**Background**

Metastatic Castration-Resistant Prostate Carcinoma (mCRC)

- 248,530 new cases of prostate cancer in US in 2021 (American Cancer Society)
- 10-20% develop CRPC within 5-7 years of follow-up, most of them having metastases at time of diagnosis
- Docetaxel (D) has reliably delayed the progression of mCRPC for a median of 7-10 months
- Second-line treatment with androgen deprivation therapy or any of several androgen signaling inhibitors (AR, anti-androgens) is unmet need
- 1st-line treatment with enzalutamide, a new anti-androgen, resulted in improved overall survival

**Methods**

**Pretreated Setting**: Phase 2/3APR-De-escalation Cycles
- 1 spiral dose, 7 days on/10 days off
- 3 cycles (9 weeks), range 1-12 cycles
- Median duration on-treatment:
  - Cohort 1: 9 weeks
  - Cohort 2: 3-4 months

**Efficacy Setting**: 21 Days each cycle
- Phase 1b/2 Treatment Cycle: 21 Days each cycle

**Exposure Duration and Subject Disposition**

**Response Evaluation**

- Response Evaluation Criteria (RECIST v 1.1)
- PSA best overall response: PSA50 = 50% decrease in PSA from baseline
- CR (complete response) defined as PSA ≤ 0.2 ng/mL
- PR (partial response) defined as PSA > 0.2 ng/mL but ≤ 50% decrease in PSA from baseline
- SD (stable disease) defined as PSA > >50% but ≤ 100% increase in PSA from baseline or no change in PSA
- PD (progressive disease) defined as PSA > 100% increase in PSA from baseline or PSA > 2 ng/mL

**Key Inclusion and Exclusion Criteria**

- **Inclusion Criteria**
  - 248,530 new cases of prostate cancer in 2021 (American Cancer Society)
  - 10-20% develop CRPC within 5-7 years of follow-up, most of them having metastases at time of diagnosis
  - Docetaxel (D) has reliably delayed the progression of mCRPC for a median of 7-10 months
  - Second-line treatment with androgen deprivation therapy or any of several androgen signaling inhibitors (AR, anti-androgens) is unmet need
  - 1st-line treatment with enzalutamide, a new anti-androgen, resulted in improved overall survival

- **Exclusion Criteria**
  - Prior treatment with an anti-PD-1, anti-PD-L1, anti- programmed death ligand 1 (PD-L1) agent or with another immunotherapy (i.e., pembrolizumab)
  - Additional active malignancy that could confound the assessment of the study endpoints
  - Brain metastases that are symptomatic and progressive on imaging
  - Significant cardiovascular or pulmonary disease

**Phases 1b & 2 Study Design**

- Phase 1b: Safety and Efficacy
  - 15 patients, 3 cohorts
    - BXCL701 alone (0.3 mg BID) or placebo
    - BXCL701 0.6 mg QD + pembrolizumab

- Phase 2a: Superiority
  - 32 enrolled
  - BXCL701 0.6 mg split dose

**Results: Study Population**

**Clinical Characteristics**

- **Baseline Characteristics**
  - Cohort 1
    - Median age: 70 years
    - ECOG PS (0-2)
    - Baseline PSA: 15 ng/mL
  - Cohort 2
    - Median age: 70 years
    - ECOG PS (0-2)
    - Baseline PSA: 25 ng/mL

**Phases 1b & 2 Phase 1b Results**

- **Reported Safety Data as of DB 01-21-21, unless otherwise noted**

**Summary of Composite Responses**

- **39 PSA evaluable enrolled 2A patients**
  - 22% PSA50 response
  - Median duration on-treatment: 3 months prior to enrollment

**Phase 2 Safety in Adenocarcinoma Population**

- **21 patients with mCRPC**
  - 2 patients with prior treatment with pembrolizumab:
    - 1 patient with progression on pembrolizumab
    - 1 patient with response to pembrolizumab

**Adenocarcinoma PSA Responses**

- **PSA Best Overall Response**
  - 2A patients evaluable
  - 22% PSA50 response

**EORTC PRO 25042**

- **EORTC PRO 25042**
  - **CRT (chemoradiotherapy)**
  - **CRT (chemoradiotherapy)**

**THANK YOU**

BioXcel Therapeutics, Inc. would like to thank all patients, their families, and caregivers who made this study possible. It is our goal to develop novel treatment options for patients with mCRPC. This study continues to enroll patients to completion as per protocol.