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A phase I first-in-human study of CLYM116 in normal healthy volunteers

Submission date 04/11/2025	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/11/2025	**Overall study status** Completed	
Last Edited 05/11/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims
Climb Bio, Inc. is developing the study drug CLYM116 as a potential new treatment for IgA nephropathy (IgAN) and other B-cell-mediated diseases. CLYM116 is a new type of medicine called a monoclonal antibody (or mAb for short). It's designed to target a protein in the body called A proliferation-inducing ligand (APRIL). APRIL helps certain immune cells, called B cells, survive and make a type of antibody called IgA. Human bodies produce different types of antibodies that have different roles in the immune system. In a kidney disease called IgA nephropathy (IgAN), the body makes too much of a harmful form of IgA (called Gd-IgA1), and APRIL levels are also higher than normal. These high levels of proteins are linked to how serious the disease gets.

CLYM116 is made to block APRIL and help the body break it down, to reduce the formation of harmful IgA related to IgAN. It smartly does this by binding tightly to APRIL in the body. Once inside cells, it lets go of APRIL in the acidic (low pH) environment, so APRIL can be destroyed. This may lead to a fast and long-lasting reduction in APRIL activity. CLYM116 also has special features to make it last longer in the body. It has also been engineered to avoid triggering immune system attacks, which can happen with some other antibodies. This makes it potentially safer. The objective of this research is to investigate the safety, tolerability (if any side effects occur), pharmacokinetics (the amount of study drug or any of its breakdown products in your body), pharmacodynamics (how the study drug affects your body), and immunogenicity (whether your body produces immune response to the study drug) of single and multiple subcutaneous (under the skin) doses of a study drug called CLYM116.

Who can participate?
Healthy adult volunteers aged 18 to 60 years (inclusive)

What does the study involve?
Volunteers will be randomly assigned to receive either CLYM116 or a placebo (a dummy treatment), and neither they nor the study team will know which one they are getting. Each person will have a 75% chance of receiving the actual study drug.

Participants will stay at the research unit for a few days after receiving the study drug so that doctors can monitor their health and take blood samples. Some participants will receive just one dose (Single Ascending Dose group), while others will receive two doses spaced two weeks apart (Multiple Ascending Dose group). The amount of CLYM116 given will increase gradually across different groups to help researchers understand how the body responds to different dose levels. Follow-up visits will continue for several weeks, and anyone whose immune system markers haven't returned to normal will be monitored monthly until they do.

What are the possible benefits and risks of participating?
There are no direct benefits to participation in this study. However, it may further research to help develop important scientific knowledge that could contribute to the development of a potential new treatment for IgA nephropathy (IgAN) and other B-cell-mediated diseases.

Risks include:
• Injection Site Reactions- A reaction at the site where the study drug is injected. This may look like redness, swelling, pain or itchiness.
• Immunogenicity- The ability of a foreign substance, such as an antigen, to provoke an immune response in the body. When you receive CLYM116, there is a small chance that your immune system may develop antibodies against the drug. If you develop these specific antibodies, it may affect your body's ability to respond to CLYM116 or other drugs of a similar type.
• Hypogammaglobulinemia- CLYM116 reduces the amount of B cells and therefore antibodies (proteins that help the body to recognize and fight off foreign invaders such as bacteria, viruses and fungi) produced by B cells. If the level of B cells and antibodies remain low after CLYM116 administration, this may predispose the participant to the risk of serious infections, including reactivation of certain viruses in your body, if you have ever been infected.
• Infection Risks- CLYM116 could decrease the activity of the immune system, it could make the participant more susceptible to contract infections. Infections may also be more severe in intensity than usual.
• Allergic reactions
o Rash
o Wheezing and difficulty breathing
o Dizziness and fainting
o Swelling around the mouth, throat, or eyes
o Fast pulse
o Sweating
o Abdominal pain
o Vomiting
o Diarrhea

Where is the study run from?
The study will be run from Q-Pharm Pty Limited (also known as Nucleus Network Brisbane) and is sponsored in Australia by Emerald Clinical Trials Pty Ltd. (local sponsor).

When is the study starting and how long is it expected to run for?
The participant's total participation in the study will last around 8 weeks (not including screening). The first dose is anticipated to take place in December 2025.

Who is funding the study?
Climb Bio Inc., USA

Who is the main contact?
Climb Bio Study Director, clinicaltrials@climbbio.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
CLYM116-NHV-101

Study information

Scientific Title
A phase I, randomized, double-blind, placebo-controlled, single-ascending-dose (SAD) and multiple-ascending-dose (MAD) study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneous injection(s) of CLYM116 in normal healthy volunteers

Study objectives
PRIMARY:
> To evaluate the safety and tolerability of single and multiple subcutaneous (SC) doses of CLYM116 in healthy volunteers
SECONDARY:
> To characterize the pharmacokinetics (PK) of CLYM116 following single and multiple SC doses
> To assess the pharmacodynamic (PD) effects of CLYM116
> To evaluate the immunogenicity of CLYM116

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/10/2025, Alfred Hospital Ethics Committee (55 Commercial Road, Melbourne VIC, 3004, Australia; +61 3 9076 2000; research@alfred.org.au), ref: Project 621/25

Primary study design
Interventional

Study design
Phase I randomized double-blind placebo-controlled single-center study

Study type(s)
Safety

Health condition(s) or problem(s) studied
Healthy volunteers

Interventions
CLYM116 is a humanized monoclonal antibody that selectively binds to a proliferation-inducing ligand (APRIL). This is a phase I, randomized, double-blind, placebo-controlled, single-center study designed to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and immunogenicity of CLYM116 in adult normal healthy volunteers (NHVs). The study will enroll up to 58 subjects across up to eight cohorts.

Normal healthy volunteers must complete the screening evaluations before enrollment. Participants will be admitted to the clinical research unit (CRU) on Day –1 for inpatient evaluations. Participants will have safety assessments as well as bioanalytical analyses performed throughout the trial.

• Randomization and Dosing:
Each cohort in this dose-escalation, placebo-controlled study will include eight eligible participants randomized in a 3:1 ratio to receive either CLYM116 (n = 6) or placebo (n = 2). The study drug dose will be escalated sequentially across cohorts. Randomization will be double-blinded, meaning neither participants nor study staff will know whether CLYM116 or a placebo is being administered. Accordingly, each participant will have a 75% (three-in-four) chance of receiving the active study drug. Planned dose levels range from 40 mg to 160 mg.

• Single Ascending Dose (SAD) Group:
Cohorts 1 to 3 received single doses subcutaneously of 40 mg, 80 mg, and 160 mg, respectively. Participants will remain in the CRU for inpatient assessments on Days 1–4, and return for outpatient visits on Days 8, 15, 22, 29, and 57.

• Multiple Ascending Dose (MAD) Group:
Cohort 4 received (subcutaneously) 80 mg every two weeks for a total of two doses, while Cohort 5 received 160 mg on the same biweekly schedule, also for two doses. Participants will be admitted on Day 1 and remain in the CRU for Days 1–4, return for an outpatient visit on Day 8, and be readmitted on Days 14–18. They will then return for outpatient visits on Days 22, 29, 36, 43, and 71.

• Safety Follow-Up:
Additional monthly follow-up visits will be conducted for participants whose IgA, IgM, or IgG levels have not recovered to at least 50% of baseline or above the lower limit of normal by the Week 8/end-of-study visit.
Cohort N CLYM116 Dose Dosing Regimen
1 8 25 mg 1 dose
2 8 80 mg 1 dose
3 8 160 mg 1 dose
4 8 Higher dose 1 TBD 1 dose
5 8 Higher dose 2 TBD 1 dose

6 8 160 mg SC once 2 doses every 2 weeks
7 8 Higher dose 3 TBD 2 doses once every 2 weeks
8 8 Higher dose 4 TBD 2 doses every 2 weeks

Intervention Type
Biological/Vaccine

Phase
Phase I

Drug/device/biological/vaccine name(s)
CLYM116

Primary outcome(s)
1. Incidence of treatment-emergent adverse events measured using data collected from electronic Case Report Forms (eCRF) from Screening through to Day 57, Day 71, or final follow-up visit
2. Number of injection site reactions measured using data collected from electronic Case Report Forms (eCRF) from Baseline through to Day 4 and Day 15 to Day 18

Key secondary outcome(s)
1. Maximum Observed Plasma Concentration (Cmax) will be assessed by measuring the concentration of study compounds in blood samples collected from Baseline through to Day 57 (excluding Day 14), Day 71, or the final follow-up visit
2. Time to Maximum Observed Concentration (Tmax) will be assessed by determining the time at which the highest concentration of study compounds occurs in blood samples collected from Baseline through to Day 57 (excluding Day 14), Day 71, or the final follow-up visit
3. Area Under the Curve (AUC) will be assessed by calculating the total exposure to the study compounds over time using blood samples collected from Baseline through to Day 57 (excluding Day 14), Day 71, or the final follow-up visit
4. Half-Life (T1/2) will be assessed by estimating the time required for the concentration of study compounds in the blood to decrease by half, based on samples collected from Baseline through to Day 57 (excluding Day 14), Day 71, or the final follow-up visit
5. Measurement of Immunoglobulins and changes over time measured using laboratory testing from Baseline through to Day 57 (except Day 14), Day 71, or final follow-up visit
6. Level of APRIL Measurement of APRIL in pg/mL and changes over time measured using laboratory testing on Day -1, Baseline, Day 1, Day 4, Day 8, Day 14, Day 15, Day 17, Day 18, Day 22, Day 29, Day 57, final follow-up visit
7. Immunogenicity Measurement of CLYM116 antidrug antibodies (ADA) measured using laboratory testing at Baseline, Day 15, Day 29, Day 43, Day 57, Day 71, final follow-up visit

Completion date
27/07/2026

Eligibility

Key inclusion criteria
1. Healthy adult males and females aged 18-60 years, inclusive
2. Body mass index (BMI) between 18 and 32 kg/m² and weight between 45 and 110 kg
3. Clinically normal medical history, physical exam, ECG, and laboratory results (or abnormalities deemed not clinically significant)

4. Willing and able to comply with study procedures and provide informed consent
5. Women of childbearing potential must use highly effective contraception and have negative pregnancy tests
6. Men must use contraception and refrain from sperm donation for 4 months post-dose
7. Completion of COVID-19 vaccination according to local guidelines, as well as influenza vaccination (within 12 months)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Key exclusion criteria
1. Prior treatment with investigational drugs within 30 days or 5 half-lives
2. Previous or current hypogammaglobulinemia
3. Current presence of allergic reactions considered clinically significant
4. Positive tests for HIV, hepatitis B/C, syphilis, or tuberculosis
5. Tobacco use (>2 cigarettes/day), alcohol abuse, or drug abuse
6. Recent live vaccination (within 21 days) or any non-live vaccine (within 14 days)

Date of first enrolment
02/12/2025

Date of final enrolment
16/02/2026

Locations

Countries of recruitment
Australia

Study participating centre
Q-Pharm Pty Ltd
Level 5, 300C Herston Rd, Herston

Brisbane, Queensland
Australia
4006

Sponsor information

Organisation
Climb Bio, Inc.

Funder(s)

Funder type
Industry

Funder Name
Climb Bio, Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study may be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		28/10/2025	05/11/2025	No	No