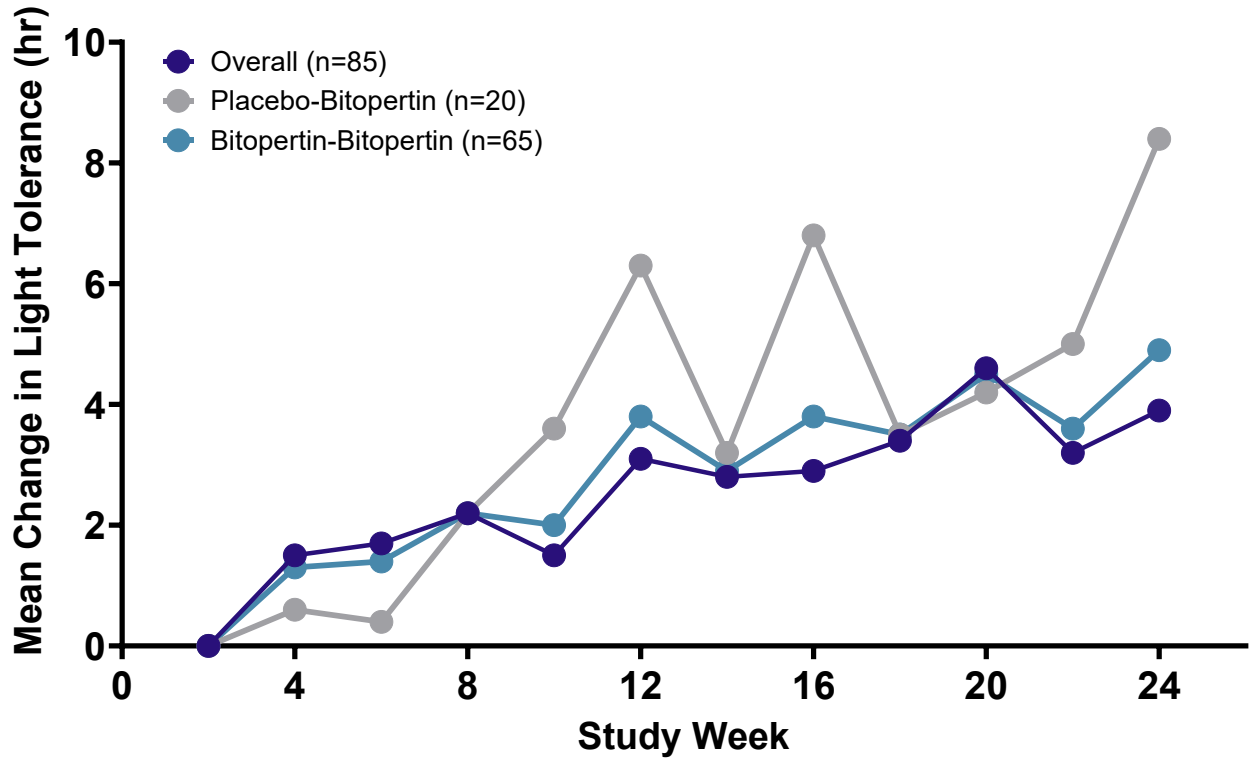
Bitopertin–Bitopertin (n)	75	71	67	68	67	59	38
Bitopertin–Bitopertin 60 mg (n)	14	14	14	14	14	12	8
Placebo–Bitopertin (n)	24	24	22	21	22	17	13

Bitopertin–Bitopertin: participants initially randomized to bitopertin (20 or 60 mg dose) in AURORA or BEACON; Bitopertin 60 mg–Bitopertin 60 mg: subset of participants who received bitopertin 60 mg continuously in AURORA or BEACON and HELIOS. Placebo–Bitopertin: participants initially randomized to placebo in AURORA. Study day calculated relative to Day 1 of AURORA or BEACON. Percent change from baseline calculated relative to baseline in AURORA or BEACON. Abbreviations: PPIX = protoporphyrin IX; SE = standard error; WB = whole blood

HELIOS Update: Light Tolerance

Sustained, significant improvements in average light tolerance

Mean Change in Light Tolerance



Week 24	Placebo Bitopertin (n=20)	Bitopertin Bitopertin (n=65)	Overall (FAS[a]) (n=85)
Total Light Tolerance (hr) over 2-Week Interval at Week 24			
LS Means (SE)	39.4 (2.6)	35.0 (1.4)	36.0 (1.1)
Change from baseline[b]	8.4 (2.5)	3.9 (1.5)	4.9 (1.3)
P-value vs baseline	0.001	0.011	<0.001

[a] FAS = full analysis set; 1 participant in the placebo – bitopertin did not receive a dose of bitopertin in HELIOS
[b] Baseline defined as the first 2-week interval in HELIOS. Change from baseline in total daily sunlight exposure from 10:00am to 6:00pm on days without pain averaged over 2-week periods and analyzed using MMRM. P-value for LS mean from the hypothesis test of 0 change from baseline at Week 24. Data as of 04 February 2025

HELIOS Update: Safety

Favorable longer-term safety profile (up to 2.5+ years exposure)

- Median exposure: 25.3 months (range: 13.8 to 32.7 months)
- 1 participant reported SAEs (unrelated) due to motor vehicle accident
- 3 Grade 3 TEAE (unrelated): hypertransaminasaemia, tendon rupture, squamous cell carcinoma
- All other TEAEs mild or moderate in severity
- Safety profile similar across adults and adolescents
- Fewer than 5 patients reported dizziness in HELIOS

	Adults (n=83)	Adolescents (n=3)	Total (n=86)
Any TEAE	59 (71%)	2 (67%)	61 (71%)
Grade 3 TEAE	4 (5%)	0	4 (5%)
Discontinuation due to AE	2 (2%)	0	2 (2%)
SAE	1 (1%)	0	1 (1%)
Common TEAEs (reported in > 5 participants)			
COVID-19	9 (11%)	1 (33%)	10 (12%)
Nasopharyngitis	8 (10%)	0	8 (9%)
Headache	6 (7%)	0	6 (7%)

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 • Percent change from baseline in whole blood metal-free PPIX after 6 months of treatment
Additional Endpoints	• Occurrence of phototoxic reactions • Cumulative total pain-free time in sunlight • Change from baseline in time to prodrome • Patient global impression of change (PGIC) • 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

APOLLO Baseline Characteristics

	Adolescent (n=34)	Adult (n=149)	Overall (n=183)
Age (years), Mean	14	42	37
Adolescent, n (%)	34	0	34 (19%)
Sex (female), n (%)	20 (59%)	87 (58%)	107 (59%)
Diagnosis			
EPP	31 (91%)	140 (94%)	171 (93%)
XLP	3 (9%)	9 (6%)	12 (7%)
Prior EPP Treatment			
Afamelanotide	2 (6%)	50 (34%)	52 (28%)
Dersimelagon	3 (9%)	29 (20%)	32 (18%)
None	29 (85%)	81 (54%)	110 (60%)
Baseline Light Tolerance			
<30 mins	15 (44%)	76 (51%)	91 (50%)
≥30 mins	19 (56%)	73 (49%)	92 (50%)
Geography			
US	17 (50%)	65 (44%)	82 (45%)
Ex-US	17 (50%)	84 (56%)	92 (55%)
North	27 (79%)	105 (70%)	132 (72%)
South	7 (21%)	44 (30%)	51 (28%)
Season of Randomization			
Fall	4 (12%)	17 (11%)	21 (12%)
Winter	11 (32%)	49 (33%)	60 (33%)
Spring	9 (27%)	48 (32%)	57 (31%)
Summer	10 (29%)	35 (24%)	45 (25%)

Northern sites are in Canada, France, Germany, Ireland, Netherlands, Norway, Sweden, United Kingdom, and any US sites north of North Carolina; Southern sites are in Australia, Italy, Spain, and any US sites in North Carolina and further south; prior EPP treatment defined as ever having received a listed treatment

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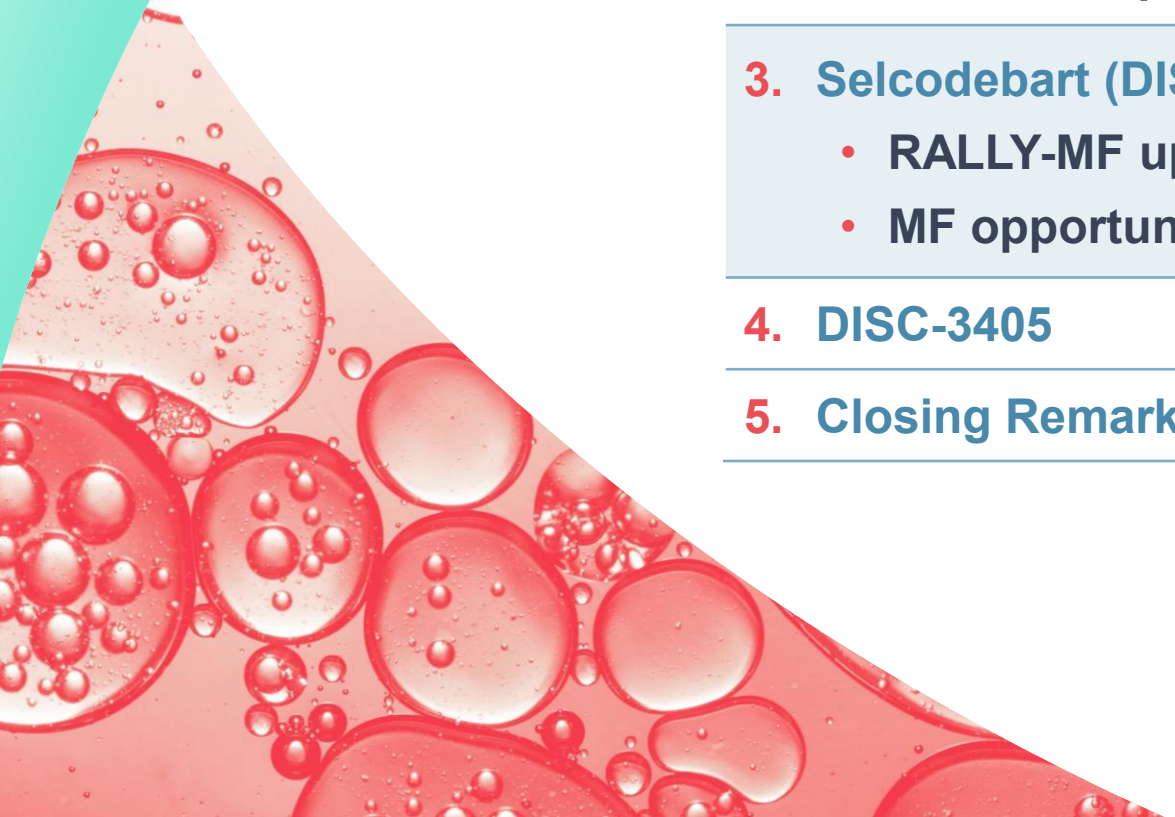
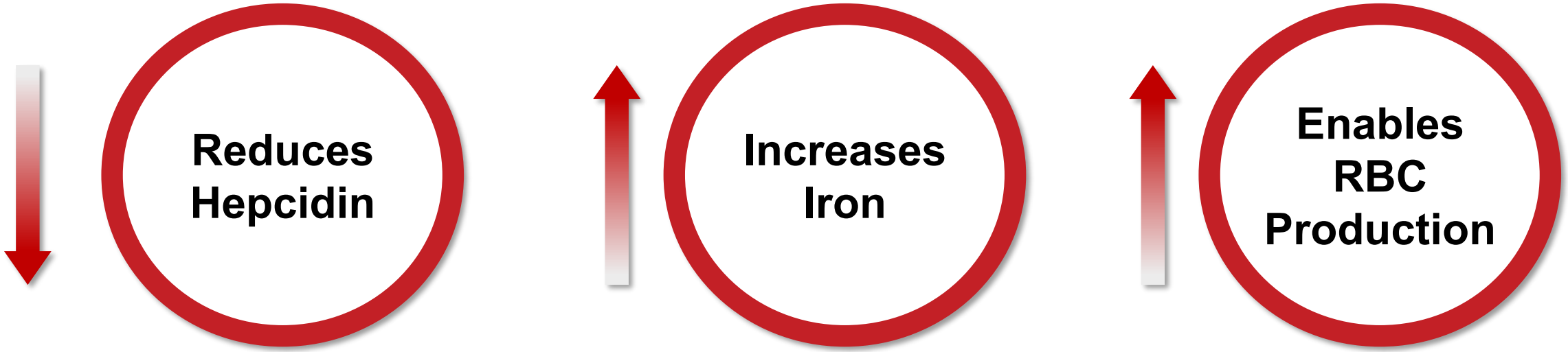


Selcodebart (DISC-0974): Novel anti-HJV mAb to suppress hepcidin

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

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; patient-reported outcomes

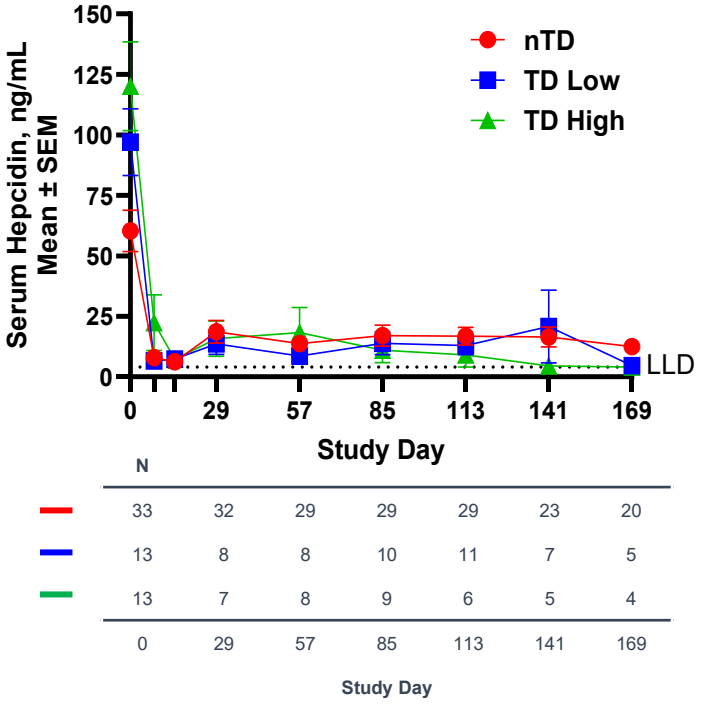
	nTD (n=35)	TD Low (n=13)	TD High (n=13)	Overall (n=61)
Age, median (range), years	70.0 (31, 83)	75.0 (60, 87)	73.0 (60, 87)	71.0 (31, 87)
Concomitant medication, n (%)	18 (51.4)	6 (46.2)	9 (69.2)	33 (54.1)
JAK inhibitor	17 (48.6)	6 (46.2)	9 (69.2)	32 (52.5)
Ruxolitinib	8 (22.9)	3 (23.1)	4 (30.8)	15 (24.6)
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

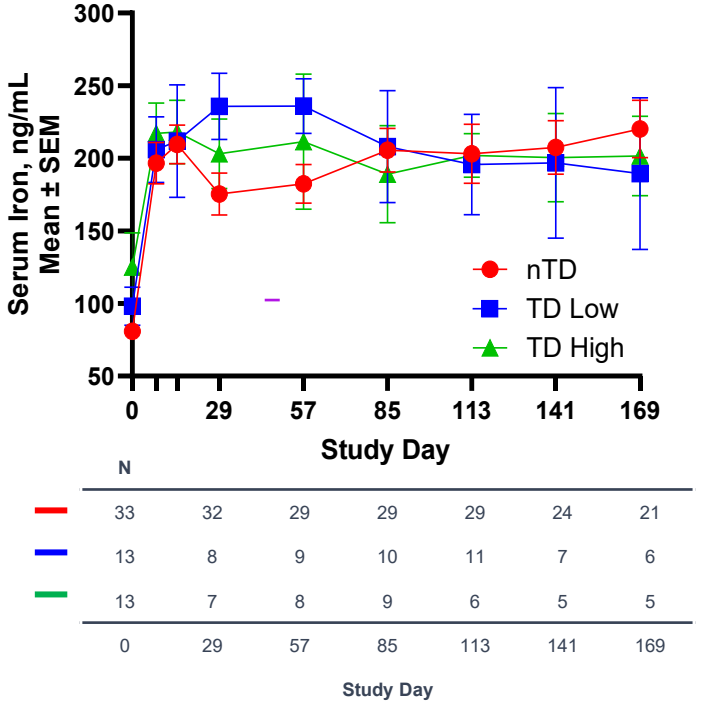
Updated RALLY-MF phase 2 data

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

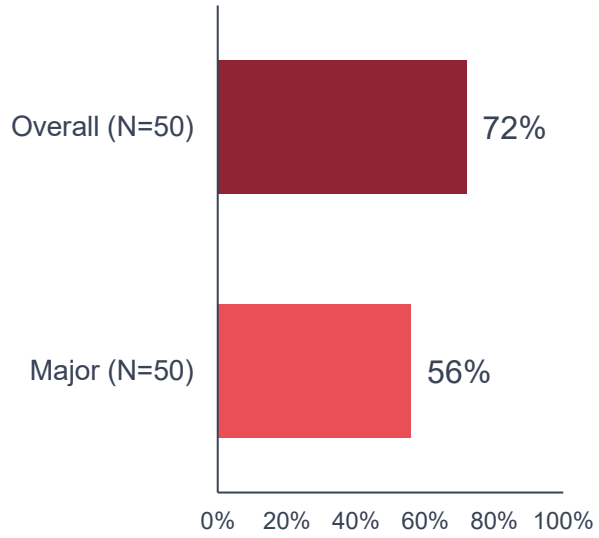
Hepcidin by Transfusion Cohort



Iron by Transfusion Cohort



Hematologic Response

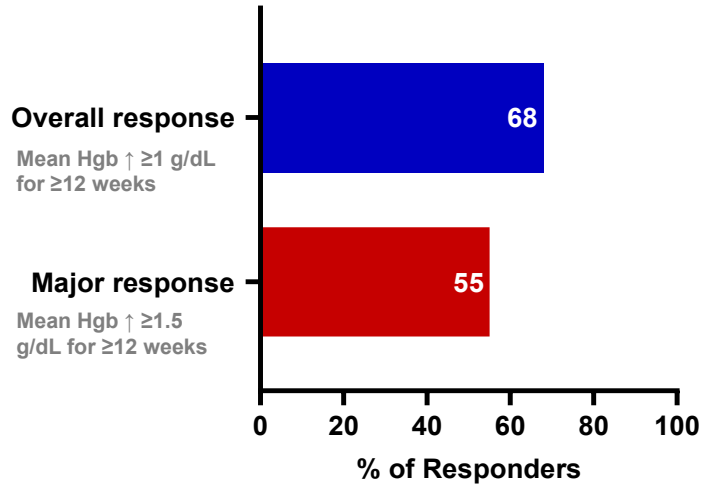


Abbreviations: LLD=lower limit of detection; TD=transfusion dependent; nTD=non-transfusion dependent; Analysis excludes values within 7 days of transfusion receipt. Overall response for NTD = Mean Hgb ↑ ≥1 g/dL for ≥12 weeks, for TD Low and TD High = ≥50% reduction in transfusion requirement; Major response for NTD = Mean Hgb ↑ ≥1.5 g/dL for ≥12 weeks, for TD Low = TI ≥16 weeks, and for TD High = TI ≥12 weeks

Updated RALLY-MF phase 2 data

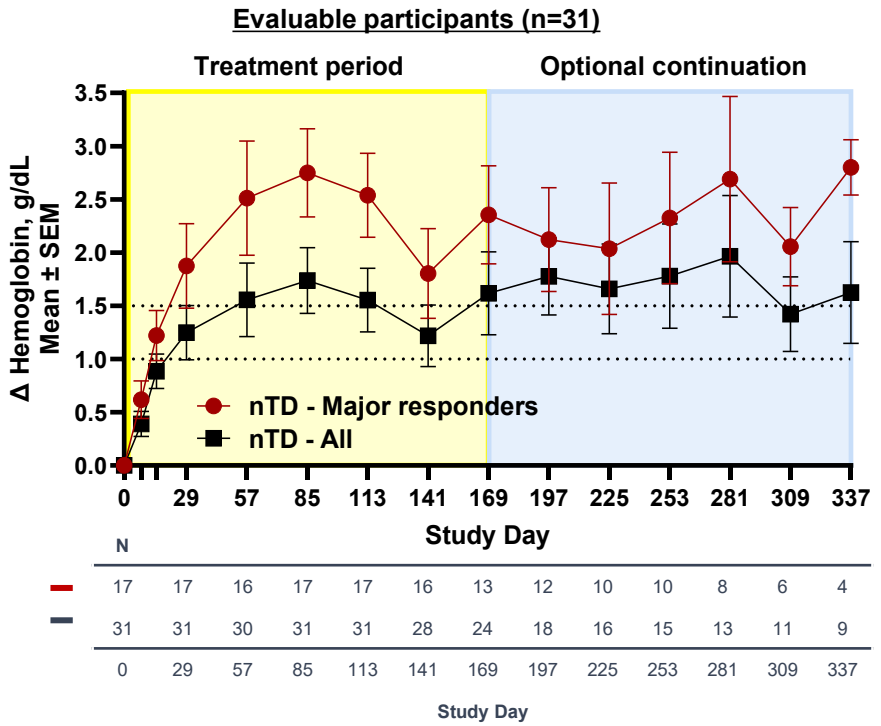
nTD (n=31): Early-acting, meaningful, and durable hemoglobin increases with 55% of patients achieving major response and 68% achieving overall response

nTD Hematologic Resposne



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

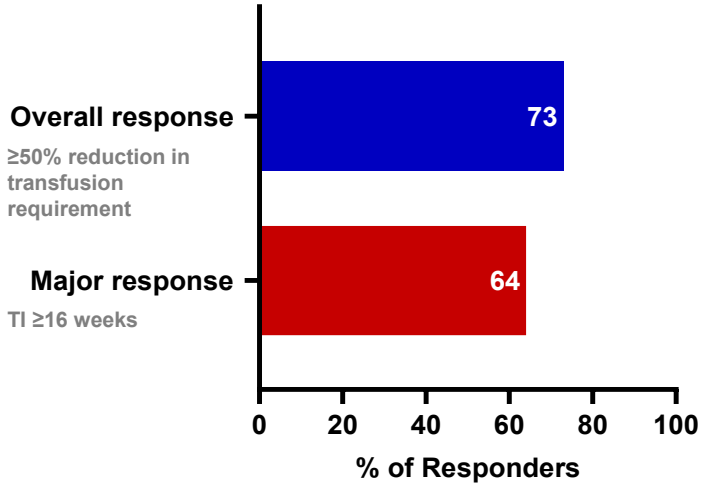


Analysis excludes values within 7 days of transfusion receipt. 9 nTD participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 8 nTD participants had a per protocol dose hold due to Hgb ≥12 g/dL. Abbreviations: EOS = end of study;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

Updated RALLY-MF phase 2 data

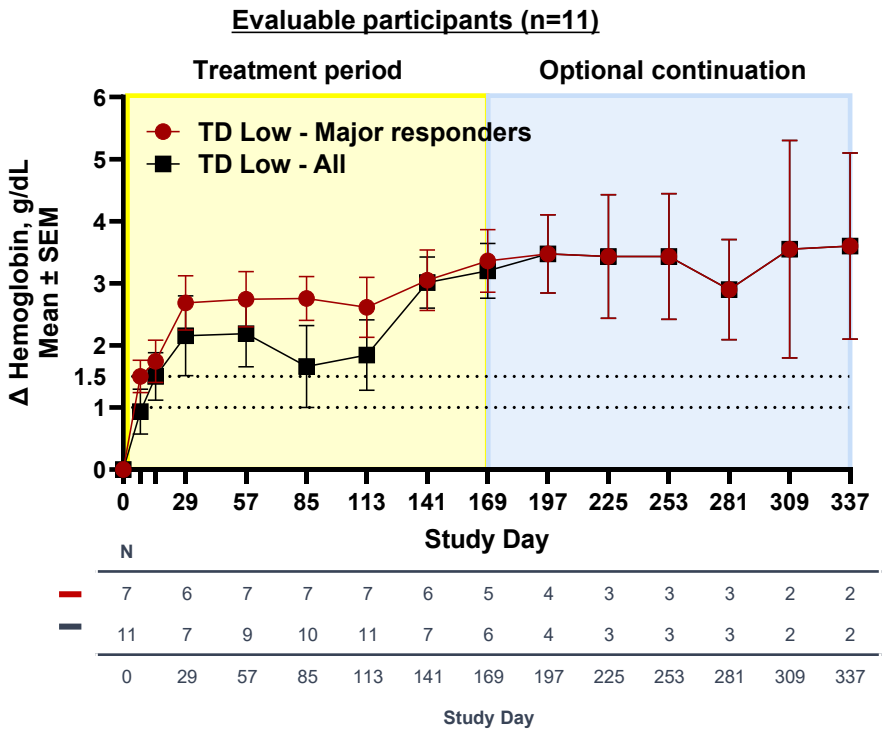
TD Low (n=11): Meaningful, and durable hemoglobin increases translating to transfusion reduction, with 64% of patients achieving major response and 73% achieving overall response

TD Low Hematologic Resposne



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

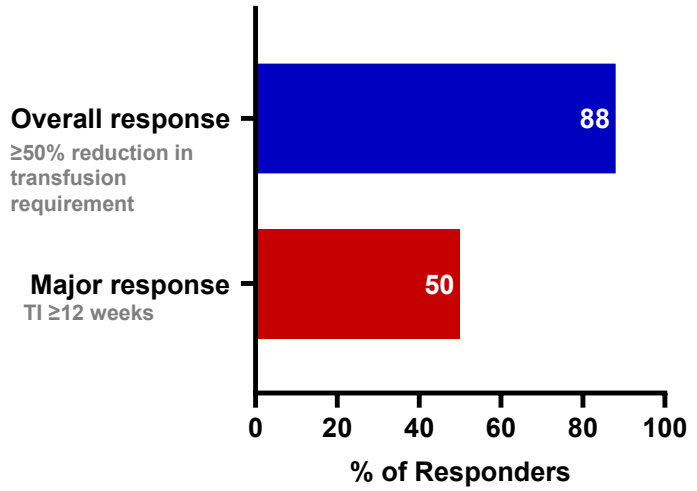


Analysis excludes values within 7 days of transfusion receipt. 5 TD Low participants with evaluable hematologic response had a per protocol dose escalation at visit Day 57 due to insufficient response. 1 TD Low participant had a per protocol dose hold due to Hgb ≥12 g/dL. Abbreviations: Hgb = hemoglobin;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

Updated 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)



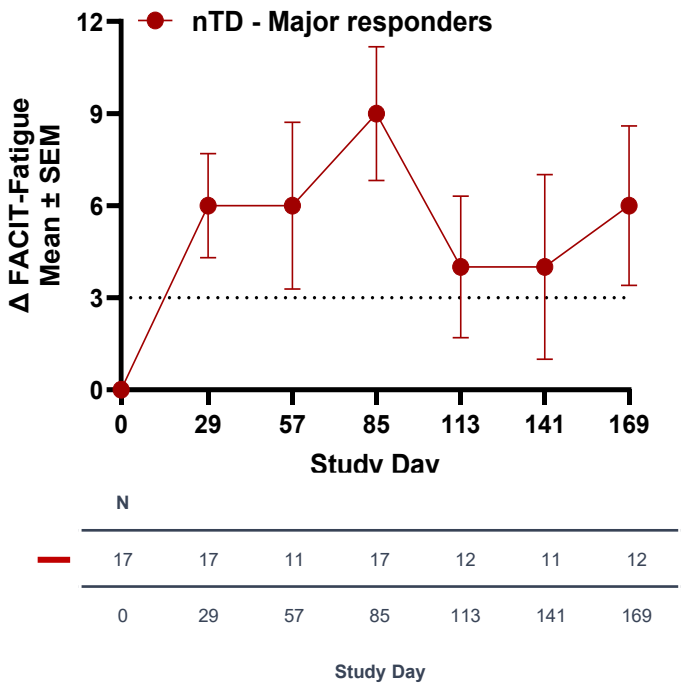
Response	Mean ± SD (days)
Time to major response (n=4)	2 ± 1
Duration of longest major response through optional continuation phase (n=2)** with ongoing follow-up	239 ± 18

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.

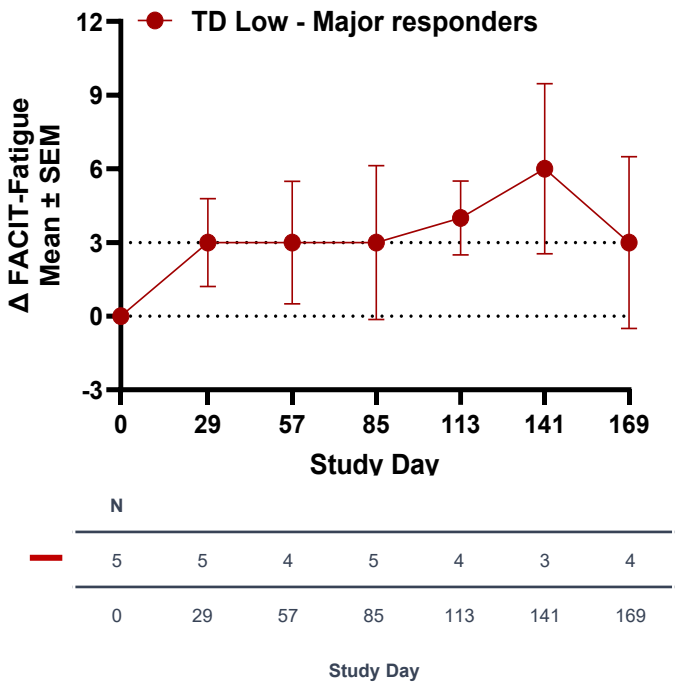
Updated RALLY-MF phase 2 data

nTD and TD Low patients experienced clinically significant improvement across multiple Patient Reported Outcomes

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

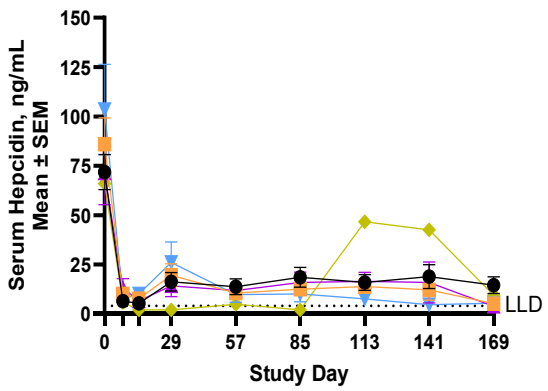
Abbreviations: EOS = end of study; Hgb = hemoglobin; MPN-SAF TSS50 = Myeloproliferative Neoplasm Assessment Total Symptom Score 50% reduction; PGIS = Patient Global Impression of Severity; TD = transfusion dependent. A 3-point change in the FACIT-Fatigue score is considered the threshold for clinical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

RALLY-MF phase 2 data update

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

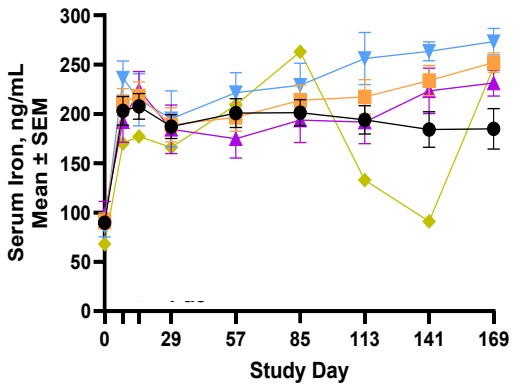
Hepcidin by JAKi Cohort

Evaluable participants (n=50)



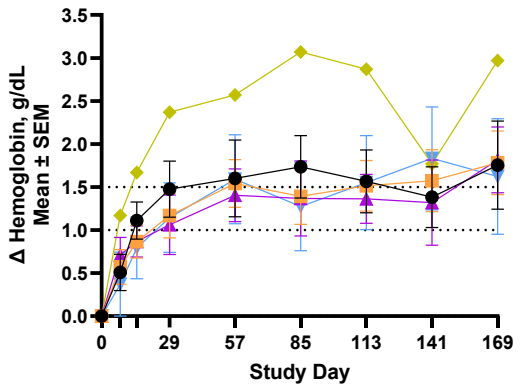
Iron by JAKi Cohort

Evaluable participants (n=50)

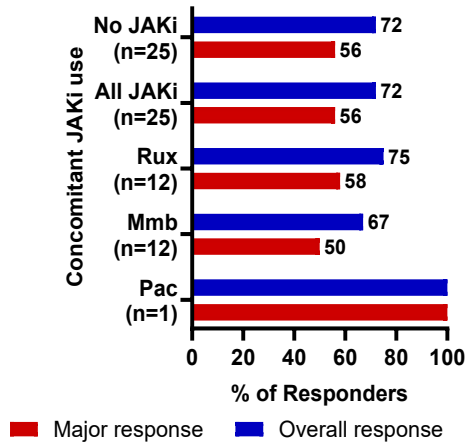


Hemoglobin by JAKi Cohort

Evaluable participants (n=50)



Response by JAKi Cohort



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.

Updated 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)

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

Emerging profile 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	✓ Updated Phase 2 data show strong hematologic responses across 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	✓ Updated Phase 2 data show strong hematologic responses 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 68-88% across all cohorts in Phase 2 ✓ Initial MRR of 50-64% across all cohorts in Phase 2

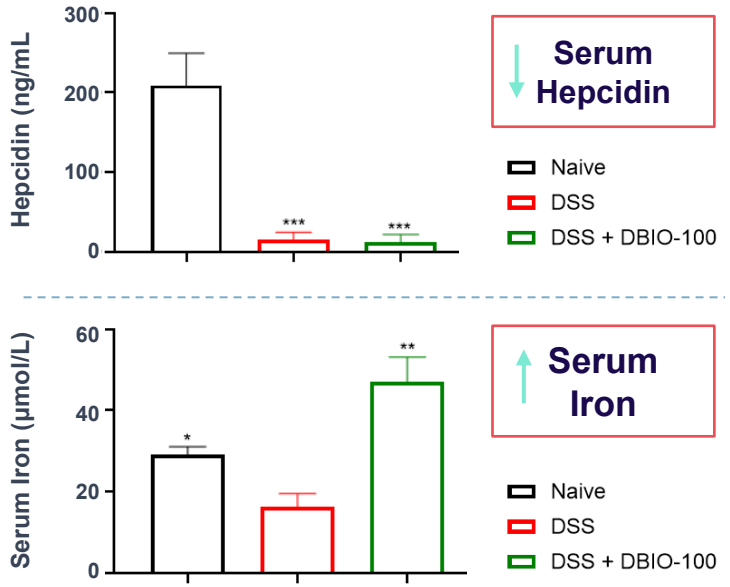
POC=Proof of concept; ORR=Overall Response Rate; MRR=Major Response Rate

Selcodebart in other anemias of inflammation

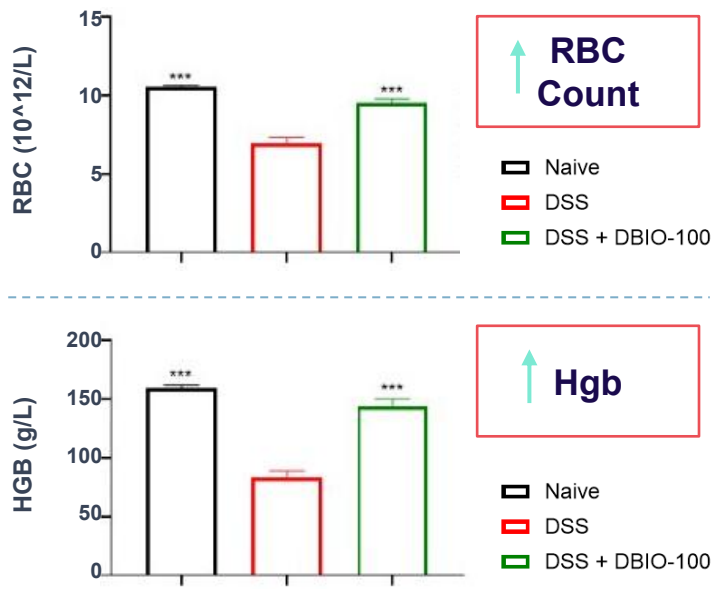
Inflammatory bowel disease mouse model

- 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

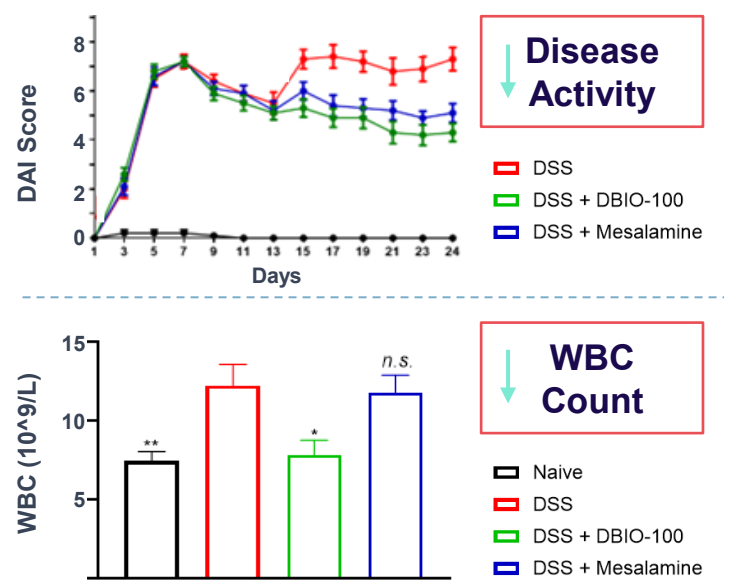
Target Engagement



Hematologic Improvement



IBD Disease Modification



DAI Score = Disease Activity Index

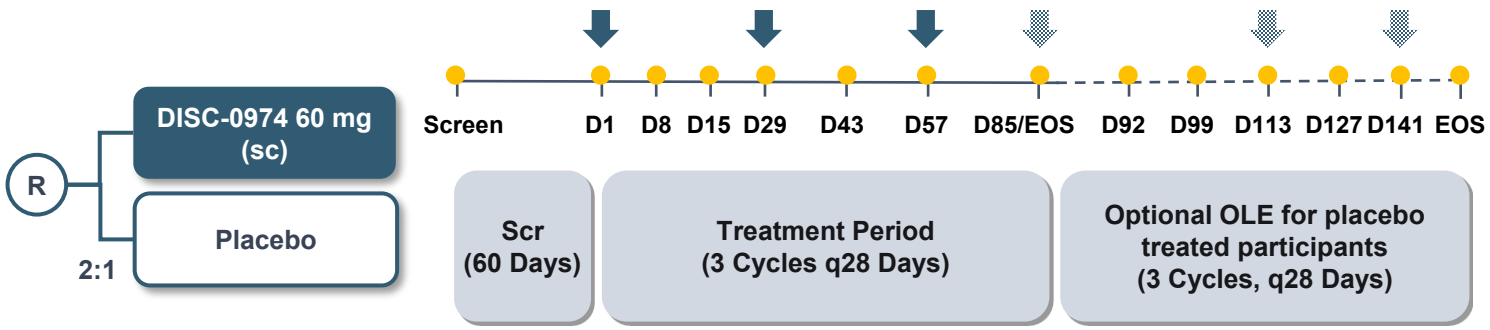
RALLY IBD: Phase 2 trial design

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 DISC-0974 initiated Q1 2026
- Exploratory work in additional anemia indications
- Continued IND-enabling activities for the long-acting anti-HJV (DISC-0998)

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1. Introduction
2. Bitopertin in EPP
   - Type A meeting summary and next steps
   - EPP data update: HELIOS open label extension
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   - RALLY-MF update
   - MF opportunity and HJV franchise next steps
4. DISC-3405
5. Closing Remarks and Q&A Session

Anti-TMPRSS6 mAb induces hepcidin

Limits 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

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

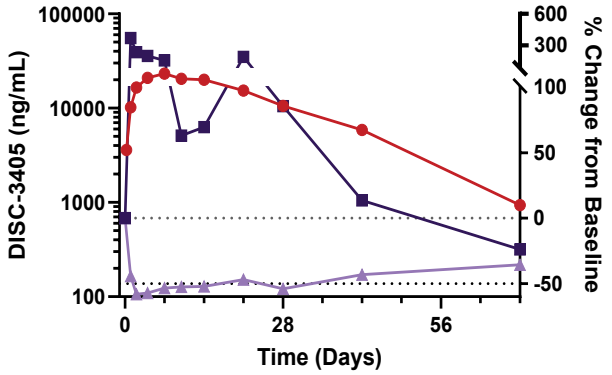
Hereditary Hemochromatosis, Beta-Thalassemia, Myelodysplastic Syndromes

Hct = hematocrit; HV = healthy volunteers

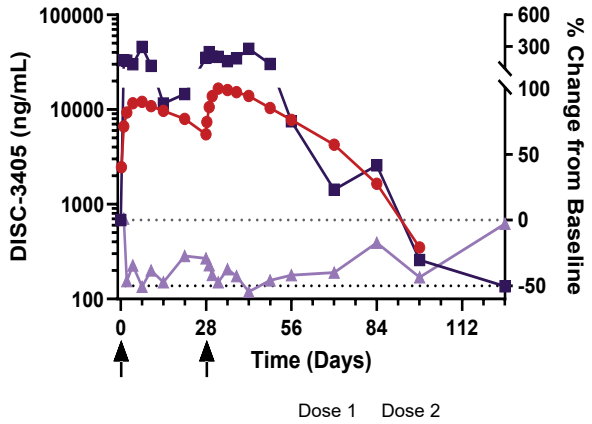
DISC-3405 healthy volunteer data

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

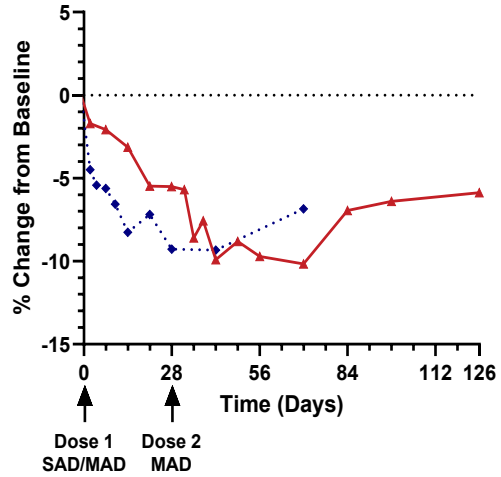
PK/PD: 300 mg SC SAD



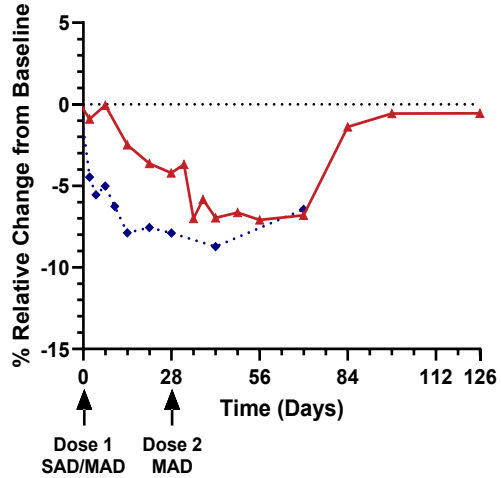
PK/PD: 150 mg SC MAD



Hemoglobin



Hematocrit



PK Hepcidin Serum Iron

150 SC, MAD 300 SC, SAD

DISC-3405: 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

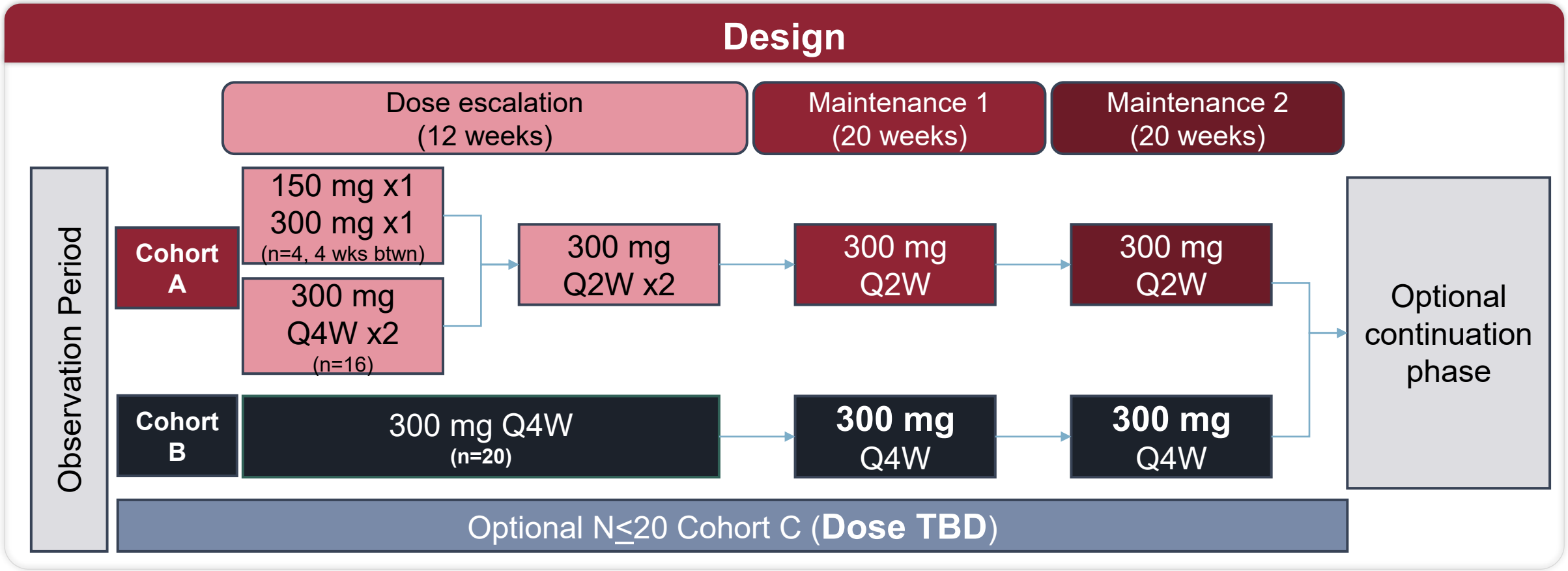
DISC-3405 is expected to be able to be used across the treatment landscape for PV

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

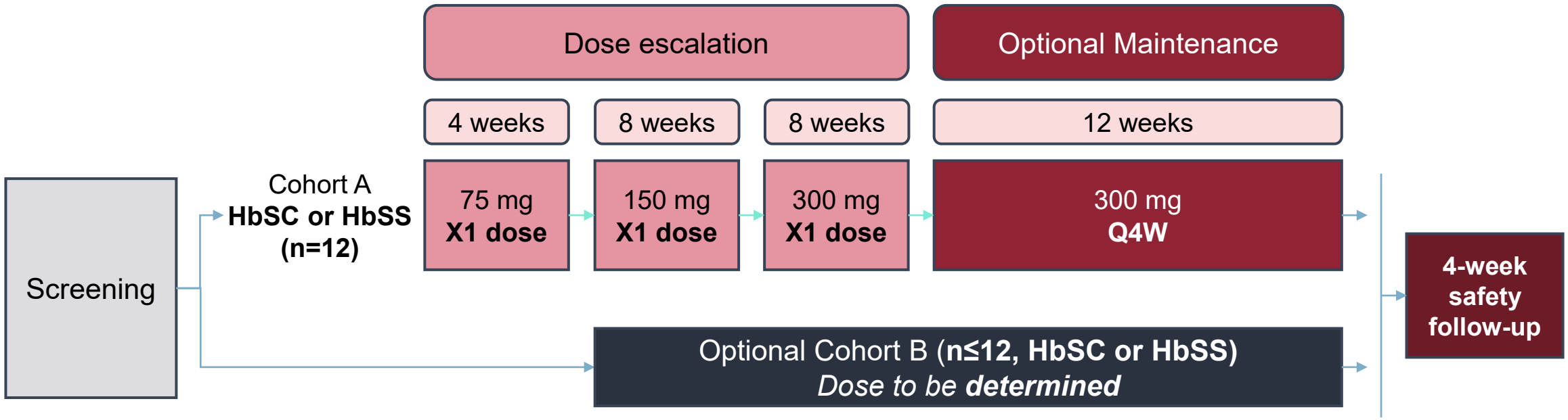
DISC-3405 in a Townes Model

- 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

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Summary and next steps

Program	Summary	Next Steps
Bitopertin Heme Synthesis Modulation	• Aligned with FDA on approach to CRL response • Sustained PPIX reductions and light tolerance improvements with bitopertin in HELIOS trial • Launched EAP program for bitopertin in EPP	› APOLLO Phase 3 topline data expected Q4 2026 › CRL response submission expected by end of 2026 › Continued EPP market development and commercial preparation
Selcodebart (DISC-0974) Hepcidin Suppression	• RALLY-MF Phase 2 data show consistently strong anemia response rates across MF subpopulations • RALLY-IBD Phase 2 trial ongoing	› Additional RALLY-MF data expected in Q4 2026 › MF End of Phase 2 meeting with FDA expected to occur by end of 2026
DISC-3405 Hepcidin Induction	• RESTORE-PV Phase 2 trial ongoing in polycythemia vera • Phase 1b trial ongoing in sickle cell disease	› Initial RESTORE-PV data expected in Q4 2026 › Initial Phase 1b sickle cell data expected in Q4 2026

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 by end of 2026

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

Selcodebart (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

Initial data for PV and SCD expected in Q4 2026

- 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

disc medicine

Q&A