

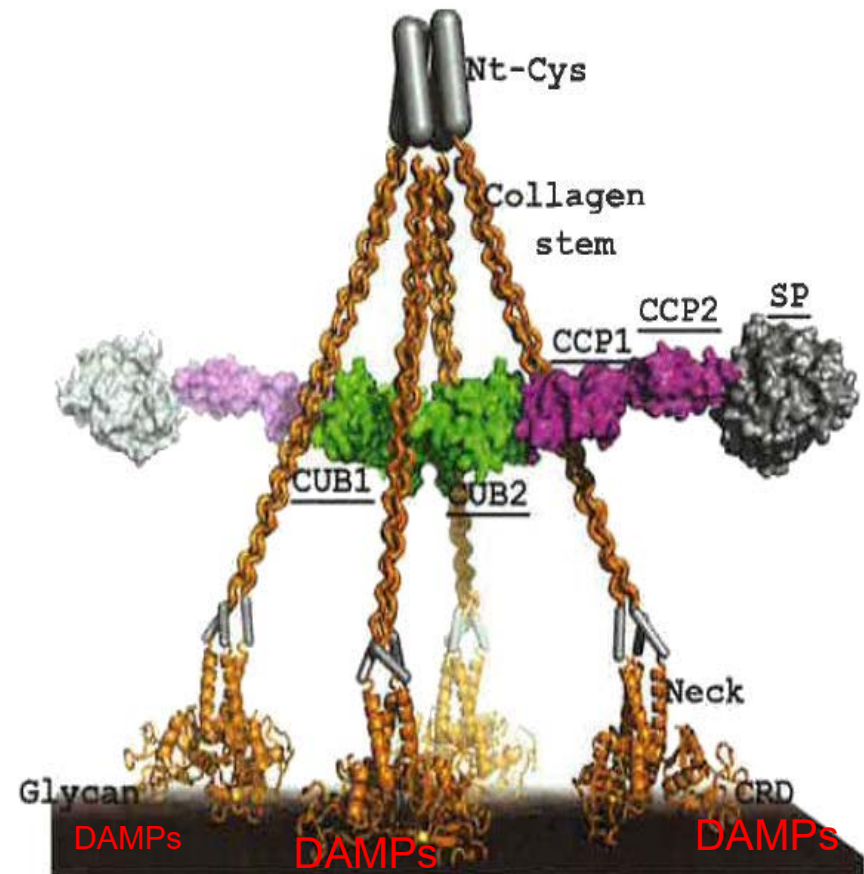


OMS906: Monoclonal Antibody Targeting MASP-3

October 2020

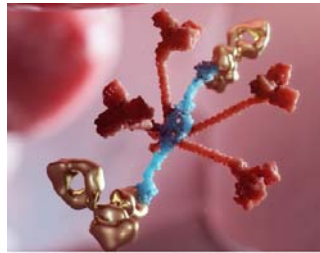
Lectin and Alternative Pathway Activation

- “MBL-associated serine proteases”
- Three MASPs can form complexes with five possible pattern recognition molecules
- Serine protease with pattern binding potential
- Lectins, via carbohydrate recognition domains (CRD), bind molecular patterns on microbes or damaged/altered host tissue
- Inhibitors expected to have broad applications in conditions involving inflammation and tissue damage



Targeting MASP Proteins

MASP Inhibitory MAb Programs



MASP-2 Inhibitor

- Narsoplimab

LECTIN
PATHWAY



Blocked Upstream

MASP-3 Inhibitor

- OMS906

ALTERNATIVE
PATHWAY



Blocked Upstream

The MASP inhibitor approach
preserves classical pathway
function

CLASSICAL
PATHWAY



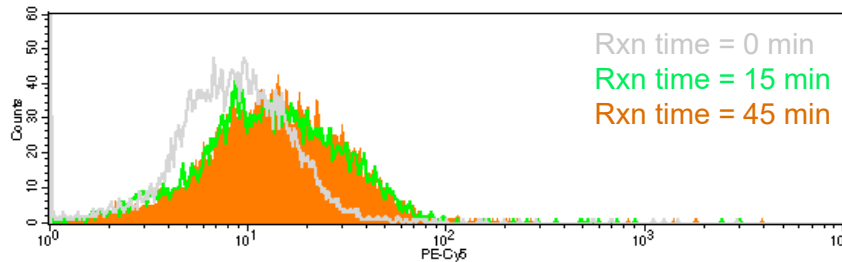
Intact

Role of MASP-3 in AP Activity of Human

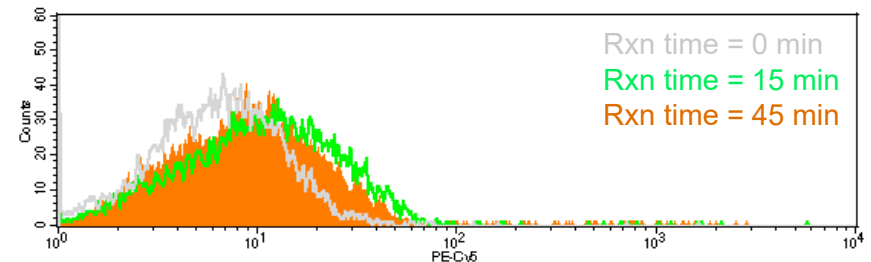


MASP-3 Deficient Individual

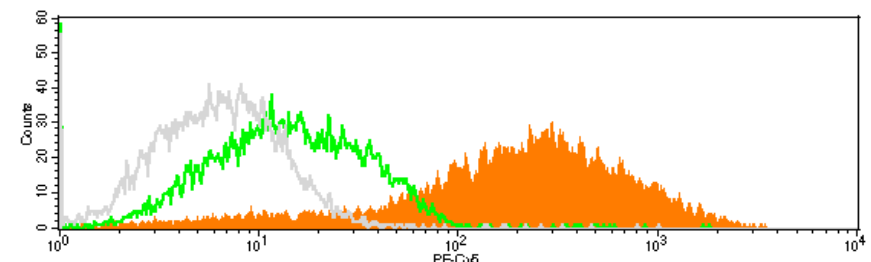
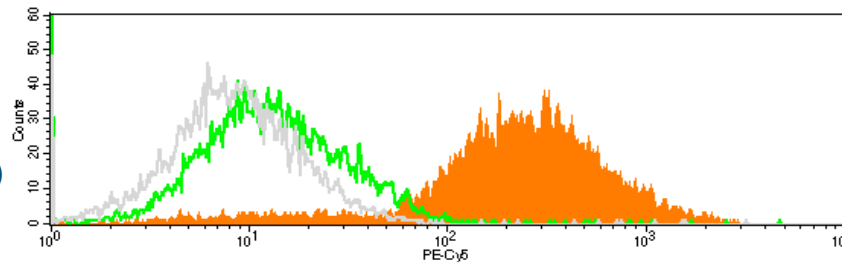
No
protein



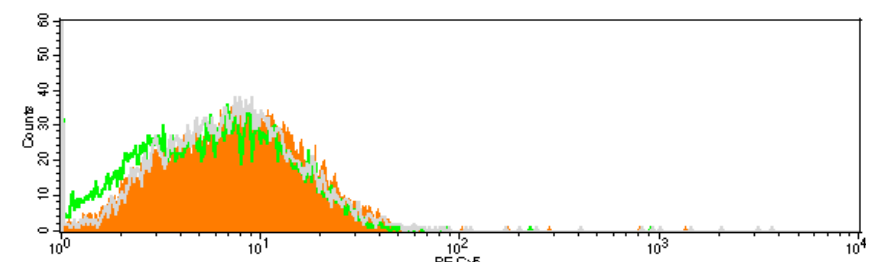
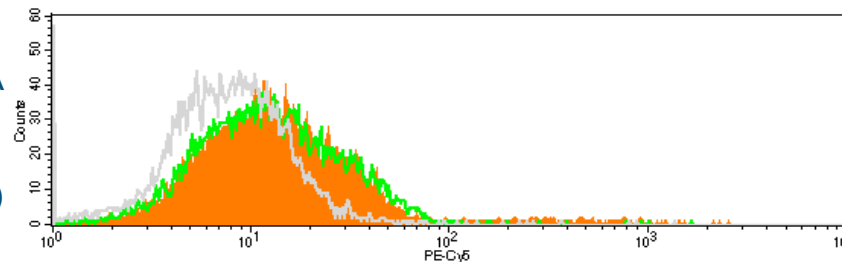
MASP-1/3 Deficient Individual



+
rMASP-3
(full-length)

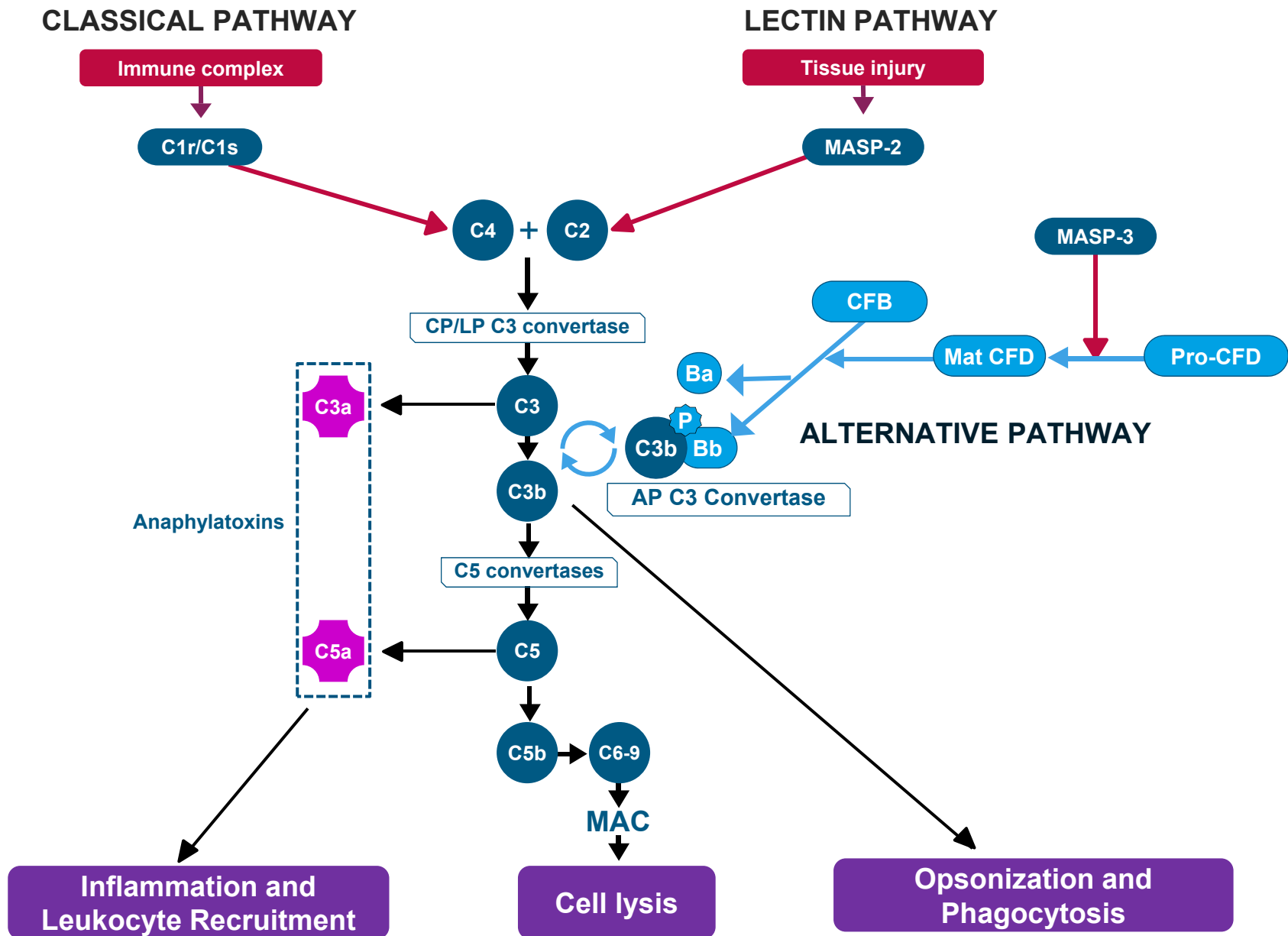


+
rMASP-3A
(catalytic
mutant;
full-length)

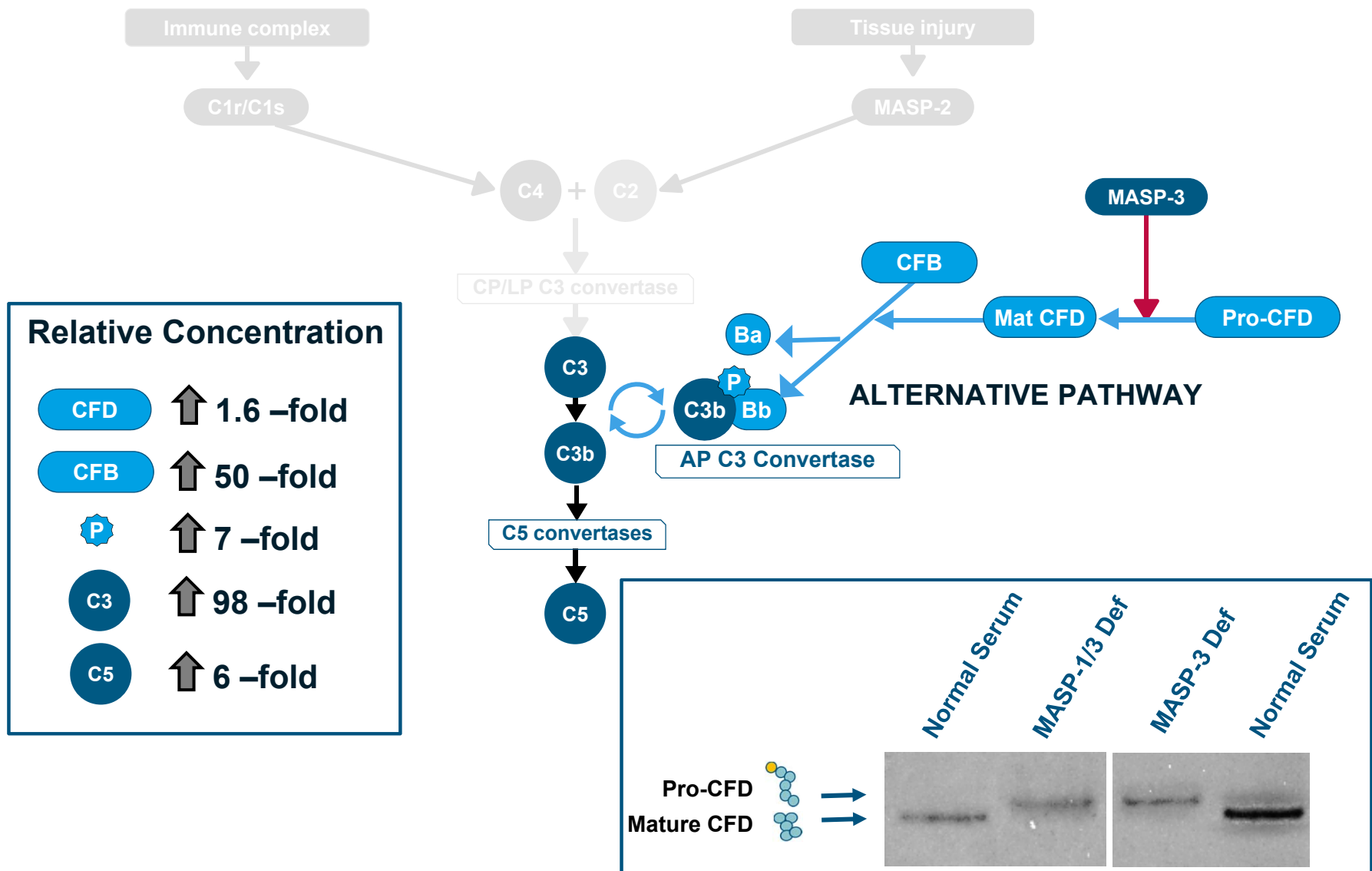


Presence of MASP-3 is required to drive AP in human serum

Three Pathways of Complement



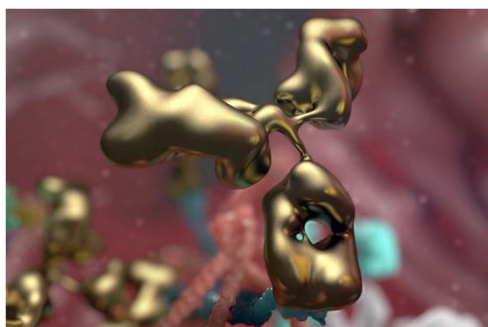
Three Pathways of Complement



Properties of OMS906



OMS906



Humanized monoclonal antibody **highly potent** and **selective** for MASP-3

Infrequent SubQ Administration



Convenient dosing regimen allows self-administration in an **outpatient setting**



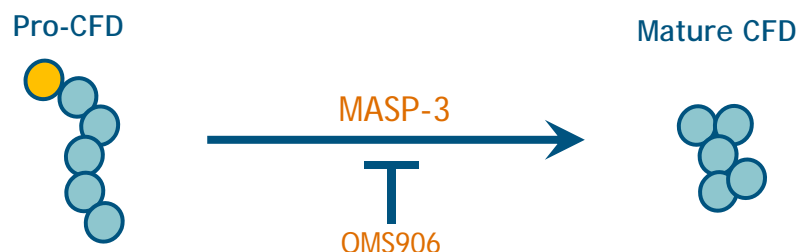
OMS906 is designed to treat multiple alternative pathway-driven diseases with infrequent, SubQ delivery

Phase 1 clinical trial initiated **3Q 2020**

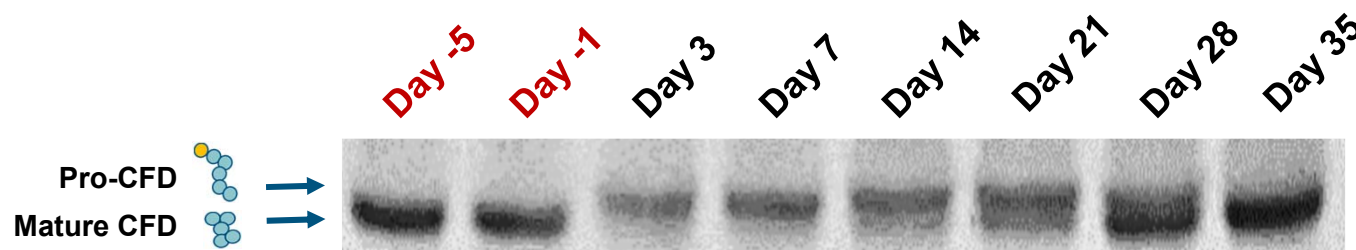
Analysis of CFD Status in a Treated Monkey



CFD is matured by cleavage and release of activation peptide on the N-terminus of the protein



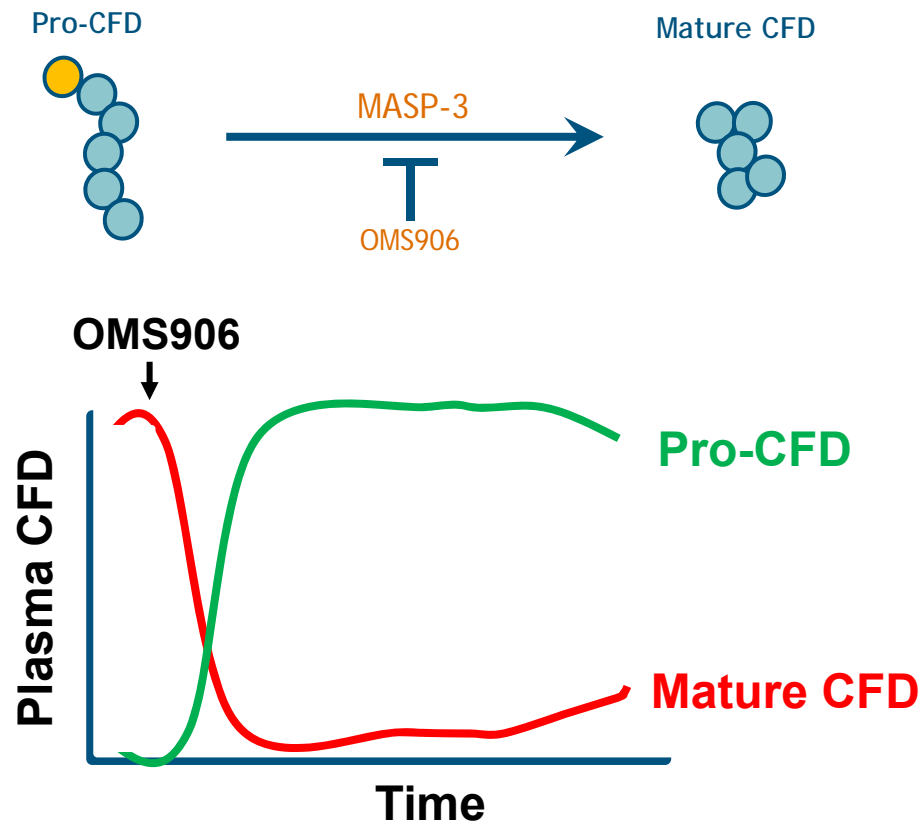
IP Ab: α CFD > Western Blot



CFD is present in plasma as pro-CFD following single dose of OMS906

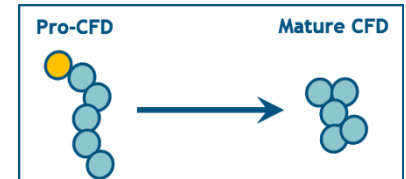
Measurement of CFD Status

CFD is matured by cleavage and release of activation peptide on the N-terminus of the protein

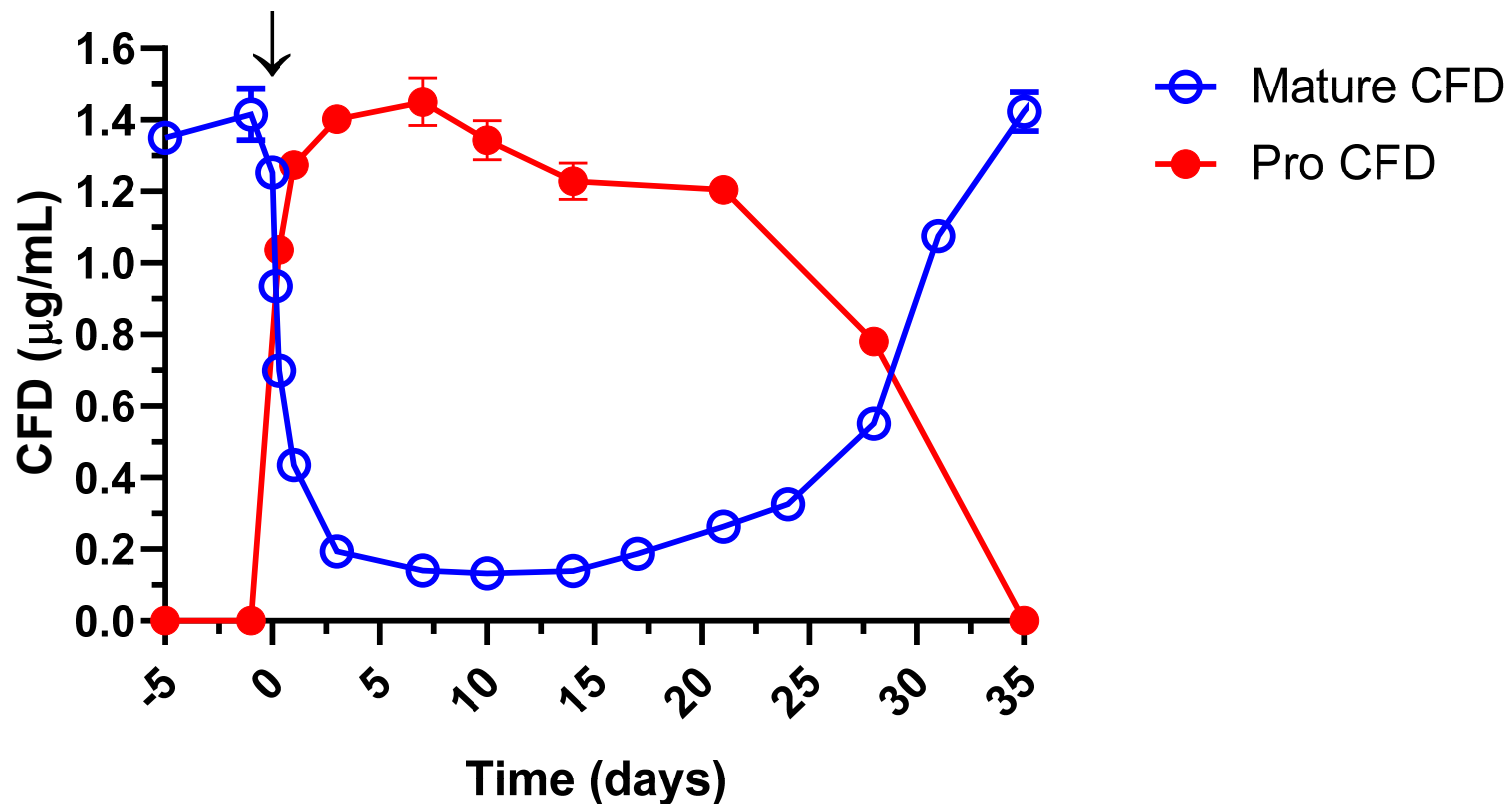


CFD status (pro vs. mature) can be used as direct measurement of MASP-3 inhibition

Measurement of CFD Status

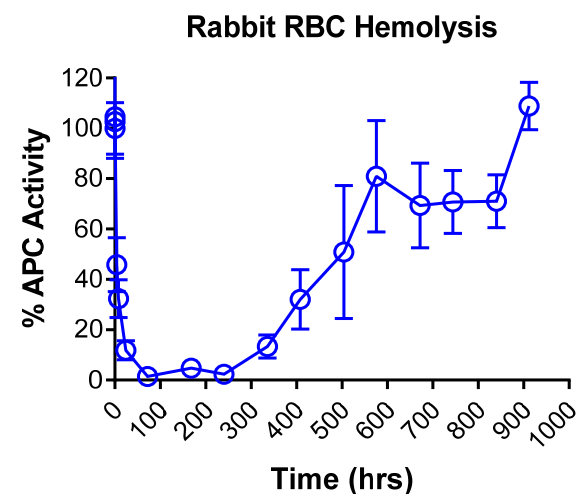
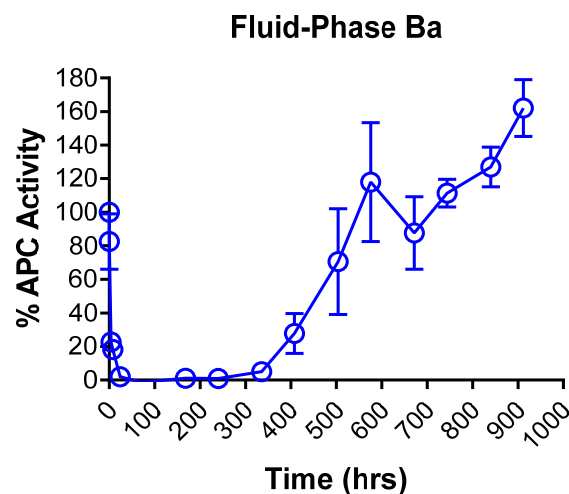
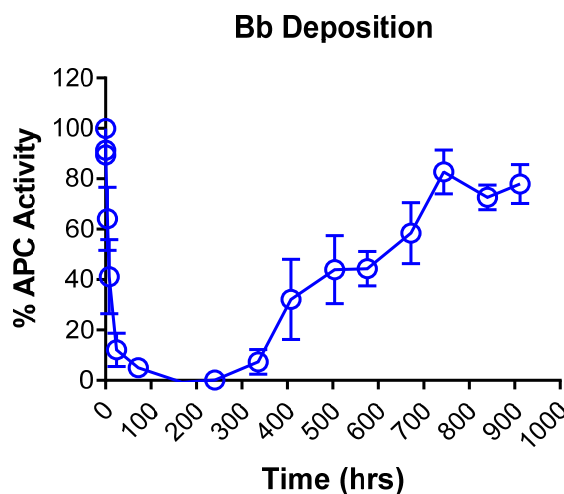


Single-Dose Monkey Study



OMS906 blocks systemic maturation of CFD and results in accumulation of Pro-CFD

Inhibition of the Alternative Pathway in Monkey



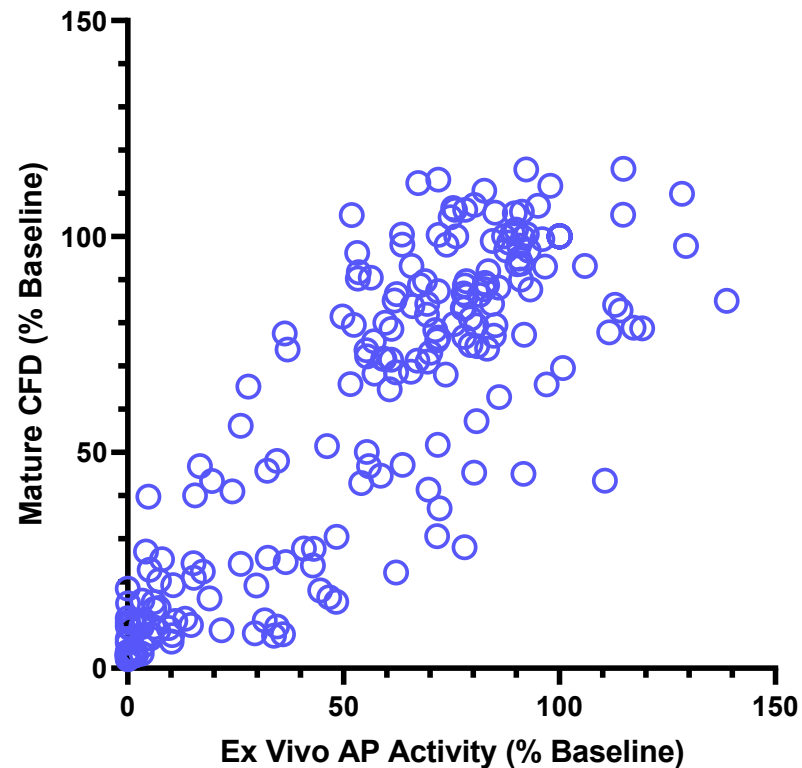
Number of Days of $\geq 90\%$ Alternative Pathway Inhibition

Bb Deposition on Zymosan	Fluid-Phase Ba	Hemolysis of Rabbit RBCs
13	14	12

Single dose is sufficient for sustained inhibition of the Alternative Pathway in monkey

Relationship of CFD Status with Activity

Mature CFD vs. AP Activity



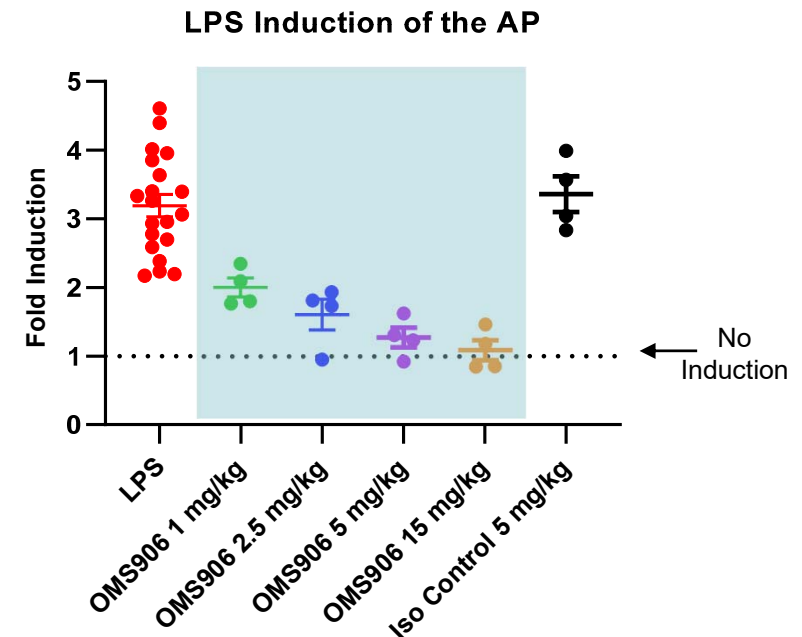
Lowest levels of detectable mature CFD correlate with complete inactivation of the AP

Demonstration of Efficacy in Mouse Disease Models



■ *In vivo* induction of AP with LPS

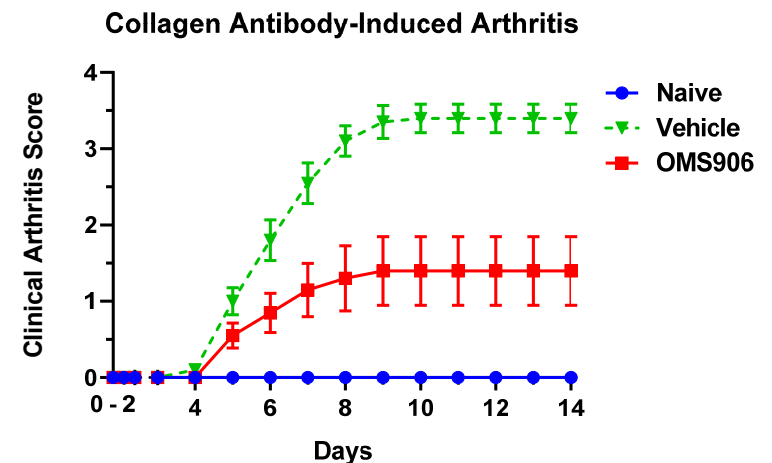
- OMS906 decreases systemic Ba levels caused by LPS injection into mice



■ Collagen antibody-induced arthritis (CAIA) model

- OMS906 decreases severity (and incidence) of arthritis

Systemic inhibition of CFD maturation is sufficient to block *in vivo* AP



OMS906 Potential in Paroxysmal Nocturnal Hemoglobinuria

Paroxysmal Nocturnal Hemoglobinuria (PNH) is a Rare, Chronic, Life-Threatening Complement-Mediated Blood Disorder



PNH is characterized by intravascular and extravascular hemolysis



Unmet Need Persists

~70%

of PNH patients continue to have
low hemoglobin levels while on a C5 inhibitor^{1,2}

~1/3

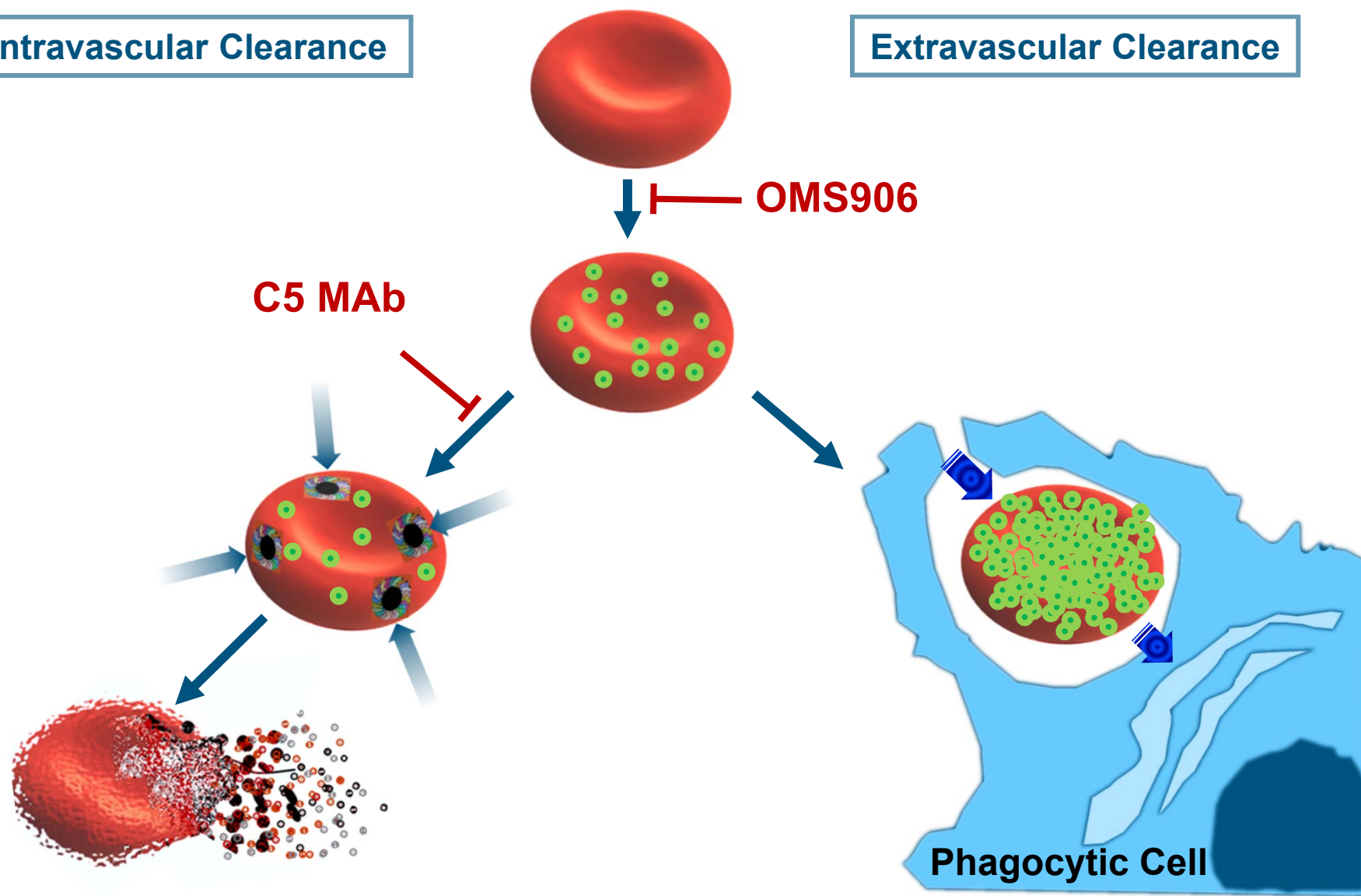
of PNH patients require
one or more transfusions a year while on a C5 inhibitor³

1. Risitano AM, Marotta S, Ricci P, et al. (2019) Anti-complement Treatment for Paroxysmal Nocturnal Hemoglobinuria: Time for Proximal Complement Inhibition? A Position Paper From the SAAWP of the EBMT. Front. Immunol. 10:1157. doi: 10.3389/fimmu.2019.01157. 2. Risitano AM, Notaro R, Marando L, et al. (2009) Complement fraction 3 binding on erythrocytes as additional mechanism of disease in paroxysmal nocturnal hemoglobinuria patients treated by eculizumab. Blood. 2009 Apr 23;113(17):4094-100. 3. McKinley C. Extravascular Hemolysis Due to C3-Loading in Patients with PNH Treated with Eculizumab: Defining the Clinical Syndrome. Blood. 2017;130:3471.

Red Blood Cell Clearance in PNH

Intravascular Clearance

Extravascular Clearance



Demonstration of Efficacy in PNH Models

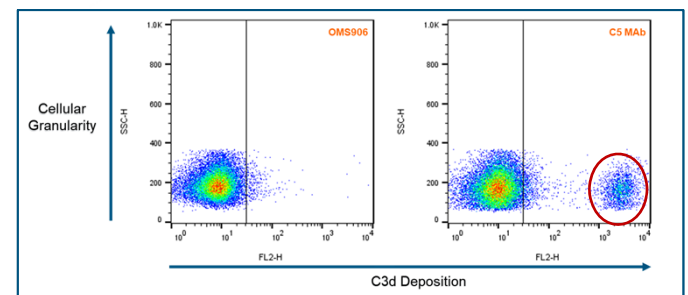
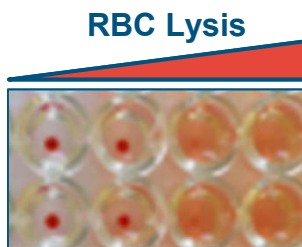
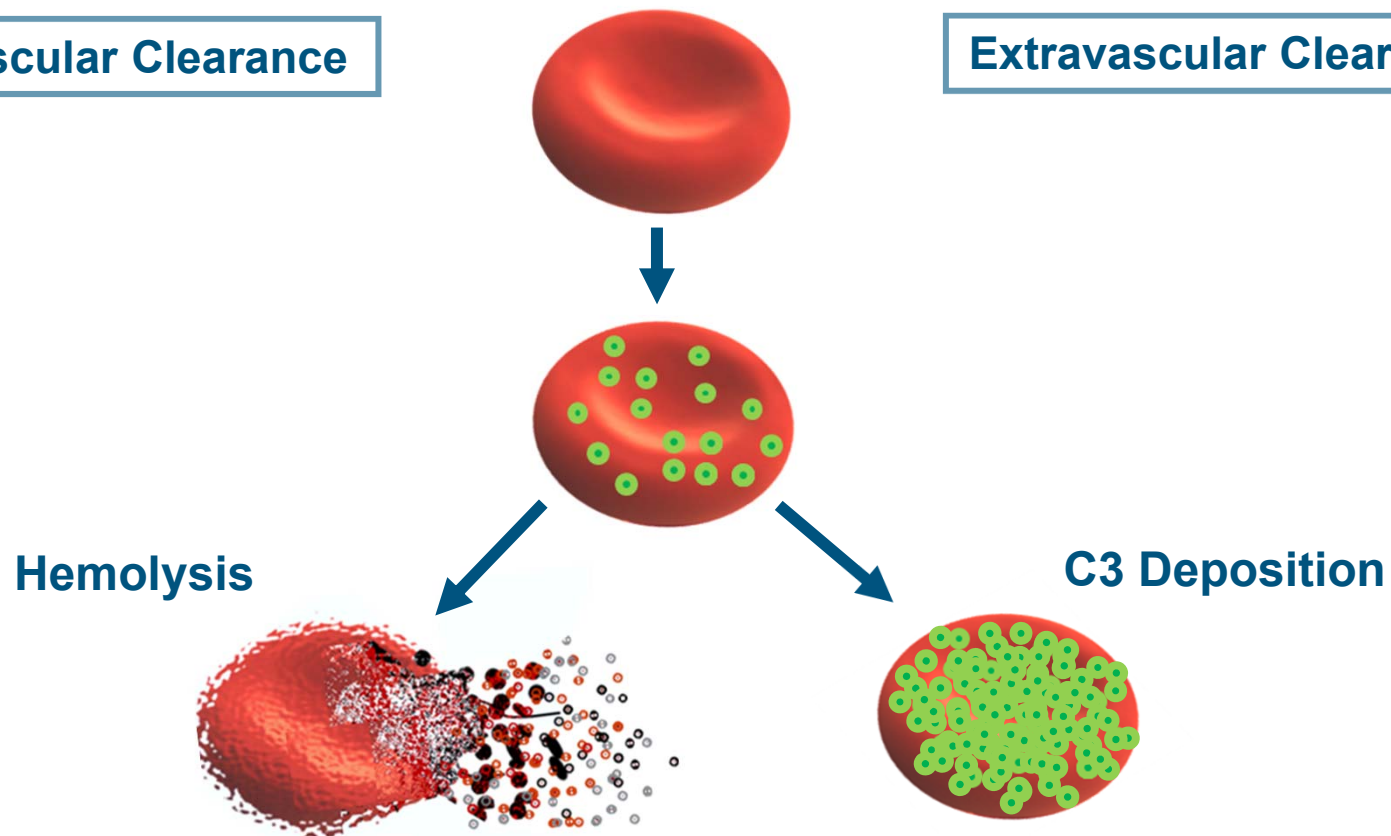
- *In vitro* destruction of human “PNH-like RBCs” (sensitized with α CD55/59 Abs)
 - Hemolysis
 - Opsonization (C3b/iC3b and C3d deposition)

- *In vivo* clearance of RBCs (Crry-/- mouse RBCs)
 - Primarily model of extravascular pathway of clearance

Red Blood Cell Clearance in PNH

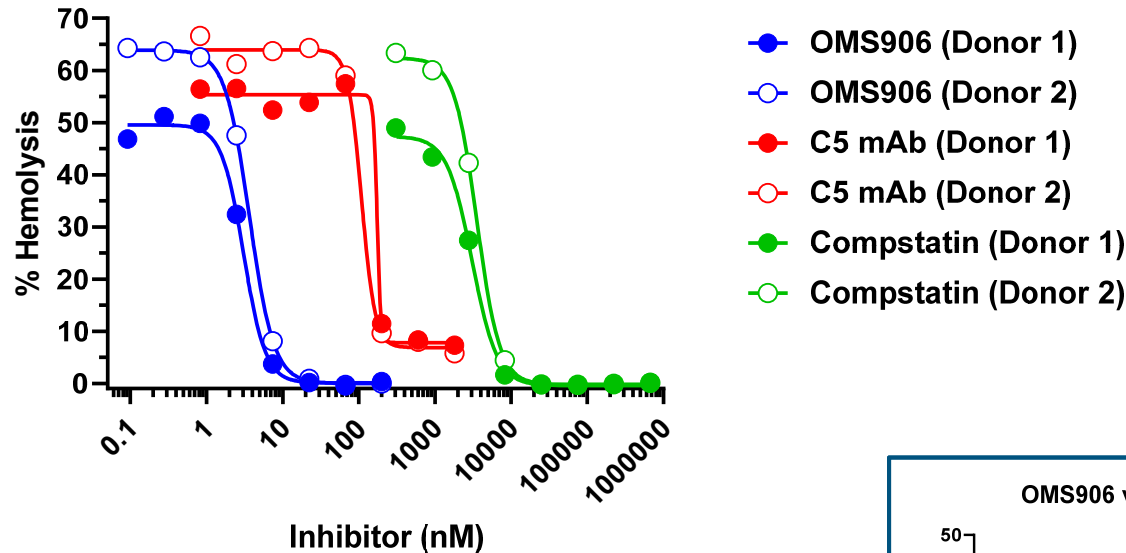
Intravascular Clearance

Extravascular Clearance

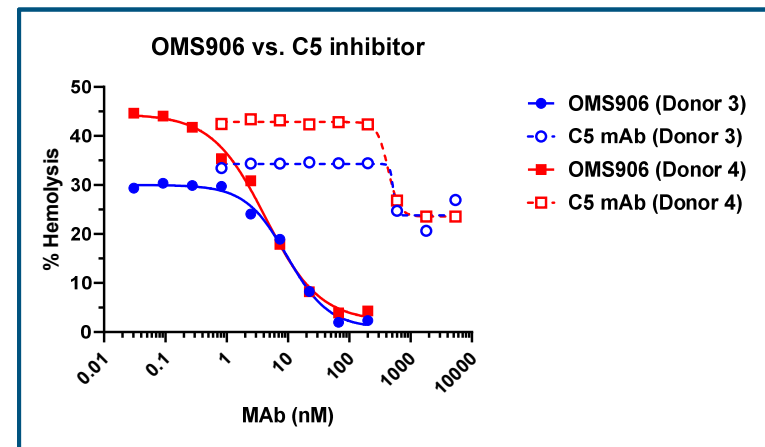


Model of Intravascular Lysis of PNH RBCs: Comparison with C3 and C5 Inhibitor

OMS906 vs. C5 and C3 Inhibitors

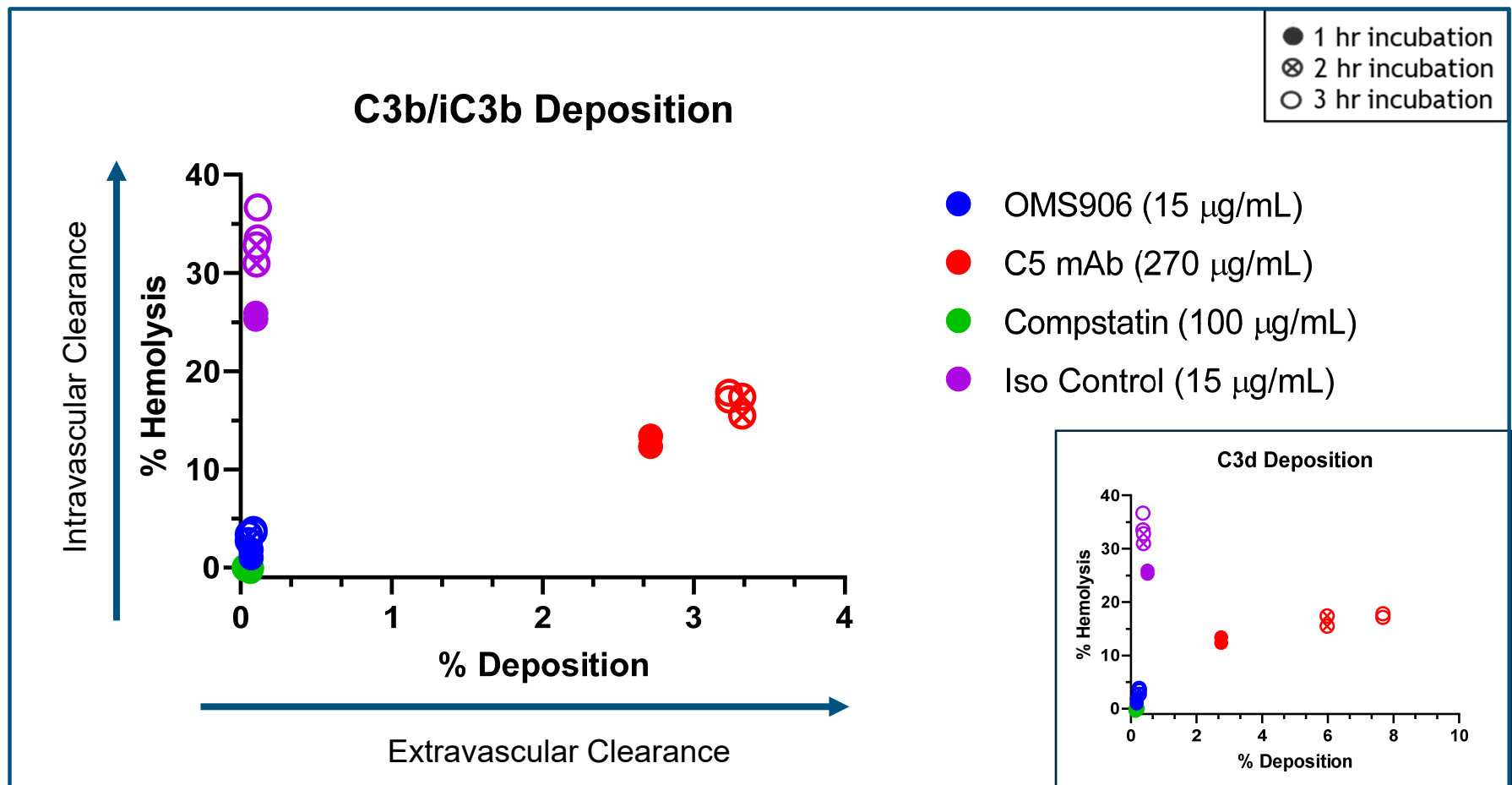


	C5 MAb	Compstatin
Relative OMS906 Potency	~30-fold	~1000-fold



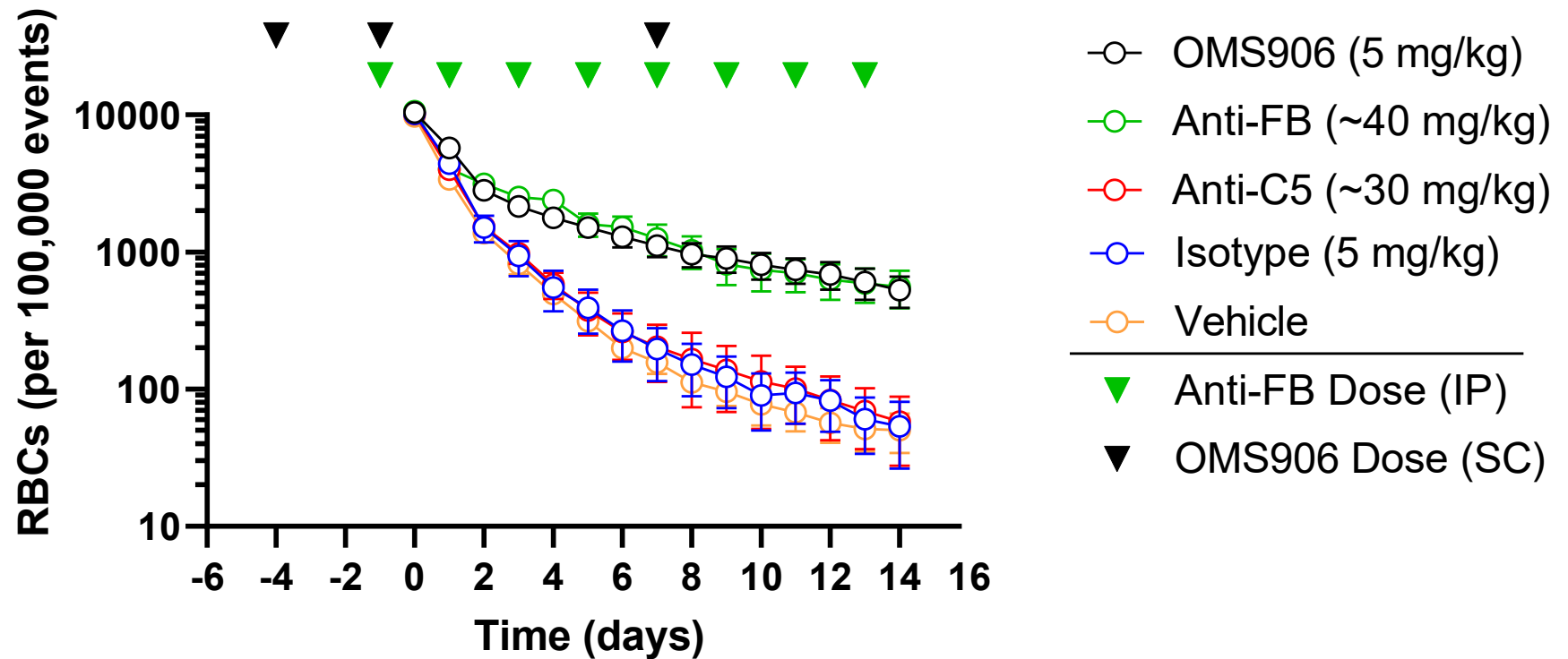
OMS906 demonstrates greater potency and greater degree of pathway inhibition than C5 mAb

Comparison to C3 and C5 Inhibition for PNH



OMS906 blocks a shared step in both pathways of PNH RBC clearance.

Crry^{-/-} RBC Survival



- Potent inhibition of the alternative pathway
- Classical pathway left intact
- Treats both intravascular and extravascular hemolysis
- Broad applications in conditions involving inflammation and tissue damage
- Phase 1 (SAD/MAD) clinical program enrolling
- Targeting monthly subcutaneous dosing

Omeros

Yi Li

Kathy Shaffer

Thomas Dudler

Munehisa Yabuki

Jeremy Freeman

Heidi Utsugi

John Atkinson

jcummings@omeros.com

