Results of Pivotal Phase 2 Trial of Tagraxofusp (SL-401) in Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)

Naveen Pemmaraju¹, Andrew A. Lane², Kendra L. Sweet³, Anthony S. Stein⁴, Sumithira Vasu⁵, William Blum⁵, David A. Rizzieri⁶, Eunice S. Wang⁷, Madeleine Duvic¹, Sharon Spence⁸, Shay Shemesh⁸, Janice Chen⁸, Christopher L. Brooks⁸, Ivan Bergstein⁸, Peter McDonald⁸, J. Mark Sloan⁹, Jeffrey E. Lancet², Hagop M. Kantarjian¹, Marina Konopleva¹

¹The University of Texas MD Anderson Cancer Center, Houston, TX; ²Dana-Farber Cancer Institute, Boston, MA; ³H. Lee Moffitt Cancer Center, Tampa, FL; ⁴City of Hope National Medical Center, Duarte, CA; ⁵The Ohio State University, Columbus, OH; ⁶Duke University Medical Center, Durham, NC; ⁷Roswell Park Cancer Institute, Buffalo, NY; ⁸Stemline Therapeutics, Inc., New York, NY; ⁹Boston University School of Medicine, Boston, MA.
BPDCN: Aggressive Malignancy of Unmet Medical Need

- Primary sites: skin, bone marrow
- Secondary sites: LN, CNS, visceral
- CD123, CD4, CD56 - “Think 123456”
- TCL-1, CD303, TCF-4
- TET2, ASXL1, RAS, TP53
- No approved therapies
- Outcomes poor; med OS ~8-14 mos
- SCT promising for select/fit patients

Tagraxofusp (SL-401): Novel Targeted Therapy Directed to the IL-3 Receptor (IL-3Rα / CD123)

- IL-3Rα/CD123 overexpressed on BPDCN and many other hematologic cancers
- Tagraxofusp (SL-401) is a targeted therapy directed to CD123
- Tagraxofusp potent vs BPDCN cells *in vitro* and *in vivo*
- Previous Phase 1 study
  - Major responses in 7/9 patients (78%): 5 CR, 2 PR (*Frankel et al. Blood, 2014*)
### Tagraxofusp: Study Design and Inclusion / Exclusion

#### Stage 1
(Lead-in, dose escalation)

- BPDCN (1L and R/R)
- Tagraxofusp (7, 9, 12, or 16 µg/kg) via IV infusion, days 1-5 of a 21-day cycle
- Key objectives: To determine optimal dose and regimen for Stage 2

#### Stage 2
(Expansion)

- BPDCN (1L and R/R)
- Tagraxofusp (12 µg/kg) via IV infusion, days 1-5 of a 21-day cycle
- Key objectives: To further define safety and efficacy

#### Stage 3
(Pivotal, confirmatory)

- BPDCN (1L)
- Tagraxofusp (12 µg/kg) via IV infusion, days 1-5 of a 21-day cycle
- Key objective: To confirm efficacy for registration

### Select inclusion criteria

- Patient Population:
  - Stage 1: BPDCN (1L or R/R)
  - Stage 2: BPDCN (1L or R/R)
  - Stage 3: BPDCN (1L)
- Age ≥ 18; ECOG PS 0-2
- Adequate organ function including: LVEF ≥ lower limit of normal, creatinine ≤ 1.5mg/dL, albumin ≥ 3.2 g/dL, bilirubin ≤ 1.5 mg/dL, AST/ALT ≤ 2.5x ULN

### Select exclusion criteria

- Persistent clinically significant toxicities from prior chemotherapy
- Received chemotherapy or other investigational therapy within the prior 14 days
- Clinically significant cardiopulmonary disease
- Receiving immunosuppressive therapy

➢ To ensure ongoing access to tagraxofusp, BPDCN patients are being enrolled in an additional cohort, Stage 4
## Tagraxofusp: Demographics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Stages 1 &amp; 2</th>
<th>Stage 3</th>
<th>Stages 1, 2 &amp; 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>32</td>
<td>13</td>
<td>45</td>
</tr>
<tr>
<td>Age: years median [range]</td>
<td>72 [28-84]</td>
<td>65 [22-84]</td>
<td>70 [22-84]</td>
</tr>
<tr>
<td>Gender: male [n, (%)]</td>
<td>26 (81)</td>
<td>11 (85)</td>
<td>37 (82)</td>
</tr>
<tr>
<td>First-line (1L) [n, (%)]</td>
<td>19 (59)</td>
<td>13 (100)</td>
<td>32 (71)</td>
</tr>
<tr>
<td>Relapsed / Refractory (R/R) [n, (%)]</td>
<td>13 (41)</td>
<td>--</td>
<td>13 (29)</td>
</tr>
<tr>
<td>Baseline sites of disease [n, (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutaneous</td>
<td>30 (94)</td>
<td>13 (100)</td>
<td>43 (96)</td>
</tr>
<tr>
<td>Bone Marrow</td>
<td>16 (50)</td>
<td>7 (54)</td>
<td>23 (51)</td>
</tr>
<tr>
<td>Extramedullary (non-cutaneous)</td>
<td>18 (56)</td>
<td>6 (46)</td>
<td>24 (53)</td>
</tr>
<tr>
<td>Dose [n]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7 µg/kg/day</td>
<td>3</td>
<td>--</td>
<td>3</td>
</tr>
<tr>
<td>12 µg/kg/day</td>
<td>29</td>
<td>13</td>
<td>42</td>
</tr>
</tbody>
</table>
# BPDCN Disease Measurements

<table>
<thead>
<tr>
<th>Site of disease</th>
<th>Assessment tool</th>
<th>Criteria</th>
<th>Key Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Skin</td>
<td>mSWAT/ biopsy</td>
<td>mSWAT calculation and pathology&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Olsen, 2011</td>
</tr>
<tr>
<td>• Bone Marrow (BM)</td>
<td>BM aspirate/biopsy, peripheral blood counts</td>
<td>AML</td>
<td>Cheson, 2003</td>
</tr>
<tr>
<td><strong>Secondary&lt;sup&gt;2&lt;/sup&gt;</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lymph nodes, viscera</td>
<td>CT or PET/CT</td>
<td>NHL</td>
<td>Cheson, 2014</td>
</tr>
</tbody>
</table>

<sup>1</sup>CR includes Clinical CR (CRc) = complete response in all non-skin disease sites, marked clearance of all skin lesions from baseline but with residual skin abnormalities not indicating active BPDCN

<sup>2</sup>Assessed at baseline and thereafter as necessary

Illustration of mSWAT surface area assessment
Tagraxofusp: Safety and Tolerability

All Tagraxofusp Clinical Trials (12 µg/kg/day) (n=148)

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>All Grades n (%)</th>
<th>TRAEs n (%)</th>
<th>TRAEs</th>
<th>All AEs</th>
<th>Gr 1-2</th>
<th>Gr 3</th>
<th>Gr 4</th>
<th>Gr 5</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TRAEs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALT increased</td>
<td>65 (43.9%)</td>
<td>80 (54.1%)</td>
<td>31 (20.9%)</td>
<td>34 (23.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST increased</td>
<td>65 (43.9%)</td>
<td>74 (50.0%)</td>
<td>30 (20.3%)</td>
<td>31 (20.9%)</td>
<td>4 (2.7%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminaemia</td>
<td>65 (43.9%)</td>
<td>73 (49.3%)</td>
<td>64 (43.2%)</td>
<td>1 (0.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>39 (26.4%)</td>
<td>48 (32.4%)</td>
<td>7 (4.7%)</td>
<td>8 (5.4%)</td>
<td>24 (16.2%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>38 (25.7%)</td>
<td>70 (47.3%)</td>
<td>37 (25.0%)</td>
<td>1 (0.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>33 (22.3%)</td>
<td>60 (40.5%)</td>
<td>33 (22.3%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>30 (20.3%)</td>
<td>67 (45.3%)</td>
<td>26 (17.6%)</td>
<td>4 (2.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight increased</td>
<td>28 (18.9%)</td>
<td>42 (28.4%)</td>
<td>28 (18.9%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chills</td>
<td>26 (17.6%)</td>
<td>40 (27.0%)</td>
<td>25 (16.9%)</td>
<td>1 (0.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capillary leak syndrome (CLS)</td>
<td>25 (16.9%)</td>
<td>25 (16.9%)</td>
<td>16 (10.8%)</td>
<td>5 (3.4%)</td>
<td>3 (2.0%)</td>
<td>1 (0.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypotension</td>
<td>23 (15.5%)</td>
<td>36 (24.3%)</td>
<td>17 (11.5%)</td>
<td>5 (3.4%)</td>
<td>1 (0.7%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oedema peripheral</td>
<td>22 (14.9%)</td>
<td>57 (38.5%)</td>
<td>21 (14.2%)</td>
<td>1 (0.7%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 As of August 2018

2 0.6% (1/166) for all trials (12 µg/kg/day) and 1.5% (3/202) for all trials (all doses) were grade 5.

A myocardial infarction, grade 5, was also reported in a patient who experienced a grade 4 CLS.

- No apparent cumulative AEs, including in the bone marrow, over multiple cycles
- CLS largely cycle 1-related and manageable with monitoring and pre-emptive measures
# Tagraxofusp: Clinical Activity – All Stages (1, 2, and 3)

Stages 1, 2, and 3: BPDCN (12 µg/kg/day) (n=42)

<table>
<thead>
<tr>
<th>Line of Therapy</th>
<th>1L</th>
<th>R/R</th>
<th>1L &amp; R/R</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>29</td>
<td>13</td>
<td>42</td>
</tr>
<tr>
<td>ORR, n (%)</td>
<td>26 (90%)</td>
<td>9 (69%)</td>
<td>35 (83%)</td>
</tr>
<tr>
<td>CR + CRc + CRi, n (%)</td>
<td>21 (72%)</td>
<td>5 (38%)</td>
<td>26 (62%)</td>
</tr>
<tr>
<td>CR</td>
<td>14</td>
<td>1</td>
<td>15</td>
</tr>
<tr>
<td>CRc</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>CRi</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>5 (17%)</td>
<td>4 (31%)</td>
<td>9 (21%)</td>
</tr>
<tr>
<td>Bridged to SCT, n (%)</td>
<td>13 (45%)</td>
<td>1 (8%)</td>
<td>14 (33%)</td>
</tr>
<tr>
<td>Allo</td>
<td>10</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Auto</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
Tagraxofusp: Clinical Activity – Stage 3

Stage 3: BPDCN (12 μg/kg/day) (n=13)

- Pivotal, confirmatory cohort met primary endpoint
- 54% rate of CR + CRc (7/13) [95% CI: 25.1, 80.8]; exceeded pre-specified rate

### Stage 3 responders

<table>
<thead>
<tr>
<th>Line of Therapy</th>
<th>First-line Dose Level 12 μg/kg</th>
<th>ORR, n (%)</th>
<th>CR + CRc + CRi, n (%)</th>
<th>CR</th>
<th>CRc</th>
<th>CRi</th>
<th>PR, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>13</td>
<td>10 (77%)</td>
<td>7 (54%)</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>3 (23%)</td>
</tr>
<tr>
<td>Bridged to SCT, n (%)</td>
<td>6 (46%)</td>
<td>6</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 3 complete responders</th>
<th>Bone Marrow (% Blasts)</th>
<th>Skin (mSWAT)</th>
<th>SCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Best Response</td>
<td>Baseline</td>
<td>Best Response</td>
</tr>
<tr>
<td>69</td>
<td>CR</td>
<td>94%</td>
<td>2%</td>
</tr>
<tr>
<td>68</td>
<td>CRc</td>
<td>70%</td>
<td>2%</td>
</tr>
<tr>
<td>57</td>
<td>CR</td>
<td>66%</td>
<td>2%</td>
</tr>
<tr>
<td>74</td>
<td>CRc</td>
<td>22%</td>
<td>1%</td>
</tr>
<tr>
<td>65</td>
<td>CR</td>
<td>12%</td>
<td>1%</td>
</tr>
<tr>
<td>32</td>
<td>CRc</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>22</td>
<td>CRc</td>
<td>1%</td>
<td>1%</td>
</tr>
</tbody>
</table>
Tagraxofusp: Bone Marrow Responses

BPDCN (12 μg/kg/day); Stages 1, 2, and 3

Stages 1 and 2 (1L)

Stages 1 and 2 (R/R)

Stage 3 (1L)
**Tagraxofusp: Best Response and Treatment Duration**

### Stages 1 and 2: First-line BPDCN (12 µg/kg/day)

- **Individual patients:**
  - Patient 1: CR
  - Patient 2: CR
  - Patient 3: CR
  - Patient 4: PR
  - Patient 5: CRc
  - Patient 6: CR
  - Patient 7: CR
  - Patient 8: CRc
  - Patient 9: CR
  - Patient 10: CR
  - Patient 11: CR
  - Patient 12: PR
  - Patient 13: CR
  - Patient 14: CRc
  - Patient 15: CR
  - Patient 16: CR

- **Responses:**
  - CR: Complete Response
  - CRc: Complete Response with count
  - PR: Partial Response
  - SD: Stable Disease

- **Treatment Duration:**
  - Patient 16: CR (Auto)
  - Patient 15: CR
  - Patient 14: CRc
  - Patient 13: CR
  - Patient 12: PR
  - Patient 11: CR
  - Patient 10: CR
  - Patient 9: CR
  - Patient 8: CRc
  - Patient 7: CR
  - Patient 6: CR
  - Patient 5: CRc
  - Patient 4: PR
  - Patient 3: CR
  - Patient 2: CR
  - Patient 1: CR

### Stage 3: First-line BPDCN (12 µg/kg/day)

- **Individual patients:**
  - Patient 29: CRc
  - Patient 28: CR
  - Patient 27: CR
  - Patient 26: CR
  - Patient 25: CRc
  - Patient 24: CRc
  - Patient 23: CRc
  - Patient 22: PR
  - Patient 21: PR
  - Patient 20: SD
  - Patient 19: SD
  - Patient 18: PR
  - Patient 17: PR

- **Responses:**
  - CR: Complete Response
  - CRc: Complete Response with count
  - PR: Partial Response
  - SD: Stable Disease

- **Treatment Duration:**
  - Patient 29: CRc (Allo)
  - Patient 28: CR (Allo)
  - Patient 27: CR (Allo)
  - Patient 26: CR (Allo)
  - Patient 25: CRc (Allo)
  - Patient 24: CRc (Allo)
  - Patient 23: CRc
  - Patient 22: PR
  - Patient 21: PR
  - Patient 20: SD
  - Patient 19: SD
  - Patient 18: PR
  - Patient 17: PR

- **Off study in remission:**
  - Patient 17: *Patient relapsed off study at 7.3 months.*

**Data cutoff:** September 1, 2018
Tagraxofusp: Overall Survival (OS)

First-line BPDCN (12 µg/kg/day) - Stages 1, 2, and 3 (n=29)

- Median OS: Not reached
- Long-term survivors
  
  (median follow up: 23.0 mos. [0.2-41\,])

Data cutoff: September 1, 2018
Tagraxofusp: Summary and Conclusions

• BPDCN: historically poor outcomes; no standard of care

• High response rates in BPDCN
  – 90% ORR in first-line (12 μg/kg; n=29); 69% ORR in R/R (n=13)
  – Majority of responses are CR/CRc

• 45% of patients treated with tagraxofusp in first-line setting (12 μg/kg) were bridged to SCT in remission (n=13)

• Tagraxofusp for BPDCN:
  – Breakthrough Therapy Designation (BTD) granted by FDA
  – BLA under Priority Review; February 21, 2019 PDUFA action date

• Tagraxofusp is also being clinically evaluated in additional malignancies
Acknowledgements

We would like to thank:

• Investigators, co-investigators, and study teams at each participating center:

• This study is sponsored by Stemline Therapeutics, Inc.