# OCEAN (OP-103): A Phase 3, Randomized, Global Study of Melflufen and Dexamethasone Versus Pomalidomide and Dexamethasone in Patients With Relapsed/Refractory Multiple Myeloma Refractory to Lenalidomide



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**Primary endpoint** 

IMWG criteria<sup>12</sup>

 $\cdot$  OS

Safety

Secondary endpoints

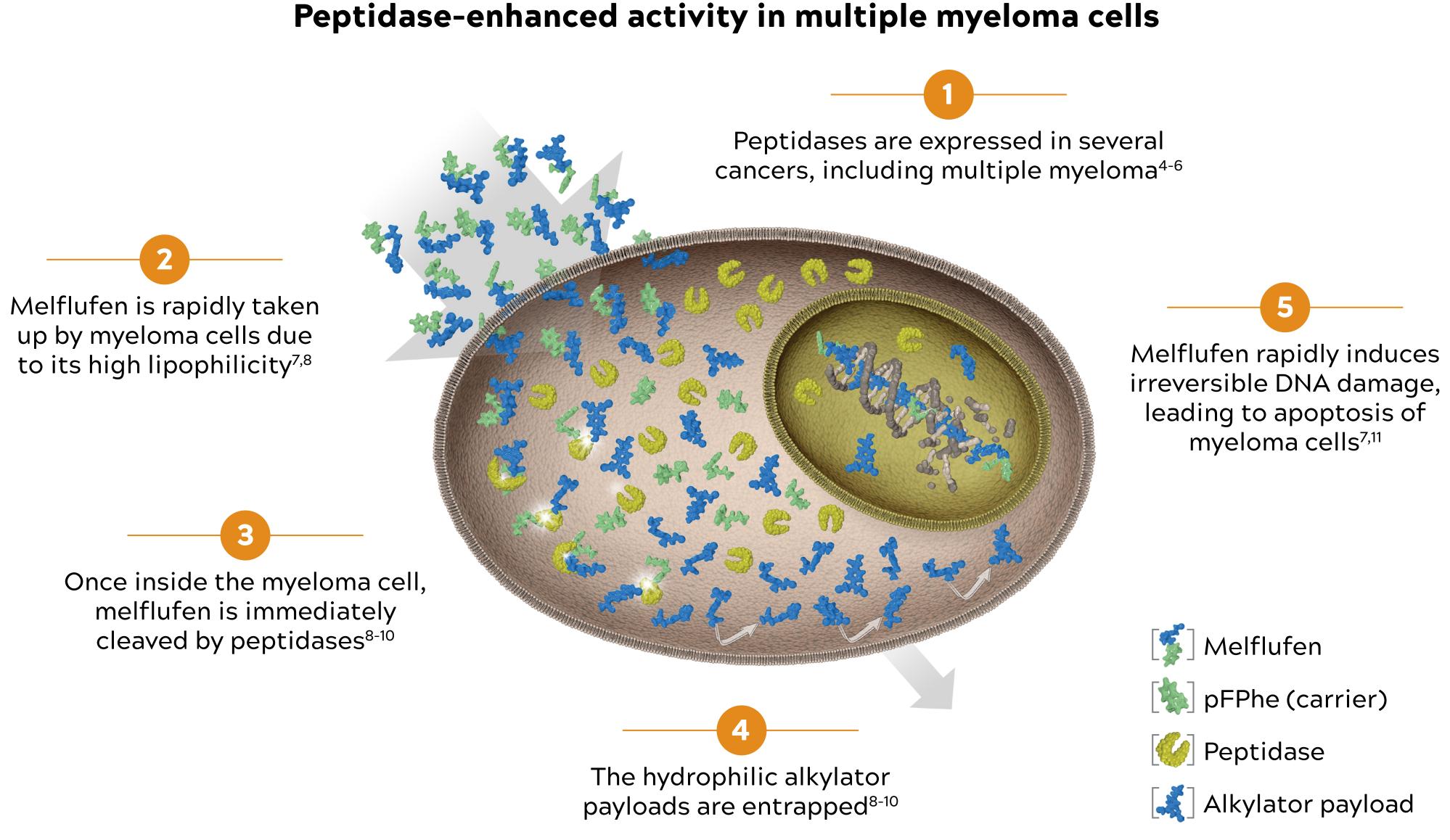
PFS assessed by IRC per

### BACKGROUND

pFPhe, p-Fluorophenylalanine

- Only ≤40% of patients with relapsed/refractory multiple myeloma (RRMM) respond to the next line of treatment, and ultimately most will relapse¹
- Melflufen is a lipophilic peptide-conjugated alkylator that rapidly delivers a highly cytotoxic payload into myeloma cells (Figure 1)
- In phase 1/2 O-12-M1 melflufen and dexamethasone (DEX) showed promising activity in patients with RRMM and a median of 4 prior lines of therapy<sup>2</sup>
- Overall response rate (ORR): 31%
- Median progression-free survival (PFS): 5.7 months
- Median overall survival (OS): 20.7 months
- Melflufen was well-tolerated, with an acceptable safety profile
- OCEAN (OP-103; NCT03151811) is a global, phase 3, randomized, open-label study of melflufen-DEX versus pomalidomide (POM)-DEX in patients with RRMM who are refractory to the last-line of therapy and to lenalidomide (LEN) within 18 months of randomization
- OCEAN is evaluating melflufen-DEX versus POM-DEX in a RRMM patient population similar to that of the pivotal phase 3 POM trial  $MM-003^3$

### Figure 1. Melflufen Mechanism of Action



Melflufen is 50-fold more potent than melphalan in myeloma cells in vitro due to increased intracellular alkylator activity<sup>4,5</sup>

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METHODS

N = 450

LEN-refractory

MM patients

DEX 40 mg PO

(days 1, 8, 15, and 22 of each 28-day cycle)<sup>a,b</sup>

Figure 2. OCEAN: Global, Randomized, Open-Label Phase 3 Study (NCT03151811)

POM 4 mg PO (days 1 to 21 of each 28-day cycle)<sup>a</sup> +

Melflufen 40 mg IV

(day 1 of each 28-day cycle)<sup>a</sup>

**DEX 40 mg PO**(days 1, 8, 15, and 22 of each 28-day cycle)<sup>a,b</sup>

<sup>a</sup>Patients will be treated until disease progression or unacceptable toxicity.

<sup>b</sup>The starting DEX dose will be reduced to 20 mg/d in patients aged ≥75 years.

DEX, dexamethasone; DOR, duration of response; IMWG, International Myeloma Working Group; IRC, Independent Review Committee; IV, intravenously; LEN, lenalidomide; MM, multiple myeloma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PO, orally; POM, pomalidomide.

### KEY ELIGIBILITY CRITERIA

<ul> <li>Diagnosis of MM with documented disease progression and requiring further treatment</li> <li>2 to 4 prior lines of therapy including LEN and a PI</li> </ul>	<ul> <li>Primary refractory disease (eg, never responded [≥MR to any prior therapy)</li> </ul>
<ul> <li>Relapsed and refractory or refractory to last line of therapy and to LEN administered within 18 months prior to randomization</li> <li>Measurable disease, defined as         <ul> <li>Serum M-protein ≥0.5 g/dL by protein electrophoresis</li> <li>Urine M-protein ≥200 mg/24 hours by protein electrophoresis</li> <li>Serum FLC ≥10 mg/dL and abnormal serum kappa-to-lambda FLC ratio</li> </ul> </li> <li>Age ≥18 years</li> <li>ECOG PS 0-2</li> <li>Adequate organ and hematologic function</li> </ul>	<ul> <li>Evidence of mucosal or internal bleeding or platelet transfusion refractory</li> <li>Any medical conditions that, in the investigator's opinion, would impose excessive risk to the patient or would adversely affect participation in this study including         <ul> <li>Significant history of cardiovascular disease (eg, myocardial infarction, significant conduction system abnormalities, uncontrolled hypertension, or grade ≥3 thromboembolic event in the last 6 months)</li> </ul> </li> <li>Prior POM</li> <li>Intolerance to IMiDs</li> <li>Prior alloSCT with active GVHD</li> </ul>

alloSCT, allogeneic stem cell transplantation; ECOG PS, Eastern Cooperative Oncology Group performance status; FLC, free-light chain; GVHD, graft-versus-host-disease; IMiDs, immunomodulatory drugs; LEN, lenalidomide; MM, multiple myeloma; MR, minimal response; PI, proteasome inhibitor; POM, pomalidomide.

### STATISTICAL ANALYSES

- Event-driven head to head superiority (and non-inferiority) study with approximately 450 patients enrolled
- PFS, DOR, and OS will be analyzed by using a 2-sided, 0.05 level stratified Cox proportional hazards regression model, and stratified by
- Age (≥75 vs <75 years)</li>
- Number of prior lines of therapy (2 vs 3-4 prior lines)
- International Staging System score (1 vs ≥2)
- ORR (≥partial response) will be compared using the Cochran-Mantel-Haenszel chi-squared test
- Incidence rates of adverse events will be summarized and analyzed for all patients who receive at least one or partial dose of melflufen, POM, or DEX and by the treatment received

### STUDY STATUS

# The study is open to accrual in 21 countries and is currently recruiting participants at 135 sites

Participating Countries	
• Austria	• Lithuania
• Belgium	• Norway
<ul> <li>Czech Republic</li> </ul>	<ul> <li>Poland</li> </ul>
<ul> <li>Denmark</li> </ul>	• Romania
• Estonia	• Russia
• France	• Spain
• Greece	• Taiwan
• Hungary	<ul> <li>The Netherlands</li> </ul>
• Israel	<ul> <li>United Kingdom</li> </ul>
• Italy	<ul> <li>United States</li> </ul>
• Korea	
	US Sites
• Arizona (AZ)	<ul> <li>Massachusetts (MA)</li> </ul>
<ul> <li>California (CA)</li> </ul>	<ul> <li>Missouri (MO)</li> </ul>
• Florida (FL)	<ul> <li>Mississippi (MS)</li> </ul>
• Idaho (ID)	<ul> <li>North Carolina (NC)</li> </ul>
	<ul><li>Pennsylvania (PA)</li></ul>
• Illinois (IL)	i Cilisyivailla (i A)

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This study is funded by Oncopeptides

### REGISTRATION

and is registered at ClinicalTrials.gov (NCT03151811)

This study is sponsored by Oncopeptides

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