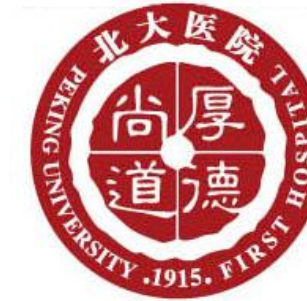


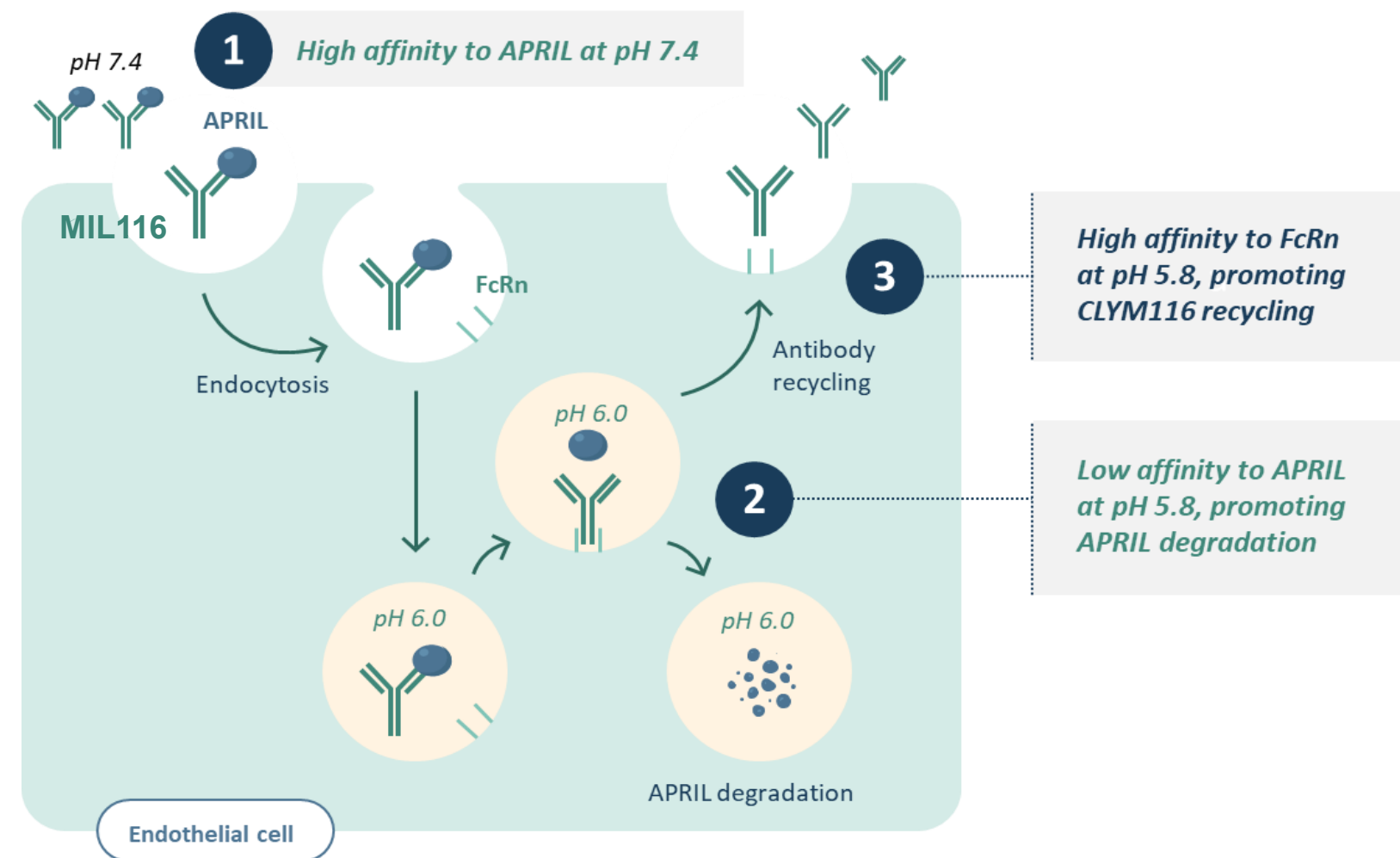


INTRODUCTION

- **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.

MIL116 ‘SWEEPER’ MOA

pH-Dependent Binding Enhances APRIL Clearance, Recycles MIL116



pH-dependent binding to APRIL provides potential for enhanced APRIL elimination through **both**:

- ➊ **potent blocking of APRIL binding to its receptors and**
- ➋ **promotion of APRIL degradation** in the lysosome
- ➌ **Efficient antibody recycling** reduces clearance of MIL116, resulting in potentially longer half-life

NAVIGATE-2: a Phase 2, Randomized, Parallel-Group, Open-Label Trial

AIMS

This **Randomized, Parallel-Group, Open-Label Phase 2 study** (NCT07375758) will characterize the efficacy, safety, tolerability, and PK/PD profile of MIL116 in patients with IgAN.

- **Screening Period:** up to 28 days
- **Treatment Period:** 72 weeks
- **Extension/Follow-up Period:** through Week 104 after first dose
- **Country/Sites:** China/~39 sites

METHODS

Participants are randomized 1:1 to two subcutaneous dosing regimens for 72 weeks. An optional cohort may be added based on model-informed drug development (MIDD) analysis. All participants are followed up to 104 weeks after first dose.

- All participants will receive MIL116 subcutaneously (SC).
- **Cohort 1:** 800 mg loading dose followed by 400 mg maintenance dosing, Q12W
- **Cohort 2:** 800 mg loading dose followed by 400 mg maintenance dosing, Q8W
- **Optional Cohort 3:** flexible design based on MIDD

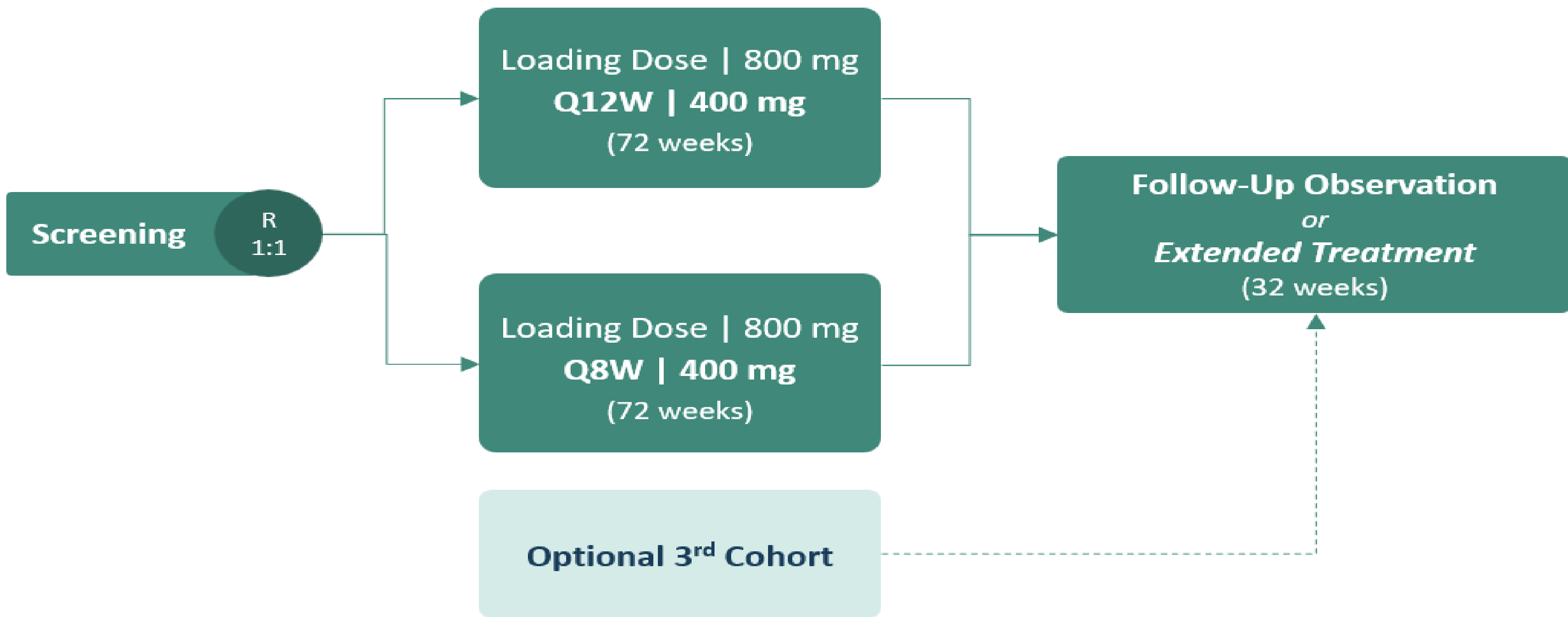
Population

- Adult with biopsy-proven IgAN
- 24-hour UPCR ≥ 0.5 g/g or 24-hour urine protein ≥ 0.75 g
- eGFR ≥ 30 mL/min/1.73 m²
- Stable, max tolerated ACEi/ARB for ≥ 12 weeks

Designed to evaluate:

- Safety and tolerability
- Gd-IgA1
- 24-hour UPCR
- eGFR slope
- Serum immunoglobulin profile
- Free APRIL

RANDOMIZED, OPEN-LABEL STUDY, N ~30 / COHORT



Note: This represents the Phase 2 portion of an ongoing study.

Key Inclusion Criteria

- **Participant Characteristics**
 - ✓ Adults aged ≥ 18 years; BMI ≥ 16 kg/m²
- **IgAN Diagnosis, Proteinuria and eGFR**
 - ✓ Biopsy-proven IgAN within 10 years before screening
 - ✓ UPCR ≥ 0.5 g/g or 24-h UP ≥ 0.75 g
 - ✓ eGFR ≥ 30 mL/min/1.73 m² by 2021 CKD-EPI
 - ✓ Stable eGFR per protocol-defined assessment
- **Background Therapy**
 - ✓ Stable, maximally tolerated RAASi for ≥ 12 weeks
 - ✓ Stable SGLT2i and/or ERA allowed if initiated ≥ 12 weeks

Key Exclusion Criteria

- **Renal Disease and Biopsy**
 - ✓ Secondary IgAN, IgA vasculitis, RPGN, or CKD other than IgAN
 - ✓ Non-IgAN renal pathology on biopsy
 - ✓ Tubulointerstitial fibrosis $>50\%$ or crescents $>25\%$
 - ✓ Nephrotic syndrome: 24-h UP >3.5 g with albumin <30 g/L
- **Prior/Concomitant Therapy**
 - ✓ Prior APRIL or APRIL/BAFF-targeted therapy
 - ✓ Biologics, immunosuppressants, Chinese herbal decoction, high-dose systemic steroids, or delayed-release budesonide within 12 weeks
- **Clinical and Laboratory Conditions**
 - ✓ BP $>150/90$ mmHg, CD4+ T cells $<200/\mu\text{L}$, IgG <6 g/L, IgA <0.7 g/L, or IgM <0.4 g/L
 - ✓ Type 1 diabetes or uncontrolled type 2 diabetes with HbA1c $>8\%$
 - ✓ Active infection

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CONTACT INFORMATION

liuxf@mab-works.com
weim@mab-works.com

Scan QR code
for more
information on
NCT07375758

