BXCL701 Key Opinion Leader Day

February 21, 2023
Forward-Looking Statements

This presentation includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. We intend such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended (the "Securities Act") and Section 21E of the Securities Exchange Act of 1934, as amended (the "Exchange Act"). Forward-looking statements in this presentation include but are not limited to: statements regarding BioXcel Therapeutics' expected timing of, and data results from, trials and clinical studies involving its product candidates, in particular BXCL701; planned discussions with regulators and potential registrational trials; strategic options for OnkosXcel; and potential market size and opportunity for product candidates. The words "anticipate," "believe," "can," "continue," "could," "designed," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. In addition, any statements or information that refer to expectations, beliefs, plans, projections, objectives, performance, or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking. All forward-looking statements are based upon BioXcel Therapeutics' current expectations and various assumptions. BioXcel Therapeutics believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain.

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Agenda and Speakers

- BioXcel Therapeutics: Corporate Overview
- Prostate Cancer Overview and Challenges with Current Immunotherapy
- BXCL701 Mechanism of Action
- Results of Phase 2 Trial of BXCL701 in Small Cell Neuroendocrine Prostate Cancer (SCNC)
- BXCL701 Current Trials and Future Direction
- Panel Q&A Session

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BioXcel Therapeutics

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OnkosXcel Therapeutics

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Director, Georgetown Lombardi Comprehensive Cancer Center
Professor of Oncology and Chair
Georgetown University Medical Center

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Associate Director for Clinical Sciences, Helen Diller Family Comprehensive Cancer Care
Associate Professor of Medicine, UCSF
BioXcel Therapeutics: Corporate Overview

Vimal Mehta
Founder & CEO
Building a Unique Biopharmaceutical Business Model
Transformative Drug Re-innovation Approach Using AI

BioXcel Therapeutics: Targeting High Unmet Needs in Neuroscience and Immuno-Oncology
- Optimize R&D, accelerate development, increase probability of success

Neuroscience (BXCL501): First-in-human trials to FDA approval in just under 3.5 years
- IGALMI™ (dexmedetomidine) sublingual film, acute treatment of agitation in schizophrenia and bipolar I and II disorder
- Multiple indications for BXCL501, $15B total market opportunity

OnkosXcel Therapeutics
Continuing Mission of Developing Transformative Medicine in Hard-to-Treat Tumors

Lead Oncology Drug Candidate: BXCL701
- Unique oral innate immune activator, designed to turn cold tumors hot via DPP8/9 inhibition
- Combination approach, BXCL701 plus KEYTRUDA®
- Extend the value of IO in large underserved patient populations
- Focusing on cold tumor types

High-Value Catalysts
- Positive Phase 2 data presented at ASCO GU, 2023
- SCNC Phase 2b trial initiation planned in 2023

*Subject to alignment with FDA | IO = Immuno-Oncology
Innovation Shaping the Immunotherapy “Cold” Solid Tumor Market
Similar to Hematological Market in the 2000s

Multiple Myeloma

Addressing underserved patient population
Disrupting the treatment paradigm
Unlocking immuno-oncology potential

BXCL701 Transformative Potential

Leadership in DPP8/9 inhibition to turn “cold” tumors into “hot” tumors

- Human POC achieved in two cold tumor subtypes
- Broad potential application in multiple cold solid tumors

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“Thalidomide is one of the drugs emerging in a promising new class of therapeutics for MDS. The recently discovered uses of thalidomide have conferred upon the once derided drug the moniker “wonder drug.” Hematologists are working to discover novel molecular pathways in which the drug and its derivatives can be used in a combination regimen to treat various forms of leukemia.” (2005)
Disruption is in Our DNA
Developing Transformative Medicines in Two Underserved Therapeutic Areas

Delivering innovation
Disrupting drug development paradigm
First drug approved and POC achieved with second drug candidate
$260m strategic financing in April 2022

Neuro franchise
Poised to potentially capture 139-million-episode1 U.S. agitation market2

First public AI company focused on neuroscience and Immuno-oncology (2018)
IND to commercial launch of IGALMI™ in under 4 years
AI-based drug development and commercialization capability
Advanced commercial launch activities and clinical pipeline development

2 For Bipolar disorders, schizophrenia & Alzheimer's-related agitation
First AI Derived Human POC for Oral Innate Immune Activator
Utilizing Extensive Data from 11 Prior Clinical Trials and ~700 Subjects

Q4 2018
- Received FDA acceptance of IND for BXCL701 in SCNC

Q2 2020
- Initiation of Phase 2 efficacy portion of Phase 1b/2 trial

Q4 2020
- Initial data from Phase 1b/2 trial

Q1 2021
- Update on efficacy data from Phase 1b/2 trial

Q1 2022
- SCNC Phase 2a interim efficacy/safety data

Q3 2022
- Durability of Phase 2a interim efficacy/safety data

Q1 2023
- SCNC full Phase 2a efficacy/safety data

2H 2023*
- Phase 2B initiation

8

Presented at ASCO Genitourinary Cancers Symposium
Presented at Prostate Cancer Foundation Curbing Together.

*Subject to FDA alignment

Acquired asset developed by Point Therapeutics (talabostat)
BXCL701: Strong Value Proposition in Hard-to-Treat Tumors

Mechanism of Action
Data Published in JITC

One of the most clinically advanced oral innate immune activators, designed to activate inflammasome via DPP8/9 inhibition*

Clinical Proof of Concept
Cold Tumors

• Demonstrated positive efficacy results in two cancer types: mCRPC small cell neuroendocrine prostate cancer (SCNC) and adenocarcinoma
• ~800-subject clinical safety database

Full Phase 2 Data for SCNC
Presented at ASCO GU

• Composite response rate: 25%
• Median duration of response: 6+ months**
• Generally well tolerated in combination with KEYTRUDA

Leadership Position in Innate Immunity
DPP8/9 Biology

Scarcity of assets in innate immunity

Exploring Strategic Options

*Source: www.clinicaltrials.gov
**As of data cutoff on December 19, 2022
Prostate Cancer Overview and Challenges with Current Immunotherapy

Daniel P. Petrylak, M.D.

Yale Medicine

Speaker is acting on behalf of and is a paid consultant to BioXcel Therapeutics, Inc. This material is intended for an investor audience only. The information contained in the following material is intended to provide background and educational information only and does not constitute medical advice. Individual results will vary among patients and depend on many factors. A patient’s healthcare provider should consider the circumstances of each patient.
Prostate Cancer 2023

• Leading male US cancer, 2\textsuperscript{nd} cancer deaths (lung #1)
• **New:** 288,300  **Deaths:** 34,700
• Prevalence of metastatic disease: 100,000
• Lifetime US risk:
  – Diagnosis: \(~17\%\)  Death: \(~3\%\)
• Every **2 Minutes** an American is diagnosed with prostate cancer and every **18 Minutes** an American dies of prostate cancer
• Since 2014, the incidence rate has increased by 3\% per year overall and by about 5\% per year for advanced-stage prostate cancer
What Was the Path to mCRPC?

Recurrent

- primary prostate cancer
- BCR → nmCRPC
- mHSPC
- mCRPC

- no ADT
- ADT

De Novo

- de novo mHSPC
- ADT
Differing Natural Histories

- OS comparable after progression to mCRCP
- De nova mHSPC has a shorter natural history than recurrent disease

Treatment of Metastatic Prostate Cancer

Androgen blockade
  + Abiraterone
  + Docetaxel
  + Apalutamide
  + Enzalutamide
  + Daralutamide

Abiraterone
  + Enzalutamide
  + Cabazitaxel
  + Radium-223

Abiraterone Sipuleucel-T

Docetaxel
Classes of Agents

• **Immunotherapeutic**
  - Sipuleucel-T
  - Pembrolizumab MSI-high

• **Hormonal**
  - Enzalutamide, apalutamide, darolutamide, abiraterone

• **Cytotoxic**
  - Docetaxel, cabazitaxel

• **DNA damage**
  - Rad223
  - Olaparib, rucaparib
Table 1 - The 2022 WHO classification of the Prostate and Seminal Vesicle

<table>
<thead>
<tr>
<th>Epithelial tumors of the prostate</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>8440/0 Cystadenoma</td>
<td></td>
</tr>
<tr>
<td>8148/2 Prostatic intraepithelial neoplasia, high grade</td>
<td></td>
</tr>
<tr>
<td>8500/2 Intraductal carcinoma</td>
<td></td>
</tr>
<tr>
<td>8140/3 Acinar adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>8490/3 Signet ring cell-like acinar adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>8140/3 Pleomorphic giant cell acinar adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>8572/3 Sarcomatoid acinar adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>8140/3 Prostatic intraepithelial neoplasia-like carcinoma</td>
<td></td>
</tr>
<tr>
<td>8500/3 Ductal adenocarcinoma</td>
<td></td>
</tr>
<tr>
<td>85743 Treatment-related neuroendocrine prostatic carcinomas</td>
<td></td>
</tr>
</tbody>
</table>

- Squamous neoplasms of the prostate
  - 8560/3 Adenosquamous carcinoma
  - 8070/3 Squamous cell carcinoma
  - 8147/3 Adenoid cystic (basal cell) carcinoma

- Mesenchymal tumors unique to the prostate
  - Stromal tumors of the prostate
    - 8935/1 Stromal tumor of uncertain malignant potential
    - 8935/3 Stromal sarcoma

- No distinction between small cell, large cell, or mixed morphologies
- No comment on the use of IHC markers
Neuroendocrine Prostate Cancer Terminology

- Morphology-based definition
  - Small cell carcinoma, large cell carcinoma, mixed/NED, other NE
Neuroendocrine Prostate Cancer Terminology

- **Morphology-based definition**
  - Small cell carcinoma, large cell carcinoma, mixed/NED, other NE

- **IHC not required for diagnosis but is often:**
  - (+) for at least 1 NE marker
    - e.g., INSM1, SYP, NSE
  - (-) androgen receptor (AR)
  - (-) Luminal markers
    - Eg, PSA, ERG, NKX3.1

Exceptions are common!
IHC is used variably
Current Diagnosis of NEPC is Imperfect

Some people report never or rarely seeing a case of NEPC

Others report up to 15–20% of CRPC tumors

POSSIBLE EXPLANATIONS:

- Repeat biopsies are not standardly done in mCRPC
- Variability amongst pathologists – evaluation and nomenclature not standardized
- Intra-patient heterogeneity
Tumors Exhibiting a T Cell–Inflamed or Non-T-Cell-Inflamed Phenotype
Sipuleucel-T: Autologous APC Cultured with PAP-Cytokine Fusion Protein

Recombinant Prostatic Acid Phosphatase (PAP) antigen combines with resting antigen presenting cell (APC)

APC takes up the antigen

Antigen is processed and presented on surface of the APC

Fully activated, the APC is now sipuleucel-T

INFUSE PATIENT

T-cells proliferate and attack cancer cells

Active T-cell

Inactive T-cell

Sipuleucel-T activates T-cells in the body

The precise mechanism of sipuleucel-T in prostate cancer has not been established.
IMPACT Overall Survival

Intent-to-Treat Population

Placebo (n = 171)
Median Survival: 21.7 months

Sipuleucel-T (n = 341)
Median Survival: 25.8 months

P = 0.032 (Cox model)
HR = 0.775 [95% CI: 0.614, 0.979]
Median Survival Benefit = 4.1 months
Key Data From Anti-PD-1 / PD-L1 Alone in mCRPC

• Phase I atezolizumab study in mCRPC cohort 1
  – Unresectable or recurrent patients with prior treatment with sipuleucel-T or enzalutamide
  – ORR (RECIST 1.1) 0%, ORR (irRECIST) 7.0%, mPFS 3.4 months, and mOS 18.6 months
  – 60% of patients had TRAEs (20% had treatment interruptions/modifications, and 7% discontinued because of TRAEs)

• KEYNOTE 199: Phase II pembrolizumab study in mCRPC cohorts post docetaxel2-4
  – N=259, Cohort 1 (PD-L1+), Cohort 2 (PD-L1–), Cohort 3 (any PD-L1, bone predominant)
  – ORR (RECIST 1.1) ranged from 3%-6%, mPFS 2.0-4.0 months, and mOS 8.0-14.0 months among all 3 cohorts
  – 15%-17% (cohorts 1-3) had grade 3-5 TRAEs*
### TABLE. Subtypes of Prostate Cancer Sensitive to Checkpoint Inhibitors

<table>
<thead>
<tr>
<th>NAME</th>
<th>INTERVENTION</th>
<th>TRIAL TYPE</th>
<th>PATIENTS</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>dMMR/MSI-H</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02312557³</td>
<td>Pembrolizumab 200 mg/kg IV/3 wk</td>
<td>Phase 2</td>
<td>10</td>
<td>PSA 50 30% PR 20%</td>
</tr>
<tr>
<td>Abida et al⁷</td>
<td>Anti–PD-1/PD-L1</td>
<td>Retrospective</td>
<td>11</td>
<td>PSA 50 55%</td>
</tr>
<tr>
<td><strong>PD-1/PD-L1 positive</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KEYNOTE-028²</td>
<td>Pembrolizumab 10 mg/kg IV/2 wk</td>
<td>Phase 1b</td>
<td>23</td>
<td>ORR 17% DOR 1.4 mo OS 8 mo</td>
</tr>
<tr>
<td>KEYNOTE-199⁴</td>
<td>Pembrolizumab 200 mg/kg IV/3 wk</td>
<td>Phase 2</td>
<td>133</td>
<td>ORR 7% DOR 17 mo OS 9.5 mo</td>
</tr>
<tr>
<td><strong>High TMB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHECKMATE-650¹⁰</td>
<td>Ipiilimumab+nivolumab</td>
<td>Phase 2</td>
<td>33</td>
<td>ORR 58%</td>
</tr>
<tr>
<td><strong>CDK12</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antonorakis et al⁶⁷</td>
<td>Pembrolizumab</td>
<td>Retrospective</td>
<td>8</td>
<td>PSA 50 38%</td>
</tr>
<tr>
<td>Antonorakis et al⁶⁷</td>
<td>Nivolumab</td>
<td>Retrospective</td>
<td>3</td>
<td>PFS 6.6 mo</td>
</tr>
<tr>
<td>Reimers et al⁷⁸</td>
<td>Anti–PD-1</td>
<td>Retrospective</td>
<td>5</td>
<td>PSA 50 40%</td>
</tr>
<tr>
<td>Antonorakis et al⁶⁸</td>
<td>Pembrolizumab</td>
<td>Retrospective</td>
<td>5</td>
<td>PSA 50 33%</td>
</tr>
<tr>
<td>Antonorakis et al⁶⁸</td>
<td>Nivolumab</td>
<td>Retrospective</td>
<td>4</td>
<td>PFS 5.5 mo</td>
</tr>
<tr>
<td><strong>POLE/POLD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al⁸⁸</td>
<td>Pembrolizumab 200 mg/kg IV/3 wk</td>
<td>Case report POLE V411L</td>
<td>1</td>
<td>PSA &lt;0.1 ng/mL DOR 17 mo OS 10 mo</td>
</tr>
<tr>
<td>Guedes et al⁹⁹</td>
<td>Pembrolizumab 200 mg/kg IV/3 wk</td>
<td>Case report POLD1 D402N</td>
<td>1</td>
<td>“Exceptional response”</td>
</tr>
</tbody>
</table>

*dMMR/MSI-H, deficient mismatch repair genes/microsatellite instability-high; DOR, duration of response; IV, intravenous; ORR, overall response rate; OS, overall survival; NR, not reached; PD-1/PD-L1, programmed death-1/PD-L1 ligand; PFS, progression-free survival; PR, partial response; PSA50, PSA decrease ≥50%; TMB, tumor mutational burden.*

*Source: Miguel Gonzalez-Velez, MD, and Alan H. Bryer, MD*
MSI in Castration-Resistant Prostate Cancer

Patient No.

P-0011155

P-0008682

P-0025952

P-0000755

P-0018147

P-0012928

P-0000964

P-0024650

P-0021355

P-0024660

P-0001071

Time, wk

Best PSA Response From Baseline, %

-99.9

-81.3

-99.9

-40.8

+88.1

-18.3

-60.3

-99.9

+108.5

-99.5

-38.8

Treatment duration

Death

Treatment ongoing

Anti-PD-L1

Anti-PD-1

Clinical trial

Combination

Monotherapy
Primary Endpoint: OS at Final Analysis, ITT Population

- **HR 0.92 (95% CI 0.78−1.09); P = 0.1677**

<table>
<thead>
<tr>
<th>Events/Participants</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.92 (0.78-1.09)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>0.95 (0.66-1.35)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>0.91 (0.75-1.09)</td>
</tr>
<tr>
<td>Age (EU categories)</td>
<td></td>
</tr>
<tr>
<td>&lt;65 years</td>
<td>0.95 (0.66-1.35)</td>
</tr>
<tr>
<td>65 to 74 years</td>
<td>0.93 (0.72-1.19)</td>
</tr>
<tr>
<td>75 to 84 years</td>
<td>0.86 (0.64-1.15)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>0.96 (0.80-1.16)</td>
</tr>
<tr>
<td>All others</td>
<td>0.78 (0.54-1.13)</td>
</tr>
<tr>
<td>Region</td>
<td></td>
</tr>
<tr>
<td>North America</td>
<td>0.75 (0.47-1.21)</td>
</tr>
<tr>
<td>Outside North America</td>
<td>0.94 (0.79-1.13)</td>
</tr>
<tr>
<td>ECOG PS</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0.93 (0.74-1.17)</td>
</tr>
<tr>
<td>≥1</td>
<td>0.93 (0.73-1.18)</td>
</tr>
<tr>
<td>Metastases at baseline</td>
<td></td>
</tr>
<tr>
<td>Bone only</td>
<td>0.85 (0.66-1.09)</td>
</tr>
<tr>
<td>Liver</td>
<td>0.98 (0.57-1.67)</td>
</tr>
<tr>
<td>Other</td>
<td>1.00 (0.79-1.26)</td>
</tr>
<tr>
<td>Prior abiraterone</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0.82 (0.66-1.03)</td>
</tr>
<tr>
<td>No</td>
<td>1.04 (0.81-1.33)</td>
</tr>
<tr>
<td>PD-L1 status</td>
<td></td>
</tr>
<tr>
<td>PD-L1 positive</td>
<td>0.71 (0.51-0.98)</td>
</tr>
<tr>
<td>PD-L1 negative</td>
<td>0.99 (0.81-1.21)</td>
</tr>
</tbody>
</table>

ITT population included all randomized participants. Data cutoff date, FA: June 20, 2022. Median (range) time from randomization to data cutoff date: 22.7 months (12.1−36.7).
Figure 1. Cabozantinib Targets Pathways Associated With Tumor Immune-Suppression

- **TAM Kinase (TYRO3, AXL, MER) Inhibition**
  - Increases numbers of circulating and tumor-infiltrating CD8+ T cells
  - Promotes macrophage phenotype transition from M2 (immune-suppressive) to M1 (immune-stimulating)

- **VEGFR2 Inhibition**
  - Decreases number/function of regulatory T cells and MDSCs

- **MET Inhibition**
  - Blocks MET-induced tumor expression of PD-L1
  - Blocks mobilization of immunosuppressive neutrophils

- **AXL Inhibition**
  - Increases tumor MHC class I expression

- **Macrophage**
- **MHC-I**
- **MDSC**
- **Regulatory T cell**
- **CD8+ T cell**
- **Neutrophil**
### Table 2: Tumour response per RECIST version 1.1

<table>
<thead>
<tr>
<th></th>
<th>Tumour response per investigator</th>
<th>Tumour response per BIRC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All patients (n=132)</td>
<td>Visceral metastases or measurable extrapelvic lymphadenopathy (n=101)</td>
</tr>
<tr>
<td>Objective response rate</td>
<td>31 (23%; 17–32)</td>
<td>27 (27%; 18–37)</td>
</tr>
<tr>
<td>Best overall response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirmed complete response</td>
<td>3 (2%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>Confirmed partial response</td>
<td>28 (21%)</td>
<td>25 (25%)</td>
</tr>
<tr>
<td>Stable disease</td>
<td>80 (61%)</td>
<td>62 (61%)</td>
</tr>
<tr>
<td>Progressive disease</td>
<td>19 (14%)</td>
<td>11 (11%)</td>
</tr>
<tr>
<td>Missing</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Disease control rate*</td>
<td>111 (84%; 77–90)</td>
<td>89 (88%; 80–94)</td>
</tr>
<tr>
<td>Duration of objective response, months†</td>
<td>8.3 (4.6–11.0)</td>
<td>6.9 (4.2–9.8)</td>
</tr>
<tr>
<td>Time to objective response, months‡</td>
<td>17 (14–28)</td>
<td>17 (14–32)</td>
</tr>
</tbody>
</table>

Data are n (%; 95% CI), n (%), or median (IQR). BIRC=blinded independent radiology committee. RECIST=Response Evaluation Criteria in Solid Tumors. *Patients with a complete response, partial response, or stable disease. †Kaplan-Meier estimate. ‡Arithmetic estimate.

Atezolizumab / Cabozantanib
CONTACT-02 Trial Design

Patients

Key eligibility
- Prior treatment with one, and only one, NHT (e.g., abiraterone, apalutamide, darolutamide, or enzalutamide)
- Surgical or medical castration
- Measurable visceral disease per RECIST 1.1; OR measurable extrapelvic adenopathy
- Progressive disease at study entry
- ECOG PS ≤1

Exclusion criteria
- Any prior nonhormonal therapy initiated for the treatment of mCRPC

Efficacy Endpoints

Primary:
- PFS per RECIST 1.1
- Overall survival (37 months after randomization)

Secondary:
- ORR per RECIST 1.1 (37 months after randomization)
Bi-Specific T Cell Engager (BiTE®)…

- Once T cells are activated by a BiTE molecule, the T cells may induce further T-cell proliferation and cytokine production
- Induces apoptosis; activated T cells release cytokines and produce additional perforin/granzymes that may allow T cells to target surrounding cancer cells
- Potentially results in the serial lysis of multiple cancer cells by a single T cell
- Sustained activation of a single activated cytotoxic T cell theoretically results in local proliferation and expansion of polyclonal memory T cells
Two flexibly linked, single-chain antibodies, with one that is specific for a selected tumor-associated antigen and the other that is specific for CD3 found on T cells.
Pasotuxizumab

- T cell binding domain (CD3)
- Peptide linker
- Tumor specific antigen binding domain
Therapeutic Targets

- DLL3 in NEPC (AMG 757)
- STEAP1 (AMG 509)
- Human Kallikrein-2 (KLK2)
- TMEFF2: ESMO 2022 poster
- PD-1 x CTLA-4 (Vudalimab = XmAb20717)
- PSMA
- PSCA
BiTE Molecules

- Pasotuxizumab - AMG 212 = BAY 2010112
- Acapatamab - AMG 160: half-life extended
- HPN424
- JNJ-081
- REGN5678
PSCA Targeted CAR T

Phase 1 Study

PSCA targeted CAR T in mCRPC: phase 1 results

- Radiographic and PSA responses have occurred (abstr #91, poster E5)
  - On-target, off-tumor toxicity = cystitis
- PSCA PET imaging feasible

Tsai WK et al. Theranostics 2018; 5903-14
**P-PSMA-101**

**PSMA Targeted CAR T, Phase 1 Study**

CAR encodes intracellular 4-1BB signaling domain and a T-cell receptor (TCR) ζ chain signaling domain expresses three major components from a transposed transgene that is stably integrated into the genome

1) An anti-PSMA Centrin™-based CAR gene,
2) Dihydrofolate reductase (DHFR) mutein gene for selection of transposed cells during manufacture,
3) (3) an inducible caspase 9 (iCasp9)-based safety switch gene (activated by the small molecule rimiducid) for rapid ablation of CAR T-cells for SAE

- **P-PSMA-101** is an autologous CAR-T therapy targeting PSMA and is made using a unique non-viral transposon system (piggyBac®) that results in a CAR-T product composed of a high percentage of stem cell memory T cells (T_{SCM})
Baseline (SUV 28.5)

4 weeks (SUV 8.3)

12 weeks (SUV 2.8)

Baseline

12 weeks

Days after infusion

PSA (ng/mL)

P-PSMA-101 /mg DNA

PSA

P-PSMA-101
copies/mg DNA in
peripheral blood

P-PSMA-101
copies/mg DNA in
biopsy tissue

Conclusions

• Sipuleucel-T is FDA approved for CRPC in patients who are minimally symptomatic/asymptomatic with non-hepatic metastases

• Checkpoint inhibition therapy is effective in the MSI high subgroup, results in unselected patients are disappointing

• Further treatment should be designed to convert a cold tumor to hot
BXCL701 Mechanism of Action

Louis M. Weiner, M.D.

Speaker is acting on behalf of and is a paid consultant to BioXcel Therapeutics, Inc. This material is intended for an investor audience only. The information contained in the following material is intended to provide background and educational information only and does not constitute medical advice. Individual results will vary among patients and depend on many factors. A patient's healthcare provider should consider the circumstances of each patient.
Disclosures

• I receive no monetary compensation from BioXcel Therapeutics*

• My laboratory has a contract for work that will be discussed

• Co-PI of open clinical trial of BXCL701 + pembrolizumab in metastatic pancreatic adenocarcinoma

*Travel was arranged by BioXcel Therapeutics
BXCL701 (Talabostat): Biochemical Activities

<table>
<thead>
<tr>
<th></th>
<th>DPP8</th>
<th>DPP9</th>
<th>DPPIV</th>
<th>FAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC50</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>(nM)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mechanism of Action of BXCL701

BXCL701 Modulates the Tumor Microenvironment by Activating the Innate Immunity Followed by Adaptive Immunity Leading to Cancer Cell Death

• DPP8/9 inhibition by BXCL701 activates inflammasome leading to proinflammatory cytokines, Th1 cytokines and CXCL9/10 increase that enhances CXCR3+ NK and CD8+ T cell infiltration to improve anti-PD1 activity resulting in tumor lysis

• CXCL9/10 increase by inhibition of DPP4 also enhances CXCR3+ NK and CD8+ T cell infiltration
DPP Inhibition by BXCL701 Reduces Tumor Growth in a Murine Pancreatic Ductal Adenocarcinoma (PDAC) Model

Tumor Growth Curves

Survival curves of mice
BXCL701 Synergizes with Anti-PD-1 in Reducing Tumor Growth in a Murine Pancreatic Ductal Adenocarcinoma (PDAC) Model

BXCL701 Increases Circulating Inflammasome and Th1-Related Cytokines in a Syngeneic PDAC Mouse Model of Pancreatic Cancer

BXCL701 Alone and in Combination with Anti-PD-1 Increases Tumor Levels of CXCR3+ and Innate Immune Cells in a Syngeneic Mouse Model (mT3-2D) of Pancreatic Ductal Adenocarcinoma
BXCL701 + Anti-PD-1 Engages Both NK and CD8+ T Cells in a Syngeneic Mouse Model (mT3-2D) of Pancreatic Ductal Adenocarcinoma

- NK and CD8+T cells both contribute to tumor growth inhibition by PD-1 / BXCL701 combination treatment
- Depletion of either immune cell type or especially both types simultaneously has a large impact on tumor growth

NK Cell and T Cell Depletion Influences Treatment Outcomes for 701 Treatment Alone

Day 18 after treatment

Day 28 after treatment
BXCL701 + Anti-PD-1 Induces Memory Response Against Rechallenge

- Tumor-free mice from previous experiment (BXCL701 + anti-PD-1 Ab) were re-challenged with 5-fold excess (i.e., $5 \times 10^5$) tumor cells compared with original challenge.
- 5 tumor-naive mice used as controls.
- Tumor growth was monitored without administering any additional treatment.
- **** $p < 0.0001$ by unpaired two-tailed t-test.
Percentage of CD45+ Cells (Effector Memory T Cells) Were Increased in Re-Challenged Mice

CD8+ CD44$^{\text{high}}$ CD62L$^{\text{low}}$

CD4+ CD44$^{\text{high}}$ CD62L$^{\text{low}}$
Well-Understood Mechanism of Action of BXCL701 and Pembrolizumab Combination

Tumor Microenvironment

**DPP8/9 INHIBITION**

- **Inflammasome Activation**
- **Proinflammatory cytokines IL-1β, IL-18...**
- **Th1 cells response stimulation**
  - **TH1 cytokines (IL-2, IL-12, IFNγ)**
  - **CCL3, CCL4**

**DPP4 INHIBITION**

- **Inhibition of CXCL9/10 Truncation**
- **CXCL9/10 ↑**
- **Anti-PD-1 releases breaks on T-cells**

**DPP8/9**

- **BXCL701**
- **Immune Cells**
- **Tumor Cell**
- **NK Cell**
- **T Cell**
- **Cytotoxicity**
- **PD-L1**
- **PD-1**
- **Anti-PD-1**

**CXCL9/10 ↑**

**BLOOD VESSEL**

**CXCR3 + Cell Recruitment**

**Tumor NK and CD8+ T cells ↑**

Adapted from Journal for ImmunoTherapy of Cancer 2021; 9:e002837. doi:10.1136/jitc-2021-002837
BSCL701 or BSCL701 + PD1 Antibody Treatment Reduces Fibrosis in Tumor Micro-Environment

(A) Masson’s Trichrome stain demonstrating intense fibrosis formation in a representative mT3-2D pancreatic tumor from a PBS treated mouse, while BSCL701 or combined Rx markedly decreased fibrosis. (B) Fibrosis scoring was performed using quantitative morphometry by Image J. BSCL701 treated mouse tumors showed significantly decreased fibrosis compared to PBS treatment (n=22 pooling results from two separate experiments).
BXCL701: Potential Combination Opportunities in Addition to Anti-PD-1
BXCL701 Synergizes with Multiple T Cell Activating Therapies

Anti-CTLA-4 (checkpoint antagonist)

Anti-PD1 (checkpoint antagonist)

Anti-OX40 (co-stimulator)

BXCL701 Has Shown Synergistic Antitumor Activity with Different Checkpoint Modulators
BXCL701 (0.01-0.03 μM) induces peak ADCC by PBMCs + Ab against A431 and SKOV3 cells with 3 days of exposure in 2 separate donors.
BXCL701: Potential Predictive Biomarker
DPP9 Copy Number Correlates with BXCL701 Cytotoxicity in Leukemic Cell Lines and is a Potential Predictive Biomarker in Leukemias

Out of total 13 cell lines 10 were AML cell lines

\[ y = 0.1357x - 0.0415 \]

\[ R^2 = 0.8131 \]

*** p-value calculated by non-parametric Mann-Whitney Test,
R – Responder Cell Lines, NR – Non-Responder Cell Lines
Results of Phase 2 Trial of BXCL701 in SCNC

Rahul Aggarwal, M.D.

Speaker is acting on behalf of and is a paid consultant to BioXcel Therapeutics, Inc. This material is intended for an investor audience only. The information contained in the following material is intended to provide background and educational information only and does not constitute medical advice. Individual results will vary among patients and depend on many factors. A patient's healthcare provider should consider the circumstances of each patient.
First-in-class Oral Innate Immune Activator BXCL701 Combined with Pembrolizumab in Patients with Metastatic Castration-resistant Prostate Cancer (mCRPC) of Small Cell Neuroendocrine (SCNC) Phenotype: Phase 2a Final Results

Rahul R. Aggarwal¹, Jingsong Zhang², Paul Monk³, Xinhua Zhu⁴, Rob Jones⁵, Mark Linch⁶, Dan Costin⁷, Johann de Bono⁸, Lawrence I. Karsh⁹, Daniel Petrylak¹⁰, Pascal Borderies¹¹, Rashmi Deshpande¹², Amir Hafeez¹³, Vincent O’Neill¹⁴, Scott T. Tagawa¹⁵

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2. Medical Oncology, Moffitt Cancer Center, Tampa, FL, USA; Paul Monk, Medical Oncology, The Ohio State University, Columbus, OH, USA
3. Medical Oncology, The Ohio State University, Columbus, OH, USA
4. Monter Cancer Center, Northwell Health Center for Advanced Medicine, New Hyde Park, NY, USA
5. Beatson West of Scotland Cancer Centre, University of Glasgow, Glasgow, UK
6. Uro-Oncology, University College London Hospital, London, UK
7. Center for Cancer Care, White Plains Hospital, White Plains, NY, USA
8. The Royal Marsden NHS Foundation Trust, Sutton, UK
9. Urology Department, The Urology Center of Colorado, Denver, CO, USA
10. Medical Oncology department, Yale University School of Medicine, New Haven, CT, USA
11. Medical & Scientific Affairs, BioXcel Therapeutics, Inc., New Haven, CT, USA
12. Clinical Scientist, BioXcel Therapeutics, Inc., New Haven, CT, USA
13. Clinical Development Oncology, BioXcel Therapeutics, Inc., New Haven, CT, USA
14. Head Oncology Unit, BioXcel Therapeutics, Inc., New Haven, CT, USA
15. Hematology and Medical Oncology, Weill Cornell Medicine, New York, NY, USA
Background

- *De novo* and treatment-emergent SCNC are associated with adverse survival outcomes
- BXCL701 modulates 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)
High Unmet Need in SCNC with no FDA Approved Therapy and Incidence is Increasing

288,300 Men Diagnosed with Prostate Cancer in U.S. in 2023*; ~20% Expected to Progress to More Aggressive mCRPC

• ~20% of these mCRPC patients will develop SCNC phenotype, characterized by poor prognosis and low survival rate

• Current treatment protocols that are sub-optimal include platinum-based cytotoxic chemotherapies despite short duration of response and considerable toxicities

• Current CPIs targeting PD-1 and CTLA-4 have not demonstrated meaningful single-agent therapeutic benefit in SCNC

* American Cancer Society’s estimates for prostate cancer in the United States for 2023
Methods

**KEY INCLUSION CRITERIA**

- Histologically confirmed *de novo* SCNC or treatment-emergent SCNC
- ≥1 prior line of systemic therapy
- Progression as defined by PCWG3 criteria
- Serum testosterone <50 ng/dL during screening, except for patients with *de novo* SCNC
- ECOG performance status of 0-2

**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

**Pembrolizumab 200 mg IV q3w Day 1 + BXCL701 0.3 mg PO BID Days 1-14 of 21-day cycle**

**Step-up dosing in Cycle 1: BXCL701 0.2 mg PO BID Days 1-7 then BXCL701 0.3 mg PO BID Days 8-14**

**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:** Duration of response, safety, and changes in circulating cytokines
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Phase 2a Cohort (n = 34)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age, years (range)</td>
<td>67.5 (54 – 80)</td>
</tr>
<tr>
<td>ECOG Performance Status (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>16 (47%)</td>
</tr>
<tr>
<td>1</td>
<td>16 (47%)</td>
</tr>
<tr>
<td>2</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Visceral Metastases (%)</td>
<td></td>
</tr>
<tr>
<td>Any site</td>
<td>21 (62%)</td>
</tr>
<tr>
<td>Liver</td>
<td>11 (32%)</td>
</tr>
<tr>
<td>Median number of lines of prior systemic therapy (range)</td>
<td>3 (1 – 8)</td>
</tr>
<tr>
<td>Prior Systemic Treatment</td>
<td></td>
</tr>
<tr>
<td>Androgen signaling inhibitor(s)</td>
<td>25 (89%)</td>
</tr>
<tr>
<td>Platinum-based Chemotherapy</td>
<td>19 (68%)</td>
</tr>
<tr>
<td>Taxane Chemotherapy</td>
<td>17 (50%)</td>
</tr>
</tbody>
</table>
• Median duration of follow up = 30.8 weeks (range 1.9 – 86.9 weeks)

• Median duration of treatment = 9 weeks (range: 0.7 to 73 weeks)

28 Evaluable Patients - Data as of 19-DEC-22
### Best Overall Response

<table>
<thead>
<tr>
<th></th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RECIST Evaluable</strong>a (%)</td>
<td>25 (89)</td>
</tr>
<tr>
<td><strong>Objective Response Rate (%)</strong></td>
<td>5 (20)</td>
</tr>
<tr>
<td><strong>Confirmed Partial Response (%)</strong></td>
<td>4 (16)</td>
</tr>
<tr>
<td><strong>Unconfirmed Partial Response (%)</strong></td>
<td>1 (4)</td>
</tr>
<tr>
<td>SD (any duration)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>PD</td>
<td>13 (52)</td>
</tr>
<tr>
<td><strong>Disease Control Rate (PR + SD)</strong></td>
<td>12 (48)</td>
</tr>
<tr>
<td><strong>Non-RECIST Evaluable</strong></td>
<td>3 (11)</td>
</tr>
<tr>
<td><strong>CTC Evaluable</strong>b</td>
<td>1</td>
</tr>
<tr>
<td><strong>CTC Response</strong>d</td>
<td>1</td>
</tr>
<tr>
<td><strong>PSA Evaluable</strong>e</td>
<td>1</td>
</tr>
<tr>
<td><strong>PSA_{50} Response</strong></td>
<td>1</td>
</tr>
<tr>
<td><strong>Composite Response Rate (%)</strong></td>
<td>7 (25)</td>
</tr>
</tbody>
</table>

**Objective response rate: 20%**
- 4 confirmed partial responses + 1 unconfirmed partial response

**Median duration of response: 6+ months**
- (range: 1.8 - 9.8 months)

---

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

e Baseline PSA >4 ng/mL and 1 on-treatment PSA assessment
Change in Tumor Size from Baseline

RECIST 1.1 Best Response n = 25

- All responders are MSS and/or TMB low

* SoD = Sum of Diameters

Data as of 08-FEB-23
# Safety

## Treatment-Emergent Adverse Events (n = 34)

<table>
<thead>
<tr>
<th>Any Grade</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Attributed to BXCL701</strong></td>
<td>29 (85)</td>
</tr>
<tr>
<td><strong>Attributed to Pembrolizumab</strong></td>
<td>23 (68)</td>
</tr>
<tr>
<td><strong>Grade 3</strong></td>
<td>16 (47)</td>
</tr>
<tr>
<td><strong>Attributed to BXCL701</strong></td>
<td>6 (18)</td>
</tr>
<tr>
<td><strong>Attributed to Pembrolizumab</strong></td>
<td>6 (18)</td>
</tr>
<tr>
<td><strong>Grade 4</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Grade 5</strong></td>
<td>1* (3)</td>
</tr>
</tbody>
</table>

## AE Leading to Treatment Discontinuation

- **BXCL701 Discontinuation** | 6 (18) |
- **Pembrolizumab Discontinuation** | 5 (15) |

## Immune Related Adverse Events Any Grade

- **Any Grade** | 14 (41) |
- **Grade ≥3** | 1^ (7) |

* Grade 5 tumor lysis
^ Grade 3 colitis

---

### Treatment-Related Adverse Events Safety Population n=34

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>2</td>
<td></td>
<td>9</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2</td>
<td></td>
<td>5</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Pruritus</td>
<td></td>
<td></td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td></td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

* At least possibly related to BXCL701 or pembrolizumab, occurring in >10% of patients

---

* Grade 5 tumor lysis
^ Grade 3 colitis
Response in a Patient with Treatment-Emergent SCNC with Liver Metastases

- Prior systemic therapies: LHRH agonist, abiraterone + prednisone, cisplatin + etoposide
- Microsatellite stable, low TMB
- 58% reduction in target lesions following three cycles of treatment

Liver – Baseline
JAN-21

Liver – Post Cycle 3
APR-21

Cytokine expression in the circulation

<table>
<thead>
<tr>
<th>Cytokine concentration (ng/ml)</th>
<th>Baseline</th>
<th>C1D14, 24hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-gamma</td>
<td>0</td>
<td>1000</td>
</tr>
<tr>
<td>TNFalpha</td>
<td>2000</td>
<td>3000</td>
</tr>
<tr>
<td>IL-18</td>
<td>4000</td>
<td>5000</td>
</tr>
</tbody>
</table>

Responders

- Responder patient 101: 926
- DPP9 overexpressed vs non-responder

Non-responders

- DPP9 PanCK

Responder

- DPP9 PanCK

Responder patient 101-926: DPP9 overexpressed vs non-responder
Results from Adenocarcinoma Cohort BXCL701 + Pembrolizumab

Best Tumor Response (n = 18)

Composite response rate: **21%**
- RECIST-defined PR*: **22%**
- Disease control rate: **83%**
- PSA\textsubscript{50}: **17%**—including 5 patients with -100% to -57% PSA decrease
- CTC response: **18%**

*Includes confirmed and unconfirmed PRs

Data cut-off date: 24-NOV-21
Conclusions

• BXCL701 + pembrolizumab demonstrated encouraging activity with durable responses observed in a subset of patients with platinum pre-treated, small cell neuroendocrine prostate cancer
  – All responders were MSS and/or TMB low, with low probability of response to pembrolizumab monotherapy

• BXCL701 + pembrolizumab demonstrated manageable safety profile
  – Split and step-up dosing to mitigate cytokine release
  – No evidence of potentiation of immune-related AEs

• BXCL701 + pembrolizumab demonstrated similar activity in adenocarcinoma

• Evaluation of DPP9 overexpression as a predictive biomarker is ongoing

• Planned Phase 2b randomized study in SCNC expected to commence in 2H23
Acknowledgements

• Patients and their families
• Co-Investigators and study staff
• BioXcel Therapeutics
BXCL701 Current Trials and Future Direction

Vincent J. O’Neill, M.D.
# BXCL701: Pipeline Within a Product Plan and Next-Generation Candidate

<table>
<thead>
<tr>
<th>Compound</th>
<th>Proposed Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Expected Upcoming Milestone</th>
<th>Collaborator</th>
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</thead>
<tbody>
<tr>
<td><strong>BXCL701</strong></td>
<td>Small Cell Neuroendocrine Prostate Cancer (SCNC)</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>Initiate Phase 2b</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Small Cell Lung Cancer (SCLC)</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>Initiate Phase 1b/2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute Myeloid Leukemia (AML) IST*</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>Initiate Phase 1b/2</td>
<td>Dana-Farber Cancer Institute</td>
</tr>
<tr>
<td></td>
<td>Metastatic Pancreatic Ductal Adenocarcinoma IST*</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>Initiate Phase 2</td>
<td>Georgetown Lombardi Comprehensive Cancer Center</td>
</tr>
<tr>
<td><strong>Next-Generation DPP8/9 Inhibitor</strong></td>
<td>Solid and Liquid Tumors</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>![Progress Bar]</td>
<td>Initiate novel candidate development</td>
<td>MERCK supply agreement</td>
</tr>
</tbody>
</table>

*Investigator Sponsored Trial
Frequency of DPP Alterations in Solid Tumors

TCGA Data; AACR 2017
SCNC Phase 2a Results Support Further Development of BXCL701 + KEYTRUDA

Phase 2b Potential Registrational Trial in SCNC Expected to Initiate in 2H 2023*

*Initial discussions with the FDA regarding the development pathway and registrational strategy for BCXL701 in SCNC expected in mid-2023.

RECIST 1.1 = Response Evaluation Criteria in Solid Tumors Version 1.1 | R = Randomization
* Additional objectives: CRR, OS, duration of response, rPFS, and PSA PFS

Biomarker evaluation to be performed retrospectively
### SCNC Clinical Development Timeline*

<table>
<thead>
<tr>
<th></th>
<th>2023</th>
<th>2024</th>
<th>2025</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1H</td>
<td>2H</td>
<td>1H</td>
</tr>
<tr>
<td></td>
<td>1H</td>
<td>2H</td>
<td>2H</td>
</tr>
</tbody>
</table>

**SCNC Phase 2b pivotal study**

**NDA Submission Under AA Program**

*Initial discussions with the FDA regarding the development pathway and registrational strategy for BCXL701 in SCNC expected in mid-2023.

| AA = Accelerated Approval |
BXCL701: Extensive Stage Small Cell Lung Cancer (SCLC)
Current Therapy Remains Sub-optimal

- SCLC is an aggressive disease with early metastasis

- 2 CPIs approved in combination with carboplatin / etoposide for Extensive Stage SCLC
  - TECENTRIQ® (atezolizumab)
  - IMFINZI® (durvalumab)

- Median overall survival remains about 1 year
  - TECENTRIQ® 12.3 months
  - IMFINZI® 13 months

U.S. Patients 2023

New SCLC patients 36K¹
75% Extensive Stage SCLC 27K
60% maintenance therapy with checkpoint inhibitor + carboplatin / etoposide 16K

¹ The American Cancer Society’s estimates for lung cancer in the United States for 2023
Planned Phase 1b/2 SCLC Clinical Trial Design*

*Trial design subject to agreement with FDA | SoC = Standard of Care

ES-SCLC Patients in Maintenance

Screening

ES-SCLC Patients in Maintenance

Screening

Determine Recommended Phase 2 Dose (RP2D)

Cohort 1

Atezolizumab IV 1,200 mg Day 1 q3week + BXCL701 0.2 mg BID 14 days

n = 3 + 3

Cohort 2

Atezolizumab IV 1,200 mg Day 1 q3week + BXCL701 0.3 mg BID 14 days

n = 3 + 3

Proof of Concept

Atezolizumab IV 1,200 mg Day 1 q3week + BXCL701 RP2D BID 14 days

n = 45

Proceed to Phase 3 if 6-month PFS rate is superior to SoC
# SCLC Clinical Development Timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>1H</th>
<th>2H</th>
<th>1H</th>
<th>2H</th>
<th>1H</th>
<th>2H</th>
</tr>
</thead>
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- **Phase 1b**
- **SCLC PoC**
- **End of Phase 2 meeting**
BXCL701: Acute Myeloid Leukemia (AML)
Significant Underserved Patient Population

• BXCL701 is directly cytotoxic in AML cell lines

• Conventional chemotherapy is a mainstay in AML therapy, response rates 35-75%

• Standard of care for patients unfit for induction chemotherapy: combination of decitabine or azacitidine and venetoclax
  – All oral combination is preferable

• BXCL701 cytotoxicity in human AML cell lines highly correlates with DPP9 copy number

2 The American Cancer Society's estimates for Acute Myeloid Leukemia (AML) in the United States for 2023  
4 V. R. Agarwal et al. (2022) Potential Predictive Biomarkers for BXCL701 in Acute Myeloid Leukemia (AML). Society for Immunotherapy of Cancer Annual Meeting 2022
Initiating Phase 1b/2 AML Clinical Trial

3 + 3 Dose Escalation Study Design
n = 12 - 30

Level (-1)  BXCL701 0.2 mg BID Pulse Dosing
Level 1     BXCL701 0.3 mg BID Pulse Dosing
Level 2     BXCL701 0.4 mg BID Pulse Dosing
Level 3     BXCL701 0.6 mg BID Pulse Dosing
Level 4     BXCL701 0.8 mg BID Pulse Dosing

BXCL701 Pulse Dosing:
dose BID on Days 1-3, 8-10, 15-17, 22-24 on a 28-day cycle

Primary objective
Determine MTD and establish recommended Phase 2 dose

MTD = Maximum Tolerated Dose | RP2D = Recommended Phase 2 Dose | SoC = Standard of Care
BXCL701: Pancreatic Cancer
Significant Underserved Patient Population

- Pancreatic cancer has among the highest levels of overexpression and amplification of DPPs
- Preclinical models demonstrate synergy between DPP inhibition with BXCL701 and anti-PD-1 antibody in PDAC tumor microenvironment
- Immunotherapy not been demonstrated to have significant clinical impact in patients with mPDAC
- 2nd line standard of care varies:
  - FOLFIRINOX: RR 2.5% - 24% and mOS 4 - 6 months
Initiating Phase 2 Pancreatic Clinical Trial

**Safety Lead-In n = 6**

- Pembrolizumab 200 mg IV q3w Day 1 + BXCL701 0.3 mg PO BID Days 1-14 of 21-day cycle

**Simon’s 2-stage, single-arm, open label n = 19-43**

- Pembrolizumab 200 mg IV q3w Day 1 + BXCL701 0.3 mg PO BID Days 1-14 of 21-day cycle
- Step-up dosing in Cycle 1:
  - BXCL701 0.2 mg PO BID Days 1-7
  - then BXCL701 0.3 mg PO BID Days 8-14

**Primary objective**
Determine 18-week progression-free survival rate of BXCL701 + pembrolizumab

**On-treatment tumor biopsy**

**Screening + pre-treatment core tumor biopsy**
BXCL701 Potential Pipeline Within a Product in Cold Tumors

SCNC  
SCLC  
Pancreatic*
Breast  
Colorectal  
Ovarian  
GBM  
Sarcoma*

BXCL701  
Sensitizing cold tumors to CPI

*Orphan Drug Designation

*
Conclusions

• **BXCL701 is an oral innate immune activator with a novel mechanism of action**, described in peer-reviewed publication

• **BXCL701 has demonstrated clinical POC, in combination with KEYTRUDA, in two cold tumor settings**
  – Adenocarcinoma
  – SCNC

• Initial discussions with the FDA regarding development pathway and registrational strategy for BCXL701 in SCNC expected in **mid-2023**.

• **Strong scientific rationale** to guide choice of indications

• Foundation for a **precision medicine strategy** (DPP9 overexpression)

• **Potentially extending the value of IO** into large underserved patient populations
Panel Discussion