Preliminary safety and efficacy of TH-302, an investigational hypoxia-targeted drug, and dexamethasone (dex) in patients (pts) with relapsed/refractory multiple myeloma (RR MM) (Laubach et al. Abstr #8534)

**Trial Design**
Relapsed / Refractory Myeloma

**Cohort 1**
240 mg/m²
n = 5

**Cohort 2**
340 mg/m²
n = 9

**Cohort 3**
480 mg/m²
n = 2

**TH-302 + dex + Bortezomib**
*Enrollment to start at completion of dose expansion*

**TH-302 + dex**
n = 24

**Prior Therapies**

<table>
<thead>
<tr>
<th>All Patients (n=24)</th>
<th>Median # Prior Lines (induction + transplant = 1 line)</th>
<th>6.5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Received IMiD Multiple IMiDs</td>
<td>100% 50%</td>
</tr>
<tr>
<td></td>
<td>Received Proteasome Inhibitor Multiple Proteasome Inhibitors</td>
<td>100% 54%</td>
</tr>
<tr>
<td></td>
<td>Received Transplant</td>
<td>58%</td>
</tr>
</tbody>
</table>
Safety (n=24)

• 2 Dose-Limiting Toxicities Reported at 480 mg/m²
  – Stomatitis (n=2)

• Grade 3/4 Non-Laboratory AEs Related to TH-302
  – Pneumonia (n=2), stomatitis (n=2), abdominal pain (n=1), cellulitis (n=1), diarrhoea (n=1), fatigue (n=1), proctalgia (n=1), pseudomonas sepsis (n=1)

• Serious Adverse Event Related to TH-302
  – Pneumonia (n=2), abdominal pain (n=1), cellulitis (n=1), proctalgia (n=1), pseudomonas sepsis (n=1), pyrexia (n=1)
### Efficacy Outcomes

<table>
<thead>
<tr>
<th></th>
<th>240 mg/m² (N=5)</th>
<th>340 mg/m² (N=17)</th>
<th>480 mg/m² (N=2)</th>
<th>Total (N=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Efficacy Evaluable</strong></td>
<td>5</td>
<td>16</td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td><strong>PR</strong></td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td><strong>MR</strong></td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>SD</strong></td>
<td>4</td>
<td>9</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td><strong>PD</strong></td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>ORR (≥PR)</strong></td>
<td>20%</td>
<td>19%</td>
<td>0%</td>
<td>17%</td>
</tr>
<tr>
<td><strong>CBR (≥MR)</strong></td>
<td>20%</td>
<td>31%</td>
<td>0%</td>
<td>26%</td>
</tr>
</tbody>
</table>
Efficacy Outcomes:
Time on Study (months)

[Bar chart showing time on study for different patients with PD, SD, MR, PR, and NA outcomes.]

PD, SD, MR, PR, NA

⇒ = ongoing
Summary

• TH-302 (a hypoxia targeted drug) + dex is well tolerated in relapsed and/or refractory myeloma with stomatitis as the dose limiting toxicity (480mg/m2)

• TH-302 + dex shows promising early efficacy in heavily pre-treated patients with a overall response rate of 19% (3/16) and clinical benefit rate (≥MR) of 31% (5/16) at the TH-302 maximum tolerated dose (340mg/m2)

• Confirmed partial responses seen in patients who failed multiple IMiDs (including pomalidomide) or proteasome inhibitors (including carfilzomib)

• TH-302 + dex expansion arm has enrolled 14 of 15 planned patients at time of presentation and a TH-302 + bortezomib + dex dose escalation arm will initiate after TH-302 + dex expansion at MTD completes enrollment