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# Mavorixafor for Patients with Chronic Neutropenic Disorders Treated with G-CSF: Preliminary Response Data and G-CSF Dose Reduction in an Ongoing Phase 2, Open-Label, Multicenter Study Support Reduction in G-CSF Dosing

Julia T. Warren, MD, PhD<sup>1,2</sup>; Kathryn E. Dickerson, MD, MS<sup>3</sup>; Anjali A. Sharathkumar, MBBS, MD, MS<sup>4</sup>; Jolan E. Walter, MD, PhD<sup>5</sup>; David B. Wilson, MD, PhD<sup>6</sup>; Christophe Arbet-Engels, MD, PhD<sup>7</sup>; Katrina P. Adell, MD<sup>7</sup>; Susan Dubuc, RN, MSN<sup>7</sup>; Rick MacLeod<sup>7</sup>; Katie Peters, MS<sup>7</sup>; Deborah J. Steiner, MD, MS<sup>7</sup>; Murray Stewart, MD<sup>7</sup>; Arthur G. Taveras, PhD<sup>7</sup>; Kelly Walkovich, MD<sup>8</sup>

<sup>1</sup>Division of Hematology, Children's Hospital of Philadelphia, Philadelphia, PA, USA; <sup>2</sup>Department of Pediatrics, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA; <sup>3</sup>Division of Hematology and Oncology, Department of Pediatrics, University of Texas Southwestern Medical Center, Dallas, TX, USA; <sup>4</sup>Stead Family Department of Pediatrics, Carver College of Medicine, University of Iowa Health Care, Iowa City, IA, USA; <sup>5</sup>Division of Allergy & Immunology, Department of Pediatrics, Morsani College of Medicine, University of South Florida at Johns Hopkins All Children's Hospital, St. Petersburg, FL, USA; <sup>6</sup>Department of Pediatrics, Washington University School of Medicine, St. Louis, MO, USA; <sup>7</sup>X4 Pharmaceuticals, Inc., Boston, MA, USA; <sup>8</sup>C.S. Mott Children's Hospital, Ann Arbor, MI, USA

## Background

- Chronic neutropenia (CN) includes blood disorders with heterogeneous causes and presentations, characterized by low levels of neutrophils (ANC <1500/ $\mu$ L for >3 months) leading to increased susceptibility to recurrent and/or severe infections<sup>1</sup>
- Injectable granulocyte colony-stimulating factor (G-CSF) is the only approved therapy for severe chronic neutropenia
  - G-CSF presents unmet needs, with burden posed by frequent injections, side effects (e.g., bone pain), and prolonged use associated with the risk of malignancies in some CN disorders<sup>2</sup>
- Mavorixafor is an investigational oral, highly-selective CXCR4 antagonist that showed:
  - Durable increases in ANC and reduction in frequency and severity of infections; apparent safety and tolerability in a phase 3 trial in WHIM syndrome<sup>3</sup>
  - Substantial ANC increases in a phase 1b trial in chronic neutropenic disorders<sup>5,4</sup>
- The phase 2 trial of mavorixafor in chronic neutropenic disorders is ongoing; these data will inform the design of the planned phase 3 study in CN<sup>5</sup>
- A phase 3 trial is planned to evaluate the efficacy (positive ANC response, infection rate) and safety of mavorixafor

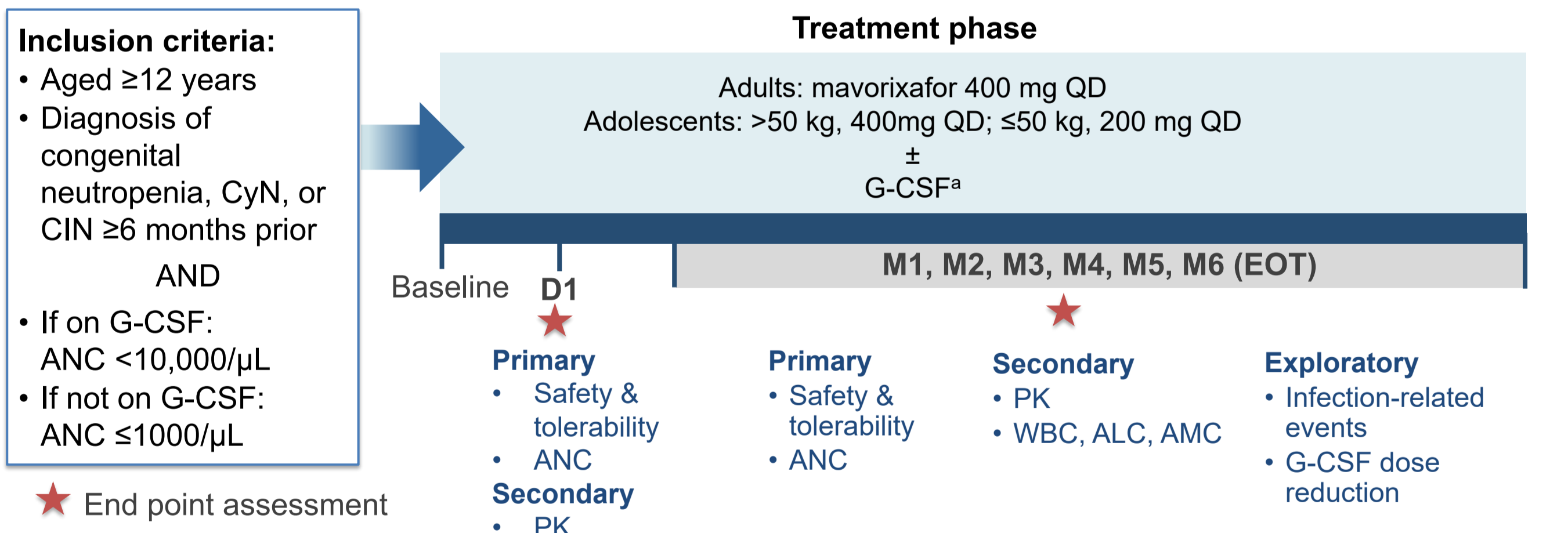
## Objectives

- To report preliminary results for 3 participants enrolled in an ongoing phase 2, open-label, multicenter trial evaluating the safety, tolerability, and proof of concept for efficacy of mavorixafor, alone or with concurrent G-CSF use, in chronic neutropenia disorders (NCT04154488; part 2)

## Methods

Primary Objectives	Secondary Objectives	Exploratory Objectives
Evaluate safety, tolerability, and effect on ANC of 6-month chronic dosing of mavorixafor	Characterize the multidose PK profile of mavorixafor during 6 months of chronic dosing Evaluate effect of 6-month chronic dosing of mavorixafor on ALC, WBC, and AMC	Assess incidence and duration of infection-related events with chronic dosing Evaluate G-CSF dose reduction in participants treated concurrently with mavorixafor and G-CSF

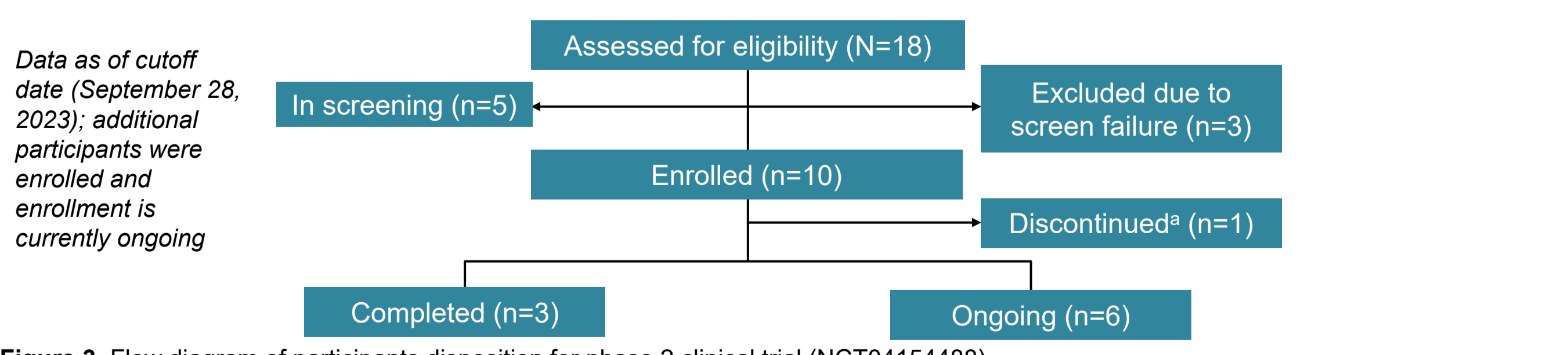
**Figure 1.** Primary, secondary, and exploratory objectives for part 2 (phase 2) of clinical trial evaluating mavorixafor for chronic neutropenia. ALC, absolute lymphocyte count; AMC, absolute monocyte count; PK, pharmacokinetic; WBC, white blood cell.



**Figure 2.** Study design schematic of phase 2 clinical trial (NCT04154488). ALC, absolute lymphocyte count; AMC, absolute monocyte count; ANC, absolute neutrophil count; CIN, chronic idiopathic neutropenia; CyN, cyclic neutropenia; D, day; EOT, end of treatment; G-CSF, granulocyte colony-stimulating factor; M, month; PK, pharmacokinetics; QD, once daily. <sup>a</sup>Participants already on G-CSF continued individualized G-CSF dosing for  $\geq 8$  weeks. Dose and/or frequency may be reduced based on monthly ANC assessments.

- Hematologic parameters, including ANC, were assessed over 8 hours on day 1 and at months 1, 3, and 6. At months 2, 4, and 5, hematologic parameters were assessed within 2 to 4 hours of dosing to reduce trial burden

### Participant Disposition: Study Flow Diagram for Phase 2 Clinical Trial (NCT04154488)



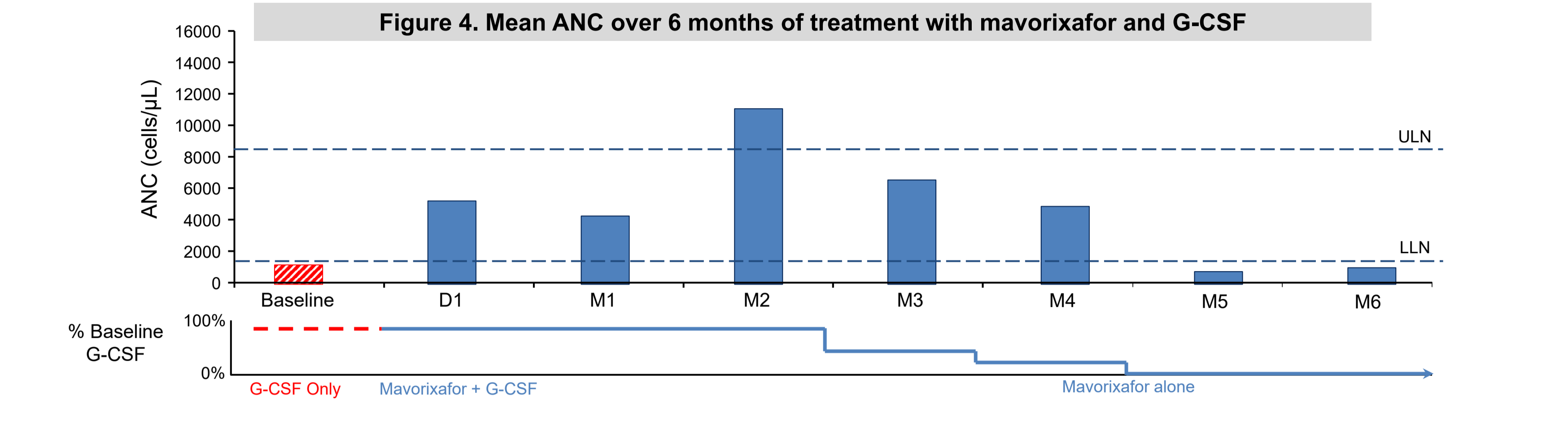
**Figure 3.** Flow diagram of participants disposition for phase 2 clinical trial (NCT04154488). <sup>a</sup>Participant withdrew consent.

- Only preliminary results for the 3 participants who have completed the study as of September 28, 2023 are presented

## Results

### Participant 1: Mavorixafor Allows for Exploratory G-CSF Dose Reduction in a Participant With Chronic Idiopathic Neutropenia

**Background:** 24 year-old female with CIN, pre-study G-CSF dosing: 0.74  $\mu$ g/kg/dose QOD



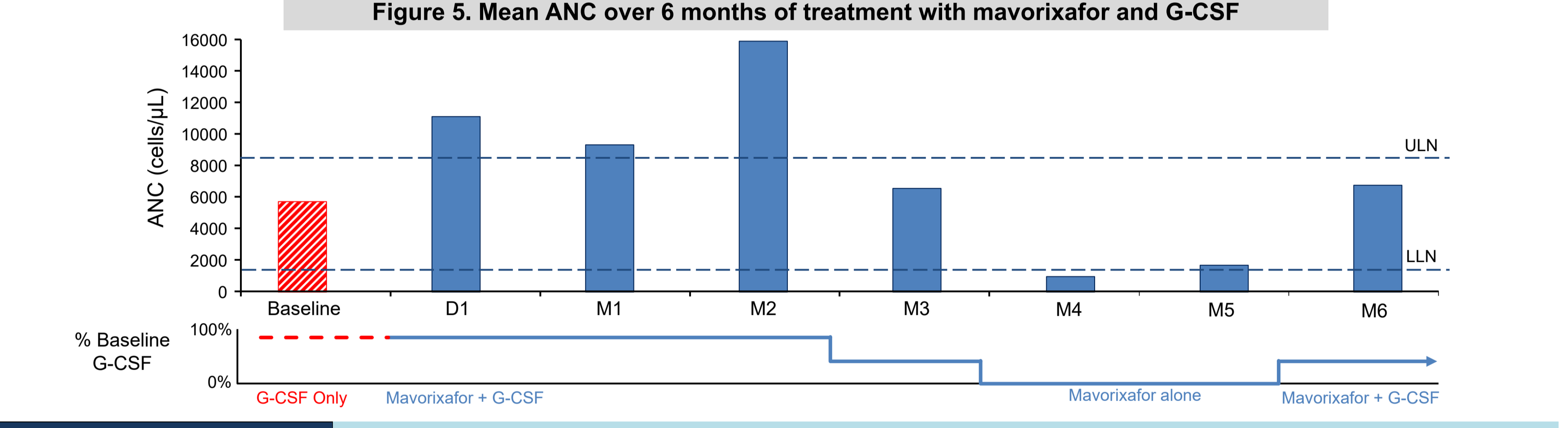
**Summary:**

- Baseline ANC in mild neutropenia range
- Normalization of ANC with mavorixafor in addition to G-CSF maintained through 4 months, including with  $\geq 75\%$  baseline G-CSF dose reduction (through decreases in dosage and frequency), as determined by the treating physician

ANC, absolute neutrophil count; CIN, chronic idiopathic neutropenia; D, day; G-CSF, granulocyte colony-stimulating factor; LLN, lower limit of normal; M, month; QOD, every other day; ULN, upper limit of normal. Note: Normal ANC:  $\geq 1500$  to  $8500$  cells/ $\mu$ L; Severe CN: ANC < $500$  cells/ $\mu$ L; Moderate CN: ANC  $\geq 500$  and < $1000$  cells/ $\mu$ L; Mild CN: ANC  $\geq 1000$  and < $1500$  cells/ $\mu$ L.

### Participant 2: Mavorixafor Allows for Exploratory G-CSF Dose Adjustment in a Participant With Chronic Idiopathic Neutropenia

**Background:** 20 year-old female with CIN, pre-study G-CSF dosing: 0.38  $\mu$ g/kg/dose QD



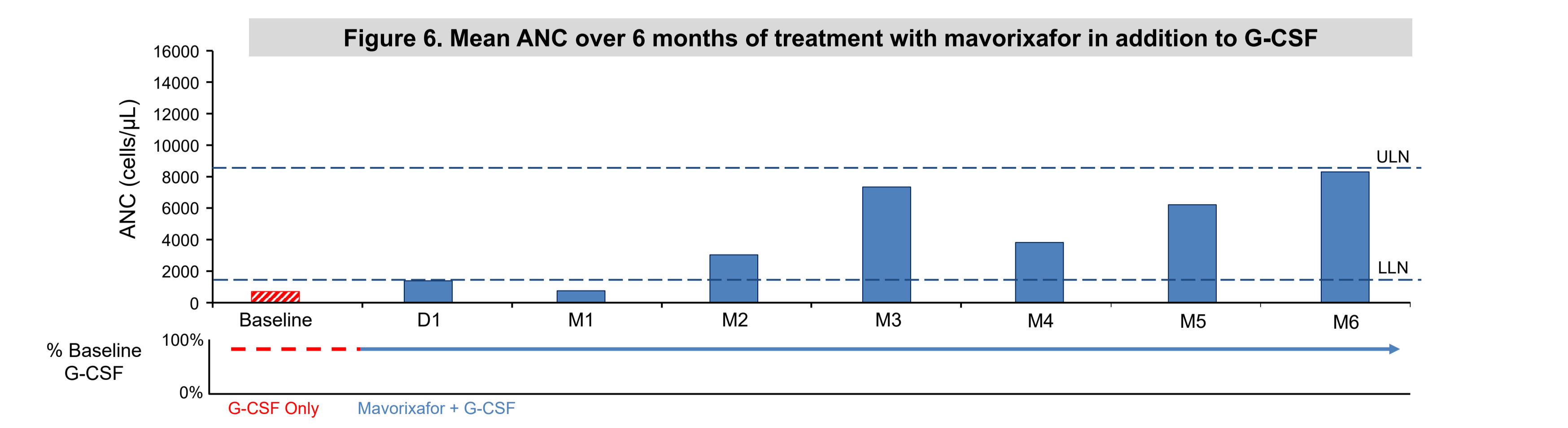
**Summary:**

- Baseline ANC in normal range
- Mavorixafor, in addition to G-CSF, increased ANC (3500 – 10,000 cells/ $\mu$ L)
- Normal or near-normal ANC maintained with 50% baseline G-CSF dose reduction (through decreases in dosage and/or frequency) and cessation, as determined by the treating physician after M2
- Treating physician increased G-CSF dose to 50% of baseline after M5 due to CN presentation (history of gingivitis)

ANC, absolute neutrophil count; CIN, chronic idiopathic neutropenia; D, day; G-CSF, granulocyte colony-stimulating factor; LLN, lower limit of normal; M, month; QD, once daily; ULN, upper limit of normal. Note: Normal ANC:  $\geq 1500$  to  $8500$  cells/ $\mu$ L; Severe CN: ANC < $500$  cells/ $\mu$ L; Moderate CN: ANC  $\geq 500$  and < $1000$  cells/ $\mu$ L; Mild CN: ANC  $\geq 1000$  and < $1500$  cells/ $\mu$ L.

### Participant 3: ANC Maintained within the Normal Range When Mavorixafor is Used in Combination with a Stable G-CSF Dose in a Participant with Cyclic Neutropenia

**Background:** 39 year-old male with CyN, pre-study G-CSF dosing: 0.53  $\mu$ g/kg/dose QD



**Summary:**

- Moderate neutropenia at baseline
- Normal ANC maintained from M2 through M6

ANC, absolute neutrophil count; CyN, cyclic neutropenia; D, day; G-CSF, granulocyte colony-stimulating factor; LLN, lower limit of normal; M, month; QD, once daily; ULN, upper limit of normal. Note: Normal ANC:  $\geq 1500$  to  $8500$  cells/ $\mu$ L; Severe CN: ANC < $500$  cells/ $\mu$ L; Moderate CN: ANC  $\geq 500$  and < $1000$  cells/ $\mu$ L; Mild CN: ANC  $\geq 1000$  and < $1500$  cells/ $\mu$ L.

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### Participants 1, 2, and 3: Infection Events and Safety/Tolerability

Among the 3 participants treated with mavorixafor for 6 months in addition to G-CSF:

- Infection reduction**
- Four (4) infections were reported within the first 2 months
    - Laryngitis, pharyngitis (Participant 1); nasopharyngitis, cystitis (Participant 2)
  - No infections were reported during the following 4 months despite some participants adjusting G-CSF dosing regimen

- Safety and Tolerability**
- Nineteen (19) adverse events
  - No events were serious, and all were Grade 1 (mild) or Grade 2 (moderate)
  - None of these events led to mavorixafor dose reduction, interruption, or cessation
  - There were no new safety adverse events
  - These preliminary data are consistent with the safety and tolerability of mavorixafor in the WHIM program, with mild and moderate gastrointestinal events, such as nausea and vomiting reported

### Chronic Neutropenia Community Insights on G-CSF Dosing Adjustments in Addition to an Oral Agent

- Due to substantial disease burden, incorporating patient perspective into the clinical research process can improve patient outcome<sup>6</sup>

CN participant feedback suggests that patients would take an oral medicine in addition to G-CSF if it reduced the dose or frequency of G-CSF, with a strong preference for reduced frequency<sup>a</sup>

Further investigation is needed to determine individual patient G-CSF dosing adjustment, and X4 is working with the scientific and clinical community to design future studies

<sup>a</sup>Preliminary results from a chronic neutropenia engagement survey in partnership with the National Neutropenia Network

“ Taking G-CSF less frequently would allow more flexibility in my life ”

“ It would be really helpful to reduce how often I need an injection even if it is only by 25% ”

“ It would be very nice to reduce both dose and frequency, or either! It would be absolutely worth it to reduce side effects, or improve medication efficacy ”

“ If I am able to decrease my dosing or the frequency of my injection it would help some of the side effects from G-CSF. I am very willing to take a medication orally to help that! ”

## Conclusions

- Sustained normal ANC levels within the first 3 months observed in all 3 participants
- Preliminary results suggest:
  - G-CSF dosing adjustments (frequency and/or dose)  $\geq 50\%$  can maintain normal or near-normal ANC
  - Early infection event reporting did not demonstrate increased infections with G-CSF reduction
  - No new safety adverse events or concerns with mavorixafor
- Further investigations are warranted to establish guidance on mavorixafor treatment, including optimizing individualized G-CSF dose and frequency adjustments for long-term maintenance of adequate ANC and improvement in clinical presentation
- G-CSF dosing represents an unmet medical need in individuals with chronic neutropenic disorders
  - Preliminary feedback from CN community suggest that G-CSF dose reductions could represent meaningful change to many patients with CN
- Overall, preliminary ANC and infection data support the primary end points of positive ANC response and infection rate, respectively, in the global phase 3 pivotal study

These early phase 2 data for mavorixafor in addition to G-CSF support the CN phase 3 study design and potential G-CSF dosing adjustment

## References

1. Fioredda F, et al. *Hemasphere*. 2023;7(4):e872. 2. Donadieu J, et al. *Expert Rev Hematol*. 2021;14(10):945-960. 3. Badolato R, Donadieu J. *Hemasphere*. 2023;7(Suppl 1):e884700a. 4. Warren J, et al. *Blood*. 2022;140 (Supp 1): 1408-1410. 5. NCT04154488. Updated October 4, 2023. Accessed November 9, 2023. <https://clinicaltrials.gov/study/NCT04154488>. 6. Mercieca-Bebber R, et al. *Patient Relat Outcome Meas*. 2018;9:353-367

## Disclosures

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