UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 20, 2025

Disc Medicine, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39438**	**85-1612845**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
321 Arsenal Street, Suite 101 **Watertown, Massachusetts** **(Address of Principal Executive Offices)**		**02472** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 674-9274

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.0001 per share	IRON	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02 Results of Operations and Financial Condition.

On October 20, 2025, Disc Medicine, Inc. (the "Company") announced that its preliminary unaudited cash, cash equivalents and marketable securities as of September 30, 2025 were approximately $615.9 million.

The Company has not yet completed its quarter-end financial close process for the quarter ended September 30, 2025. This estimate of the Company's cash, cash equivalents and marketable securities as of September 30, 2025 is preliminary, has not been audited and is subject to change upon completion of the Company's financial statement closing procedures. Additional information and disclosure would be required for a more complete understanding of the Company's financial position and results of operations as of September 30, 2025. The Company's independent registered public accounting firm has not audited, reviewed or performed any procedures with respect to this preliminary result and, accordingly, does not express an opinion or any other form of assurance about it. The information presented herein should not be considered a substitute for the financial information the Company files with the Securities and Exchange Commission (the "SEC") in its quarterly report on Form 10-Q for the quarter ended September 30, 2025. The Company has no intention or obligation to update preliminary estimates of its cash, cash equivalents and marketable securities set forth above.

The information contained in Item 2.02 of this Current Report on Form 8-K is intended to be furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities and Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or the Exchange Act, except as expressly provided by specific reference in such filing.

Item 7.01 Regulation FD Disclosure

On October 20, 2025, the Company issued a press release providing an update on its hematology portfolio and outlining near-term business objectives and anticipated milestones. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K (including Exhibit 99.1 attached hereto) is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly provided by specific reference in such filing. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.1.

Item 8.01 Other Events.

Corporate Presentation

On October 20, 2025, the Company updated its corporate presentation. A copy of the updated corporate presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference. The corporate presentation will also be available in the investor relations section of the Company's website at https://ir.discmedicine.com. Information contained on the Company's website is not incorporated by reference into this Current Report on Form 8-K, and you should not consider any information on, or that can be accessed from, the Company's website as part of this Current Report on Form 8-K.

Recent Developments

On October 20, 2025, the Company provided an update on its hematology portfolio and outlined its near-term business objectives and anticipated milestones for the rest of 2025 and 2026:

Bitopertin: GlyT1 Inhibitor (Heme Synthesis Modulator)

- Accelerate activities to support a potential US approval and launch in late 2025 or early 2026 based on accelerated review timeline associated with receipt of the FDA Commissioner's National Priority Voucher ("CNPV"), which is designed to shorten the New Drug Application review process to 1-2 months
- Drive enrollment of ongoing APOLLO confirmatory trial of bitopertin in erythropoietic protoporphyria that is intended to also support potential approval of bitopertin in territories outside the US

DISC-0974: Anti-hemojuvelin Antibody (Hepcidin Suppression)

- Progress and position DISC-0974 to be advanced into potential late-stage clinical development for anemia of myelofibrosis ("MF")
- Initial data from ongoing Phase 2 study in anemia of MF to be reported by year end; topline data expected in 2026, if positive, is anticipated to support discussion with regulatory agencies on registrational path
- Demonstrate role of hepcidin suppression and anti-hemojuvelin ("HJV") mechanism in other anemias of chronic disease:
  - Recently completed Phase 1b double-blind, placebo-controlled study of DISC-0974 demonstrated engagement of mechanism in anemia of non-dialysis dependent chronic kidney disease with variable effects on hemoglobin
    - DISC-0974 was generally well-tolerated with substantial decreases in hepcidin, increases in iron, and improvements in markers of erythropoiesis
    - Meaningful hemoglobin increases observed in only a subset of patients were in part driven by those with higher baseline erythropoietin ("EPO") levels
    - Full data will be shared at the upcoming 2025 ASN Kidney Week; the Company is assessing options for the program based on full analysis of the data
  - Initiation of a Phase 2 study in patients with inflammatory bowel disease and anemia anticipated in Q1 2026, and planning exploratory studies in additional patient populations with anemia of chronic disease.
- Plans to accelerate next-generation, long-acting anti-HJV antibody into IND-enabling studies

DISC-3405: Anti-TMPRRS6 Antibody (Hepcidin Induction)

- Establish Phase 2 proof-of-concept of DISC-3405 for polycythemia vera ("PV") and support potential development into later stage development
  - Topline data from ongoing Phase 2 study in PV expected in 2026
- Initiation of Phase 1b study in patients with sickle cell disease anticipated by year end
- Plans to explore the role of therapeutic iron restriction in other indications

This Current Report on Form 8-K contains forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act. Any statements about the Company's expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as "may," "will," "could," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "projects," "seeks," "endeavor," "potential," "continue," and similar expressions, or the negative of these terms, or similar expressions. These forward-looking statements include statements about the Company's expectations with respect to the next stages of its development programs for bitopertin, DISC-0974 and DISC-3405, including projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; the registrational pathway for bitopertin, including the potential for accelerated approval, benefits of the CNPV and expected review period; anticipated discussions with regulatory agencies; ongoing preparations for the potential launch of bitopertin; and the potential of its development programs in new indications. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them, including the uncertainties related to market conditions and the completion of the public offering on the anticipated terms or at all. The Company's forward-looking statements also involve assumptions that, if they prove incorrect, would cause its results to differ materially from those expressed or implied by such forward-looking statements. These and other risks concerning the Company's business are described in additional detail in the Company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025 and other documents filed by the Company from time to time with the SEC. The Company is under no obligation to, and expressly disclaims any such obligation to, update or alter its forward-looking statements, whether as a result of new information, future events or otherwise.

Item 9.01. Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by Disc Medicine, Inc. on October 20, 2025, furnished herewith.
99.2	Disc Medicine, Inc. Investor Presentation, filed herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

DISC MEDICINE, INC.

Date: October 20, 2025

By: /s/ John Quisel
Name: John Quisel, J.D., Ph.D.
Title: Chief Executive Officer

Disc Medicine Provides Update on Hematology Portfolio and Outlines Near-Term Business Objectives and Anticipated Milestones

- *Submitted a New Drug Application (NDA) for accelerated approval of bitopertin in erythropoietic protoporphyria (EPP) on September 29, 2025, and subsequently was awarded the FDA Commissioner's National Priority Voucher (CNPV), a program designed to shorten the expected NDA review period to 1-2 months*
- *Acceleration of ongoing efforts to support the potential earlier approval and commercialization of bitopertin for EPP in the US, expected in late 2025 or early 2026*
- *Plans to advance DISC-0974 for anemia of myelofibrosis (MF) and DISC-3405 for polycythemia vera (PV) deeper into development and to continue exploring potential role of hepcidin in additional indications*
- *Strong financial position ending Q3 with approximately $616 million in cash, cash equivalents, and marketable securities*

WATERTOWN, Mass., October 20, 2025 – Disc Medicine, Inc. (NASDAQ:IRON), a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel treatments for patients suffering from serious hematologic diseases, today outlined its recent pipeline and operational progress and strategic priorities for the rest of 2025 and 2026.

"2025 has been another eventful year for Disc Medicine, and we are accelerating development across three key indications—EPP and our myeloproliferative neoplasm portfolio, MF and PV. For bitopertin, with the recent grant of the FDA's CNPV, our focus is on accelerating our commercial readiness to ensure access to patients as quickly as possible upon approval, if granted," said John Quisel, J.D., Ph.D., Chief Executive Officer and President of Disc Medicine.

We're also excited about the progress across our iron homeostasis portfolio, DISC-0974 and DISC-3405, as these programs will be important drivers of Disc's future growth. We're positioning DISC-0974 for development in anemia of MF and look forward to providing an initial set of data from the Phase 2 RALLY-MF trial of DISC-0974 in its lead indication, anemia of MF, by the end of this year. Additionally, we are advancing the development of DISC-3405 in PV with data expected next year. We also continue to drive our expansion strategy for both of these programs with a plan to initiate a Phase 2 trial of DISC-0974 in anemia of inflammatory bowel disease in 2026 and a Phase 1b trial of DISC-3405 in sickle cell disease by year end."

Key Near-Term Business Objectives

Bitopertin: GlyT1 Inhibitor (Heme Synthesis Modulator)

- Accelerate activities to support a potential US approval and launch in late 2025 or early 2026 based on accelerated review timeline associated with receipt of the CNPV, which is designed to shorten the NDA review process to 1-2 months
- Drive enrollment of ongoing APOLLO confirmatory trial of bitopertin in EPP that is intended to also support potential approval of bitopertin in territories outside the US

DISC-0974: Anti-hemojuvelin Antibody (Hepcidin Suppression)

- Progress and position DISC-0974 to be advanced into potential late-stage clinical development for anemia of MF

- Initial data from ongoing Phase 2 study in anemia of MF to be reported by year end; topline data expected in 2026, if positive, is anticipated to support discussion with regulatory agencies on registrational path
- Demonstrate role of hepcidin suppression and anti-hemojuvelin (HJV) mechanism in other anemias of chronic disease:
    - Recently completed Phase 1b double-blind, placebo-controlled study of DISC-0974 demonstrated engagement of mechanism in anemia of non-dialysis dependent chronic kidney disease (NDD-CKD) with variable effects on hemoglobin
        - DISC-0974 was generally well-tolerated with substantial decreases in hepcidin, increases in iron, and improvements in markers of erythropoiesis
        - Meaningful hemoglobin increases observed in only a subset of patients were in part driven by those with higher baseline erythropoietin (EPO) levels
        - Full data will be shared at the upcoming 2025 ASN Kidney Week; we are assessing options for the program based on full analysis of the data
    - Initiation of a Phase 2 study in patients with IBD and anemia anticipated in Q1 2026, and planning exploratory studies in additional patient populations with anemia of chronic disease.
- Plans to accelerate next-generation, long-acting anti-HJV antibody into IND-enabling studies

DISC-3405: Anti-TMPRRS6 Antibody (Hepcidin Induction)

- Establish Phase 2 proof-of-concept of DISC-3405 for PV and support potential development into later stage development
    - Topline data from ongoing Phase 2 study in PV expected in 2026
- Initiation of Phase 1b study in patients with SCD anticipated by year end
- Plans to explore the role of therapeutic iron restriction in other indications

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

About Disc Medicine

Disc Medicine (NASDAQ:IRON) is a clinical-stage biopharmaceutical company committed to discovering, developing, and commercializing novel treatments for patients who suffer from serious hematologic diseases. We are building a portfolio of innovative, potentially first-in-class therapeutic candidates that aim to address a wide spectrum of hematologic diseases by targeting fundamental biological pathways of red blood cell biology, specifically heme biosynthesis and iron homeostasis. For more information, please visit www.discmedicine.com.

Disc Cautionary Statement Regarding Forward-Looking Statements

This press release 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 the next stages of its development programs for bitopertin, DISC-0974 and DISC-3405, including projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; the registrational pathway for bitopertin, including the potential for accelerated approval, benefits of the CNPV and expected review period; anticipated discussions with regulatory agencies; ongoing preparations for the potential launch of bitopertin; the potential of its development programs in new indications; and the strength of its financial position and its anticipated cash runway. 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, 2024, 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.

Media Contact

Peg Rusconi
Deerfield Group
peg.rusconi@deerfieldgroup.com

Investor Relations Contact

Christina Tartaglia
Precision AQ
christina.tartaglia@precisionaq.com

Exhibit 99.2

Corporate Presentation

October 2025

disc medicine

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, DISC-0974 and DISC-3405, and any developments or results in connection therewith; projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; the registrational pathway for bitopertin, including the potential for accelerated approval, benefits of the CNPV and expected review period; anticipated discussions with regulatory agencies; ongoing preparations for the potential launch of bitopertin; the potential of Disc’s development programs in new indications; the market and potential opportunities for bitopertin, DISC-0974 and DISC-3405; 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, 2024, 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.

disc medicine

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

Bitopertin selected for the FDA's Commissioner's National Priority Voucher (CNPV) Pilot Program

New program announced June 2025 offering accelerated reviews for drug product applications that support US national interests

FDA's Stated Program Priorities	Key Program Benefits
• Addressing a US public health crisis • Delivering more innovative cures for the American people • Addressing a large unmet medical need • Onshoring drug development and manufacturing • Increasing affordability	• Faster review times (expected 1-2 months) • Enhanced communication throughout the process • Multidisciplinary team-based evaluation • Potential for accelerated approval if applicable requirements are met • Maintains FDA's rigorous safety and efficacy standards

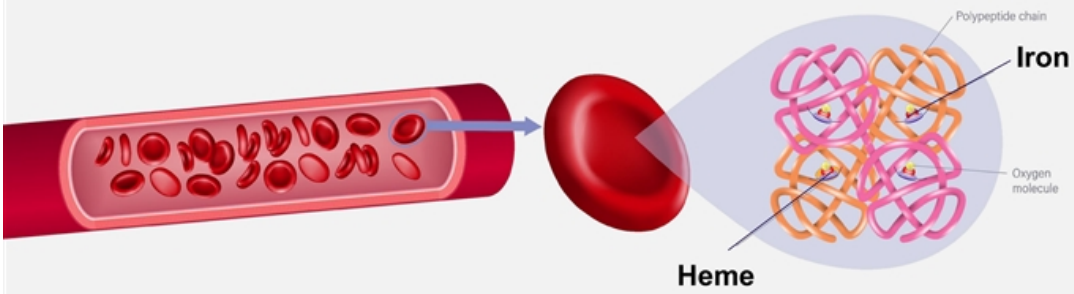
NDA Submitted*
September 29

Anticipated Review Period Under CNPV Program
1-2 months

Disc is committed to ensuring access to bitopertin for patients as quickly as possible and is advancing commercial readiness activities to support potential launch of bitopertin on accelerated timeline, if approved

*FDA acceptance of NDA submission expected on or before November 28; NDA=New Drug Application

Targeting Fundamental Pathways of Red Blood Cell Biology using Validated Mechanisms



Iron and heme metabolism are critical pathways in hematology with genetically-validated targets

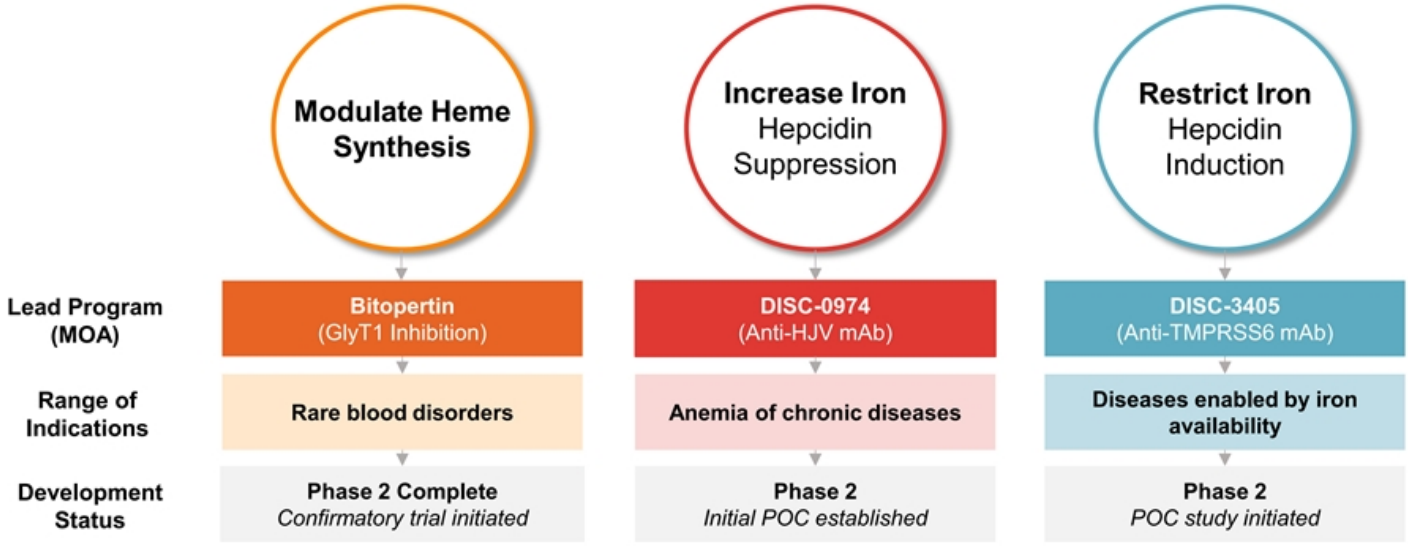
Key points of intervention across a wide range of diseases

Spectrum of Hematologic Diseases Addressable by Disc Portfolio

Severe Rare (000s)			*Moderate Prevalence (100K+)*				*Widely Prevalent (MMs)*		
Diamond-Blackfan Anemia	**Erythropoietic Porphyrias**	Beta-Thalassemia	**Anemia of Myelofibrosis**	**Myelodysplastic Syndromes**	**Sickle Cell Disease**	**Polycythemia Vera**	Hereditary Hemochromatosis	IBD Anemia	**CKD Anemia**

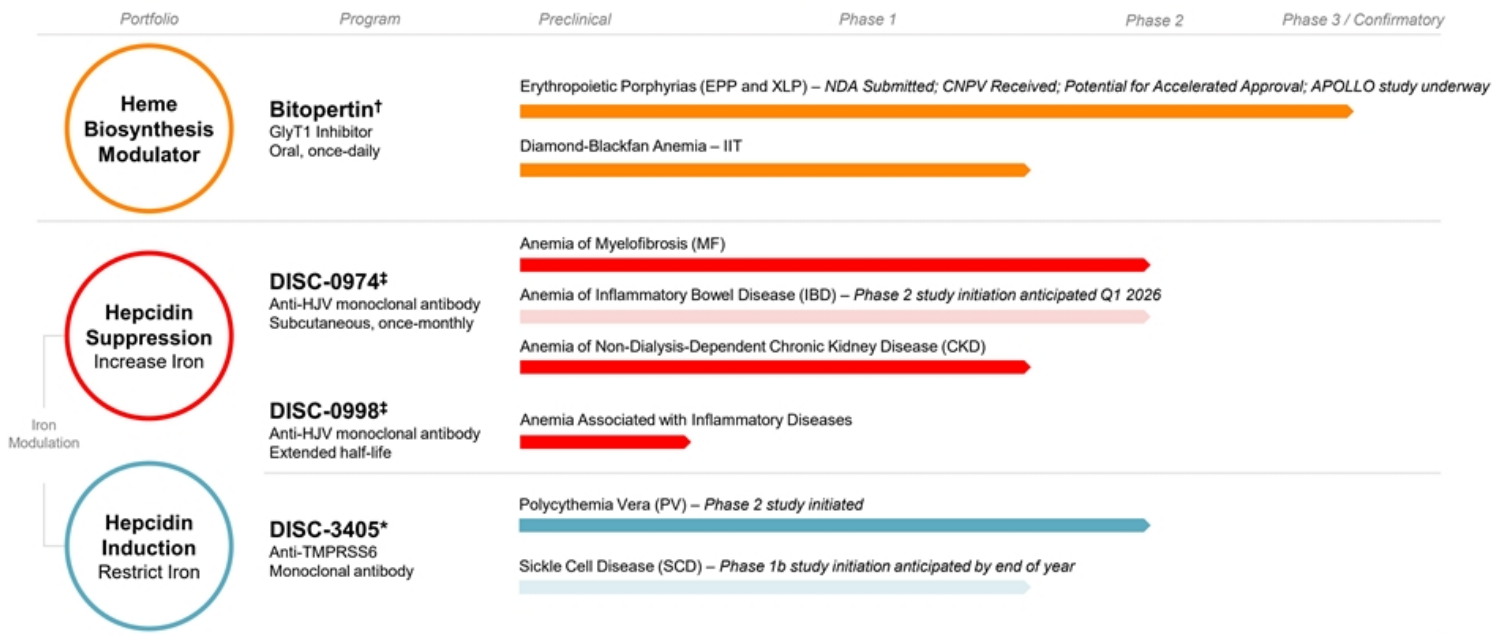
Bold = ongoing Disc trial

By Targeting Heme and Iron, Disc's Portfolio Can Address a Wide Range of Hematologic Disorders



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); CNPV = Commissioner's National Priority Voucher

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 initiated	✓ NDA Submission ✓ CNPV Received • NDA Filing Decision	Potential Approval (late '25 - early '26)
	Diamond-Blackfan Anemia (DBA)	• IIT ongoing →		
DISC-0974 Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**		• Initial RALLY-MF Phase 2 Data	• Topline RALLY-MF Phase 2 Data
	Anemia of Inflammatory Bowel Disease (IBD)			• Phase 2 initiation
	Anemia of Chronic Kidney Disease (CKD)		• Phase 1b Multiple-Dose Data	• Next study*
DISC-3405 Hepcidin Induction	**Polycythemia Vera (PV)**	✓ Phase 2 Study Initiated		• Initial Phase 2 Data
	Sickle Cell Disease (SCD)		• Phase 1b Study Initiation	• Initial Phase 1b Data

*assessing options for the program based on full analysis of the data

Supported by a strong cash position with runway into 2028

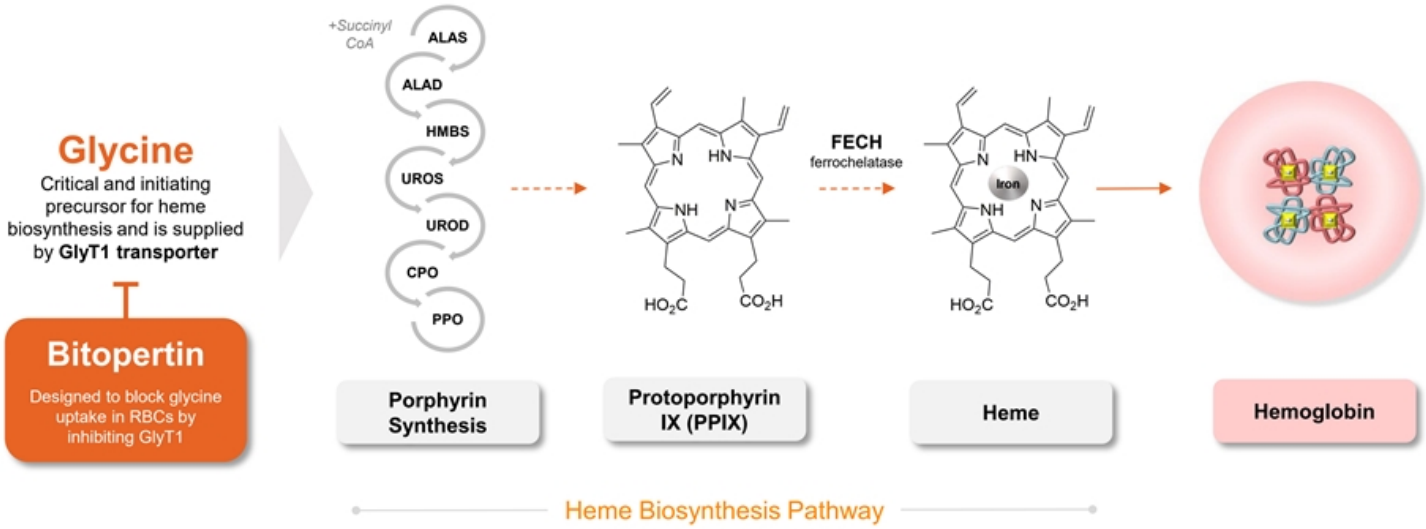
Bitopertin

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



Erythropoietic Protoporphyria (EPP)

Rare, debilitating and lifelong condition characterized by extreme pain and damage to skin caused by light

Genetic condition caused by defective heme biosynthesis – deficient enzyme ferrochelatase

- Lifelong and presents in early childhood
- Caused by accumulation of toxic metabolite PPIX
- XLP, mechanistically similar disease, also PPIX-related

Debilitating and potentially life-threatening

- Skin: severe, disabling pain attacks (days), edema, burning
- Hepatobiliary disease: gallstones, liver dysfunction or failure
- Psychosocial well-being (fear, anxiety) and development

No cure or disease-modifying treatment

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

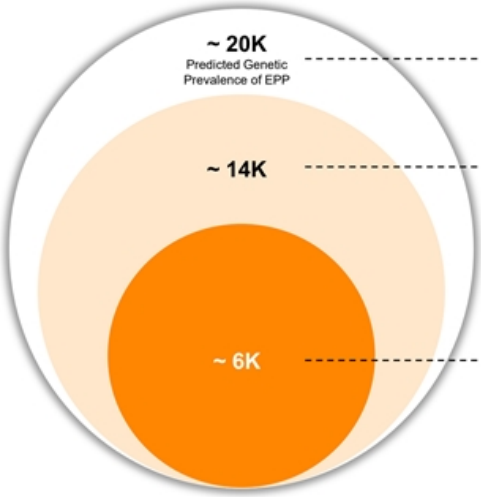


Image sources: *Daily Mail Australia* (2019); FDA Scientific Workshop on EPP (2016); Buonuomo et al. (2014) *Arch Dis Child*

Sources: Deybach et al (2009) Orphanet Journal of Rare Diseases; American Porphyria Foundation; Dickey et al (2021) Genet. Med.

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

Prevalence of EPP Patients in the US

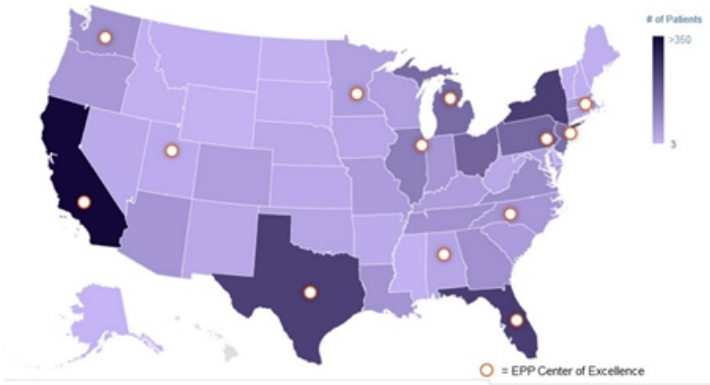


Expansion
Misdiagnosed or have not sought treatment for EPP

Growth
Diagnosed EPP patients with lower degree of engagement with healthcare system

INITIAL LAUNCH FOCUS
Diagnosed EPP patients with recent or recurring claims

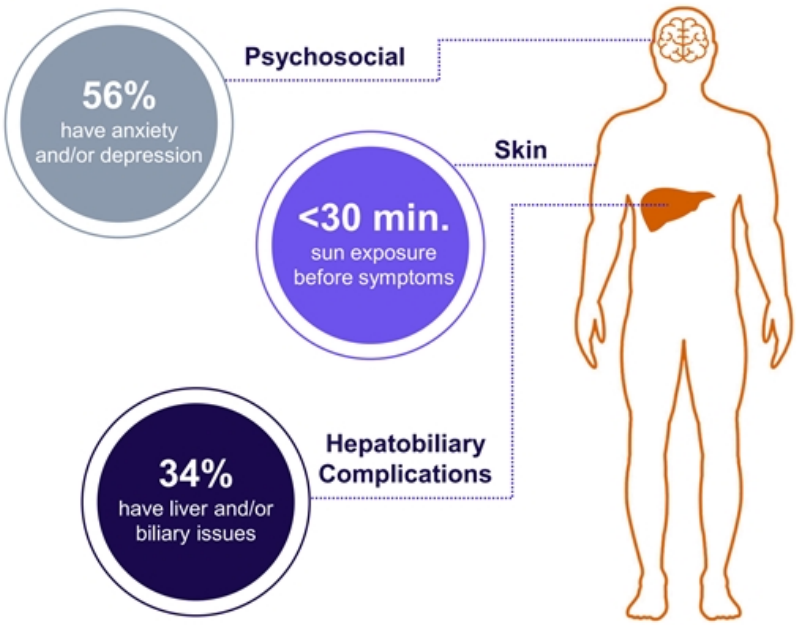
Distribution of EPP Treatment Centers



Mapping diagnostic codes enables a targeted and efficient field force

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

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



Concomitant Medication

- **57%** receive steroid treatment
- **30%** treated with narcotics
- **19%** get prescription Vitamin D

Healthcare Utilization

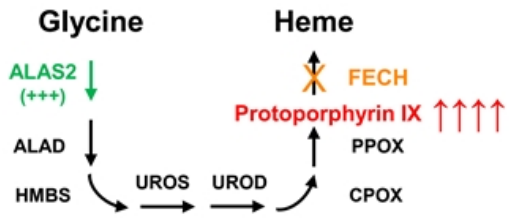
- **38%** inpatient stay in past 3 years
- **32%** visit the ER each year

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

Bitopertin: Potential Disease-Modifying Treatment

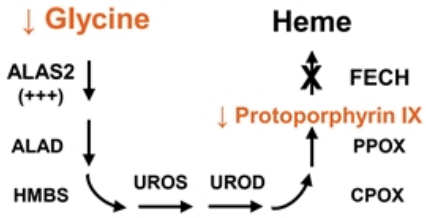
Designed to reduce disease-causing PPIX by limiting uptake of glycine into developing erythrocytes

EPP and XLP Patients
High PPIX Levels



Mutations result in reservoir of pathologically high levels of PPIX

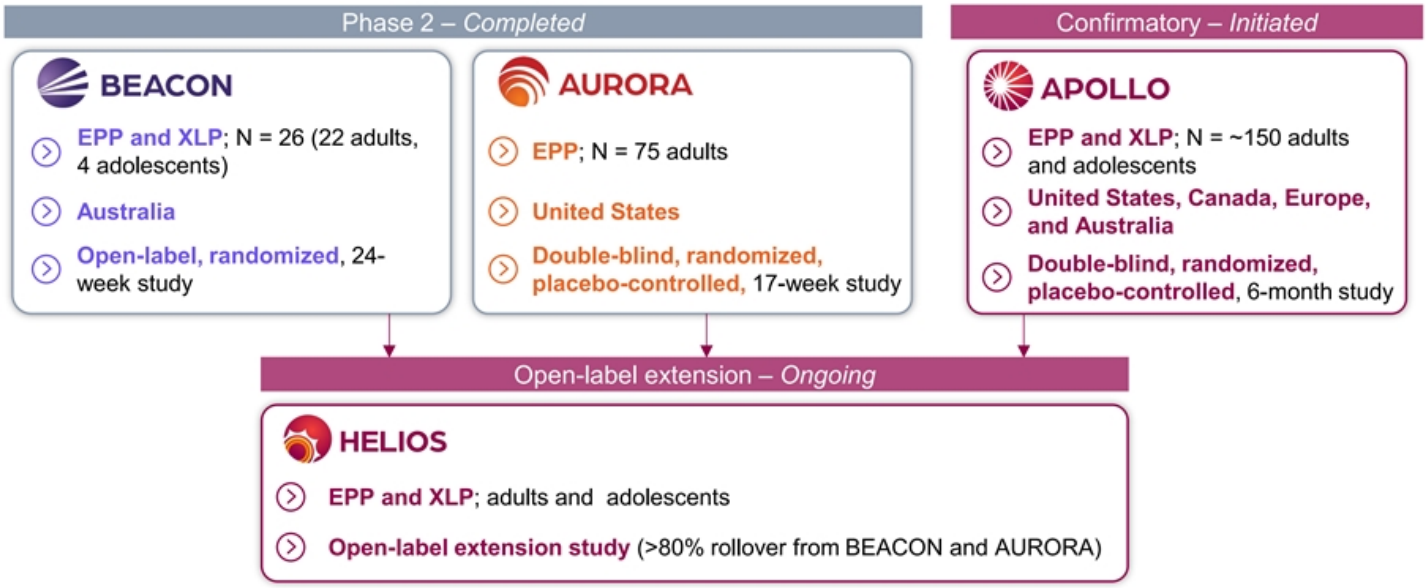
Bitopertin Treatment
Designed to Reduce PPIX Levels



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



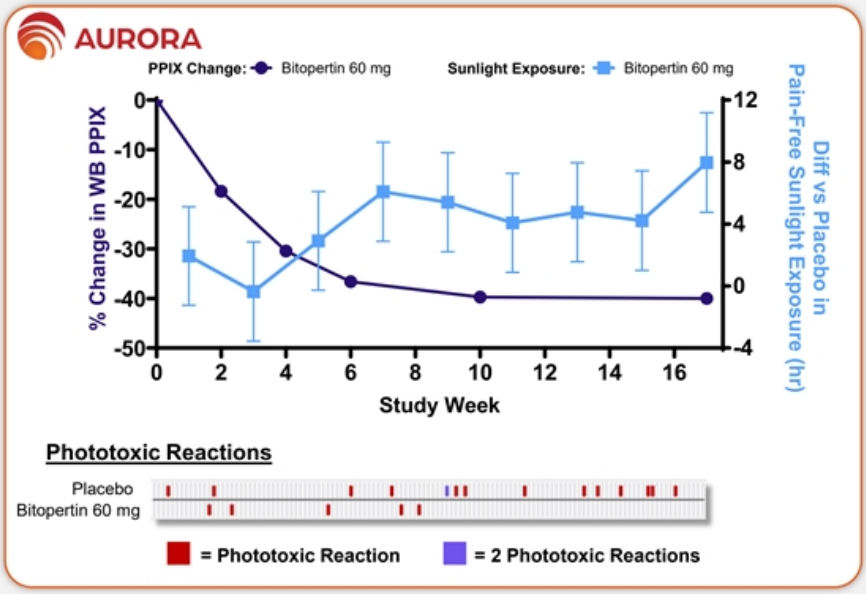
APOLLO Trial

Post marketing confirmatory trial required for US full approval

N Size	~150* patients across sites in the US, Canada, Europe, and Australia
Trial Duration	6-month treatment period; Expected to fully enroll within ~12 months
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 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 • Patient global impression of change (PGIC) • Cumulative total pain-free time in sunlight • Time to prodrome • Safety and tolerability

*Subject to blinded sample size recalculation; XLP=X-linked protoporphyria

Summary of AURORA Results
Bitopertin 60 mg

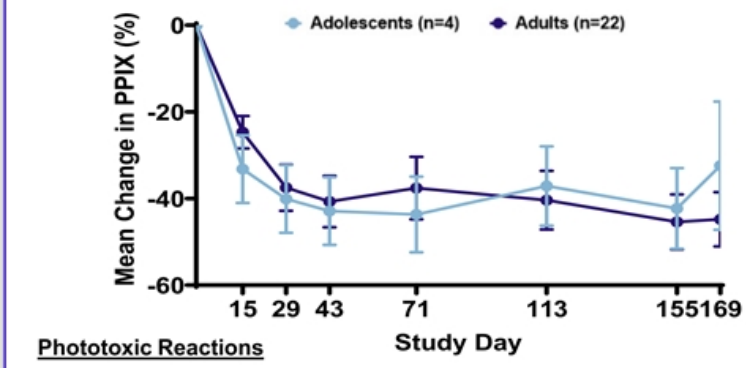


- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent, improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant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

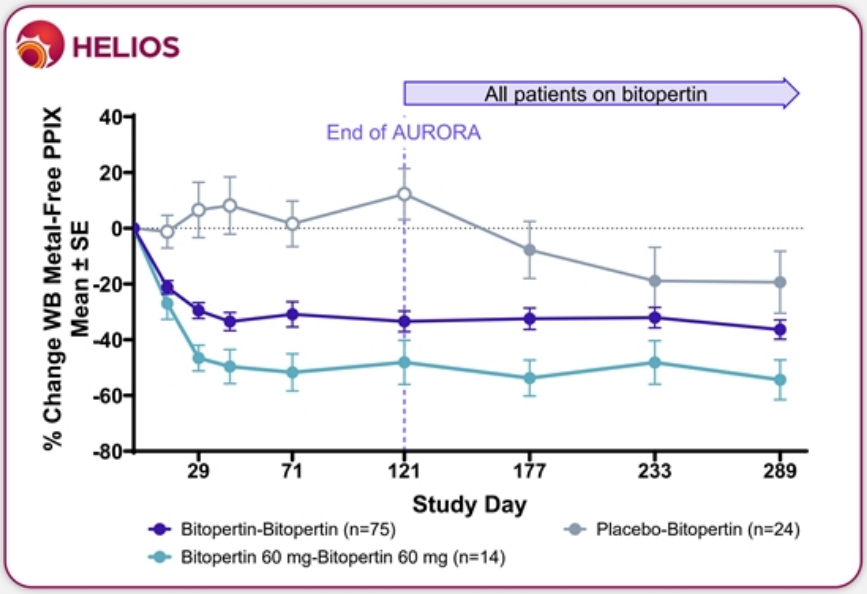
PPIX Increased ← → **PPIX Decreased**

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

- PPIX reduction associated with **significant reduction in phototoxic reactions** from baseline
- PPIX reduction associated with **significant improvement in pain-free time in sunlight**

Summary of HELIOS Initial Results

Favorable long-term efficacy and safety



- **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 Next Steps

- Collaborate with FDA throughout their review
- Accelerate activities to support a potential US approval and launch in late 2025 or early 2026
- Drive enrollment of ongoing APOLLO confirmatory trial ongoing in US and Europe

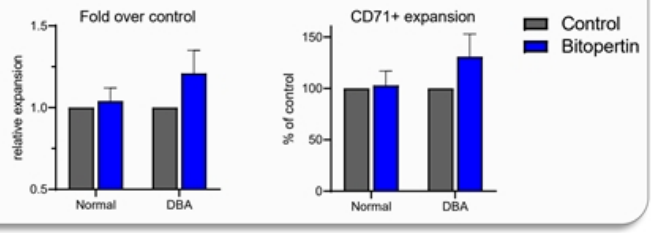
Disc is committed to ensuring access to bitopertin for patients as quickly as possible upon approval, if granted

Bitopertin in Diamond Blackfan Anemia

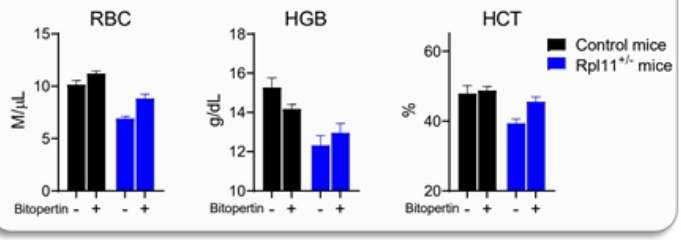
By slowing the influx of glycine, bitopertin lowers heme production, reducing the amount of excess heme and preventing cell death



Primary human marrow in erythroid differentiation cultures treated with 10 ng/ml bitopertin for 7 days



Rpl11 haploinsufficient mice were treated with 100 ppm bitopertin in chow (20 mg/kg/d) for 8 weeks



Phase 2 trial is underway – sponsored by NIH

Multiple Additional Potential Applications of Bitopertin

Inhibiting heme synthesis with bitopertin has potential to address a wide range of hematologic diseases



Porphyrin Toxicity

Erythropoietic Protoporphyria
X-Linked Protoporphyria
Congenital Erythropoietic Porphyria
Hepatic Porphyrias

Heme Toxicity

Diamond-Blackfan Anemia
Myelodysplastic Syndromes

Globin Toxicity

Beta-Thalassemia
Sickle Cell Disease

Excess RBCs

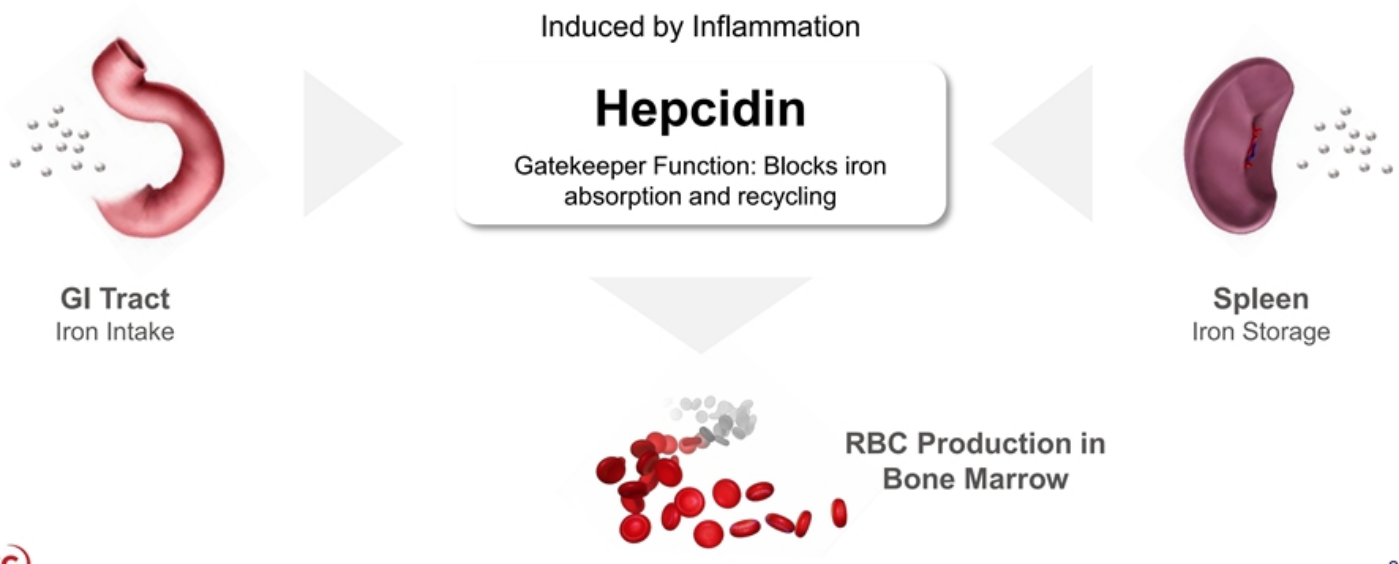
Polycythemia Vera

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

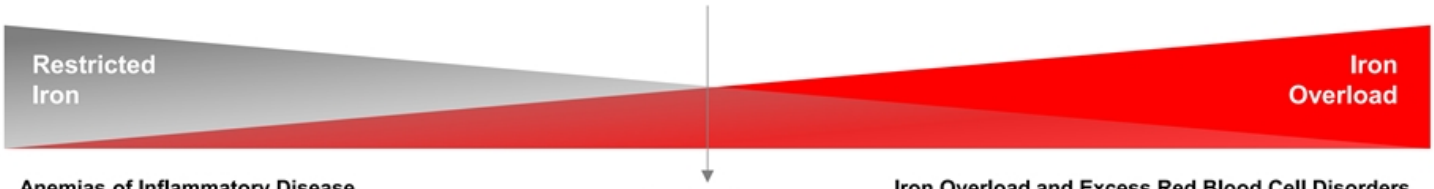


Hepcidin is a Therapeutic Target for Diseases

Dysregulated hepcidin drives a wide range of hematologic diseases

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

Regulated erythropoiesis



Regulated iron

Anemias of Inflammatory Disease

- Myelofibrosis
- Chronic Kidney Disease
- Autoimmune / Inflammatory Disorders

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

Iron Overload and Excess Red Blood Cell Disorders

- Polycythemia Vera
- Sickle Cell Disease
- Hereditary Hemochromatosis

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

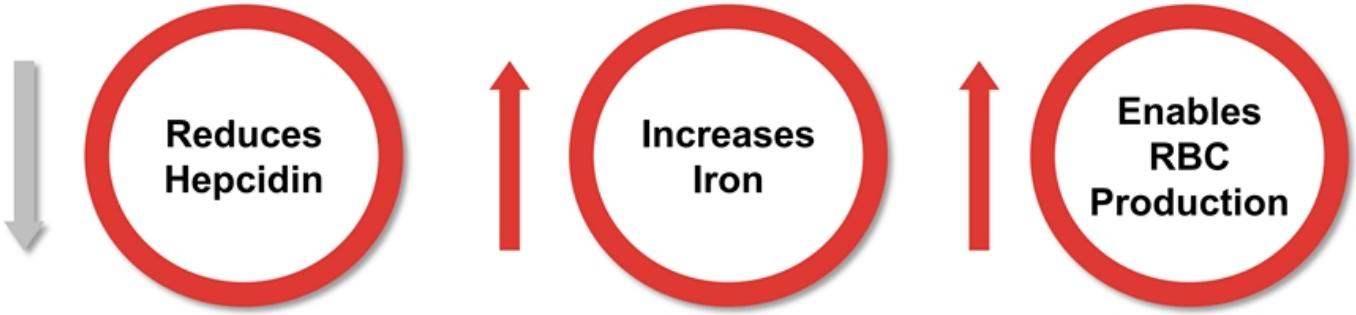
DISC-0974

Anti-HJV mAb

Hepcidin Suppression

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

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



Inhibits endogenous production of hepcidin

Releases iron stores
Enables GI absorption

Potential to treat wide range of anemias

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%
Chronic Kidney Disease (CKD)	37 MM	17-50%
Inflammatory Bowel Disease	1.6 MM	25-35%
Anemia of Cancer	17 MM	35-80%
Systemic Lupus Erythematosus	210K	50%

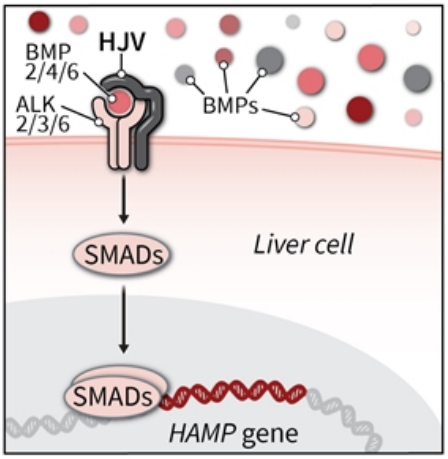
- **Anemia of inflammation** is the 2nd most common form of anemia
- **Estimated 40% of all anemias** are driven by or have an inflammatory component
- **Hepcidin is up-regulated** and correlates with anemia, driven by inflammation

Bold = ongoing Disc trial

Sources: Weiss (2019); Maccio (2014); Barraco (2016); Lupus Foundation; Stauffer (2014); Filmann (2014); Koutroubakis (2015); Crohn's and Colitis Foundation

Targeting Hemojuvelin (HJV) to Suppress Hepcidin

Critical and specific target for hepcidin expression



Inhibiting Hemojuvelin (HJV) Prevents Hepcidin Expression and Increases Iron

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

Sources: Finberg et al, (2010) Blood; Zhang et al, (2010) J Biol Chem

Phase 1 SAD Trial in Healthy Volunteers

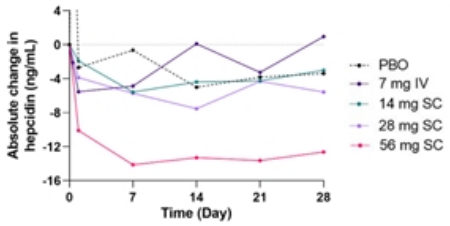
Established proof-of-mechanism based on hepcidin and iron parameters

Trial Design

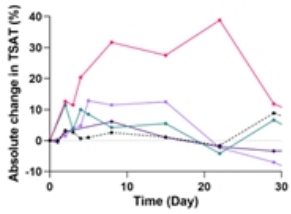
- Single-ascending dose in ≥32 healthy volunteers
- Key outcome measures:
  - Safety and PK
  - Hepcidin level, serum iron level, % TSAT
- Dose escalation until TSAT > 40% for at least 2 weeks
- Dose levels: 7 mg dose (IV); 14, 28 and 56 mg doses (SC)

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

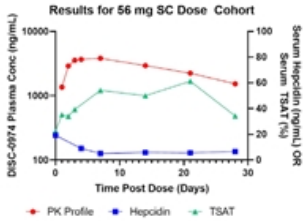
DISC-0974 Reduced Hepcidin Production

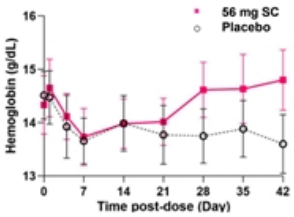


DISC-0974 Increased TSAT



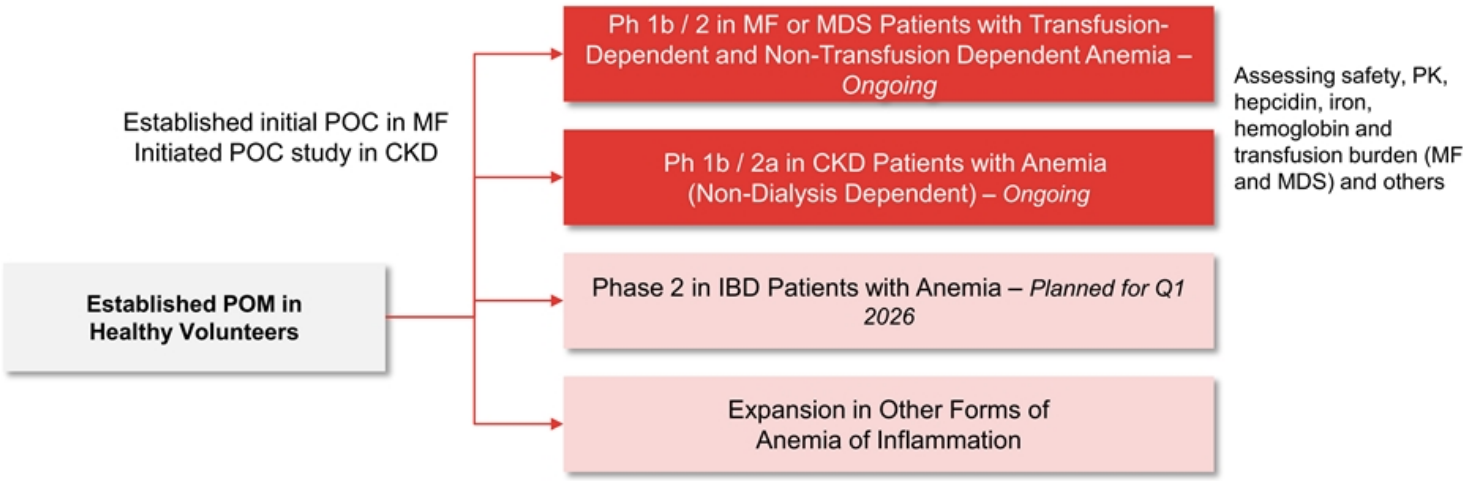
56 mg pharmacodynamic activity improved key clinical parameters (> 1g/dL Hgb)





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

DISC-0974 Development Strategy

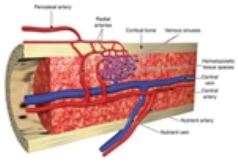


CKD = chronic kidney disease; MDS = myelodysplastic syndrome; MF = myelofibrosis; POC = proof of concept; POM = proof of mechanism

Hepcidin is a Key Driver of Myelofibrosis (MF) Anemia

Anemia is severe and prevalent in MF and can limit treatment

Anemia of MF



Est. # Patients

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

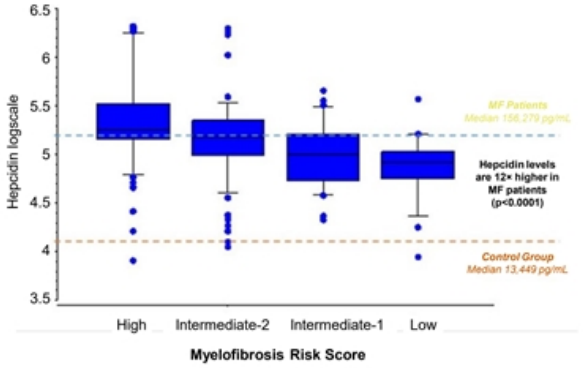
Etiology of Anemia

- 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

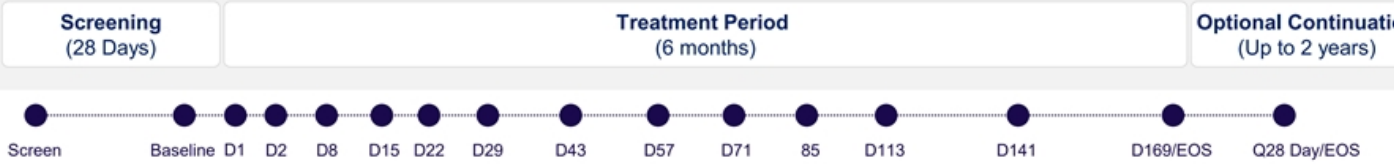
Hepcidin Levels are Elevated in MF
~ 12× higher than control and associated with severity of anemia and transfusion burden



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

DISC-0974 Anemia of MF Phase 1b

Study overview – enrollment data as of October 17, 2024



	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

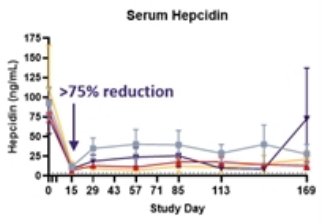
*Reason for early withdrawal: Physician decision due to inadequate response (n=2)
Source: ASH DISC-0974 MF Presentation

DISC-0974 Anemia of MF Phase 1b Results

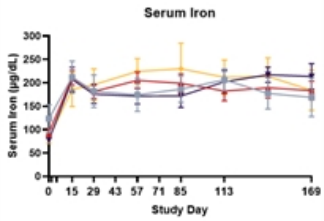
Pharmacodynamics

- 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

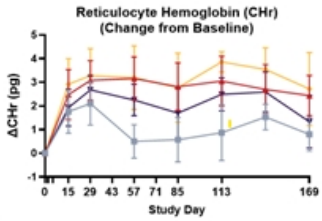
↓ Serum Hepcidin



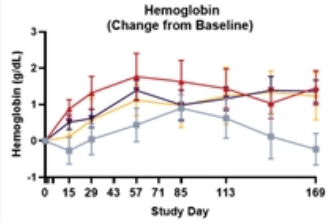
↑ Serum Iron



↑ Reticulocyte Hemoglobin



↑ Hemoglobin



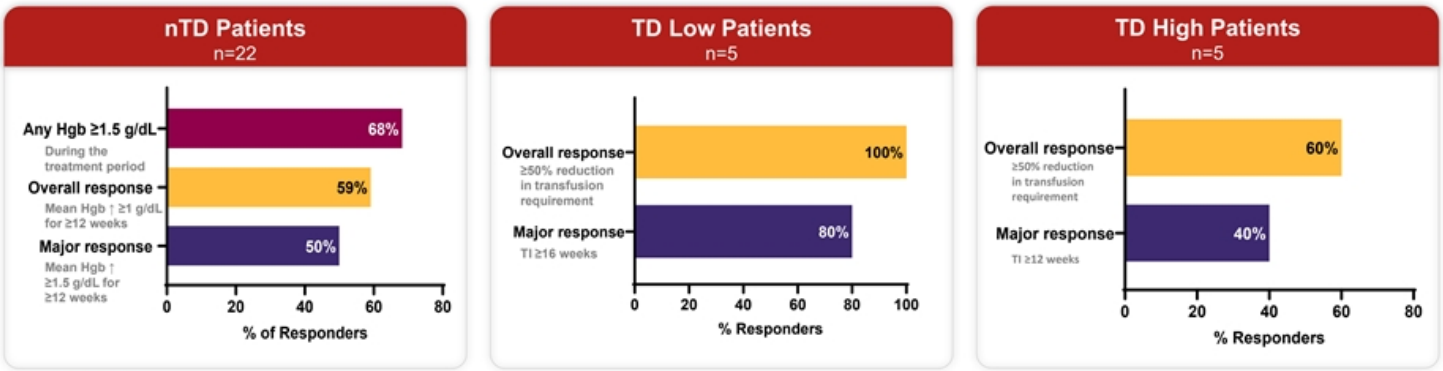
28 mg 50 mg 75 mg 100 mg

Source: ASH DISC-0974 MF Presentation

DISC-0974 Anemia of MF Phase 1b Results

Hematologic response: 14, 28, 50, 75, and 100 mg

- 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



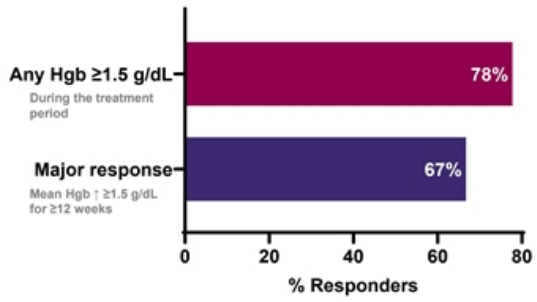
Safety: DISC-0974 demonstrated acceptable safety and tolerability at all evaluated dose levels; most adverse events were deemed not related to DISC-0974, and all adverse events assessed as treatment-related were Grade 1 or 2

nTD: Hemoglobin <10 g/dL and 0 RBC units transfused over 12 weeks at baseline; TD Low: 1-2 RBC units transfused over 12 weeks at baseline; TD High: 3-12 RBC units transfused over 12 weeks at baseline

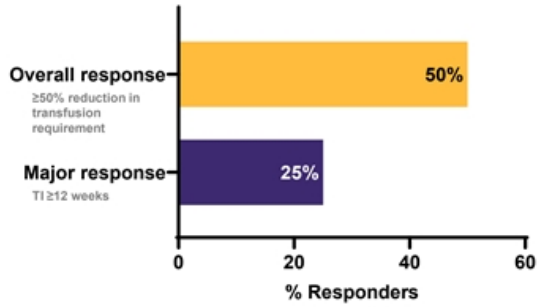
DISC-0974 Anemia of MF Phase 1b Results

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

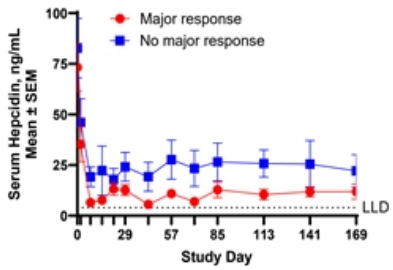
Source: ASH DISC-0974 MF Presentation

DISC-0974 Anemia of MF Phase 1b Results

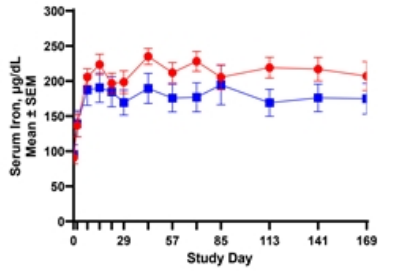
Biomarker analysis – major responders vs non-major responders

- Sustained hepcidin suppression and iron mobilization, consistent with mechanism and previous results
- Also showed sustained reduction in Zinc PPIX, a measure of iron restricted hemoglobin production

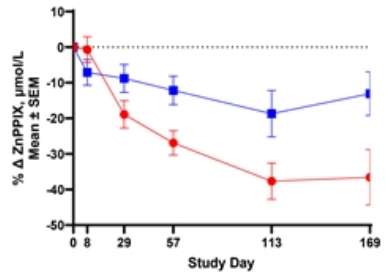
↓ Serum Hepcidin



↑ Serum Iron



↓ Zinc PPIX



Other measures: Major responders treated with DISC-0974 also experienced a 43% and 29% reduction from baseline at Day 113 in erythropoietin and ferritin, respectively

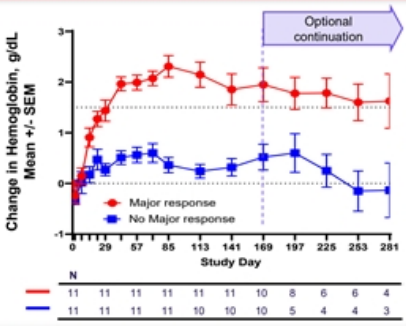
Includes participants dosed at 28-100 mg. Excludes 2 TD High participants considered not evaluable due incomplete data entry at time of data cut. LLD = lower limit of detection. No major response includes participants achieving either minor or no hematologic response.

DISC-0974 Anemia of MF Phase 1b Results

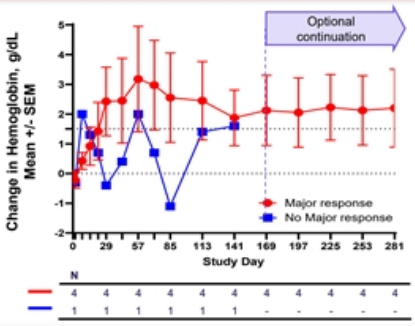
Durability of hematologic response – major responders vs non-major responders

- Anemia response is durable in continuation phase for major responders
- No nTD or TD Low major responders received a transfusion during continuation phase

Hemoglobin Change from Baseline
nTD Participants



Hemoglobin Change from Baseline
TD Low Participants



TD High Participants: 1 of 2 participants with major response entered continuation phase and remained transfusion independent at Day 225 with follow-up ongoing

Includes participants dosed at 28-100 mg. No major response includes participants achieving either minor or no hematologic response

DISC-0974 Anemia of MF Phase 1b Results

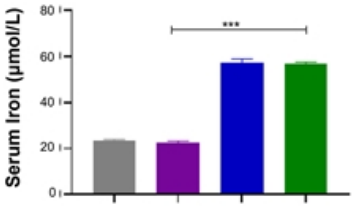
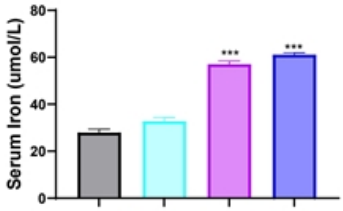
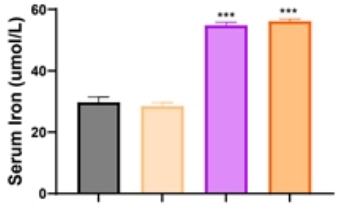
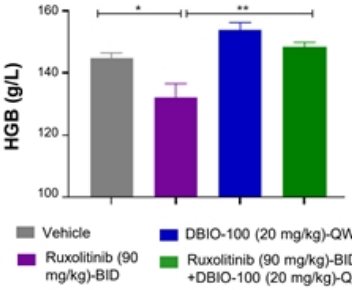
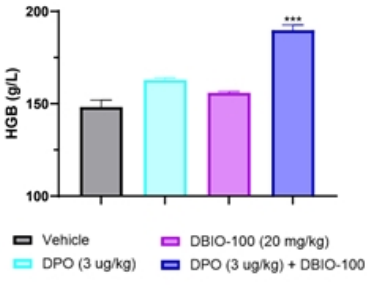
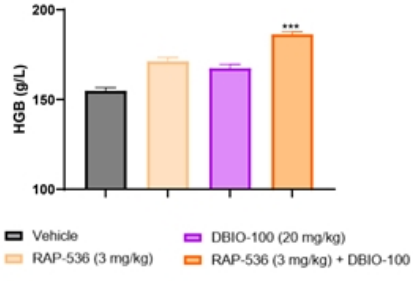
Safety

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.; Source: ASH DISC-0974 MF Presentation

DISC-0974 in Combination Regimens

Wild-type mouse models

	Mouse analog: DISC-0974 + ruxolitinib	Mouse analog: DISC-0974 + ESA	Mouse analog: DISC-0974 + luspatercept
Target Engagement ↓ Hepcidin ↑ Serum Iron			
Hematologic Improvement ↑ Hemoglobin			

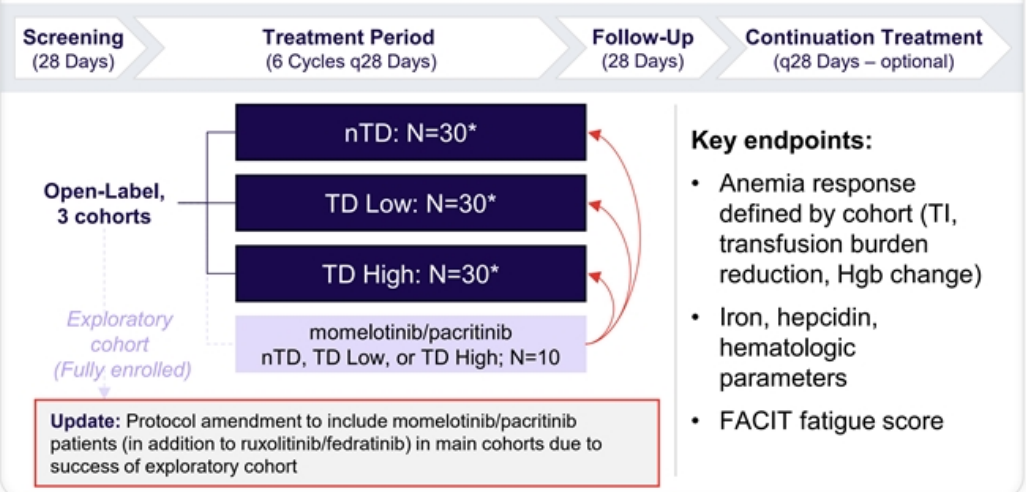
RALLY-MF: Phase 2 Study Overview

RALLY MF

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



Update: Protocol amendment to include momelotinib/pacritinib patients (in addition to ruxolitinib/fedratinib) in main cohorts due to success of exploratory cohort

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. DIPSS = Dynamic International Prognostic Scoring System; FACIT = Functional Assessment of Chronic Illness Therapy; Hgb = hemoglobin; PRBC = packed red blood cells; TI = transfusion independent

MF Anemia Opportunity

Anemia remains a high unmet need within an established field

~22K US addressable MF patients with anemia

Severe Condition

Progressive in nature, with significant impact on prognosis and QoL

Clear Unmet Need

HCPs and patients recognize importance of treating anemia and lack of effective options

Well-Characterized Market

MF expert network and treatment pathway are well-established

Differentiated Product

Aiming to address anemia in any patient on any MF treatment regimen

> *Anemia is a prevalent, severe, and prognostic manifestation of myelofibrosis…we need additional and better therapies"*
>
> *- KOL, Disc Medicine MF Anemia KOL Day*

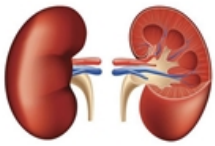
> *There is a dramatic need for this agent…an agent like this can help us maximize [anemia benefit and JAK inhibition] no matter what JAK inhibitor is used"*
>
> *- KOL, Disc Medicine MF Anemia KOL Day*

HCP = healthcare providers; QoL = quality of life

Hepcidin is a Key Driver of CKD Anemia

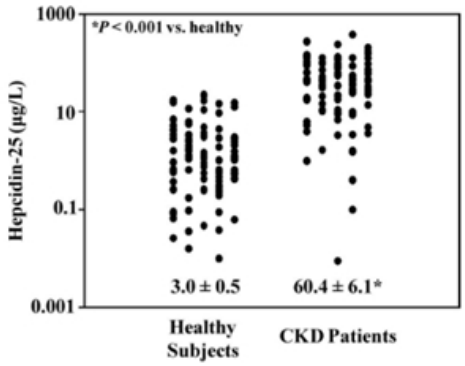
Pervasive issue that is currently highly under-treated

Anemia of CKD



- **Est. # Patients**
  - 5 to 6 million anemic NDD-CKD patients in the US alone
- **Etiology of Anemia**
  - High hepcidin from inflammation & poor renal clearance
  - Compromised erythropoietin production
- **Unmet Medical Needs**
  - Majority patients untreated or under-treated
  - ESAs restricted due to safety and black box
  - Mean Hb 9.3 g/dL in patients initiating dialysis

Hepcidin Levels Elevated in CKD Patients
~20x higher than healthy subjects and increases with disease severity

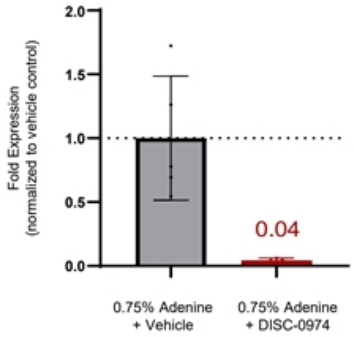


Sources: Troutt et al. (2013), J Clin Lab Analy; Sheetz et al. (2019) Br J Clin Pharmacol. (2019); *from third party; NDD: Non-Dialysis Dependent; DD: Dialysis Dependent

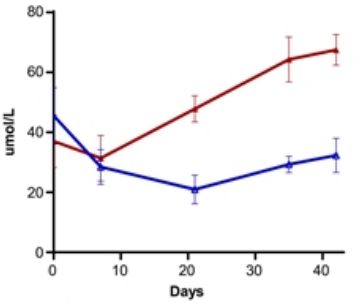
DISC-0974 Improved Anemia in Model of CKD

Rat Model of Adenine Diet-Induced CKD

DISC-0974 Reduced Hepcidin Expression

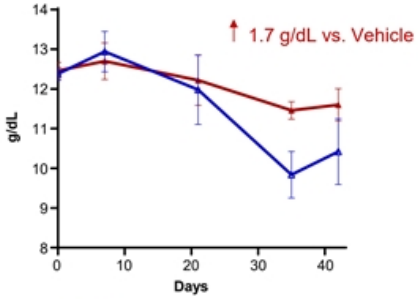


DISC-0974 Increased Serum Iron



Red: 0.75% Adenine + DISC-0974 (20 mg/kg)
Blue: 0.75% Adenine + Vehicle

DISC-0974 Increased Hemoglobin Levels



Red: 0.75% Adenine + DISC-0974 (20 mg/kg)
Blue: 0.75% Adenine + Vehicle

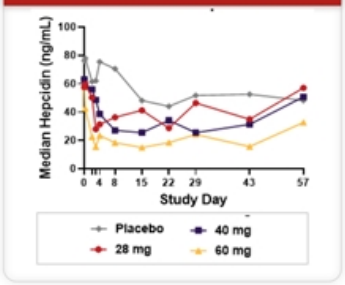
DISC-0974 Anemia of NDD-CKD: Hepcidin, Iron, and Hgb

28 mg, 40 mg, and 60 mg SAD cohorts (ASN 2024)

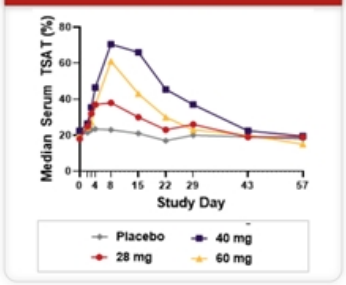
Substantial, durable, dose-dependent reduction in hepcidin and sustained increase in TSAT from baseline

SAD Cohorts

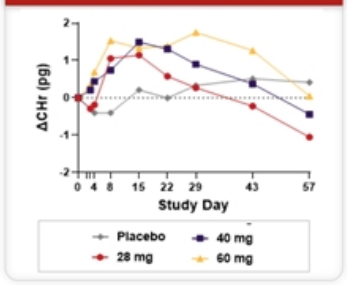
↓ Serum Hepcidin



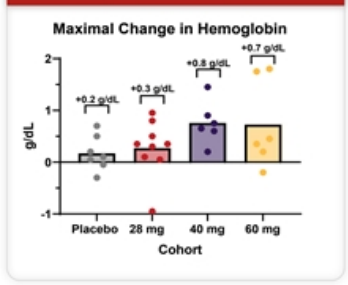
↑ Serum TSAT



↑ 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

- In recently completed Phase 1b study including multiple dose cohorts, DISC-0974 was generally well-tolerated with substantial decreases in hepcidin, increases in iron, and improvements in markers of erythropoiesis; meaningful hemoglobin increases in only a subset of patients, in part driven by those with higher baseline EPO
- Full data to be shared at upcoming 2025 ASN Kidney Week; assessing options for the program based on full analysis of the data

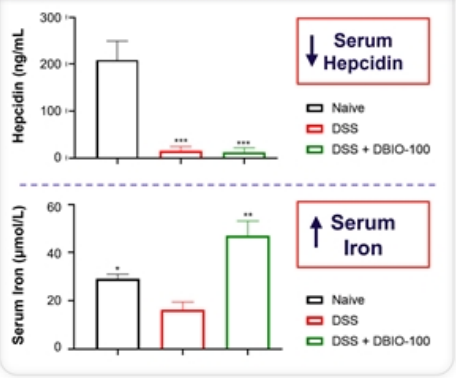
EPO = erythropoietin

DISC-0974 in Other Anemias of Inflammation

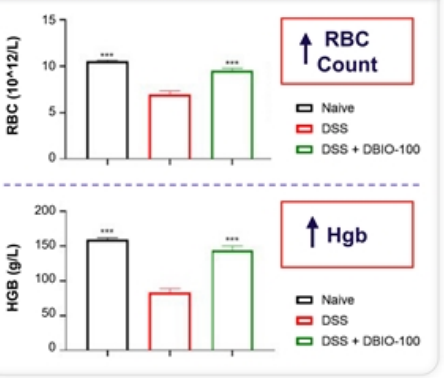
Inflammatory bowel disease mouse model

- 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

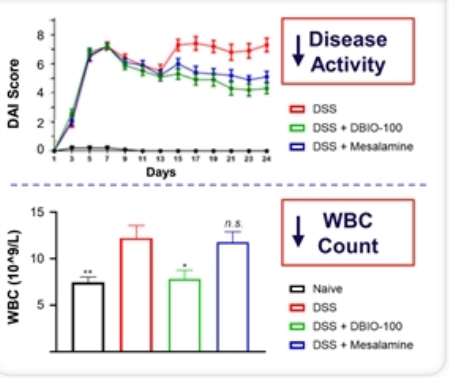
Target Engagement



Hematologic Improvement



IBD Disease Modification



Plan to initiate a Phase 2 study in patients with IBD and anemia in 2026

DAI Score = Disease Activity Index

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



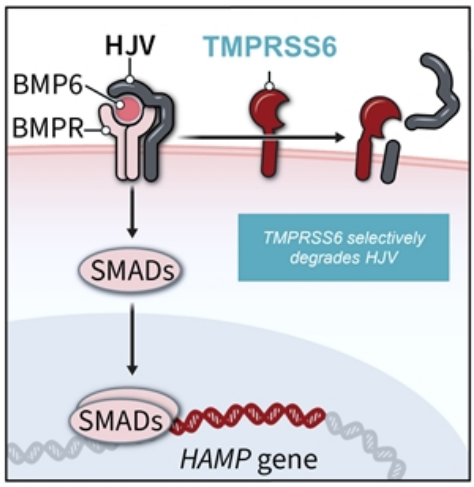
Enables Endogenous Production of Hepcidin

Promotes Iron Restriction
Decreases GI Absorption

Erythrocytosis (PV)
Ineffective Erythropoiesis
Iron Overload

Targeting TMPRSS6 to Increase Hepcidin

Potent, specific target controls endogenous hepcidin production



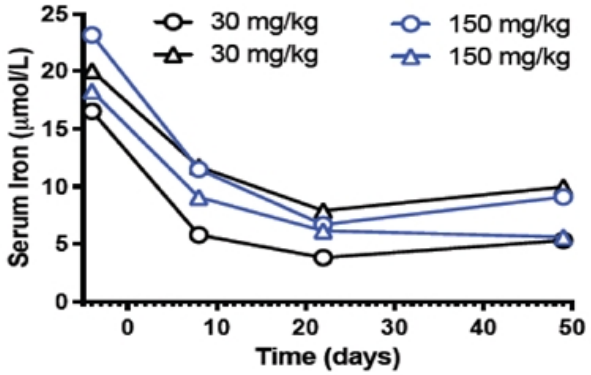
Inhibiting TMPRSS6 with an Antibody Enables Hepcidin Production to Suppress Iron

- **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 Effects in Non-Human Primates

Resulted in deep and sustained suppression of serum iron levels

Single dose of DISC-3405 resulted in ~ 70% suppression of serum iron lasting 3 weeks



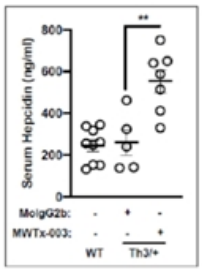
- Potent PD effects observed across multiple preclinical studies consistent with TMPRSS6 inhibition
  - Hepcidin: 3-4 fold induction
  - Serum iron: ~60-70% suppression
- DISC-3405 demonstrated excellent safety profile in non-clinical GLP safety studies

DISC-3405 in Beta Thalassemia and Polycythemia Vera

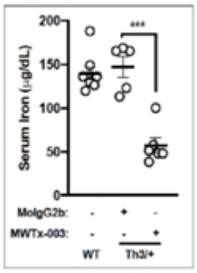
Significant effects on hallmarks of disease

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

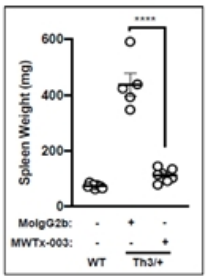
↑ Hepcidin Production



↓ Iron

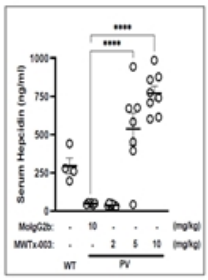


↓ Spleen Weight

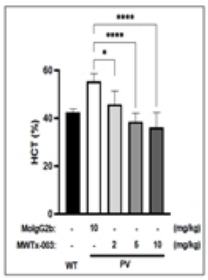


$Jak2^{V617F}$ model of Polycythemia Vera

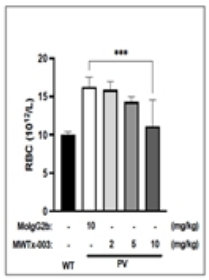
↑ Hepcidin Production



↓ 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

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 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
Initiated October 2023

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

Phase 2 Proof-of-Concept Study in Polycythemia Vera

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

Phase 1b in Sickle Cell Disease

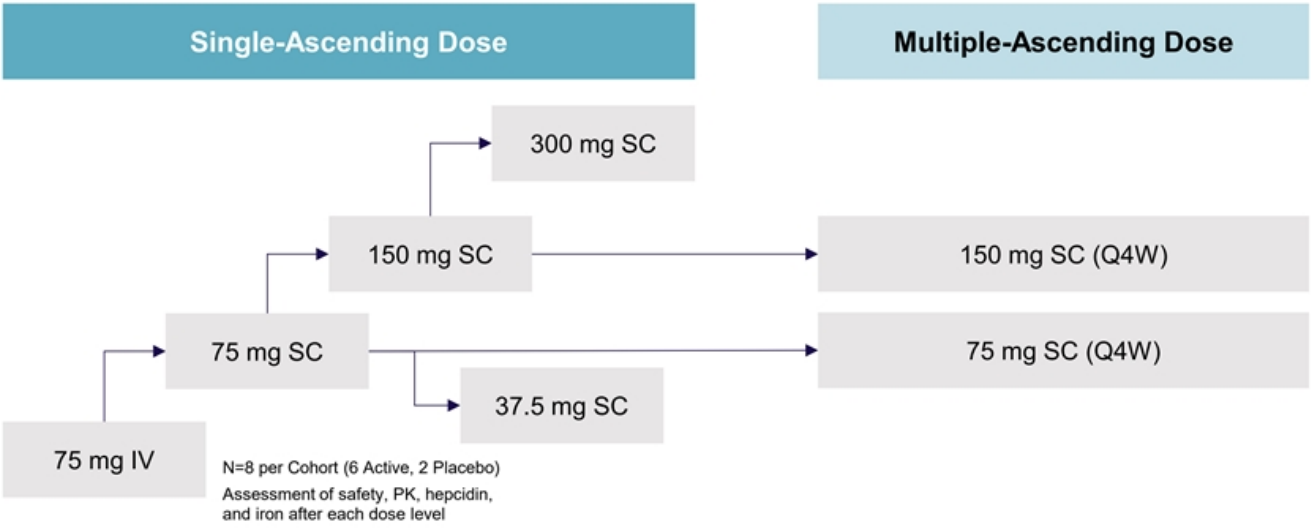
- Mechanistic rationale for iron restriction as a disease-modifying therapy for SCD
- Assess safety, PK, hepcidin, iron, hematologic parameters, hemolysis markers, and exploratory PROs

Exploration of Other Indications

Hereditary Hemochromatosis, Beta-Thalassemia, Myelodysplastic Syndromes

Hct = hematocrit; HV = healthy volunteers

DISC-3405 Phase 1 Healthy Volunteer Study Overview

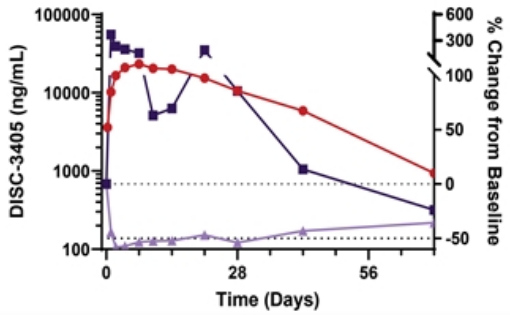


Key Endpoints/Measures: Iron, hepcidin, and other hematologic parameters, safety/tolerability

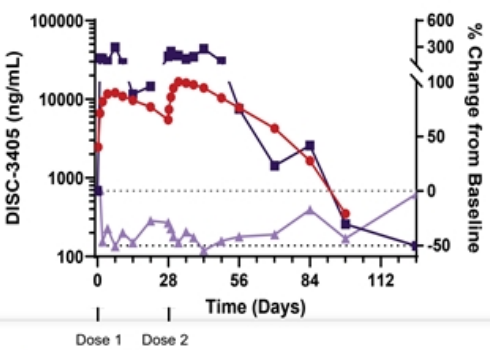
Updated DISC-3405 HV Data: Hepcidin, Iron, and PK

- DISC-3405 produced dose-related increases in serum hepcidin, with corresponding reductions in serum iron across all dose levels
- DISC-3405 resulted in deep reductions in serum iron (ranging from 50-80% from baseline) that were sustained and support a once-monthly SC dosing regimen

PK/PD: 300 mg SC SAD



PK/PD: 150 mg SC MAD



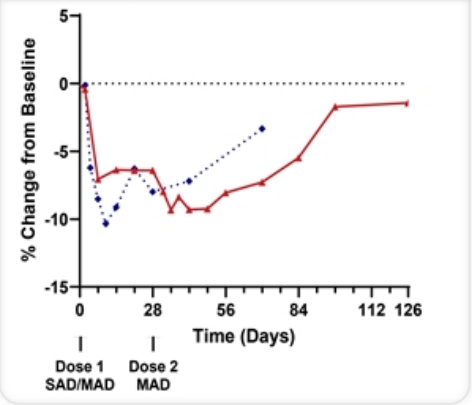
PK Hepcidin Serum Iron

Source: EHA 2025 Poster

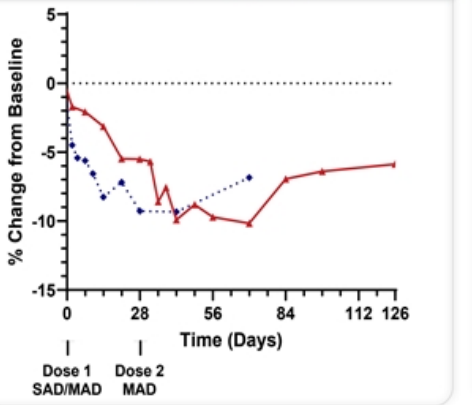
Updated DISC-3405 HV Data: Hematologic Response

- Single and repeat dosing of DISC-3405 demonstrated meaningful reductions in hematologic parameters (reticulocyte hemoglobin, hemoglobin, and hematocrit)

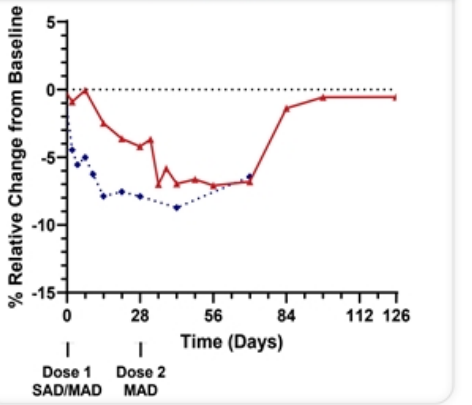
Reticulocyte Hemoglobin



Hemoglobin



Hematocrit



150 SC, MAD 300 SC, SAD

Source: EHA 2025 Poster

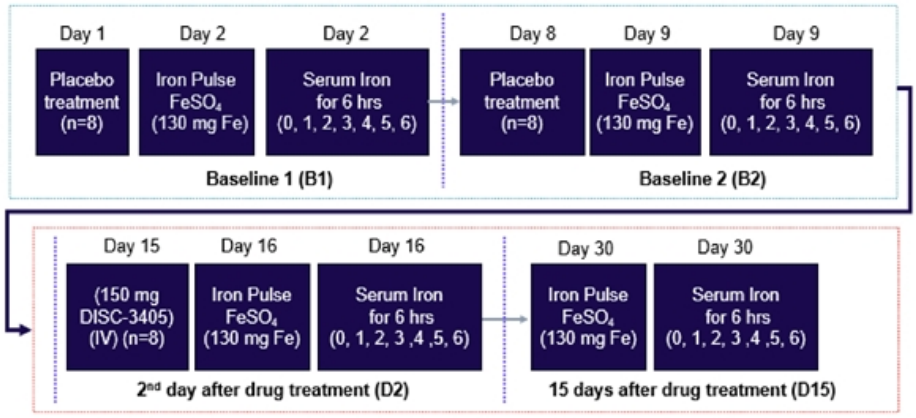
DISC-3405: Iron Pulse Study in Healthy Volunteers

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

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

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

Study Design

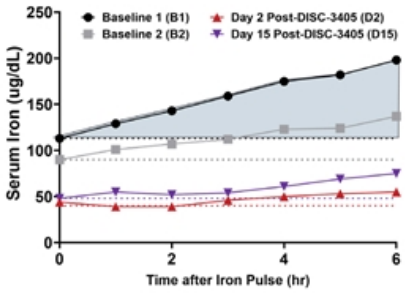


DISC-3405: Iron Pulse Study in Healthy Volunteers

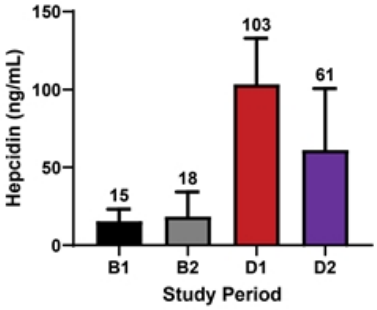
Strong inhibition of iron absorption with DISC-3405

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

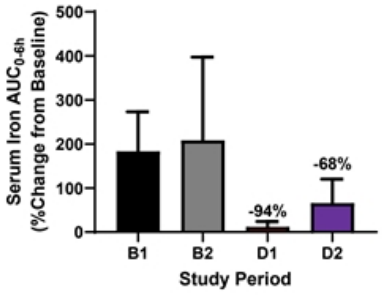
Representative Serum Iron Profiles of One Participant*



Average Hepcidin**



Average Serum Iron**

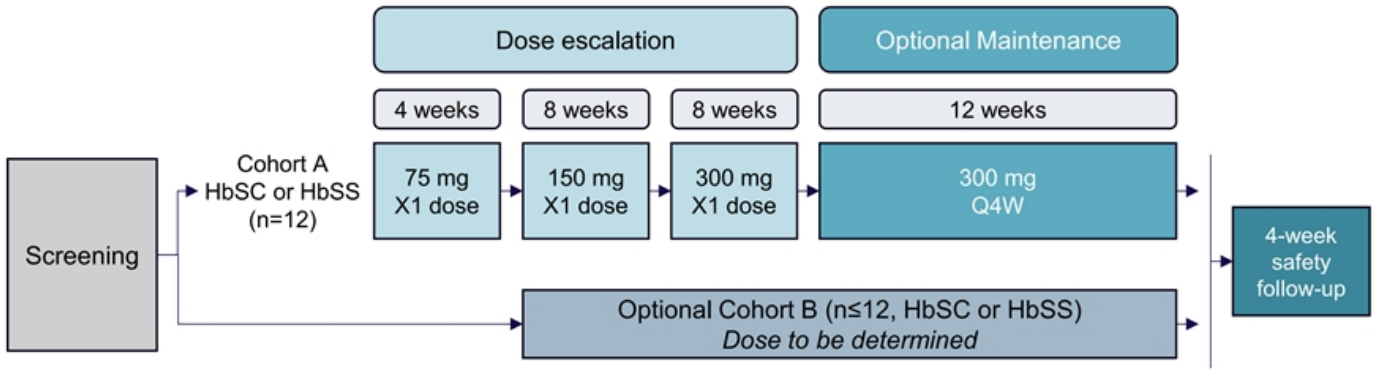


*Each dotted line represents the baseline for each group. AUC_{0-6h} was determined for each group using respective baselines. A shaded example is shown for the B1 group.
**Data presented as mean ± SD. Value above bars are means/mean change from average baseline; Source: EHA 2025 Poster

Sickle Cell Disease Phase 1b Study

Initiation anticipated by year end

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

Summary and Upcoming Objectives and Catalysts

	Summary	Objectives and Catalysts
Bitopertin Heme Synthesis Modulator	• Positive data across two Phase 2 studies and HELIOS data supports the durability of efficacy • Confirmatory APOLLO study initiated in May 2025 • NDA submitted September 29, 2025; CNPV designed to shorten review time to 1-2 months	• Potential approval late 2025-early 2026 • Accelerated commercialization activities
DISC-0974 Hepcidin Suppression	• Positive Phase 1b data in MF anemia with durable anemia responses in continuation phase • RALLY-MF Phase 2 study ongoing • Engaged mechanism in NDD-CKD anemia with variable hemoglobin; assessing options for program	• Initial data from RALLY-MF Phase 2 study in MF anemia • Initiation of Phase 2 study in IBD anemia anticipated in Q1 2026
DISC-3405 Hepcidin Induction	• Proof of mechanism achieved in healthy volunteers; data supportive of monthly SC dosing • Phase 2 PV study initiated • Iron pulse shows potential in iron overload diseases	• Initiation of Phase 1b study in SCD anticipated by end of year • Initial PV data expected in 2026 • Initial SCD data expected in 2026

Thank You

disc medicine