LIGAND-INDUCIBLE, PROSTATE STEM CELL ANTIGEN (PSCA)-DIRECTED GoCAR-T® CELLS IN ADVANCED SOLID TUMORS: PRELIMINARY RESULTS FROM A DOSE ESCALATION STUDY

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DISCLOSURE SLIDE

Dr. Becerra has received honoraria from Taiho Pharmaceutical; has consulted for Agenus, Bayer, Heron, Ipsen, SOBI, and Takeda; and has participated in speakers’ bureaus for Bristol-Myers Squibb, Celgene, Merck Serono, and Taiho Pharmaceutical.

This study was sponsored by Bellicum Pharmaceuticals.
**INDUCIBLE MYD88/CD40 (iMC)**

Proinflammatory cytokines, Type I IFNs, T Cell Proliferation and Persistence
Other immune functions

IFN, interferon; iMC, inducible MyD88/CD40; TIR, toll/interleukin-1 receptor; TLR, toll-like receptor.
GoCAR-T®: BPX-601 OVERVIEW

- Autologous T cell product candidate
- Antigen-specific activation through PSCA-CD3ζ CAR
- Rimiducid-dependent costimulation through inducible MyD88/CD40 domain

**Hypothesis:** GoCAR-T design optimizes BPX-601 for antigen-directed and -independent T cell activation, proliferation, and persistence, which may afford BPX-601 enhanced clinical activity relative to traditional CAR-T cell therapies for solid tumors

CAR, chimeric antigen receptor; iMC, inducible MyD88/CD40; PSCA, prostate stem cell antigen; Rim, rimiducid; TCR, T cell receptor.
PROSTATE STEM CELL ANTIGEN (PSCA) TARGET RATIONALE

- Small, GPI-anchored cell-surface protein of the Thy-1/Ly-6 family
- Expressed in 60–80% of pancreatic ductal adenocarcinomas
- Also expressed in prostate, bladder, gastric, and other solid tumors and correlates with disease stage
- Low basal expression on normal prostate epithelium, urinary bladder, kidney, esophagus, stomach, and placenta
- Low toxicity profile with PSCA-targeted antibodies in prostate and pancreatic cancer

GPI, glycosylphosphatidylinositol; hACTB, human beta-actin; LoQ, limit of quantification.

• Part 1 objectives: safety, tolerability, MTD and/or RDE for use in Part 2
• Part 1 status: enrollment ongoing in Cohort 5

MTD, maximum tolerated dose; PSCA, prostate stem cell antigen; RDE, recommended dose expansion.
## PATIENT DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Tumor Type</th>
<th>BPX-601 Dose (10^6 cells/kg)</th>
<th>Rim (Y/N)</th>
<th>LD Regimen*</th>
<th># Prior Systemic Therapies</th>
<th>PSCA (copies)†</th>
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</table>

* Cytoxan 1 g/m² by IV infusion on Day −3; † PSCA (copies per 10⁶ copies hACTB) was measured at screening.
CTX, cyclophosphamide; hACTB, human beta-actin; LD, lymphodepletion; PSCA, prostate stem cell antigen; Rim, rimiducid.
### SAFETY SUMMARY

<table>
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<tr>
<th>Most common AEs reported by &gt; 1 patient</th>
<th>Total (N=12)</th>
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<tbody>
<tr>
<td>Any Event, n (%)</td>
<td>12 (100)</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Abdominal pain upper</td>
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<tr>
<td>Hypotension</td>
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<tr>
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<td>Back pain</td>
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<tr>
<td>Diarrhea</td>
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<td>Flatulence</td>
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<tr>
<td>Nausea</td>
<td>2 (17)</td>
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<tr>
<td>Pyrexia</td>
<td>2 (17)</td>
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- No DLTs, neurotoxicity, or events of cytokine release syndrome were observed
- Pyrexia is the only treatment-related AE reported by >1 patient (n=2)
  - Grade 1–2 on Day 0 following BPX-601 infusion
  - Both events resolved within 24–36 hours with supportive care

AE, adverse event; DLT, dose-limiting toxicity.
BPX-601 T CELL EXPANSION AND PERSISTENCE

Cohort 0
1.25x10⁶/kg

Cohort 3
1.25x10⁶/kg + Rim

Cohort 4
2.5x10⁶/kg + Rim

Cohort 5
5x10⁶/kg + Rim

- Limited evidence of LD with CTX-only regimen (79% ± 25% of cells remained)
- Rapid cell expansion by Day 4, but no persistence without Rim
- With single-dose Rim:
  - Cell expansion of 3- to 20-fold within 7 days in 4 patients
  - Cell persistence of >3 weeks in 3 patients

* Vector copy number < limit of quantification.
CTX, cyclophosphamide; LD, lymphodepletion; PSCA, prostate stem cell antigen; Rim, rimiducid.
PERIPHERAL CYTOKINE PROFILES OVER TIME

The orange, black, and blue lines represent data for an individual patient in the indicated cohort for multiple cytokines. Rim, rimiducid.

**Cohort 0**
1.25x10^6/kg

**Cohort 3**
1.25x10^6/kg + Rim

**Cohort 4**
2.5x10^6/kg + Rim

**Cohort 5**
5x10^6/kg + Rim

**Serum cytokines (pg/mL)**

Days post-BPX-601 infusion

ESMO
EVIDENCE OF ANTI-TUMOR ACTIVITY IN BPX-601–TREATED PATIENTS

<table>
<thead>
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<th>Cohort</th>
<th>Best Response (RECIST)</th>
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</tbody>
</table>

Two patients with SD had tumor shrinkage >20%

Patient 3A: 2 prior therapies; PSCA = 34,000 copies

Baseline
- Lesion longest diameter: 70 mm
- CA19-9: 294

Month 1
- Lesion longest diameter: 57 mm
- CA19-9: 152.6
- Overall response: SD (~15%)

Month 2
- Lesion longest diameter: 49 mm
- CA19-9: 207.2
- Possible new lesion
- Overall response: SD (~25%)

Month 4
- Lesion longest diameter: 40 mm
- CA19-9: 641.4
- New lesion confirmed
- Overall response: PD

CA19-9, cancer antigen 19-9; CR, complete response; PD, progressive disease; PR, partial response; PSCA, prostate stem cell antigen; SD, stable disease.
EVIDENCE OF ANTI-TUMOR ACTIVITY IN BPX-601–TREATED PATIENTS

Patient 4B: 4 prior therapies; PSCA = 8,243 copies

Baseline

Month 1

Month 2

- Slightly enlarged lesion with ring enhancement characteristic of pseudoprogression
- Similar lesion size
- Increased density
- Continued ring enhancement

- At Month 4, no clinical symptoms of worsening disease
- Ongoing treatment-free interval >19 weeks

PSCA, prostate stem cell antigen.
SWIM PLOT AFTER BPX-601 ADMINISTRATION

Disease control without new therapy was 16 and >18 weeks (ongoing) in 1 and 3 patients, respectively.

PD, progressive disease; pseudo PD, pseudoprogression, progressive disease; SD, stable disease.
SUMMARY AND CONCLUSIONS

- Administration of BPX-601 with single-dose rimiducid was well tolerated
  - No observed cytokine release syndrome or neurotoxicity of any grade
  - Most frequent AEs were consistent with those experienced by advanced cancer patients undergoing cytotoxic chemotherapy or other cancer immunotherapies
  - Treatment-related AEs were limited, mild to moderate in intensity, and resolved with supportive care
- Despite inadequate lymphodepletion with cyclophosphamide alone, BPX-601 displayed enhanced expansion and prolonged persistence in some patients treated with rimiducid
- Evidence of biological activity/stable disease have been observed in this heavily pre-treated patient population
- Part 2 (opening soon) will include more intense lymphodepletion with cyclophosphamide/fludarabine, a repeat-dose rimiducid infusion schedule, and gastric and prostate cancer patients