A Phase 2 Trial of Prostate Specific Membrane Antigen Antibody Drug Conjugate (PSMA ADC) in Taxane-Refractory Metastatic Castration-Resistant Prostate Cancer (mCRPC)

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Background: The abundant expression of PSMA on prostate cancer cells provides a rationale for antibody therapy. PSMA ADC is a fully human antibody to PSMA linked to the microtubule disrupting agent monomethyl auristatin E (mVMAE). It binds PSMA and is internalized and cleaved by lysosomal enzymes releasing toxic MMAE causing cell cycle arrest and apoptosis. We have enrolled 70 pts in a phase 2 trial of PSMA ADC in taxane-refractory mCRPC.

Methods: Pts with progressive mCRPC following taxane and ECOG PS <1 were eligible. PSMA ADC was administered Q3 wks or up to 8 cycles. Safety, tumor response by PSA, circulating tumor cells (CTC), imaging, biomarkers and clinical progression were assessed. Dosing was initiated at 2.5 mg/kg and adjustment for tolerability was allowed.

Results: 35 pts began treatment at 2.5 mg/kg. Due to neutropenia, the remaining 35 pts began at 2.3 mg/kg. All pts received prior docetaxel and abiraterone and/or enzalutamide. 15% also received cabazitaxel. Adverse events (AEs) were observed at both dose levels. AEs of grade 3 or worse included fatigue, anemia, neutropenia, peripheral neuropathy, hypoalbuminemia, and nausea.

Study Schema

Study Objectives & Key Eligibility Criteria

Objective: To assess the anti-tumor activity and tolerability of PSMA ADC

Inclusion:
- mCRPC progressed on abiraterone and/or enzalutamide, and
- Treatment with >2 prior cytotoxic chemotherapies

Exclusion:
- Treatment of mCRPC has changed dramatically and
- Includes multiple FDA-approved agents

Demographics & Baseline Characteristics

<table>
<thead>
<tr>
<th>Initial Dose Level (n)</th>
<th>Baseline PSA (n=41)</th>
<th>PSMA Expression (n=25)</th>
<th>PSA Responses</th>
<th>CTC Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3 mg/kg (37)</td>
<td>177.5 (7.5-1749.6)</td>
<td>96.8 (15.1-2618.1)</td>
<td>72.97% (27)</td>
<td>45.45% (15/33)</td>
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<td>2.5 mg/kg (14)</td>
<td>121.4 (7.5-1749.6)</td>
<td>74.1 (15.1-2618.1)</td>
<td>52.24% (7)</td>
<td>30.43% (4/13)</td>
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<td>All Subjects (n=41)</td>
<td>149.5 (7.5-1749.6)</td>
<td>85.4 (15.1-2618.1)</td>
<td>54.88% (22)</td>
<td>34.88% (14/40)</td>
</tr>
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Adverse Events Grade 3 and Above

- Fatigue 8 (17.4%)
- Dyspnea 1 (2.2%)
- Nausea 2 (4.3%)
- Diarrhoea 1 (2.2%)
- Myalgia 0 (0.0%)
- Pain 0 (0.0%)

Conclusions: PSMA ADC at 2.3 mg/kg was generally well tolerated and appears to be better tolerated than 2.5 mg/kg. Updated safety, tumor response and radiographic assessments from the full cohorts of 2.3 and 2.5 mg/kg will be presented. Testing in taxane naïve pts is also ongoing.

This study was funded by Progenics Pharmaceuticals, Inc., which has a proprietary commercial interest in PSMA ADC. The antibody-drug linker technology is licensed from4 Liberta Biosciences, Inc.