Abstract #: 3004
Safety and clinical activity of adenosine A2a receptor (A2aR) antagonist, CPI-444, in anti-PD1/PDL1 treatment-refractory renal cell (RCC) and non-small cell lung cancer (NSCLC) patients

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Co-Director, Parker Institute of Cancer Immunotherapy @ UCSF
University of California, San Francisco
This presentation contains forward-looking statements, including statements related to the potential safety and efficacy of CPI-444, both as a single agent and in combination with anti-PD-1 and anti-PD-L1, and the Company’s ability to develop and advance product candidates into and successfully complete clinical trials, including the Company’s Phase 1/1b clinical trial of CPI-444. All statements other than statements of historical fact contained in this press release are forward-looking statements. These statements often include words such as “believe,” “expect,” “anticipate,” “intend,” “plan,” “estimate,” “seek,” “will,” “may” or similar expressions. Forward-looking statements are subject to a number of risks and uncertainties, many of which involve factors or circumstances that are beyond the Company’s control. The Company’s actual results could differ materially from those stated or implied in forward-looking statements due to a number of factors, including but not limited to, risks detailed in the Company’s Quarterly Report on Form 10-Q for the three months ended March 31, 2017, filed with the Securities and Exchange Commission on May 4, 2017, as well as other documents that may be filed by the Company from time to time with the Securities and Exchange Commission. In particular, the following factors, among others, could cause results to differ materially from those expressed or implied by such forward-looking statements: the Company’s ability to demonstrate evidence of efficacy and safety for CPI-444 during its Phase 1/1b clinical trial; the results of early clinical trials may not be predictive of future results; the unpredictability of the regulatory process; and regulatory developments in the United States and foreign countries. Although the Company believes that the expectations reflected in the forward-looking statements are reasonable, it cannot guarantee that the events and circumstances reflected in the forward-looking statements will be achieved or occur, and the timing of events and circumstances and actual results could differ materially from those projected in the forward-looking statements. Accordingly, you should not place undue reliance on these forward-looking statements. All such statements speak only as of the date made, and the Company undertakes no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise. Additional information may be available in press releases or other public announcements and public filings made after the date of this presentation.

This presentation concerns products that have not yet been approved for marketing by the U.S. Food and Drug Administration (“FDA”). No representation is made as to their safety or effectiveness for the purposes of which they are being investigated.
Safety and clinical activity of adenosine A2a receptor (A2aR) antagonist, CPI-444 in anti-PD(L)1 treatment-refractory renal cell (RCC) and non-small cell lung cancer (NSCLC) patients


University of California, San Francisco, San Francisco, CA; Johns Hopkins Kimmel Cancer Center and Bloomberg-Kimmel Institute for Cancer Immunotherapy, Baltimore, MD; Carolina BioOncology Institute, Huntersville, NC; David Geffen School of Medicine at UCLA, Los Angeles, CA; Mary Crowley Cancer Research Centers, Dallas, TX; University of Chicago, Chicago, IL; Memorial Sloan Kettering Cancer Center, New York, NY; Stanford University School of Medicine, Stanford, CA; University of Colorado Anschutz Medical Campus, Aurora, CO; The University of Arizona, Phoenix, AZ; Karmanos Cancer Institute/Wayne State University, Detroit, MI; Royal Brisbane Hospital, Chapel Hill, Australia; Monash Health and Monash University, Melbourne, Australia; Med Coll of Wisconsin, Milwaukee, WI; Icahn School of Medicine at Mount Sinai, New York, NY; The Johns Hopkins University, Baltimore, MD; Corvus Pharmaceuticals, Burlingame, CA
Background

- Anti-PD-(L)1 antibodies are approved for treatment of RCC and NSCLC but a small proportion of patients benefit.
- No approved agents overcome resistance to anti-PD-(L)1 with few reporting benefit in PD-1 resistant/ refractory setting.
- Converting tumors devoid of T cell infiltration ("cold tumors") into T cell inflamed tumors ("hot tumors") could improve response to immunotherapies.
- Adenosine is a mediator of immunosuppression within the tumor microenvironment.
- CPI-444 is an oral small molecule antagonist of the adenosine A2A receptor (A2AR) (Emens, AACR 2017).
Adenosine Suppresses Immunity and is a Potential Mechanism of Resistance to PD-(L)1 Therapy

Adenosine in the tumor microenvironment

Tumors can generate adenosine in response to anti-PD-(L)1

(Beavis et al, Can Immunol Res 2015)

CD73 expression in baseline tumor biopsies from the CPI-444 phase 1 trial

Anti-PD-(L)1

N=17

N=19

p=0.001
### Phase 1/1b Clinical Study with Oral Drug CPI-444

**Expansion cohorts:** renal cell and non-small cell lung cancer

#### CPI-444 Monotherapy

<table>
<thead>
<tr>
<th>Dose Selection</th>
<th>Cohort Expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 mg BID or 200 mg QD, 14 or 28 days</td>
<td>100 mg BID 28 days</td>
</tr>
</tbody>
</table>

#### CPI-444 with atezolizumab (anti-PD-L1)

<table>
<thead>
<tr>
<th>Dose Selection</th>
<th>Cohort Expansion</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 mg BID or 100 mg BID + 840 mg atezo Q2W</td>
<td>100 mg BID 28 days + 840 mg atezo Q2W</td>
</tr>
</tbody>
</table>

### Eligibility

- **Tumor types:** RCC, NSCLC, Melanoma, TNBC, Others
- **Prior anti PD-(L)1 allowed**
  - Resistant: SD or better > 3 months of treatment
  - Refractory: progression within 3 months
- **Must have progressive disease on prior therapy**
- **No selection for PD-L1 expression**
CPI-444 Blocks A2A Receptor Signaling

Adenosine → CPI-444 → A2AR → ↑ cAMP → ↑ pCREB

CD4+ T cell

Analysis of pCREB by flow cytometry

Adenosine (NECA) stimulation ex vivo

A2AR Pathway Activity (% Relative to Baseline)

Plasma CPI-444 (ng/ml)

- 50mg BID
- 100mg BID
- 200mg QD
## Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Non-Small Cell Lung Cancer (N=45)</th>
<th>Renal Cell Cancer (N=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prior anti-PD-(L)1 exposure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naive</td>
<td>8 (18%)</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>Resistant/Refractory</td>
<td>37 (82%)</td>
<td>22 (73%)</td>
</tr>
<tr>
<td><strong>PD-L1 Negative</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>54%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>Median time since IO agent, months (range)</strong></td>
<td>2.8 (0.6 – 24)</td>
<td>1.7 (1 – 71)</td>
</tr>
<tr>
<td><strong>Histology</strong></td>
<td>28 (62%) Non squamous 17 (38%) Squamous</td>
<td>28 (93%) Clear cell 2 (7%) Papillary</td>
</tr>
<tr>
<td><strong>Median age, years (range)</strong></td>
<td>70 (41-85)</td>
<td>65 (44-76)</td>
</tr>
<tr>
<td><strong>No. of patients single agent / No. of patients combination</strong></td>
<td>22/23</td>
<td>14/16</td>
</tr>
<tr>
<td><strong>Median number prior therapies</strong></td>
<td>2 (1-5)</td>
<td>3 (1-5)</td>
</tr>
</tbody>
</table>

*Archive samples data available on 19 RCC and 28 NSCLC patients based on FDA-approved test*
Treatement-Related Adverse Events

<table>
<thead>
<tr>
<th>Adverse Events (Gr1/2) &gt; 5% Frequency (n=75)</th>
<th>Single Agent (%)</th>
<th>Combination (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Nausea</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Pruritus</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Constipation</td>
<td>6</td>
<td>---</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6</td>
<td>---</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6</td>
<td>---</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6</td>
<td>---</td>
</tr>
<tr>
<td>Rash</td>
<td>---</td>
<td>5</td>
</tr>
<tr>
<td>AST increased</td>
<td>---</td>
<td>5</td>
</tr>
<tr>
<td>ALT increased</td>
<td>---</td>
<td>5</td>
</tr>
</tbody>
</table>

**Grade > 3 AEs:**
- **Single agent:** none
- **Combination CPI-444 + atezolizumab**
  - One patient with Gr 3 immune related hepatitis, pneumonitis, mucositis and dermatitis

Prepared by: Lawrence Fong, M.D.
Phase 1/1b Trial with CPI-444: Disease Control in NSCLC

Partial responses can be seen in anti-PD-1 progressors

Disease Control Duration

- Resistant/refractory to prior IO
- Naïve to prior IO
- PD-L1 Positive / Negative
Phase 1/1b Trial with CPI-444: Disease Control in Renal Cell Cancer
Partial responses can be seen in an anti-PD-1 progressing and naïve patients

- Partial responses can be seen in anti-PD-1 progressing and naïve patients
- Resistant/refractory to prior IO
- Naïve to prior IO
- PD-L1 Positive / Negative

Disease Control Duration

<table>
<thead>
<tr>
<th>Patients</th>
<th>Treatment (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>-</td>
<td>10</td>
</tr>
<tr>
<td>-</td>
<td>12</td>
</tr>
</tbody>
</table>

- Partial Response (PR)
- Stable Disease (SD)
- Progressive Disease (PD)
- Ongoing at Data Cutoff

Presented by: Lawrence Fong, M.D.
Tumor Growth Kinetics in “Stable” RCC Patients

CPI-444 Single Agent

- Prior to CPI-444
- On CPI-444

Percent Change in Target Lesion(s)

Days

CPI-444 in Combination with Atezolizumab

- Anti-PD-1 Naïve
- Pembrolizumab Resistant
- Nivolumab Refractory

Percent Change in Target Lesion(s)

Days

CPI-444

- Anti-PD-1 Naïve

Percent Change in Target Lesion(s)

Days

Anti-PD-1 Naïve

Percent Change in Target Lesion(s)

Days

Anti-PD-1 Naïve

Percent Change in Target Lesion(s)

Days

Anti-PD-1 Naïve

Percent Change in Target Lesion(s)

Days

Anti-PD-1 Naïve

Percent Change in Target Lesion(s)

Days

Anti-PD-1 Naïve
Tumor Regression in Nivolumab Refractory Renal Cancer
Single Agent CPI-444

Five prior regimens including TKIs, mTOR inhibitor, and nivolumab

Pre-treatment vs. 3 months of treatment:
- Pre-treatment:
  - H&E: 14%
  - CD8 IHC: >70%
- Post Dose (8w):
  - H&E: >70%
  - CD8 IHC: 14%

Presented by: Lawrence Fong, M.D.
06/05/2017
CPI-444 Induces CD8 T Cell Infiltration and Th1 Gene Expression in Tumor Tissues

CD8 T Cell Change (IHC)

- NSCLC
- RCC

Immune Gene Expression (paired biopsies)

- Log Fold Change Gene Expression
- Log P value

- Gene Expression Changes:
  - CXCL10
  - GZMB
  - PD-L1
  - OPG
  - CXCL11
  - CXCL16
  - GZMA
  - CCL17
  - TEFF_SIG
  - PD-L2
  - IL2RA
  - EOTAXIN
  - CCL13
  - CD44
  - IL7R
  - CXCL9
  - CD8A

- Median 95% CI

Presented by: Lawrence Fong, M.D.
CPI-444 Expands New T Cell Clones in Blood and Tumor

- RCC patient with PR on single-agent CPI-444
- T cell receptor (TCR) sequencing of blood and tumor biopsies pre- and post-treatment
- T cell clonotypes can be matched between blood and tumor

Treatment induces expansion of identical T cell clones in blood and tumor
Phase 1/1b Trial with CPI-444: Summary

- CPI-444 is well-tolerated as a monotherapy and in combination with atezolizumab
- CPI-444 has clinical activity alone and in combination with atezolizumab
- Anti-tumor activity seen in:
  - Patients who have progressed on prior anti-PD-(L)1
  - Patients with PD-L1 negative tumors
- CPI-444 can induce CD 8 T cell infiltration and expression of T cell activation genes within the tumor microenvironment
- CPI-444 induces new T cell clonotypes in the blood, which are capable of migrating to tumors
- Accrual of patients into the expansion cohorts for NSCLC and RCC is ongoing
Acknowledgements

• The patients and their families

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• Colleagues at Corvus

• Colleagues at Roche Genentech