**Results from Phase 1/2 Trial of Tagraxofusp in Combination with Pomalidomide and Dexamethasone in Relapsed or Refractory Multiple Myeloma**

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**Introduction and Highlights**

Tagraxofusp: Novel-targeted therapy directed to CD123
- CD123 approved for the treatment of adult and pediatric patients, 2 years and older, with select myeloid malignancies (cHL/DR) and chronic myelomonocytic leukemia
- Brownstone Transplantation Designation (BTD)
- Marketing Authorization Application (MAA) for BTD is under review by the European Medicines Agency

CD123 target: Expressed by multiple malignancies, including certain myeloproliferative neoplasms such as multiple myeloma (MM), chronic myelomonocytic leukemia, and myelofibrosis, certain B-cell lymphomas, and leukemia

Tagraxofusp and MM
- This bone marrow microenvironment of many multiple myeloma (MM) patients contains high levels of CD123-expressing plasma-activated dendritic cells (pDCs), which have been shown to augment MM growth and contribute to drug resistance
- Tagraxofusp was well-tolerated, with a predictable and manageable safety profile, when dosed in combination with pomalidomide (POM) and dexamethasone (DEX) in patients with relapsed or refractory (R/R) MM
- Evidence of CD123 suppression in peripheral blood and bone marrow was observed in this patient population

**Background: Multiple Myeloma**
- Multiple myeloma (MM) is a heterogeneous bone marrow malignancy characterized by the accumulation of abnormal plasma cells in the bone marrow (BM)
- The disease is associated with a variety of clinical manifestations including lytic bone lesions, hypercalcemia, renal impairment, and anemia
- MM is the second most common hematologic malignancy, with an estimated 12,000 new cases and approximately 13,000 deaths per year in the US (SEER 2019)
- Current treatment options for MM, including combinations with proteasome inhibitors (bortezomib, carfilzomib, ixazomib, and delphamide), immunomodulatory drugs (thalidomide, lenalidomide), and anti-CD38 antibodies (belizumab, isatuximab), have not changed the natural history of MM
- However, despite these treatment options, most patients relapse as the MM clone cannot be permanently eradicated, thus showing the necessity for new treatment modalities

**Study Design and Inclusion Exclusion Criteria**

**Dosing Schedule**

**Response Evaluation and Treatment Duration**

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**Baseline Demographics**

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<th>Age, years</th>
<th>Male/Female</th>
<th>Median [rang]</th>
<th>65 [57-70]</th>
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<tbody>
<tr>
<td>65 [57-70]</td>
<td>Male</td>
<td>5 (96)</td>
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<tr>
<td>65 [57-70]</td>
<td>Female</td>
<td>7 (96)</td>
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**Number of Prior Therapies**

| Median [rang] | 3 (10) |

**Prior Therapies**

- Dexamethasone: 9 (100%)
- Bortezomib: 8 (100%)
- Lenalidomide: 7 (78%)
- Cyclophosphamide: 7 (78%)

**Safety and Tolerability**

**Predictable and manageable safety profile both as a single agent and when combined with POM-DEX**

**MM all classes, n=9**

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
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<tr>
<td>Neutropenia</td>
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<tr>
<td>Thrombocytopenia</td>
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<td>Fatigue</td>
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**References**


**Summary of Tagraxofusp Trial Results**

- In this Phase 1/2 trial, tagraxofusp was well-tolerated, with a predictable and manageable safety profile, when dosed in combination with pomalidomide (POM) and dexamethasone (DEX) in patients with heavily pretreated R/R MM
- Most common grade 3/4 TEAEs were thrombocytopenia and neutropenia
- 5 patients who achieved tagraxofusp-POM-DEX combination had partial responses (PRs) and decreases in POC levels while on treatment with tagraxofusp
- These patients also experienced decreased levels of myeloma-related laboratory assessments values after 1 cycle of treatment with tagraxofusp combined with POM and DEX
- Evidence of DEX suppression in peripheral blood and BM was observed in this patient population
- All 5 patients experienced decreases in DEX levels
- Given CD123 suppression on pDCs in the tumor microenvironment and the potential synergistic effect of targeting both pDCs, including BTK inhibitors, and POM, tagraxofusp may offer a novel mechanism of action in MM
- Further research for better development include in other patient populations, combination with daratumumab, and/or novel agents such as BTK inhibitors