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): June 14, 2024

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 7.01 Regulation FD Disclosure

On June 14, 2024, Disc Medicine, Inc. (the "Company") issued a press release announcing (i) updated analyses of data from its ongoing Phase 2 open-label AURORA and BEACON trials evaluating bitopertin in patients with erythropoietic protoporphyria ("EPP"), (ii) additional data from its ongoing Phase 1b study of DISC-0974 in patients with myelofibrosis ("MF") anemia, and (iii) initial data from single ascending dose ("SAD") cohorts in its ongoing Phase 1 study of DISC-3405 in healthy adult volunteers, all at the European Hematology Association 2024 Congress. The Company will host a live webcast on June 14, 2024 at 8:00 a.m. ET. An archived webcast will be available for 30 days on the events & presentations section of the Company's website. The Company also updated its corporate presentation. Copies of the press release and the Company's updated corporate presentation are attached as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K. 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.

The information contained in Item 7.01 of this Current Report on Form 8-K (including Exhibits 99.1 and 99.2 attached hereto) is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities 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, 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 Exhibits 99.1 and 99.2.

Item 8.01 Other Events.

On June 14, 2024, the Company announced (i) updated analyses of data from its ongoing Phase 2 open-label AURORA and BEACON trials evaluating bitopertin in patients with EPP, (ii) additional data from its ongoing Phase 1b study of DISC-0974 in patients with MF anemia, and (iii) initial data from SAD cohorts in its ongoing Phase 1 study of DISC-3405.

Bitopertin in EPP

The AURORA study is a randomized, double-blind, placebo-controlled Phase 2 clinical trial that enrolled 75 adult subjects with EPP. Subjects were randomized 1:1:1 to receive 20 mg of bitopertin (n=26), 60 mg of bitopertin (n=25), or placebo (n=24) once daily for 17 weeks. Key AURORA data presented include:

- Significant reductions in protoporphyrin IX (PPIX) (40% for the 60 mg group) compared to placebo
- Meaningful improvements on key aspects of EPP
    - Time-dependent improvement in light tolerance that was nominally significant compared to placebo in both the 20 mg (p=0.026) and 60 mg (p=0.013) dose groups
    - ~2x improvement in light tolerance relative to baseline in both 20 mg and 60 mg dose groups as evaluated in a post-hoc longitudinal analysis
    - Substantial, dose-dependent reductions in rate of phototoxic reactions compared to placebo, reaching statistical significance in the 60 mg dose group (75.3% reduction, p=0.011)
    - Dose-dependent improvements in Patient Global Impression of Change (PGIC), which were statistically significant for the 60 mg dose (p=0.022)
- Evaluation of the time course of phototoxic reactions and sunlight exposure showed greater treatment effect in the time period after PPIX nadir was reached, including elimination of observed phototoxic reactions in the 60 mg dose group
- Greater PPIX reductions were associated with improvements in multiple light tolerance measures, including cumulative total time in light, average time in sunlight without pain, change from baseline in time to prodrome, as well as PGIC
- Bitopertin was generally well-tolerated with no reported serious adverse events (SAEs) to date
- Disc also presented the full adult data set from BEACON, which was consistent with previously-presented results and demonstrated similar clinical activity to that observed in AURORA

DISC-0974 in MF

The Phase 1b/2a multi-center, open-label, ascending-dose clinical trial of DISC-0974 is enrolling patients with MF and severe anemia, including both transfusion and non-transfusion dependent patients. In the phase 1b dose-escalation phase, DISC-0974 is administered subcutaneously every 4 weeks for up to 6 treatments. Updated data from 34 patients with an April 29, 2024 cutoff include:

- Substantial and sustained reductions in hepcidin levels and increases in iron were observed in patients for several weeks after each dose
- Strong hematologic response was observed across all patient types at 28-100 mg doses:
  - 68.9% of non-transfusion dependent (nTD) participants demonstrated a hemoglobin response of ≥1.5 g/dL (n=29)
  - 60% of nTD participants who have completed at least 16 weeks of treatment had a mean hemoglobin response of ≥1.5 g/dL above baseline sustained for at least 12 weeks (n=15)
  - One of two evaluable transfusion dependent (TD) participants became transfusion independent (TI) by the end of the trial
  - Hemoglobin response of ≥1.5 g/dL above baseline was achieved in 6 of 10 participants with concomitant JAK inhibitor therapy
  - All evaluable participants with baseline transfusion requirements demonstrated at least a 50% reduction in transfusions over a rolling 8-week window on trial compared to baseline (n=8)
- DISC-0974 was generally well-tolerated at all evaluated dose levels

DISC-3405

Initial data were also presented from the SAD portion of the Phase 1 clinical trial of DISC-3405 in healthy volunteers. In this trial, healthy males and females ages 18 to 65 were given a single dose of placebo (n=10) or DISC-3405 at 75 mg intravenously (IV) (n=6), 37.5 mg subcutaneously (SC) (n=6), 75 mg SC (n=6), 150 mg SC (n=6), or 300 mg SC (n=6). This initial data showed:

- A meaningful dose-dependent increase in hepcidin and corresponding reduction in serum iron across all dose levels
- Mean serum iron reduction in excess of 50% from baseline was achieved in the150- and 300-mg dose groups
- Mean serum iron reduction in excess of 50% was sustained for at least 4 weeks for the 300-mg dose group, with meaningful reduction observed in selective hematological parameters (CHr, hemoglobin, and hematocrit)
- PK/PD profile is supportive of monthly subcutaneous dosing.
- DISC-3405 was generally well-tolerated with no SAEs, AEs higher than Grade 2, or AEs leading to trial withdrawal reported to date

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

Item 9.01. Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by Disc Medicine, Inc. on June 14, 2024, furnished herewith.
99.2	Disc Medicine, Inc. Investor Presentation, furnished 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: June 14, 2024

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

Disc Medicine Presents Positive Clinical Data Across Portfolio at the European Hematology Association (EHA) 2024 Congress

- *Updated analyses of data from AURORA and BEACON studies further demonstrate clinical activity of bitopertin across multiple measures of erythropoietic protoporphyria (EPP) and support development path forward*
- *Additional data from the ongoing Phase 1b trial of DISC-0974 in myelofibrosis (MF) patients continued to demonstrate greater than 60% hematologic response rates, with durable increases in hemoglobin levels and reductions in transfusion burden*
- *Positive data from initial single-ascending dose (SAD) cohorts of a Phase 1 trial of DISC-3405 in healthy volunteers demonstrated sustained, meaningful induction of hepcidin and >50% suppression of mean serum iron*

WATERTOWN, Mass. (June 14, 2024) – 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 announced positive additional data for bitopertin in erythropoietic protoporphyria (EPP), including additional analyses of AURORA data that further demonstrated the clinical activity of bitopertin and highlighted meaningful improvements in light tolerance, phototoxic reactions, and quality of life. Additionally, Disc shared updated data from a Phase 1b trial of DISC-0974 in MF anemia which demonstrated durable increases in hemoglobin and reduced transfusion burden in a majority of evaluable patients. Disc also shared initial SAD data from a Phase 1 healthy volunteer trial of DISC-3405 that provided proof of mechanism, showing that the drug has the potential to provide deep and sustained increases in hepcidin and reductions in iron. The data were presented at the European Hematology Association (EHA) 2024 Congress.

“This has been a tremendously exciting EHA meeting for Disc, where we had the opportunity to present data from ongoing clinical studies across our entire portfolio, showcasing the activity and therapeutic potential of each of our programs,” said John Quisel, J.D., Ph.D., President and Chief Executive Officer of Disc. “At this meeting, we shared a deeper analysis of data from AURORA that underscores our confidence in bitopertin’s potential in EPP and supports a development path forward. We also provided an update from our study of DISC-0974 in anemia of myelofibrosis, which continues to demonstrate promising hematologic activity similar to what we showed at ASH. And, finally, we’re excited to share for the first time, data from our third program, DISC-3405, in healthy volunteers, demonstrating clinical proof-of-mechanism as an iron restriction agent with the potential for a differentiated profile.”

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    - Substantial, dose-dependent reductions in rate of phototoxic reactions compared to placebo, reaching statistical significance in the 60 mg dose group (75.3% reduction, p=0.011)
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- PK/PD profile is supportive of monthly subcutaneous dosing.
- DISC-3405 was generally well-tolerated with no SAEs, AEs higher than Grade 2, or AEs leading to trial withdrawal reported to date

Management will host a call to review the presented data on Friday, June 14th at 8:00 am ET. Please register for the event on the Events and Presentations page of Disc's website (https://ir.discmedicine.com/).

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About Disc Medicine

Disc Medicine 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 Medicine 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 its AURORA Phase 2 and BEACON Phase 2 clinical trials of bitopertin and the results thereof, its Phase 1b/2 clinical trial of DISC-0974 in patients with MF and NDD-CKD patients with anemia, its initial SAD data in its Phase 1 clinical trial of DISC-3405 in healthy volunteers; and projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities. 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 other risks and uncertainties described in the "Risk Factors" section of our Quarterly Report for the quarter ended March 31, 2024, and other documents filed by Disc from time to time with the Securities and Exchange Commission (SEC), as well as discussions of potential risks, uncertainties, and other important factors in Disc's subsequent filings with the SEC. 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
Verge Scientific Communications
prusconi@vergescientific.com

Investor Relations Contact

Christina Tartaglia
Stern Investor Relations
christina.tartaglia@sternir.com

Exhibit 99.2

2024 EHA Management Call

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

June 14, 2024

disc medicine

Disclaimer and FLS

This presentation includes “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. These forward-looking statements include express or implied statements relating to Disc's management team's expectations, hopes, beliefs, intentions or strategies regarding Disc’s expectations with respect to its AURORA Phase 2 and BEACON Phase 2 clinical studies of bitopertin and the results thereof, its Phase 1b/2 clinical studies of DISC-0974 in patients with MF and NDD-CKD patients with anemia, its Phase 1 clinical study of DISC-3405 in healthy volunteers; projected timelines for the initiation and completion of its clinical trials, anticipated timing of release of data, and other clinical activities; Disc’s business plans and objectives; Disc's analysis of market potential for patients with EPP; and Disc’s beliefs about operating expenses and that it will have capital to fund Disc well into 2026. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intends,” “may,” “might,” “plan,” “possible,” “potential,” “predict,” “project,” “should,” “suggest,” “will,” “would” and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. 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. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond Disc's control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are 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 other risks and uncertainties described in our Annual Report on Form 10-K for the year ended December 31, 2022, Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023 and September 30, 2023, and other documents filed by Disc from time to time with the Securities and Exchange Commission. 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.

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Agenda

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

02 **Bitopertin in EPP**
- **Updated AURORA Data**
  Will Savage, MD, PhD, Chief Medical Officer

03 **DISC-0974**
- **Updated Data in Anemia of Myelofibrosis**
  Will Savage, MD, PhD, Chief Medical Officer

04 **DISC-3405**
- **Healthy Volunteer SAD Data**
  Will Savage, MD, PhD, Chief Medical Officer

05 **Closing Remarks**
John Quisel, JD, PhD, Chief Executive Officer

06 **Q&A Session**

Bitopertin: Summary of Phase 2 AURORA and BEACON Data Updates

Additional analysis of AURORA data confirmed bitopertin drug activity and meaningful impact on multiple aspects of EPP. Key findings:

Confirmed drug activity with significant reduction in PPIX, phototoxic reactions, and improved QoL

Time course of phototoxic reactions and sunlight exposure showed **greater treatment effect after PPIX nadir established**

Greater **PPIX reductions associated with improvements in multiple light-tolerance measures**

Generally well tolerated with stable mean hemoglobin levels

DISC-0974: Summary of Updated Data from Phase 1b Study in MF

Updated data from Phase 1b study in MF continued to demonstrate positive impacts on anemia with high response rates. Key findings:

- Substantial **reduction in hepcidin levels and increase in iron levels**
- Positive impact on **hemoglobin and transfusion burden** across a broad range of participants
- **Durable response** in the majority of participants
- **Generally well tolerated** at all evaluated dose levels

DISC-3405: Summary of Healthy Volunteer SAD Data

Single-ascending dose portion of the healthy volunteer study of DISC-3405 demonstrated proof of mechanism. Key findings:

- Substantial **increase in hepcidin levels**
- **Sustained reductions in iron levels; >50% at the highest dose levels**, supportive of SC monthly dosing
- Positive impact on **hematologic parameters** at the highest dose
- **Generally well tolerated** at all evaluated dose levels

SC = subcutaneous

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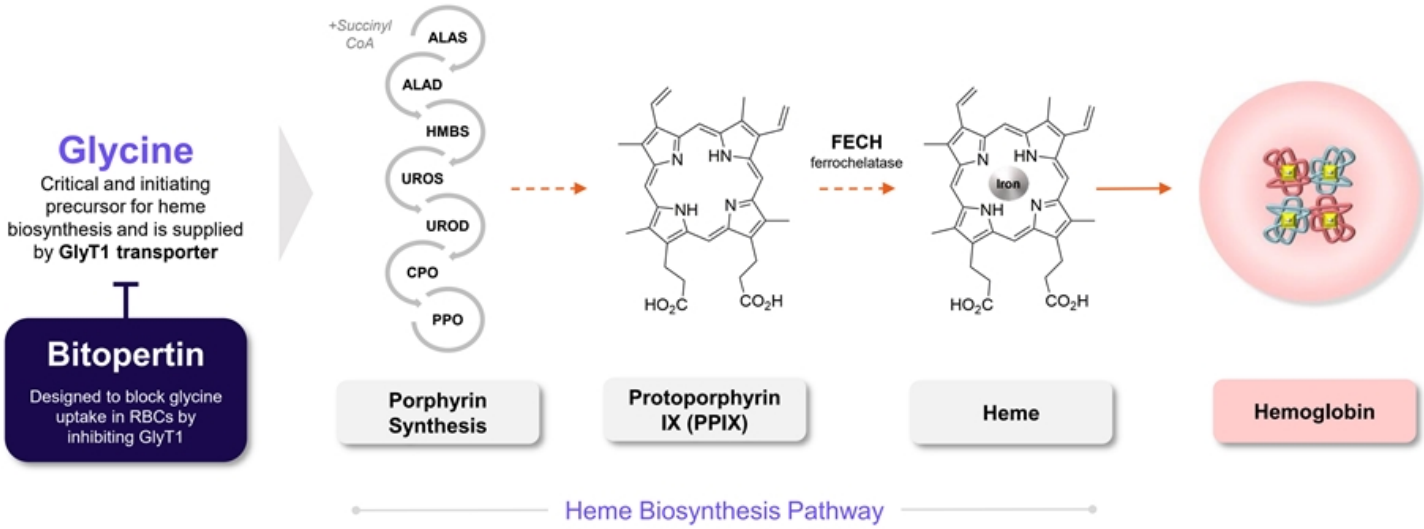
Bitopertin: Investigational Oral, Selective GlyT1 Inhibitor

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



Heme Biosynthesis Pathway

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 phototoxic reactions (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

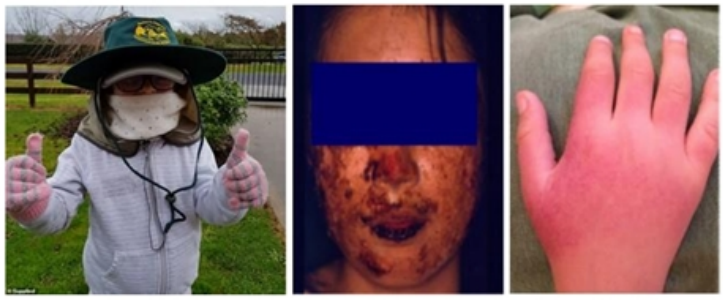


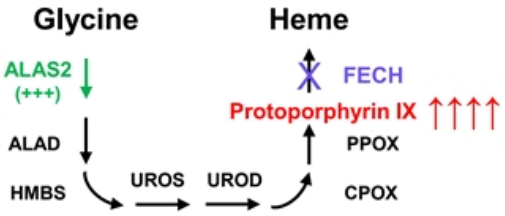
Image sources: *Daily Mail Australia* (2019); FDA Scientific Workshop on EPP (2016); Buonuomo et al. (2014) *Arch Dis Child*

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

Bitopertin: Potential Disease-Modifying Treatment

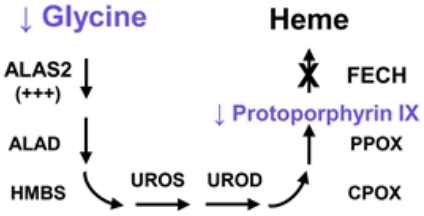
Designed to reduce disease-causing PPIX by limiting uptake of glycine into developing erythrocytes

EPP and XLP Patients
High PPIX Levels



Mutations result in reservoir of pathologically high levels of PPIX

Bitopertin Treatment
Designed to Reduce PPIX Levels



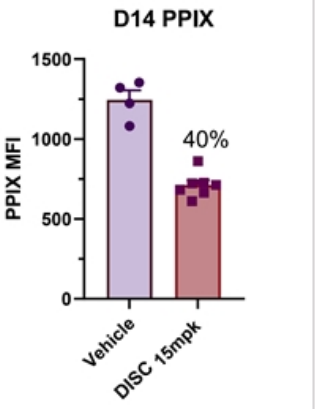
Potential first disease-modifying treatment for EPP and XLP

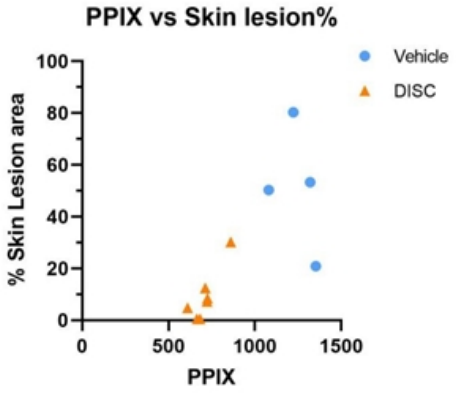
Reductions in PPIX levels of ≥30% reported in literature to have a major impact on photosensitivity in patients

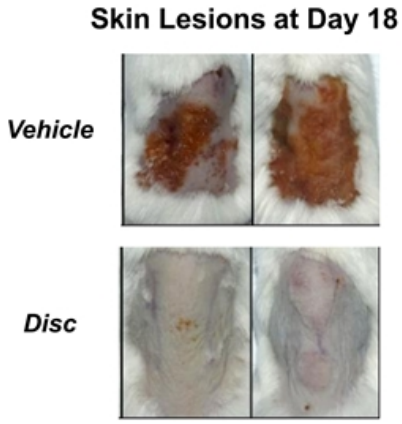
Figures adapted from Halloy et al. (2021) Cell Chem Biol

PPIX in EPP: Phototoxicity in Mice

GlyT1 inhibition significantly ameliorated skin lesions after UV exposure and degree of skin lesion correlated with PPIX levels







Note: Initial study data; EPP mice were dosed with either vehicle (N=4) or DISC (N=7) 15 mpk BID for 18 days; mice were exposed to UV light on Day 14; study measured PPIX, skin lesions, and pain sensitivity; DISC is a research-grade GlyT1 inhibitor; This study was performed with approval from an IACUC. Adequate measures were taken to minimize pain and distress for the animals and still accomplish the objectives for the study.

EPP Phase 2 Development Program
BEACON and AURORA Studies

BEACON

- **EPP and XLP**; N = >22
- **Australia** (study opened July '22)
- **Open-Label, randomized, 24-week study**

AURORA

- **EPP**; N = 75 (fully enrolled)
- **US** (study opened October '22)
- **Double-blind, placebo-controlled, 17-week study**

AURORA Study: Disposition and Baseline Characteristics

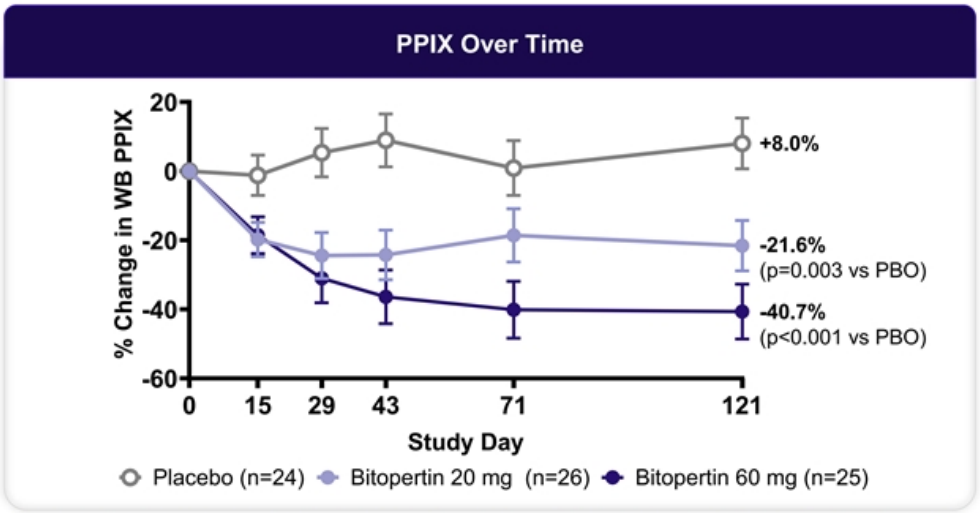
	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Randomized	24	26	25
Completed Study	24	26	22
Discontinued Prior to Day 121	0	0	3
Characteristic			
Mean Age, years	42.3	45.0	47.8
Female, n (%)	12 (50%)	14 (54%)	12 (48%)
White, n (%)	24 (100%)	24 (92%)	24 (96%)
Baseline PPIX, Mean ± SE (ng/mL)	8,691 ± 903	8,155 ± 1,337	10,597 ± 983
Daily Sunlight Exposure (hr), Mean (range)	1.29 (0.18, 3.31)	1.17 (0.26, 4.03)	1.07 (0.04, 2.78)
Time to Prodrome, n (%)			
< 30 min	9 (38%)	9 (35%)	8 (32%)
≥ 30 min	15 (63%)	17 (65%)	17 (68%)

[a] Season that encompasses majority of participant's double-blind treatment period

AURORA Met Primary Endpoint

Statistically significant reductions in whole-blood (WB) metal-free PPIX

- Bitopertin reduced PPIX levels consistent with BEACON, taking ~6-8 weeks to reach max reduction
- Significant reductions observed in both 20 mg and 60 mg doses

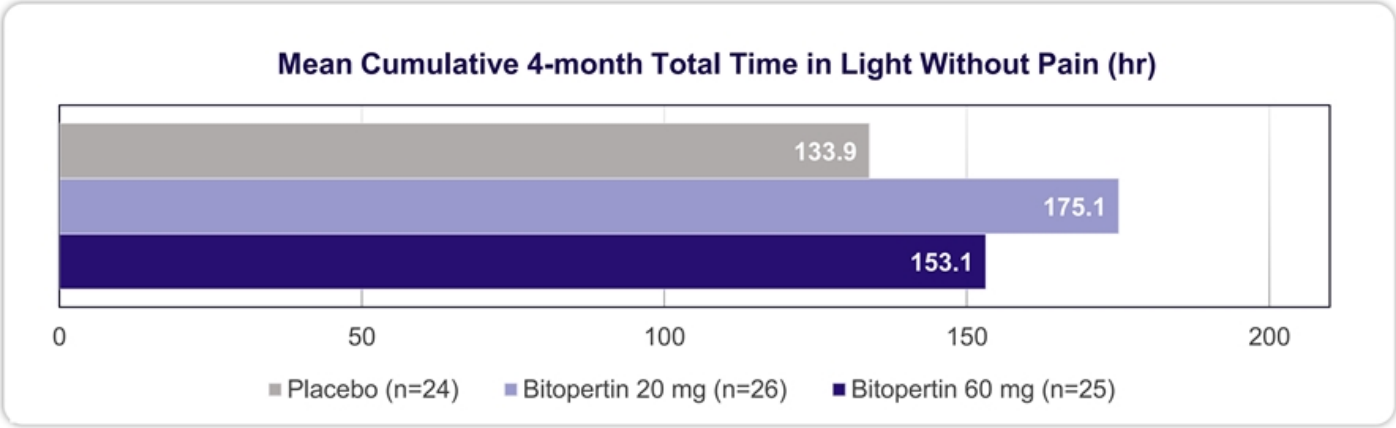


Least-squares means and p-values for percent changes in PPIX analyzed using a mixed model repeated measures (MMRM) to compare 20 mg and 60 mg bitopertin dose groups versus placebo.

Updated AURORA Data: Key Secondary Endpoint

Cumulative time in light without pain

- Bitopertin treatment effect similar to BEACON results
- Did not meet statistical significance due to strong performance of placebo arm

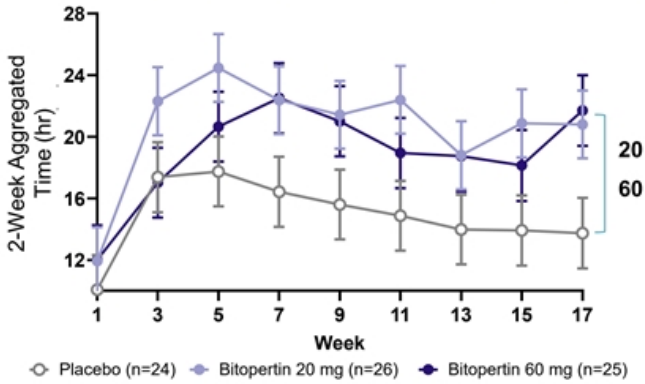


Least-squares means for cumulative time in light measured via daily diary, adding all time in light between the hours of 10:00 am and 6:00 pm on days without any pain, and analyzed using an analysis of variance model to compare 20 mg , 60 mg bitopertin dose groups versus placebo.

Updated AURORA Data: Time in Light Without Pain

Post-hoc longitudinal analysis adjusted for baseline

- Statistically significant improvements in daily time in light compared to placebo
- Meaningful changes in daily time in light relative to baseline



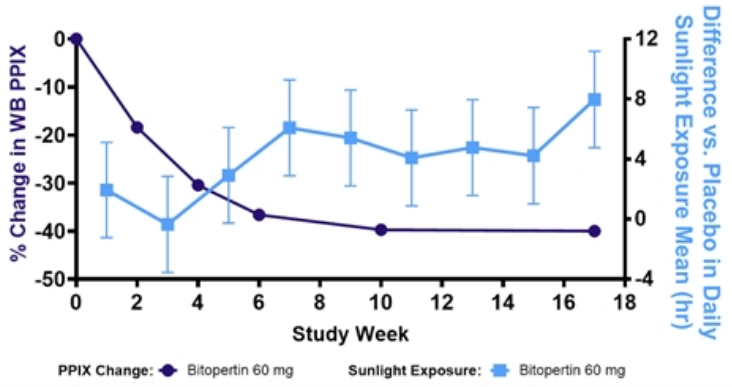
Change from Baseline	
Bitopertin 60 mg (n=25)	2.0x
Bitopertin 20 mg (n=26)	1.9x
Placebo (n=24)	1.1x

Total daily sunlight exposure from 10:00am to 6:00pm on days without pain aggregated over 2-week periods and analyzed using MMRM to compare 20 mg and 60 mg bitopertin dose groups vs placebo. Mean ± SE baseline daily sunlight exposure (hr) during 14-day screening period: 11.1 ± 1.9 for 20 mg, 10.7 ± 1.7 for 60 mg, 12.2 ± 2.1 for placebo.

Updated AURORA Data: Light Tolerance

- Timing of PPIX reduction aligns with the time course of increases in sunlight tolerance

Change in PPIX and Placebo-Corrected Sunlight Exposure for 60 mg Group



Updated AURORA Data: Phototoxic Reactions with Pain

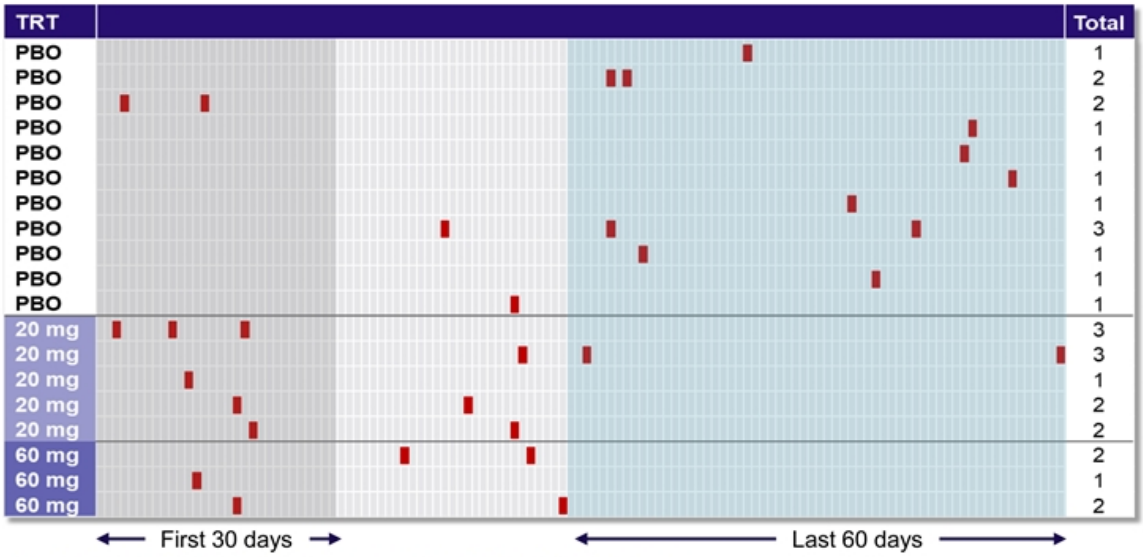
- Dose-dependent reduction in rate of phototoxic reactions with pain, reaching statistical significance in the 60 mg dose group
- Max pain score reduced with bitopertin

Incidence Rate Ratio of New Phototoxic Reactions with Pain vs. Placebo

	Screening (2-4 weeks)		Double-Blind Period (17 weeks)		
	# of New Reactions	# of Participants	# of New Reactions	# of Participants	Median Max Pain Score
Placebo (n=24)	4	2 (8%)	15	11 (46%)	5.0
Bitopertin 20 mg (n=26)	11	8 (31%)	11	5 (19%)	4.0
Bitopertin 60 mg (n=25)	8	6 (24%)	5	3 (12%)	3.5

Updated AURORA Data: Phototoxic Reactions with Pain

- Consistent with profile for PPIX reductions reaching a nadir, time course of phototoxic reactions showed greater bitopertin treatment effect during the last 60 days of study



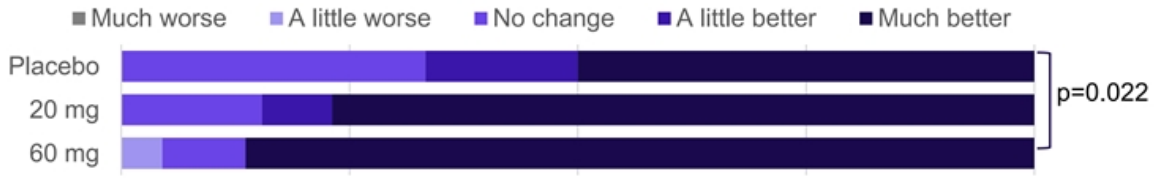
Participants reporting new phototoxic reactions during double-blind period and corresponding study day for new reaction (shown in red)

■ = New Phototoxic Reaction

Updated AURORA Data: Patient-Reported Outcomes

- Dose-dependent improvements in Patient Global Impression of Change (PGIC), reaching statistical significance in the 60 mg dose group at end of study
- Improved PGIC responses are associated with greater reductions in PPIX

PGIC: *"Since the start of the study, how would you rate the change in your EPP?"*



% PPIX Change	PGIC Response				
	Much worse	A little worse	No change	A little better	Much better
N	0	1	14	6	48
Mean (SD)	-	43.8	6.7 (64.9)	-0.4 (15.2)	-25.9 (31.7)

Percentages calculated using data for PGIC from participants who completed the study (D121): n=26 for 20 mg bitopertin, n=22 for 60 mg bitopertin; n=24 for placebo

Updated AURORA Data: PPIX Change and Light Tolerance

- Greater PPIX reductions in bitopertin participants reporting no phototoxic reactions (-36.5%) vs phototoxic reactions (-4.0%)
- PPIX reductions associated with improvements in multiple measures of light tolerance

Tertiles of PPIX Change

PPIX Decreased ← → PPIX Increased

Light Tolerance Measure (Mean ± SD)	Tertile 1 (-88% to -38%)	Tertile 2 (-38% to -7%)	Tertile 3 (-7% to 190%)
Cumulative total time in sunlight without pain (hr)	161.1 ± 142.6	124.5 ± 68.3	117.5 ± 83.2
Average time in sunlight without pain (hr)	1.61 ± 1.32	1.20 ± 0.72	1.16 ± 0.83
Change from baseline in time to prodrome (min)	117.4 ± 148.6	109.4 ± 121.1	64.1 ± 123.8

Tertile 1 = 6 participants at 20 mg, 16 at 60 mg, and 2 on placebo; Tertile 2 = 13 participants at 20 mg, 6 at 60 mg, and 5 on placebo; Tertile 3 = 7 participants at 20 mg, 1 at 60 mg, and 17 at placebo

Safety and Tolerability

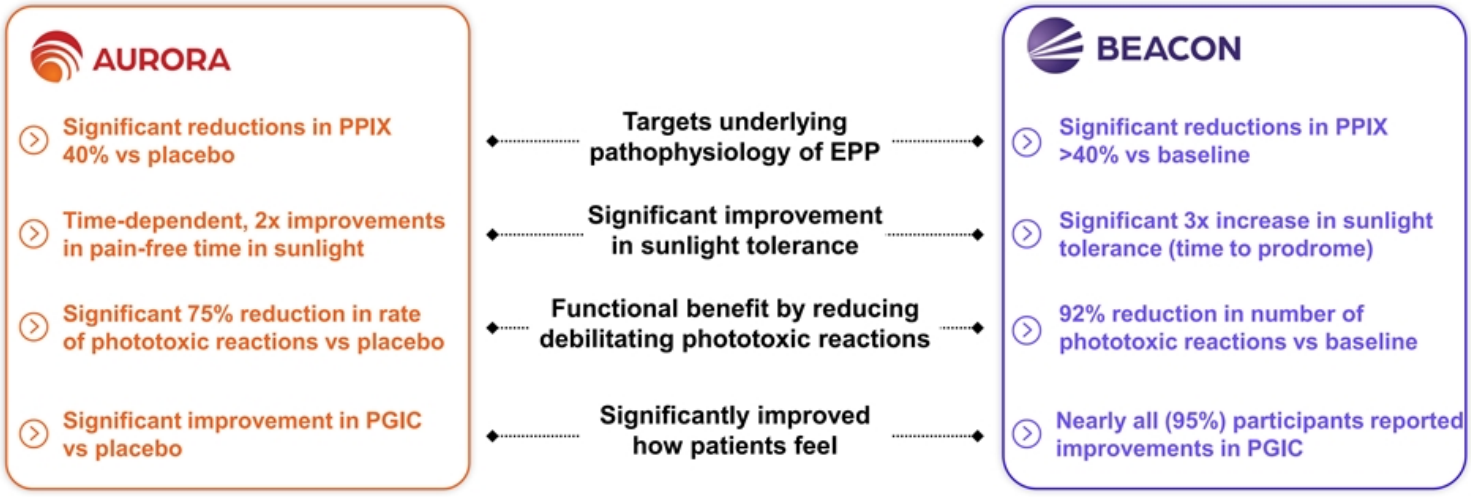
- No serious adverse events reported with bitopertin
- Stable hemoglobin levels
- Favorable safety profile consistent with prior studies enrolling >4000 participants

	Placebo (n=24)	Bitopertin 20 mg (n=26)	Bitopertin 60 mg (n=25)
Participants with any TEAE, n (%)	18 (75%)	20 (77%)	22 (88%)
TEAEs leading to discontinuation, n (%)	0	0	2 (8%)
SAEs, n (%)	1 (4%)	0	0
Common TEAEs			
Dizziness, n (%)	4 (17%)	4 (15%)	11 (44%)
Median Duration (days)	2.0	4.5	5.0
Nausea, n (%)	2 (8%)	1 (4%)	4 (16%)
Alanine aminotransferase increased, n (%)	3 (13%)	1 (4%)	2 (8%)

TEAEs leading to discontinuation: rash and dizziness; common TEAEs include those reported in >5 participants during study regardless of treatment assignment.
SAE = serious adverse event; TEAE = treatment-emergent adverse event

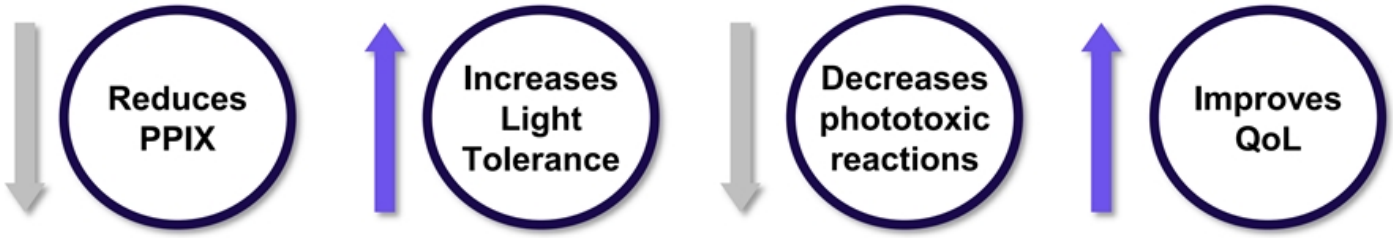
Summary of EPP Bitopertin Data

BEACON and AURORA Studies



Summary of Updated Bitopertin Data

Bitopertin demonstrated meaningful impact on key aspects of EPP



➢ **Next Steps**

- End of Phase 2 meeting in second half of 2024; initiation of a pivotal study in 1H 2025
- Range of available endpoints to bring to regulators that address the placebo effect
  - *Options include*: longitudinal analysis of time in sunlight, phototoxic pain reactions, PPIX, composites of multiple endpoints, and others

Agenda

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

02 **Bitopertin in EPP**
- **Updated AURORA Data**
  Will Savage, MD, PhD, Chief Medical Officer

03 **DISC-0974**
- **Updated Data in Anemia of Myelofibrosis**
  Will Savage, MD, PhD, Chief Medical Officer

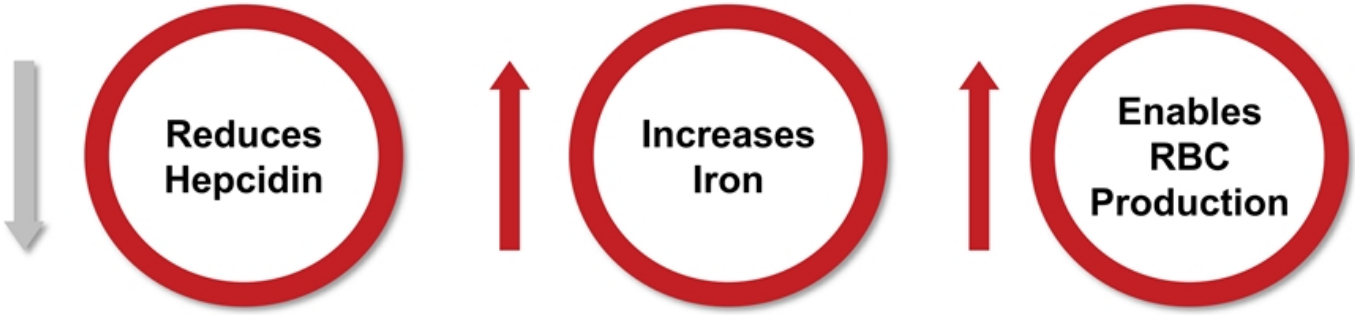
04 **DISC-3405**
- **Healthy Volunteer SAD Data**
  Will Savage, MD, PhD, Chief Medical Officer

05 **Closing Remarks**
John Quisel, JD, PhD, Chief Executive Officer

06 **Q&A Session**

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

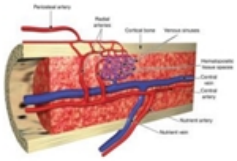
Releases iron stores
Enables GI absorption

Potential to treat wide range of anemias

Hepcidin is a Key Driver of Myelofibrosis (MF) Anemia

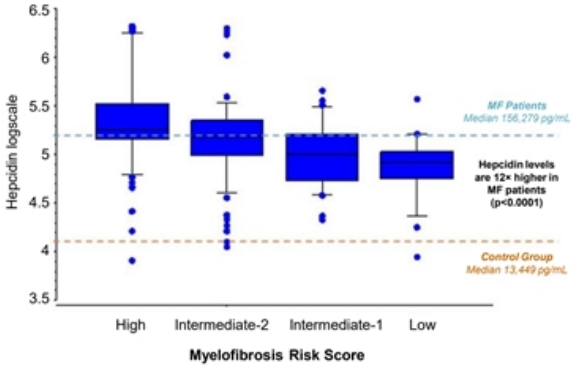
Anemia is severe and prevalent in MF and can limit treatment

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

Updated DISC-0974 MF Data: Baseline and Demographics

Data as of April 29, 2024

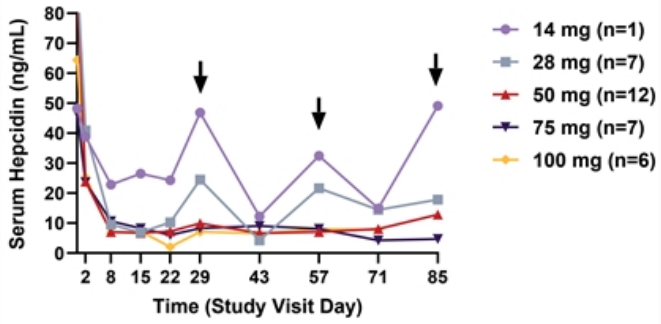
	DISC-0974 14 mg (N=1)	DISC-0974 28 mg (N=7)	DISC-0974 50 mg (N=12)	DISC-0974 75 mg (N=8)	DISC-0974 100 mg (N=6)
Age, median (range), years	70	71 (57, 89)	70.5 (31, 83)	74 (58, 84)	67.5 (53, 79)
Time since MF diagnosis, median (range), years	1	6 (0,18)	2.5 (0,14)	4 (0, 12)	1 (0,2)
Concomitant medication, n (%)					
JAK inhibitor	0	4 (57.1)	5 (41.7)	1 (12.5)	0
Hydroxyurea	1 (100)	0	0	1 (12.5)	0
Transfusion dependent, n (%)*	0	2 (28.6)	1 (8.3)	0	1 (16.7)
Baseline hepcidin, median (range), ng/mL	48.2	93.3 (21.4, 171.1)	90.2 (8.7, 155.7)	46.6 (23.7, 188.2)	64.4 (11.5, 374.7)
Baseline hemoglobin, median (range), g/dL	8.2	8.4 (6.8, 9.3)	8.6 (6.1, 10.3)	8.9 (6.7, 9.9)	8.2 (5.5, 9.4)

Defined as an RBC transfusion frequency of ≥6 units PRBC over the 84 days immediately prior to Screening. There must not be any consecutive 42-day period without an RBC transfusion in the 84-day period, and the last transfusion must be within 28 days prior to Screening. One participant treated with 28 mg discontinued DISC-0974 early due to physician decision. JAK = Janus kinase. Baseline is defined as: (1) Participants transfused within 84 days of screening; (1.a) transfusion dependent then use lowest hemoglobin level recorded in the 84 days before screening initiation (one reading). (1.b) Non-transfusion dependent then {1.b.i} participants transfused within 30 days before screening use the lowest pre-transfusion hemoglobin level (one reading). {1.b.ii} participants transfused within 84 days but not within the month before screening use average of the pre-transfusion hemoglobin level, screening hemoglobin level, and Day -1 level (3 readings); (2) Participants not transfused within 84 days of Screening use Screening and Day -1 average

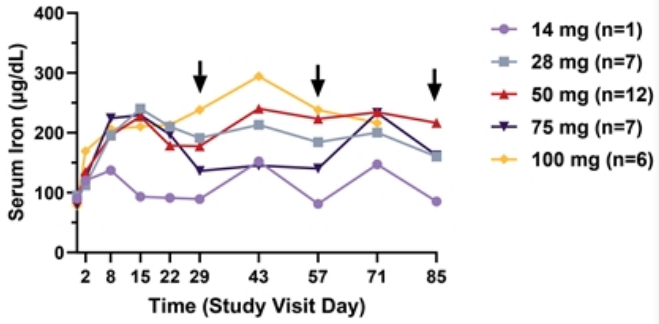
Updated DISC-0974 Anemia of MF Data: Hepcidin and Iron

- DISC-0974 demonstrated decreases in hepcidin and increases in serum iron
- Impact was consistent across all treated participants

Median Serum Hepcidin



Median Serum Iron

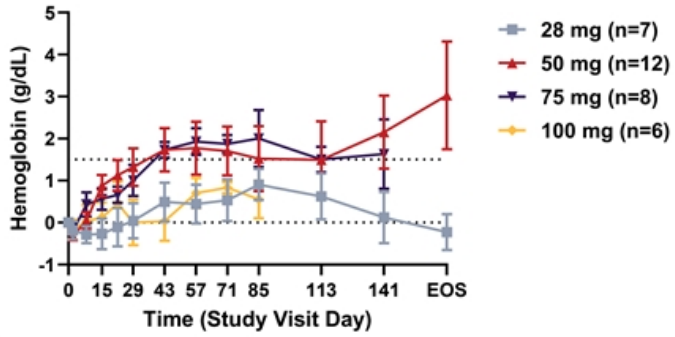


Arrows represent dosing days

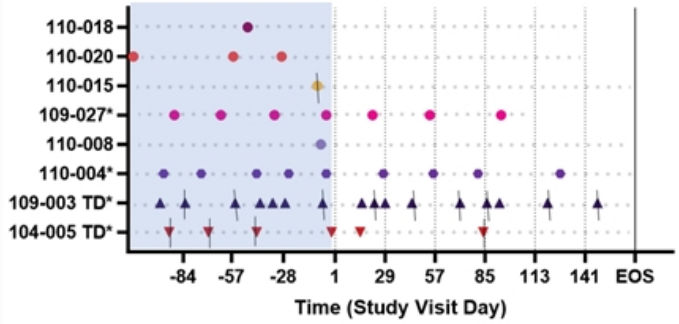
Updated DISC-0974 Anemia of MF Data: Hematologic Response

- DISC-0974 demonstrated sustained increases in hemoglobin across dose groups
- All evaluable participants with baseline transfusion requirement had at least a 50% reduction in transfusions over a rolling 8-week window on study compared to baseline

Hemoglobin Increase from Baseline in All Patients



Transfusion Frequency Over Time[1]

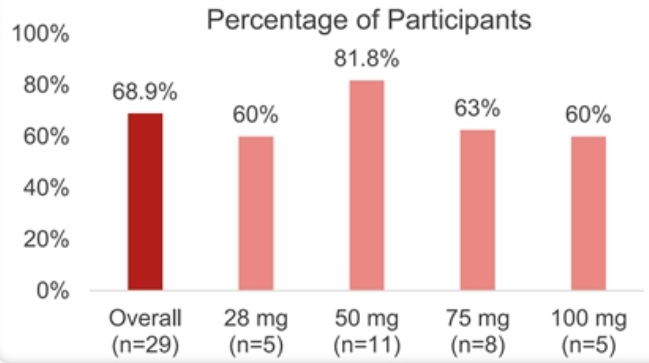


[1]Transfusion frequency of participants with baseline transfusion requirement and at least 12-weeks of follow up. I indicates 2 units transfused; all other transfusions are 1 unit. One of 2 evaluable TD participants (104-005) achieved a TI per Gale criteria. * denotes concomitant MF-directed therapy. EOS = end of study; TD = transfusion dependent; TI = transfusion independent.

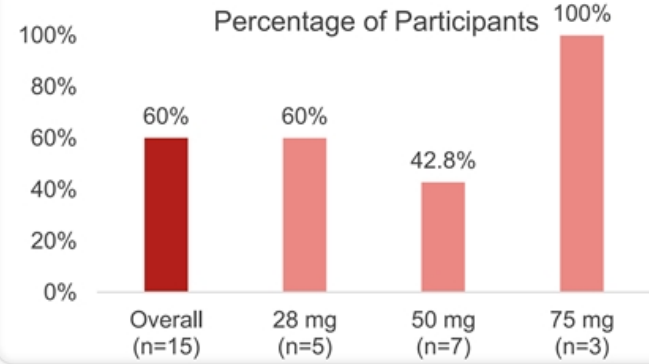
Updated DISC-0974 Anemia of MF Data: Hemoglobin Response in NTD Participants

- Hemoglobin responses of ≥1.5 g/dL increase were achieved in 68.9% of NTD participants
- For participants who have completed at least 16 weeks of the study, 60% of NTD had a mean hemoglobin response of 1.5 g/dL above baseline sustained for at least 12-weeks

NTD Participants with Hgb Δ ≥1.5 g/dL



NTD Participants with Hgb Δ ≥1.5 g/dL for ≥12 Weeks[1]



[1]Percent of non-transfusion dependent participants with mean hemoglobin ≥ 1.5 g/dL above baseline for at least 12 weeks (minimum of 16 week follow up required for inclusion and maximal follow up of 169 days). NTD = non-transfusion dependent; Hemoglobin response was achieved in 62.5% of participants on concomitant JAKi and 71.4% in those not on concomitant JAKi

Updated DISC-0974 Anemia of MF Data: Safety

- Generally well tolerated at all evaluated dose levels

Adverse events at least possibly related to DISC-0974	14 mg (N=1)	28 mg (N=7)	50 mg (N=12)	75 mg (N=8)	100 mg (N=6)
Participants with event (n)	**0**	**3**	**5**	**1**	**1**
Diarrhea	0	1	2	1	0
Injection site bruising	0	1*	0	0	0
Pyrexia	0	1*	0	0	0
Blood bilirubin increased	0	0	0	0	1
Platelet count decreased	0	0	1*	0	0
Anemia	0	0	1*	0	0
Urinary tract infection	0	1*	0	0	0
Headache	0	0	1	0	0
Hot flush	0	0	1	0	0

AE = adverse event; JAKi = Janus kinase inhibitor
Grade 3 AEs include headache reported in 1 participant treated at 28 mg (unlikely related to DISC-0974) and Grade 3 anemia reported in 2 participants treated at 28 mg and 4 participants treated at 50 mg (one at 50 mg was deemed related to DISC-0974; all others were deemed not related). Serious AE: Grade 2 arthralgia was reported in 1 participant treated at 28 mg (not related to DISC-0974). There were no ≥ Grade 4 AEs reported. Liver iron concentration was obtained at baseline and end of study; for available participants (n=10), median change from baseline was 0.3 mg/g dry weight, range (-0.5 to 16.2). * indicates AE in a participant receiving concomitant JAKi therapy.

Summary of Updated DISC-0974 MF Data

Decreased hepcidin & increased iron

68.9% of NTD pts had Hgb response ≥1.5g/dL

60% of NTD pts had Hgb response sustained for ≥12 weeks*

100% of pts with baseline transfusions had ≥50% reduction

1 of 2 TD pts reached TI

Generally well tolerated

*for participants who have completed at least 16 weeks on study

Summary of DISC-0974 in MF Anemia

DISC-0974 demonstrated improved hemoglobin response and transfusion burden in MF

➢ **Next Steps**

- End of Phase 1b meeting with regulators in H2 2024
- Initiation of Phase 2 study by the end of 2024

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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 Development Plans

Phase 1 in healthy volunteers ongoing; aim to advance program into POC studies with focus on polycythemia vera

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

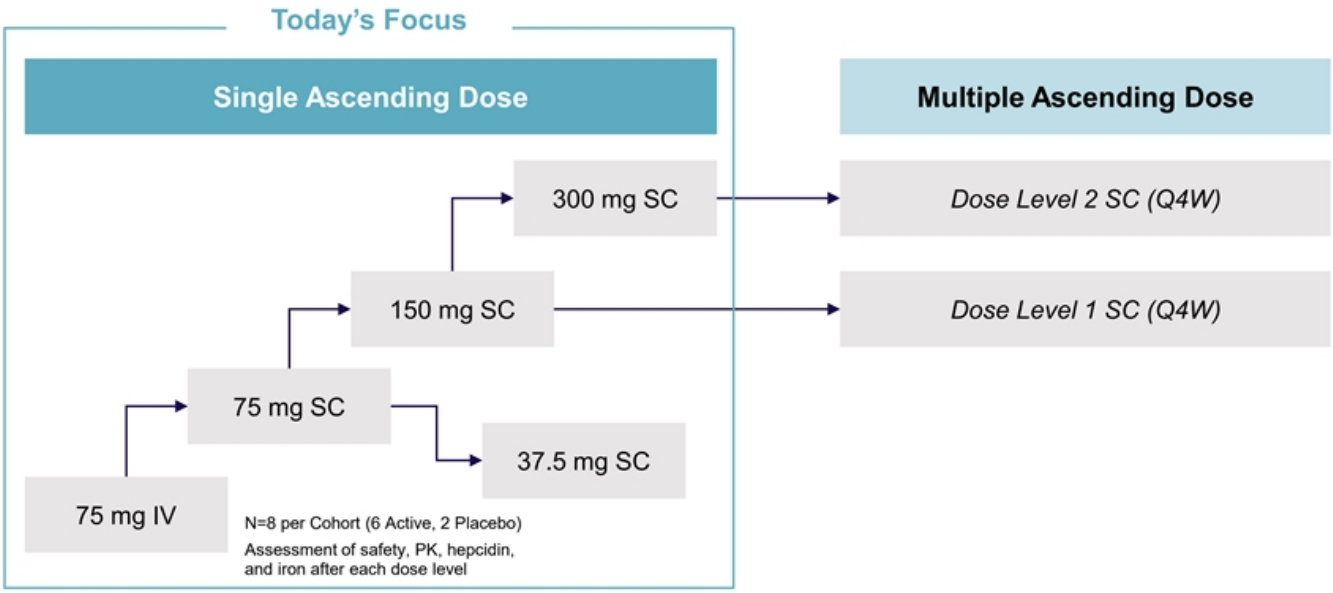
- Strong proof of therapeutic hypothesis; clarity on regulatory development path
- Assess safety, PK, hepcidin, iron, hematologic parameters; % Hct and requirement for phlebotomy

Additional POC Studies in a Range of Indications

- Hereditary Hemochromatosis
- Beta-Thalassemia
- Myelodysplastic Syndromes

Hct = hematocrit; HV = healthy volunteers

DISC-3405 Phase 1 Healthy Volunteers Study Overview



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

DISC-3405 Phase 1 Healthy Volunteer SAD: Baseline and Demographics

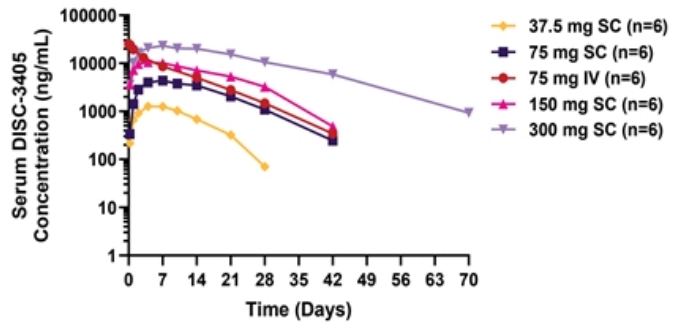
Characteristic	Placebo n = 10	37.5 mg SC n = 6	75 mg IV n = 6	75 mg SC n = 6	150 mg SC n = 6	300 mg SC n = 6
Age, years	48.6 (39-62)	52.7 (42-64)	36.8 (23, 49)	57.3 (49, 61)	44.0 (25, 57)	34.0 (22, 38)
Gender, Female, n (%)	2 (20)	5 (83.3)	3 (50.0)	4 (66.7)	2 (33.3)	0 (0)
Hepcidin, ng/mL	14.1 (5.2, 28.8)	41.7 (6.1, 177.2)	19.4 (2.0, 36.6)	32.6 (7.2, 69.8)	15.2 (8.7, 20.2)	18.7 (8.6, 45.0)
Serum Iron, ug/dL	97.2 (50, 180)	88.7 (43, 127)	99.2 (74, 127)	95.7 (67, 137)	85.7 (43, 138)	106.2 (54, 135)
Hemoglobin, g/dL	14.9 (13.1, 16.0)	13.2 (10.7, 17.7)	13.8 (12.1, 15.6)	13.8 (12.7, 16.0)	14.2 (13.0, 14.9)	15.4 (14.4, 16.7)
Hematocrit, %	43.6 (38.9, 47.1)	39.7 (34.3, 50.2)	41.5 (37.1, 45.5)	41.0 (38.7, 45.0)	42.3 (39.4, 46.2)	45.2 (42.3, 48.2)
RBC, 10^{12}/L	4.9 (4.2, 5.8)	4.5 (3.9, 5.7)	4.6 (3.8, 5.2)	4.5 (4.2, 5.0)	4.7 (3.9, 5.1)	5.1 (4.8, 5.8)

IV = intravenous; RBC = red blood cell; SC = subcutaneous

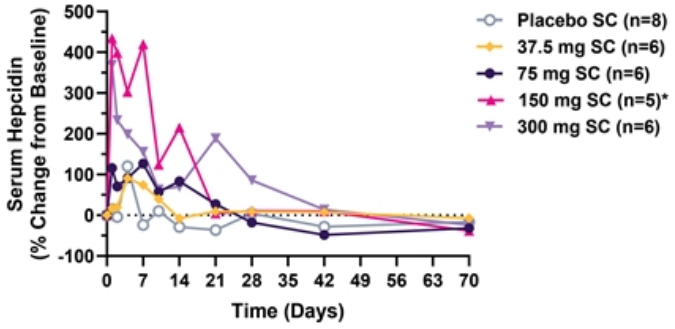
Initial DISC-3405 HV Data: PK and Hepcidin

- Dose-dependent PK profiles
- DISC-3405 demonstrated dose-related hepcidin increases

Pharmacokinetics



Mean Change from Baseline in Serum Hepcidin

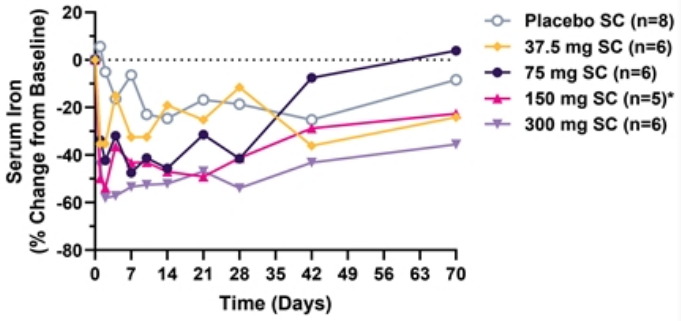


*One participant randomized to 150 mg SC was excluded from PD analysis due to history of anemia and recent hemorrhoidal bleeding, not disclosed prior to enrollment, deeming the participant ineligible; data as of 19 April 2024

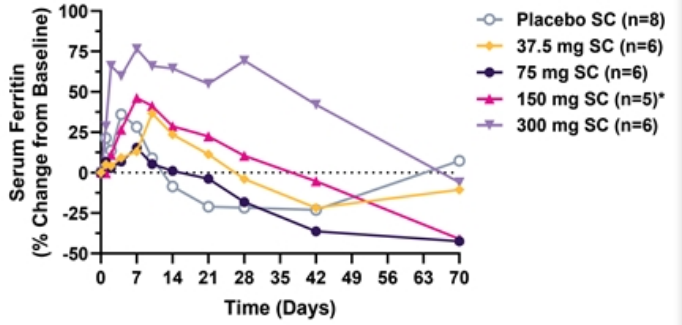
Initial DISC-3405 HV Data: Iron Parameters

- Mean serum iron reduction of more than 50% from baseline was achieved for both 150- and 300-mg doses
- Serum iron reductions were sustained for at least 4 weeks, supportive of monthly SC dosing

Mean Change from Baseline in Serum Iron



Mean Change from Baseline in Serum Ferritin

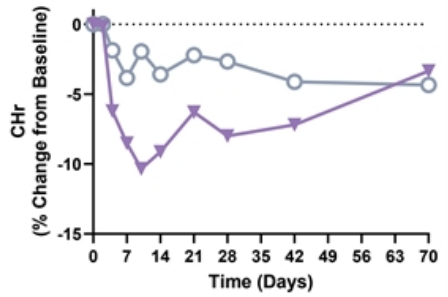


*One participant randomized to 150 mg SC was excluded from PD analysis due to history of anemia and recent hemorrhoidal bleeding, not disclosed prior to enrollment, deeming the participant ineligible; SC = subcutaneous

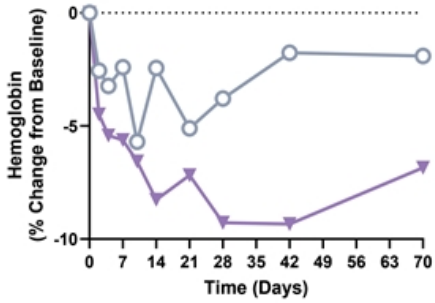
Initial DISC-3405 HV Data: Hematologic Response

- A single 300-mg dose of DISC-3405 demonstrated meaningful reductions in hematologic parameters (reticulocyte hemoglobin, hemoglobin, and hematocrit)

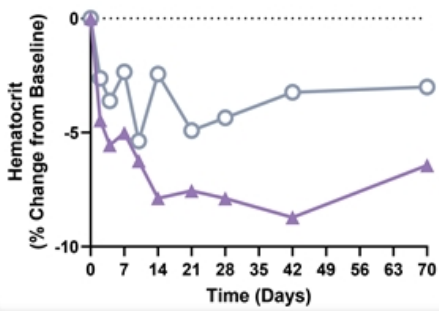
Reticulocyte Hemoglobin (300 mg)



Hemoglobin (300 mg)



Hematocrit (300 mg)



300 mg SC (n=6) Placebo SC (n=8)

CHr = reticulocyte hemoglobin; SC = subcutaneous

Initial DISC-3405 HV Data: Safety

- Generally well tolerated at all evaluated dose levels; no serious AEs, > Grade 2 AEs, or AEs leading to study withdrawal were reported

Adverse Event	Placebo n = 10	37.5 mg SC n = 6	75 mg IV n = 6	75 mg SC n = 6	150 mg SC n = 6	300 mg SC n = 6
Sore Throat	0	0	1	0	0	0
Nausea	0	1	0	1	0	0
Headache	1	1*	0	0	0	0
Cough	0	0	0	0	1	0
Rhinorrhea	0	0	0	0	1	0
Lightheadedness	0	0	0	1	0	0
Increased ALT	0	0	0	0	1*	0
Increased AST	0	0	0	0	1*	0

*Grade 2 AEs; one participant reported a self-limited headache; one participant observed to have isolated, self-limited elevations of AST and ALT.

Summary of Phase 1 Healthy Volunteer SAD Data

- Single-dose SC administration of DISC-3405 demonstrated dose-dependent increases in hepcidin and corresponding reductions in serum iron levels across all dose levels
- >50% reductions in mean serum iron were observed in patients that received 150 mg and 300 mg doses
- PK/PD profile is supportive of monthly subcutaneous dosing in polycythemia vera and iron overload conditions
- DISC-3405 was well tolerated
- **Next Steps**: Phase 1 multiple-ascending dose (MAD) data expected by EOY; initiation of a Phase 2 study in PV expected in 1H 2025

Agenda

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

02 **Bitopertin in EPP**
- **Updated AURORA Data**
  Will Savage, MD, PhD, Chief Medical Officer

03 **DISC-0974**
- **Updated Data in Anemia of Myelofibrosis**
  Will Savage, MD, PhD, Chief Medical Officer

04 **DISC-3405**
- **Healthy Volunteer SAD Data**
  Will Savage, MD, PhD, Chief Medical Officer

05 **Closing Remarks**
John Quisel, JD, PhD, Chief Executive Officer

06 **Q&A Session**

Summary of EHA Data

Bitopertin
Heme Synthesis Modulator

- Meaningful improvements on key aspects of EPP consistent across studies
  - Significant reduction in PPIX
  - 2x improvement in light tolerance
  - Significant reduction in phototoxic reactions and improvement in QoL
- Range of viable endpoints that could be brought to regulators

DISC-0974
Hepcidin Suppression

- Decreased hepcidin and increased iron sustained for several weeks
- Durably increased hemoglobin
- Reduced transfusion burden
- Generally well tolerated

DISC-3405
Hepcidin Induction

- Increased hepcidin and reduced serum iron across all dose levels
- Serum iron reduction of more than 50% from baseline at top doses
- Supportive of SC monthly dosing
- Generally well tolerated

Projected Upcoming Milestones and Events

Multiple additional data catalysts anticipated through the rest of the year

Program	Indication	H1 2024	H2 2024	2025
Bitopertin Heme Synthesis Modulator	**Erythropoietic Porphyrias (EPP and XLP)**	• Phase 2 AURORA Data (March-April)	• End of Ph 2 Meeting / Other Regulatory Interaction	• Phase 3 Initiation Pending Regulatory Feedback
	Diamond-Blackfan Anemia (DBA)		• Initial Phase 2 Data	
DISC-0974 Hepcidin Suppression	**Anemia of Myelofibrosis (MF)**	• Updated Phase 1b Data	• Final Phase 1b Data • Initiate Phase 2 Study	• Phase 2 Topline Data
	Anemia of Chronic Kidney Disease (CKD)		• Phase 1b Data (hemoglobin)	• Phase 2a Topline Data
DISC-3405 Hepcidin Induction	**Polycythemia Vera and Diseases of Iron Overload/ Ineffective Erythropoiesis**	• Phase 1 SAD Data	• Phase 1 SAD/MAD Data	• Phase 2 in PV Initiation

SAD = single ascending dose; MAD = multiple ascending dose; PV = polycythemia vera

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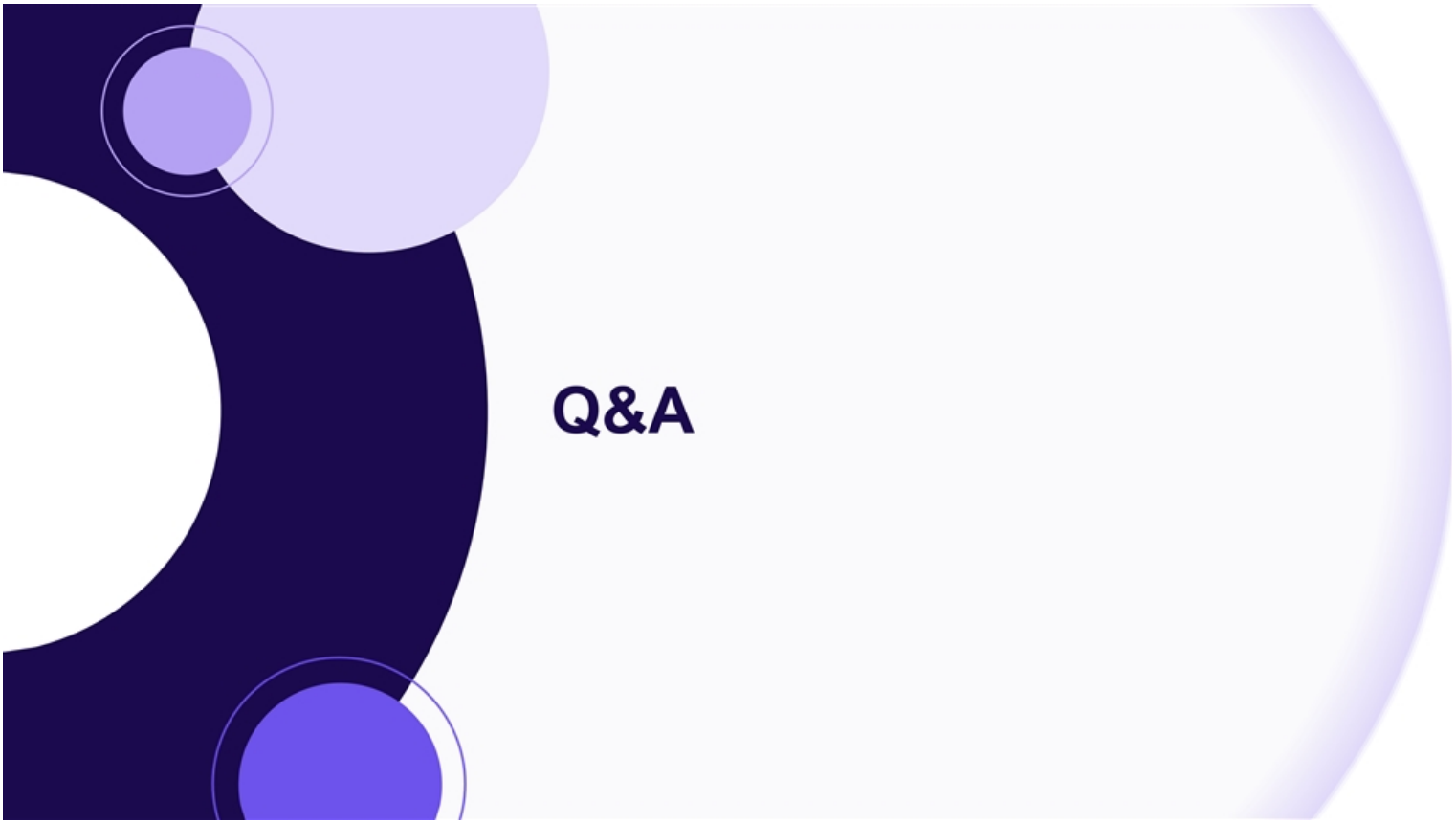
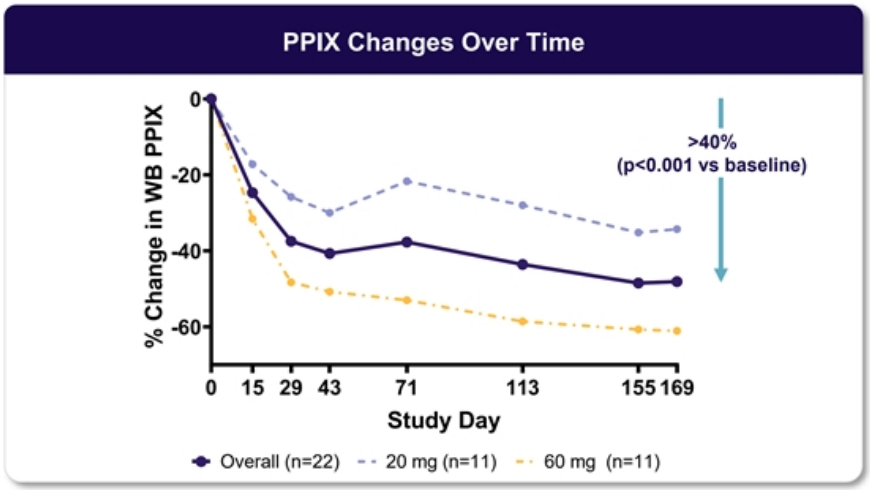

Q&A

Updated BEACON Data: % Change in Whole-Blood PPIX

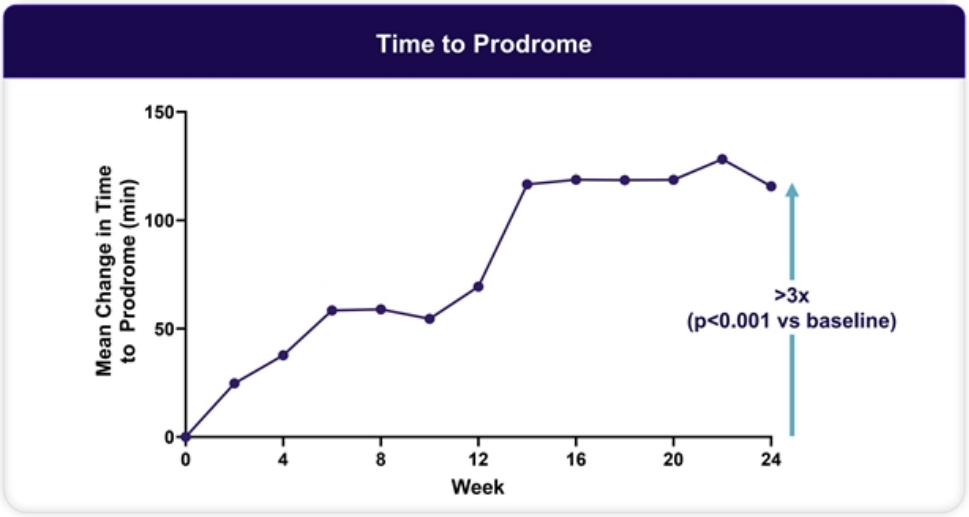
- Bitopertin significantly reduced WB metal-free PPIX levels by >40%
- Dose-dependent reductions were observed across broad range of baseline whole-blood PPIX levels (140-3075 µg/dL)



Least-squares means and p-value for percent changes in PPIX analyzed using a mixed model repeated measures (MMRM). PPIX = protoporphyrin IX; WB = whole blood

Updated BEACON Data: Time to Prodrome

- Significant, time-dependent improvements in light tolerance during weekly sun exposure challenges

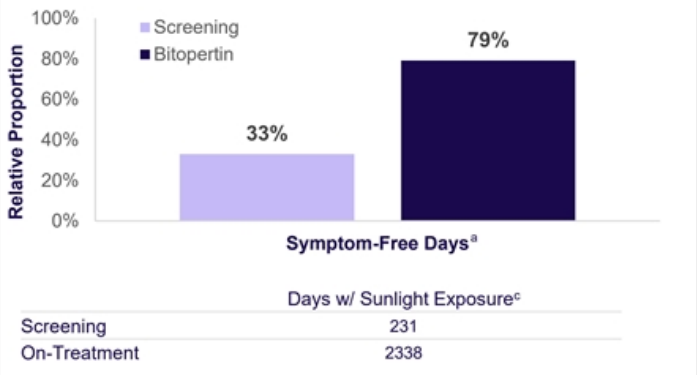


Time to prodrome data from weekly sunlight-exposure challenges were averaged over a 2-week period, including cumulative time in sunlight challenges where the participant did not report a prodrome, and were analyzed using MMRM for both 20 mg and 60 mg bitopertin dose groups combined (n=22).

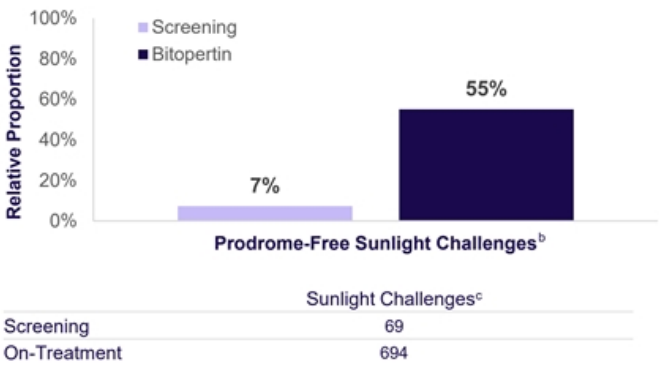
Updated BEACON Data: Light Tolerance

Days without Symptoms or Prodromes

- 92% reduction in patient-reported full phototoxic reactions[a]
- An increase in the proportion of total symptom-free days (no prodrome/early warning symptoms or full phototoxic reactions) with sunlight exposure was observed



	Days w/ Sunlight Exposure[c]
Screening	231
On-Treatment	2338

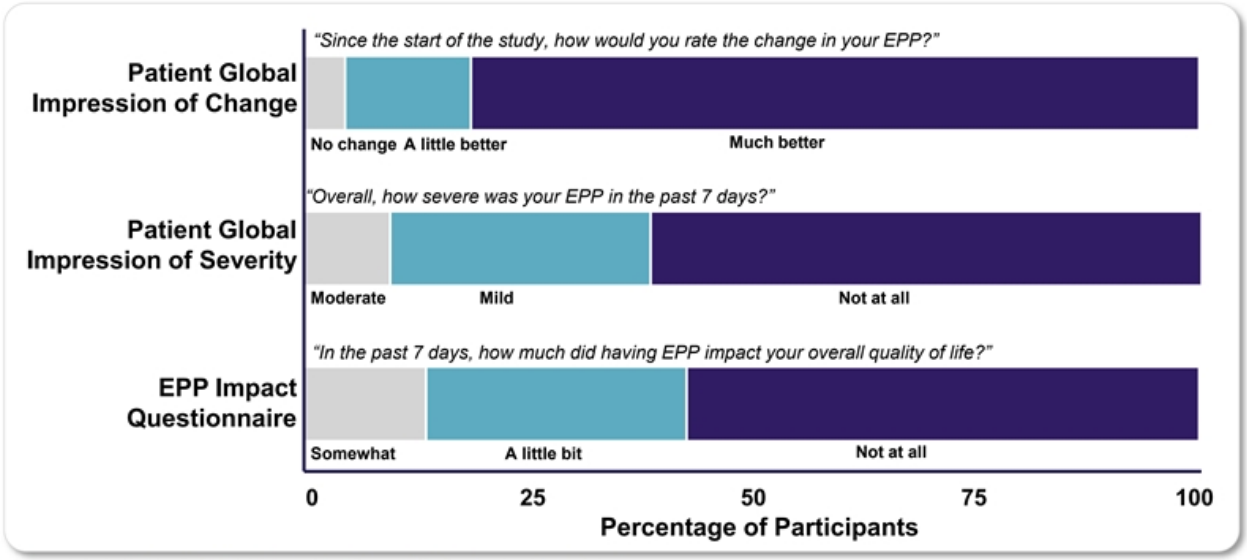


	Sunlight Challenges[c]
Screening	69
On-Treatment	694

[a] As assessed with a daily diary; [b] As assessed with a weekly sunlight challenge; [c] Summed across all participants. Percentages calculated relative to total number of days with sunlight exposure (left) or total number of weekly sunlight exposure challenges (right) from all study participants (n=22) during screening or while receiving bitopertin (20 mg and 60 mg dose groups combined).

Updated BEACON Data: Measures of Quality of Life

- Nearly all participants reported improvements in multiple quality-of-life measures at end of study

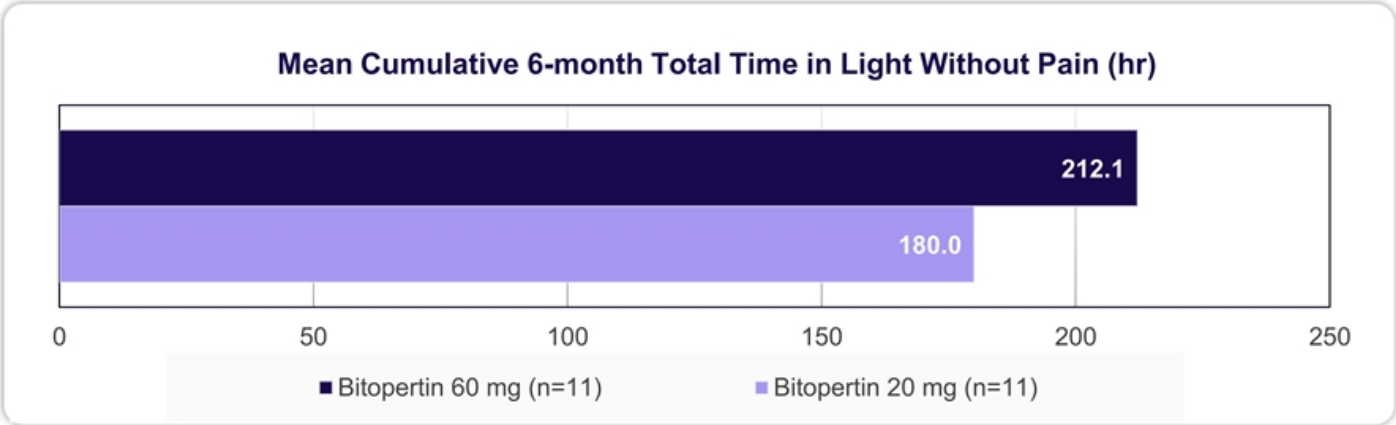


Includes responses from EOS/D169 or Week 8 of open-label extension study (n=21).

Updated BEACON Data: Precedented Pivotal Endpoint

Cumulative Time in Light on Days without Pain

- Cumulative total time in light observed over 6-month treatment period with bitopertin represents >3x increase relative to historical control
- Improvements in average daily light tolerance with bitopertin increased with time



Least-squares means for cumulative time in light measured via daily diary, adding all time in light between the hours of 10:00 am and 6:00 pm on days without any pain, and analyzed using an analysis of variance model.

Updated BEACON Data: Safety and Tolerability

- No serious adverse events
- Stable mean Hgb levels; no anemia AEs reported
- Favorable safety profile consistent with prior studies enrolling >4000 participants

	Bitopertin 20 mg (n=11)	Bitopertin 60 mg (n=11)	Total (n=22)
Participants with any TEAE	9 (82%)	11 (100%)	20 (91%)
TEAEs leading to discontinuation	1 (9%)[a]	0	1 (5%)
TEAEs reported in >2 participants			
Dizziness	6 (55%)	7 (64%)	13 (59%)
Headache	3 (27%)	1 (9%)	4 (18%)
Nausea	1 (9%)	2 (18%)	3 (14%)

[a] Grade 3 TEAE of cluster headache; AE = adverse event; Hgb = hemoglobin; TEAE = treatment-emergent adverse event