



INVESTOR PRESENTATION
JUNE 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 May 7, 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 Cambridge, MA with R&D facility in Vienna, Austria



LEADERSHIP: PROVEN TEAM WITH RARE DISEASE EXPERTISE



MANAGEMENT



PAULA RAGAN, Ph.D.
CEO



MARY DIBIASE, Ph.D.
SVP of Technical Operations & Quality



ADAM MOSTAFA
CFO



NIC SCALFAROTTO, D.V.M.
SVP of Regulatory Affairs



DEREK MEISNER, J.D.
General Counsel



SHARIQ ALI, Ph.D.
VP of Medical Affairs



RENATO SKERLJ, Ph.D.
SVP of Research and Development



CELESTE DIJOHNSON, M.A.
VP of Clinical Operations

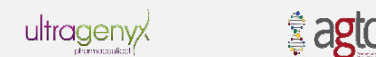


BOARD OF DIRECTORS

MICHAEL WYZGA, Board Chair



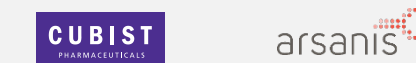
BILL ALISKI, Director



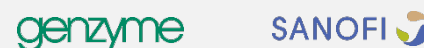
GARY BRIDGER, PhD, Director



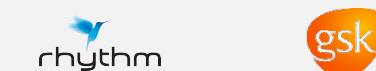
DAVID MCGIRR, MBA, Director



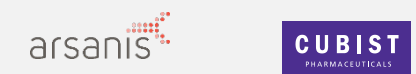
PAULA RAGAN, PhD, Director



MURRAY STEWART, MD, Director

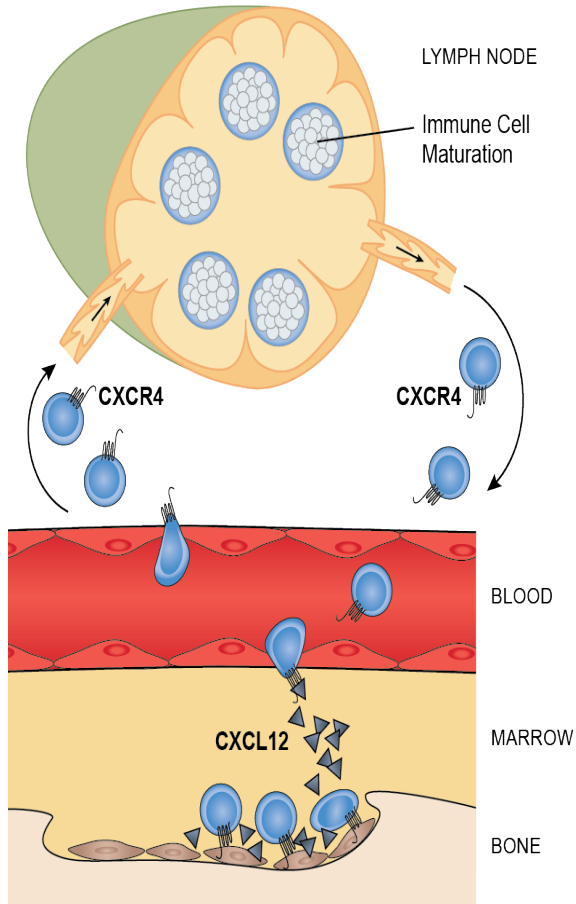


RENE RUSSO, PharmaD, BCPS, Director



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

FIRST-IN-CLASS ORAL CXCR4 ANTAGONIST

- 350 Da small molecule with high potency (<10 nM) and selectivity
 - Administered as an oral capsule, once daily
 - Terminal half-life of 22 hours
- Previous clinical trials with >100 patients demonstrated dose-dependent mobilization of neutrophils and lymphocytes and favorable safety profile
- Orphan Drug Designation for WHIM syndrome received from FDA and EMA
- IP: X4 was issued patents that are expected to provide exclusivity through 2038 for mavorixafor, the company's lead therapeutic candidate, with additional protection for WHIM.
- Breakthrough Therapy Designation granted by FDA for treatment of adult WHIM patients

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

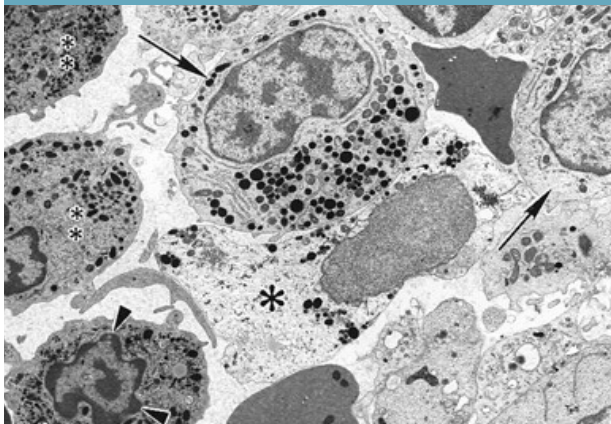
³ Intend to enter into a strategic partnership for future development and potential commercialization for mavorixafor for ccRCC and other potential solid tumor immuno-oncology indications

LEAD INDICATIONS: CXCR4 MUTATIONS AS A DRIVER OF DISEASE

WHAT IS WHIM SYNDROME?

Warts **H**ypogammaglobulinemia **I**nfections **M**yelokathexis

MYELOKATHEXIS



HPV-WARTS



WHIM PATIENT:
ORAL HPV-ASSOCIATED CANCER



WHIM SYNDROME CARRIES A SIGNIFICANT UNMET MEDICAL NEED

NO THERAPIES ARE APPROVED TO ADDRESS THE UNDERLYING CAUSE OF WHIM: A GENETIC DEFECT OF THE CXCR4 RECEPTOR

- Immuno-deficiency caused by “gain-of-function” mutations in the CXCR4 receptor
 - Bone marrow filled with degenerating white blood cells including apoptotic neutrophils, due to defective trafficking caused by CXCR4 mutations
- Clinical impact of the genetic root cause
 - Critically low white blood cell counts, including neutrophils and lymphocytes, results in insufficient ability to clear serious bacterial and viral infections
 - Long-term impact of increased incidence of bronchiectasis (loss of lung function), HPV and EB related cancers, hearing loss
 - FDA’s March 2019 industry guidance is that WHIM Syndrome is a “Severely Debilitating or Life-Threatening Hematologic Disorder”
- Symptomatic treatments don’t address underlying disease
 - Antibiotics, G-CSF, and immunoglobulins can be used; none tested in WHIM trials

Breakthrough Therapy Designation granted by FDA for treatment of adult WHIM patients

PHASE 2 TRIAL INFORMS PHASE 3 TRIAL

PHASE 2 TRIAL DESIGN

INTRA-PATIENT DOSE ESCALATION

- Open label
- 50mg to 400mg oral capsule once daily (QD)
- n = 8 patients
- Daily, assessed at one month and beyond

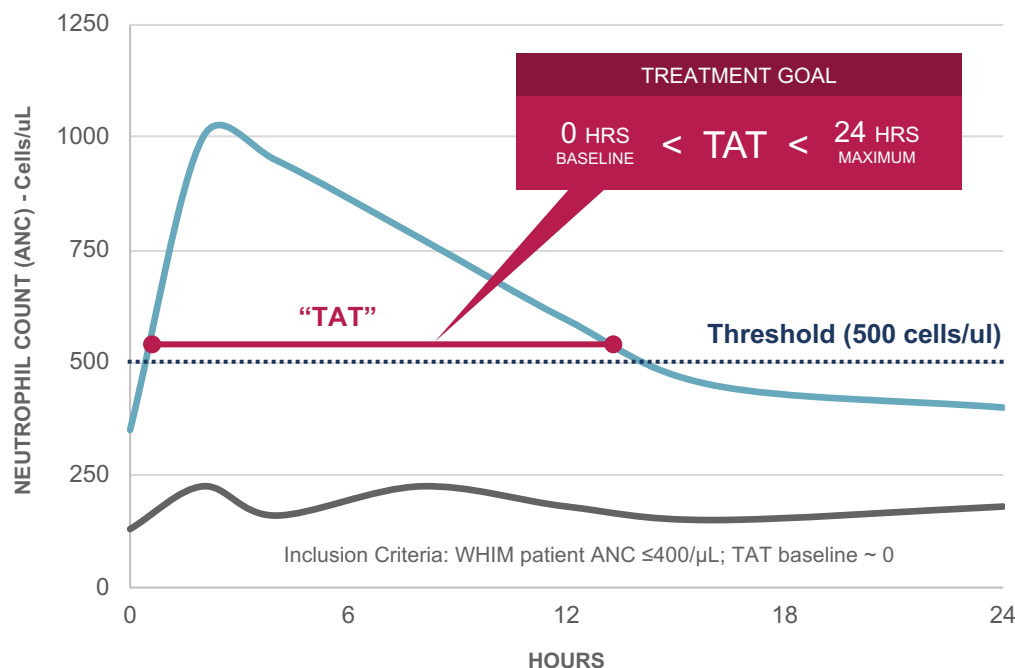
INCLUSION

- Neutrophil count: ANC $\leq 400/\mu\text{L}$ *and/or*
- Lymphocyte count: ALC $\leq 650/\mu\text{L}$ *or both*

ENDPOINTS & ASSESSMENTS

- Safety (infections, warts), pharmacokinetics (PK) / pharmacodynamics (PD)
- **Biomarker:** 24-hr Blood Counts of Neutrophils– Time (hrs.) Above Threshold

ILLUSTRATIVE TRIAL ENDPOINT EXAMPLE

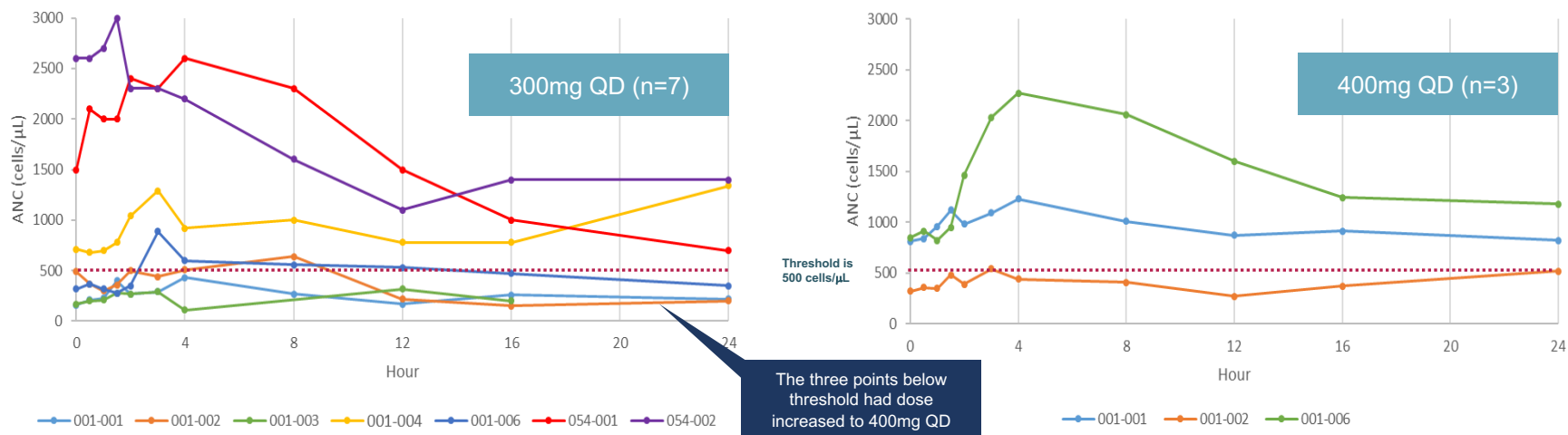


OBJECTIVE: INCREASE DAILY NEUTROPHIL COUNTS (ANC) ABOVE THRESHOLD AS MEASURED OVER 24 HOURS: TIME ABOVE THRESHOLD (TAT)

WHIM PHASE 2: ACHIEVED MAXIMUM TAT IN MOST PATIENTS

NEUTROPHILS AND LYMPHOCYTES MOBILIZED; PAN-LEUKOPENIA ADDRESSED

Patients' baseline with an ANC of 50 – 200 cells/ μ L prior to treatment. Patients **dosed daily** and assessed at one month and beyond.



ASSESSMENTS		RESULTS
Neutrophil Counts > Threshold	✓	5 of 7 patients (71%): maximum TAT
Lymphocyte Counts > Threshold	✓	6 of 7 patients (85%): maximum TAT
Safety	✓	Acceptable; no Grade 3/4

400mg QD: Dose being tested in ongoing pivotal Phase 3 clinical trial

WHIM PHASE 2 AND OLE CLINICAL DATA SHOWS FAVORABLE CLINICAL EVIDENCE OF DISEASE MODIFICATION

- Sustained, dose-dependent increases in absolute neutrophil count (ANC) and absolute lymphocyte count (ALC)
- ANC/ALC increases correlated with fewer infections and improved cutaneous warts
- Patients treated with 300 mg or 400 mg once-daily doses of mavorixafor for up to 28.6 months; dosing was well tolerated for the extended duration of treatment with no SAEs

INFECTION RATES¹

- Clinical yearly infection rates decreased from 4.63 in the 12 months prior to the trial, to:
 - 2.41 (a 48% reduction) at 300 mg
 - 2.14 (a 54% reduction) at 400 mg

WART BURDEN¹

- Cutaneous warts on hands and/or feet demonstrated >50% reduction in the number of warts over baseline

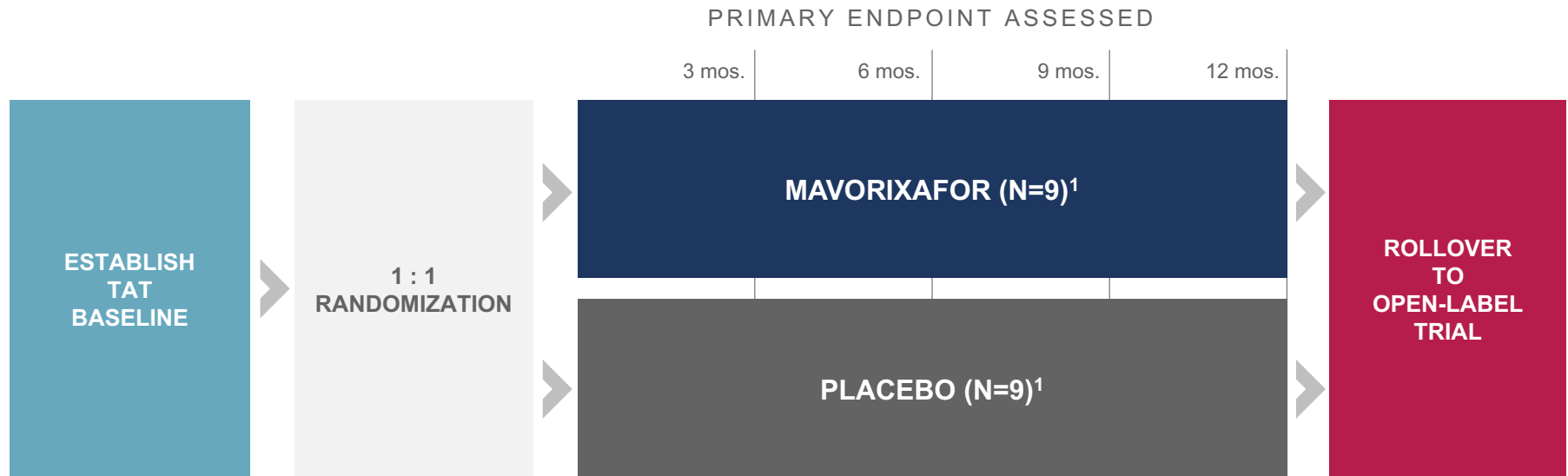
Two key secondary endpoints in ongoing pivotal Phase 3 trial

PRE-TREATMENT



55 WEEKS POST-TREATMENT²





Primary Endpoint: Biomarker of absolute neutrophil count time above threshold (TAT_{ANC}) 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

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

OVERVIEW: WALDENSTRÖM'S MACROGLOBULINEMIA (WM)

- Rare form of Non-Hodgkin's Lymphoma
- Estimated prevalence of >13,000 in US and EU^{1,2}
 - Annual incidence: 1,000-1,500 in US; ~1,800 in EU ^{1,2}
- Signs and symptoms
 - Elevated IgM and other blood-markers
 - Hepatomegaly, splenomegaly, skin purpura
- ~8-year survival rate post-diagnosis ^{1,2}
- Current treatment
 - Imbruvica (\$136,000 per year)
 - Chemo and Rituxan in certain lines/settings
- Mechanism: genetic drivers in WM
 - >90% have mutations in MYD88 gene
 - 30-40% have WHIM-like mutations in CXCR4 gene

**CXCR4 MUTATIONS DRIVE POOR RESPONSE
IN RARE LYMPHOMA**



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;

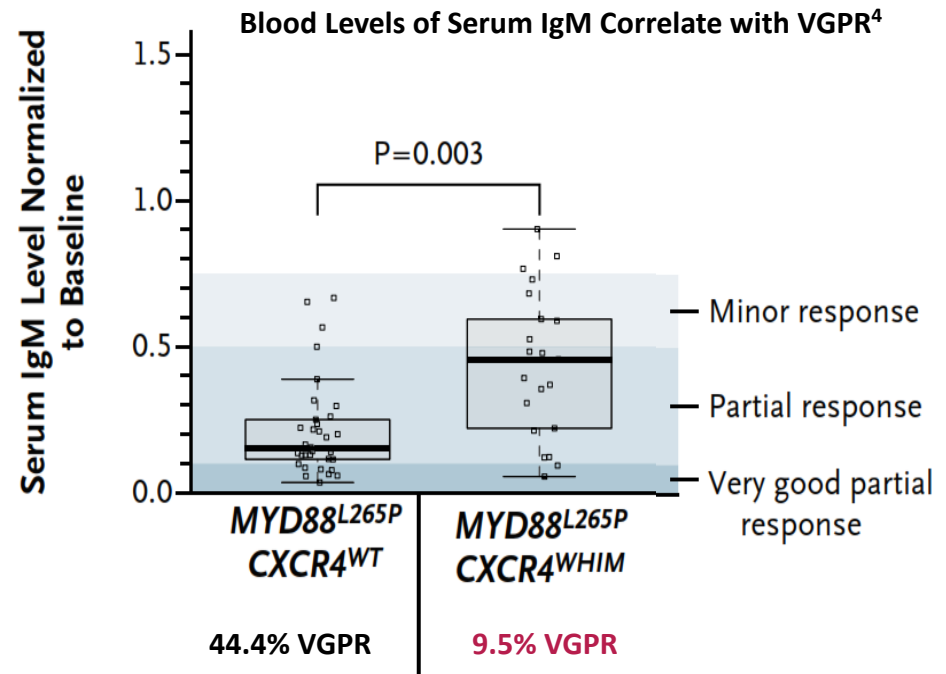
² https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=33226

CXCR4^{WHIM} REFRACTORY/RECURRENT WM: POOR CLINICAL OUTCOMES VS. WILD-TYPE

- Very Good Partial Response (VGPR) Rates: **9.5% for CXCR4-mutant vs. 44.4% for wild-type**¹
- Median Progression Free Survival (mPFS) for CXCR4^{WHIM} is less than half that of mPFS for wild-type²
- ~4-fold likelihood ibrutinib discontinuation in CXCR4^{WHIM} WM³

RESPONSE PROFILE IN REFRACTORY/RECURRENT WM (IBRUTINIB TREATMENT ONLY)

	MYD88 ^{Mut} CXCR4 ^{WT}	MYD88 ^{Mut} CXCR4 ^{Mut}	P- Value
Patients (n) =	36	21	
ORR	100%	85.7%	0.005
Major (>PR)	97.2%	66.6%	<0.001
VGPR	44.4%	9.5%	0.007
Time to Minor Response (mos.)	1.0	1.0	0.10
Time to Major Response (mos.)	2.0	6.0	0.05



1. Table Recreated from: Treon et al, EHA 2018; 2. Treon et al, EHA 2018 ; 3. Gustine J. Am J Hematol. 2018; 4. Figure extracted and adapted from Treon et al, NEJM, 2015

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



Inclusion: Patients with MYD88 + CXCR4 mutations who have failed prior Rx

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

- Inpatient 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 2H 2020



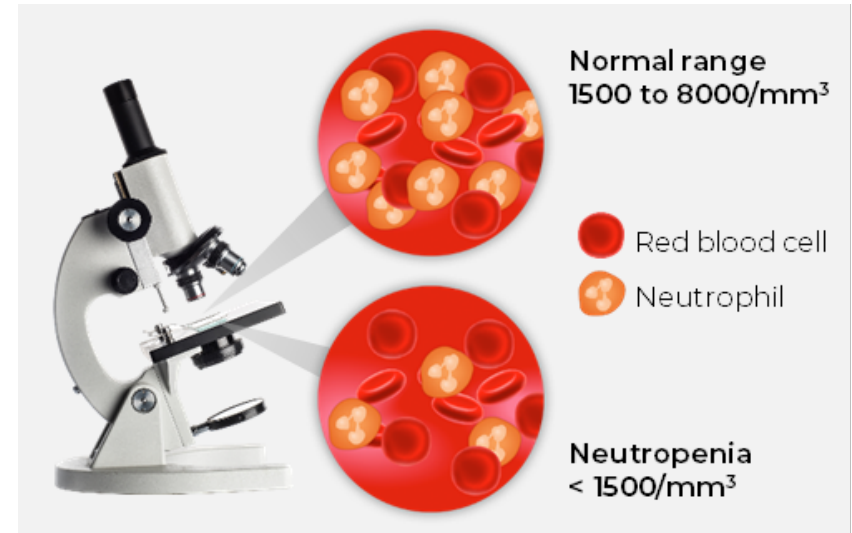
LEUKEMIA &
LYMPHOMA
SOCIETY®

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

LABEL EXPANSION OPPORTUNITIES

OVERVIEW: SEVERE CONGENITAL NEUTROPENIA (SCN)

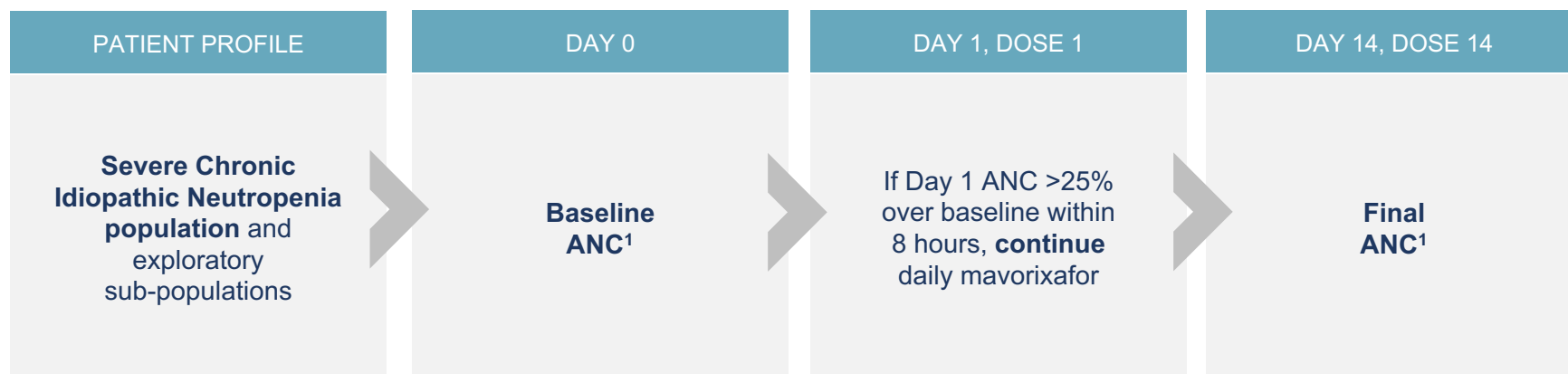
- Rare blood disorder
- Characterized by abnormally low levels of certain white blood cells (neutrophils $<1,500$ cell/ μl)¹
 - From birth, fevers, severe bacterial infections (at times life-threatening), pneumonias, oral ulcers, premature tooth loss
 - Treatment options: antibiotics and G-CSF
- Prevalence 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



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



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

INTRODUCING PATH4WARD



- Genotyping initiative for Congenital Neutropenia including WHIM
- Collaboration with  INVITAE
- Individuals with history of chronic severe neutropenia (ANC < 500/uL)
- Permanent or intermittent (cyclical) neutropenia of unknown origin and with a clinical presentations of SCN or Congenital Idiopathic Neutropenia (CIN)
- Genotyping panel of up to ~200 genes related to immuno-deficiencies
- Individuals with CXCR4 mutations may enroll in WHIM Phase 3 trial or SCN Phase 1b trial

**EXPLORING THE CAUSES OF NEUTROPENIA AND
POTENTIAL FOR TREATMENT WITH MAVORIXAFOR**

CLINICAL EPIDEMIOLOGY SUGGESTS SIGNIFICANT MARKET OPPORTUNITY

1,000-1,300¹

DIAGNOSED

+

800-2,400²

UNDIAGNOSED

WHIM
SYNDROME

2,000 - 3,000

SEVERE CONGENITAL
NEUTROPENIA
(SCN)

4,000 - 5,000

WALDENSTRÖM'S
MACROGLOBULINEMIA
(WM)³

Total estimated diagnosed &
undiagnosed WHIM patients ~1,800 – 3,700

WORLD-CLASS PARTNERSHIPS TO INCREASE PATIENT AND CLINICIAN AWARENESS



¹ Qessential Market Research 2019; ² IPM.ai, 2020 - number of potential undiagnosed represents estimates from AI study

³ Represents CXCR4-mutant patients; 30% to 40% of total WM estimate of 13,000 patients

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

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 
Mid-2020	Phase 2 open-label extension update for WHIM to be presented at EHA
2H 2020	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

\$117.0M¹

Cash Expected to Fund Operations into 2022

Share and Warrant Information:

- **20.0M shares outstanding**
(16.1M 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

ANALYST COVERAGE

citi

cg/Canaccord
Genuity

COWEN

STIFEL

OPPENHEIMER

B | RILEY FBR

ROTH Capital Partners

HCW
H.C.WAINWRIGHT & CO.

¹ As of March 31, 2020, as reported in the Company's form 10-Q filed with the SEC on May 7, 2020. Cash figure does not include potential additional borrowing availability of \$25 million under amended credit agreement with Hercules Capital, Inc. and \$3.0 million milestone payment received from Abbisko Therapeutics in April 2020.



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