# CLYM116, A NOVEL 'SWEEPER' ANTI-APRIL mAb IN DEVELOPMENT FOR IgAN: PHASE 1 SAFETY, TOLERABILITY, PK, AND PD RESULTS IN HEALTHY VOLUNTEERS


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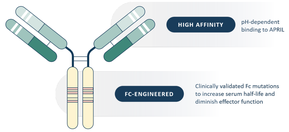
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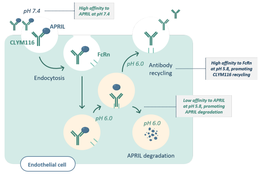

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## INTRODUCTION

### CLYM116 (MIL116) – ANTI-APRIL WITH 'SWEEPER' MECHANISM

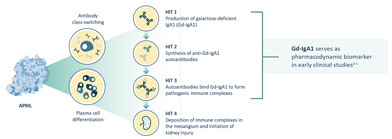
- **CLYM116** is an investigational, **novel 'sweeper' anti-APRIL mAb** engineered with **pH-dependent antigen binding** to enhance APRIL degradation and antibody recycling, and with **Fc mutations to extend half-life** and reduce effector function.
- **pH-dependent binding to APRIL** provides potential for enhanced APRIL elimination through both:
  - **Potent blocking of APRIL binding to its receptors** *and*
  - **Promotion of APRIL degradation** in the lysosome
- **Efficient antibody recycling** reduces clearance of CLYM116, resulting in potentially longer half-life.




### APRIL RATIONALE IN IgA NEPHROPATHY

- **APRIL is a key driver of IgAN pathogenesis, promoting production of Gd-IgA1** that forms immune complexes with anti-glycan antibodies and deposits in the glomeruli, triggering inflammation and progressive loss of kidney function.[1]

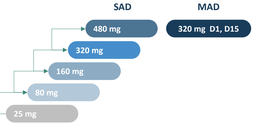



*APRIL = a proliferation-inducing ligand*
*Adapted from Mathur J Clin Med 2023.[1] Mathur Kl Reports 2022,[2] Davies Clin Transl Sci 2024,[3] Kooienga Kid Int'l 2025*

## STUDY OVERVIEW

**ASCENDING DOSE COHORTS, N = 46**

Subcutaneous administration
Planned 8 participants per cohort (6 CLYM116: 2 placebo)




- Randomized, placebo-controlled ascending-dose study in healthy volunteers
- Conducted at one site in Australia
- NCT07248865

**STUDY OBJECTIVES**

- Safety and tolerability
- Pharmacokinetics
- Pharmacodynamics, including the effects on serum APRIL and immunoglobulins (Gd-IgA1, IgA, IgM, IgG, IgE)

- A parallel study in China is being conducted by Beijing Mabworks Biotech (ASN 2026 poster FR-PO0838, NCT07375758)

## RESULTS

### PARTICIPANT DEMOGRAPHICS

| | 25 mg | 80 mg | 160 mg | 320 mg | 480 mg | 320 mg D1, D15 | Pooled CLYM116 | Pooled Placebo |
|---|---|---|---|---|---|---|---|---|
| **N** | 6 | 6 | 5 | 6 | 6 | 6 | **35** | **11** |
| **Age**, years | 30.3 (7.4) | 33.2 (14.3) | 34.6 (10.1) | 30.3 (4.6) | 43.7 (14.6) | 41.2 (15.8) | **35.6 (12.2)** | **35.6 (11.8)** |
| **Female** (n, %) | 1 (17%) | 5 (83%) | 4 (80%) | 3 (50%) | 3 (50%) | 4 (67%) | **20 (57%)** | **8 (73%)** |
| **Race** (n, %) | | | | | | | | |
| White | 2 (33%) | 3 (50%) | 4 (80%) | 5 (83%) | 4 (67%) | 5 (83%) | **23 (66%)** | **5 (45%)** |
| Asian | 4 (67%) | 1 (17%) | 1 (20%) | 0 | 2 (33%) | 1 (17%) | **9 (26%)** | **5 (45%)** |
| Other | 0 | 2 (33%) | 0 | 1 (17%) | 0 | 0 | **3 (9%)** | **1 (9%)** |
| **Body Weight**, kg | 76.0 (17.0) | 60.2 (10.6) | 67.9 (8.0) | 75.1 (11.4) | 70.7 (10.4) | 78.0 (16.9) | **71.4 (13.5)** | **62.6 (11.2)** |
| **BMI**, kg/m$^2$ | 25.0 (3.3) | 21.6 (2.1) | 25.4 (2.5) | 25.4 (3.7) | 24.3 (2.3) | 27.3 (4.2) | **24.8 (3.4)** | **22.8 (2.7)** |
| **IgA**, g/L | 2.95 (1.2) | 1.87 (0.6) | 2.04 (1.0) | 1.35 (0.4) | 2.37 (0.5) | 1.73 (0.3) | **2.05 (0.9)** | **2.36 (0.7)** |
| **Gd-IgA1**, µg/mL | 4.435 (4.0) | 4.141 (2.5) | 3.841 (1.4) | 2.176 (0.8) | 3.539 (1.5) | 2.119 (0.7) | **3.362 (2.2)** | **5.410 (4.2)** |

Mean (SD) used for age, body weight, body mass index (BMI), serum IgA and Gd-IgA1; all participants had to have normal kidney function

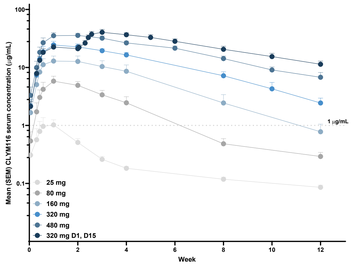
- Cohorts were generally well balanced, with participant characteristics consistent with an HV population

### SAFETY

| | 25 mg | 80 mg | 160 mg | 320 mg | 480 mg | 320 mg D1, D15 | Pooled CLYM116 | Pooled Placebo |
|---|---|---|---|---|---|---|---|---|
| **N** | 6 | 6 | 5 | 6 | 6 | 6 | 35 | 11 |
| **TEAE**, n (%) | 4 (67%) | 5 (83%) | 3 (60%) | 4 (67%) | 5 (83%) | 5 (83%) | 26 (74%) | 5 (45%) |
| **TRAE**, n (%) | 0 | 1 (17%) | 3 (60%) | 1 (17%) | 3 (50%) | 0 | 8 (23%) | 2 (18%) |
| **≥Gr3 TEAE**, n | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| **Discontinued due to AE**, n | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

- No dose-limiting AEs, SAEs, Grade ≥3 AEs, or discontinuations
- All AEs mild to moderate (Grades 1-2), transient, and self-resolving
- TEAEs occurring in >2 participants in the CLYM116 cohorts included upper respiratory tract infection (17%), headache (14%), and injection-site reactions (14%)
- Injection-site reactions observed in 5 participants, all Grade 1 and resolved without intervention
- No hypogammaglobulinemia (IgG < 3 g/L)

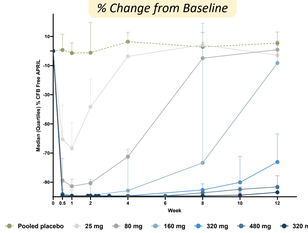
### PHARMACOKINETICS



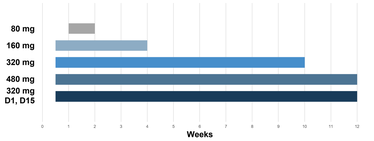

- Dose-dependent exposure
- Terminal half-life of 32.9 days for 320 mg D1, D15, compared to 9.3 days for sibeprenlimab[2,3]
- Linear clearance observed at concentrations above 1 µg/mL
- No TMDD observed during the 12-week follow-up at doses ≥ 160 mg, likely reflective of APRIL degradation due to the sweeper mechanism
- **Supportive of Q12W dosing schedule**

### PHARMACODYNAMICS: FREE APRIL

**Free APRIL**
*% Change from Baseline*



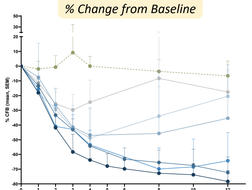

***Duration of ≥90% free APRIL suppression***




- >99% suppression by Day 4 with doses ≥ 160 mg
- ≥90% suppression ongoing through Week 12 in the 480 mg and 320 mg D1, D15 cohorts

### PHARMACODYNAMICS: Gd-IgA1

**Gd-IgA1**
*% Change from Baseline*

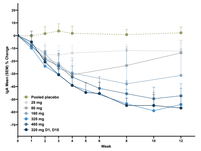



**Substantial Gd-IgA1 reduction observed:**

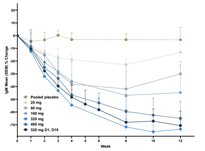
- 480 mg: 72% at 12 weeks
- 320 mg D1, D15: 78% at 12 weeks

### PHARMACODYNAMICS: OTHER IMMUNOGLOBULINS

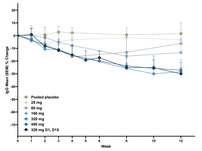
**IgA**
*% Change from Baseline*




**IgM**
*% Change from Baseline*




**IgG**
*% Change from Baseline*



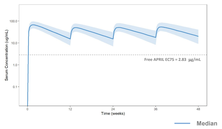

- Robust IgA and IgM reduction observed
- IgG reduction did not exceed 30%, even at the highest dose evaluated; lowest IgG value reported across all cohorts was 5.8 g/L
- No meaningful changes in IgE observed

## CONCLUSIONS

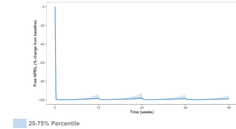
1. **Favorable safety and tolerability**
   - No dose-limiting AEs, SAEs, Grade ≥3 AEs, or discontinuations; no hypogammaglobulinemia
2. **Long terminal half-life (~33 days)**
   - CLYM116 exhibited a ~33-day half-life, >3.5x longer than sibeprenlimab, with linear clearance throughout the effective dose range
3. **Profound and durable PD activity through 12 weeks**
   - ≥90% free APRIL suppression
   - >70% Gd-IgA1 reduction
4. **PK/PD modeling supports Q12W dosing in IgAN**
   - PK/PD modeling shows potential for sustained APRIL suppression, supporting a Q12W dosing regimen in IgAN patients
   - NAVIGATE-2, a Phase 2 study in IgAN, is enrolling

### PK/PD MODELING SUPPORTS Q12W DOSING

**Simulated serum concentration over time**
*800 mg LD on Day 1, then 400 mg Q12W starting Week 12*




**Simulated free APRIL over time**
*800 mg LD on Day 1, then 400 mg Q12W starting Week 12*




- Modeled 800 mg LD, followed by 400 mg Q12W regimen, predicted to maintain exposure above APRIL EC75 throughout the dosing interval and produce near-complete APRIL suppression out to 48 weeks
- Recommended Phase 3 dose will be selected based on near-complete APRIL suppression over the dosing interval
- NAVIGATE-2 Phase 2 study in IgAN ongoing to assess Q12W dosing regimen in patients
- *For more information on NAVIGATE-2, please scan the QR code*

NavIgAte-2

**Abbreviations:** AE=adverse event; D=day; EC75=concentration giving 75% of maximal effect; Fc=fragment crystallizable; Gd-IgA1=galactose-deficient IgA1; Gr=grade; HV=healthy volunteer; Ig=immunoglobulin; LD=loading dose; mAb=monoclonal antibody; MAD=multiple ascending dose; PD=pharmacodynamics; PK=pharmacokinetics; Q12W=every 12 weeks; SAD=single ascending dose; SAE=serious adverse event; SD=standard deviation; TEAE=treatment-emergent adverse event; TMDD=target-mediated drug disposition; TRAE=treatment-related adverse event


**REFERENCES** 1. Wyatt & Julian N Engl J Med 2013; 2. Zhang Clin Pharmacol Drug Dev 2023; 3. Sibeprenlimab US Prescribing Information


**ADDITIONAL INFORMATION**

Scan the QR code to download the poster


**CONTACT**
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