

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): **November 7, 2022**

XENCOR, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation)

001-36182

(Commission File Number)

20-1622502

(IRS Employer Identification Number)

**111 West Lemon Avenue
Monrovia, California**

(Address of principal executive offices)

91016

(Zip Code)

(626) 305-5900

(Registrant's telephone number, including area code)

N/A

(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.01 per share	XNCR	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 2.02. Results of Operations and Financial Condition.

On November 7, 2022, Xencor, Inc. announced its financial results for the quarter ended September 30, 2022 in the press release attached hereto as Exhibit 99.1 and incorporated herein by reference.

The information in “Item 2.02. Results of Operations and Financial Condition” of this Current Report on Form 8-K and in Exhibit 99.1 attached hereto is being furnished and shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 7.01. Regulation FD

On November 7, 2022, the Company posted a presentation on the “Investors” section of the Company’s website (www.xencor.com). The information contained in, or that can be accessed through, the Company’s website is not a part of this filing. A copy of the presentation is attached as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information in “Item 7.01”. and in Exhibit 99.2 attached hereto is being furnished and shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing

Item 9.01. Financial Statements and Exhibits.**(d) Exhibits.**

Exhibit No.	Description
99.1	Press Release dated November 7, 2022.
99.2	Presentation dated November 7, 2022.
104	Cover Page Interactive Data File (formatted as inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: November 7, 2022

XENCOR, INC.

By: /s/ Celia Eckert
Celia Eckert
General Counsel & Corporate Secretary



Xencor Reports Third Quarter 2022 Financial Results

-- XmAb564, engineered IL-2 cytokine, is well-tolerated and generates a durable, dose-dependent and selective expansion of Tregs in single-dose, healthy volunteer study --

-- Management to host conference call at 4:30 p.m. ET Today --

MONROVIA, Calif.-- Nov. 7, 2022-- Xencor, Inc. (NASDAQ:XNCR), a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of cancer and autoimmune diseases, today reported financial results for the third quarter ended September 30, 2022 and provided a review of recent business and clinical highlights.

"Xencor's XmAb® technologies and protein engineering capabilities enable us to address challenging areas of biology and to continually grow our portfolio, both internally and together with our many partners. Today we presented very encouraging data from our second clinical-stage cytokine program, XmAb564, a regulatory T-cell targeting IL2-Fc fusion protein for development in autoimmune disease. The selective T-cell increases, their durability and the tolerability in our data provide us additional clinical validation for Xencor's long-acting, low-potency approach to cytokine engineering and offers a potentially differentiated profile for this autoimmune program," said Bassil Dahiyat, Ph.D., president and chief executive officer at Xencor. "In the coming weeks, we will also present new data from two additional clinical programs—for vudalimab, data from the safety run-in portion of our Phase 2 prostate cancer study at SITC and, for plamotamab, updated Phase 1 expansion data in patients with lymphoma at ASH—as well as preclinical data from emerging platforms."

Dr. Dahiyat continued, "Altogether, these updates reflect Xencor's steady commitment to the priorities we laid out at the beginning of this year: to execute on development plans for our mid-stage bispecific antibodies, vudalimab and plamotamab; to advance potency-reduced cytokines for oncology and autoimmune disease; and to expand our portfolio with novel formats enabled by our protein engineering expertise and suite of leading XmAb technologies."

Recent Portfolio Highlights

- **XmAb564 (IL2-Fc):** Today, Xencor announced initial results from its single-dose Phase 1a study of XmAb564, administered subcutaneously in healthy volunteers. XmAb564 is a wholly owned, monovalent interleukin-2 Fc (IL-2-Fc) fusion protein, engineered to selectively activate and expand regulatory T cells (Tregs) for the potential treatment of patients with autoimmune diseases. XmAb564 is engineered with reduced binding affinity for IL-2's beta receptor and increased binding affinity for its alpha receptor (CD25). The study enrolled 48 subjects, with six dose-level cohorts each randomizing six subjects to XmAb564 and two subjects to placebo.

The study demonstrated that a single dose of XmAb564 is well tolerated and generates durable, dose-dependent and selective expansion of Tregs. In the highest dose cohort (0.065 mg/kg; Cohort 6), a 117-fold mean peak expansion over baseline in CD25^{bright} cells was observed, with an 8-fold expansion in the bulk Treg population. The ratio of Tregs to conventional T cells also

increased significantly in a dose-dependent manner. At day 21, both CD25^{bright} and total Treg counts remained markedly elevated, potentially supporting a multi-week dosing profile. All adverse events (AEs) were either Grade 1 or 2 and resolved without intervention. Injection site reaction was the most reported AE.

Xencor has dosed the first patient in a newly initiated Phase 1b, multiple-ascending dose study of XmAb564 in patients with atopic dermatitis and psoriasis.

- **Vudalimab (PD-1 x CTLA-4):** Xencor is advancing vudalimab, a selective dual checkpoint inhibitor, in multiple Phase 2 clinical studies. Xencor is conducting a Phase 2 study of vudalimab in patients with metastatic castration-resistant prostate cancer (mCRPC), as a monotherapy or in combination with standard-of-care chemotherapy or a PARP inhibitor. Initial data from the first patients in the study will be presented in a trials-in-progress poster at the Annual Meeting of the Society for Immunotherapy of Cancer (SITC) this month. Xencor is also conducting a Phase 2 monotherapy study in patients with advanced gynecologic and clinically-defined high-risk mCRPC.
- **Plamotamab (CD20 x CD3):** Xencor is advancing plamotamab as part of highly active chemotherapy-free regimens across B-cell cancers. The Phase 2 study of plamotamab in combination with tafasitamab plus lenalidomide is currently enrolling patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL).

Data from expansion cohorts in the first-in-human, Phase 1 monotherapy study in patients with relapsed or refractory non-Hodgkin's lymphoma will be presented at the 64th American Society of Hematology Annual Meeting on Monday, December 12, 2022. These expansion cohorts are actively recruiting patients with relapsed or refractory DLBCL and follicular lymphoma and are dosing using the intravenous recommended Phase 2 regimen to evaluate the safety and efficacy of plamotamab monotherapy. Subcutaneous administration of plamotamab is currently being incorporated into the study.

- **Preclinical Data Presentations:** New data from four preclinical-stage programs, including Xencor's IL-18-Fc and LAG3-targeted IL-15-Fc cytokine programs, CD28 trispecific antibodies targeting PDL1 and PDL2 and its NK cell engager platform, will also be presented at the SITC Annual Meeting.

Progress Across Partnerships

- **Vir Biotechnology, Inc.:** In the third quarter of 2022, Xencor reported \$17.8 million in royalty revenue under the Company's agreement with Vir. Sotrovimab, an antibody that targets the SARS-CoV-2 virus and incorporates Xencor's Xtend™ Fc domain for longer duration of action, has been made available by Vir and its partner GSK. Sotrovimab currently has emergency use authorization, temporary authorization or marketing approval (under the brand name Xevudy®) for early treatment of COVID-19 in more than 40 countries, and remains in use outside of the U.S. For the first nine months of 2022, the Company has received \$110.1 million in royalty revenue under the Vir Agreement.
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- **Zenas Biopharma Ltd.:** Today, Zenas announced that it raised \$118 million in additional capital in connection with the issuance of Series B shares. Xencor had owned a warrant and a convertible note in Zenas, which as a result of the financing converted into additional equity. Zenas also announced plans to initiate a global Phase 3 registration study of obixelimab, which was acquired from Xencor, in patients with IgG4-related disease in late 2022.

Corporate: In September, Xencor appointed Nancy Valente, M.D., to its board of directors. Dr. Valente is a recognized and accomplished biotechnology executive with broad expertise in late-stage oncology clinical development, and she served a critical role for numerous product launches. She most recently served as a senior vice president at Genentech, a member of the Roche Group, and as its global head and co-lead of global product development of its oncology and hematology therapeutic area.

Xevudy® is a registered trademark of the GSK group of companies.

Financial Results for the Third Quarter Ended September 30, 2022

Cash, cash equivalents, receivables and marketable debt securities totaled \$654.6 million as of September 30, 2022, compared to \$664.1 million on December 31, 2021. During the first nine months of 2022, the Company received royalty and milestone payments from partners of \$140.9 million, which offset net spending on operations of \$170.3 million through September 30, 2022.

Total revenue for the third quarter ended September 30, 2022 was \$27.3 million, compared to \$19.7 million for the same period in 2021. Revenues earned in the third quarter of 2022 were primarily royalties from the Alexion and Vir agreements, compared to the same period in 2021, which were primarily from the Janssen collaboration, and royalty revenue from Alexion and Vir. Revenues for the nine months ended September 30, 2022 were \$143.0 million, compared to \$121.1 million for the same period in 2021. Revenues for the nine-month period in 2022 were primarily from milestone revenue from Astellas and royalty revenue from Alexion, MorphoSys and Vir, compared to the same period in 2021, which were earned primarily from the collaborations with Janssen and Novartis, milestone revenue from MorphoSys and the royalties from Alexion and Vir.

Research and development (R&D) expenses for the third quarter ended September 30, 2022 were \$53.3 million, compared to \$50.6 million for the same period in 2021. Increased R&D spending for third quarter of 2022 compared to 2021 reflects increased spending on IL-12 and IL-18 cytokine programs offset by lower spending on CD3 programs. R&D expenses for the nine months ended September 30, 2022 were \$148.1 million, compared to \$141.5 million for the same period in 2021. Increased R&D spending for the first nine months of 2022 reflects additional spending on XmAb808 (B7-H3 x CD28) and cytokine programs offset by lower spending on CD3 programs.

General and administrative (G&A) expenses for the third quarter ended September 30, 2022 were \$12.4 million, compared to \$10.4 million for the same period in 2021. G&A expenses for the nine months ended September 30, 2022 were \$34.7 million, compared to \$27.5 million for the same period of 2021. Increased G&A spending for the third quarter and first nine months of 2022 compared to amounts for the same periods in 2021 reflects additional general and administrative staffing and increased spending on professional services and facility costs.

Other income for the third quarter ended September 30, 2022 was \$6.7 million compared to \$1.1 million in the same period in 2021. Other income for these periods represents unrealized gain from the change in

fair value of equity securities and interest income earned on investments. Other expenses for the nine months ended September 30, 2022 were \$2.2 million, compared to other income of \$57.5 million in the same period in 2021. Other expenses for nine months ended September 30, 2022 consists of unrealized losses from the change in the fair value of equity investments and interest income earned, while other income for the first nine months of 2021 includes realized gains on the sale of an investment equity security and an increase in unrealized gains on the Company's marketable equity investments.

Non-cash, stock-based compensation expense for the nine months ended September 30, 2022 was \$36.2 million, compared to \$26.6 million for the same period in 2021.

Net loss for the third quarter ended September 30, 2022 was \$32.8 million, or \$(0.55) on a fully diluted per share basis, compared to net loss of \$40.2 million, or \$(0.69) on a fully diluted per share basis, for the same period in 2021. For the nine months ended September 30, 2021, net loss was \$43.1 million, or \$(0.72) on a fully diluted per share basis, compared to net income of \$9.6 million, or \$0.16 on a fully diluted per share basis, for the same period in 2021. Net loss reported for the third quarter ended September 30, 2022 compared to the net loss reported for the same period in 2021 is lower due to increased revenue and interest income in 2022 compared to 2021. Net loss for the first nine months of 2022, compared to the net income reported for the same periods in 2021, is primarily due to realized gain on an equity investment and an increase in unrealized gains on marketable equity securities during the nine months ended September 30, 2021.

The total shares outstanding were 59,773,337 as of September 30, 2022, compared to 58,454,811 as of September 30, 2021.

Financial Guidance

Based on current operating plans, Xencor expects to have cash to fund research and development programs and operations through the end of 2025. The Company expects to end 2022 with between \$575 million and \$600 million in cash, cash equivalents, receivables and marketable debt securities.

Conference Call and Webcast

Xencor will host a conference call today at 4:30 p.m. ET (1:30 p.m. PT) to discuss the third quarter 2022 financial results, provide a corporate update and present results from the Phase 1a study of XmAb564.

The live webcast will be available under "Events & Presentations" in the Investors section of the Company's website at investors.xencor.com and will be archived for at least 30 days. Active participants in the conference call may receive credentials for telephone access by registering at the following link:
<https://register.vevent.com/register/B1b8a7d450f24d42068f4bb86e717257fe>.

About Xencor

Xencor is a clinical-stage biopharmaceutical company developing engineered antibodies and cytokines for the treatment of patients with cancer and autoimmune diseases. More than 20 candidates engineered with Xencor's XmAb® technology are in clinical development, and three XmAb medicines are marketed by partners. Xencor's XmAb engineering technology enables small changes to a protein's structure that result in new mechanisms of therapeutic action. For more information, please visit www.xencor.com.

Forward-Looking Statements

Certain statements contained in this press release may constitute forward-looking statements within the meaning of applicable securities laws. Forward-looking statements include statements that are not purely statements of historical fact, and can generally be identified by the use of words such as “potential,” “can,” “will,” “plan,” “may,” “could,” “would,” “expect,” “anticipate,” “seek,” “look forward,” “believe,” “committed,” “investigational,” and similar terms, or by express or implied discussions relating to Xencor’s business, including, but not limited to, statements regarding planned presentations of clinical data, planned additional clinical trials, the quotations from Xencor’s president and chief executive officer, our projected financial resources and other statements that are not purely statements of historical fact. Such statements are made on the basis of the current beliefs, expectations, and assumptions of the management of Xencor and are subject to significant known and unknown risks, uncertainties and other factors that may cause actual results, performance or achievements and the timing of events to be materially different from those implied by such statements, and therefore these statements should not be read as guarantees of future performance or results. Such risks include, without limitation, the risks associated with the process of discovering, developing, manufacturing and commercializing drugs that are safe and effective for use as human therapeutics and other risks, including the ability of publicly disclosed preliminary clinical trial data to support continued clinical development and regulatory approval for specific treatments, in each case as described in Xencor’s public securities filings. For a discussion of these and other factors, please refer to Xencor’s annual report on Form 10-K for the year ended December 31, 2021 as well as Xencor’s subsequent filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended to date. All forward-looking statements are qualified in their entirety by this cautionary statement and Xencor undertakes no obligation to revise or update this press release to reflect events or circumstances after the date hereof, except as required by law.

Contacts

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Xencor, Inc.
Condensed Balance Sheets
(in thousands)

	September 30, 2022 <u>(Unaudited)</u>	December 31, 2021
Assets		
Current assets		
Cash and cash equivalents	\$ 52,654	\$ 143,480
Marketable debt securities	515,398	153,767
Marketable equity securities	32,184	36,860
Accounts receivable	44,876	66,384
Prepaid expenses	22,886	23,877
Total current assets	667,998	424,368
Property and equipment, net	51,040	28,240
Intangible assets, net	18,094	16,493
Marketable debt securities - long term	41,720	300,465
Marketable equity securities - long term	31,124	31,262
Notes receivable - long term	5,000	5,000
Right of use asset	19,680	31,730
Other assets	613	653
Total assets	\$ 835,269	\$ 838,211
Liabilities and stockholders' equity		
Current liabilities		
Accounts payable and accrued liabilities	\$ 33,907	\$ 33,444
Deferred revenue	35,186	37,294
Lease liabilities	20,551	—
Income tax liability	388	—
Total current liabilities	90,032	70,738
Lease liabilities, net of current portion	22,539	33,969
Total liabilities	112,571	104,707
Stockholders' equity	722,698	733,504
Total liabilities and stockholders' equity	\$ 835,269	\$ 838,211

Xencor Inc.
Condensed Statements of Comprehensive Income (Loss)
(unaudited)
(in thousands, except share and per share data)

	<u>Three months ended September 30,</u>		<u>Nine months ended September 30,</u>	
	<u>2022</u>	<u>2021</u>	<u>2022</u>	<u>2021</u>
Revenues	\$ 27,299	\$ 19,683	\$ 142,969	\$ 121,096
Operating expenses:				
Research and development	53,273	50,610	148,111	141,519
General and administrative	12,374	10,373	34,738	27,462
Total operating expenses	65,647	60,983	182,849	168,981
Loss from operations	(38,348)	(41,300)	(39,880)	(47,885)
Other income (expense), net	6,677	1,109	(2,171)	57,455
Income (loss) before income taxes	(31,671)	(40,191)	(42,051)	9,570
Income tax expense	1,088	—	1,088	—
Net income (loss)	(32,759)	(40,191)	(43,139)	9,570
Other comprehensive loss				
Net unrealized loss on marketable securities	(931)	(59)	(8,366)	(149)
Comprehensive income (loss)	\$ (33,690)	\$ (40,250)	\$ (51,505)	9,421
Net income (loss) per share:				
Basic net income (loss) per share	\$ (0.55)	\$ (0.69)	\$ (0.72)	\$ 0.16
Diluted net income (loss) per share	\$ (0.55)	\$ (0.69)	\$ (0.72)	\$ 0.16
Weighted-average number of common shares used in net income (loss) per share applicable to common stockholders - basic				
	59,716,594	58,350,647	59,564,985	58,199,928
Weighted-average number of common shares used in net income (loss) per share applicable to common stockholders - diluted				
	59,716,594	58,350,647	59,564,985	60,346,480

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

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

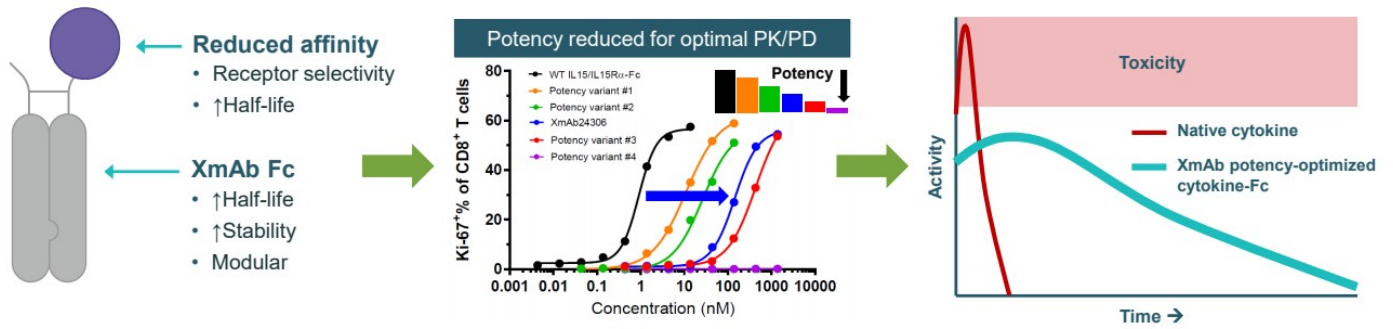


Reduced potency IL2-Fc

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

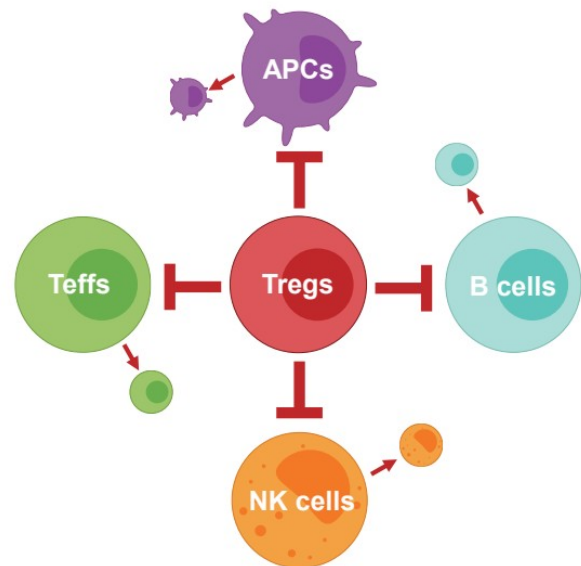
- Single ascending dose of subcutaneously administered XmAb564 in healthy volunteers
- Well tolerated; no serious adverse events or dose limiting toxicities observed
- Selective expansion of CD25^{bright} regulatory T cells (Tregs) of 10x and higher beginning at 3rd dose level and reaching 117x increase 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-IL15R α -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

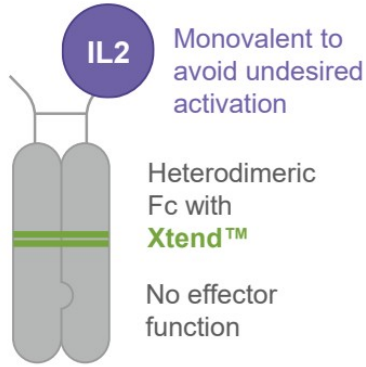
- Regulatory T cells (Tregs) are CD4⁺FoxP3⁺ cells expressing CD25 (IL-2R α) that maintain immune tolerance in tissues by suppressing the function of both CD4 and CD8 effector T cells
- Tregs are dysfunctional in most autoimmune diseases
- A therapeutic approach has been to restore Treg numbers and function 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



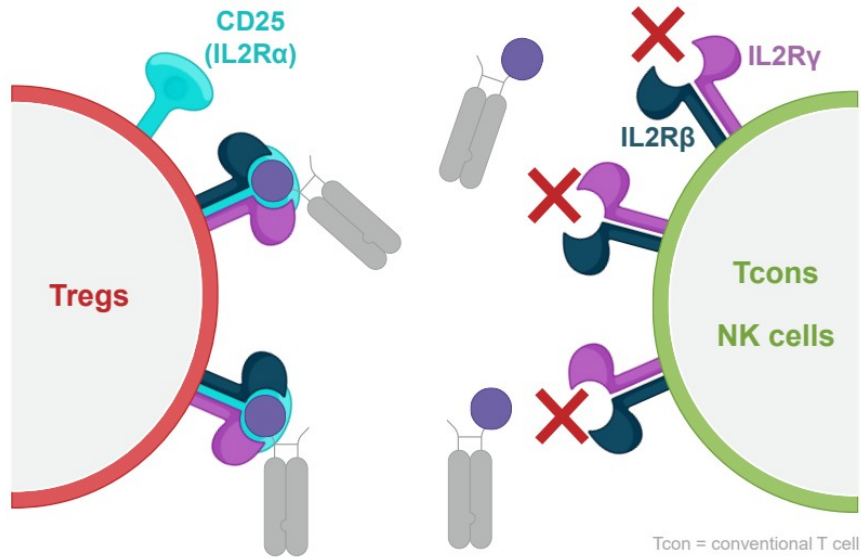
IL-2 Activates Multiple T Cell Types

XmAb564 is Engineered to Improve for Treg Selectivity

2x increase to **CD25 (IL2R α)** binding and reduced affinity for IL2R β



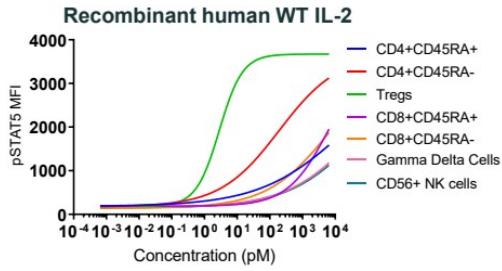
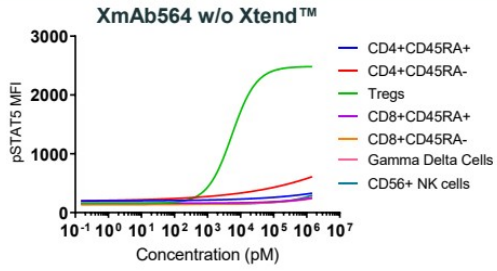
Overall 400-1000x reduced potency



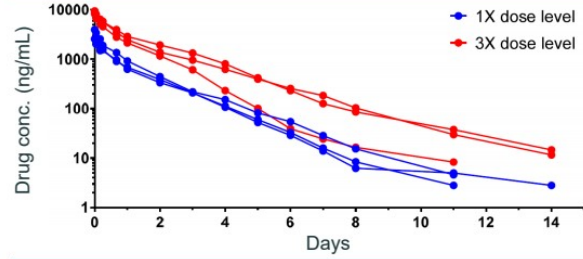
Tcon = conventional T cell
WT = wild-type

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

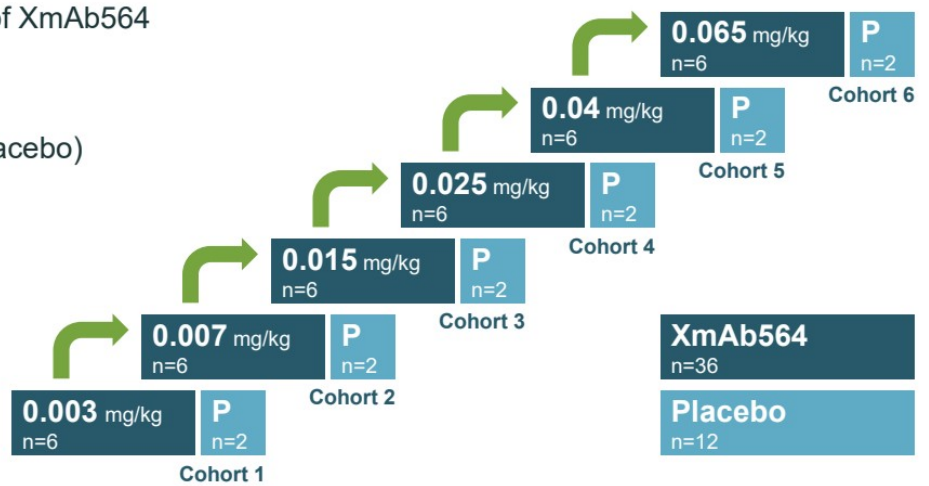
XmAb564 Phase 1a Healthy Volunteer Study Design

Phase 1a single-ascending dose (SAD) study

- Randomized and double-blinded
- Subcutaneous administration of XmAb564
- Healthy 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)



XmAb564 Was Well Tolerated

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

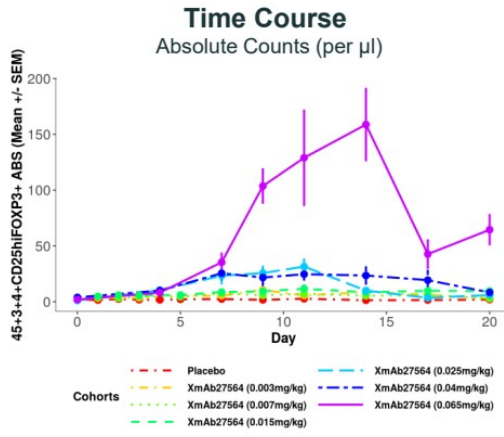
- All adverse events (AEs) were grade 1 or 2 (mild-to-moderate) and self-limited
- Injection site reaction was the most reported AE
- No serious AEs, dose-limiting toxicities or early discontinuations due to AEs
- No clinically significant abnormalities in laboratory values, vital signs and ECGs

Laboratory findings and pharmacokinetics

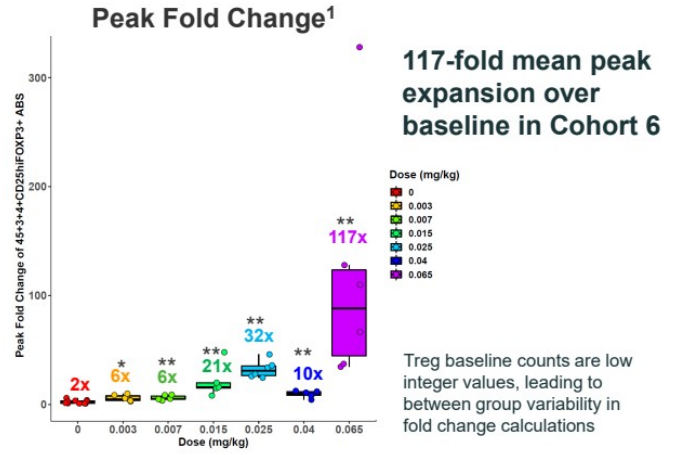
- Some subjects had transient, reversible elevations in blood eosinophils
 - No eosinophil-related AEs were observed
 - Possibly related to mechanism-of-action, reported in other third-party CD25-targeting IL-2 programs
- No other clinically significant abnormalities in safety laboratory studies were 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



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



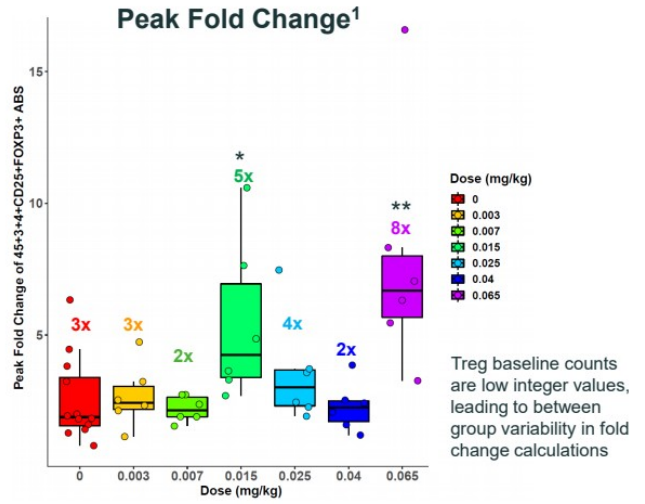
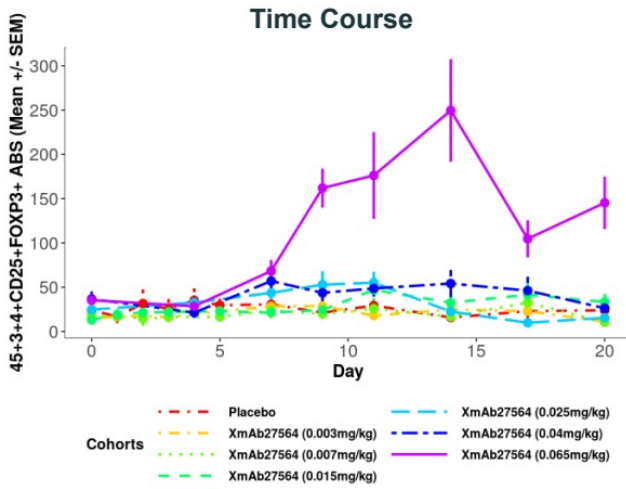
Highest reported CD25^{bright} Treg expansion

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 \le 0.05, **: p \le 0.01, ***: p \le 0.001 compared with placebo treated cohort, Wilcoxon test

XmAb564 Promotes Robust & Durable Expansion of Total Tregs



Numeric values in "Peak Fold Change" plot are Mean

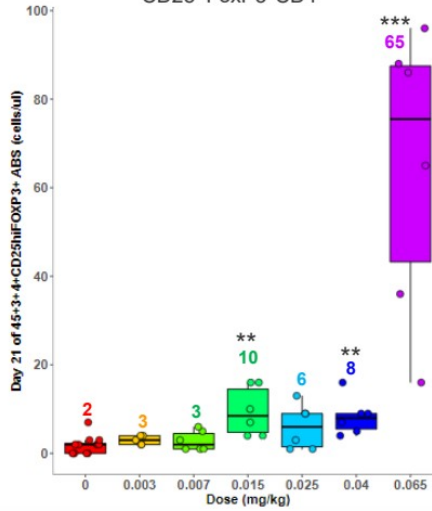
¹ Peak fold change: Peak CD25⁺FoxP3⁺ CD4 Treg cell absolute count at a post-treatment time point divided by absolute count at baseline

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

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

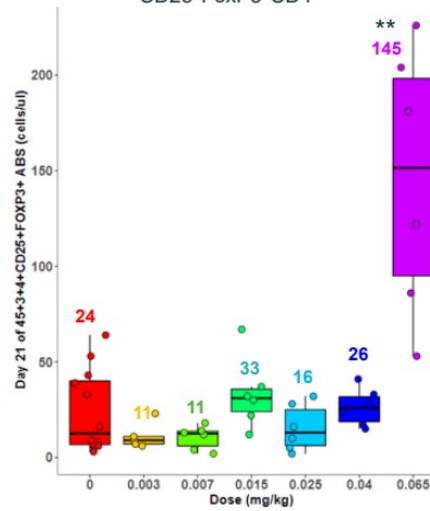
Day 21 CD25^{bright} Treg Cell Count

CD25^{hi}FoxP3⁺CD4⁺



Day 21 Total Treg Cell Count

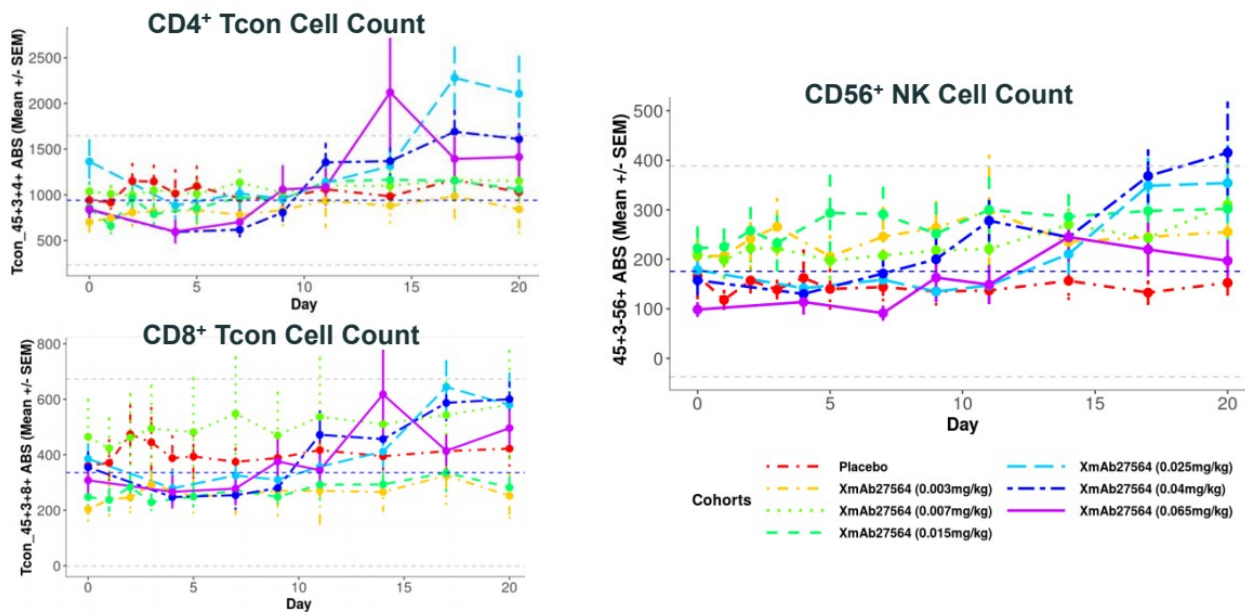
CD25⁺FoxP3⁺CD4⁺



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

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 $\pm 2SD$ shown in grey lines

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-15R α
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

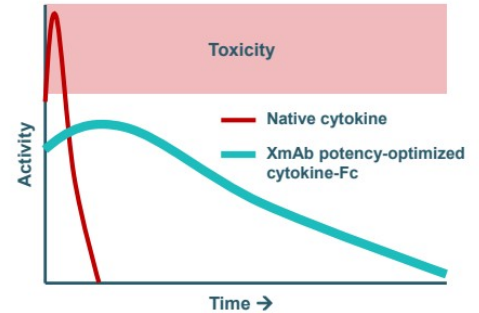
WHOLLY OWNED

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



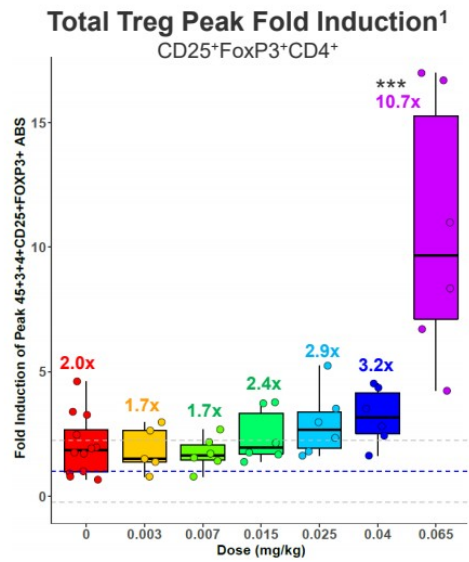
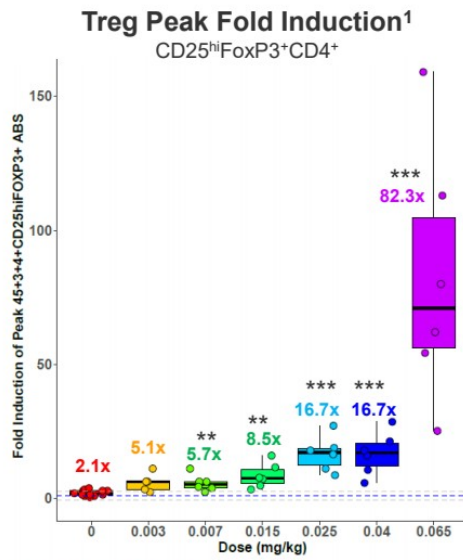
Q&A



Data Appendix



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

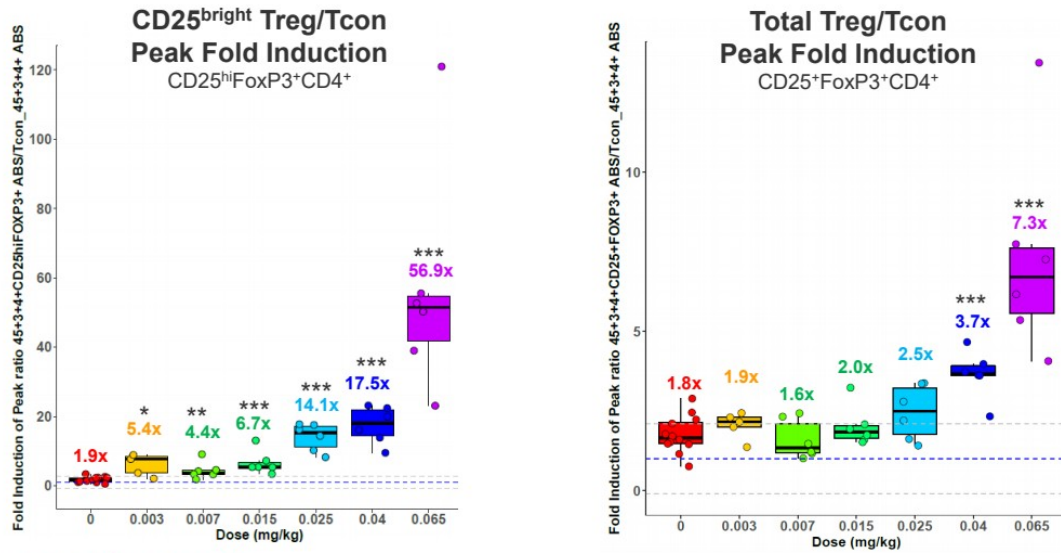


Numeric value in "Peak Fold Change" plot is Mean

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

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