Bitopertin End of Phase 2 Meeting Feedback

November 4, 2024

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 proposed APOLLO clinical trial of bitopertin, including the primary endpoint and other study parameters, its AURORA Phase 2, BEACON Phase 2 and HELIOS 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, and its HVOL MAD data in its Phase 1 clinical trial 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; the possible regulatory path for bitopertin in EPP, including the potential to seek approval under the Accelerated Approval pathway and the timeline of related discussions with the FDA; and commercialization plans for bitopertin. The use of words such as, but not limited to, “believe,” “expect,” “estimate,” “project,” “intend,” “future,” “potential,” “continue,” “may,” “might,” “plan,” “will,” “should,” “seek,” “anticipate,” or “could” or the negative of these terms and other similar words or expressions that are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on Disc’s current beliefs, expectations and assumptions regarding the future of Disc’s business, future plans and strategies, clinical results and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Disc may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and investors should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements as a result of a number of material risks and uncertainties including but not limited to: the adequacy of Disc’s capital to support its future operations and its ability to successfully initiate and complete clinical trials; the nature, strategy and focus of Disc; the difficulty in predicting the time and cost of development of Disc’s product candidates; Disc’s plans to research, develop and commercialize its current and future product candidates; the timing of initiation of Disc’s planned preclinical studies and clinical trials; the timing of the availability of data from Disc’s clinical trials; Disc’s ability to identify additional product candidates with significant commercial potential and to expand its pipeline in hematological diseases; the timing and anticipated results of Disc’s preclinical studies and clinical trials and the risk that the results of Disc’s preclinical studies and clinical trials may not be predictive of future results in connection with future studies or clinical trials and may not support further development and marketing approval; and the other risks and uncertainties described in Disc’s filings with the Securities and Exchange Commission, including in the “Risk Factors” section of our Annual Report on Form 10-K for the year ended December 31, 2023, and in subsequent Quarterly Reports on Form 10-Q. Any forward-looking statement speaks only as of the date on which it was made. None of Disc, nor its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law.

Agenda

01 **Introduction and Summary**
John Quisel, J.D., PhD, Chief Executive Officer

02 **Detailed Review of End of Phase 2 Feedback**
Steve Caffé, M.D., Chief Regulatory Officer

03 **Proposed APOLLO Study Parameters**
Will Savage, M.D., PhD, Chief Medical Officer

04 **Closing Remarks**
John Quisel, J.D., PhD, Chief Executive Officer

05 **Q&A Session**

Key Takeaways from Positive End of Phase 2 Meeting

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

EPP Phase 2 Development Program

BEACON, AURORA, and HELIOS Studies

BEACON

- **EPP and XLP**; N = 26 (22 adults, 4 adolescents)
- **Australia**
- **Open-label, randomized, 24-week study**

AURORA

- **EPP**; N = 75 adults
- **United States**
- **Double-blind, randomized, placebo-controlled, 17-week study**

HELIOS

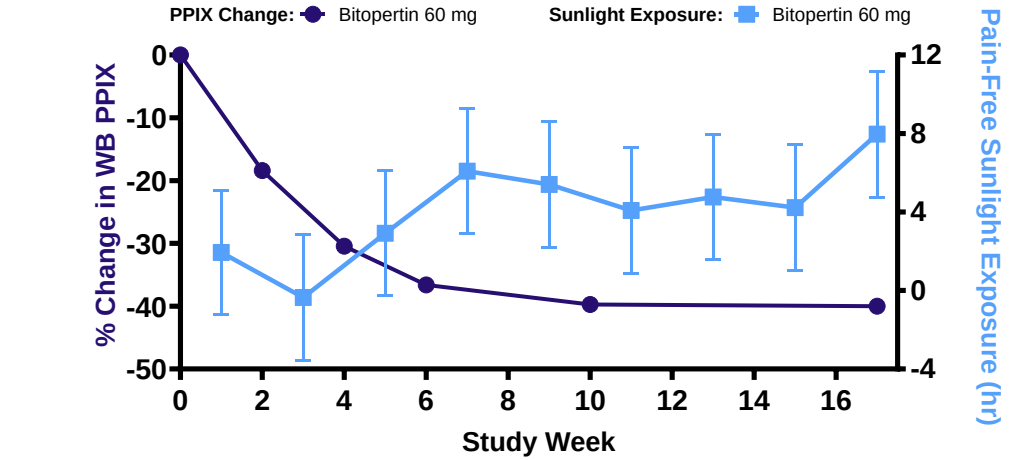
- **EPP and XLP**; adults and adolescents
- **US and Australia**
- **Open-label extension study** (>80% rollover from BEACON and AURORA)

Successful end of Phase 2 meeting with the FDA acknowledging the high unmet need in EPP and supporting our chosen trial parameters; clear development path to registration

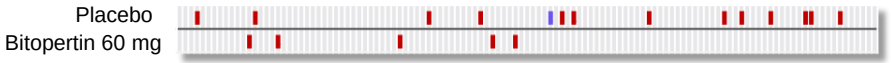
Summary of AURORA Results

Bitopertin 60 mg

AURORA



Phototoxic Reactions



= Phototoxic Reaction = 2 Phototoxic Reactions

- **Significant reductions in PPIX**
  40% reduction vs baseline
- **Time-dependent, improvements in pain-free time in sunlight vs placebo**
  2x more light time vs baseline
- **Significant 75% reduction in rate of phototoxic reactions vs placebo**
  Phototoxic reaction-free in last 60 days
- **Significant improvement in PGIC vs placebo**
  86% reported EPP was ‘much better’
- **Clear association between PPIX reduction and clinical endpoints**

Agenda

01 **Introduction and Summary**
John Quisel, J.D., PhD, Chief Executive Officer

02 **Detailed Review of End of Phase 2 Feedback**
Steve Caffé, M.D., Chief Regulatory Officer

03 **Proposed APOLLO Study Parameters**
Will Savage, M.D., PhD, Chief Medical Officer

04 **Closing Remarks**
John Quisel, J.D., PhD, Chief Executive Officer

05 **Q&A Session**

Detailed FDA Feedback

FDA agreed to all study parameters Disc requested prior to the meeting

	Disc Request	***FDA Agreement***
Primary Endpoint	Average monthly total time in sunlight without pain between 10:00 and 18:00 after 6 months of treatment is clinically meaningful and can serve as a primary endpoint	✓
Additional Endpoints	Change in PPIX, occurrence of phototoxic reactions, cumulative total pain-free time in sunlight, and patient global impression of change (PGIC)	✓
Dose and Duration	Proceed with 60 mg dose of bitopertin and 6-month study duration	✓
Study Population	Patients aged 12 years and older with EPP, including XLP	✓

Accelerated Approval

Accelerated approval pathway allows for earlier marketing authorization using a surrogate endpoint. Full approval is subject to demonstration of clinical benefit in a confirmatory trial

- FDA acknowledged PPIX reduction, as demonstrated in AURORA, may serve as surrogate endpoint to support accelerated approval
- An accelerated NDA package would include data from BEACON, AURORA, HELIOS, and a >4,000 participant safety database
- Will meet with FDA to finalize confirmatory trial design
- Expect to provide an update on this process in Q1 2025, while simultaneously moving forward with preparations for trial initiation by mid-2025

Agenda

01 **Introduction and Summary**
John Quisel, J.D., PhD, Chief Executive Officer

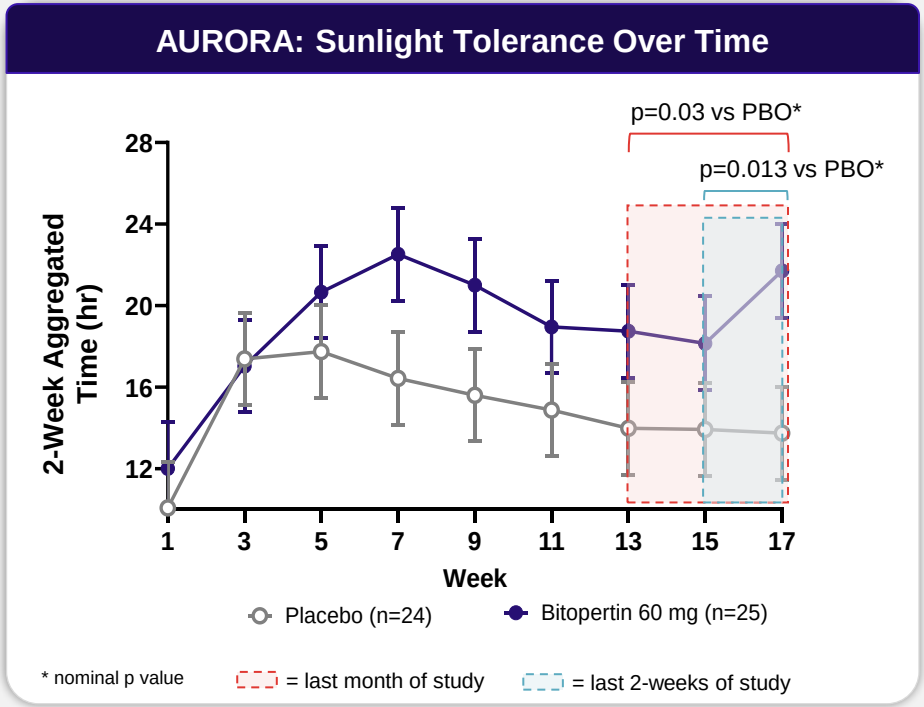
02 **Detailed Review of End of Phase 2 Feedback**
Steve Caffé, M.D., Chief Regulatory Officer

03 **Proposed APOLLO Study Parameters**
Will Savage, M.D., PhD, Chief Medical Officer

04 **Closing Remarks**
John Quisel, J.D., PhD, Chief Executive Officer

05 **Q&A Session**

Primary Endpoint: Average Monthly Time in Light without Pain After 6 Months of Treatment



Robust Endpoint

- Longitudinal analysis leverages robust model that demonstrated significance in AURORA
- Accounts for time-dependent PPIX lowering effects with bitopertin and for waning of a placebo effect
- Endpoint has >80% power with 150 patients

Strong Study Design

- Rigorous evaluation of baseline light tolerance required during screening and factored into analysis of the primary endpoint
- Stratification by geography to minimize confounding factors affecting light exposure across study arms

Post-hoc longitudinal analysis adjusted for baseline

APOLLO Study Parameters

N Size	~150 patients across sites in the US and Europe
Trial Duration	6-month treatment period
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
Primary Endpoint	Average monthly total time in sunlight without pain between 10:00 and 18:00 after 6 months of treatment
Additional Endpoints	• Change from baseline in whole blood metal-free PPIX • Occurrence of phototoxic reactions • Patient global impression of change (PGIC) • Cumulative total pain-free time in sunlight • Safety and tolerability

Pending regulatory feedback on final protocol design

Agenda

01 **Introduction and Summary**
John Quisel, J.D., PhD, Chief Executive Officer

02 **Detailed Review of End of Phase 2 Feedback**
Steve Caffé, M.D., Chief Regulatory Officer

03 **Proposed APOLLO Study Parameters**
Will Savage, M.D., PhD, Chief Medical Officer

04 **Closing Remarks**
John Quisel, J.D., PhD, Chief Executive Officer

05 **Q&A Session**

Key Takeaways from End of Phase 2 Meeting

Endpoint Alignment

Alignment with FDA on clinically meaningful endpoints

Target Population Included

Study can be conducted in adults and adolescents (ages 12+) with EPP and XLP

Desired Dose Endorsed

Endorsement of 60 mg dose for 6-month study

Accelerated Approval Potential

PPIX may serve as a surrogate endpoint to support accelerated approval

Next Steps and Upcoming Catalysts

Bitopertin Next Steps

- Discussion of confirmatory trial design with FDA, with updates provided in Q1 2025
- Trial initiation by mid-2025
- European protocol assistance and confirmation of regulatory path with EMA
- Commercialization and launch preparation

Q4 2024 Catalysts

- **ASN**: Presented positive Phase 1 SAD data for DISC-0974 in CKD

Additional data updates by EOY

- **Bitopertin:** Additional analyses from BEACON and AURORA
- **DISC-0974**: Complete Phase 1b data in MF anemia
- **DISC-3405**: Phase 1 HVOL MAD data

HVOL = healthy volunteers; SAD = single ascending dose; MF = myelofibrosis; MAD = multiple ascending dose

Agenda

01 **Introduction and Summary**
John Quisel, J.D., PhD, Chief Executive Officer

02 **Detailed Review of End of Phase 2 Feedback**
Steve Caffé, M.D., Chief Regulatory Officer

03 **Proposed APOLLO Study Parameters**
Will Savage, M.D., PhD, Chief Medical Officer

04 **Closing Remarks**
John Quisel, J.D., PhD, Chief Executive Officer

05 **Q&A Session**