

Investor Presentation

March 2022



Forward-Looking Statements

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X4: Strategy of Building on Success and Delivering Long-Term Growth



Advancing innovative treatments for rare diseases caused by dysregulation of the immune system

Phase 3 Candidate (PRV* Eligible): Mavorixafor – Once-daily oral CXCR4 antagonist

Advancing Mavorixafor to potentially treat >30,000 patients (U.S. and EU Markets) in multiple indications

Building a sustainable rare disease company with a growing pipeline

Key Business Drivers

- ✓ Encouraging Phase 2 trial data; Breakthrough Therapy Designation in lead indication (WHIM syndrome)
- ✓ Fully enrolled global Phase 3 trial in WHIM; **top-line data expected in 4Q 2022**
- ✓ Positive Phase 1b data in Waldenstrom's Macroglobulinemia (lymphoma); **additional data expected in 2H 2022**
- ✓ Positive Phase 1b data in chronic neutropenia; **interim data expected in 2Q/3Q 2022**
- ✓ Pipeline of multiple pre-clinical compounds

*PRV: priority review voucher

Advancing a Pipeline of Oral CXCR4 Antagonists

Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Expected Milestones	Target Patient Populations
Mavorixafor	WHIM (Warts, Hypogammaglobulinemia, Infections and Myelokathexis) syndrome ¹	Phase 3				Top-line data 4Q 2022 2H 2023 NDA	> 1,000 U.S. ²
	Chronic Neutropenia (CN)	Phase 1b				Add'l data / clinical update in 2Q/3Q 2022	> 5,000 U.S. ³
	Waldenström's Macroglobulinemia (WM)	Phase 1b				Add'l data / clinical update in 2H 2022	> 2,000 U.S. ⁴
X4P-002	Oncology indications	IND-enabling				IND in 2H 2022	Other leukemias and lymphomas > 25,000 U.S. ³
X4P-003	Primary immuno-deficiencies (PIDs)						Undisclosed

Potential to address the needs of >30,000 patients across multiple indications ^{2,3,4}

Seasoned Executive Leadership Team



PAULA RAGAN, Ph.D.
President & CEO

genzyme

SANOFI



DIEGO CADAVID, M.D.
Chief Medical Officer



Fulcrum
Therapeutics



Biogen



ADAM MOSTAFA
Chief Financial Officer

abpro

CANTOR
Fitzgerald



ART TAVERAS, Ph.D.
Chief Scientific Officer



Schering-Plough



Biogen



MARY DIBIASE, Ph.D.
Chief Operating Officer



Biogen



EPIRUS
BIOPHARMACEUTICALS



DEREK MEISNER, J.D.
Chief Legal Officer



genocea

RACapital

Dysregulation of white blood cells (leukocytes) contributes to a broad range of serious diseases with significant unmet needs



Primary Immunodeficiencies

Life-threatening infections & deaths

- >\$3.3 billion WW annual Rx sales¹
- Few options (G-CSF & IVIG)
- Injectable or infusion only



Lymphomas

Cancer progression and deaths

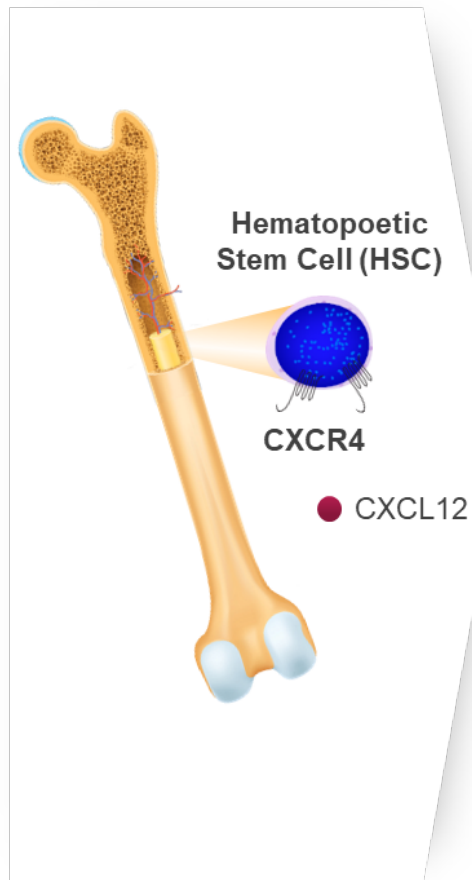
- >\$7 billion WW annual Rx sales²
- Multiple therapies and lines of treatment
- Few cures

1. Allied Market Research 2019.

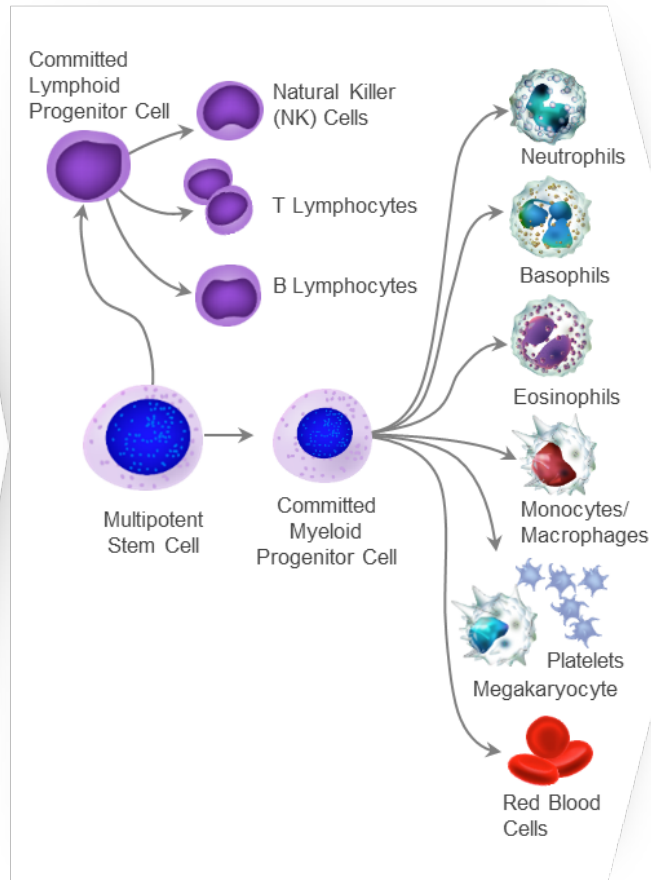
2. Business Insight, Market Research Report, 2018.

CXCR4/CXCL12 Pathway: Master Regulator of Healthy Immune System Function

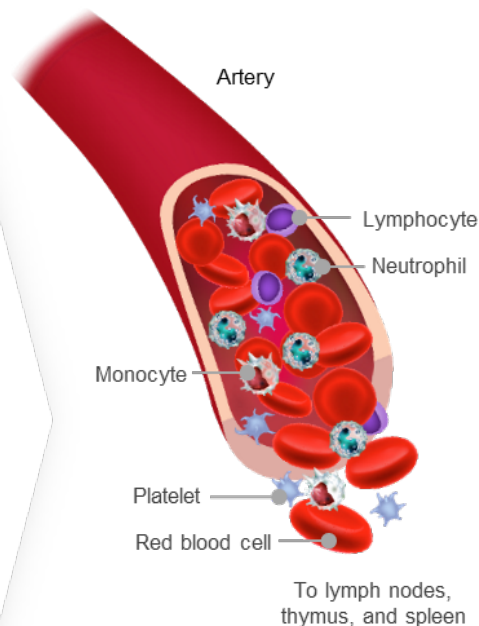
EXPANSION



MATURATION



TRAFFICKING



CXCR4 Antagonism Clinically Shown to:

- ✓ Increase maturation and mobilization of WBCs in all those dosed
- ✓ Increase circulating neutrophils, lymphocytes, and monocytes in patients with immunodeficiencies and certain cancers
- ✓ Reduce bacterial and viral infections
- ✓ Reduce lymphoma burden in combination with oncology Rx

CXCR4 Plays Key Role in Regulating Expansion, Maturation, and Trafficking of Leukocytes

Mavorixafor: Realizing the Potential of CXCR4 Antagonism in an Oral Capsule



The only oral CXCR4 antagonist in development

- Small molecule with high potency and selectivity
- Durable half-life supporting once daily dosing
 - 2 or 4 capsules, once per day (WHIM)

Antagonizes Both Wild-Type and Mutant CXCR4

- Broad applicability to various disease states with high unmet needs

Safety Profile Supports Chronic Use

- >200 patients/subjects treated to date
- Some patients on Rx for several years

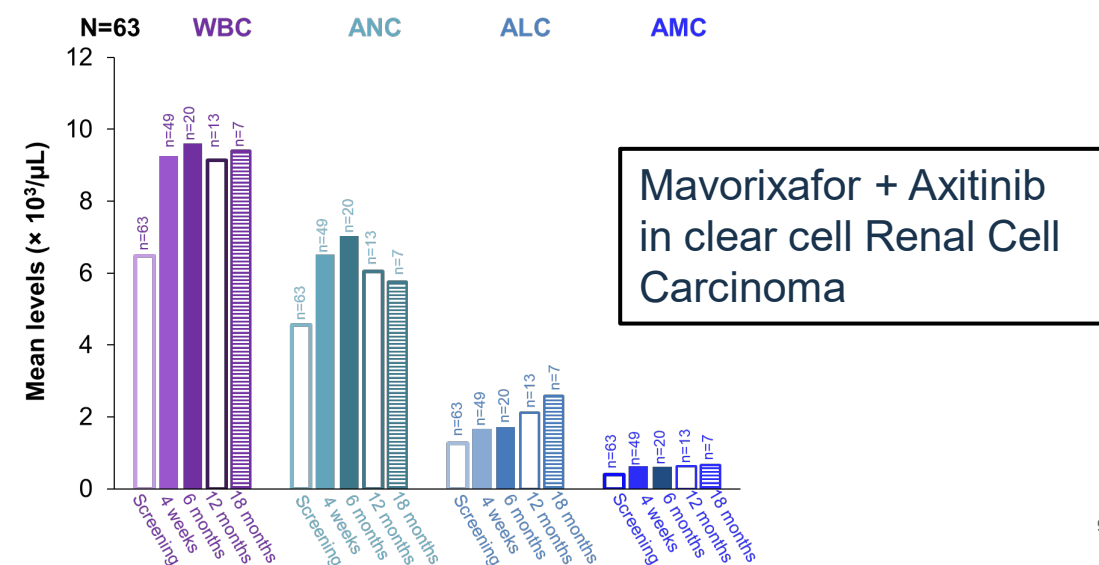
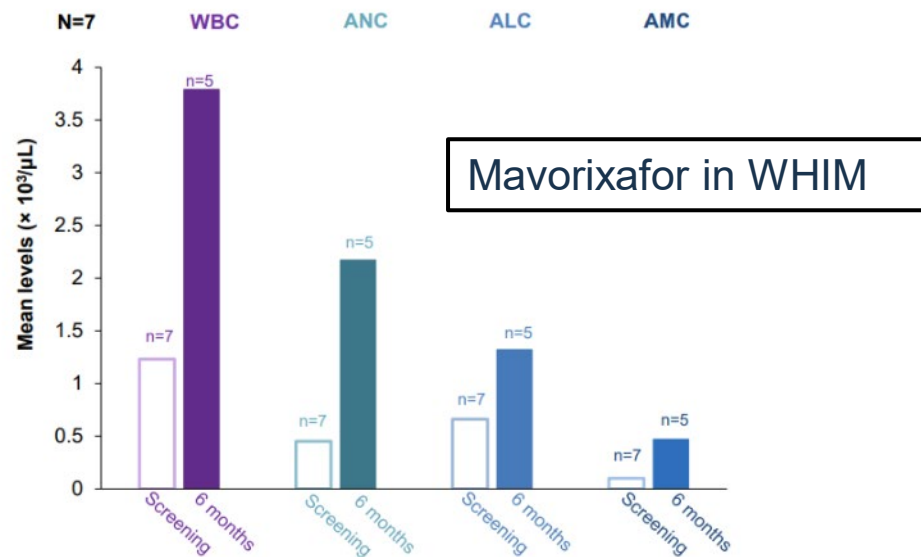
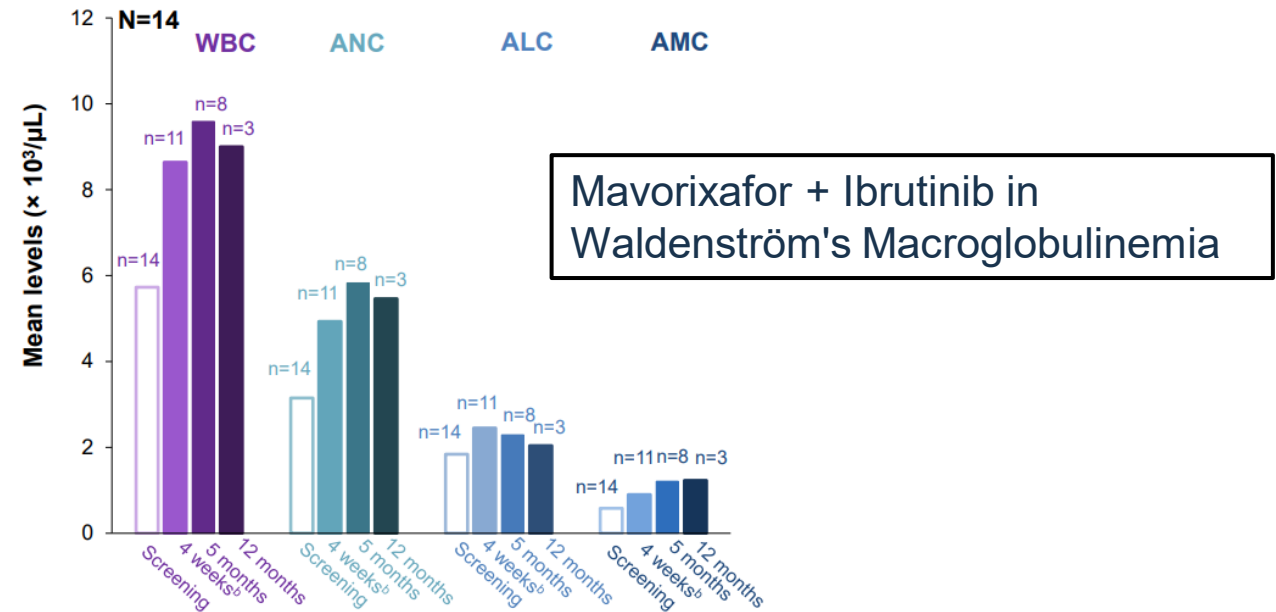
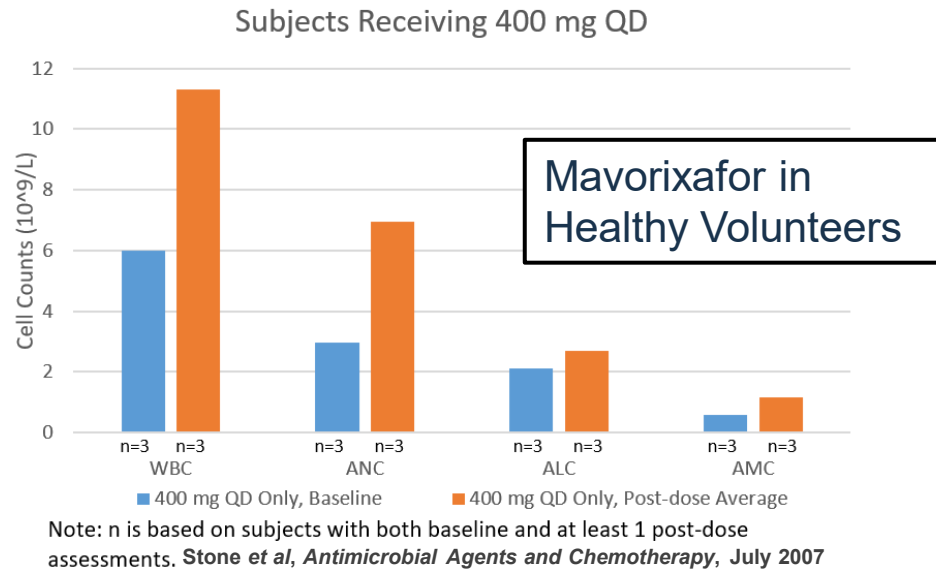
Favorable Regulatory Designations (WHIM)

- Breakthrough Therapy Designation (U.S.)
- Fast Track Designation (U.S.)
- Rare Pediatric Disease Designation (PRV eligible)
- Orphan Drug Status in U.S. and Europe

Patent Protection Expected Through 2038 and Beyond



Mavorixafor Clinical Trial Data: First Oral Treatment to Demonstrate a Durable Increase in Peripheral White Blood Cell Counts Across All Populations Studied



Dysregulation of white blood cells (leukocytes) contributes to a broad range of serious diseases with significant unmet needs



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Lymphomas

Cancer progression and deaths

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- Multiple therapies and lines of treatment
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1. Allied Market Research 2019.

2. Business Insight, Market Research Report, 2018.

The Dysregulated Immune System: Immunodeficiencies

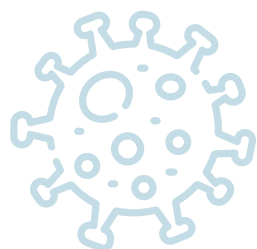
Immunodeficiencies (U.S. Prevalence)



**Common Variable
Immunodeficiency (CVID)¹**
>10,000



Chronic Neutropenias²
5,000 - 10,000
(severe and moderate)



WHIM Syndrome³
~1,000 to 3,700

Chronic Immunosuppression

- Life-long severe and/or life-threatening infections
- Reduced/no response to vaccines
- Increased cancer risk
- High morbidity (bronchiectasis, hearing loss) and life-threatening sepsis

Caused By

- Low white blood cell counts (cytopenias) and/or
- Dysregulated or dysfunctional immune cells

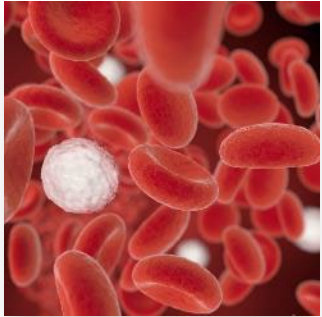
Treated With Injectables

- Antibiotics for acute infections
- G-CSF for those with severe neutropenia
- IVIG for those with hypogammaglobulinemia (prevention)
 - Stem cell transplant in rare/severe cases

Unmet need: Oral treatment that corrects and regulates a range of immune system deficiencies

Introduction to WHIM Syndrome

An Immunodeficiency Affecting Children and Adults



Pancytopenia: All White Blood Cells Affected & Reduced



Severe bacterial infections

In multiple organ systems: bronchiectasis (lung), hearing loss (ear), cellulitis (skin)



Viral infections & cancer risk

Disfiguring recalcitrant warts; EBV and HPV-associated cancers

0

Approved targeted therapies; symptomatic treatment with G-CSF and IVIG

www.whimsyndrome.com

Leanne's Story - *Living with WHIM Syndrome*



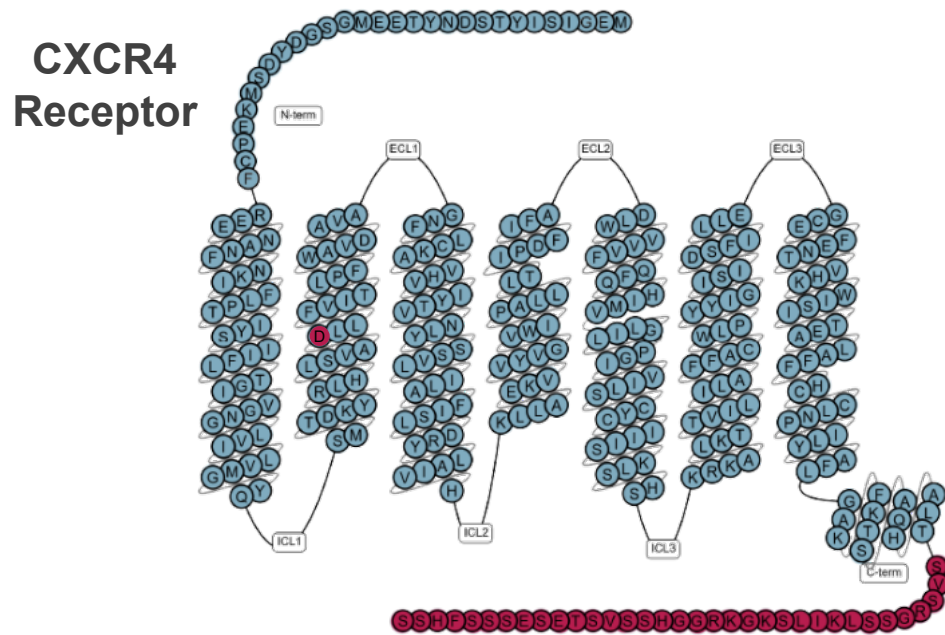
WHIM Patient
New South Wales, Australia

[In early marriage], I had 8 episodes of pneumonia in 8 months, more likely one continual episode of pneumonia. I had a PICC line, I was having intravenous antibiotics.

Every time I was better, they'd stop the antibiotics and almost immediately I'd become unwell again.

Root Cause of WHIM Syndrome: Over-Signaling of CXCR4

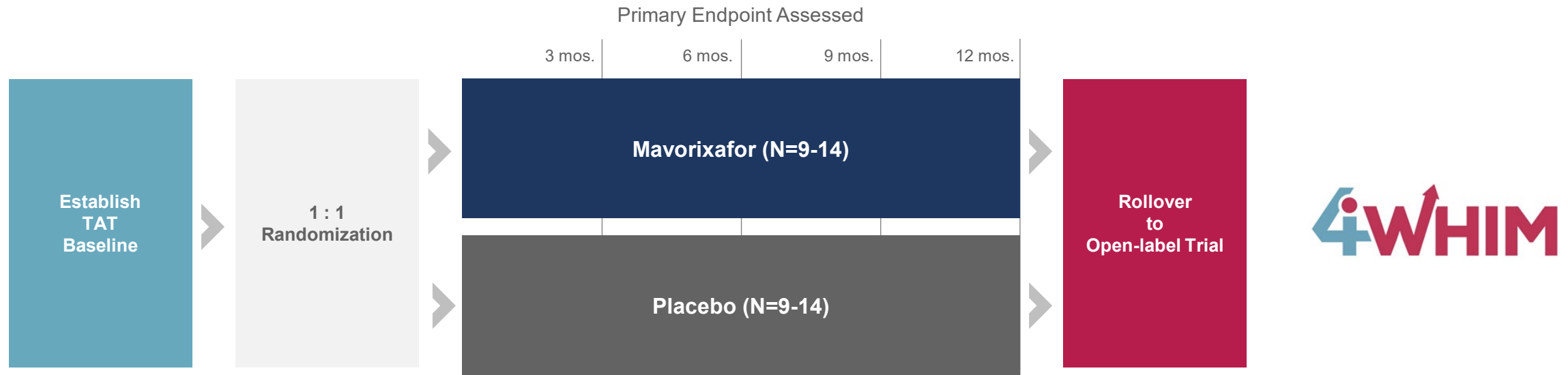
**Mutations
cause over-signaling**



**Impacting immune cell expansion,
maturation, and trafficking**

- **WHIM Syndrome:** spectrum of clinical presentations mostly with (and sometimes without) CXCR4 mutations
 - **W:** warts
 - **H:** hypogammaglobulinemia
 - **I:** infections
 - **M:** myelokathexis (hyper-cellular bone marrow)
- In most cases, **autosomal dominant disease** driven by pathogenic CXCR4 mutations; mostly located in "tail" (c-terminus) of receptor
 - ~16 identified to date; # increasing with research
- Results in **over-signaling of CXCR4 impacting all white blood cells**

Design of Mavorixafor Global Phase 3 Trial in WHIM (*Patients 12 years of age and older*)



- **Primary Endpoint:** Biomarker of time above threshold (>500 cells per microliter) for absolute neutrophil count (TAT_{ANC}); average of four assessment timepoints
- **Secondary Endpoints:** TAT_{ALC} , infections, wart burden, infection score composite, QoL assessment and others
- **Dosing:** 400mg QD in patients for subjects above 50 kg; 200 mg QD for those below 50 kg
- **Enrollment Complete:** Over-enrolled with 31 patients

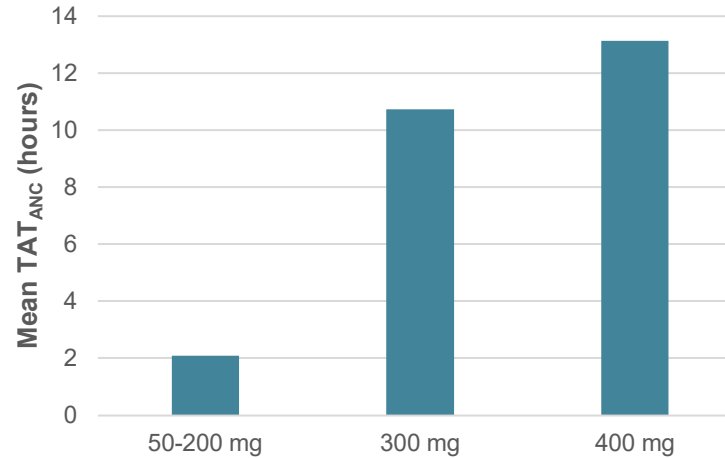
Phase 3 Top-line Data Expected in 4Q 2022

EHA 2020: Phase 2 Trial Demonstrates Clinical Activity Based on Endpoints in Phase 3 Trial

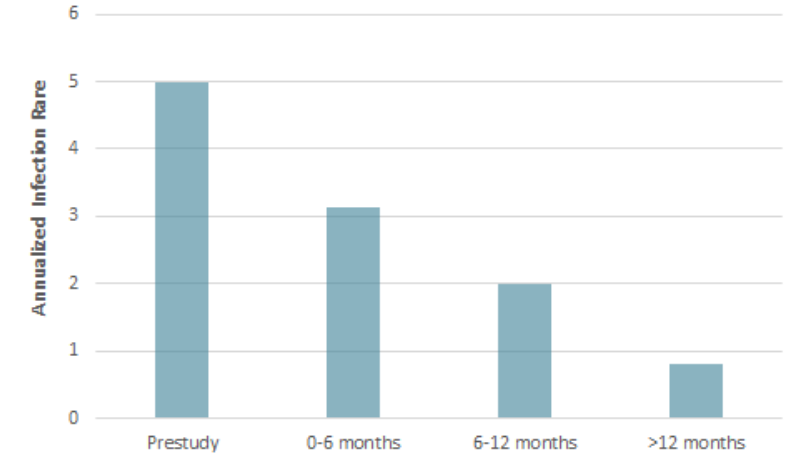
Phase 2 Trial Design

- Intra-patient dose-escalation: safety, PK
- Endpoint: clinically relevant blood measurement: **"Time above threshold for absolute neutrophil count" (TAT_{ANC})**
 - FDA & EMA agreement on use as P3 endpoint
 - Wart burden and infection rates also examined

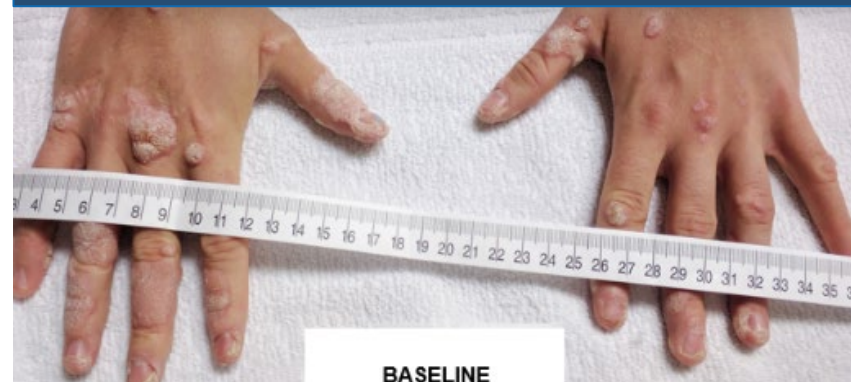
Major (>600%) Increase in Neutrophil Counts (TAT_{ANC})



>80% Reduction in Annualized Infection Rates

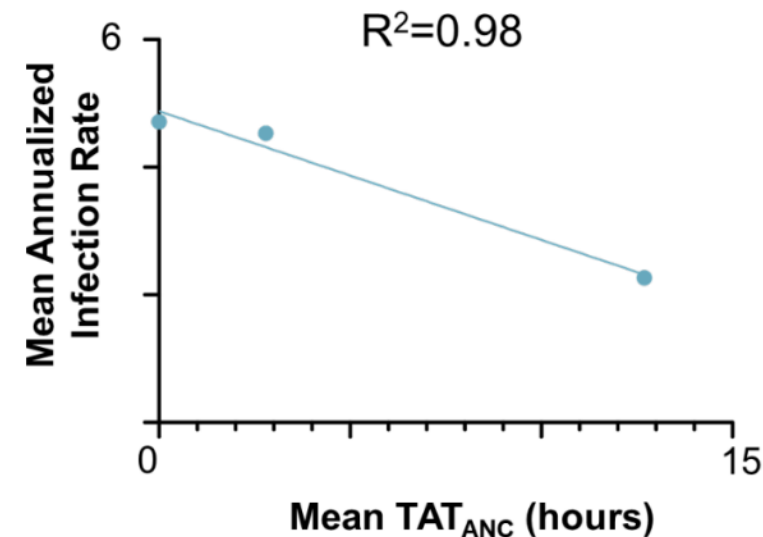
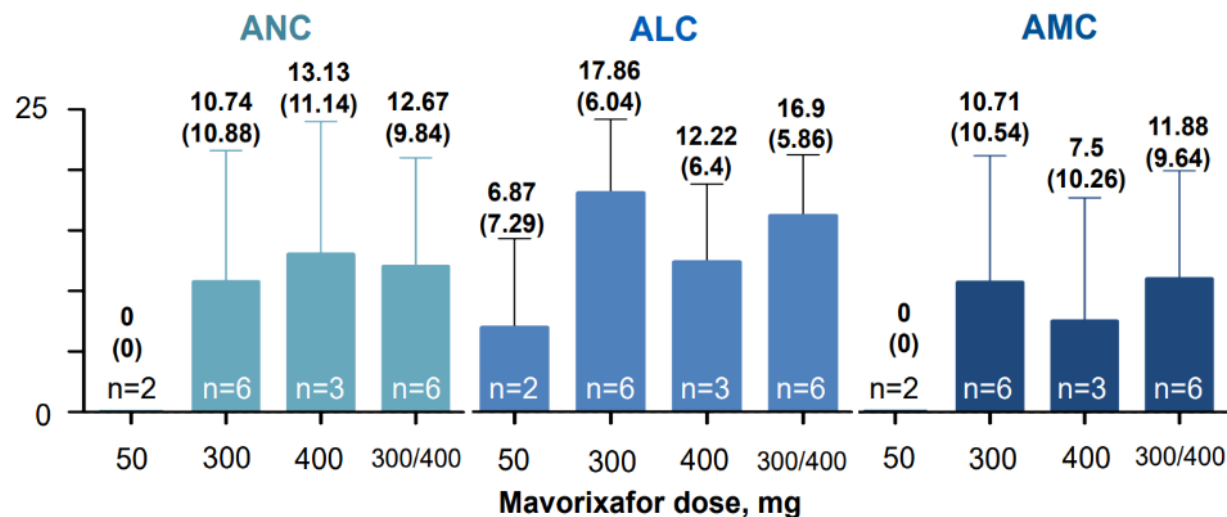


>75% reduction in the number of warts while on treatment



ASH 2021: Phase 2 WHIM Trial Shows Continued Benefit

Mean Time Above Threshold (TAT, hours) for ANC, ALC, and AMC



Datapoints (L to R): pre-treatment, low dose (50-150mg), high dose (300/400mg) mavorixafor

- **Patient interviews** revealed long-term treatment with mavorixafor to be well tolerated and continuing to demonstrate beneficial treatment effects, including:
 - Decreased frequency, severity, and duration of infections and
 - Fewer hospital/doctor visits
- **Decreases in mean annualized infection rates correlate well with TAT_{ANC}, the primary endpoint in our ongoing, fully enrolled, global, Phase 3 registrational trial**
- Data continue to support the potential of mavorixafor to be a safe, effective, and long-term oral therapy targeting the underlying cause of WHIM syndrome

"ALC" represents absolute lymphocyte count. "AMC" represents absolute monocyte count.

Understanding the Definition and Diagnosis of WHIM Syndrome

Mavorixafor
Potential Label

For the treatment of WHIM Syndrome in patients ≥ 12 years

**Diagnosis of
WHIM Syndrome:**

*Combined
Immunodeficiency¹
w/ clinical
presentation*

One or more of the following:

1. **CXCR4 gain-of-function mutation**
2. **Confirmed Myelokathexis**
3. **Novel genes/mutations** impacting WBC maturation & trafficking – *but no CXCR4 mutations*²

The Different Faces of WHIM



1. "Combined Immunodeficiency" is defined as one or more of abnormal neutrophils (ANC) lymphocytes (ALC) and monocytes (AMC) and hypogammaglobulinemia. Clinical presentation of infections (bacterial and/or viral including HPV) is also required.

2. WHIM syndrome has been diagnosed without CXCR4 mutations or myelokathexis.

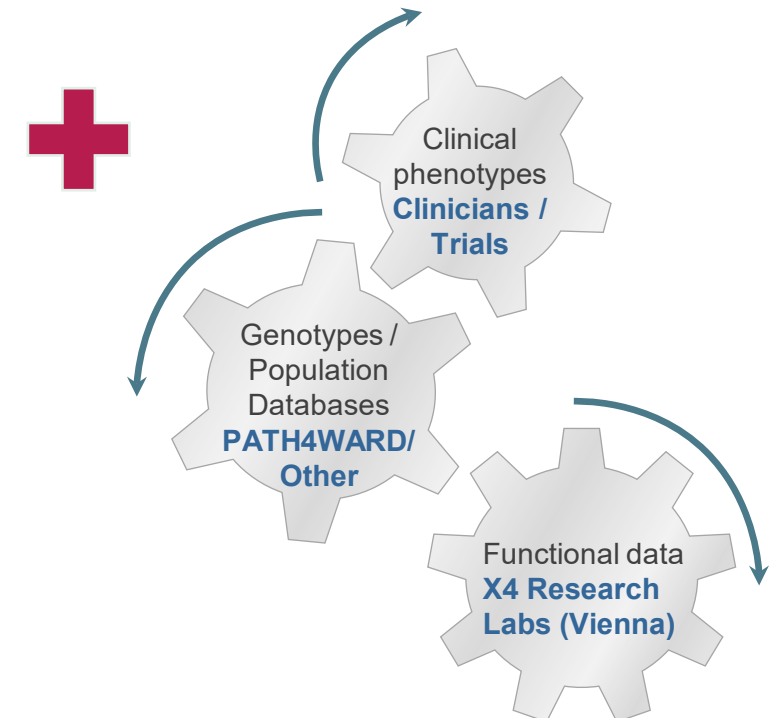
WHIM Prevalence: 1,000 – 3,700¹ in the U.S.

Market and AI Research Results: Estimated Prevalence



Bench-to-Bedside Research Expanding the Definition and Estimated Prevalence of WHIM

Newly identified D84H CXCR4
mutation suggests additional
~1,250-2,500 WHIM patients



What is Chronic Neutropenia (CN)?

Chronically immunocompromised patients due to sustained, low neutrophil counts (neutropenia)

Danish Study: Prevalence and Mortality Risk¹

- 0.06% of population with chronic neutropenia (<1,500 cells/microliter), or about 6 in 10,000
- All-cause mortality: 2.5-6.5X hazard ratio vs. non-neutropenic population

The magnitude of neutropenia correlates with higher risk of severe infections and greater frequencies of infections

- Mild if ANC between 1,000 and 1,500/ μ L
- Moderate if ANC between 500 and 1,000/ μ L
- Severe if ANC <500/ μ L

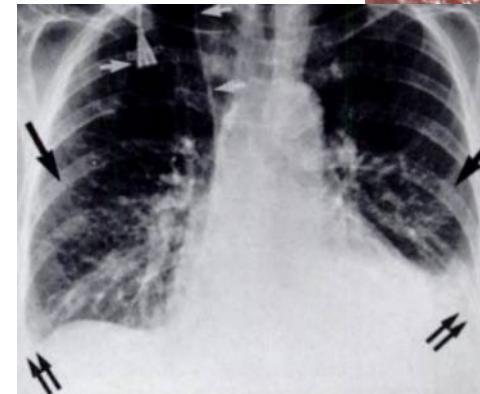
Skin Abscesses



Oral Ulcerations

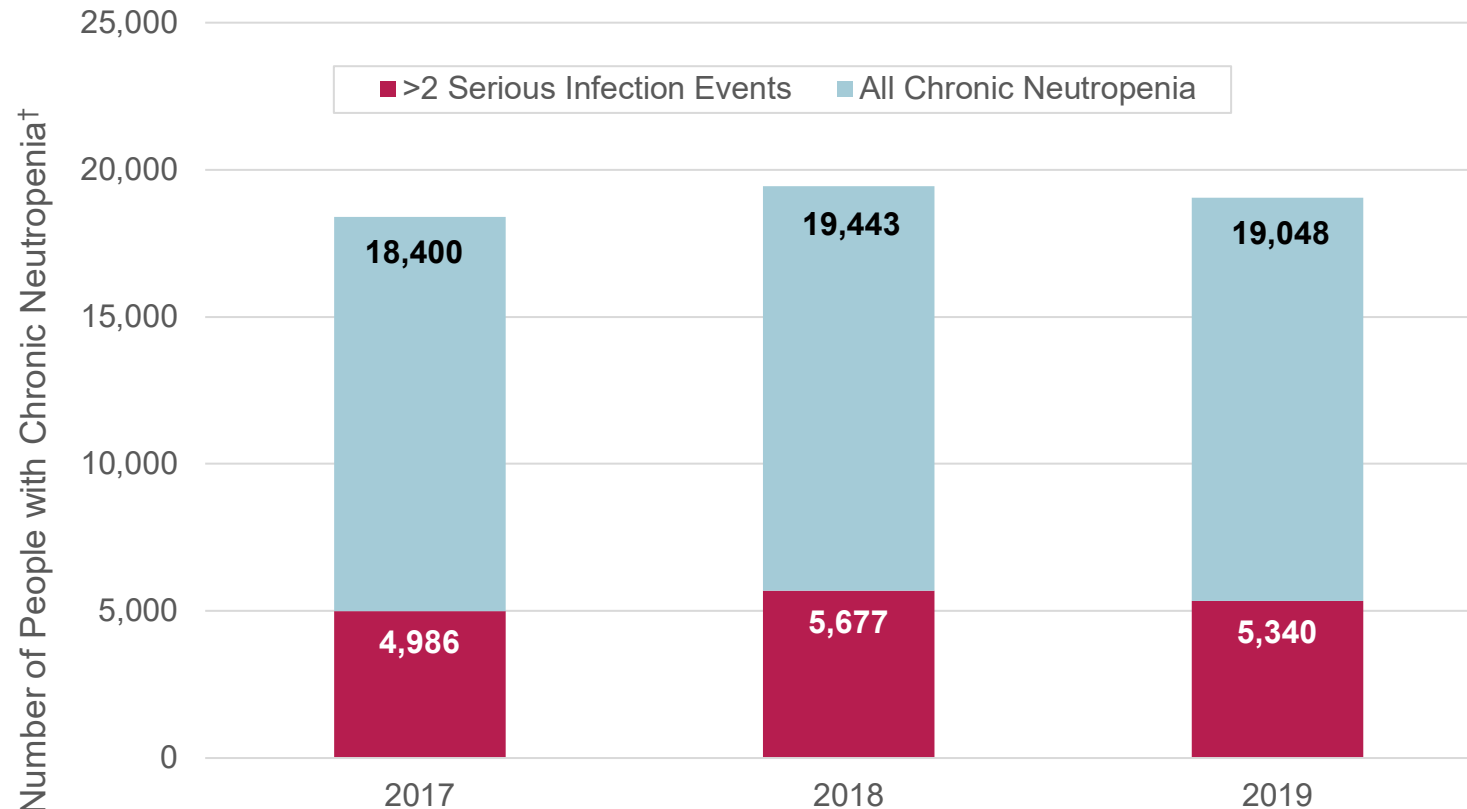


Pneumonia



~20,000 With Chronic Neutropenia In the U.S.¹:
Thousands Have Major Health Impact With >2 Serious Infection Events per Year

CN Patients Experience Serious Infection Events (SIEs): Any infection that required **hospitalization, intravenous antibiotics and/or resulted in disability or death**



~25% of all CN patients have two or more SIEs² per year

Source: X4 Data on file; TriNetX USA EMR Database analysis using inclusion criteria and medical record coding, data and confirmation. Patients 12 years of age and above.

¹ Eligible patients in the TriNetX USA database who had an ANC <1500 cells/μl in calendar year of interest and two additional ANC <1500 cells/μl in the subsequent two years.

² Numbers are extrapolated to reflect the total U.S. population each year (multipliers ranged from x6.4 in 2017 to x5.2 in 2019).

Chronic Neutropenia Management: Currently Approved Treatments Have Significant Drawbacks

Injections of G-CSF

- **Once or twice-daily at 5-6 $\mu\text{g/kg}$** to reduce severe neutropenia and risk of infections
- “Dose down-titration” and reduced frequency often implemented to aid with tolerability for chronic use
- Neutrophil target: $\sim 1,000\text{-}2,000$ cells/ μL

Challenges for patients on G-CSF

- 25% continue to experience severe bacterial infections *while on chronic treatment*¹
- Increasing risk of myelodysplastic syndromes (MDS)²
- $\sim 70\%$ have moderate or severe bone-pain impacting compliance and QoL³

No alternate therapies, except for bone marrow transplantation



U.S. G-CSF Market For Severe Chronic Neutropenia: Estimated \$120-460 Million

- **Injectable treatment** with a growth factor
- Chronic treatment with G-CSF has been approved for certain types of **severe chronic neutropenia (ANC < 500 μ L)** and has been shown to reduce infections
- **>2,000 patients with chronic neutropenia estimated to be on regular G-CSF treatment in the U.S.**²
- Annual cost of treatment at generic prices ranges **\$60,000 to \$230,000 per patient**³
 - Range depends on dose frequency and weight; some intermittent use

1. IQVIA Sales Audit – G-CSF.

2. Based on research of U.S. claims data, EMR and SCNIR registry data; excludes all cancer/chemotherapy-related uses of G-CSF.

3. Based on labeled dosing for SCN and ASP for biosimilar products.

Ongoing Phase 1b Trial: Assessing Mavorixafor in Patients with CN

Phase 1b trial: Activity in Broad CN Population

- Severe and moderate CN
- With or without genetic causes
- With or without G-CSF

Endpoints: Safety and tolerability, change in ANC (and other WBCs) vs. pre-treatment baseline

Goal: Achieve proof of concept to support FDA interactions regarding proposed registrational trial

*Studying mavorixafor
across broader chronic
neutropenia populations*

12 years or older; on or off G-CSF

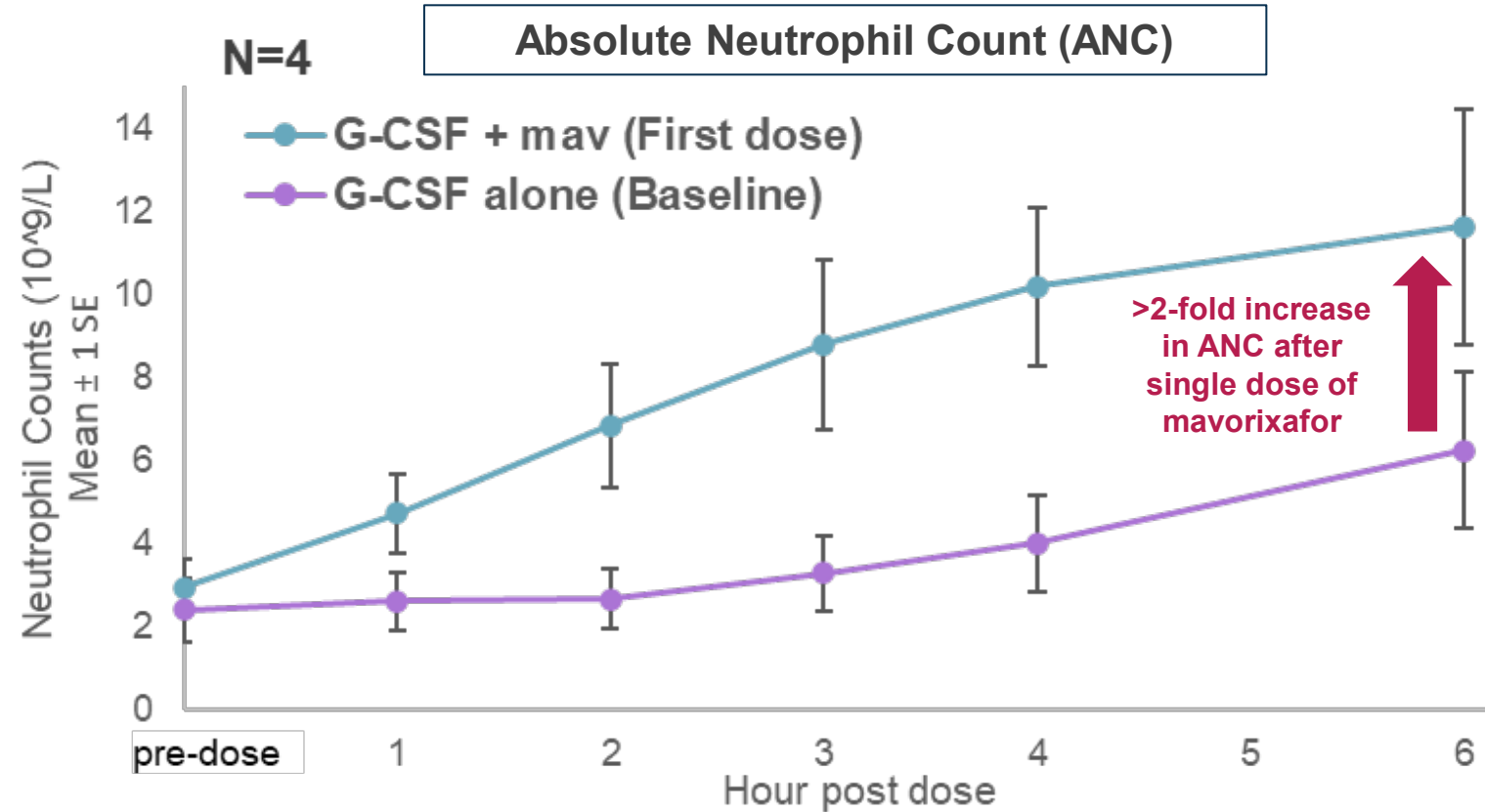
Cohort A

- 14 days of treatment
- Chronic idiopathic neutropenias
- Neutrophil count $<500 \mu\text{L}$

Cohort B

- 1 day of treatment
- Congenital, cyclic or idiopathic neutropenia
- Neutrophil count $<1,000 \mu\text{L}$

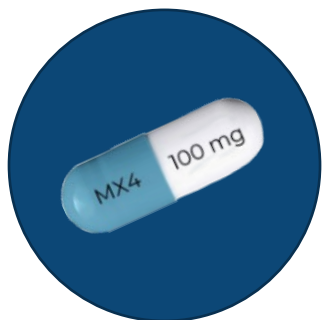
Meaningful Responses* to Single Dose in Idiopathic Chronic Neutropenia Patients



Similar increases in:

- ✓ Total White Blood Cell Counts (WBCs)
- ✓ Absolute Lymphocyte Counts (ALC)
- ✓ Absolute Monocyte Counts (AMC)

Significant Opportunity for Mavorixafor in Chronic Neutropenia



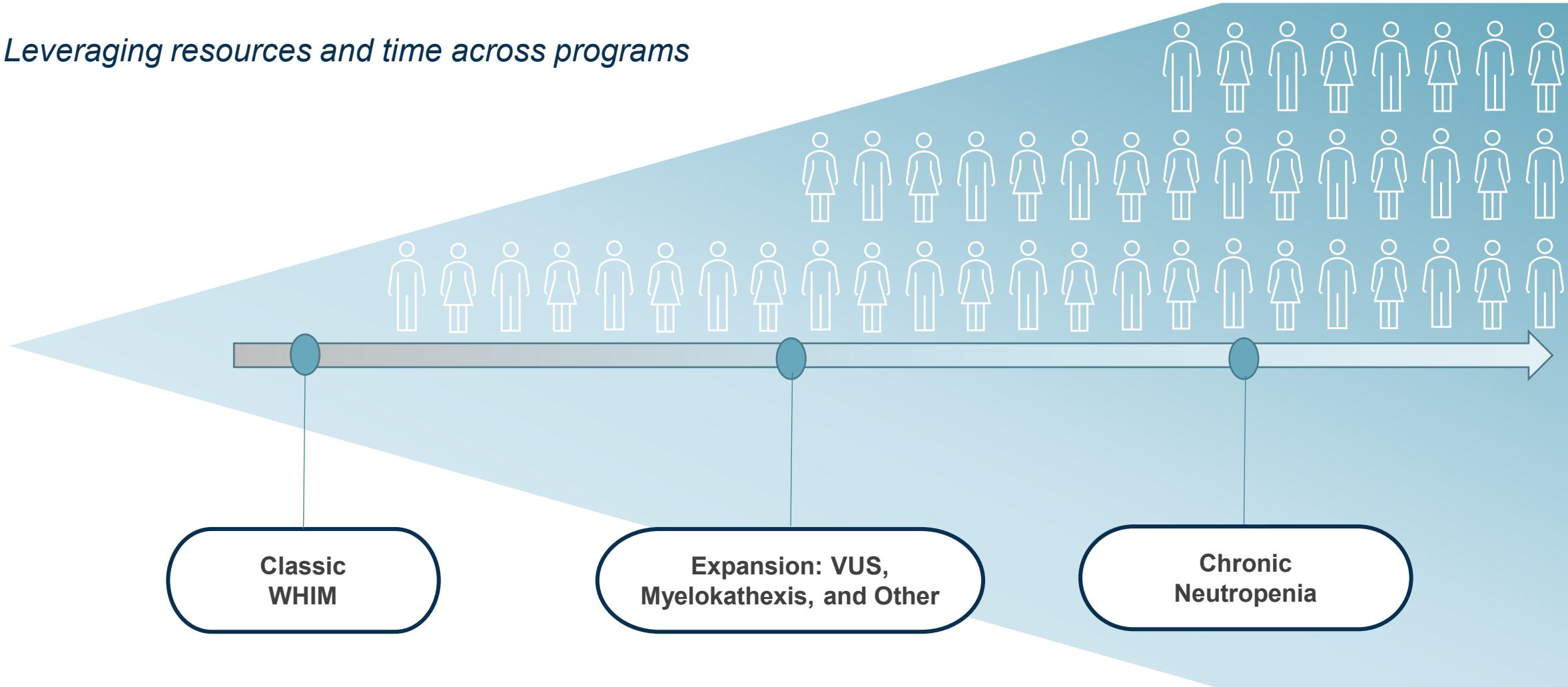
- ✓ **More than 5,000 patients in the U.S. with neutropenia** at significantly increased rates of hospitalization with severe infections
- ✓ Only available treatment is injectable, with limited tolerability and frequent injections
- ✓ **Mavorixafor single dose activity:** Initial data from the ongoing Phase 1b trial in adult patients with idiopathic CN shows clear elevation of neutrophils and all other WBCs
- ✓ Further positive data from this ongoing trial will inform for a pivotal trial to investigate mavorixafor as the potential first oral treatment to reduce the burden of infections in patients with chronic neutropenia

Ongoing Phase 1b trial enrolling; 2Q/3Q 2022 readout expected



Building Our PI Business To Support A Continuum of Mavorixafor-Treatable Patients

Leveraging resources and time across programs



Dysregulation of white blood cells (leukocytes) contributes to a broad range of serious diseases with significant unmet needs



Primary Immunodeficiencies

Life-threatening infections & deaths

- >\$3.3 billion WW annual Rx sales¹
- Few options (G-CSF & IVIG)
- Injectable or infusion only



Lymphomas

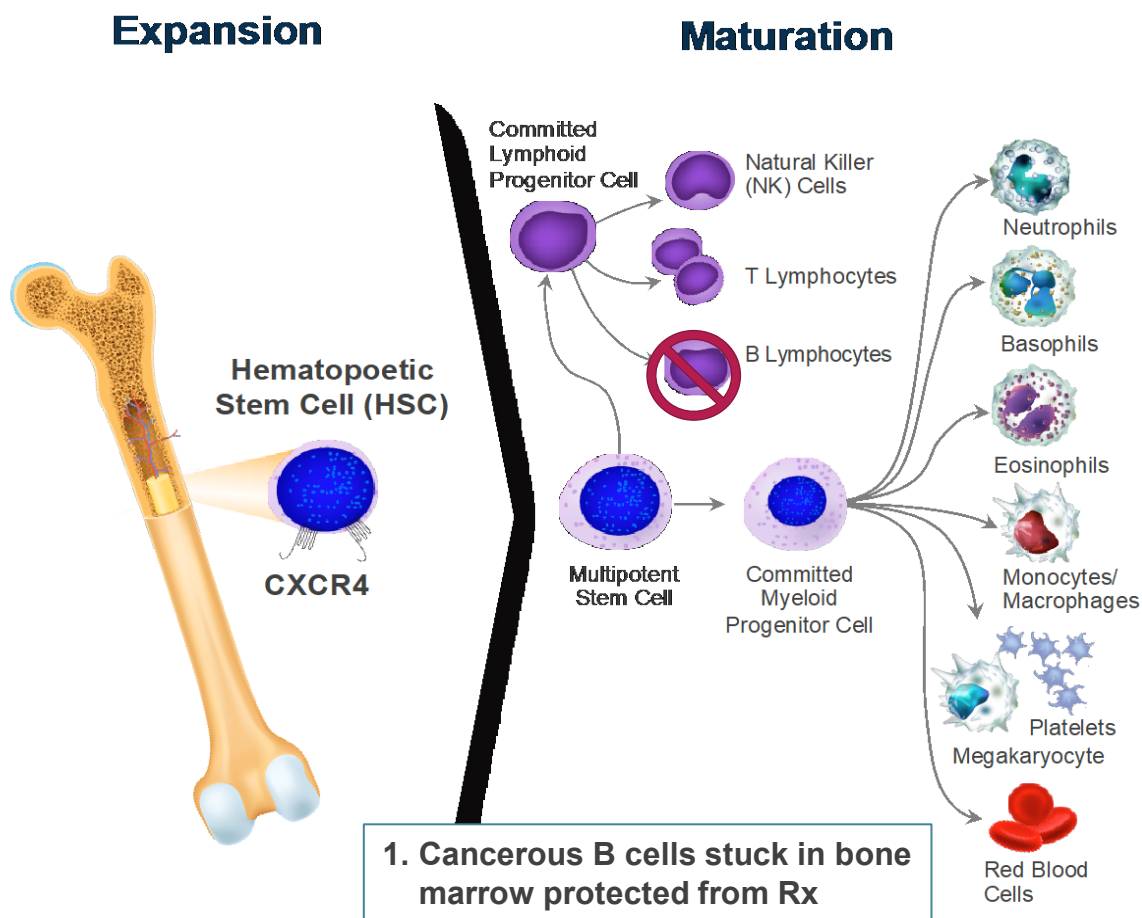
Cancer progression and deaths

- >\$7 billion WW annual Rx sales²
- Multiple therapies and lines of treatment
- Few cures

1. Allied Market Research 2019.

2. Business Insight, Market Research Report, 2018.

The Dysregulated Immune System: Lymphomas



2. CXCR4 antagonism mobilizes cancer cells to increase susceptibility to Rx

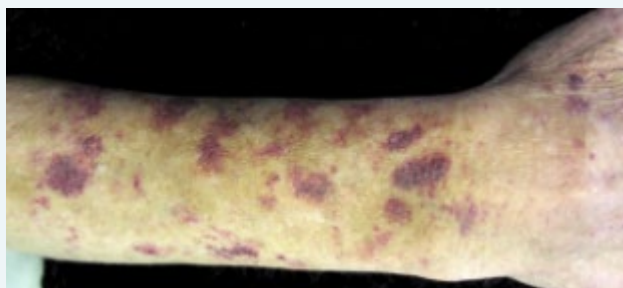
3. “Chemosensitization” by CXCR4 antagonist combination to improve efficacy in leukemias and lymphomas

CXCR4 Antagonism Proof of Concept

B-Cell Lymphomas	U.S. Prevalence	Combinations Studies
Diffuse Large B-Cell Lymphoma (DLBCL)	~20,000 ²	Plerixafor + Rituximab (Preclinical)
Mantle Cell Lymphoma (MCL)	>4,000 ³	Plerixafor + Bortezomib (Preclinical)
Waldenström's Macroglobulinemia (<i>non-CXCR4 mutation</i>)	~8,000-10,000 ⁴	Mavorixafor + SOC Preclinical in WT CXCR4
Waldenström's Macroglobulinemia (<i>CXCR4-mutation sub-population</i>)	~2,000-3,000 ⁴	Ulocuplumab + ibrutinib (Clinical) Mavorixafor + Ibrutinib (Clinical)

Waldenström's Macroglobulinemia: a Rare B-Cell Lymphoma

A rare B-cell blood cancer of the bone marrow; most often (>90%) caused by mutations in the MYD88 gene, which is involved in innate immune response system



30-40%

Patients with identified WHIM-like CXCR4 mutations in addition to MYD88 mutation

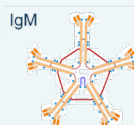


~8-10

year survival rate post diagnosis^{1,2}

Signs and symptoms

- **Elevated IgM**
- Hyperviscosity syndrome
- Cryoglobulinemia – IgM clumping
- Pancytopenia, anemia
- Peripheral neuropathy
- Fever, night sweats, weight loss, fatigue



Limited Current Treatments

- Ibrutinib, zanubrutinib
- Chemo (bendamustine, R-CHOP)
- Rituximab
- Combinations and others

<50%

Mean progression-free survival (PFS) in CXCR4-mutation Waldenström's patients versus CXCR4-wild type³

1. Sekhar J, et.al., Waldenström macroglobulinemia: a Surveillance, Epidemiology, and End Results database review from 1988 to 2005. *Leuk Lymphoma* 2012;53(8):1625-1626.

2. www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=33226. 3. Treon et al, EHA 2018.



Improvements in serum levels of IgM and hemoglobin

- *Reductions in IgM* changes correlated with response definitions
- *Increases in hemoglobin* indicate reduction in cancer burden

Improvements in Response Rates

- Responses correlate with progression free survival and overall survival

Mavorixafor Phase 1b Trial in Double-Mutation WM Patients

Inclusion: Patients with *MYD88* + *CXCR4* mutations who are naïve to ibrutinib

Design: Multi-national Phase 1b trial of mavorixafor in combination with ibrutinib (n=12 to 18)

- **Inpatient dose-escalation:** cycles of 200 mg, 400 mg, and 600 mg QD
- **3 cohorts supporting dose selection of mavorixafor:**
 - ✓ Cohorts A & B: minimum of 6 patients enrolled in each
 - ✓ Cohort C (expansion): potential for additional 6 patients dosed up to 600 mg
- **Endpoints**
 - Safety, PK/PD
 - Assessments of serum IgM levels, hemoglobin, and clinical response

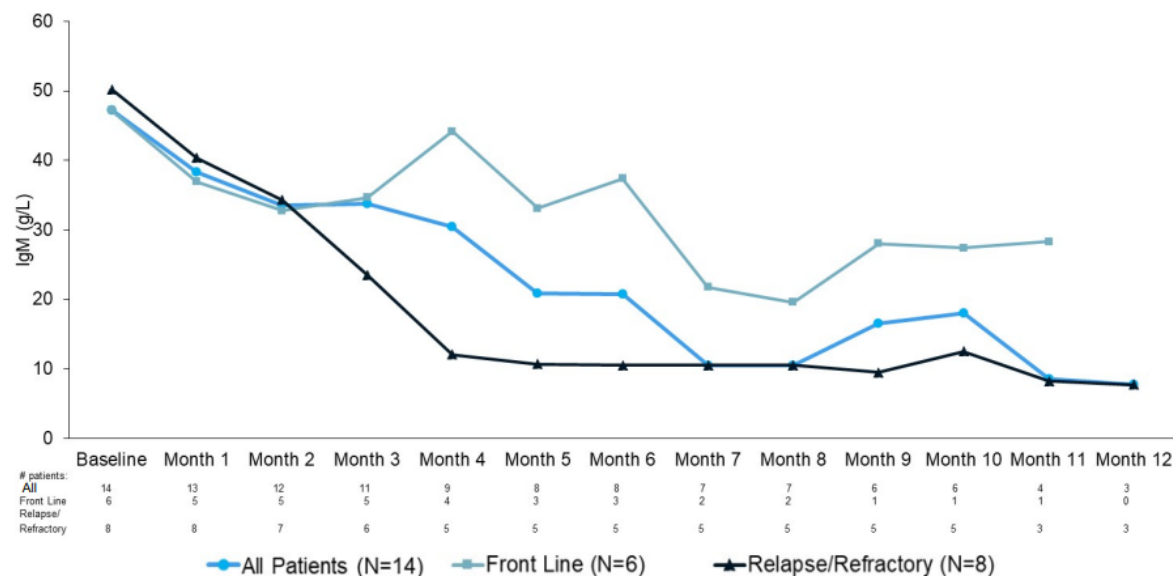


- Strategic collaboration with Leukemia & Lymphoma Society (LLS)
- Selected for LLS' Therapy Acceleration Program

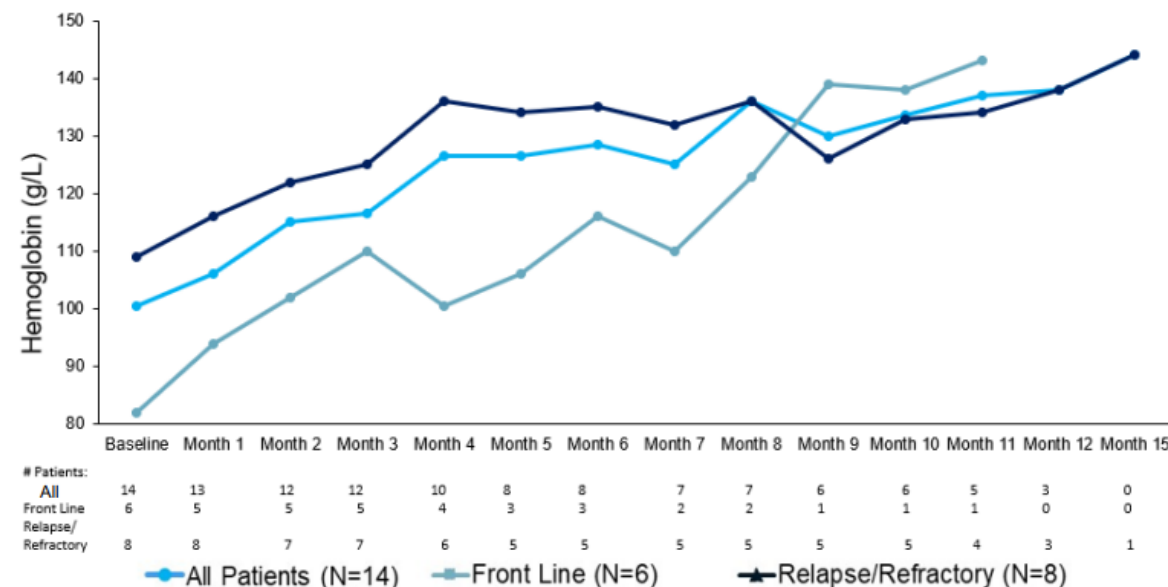
ASH 2021: Interim Data Support Potential of Mavorixafor for the Treatment of Waldenström's

- 100% overall response rate (n=10)
 - 4 achieving a Major Response (>50% reduction in serum IgM)
 - 1 achieving Very Good Partial Response (VGPR) (>90% reduction in serum IgM)
- Mavorixafor + ibrutinib led to rapid, clinically meaningful, and durable decrease in IgM levels and increase in Hgb levels

Median Serum IgM Levels^{a,b}



Median Change From Baseline in Hgb^{a,b}



^aData cut as of October 12, 2021.

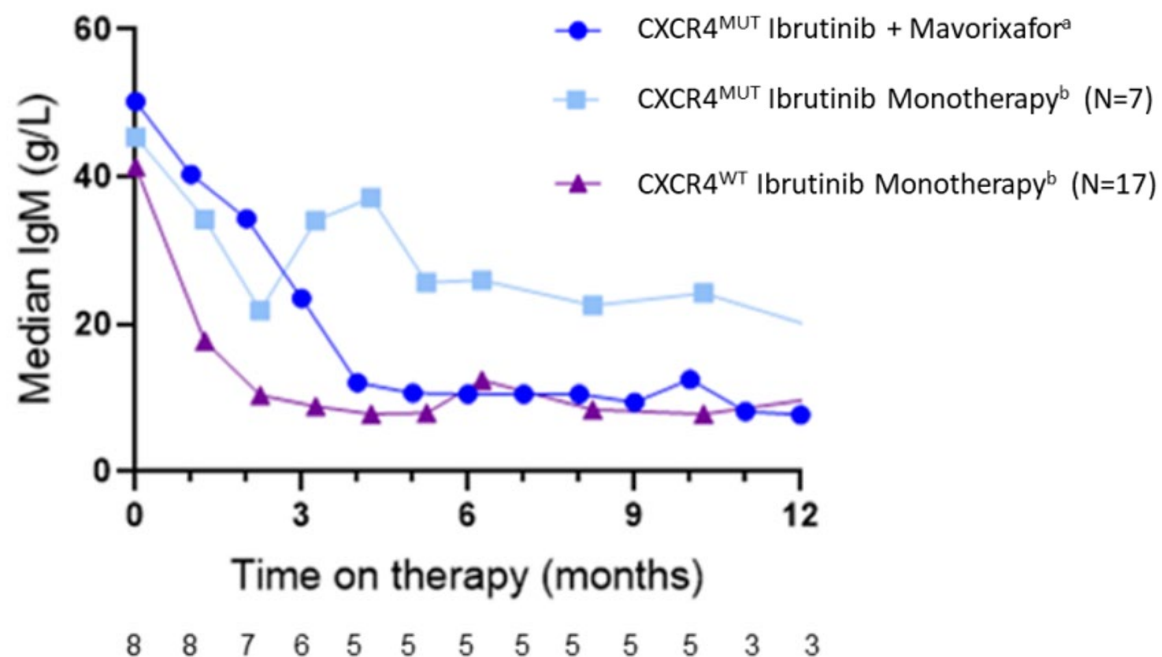
^bFor 1 participant receiving frontline therapy, study treatment was temporarily withheld due to an AE the week prior to Month 4 IgM sample collection; the subject subsequently restarted on a reduced dose and then discontinued from the study at Month 6. Another participant discontinued study treatment after Month 2.

^aInterim early data analysis performed with data cutoff at Oct 12, 2021.

^bMissing data imputed using last observation carried forward.

ASH 2021: Positive Initial Results with Mavorixafor in WM Refractory Patient Population

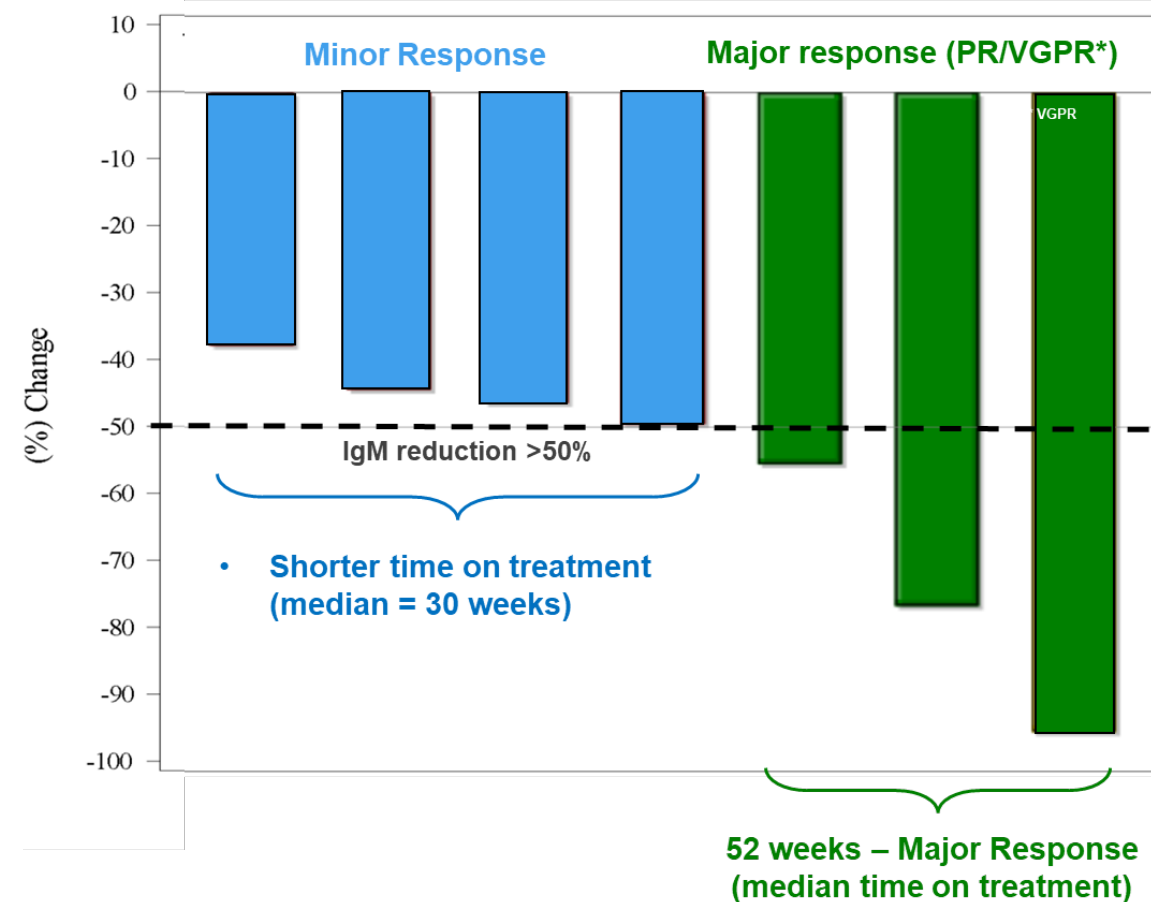
Refractory Patients' Serum IgM Levels After Treatment with Mavorixafor + Ibrutinib vs. Ibrutinib Monotherapy With or Without CXCR4 Mutations



Refractory Patients on Ibrutinib + Mavorixafor

^a Refractory patients in study
^b This study included adults with WM requiring treatment / refractory to their last therapy

Clinical Responses in Individual R/R Patients (N=7) (based on Best IgM Response)



Differentiated Next-Generation CXCR4 Antagonists Progressing into the Clinic

Supporting Corporate Growth

Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Expected Milestones
Mavorixafor	WHIM (Warts, Hypogammaglobulinemia, Infections and Myelokathexis) syndrome ¹	Phase 3				Top-line data 4Q 2022 2H 2023 NDA
	Chronic Neutropenia (CN)	Phase 1b				Add'l data / clinical update in 2Q/3Q 2022
	Waldenström's Macroglobulinemia (WM)	Phase 1b				Add'l data / clinical update in 2H 2022
X4P-002	Oncology indications	IND-enabling				IND in 2H 2022
X4P-003	Primary immuno-deficiencies (PIDs)					

- **Milestones Achieved During the Second Half of 2021**

- ✓ WHIM Phase 3 trial enrollment complete with 31 patients
- ✓ ASH abstracts with data updates across all programs
- ✓ Positive initial data in Waldenström's Phase 1b trial
- ✓ Positive initial data in Chronic Neutropenia (CN) Phase 1b trial
- ✓ Positive long-term outcomes in ongoing WHIM Phase 2 trial
- ✓ Bench to bedside research: WHIM prevalence/patient ID

- **Expected Milestones in 2022 and Beyond**

- Data & regulatory updates in CN in 2Q/3Q 2022 and WM in 2H 2022
- Pipeline candidate IND filing in 2H 2022
- Preclinical PoC in lymphoma and neutropenia models in 2022
- Continued reporting on expanding market opportunity in WHIM
- ***WHIM Phase 3 top-line data in 4Q 2022***
- ***Potential mavorixafor WHIM NDA filing in 2H 2023***

\$83M¹

Cash Expected to Fund Operations into 4Q 2022²

Share and Warrant Information:

**31.9 M shares
outstanding**

(28.1M common shares
and 3.8M pre-funded
warrants)

**5.4M class B
warrants**

(expiry **30 days** post
WHIM P3 data)

**3.9M class A
warrants**

(2024 expiry)

Biotech-focused Institutional Shareholder Base

Analyst Coverage

STIFEL

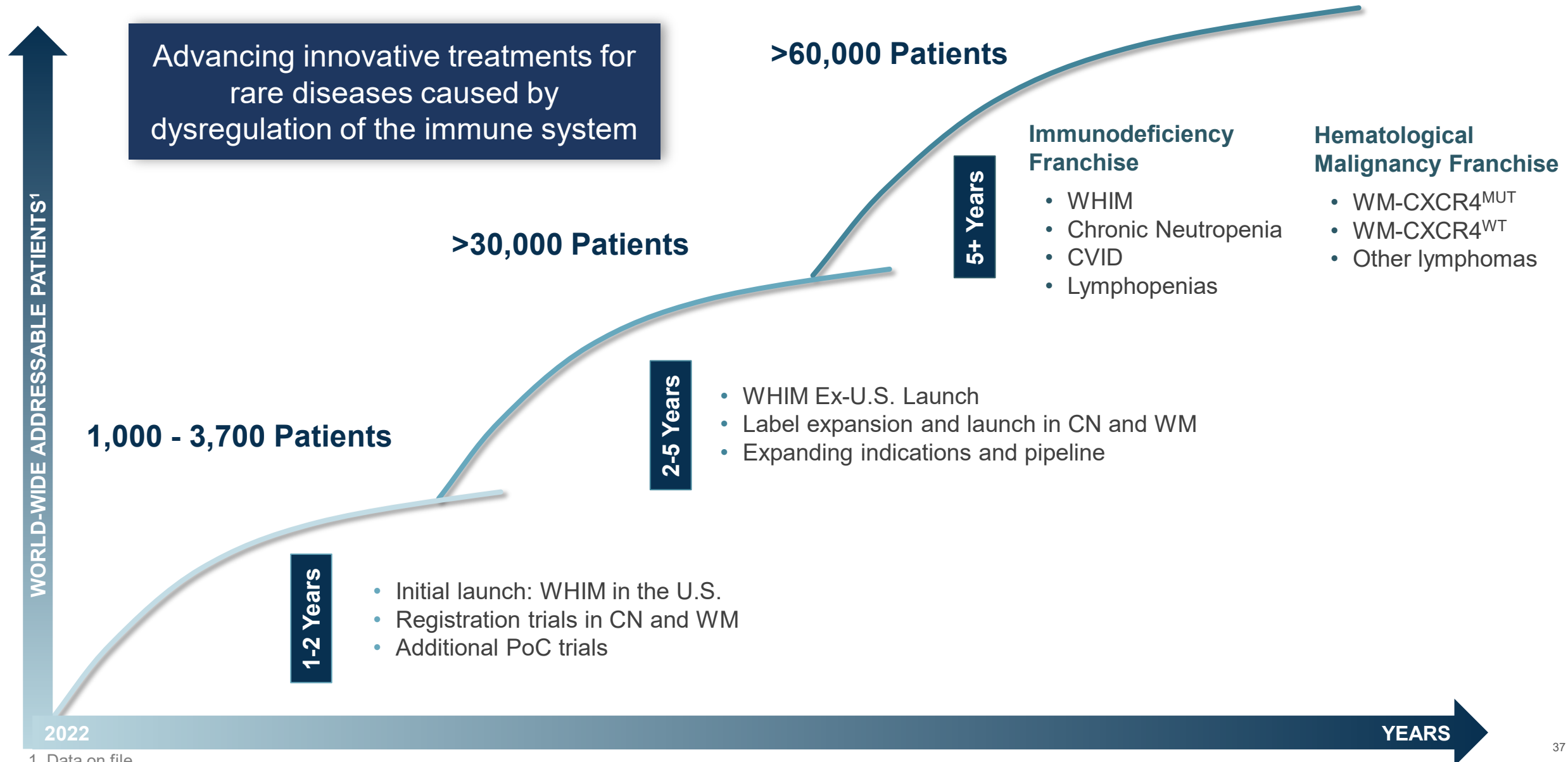


**BROOKLINE
CAPITAL MARKETS**



¹ As of December 31, 2021. ² As described in detail in our most recent Form 10-K, our agreement with Hercules Capital, Inc. contains a minimum cash covenant that becomes effective on September 1, 2022, subject to certain exceptions. We will require additional funding to satisfy this covenant. Our current cash runway projections assume continued compliance with this covenant. Failure to satisfy this covenant could result in accelerated principal and interest payments due that could shorten our cash runway. Outstanding debt balance as of 12/31/2021 is \$32.5 million.

X4: Preparing to Deliver Long-Term Growth



1. Data on file.



Thank you!



61 North Beacon Street
4th Floor
Boston, MA 02134

www.x4pharma.com