OMEROS: *The premier complement franchise*

MASP-2 and MASP-3 Programs

April 2023

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Safe Harbor

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ABOUT OMEROS

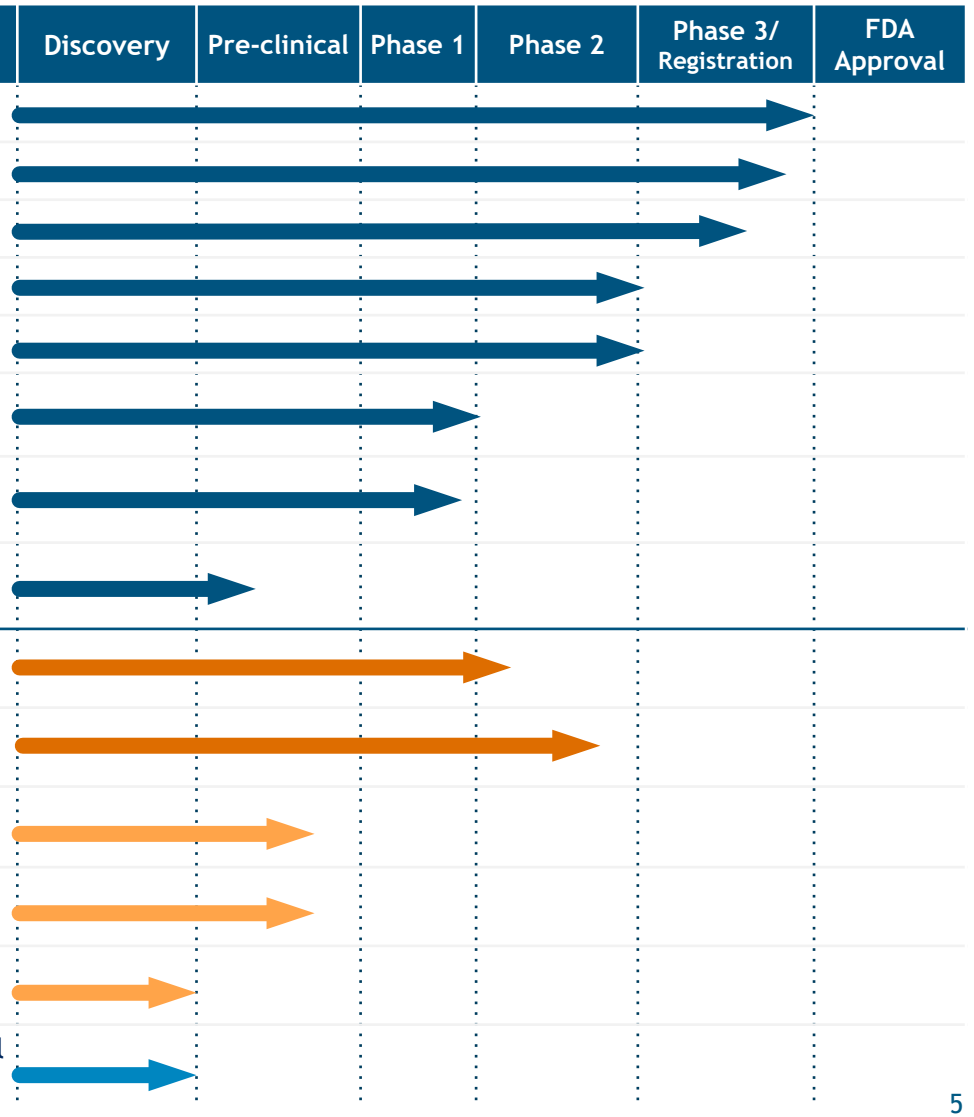
Our cutting-edge science serves as the foundation for a deep and diverse pipeline of first-in-class drugs with new mechanisms of action that target previously untapped receptors and enzymes.

Omeros Believes that It Has the Premier Complement Franchise in the Industry

- **Narsoplimab** – IgG4 mAb against MASP-2, the effector enzyme of the lectin pathway
  - Commercial preparations underway for anticipated US launch in HSCT-TMA
  - Clinical efficacy observed in HSCT-TMA, IgA Nephropathy (IgAN), lupus nephritis (LN), aHUS and broader endothelial injury syndromes; no significant safety concerns
  - Pivotal Global Phase 3 trial in IgAN nearing data readout
- **OMS1029** - Long-acting MASP-2 inhibitor (IV or SC once quarterly)
  - Designed for life-cycle management with same efficacy and safety as narsoplimab
  - Ideally suited for chronic administration
- **OMS906** – Long-acting mAb targeting MASP-3, the key activator of the alternative pathway
  - Once quarterly IV or SC administration, ideal for patient adherence
  - Designed to prevent PK/PD breakthrough of underlying disease
- **MASP-2 and MASP-3 small-molecule programs**
  - Designing for life-cycle management with same efficacy and safety as narsoplimab and OMS906, respectively
  - Ideally suited for chronic administration in indications segmented from those of OM1029 and OMS906 (e.g., preventive)

Omeros Pipeline

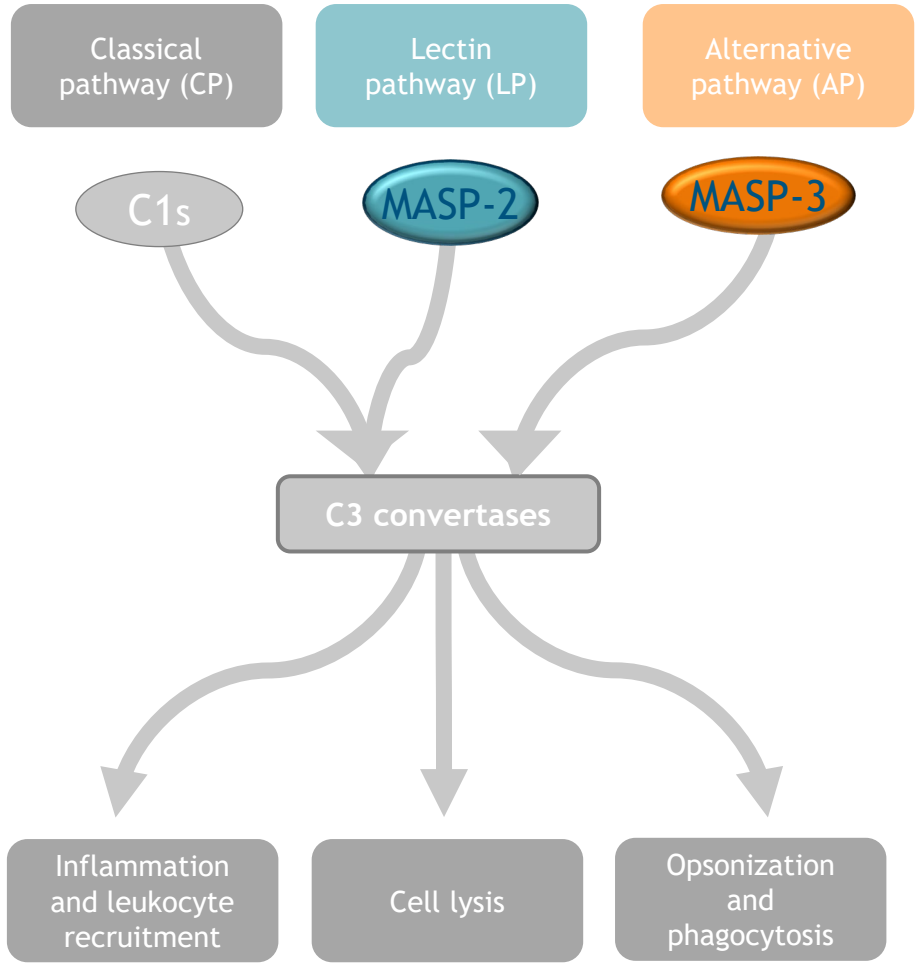
	Program / (Candidate)	Molecule	Targeted Disease
Complement Franchise	MASP-2, lectin pathway (narsoplimab [OMS721])*	LM	Stem cell transplant-associated TMA
			IgA nephropathy
			Atypical hemolytic uremic syndrome
			Lupus nephritis & other renal diseases
			COVID-19
	MASP-3, alternative pathway (OMS906)*	LM	PNH, C3 glomerulopathy, and other alternative pathway disorders
	MASP-2 (OMS1029)*	LM	Long-acting 2nd generation antibody targeting lectin pathway disorders
	MASP-2, MASP-3, MASP-2/3*	SM	Disorders of the lectin and alternative pathways of complement
Addiction	PDE7 (OMS527)*	SM	Addictions and compulsive disorders; movement disorders
	PPARγ (OMS405)	SM	Opioid and nicotine addiction
Immuno-oncology	Adoptive T cell therapies/CAR-T	SM/LM	Cancer
	Biologic therapeutics	LM	Cancer
	GPR174*	SM	Cancer
Other	GPCR platform	SM	Immunologic, CNS, metabolic, CV, musculoskeletal & other disorders



Notes: LM, large molecule; SM, small molecule; *Program directed to inhibiting associated target

Our Innovative Inhibitors Selectively Target the Key Activators of the Complement System's Lectin and Alternative Pathways

ROLE OF MASP-2 AND MASP-3 IN THE COMPLEMENT SYSTEM

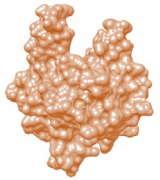


MASP-2
Effector enzyme of the LP

The LP is a pattern recognition system, and its dysregulation is associated with many diseases (e.g., TA-TMA, IgAN, aHUS)

Narsoplimab is a first-in-class, potent and selective inhibitor of MASP-2, a target for treatment of LP-related diseases

OMS1029 is a potent and selective, long-acting inhibitor of MASP-2, ideally suited for chronic administration; SM inhibitor also moving toward clinic



MASP-3
Key activator of the AP

The AP amplifies the LP and/or CP signaling cascade and its dysregulation is associated with a wide range of diseases (e.g., PNH, C3G, LN)

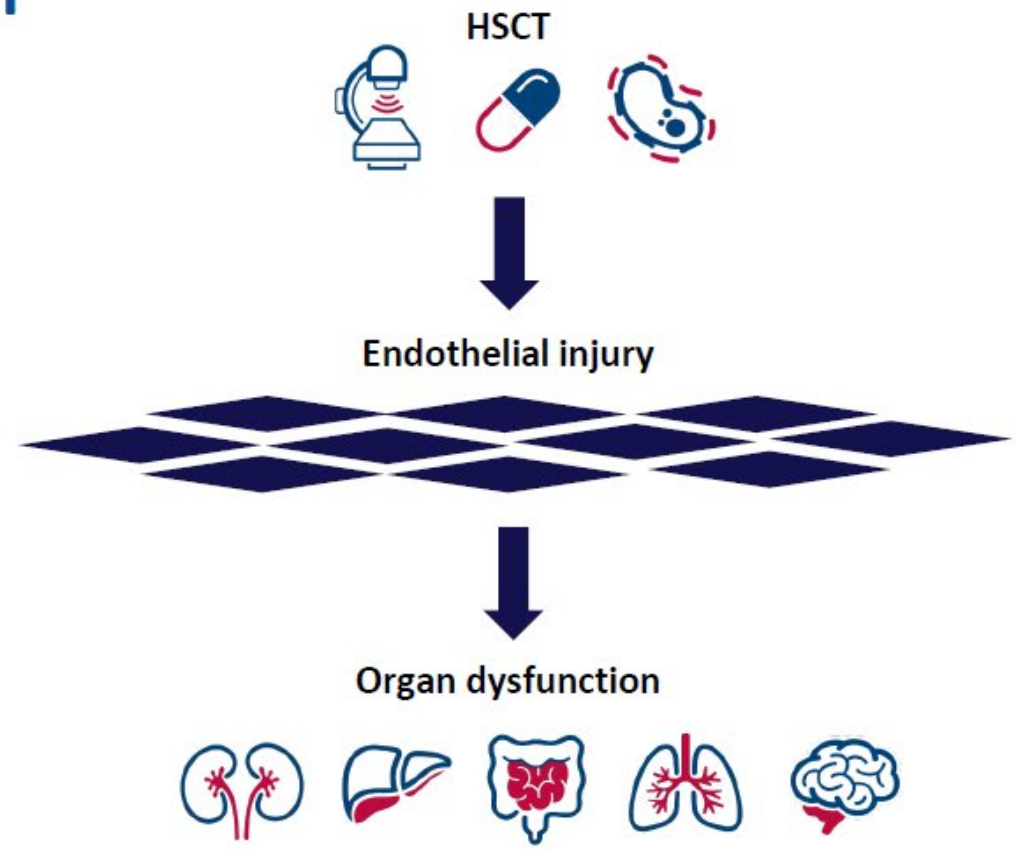
OMS906 is a first-in-class, potent and selective inhibitor of MASP-3, a target for treatment of AP-related diseases

Notes: TA-TMA, transplant associated thrombotic microangiopathy; IgAN, IgA nephropathy; aHUS, atypical hemolytic uremic syndrome; SM, small molecule; PNH, paroxysmal nocturnal hemoglobinuria; C3G, complement 3 glomerulopathy; LN, lupus nephritis; Narsoplimab issued method-of-treatment patents extending to 2038, others pending; OMS906 composition-of-matter patent extends to 2037, Clinical/MOU/orphan extensions apply

Source: Dunkelberger, J et al. *Nat. Cell Biol.* 2010

HSCT-TMA is initiated by endothelial injury associated with transplantation

- Endothelial injury activates the lectin pathway of the complement system
- Complement activation leads to inflammation and thrombus formation that result in organ dysfunction and failure
- HSCT-TMA has been reported to occur in up to 39% of patients undergoing allogeneic HSCT but remains under-recognized

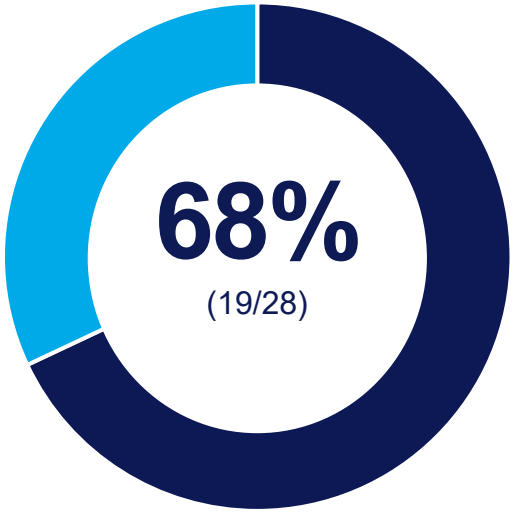


HSCT, hematopoietic stem cell transplantation; HSCT-TMA hematopoietic stem cell transplantation-associated thrombotic microangiopathy.

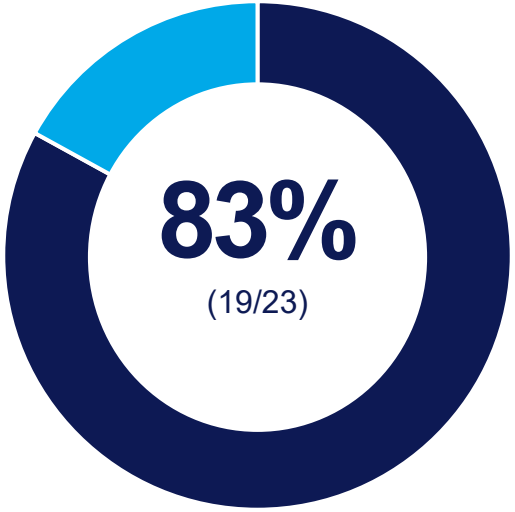
Carreras E, Diaz-RicartM. *Bone Marrow Transplantation*. 2011;46:1495-1502. Jodele S, Davies SM, Lane A, et al. *Blood*. 2014;124:645-653.

Narsoplimab HSCT-TMA Pivotal Study - 100-day Survival

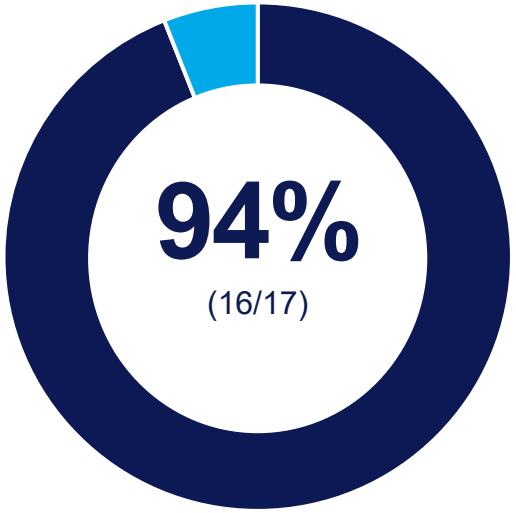
All treated patients
ITT
(N=28)



Patients treated
Per Protocol
(≥ 4 weeks of dosing)
(n=23)



Complete Responders only
(n=17)



IgA Nephropathy (IgAN) Global Overview

IgAN is a chronic progressive disease of the kidney that occurs when immunoglobin A (IgA)-containing immune complexes accumulate in the kidneys

Most common form of primary glomerulo-nephritis globally

10% of patients on dialysis have IgAN

Up to 50% of patients with IgAN develop ESRD and require dialysis[1,2]

60% of IgAN patients with ESRD will receive ≥1 kidney transplant[3,4]

150,000 - 200,000 people with IgAN in US

818,000 people with IgAN in China

160,000 - 200,000 people with IgAN in EU5

130,000 people with IgAN in Japan

No complement-targeting therapy is approved for treatment of IgAN

1. Cattran, Daniel C, et al. “Treatment and Prognosis of IgA Nephropathy.” UpToDate, Wolters Kluwer, https://www.uptodate.com/contents/treatment-and-prognosis-of-iga-nephropathy. 2. McGrogan A, Franssen CF, de Vries CS: The incidence of primary glomerulonephritis worldwide: a systematic review of the literature. Nephrol Dial Transplant 2011; 26: 414–430. 3. KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (Suppl 3): S14–S15. 4. Hastings, M. Colleen, et al. “Life Expectancy for Patients From the Southeastern United States With IgA Nephropathy.” Kidney International Reports, vol. 3, no. 1, 2018, pp. 99–104., doi:10.1016/j.ekir.2017.08.008

Narsoplimab Clinical Program in IgAN

Phase 2 Clinical Trial

- Substudy 1: Narsoplimab in patients receiving corticosteroids
- Substudy 2: Narsoplimab in patients NOT receiving corticosteroids

Phase 3 Clinical Trial: ARTEMIS-IGAN

- A randomized, double-blind, placebo-controlled, study of the safety and efficacy of Narsoplimab in patients with IgAN
- ARTEMIS-IGAN Trial Design agreed to with FDA
  - Primary endpoint – reduction in proteinuria @ 36 weeks, read-out slated for 3Q 2023
  - Patients continue in trial for long-term eGFR data

Potential Advantages of Narsoplimab over Other Complement Inhibitors

- Narsoplimab designed to leave classical and alternative pathways fully functional
  - Leaves the effector function of adaptive immune response intact
  - Maintains antigen-antibody complex-mediated lytic response and killing of microbe-infected cells
  - No evidence of increased infection risk
- In addition to lectin pathway inhibition, narsoplimab has anticoagulation effects
  - Inhibits MASP-2-mediated cleavage of prothrombin to thrombin and activation of factor XII to XIIa, blocking thrombus formation
  - No prolongation of PT, aPTT or bleeding time
  - Inhibits MASP-2 activation of kallikrein

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MASP-3 Inhibitor Program OMS906

Our Innovative Inhibitors Selectively Target the Key Activators of the Complement System's Lectin and Alternative Pathways

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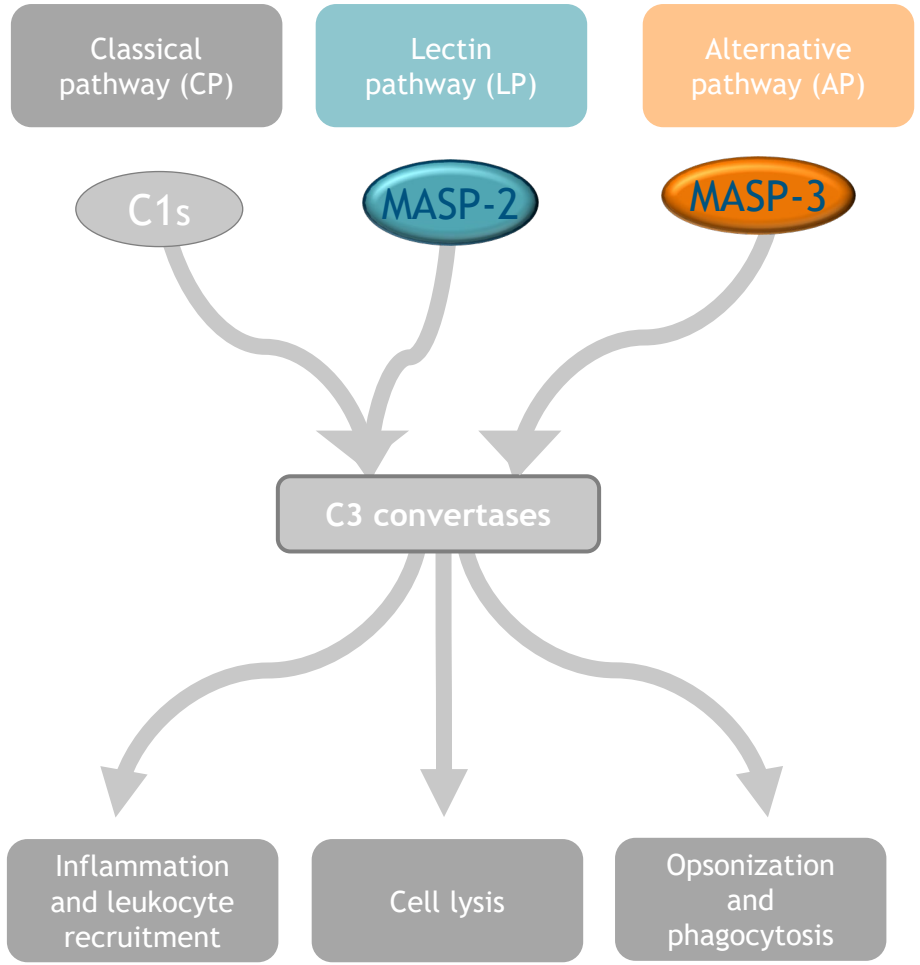

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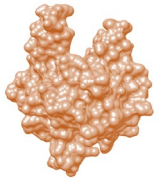

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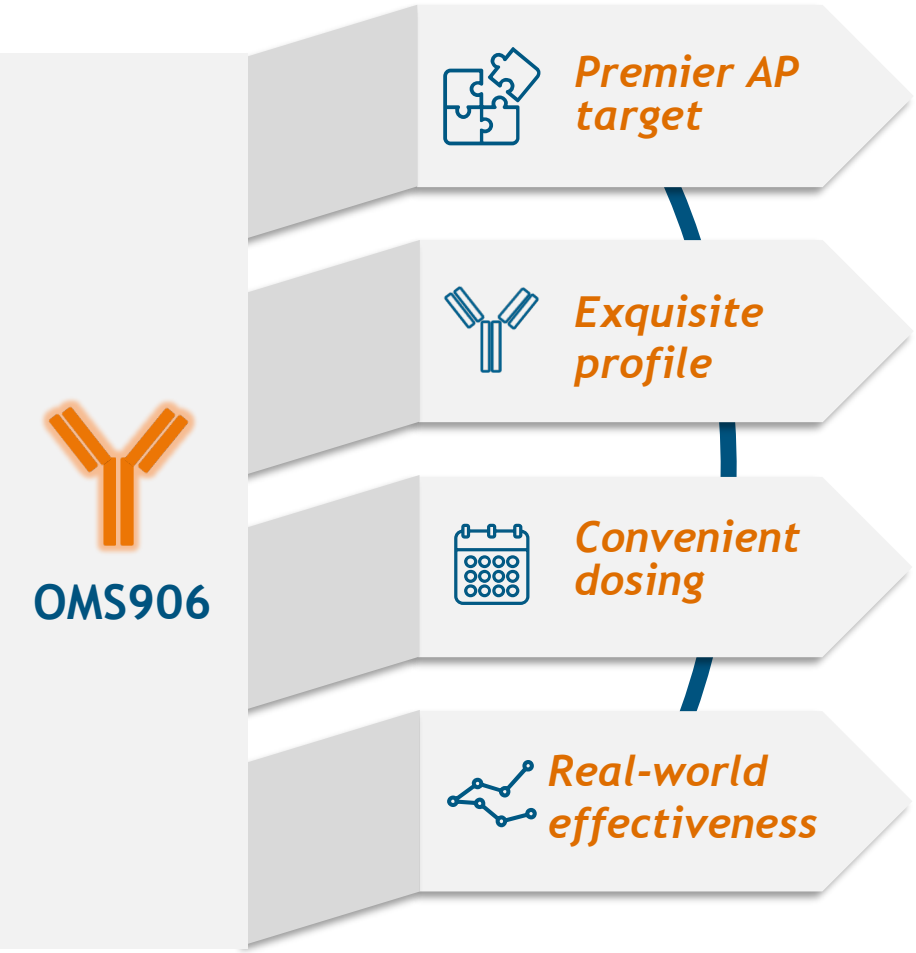
Source: Dunkelberger, J et al. *Nat. Cell Biol.* 2010

OMS906 Is an Ideal Therapeutic for Targeting MASP-3 and AP-Associated Indications



Favorable target properties, dynamics and **preserved lytic function** of the CP should enable better disease control and reduced adverse events

Long-acting, highly specific mAb ensures a consistent and favorable PK profile and, relative to small-molecule AP inhibitors, reduces the risk of off-target effects

Convenient dosing (once quarterly IV or SC) is designed to drive **favorable adherence, reducing risk** of **breakthrough disease***

Expected to provide **superior efficacy** and **safety** in **real-world settings**

Notes: *Short half-life agents can have dramatic breakthrough disease
Source: Castelli, M. et al. *Pharmacol. res. Perspect.* 2019; Shepard, M. et al. *Clin. Med. (Lond).* 2017; Notaro, R. *N. Engl. J. Med.* 2022

OMS906: A First-in-Class, Potent and Selective Inhibitor of MASP-3, Is Expected to Provide Superior Efficacy and Safety in Real-World Settings

TARGETING MASP-3 HAS ADVANTAGES OVER OTHER CLINICALLY VALIDATED COMPLEMENT TARGETS

By targeting MASP-3,
OMS906 is designed to provide…

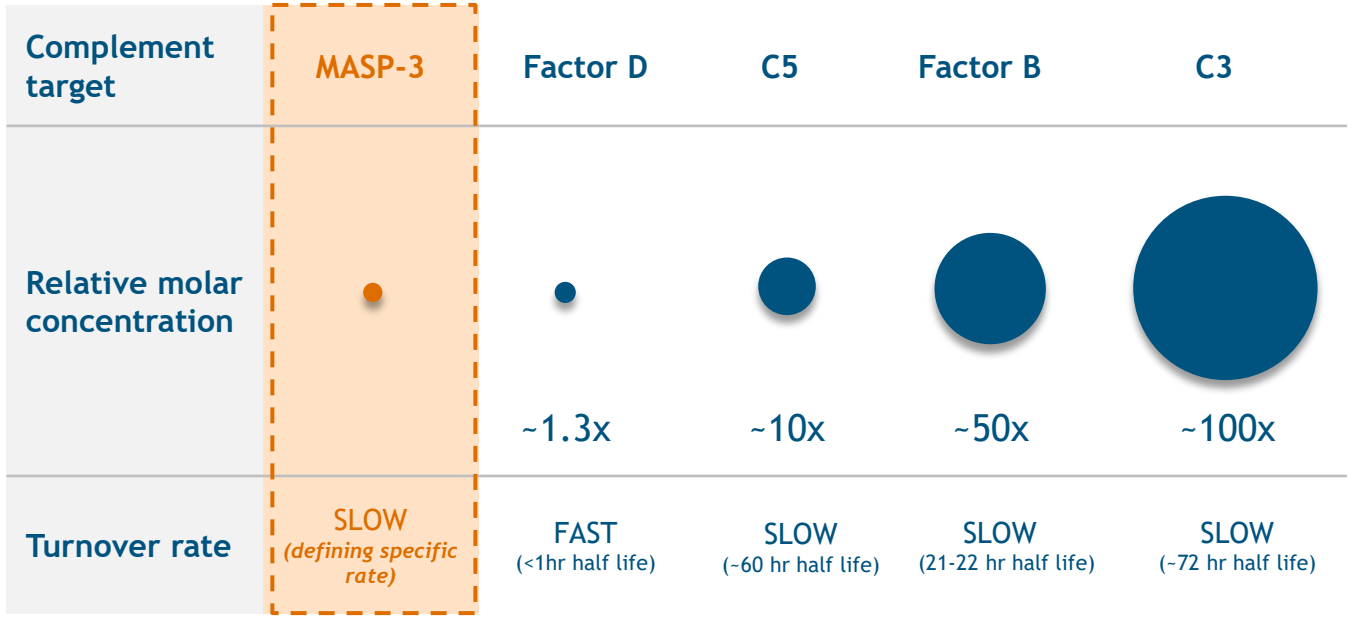
	Rationale	MASP-3	Factor D	Factor B	C3	C5a	C5
		Alternative Pathway				Terminal Pathway	
BETTER disease control	**Favorable resting target properties** *MASP-3 has lower plasma concentrations and slower turnover, allowing a longer/more consistent dosing profile — resulting in lower risk of PK/PD breakthrough*	✓	✗	✗	✗	✗	✗
	Favorable target dynamics *Based on available data, MASP-3 is not an acute phase reactant, which is important for chronic disease treatment in the setting of inflammation (e.g., infection)*	✓	✓	✗	✗	✗	✗
LOWER RISK of adverse events	**Preserves complement's lytic function** *Classical, lectin, and terminal pathway functions retained to mount appropriate response to infection*	✓	✓	✓	✗	✓	✗
BETTER adherence	**Designed for convenience** *The dosing amount and frequency should improve patient adherence*	✓	✗	✗	✗	✗	✓*

Note: *Ravulizumab (Q8W regimen), but not eculizumab (Q2W regimen), has convenient dosing

MASP-3 Has Inherent Advantages over Other AP and Terminal Pathway Targets, Reducing Risk of Breakthrough Disease

RELATIVE CONCENTRATION AND TURNOVER RATE OF COMPLEMENT TARGETS IN SERUM / PLASMA

Indexed to MASP-3 molar concentration



MASP-3 is a **superior therapeutic target** with low native circulating concentration and slow turnover

Other AP and TP targets face **high target burden** (Factor B, C3, C5) or **fast turnover** rate (Factor D), necessitating **frequent** or **large doses**

MASP-3 is not an acute phase reactant, **reducing risk of breakthrough — long-acting OMS906** ensures a consistent and favorable PK profile, further reducing that risk

Additionally, **highly specific mAb OMS906** reduces risk of off-target effects

Source: Dobo, J. et. al. *Front. Immunol.* 2018; Pascual, M. et al. *KI.* 1988; Bereman, M. et al. *Anal. Bioanal. Chem.* 2012; Ekdahl, K. et al. *Mol. Immunol.* 2019; Sissons JG, Liebowitch J, Amos N, Peters DK. Metabolism of the fifth component of complement, and its relation to metabolism of the third component, in patients with complement activation. *J Clin Invest.* 1977; Bokisch, V. et al. *Proc. Natl. Acad. Sci. USA.* 1975; Skjoedt, M. et al. *Immunobiology* 2010; Barratt, J. et al. *Front. Immunol.* 2021; Schnabolk, G. et al. *Investig. Ophthalmol.* Vis. Sci. 2015; Yuhong, S. et al. *Investig. Ophthalmol. Vis. Sci.* 2017; Andoh, A. et al. *J. Clin. Immunol.* 1997

Ongoing Trials in PNH and C3G Are Expected Soon to Provide Early Safety and Efficacy Evidence In High-Unmet-Need Patients

OMS906 CLINICAL TRIAL DESIGNS IN PNH AND C3G

	PNH		C3G
Study #	1	2	3
Population	Patients with inadequate response to C5 inhibitor (ravulizumab)	Naïve patients or patients who are poor responders to C5 inhibitor	Naïve patients or poor responders to current treatment
Study design	Single-arm sequential-dose cohorts	Single-arm	Single-arm
Estimated enrollment (N)	Up to 12 patients	Up to 10 patients	Up to 10 patients
Cohorts	**2 cohorts:** IV	**1 cohort:** SC	**1 cohort:** SC

OMS906 Has a Validated and Efficient Development Pathway in PNH, C3G, and Beyond

OMS906 POTENTIAL INDICATIONS

Initiated Clinical Development

PNH*

C3G

*Potential Follow-on Indications***

Age-related macular degeneration

Lupus nephritis

Atypical hemolytic uremic syndrome

IgA nephropathy

Sickle cell disease

Rheumatoid arthritis

Likely orphan condition

Notes: *OMS906 has received orphan drug designation for paroxysmal nocturnal hemoglobinuria (PNH) from FDA; **Not exhaustive

OMS906, a First-in-Class, Potent and Selective Inhibitor of MASP-3, Is the Complete Package for Treating AP-Associated Diseases

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OMS906 VALUE PROPOSITION:

- *Targeting the AP is a de-risked CLINICALLY VALIDATED APPROACH to address diseases with AP involvement*
- *Targeting MASP-3 has MEANINGFUL ADVANTAGES over other AP targets, including lower risk of adverse events and breakthrough disease*
- *MASP-3 inhibition should provide BETTER DISEASE CONTROL in real-world settings over other efficacious AP inhibitors*
- *OMS906 is an EXCEPTIONAL THERAPEUTIC for targeting MASP-3 and AP-associated indications*
- *OMS906 has an achievable DEVELOPMENT PATHWAY in orphan indications; clinical development has been initiated in C3G and PNH*