### Objectives

- To assess the capacity of the excipient content of the current ORMD-0801 formulation to support delivery higher concentrations of insulin.
- To assess the pharmacodynamics (PD) of orally administered insulin in healthy subjects
- To compare PD responses to equal amounts of insulin delivered in one versus two capsules.

### Design

Following informed consent, a single capsule containing 8 mg or 16 mg insulin, or two capsules containing 8 mg insulin each, were administered to ten fasting, healthy, male subjects. This interim analysis focused on blood glucose concentrations, which were monitored over the ensuing 300-minute period. Subjects demonstrating a PD response in any of the three treatment sessions were included in the analyses. A PD response was defined as a Cmin ≥15% lower than baseline blood glucose values.

### Results

No adverse events were observed or reported for any of the treatment regimens. PD responses were observed in 7/10 subjects. Maximal glucose responses for all treatments were observed following a ≥60-min lag period, as expected of enteric-coated capsules (Table 1, Figure 1). Dose responses were manifested by significantly lower mean blood glucose Cmin following the 8+8 mg (47.9 ± 11.3 mg/dL, p=0.006) and 16 mg (57.3 ± 8.4 mg/dL, p=0.001) treatments, when compared to that followed 8 mg dosing (64.6 ± 6.2 mg/dL) (Table 1, Figure 1). Moreover, glucose area under the curve (AUC) was significantly lower following both 8+8mg and 16mg treatments (13.2% and 8.1%, respectively), when compared to 8 mg (p=0.003 and 0.008, respectively) (Table 1).

### Conclusions

- The ORMD-0801 excipient ratios effectively deliver doses higher than those tested to date.
- Blood glucose response intensity positively correlated with the insulin content in ORMD-0801.
- One and two-capsule regimens for delivery of 16 mg insulin were equally effective in lowering blood glucose concentrations.

---

**Table 1. Mean glucose responses to ORMD-0801**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cmin [SD] (mg/dL)</th>
<th>Tmin [SD] (min)</th>
<th>AUC [SD] (mg/dL*min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 mg</td>
<td>64.6 [6.2]</td>
<td>169.3 [67.5]</td>
<td>22425.0 [2152.6]</td>
</tr>
<tr>
<td>8+8 mg</td>
<td>47.9 [11.3]</td>
<td>188.6 [72.9]</td>
<td>19470.7 [2126.5]</td>
</tr>
<tr>
<td>16 mg</td>
<td>57.3 [8.4]</td>
<td>139.3 [48.0]</td>
<td>20610.4 [1427.6]</td>
</tr>
</tbody>
</table>

**Figure 1. Blood glucose profiles of two healthy subjects following treatment with ORMD-0801.** ORMD-0801 capsules, containing 8 or 16 mg insulin were administered to fasting healthy subjects. Blood glucose concentrations were monitored for 5 hours thereafter.

---

For more information: aviva@oramed.com

U.S.:1-646-240-4193; Intl.:+972-2-566-0001