2024 ASH Management Call

Clinical Data Updates:
Bitopertin, DISC-0974, and DISC-3405

December 8, 2024

disc medicine

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This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, express or implied statements regarding Disc’s expectations with respect to: (i) the timing, progress and results of preclinical studies and clinical trials for bitopertin, DISC-0974, DISC-3405 and other product candidates Disc may develop, including statements regarding the timing of initiation and completion of studies or trials and related preparatory work and the period during which results will become available; (ii) Disc’s research and development plans, including plans to explore the therapeutic potential of DISC-0974 in other anemias of inflammation; (iii) the possible regulatory path for bitopertin in EPP, including the potential to seek approval under the Accelerated Approval pathway and the timeline of related discussions with the FDA; (iii) Disc’s analysis of the market potential for its product candidates; (iv) Disc’s commercialization plans for bitopertin; and (v) Disc’s future cash position. 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; and the other risks and uncertainties described in Disc’s filings with the Securities and Exchange Commission, including in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2023, 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, DISC-0974, and DISC-3405 are investigational agents and are not approved for use as therapies in any jurisdiction worldwide

Agenda

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

02 **Bitopertin in EPP**
- **Review of Updated Data and Regulatory Path**
  Will Savage, MD, PhD, Chief Medical Officer
- **EPP Market Opportunity and Commercialization Approach**
  Pamela Stephenson, MPH, Chief Commercial Officer

03 **DISC-0974**
- **Updated Data in Anemia of MF and Phase 2 Study Plan**
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- **Preclinical Data in Anemia of IBD**
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04 **DISC-3405**
- **Phase 1b MAD and Preclinical SCD Data**
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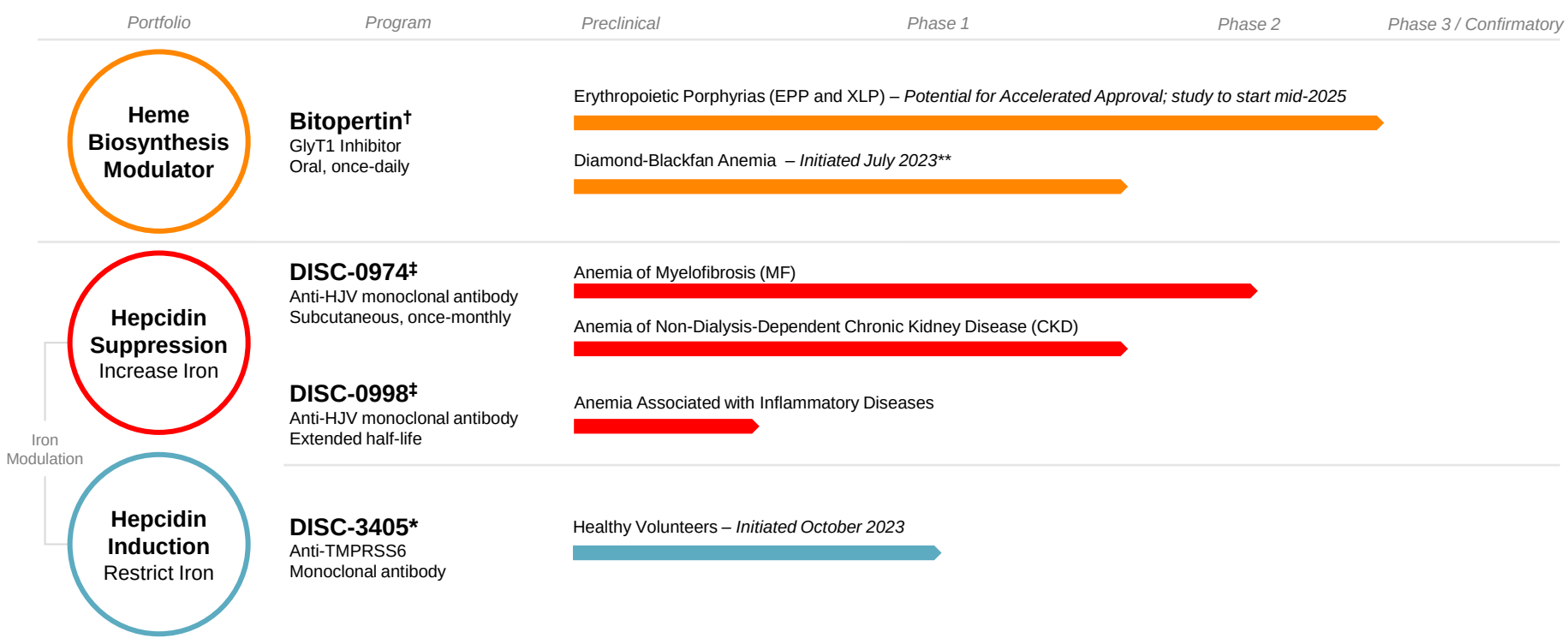
05 **Closing Remarks**
John Quisel, JD, PhD, Chief Executive Officer

06 **Q&A Session**

Disc's Hematology-Focused Pipeline

Multiple programs in development with pipeline-in-a-product potential



† Bitopertin in-licensed from Roche; ‡ DISC-0974 and DISC-0998 in-licensed from AbbVie; *DISC-3405 in-licensed from Mabwell (formerly MWTX-003); **IIT with the NIH

Bitopertin: Summary of Updates

Strong data package and high unmet need in EPP support a potential path to accelerated approval

BEACON data show **similar results between adults and adolescents** with **clear correlation between PPIX reduction and clinical outcomes**

Patient survey highlights **the burden of EPP and its impacts on multiple aspects of daily life**

Positive feedback from EOP2 meeting with the FDA setting up a **path to accelerated approval**

Strong market potential due to engaged patient and KOL community; **commercial readiness activities well underway**

DISC-0974: Summary of Updates for Multiple Indications

Final results from the Phase 1b study in MF anemia demonstrate efficacy across patient types; clinical data in CKD and preclinical data in IBD provide evidence of broad potential in anemias of inflammation. Key findings:

Substantial reductions in hepcidin and increases in iron levels translating to **hematologic response**

Positive impact on **clinically meaningful measures of anemia** across a broad range of MF patients

Development path aligned on with regulators; **Phase 2 study initiated**

Initial proof of concept in **anemia of CKD** and preclinical evidence in **broader anemias of inflammatory disease**

DISC-3405: Summary of ASH Data

Multiple-ascending dose portion of the DISC-3405 healthy volunteer study confirmed proof of mechanism, and preclinical data demonstrated potential for use in sickle cell disease. Key findings:

Substantial, dose-dependent **increase in hepcidin levels**

Deep, sustained reductions in serum iron (50-80% from baseline) supportive of SC monthly dosing

Meaningful changes in **hematologic parameters,** supporting initiation of a Phase 2 study in PV in 2025

Preclinical SCD data showing **decreased HbS concentration and improved markers of inflammation and hemolysis**

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EPP Phase 2 Development Program

BEACON, AURORA, and HELIOS Studies

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**

HELIOS

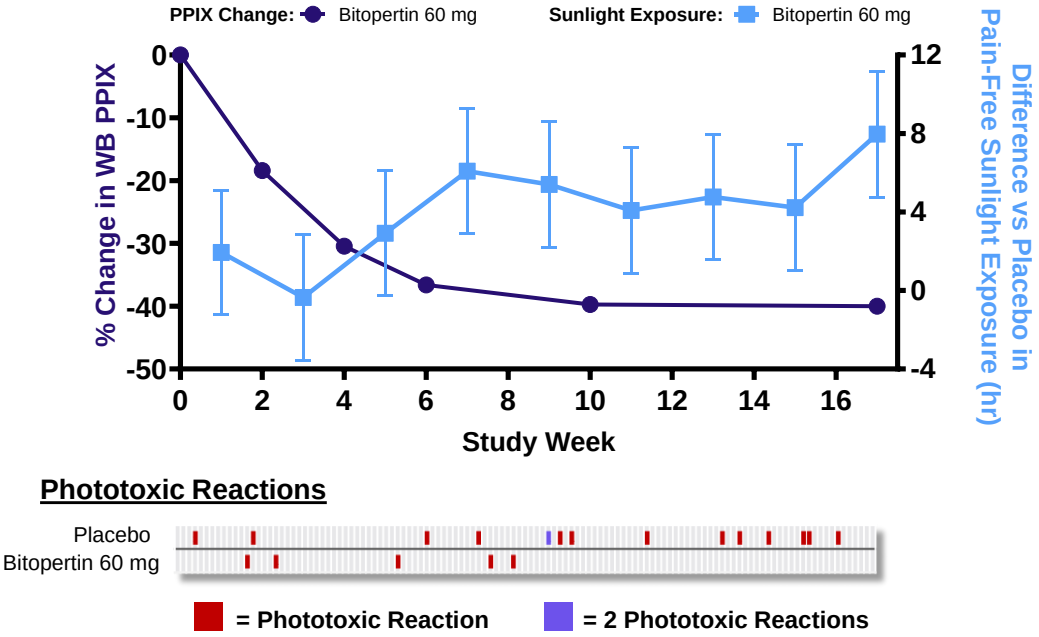
- **EPP and XLP**; adults and adolescents
- **US and Australia**
- **Open-label extension study** (>80% rollover from BEACON and AURORA)

Successful End of Phase 2 meeting with the FDA puts bitopertin on a path to potential accelerated approval, with the confirmatory APOLLO study starting by mid-2025

Summary of AURORA Results

Bitopertin 60 mg

AURORA

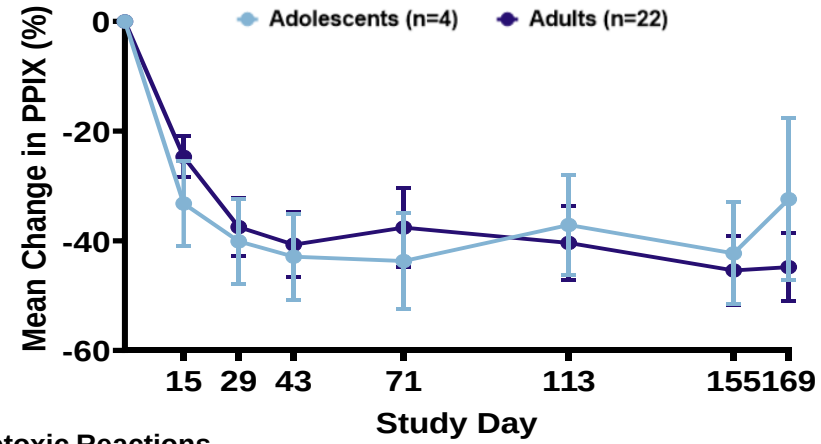


- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant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

Tertiles of PPIX Change

PPIX Increased **PPIX Decreased**

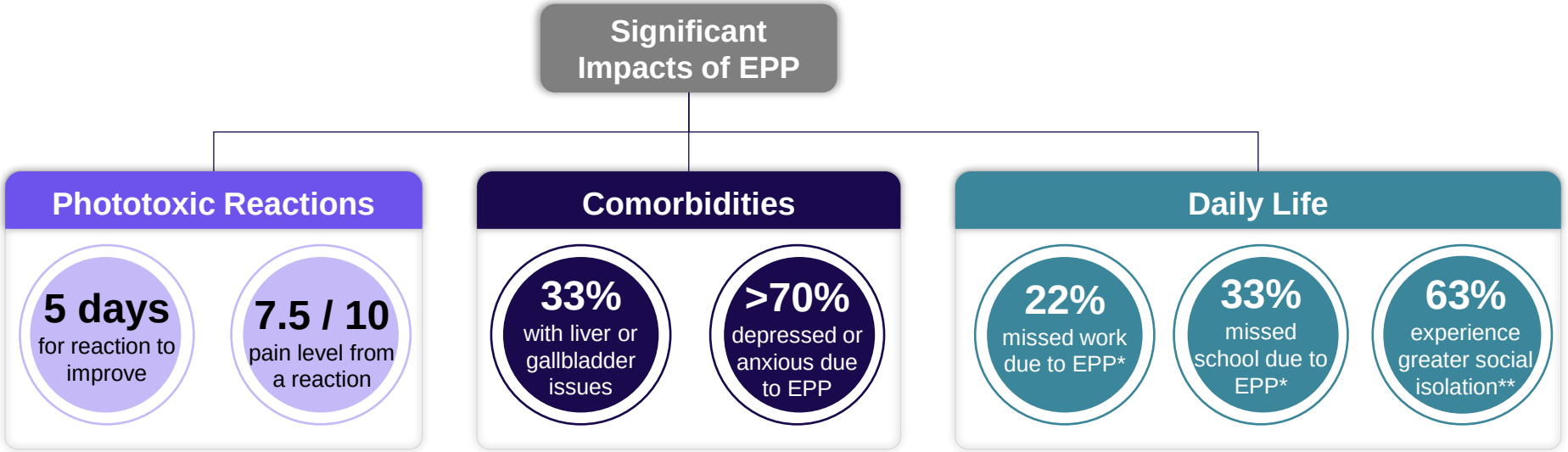
Light Tolerance Measure (Mean ± SD)	Tertile 3 (-43% to 25%)	Tertile 2 (-53% to -43%)	Tertile 1 (-98% to -53%)
Cumulative total time in sunlight without pain (hr)	145.6 ± 99.5	190.5 ± 111.6	262.1 ± 160.6
Average time in sunlight without pain (hr)	0.86 ± 0.6	1.1 ± 0.7	1.6 ± 1.0
Change from baseline in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

Significant reductions in PPIX, improvements in pain-free time in sunlight, reductions in rate of phototoxic reactions, and improvement in QoL with clear association between PPIX reduction and clinical endpoints

EPP LIGHT Survey

Highlights the significant burden of illness and unmet need in EPP

Quantitative survey conducted with 197 EPP patients (164 adults, 33 adolescents) from May to July 2024 reinforces the severity of phototoxic reactions, the high rate of comorbidities, and the overall impact EPP has on daily life



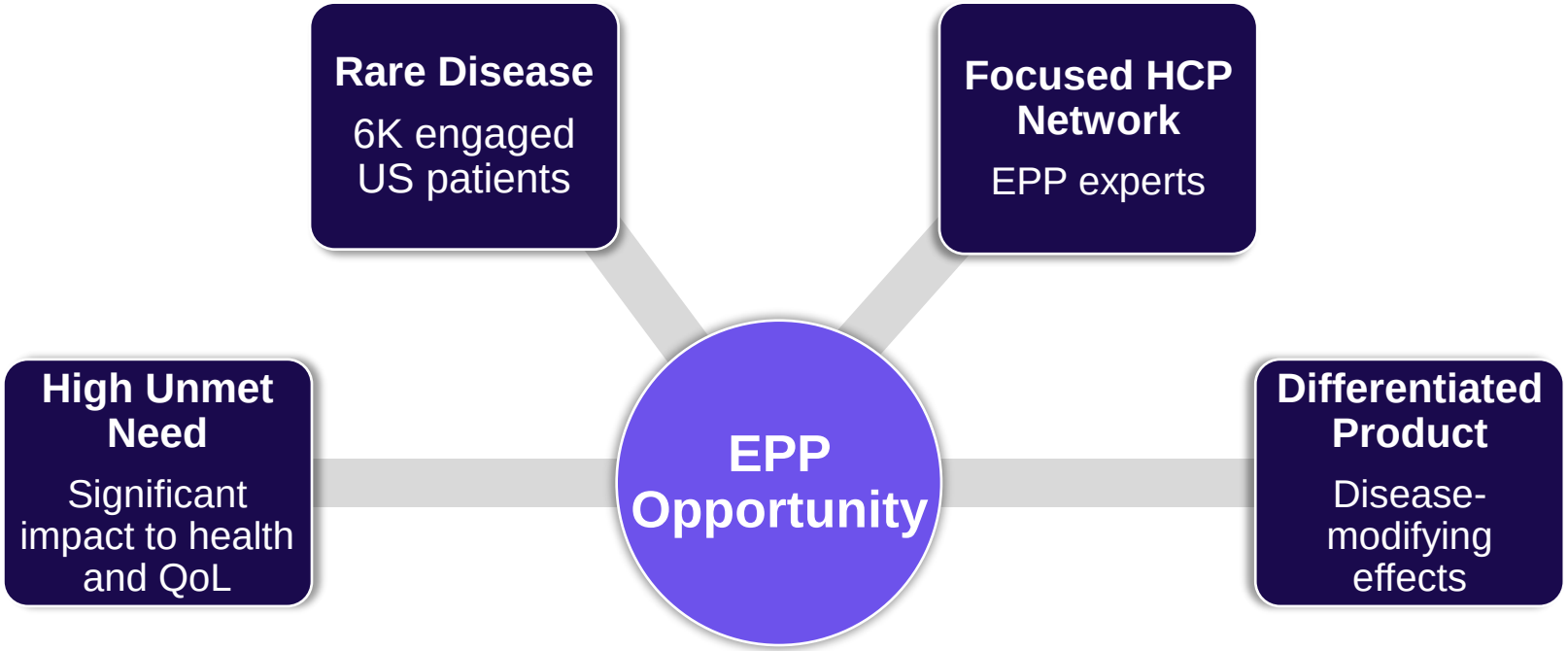
*of those who work (n=114) / are in school (n=45); **of adults, compared to the general population. Source: EPP LIGHT Survey, ASH 2024 Abstract #3631

Key Takeaways from Positive End of Phase 2 Meeting

- **Alignment with the FDA on all proposed study parameters**
- **FDA acknowledged that EPP is a serious and potentially life-threatening disease with significant unmet medical need**
- **FDA agreed that average monthly time in sunlight without pain at the end of a 6-month treatment period can be used as a primary endpoint**
- **PPIX reduction may be sufficient as a surrogate endpoint supportive of accelerated approval**
- **Proceeding to APOLLO, a 6-month study with a 60 mg dose of bitopertin in EPP and XLP patients ages 12+ by mid-2025**

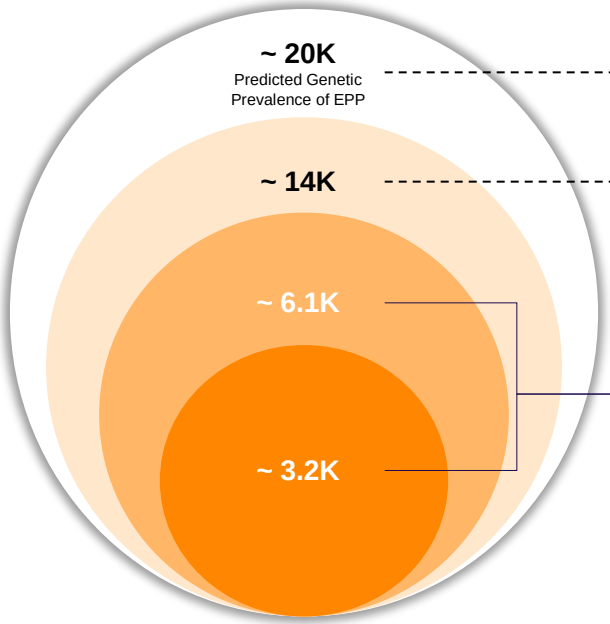
EPP Opportunity

Engaged, concentrated patient and KOL community eager for a disease-modifying therapy



The EPP patient population is well-defined and relatively concentrated, enabling an efficient commercial model

Prevalence of EPP Patients in the US

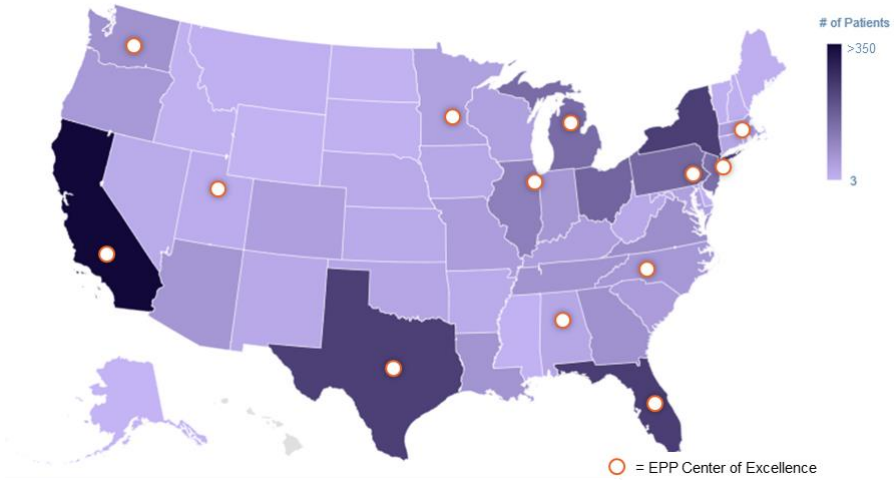


Expansion
Misdiagnosed or have not sought treatment for EPP

Growth
Patients with lower degree of engagement with HC system

Focus
Engaged EPP patients recent or recurring claims

Distribution of EPP Treatment Centers



Concentration of patients in key accounts enables a targeted and efficient field force

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

Building strong relationships with patient advocacy groups and physician organizations worldwide

Commercial Readiness Activities Well Underway

Patient Identification and Account Mapping	✓	Disease State Education and Brand Proposition	✓
Payer Engagement and Pricing Assessments	✓	Operational Readiness	✓
Evidence Generation, including HEOR and Burden of Illness	✓	Commercial Manufacturing and Supply	✓

Bitopertin Summary and Next Steps

Bitopertin Summary

- Positive EOP2 meeting sets up the path toward potential accelerated approval
- Additional data from BEACON supportive of drug activity and use of bitopertin in adolescents
- Robust market opportunity with a clearly defined population of 3-6K patients with the opportunity to expand to 14K
- DBA Study: 14 patients have been enrolled; bitopertin has been well-tolerated with safety consistent with prior studies; efficacy evaluation is ongoing

Next Steps

- Discussion of confirmatory study design with FDA, with updates provided in Q1 2025
- APOLLO study initiation by mid-2025
- European protocol assistance and confirmation of regulatory path with EMA
- Continued commercialization and launch preparation

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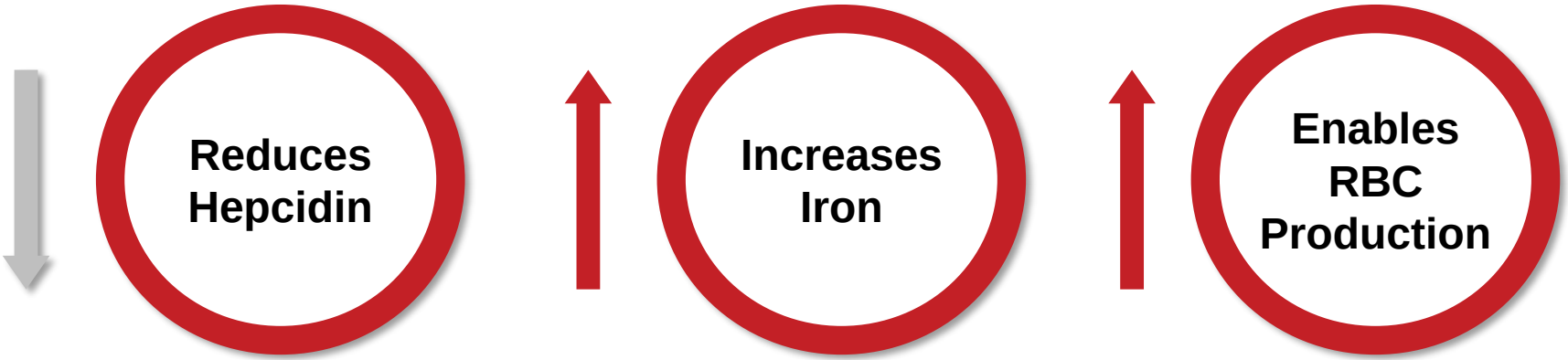
DISC-0974: Novel Anti-HJV mAb to Suppress Hepcidin

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



Inhibits endogenous production of hepcidin

Releases iron stores
Enables GI absorption

Potential to treat wide range of anemias

HJV = hemojuvelin

DISC-0974 Anemia of MF Phase 1b

Study overview – enrollment data as of October 17, 2024

Screening (28 Days) | **Treatment Period** (6 months) | **Optional Continuation** (Up to 2 years)

	14 mg	28 mg	50 mg	75 mg	100 mg	Overall
Treated, N	1	7	12	9	6	35
Completed study, N (%)	1 (100)	6 (86)	12 (100)	8 (89)	5 (83)	32 (91)
Subjects with early withdrawal (N)*	0	1	0	0	1	2
Participating in continuation, N (%)	0	2 (29)	10 (83)	8 (89)	4 (67)	24 (69)
Concomitant JAK inhibitor, N (%)	0	4 (57)	6 (50)	2 (22)	1 (17)	13 (37)
Baseline hepcidin, median (min, max), ng/mL	48	93 (21, 171)	90 (9, 156)	47 (23, 188)	64 (12, 375)	69 (9, 375)
Baseline hemoglobin, median (min, max), g/dL	8.2	8.4 (6.7, 9.3)	8.4 (5.5, 10)	8.8 (6.7, 9.9)	8.3 (5.5, 9)	8.4 (5.5, 10)

Study Endpoints

Primary: Safety and tolerability; **Secondary:** Hematologic response, pharmacodynamic markers of mechanism engagement

*Reason for early withdrawal: Physician decision due to inadequate response (n=2)

DISC-0974 Anemia of MF Phase 1b

Overview of patient segmentation

Shift informed by **FDA feedback** on clinically meaningful measures for MF anemia patient types and **new clinical response criteria**[1]

Previous Data Readouts

Non-Transfusion Dependent (NTD)	Transfusion Dependent (TD)
Hgb <10 and not TD	≥6 units transfused / 12 weeks

Today

nTD	TD Low	TD High
Hgb <10 and 0 units transfused / 12 weeks	**1-2 units transfused / 12 weeks**	**3-12 units transfused / 12 weeks**

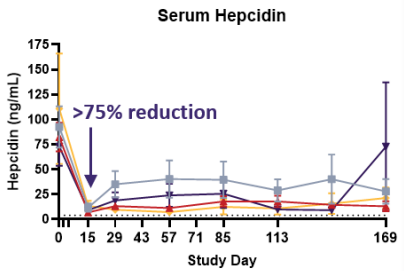
Source: [1]Tefferi A, et al. Blood. 2024.

DISC-0974 Anemia of MF Phase 1b Results

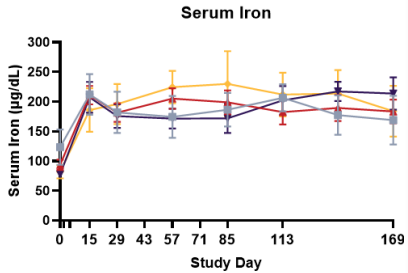
Pharmacodynamics

- DISC-0974 demonstrated consistent decreases in hepcidin and increases in serum iron across patients
- Iron mobilization translated to increased reticulocyte hemoglobin and hemoglobin from baseline

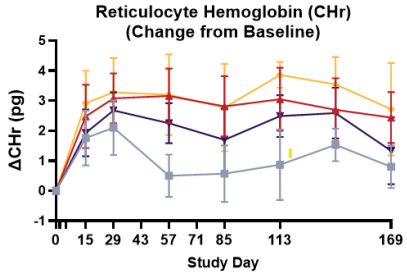
↓ Serum Hepcidin



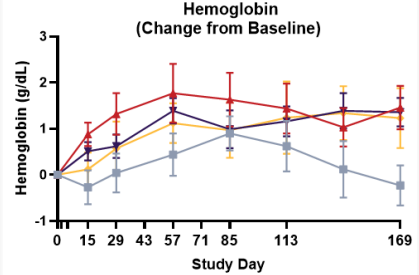
↑ Serum Iron



↑ Reticulocyte Hemoglobin



↑ Hemoglobin

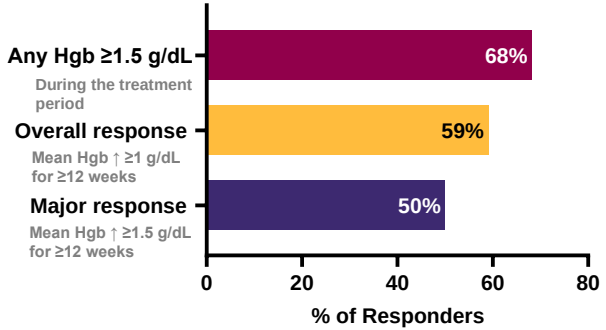


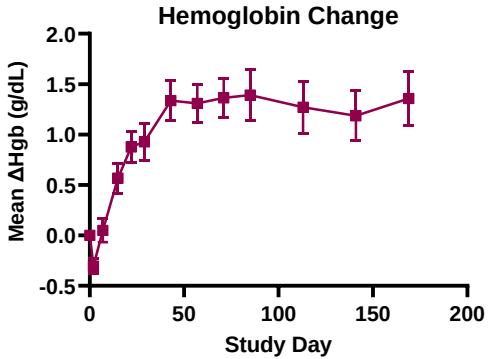
28 mg 50 mg 75 mg 100 mg

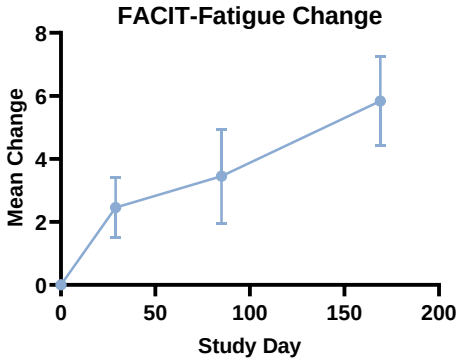
DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: nTD participants* (n=22)

68% of nTD[1] participants achieved a Hgb Increase of ≥1.5 g/dL during study period; 50% achieved a sustained Hgb response for ≥12 weeks







67% of participants (n=9) receiving concomitant JAKi therapy achieved durable response

Response	Mean ± SD (days)
Time to first Hgb increase for major response	36 ± 18
Duration of response during treatment period	150 ± 27

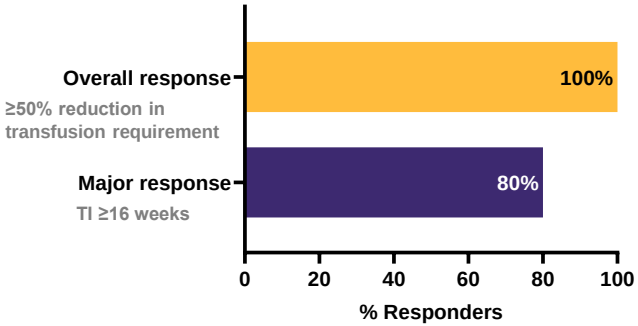
17 of 22 nTD participants have received continuation treatment with median response not reached. Follow-up ongoing (maximum 14.7 months).

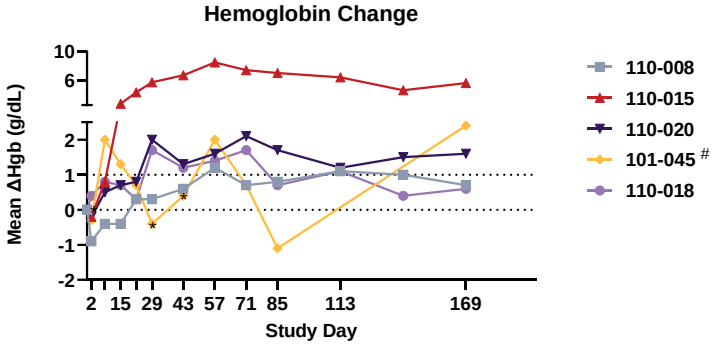
[1]nTD participants: Baseline Hgb <10 with 0 units PRBC in the 84 days prior to screening. * Participants dosed at 28-100 mg dose levels.

DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: TD Low participants (n=5)

100% of TD Low[1] participants achieved a ≥50% reduction in transfusion requirement; 80% of participants achieved TI-16 weeks^





No TD Low participants were receiving concomitant JAKi therapy

*Indicates transfusion; #Indicates patient receiving transfusion during treatment period.

Response	Mean ± SD (days)
TD Low duration of major response during treatment period	171 ± 4

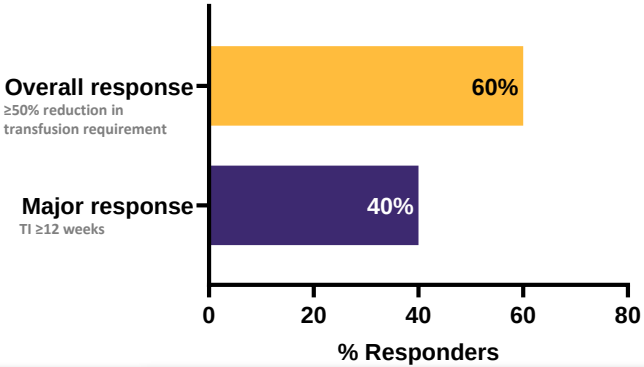
5 of 5 TD Low participants have received continuation treatment with median response not reached. Follow-up ongoing (maximum 16.6 months).

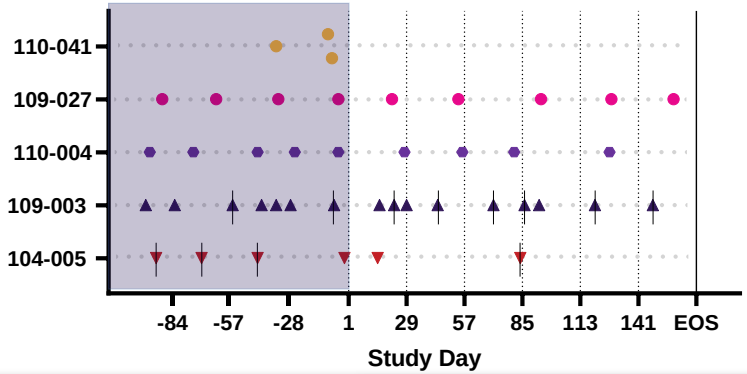
[1]TD Low: Participants receiving 1-2 units PRBC in the 84 days prior to screening. ^ with a minimum Hgb of 7 g/dL.

DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: TD High participants (n=5)

60% of TD High[1] participants achieved a ≥50% reduction in transfusion requirement; 40% of participants achieved TI-12 weeks^





50% of participants (n=4) receiving concomitant JAKi therapy achieved ≥50% transfusion reduction; 25% achieved TI-12

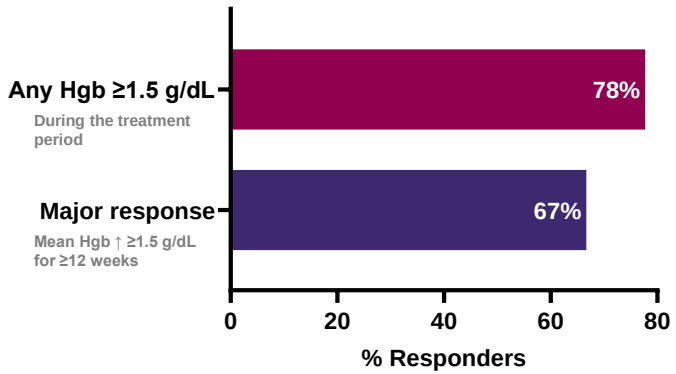
Response	Mean ± SD (days)
TD High duration of major response during treatment period	127 ± 60

[1]TD High: Participants receiving 3-12 units PRBC in the 84 days prior to screening. ^ with a minimum Hgb of 7 g/dL; 2 TD-high participants were considered not evaluable due to incomplete data entry at time of data cut.

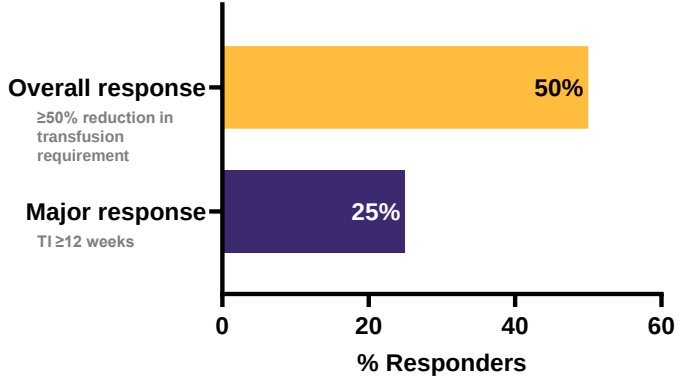
DISC-0974 Anemia of MF Phase 1b Results

Hematologic response with concomitant JAKi therapy (n=13)

nTD Response (n=9)



TD High Response (n=4)



Overall, 54% of participants receiving concomitant JAKi therapy achieved a major hematologic response

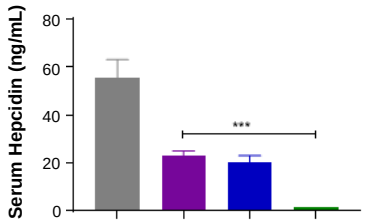
DISC-0974 Alleviated Ruxolitinib-Induced Anemia in Mice

Wild-type mouse model

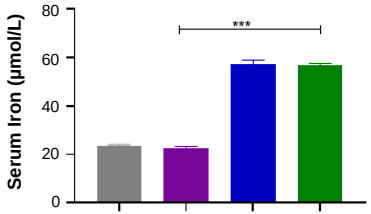
- Treating wild-type mice with ruxolitinib reduced hemoglobin and induced anemia
- Adding a mouse analog of DISC-0974 reversed these effects, further decreasing hepcidin, increasing serum iron, and increasing hemoglobin

Target Engagement

↓ Serum Hepcidin



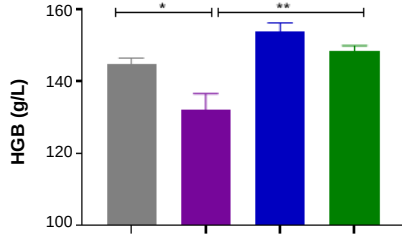
↑ Serum Iron



Vehicle | Ruxolitinib (90 mg/kg)-BID | DBIO-100 (20 mg/kg)-QW | Ruxolitinib (90 mg/kg)-BID +DBIO-100 (20 mg/kg)-QW

Hematologic Improvement

↑ Hemoglobin



- Ruxolitinib alone reduced Hgb by **~1.1 g/dL**
- Adding DISC-0974 analog increased Hgb by **~0.9 g/dL**

Vehicle | Ruxolitinib (90 mg/kg)-BID | DBIO-100 (20 mg/kg)-QW | Ruxolitinib (90 mg/kg)-BID +DBIO-100 (20 mg/kg)-QW

DISC-0974 Anemia of MF Phase 1b Results

Safety

Preferred Term	28 mg (n=7)	50 mg (n=12)	75 mg (n=9)	100 mg (n=6)	Overall (n=35)
Any TEAE	6 (85.7)	12 (100)	8 (88.9)	6 (100)	32 (94.1)
Related AE	4 (57.1)	6 (50)	5 (55.6)	1 (16.7)	16 (47.1)
SAE	1 (14.3)	2 (16.7)	0	1 (16.7)	4 (11.8)
Common TEAEs in ≥5 participants					
Diarrhea	3 (42.9)	5 (41.7)	5 (55.6)	1 (16.7)	14 (41.2)
Nausea	2 (28.6)	2 (16.7)	2 (22.2)	2 (33.3)	8 (23.5)
Vomiting	1 (14.3)	2 (16.7)	0	3 (50.0)	6 (17.6)
Constipation	0	4 (33.3)	1 (11.1)	0	5 (14.7)
Fatigue	3 (42.9)	3 (25.0)	1 (11.1)	3 (50.0)	10 (29.4)
Lymphocyte count decreased	1 (14.3)	2 (16.7)	2 (22.2)	1 (16.7)	6 (17.6)
Dizziness	0	2 (16.7)	2 (22.2)	3 (50.0)	7 (20.6)
Headache	1 (14.3)	1 (8.3)	1 (11.1)	2 (33.3)	5 (14.7)
Dyspnea	0	1 (8.3)	2 (22.2)	2 (33.3)	5 (14.7)
Hyperhidrosis	1 (14.3)	1 (8.3)	1 (11.1)	2 (33.3)	5 (14.7)
Anemia	5 (71.4)	4 (33.3)	0	0	9 (26.5)
Hypertension	0	3 (25.0)	3 (33.3)	0	6 (17.6)

No TEAEs were reported at the 14 mg dose level. Related AEs occurring in ≥2 participants: diarrhea (n=6); SAEs: arthralgia, cellulitis related to cat scratch, cellulitis related to cat bite, and kidney infection; ≥Grade 3 AEs: anemia, lymphocyte count decreased, platelets decreased, cellulitis, kidney infection (same as SAE), muscular weakness, and headache.

Overview of MF Anemia Market

DISC-0974 positioned to address all clinically significant patient types

>20K
MF patients with anemia

Transfusion Status			JAK Inhibitor Experience	
nTD	TD Low	TD High	On JAKi	Not on JAKi

DISC-0974 Efficacy

Any transfusion status			With or without disease-directed treatment	
50% Major response	80% Major response	40% Major response	54% Major response	53% Major response

Unmet Need

- Anemia and transfusions are associated with **high burden and poor survival**, regardless of other risk factors[1]
- 87% of MF patients develop anemia; most MF patients become more transfusion dependent over time
- Anemia symptoms **worsen QoL** regardless of transfusions
- JAKi can **worsen anemia**
- Anemia can drive JAK **discontinuation** or **suboptimal treatment choice / dose**
- Treating anemia separately may allow **JAKi regimen to be optimized**

Source: [1]Elena C, et al, Haematologica, 2010.

Phase 2 MF Anemia Study Overview

Study Population

- N= ~90 (30 per cohort)
  - 12 patients carried over from Phase 1b*
- Adult patients with MF and anemia
  - Hgb <10 g/dL on ≥3 assessments over 12 weeks, or
  - 1 or more PRBC units transfused in 12 weeks
- Severity: DIPSS INT-1/High
- +/- JAK inhibitor permitted

Design

Screening (28 Days) → **Treatment Period** (6 Cycles q28 Days) → **Follow-Up** (28 Days) → **Continuation Treatment** (q28 Days – optional)

Open-Label, 3 cohorts

- nTD: N=30*
- TD Low: N=30*
- TD High: N=30*

Exploratory cohort

momelotinib / pacritinib
nTD, TD Low, or TD High; N=10

Flexibility to add exploratory cohorts

Key endpoints:

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

Phase 2 Dosing: 50 mg, SC, q28 days

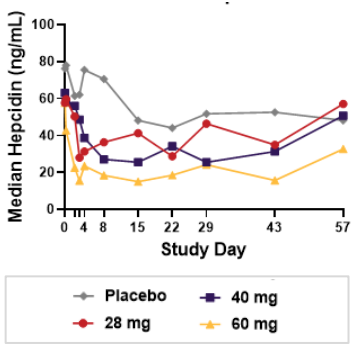
*Patients carried over from Phase 1b: nTD n=8, TD (Low + High) n=4

DISC-0974 Anemia of NDD-CKD: Hepcidin, Iron, and Hgb

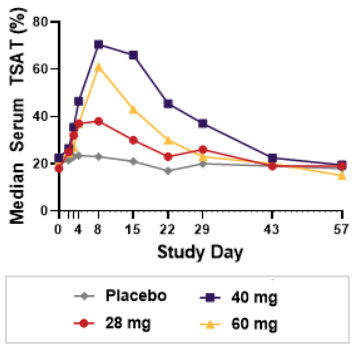
28 mg, 40 mg, and 60 mg SAD cohorts

- Substantial, durable, dose-dependent reduction in hepcidin and sustained increase in TSAT from baseline
- Early and sustained increase in mean reticulocyte hemoglobin across dose groups
- Increase in mean hemoglobin from baseline across dose groups, with maximal observed individual increases in hemoglobin up to +0.95 g/dL at 28 mg, +1.5 g/dL at 40 mg, and +1.8 g/dL at 60 mg

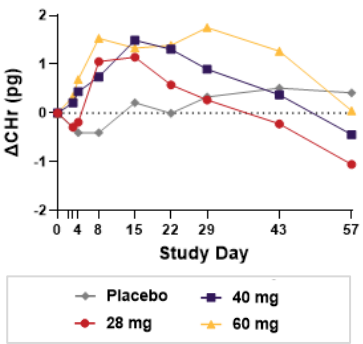
↓ Serum Hepcidin



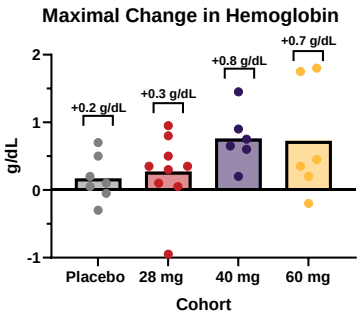
↑ Serum TSAT



↑ Reticulocyte Hemoglobin



↑ Hemoglobin



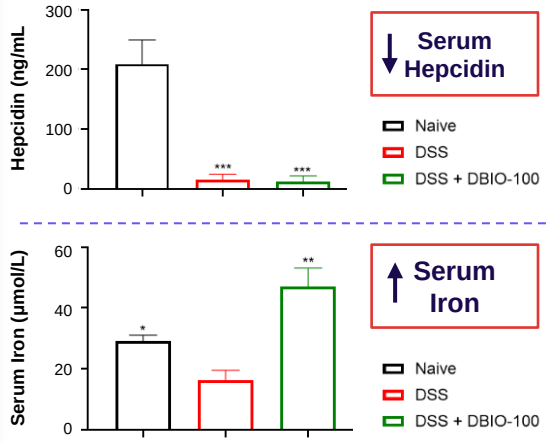
Safety: DISC-0974 demonstrated acceptable safety and tolerability at all evaluated dose levels; the majority of adverse events were deemed not related to DISC-0974, and all adverse events assessed as treatment-related were Grade 1 or 2

DISC-0974 in Other Anemias of Inflammation

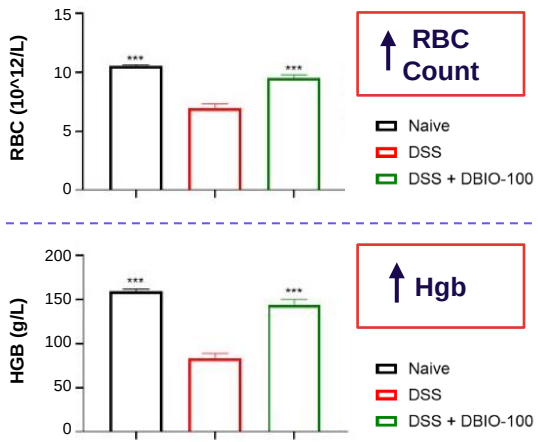
Inflammatory bowel disease mouse model

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

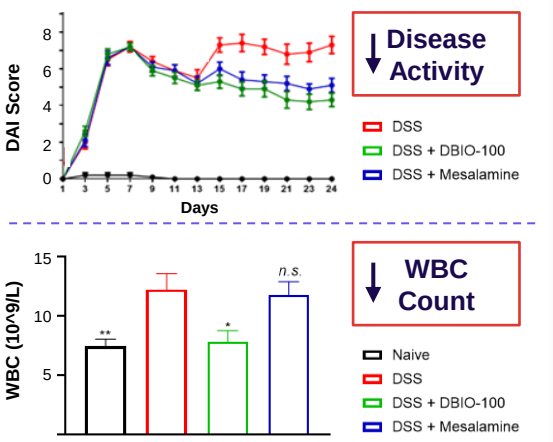
Target Engagement



Hematologic Improvement



IBD Disease Modification



DAI Score = Disease Activity Index

DISC-0974 Summary and Next Steps

DISC-0974 Summary

- MF Phase 1b data demonstrate proof of concept for DISC-0974 across all clinically meaningful patient segments
- CKD Phase 1b SAD data demonstrate sustained pharmacologic activity and initial hematologic response with a single dose
  - Multiple-dose portion will further explore optimal dose regimen to inform Phase 2a
- Preclinical IBD data provide further support for DISC-0974's potential in anemias of inflammation

Next Steps

- **MF Anemia** Phase 2 study has been initiated with initial data expected H2 2025
- **CKD Anemia** Phase 1b multiple-dose portion initiation by end of year, with data expected by end of 2025

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  Will Savage, MD, PhD, Chief Medical Officer
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06 **Q&A Session**

Anti-TMPRSS6 mAb Induces Hepcidin

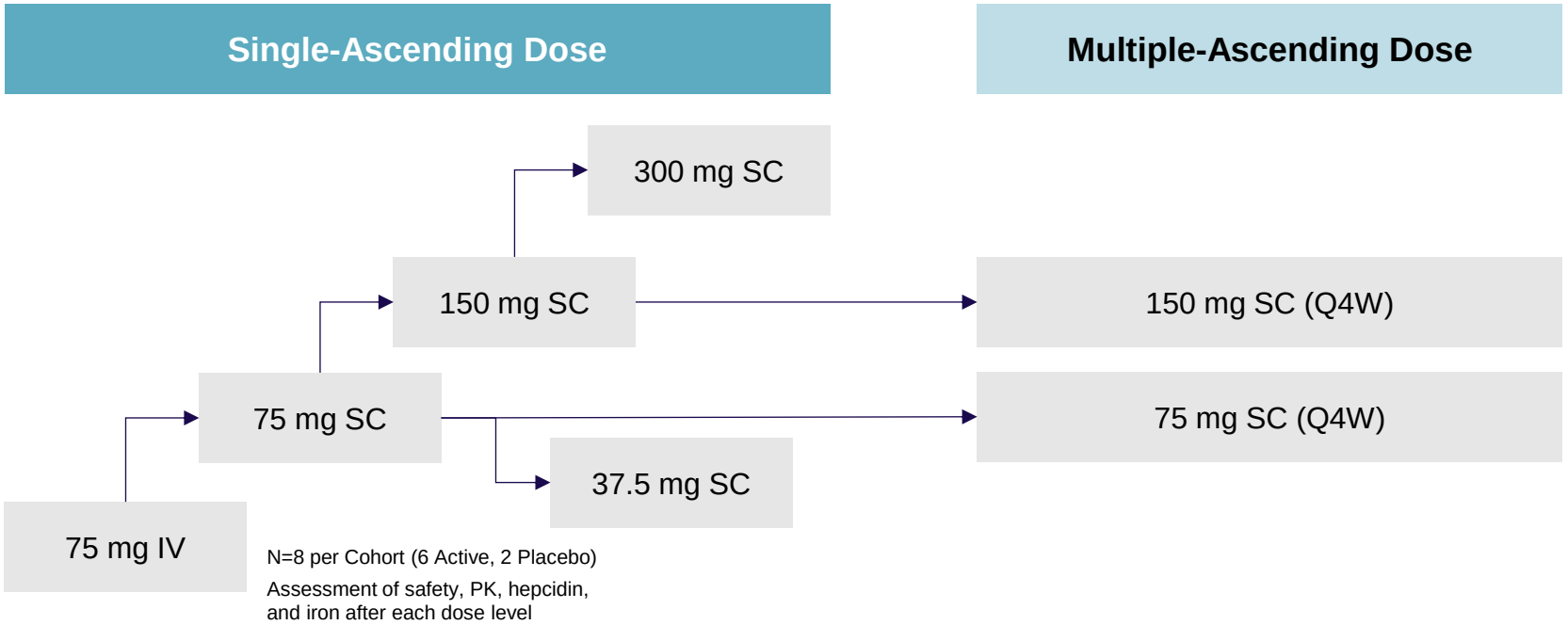
Designed to limit iron levels with potential to address a wide range of hematologic disorders

Enables Endogenous Production of Hepcidin

Promotes Iron Restriction
Decreases GI Absorption

Erythrocytosis (PV)
Ineffective Erythropoiesis
Iron Overload

DISC-3405 Phase 1 Healthy Volunteer Study Overview



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

DISC-3405 Phase 1 Healthy Volunteer Study Summary

- Dose-dependent increases in hepcidin and corresponding reductions in serum iron levels across all dose levels
- Deep and sustained reductions in serum iron (50-80% from baseline)
- Meaningful reductions in reticulocyte hemoglobin, hemoglobin, and hematocrit in both SAD and MAD cohorts
- Data set supportive of a once-monthly subcutaneous dosing regimen in polycythemia vera and iron-overload conditions
- DISC-3405 was well tolerated with no injection-site reactions

Iron Restriction in Sickle Cell Disease

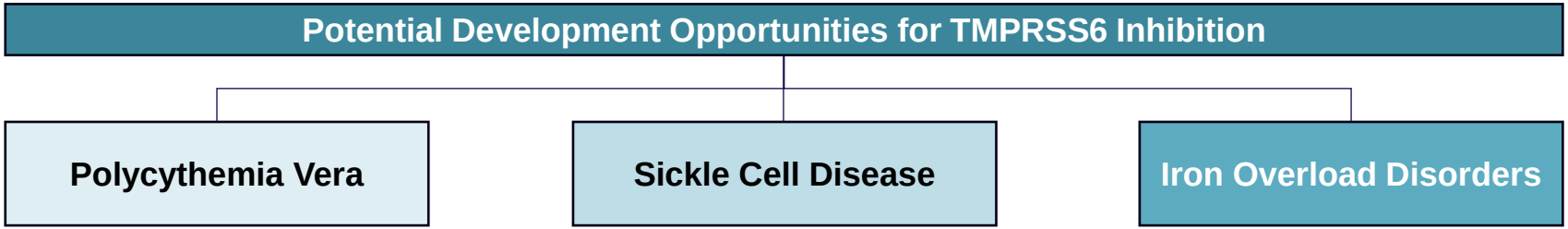
Potential for iron restriction through inhibition of TMPRSS6 to benefit SCD by reducing HbS concentration

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

DISC-3405 in a Townes Model

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

DISC-3405 Summary and Next Steps



ASH Data Summary

- Proof of mechanism in HVOL with reductions in hepcidin and increases in serum iron supportive of monthly dosing
- Preclinical SCD data showing decreased HbS concentration and improved markers of inflammation and hemolysis

Next Steps

- Phase 2 study initiation in polycythemia vera in 1H 2025

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Summary of ASH Updates

Bitopertin
Heme Synthesis Modulator

- Consistent, strong efficacy across BEACON and AURORA in adults and adolescents
- Patient survey highlights high burden of disease in EPP
- Defined path to registration with potential for accelerated approval
- Commercial readiness activities are well underway

DISC-0974
Hepcidin Suppression

- Positive, durable benefits on hemoglobin and transfusion burden in anemia of MF across all meaningful patient types
- Preclinical data demonstrate potential to reverse the Hgb-lowering effects of ruxolitinib
- Demonstrated potential to treat additional anemias of inflammation with efficacy in a mouse model of IBD anemia
- Phase 2 study in MF initiated

DISC-3405
Hepcidin Induction

- Increased hepcidin and reduced serum iron across all dose levels supportive of subcutaneous monthly dosing
- Meaningful changes in hematologic parameters with multiple doses
- Positive preclinical data in SCD demonstrating potential for disease modification
- Phase 2 study in PV to start in 2025

Projected Upcoming Milestones and Events

Multiple additional data catalysts anticipated in the next 18 months

Program	Indication	H1 2025	H2 2025	2026
Bitopertin Heme Synthesis Modulator	**Erythropoietic Porphyrias (EPP and XLP)**	• Feedback from Type C Meeting with FDA • APOLLO Study Initiation	*Guidance on NDA timing to be provided in Q1 2025*	
	Diamond-Blackfan Anemia (DBA)	• IIT ongoing →		
DISC-0974 Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**		• Initial Phase 2 Data	• Final Phase 2 Data
	Anemia of Chronic Kidney Disease (CKD)		• Phase 1b Multiple-Dose Data	• Phase 2a Initiation • Initial Phase 2a Data
DISC-3405 Hepcidin Induction	**Polycythemia Vera**	• Phase 2a Study Initiation		• Phase 2a Data

Supported by a strong cash position with runway well into 2027

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