Phase 2 trial of SL-701, a novel immunotherapy comprised of synthetic short peptides against GBM targets IL-13Rα2, EphA2, and Survivin, in adults with second-line recurrent GBM: Interim results

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SL-701 Background

- SL-701 is a subcutaneously-delivered immunotherapy
- Comprised of short synthetic peptides engineered to generate T cell response against GBM
- Co-administered with immunostimulants

**GBM targets:**
- IL-13Ra2, Survivin, Ephrin A2

**Overexpression of SL-701 targets on GBM**

**Normal brain**
- IL-13Ra2
- EphA2
- Survivin

**GBM**
- IL-13Ra2
- EphA2
- Survivin

**Mechanism of Action**
- SL-701 (subcutaneously administered)
- Immunostimulants co-administered
- Antigen presentation
- Immune activation
- GBM cells
- Tumor cell killing
- CD8+ T cell activation
- CD8+ T cell proliferation and differentiation

**Directs T cells to GBM**
- Inflammatory response in post-therapy brain biopsy
- Abundant CD8+ T cells
- Numerous CD68+ macrophages


From: JCO, 2011; ASCO, 2011
SL-701 Clinical Trials Summary

• Previous Phase 1/2 Trial for safety; completed
  - Earlier version of SL-701 + poly-ICLC (T cell and NK cell activator)
  - Safe and well-tolerated
  - Single-agent activity (major responses in relapsed/refractory GBM)
    (JCO, 2011; ASCO, 2011 Poster#2506; AACR, 2012 Poster#LB-135)

• Phase 2 Trial (STML-701-0114), Stage 1 (single agent proof-of-concept); completed
  - SL-701 + GM-CSF + Imiquimod
  - Single agent activity observed in second-line GBM
    Bevacizumab and poly-ICLC introduced in combination study (Stage 2) to potentially enhance immune activity & optimize long-term anti-tumor effect of SL-701 (i.e. survival)

• Phase 2 Trial (STML-701-0114), Stage 2 (combination study); ongoing
  - SL-701 + poly-ICLC + bevacizumab
    - Major responses observed in second-line GBM
    - Overall survival trending favorably, median not reached

PR=partial response; SD=stable disease
SL-701: Phase 2 Trial Design (STML-701-0114)

Eligibility: Second-line GBM

### Stage 1

- **SL-701**
- **GM-CSF** + **Imiquimod**

<table>
<thead>
<tr>
<th>Week:</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
<th>18</th>
<th>20</th>
<th>22</th>
</tr>
</thead>
</table>

After week 22: **SL-701 / GM-CSF / imiquimod every 4 weeks thereafter until disease progression**

### Stage 2

- **SL-701**
- **poly-ICLC**
- **Bevacizumab**

<table>
<thead>
<tr>
<th>Week:</th>
<th>0</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>14</th>
<th>16</th>
<th>18</th>
<th>20</th>
<th>22</th>
</tr>
</thead>
</table>

After week 22: **SL-701 / poly-ICLC every 4 weeks and bevacizumab (as per label) every 2 weeks thereafter until disease progression**
**SL-701: Demographics and Baseline Disease**

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Stage 1 (n=46)</th>
<th>Stage 2 (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender [n, (%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>36 (65)</td>
<td>18 (64)</td>
</tr>
<tr>
<td>Time from initial diagnosis, months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median [range]</td>
<td>14.4 [0.9-99]</td>
<td>11.2 [1.1-176]</td>
</tr>
<tr>
<td>IDH1 mutation [n,(%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mutation</td>
<td>2 (4)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>No mutation</td>
<td>16 (35)</td>
<td>17 (61)</td>
</tr>
<tr>
<td>Unknown / not available</td>
<td>28 (61)</td>
<td>9 (32)</td>
</tr>
<tr>
<td>KPS score at screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median [range]</td>
<td>90% [70-100]</td>
<td>80% [70-100]</td>
</tr>
<tr>
<td>Duration on treatment, months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median [range]</td>
<td>1.9 [0.1-23]</td>
<td>3.1 [0.9-10]</td>
</tr>
<tr>
<td>Salvage surgeries [n, (%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross Total Resection (GTR)</td>
<td>15 (33)</td>
<td>6 (21)</td>
</tr>
<tr>
<td>Sub Total Resection (STR)</td>
<td>10 (22)</td>
<td>3 (11)</td>
</tr>
<tr>
<td>Non-surgical anti-GBM therapies [n, (%)]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stupp protocol for GBM</td>
<td>42 (91)</td>
<td>26 (93)</td>
</tr>
<tr>
<td>TMZ chemotherapy</td>
<td>40 (87)</td>
<td>24 (86)</td>
</tr>
<tr>
<td>Investigational agent</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>Other (Gliadel wafer, Nivolumab, Vorinostat)</td>
<td>1 (2)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Radiotherapy only</td>
<td>1 (2)</td>
<td>1 (4)</td>
</tr>
</tbody>
</table>
## SL-701: Adverse Events

### Most common adverse events (≥ 15% treatment-related adverse effects, TRAEs)

<table>
<thead>
<tr>
<th>Stage 1 (N=46)</th>
<th>All Grades (% of patients)</th>
<th>Grade ≥ 3 (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TRAEs</td>
<td>All AEs</td>
</tr>
<tr>
<td>Injection site disorders¹</td>
<td>41</td>
<td>46</td>
</tr>
<tr>
<td>Fatigue</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Headache</td>
<td>7</td>
<td>28</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage 2 (N=28)</th>
<th>All Grades (% of patients)</th>
<th>Grade ≥ 3 (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TRAEs</td>
<td>All AEs</td>
</tr>
<tr>
<td>Injection site disorders²</td>
<td>54</td>
<td>61</td>
</tr>
<tr>
<td>Fatigue</td>
<td>32</td>
<td>50</td>
</tr>
<tr>
<td>Nausea</td>
<td>7</td>
<td>18</td>
</tr>
</tbody>
</table>

¹Includes: injection site cellulitis, erythema, induration, pain, pruritus, rash, swelling and general reaction
²Includes: injection site erythema, hemorrhage, infection, pain, pruritus, rash and general reaction
SL-701: Efficacy Results

- **Stage 1 (single agent proof-of-concept)**
  - 1 PR of 13+ months duration, ongoing
  - 2 SDs of 18+ and 20+ months duration, both ongoing

- **Stage 2 (combination study)**
  - 7 responses (2 CR, 5 PR)
    - 4 confirmed with 2nd response assessment
    - 2 with pending 2nd response assessment
    - 1 progressed prior to 2nd response assessment
  - 28 patients enrolled; 21 patients currently evaluable, which excludes:
    - 4 with pending 1st response assessment
    - 3 with pending 2nd response assessment (SD at 1st assessment)

**Duration of Response:** 0.9+ – 13.3+ months, ongoing
SL-701: Stage 2 Overall and Progression Free Survival (n=28)

Median follow-up: 4.1 months (0.7-10.6)

OS probability

Median follow-up:
4.1 months (0.7-10.6)

PFS probability

Median follow-up:
4.1 months (0.7-10.6)
Stage 1 (single agent)

- 30 yr male, grade IV GBM, KPS 90%
- Prior treatment: 2 resections + Stupp
- SL-701 for 23+ months (ongoing)
  - PR after 11 months (confirmed by 2nd assessment)
- Patient continues to receive SL-701 on study in remission
SL-701: Major Responders, Combination (Stage 2)

Stage 2 (combination study)
- 51 yr male, grade IV GBM, KPS 90%
- Prior treatment: 2 resections + Stupp
- SL-701 for 6+ months (ongoing)
  - PR after 2 months (confirmed by 2nd assessment); subsequently converted to CR (2nd assessment pending)
- Patient continues to receive SL-701 on study in remission

Stage 2 (combination study)
- 60 yr male, grade IV GBM, KPS 90%
- Prior treatment: 1 resections + Stupp + Veliparib
- SL-701 for 10+ months (ongoing)
  - CR after 4 months (confirmed by 2nd assessment)
- Patient continues to receive SL-701 on study in remission
SL-701: Phase 2 Trial Summary and Conclusions

- SL-701 is safe and well-tolerated as both a single agent and in combination with bevacizumab
- SL-701 has demonstrated clinical activity, including major responses, in relapsed/refractory GBM when used either alone or in combination with bevacizumab
- Key efficacy outcomes observed in the Phase 2 (STML-701-0114) trial:
  - Major objective responses
  - Response duration encouraging, with 4 responses of 6+ months in duration, all ongoing
  - Overall survival data maturing and appear promising; median not reached
- Patients continue to be followed for response and survival, and additional clinical data updates are expected next year, as well as immunocorrelative analyses
- Next steps include a potential Phase 3 pivotal trial and evaluation of additional combination regimens
• We would like to thank investigators, co-investigators, and study teams at each participating center:

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  • UC San Francisco
  • Barrow Neurological Institute
  • University of Minnesota
  • Columbia University Medical Center
  • George Washington University

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