Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of MIL116, a Novel 'Sweeper' Anti-APRIL Monoclonal Antibody in Healthy Volunteers: Preliminary Phase 1 Results

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INTRODUCTION

- **Immunoglobulin A Nephropathy (IgAN) is a progressive immune-mediated kidney disease** with persistent risk of kidney failure despite optimized supportive care.
- **A Proliferation-Inducing Ligand (APRIL),** as a **key regulator of pathogenic Gd-IgA1 production** and **plasma cell survival,** is a central driver of IgAN pathogenesis.
- **MIL116 (also known as CLYM116)** is a **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.

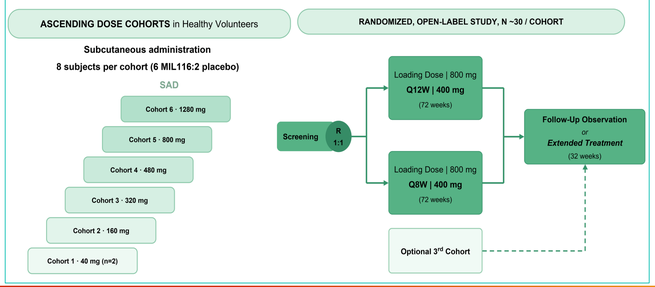
AIMS

This Phase 1/2 trial (NCT07375758) in healthy adult volunteers and adult patients with IgAN comprises a double-blind, placebo-controlled, single-ascending-dose (SAD) Phase 1 part designed to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of MIL116 in healthy adult volunteers, followed by a randomized, parallel-group, open-label Phase 2 part designed to evaluate the efficacy, safety, tolerability, PK, and PD of at least two MIL116 dosing regimens in adult patients with IgAN.

METHODS

- The Phase 1 part of the study enrolled 42 healthy volunteers in 6 cohorts. The MIL116 dose levels are 40 mg, 160 mg, 320 mg, 480 mg, 800 mg, and 1280 mg. As follow-up is ongoing, participants and study personnel remain blinded to treatment assignment.
- The Phase 2 part of the study is enrolling 60 to 90 adults with IgAN; randomized 1:1 to one of two subcutaneous dosing regimens for 72 weeks. An optional cohort may be added based on model-informed drug development (MIDD) analyses. All participants will be followed through Week 104 after first dose.

Phase 1 in Healthy Volunteers | **NAVIGATE-2: Phase 2 in IgAN Patients**



RESULTS: PHASE 1 PHARMACOKINETICS (PK), PHARMACODYNAMICS (PD), AND SAFETY IN HEALTHY VOLUNTEERS

- Data cutoff Oct 13, 2026, 42 participants received study drug (32 MIL116, 10 placebo). Follow-up through EOS visit continues. Safety Population = all participants exposed to study drug. For the 1280 mg cohort only baseline characteristics and safety/tolerability are provided, as the cohort had not yet reached Week 12 as of the data cutoff.

✓ Baseline Characteristics

	40 mg	160 mg	320 mg	480 mg	800 mg	1280 mg	Pooled MIL116	Pooled Placebo
N	2	6	6	6	6	6	**32**	**10**
Age, years	31.0 (2.8)	34.8 (8.4)	35.7 (6.7)	33.8 (8.6)	36.5 (2.2)	31.5 (8.3)	**34.3 (6.8)**	**38.5 (6.1)**
Female (n, %)	0	3 (50%)	3 (50%)	1 (17%)	2 (33%)	4 (67%)	**13 (41%)**	**8 (80%)**
Body Weight, kg	66.0 (13.1)	66.5 (12.2)	72.5 (7.9)	69.0 (10.6)	67.3 (4.2)	59.2 (6.7)	**66.9 (9.3)**	**62.8 (9.3)**
BMI, kg/m^2	22.7 (3.5)	23.4 (2.4)	24.5 (1.7)	24.2 (2.3)	25.4 (2.5)	22.3 (2.1)	**23.9 (2.3)**	**24.6 (2.3)**
IgA, g/L	2.55 (0.29)	2.80 (1.07)	3.15 (0.31)	2.31 (0.34)	2.18 (0.66)	2.60 (0.46)	**2.60 (0.67)**	**2.29 (0.89)**
Gd-IgA1, µg/mL	2.78 (0.01)	4.23 (2.39)	5.88 (1.18)	4.69 (1.67)	5.02 (1.90)	4.82 (1.76)	**4.79 (1.80)**	**4.04 (2.66)**

Note: 41/42 participants were of Han ethnicity. Mean (SD) used for age, body weight, body mass index (BMI), serum IgA and Gd-IgA1.

✓ Safety

- As of the Oct 13, 2026 data cutoff*, MIL116 was generally well tolerated across all evaluated single subcutaneous (SC) dose levels (40 mg, 160 mg, 320 mg, 480 mg, 800 mg, and 1280 mg). No dose-limiting adverse events (AEs), deaths, treatment-related serious adverse events (SAEs), or AE-related discontinuations were reported. No hypogammaglobulinemia (HGG, IgG<3 g/L) or injection site reactions (ISRs) were observed.

	40 mg	160 mg	320 mg	480 mg	800 mg	1280 mg	Pooled MIL116	Pooled Placebo
N	2	6	6	6	6	6	**32**	**10**
TEAE, n (%)	1 (50%)	4 (67%)	3 (50%)	3 (50%)	4 (67%)	2 (33%)	**17 (53%)**	**5 (50%)**
TRAE, n (%)	0	3 (50%)	1 (17%)	1 (17%)	2 (33%)	0	**7 (22%)**	**4 (40%)**
≥Gr3 TRAE, n	0	0	0	0	0	0	**0**	**0**
Discontinued due to AE, n	0	0	0	0	0	0	**0**	**0**

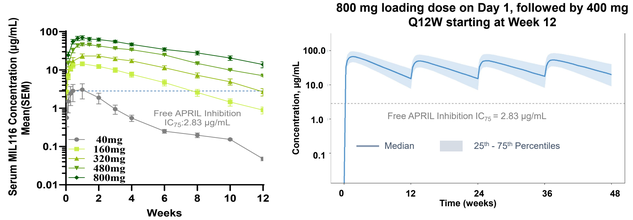
*Participants in the 40mg-800mg cohorts had been followed through Week 12, and the 6 patients in 1280mg had been followed through Week 4

- 1/42 participants had a Gr3 TEAE: lumbar vertebral fracture due to a traffic accident; not related to study drug; resolved.
- TEAEs occurring in >2 participants in each cohort included creatine kinase increased (16%), alanine aminotransferase increased (13%), upper respiratory tract infection (13%), and White blood cells urine positive (9%).
- As follow-up is ongoing, data were analyzed by an unblinded data analysis team while the study remained blinded.

✓ PK

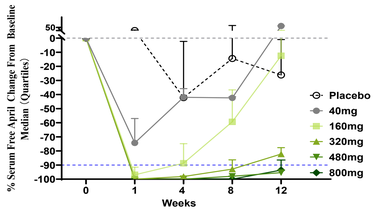
- The median half-life for the 800 mg dose level is 32.8 days. Phase 1 PK data were used to develop the popPK model and simulate the regimens for Phase 2 dose selection.

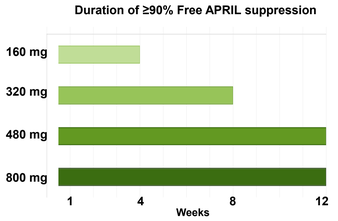
Simulated Serum Concentration Over Time
800 mg loading dose on Day 1, followed by 400 mg Q12W starting at Week 12



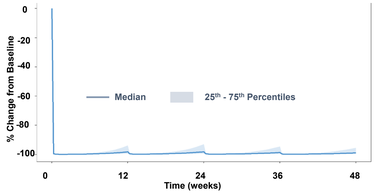
✓ Free APRIL Inhibition

- MIL116 elicited robust, durable free APRIL suppression: single 480 mg and 800 mg doses maintained >90% suppression through Week 12. PopPK-PD simulations based on Phase 1 data indicate Q12W dosing sustains profound (>90%) free APRIL suppression over repeated cycles.





Simulated Free APRIL Over Time
800 mg loading dose on Day 1, followed by 400 mg Q12W starting at Week 12



✓ PopPK Simulation for Phase 2 Cohorts

- PopPK-simulated Phase 2 exposures are comparable to observed Phase 1 exposures: the 800 mg loading dose approximates Phase 1 800 mg, and 400 mg at steady state approximates Phase 1 480 mg, supporting the Q12W dosing interval for Phase 2.

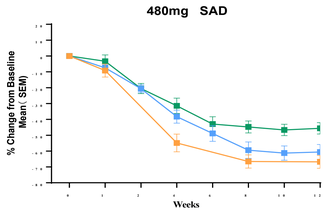
Phase 2 regimen	Parameter	Phase 2 — Arm 1: Q12W popPK-estimated, median [5%, 95%] C_{trough} at Week 12		Phase 1 dose	Phase 1 observed, median [min, max] C_{trough} at Week 12
800 mg Loading dose	C_{max} (µg/mL)	72.60 [36.28, 118.21]	⇔	**800 mg**	78.14 [41.08, 83.40]
	C_{trough}(µg/mL)	12.22 [0.99, 41.76]	⇔		14.22 [4.30, 22.12]
400 mg Steady state	C_{max} (µg/mL)	45.68 [19.49, 99.15]	⇔	**480 mg**	44.97 [35.28, 56.60]
	C_{trough}(µg/mL)	11.26 [0.90, 46.94]	⇔		7.01 [6.19, 8.44]

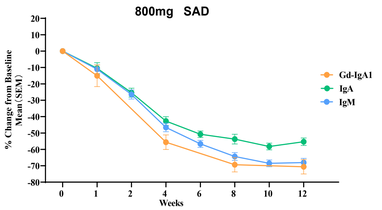
800 mg loading dose vs. Phase 1 800 mg 400 mg steady state vs. Phase 1 480 mg

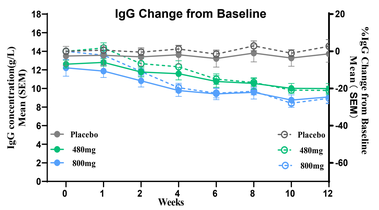
Abbreviations: C_{max} = maximum serum concentration; C_{trough} = trough serum concentration; Q12W = every 12 weeks; popPK = population pharmacokinetics.
Notes: Phase 2 values are model-simulated, summarized as median [5th, 95th percentiles]; Phase 1 values are observed, summarized as median [min, max].

✓ PD Marker Assessments in Phase 2 Relevant Dose Cohorts

- Gd-IgA1: Mean reduction from baseline of 66.8% (480 mg) and 70.6% (800 mg) at Week 12 (Nadir).Robust IgA and IgM lowering was observed. IgG: Mean reduction from baseline of 21.0% (480 mg) and 27.9% (800 mg) at Nadir with a minimum observed IgG of 6.5 g/L.







★ CONCLUSIONS

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1. **Favorable safety & tolerability**
   MIL116 was generally well tolerated across all SC dose levels evaluated (40–1280 mg): TEAEs were mild-to-moderate, with no deaths or treatment-related discontinuations,and no HGG or ISRs were reported.
2. **Long terminal half-life (~33 days)**
   The ~33-day t½ supports extended-interval subcutaneous dosing and less frequent administration.
3. **Profound & durable PD activity**
   Sustained, deep suppression of free APRIL with marked, dose-dependent reductions in Gd-IgA1 and total IgA, consistent with target engagement of a central IgAN driver.
4. **PopPK / PK–PD simulation support Q12W dosing**
   Simulated Phase 2 exposure and APRIL suppression profiles are comparable to pharmacodynamically active Phase 1 regimens, supporting adoption of the Q12W dosing schedule in the Phase 2 IgAN study.