Phase 1/2 Study to Assess Safety, Tolerability, and Efficacy of XmAb942 (anti-TL1A) in Healthy Participants and Participants With Ulcerative Colitis

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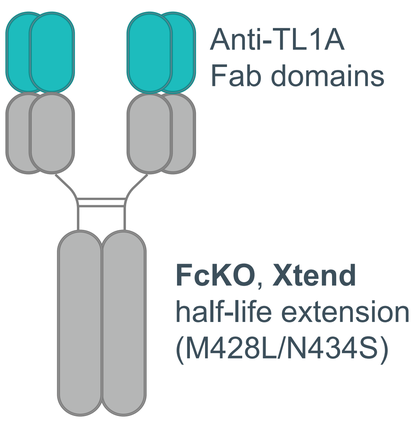
BACKGROUND

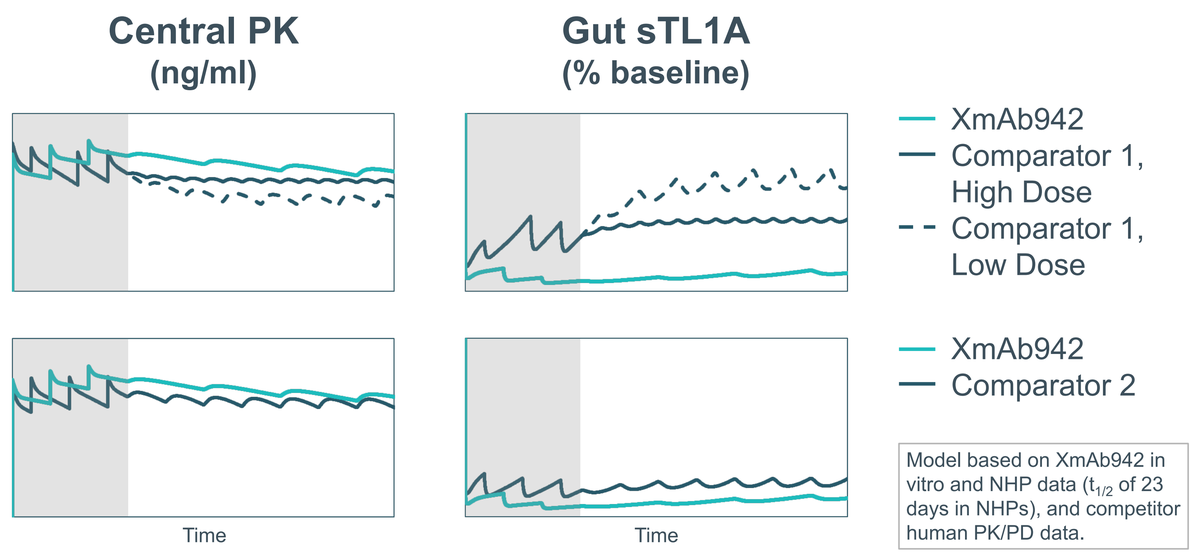
- TL1A mediates pro-inflammatory and pro-fibrotic effects that have been linked to the pathogenesis of IBD, including UC and CD.
- Recent clinical trials have demonstrated early efficacy of antagonist anti-TL1A antibodies for UC and CD.[1]
- XmAb942 (**Figure 1**) is an effector-less (FcKO) anti-TL1A IgG1 antibody that incorporates Xtend™ half-life extension technology. XmAb942 binds trimeric TL1A with high affinity and specificity and is highly potent across multiple preclinical assays.[2]

Figure 1. XmAb942 Characteristics



- ✓ High affinity (K_D ~10 pM), potent and selective TL1A binding
- ✓ Proprietary half-life extension provides a predicted $t_{1/2} \geq 70$ days in humans[3]
- ✓ QSP simulations suggest best-in-class TL1A suppression (**Figure 2**)
- ✓ Modeling supports less frequent dosing (Q8-12W SC; **Figure 2**)
- ✓ High concentration formulation with low viscosity (<10 cp) for SC administration
- ✓ Predicted low immunogenicity

Figure 2. QSP Simulations: XmAb942 vs. Comparators

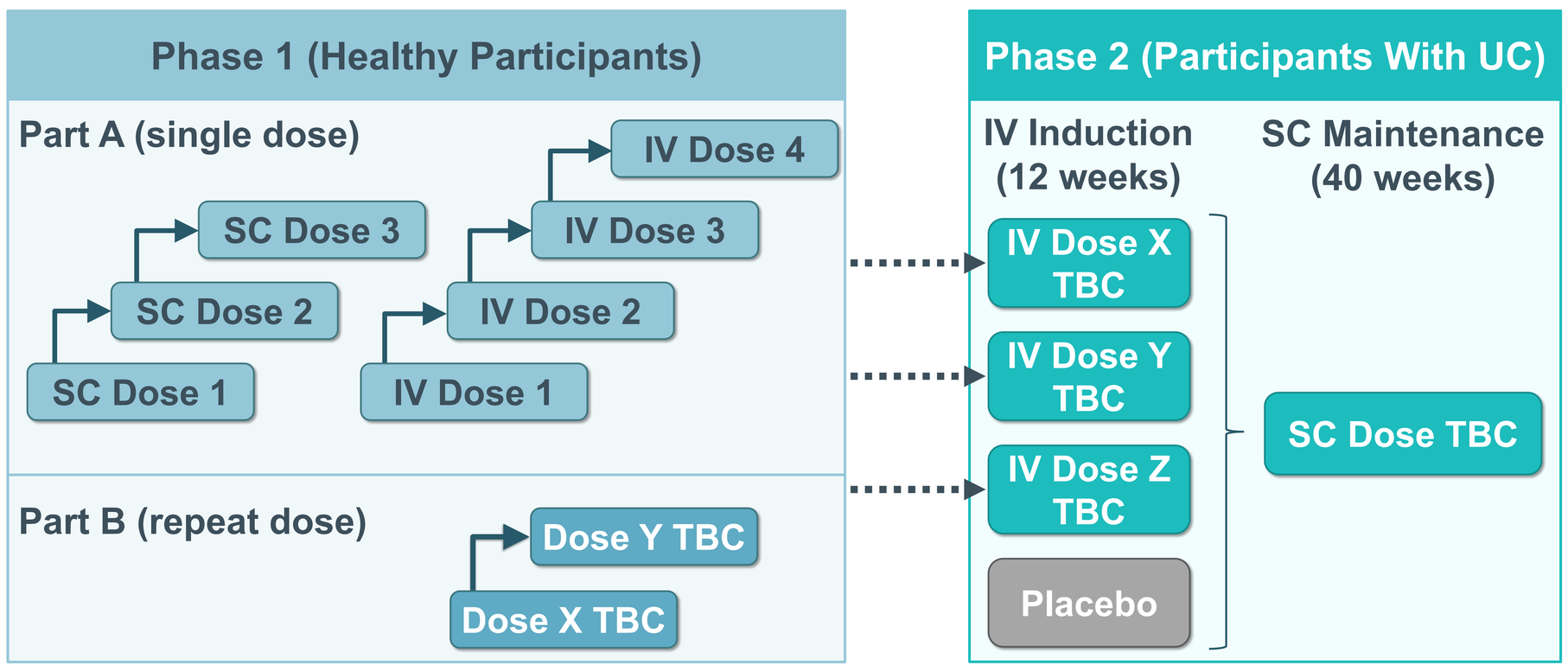


- Here, we present details of the ongoing seamless Phase 1/2 study (NCT06619990) assessing XmAb942 in healthy participants and participants with UC.

METHODS

- This study is a seamless Phase1/2 randomized, double-blind, placebo-controlled trial (**Table 1, Figure 3**).
  - The Phase 1 in healthy participants (Parts A and B) consists of a single ascending-dose study, followed by a repeat-dose study.
  - The Phase 2 (Part C) evaluates participants with UC at dose levels determined by the emerging Phase 1 data.
- Approximately 300 participants will be enrolled.

Figure 3. Study Design



RESULTS

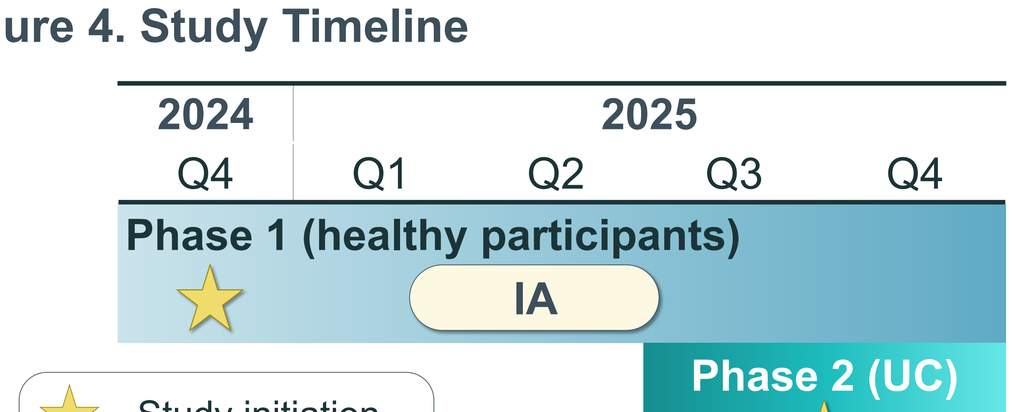
Table 1. Objectives

	Parts A and B *Healthy participants*	Part C *Participants with UC*
Objectives		
Primary	Safety and tolerability	Clinical remission
Secondary	PK	• Safety and tolerability • PK • Endoscopic improvement • Endoscopic remission • Clinical response • Histologic-endoscopic improvement • Histologic-endoscopic remission
Exploratory	• Immunogenicity • PD	• Immunogenicity • PD

CONCLUSIONS

- This seamless Phase 1/2 study is designed to assess XmAb942 as a next-generation, potent, and long-acting anti-TL1A antibody therapeutic with potential best-in-class target neutralization and less frequent dosing.
- This study is currently enrolling in Australia, with Phase 2 to be expanded globally (**Figure 4**).
- Interim Part A data are expected in the first half of 2025.

Figure 4. Study Timeline



Abbreviations: CD Crohn's disease **FcKO** Fc knockout **IBD** inflammatory bowel disease **IgG** immunoglobulin G **IV** intravenous **Q8-12W** every 8-12 weeks **NHP** non-human primate **PD** pharmacodynamic(s) **PK** pharmacokinetic(s) **QSP** quantitative systems pharmacology **$t_{1/2}$** half-life **SC** subcutaneous **TBC** to be confirmed **TL1A** tumor necrosis factor-like ligand 1A **UC** ulcerative colitis.

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References: 1. Solitano V, et al. *Med.* 2024;5(5):386-400. **2.** Ernst JA, et al. *UEG J.* 2025;12: 554 (Poster MP568). **3.** Haraya K, Tachibana T. BioDrugs. 2023;37(1):99-108.

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