Xencor Q3 2022 Financial Results

XmAb®564 Data Presentation

November 7, 2022

Speakers

Bassil Dahiyat, Ph.D.
President
Chief Executive Officer
Director

John Desjarlais, Ph.D.
Senior Vice President
Chief Scientific Officer

John Kuch
Senior Vice President &
Chief Financial Officer

Allen Yang, M.D., Ph.D.
Senior Vice President
Chief Medical Officer

Ralph Zitnik, M.D.
Executive Medical Director

xencor

Forward-Looking Statements

Certain statements contained in this presentation, other than statements of historical fact, may constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements include, but are not limited to, statements regarding Xencor's development plans and timelines; potential regulatory actions; expected use of cash resources; the timing and results of clinical trials; the plans and objectives of management for future operations; and the potential markets for Xencor's product and development candidates. Forward-looking statements are based on the current expectations of management and upon what management believes to be reasonable assumptions based on information currently available to it, and involve numerous risks and uncertainties, many of which are beyond Xencor's control. These risks and uncertainties could cause future results, performance or achievements to differ significantly from the results, performance or achievements expressed or implied by such forward-looking statements. Such risks include, but are not limited to, potential delays in development timelines or negative preclinical or clinical trial results, reliance on third parties for development efforts and changes in the competitive landscape including changes in the standard of care, as well as other risks described in Xencor's filings with the Securities and Exchange Commission (SEC). Xencor expressly disclaims any duty, obligation or undertaking to update or revise any forward-looking statements contained herein to reflect any change in Xencor's expectations with regard thereto of any subsequent change in events, conditions or circumstances on which any such statements are based, except in accordance with applicable securities laws. For all forward-looking statements, we claim the protection of the safe harbor for forward looking statements contained in the Private Securities Litigation Reform Act of 1995.

Agenda for Today's Call

1. Recent Business Updates and Financial Results
2. XmAb®564 Data Presentation
3. Q&A

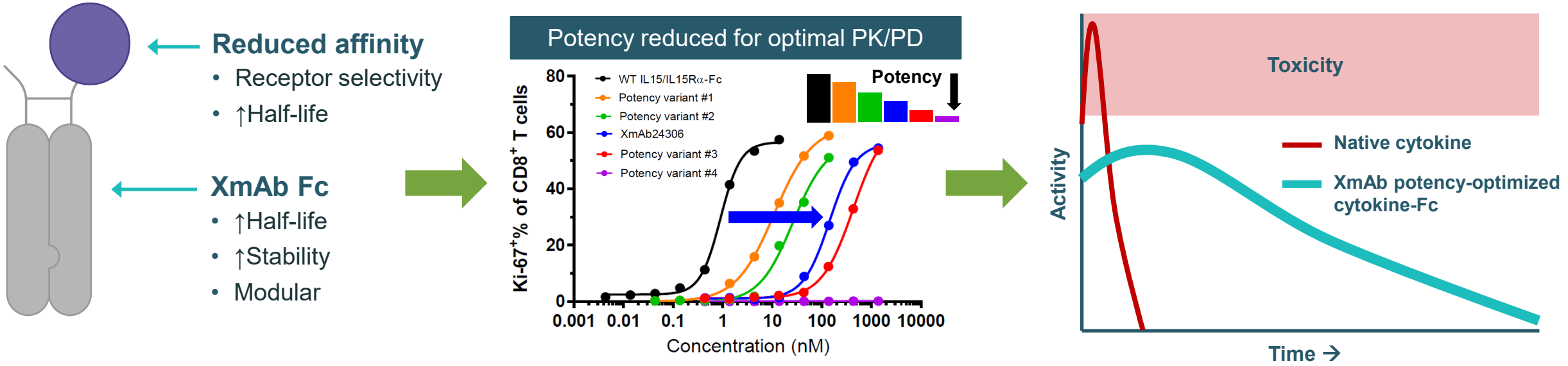
XmAb®564 Single Dose Phase 1a Data Presentation

Reduced potency IL2-Fc

For selective expansion of regulatory T cells

In development for patients with autoimmune diseases

XmAb® Cytokines: Potency-tuned to Enhance Half-life and Tolerability



Xencor's general approach for creating cytokine therapies

- Overcomes native cytokine short half-life and high toxicity
- Systematically engineer a broad portfolio of cytokines

XmAb®564 Phase 1a Clinical Trial Top-line Data Summary

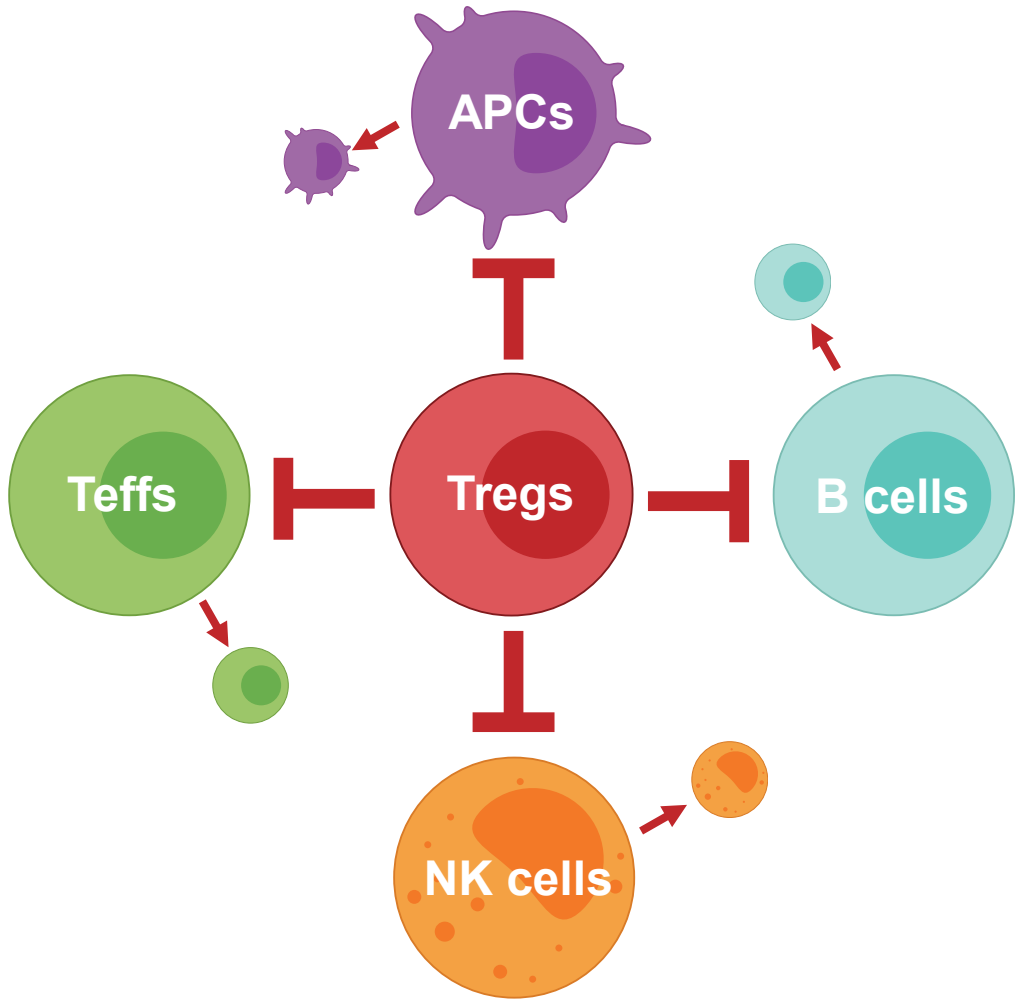
- Single ascending dose of subcutaneously administered XmAb564 in healthy volunteers
- Well tolerated; no serious adverse events or dose limiting toxicities observed
- Selective expansion of $CD25^{bright}$ regulatory T cells (Tregs) of 10x and higher beginning at 3rd dose level and reaching 117x increase over baseline at highest dose
- Exceptional durability of Treg expansion relative to reported third-party data
  - Provides opportunity to explore differentiated multi-week dosing schedules
- Minimal increases in natural killer (NK) cells and conventional T cells (Tcons)

Second potency-tuned XmAb Cytokine program showing marked target cell expansion and good tolerability in human clinical trials

- XmAb306, an IL15-IL15Rα-Fc fusion in oncology, showed consistent and robust dose-dependent NK cell expansion and accumulation upon repeat dosing, reaching 40-100x higher than baseline in higher dose cohorts (Nov. 2021)

Tregs Important Role in Homeostasis and in Autoimmune Disease

- Regulatory T cells (Tregs) are $CD4^{+}FoxP3^{+}$ cells expressing CD25 (IL-2Rα) that maintain immune tolerance in tissues by suppressing the function of both CD4 and CD8 effector T cells
- Tregs are dysfunctional in most autoimmune diseases
- A therapeutic approach has been to restore Treg numbers and function via a low-dose IL-2 regimen
  - Treg homeostasis depends on IL-2
  - IL-2 as a drug suffers from fast *in vivo* clearance and a narrow therapeutic index



xencor

IL-2 Activates Multiple T Cell Types
XmAb564 is Engineered to Improve for Treg Selectivity

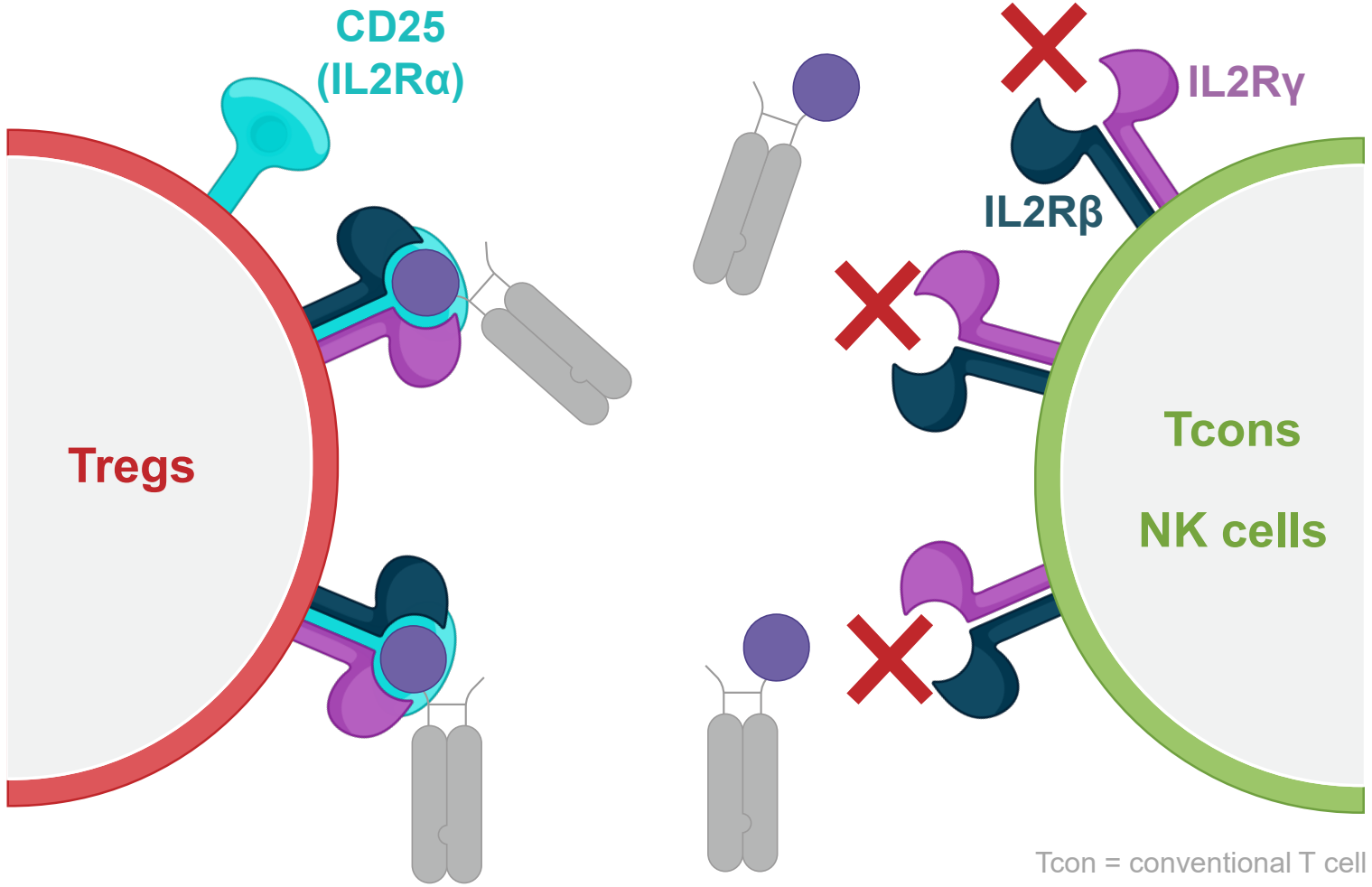
2x increase to **CD25 (IL2Rα)** binding and reduced affinity for IL2Rβ

Monovalent to avoid undesired activation

Heterodimeric Fc with **Xtend™**

No effector function

Overall 400-1000x reduced potency



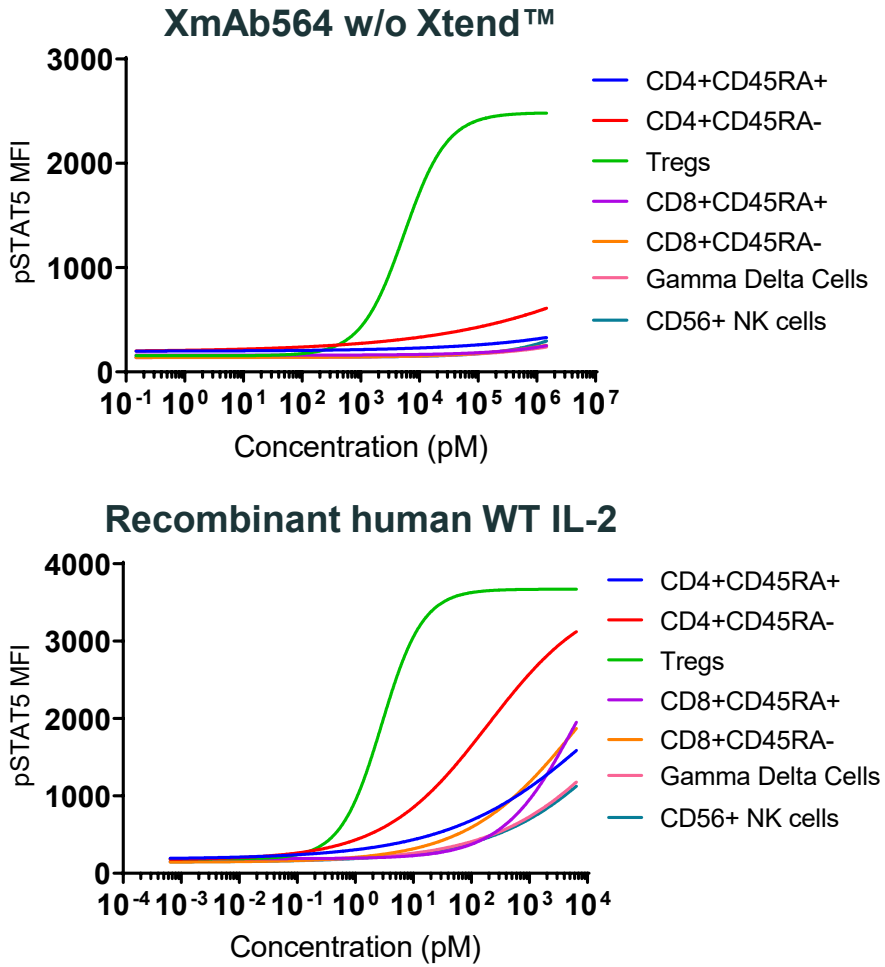
Tcon = conventional T cell

WT = wild-type

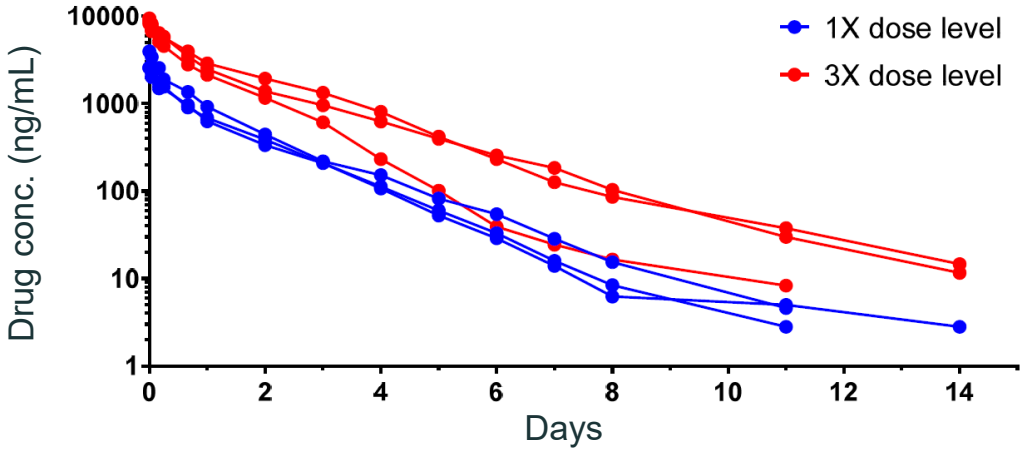
xencor

XmAb564 Design Reduces Potency and Improves Treg Selectivity

XmAb564 Selectively Promotes Treg Signaling in Human T Cells



Sustained PK up to Several Days in Non-Human Primates



XmAb564 exhibits extended half-life and good tolerability in NHPs (not shown)

XmAb564 selectively promotes Tregs and has extended half-life due to low potency and Xtend™ Fc domain

xencor

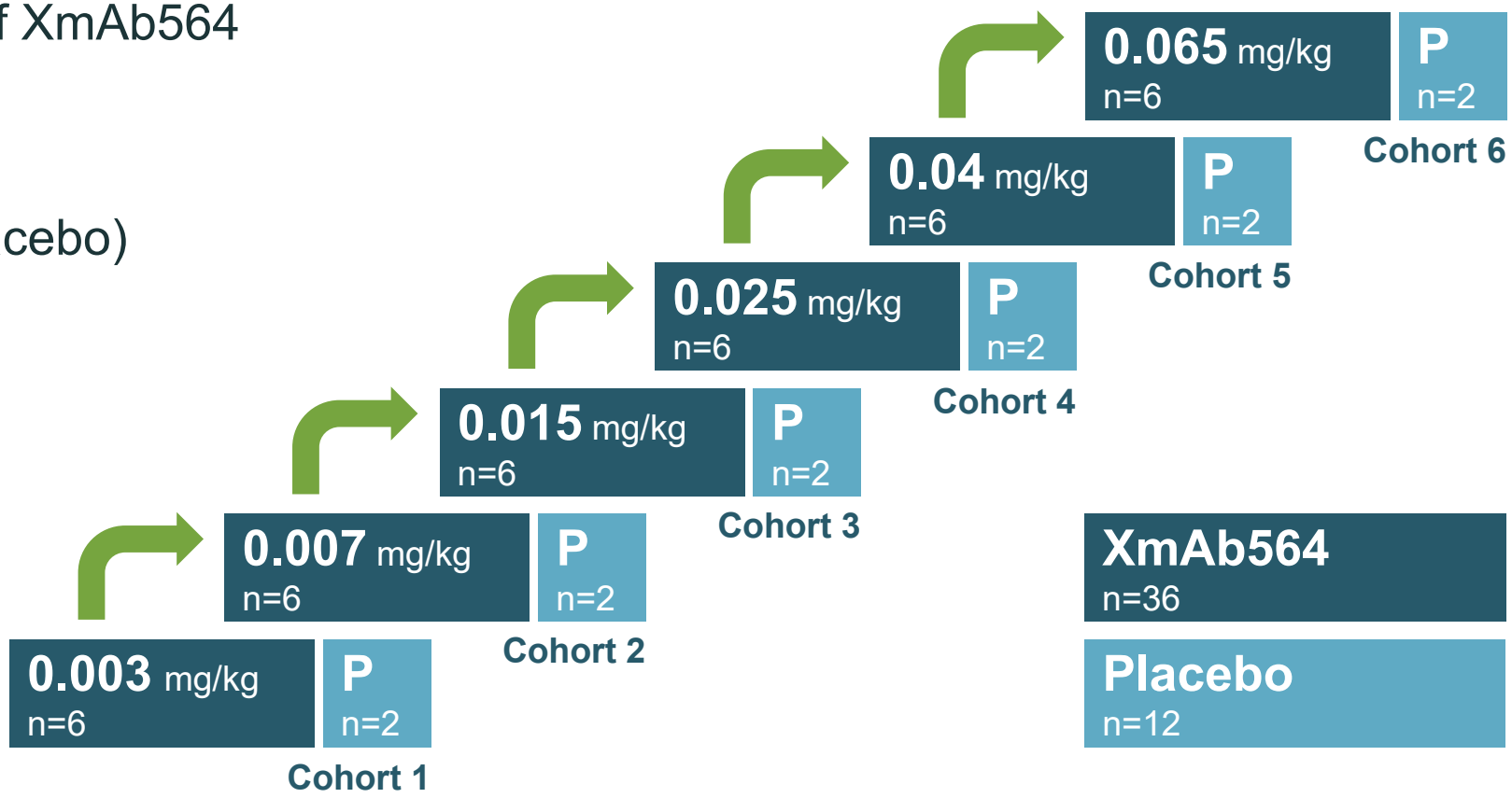
XmAb564 Phase 1a Healthy Volunteer Study Design

Phase 1a single-ascending dose (SAD) study

- Randomized and double-blinded
- Subcutaneous administration of XmAb564
- Heathy volunteers (n=48)
- 6 dose level cohorts
- Randomized 6:2 (XmAb564:placebo)

Outcome measures

- Safety and tolerability
- Pharmacokinetics and activity biomarkers (e.g., T-cell populations)



xencor

XmAb564 Was Well Tolerated

Well tolerated including at the highest dose evaluated (0.065 mg/kg)

- All adverse events (AEs) were grade 1 or 2 (mild-to-moderate) and self-limited
- Injection site reaction was the most reported AE
- No serious AEs, dose-limiting toxicities or early discontinuations due to AEs
- No clinically significant abnormalities in laboratory values, vital signs and ECGs

Laboratory findings and pharmacokinetics

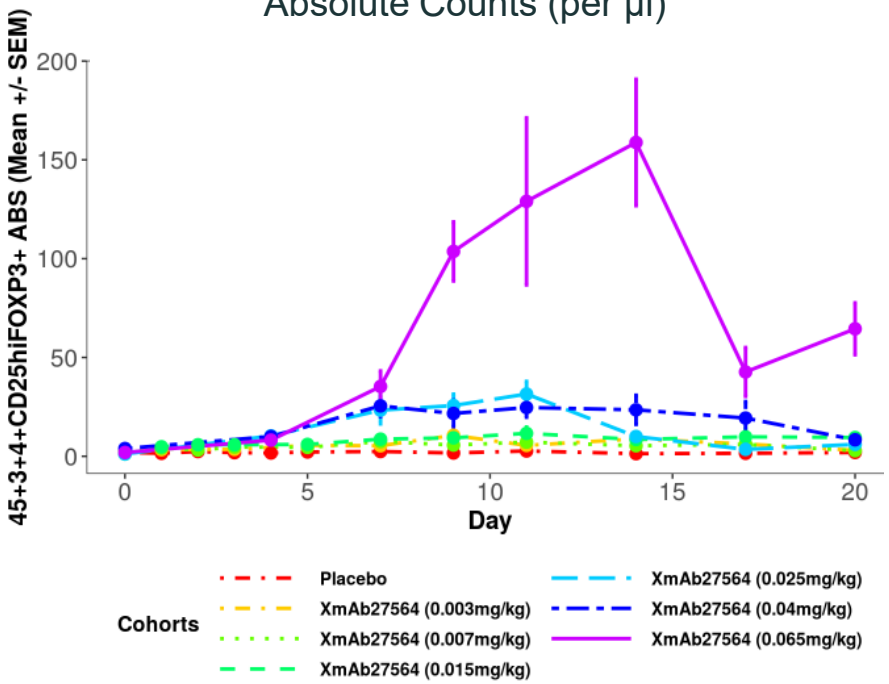
- Some subjects had transient, reversible elevations in blood eosinophils
  - No eosinophil-related AEs were observed
  - Possibly related to mechanism-of-action, reported in other third-party CD25-targeting IL-2 programs
- No other clinically significant abnormalities in safety laboratory studies were observed
- Terminal half-life is estimated to be 9-10 days at lower doses and 6-7 days at the highest dose, consistent with an increase in CD25 target-mediated clearance on the expanding Treg population

Study remains blinded

XmAb564 Promotes Robust & Durable Expansion of CD25^{bright} Tregs

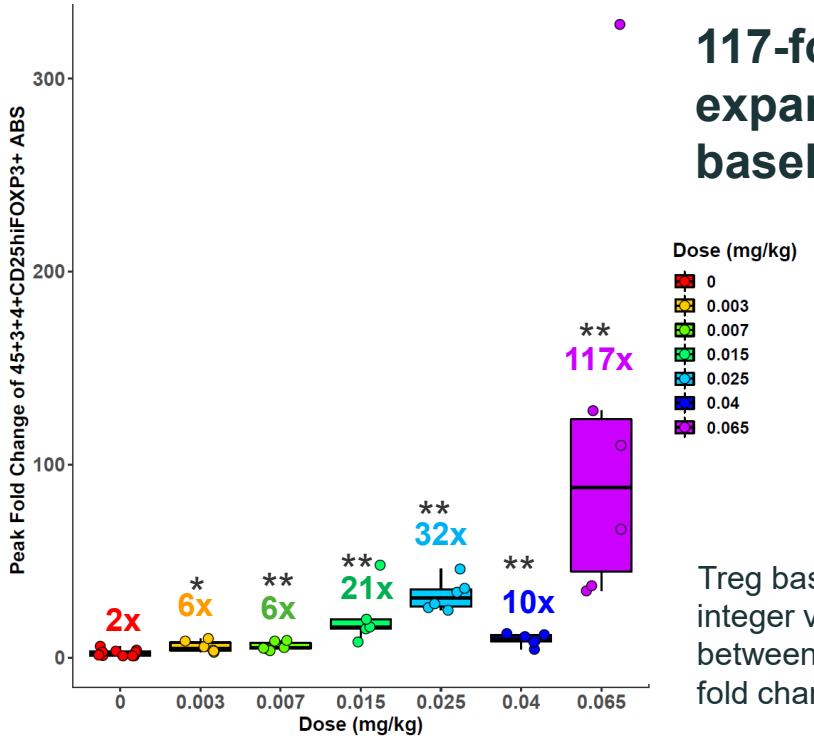
Time Course

Absolute Counts (per µl)



Durable, dose-dependent increases in CD25^{bright} Tregs

Peak Fold Change[1]



117-fold mean peak expansion over baseline in Cohort 6

Treg baseline counts are low integer values, leading to between group variability in fold change calculations

Highest reported CD25^{bright} Treg expansion

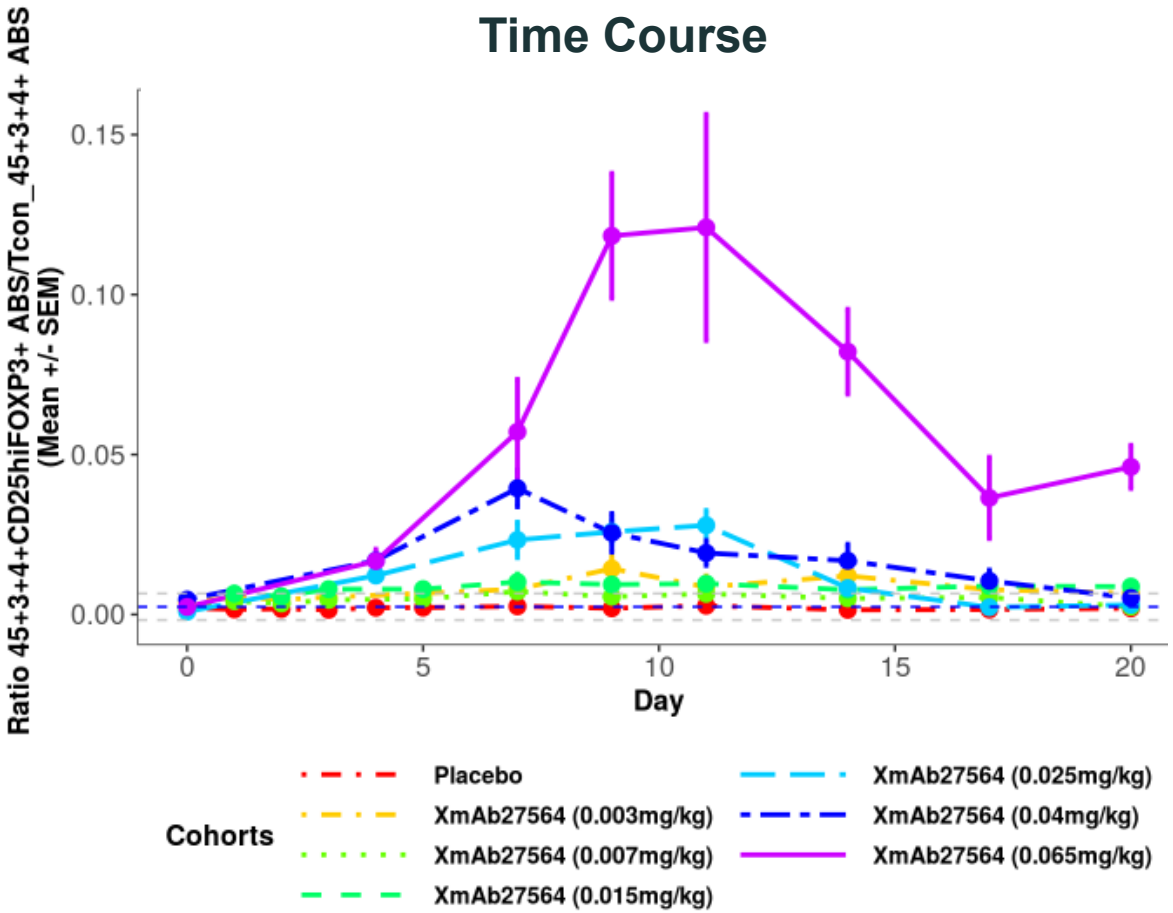
Numeric values in “Peak Fold Change” plot are Mean

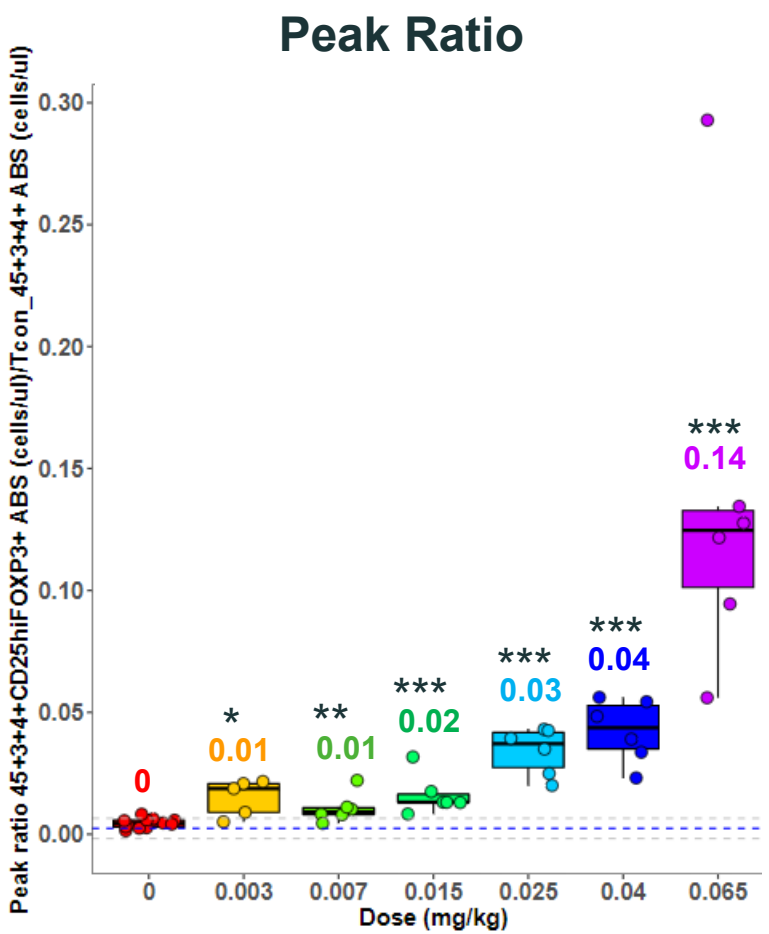
[1] Peak fold change: Peak CD25^{bright}FoxP3^{+} CD4 Treg cell absolute count at a post-treatment time point divided by absolute count at baseline

NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor

XmAb564 Promotes Robust & Durable Increases in CD25^{bright} Treg/Tcon ratio



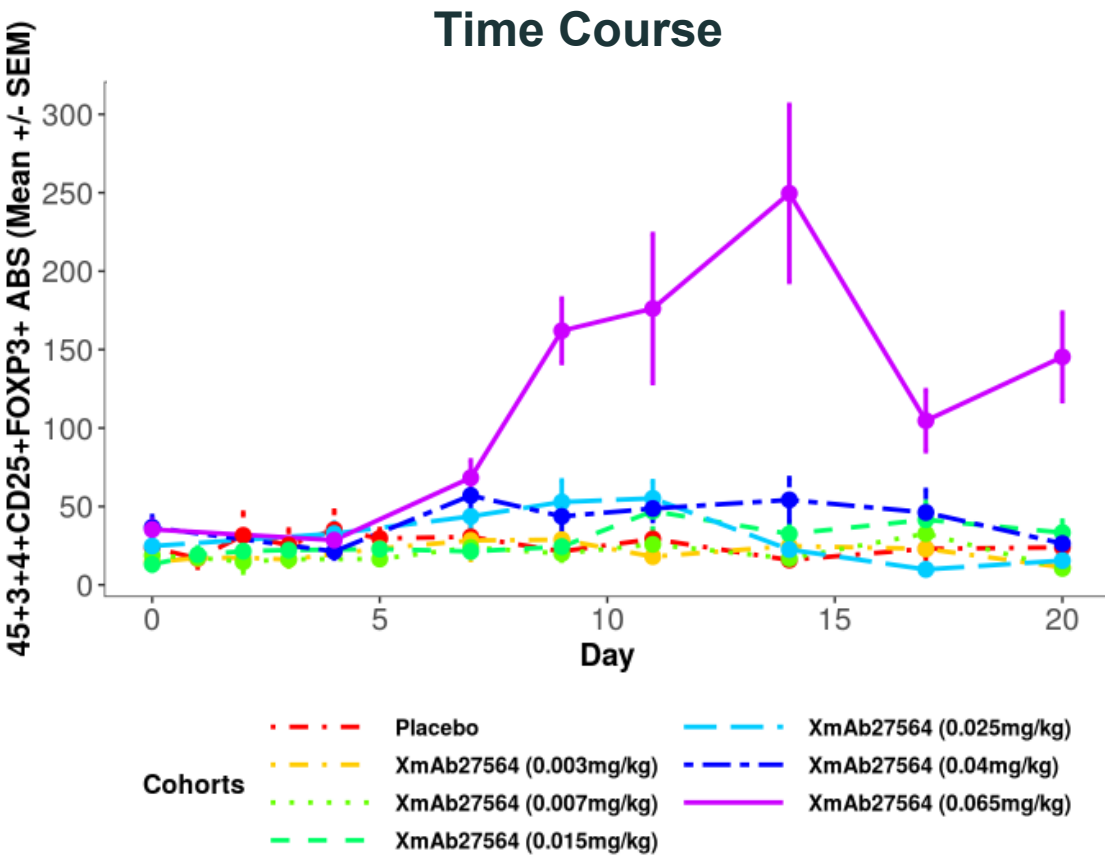


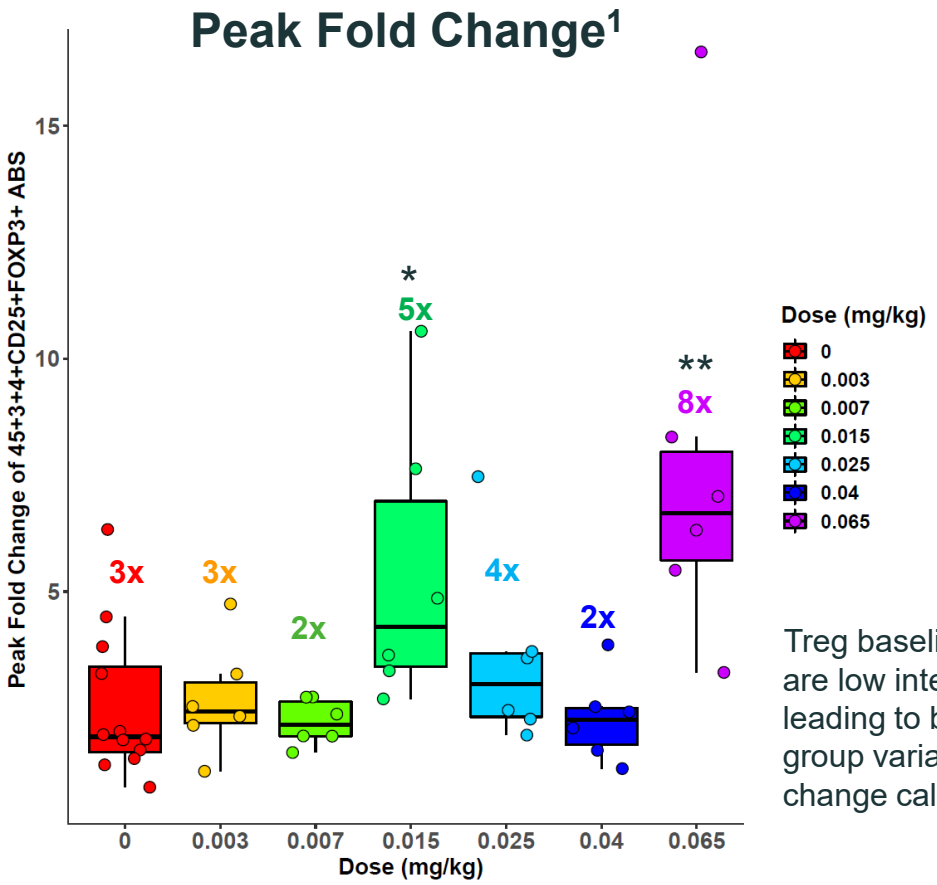
Treg baseline counts are not used in Treg/Tcon ratio calculations, leading to less variability in ratio values

Numeric values in “Peak Fold Change” plot are Mean
Dashed horizontal blue line represents the average of pre-dose values from all 48 subjects with ±2SD shown in grey lines
NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor

XmAb564 Promotes Robust & Durable Expansion of Total Tregs





Treg baseline counts are low integer values, leading to between group variability in fold change calculations

Numeric values in “Peak Fold Change” plot are Mean

[1] Peak fold change: Peak CD25⁺FoxP3⁺ CD4 Treg cell absolute count at a post-treatment time point divided by absolute count at baseline

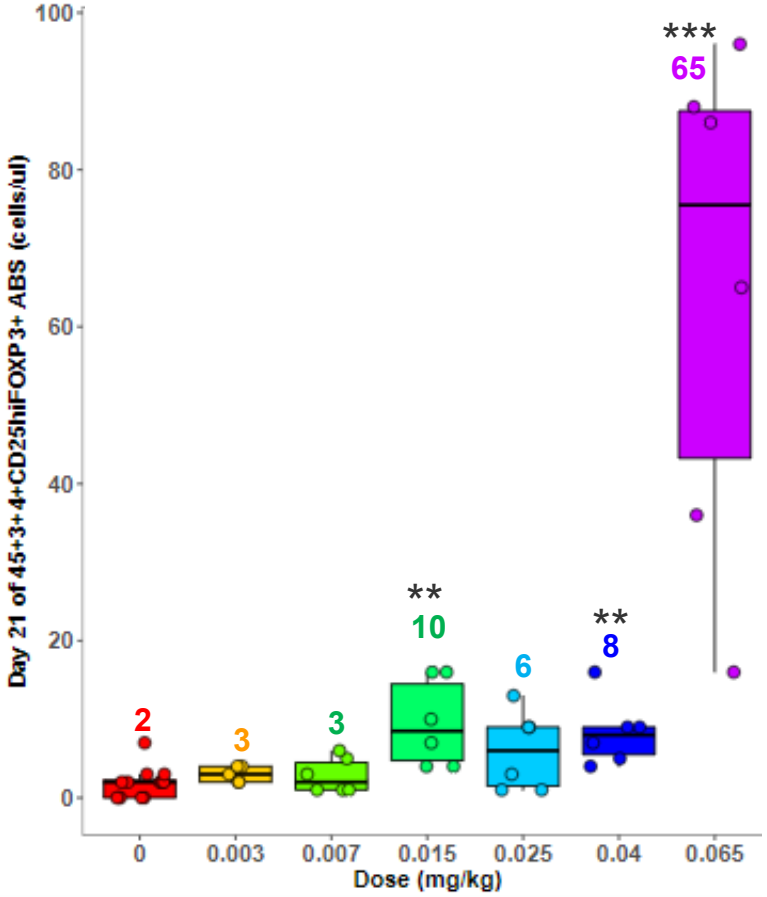
NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor

CD25^{bright} and Total Treg Remain Elevated for at Least 3 Weeks

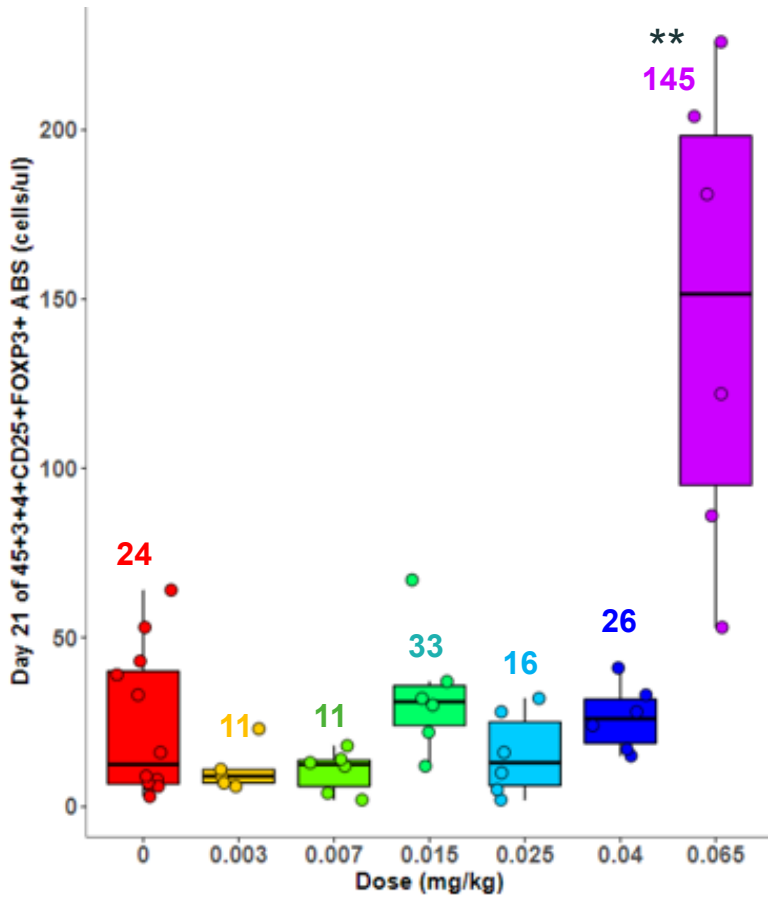
Day 21 CD25^{bright} Treg Cell Count

CD25^{hi}FoxP3^{+}CD4^{+}



Day 21 Total Treg Cell Count

CD25^{+}FoxP3^{+}CD4^{+}

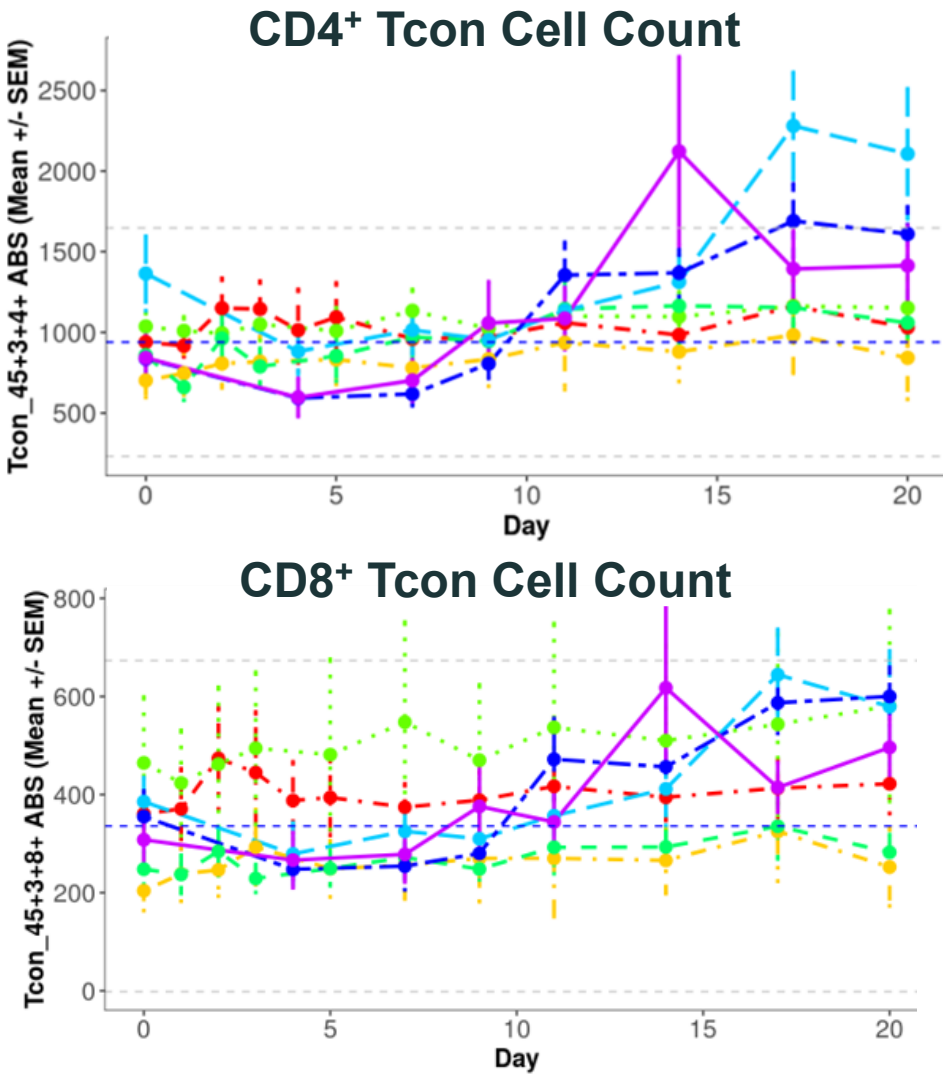


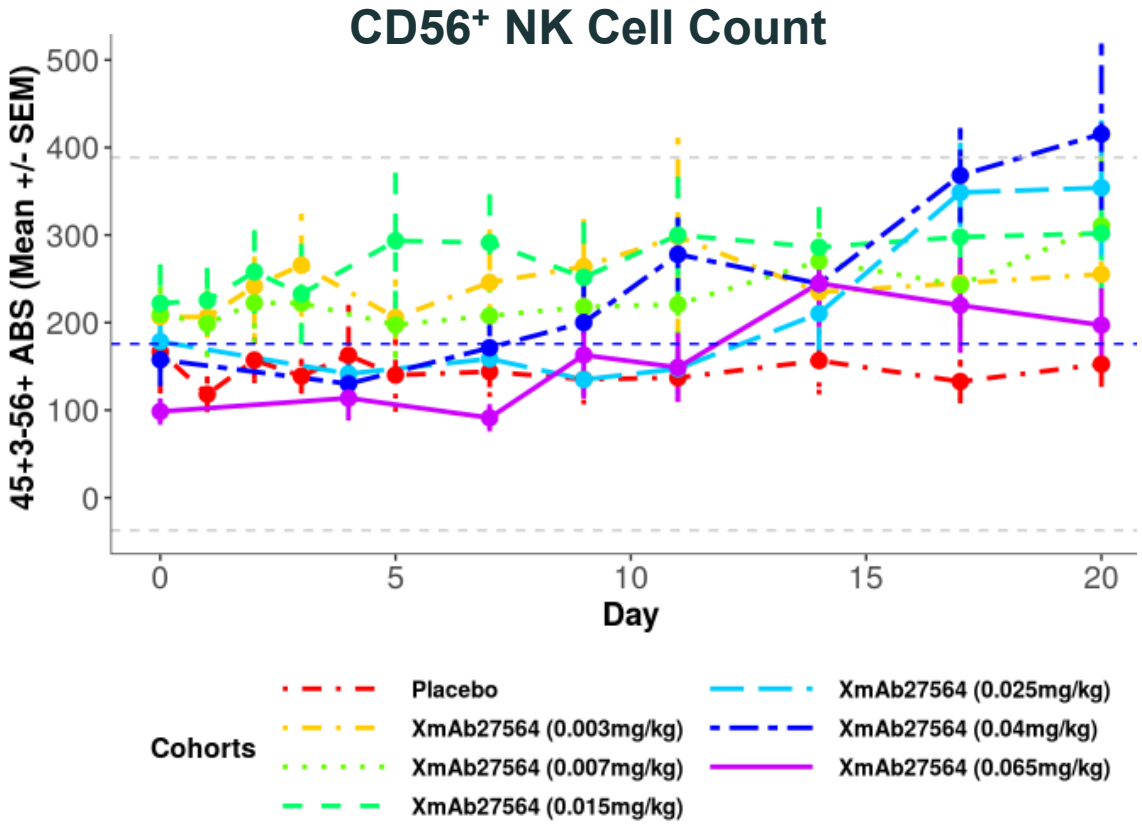
Numeric values in plots are Mean

NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor

XmAb564 Induces Minimal Increases in Conventional T cells and NK Cells





Dashed horizontal blue line represent the average of pre-dose values from all 48 subjects with ±2SD shown in grey lines

xencor

XmAb564 Phase 1a Topline Summary

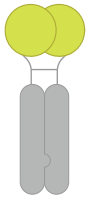
XmAb564 is well tolerated and generates a durable, dose-dependent and selective expansion of Tregs with a single dose

- 117-fold mean peak expansion over baseline in $CD25^{bright}$ Tregs and 8-fold mean peak expansion in total Tregs at highest dose
- Marked elevation of Tregs sustained through at least day 21: $CD25^{bright}$ and total Tregs increased 44-fold and 4.5-fold at highest dose, respectively
- Treg/Tcon ratio increased significantly in a dose-dependent manner
- All AEs Grade 1/2 and resolved without intervention

Phase 1b study in patients

- First patient dosed in a newly initiated Phase 1b, multiple-ascending dose (MAD) study of XmAb564 in patients with atopic dermatitis and psoriasis
- Multiple dosing schedules to be explored based on pharmacodynamic data

Xencor's Growing Portfolio of Potency-Optimized XmAb® Cytokines



IL-15/IL-15Rα
XmAb306
Phase 1

IL-2 (Treg selective)
XmAb564
Phase 1b

IL12-p40/IL12-p35
XmAb662
Phase 1 in 2023

Decoy resistant IL-18
Preclinical stages

LAG3-targeted IL-15
Preclinical stages

GENENTECH COLLABORATION
45% Xencor economics

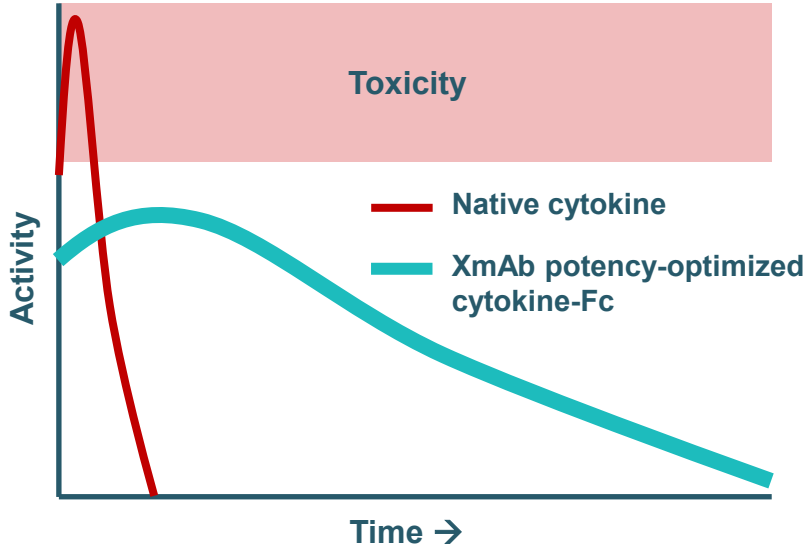
WHOLLY OWNED

Second validation of Xencor's approach to cytokine therapeutics

- XmAb306 (IL-15) Phase 1 demonstrated 40- to 100-fold increases in activated NK cells and accumulation upon multiple doses
- In two first-in-human studies, reduced potency and long half-life has translated to improved tolerability compared to the high toxicities generated by native cytokines

XmAb Cytokines

- Engineered to expand select immune cell populations
- Designed to be tolerable, active and easy to use

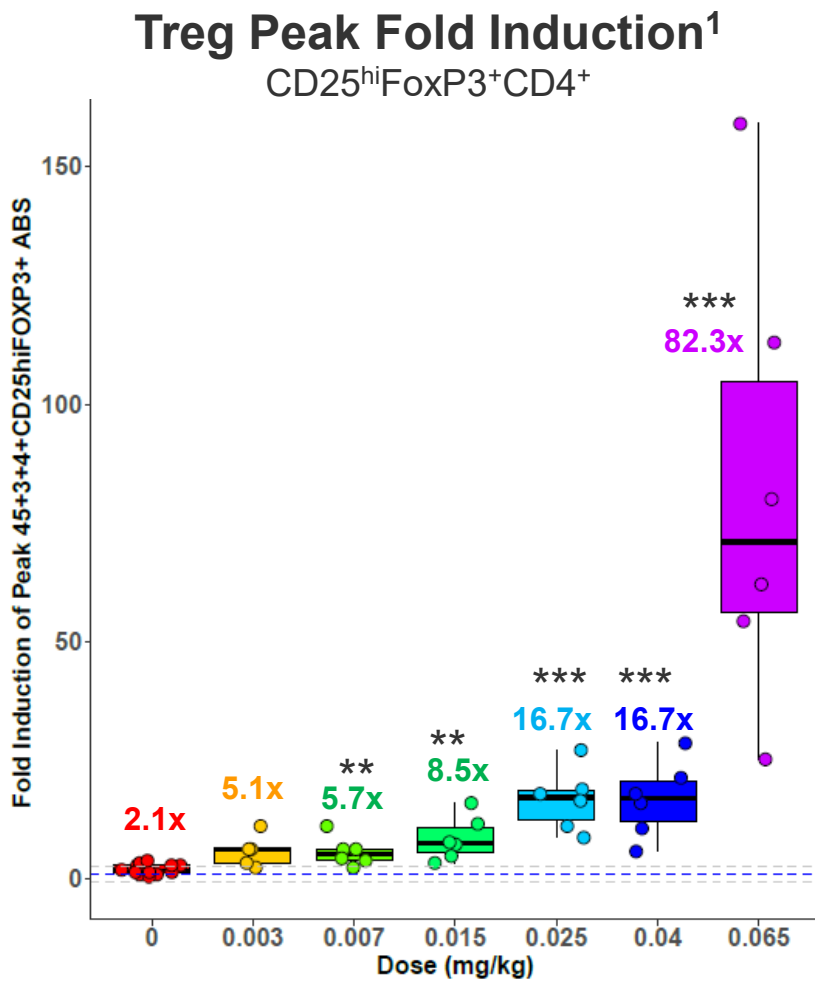


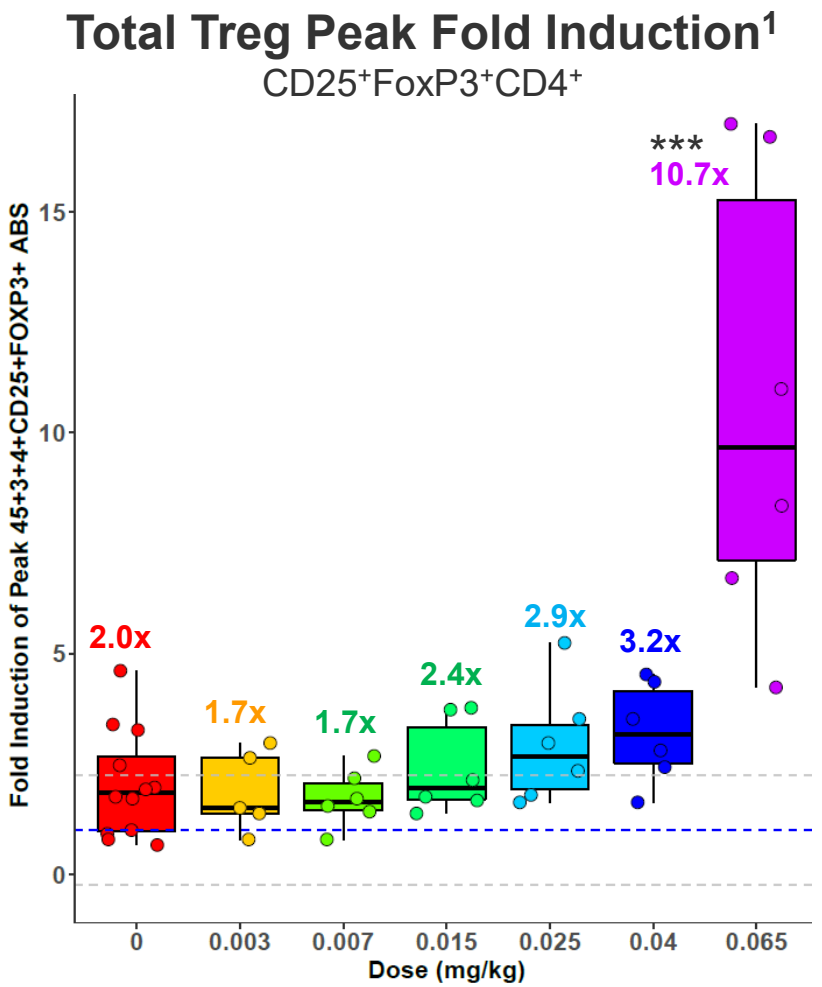
xencor

Q&A

Data Appendix

Peak Fold Induction of CD25^{bright} and Total Treg Cells Shows Consistent Dose Response of Treg Populations to XmAb564





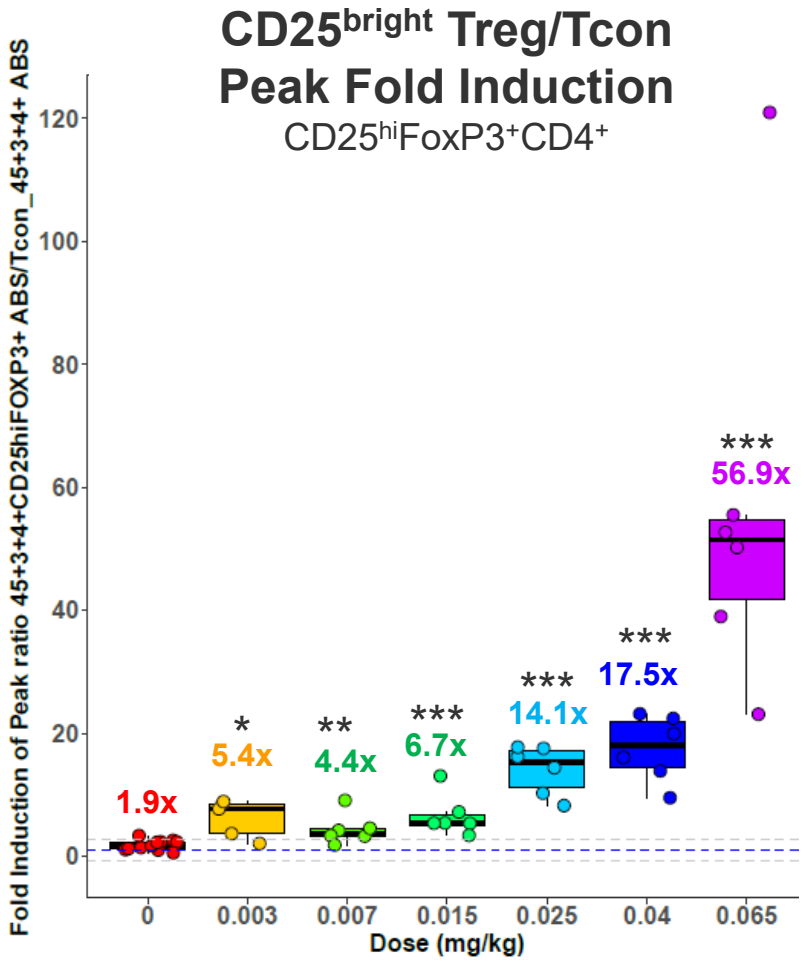
Numeric value in "Peak Fold Change" plot is Mean

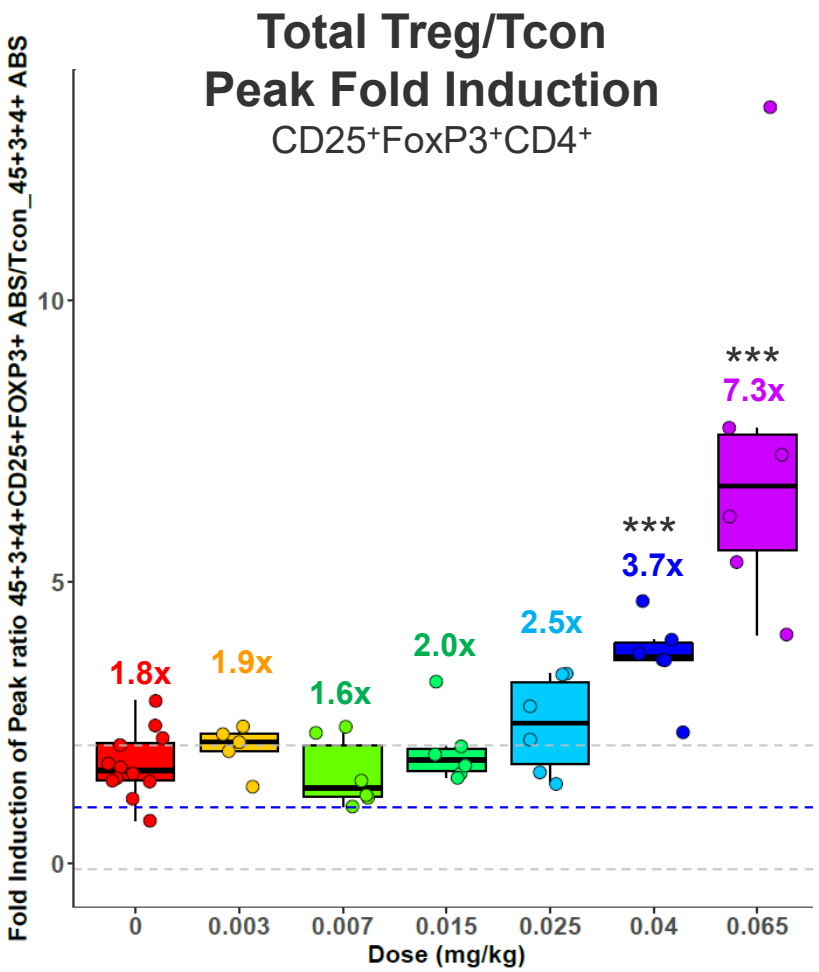
[1] Peak fold induction: Peak CD25^{bright} Treg or total Treg cell absolute counts of each subject divided by the average of all pre-dose values from all subjects (n=48)

NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor

Ratio of CD25^{bright}/Tcon and Total Treg/Tcon Peak Fold Induction Shows Consistent Dose Response of Treg Populations to XmAb564





Numeric value in “Peak Fold Change” plot is Mean
Peak fold induction: Peak CD25^{bright} Treg/Tcon or total Treg/Tcon ratios of each subject divided by the average of all pre-dose values from all subjects (n=48)
NS: p>0.05, *: p≤0.05, **: p≤0.01, ***:p≤0.001 compared with placebo treated cohort, Wilcoxon test

xencor