Update of The P-BCMA-101-001 Phase 1 Clinical Trial: A Novel Stem Cell Memory CAR-T for Relapsed/Refractory Multiple Myeloma

Eric Ostertag, MD, PhD
Chief Executive Officer
September 5th, 2018
piggyBac™ Enables Multiple Differentiated CAR-T Product Attributes

piggyBac™ is a superior DNA delivery system for developing CAR-T and other gene therapy products

- **Unprecedented cargo capacity (>30X lentivirus)** – three-in-one transgene and possibility of multiple CAR or TCR molecules
- Creates highly desirable **T Stem Cell Memory (Tscm) Phenotype**
- Non-viral delivery system – **non-oncogenic and non-mutagenic**
- **High insertion efficiency** and stable transgene expression
- Faster to clinic with **lower cost** than viral methods
- **Substantial IP portfolio** with no dominant or competing IP
Massive piggyBac™ Cargo Capacity Allows for Delivery of Three-In-One Transgene for P-BCMA-101

1. **CAR-T MOLECULE**
   - Superior binding molecule
     - Centyrin molecule with high-specificity binding to BCMA
     - Fully human and not susceptible to tonic signaling

2. **POSITIVE SELECTION**
   - Drug resistance gene permits positive selection
     - All T-cells in final product express the CAR molecule
     - Predicted to result in better therapeutic index

3. **SAFETY SWITCH**
   - Incorporates proprietary safety switch
     - Rapid, dose-dependent elimination of engineered T-cells if needed
     - Management of Cytokine Release Syndrome (CRS) or other AEs
piggyBac™ Unmatched Cargo Capacity Increases Optionality

piggyBac™ effectively delivers multiple full-length CARs in single transposon system

# Full-length CARs*

1. BCMA
2. BCMA + PSMA
3. BCMA + PSMA + CD19
4. BCMA + PSMA + CD19 + GD2

* Plus selection gene and marker gene
Poseida CAR-T Products Comprised of Highly Favorable Stem Cell Memory T Cells

- Ability to develop product with **high percentage of Tscm cells** is a distinct competitive advantage
- piggyBac™ preferentially transposes in Tscm cells
- **Tscm cells persist and live longer** than effector cells
- Tscm cells can produce potentially unlimited effectors cells
- Tscm-rich product should lead to **better engraftment and better duration** of response with the potential for re-response

Lentivirus-produced products have not achieved high Tscm **published** percentages ranging from less than 1% to ~14%
Stem Cell Memory Phenotype

Adapted from Gattinoni et al. (2017) Nat. Med.

- Naïve/Tscm
- Tcm
- Tem
- Teff
- P-BCMA-101

- CD62L
- CD45RA

Perforin

CD45RA

CD45RO

CCR7

CD62L

CD28

CD27

IL-7Rα

CXCR3

CD95

CD11a

IL-2Rβ

CD58

CD57

Stemness

Proliferative potential

Lymphoid homing

Antigen independence

Lipid metabolism

Low Δψm

Senescence

Cytotoxicity

Tissue tropism

Antigen addiction

Glycolytic metabolism

Oxidative stress

Adapted from Gattinoni et al. (2017) Nat. Med.
piggyBac™ and Lentivirus Modify Different T Cell Subsets

piggyBac™ preferentially transposes early Tscm cells, while lentivirus prefers differentiated T cells

We purified donor cells to these T-cell subsets and then performed optimized piggyBac™ or optimized lentivirus manufacturing on each subset.
P-BCMA-101 Efficacy & Control of Tumor Recurrences

Unprecedented efficacy in preclinical MM.1S xenograft model

- Some tumor relapse, but subsequent elimination of tumor
  - First observed in MDACC pilot study
  - Many examples of same phenomenon
  - Possibly due to stem-like ($T_{SCM}$) quality of product

Days Post P-BCMA-101 Administration

Days Post P-BCMA-101 Administration
Phase 1 Relapsed/Refractory Multiple Myeloma Clinical Trial

**P-BCMA-101-001 Phase 1 Trial Design**
- Open Label, 3+3 Design, Single Ascending Dose Study
- Up to 6 dose levels
- 30 mg/m2 fludarabine + 300 mg/m2 cyclophosphamide x 3d lymphodepletion regimen
- P-BCMA-101 administered intravenously as a single dose
- Up to 40 subjects

**Clinical Sites / Investigators**
- Johns Hopkins – Syed Abbas Ali
- MD Anderson – Krina Patel & Bob Orlowski
- Sarah Cannon (SCRI) – Tara Gregory & Jesus Berdeja
- U. of California at San Diego (UCSD) – Caitlin Costello
- University of Pennsylvania – Adam Cohen

**Timeline**
- 2017: Complete IND Enabling Studies
- 2018: Phase 1/2 First Patient Dosed
- 2018: Phase 1/2 Data Readouts (Open Label Trial)
## P-BCMA-101-001 Enrollment

11 patients treated in 3 dose groups

<table>
<thead>
<tr>
<th>Dose levels assessed</th>
<th>cells/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.75 x 10^6</td>
</tr>
<tr>
<td>2</td>
<td>2 x 10^6</td>
</tr>
<tr>
<td>3</td>
<td>6 x 10^6</td>
</tr>
</tbody>
</table>

Potential additional dose levels

<table>
<thead>
<tr>
<th></th>
<th>cells/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>10 x 10^6</td>
</tr>
<tr>
<td>5</td>
<td>15 x 10^6</td>
</tr>
</tbody>
</table>

Total CAR-T cell administered per group (mean)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Patients (###)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>51 x 10^6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>152 x 10^6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>430 x 10^6</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
## Baseline Demographics and Clinical Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (min, max) age, y</td>
<td>60 (48, 72)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>7 (64)</td>
</tr>
<tr>
<td>Median (min, max) time since diagnosis, y</td>
<td>5 (2, 12)</td>
</tr>
<tr>
<td>High-risk, n (%)</td>
<td>73</td>
</tr>
<tr>
<td>ECOG PS</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7 (64)</td>
</tr>
<tr>
<td>1</td>
<td>4 (36)</td>
</tr>
<tr>
<td>Median (min, max) prior regimens</td>
<td>6 (3, 9)</td>
</tr>
<tr>
<td>proteasome inhibitor, n (%)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>bortezomib</td>
<td>11 (100)</td>
</tr>
<tr>
<td>carfilzomib</td>
<td>10 (91)</td>
</tr>
<tr>
<td>IMiD, n (%)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>lenalidomide</td>
<td>11 (100)</td>
</tr>
<tr>
<td>pomalidomide</td>
<td>10 (91)</td>
</tr>
<tr>
<td>daratumumab, n (%)</td>
<td>11 (100)</td>
</tr>
<tr>
<td>Prior autologous SCT</td>
<td>9 (82)</td>
</tr>
</tbody>
</table>

## Adverse Events

### Treatment-Emergent Adverse Events (N=11)

<table>
<thead>
<tr>
<th>TEAE, n (%)</th>
<th>Overall</th>
<th>≥ Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Limiting Toxicity (DLT) (^a)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cytokine Release Syndrome (^a)</td>
<td>1 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Neurotoxicity (^a)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia/Neutrophil count decreased (^b)</td>
<td>8 (73)</td>
<td>8 (73)</td>
</tr>
<tr>
<td>Thrombocytopenia/Platelet count decreased (^b)</td>
<td>5 (45)</td>
<td>2 (18)</td>
</tr>
<tr>
<td>Anemia</td>
<td>4 (36)</td>
<td>2 (27)</td>
</tr>
<tr>
<td>Infection (^c)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>5 (45)</td>
<td>2 (18)</td>
</tr>
<tr>
<td>First month</td>
<td>4 (36)</td>
<td>2 (18)</td>
</tr>
</tbody>
</table>

\(^a\) by investigator assessment
\(^b\) subject counted once for either term
\(^c\) includes events in the SOC Infections and Infestations. Subject counted once for any PT within the SOC. Events reported include upper respiratory tract infection (3 subjects), pneumonia, sinusitis, wound infection, candida infection. Not including orthostatic dizziness or peripheral neuropathy/tremor

### Cytokine Release Syndrome By Dose Level

<table>
<thead>
<tr>
<th>Dose Level</th>
<th>Patients, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 2 x 10^-6</td>
<td>0%</td>
</tr>
<tr>
<td>15 2 x 10^-6</td>
<td>14%</td>
</tr>
<tr>
<td>4 3 x 10^-6</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Mean Dose:**

*5.2 x 10^-6 (n = 3)*

*15.2 x 10^-6 (n = 7)*

*4.3 x 10^-6 (n = 1)*

**Not including orthostatic dizziness or peripheral neuropathy/tremor**
**Cytokine Release Syndrome: Negligible**  
No Tocilizumab or Steroid Required, Low IL-6 Peaks

**Cytokine Release Syndrome Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Dosed Patients (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with a CRS event, n</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Maximum CRS grade</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10 (91%)</td>
</tr>
<tr>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>1 (9%)</td>
</tr>
<tr>
<td>Median time to onset, d</td>
<td>11</td>
</tr>
<tr>
<td>Median duration, d</td>
<td>4</td>
</tr>
<tr>
<td>Tocilizumab use, n</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Corticosteroid use, n</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Peak IL-6 Levels After P-BCMA-101**

![Graph showing peak IL-6 levels](image-url)
P-BCMA-101 CAR-T Cell Expansion

P-BCMA-101 in Peripheral Blood (PB)

- P-BCMA-101 shows peak expansion between 14-21 days
- CAR-T products generally show peak expansion between 5-14 days
- Peak expansion of CAR-Ts often associated with CRS
- P-BCMA-101 reaches peak expansion gradually without CRS
Tumor Response: High From The Lowest Dose Level Up

Tumor Response in Evaluable Patients by Dose

Data cutoff: August 10th, 2018. mDOR, median duration of response; ORR, objective response rate, attaining sCR, CR, VGPR, or PR, including confirmed and unconfirmed responses. Evaluable patients: reached first response assessment by IMWG m-protein criteria or PD/death.
Acknowledgements

P-BCMA-101 Patients

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Satva Neelapu, M.D.

P-BCMA-101-001 Investigators

Adam Cohen, M.D. UP
Abbas Ali, M.D. JHU
Jesus Berdeja, M.D. SCRI
Caitlin Costello, M.D. UCSD
Tara Gregory, M.D. SCRI/CBCI
Krina Patel, M.D. MDACC
Summary

- P-BCMA-101 at all doses induces deep and durable responses in a heavily pretreated population with R/R MM

- To date, the safety profile of P-BCMA-101 has been extremely good
  - Only one case of CRS observed
  - No tocilizumab or corticosteroid use
  - No neurotoxicity

- **Best-in-class** gene engineering and CAR-T platforms

- **Advantages** in efficacy, safety, speed to clinic and cost
  - Purity may give a better therapeutic index
  - Tscm phenotype may give a delayed and less toxic response