X4 PHARMACEUTICALS

# INVESTOR PRESENTATION

OCTOBER 2020

# FORWARD LOOKING STATEMENTS

The statements herein are subject to various risks and uncertainties. These risks and uncertainties include, without limitation, the risk that trials and studies may be delayed and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of mavorixafor or other product candidates; the risk that costs required to develop mavorixafor or other product candidates or to expand our operations will be higher than anticipated; the ongoing direct and indirect effects of the ongoing COVID-19 pandemic on various aspects and stages of X4's clinical development process including the impact to expected site initiation, enrollment and participation in X4's clinical trials; and the risk that the PATH4WARD program and X4's relationship with Invitae will not be successful. Any forward-looking statements herein are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained herein, including, without limitation, the risks and uncertainties described in the section entitled "Risk Factors" in X4's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 4, 2020, and in other filings X4 makes with the SEC from time to time. X4 cautions investors not to place undue reliance on the forward-looking statements herein and undertakes no obligation to update the information contained in this presentation to reflect subsequently occurring events or circumstances.

**Developing treatments designed to have a clear and profound impact for patients suffering from rare diseases, including WHIM syndrome and uncommon cancers**

# **OVERVIEW:** BUILDING A GLOBAL RARE DISEASE COMPANY

- Leading discovery and development of novel therapies targeting diseases resulting from CXCR4 pathway dysfunction
- Novel therapeutics designed to improve immune cell trafficking
- Lead product candidate mavorixafor (X4P-001), first-in-class, oral, small molecule allosteric antagonist of chemokine receptor CXCR4
- Multiple clinical trials underway, including ongoing global registrational Phase 3 trial of mavorixafor in WHIM syndrome, a Phase 1b trial in Waldenström's macroglobulinemia and a Phase 1b trial in Severe Congenital Neutropenia
- Potential expansion opportunities across rare disease landscape
- Experienced leadership team in rare disease – includes several former members of Genzyme leadership team
- Headquarters in Boston, MA with R&D facility in Vienna, Austria

# LEADERSHIP:
## PROVEN TEAM WITH RARE DISEASE EXPERTISE

### MANAGEMENT

**PAULA RAGAN, Ph.D.**
CEO
genzyme SANOFI

**ADAM MOSTAFA**
CFO
abpro CANTOR Fitzgerald

**DEREK MEISNER, J.D.**
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gsk TESARO KURA ONCOLOGY EMD SERONO

**MARY DIBIASE, Ph.D.**
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Biogen EPIRUS BIOPHARMACEUTICALS

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Aegerion Pharmaceuticals GE Healthcare

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VP of Patient Advocacy
ENZYVANT Takeda ONCOLOGY

**SHARIQ ALI, Ph.D.**
VP of Medical Affairs
WAVE SANOFI genzyme

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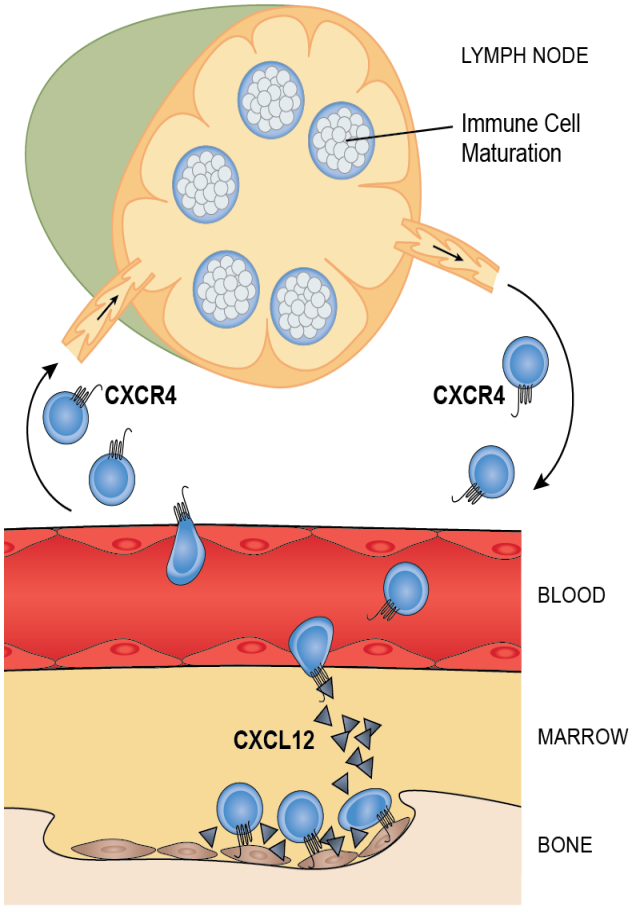
rhythm gsk

**RENE RUSSO, PharmD, BCPS**
arsanis CUBIST PHARMACEUTICALS

**ALISON LAWTON**
kaleido genzyme

# **MAVORIXAFOR:** TARGETED TREATMENT FOR DISEASES DRIVEN BY IMMUNE-CELL TRAFFICKING DEFICITS

## MECHANISM OF ACTION




## LEAD INDICATIONS

**PHASE 3:**
WHIM Syndrome

**PHASE 1B**:
Waldenström's Macroglobulinemia

Validated by blocking **"Gain-of-Function" CXCR4 genetic mutations**

## LABEL EXPANSION OPPORTUNITIES

**PHASE 1B:**
Severe Congenital Neutropenia

**PHASE 2A:**
Renal Cell Carcinoma*

Immune-suppression corrected by **blocking CXCR4 Signaling**

## PIPELINE

**PRECLINICAL PROGRAMS:**
Additional primary immuno-deficiencies

Established linkages to **immune-system genetics/pathways**

** Exploring potential strategic partnership(s) for future development and potential commercialization for mavorixafor for ccRCC and other potential immuno-oncology indications*

# **OVERVIEW:** MAVORIXAFOR

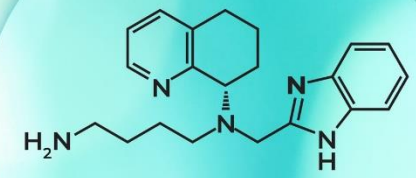
First-in-class CXCR4 antagonist
- Small molecule with high potency and selectivity
- Terminal half-life of 22 hours
- Formulated as a once-daily oral capsule

Clinical trial experience in nearly 200 patients

Alignment on global Phase 3 trial design and regulatory path for WHIM
- **Breakthrough Therapy Designation in U.S**.
- **Fast Track Designation in U.S.**

Orphan Drug Status in U.S. and Europe

Critical U.S. composition of matter patents expected to provide protection through 2038



# PRODUCT PIPELINE

| CANDIDATE | INDICATION | PRECLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|
| **Mavorixafor (X4P-001)** | Warts, Hypogammaglobulinemia, Infections and Myelokathexis (WHIM) syndrome[1] | | | | PHASE 3 |
| | Waldenström's Macroglobulinemia (WM) | | PHASE 1B | | |
| | Severe Congenital Neutropenia (SCN) | | PHASE 1B | | |
| | Clear cell renal cell carcinoma[2,3] (ccRCC) *(Combination with Inlyta®)* | | | PHASE 2A | |
| **X4P-002** | Glioblastoma multiforme (GBM) | | | | |
| **X4P-003** | Primary immuno-deficiencies (PID) | | | | |

[1] *Phase 2 open label extension trial for WHIM ongoing and Phase 3 trial initiated*
[2] *Two oncology trials have concluded: Phase 1b biomarker in melanoma and Phase 1b in ccRCC. Positive data from ccRCC Phase 2a trial reported at ESMO 2019*
[3] *Intend to enter into a strategic partnership for future development and potential commercialization for mavorixafor for ccRCC and other potential solid tumor immuno-oncology indications*

# LEAD INDICATIONS:
# CXCR4 MUTATIONS AS A DRIVER OF DISEASE

# ABOUT WHIM SYNDROME

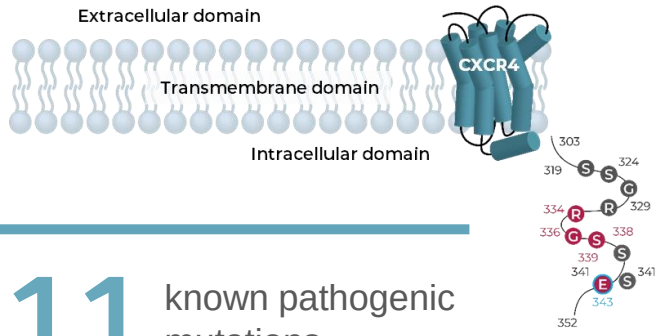
**W** **Warts** – can lead to HPV-related cancers

**H** **Hypogammaglobulinemia**

**I** **Infections**

**M** **Myelokathexis** – retention of mature neutrophils in the bone marrow

Immunodeficiency caused by gain-of-function mutations in the CXCR4 receptor that lead to excessive "on-signaling," compromising immune cell trafficking and the ability to mount a healthy immune response




**>3,500**[1]

estimated U.S. WHIM population

**0**

Approved targeted therapies

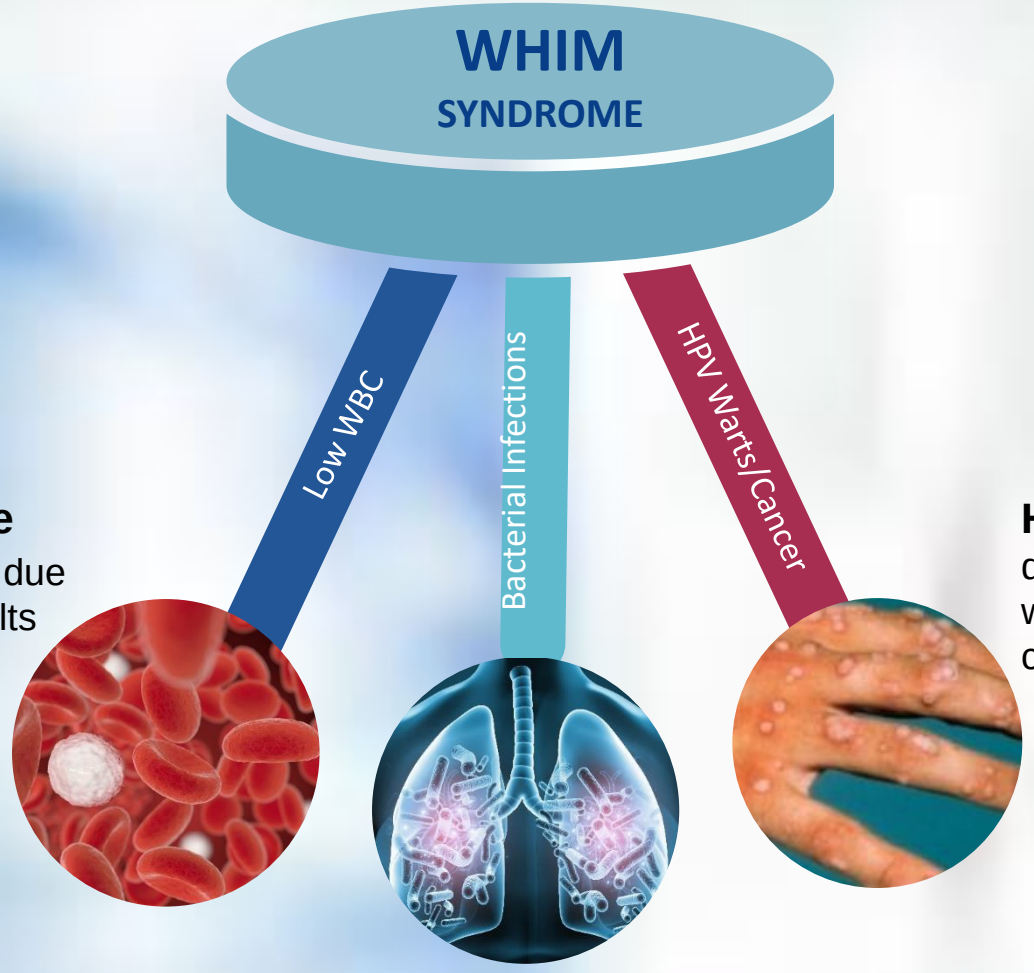
Symptomatic Rx; antibiotics, G-CSF, immunoglobulins

**11** known pathogenic mutations

Genetic test to diagnose

1. Qessential Market Research 2019; IPM.ai AI research study, 2020

# UNMET NEEDS IN WHIM




**Critically low white blood cell counts**, due to *myelokathexis*, results in immunosuppression

**HPV infections** disfiguring recalcitrant warts; HPV-associated cancers

**Severe bacterial infections in multiple organ systems**
Bronchiectasis (lung), hearing loss (ear), cellulitis (skin)

# PHASE 2 TRIAL INFORMS PHASE 3 TRIAL

## PHASE 2 TRIAL DESIGN

### INCLUSION

- Neutrophil count: ANC ≤400/µL *and/or*
- Lymphocyte count: ALC ≤650/µL *or* both

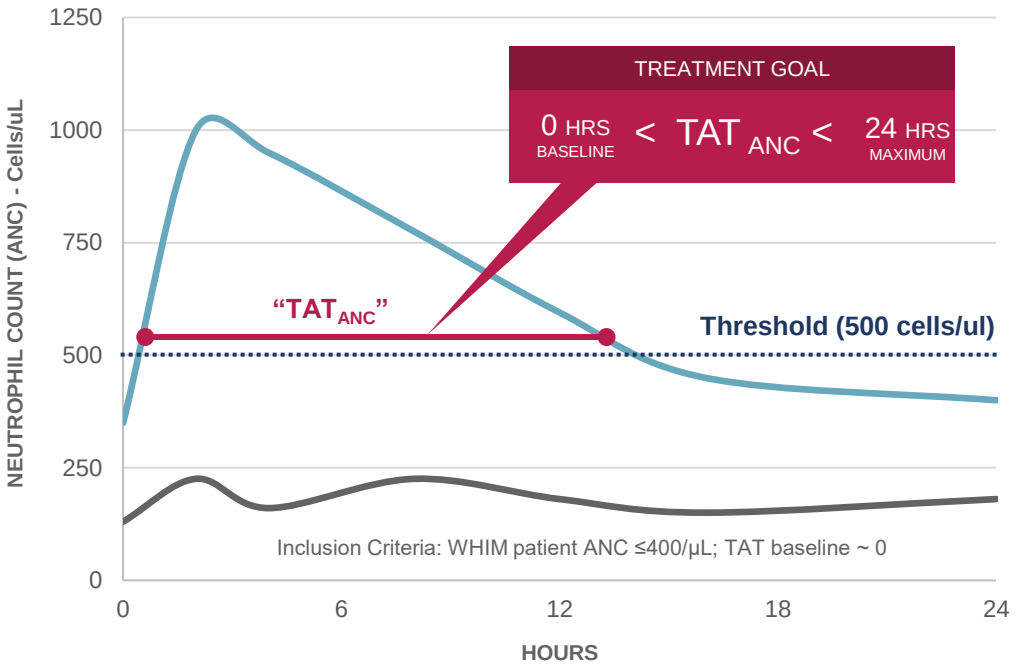
### DOSE ESCALATION + OPEN-LABEL EXPANSION

- Dose Escalation: 50 to 400mg oral capsule once daily (QD), N = 8 patients
- Open-Label Expansion: If completed >24 weeks of dose escalation (N=5)

### ENDPOINTS & ASSESSMENTS

- Safety, infections, warts, pharmacokinetics (PK) / pharmacodynamics (PD) to support dose-selection
- Open label extension examined infection rates, warts, long-term safety
- **Primary Endpoint for Phase 3:** 24-hr Time (hrs.) Above Threshold of Absolute Neutrophils Count ($TAT_{ANC}$)

## ILLUSTRATIVE TRIAL ENDPOINT EXAMPLE

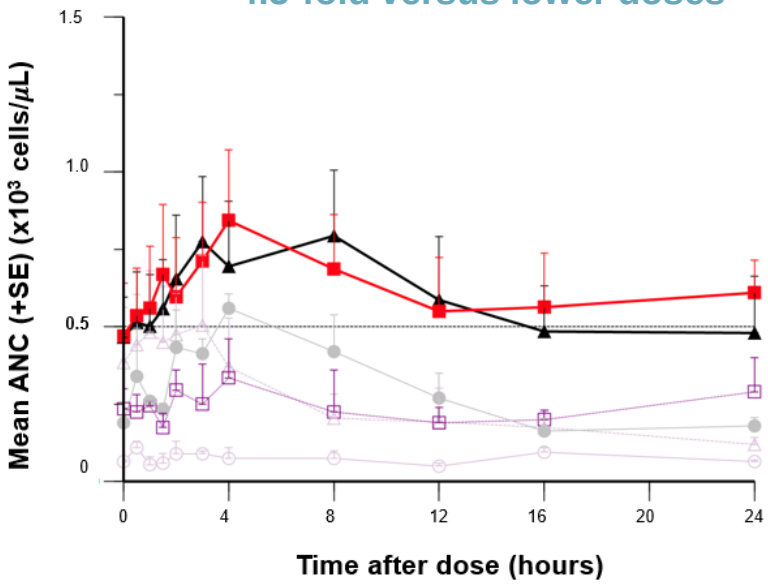



**OBJECTIVE: INCREASE DAILY NEUTROPHIL COUNTS (ANC) ABOVE THRESHOLD AS MEASURED OVER 24 HOURS: TIME ABOVE THRESHOLD (TAT)**

# WHIM PHASE 2: OPEN-LABEL EXTENSION
## SUCCESSFULLY ADDRESSED ALL 3 UNMET NEEDS

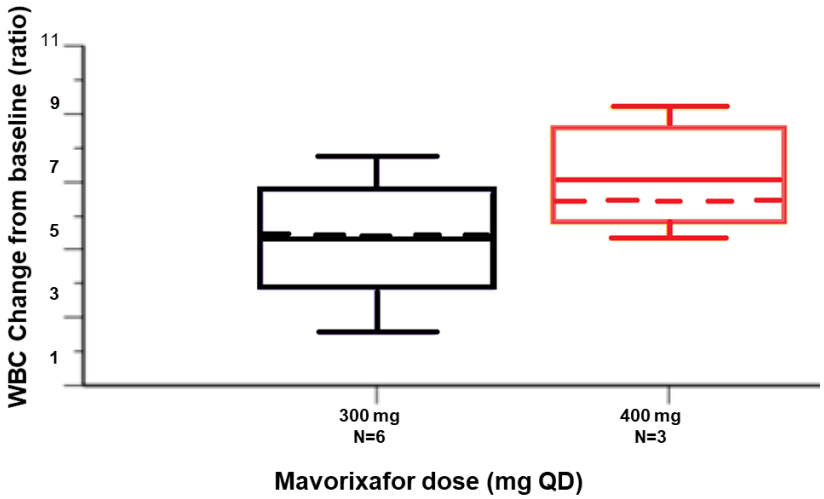
- Mavorixafor 400 mg orally once daily was well tolerated for >2 years without attributable serious AEs
- Durable, dose-dependent increases of WBC, ANC, and ALC counts
- $TAT_{ANC}$ is an objective and consistent biomarker of clinical response to CXCR4 antagonist therapy
  - Primary endpoint in ongoing Phase 3 global clinical trial

### Demonstrated increase in $TAT_{ANC}$ at least 4.5-fold versus lower doses




**At 300/400 QD Doses: Mean $TAT_{ANC}$ was 12.6 hours**

### Increased total white blood cell counts




**400 mg QD: largest WBC increase vs. baseline**



Data from X4 poster presentation at 2020 EHA

# WHIM PHASE 2: OPEN-LABEL EXTENSION
## SUCCESSFULLY ADDRESSED ALL 3 UNMET NEEDS

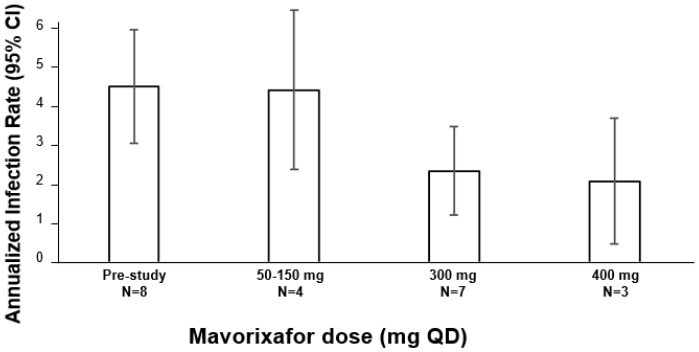
- Durable, dose-dependent increases of WBC, ANC, and ALC counts led to clinical benefits

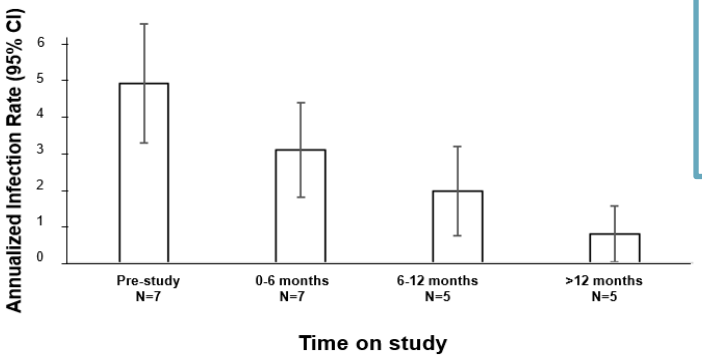
### INFECTION RATES

- Infection rates decreased from 4.63 in the 12 months prior to the trial, to 2.14 (a 54% reduction) at 400 mg
- Deepening reductions in infection rates with time

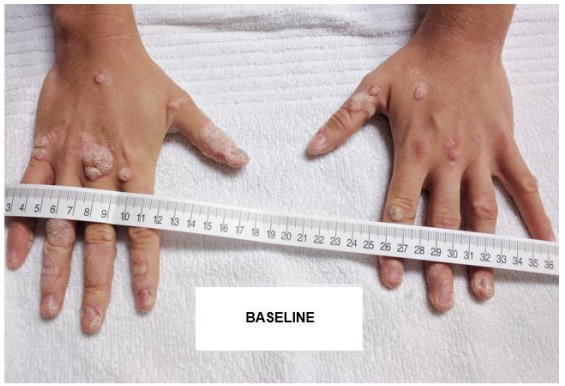
### WART BURDEN

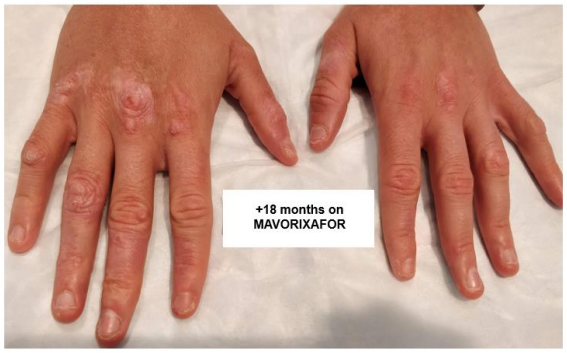
- Average 75% reduction in the number of warts
- Baseline vs. 18 months, following 14 months on 400 mg mavorixafor




**Two key secondary endpoints in ongoing pivotal Phase 3 trial**

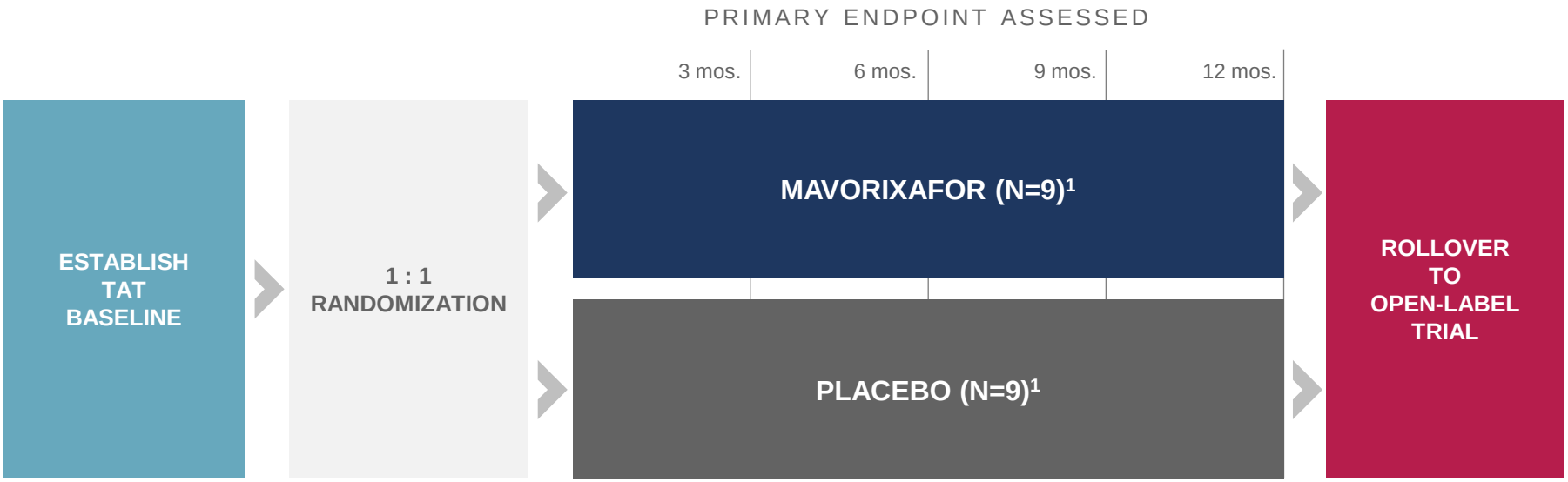





Data from X4 poster presentation at 2020 EHA

# GLOBAL REGISTRATIONAL PHASE 3 TRIAL IN WHIM SYNDROME

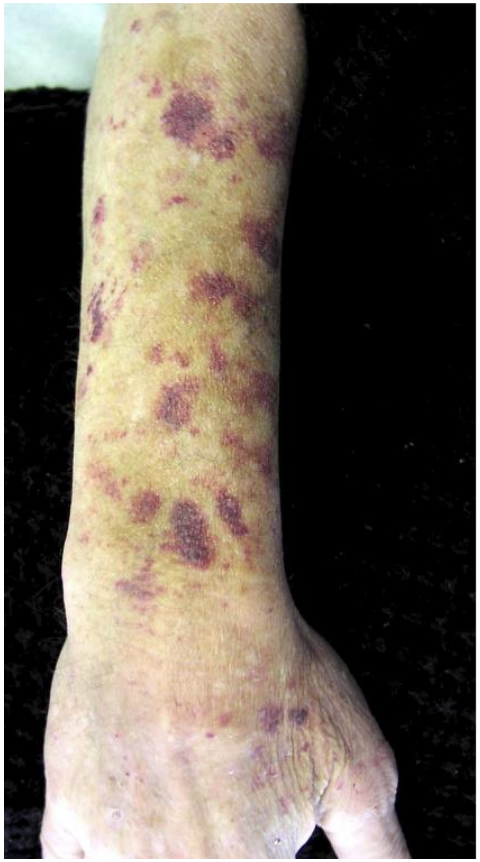



- **Primary Endpoint:** Biomarker of neutrophil count time above threshold (TAT) where the threshold is defined as 500 cells/uL; average of four assessment timepoints
- **Secondary Endpoints:** Infection rates and wart burden assessments
- **Dosing:** 400mg QD in patients 12 years of age or older
- **Enrollment:** Plan to enroll 18 to 28 subjects and activate approximately 20 to 25 sites globally
- **Phase 3 Top-line Data:** expected in 2022

1. Allowed to enroll up to 14 patients on drug and 14 patients on placebo

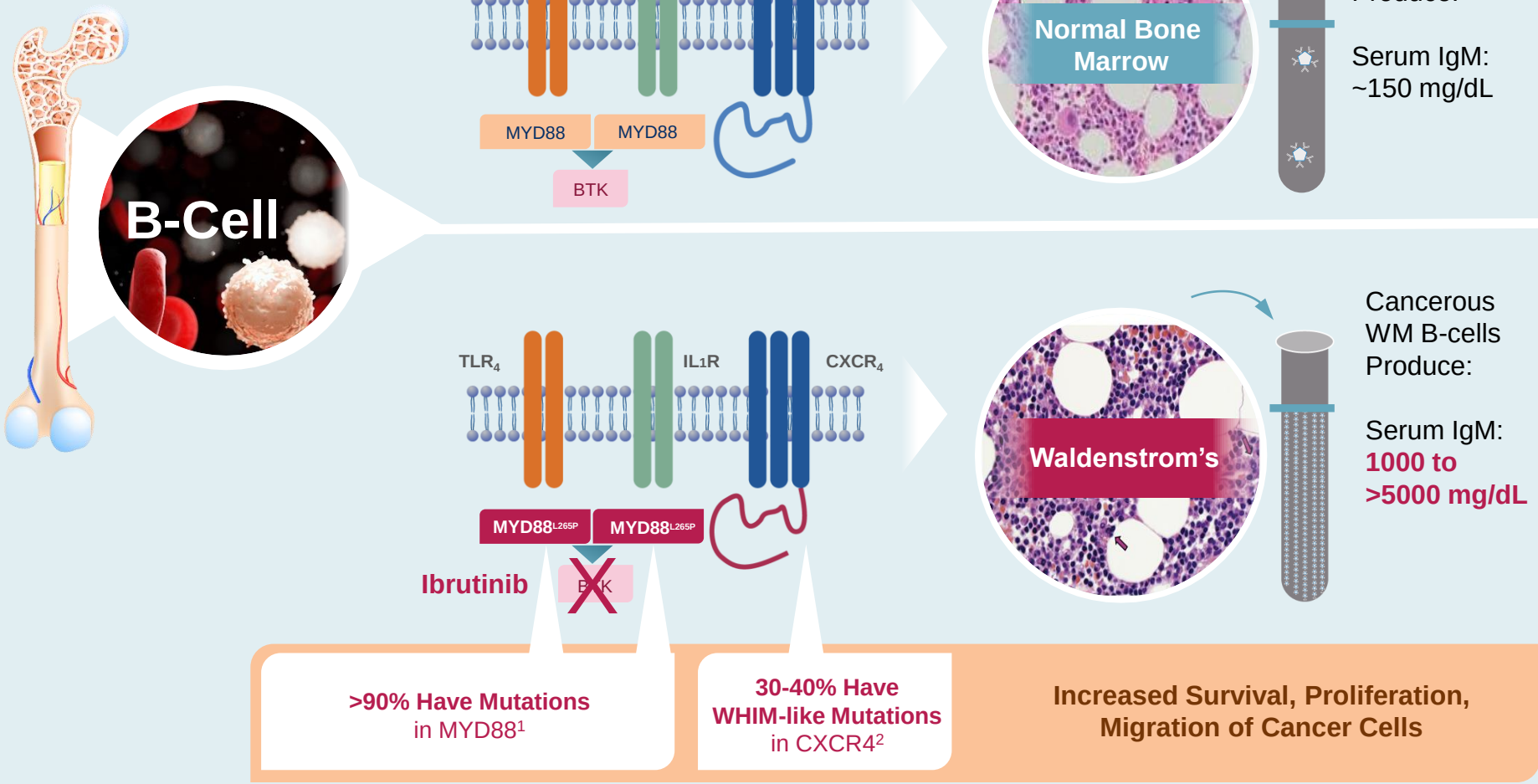
# **OVERVIEW:** WALDENSTRÖM'S MACROGLOBULINEMIA (WM)

- Rare blood cancer: form of Non-Hodgkin's Lymphoma
- Manifestations[1]
  - Hyperviscosity syndrome
  - Cryoglobulinemia/skin lesions
  - Cold agglutinemia
  - IgM neuropathy
  - Reduced iron/anemia
  - Enlarged lymph nodes/spleen
  - Bing Neal Syndrome (CNS infiltration)
- ~8-year survival rate post-diagnosis[2,3]



[1] https://www.iwmf.com/about-wm/signs-and-symptoms
[2] *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;*
[3] https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=33226

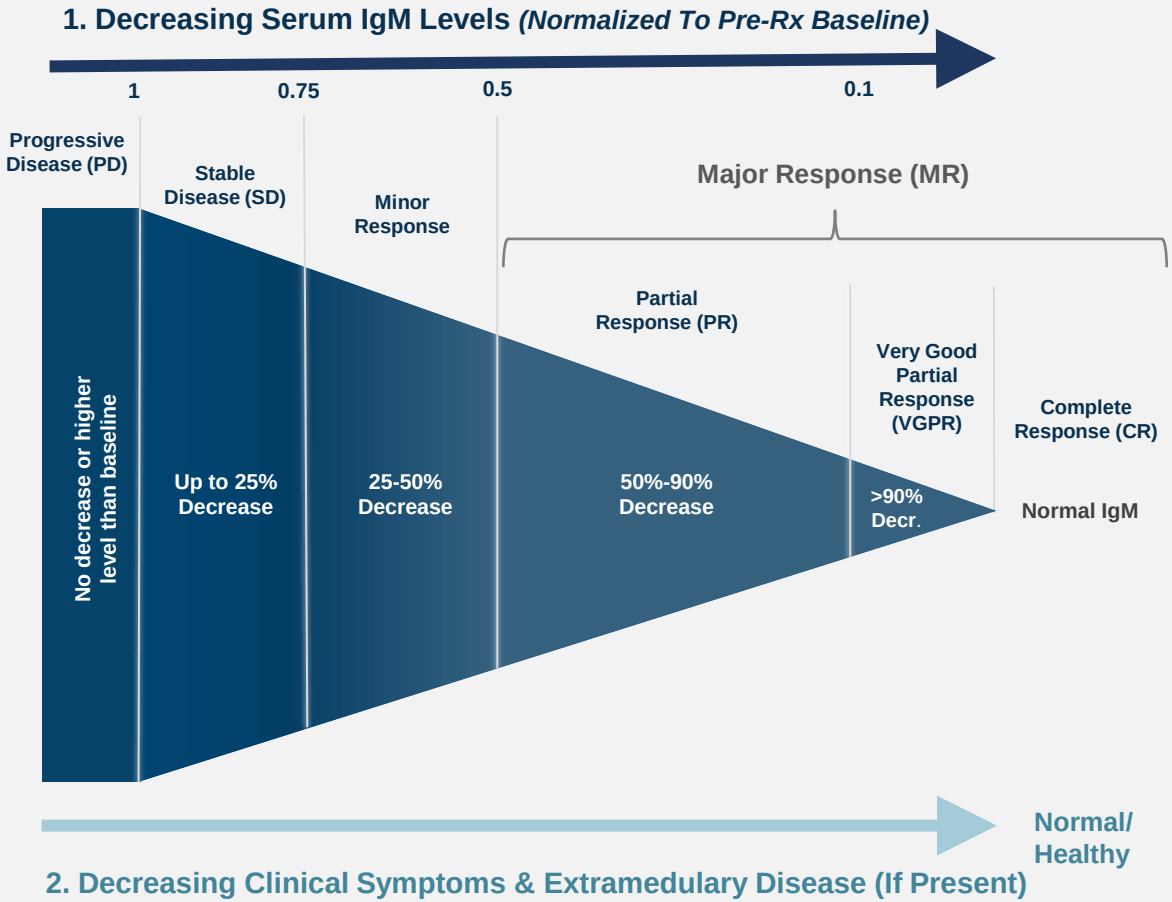
# INCREASE IN CANCEROUS B-CELLS AND SERUM IGM IN WM: DRIVEN BY GENETIC MUTATIONS IN MYD88 & CXCR4




1. Treon et al. 2012. *New England Journal of Medicine,* 367, 826-833; 2. Hunter et al. 2014. *Blood*, 123, 1637–1646.

# **IgM LEVELS:** MAJOR METRIC IN "RESPONSE RATES" FOR REGISTRATION TRIALS

*"Response" Definitions in WM – Two Components*




***Current Treatment Options - Response Rates[1]***

- *~No CRs*
- *13%-27% VGPR rates*
- *71-84% MR rates*

***WM Patients with CXCR4 mutations - Response Rates with Ibrutinib[2,3]***

- *~No CRs*
- *~10% VGPR rates*
- *~60% MR rates*
- *~4-fold likelihood ibrutinib discontinuation*

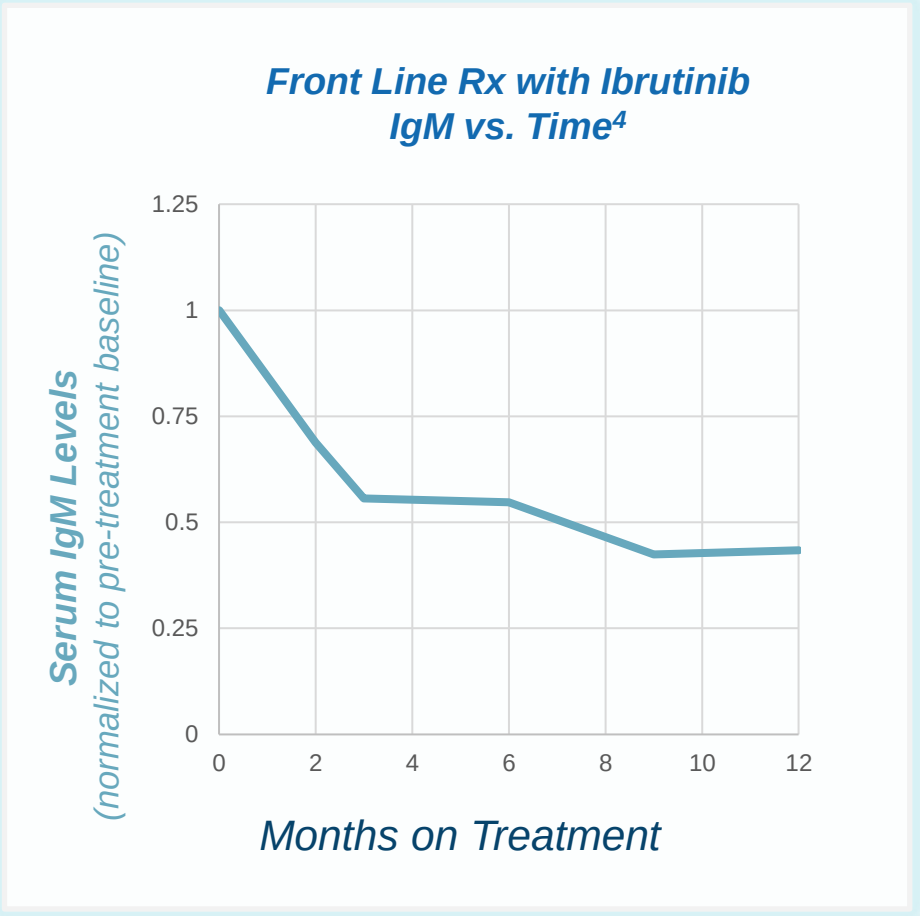
*1. Castillo and Treon, Leukemia, 2019. 2. Treon et al, EHA 2018; 3. Treon et al, EHA 2018*

# CXCR4-MUTANT WM PATIENTS:
## EARLY IGM KINETICS & EARLY RESPONSE RATES

**New Therapies Should Deliver**

- Faster Time to Major Response
- Increased Major Response Rates within the first 24 weeks and beyond

| | *PREVIOUSLY TREATED – Rx w/ Ibrutinib[3,5]* | *FRONT LINE Rx w/ Ibrutinib[4]* |
|---|---|---|
| ***Time to Major Response[1] (months)*** | *6.0* | *7.3* |
| ***Major Response Rate[2](%) at 12 weeks*** | *28.6%* | *28.6%* |
| ***Major Response (%) at 24 weeks*** | *38.1%* | *28.6%* |




1. Time (months) Major Response is time (months) until serum IgM levels drop by 50% or more.
2. Major Response defined as Partial Response (PR) or better as best response on treatment.
3. Treon et al, NEJM, 2015; 372:1430-40. (Rx -second thru 4th line)
4. Treon et al, JCO, 2018; 36:2755-2761. (Rx -first line)
5. Treon et al, EHA abstract PS1185, 2018.

# WM PHASE 1B TRIAL UNDERWAY:
## FOCUS ON DOUBLE-MUTANT REFRACTORY/RECURRENT

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

**Design:** Multi-national Phase 1b trial of mavorixafor in combination with ibrutinib

- Intrapatient dose-escalation with extension on highest tolerated dose for additional 3 months
- Endpoints: safety, PK/PD, and **assessments of serum IgM levels and other blood parameters**

**Timing:** Initial data in 1H 2021

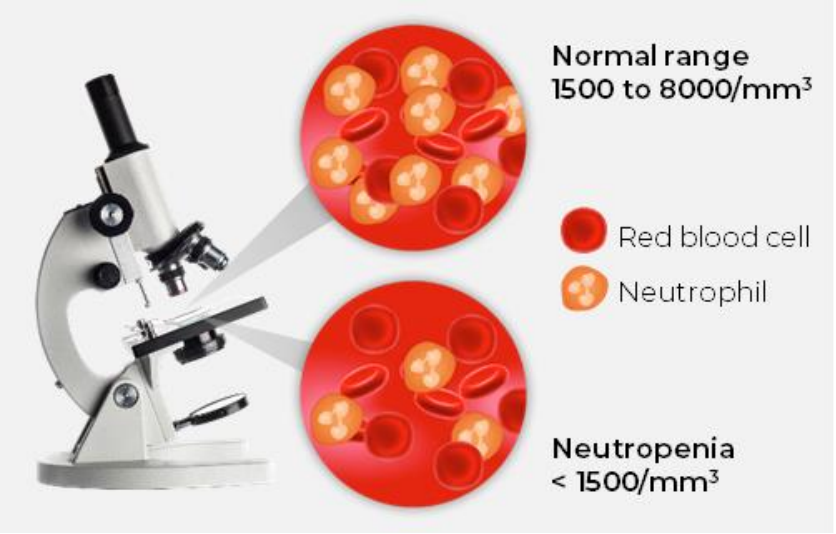
LEUKEMIA & LYMPHOMA SOCIETY®

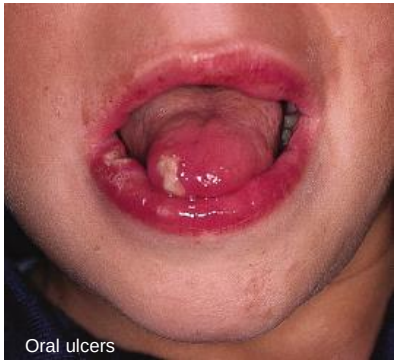
- Strategic collaboration with Leukemia & Lymphoma Society (LLS)
- Selected for LLS' Therapy Acceleration Program

# LABEL EXPANSION OPPORTUNITIES

# **OVERVIEW:** SEVERE CONGENITAL NEUTROPENIA (SCN)

- Rare blood disorder
- Characterized by abnormally low levels of certain white blood cells (neutrophils <1,500 cell/ul)[1]
  - From birth, fevers, severe bacterial infections
    (at times life-threatening), pneumonias, oral ulcers, premature tooth loss
  - Treatment options: antibiotics and G-CSF
- Prevalence estimated 2,000-3,000 patients (US & EU)[2]
- Genetic drivers:
  - May be inherited as either an autosomal dominant or an autosomal recessive genetic trait
  - Many cases of SCN are the result of spontaneous, random mutations





Oral ulcers


1. https://rarediseases.org/rare-diseases/severe-chronic-neutropenia/ 2. https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=42738

# PHASE 1B SCN TRIAL UNDERWAY:
## FOCUS ON NEUTROPHIL RESPONDERS

**14-DAY EXPLORATORY TRIAL ASSESSING FOR RESPONDERS TO MAVORIXAFOR**

| PATIENT PROFILE | DAY 0 | DAY 1, DOSE 1 | DAY 14, DOSE 14 |
|---|---|---|---|
| **Severe Chronic Idiopathic Neutropenia population** and exploratory sub-populations | **Baseline ANC[1]** | If Day 1 ANC >25% over baseline within 8 hours, **continue** daily mavorixafor | **Final ANC[1]** |

**Inclusion:** Up to 45 patients total (30 SCN, 15 exploratory sub-populations)

**Endpoints:** Safety and tolerability, percentage of patients with ANC >50% baseline

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

[1] *Measured over first 8-hours of baseline assessment or dose*

# **CLINICAL EPIDEMIOLOGY** SUGGESTS SIGNIFICANT MARKET OPPORTUNITY

## De-risked MOA targeting the CXCR4 pathway positions X4 to treat >10,000 total patients with rare diseases


- Strong Phase 2 results de-risk ongoing Phase 3
- Favorable Breakthrough Therapy Designation

- Near-term inflection point
- Large, well defined market opportunity

Neutropenia expansion opportunities

[1] Qessential Market Research 2019 and IPM.ai, 2020 - number of potential undiagnosed represents estimates for US only from AI study
[2] Represents CXCR4-mutant patients; 30% to 40% of total WM estimate of 13,000 patients in the U.S. and EU;
[3] Estimated U.S. and EU https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=42738

# EFFORTS TO MAXIMIZE MAVORIXAFOR POTENTIAL

Sponsored Genetic Testing

MSL Deployment to engage concentrated, targeted physician population

Disease Education on WHIM and Waldenstrom's

Ongoing Collaboration with key Patient Advocacy Groups

# COMPLETED AND ANTICIPATED MILESTONE ACHIEVEMENTS

| TARGET DATE | MILESTONES |
|---|---|
| 2019 | Phase 1b trial in SCN: initiated ✓ |
| 2019 | Breakthrough Therapy Designation granted by FDA for treatment of adult WHIM patients ★ |
| 2019 | Phase 1b trial in Waldenström's: initiated ✓ |
| 1H 2020 | WHIM prevalence update: raised guidance ✓ |
| Mid-2020 | Positive WHIM Phase 2 open-label extension data presented at EHA ✓ |
| 1H 2021 | Phase 1b trial in Waldenström's: initial data readout |
| 2021 | Phase 1b trial in SCN: initial results |
| 2022 | Phase 3 trial in WHIM: topline results |

# SELECTED FINANCIAL INFORMATION

# $105.6M[1]

**Cash Expected to Fund Operations into 2022**

## Share and Warrant Information:

- **20.1M shares outstanding**
  (16.2M common shares and 3.9M pre-funded warrants)
- **5.4M class B cash-only warrants at $15.00**
  ($80M / expiry just post WHIM P3 data)
- **3.9M class A warrants at $13.20**
  ($50M / 2024 expiry)

**BIOTECH-FOCUSED INSTITUTIONAL SHAREHOLDER BASE**

**~ ATM Program on File ~**

ANALYST COVERAGE

citi
Canaccord Genuity
COWEN
STIFEL
OPPENHEIMER
B RILEY FBR
ROTH Capital Partners
HCW H.C.WAINWRIGHT&CO.

[1] As of June 30, 2020, as reported in the Company's form 10-Q filed with the SEC on August 4, 2020. Cash figure does not include potential additional borrowing availability of $25 million under amended credit agreement with Hercules Capital, Inc.

X4 PHARMACEUTICALS

# INVESTOR PRESENTATION

OCTOBER 2020

# APPENDIX

# IMMUNO-ONCOLOGY STRATEGY:
## PARTNERSHIPS TO CAPTURE GLOBAL VALUE

**COMPLETED TRIALS DEMONSTRATE SINGLE AGENT ACTIVITY & PROOF OF MECHANISM**

### POSITIVE DATA FROM PHASE 2A ccRCC TRIAL: MAVORIXAFOR + AXITINIB PRESENTED AT ESMO 2019

- **Phase 2a Trial:**
  - Inclusion: 65 patients, multi-national, fully enrolled
  - Assessment: 4.8 months mPFS with axitinib in patients with immediate prior TKI
  - Objective: >50% improvement in medium PFS
- **Conclusions:**
  - Combination therapy with 400mg QD mavorixafor + 5mg BID axitinib observed to be generally well-tolerated with a manageable safety profile
    - Overall mPFS across clinically evaluable patients (n=62): 7.4 months
  - Demonstrated encouraging mPFS in this heavily pretreated advanced RCC patient population
    - mPFS with immediate prior IO therapy (n=18): 11.6 months
    - mPFS with immediate prior TKI therapy (n=34): 7.4 months
    - 8 patients remain on study > 17 months
  - Results suggest that mavorixafor may enhance clinical responses to axitinib and other TKIs that target tumor angiogenesis, as well as immunotherapy agents, such as CPIs
- **Strategy: Identify strategic collaborators to advance in IO**
  - Entered into partnership with Abbisko Therapeutics to develop mavorixafor in solid tumor oncology indications. We have retained all ex-China rights and can leverage data generated by Abbisko

# IGM LEVELS: MAJOR METRIC IN "RESPONSE RATES" FOR REGISTRATION TRIALS

## ***Based on Best Responses:*** *typically 6 months or later in trials*

| Response Category | Response Requirements |
|---|---|
| **Complete Response (CR)** | • Absence of serum monoclonal IgM protein by immunofixation<br>• **Normal serum IgM level**<br>• Complete resolution of extramedullary disease<br>• Morphologically normal bone marrow aspirate trephine biopsy |
| **Very Good Partial Response (VGPR)** | • **Monoclonal IgM protein is detectable >/= 90% reduction in serum IgM level from baseline**<br>• Complete resolution of extramedullary disease<br>• No new signs or symptoms of active disease |
| **Partial Response (PR)** | • **Monoclonal IgM protein is detectable >/= 50% but <90% reduction in serum IgM level from baseline**<br>• Reduction in extramedullary disease<br>• No new signs or symptoms of active disease |
| **Minimal Response (MR)** | • **Monoclonal IgM protein is detectable >/= 25% but <50% reduction in serum IgM level from baseline**<br>• No new signs or symptoms of active disease |
| **Stable Disease (SD)** | • **Monoclonal IgM protein is detectable <25% reduction and <25% increase in serum IgM level from baseline**<br>• No progression is extramedullary disease<br>• No new signs or symptoms of active disease |
| **Progressive Disease (PD)** | • **>/= 25% increase in serum IgM level from lowest nadir (requires confirmation)***<br>• And/or progression in clinical features attributable the disease |

*An absolute increase of >5 g/L (0.5 g/dL) is required when the increase of IgM component is the only applicable criterion

### ***Current Treatment Options - Response Rates[1]***

- *~No Complete Responses*
- *13%-27% VGPR Rates (IgM decrease of >90%)*
- *71-84% Major Response Rates (MRR) (IgM decrease of >50%)*

### ***WM Patients with CXCR4 mutations - Response Rates w/Ibrutinib[2,3]***

- *~No Complete Responses*
- ***~10% VGPR & ~60% MRR***
- *Progression Free Survival (mPFS) for $CXCR4^{WHIM}$ less than half that for wild-type*
- ***~4-fold likelihood ibrutinib discontinuation***

1. Castillo and Treon, Leukemia, 2019. 2. Treon et al, EHA 2018; 3. Treon et al, EHA 2018