Imetelstat is a 13-mer lipid-conjugated NPS oligonucleotide that specifically targets the RNA template of human telomerase and is a potent, first-in-class competitive inhibitor of telomerase enzymatic activity. It has demonstrated clinical activity in myeloid malignancies, including T- and B-ALL patients.

Imetelstat is an ongoing global two-part, Phase 2/3 study of imetelstat in RBC TD patients with L-R-MDS with a primary endpoint of 8-week RBC Transfusion Independence (TI). Patients in Phase 2 received open-label treatment with imetelstat of 7.5 mg/kg IV q 4 weeks. Phase 2 enrolled 57 patients: an initial cohort of 32 patients and an expansion cohort of 25 lenalidomide (Len) and hematopoietic growth factor (HGF) naïve patients with del(5q) based on the results from the initial cohort (Figure 2).

The results from Phase 2 of Immerge demonstrated clinical benefit of imetelstat treatment in Len-R-MDS patients, supporting initiation of the Phase 3 (Figure 3).

RESULTS FROM PHASE 2 OF Immerge

- Imetelstat treatment showed meaningful and durable TI in 38 (67%) TD, non-del(5q), HMA/Len naïve, L-R-MDS patients (Table 1).
- Transfusion independence was observed across different clinical subgroups (Figure 4).
- No new safety signal was identified. Reversible cytopenias were the most frequent AES, without significant clinical consequences (Figure 5). 11% of infusion related reactions with 5% >Grade 3 were observed.
- Biomarker data suggested potential impact on malignant clone and disease modification by imetelstat treatment.

Table 1. Meaningful & Durable Transfusion Independence

<table>
<thead>
<tr>
<th>Feature</th>
<th>n = 38</th>
<th>Mean (SD) or Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline TI &gt;4 units</td>
<td>24 (62)</td>
<td></td>
</tr>
<tr>
<td>Baseline Hgb &lt;8 g/dL</td>
<td>26 (68)</td>
<td></td>
</tr>
<tr>
<td>Baseline Hct &lt;33%</td>
<td>25 (66)</td>
<td></td>
</tr>
<tr>
<td>Transfusion independence</td>
<td>26 (68)</td>
<td></td>
</tr>
<tr>
<td>Del(5q)</td>
<td>22 (58)</td>
<td></td>
</tr>
<tr>
<td>Have received prior ESA</td>
<td>7 (18)</td>
<td></td>
</tr>
<tr>
<td>Hematopoietic chemo</td>
<td>15 (39)</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>19 (50)</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>19 (50)</td>
<td></td>
</tr>
</tbody>
</table>

RESULTS FROM PHASE 3 OF Immerge

- 26 patients with baseline SF3B1 mutations had reduction in variant allele frequency and maintained TI lasting over a year.
- 3/6 (50%) intermediate or poor cytogenetic risk patients achieved 8-week TI and all had a ringed sideroblast WHO subtype.
- 3/3 with thrombocytosis achieved 8-week TI and 2/3 achieved 24-week TI.

METHODS FOR PHASE 3 OF Immerge

- Phase 3 received open-label treatment with imetelstat at 7.5 mg/kg IV q 4 weeks.
- Enrollment open for Phase 3 in August 2019.

TRIAL REGISTRATION

- This study is registered at ClinicalTrials.gov (NCT02598661).
- For further information please contact: MDS3001-info@Geron.com

REFERENCES