**Multiple myeloma (MM)** is characterized by the expansion of malignant plasma cells which express the cell surface protein B-cell maturation antigen (BCMA).

**REGN458** is an anti-BCMA x anti-CD3 bispecific antibody (BCMAxCD3 bsAb), designed to enable co-stimulatory natural human antibodies, using Regeneron’s proprietary human antibody mouse “recombine” (VH/VLm8)**1** and full-length bispecific antibody technology (VH/VLm8)**2**.

**REGN458** binds to both BCMA on plasma cells and to CD3 on T-cells, thereby allowing BCMA to redirect T-cell effector function to multiple myeloma (MM) cells (Figure 1).

### Clinical study design

- This is a Phase 1/2, open-label, first-in-human study of REGN458 (NCT02761126) in patients with relapsed/refractory (R/R) MM.
- The Phase 1 portion explores enrols patients with R/R MM in a 4+3 dose escalation design.
- REGN458 is administered according to the treatment schedule shown in Figure 4.

### Phase 1 Primary objectives

- To assess safety, tolerability, and dose-limiting toxicities (DLTs) and to determine the recommended Phase 2 dose of REGN458 as monotherapy in patients with R/R MM.

### Phase 1 Secondary objectives

- To evaluate pharmacokinetics, pharmacodynamics, immunogenicity, assess preliminary antitumor activity.

### Methods

**Key inclusion criteria**

- Age ≥18 years.
- Eastern Cooperative Oncology Group performance status (ECOG PS) ≤1.
- Progression on or after ≥3 prior lines of therapy including proteasome inhibitor (PI), IMiD, and monoclonal antibody treatment (including antibody drug conjugate or bispecific antibody) or BCMA-directed CAR T therapy.

### Results

- Seven patients, with a median of seven lines of prior systemic therapy, all failing anti-CD38 antibody treatment, were enrolled in two dose groups with REGN458 (3 mg and 6 mg weekly doses) and had opportunity for assessment at 4 weeks; clinical cut-off November 17, 2018.
- Responses were observed in four of seven (57%) patients, including three of four (75%) in the 6 mg dose group. Two patients (50%) in the 6 mg dose group were ongoing responses (duration of response range 1–7 weeks).

### Table 1. Patient demographics and baseline characteristics

<table>
<thead>
<tr>
<th>Median age (range), years</th>
<th>n</th>
<th>3 mg (N=3)</th>
<th>6 mg (N=3)</th>
<th>Total (N=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57.1 (40–75)</td>
<td>3</td>
<td>78 (66–81)</td>
<td>74 (59–79)</td>
<td>78 (59–81)</td>
</tr>
</tbody>
</table>

### Table 2. Summary of adverse events

<table>
<thead>
<tr>
<th>N. patients</th>
<th>Any Grade</th>
<th>Grade 3 or 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one adverse event</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>N. patients</td>
<td>Any Grade</td>
<td>Grade 3 or 4</td>
</tr>
<tr>
<td>At least one AE</td>
<td>12</td>
<td>7</td>
</tr>
</tbody>
</table>

### Pharmacokinetics and biometrics

- Preliminary data suggest that the mean concentrations of REGN458 in serum in patients with MM appear increased with dose from 3 mg to 6 mg (Figure 6).
- The Phase 1 dose escalation was reached at 6 mg dose with no DLTs reported.

### Figure 6. Pharmacokinetics

**Summary**

- A total of seven patients (median age 78 years) with R/R MM (median seven lines of prior systemic therapy, all of whom failed anti-CD38 treatment) have been treated with REGN458, an MM antibody x anti-CD38 bispecific antibody (NCT0761106).
- As of data cut-off, no DLTs were reported.
- Antitumor activity was observed at initial dose levels in patients with predominantly myeloma and secretory MM.

### Acknowledgments

The authors would like to thank the patients, their families, all other investigators, and all investigational sites that participated in the study. Funding: Regeneron Pharmaceuticals, Inc. Medical writing support: Cindi House, PhD, of Prime (Kidder, UK).

### References


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