Interim Results from First-in-Human Study of XmAb942 & TL1A Pipeline Update

April 29, 2025

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 for treatment of diseases for which we are developing product candidates, as well as other risks described in Xencor's filings with the Securities and Exchange Commission. 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.

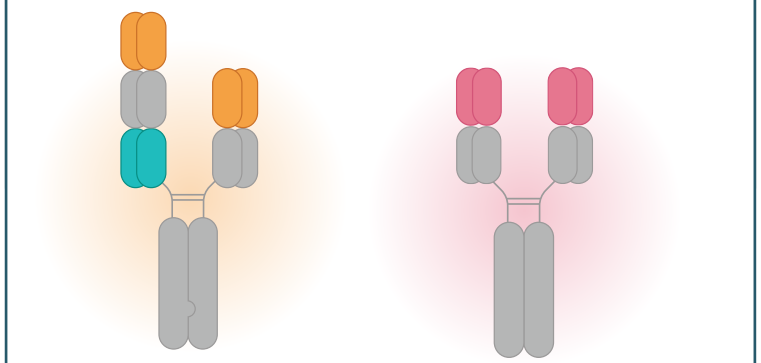
Proven Power of XmAb® Engineering: Proteins By Design®

Small changes, big functional impacts

- XmAb Fc Domains augment native immune functions in molecules and/or control their structure, while preserving desired attributes
- XmAb engineered antibodies are designed to solve complex biologic problems
- Strong patent portfolio

Advancing an optimized portfolio of XmAb drug candidates

- **Oncology:** 2 novel CD3 TCEs advancing in Phase 1 studies
- **Autoimmune**: Study initiations and plans
  - ✓ 4Q'24: XmAb942 (Xtend™ TL1A)
  - 1H'25: Plamotamab (CD20xCD3) in RA
  - 2H'25: XmAb657 (CD19xCD3)



XmAb Bispecific T-cell Engagers (TCEs)

Xtend™ Antibodies With Potential Best-in-Class Half-Life Extension

Partnerships leverage modular XmAb technology

- More than 15 technology license partnerships greatly broadens scope with little-to-no effort
- Multiple commercialized XmAb antibodies

ULTOMIRIS® **MONJUVI®/MINJUVI®**

COLLABORATION PORTFOLIO INCLUDES

Johnson&Johnson Innovative Medicine · AMGEN · ALEXION AstraZeneca Rare Disease · Incyte · Genentech A Member of the Roche Group · GILEAD · VIR · astellas

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Next-Gen XmAb® Drug Design in Oncology & Autoimmune Diseases

Pipeline focus on T-cell engagers and bispecific mechanisms

Program	Targets	XmAb® Platforms	Indications	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: T-cell Engagers (CD3 & CD28)								
XmAb819	ENPP3 x CD3	2+1 Bispecific	ccRCC					
XmAb541	CLDN6 x CD3	2+1 Bispecific, Xtend™	Ovarian cancer, oncology					
XmAb808	B7-H3 x CD28	2+1 Bispecific, Xtend	Prostate cancer, oncology					
XmAb Program	Undisclosed TCE	Bispecific, Xtend	Solid tumor oncology					
Immunology Programs (TL1A & CD3)								
XmAb942	TL1A	Xtend, FcKO	IBD				2H'25	
XENP53* **	TL1A x IL23p19	Bispecific, Xtend	IBD					
Plamotamab	CD20 x CD3	Bispecific	Rheumatoid Arthritis				1H'25	
XmAb657	CD19 x CD3	2+1 Bispecific, Xtend	Autoimmune Diseases				2H'25	

ccRCC clear cell renal cell carcinoma **FcKO** Fc knock out **IBD** Inflammatory bowel disease

Key: Solid tumors | Immunology | Planned Study Initiation

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Potential Inflection Points for Xencor's Clinical Portfolio in 2025

XmAb Drug Candidate		Indication	1H'25	2H'25
Oncology Portfolio				
XmAb819	ENPP3 x CD3	ccRCC		**Present initial Phase 1 data at a medical meeting**
XmAb541	CLDN6 x CD3	CLDN6+ tumor types, including ovarian	**Characterization of target dose levels**	
Immunology Portfolio				
XmAb942	Xtend™ TL1A	IBD+	**Initial SAD & MAD readout** ✓	**Phase 2 start in UC**
XENP53* **	TL1A x IL23p19	IBD+	**Lead candidate selection; prepare to initiate FIH study in 2026**	
Plamotamab	CD20 x CD3	Rheumatoid arthritis	**Initiate Phase 1/2 study**	
XmAb657	CD19 x CD3	Autoimmune		**Initiate FIH study**

As of 29-Apr-2025 **SAD** Single ascending dose **MAD** multiple ascending dose **FIH** first-in-human

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IBD Remains a Significant Opportunity for Novel Therapy

+3.3m
Estimated diagnoses in the U.S. and EU5[1]

Global IBD drug spend projected to be $23bn+ by 2030[2]

Two common forms:
Crohn's disease
Ulcerative colitis

Chronic High-Burden Disease

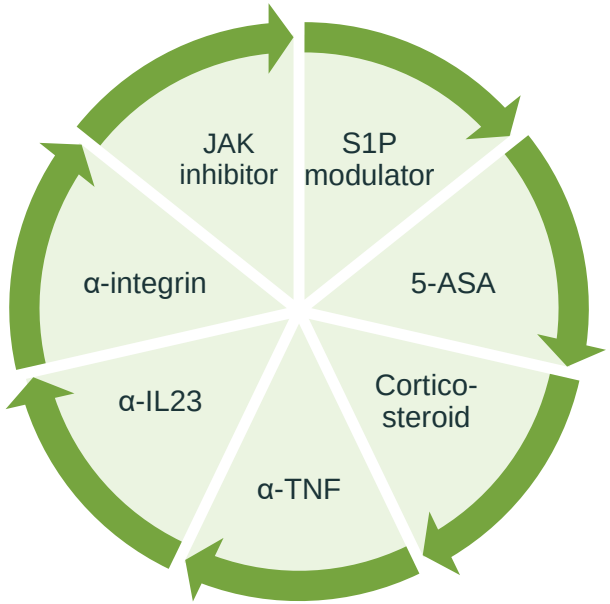
Severe Symptoms

- Diarrhea and rectal bleeding
- Fever and fatigue
- Reduced appetite and weight loss
- Mental health burden

Significant Health Burden

- Impaired quality of life
- Lower life expectancy
- Surgeries, hospitalization
- Increased risk for intestinal resection
- Increased risk for colorectal cancer

Current Standards of Care

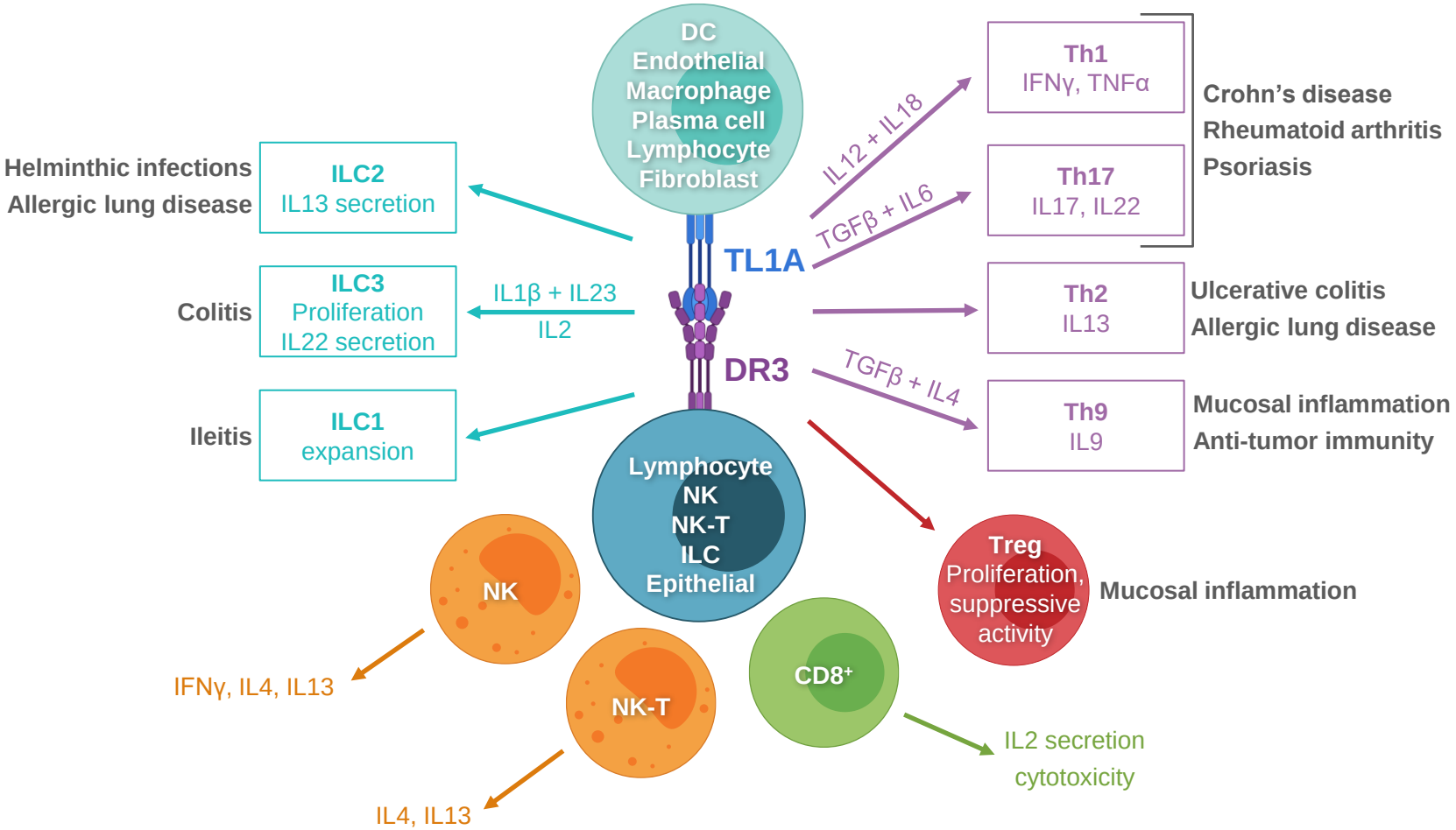


Patients cycle through multiple treatments

- **Suboptimal efficacy:** ~10-20% disease remission[3]
- **Adverse events:** Infection, malignancy, thromboembolism, cardiac
- **Burdensome regimens:** Poor patient compliance

1 GlobalData, EU5: France, Germany, Italy, Spain, UK **2** GlobalData **3** Drug Labels

TL1A Has Emerged As a Critical Node in IBD Pathophysiology



TL1A is expressed primarily by monocytes, macrophages, and dendritic cells.

TL1A amplifies innate and adaptive immune signaling and fibrogenesis through ILC, Th1, Th2, and Th17 cells, and myofibroblasts.

TL1A risk SNPs are associated with UC and CD disease severity, such as fibrostenosis.

TL1A, DR3, and DcR3 are elevated at sites of disease activity.

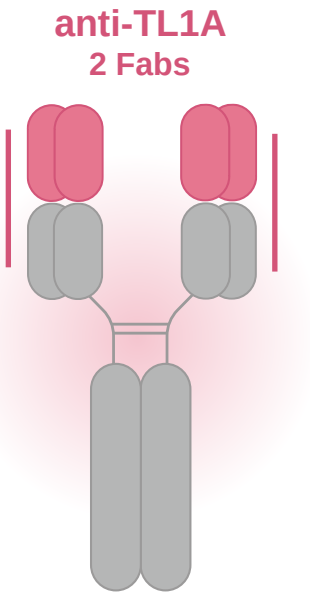
Murine TL1A models recapitulate IBD phenotypes, including fibrostenotic disease.

Neutralization of TL1A reverses disease phenotype, including fibrostenosis.

Image adapted from Valatas, et al. Front. Immunol., 2019. TL1A and DR3 receptors via BioRender.

XmAb® Protein Engineering for Differentiated, Potentially Best-in-Class Treatment Options for IBD

XmAb942 Design for a Novel Next-Gen Anti-TL1A

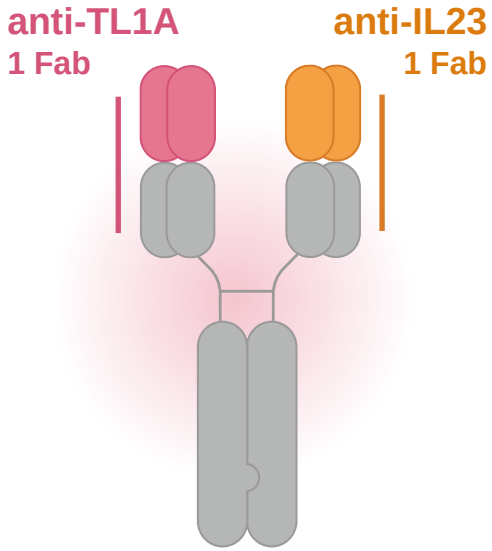


Xtend™ + FcKO

Objectives

- Class-leading potency for superior inhibition of TL1A within the GI tract
- XmAb stability and solubility engineering for high concentration formulation and lower immunogenicity risk
- Long half-life from Xtend™ Fc domain designed to enable extended subcutaneous dosing intervals in maintenance

XENP53*** Design for TL1A x IL-23p19 Bispecific



Bispecific Fc Domain

Xtend™ + FcKO

Objectives

- Highly stable monovalent format to allow subcutaneous formulation and avoid large immune complexes
- Very high affinity TL1A and IL23p19 binders to deliver equivalent target inhibition as monospecific antibodies
- Long half-life from Xtend Fc domain

Blocking IL23p19 gives consistently superior clinical outcomes across indications versus IL23p40[1,2]

1 Week 47 Efficacy of Guselkumab and Ustekinumab in Crohn's Disease Based on Prior Response/Exposure to Biologic Therapy: Results from the GALAXI 2 & 3 Phase 3 Studies; Danese and Rubin et al; JNJ Presentation.
2 Comparing Efficacy of Guselkumab versus Ustekinumab in Patients with Psoriatic Arthritis: An Adjusted Comparison Using Individual Patient Data from the DISCOVER and PSUMMIT Trial; Thilakarathne and Hassan et al.; Rheumatol Ther. 2024 Feb 28.

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XmAb942: Novel High-Affinity Anti-TL1A mAb Designed for Extended Half-Life, Under Development for the Treatment of IBD

Class Leading Target Inhibition XmAb942 utilizes Xtend™ Fc domain technology with potentially class-leading target neutralization

Class Leading Clinical Convenience High concentration formulation for subcutaneous dosing with +71 day estimated half-life in humans supporting Q12W maintenance dosing frequency

Execution of Efficient Clinical Development Plan First-in-human clinical study in healthy volunteers initiated 4Q'24 with planned Phase 2 study start during 2H'25

Program[1]	Potent	TL1A Suppression[2]	Convenient SC Dosing	Q12W Dosing	Half-Life Extension	Low Immunogenicity
XmAb942	✓	✓	✓	✓	✓	✓ Predicted[8]
Tulisokibart[3,4]	–	–	✓	✗	✗	✓
Afimkibart[5,6]	✓	✓	✓	✗	✗	✗
Duvakitug[7]	✓	✓	–	✗	✗	✓

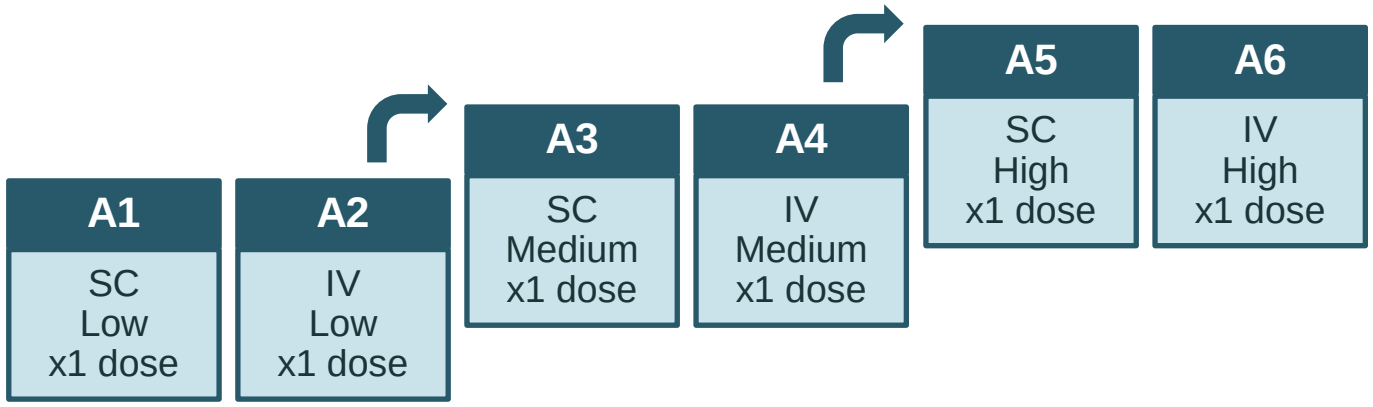
1 No head-to-head trial has been conducted evaluating XmAb942 against other data included herein. Differences exist between clinical trial design, patient populations and the product candidates themselves, and caution should be exercised when comparing data across trials **2** As predicted by quantitative systems pharmacology (QSP) modeling based on human and non-human primate (NHP) pharmacokinetic (PK)/ pharmacodynamic (PD) data **3** PRA023 Progress Update (Prometheus presentation) **4** Feagan et al. Journal of Crohn's and Colitis, 2023;17:Supplement_1, i162-i164 **5** Banfield et al. Br J Clin Pharmacol. 2020;86:812–824 **6** Clarke et al. mAbs. 2018;10:4, 664-677 **7** Danese et al. Clin Gastroenterology and Hepatology. 2021;19:11, 2324-32.e6 **8** Preliminary prediction based on no apparent impact of immunogenicity on pharmacokinetics or pharmacodynamics in initial single-ascending dose (SAD) and multiple-ascending dose (MAD) data in healthy volunteers and pre-clinical assays

XmAb942 Phase 1 Study in Healthy Volunteers

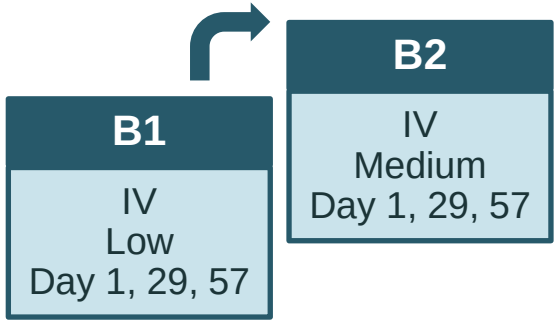
Interim Results

Interim Results From Phase 1 Study

Single Ascending Dose
6 active:2 placebo per cohort



Multiple Ascending Dose
6 active:2 placebo per cohort



SC subcutaneous administration **IV** intravenous administration

Highly efficient study design leverages known safety profile of anti-TL1A class

Study Design Elements

- Double-blind, placebo-controlled, first-in-human
- SAD and MAD cohorts
- SC and IV administration in SAD cohorts

Population

- Healthy volunteers

Endpoints

- Primary: Safety
- Secondary: Pharmacokinetics
- Exploratory: Immunogenicity, PD profile

Baseline Characteristics

	Single Dose						Multiple Dose	
Blinded Interim Data (XmAb942 + Placebo)	**Cohort A1** SC, Low	**Cohort A2** IV, Low	**Cohort A3** SC, Med	**Cohort A4** IV, Med	**Cohort A5** SC, High	**Cohort A6** IV, High	**Cohort B1** IV, Low	**Cohort B2** IV, Med
N	8	8	8	8	8	8	8	8
Age in years (Mean, SD)	39, 9	32.5, 6	39.7, 11	36, 12	36.5, 13	26, 2	31, 10	34.5, 7
Female (Percent)	50%	62.5%	37.5%	37.5%	75%	37.5%	62.5%	50%
BMI in kg/m^2 (Mean, SD)	24.8, 4	26.2, 4	26.0, 4	26.3, 3	25.6, 5	26.8, 4	26.4, 5	23.3, 3

SD standard deviation **BMI** body mass index

Blinded Interim Safety Analysis from Healthy Volunteers In-Line With Expectations for Anti-TL1A Class

	Single Dose						Multiple Dose	
Blinded Interim Data (XmAb942 + Placebo)	**Cohort A1** SC, Low	**Cohort A2** IV, Low	**Cohort A3** SC, Med	**Cohort A4** IV, Med	**Cohort A5** SC, High	**Cohort A6** IV, High	**Cohort B1** IV, Low	**Cohort B2** IV, Med
N	8	8	8	8	8	8	8	8
Participants with TEAE	3	3	5	2	3	4	3	6
Participants with TEAE Probably/Definitely Related*	1	-	-	-	2	-	-	-
Participants with SAE	-	-	-	-	-	-	-	-
Participants discontinued due to TEAE	-	-	-	-	-	-	-	-
Participants with dose decreased							-	-

* **Treatment Emergent Adverse Event (TEAE) Probably/Definitely Related:** Probably related to administration: Headache (Gr 2, Cohort A1); Definitely related to administration: Injection Site Bruise (Gr 1, Cohort A5); Injection Site Reaction (Gr 1, Cohort A5)

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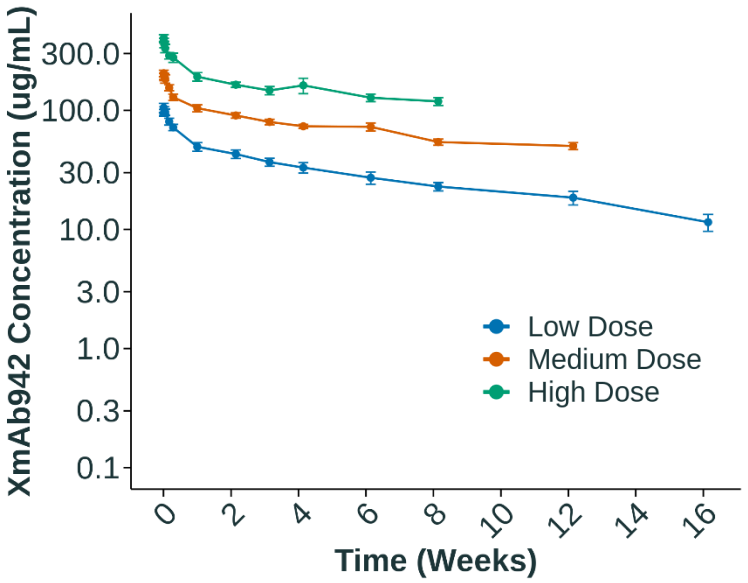
XmAb942 Has Prolonged Serum Exposure in Humans

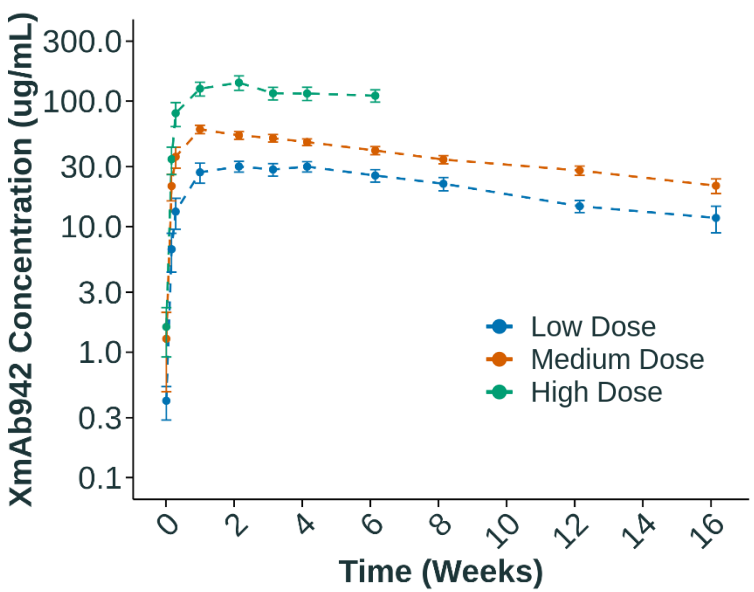
- Estimated terminal half-life is +71 days from pooled analysis of single-dose cohorts
- No apparent impact of ADA on PK profile up to 16 weeks after single dose or 10 weeks after multiple Q4W dosing
- Early multiple dose PK data consistent with single dose

Mean Drug Concentration vs. Nominal Time

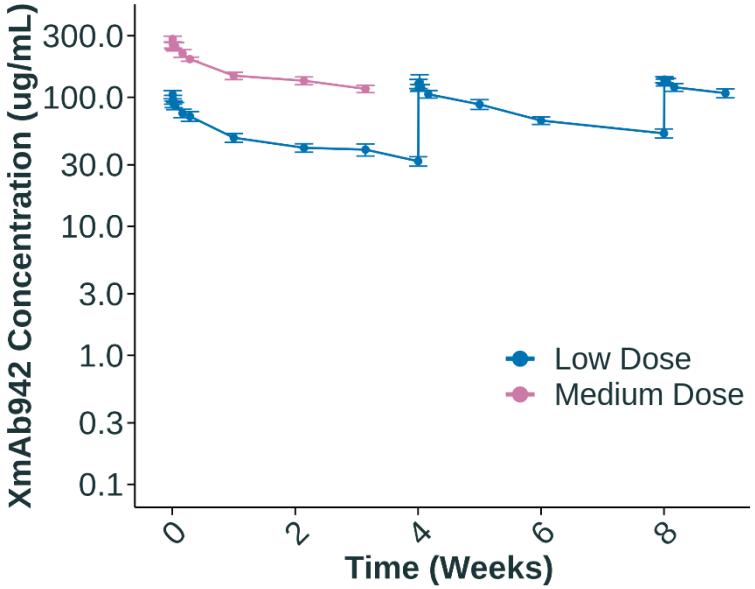
Single dose IV



Single dose SC



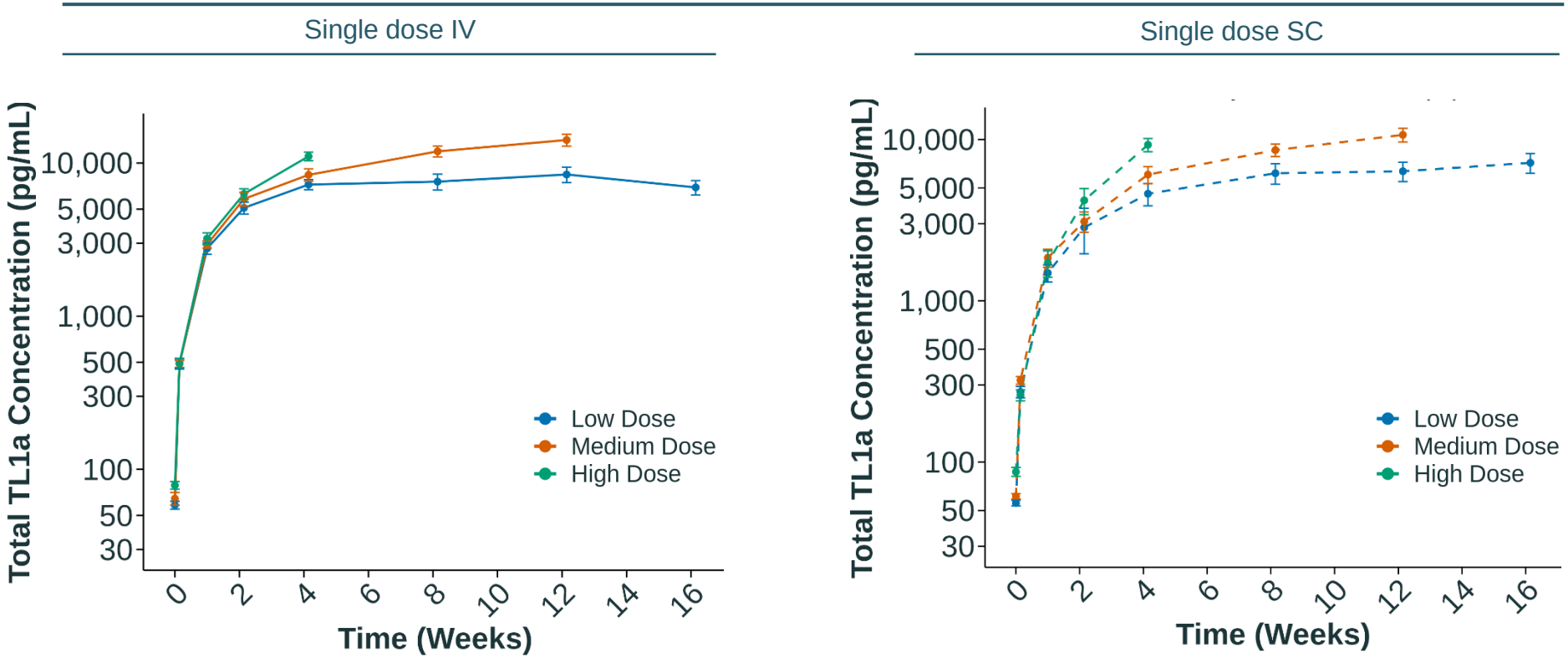
Multiple dose IV



XmAb942 Increases Total TL1A as Expected With Long Durability

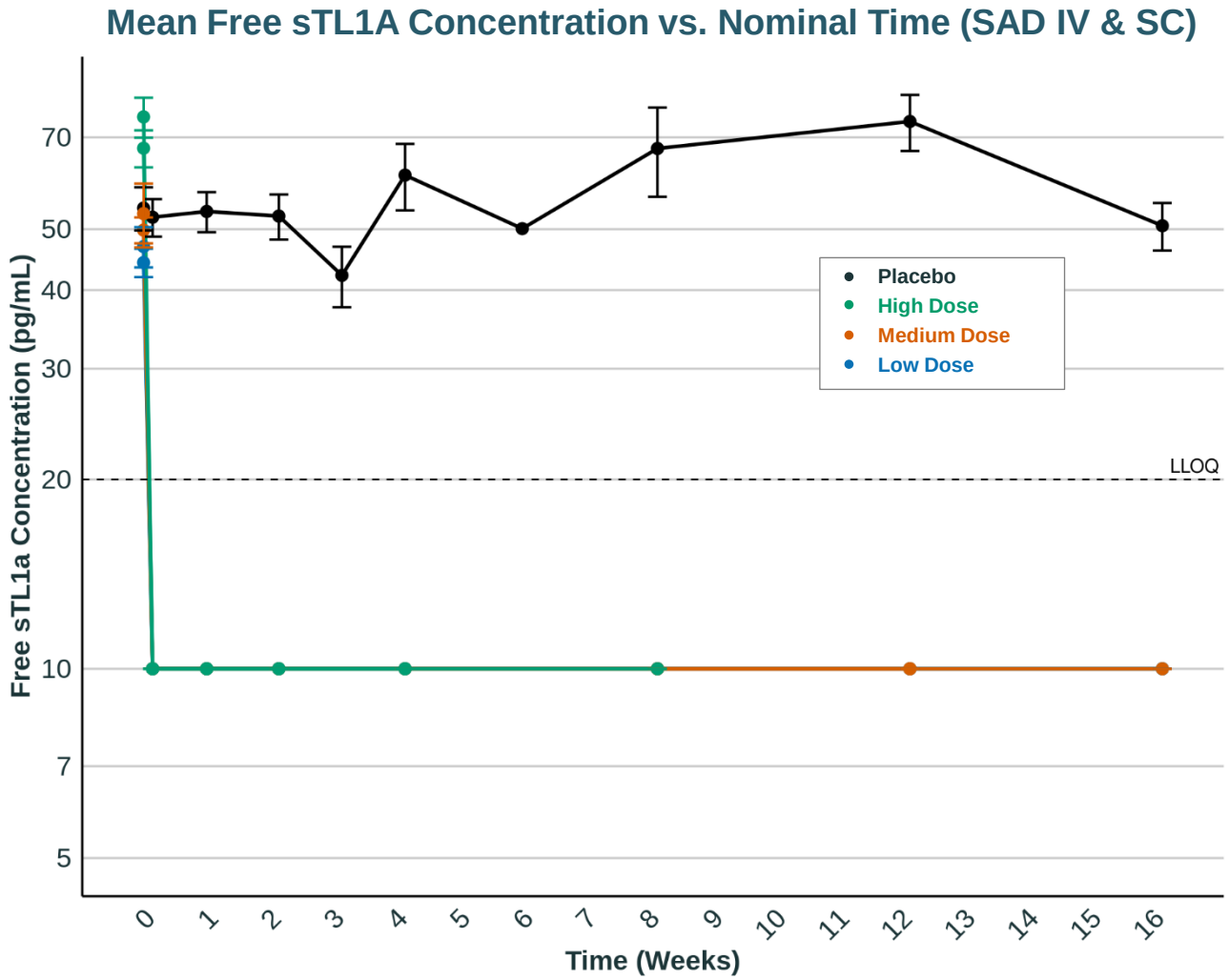
- Dose-dependent and durable increases in total TL1A , at least 16 weeks after a single dose of XmAb942, are consistent with high binding potency and extended serum exposure
- Interim results support lower frequency of dosing compared to first-generation TL1As

Total TL1A Concentration vs. Days Since Treatment Start



Free sTL1A in Serum Drops and Stays Below Quantitative Thresholds in Healthy Participants for At Least 16 Weeks

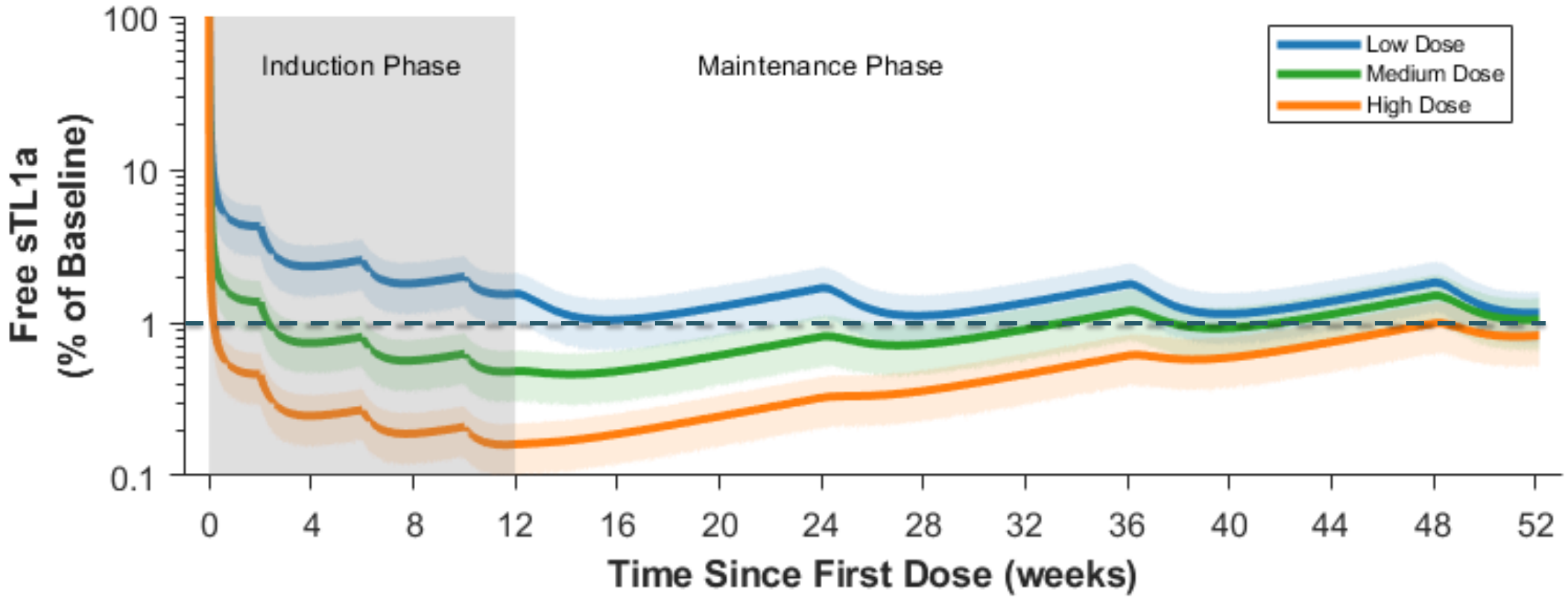
- All IV and SC dose levels had rapid and sustained reduction of free sTL1A below LLOQ for at least 16 weeks from a single dose
- All data points were below LLOQ of 20 pg/mL (plotted at one-half LLOQ value per PD plotting convention)
- Interim results support lower dosing frequency than first-generation TL1As



LLOQ lower limit of quantification (values plotted as LLOQ/2 per convention)

XmAb942 Model Predicts Sustained Effective Suppression of TL1A in the Gut in the Planned Phase 2 Dose Regimen

- Phase 2 program is designed to maximize potential for greater efficacy than other anti-TL1A drugs in the clinic
- Model predicts >90-95% inhibition at the lowest Phase 2 dose, >98-99% inhibition at medium dose and >99% inhibition at all time points for the high dose during the induction phase



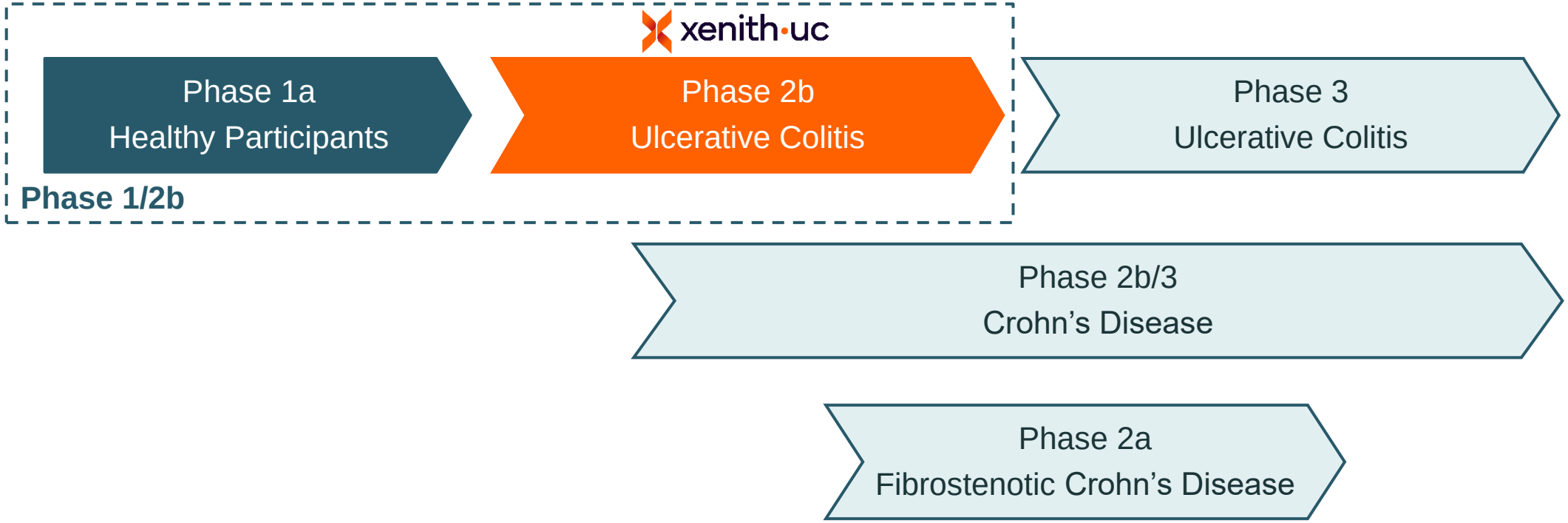
Interim SAD/MAD Data for XmAb942 Support Key Objectives for a Potential Best-in-Class Anti-TL1A Antibody

- Higher consistency of adequate drug exposure for better clinical outcomes in both induction and maintenance
- Single subcutaneous injection maintenance dose
- Maintenance period dosing every 12 weeks
- No apparent impact of immunogenicity on PK or PD[1]

1 Preliminary prediction based on no apparent impact of immunogenicity on pharmacokinetics or pharmacodynamics in initial single-ascending dose (SAD) and multiple-ascending dose (MAD) data in healthy volunteers

XmAb942 Phase 2 Study in Ulcerative Colitis

XmAb942 Clinical Development Plan – XENITH



Expansion Opportunities May Include

Atopic Dermatitis
Primary Biliary Cholangitis
Primary Sclerosing Cholangitis
Rheumatoid Arthritis
Systemic Sclerosis/Interstitial Lung Disease

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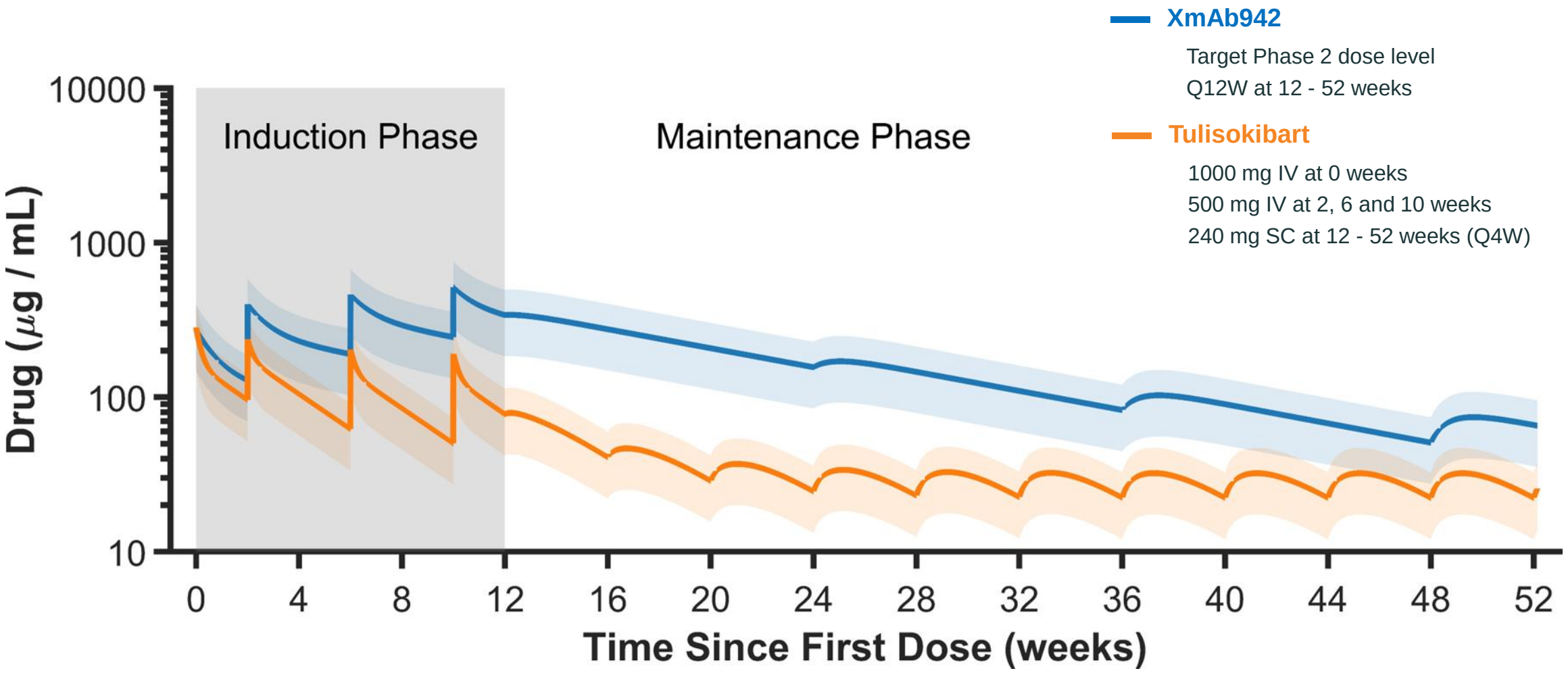
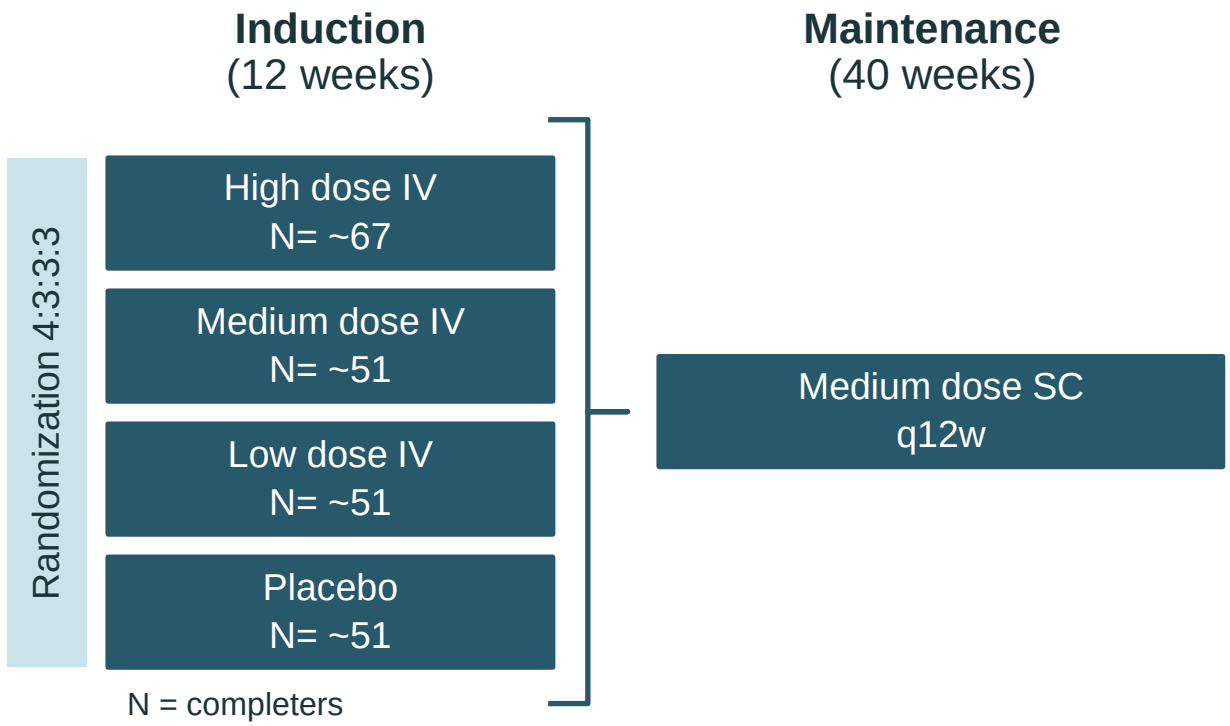
XmAb942 Predicted to Maintain Higher Exposure Than Tulisokibart at Phase 2 Target Dose Levels During Both Induction and Maintenance



XENITH-UC Study: Phase 2b Design



Study Design Elements

- Double-blind, placebo-controlled
- IV administration in induction
- SC administration in maintenance

Population

- Moderate to severely active ulcerative colitis
  - Failed ≥1 conventional or advanced therapy
- N=~220, randomized 4:3:3:3 active:placebo

Primary Endpoint

- Remission at Week 12 per modified Mayo score

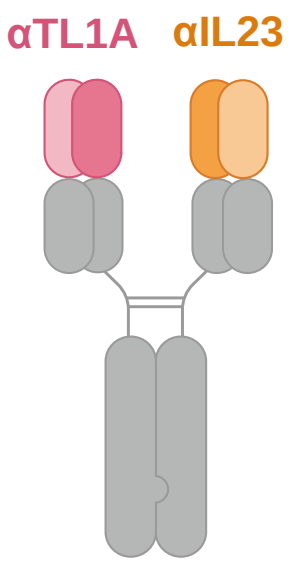
- Drug exposure maximized to potentially achieve greater induction efficacy than observed in competitor trials
- Long half-life supports every 12-week dosing (q12w) during maintenance
- Asymmetric randomization ratio will minimize number of participants receiving induction placebo
- All induction placebo participants will receive active treatment during maintenance

Summary of XENITH Program Strategy

- Well-powered with achievable enrollment goals to support differentiated clinical outcomes
- Thorough Phase 2 dose characterization supports efficient pivotal design
- Rational program gating to XENITH expansion into Crohn's disease and other disease indications beyond IBD

TL1A x IL23p19
Lead Candidate Update

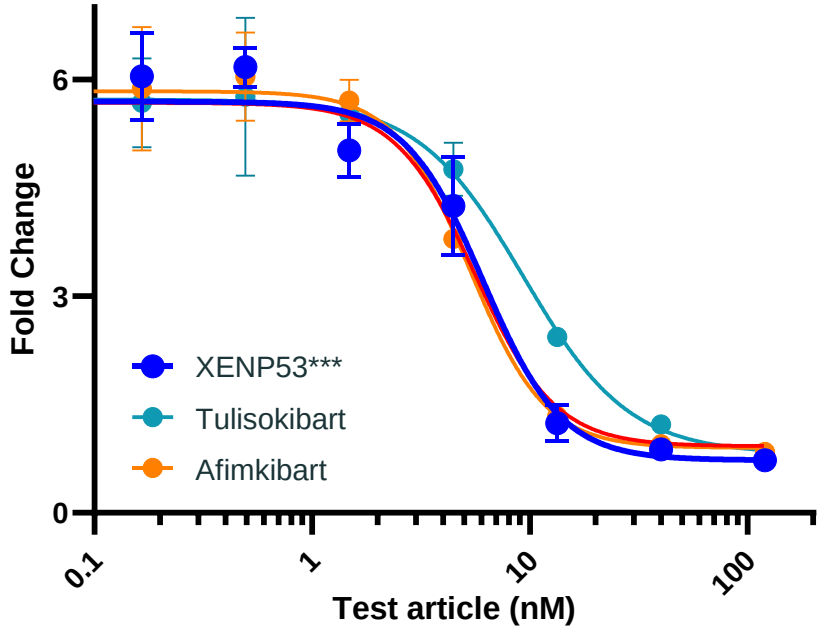
XmAb TL1A x IL23p19 Bispecific Leads Have Competitive Functional Potency for TL1A and IL23 Inhibition



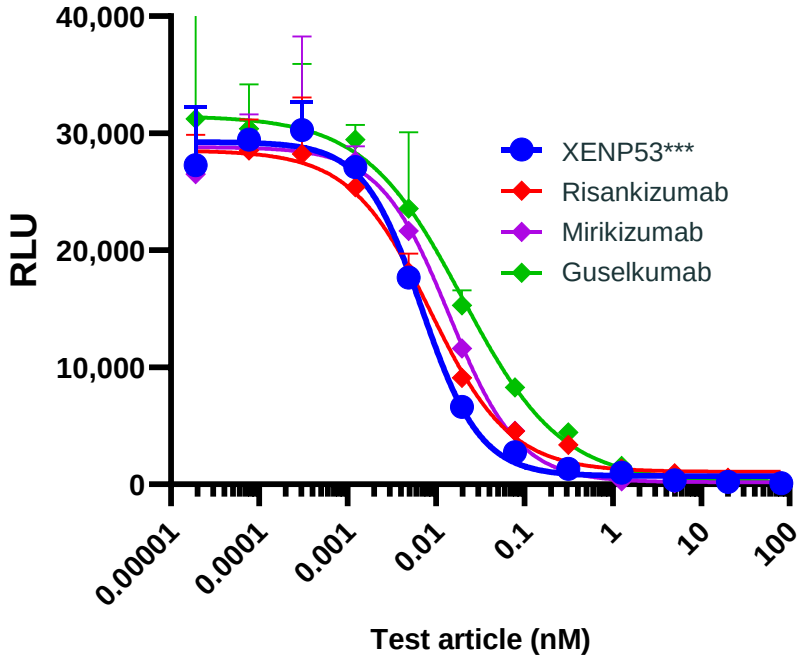
Full length bispecific antibody

Xtend™ + FcKO

DR3-mediated apoptosis



IL23 reporter assay



XENP53*** (shown above) is one of several XmAb TL1A x IL23 candidates currently undergoing lead selection studies & GMP production in parallel to prepare for first-in-human study planned in 2026

GMP Good manufacturing process **FcKO** Fc knock out **RLU** relative light unit

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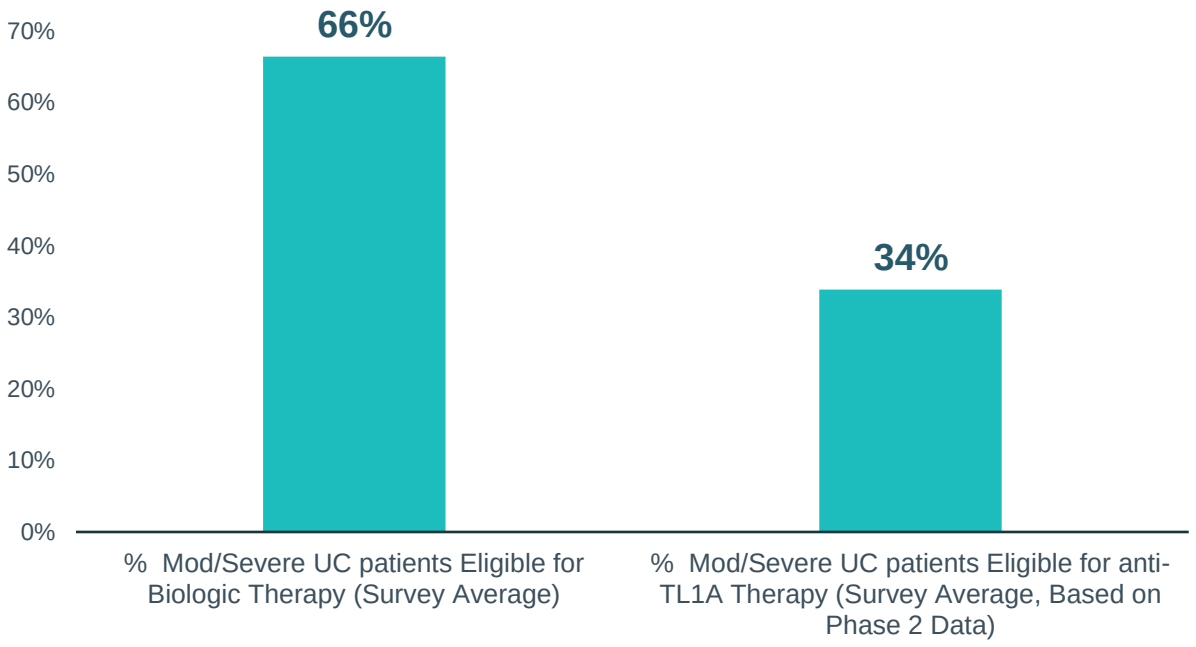
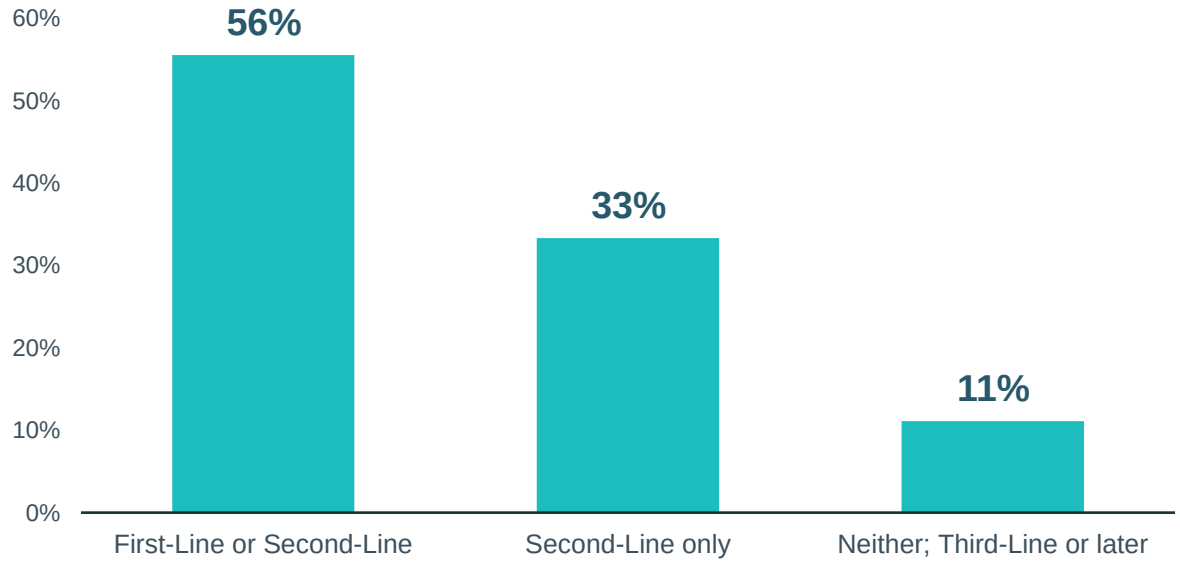
XmAb942 Potential to Address Unmet Needs in Current Care for Patients With IBD

Survey of Gastroenterologists[1] Supports High Expected Utilization of Anti-TL1A Class for IBD Treatment in the United States (>$17bn Market by 2030E[2])

Anti-TL1A class could capture ~1/3 of total market for advanced therapy in IBD



~9 out of 10 gastroenterologists surveyed expect to use anti-TL1A drugs as the first or second line of advanced therapy



1 Xencor-sponsored survey of 27 U.S.-based gastroenterologists covering treatment of >6000 patients with ulcerative colitis annually. **2** GlobalData.

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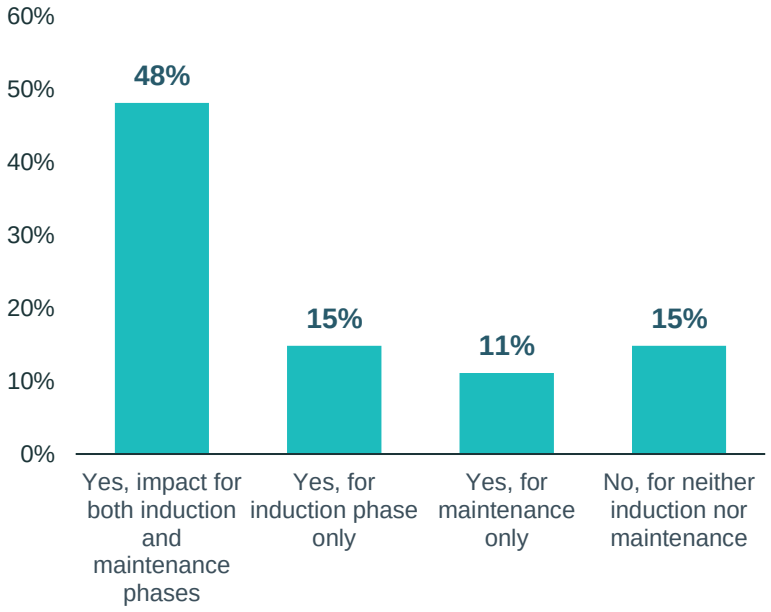
Opportunity for Next-Gen Best-in-Class Anti-TL1A Xmab942 to Differentiate on What Matters Most to Clinicians and Patients[1]

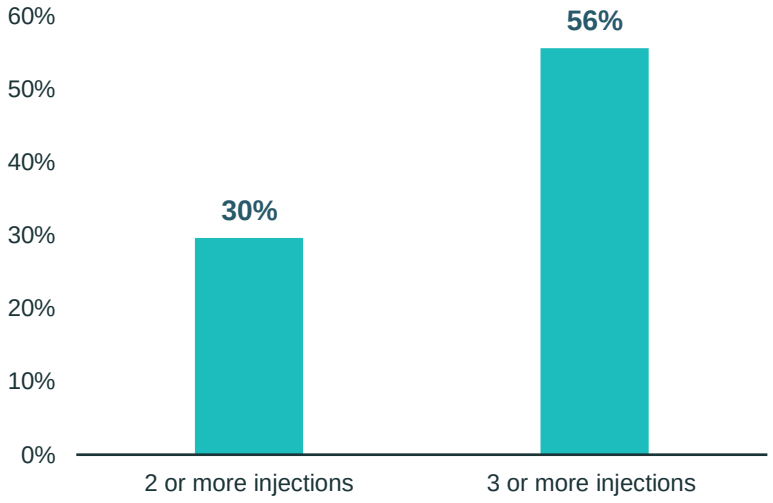
Drug Exposure Matters

>70% of gastroenterologists surveyed recognize that **inadequate drug exposure** negatively impacts clinical outcomes of **induction, maintenance or both** in UC patient.



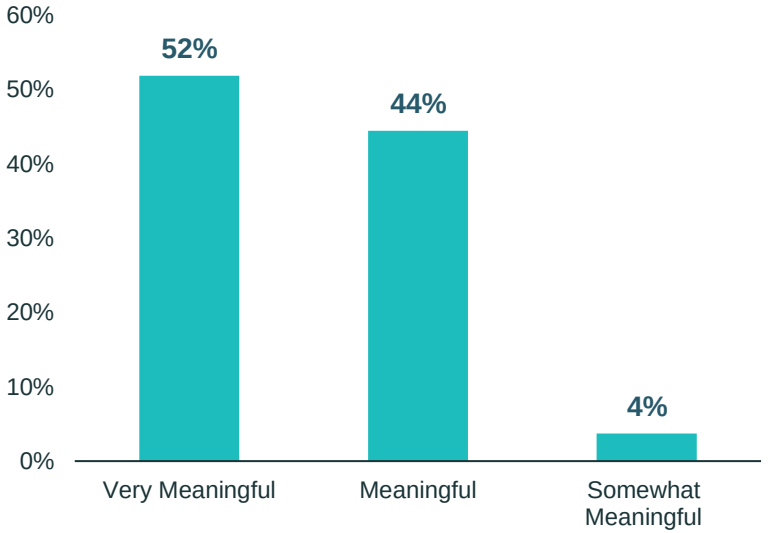
Injection Burden Matters

>80% of gastroenterologists surveyed consider **2-3+ subcutaneous injections** per visit as a **burden**



Dosing Frequency Matters

>90% of gastroenterologists surveyed rate **Q12W dosing** as a meaningful improvement in convenience versus Q2-4W



1 Xencor-sponsored survey of 27 U.S.-based gastroenterologists covering treatment of >6000 patients with ulcerative colitis annually.

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Future of Anti-TL1As in IBD Is Combination With Current SOC Therapy & Dual MoAs With Bispecifics (e.g., TL1A x IL23p19)

CLINICAL RATIONALE

Synergistic potential with established targets (IL23, α4β7), and existing MoAs:
TL1A is a differentiated inflammatory axis

High unmet need in induction and refractory settings:
Anti-TL1A safety profile enables combination flexibility

Early 2030s patent expiry of current standard-of-care biologics:
Provides pathway for affordable combination therapy[1]

COMMERCIAL STRATEGY

Bispecifics leverage existing biologic infrastructure with efficient single molecule manufacturing processes

Dual-agent monospecific combos offer modular clinical development and co-positioning with biosimilar or branded standard-of-care

Flexible opportunities across payer segments and formulary access

PHYSICIANS' SENTIMENT[2]

~90% of gastroenterologists surveyed find TL1A combos promising

"Dual therapy with advanced agents is the future for refractory patients. Especially in the induction phase, combining two different mechanisms of action is very important, as your first shot is your best shot."

"Combination of biologics can significantly increase efficacy without necessarily increasing side effects."

1 Takeda FY2024 20-F: ENTYVIO, will face loss of regulatory exclusivity in the latter half of this decade and certain patents covering various aspects of this product are expected to expire in 2032; AbbVie FY2024 10-K: The United States composition of matter patents covering risankizumab (SKYRIZI) are expected to expire in 2033. **2** Xencor-sponsored survey of 27 U.S.-based gastroenterologists covering treatment of >6000 patients with ulcerative colitis annually.

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Xencor's Roadmap for Innovation in IBD and TL1A Program Expansion

XmAb942
First-in-human study

XmAb TL1A x IL23
Lead candidate development

2024

xenith·uc

XmAb942
Interim SAD & MAD data with expected XENITH-UC study start

XmAb TL1A x IL23
Lead candidate selection

2025

XmAb942
Potential indication expansion

XmAb TL1A x IL23
First-in-human study initiation

2026

XmAb942
XENITH-UC readout

XmAb TL1A x IL23
Phase 2 study start(s)

2027+

Current cash runway supports TL1A program development and expansion

$706.7 million in cash, cash equivalents and marketable debt securities as of December 31, 2024, which does not include $34 million in milestone revenue earned in Q4 2024.

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Xencor Programs Targeting TL1A Have Achieved Key Milestones

XmAb942 interim SAD/MAD results support the thesis of delivering effective drug exposure with convenient maintenance dosing

TL1A and IL23p19 binder potency used for XENP53*** program supports effective bispecific target engagement

XmAb942 and XENP53*** program timelines are on-track with roadmap to efficient and differentiated Phase 2 clinical development

Strong cash position supports the next milestones in clinical development without the requirement for additional capital

Interim Results from First-in-Human Study of XmAb942 & TL1A Pipeline Update

April 29, 2025