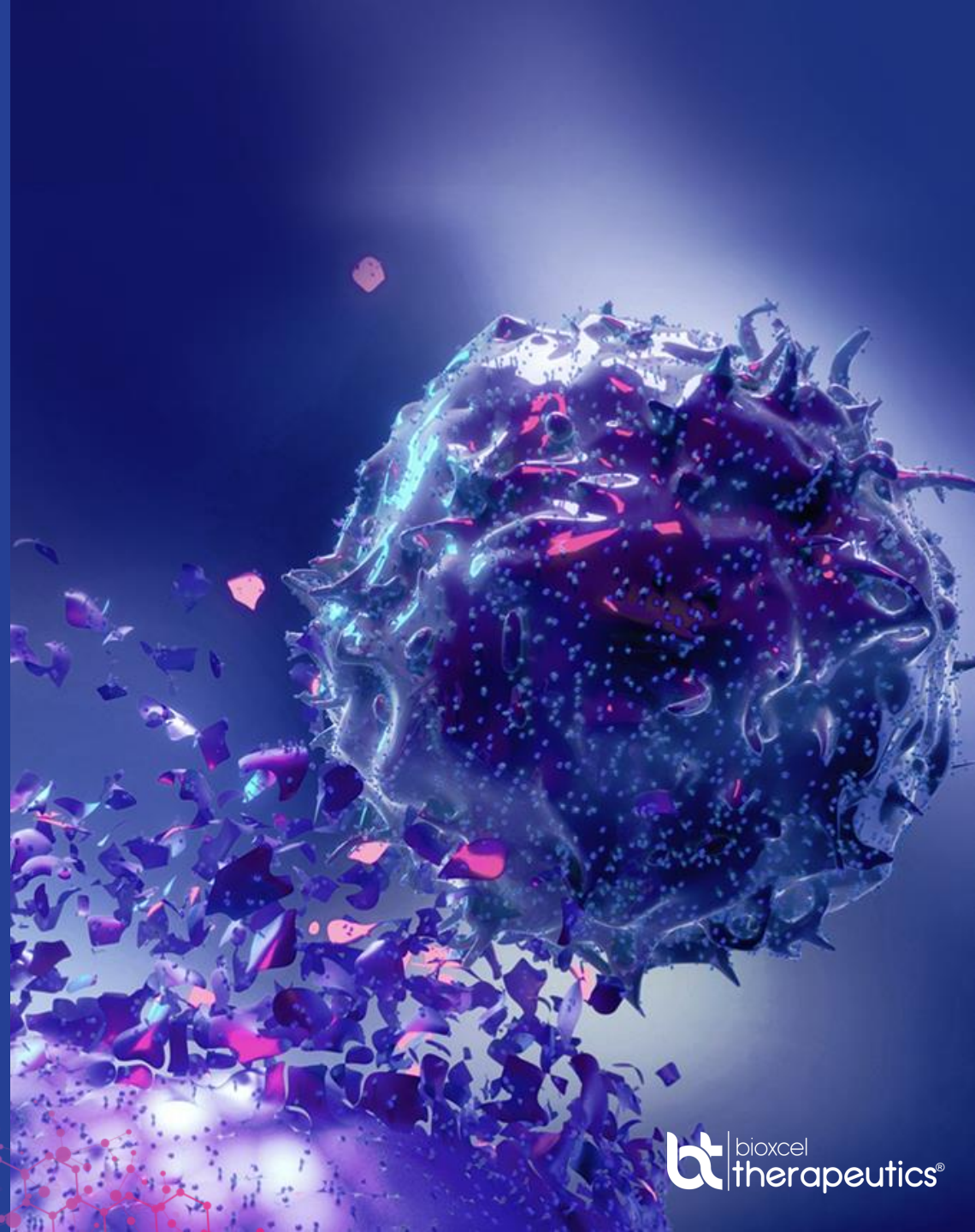


# BXCL701 Full Data Results From Phase 2 Trial in Rare, Aggressive Form of Prostate Cancer—SCNC

**Presented at:** ASCO<sup>®</sup> Genitourinary  
Cancers Symposium

February 13, 2023



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# 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; planned discussions with regulators; 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.

BioXcel Therapeutics may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important factors, including, without limitation: its limited operating history; its incurrence of significant losses; its need for substantial additional funding and ability to raise capital when needed; its limited experience in drug discovery and drug development; its dependence on the success and commercialization of IGALMI™, BXCL501, BXCL502 and BXCL701 and other product candidates; the Company has no experience in marketing and selling drug products; IGALMI™ or the Company's product candidates may not be accepted by physicians or the medical community in general; the failure of preliminary data from its clinical studies to predict final study results; failure of its early clinical studies or preclinical studies to predict future clinical studies; its ability to receive regulatory approval for its product candidates; its ability to enroll patients in its clinical trials; undesirable side effects caused by the Company's product candidates; its novel approach to the discovery and development of product candidates based on EvolverAI; its exposure to patent infringement lawsuits; its ability to comply with the extensive regulations applicable to it; impacts from the COVID-19 pandemic; its ability to commercialize its product candidates; and the other important factors discussed under the caption "Risk Factors" in its Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2022, as such factors may be updated from time to time in its other filings with the SEC, which are accessible on the SEC's website at [www.sec.gov](http://www.sec.gov) and the Investors section of our website at [www.bioxceltherapeutics.com](http://www.bioxceltherapeutics.com).

These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management's estimates as of the date of this presentation. While BioXcel Therapeutics may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing BioXcel Therapeutics' views as of any date subsequent to the date of this presentation.

# 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): FDA Approval

- IGALMI™ (dexmedetomidine) sublingual film, acute treatment of agitation in schizophrenia and bipolar I and II disorder
- Multiple indications for BXCL501, \$15B market opportunity



### Immuno-Oncology (BXCL701): Human Proof of Concept

- Unique innate immune activator, turning cold tumors hot
- Established OnkosXcel Therapeutics to focus on oncology assets

### High-Value Near-Term Catalysts

- 2 pivotal readouts for BXCL501 anticipated in 1H23
- Phase 2 readout for BXCL701 announced February 13, 2023

### Compelling Long-term Value

- Integrated AI-drug development & commercialization capability to build a leading neuroscience company



# BXCL701 Overview and Phase 2 Data Results

## OnkosXcel Therapeutics™

A subsidiary of BioXcel Therapeutics, Inc.



# 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

## 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®

## 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

## Leadership Position in Innate Immunity DPP8/9 Biology



Acquired for ~\$5B by



Scarcity of assets  
in innate immunity



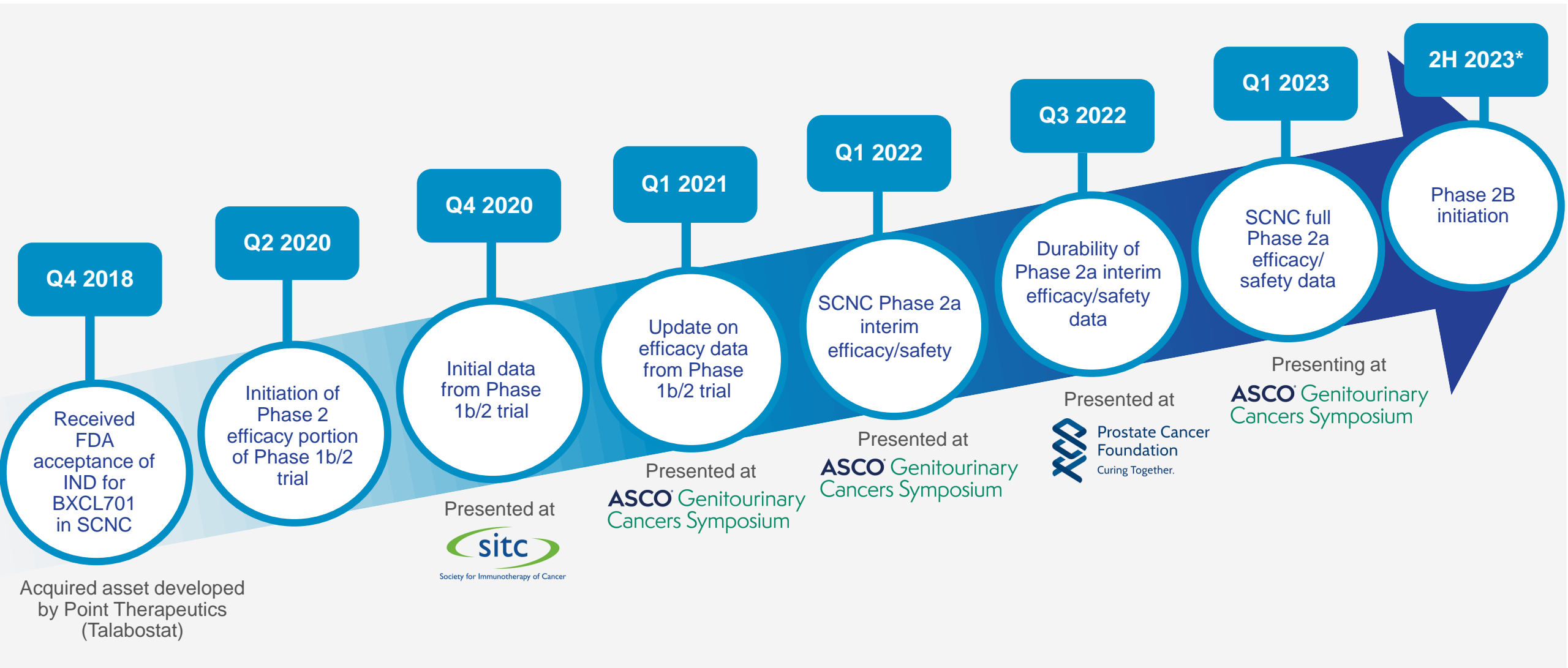
Acquired for ~\$2.3B by



\*As of data cutoff on December 19, 2022

# First AI Derived Human POC for Oral Innate Immune Activator

Proven AI Platform and Domain Expertise



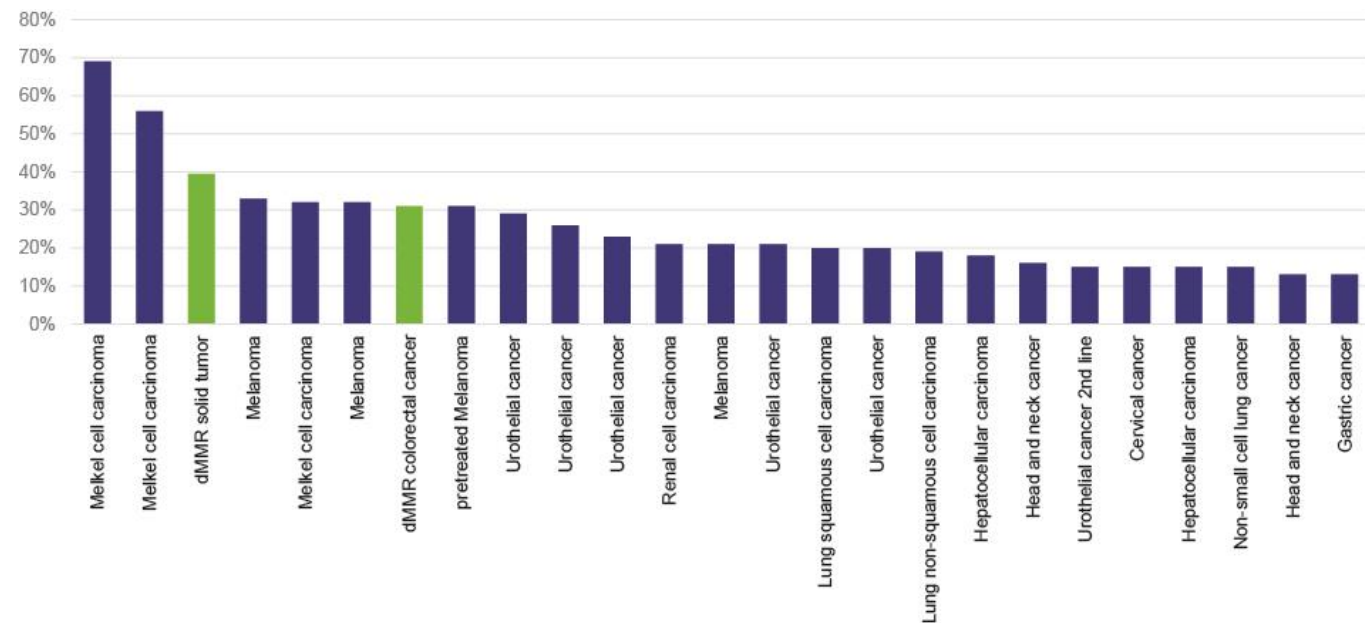
Acquired asset developed by Point Therapeutics (Talabostat)

\*Subject to FDA alignment

# Immune Checkpoint Inhibitors (ICIs) Are Not Reaching Their Full Potential

## Cold Tumors Remain One of The Most Challenging Unmet Needs in Oncology

- ICI largest drug class by 2025: >\$50B
- Significant clinical gaps:
  - Clinical benefit between 13% to 30% of cancer patients
- Cold tumors: do not respond by definition (ORR <<10%)
  - e.g., KEYTRUDA ORR in mCRPC 3-5%



Objective response rate with PD-1/PD-L1 inhibitors by cancer type and trial. Note: each bar represents one clinical trial (green bar: dMMR tumor)

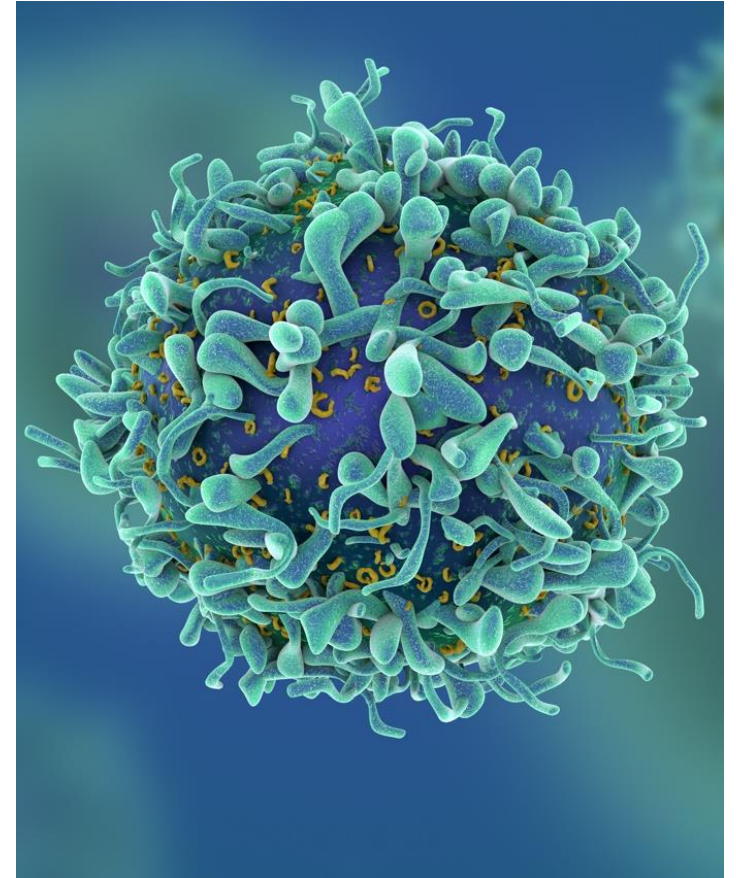
**BXCL701 immunomodulatory mechanism may convert a “cold” tumor to “hot,” unleashing checkpoint inhibitors’ potential**



# High Unmet Need in SCNC with no FDA Approved Therapy and Incidence is Increasing

268,500 men diagnosed with prostate cancer in U.S. in 2022\*, ~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 ICIs targeting PD-1 and CTLA-4 have not demonstrated meaningful single-agent therapeutic benefit in SCNC

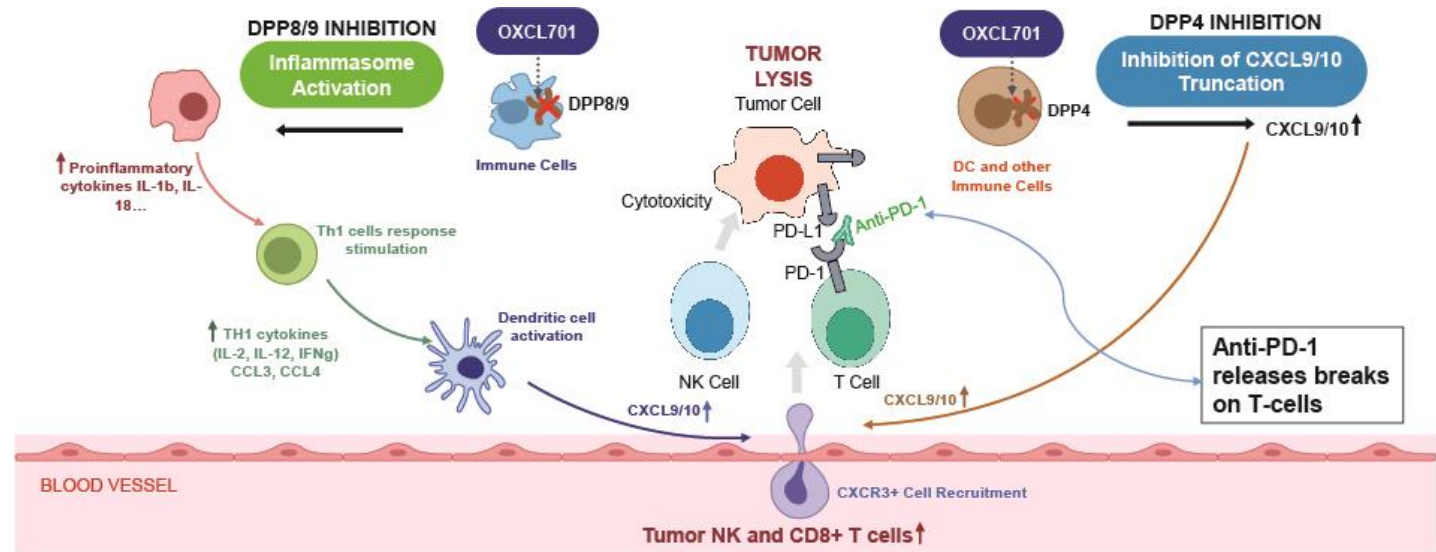


\* American Cancer Society's estimates for prostate cancer in the United States for 2022

# BXCL701 Offers Unique Proposed Mechanism of Action

Designed to Modulate Tumor Microenvironment by Activating Innate Immunity Followed by Adaptive Immunity

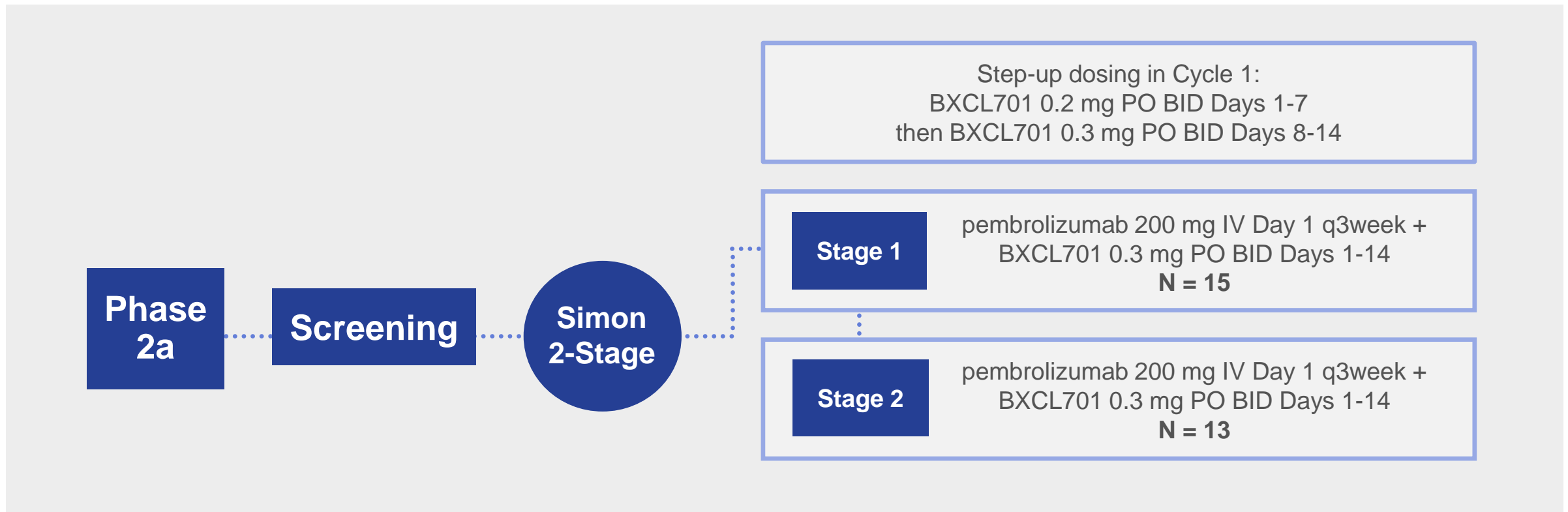
- Devised to **initiate inflammation** in the tumor microenvironment to:
  - Activate inflammasome via DPP8/9, followed by proinflammatory cytokines release\*
  - Induce an inflammatory form of cell death called pyroptosis in immune cells
- Preclinical data suggests potential **synergies** with both current ICI-based therapies and other immunotherapies
- DPP8/9 inhibition approach supported in clinic (PoC of BXCL701) with large, ~800-subject safety database
- Potential **predictive biomarker has been identified** (presented at SITC 2022)



Adapted from Journal for ImmunoTherapy of Cancer 2021; 9:e002837. doi:10.1136/jitc-2021-002837

# BXCL701 Phase 2 Trial Design for SCNC

**Primary endpoint\*: Composite Response Rate**  
**Either Objective Response by RECIST 1.1 criteria and/or**  
**CTC conversion from  $\geq 5/7.5$  mL to  $< 5/7.5$  mL and/or**  
 **$\geq -50\%$  PSA decline from baseline**



RECIST 1.1 = Response Evaluation Criteria in Solid Tumors Version 1.1

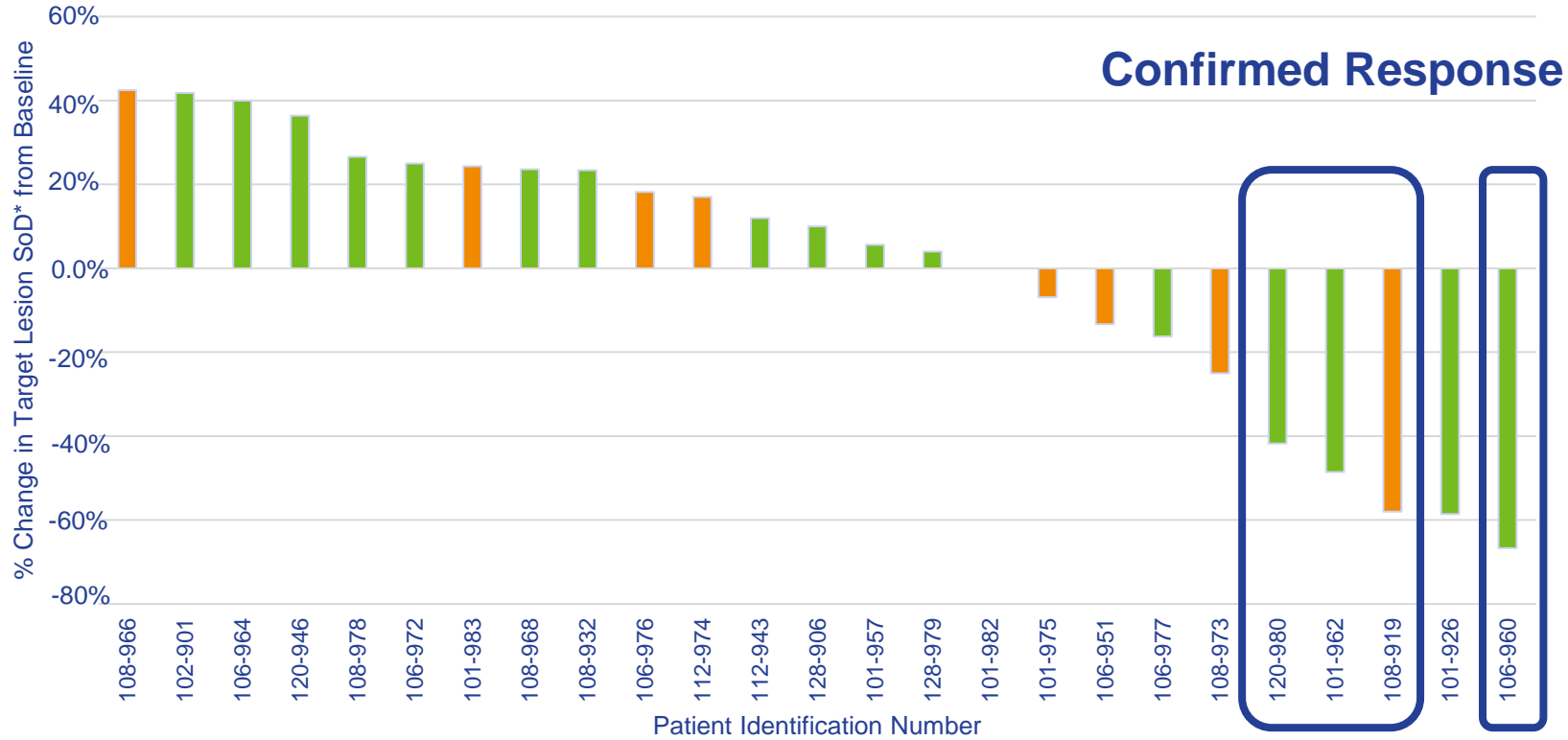
CTC = Circulating Tumor Cell

\* Additional objectives: Duration of response, PFS, changes in circulating cytokines, correlation of outcome with baseline tumor characteristics

# Efficacy Results Show Potential in SCNC in Combination with KEYTRUDA After Chemotherapy Failure

60%

RECIST 1.1 Best Response n = 25



\* SoD = Sum of Diameters

Data as of 08-FEB-23

**Composite Response Rate: 25%**  
 RECIST response rate: **20%**  
 4 confirmed PR + 1 uPR  
 Disease control rate: **48%**

**Median DoR\* (composite) = 6+ months**  
 (range: 1.3 - 17.4 months)

**Median DoR\* (RECIST 1.1) = 6+ months**  
 (range: 1.8 - 9.8 months)

## All responders are MSS and/or TMB low

Prior Platinum Chemotherapy

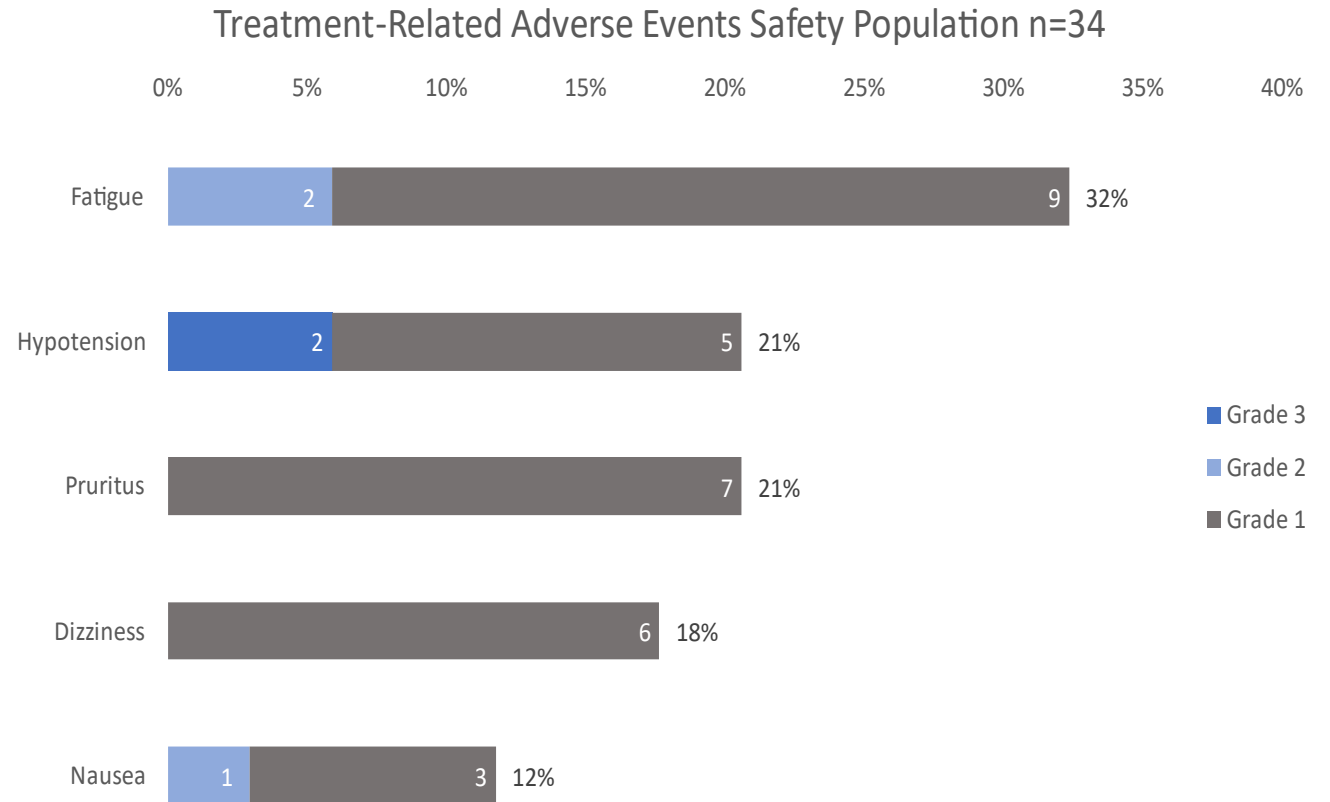
\* DoR = Duration of Response

# BXCL701 + KEYTRUDA Has a Generally Manageable Safety Profile

| Treatment-Emergent Adverse Events<br>n = 34    | n (%)           |
|--|-----------------|
| <b>Any Grade</b>                               | <b>33 (97%)</b> |
| Attributed to BXCL701                          | <b>29 (85%)</b> |
| Attributed to Pembrolizumab                    | <b>23 (68%)</b> |
| <b>Grade 3</b>                                 | <b>16 (47%)</b> |
| <b>Grade 4</b>                                 | <b>0</b>        |
| <b>Grade 5</b>                                 | <b>1* (3%)</b>  |
| <b>AE Leading to Treatment Discontinuation</b> | <b>6 (18%)</b>  |
| BXCL701 Discontinuation                        | <b>6 (18%)</b>  |
| Pembrolizumab Discontinuation                  | <b>5 (15%)</b>  |
| <b>Immune Related Adverse Events Any Grade</b> | <b>14 (41%)</b> |
| Grade ≥3                                       | <b>1^ (7%)</b>  |

\* Grade 5 tumor lysis syndrome

^ Grade 3 Colitis



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



# Responder Patient Vignette

- 69 years old
- Prior systemic therapies: LHRH agonist, abiraterone + prednisone, cisplatin + etoposide
- **Microsatellite stable**, low TMB
- Visceral (**liver** and lung) metastases, poor prognostic finding

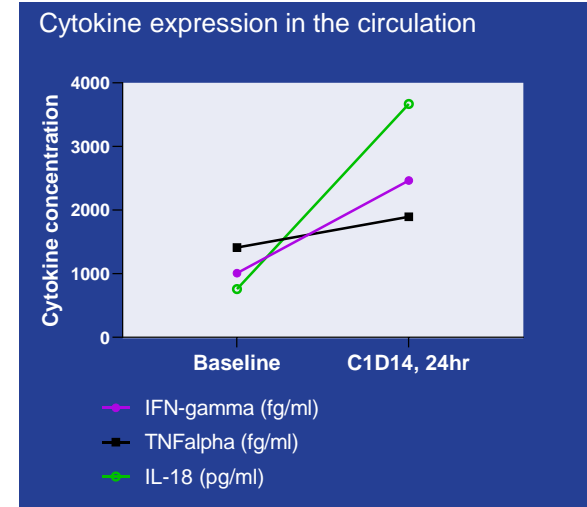
Liver – Baseline  
JAN-21



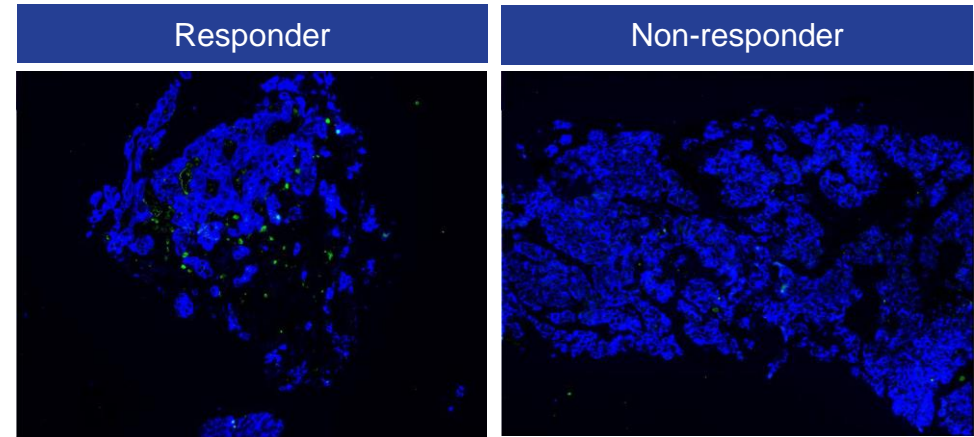
Liver – Post Cycle 3  
APR-21



58% reduction in target lesions following three cycles of treatment



Increase in key cytokines with treatment



DPP9 PanCK

Responses may be associated with DPP9 overexpression

# BXCL701 Phase 2 Data Summary of Results

## Efficacy:

- In the evaluable patient cohort (n = 28), **7 (25%) patients achieved a composite response, the primary endpoint of the trial**
- In patients with RECIST 1.1-defined measurable disease (n = 25):
  - **Partial response (PR) was observed in 5 (20%) patients** (4 confirmed PR, 1 unconfirmed PR)
  - **The disease control rate\* was 48% (12 patients)**
- The median duration of response for both composite responses and RECIST 1.1-defined partial responses was **6+ months\*\***

## Safety:

- 6 out of 34 patients (18%) in the safety population experienced serious adverse events (SAEs) possibly related or related to BXCL701 or pembrolizumab
- 6 (18%) patients discontinued any drug due to a treatment-related AE
- No evidence that BXCL701 potentiates immune-related AEs related to ICIs

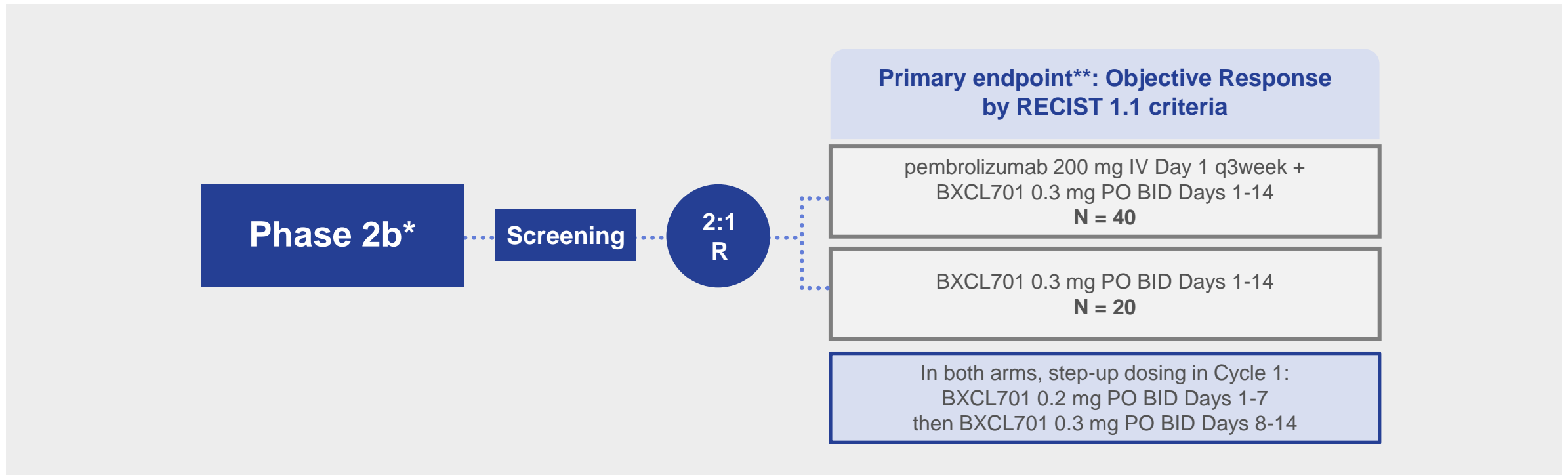
DPP9 overexpression was identified as a potential predictive biomarker for BXCL701 response and will be further evaluated

\*Disease control rate defined as: complete response + partial response + stable disease

\*\*As of the data cutoff on December 19, 2022.

# Results Support Further Development of BXCL701 + KEYTRUDA

Phase 2b Potential Registrational Trial in SCNC Expected to Initiate in H2 2023



Biomarker evaluation is ongoing and additional findings will be **presented at an upcoming medical meeting**

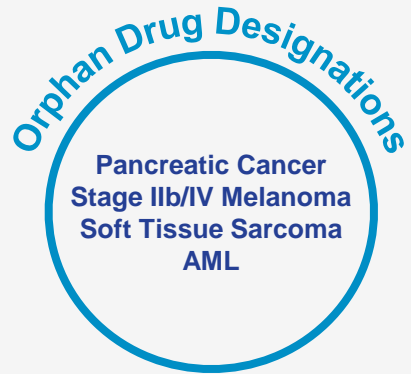
RECIST 1.1 = Response Evaluation Criteria in Solid Tumors Version 1.1

\* Final trial design may be updated as we seek regulatory guidance

\*\* Additional objectives: CRR, OS, duration of response, rPFS, and PSA PFS

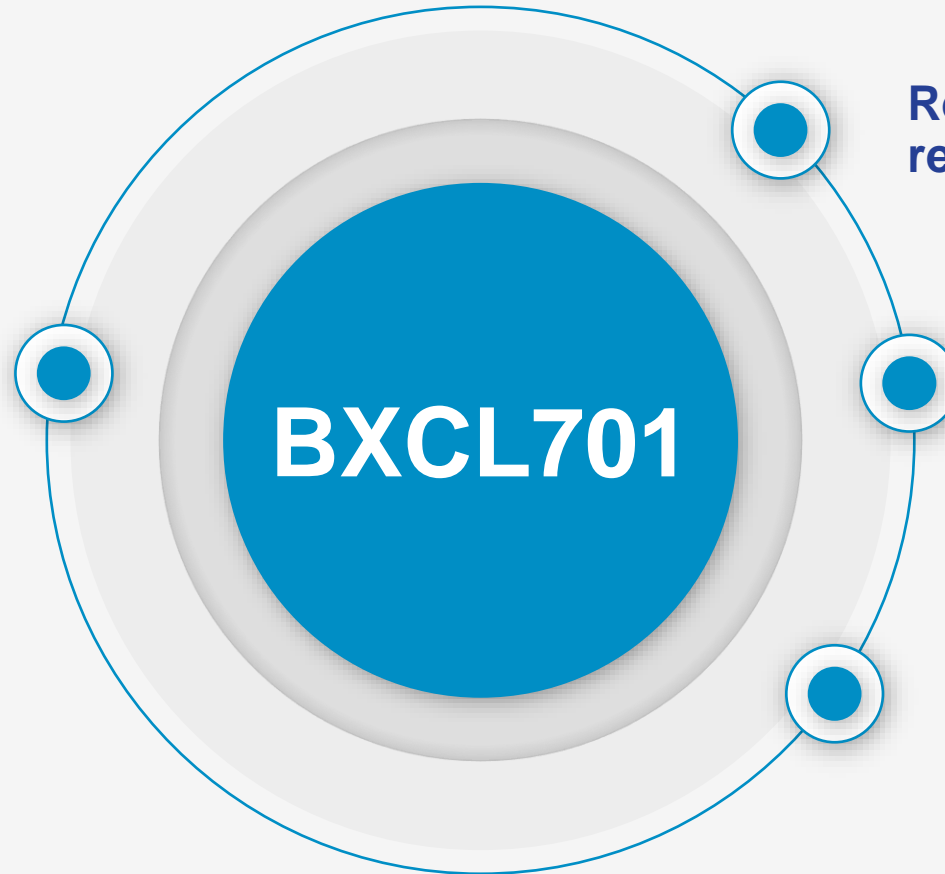
Phase 2b trial design and initiation subject to FDA alignment

# BXCL701 Pipeline Within a Product



**Sensitizing cold tumors to ICI**

- ER+ Breast Cancer
- Colorectal Cancer
- Ovarian cancer
- Glioblastoma
- Multiforme
- Pancreatic Cancer



**Reversing resistance to ICI**

**Deepening responses to ICI in hot tumors**

Sensitive settings

**Direct cytotoxicity in myeloid tumors**

Acute Myeloid Leukemia

# Further Development, Strategy, and Plan of BXCL701 in SCNC

Renown Experts at Upcoming BXCL701 Key Opinion Leader Day

## Daniel P. Petrylak, M.D.

Professor of Medicine and Urology



Yale Medicine

*Prostate Cancer Overview and Challenges  
with Current Immuno-Therapy*

## Louis M. Weiner, M.D

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



Georgetown | Lombardi  
COMPREHENSIVE CANCER CENTER



*BXCL701 Mechanism of Action*

## Rahul Aggarwal, M.D.

Associate Director for Clinical  
Sciences, Helen Diller Family  
Comprehensive Cancer Center, and  
Associate Professor of Medicine



UCSF

*Results of Phase 2 Trial of  
BXCL701 in SCNC*

KOL Event Scheduled for Tuesday, February 21, 2023: 1:00 to 3:00 p.m. ET 



## Value Creation

Exploring our strategic options to unlock value

## Clear Focus

Hard-to-treat tumors with focus on innate immunity (BXCL701 lead asset with ~800-subject safety database) and utilizing artificial intelligence platform

## Proven Expertise

Led by a world-class management team

## Established Infrastructure

Well-positioned to deliver on key milestones and fulfill our mission

# Appendix

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# Efficacy Results Show Potential in SCNC in Combination with KEYTRUDA After Chemotherapy Failure

| Best Response  | SCNC/t-SCNC Evaluable Patients<br>n = 28 (%) [95% Exact CI] |
|--|---|
| <b>Composite Response</b> (includes unconfirmed PR)        | <b>7 (25%)</b> [8.3%-41%]                                   |
| <b>Best RECIST 1.1 Response by Investigator Assessment</b> |   |
| <b>RECIST Evaluable<sup>a</sup></b>                        | <b>25 (89%)</b>   |
| <b>Partial Response</b>                                    | <b>5 (20%)</b> [6.8%-40.7%]                                 |
| <i>Confirmed PR</i>  | 4 (16%)   |
| <i>Unconfirmed PR</i>                                      | 1 (4%)  |
| SD (any duration)  | 7 (28%)   |
| PD   | 13 (52%)  |
| <b>Disease Control Rate (CR + PR + SD)</b>                 | <b>12 (48%)</b>   |
| <b>CTC<sup>b</sup></b>                                     |   |
| <b>CTC Evaluable<sup>c</sup></b>                           | <b>4</b>  |
| <b>CTC Response<sup>d</sup></b>                            | <b>1 (25%)</b> [0.6%– 80.6%]                                |
| <b>PSA</b>   |   |
| <b>PSA Evaluable<sup>e</sup></b>                           | <b>27 (96%)</b>   |
| <b>PSA<sub>50</sub> Response</b>                           | <b>3 (11%)</b> [2.4%- 29%]                                  |

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

Results as of Dec 19., 2022

# BXCL701 Clinical Proof of Concept Interim Phase 2a Data as of Sept. 12, 2022



## SCNC—aggressive variant of metastatic castration-resistant prostate cancer

93% enrolled SCNC patients pre-treated with platinum

### Preliminary results

33% RECIST-defined PR (3 confirmed, 1 unconfirmed, n = 12)—all responders MSS and/or TMB low

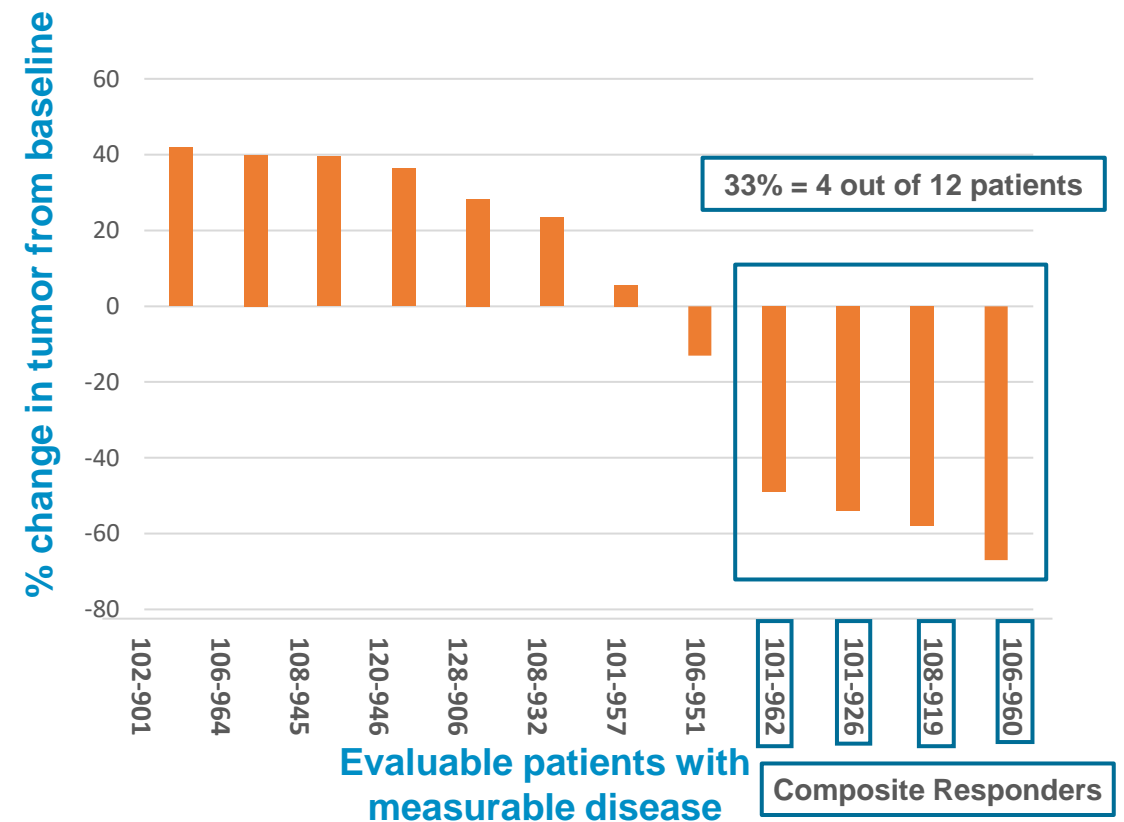
### PD-L1 inhibitor single agent historic data in SCNC

Objective response rate 6.7%—1/15 patients  
Responder was microsatellite instability-high<sup>1</sup>\*

No response observed in microsatellite stable patients

\* FOR ILLUSTRATIVE PURPOSES ONLY: no head-to-head studies have been conducted comparing BXCL701 to checkpoint inhibitors as a single agent. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

## SCNC Tumor Best Response (n = 12)



# Efficacy Results Adenocarcinoma Cohort

| Best Response  | Phase 2a Adenocarcinoma Patients<br>N = 29 (%) [95% Exact CI] |
|--|---|
| Composite Response   | 6 (21) [8.0 – 39.7]   |
| <b>Best RECIST 1.1 Response by Investigator Assessment</b> |   |
| RECIST Evaluable <sup>a</sup>                              | 18 (62)   |
| <b>Partial Response</b>                                    | <b>4 (22) [6.4 – 47.6]</b>                                    |
| <i>Confirmed PR</i>  | 3 (75)  |
| <i>Unconfirmed PR</i>                                      | 1 (25)  |
| SD (any duration)<br>including Minor Response              | 11 (61)   |
| Non-CR / Non-PD  | 15 (83)   |
| PD   | 3 (17)  |
| <b>Disease Control Rate (CR + PR + SD)</b>                 | <b>83%</b>  |
| <b>PSA</b>   |   |
| PSA Evaluable <sup>b</sup>                                 | 29 (100)  |
| <b>PSA<sub>50</sub> Response</b>                           | <b>5 (17) [5.8 – 35.8]</b>                                    |
| <b>CTC<sup>c</sup></b>                                     |   |
| CTC Evaluable <sup>d</sup>                                 | <b>11 (38)</b>  |
| <b>CTC Response<sup>e</sup></b>                            | <b>2 (18)</b>   |

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

ASCO<sup>®</sup> Genitourinary  
Cancers Symposium

2022

**Composite response rate: 21%**

- RECIST-defined PR\*: **22%**
- Disease control rate: **83%**
- PSA<sub>50</sub>: **17%**—including 5 patients with -100% to -57% PSA decrease
- CTC response: **18%**

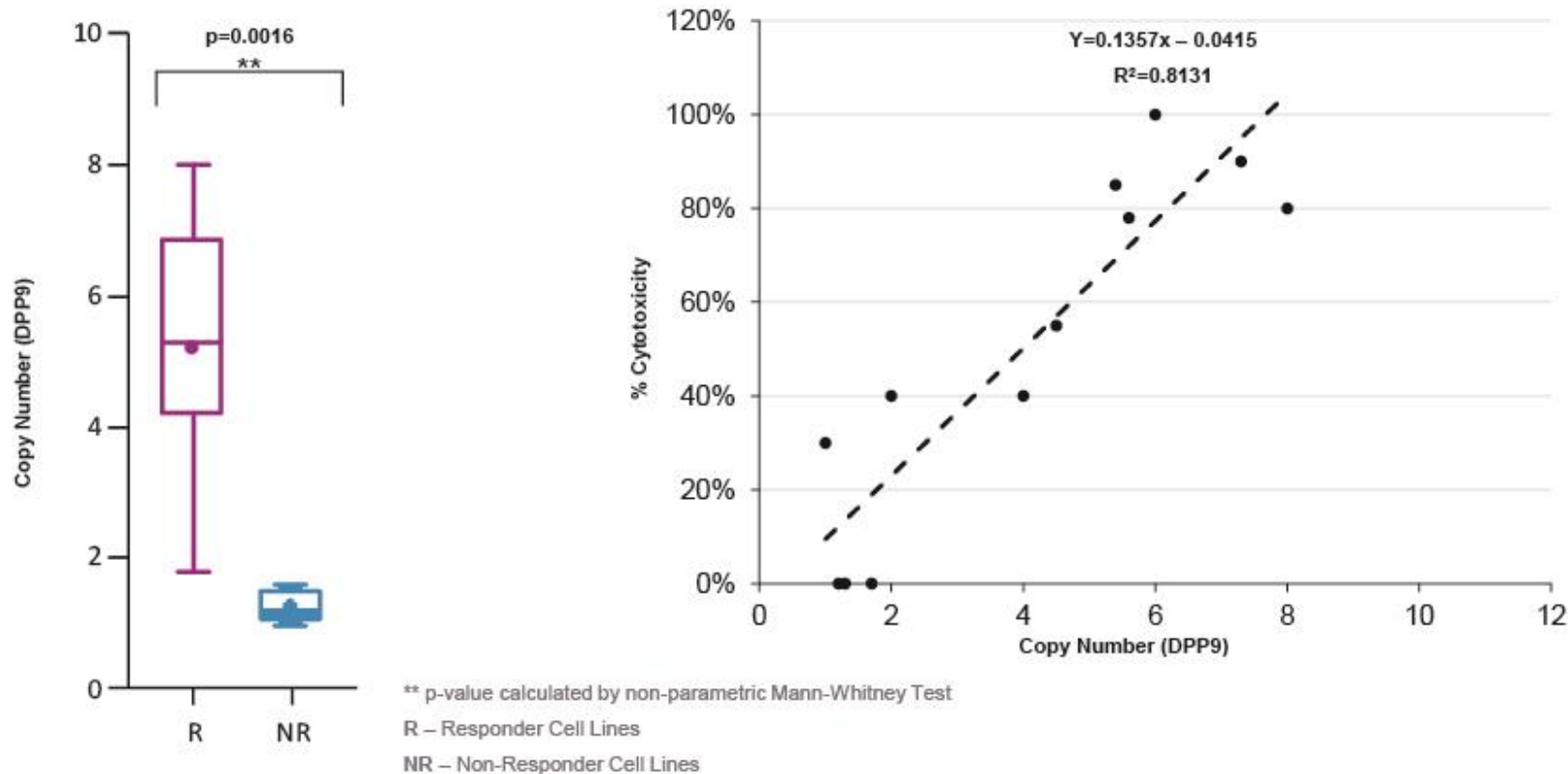
\* Includes confirmed and unconfirmed PRs

**Data cut-off date: 24-Nov-21**



# Potential Predictive Biomarker Has Been Identified

DPP9 Copy Number Variation Highly Correlated with BXCL701 Cytotoxicity in Human AML Cell Lines



Potentially applicable to liquid and solid tumors  
 Can be assayed by standard assay approaches: NGS, FISH/CISH, RT-PCR

# Point Therapeutics' Talabostat Clinical Trial History

Talabostat developed prior to immunotherapy revolution, generally in combination with chemotherapy, with limited success

- **Phase 1 Studies in Patients with Cancer**

- Study PTH-101 MTD in patients with solid tumors receiving myelosuppressive chemotherapy: n = 34, no evaluation of antitumor activity
- Study PTH-201 safety, MTD, and activity of combination with rituximab in patients with B- cell malignancies: n = 20, 10% PR
- National Cancer Institute to find optimal dose of talabostat in combination with temozolomide or carboplatin in children with relapsed or refractory solid tumors: no evaluation of antitumor activity

- **Phase 2 Studies in Patients with Malignancies**

- Study PTH-301 Stage IV melanoma monotherapy: n = 42, OR 2/33 (6%)
- Study PTH-302 Stage IIIB/IV NSCLC + docetaxel: n = 55, PR 7.1%
- Study PTH-303 Stage IV melanoma + cisplatin: n = 74, PR 8.1%
- Study PTH-320 Stage IV adenocarcinoma of the pancreas + gemcitabine: n = 68, ORR 11.8%
- Study PTH-203 advanced CLL + rituximab: n = 54, 6 PR 11.1%

- **Phase 3 Studies in Patients with Malignancies**

- Study PTH-304 talabostat and docetaxel versus docetaxel and placebo in advanced (Stage IIIB/IV) NSCLC: n = 65, negative study
- Study PTH-305 talabostat and pemetrexed versus pemetrexed and placebo in advanced (Stage IIIB/IV) NSCLC: n = 139, negative study

# IGALMI™ Indication and Important Safety Information

## INDICATION

IGALMI is indicated for the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder in adults. Limitations of Use: The safety and effectiveness of IGALMI have not been established beyond 24 hours from the first dose.

## IMPORTANT SAFETY INFORMATION

IGALMI can cause serious side effects, including:

- Decreased blood pressure, low blood pressure upon standing, and slower than normal heart rate, which may be more likely in patients with low blood volume, diabetes, chronic high blood pressure, and older patients. IGALMI is taken under the supervision of a healthcare provider who will monitor vital signs (like blood pressure and heart rate) and alertness after IGALMI is administered to help prevent falling or fainting. Patients should be adequately hydrated and sit or lie down after taking IGALMI and instructed to tell their healthcare provider if they feel dizzy, lightheaded, or faint.
- Heart rhythm changes (QT interval prolongation). IGALMI should not be given to patients with an abnormal heart rhythm, a history of an irregular heartbeat, slow heart rate, low potassium, low magnesium, or taking other drugs that could affect heart rhythm. Taking IGALMI with a history of abnormal heart rhythm can increase the risk of torsades de pointes and sudden death. Patients should be instructed to tell their healthcare provider immediately if they feel faint or have heart palpitations.
- Sleepiness/drowsiness. Patients should not perform activities requiring mental alertness, such as driving or operating hazardous machinery, for at least 8 hours after taking IGALMI.
- Withdrawal reactions, tolerance, and decreased response/efficacy. IGALMI was not studied for longer than 24 hours after the first dose. Physical dependence, withdrawal symptoms (e.g., nausea, vomiting, agitation), and decreased response to IGALMI may occur if IGALMI is used longer than 24 hours.

The most common side effects of IGALMI in clinical studies were sleepiness or drowsiness, a prickling or tingling sensation or numbness of the mouth, dizziness, dry mouth, low blood pressure, and low blood pressure upon standing.

These are not all the possible side effects of IGALMI. Patients should speak with their healthcare provider for medical advice about side effects.

Patients should tell their healthcare provider about their medical history, including if they suffer from any known heart problems, low potassium, low magnesium, low blood pressure, low heart rate, diabetes, high blood pressure, history of fainting, or liver impairment. They should also tell their healthcare provider if they are pregnant or breastfeeding or take any medicines, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Patients should especially tell their healthcare provider if they take any drugs that lower blood pressure, change heart rate, or take anesthetics, sedatives, hypnotics, and opioids.

Everyone is encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088. You can also contact BioXcel Therapeutics, Inc. at 1-833-201-1088 or [medinfo@bioxceltherapeutics.com](mailto:medinfo@bioxceltherapeutics.com).

Please see full [Prescribing Information](#).

# Thank you!

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