

OMS906, a Mannan-Binding Lectin-Associated Serine Protease-3 (MASP-3) Inhibitor, Normalizes Hemoglobin Levels in Treatment-Naïve PNH Patients: Interim Data From a Proof-of-Concept Clinical Trial

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- **EG:** Consultancy – Astra Zeneca, Novartis, and Omeros Corporation.
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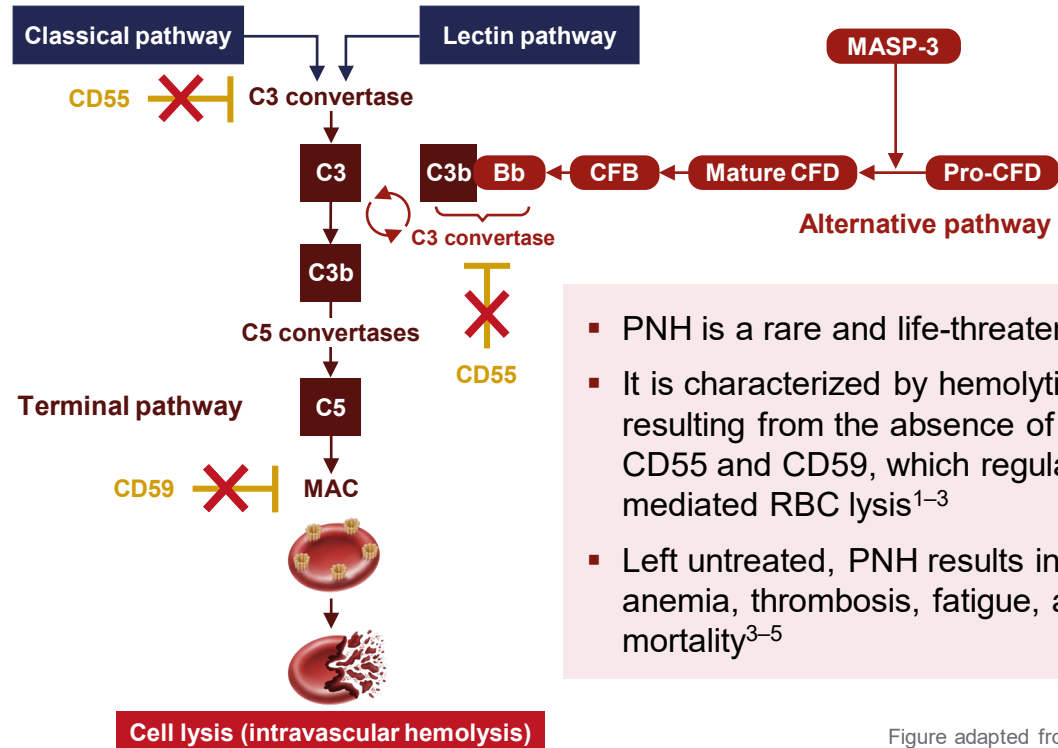
DISCLAIMER

- OMS906 is an investigational agent and has not been approved by any regulatory agency



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Clinical Presentation of PNH is Driven by Intravascular Hemolysis due to Dysregulation of the Complement System



- PNH is a rare and life-threatening disorder¹⁻³
- It is characterized by hemolytic anemia resulting from the absence of surface proteins CD55 and CD59, which regulate complement-mediated RBC lysis¹⁻³
- Left untreated, PNH results in debilitating anemia, thrombosis, fatigue, and increased mortality³⁻⁵

Figure adapted from Belcher *et al.* (2022)⁶

CFB, complement Factor B; CFD, complement Factor D; MAC, membrane attack complex; MASP-3, mannan-binding lectin-associated serine protease-3; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell.

1. Risitano AM *et al.* *Front Immunol.* 2019;10:1157. 2. Notaro R *et al.* *N Engl J Med.* 2022;387:160-6. 3. Risitano AM *et al.* *Immunol Rev.* 2023;313:262-78.

4. Loschi M *et al.* *Am J Hematol.* 2016;91:366-70. 5. Fattizzo B *et al.* *J Blood Med.* 2022;13:327-35. 6. Belcher JD *et al.* *Transl Res.* 2022;249:1-12.

Terminal Complement Inhibition in PNH Inhibits Intravascular Hemolysis but Inevitably Leads to Extravascular Hemolysis^{1,2}

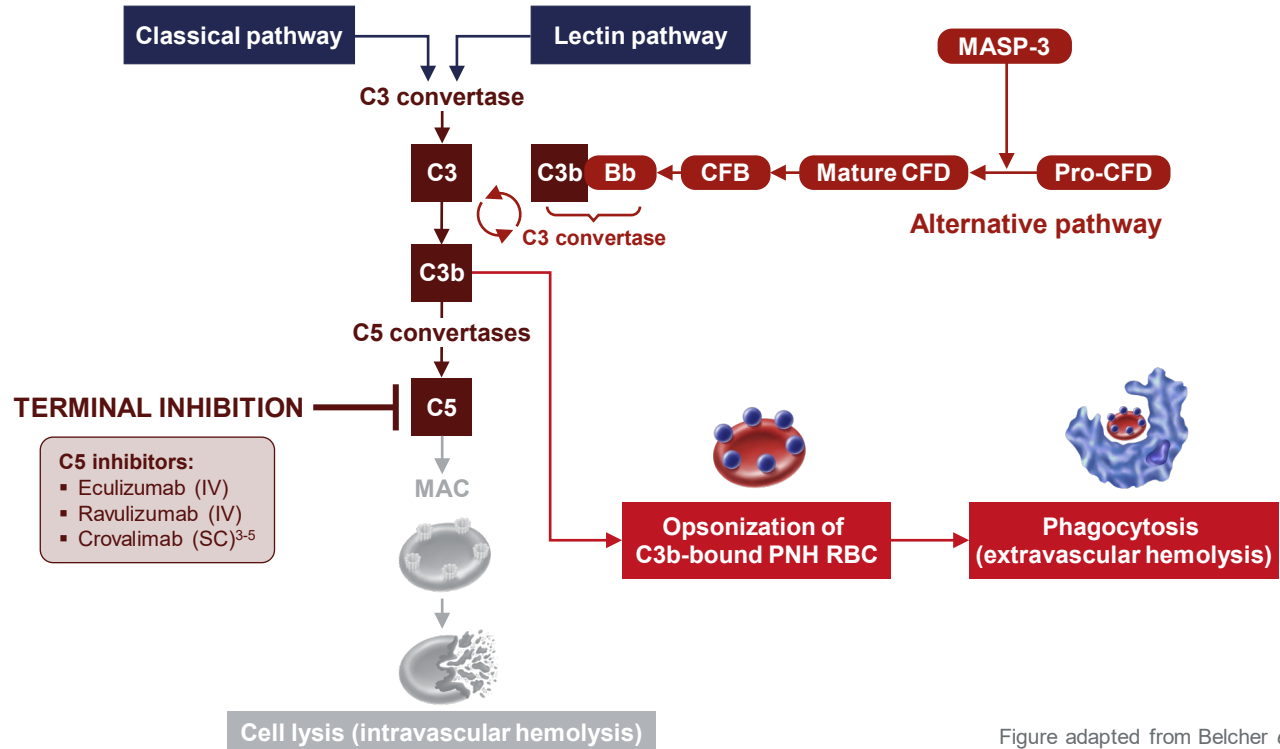


Figure adapted from Belcher *et al.* (2022)⁶

CFB, complement Factor B; CFD, complement Factor D; IV, intravenous; MAC, membrane attack complex; MASP-3, mannan-binding lectin-associated serine protease-3; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; SC, subcutaneous.

1. Notaro R *et al.* *N Engl J Med.* 2022;387:160–6.
2. Risitano AM *et al.* *Immunol Rev.* 2023;313:262–78.
3. Röth A *et al.* *HemaSphere* 2023;7(S3):S181.
4. Kulasekararaj A *et al.* *HemaSphere* 2023;7(S3):S183.
5. Chang A *et al.* *HemaSphere* 2023;7(S3):P785.
6. Belcher JD *et al.* *Transl Res.* 2022;249:1–12.

MASP-3 is a Key Activator of the Alternative Pathway and a Novel Target for Treatment of PNH^{1,2}

- MASP-3 is the exclusive activator of pro-CFD, thereby continuously generating mature CFD¹
- Inhibition of MASP-3 blocks the entire alternative pathway, including CFD, CFB, and C3¹

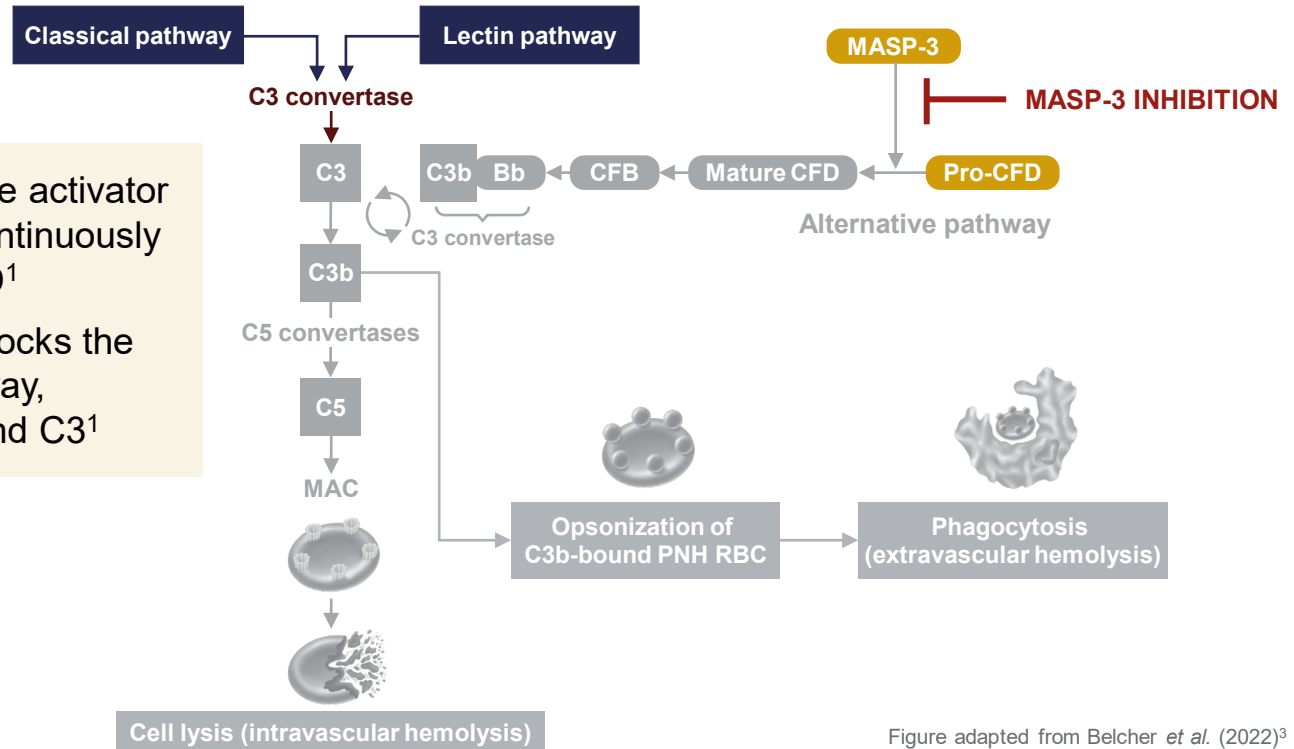
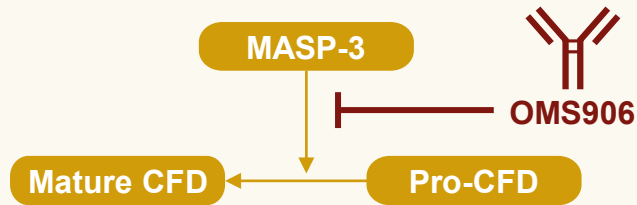


Figure adapted from Belcher *et al.* (2022)³

CFB, complement Factor B; CFD, complement Factor D; MAC, membrane attack complex; MASP-3, mannan-binding lectin-associated serine protease-3; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; SC, subcutaneous.

1. Sekine H *et al. Immunol Rev.* 2023;313:15–24. 2. Barratt J, Weitz I. *Front Immunol.* 2021;12:712572. 3. Belcher JD *et al. Transl Res.* 2022;249:1–12.

OMS906 Selectively Targets MASP-3



- OMS906 is a highly selective humanized IgG4 mAb that binds to and inhibits MASP-3^{1,2}
- It can be administered SC or IV:²
 - T_{1/2} (geometric mean): 239–406 h (SC)
 - T_{1/2} (geometric mean): 94–399 h (IV)
- In a Phase 1 study in healthy subjects, OMS906 was well tolerated, with 5 mg/kg SC providing substantial MASP-3 inhibition through Day 42²

- For further information on OMS906 in healthy subjects, please see EHA Poster P787 or scan the below QR code:

Alternative Pathway MASP-3 Inhibitor OMS906: Results From a First-in- Man Phase 1 Study in Healthy Subjects and Study Design of Two Ongoing Clinical Trials in Patients With PNH

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OBJECTIVE

To demonstrate that suppression of mature CFD with OMS906 in a Phase 1 study provides scientific rationale for evaluating MASP-3 inhibition for the treatment of PNH

CONCLUSIONS

- In this Phase 1 study of healthy subjects, MASP-3 inhibitor OMS906 was well tolerated with no safety concerns
- OMS906 PK and PD profiles showed predictable systemic exposure, evidence of MASP-3 inhibition, and a long duration of action
- In PNH, targeting the alternative pathway via MASP-3 inhibition is predicted to block intravascular hemolysis and prevent extravascular hemolysis caused by CS inhibitors
- Two ongoing open-label clinical trials are currently evaluating OMS906 in adults with PNH (EudraCT numbers: 2021.000930.3.1, 2022.002405.0.2)



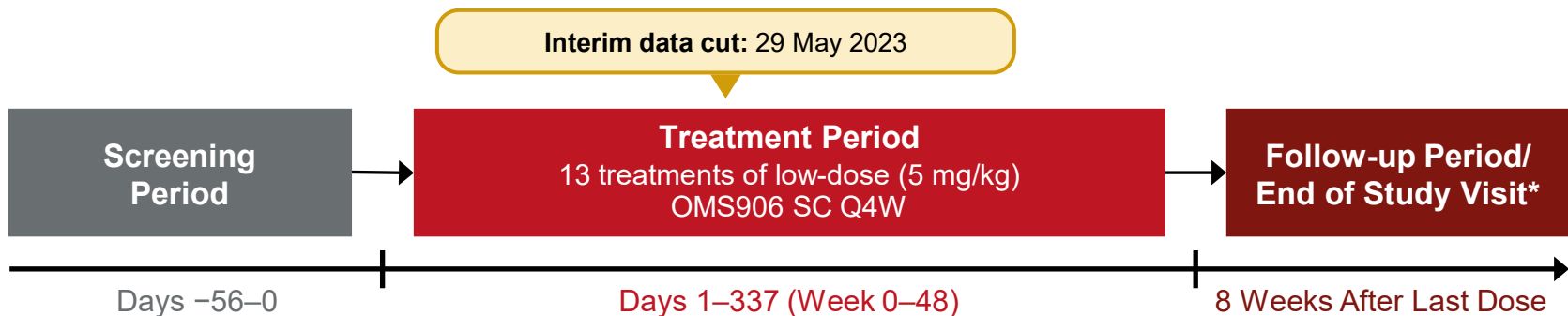
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IgG, immunoglobulin G; IV, intravenous; mAb, monoclonal antibody; MASP-3, mannan-binding lectin-associated serine protease 3; QR, quick response; SC, subcutaneous; T_{1/2}, terminal elimination half-life.

1. Cummings WJ *et al. Mol Immunol* 2022;150:145. 2. Griffin M *et al. HemaSphere* 2023;7(S3):P787.

Study Design for the Treatment-Naïve Cohort in an Ongoing Phase 1b Trial of OMS906 (NCT05889299; EudraCT 2022-002450-22)



Key Inclusion Criteria:

- Adults with confirmed PNH diagnosis by flow cytometry (RBC clone size >10%)
- Complement inhibitor treatment naïve[†]
- Hgb <10.5 g/dL
- LDH >1.5 × ULN
- *Neisseria meningitidis* vaccination



Primary Endpoint:

- Safety and tolerability



Key Secondary Endpoints:

- Preliminary efficacy by effect on hemolysis and anemia:
 - Change from baseline in Hgb and LDH levels, absolute reticulocyte count, RBC transfusion burden
 - Proportion of patients achieving Hgb ≥12 g/dL or increase in Hgb ≥2 g/dL

*If patient discontinues from study for any reason; [†]Patients treated with any complement pathway inhibitor within 6 months prior to screening were excluded. Hgb, hemoglobin; LDH, lactate dehydrogenase; PNH, paroxysmal nocturnal hemoglobinuria; Q4W, every 4 weeks; RBC, red blood cell; SC, subcutaneous; ULN, upper limit of normal.

Thus Far, All Enrolled Patients Are Complement Inhibitor Treatment Naïve

- This study enrolled patients between 20 December 2022 and 3 April 2023
 - Interim analysis data cut: 29 May 2023
- 10 patients have received low-dose OMS906 (5 mg/kg)

No of Patients	Doses received
10	≥1
9	≥2
8	≥3
4	≥4
3	6

- This study provided treatment access for patients with PNH who had no other options available

The Majority of Patients Received RBC Transfusions in the 12 Months Prior to OMS906 Treatment

	OMS906 5 mg/kg SC N=10	
Baseline demographics	Mean (SD)	Median (range)
Age, years	42.3 (15.8)	38.5 (27–72)
Weight, kg	72.6 (12.1)	68.5 (59–91)
Female, n (%)		5 (50)
Caucasian, n (%)		10 (100)
PNH disease characteristics	Mean (SD)	Median (range)
Time since PNH diagnosis, years	3.2 (3.7)	0.8 (0.02–7.8)
PNH RBC clone size, % [n=7]	52.4 (23.9)	60.3 (15–88)
Patients receiving RBC transfusions*, n (%)		7 (70)
Patients receiving steroids for PNH, n (%)		4 (40)
Laboratory marker at baseline	Mean (SD)	Median (range)
Hgb, g/dL	7.1 (2.3)	7.2 (3.9–10.4)
LDH, U/L	1828 (789)	1748 (905–3480)
Absolute reticulocytes, ×10 ⁹ /L	175 (69)	151 (107–307)

	OMS906 5 mg/kg SC N=10
Medical history, n (%)	
Iron deficiency	5 (50)
Chronic kidney disease	3 (30)
MDS	2 (20)
Aplastic anemia	2 (20)
Folate deficiency	2 (20)
B12 deficiency	1 (10)
Concomitant medications, n (%)	
Ursodiol	8 (80)
Rivaroxaban	7 (70)
Iron	4 (40)
Folate	3 (30)
Enoxaparin	3 (30)
Vitamin B12	1 (10)

Data shown are from interim data cut as of 29 May 2023. *In the 12 months prior to OMS906 treatment.

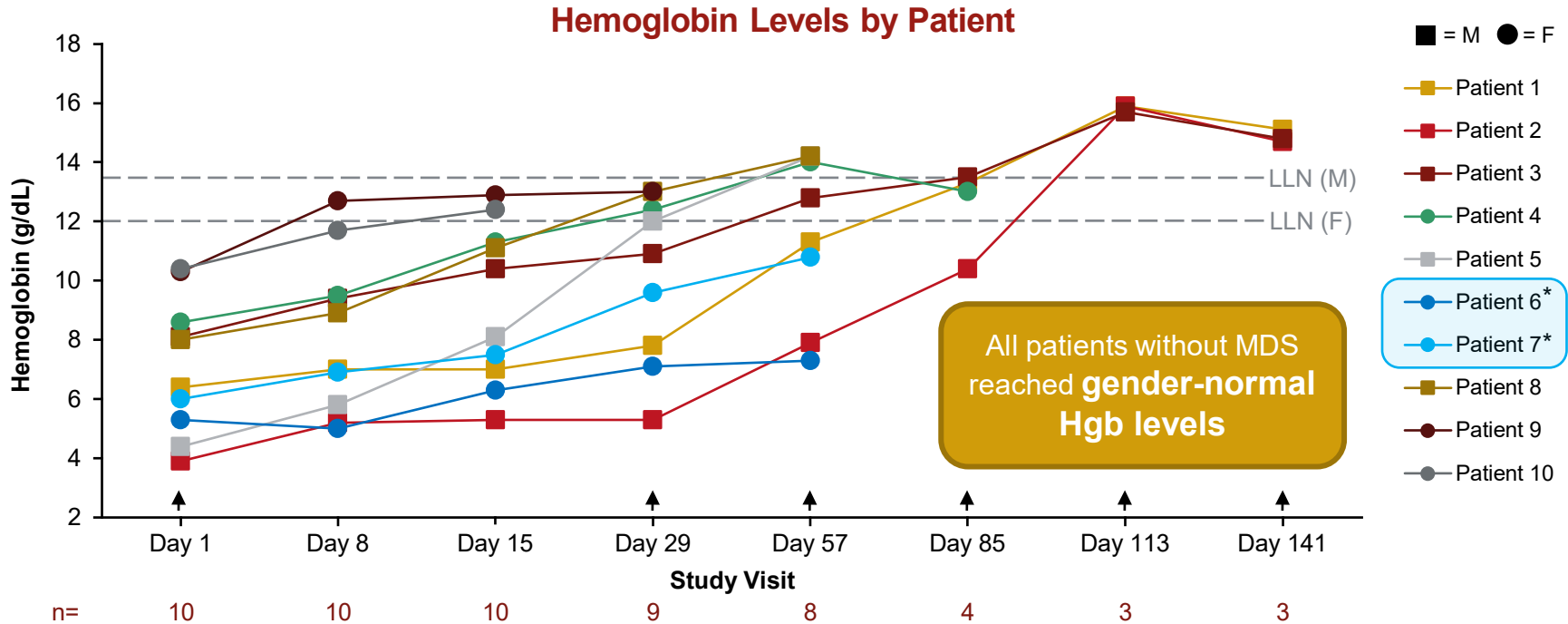
Hgb, hemoglobin; LDH, lactate dehydrogenase; MDS, myelodysplastic syndrome; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell; SC, subcutaneous; SD, standard deviation.

OMS906 Treatment Was Well Tolerated in Patients with PNH

Adverse Events in $\geq 20\%$ of Patients	n (%)	CTCAE Grade
Headache	2 (20)	All Grade 2
Itching	3 (30)	All Grade 1
Increased thrombocytopenia	3 (30)	1 patient Grade 2* 1 patient Grade 3* 1 patient Grade 4†
Transient neutropenia	2 (20)	2 patients Grade 3
Reduction in neutrophils	2 (20)	1 patient Grade 2 1 patient Grade 3

- Patients with reported cytopenia had evidence of underlying bone marrow failure
- No clinical breakthrough hemolysis
- No MAVEs
- No SAEs, discontinuations, or deaths

Treatment with Low-Dose OMS906 Rapidly Improved Hemoglobin Levels

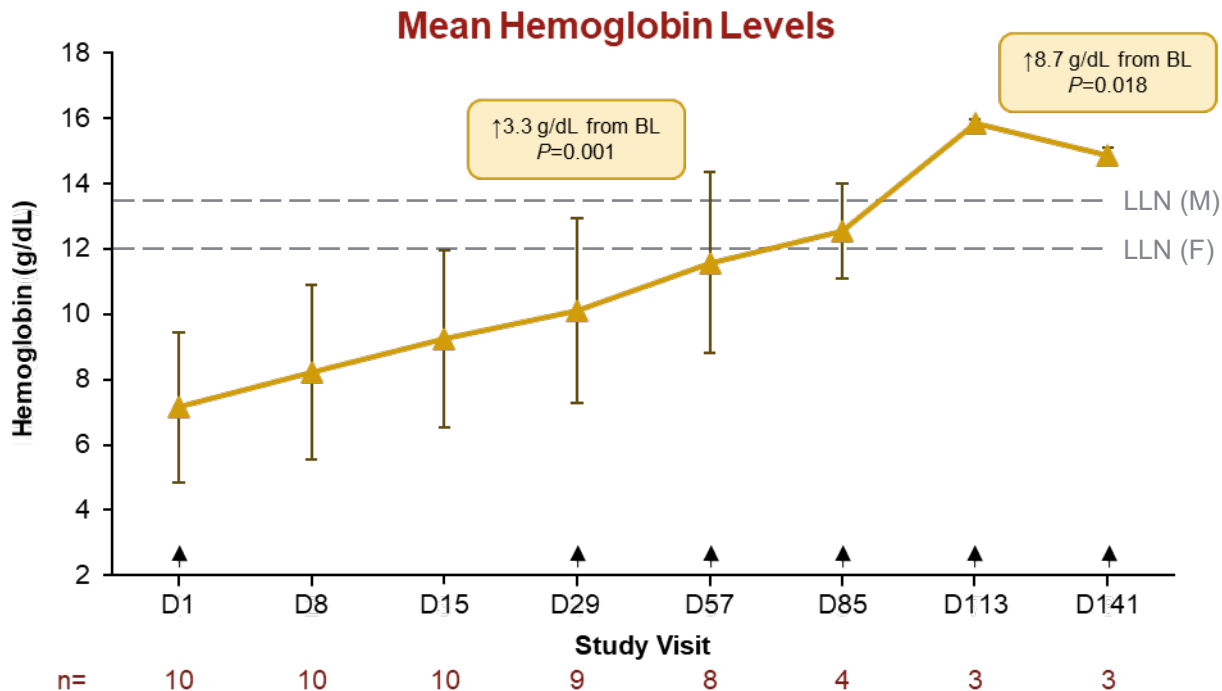


- No patients required transfusions following initiation of OMS906 treatment

Data shown are from interim data cut as of 29 May 2023. Black arrows indicate OMS906 administration following laboratory marker collection.

*Patients 6 and 7 had MDS. F, female; LLN, lower limit of normal; M, male; MDS, myelodysplastic syndrome.

Treatment with Low-Dose OMS906 Rapidly Improved Hemoglobin Levels



10/10 patients had an increase in Hgb ≥ 2 g/dL

8/10* patients achieved Hgb ≥ 12 g/dL

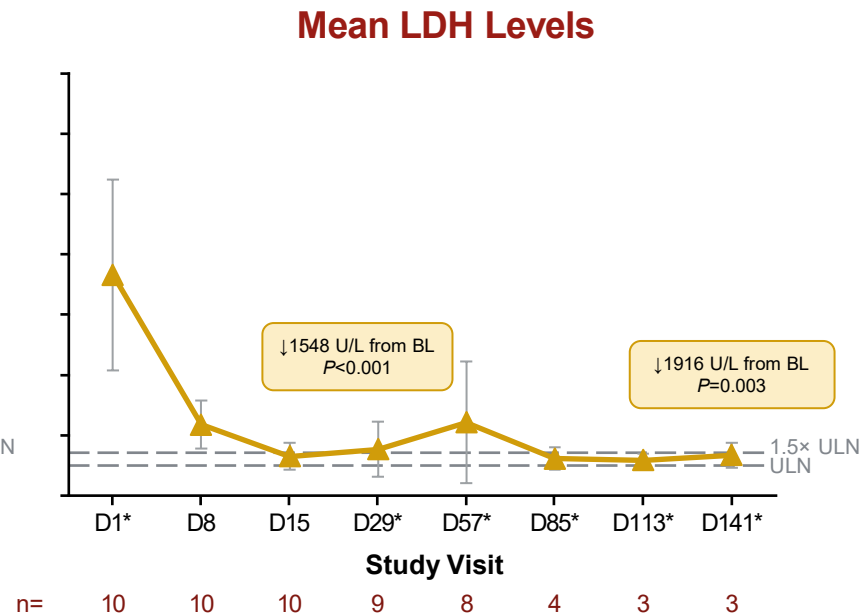
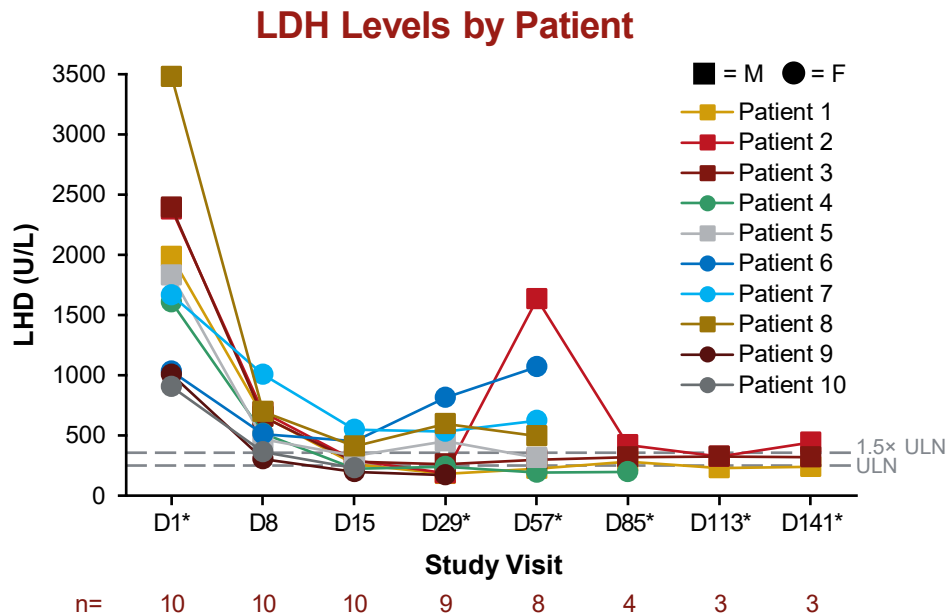
*The remaining 2 patients had MDS

- No patients required transfusions following initiation of OMS906 treatment

Data shown are from interim data cut as of 29 May 2023. *P*-values are for testing change from zero using t-test; *P*-values may not be valid for small N.

Black arrows indicate OMS906 administration following laboratory marker collection. BL, baseline; Hgb, hemoglobin; LLN, lower limit of normal; MDS, myelodysplastic syndrome.

Treatment with Low-Dose OMS906 Reduced LDH Levels

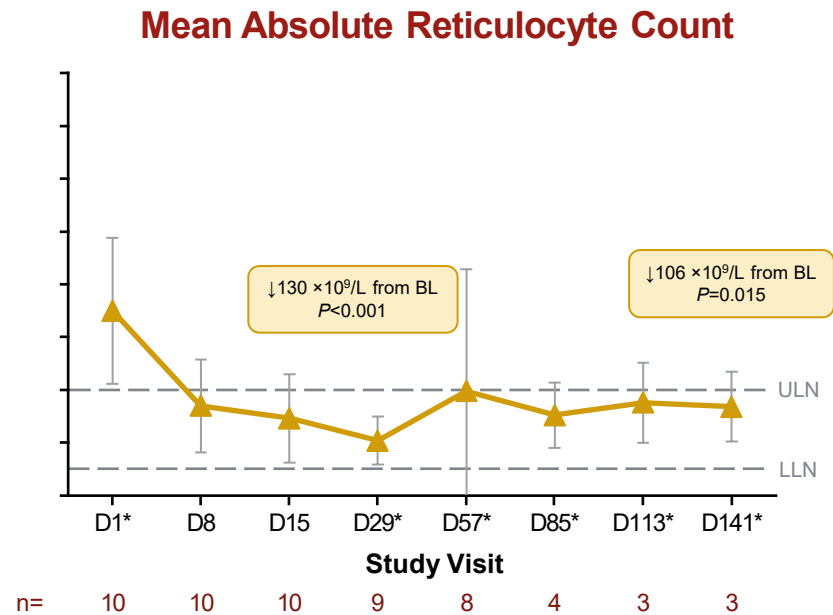
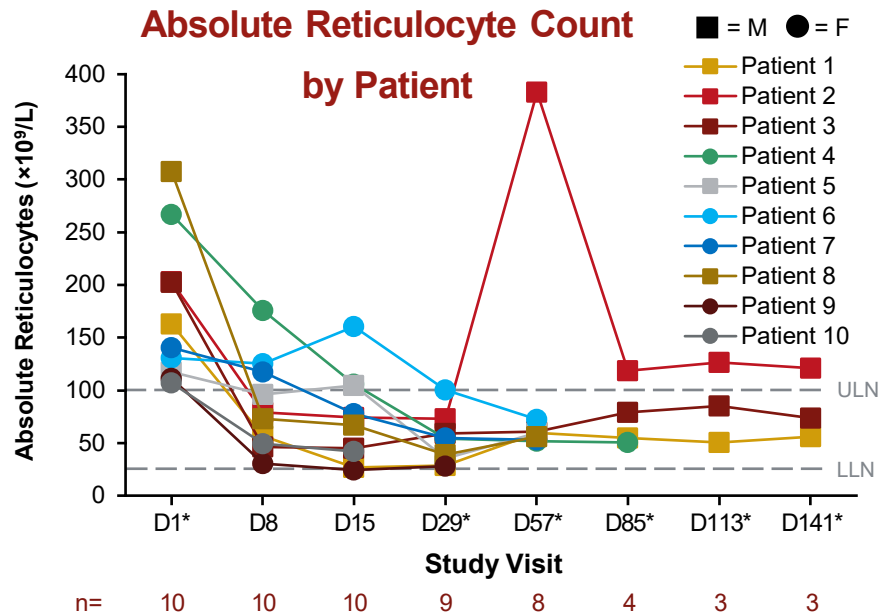


- Two patients had increases in LDH suggesting initiation of hemolysis at the end of a dosing period, although hemoglobin was not reduced in either
- PK and PD from these patients will help inform planned dose escalation to achieve once-quarterly dosing

Data shown are from interim data cut as of 29 May 2023. *P*-values are for testing change from zero using t-test; *P*-values may not be valid for small N.

*OMS906 administered following laboratory marker collection. BL, baseline; LDH, lactate dehydrogenase; LLN, lower limit of normal; ULN, upper limit of normal.

Absolute Reticulocyte Count Decreased Overall with OMS906 Treatment

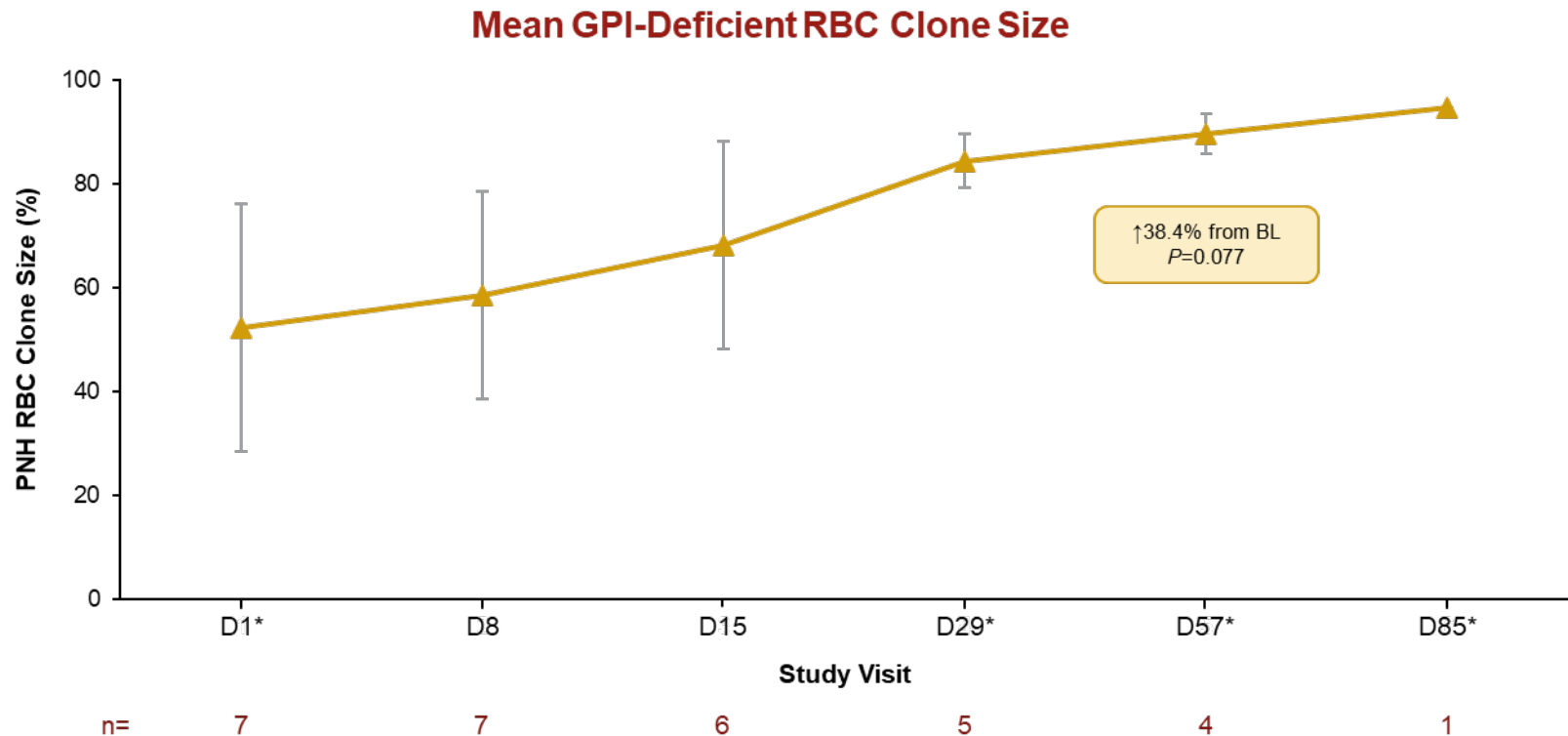


- Mean absolute reticulocyte counts were reduced from baseline by 90–133 × 10⁹/L at all timepoints

Data shown are from interim data cut as of 29 May 2023. *P*-values are for testing change from zero using *t*-test; *P*-values may not be valid for given small *N*.

*OMS906 administered following laboratory marker collection. BL, baseline; F, female; LLN, lower limit of normal; M, male; ULN, upper limit of normal.

PNH Clone Size Increased Over Time with OMS906 Treatment, Indicating Protection of PNH RBCs



Data shown are from interim data cut as of 29 May 2023. *P*-values are for testing change from zero using t-test; *P*-values may not be valid for small N.

*OMS906 administered following laboratory marker collection. BL, baseline; GPI, glycosylphosphatidylinositol; PNH, paroxysmal nocturnal hemoglobinuria; RBC, red blood cell.

Conclusions

- MASP-3 is a key activator of the alternative pathway and a novel target for PNH treatment
- OMS906, a MASP-3 inhibitor, showed promising efficacy in this interim analysis:
 - Normalization of Hgb (8/10 patients) was achieved with monthly SC dosing without clinical breakthrough hemolysis
 - Normalization of LDH (7/10 patients $<1.5 \times$ ULN), normalization of reticulocytes (9/10 patients), and transfusion independence were achieved
 - OMS906 was well tolerated with no safety signals of concern
- OMS906 dose escalation guided by the PK / PD of patients experiencing subclinical hemolysis is underway to inform achievement of quarterly dosing
- Further evaluation of OMS906 for PNH will explore GPI-deficient patients who have a suboptimal response to C5 inhibitors or are complement inhibitor treatment-naïve
- C5-switchover PNH trials and C3G trials are underway; additional alternative pathway-mediated indications are being evaluated

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GPI, glycosylphosphatidylinositol; Hgb, hemoglobin; LDH, lactate dehydrogenase; MASP-3, mannan-binding lectin-associated serine protease 3; PD, pharmacodynamics; PK, pharmacokinetics; PNH, paroxysmal nocturnal hemoglobinuria; SC, subcutaneous; ULN, upper limit of normal.

Special Thanks to the Patients and Healthcare Professionals in Ukraine Who Participated in This Study!

