Tagraxofusp is a novel targeted therapy directed to CD123, the alpha chain of the interleukin-3 (IL-3) receptor. It is FDA-approved for treatment of adult and pediatric patients, 2 years and older, with blastic plasmacytoid dendritic cell neoplasm (BPDCN) who have received prior systemic therapy and for whom the disease remains active.

### Results of Pivotal Tower Trial of Tagraxofusp (SL-401) in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

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#### Introduction and Highlights

- **Tagraxofusp** is a novel targeted therapy directed to CD123, the alpha chain of the interleukin-3 (IL-3) receptor.
- **CD123** is upregulated on multiple malignancies including blastic plasmacytoid dendritic cell neoplasm (BPDCN), acute myeloid leukemias (AML), cutaneous mycosis fungoides (CMF), monocytic myeloid neoplasms (MMN), multiple myelomas, and a variety of other highly aggressive and refractory cancers.
- **BPDCN** is a highly aggressive hematologic malignancy, often with cutaneous and other extramedullary involvement, in lymph node, skin, etc. manifestations.
- Prior progression, with a median overall survival (OS) of 4-8 months from diagnosis.
- **Tagraxofusp Phase 2 Pivotal Trial (STML-0114)**
  - Tagraxofusp demonstrated high levels of clinical activity, with a predictable and manageable safety profile, in patients with BPDCN.
  - Pivotal trial results of tagraxofusp in BPDCN served as the basis for U.S. approval.

#### Tagraxofusp: Study Design and Inclusion/Exclusion

- **Patient Population**
  - Stage 1 BPDCN (≤ 80% BM involvement) and Stage 2 BPDCN (>80% BM involvement)
  - Age ≥ 18 years
  - Prior chemotherapy or prior investigational therapy
- **Objectives**
  - To confirm clinical activity of tagraxofusp in patients with BPDCN
  - To confirm safety profile of tagraxofusp in patients with BPDCN
- **Study Design**
  - Phase 1: Dosing to determine safety and recommended Phase 2 dose (RP2D) of 12 mcg/kg IV on days 1 through 21 of a 28-day cycle.
  - Phase 2: Open-label, 2-stage, randomized, controlled trial in patients with BPDCN.
  - Control arm: Best supportive care (BSC)
- **Inclusion Criteria**
  - Patients are treated with tagraxofusp at the labeled dose and schedule.
- **Exclusion Criteria**
  - Prior treatment with any other BPDCN targeted therapy
  - < 18 years of age
  - Hematopoietic stem cell transplant (HSCT) within the past 6 months
  - History of malignancy
- **Safety**
  - Safety of tagraxofusp at the labeled dose and schedule
  - Most common adverse reactions (incidence ≥30%): capillary leak syndrome (CLS), nausea, fatigue, peripheral pain, vomiting, and decreased appetite.

#### Tagraxofusp: Demographics

- **Overall Survival (OS)**
  - Median OS: Not reached
  - Long-term survivors (median follow-up: 6 months)

#### Tagraxofusp: Clinical Activity

- **Efficacy Measures**
  - Overall response rate (ORR): 54% (95% CI 47-61%)
  - Complete response (CR): 20% (95% CI 13-29%)
  - Clinical complete response (CRc): 7% (95% CI 4-12%)

- **Response Rates in BPDCN Patients (n=44)**
  - ORR: 90% (36/40)
  - CR: 27% (12/44)
  - CRc: 27% (12/44)

- **Survival Probability (days)**
  - Median OS: Not reached
  - 1-year OS: 67% (95% CI 54-77%)

#### Tagraxofusp: Safety Profile in Patients in Pivotal Trial

- **Safety of tagraxofusp assessed in 91 adults with treatment naïve or previously treated malignancies treated with tagraxofusp at the RP2D of 12 mcg/kg IV on days 1 through 21 of a 28-day cycle.
  - Most common adverse reactions (incidence ≥30%): capillary leak syndrome (CLS), nausea, fatigue, peripheral pain, vomiting, and decreased appetite.
  - Most common laboratory abnormalities (incidence ≥30%): increase in albumin, platelets, hemoglobin, calcium, sodium, and potassium in patients with advanced cancer (ACC) and acute myeloid leukemia (AML).
  - G3 or grade 4 toxicities were seen in 15% (G3 = 10% and G4 = 5%) of patients at the RP2D.

#### Tagraxofusp: Best Response and Treatment Duration

- **Median duration of CR/CRc**: 24 months (range 0.2-55)
- **ORR, CR, and CRc**
  - ORR: 72% (31/43)
  - CR: 15% (6/43)
  - CRc: 13% (5/39)

#### Tagraxofusp: Summary and Conclusions

- **Pivotal Trial Results**
  - Tagraxofusp, a novel targeted therapy directed to CD123, demonstrated high levels of clinical activity in patients with BPDCN.
  - In treatment-naïve patients:
    - 90% overall response rate (ORR)
    - 45% of patients were bridged to stem cell transplantation, including older patients who might have been excluded from chemotherapy.
- Overall survival rate of 59% at 18 months and 52% at 24 months.
- **Tagraxofusp demonstrated a predictable and manageable safety profile**
- Most common adverse reactions in patients with treatment naïve to previously treated malignancies treated with tagraxofusp at the labeled dose and schedule include capillary leak syndrome (G3: nausea, fatigue, peripheral pain, vomiting, and decreased appetite (APD) G4: albumin, calcium, sodium, and potassium in patients with advanced cancer (ACC) and acute myeloid leukemia (AML)).
- Tagraxofusp approved and commercially available in the U.S. for BPDCN.
- Tagraxofusp is the first and only approved treatment for BPDCN.
- **Tagraxofusp** is an approved treatment for BPDCN.
- **Tagraxofusp** is an approved treatment for BPDCN.

#### References

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- **EHA 2019 #PS1063**
- **Tagraxofusp: Mechanism of Action and Rational in BPDCN**
- **Tagraxofusp skin biopsy (H&E)**