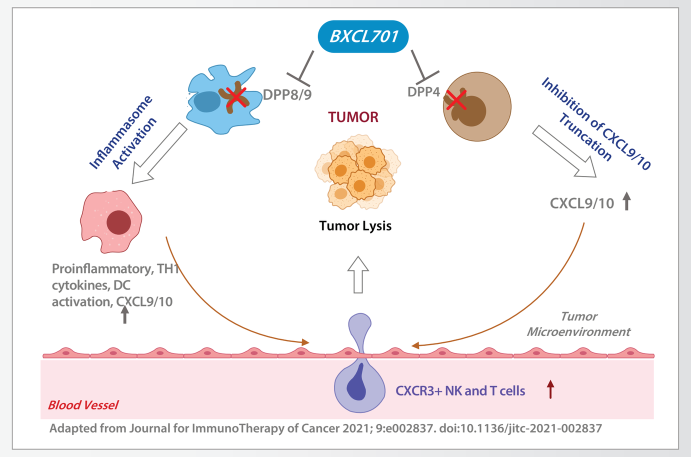
FIRST-IN-CLASS ORAL INNATE IMMUNE ACTIVATOR BXCL701 COMBINED WITH PEMBROLIZUMAB IN PATIENTS WITH METASTATIC CASTRATION-RESISTANT PROSTATE CANCER (mCRPC) OF ADENOCARCINOMA PHENOTYPE: PHASE 2 UPDATED EFFICACY RESULTS

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BXCL701 BACKGROUND

- 288,300 men diagnosed with prostate cancer in U.S. in 2023
- ~20% expected to progress to more aggressive mCRPC
- ~80% adenocarcinoma (~20% will develop SCNC)
- BXCL701 modulates the tumor microenvironment by activating innate immunity followed by adaptive immunity leading to cancer cell death
- Phase 1b safety lead-in tested 2 total daily doses of BXCL701 (0.4 mg and 0.6 mg) [SITC 2020]
 - On-target AEs consistent with cytokine activation seen at highest daily dose (0.6 mg)
 - Splitting daily dose + step-up dosing improved tolerability (no reported DLTs and lower rates of AEs of interest hypotension and peripheral edema)


BXCL701
DPP8/9
DPP4
TUMOR
Inflammasome Activation
Inhibition of CXCL9/10 Truncation
Tumor Lysis
CXCL9/10
Proinflammatory, TH1 cytokines, DC activation, CXCL9/10
Tumor Microenvironment
Blood Vessel
CXCR3+ NK and T cells
Adapted from Journal for ImmunoTherapy of Cancer 2021; 9:e002837. doi:10.1136/jitc-2021-002837

METHODS

KEY INCLUSION CRITERIA

- Histologically confirmed adenocarcinoma
- Measurable disease by RECIST 1.1 or bone metastases
- Progression as defined by PCWG3 criteria
- Serum testosterone <50 ng/dL during screening
- ECOG performance status of 0-2
- 1 or 2 androgen signaling inhibitors (ASI) + ≥1 prior line of taxane containing chemotherapy

KEY EXCLUSION CRITERIA

- >2 cytotoxic chemotherapy regimens for mCRPC
- Prior treatment with anti-PD-1, anti-PD-L1, anti-programmed death-ligand 2 (PD-L2) agent or with agent directed to another co-inhibitory T-cell receptor
- History of symptomatic orthostatic hypotension within 3 months prior to enrollment

PEMBROLIZUMAB 200 MG IV Q3W DAY 1 + BXCL701 PO BID DAYS 1-14 OF 21-DAY CYCLE
CYCLE 1, BXCL701 STEP-UP DOSING: 0.2 MG BID PO DAYS 1-7 + 0.3 MG BID PO DAYS 8-14
SUBSEQUENT CYCLES: BXCL701 0.3 MG BID PO DAYS 1-14

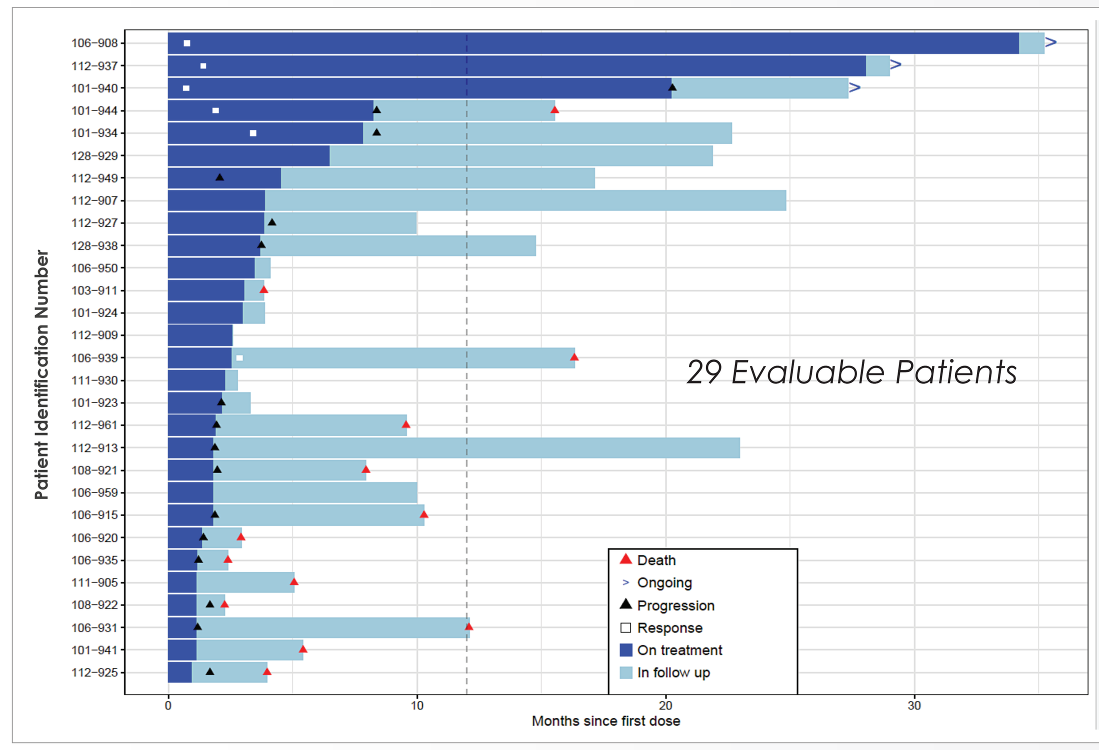
PRIMARY OBJECTIVE: Composite Response Rate, either objective response by RECIST 1.1 criteria, and/or CTC Conversion from ≥5/7.5 mL to <5/7.5 mL, and/or ≥-50% PSA decline from baseline

SECONDARY OBJECTIVES: DoR, OS, PFS, changes in circulating cytokines and predictive biomarker identification

PATIENTS BASELINE CHARACTERISTICS

Phase 2a Cohort (n = 42 enrolled)	n (%)
Median Age (range)	**69.5** (51-87)
ECOG Performance Status (%)	
0	**13** (31)
1	**25** (60)
2	**3** (7)
Bone Only disease	**17** (40)
Median lines of prior systemic therapy (range)	**5** (1 – 11)
Prior Systemic Treatment	
Previous targeted endocrine therapy	
Enzalutamide only	**5** (17)
Abiraterone only	**6** (21)
Enzalutamide and abiraterone	**17** (59)
Taxane Chemotherapy	**29** (100)
Provenge (sipuleucel-T)	**7** (24)
Radiation Therapy	**12** (41)

TREATMENT DURATION


Patient Identification Number
106-908
112-937
101-940
101-944
101-934
128-929
112-949
112-907
112-927
128-938
106-950
103-911
101-924
112-909
106-939
111-930
101-923
112-961
112-913
108-921
106-959
106-915
106-920
106-935
111-905
108-922
106-931
101-941
112-925
0
10
20
30
Months since first dose
29 Evaluable Patients
Death
Ongoing
Progression
Response
On treatment
In follow up

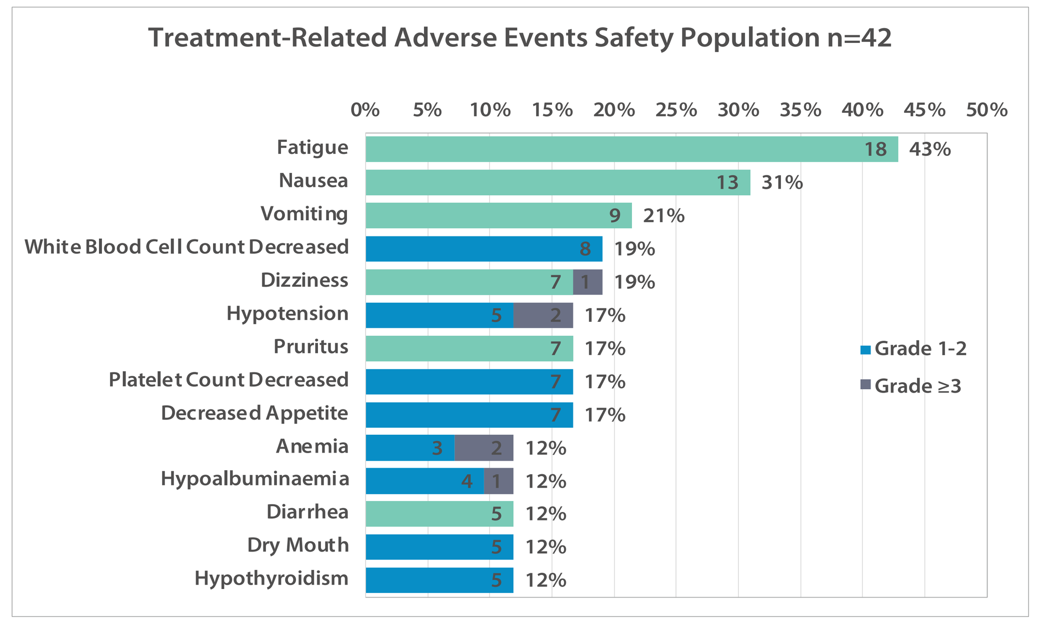
Median duration of follow-up
29 months
(range, 22 – 34)

Data as of 30-AUG-23

SAFETY

Treatment-Emergent Adverse Events	n = 42 n (%)
Any Grade	39 (93)
Attributed to BXCL701	*36 (86)*
Attributed to Pembrolizumab	*32 (76)*
Grade 3	22 (52)
Grade 4	2 (5)
Grade 5	1* (2)
AE Leading to Treatment Discontinuation	2 (5)
Attributed to BXCL701	*2 (5)*
Attributed to Pembrolizumab	*2 (5)*

** Grade 5 Disease Progression Not Related to Drug Treatment | n = number of patients experiencing an AE*


Treatment-Related Adverse Events Safety Population n=42
0% 5% 10% 15% 20% 25% 30% 35% 40% 45% 50%
Fatigue 18 43%
Nausea 13 31%
Vomiting 9 21%
White Blood Cell Count Decreased 8 19%
Dizziness 7 1 19%
Hypotension 5 2 17%
Pruritus 7 17%
Platelet Count Decreased 7 17%
Decreased Appetite 7 17%
Anemia 3 2 12%
Hypoalbuminaemia 4 1 12%
Diarrhea 5 12%
Dry Mouth 5 12%
Hypothyroidism 5 12%
Grade 1-2
Grade ≥3

AEs consistent with cytokine activation were observed

TRAEs at least possibly related to BXCL701 or pembrolizumab, occurring in >10% of patients

EFFICACY RESULTS

Best Response	Phase 2a Adenocarcinoma Patients n = 29 (%) [95% Exact CI]
Composite Response	**6 (21) [8.0– 39.7]**
Best RECIST 1.1 Response by Investigator Assessment	
RECIST Evaluable[a]	18 (62)
Partial Response	**5 (28) [9.7– 53.5]**
Confirmed PR	*4 (80)*
Unconfirmed PR	*1 (20)*
SD (any duration) including Minor Response	7 (39)
Non-CR / Non-PD	12 (67)
PD including 2 bony progressions	6 (33)
Disease Control Rate (PR + SD)	**67%**
PSA	
PSA Evaluable[b]	29 (100)
PSA_{50} Response	**5 (17) [5.8– 35.8]**
CTC[c]	
CTC Evaluable[d]	**11 (38)**
CTC Response[e]	2 (18)

Composite response rate: **21%**

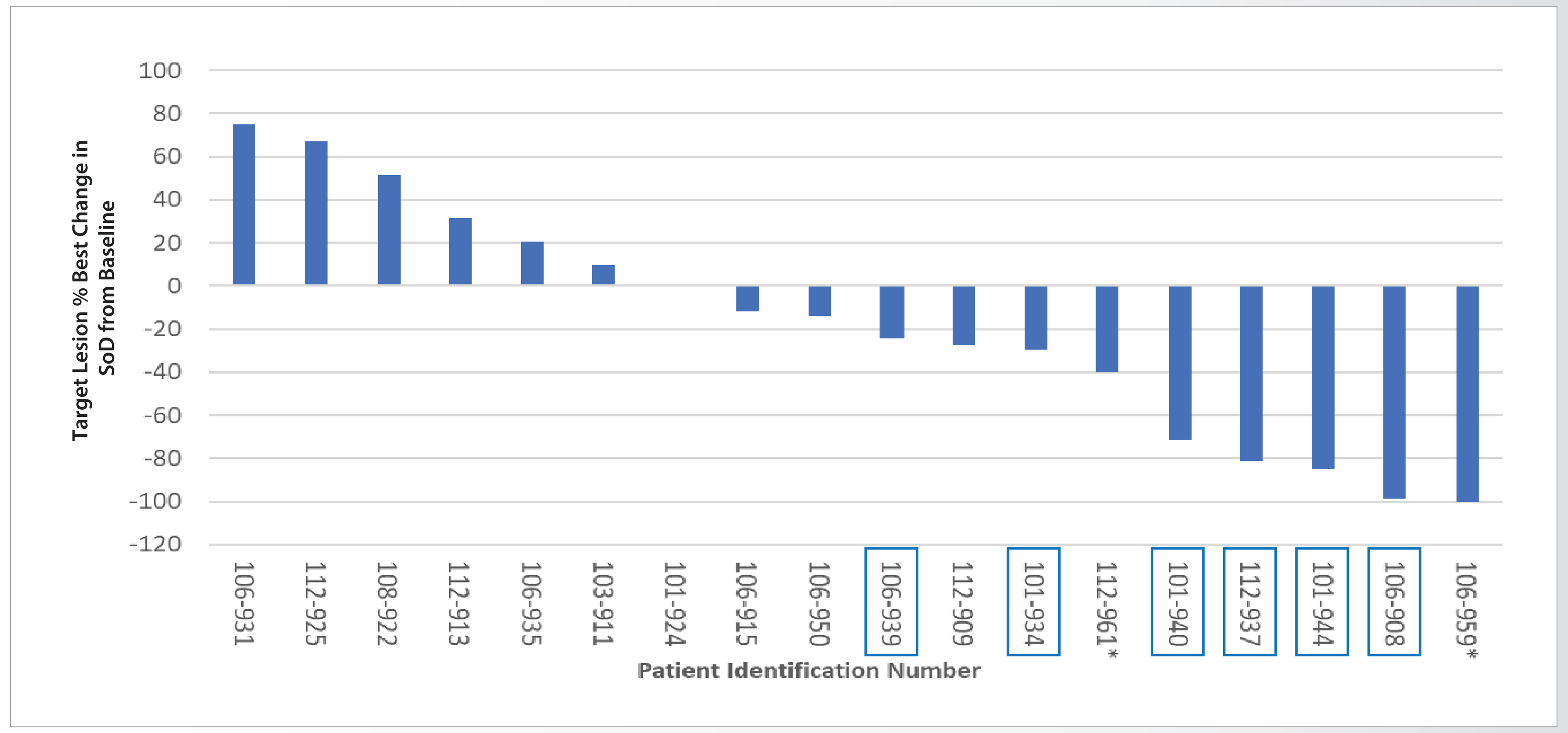
- RECIST-defined PR*: **28%**
- Disease control rate: **67%**
- PSA_{50}: **17%**—including 5 patients with -100% to -57% PSA decrease
- Median duration of response for both RECIST confirmed and PSA_{50} responses increased to **19 months**
- CTC response: **18%**

** Includes confirmed and unconfirmed PRs*

Data as of 30-AUG-23

a *Patients who received ≥2 cycles of study therapy and had 1 on-treatment tumor assessment* **b** *Baseline PSA >4 ng/mL and 1 on-treatment PSA assessment*
c *Circulating tumor cell* **d** *Baseline CTC value ≥5/7.5 mL and 1 measurable on-treatment assessment* **e** *CTC conversion from ≥5/7.5 mL to <5/7.5 mL*

BEST TUMOR RESPONSE n = 18 RECIST 1.1 EVALUABLE PATIENTS


Target Lesion % Best Change in SoD from Baseline
100
80
60
40
20
0
-20
-40
-60
-80
-100
-120
106-931
112-925
108-922
112-913
106-935
103-911
101-924
106-915
106-950
106-939
112-909
101-934
112-961*
101-940
112-937
101-944
106-908
106-959*
Patient Identification Number

not shown 11 patients with only non-target lesions
5 responders were MSS and/or TMB low, 1 responder was MSI-High / TMB High

Composite Responders

*Bony Progression

Data as of 30-AUG-23

CONCLUSIONS

- BXCL701 + pembrolizumab demonstrated encouraging activity with durable responses observed in this end stage group of mCRPC patients with adenocarcinoma histology and limited treatment options
 - Low single digit response rates expected with pembrolizumab alone in this patient population
 - Significant minority of patients in study had bone only disease, a group with very low activity to single agent pembrolizumab
 - Vast majority of study patients did not have predictive markers associated with pembrolizumab activity
- Combination of BXCL701 + pembrolizumab demonstrated manageable safety profile
 - Split and step-up dosing to mitigate cytokine release
 - No evidence of potentiation of immune-related AEs
- Biomarker work continues and will be presented in a future scientific meeting

THANK YOU

BioXcel Therapeutics, Inc. would like to thank all patients, their families, and caregivers who made this study possible. BioXcel Therapeutics, Inc. would also like to thank the participating investigators and their staff for their support on this study and their dedication to their patients, despite the additional challenges as a circumstance of the COVID-19 pandemic.

CONFLICT OF INTEREST DECLARATION

Primary author Vincent J. O'Neill M.D. <VOneill@BioXcelTherapeutics.com> is Senior Vice President & Chief Medical Officer at BioXcel Therapeutics, Inc., sponsor of study BXCL701-201

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