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 in 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 C5 inhibitors.

Two ongoing open-label clinical trials are currently evaluating OMS906 in adults with PNH (EudrACT numbers: 2021-009503-37, 2022-002450-22)

METHODS
Design
• This was a first-in-man, randomized, double-blind, single-center, placebo-controlled Phase 1 study of OMS906.
• Subjects were randomized (8:2) into 9 escalating SAD cohorts (0.1-0.5 mg/kg IV and 3-8 mg/kg SC) receiving either placebo or OMS906 via infusion.
• Eligible subjects for inclusion were healthy males or females aged 18–64 years at screening with a BMI of 20–32 kg/m² and weight of ≥50 kg.

Trial Objectives
• The aim of this study was to assess the safety, tolerability, PK, and PD of OMS906 in healthy subjects.

RESULTS
Subject Demographics
• In total, 72 subjects with a median age of 42 years (range, 20–63) and median BMI of 27.2 kg/m² (range, 21.0–31.4) were studied; 51.4% of subjects were female.
• Demographics were generally balanced between the dosing cohorts and between the OMS906 versus placebo groups.

Table 1. Pharmacokinetic Properties of OMS906 (PK Set)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>OMS906</th>
<th>Placebo</th>
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<tbody>
<tr>
<td>IV cohorts (n=30)</td>
<td>SC cohorts (n=24)</td>
<td>IV cohorts (n=30)</td>
</tr>
<tr>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
<td>Mean ± SD (range)</td>
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<tr>
<td>Cmax</td>
<td>2.3 ± 1.9 (0.5–6.5)</td>
<td>2.0 ± 1.9 (0.5–6.5)</td>
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<tr>
<td>Tmax</td>
<td>1.7 ± 0.9 (0.5–3.7)</td>
<td>1.7 ± 0.9 (0.5–3.7)</td>
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<tr>
<td>CLz/F</td>
<td>0.05 ± 0.02 (0.01–0.1)</td>
<td>0.05 ± 0.02 (0.01–0.1)</td>
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<tr>
<td>T1/2z</td>
<td>7.7 ± 3.2 (2.1–20.2)</td>
<td>7.7 ± 3.2 (2.1–20.2)</td>
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<tr>
<td>Mean ± SD (range)</td>
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Presence of ADA
• The overall confirmed positive rate of AADAs was 14.8% in subjects receiving OMS906 (n=54).
- There was no evidence of impact on PK or PD.
- There were no incidences of hypersensitivity reactions or anaphylaxis.

ACKNOWLEDGMENTS
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DISCLAIMER
• OMS906 is an investigational agent and has not been approved by any regulatory agency.

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