R&D Spotlight: CLYM116 and the IgAN Opportunity

SEPTEMBER 29, 2025

CLIMBBIO

Forward Looking Statements

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, including without limitation statements regarding: future expectations, plans and prospects for Climb Bio, Inc. (“Climb Bio”); expectations regarding the therapeutic benefits, clinical potential and clinical development of budoprutug and CLYM116; the trial design for the planned clinical trials of budoprutug and CLYM116; the anticipated timelines for initiating clinical trials of budoprutug for primary membranous nephropathy and CLYM116 for IgA nephropathy; plans to optimize the administration of budoprutug; the anticipated benefits of Climb Bio’s license agreement with Beijing Mabworks Biotech Co., Ltd. (“Mabworks”); expectations regarding the timing of an investigational new drug application or clinical trial application submission for CLYM116; anticipated timelines for announcing data from Climb Bio’s ongoing and planned clinical trials; the sufficiency of Climb Bio’s cash resources for the period anticipated and other statements containing the words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” “will,” “working” and similar expressions. Forward-looking statements are based on management’s current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. Climb Bio may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. These risks and uncertainties include, but are not limited to, important risks and uncertainties associated with: the ability of Climb Bio to timely and successfully achieve or recognize the anticipated benefits of its acquisition of Tenet Medicines, Inc. and its license agreement with Mabworks; changes in applicable laws or regulation; the possibility that Climb Bio may be adversely affected by other economic, business and/or competitive factors; Climb Bio’s ability to advance budoprutug and CLYM116 on the timelines expected or at all and to obtain and maintain necessary approvals from the U.S. Food and Drug Administration and other regulatory authorities; obtaining and maintaining the necessary approvals from investigational review boards at clinical trial sites and independent data safety monitoring boards; replicating in clinical trials positive results found in early-stage clinical trials and preclinical studies; competing successfully with other companies that are seeking to develop treatments for primary membranous nephropathy, immune thrombocytopenia, systemic lupus erythematosus, IgA nephropathy and other immune-mediated diseases; maintaining or protecting intellectual property rights related to budoprutug, CLYM116 and/or its other product candidates; managing expenses; and raising the substantial additional capital needed, on the timeline necessary, to continue development of budoprutug, CLYM116 and any other product candidates Climb Bio may develop. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Climb Bio’s actual results to differ materially from those contained in the forward-looking statements, see the “Risk Factors” section, as well as discussions of potential risks, uncertainties and other important factors, in Climb Bio’s most recent filings with the U.S. Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent Climb Bio’s views as of the date hereof and should not be relied upon as representing Climb Bio’s views as of any date subsequent to the date hereof. Climb Bio anticipates that subsequent events and developments will cause Climb Bio’s views to change. However, while Climb Bio may elect to update these forward-looking statements at some point in the future, Climb Bio specifically disclaims any obligation to do so, except as required by law.

Webcast Agenda

Corporate Strategy & CLYM116 Opportunity

Aoife Brennan, M.B., Ch.B.

President and CEO, Climb Bio

IgAN Disease Overview & Evolving Treatment Landscape

Craig Gordon, M.D., M.S.

Nephrologist; Professor, Tufts University School of Medicine

Co-director, Evidence Review Team for KDIGO clinical practice guideline for the treatment of IgAN

CLYM116 Preclinical Data & Development Plan

Edgar Charles, M.D.

Chief Medical Officer, Climb Bio

Q&A session

including Dr. Gordon and management

OUR MISSION

Deliver high impact, disease-modifying medicines for individuals living with immune-mediated diseases

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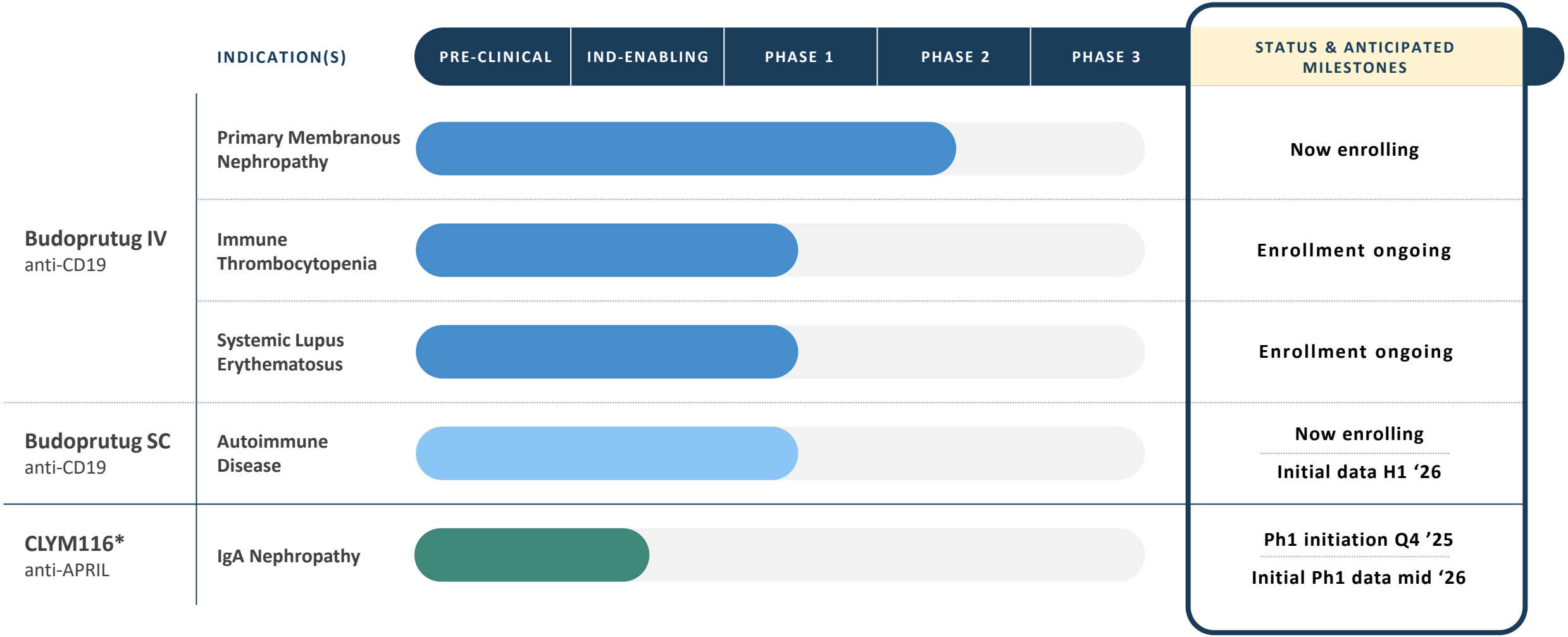
Scaling New Heights in the Development of Transformative Immune Medicines

Pipeline of Highly Differentiated mAbs

Strong execution in 2025 to date; anticipate initial readouts from multiple clinical studies in 2026



*Climb Bio has worldwide rights outside Greater China (defined as mainland China, Hong Kong, Macau, and Taiwan); Partner: Beijing Mabworks Biotech Co., Ltd.
CLYM116 Phase 1 initiation subject to regulatory clearance.
APRIL = a proliferation-inducing ligand, H = half, IV = intravenous, mAbs = monoclonal antibodies, Q = quarter, SC = subcutaneous

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CLYM116: History and Perspective

Program aligns closely with our strategy and is complementary to our lead program

CLYM116 has many attractive features, which made it the right fit for Climb Bio

• Complementary to budoprutug, from a target and indication perspective	✓ ***Synergistic***
• APRIL inhibition is clinically validated; first-generation approaches leave room for improvement	✓ ***Derisked Target***
• IgAN is a serious disease and represents a potentially large commercial opportunity	✓ ***Large Market***
• Clear regulatory path; established endpoints with opportunity for approval based on single pivotal study	✓ ***Regulatory Path***
• Potential best-in-class profile and the only sweeper mAb targeting APRIL in development	✓ ***Differentiated***

CLYM116 in-licensed from Mabworks in January 2025

- Climb Bio has rights in markets outside of Greater China, including the United States and Europe; Mabworks retains rights in Greater China
- Program is being co-developed by both companies

APRIL = a proliferation-inducing ligand, IgAN = IgA nephropathy, mAb = monoclonal antibody
Greater China defined as mainland China, Hong Kong, Macau, and Taiwan.

IgAN Represents a Significant Opportunity

IgAN is an estimated ~$10-20B market opportunity, with the majority of patients requiring lifelong treatment

Progressive, lifelong renal disease

- Most common primary glomerular disease worldwide – **~170,000 patients** in the US alone[1,2]
- Diagnosed **early in life** (typically, ages 15-40)[3]; patients at **risk for renal failure** as disease progresses
- **Lifelong disease** – patients likely to require chronic therapy

Majority of patients require treatment

- Treatment goals are to **normalize proteinuria and preserve kidney function** (stabilize eGFR)[4]
- KDIGO 2025 Guideline recommend **treatment initiation** in patients with **proteinuria >=0.5 g/day**[4] (~60-75% patients)
- KDIGO updates set a revised treatment goal: proteinuria maintained at <0.5 g/day, preferably <0.3 g/day[4], recognizing that:
  - **Even** patients with **low-grade proteinuria** (0.5-1.0 g/day) have significantly **increased risk** of kidney function decline[5,6]

~$10-20B

Estimated US Market Opportunity[7-9]

Assuming pricing of >$150k/year[10]

eGFR = estimated glomerular filtration rate, IgAN = IgA nephropathy, KDIGO = Kidney Disease Improving Global Outcomes

[1] Tarpeyo CDER Integrated Review 2021, [2] Filspari CDER Integrated Review 2022, [3] Schena Semin Nephrol 2018, [4] KIDGO 2025 Clinical Practice Guideline for the Management of IgAN, [5] Yamaguchi medRxiv 2025, [6] Le Nephrol Dial Transplant 2012, [7] Cantor IgAN Report Mar 2025, [8] Goldman Sachs IgAN Report Aug 2025, [9] Oppenheimer IgAN Report Aug 2025, [10] Based on Tarpeyo/ Filspari

CLYM116 is Rapidly Advancing to the Clinic

Initial clinical data expected mid-year 2026

- NHP data demonstrated potential for deep and durable IgA suppression, long half-life, and acceptable safety profile
- Additional preclinical data to be presented at an upcoming medical meeting

- CLYM116 has the potential to provide:
  - ✓ Improved activity
  - ✓ Less frequent dosing
  - ✓ Favorable safety profile

- CTA submission and Phase 1 initiation anticipated in Q4 2025
- Initial Phase 1 HV data expected mid-year 2026

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CLYM116 Phase 1 initiation subject to regulatory clearance.

CTA = clinical trial application, HV = healthy volunteer, NHP = nonhuman primate, Q = quarter

IgA nephropathy – an overview of pathogenesis and treatment

Craig E. Gordon, MD MS, FASN

Professor of Medicine

Tufts University School of Medicine

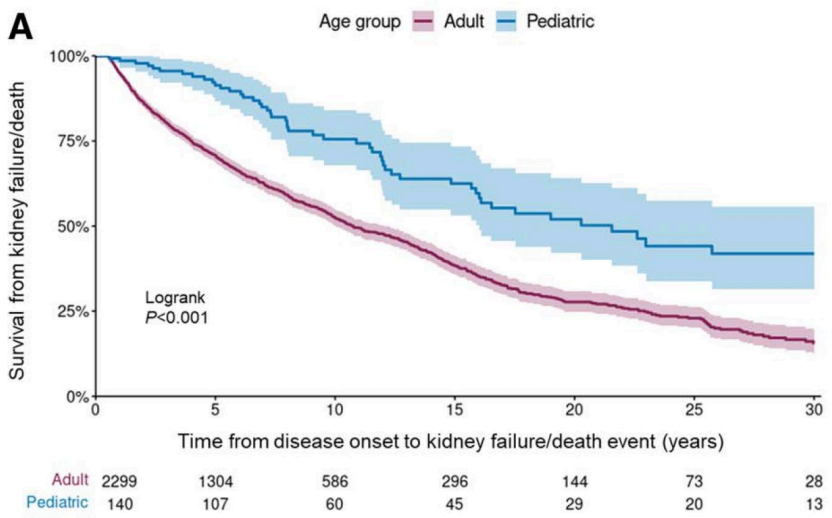
IgA nephropathy

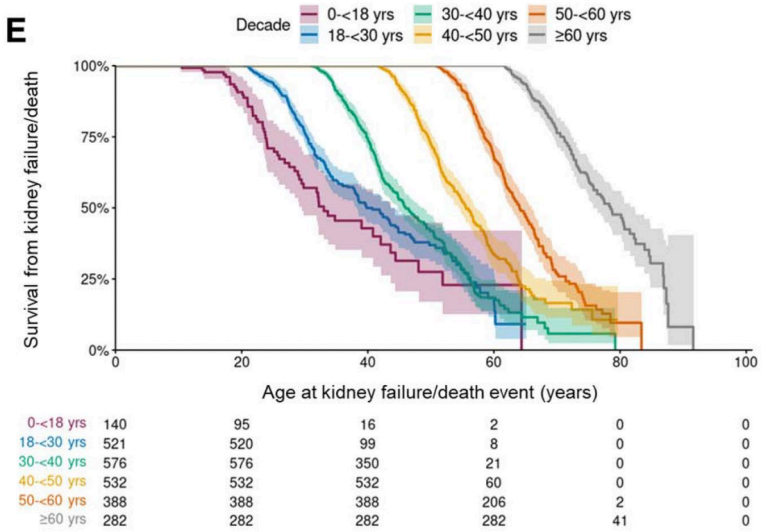
- Common condition compared with other glomerular diseases
  - Incidence: >2.5 per 100,000 individuals
    - Higher in Asian Pacific populations
  - Median age of diagnosis: 40 years of age
- UK National Registry of Rare Kidney Diseases (RaDaR)
  - Median kidney survival time of 11.4 y (10.5-12.5y)
- Consequently, IgA nephropathy is a major cause of kidney failure
- Can we do better than ACE-I/ARB?

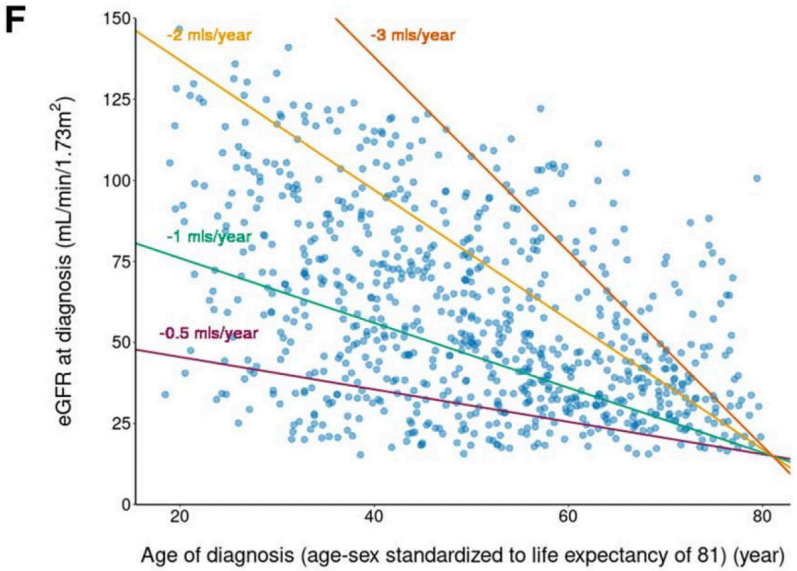
KDIGO 2025 CPG on IgA; Pitcher, CJASN 2023

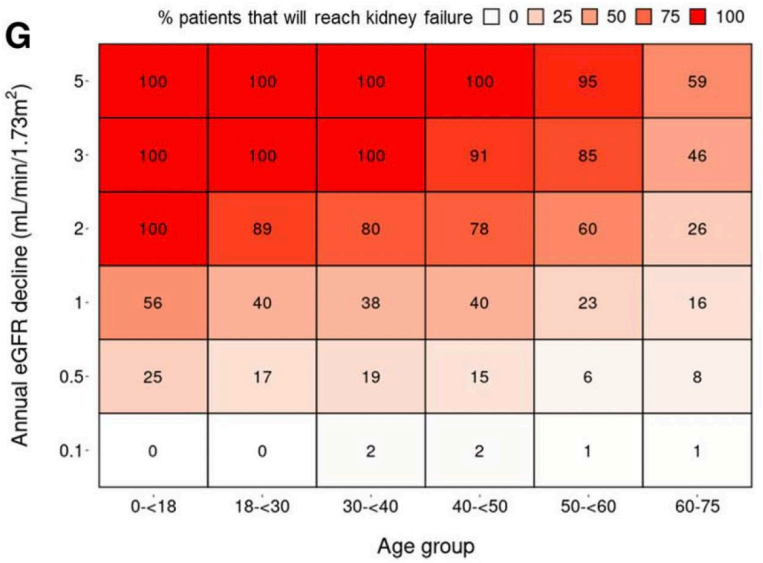
- The answer is an emphatic “yes”… with so many new treatment options available…
  - Hemodynamic treatments like SGLT2i, dual endothelin angiotensin receptor antagonists (DEARA), endothelin receptor antagonists
  - Immunosuppressive treatments like corticosteroids, TRF budesonide, complement blockade (iptacopan), or BAFF/APRIL antagonists
- The question remains which combinations?
- Hemodynamic and immunosuppressive treatments?
- What about multiple immunomodulating treatments?
- And for which patients? And when in the disease course?

UK RaDaR – high risk of kidney failure with IgAN







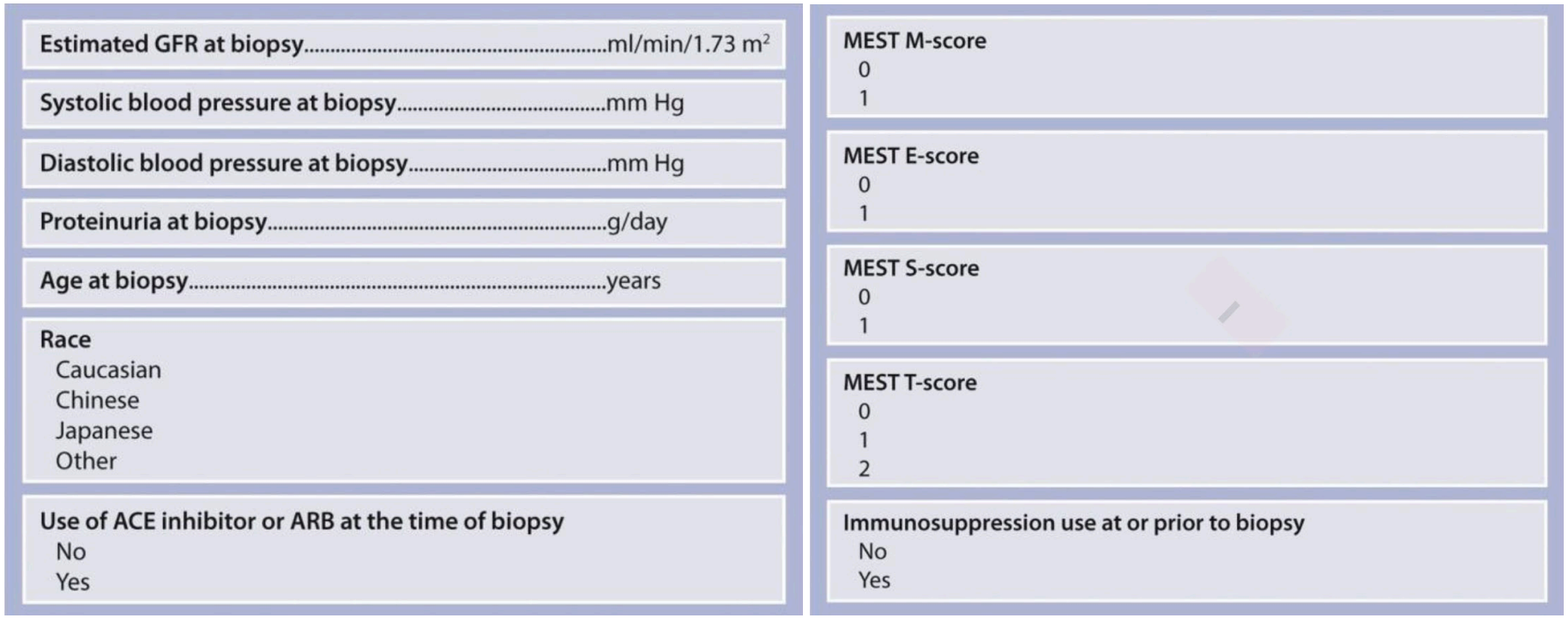


Pitcher, CJASN 2023

A patient case to highlight the challenges…

- 46 yo M referred for hematuria, proteinuria, decreased GFR, no symptoms
  - Blood pressure 138/84 mmHg
  - Urinalysis revealed 3+ blood, 3+ protein
  - UPCR 2.9 g/g
  - eGFR 58 ml/min/1.73m2
- Note the disease progression (i.e. decreased GFR) in absence of symptoms
- Underwent kidney biopsy which showed changes c/w IgA nephropathy
- Oxford classification (MEST-C): M1 EO S1 T0 C0
  - Mesangial hypercellularity and Segmental sclerosis were present but Endocapillary hypercellularity and Tubular atrophy were absent
- Started on ARB
- Discussions held with patient re: treatment options

The International IgA Nephropathy Prediction Tool



For our patient:

At 5 years:

Risk of a 50% decline in eGFR or progression to kidney failure

= **46.5%**

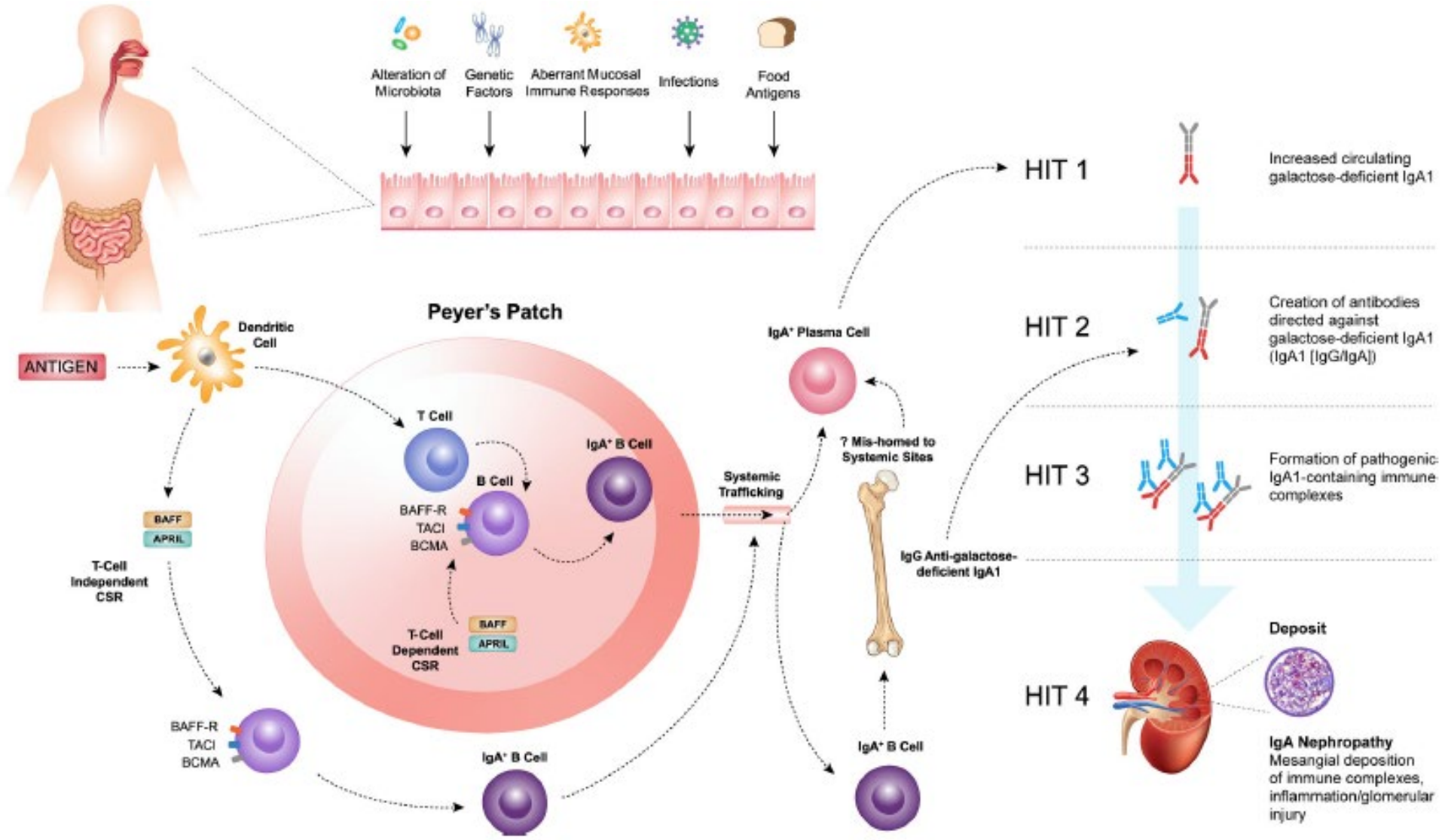
Figure 1 | The data elements included in the International Immunoglobulin A Nephropathy (IgAN) Prediction Tools.

Modified from Barbour, JAMA Int Med, 2019; KDIGO 2025 CPG on IgAN

Pathogenesis of IgAN

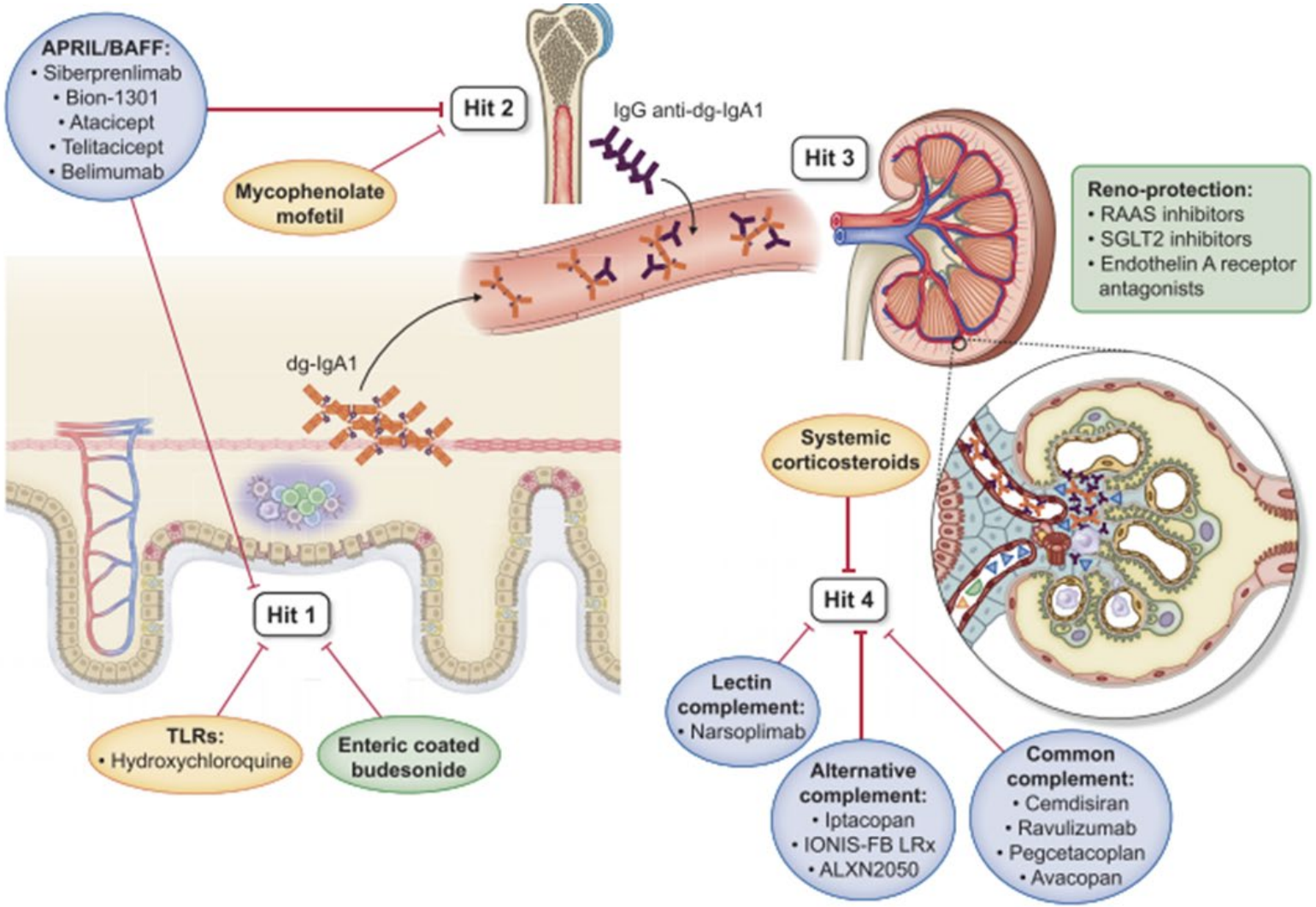
Current disease model in 2025

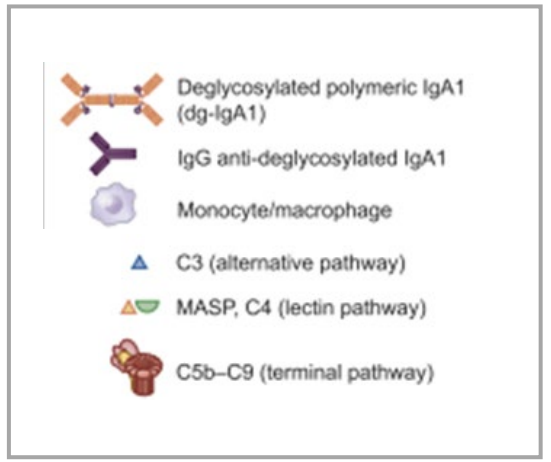
“Four hit” model



Cheung, Front in Nephr, 2024

Treatments impacting the four hit model





Gleeson, NDT, 2023

Surrogate outcomes in IgA nephropathy

- FDA recognized need for surrogate outcomes in studies of IgA nephropathy (slowly progressive disease)
- Recent accelerated approval by FDA of treatments based on improvement in proteinuria
  - True of TRF-budesonide, sparsentan, iptacopan
  - Presumably will be the pathway for all new agents studied in IgAN
- Full FDA approval based on improvement kidney function (eGFR)
- Outcomes of interest scientifically may include decreases in:
  - gd-IgA1
  - APRIL
  - Others?

SUPPLEMENT TO

kidney INTERNATIONAL

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES

KDIGO

Executive summary of the KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV)

Jürgen Floege[1], Jonathan Barratt[2], H. Terence Cook[3], Irene de Lourdes Noronha[4], Heather N. Reich[5], Yusuke Suzuki[6], Sydney C.W. Tang[7], Hernán Trimarchi[8], Ethan M. Balk[9], Craig E. Gordon[10], Gaelen P. Adam[9], Marcello A. Tonelli[11], Amy Earley[12] and Brad H. Rovin[13]

Diagnosis of IgAN

1.2 Diagnosis

Practice Point 1.2.1:

Considerations regarding the diagnosis of immunoglobulin A nephropathy (IgAN):

- **IgAN can be diagnosed only with a kidney biopsy, as there are no validated serum or urine biomarkers for the diagnosis of IgAN.**
- **To ensure an early diagnosis and prompt treatment of IgAN, a kidney biopsy should be considered in all adults with proteinuria ≥0.5 g/d (or equivalent) in whom IgAN is a possible diagnosis and kidney biopsy is not contraindicated.**

Treatment of IgAN

1.4 Treatment

1.4.1 Defining patients with IgAN at risk of progressive loss of kidney function requiring treatment

Practice Point 1.4.1.1: Because patients with IgAN are at risk of progressive loss of kidney function if they have proteinuria ≥0.5 g/d (or equivalent) while on or off treatment of IgAN, treatment or additional treatment should be considered in all such cases.

1.4.2 Defining a treatment goal in patients with IgAN at risk of progressive loss of kidney function

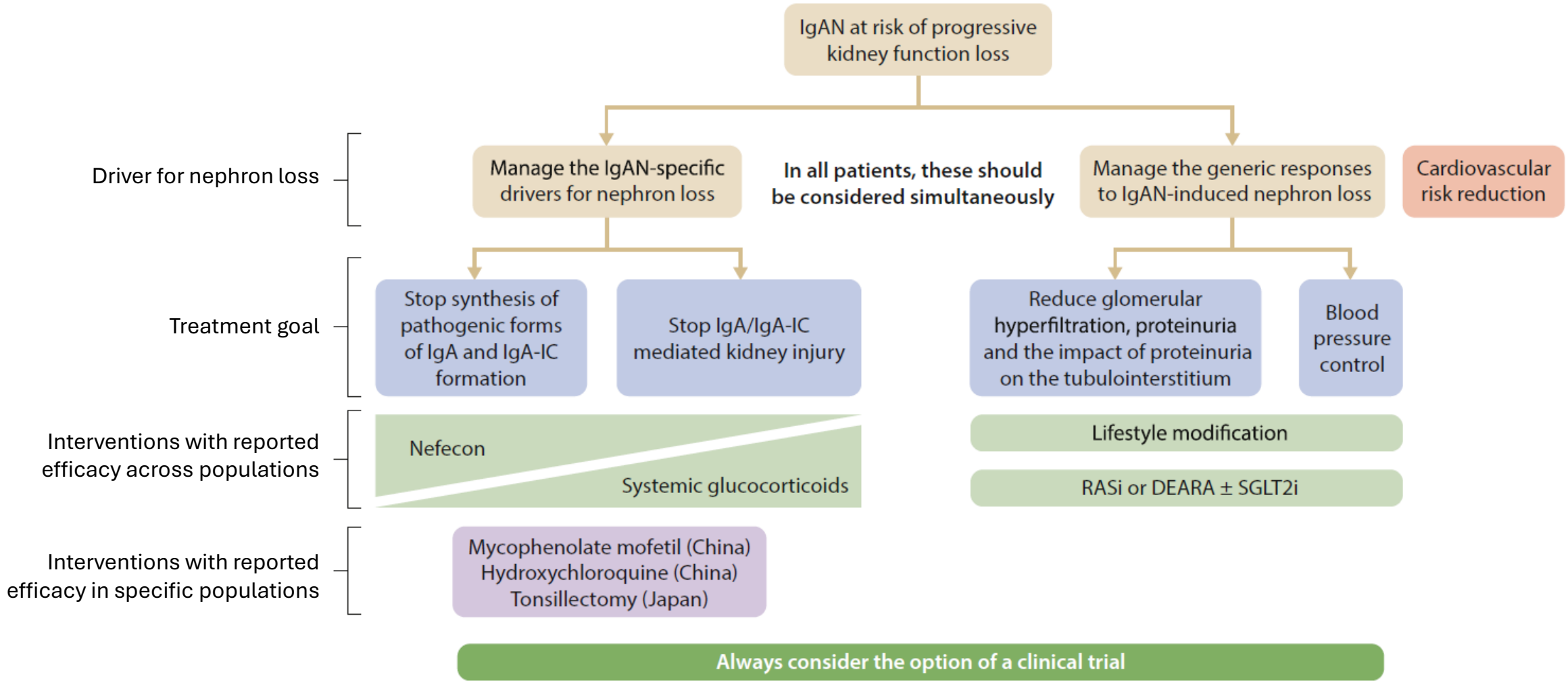
Practice Point 1.4.2.1: The treatment goal in patients with IgAN at risk of progressive loss of kidney function is to reduce the rate of loss of kidney function to the physiological state (i.e., <1 ml/min/yr for most adults) for the rest of the patient's life. The only validated early biomarker to help guide clinical decision-making is urine protein excretion, which should be maintained at a minimum of <0.5 g/d (or equivalent), and ideally at <0.3 g/d (or equivalent), accepting that in some patients with extensive kidney scarring, this may not be possible and that multiple treatment strategies, including non-pharmacologic interventions, may be needed to achieve this.

Treatment of IgAN

Practice Point 1.4.2.2:

Treatment of patients with IgAN who are at risk of progressive loss of kidney function and do not have a variant form (Section 1.5) of primary IgAN (Figure 3):

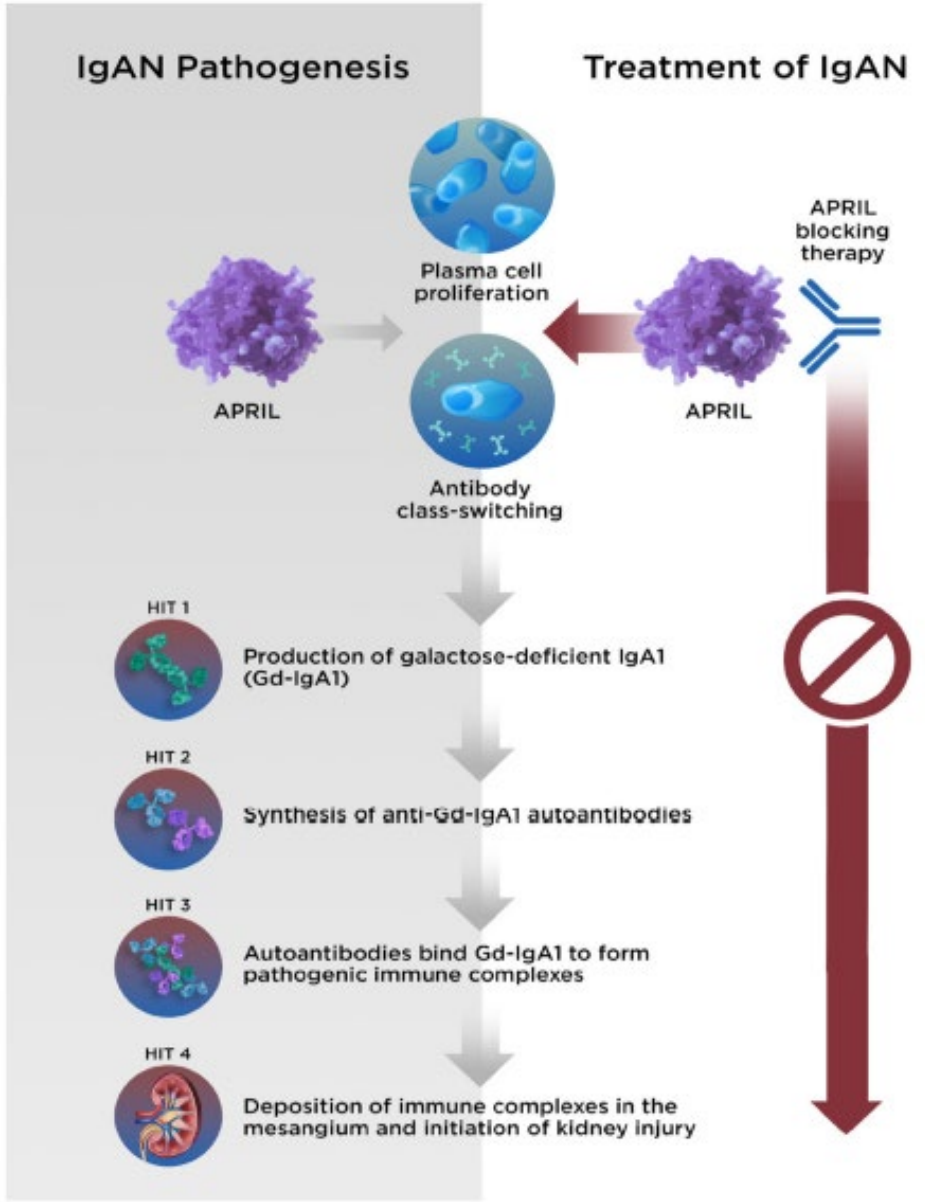
- **The focus of management in most patients should be to *simultaneously*:**
  - **Prevent or reduce immunoglobulin A–containing immune complex (IgA-IC) formation and IgA-IC–mediated glomerular injury (whether this requires lifelong or intermittent therapy is currently unknown)**
  - **Manage the consequences of existing IgAN-induced nephron loss (likely lifelong)**
- **Reduction or prevention of IgA-IC formation should incorporate treatments that have been proven to reduce pathogenic forms of IgA (commonly measured as galactose-deficient IgA1 [gd-IgA1]).**
- **Prevention of IgA-IC–mediated injury should incorporate treatments with proven anti-inflammatory and/or antifibrotic effects and ideally should be used in combination with, and not as a replacement for, treatments that prevent or reduce IgA-IC formation.**



KDIGO 2025 CPG on IgA nephropathy

Current understanding of BAFF/APRIL pathways

Downstream impact of APRIL blockade



Mathur, J Clin Med, 2023

BAFF and/or APRIL antagonists

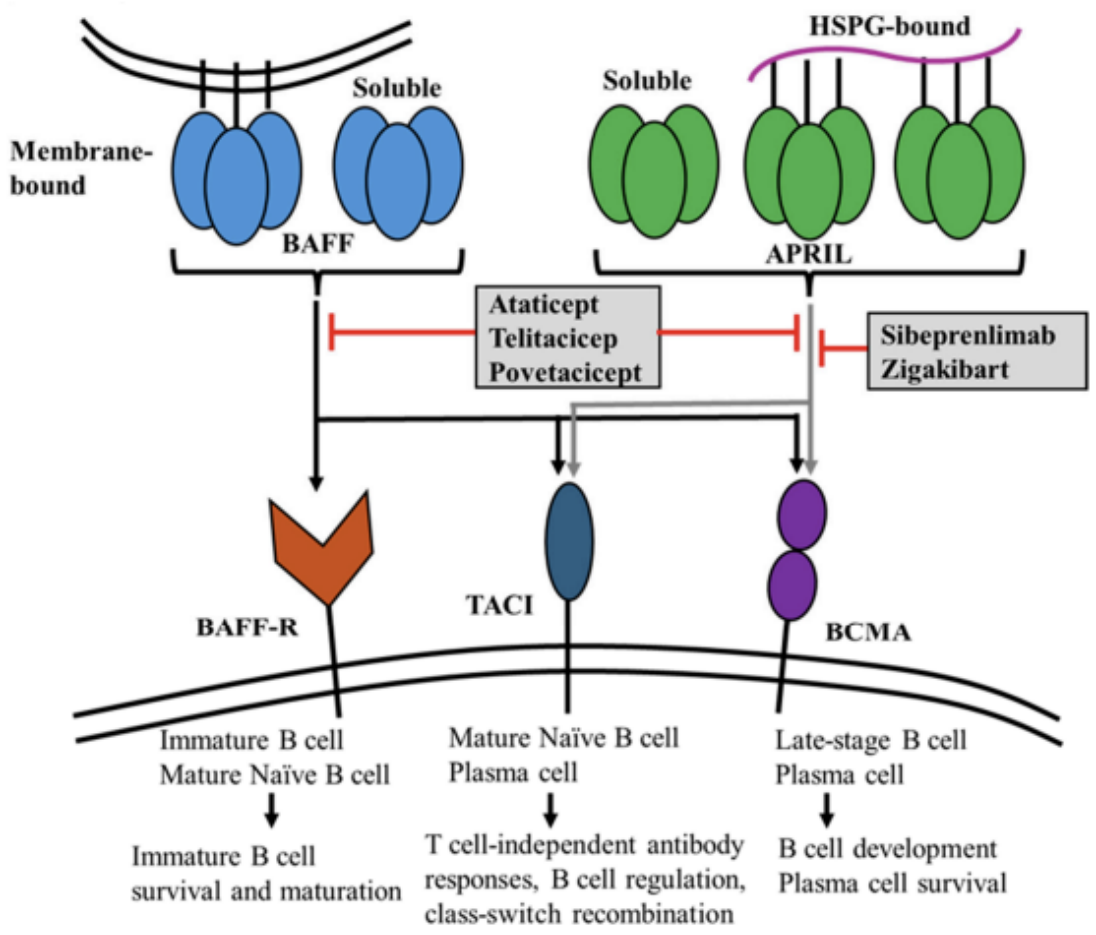


Figure 2. APRIL and BAFF signaling, their main physiological functions, and specifically targeted immunomodulatory agents. A proliferation-inducing ligand (APRIL) and B-cell activating factor (BAFF) both interact with two receptors: B-cell maturation antigen (BCMA) and transmembrane activator and calcium-modulator and cyclophilin-ligand interactor (TACI). BCMA is predominantly expressed on plasma cells, whereas TACI is expressed on both mature B cells and plasma cells. BAFF is distinct from APRIL due to its unique capacity to bind to the BAFF receptor (BAFF-R), which is predominantly found on both immature and mature naïve B cells. The heparan sulfate proteoglycan (HSPG), which serves as a receptor for APRIL, allows APRIL to interact with target cells, facilitating efficient signaling through TACI. Atacicept, telitacicept, and povetacicept are dual APRIL/BAFF antagonists, whereas sibeprenlimab and zigakibart exclusively inhibit APRIL signaling.

Muto, Int J Mol Sci, 2024

Comparison of current treatment (2025)

	Administration	Efficacy data	Safety considerations
Corticosteroids	Oral	UPCR/GFR	PJP, infections
TRF budesonide	Oral	UPCR/GFR	Acne, HTN, edema
Endothelin antagonists	Oral	UPCR/GFR	LFTs*, pregnancy* hyperkalemia, hypotension
Iptacopan	Oral (twice daily)	UPCR	Encapsulated organisms*, cholesterol
BAFF/APRIL**	SQ (generally)	TBD	TBD

Remember that based on slow progression, treatments will likely be long-term (those targeting hit 1 and hit 4, particularly).

*REMS required with sparsentan (DEARA) but not atrasentan, REMS with iptacopan
**Investigational therapies, not FDA approved

Prescribing information for TRF-budesonide, sparsentan, atrasentan, iptacopan

Where are we going in the future?

the updated guideline could have been very brief; at this time, it is reasonable to say that any of the approved therapies can be used in any patient with IgAN who has proteinuria and is at risk of progressive disease. We believe that this is a nihilistic point of view. These drugs have presumptive mechanisms of action that we think we understand, at least in part; so, in an effort to bring some order to the choice of therapies, this IgAN and IgA vasculitis (IgAV) guideline update takes some license to propose what we consider rational ways to use the new medications. We also propose that suggested combinations of medications targeting different points in the IgAN pathogenic pathways may be more effective and that maintenance immunologic treatment, as used in most other immune-mediated glomerular diseases, may be required. The idea of combination and maintenance therapies is reasonable because we have already seen that none of the newly approved drugs achieve the proteinuria or glomerular filtration rate goals that seem to be needed to prevent dialysis over the lifetime of a patient with IgAN. In addition, trial experience to date shows that when some medications are stopped, proteinuria quickly returns. As more data are gathered, this IgAN guideline will be appropriately updated, ideally moving toward a fully evidence-based set of recommendations.

DIAGNOSIS OF IgAN

As in the 2021 guideline, the 2025 IgAN and IgAV guideline notes that IgAN can only be diagnosed with a kidney biopsy, that there are no validated diagnostic serum or urine biomarkers for IgAN, that the mesangial (M) and endocapillary (E) hypercellularity, segmental sclerosis (S), interstitial fibrosis/tubular atrophy (T), and crescents (C) (MEST-C) score should be determined, and that secondary causes should be excluded (Figure 1). However, the 2025 guideline encourages a more liberal biopsy policy, noting that to ensure an early diagnosis and prompt treatment of IgAN, a kidney biopsy should be considered in all adults with proteinuria ≥0.5 g/d (or equivalent) in whom IgAN is suspected.

PROGNOSIS OF IgAN

Clinical and histologic data at the time of biopsy should be used to risk stratify patients by the International IgAN Prediction Tools, which are now available in different versions, depending on age (adult vs. children) and the time elapsed since the kidney biopsy. In addition to the lack of diagnostic biomarkers for IgAN, we do not have novel validated biomarkers for IgAN prognosis, except for estimated glomerular filtration rate (eGFR) and proteinuria.

The updated 2025 guideline again states that the International IgAN Prediction Tools and the Oxford Classification

KDIGO 2025 CPG on IgA nephropathy

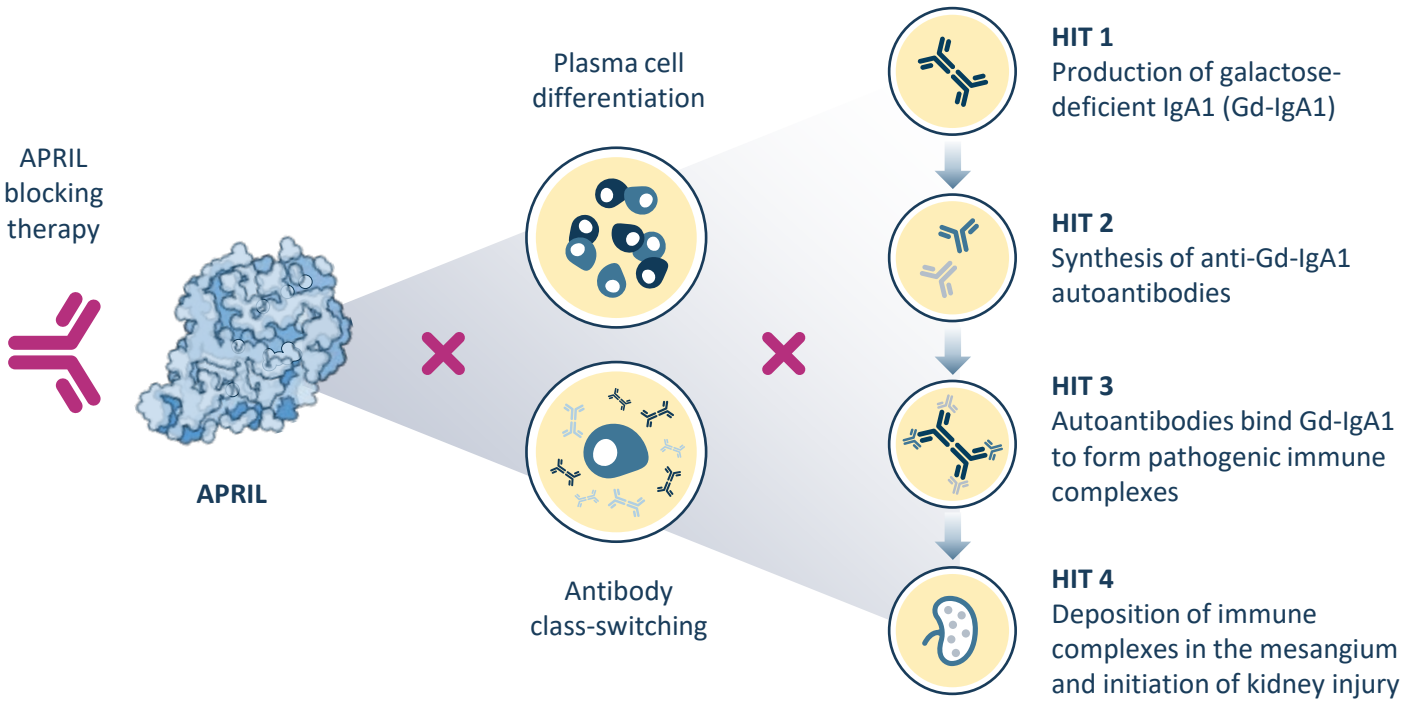
Thanks!

CLYM116

Anti-APRIL monoclonal antibody

APRIL is a Potentially Disease Modifying Approach in IgAN

In IgAN, APRIL inhibition has been demonstrated to prevent the production of pathogenic IgA and the consequent immune complex formation that leads to kidney damage



Clinical endpoints in IgAN assess key measures of disease activity

IgA and **Gd-IgA1** serve as pharmacodynamic biomarkers in early clinical studies[1-3]

Proteinuria reductions and **eGFR** stabilization reflect potential to preserve kidney function and support accelerated and full approval, respectively[4,5]

APRIL = a proliferation-inducing ligand, eGFR = estimated glomerular filtration rate, IgAN = IgA nephropathy
Adapted from Mathur J Clin Med 2023. [1] Mathur KI Reports 2022, [2] Davies Clin Transl Sci 2024, [3] Kooienga Kid Intl 2025, [4] Thompson CJASN 2019, [5] Pitcher CJASN 2023

Selective APRIL Inhibition Has Been Clinically Validated in IgAN

Anti-APRIL mAb, sibeprenlimab, demonstrated numerically better proteinuria (UPCR) reductions as compared to anti-BAFF/APRIL antagonist, atacicept, in Phase 3 IgAN studies

	Sibeprenlimab[1] (anti-APRIL mAb)	**Atacicept[2]** (TACI-IgG Fc)
Dose	400 mg SC, Q4W	150 mg SC, QW
N	320*	203**
UPCR change at 9 months	**-50.2%** vs. +2.1% for placebo	-46% vs. +7% for placebo
UPCR reduction at 9 months (placebo-adjusted)	**51.2%** p<0.0001	**42%** p<0.0001

- **Dual BAFF/APRIL inhibition does not appear to provide an efficacy benefit** beyond APRIL inhibition alone in IgAN
- APRIL only approach avoids potential immunosuppression associated with BAFF inhibition

Table above reflects cross-trial comparisons and not data from head-to-head studies; differences exist between trial designs and participant characteristics and caution should be exercised when comparing data across trials.

*Interim analysis of 320 patients, total of 530 enrolled; **Interim analysis of 203 patients, total of 431 enrolled; [1] Perkovic ERA 2025, 40 week endpoint, [2]Vera Corporate Presentation, June 2025, 36 week endpoint. APRIL = a proliferation-inducing ligand, BAFF = B-cell activating factor, IgAN = IgA nephropathy, mAb = monoclonal antibody, QW = once weekly, Q4W = once every four weeks, SC = subcutaneous, UPCR = urine protein creatinine ratio

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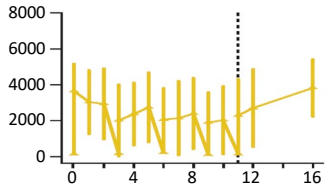
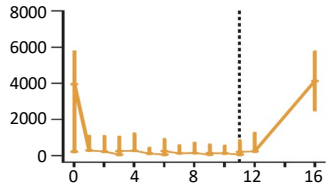
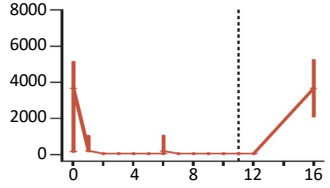
Next Gen Anti-APRILs Have Potential to Deliver Improved Profiles

Clinical data suggest that Phase 3 sibeprenlimab dose may not completely suppress APRIL or provide optimal proteinuria control, leaving opportunity for next generation agents

Sibeprenlimab Phase 2 Results*

Dose (IV, Q4W)	APRIL levels over 16 wks	Change in UPCR at 12 mo	Clinical Remission % patients with UPCR < 0.3 g/d at 12 mo
2 mg/kg		-47.2%	7.9%
4 mg/kg		-58.8%	12.2%
8 mg/kg		**-62.0%**	**26.3%**

Sibeprenlimab Phase 3 dose (400 mg SC, Q4W) roughly equivalent to 4 mg/kg IV

Opportunity for next generation approach

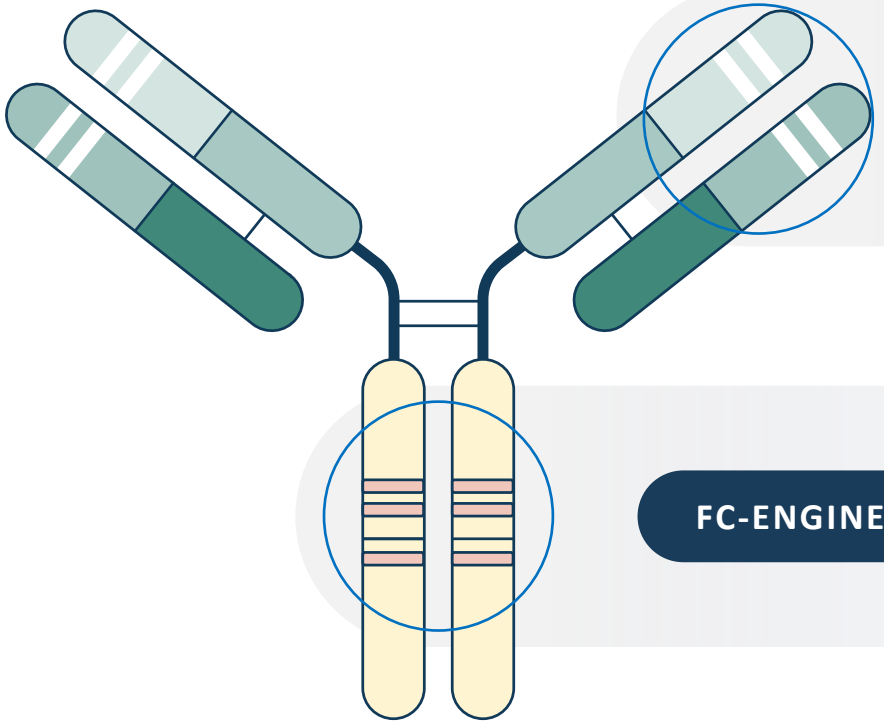
- **Improved efficacy:** more robust proteinuria reductions through deeper APRIL suppression, getting more patients to clinical remission
- **Less frequent dosing:** reduced injection frequency through more prolonged APRIL suppression
- **Favorable safety profile:** supporting chronic administration

*Adapted from Mathur NEJM 2024. Sibeprenlimab Phase 3 dose (400 mg SC) equivalency based on average 80 kg weight and 75% bioavailability (Zhang Clin Pharm Drug Dev 2023).
APRIL = a proliferation-inducing ligand, IV = intravenous, mo = months, Q4W = once every four weeks, SC = subcutaneous, UPCR = urine protein creatinine ratio, wks = weeks

CLYM116 Is The Only Known “Sweeper” Anti-APRIL In Development

Potential best-in-class anti-APRIL mAb, designed for improved activity, less frequent dosing, and favorable safety profile

KEY FEATURES



HIGH AFFINITY

pH-dependent binding to APRIL

FC-ENGINEERED

Clinically validated Fc mutations to increase serum half-life and diminish effector function

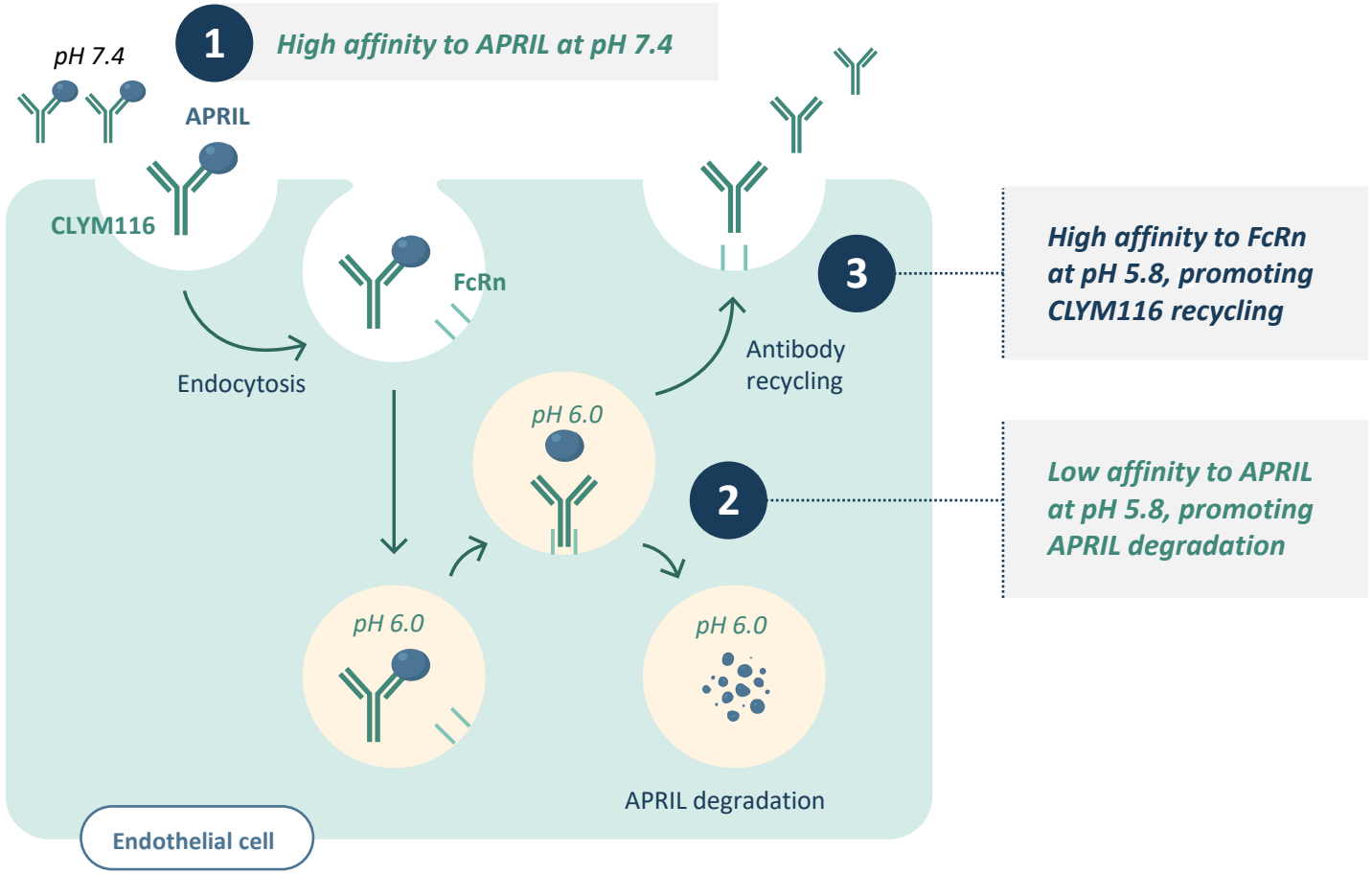
SWEEPER MECHANISM

Facilitates recycling of CLYM116 and elimination of APRIL

APRIL = a proliferation-inducing ligand, mAb = monoclonal antibody

CLYM116 “Sweeper” MoA Provides Potential for Clinical Benefits

CLYM116’s recycling degrader ‘sweeper’ mechanism of action provides potential for improved activity and less frequent dosing vs. first generation approaches or half-life extension alone



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

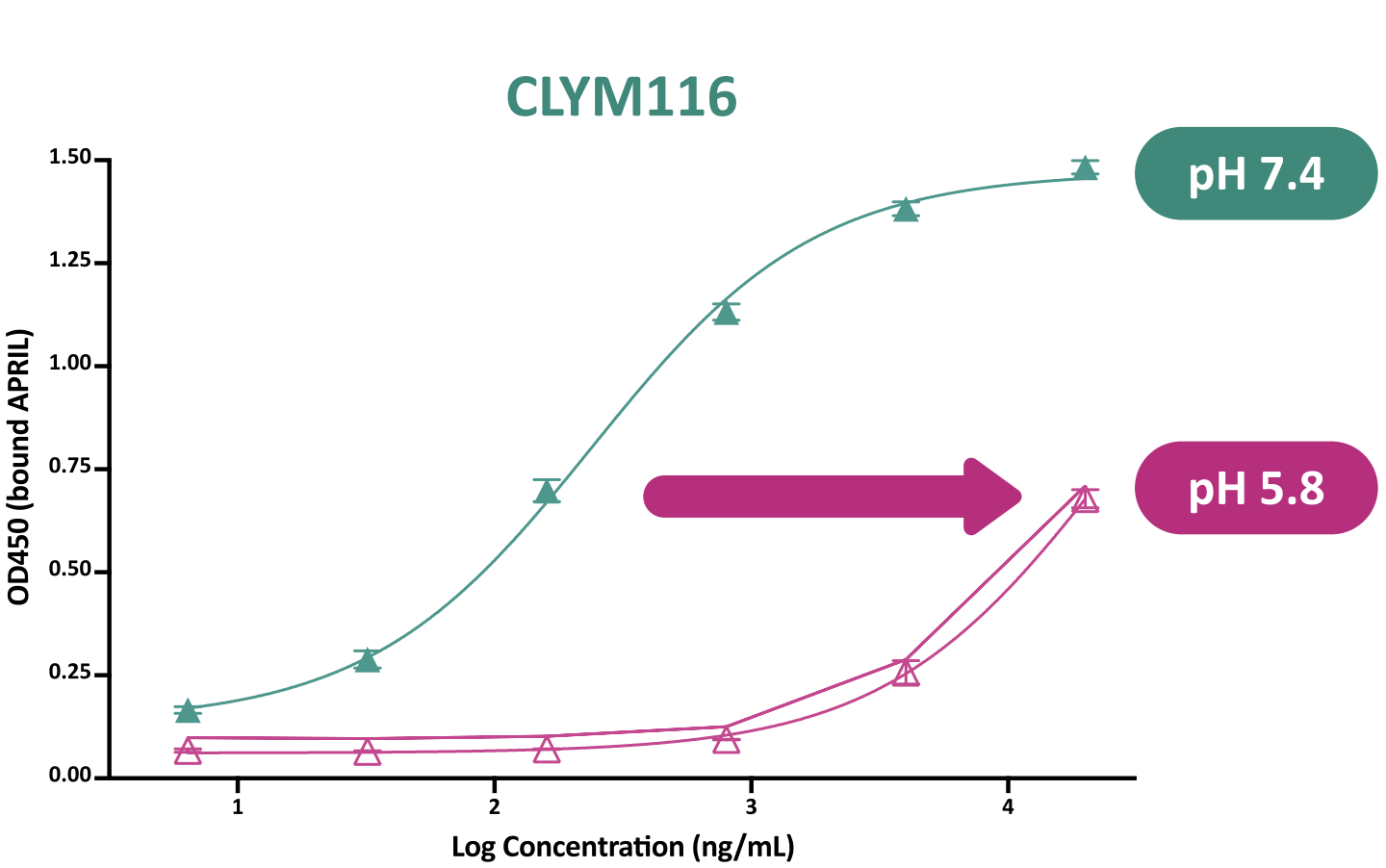
1. **potent blocking of APRIL** binding to its receptors ***and***
2. **promotion of APRIL degradation** in the lysosome

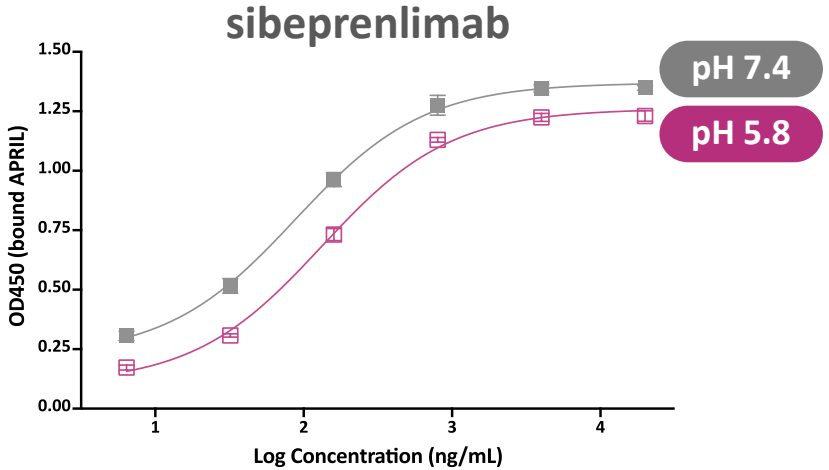
Efficient antibody recycling 3 reduces clearance of CLYM116, resulting in potentially longer half-life

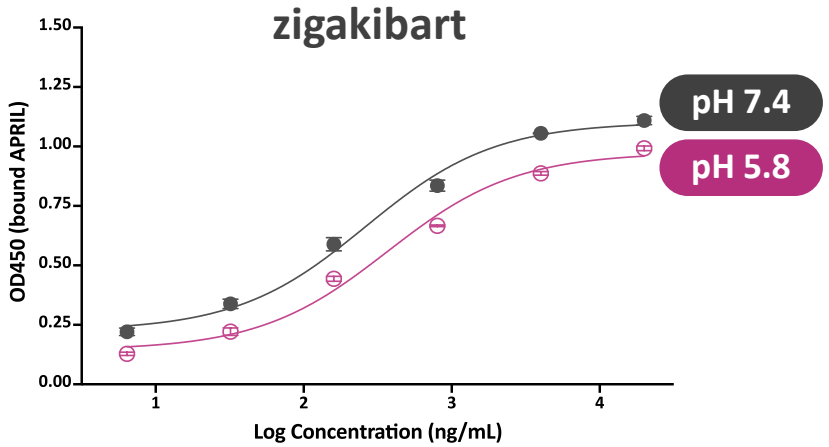
APRIL = a proliferation-inducing ligand, MoA = mechanism of action

CLYM116 Demonstrated Potent, pH-Dependent Binding of APRIL

In vitro binding assay showed CLYM116 potently bound APRIL at neutral pH, but not acidic pH, supporting sweeper mechanism, whereas first gen anti-APRIL mAbs did not demonstrate this profile





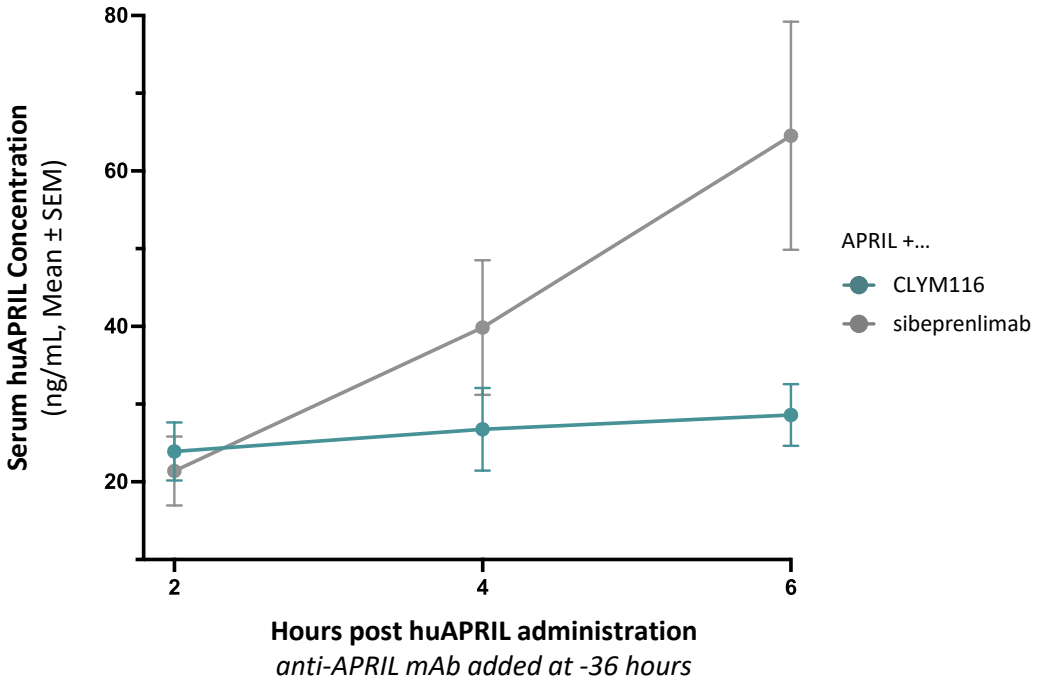


APRIL = a proliferation-inducing ligand, gen = generation, mAbs = monoclonal antibodies, OD = optical density; pH dependent binding assay: Binding profiles of CLYM116, sibeprenlimab and zigakibart were assessed via ELISA (enzyme-linked immunosorbent assay) at neutral and acidic pH. Sibeprenlimab and zigakibart analogs generated from publicly available sequences.

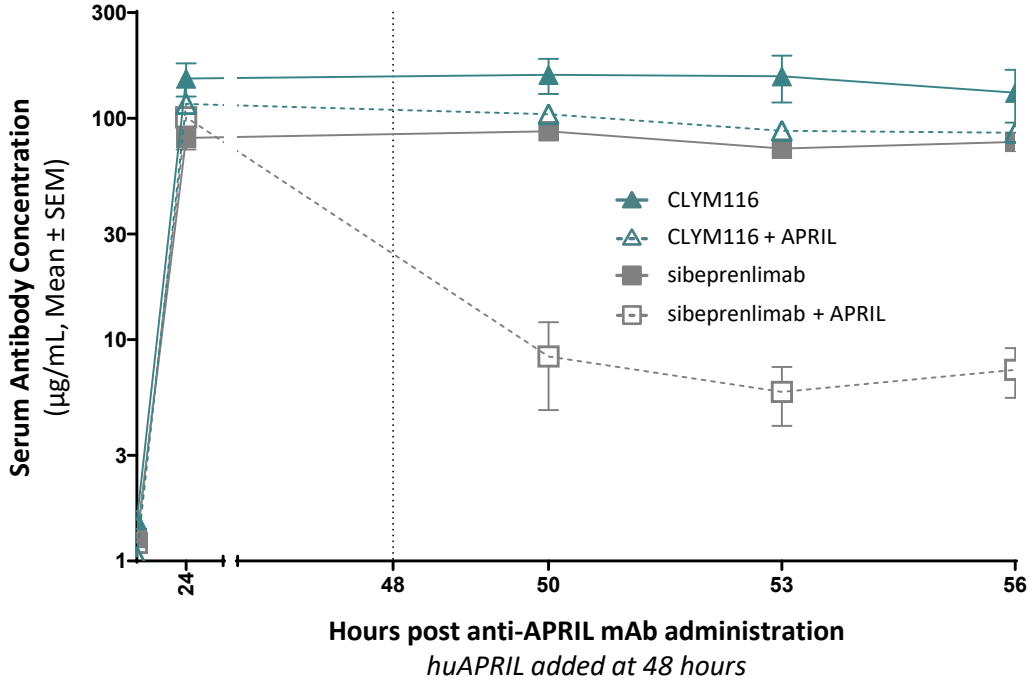
CLYM116 Showed Enhanced APRIL Elimination and Ab Recycling

In vivo APRIL degradation assay (left) and antibody exposure assay (right) support potential for enhanced APRIL elimination and antibody recycling through sweeper mechanism of action

CLYM116 demonstrated more effective APRIL depletion and clearance in a C57BL/6 mouse model



CLYM116 demonstrated more efficient antibody recycling in a humanized FcRn transgenic mouse model

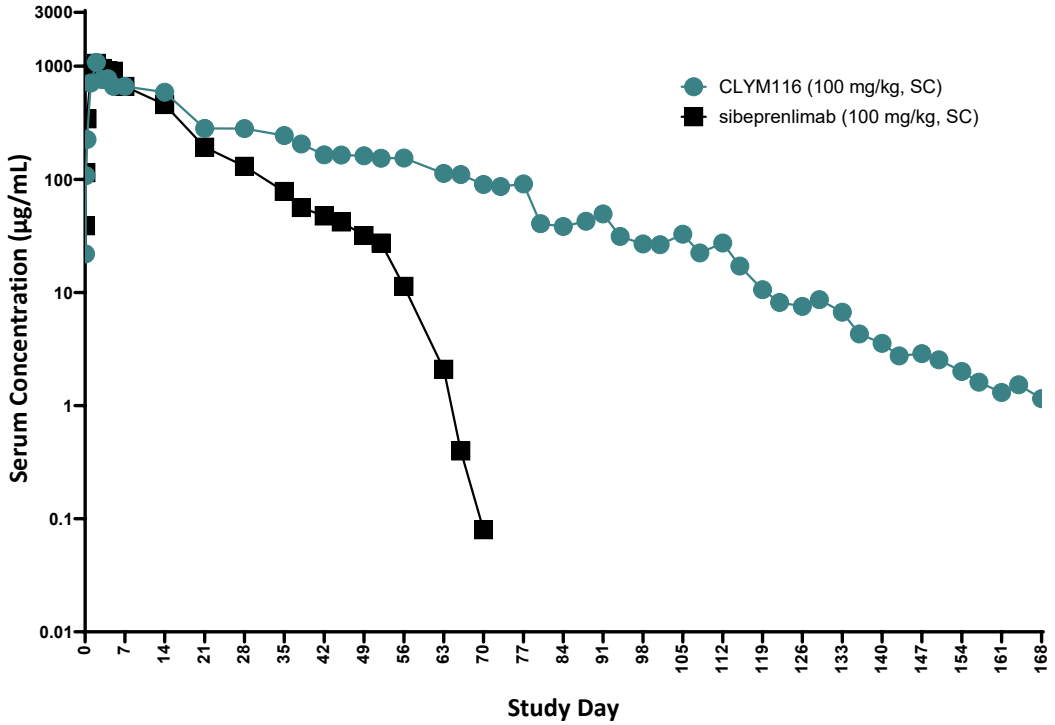


Ab = antibody, APRIL = a proliferation-inducing ligand, hu = human, mAb = monoclonal antibody, sc = subcutaneous; APRIL degradation assay (left): Wild type C57BL/6 mice were administered 10 mg/kg of antibody sc at time 0 and human APRIL (15 mg/kg sc) at 36 hours; APRIL concentration assessed every 2 hours thereafter. Antibody exposure assay (right): Humanized FcRn transgenic mice were administered 10mg/kg of antibody sc at time 0 and human APRIL (15 mg/kg sc) at 48 hours. Antibody concentration assessed thereafter. Sibeprenlimab analog generated from publicly available sequences.

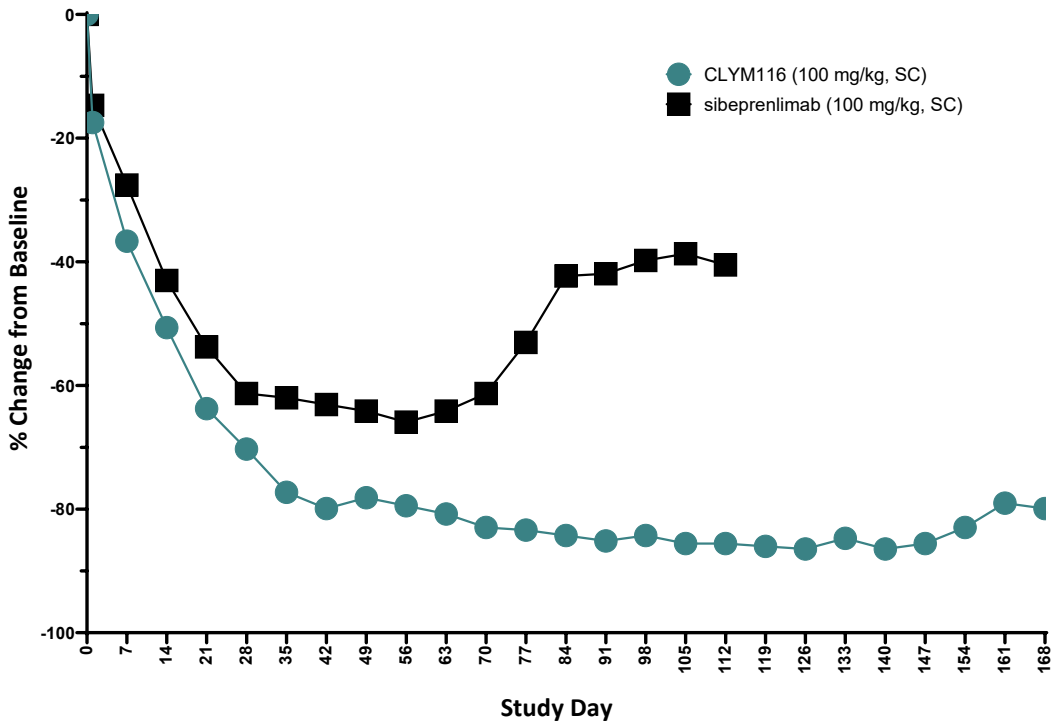
Early CLYM116 SC NHP Data Signaled Potential for Differentiation

In a pilot NHP study, CLYM116 demonstrated potential for a longer half-life and deeper, more durable IgA reductions as compared to benchmark first generation anti-APRIL antibody

CLYM116 showed prolonged exposure in NHPs at matched single SC doses



CLYM116 showed deep and durable IgA reductions out to 24 weeks following a single SC administration



Confirmed ADA+ animals were excluded from the analysis

CLIMBBIO

ADA = anti-drug antibody, APRIL = a proliferation-inducing ligand, NHPs = nonhuman primates, SC = subcutaneous
Data from a head-to-head study in nonhuman primates, 2 animals per cohort, single subcutaneous administration. Sibeprenlimab analog generated from publicly available sequence.

Larger Study in NHPs Further Evaluated CLYM116 Profile

Additional head-to-head comparative study in NHPs conducted to further assess CLYM116 exposure, activity and tolerability profile

OBJECTIVES

- Confirm SC bioavailability and tolerability profile
- Assess pharmacokinetics, dose response, and potential effect of TMDD on exposure
- Replicate pilot NHP study results in a more robust sample
- Assess biomarkers in NHPs that have shown translatability to human clinical efficacy
- Support initiation of clinical development

STUDY DESIGN

- 4-6 animals per arm per dose
- Single dose administration
- CLYM116 SC and IV at matched doses
- CLYM116 SC and sibeprenlimab SC at matched doses
- Pharmacokinetic and pharmacodynamic measures assessed daily through day 8 and weekly thereafter

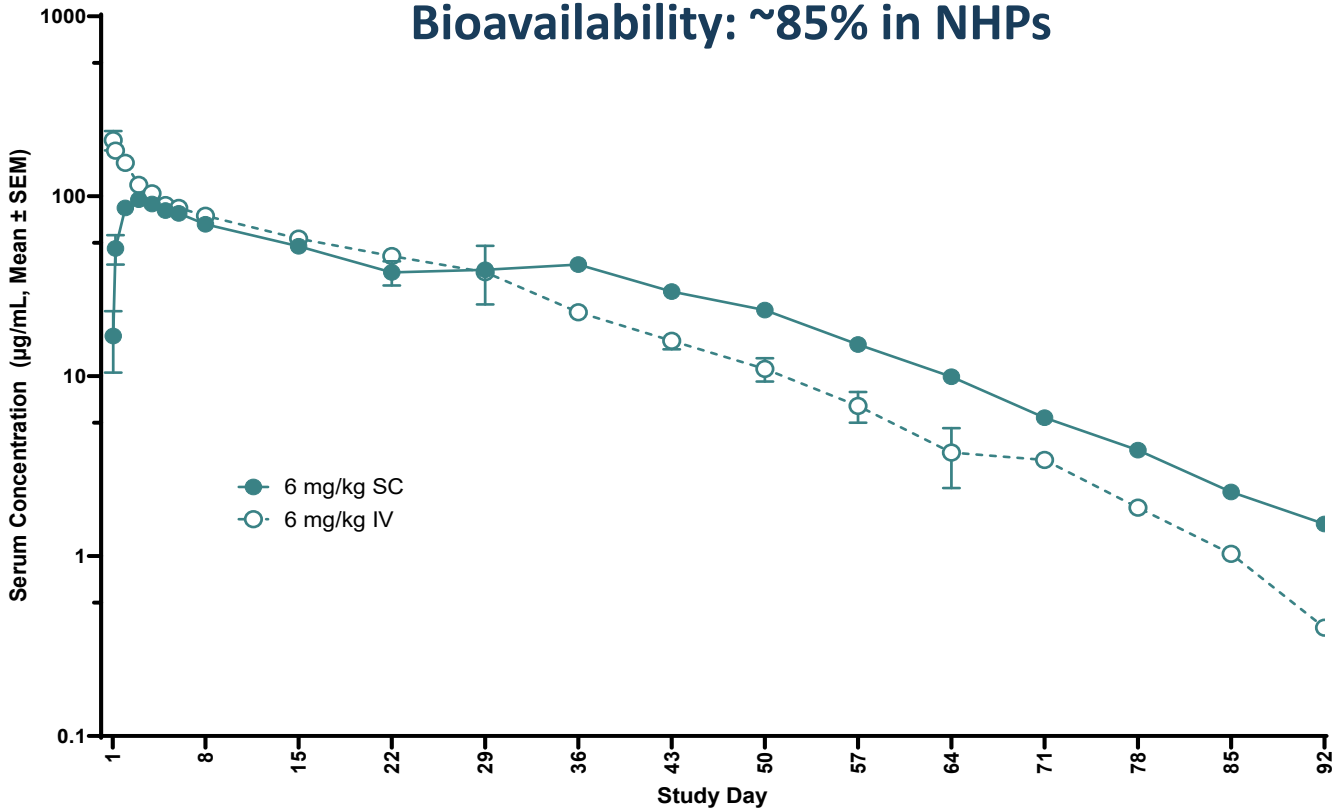
CLIMBBIO

NHP = nonhuman primate, , IV = intravenous, SC = subcutaneous, TMDD = target mediated drug disposition

CLYM116 Showed a Favorable Subcutaneous Profile in NHPs

CLYM116 SC demonstrated high bioavailability and favorable tolerability; formulation optimized to support potential for convenient, at-home dosing

Bioavailability: ~85% in NHPs



Confirmed ADA+ animals were excluded from the analysis

Favorable tolerability observed in this and other NHP studies:

- No local tolerance issues identified on histopathology
- No CLYM116-related safety findings

CLYM116 SC formulation features support potential for convenient, at-home dosing:

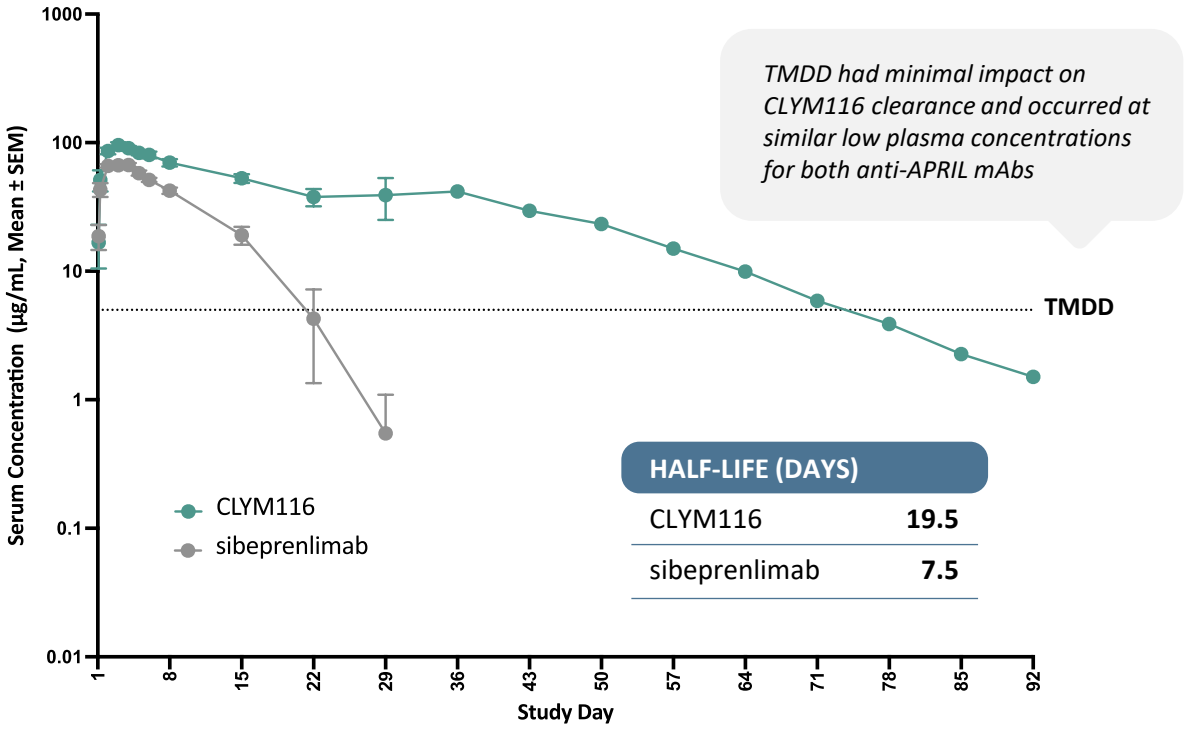
- ✓ High concentration
- ✓ Low viscosity
- ✓ Good thermal stability

ADA = anti-drug antibody, IV = intravenous, NHPs = nonhuman primates, SC = subcutaneous
Data from a head-to-head study in nonhuman primates; single subcutaneous administration. Bioavailability estimate derived from model-based analysis.

CLYM116 Showed Dose-Dependent, Prolonged Exposure in NHPs

CLYM116 demonstrated a ~2-3x longer half-life across doses as compared to sibeprenlimab, supporting potential for improved exposure and less frequent dosing in humans

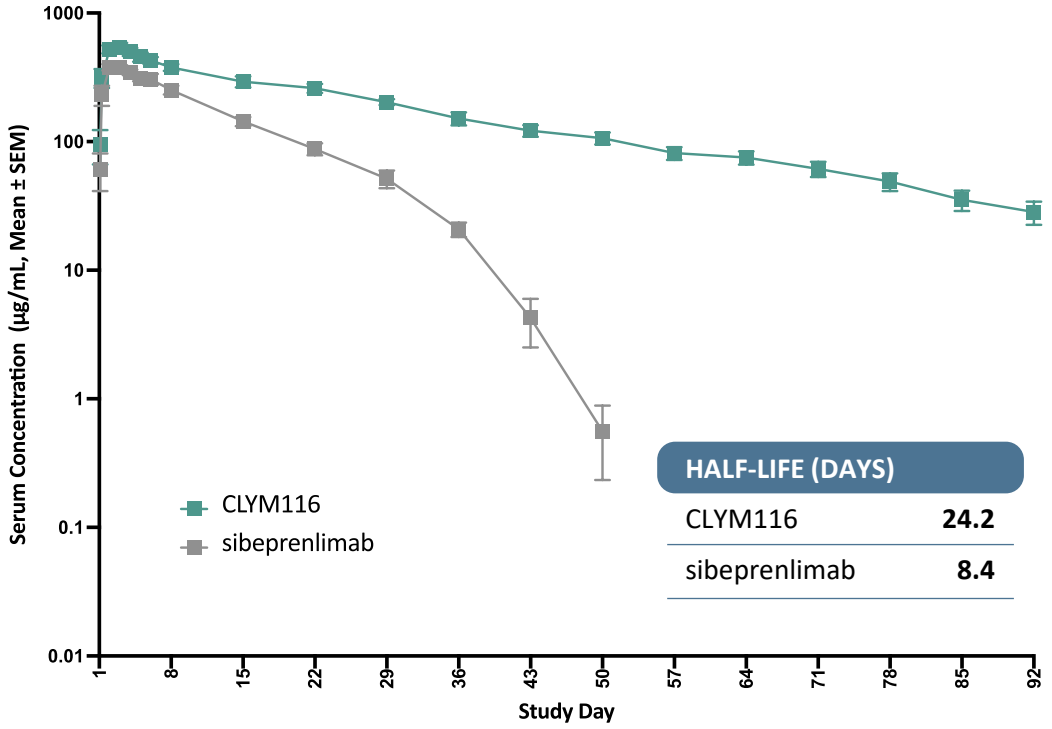
6 mg/kg SC, single administration



TMDD had minimal impact on CLYM116 clearance and occurred at similar low plasma concentrations for both anti-APRIL mAbs

HALF-LIFE (DAYS)	
CLYM116	**19.5**
sibeprenlimab	**7.5**

30 mg/kg SC, single administration



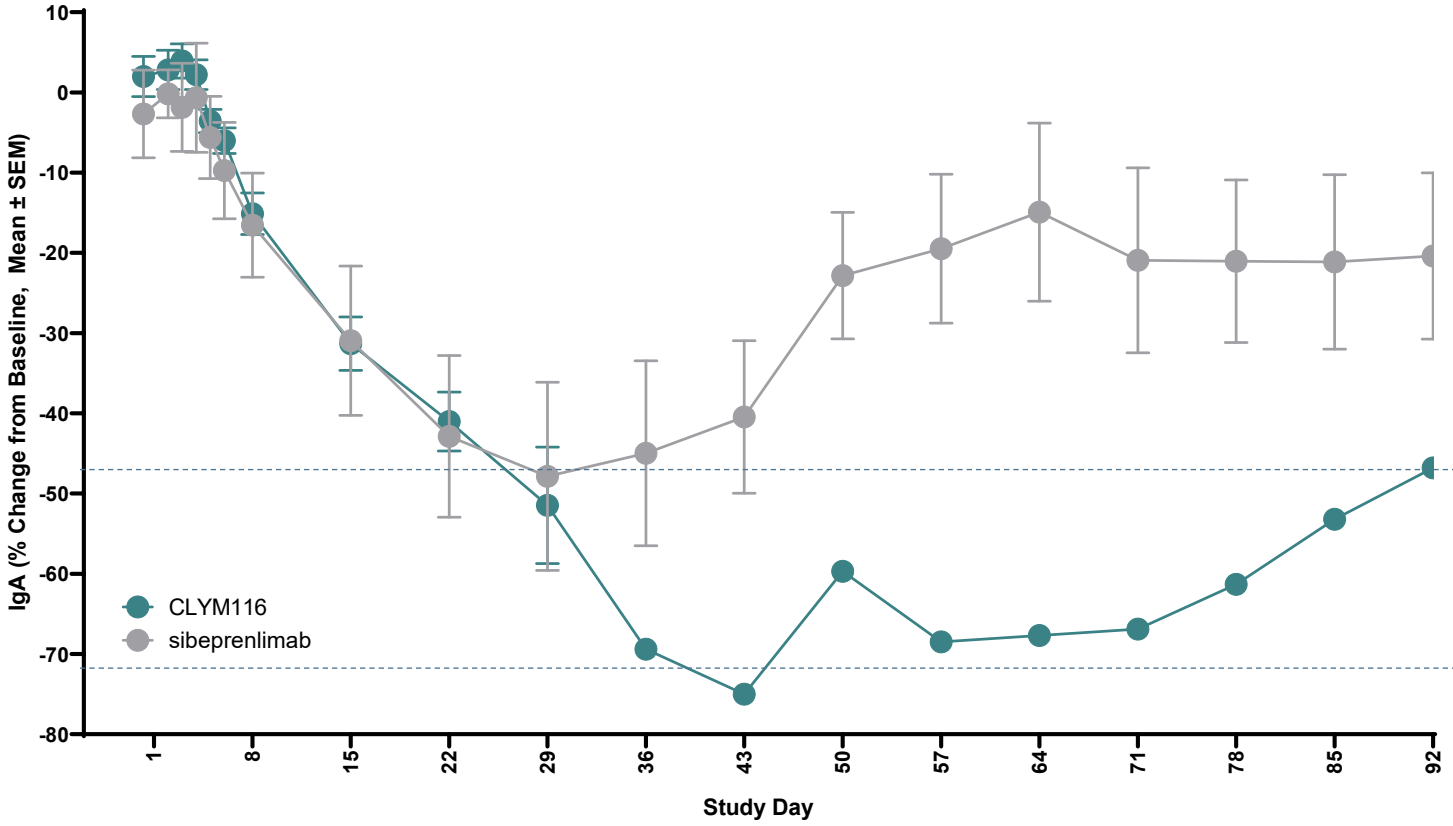
HALF-LIFE (DAYS)	
CLYM116	**24.2**
sibeprenlimab	**8.4**

Confirmed ADA+ animals were excluded from the analysis

ADA = anti-drug antibody, APRIL = a proliferation-inducing ligand, mAbs = monoclonal antibodies, NHPs = nonhuman primates, SC = subcutaneous, TMDD = target mediated drug disposition; Data from a head-to-head study in nonhuman primates; single subcutaneous administration. Sibeprenlimab analog generated from publicly available sequence.

CLYM116 Showed Robust and Durable IgA Reduction in NHPs

CLYM116 demonstrated deeper and more prolonged IgA reduction compared to sibeprenlimab after a single subcutaneous administration at equivalent doses (6 mg/kg)



Confirmed ADA+ animals were excluded from the analysis

CLYM116 demonstrated >50% reduction in IgA out to 3 months after a single 6 mg/kg SC dose

sibeprenlimab: ~50% maximal reduction

CLYM116: >70% maximal reduction

ADA = anti-drug antibody, NHPs = nonhuman primates, SC = subcutaneous
Data from a head-to-head study in nonhuman primates; single subcutaneous administration. Sibeprenlimab analog generated from publicly available sequence.

CLYM116 Has The Potential For A Best-in-Class Profile in IgAN

CLYM116 development ongoing, NHP data support potential for a differentiated profile

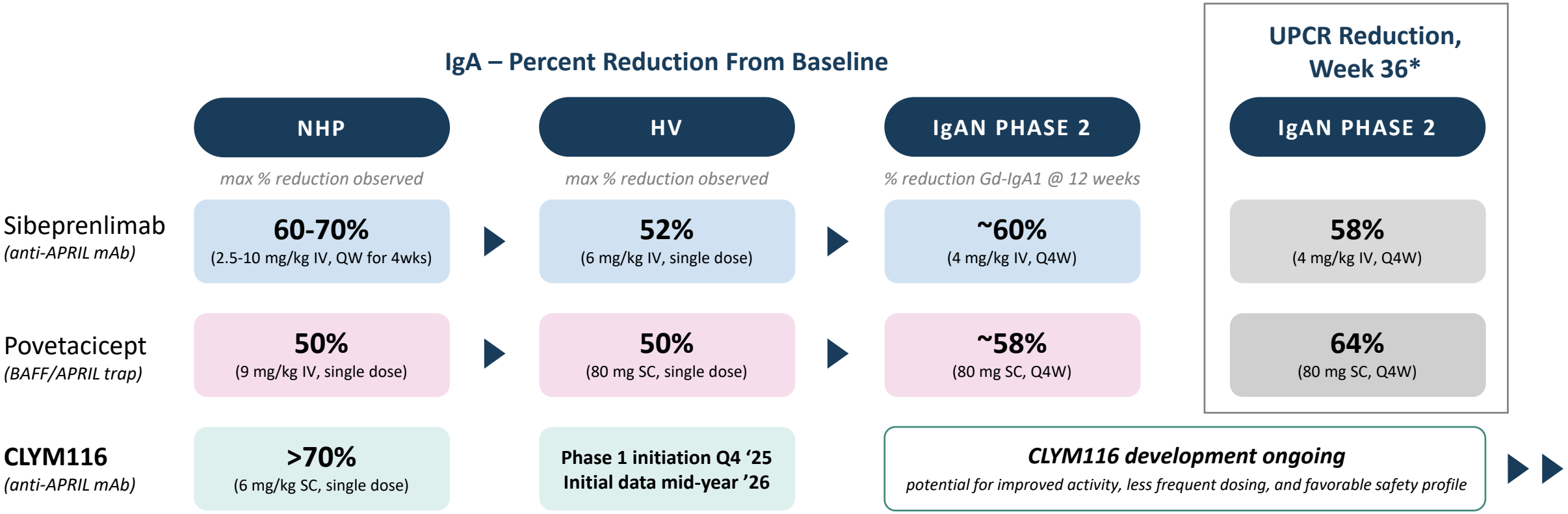


Table above reflects cross-study and cross-trial comparisons and not data from head-to-head studies; differences exist between trial designs and participant characteristics and caution should be exercised when comparing data across trials.

CLYM116 Phase 1 initiation subject to regulatory clearance. *Primary endpoint for accelerated approval.
Sibeprenlimab: Myette Kid Intl 2019, Mathur Kid Intl Reports 2022, Mathur NEJM 2024. Povetacicept: Evans Arthritis & Rheumatology 2023, Davies Clin Transl Sci 2024, Tumlin WCN 2024.
APRIL = a proliferation-inducing ligand, BAFF = B-cell activating factor, HV = healthy volunteers, IgAN = IgA nephropathy, IV = intravenous, mAb = monoclonal antibody, NHPs = nonhuman primates, Q = quarter, QW = once weekly, Q4W = once every 4 weeks, SC = subcutaneous, UPCR = urine protein creatinine ratio, wks = weeks.

CLIMBBIO

Planned CLYM116 Phase 1 Study In Healthy Volunteers

Pharmacodynamic biomarker data (APRIL, IgA) expected to guide dose and dose frequency for studies in IgAN patients; Phase 1 study expected to initiate in Q4 2025

Randomized, double-blind, placebo-controlled, ascending dose study

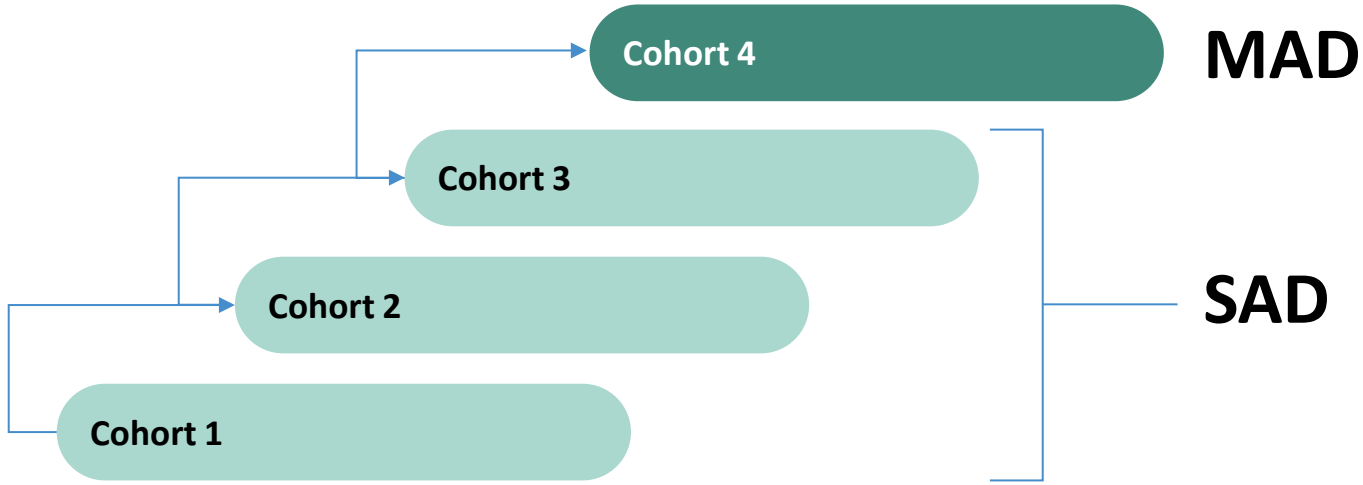
Population
- Healthy volunteers

Primary Objective
- Safety and tolerability

Secondary Objectives
- Pharmacokinetic profile
- Effect on immunoglobulins (IgA, IgM, and IgG) and APRIL levels (pharmacodynamic response)

ASCENDING DOSE COHORTS

(additional cohorts may be included as study progresses)



Additional details to be provided following study initiation

CLYM116 Phase 1 initiation subject to regulatory clearance.

APRIL = a proliferation-inducing ligand, IgAN = IgA nephropathy, MAD = multiple ascending dose, Q = quarter, SAD = single ascending dose

CLYM116 Development Strategy and Path Forward

Development strategy aimed at rapid progression into a registrational program, with streamlined phase transitions; initial data from Phase 1 trial in HVs anticipated mid-year 2026

Our Goal: Quickly progress from Phase 1 study in healthy volunteers to studies in IgAN patients

Decision to progress based upon PD (depth and duration of APRIL and IgA suppression) and safety readouts, which will inform:

- Dosing regimen/frequency
- Predicted efficacy
- Predicted safety/tolerability in IgAN patients

Opportunities for development program efficiencies provided by:

- Internal and external biomarker data (correlations between APRIL suppression, IgA suppression and UPCR reduction, and link to eGFR stabilization)
- Observed safety/tolerability profile of anti-APRIL mAbs
- Parallel execution of early-stage studies by Mabworks (China), providing a complementary, independent dataset that will allow fulsome stage-gate decisioning
- Regulatory precedent

CLYM116 Phase 1 initiation subject to regulatory clearance; APRIL = a proliferation-inducing ligand, eGFR = estimated glomerular filtration rate, HV = healthy volunteers, IgAN = IgA nephropathy, mAbs = monoclonal antibodies, PD = pharmacodynamic, UPCR = urine protein creatinine ratio

CLYM116 is a Potential Best-in-Class anti-APRIL mAb for IgAN

CLYM116 is a promising investigational therapy for IgAN, with a unique ‘sweeper’ mechanism of action

- APRIL represents a validated target with potential to address underlying IgAN pathology
- CLYM116 is the only known ‘sweeper’ anti-APRIL mAb in development

New CLYM116 NHP data demonstrated improvement versus sibeprenlimab (first-generation anti-APRIL mAb)

- Deeper and more durable IgA reductions – supporting potential for differentiated activity profile
- ~2-3x longer half-life – supporting potential for less frequent dosing

Potential for CLYM116 to be a leading therapy in the large and growing IgAN market (est. $10-20B in US alone)

- IgAN typically diagnosed early in life and may require lifelong management
- New treatment guidelines recommend earlier treatment, indicating potential for further market expansion

Derisked development opportunity, given established biology and regulatory path

- Established FDA pathway; endpoints of proteinuria and eGFR can potentially support product approval
- Biomarkers provide rapid assessment of clinical profile during early development

Meaningful near-term CLYM116 anticipated milestones

- Initiation of Phase 1 HV study expected Q4 2025, with initial data (biomarkers, projected dosing interval) anticipated mid-year 2026
- Parallel execution by Mabworks in China is expected to provide a complementary Phase 1 dataset

CLIMBBIO

CLYM116 Phase 1 initiation subject to regulatory clearance; APRIL = a proliferation-inducing ligand, eGFR = estimated glomerular filtration rate, HV = healthy volunteers, IgAN = IgA nephropathy, mAb = monoclonal antibody, NHP = nonhuman primate, Q = quarter

Q&A Session

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Edgar Charles, M.D.
Chief Medical Officer, Climb Bio

Craig Gordon, M.D., M.S.
Professor, Tufts University School of Medicine

Perrin Wilson, Ph.D.
Chief Business Officer, Climb Bio