

# Investor Presentation

Building a powerful new future in cellular IO

February 2023



# Forward Looking Statement

This presentation contains estimates, projections and other forward-looking statements, concerning, among other things: our research and development activities relating to our GoCAR™ platform, our CaspaCIDE safety switch, and related technologies; our product candidates including BPX-601, BPX-603, and rimiducid; the timing and success of our current and planned clinical trials, including the timing of receipt of data from such clinical trials and the timing of our reports of such data; the possible range of applications of our cell therapy programs and potential curative effects and safety in the treatment of diseases, including as compared to other treatment options and competitive therapies; our expected cash runway; and the potential to expand the use of our switch technology through additional license opportunities. Our estimates, projections and other forward-looking statements are based on management's current assumptions and expectations of future events and trends, which affect or may affect our business, strategy, operations or financial performance. Although we believe that these estimates, projections and other forward-looking statements are based upon reasonable assumptions, they are subject to numerous known and unknown risks and uncertainties and are made in light of information currently available to us. Many important factors, in addition to the factors described in this presentation, may adversely and materially affect our results as indicated in forward-looking statements. All statements other than statements of historical fact are forward-looking statements.

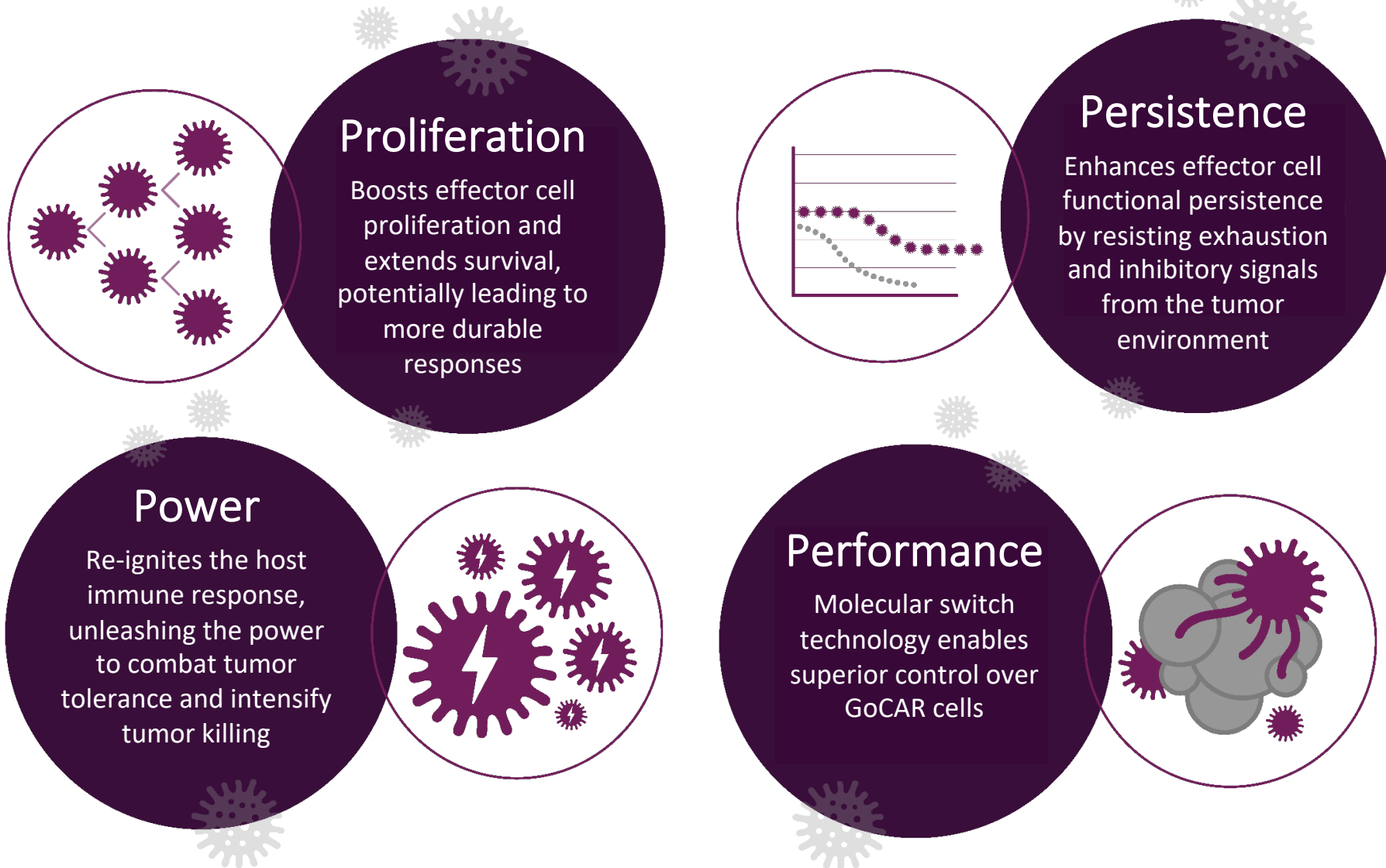
Estimates, projections and other forward-looking statements speak only as of the date they were made, and, except to the extent required by law, we undertake no obligation to update any forward-looking statement. These statements are also subject to a number of material risks and uncertainties that are described more fully in Bellicum's filings with the Securities and Exchange Commission, including without limitation our annual report on Form 10-K for the year ended December 31, 2021 and our quarterly report on Form 10-Q for the period ended September 30, 2022.



# Technology Overview

# Building a Powerful New Future in Cellular IO

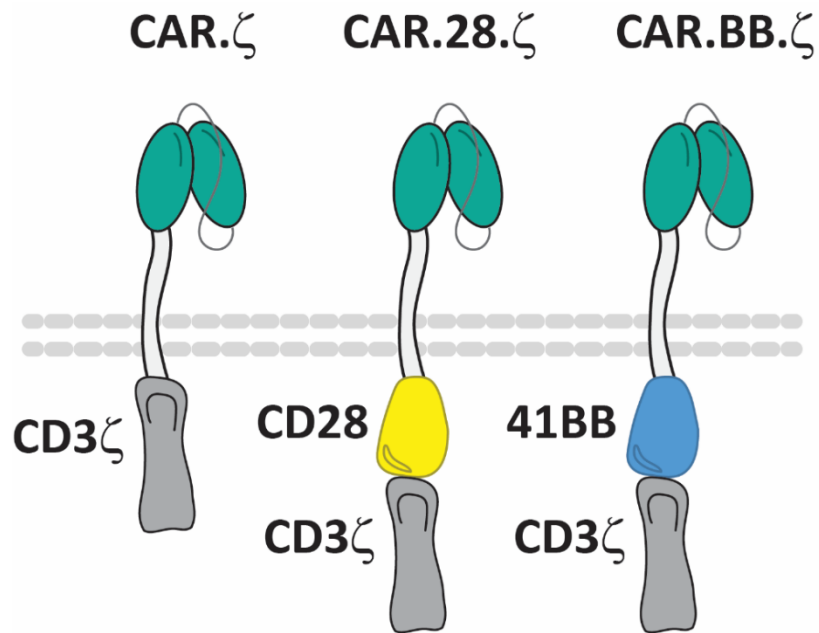
*Our GoCAR platform is engineered to break through the limitations of current cell therapies*



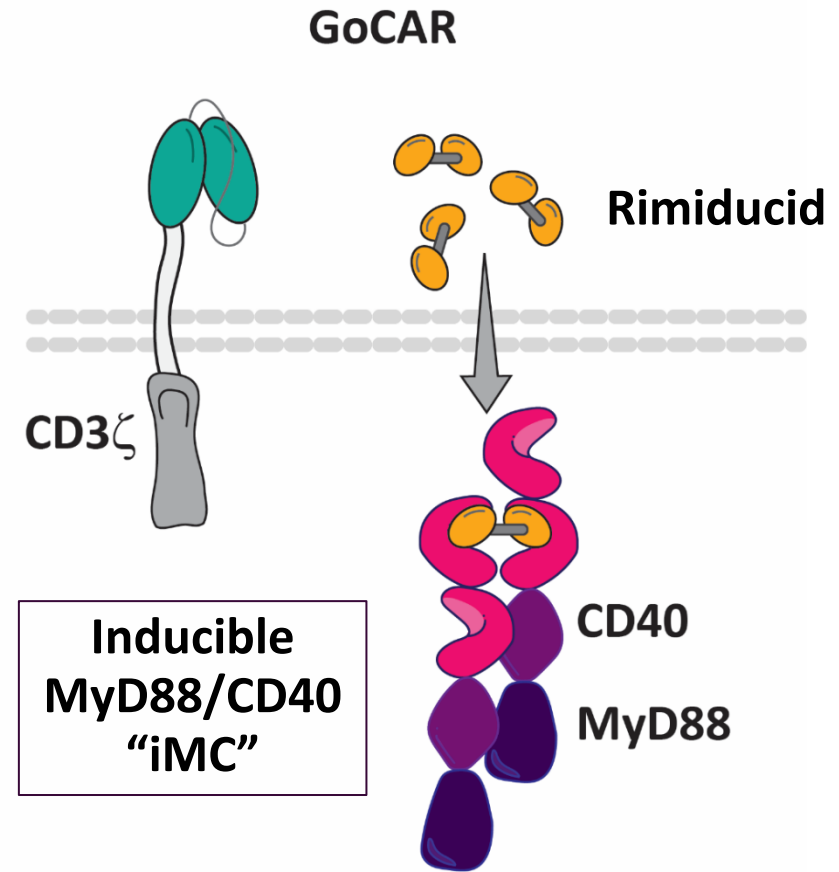


# GoCAR: Differentiated Technology Platform

## Current Generation CAR Technology



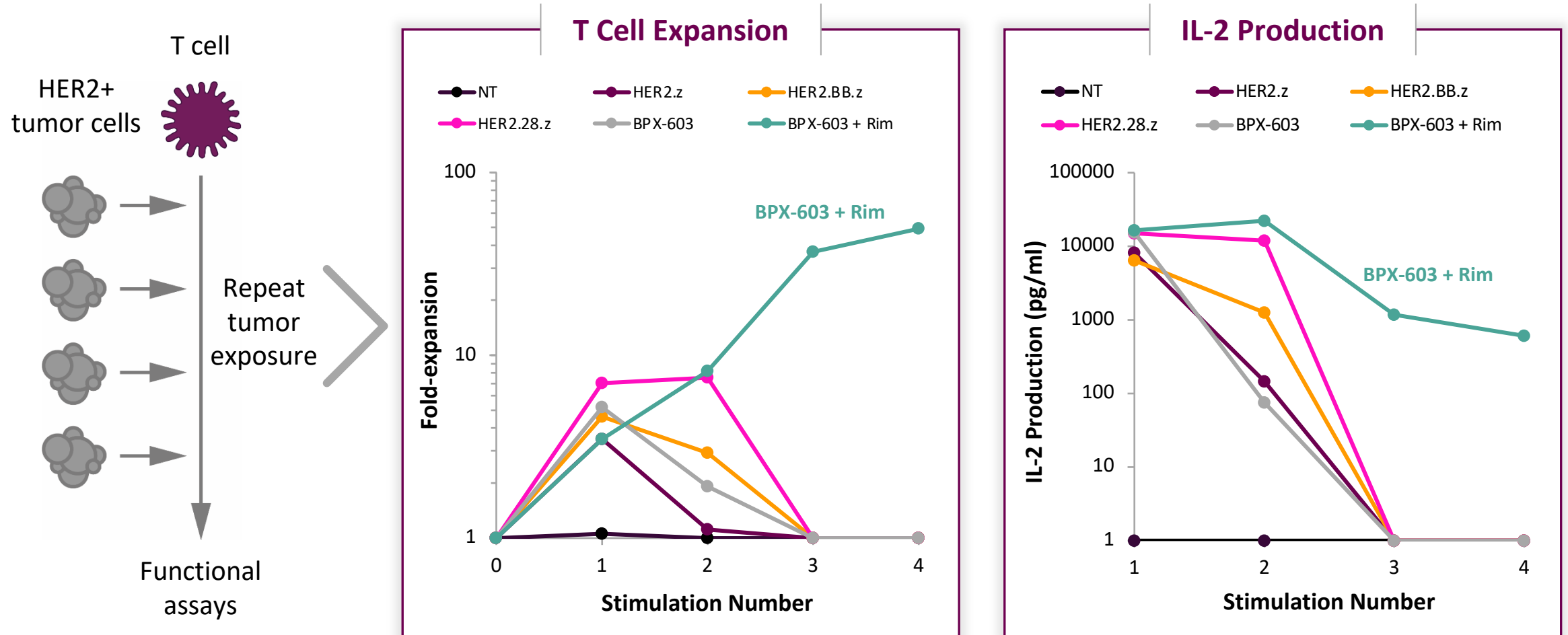
## Next Generation GoCAR Technology



Lead Program:  
BPX-601  
(PSCA)

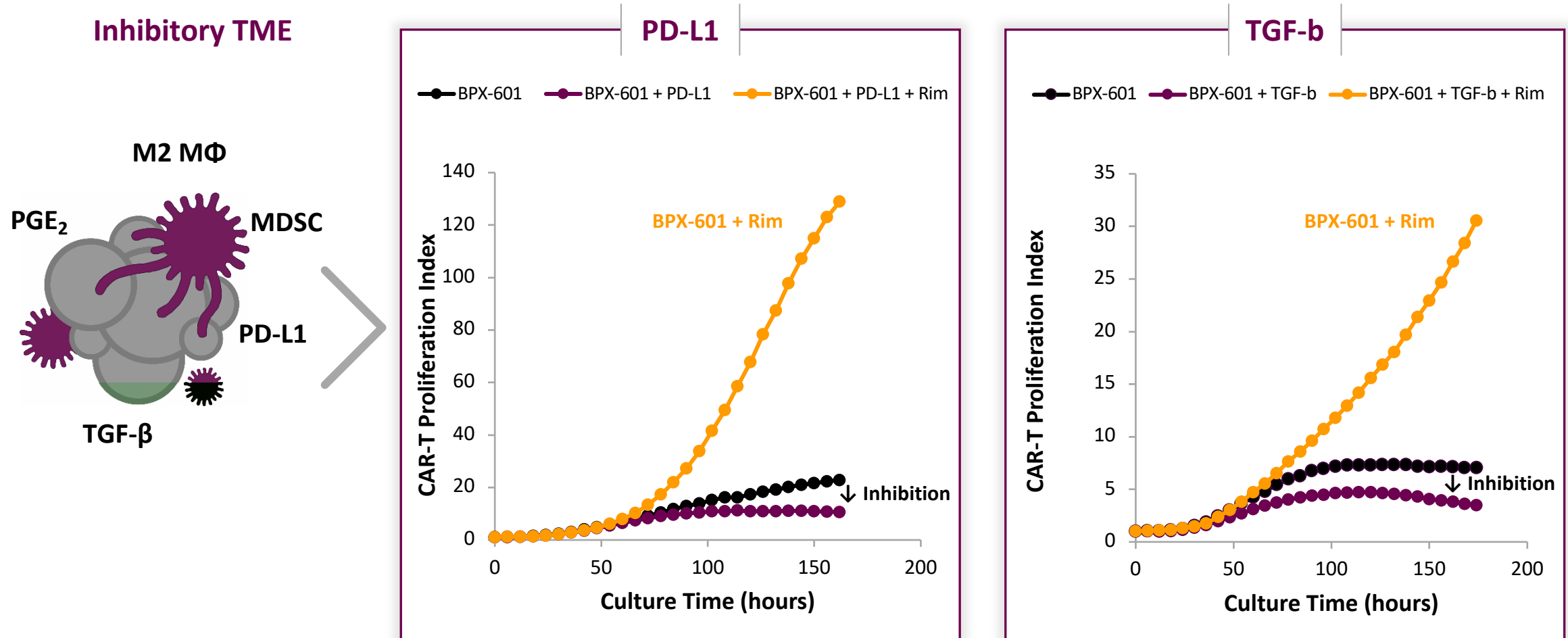
# GoCAR Proliferation: Superior Expansion and Resistance to T Cell Exhaustion

*iMC activation limits T cell dysfunction in repeat tumor stimulation exhaustion assay*



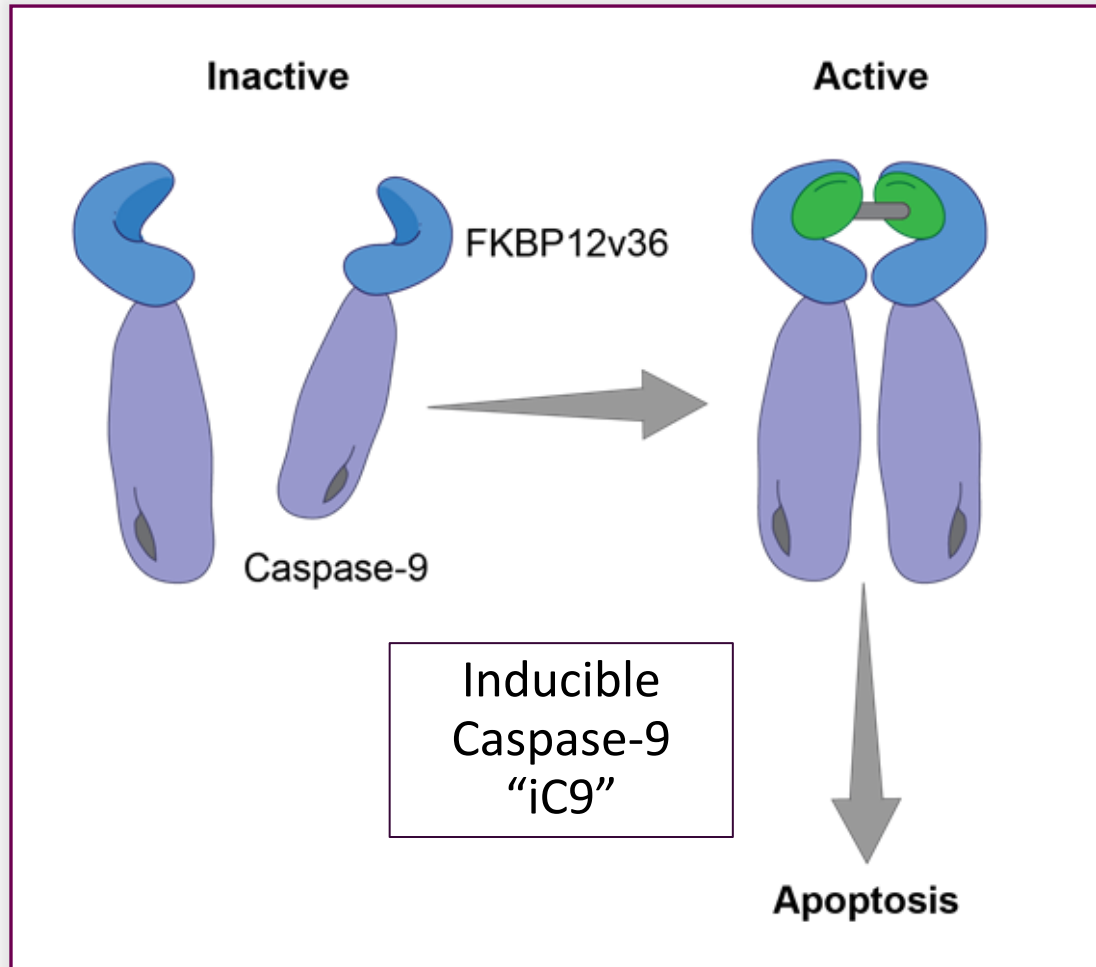
# GoCAR Persistence: Resistance to Immune Suppressive TME

*iMC overrides common inhibitory molecules in the tumor microenvironment*



# CaspaCIDE Safety Switch

*Inducible apoptosis to mitigate cell therapy-mediated adverse events*



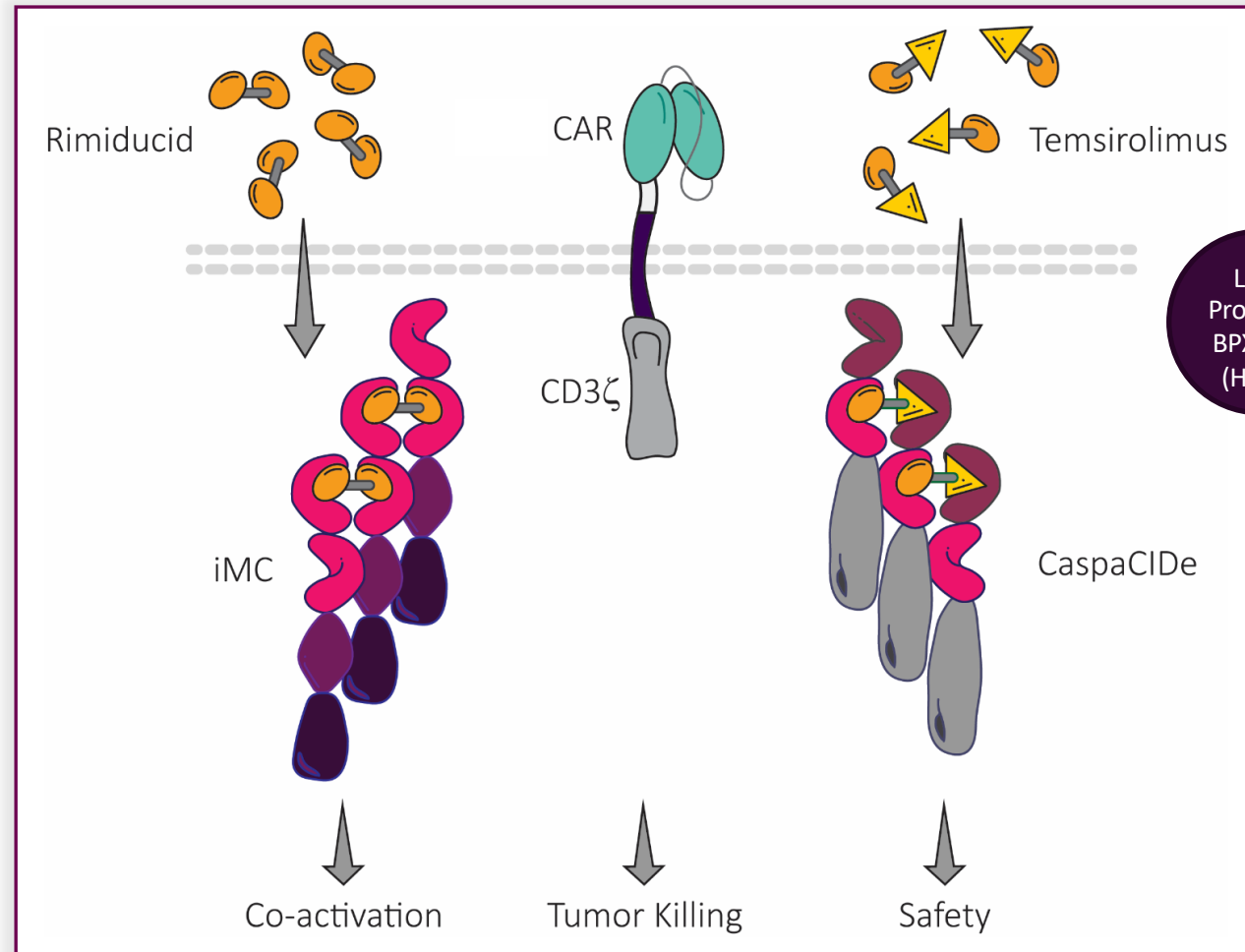
## Potential Applications

- Controlling toxicity associated with cell therapies
  - Cytokine Release Syndrome
  - ICANS
- Targeting antigens with known or potential high-risk side effects
- Developing next-generation, higher-potency cell therapy constructs
- Protecting against the risk of tumorigenesis
- Managing GvHD associated with adoptive T cell therapy with allogeneic T cells



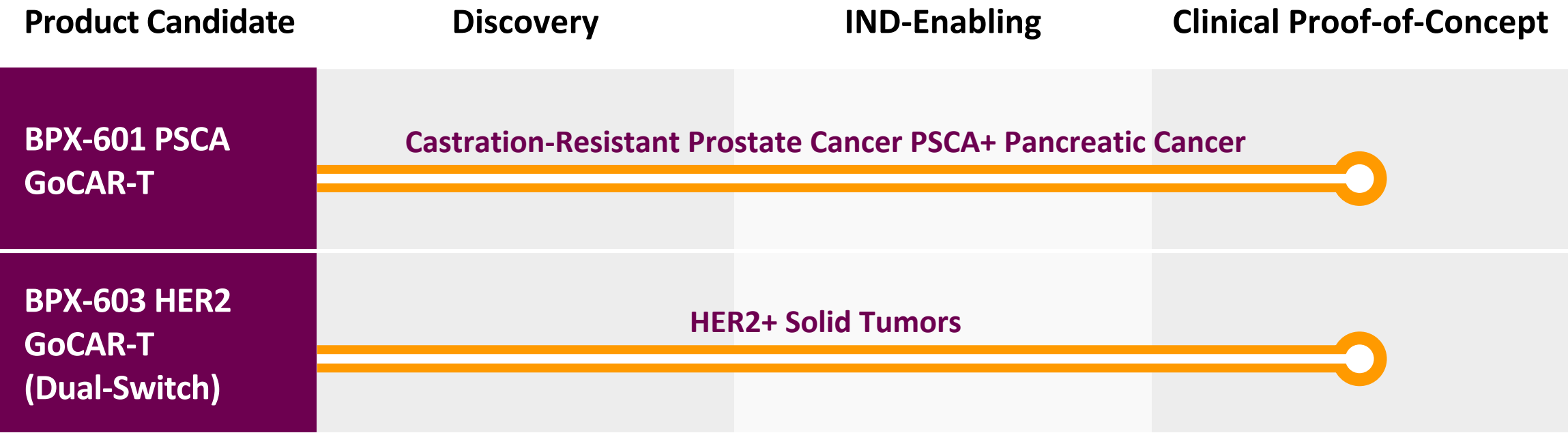
# Dual-Switch GoCAR-T

*A controllable system to manage CAR-T proliferation, persistence, and safety*



# Product Pipeline

*Establishing the clinical value of GoCAR-T in solid tumors to propel cellular IO forward*





# BPX-601 PSCA GoCAR-T

# BPX-601 GoCAR-T Targeting PSCA in mCRPC

## Product Summary

- Attractive first-in-class solid tumor CAR-T opportunity; first-in-human experience with iMC
- Initial cell dose escalation, lymphodepletion optimization, and safety assessment of rimiducid dosing in pancreatic cancer complete
- Data presented at ASCO GU 2023 demonstrate:
  - Encouraging biochemical and radiographic responses in heavily pre-treated mCRPC patients
  - >PSA50 in 50% of patients (4/8) treated
  - Consistent BPX-601 expansion with persistence >200 days

## Program Update

- Rimiducid dose escalation ongoing
- Data update planned for 1Q'2024

## Unmet Need

Unmet need in mCRPC remains, particularly in patients who have progressed after androgen deprivation therapy, chemotherapy, and radiotherapy

	Annual Incidence (U.S.)*	Annual Deaths (U.S.)	% Expressing PSCA
Prostate	249k	34k	75-90%

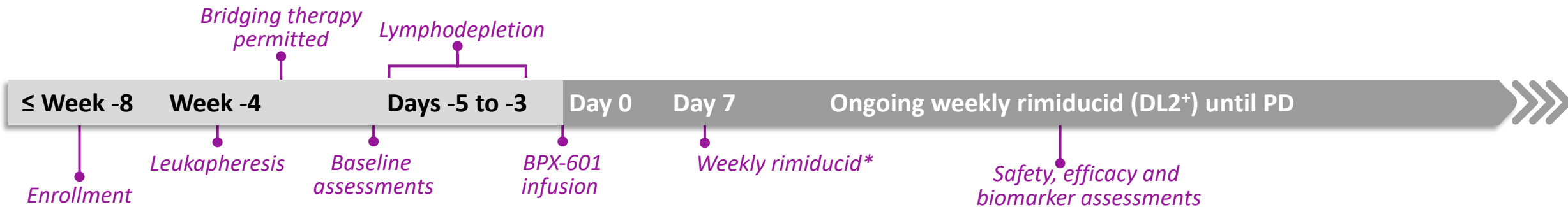
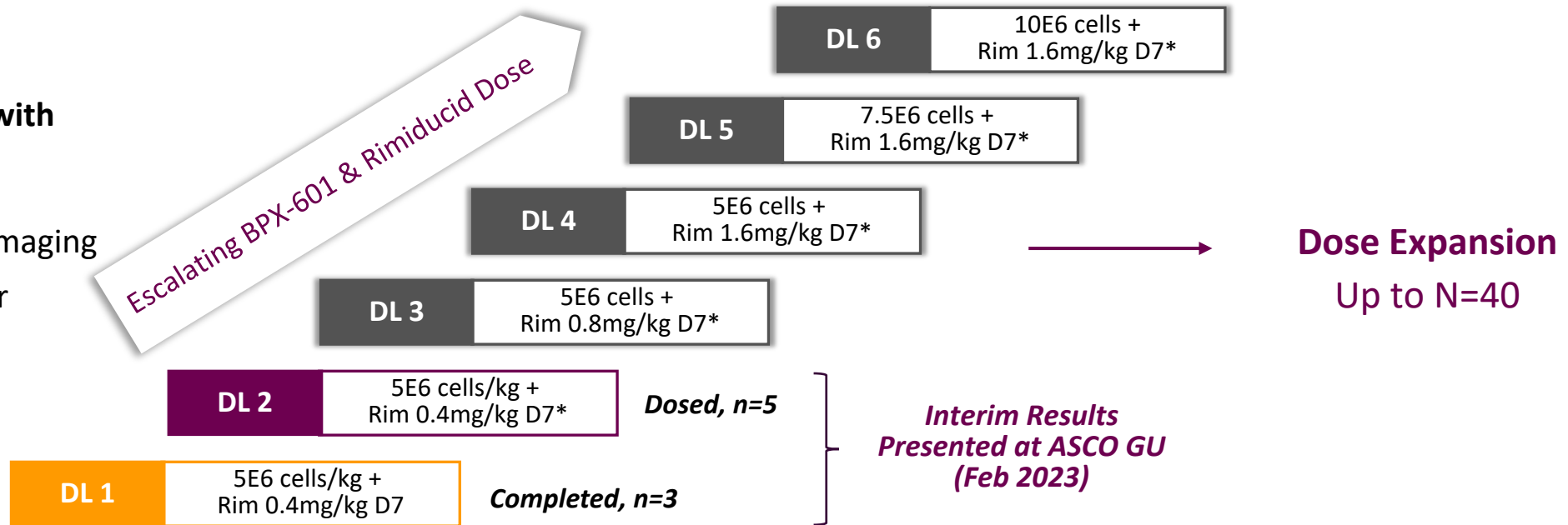
\* Incidence includes all newly diagnosed prostate cancer



# BPX-601 Phase 1/2 Trial Design in mCRPC

## Eligible subjects with mCRPC with PD:

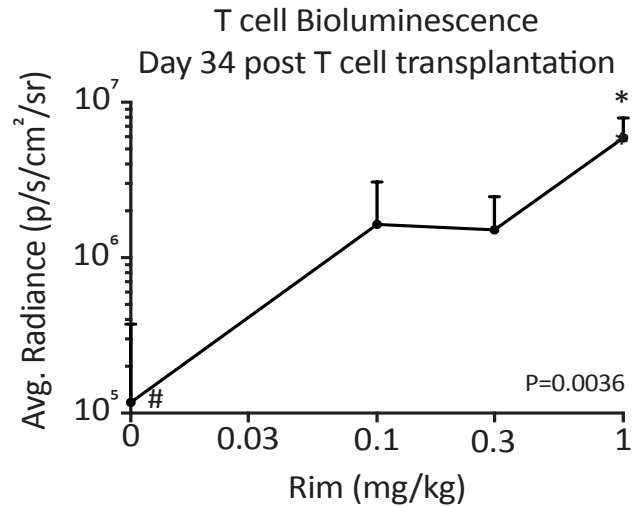
- Rising PSA or radiographic imaging
- At least 2 prior regimens
- Measurable disease at baseline



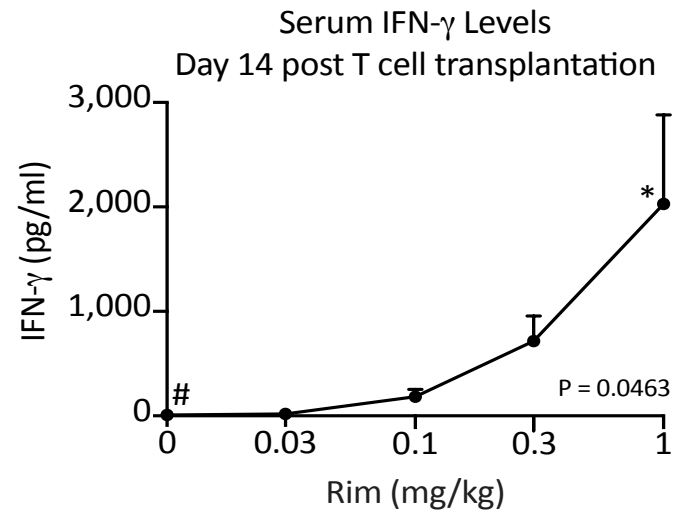
# Rationale for Rimiducid Dose Escalation

*In non-clinical models, increasing exposure to rimiducid leads to...*

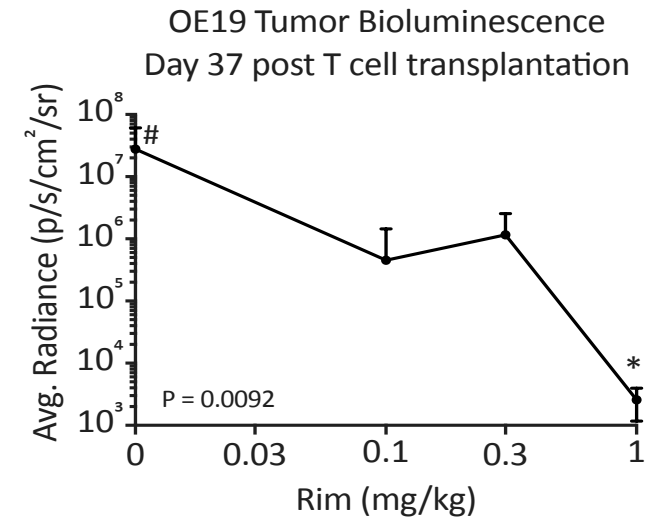
## Increased GoCAR-T Cell Persistence



## Enhanced Cytokine Production



## Improved Anti-Tumor Efficacy



# Patient Demographics and Characteristics

Baseline Characteristic	All Patients (N=8)
Age, median (range) – yr	66.5 (56 - 75)
ECOG performance score, no. (%)	
0	4 (50%)
1	4 (50%)
Site of Disease – no. (%) <sup>¥</sup>	
Liver	2 (25%)
Lung	2 (25%)
LNs	5 (62.5%)
Bone	4 (50%)
Bone only	2 (25%)
PSA level (ng/mL), median (range)	186 (29-331)
Prior lines of treatment, median (range)	6 (5-9)

- Patients received BPX-601 dose of  $5 \times 10^6$  cells/kg and rimiducid 0.4 mg/kg (range: 1-40 doses)
- Tumor of all patients tested (n=5) expressed PSCA mRNA\*
- All patients received prior ADT and chemotherapy
  - 87.5% received docetaxel
  - 75% received immune-based therapies

# Adverse Event Summary

	All Patients (N=8)	
	All Grades n (%)	Grade 3+ n (%)
<b>TEAE</b>	8 (100%)	7 (87.5%)
<b>Serious TEAE</b>	5 (62.5%)	5 (62.5%)
<b>Cytokine Release Syndrome</b>	8 (100%)	2 (25%)
<b>Neurotoxicity/ICANS<sup>‡</sup></b>	2 (25%)	1 (12.5%)
<b>Dose Limiting Toxicity</b>	1 (12.5%)*	1 (12.5%)*
<b>TEAE Leading to Death</b>	1 (12.5%)*	1 (12.5%)*

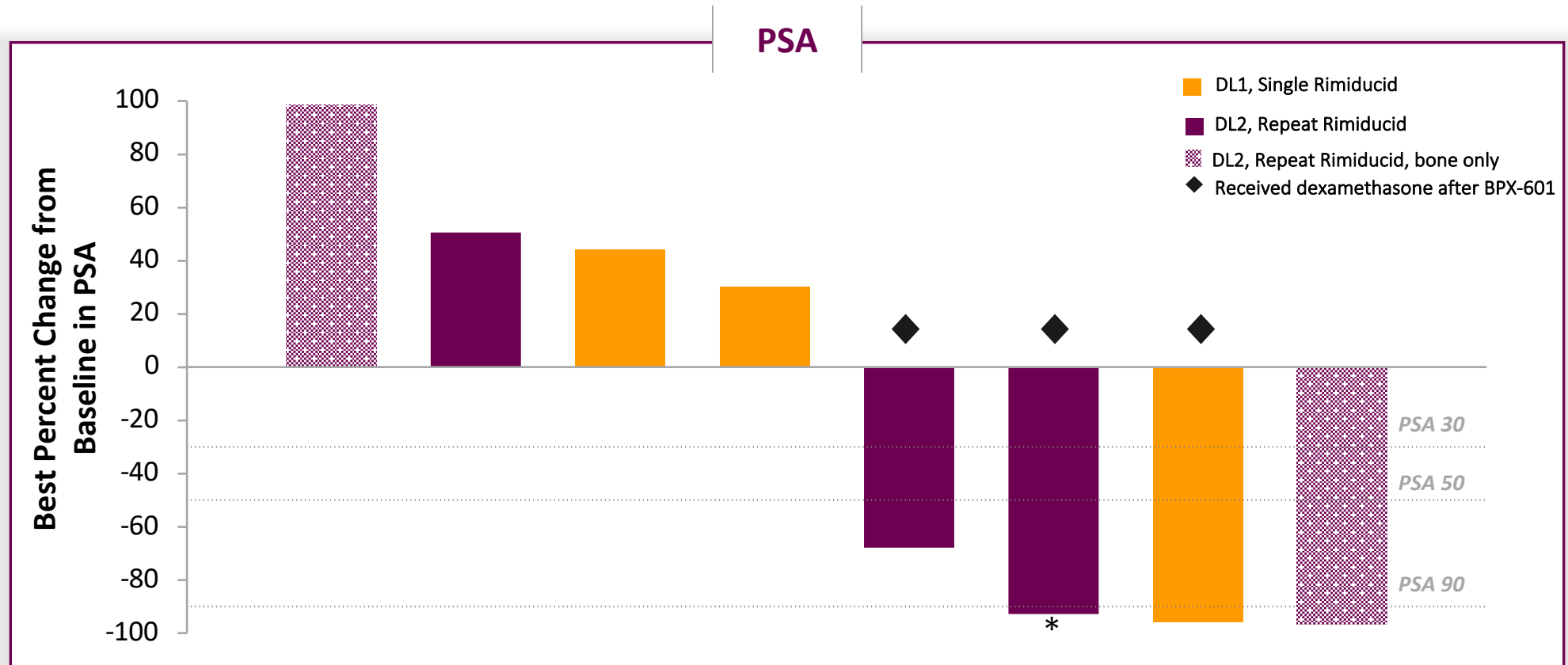
- 2 patients experienced grade 3 CRS managed with tocilizumab and dexamethasone
- 1 patient experienced grade 4 ICANS on study day 13 with concurrent HLH; ICANS event resolved to grade 1
  - Management included standard of care and withholding rimiducid
  - Patient died on study day 20 due to sepsis; confounded by baseline renal impairment, increased fludarabine exposure and CMV reactivation during lymphodepletion

- Grade 3+ adverse events occurred in 87.5% of patients, predominately myelosuppression due to lymphodepleting chemotherapy: anemia (75%), neutropenia (62.5%) and leukopenia (37.5%)
- Other grade 3+ events occurring in 2 or more patients (25% each) included AST increase, alkaline phosphatase increase, hypocalcemia, hypokalemia and dyspnea



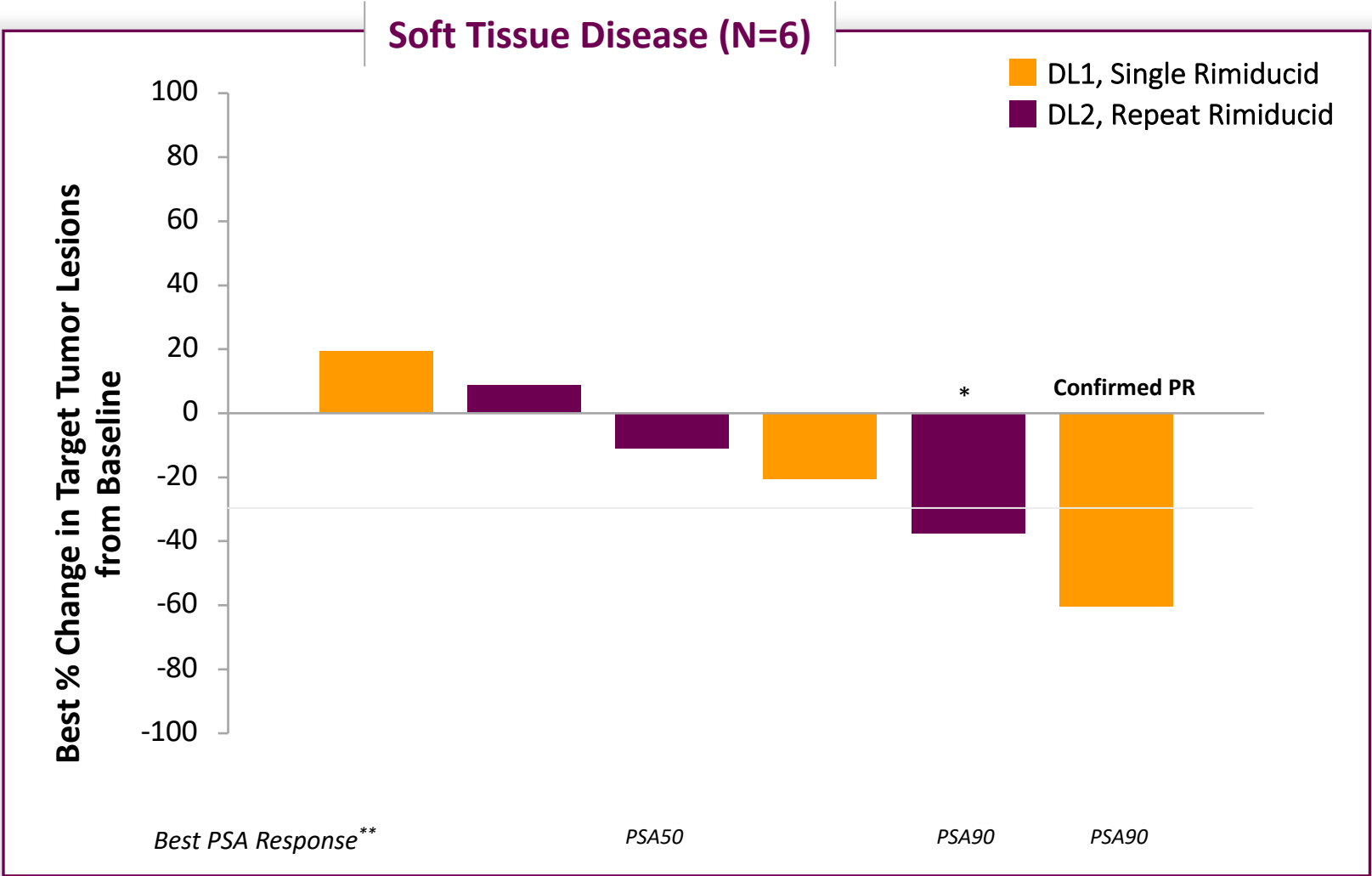
## > PSA50 Response in 50% of Patients

- PSA90 reductions in 3 patients within first 28 days following BPX-601 and rimiducid
- Marked decreases in PSA despite administration of dexamethasone



\* Death day 20 due to sepsis; received 1 dose of rimiducid.

# Radiographic Responses in Soft Tissue and Bone Only<sup>¥</sup> Disease



**Bone Only (N=2)**

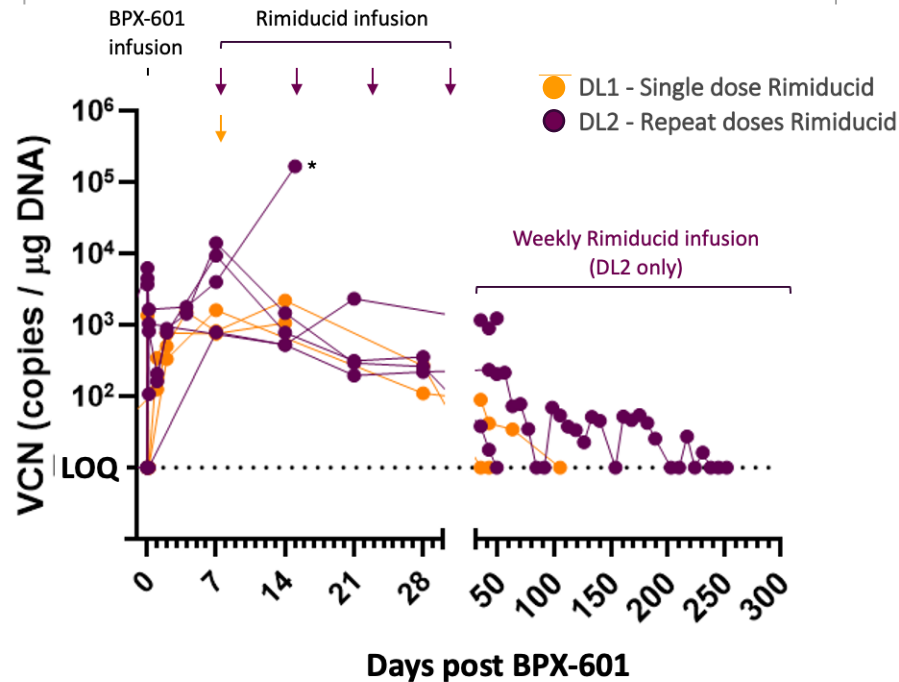
- 50% (1 of 2) patients with bone only disease and a PSA90 response at Day 28 demonstrated improvement on week 8 bone scan (3 of 4 lesions showed decreased enhancement)

\*Death day 20 due to sepsis. \*\* As defined in prior slide; best percent change from baseline in PSA.

# BPX-601 Expansion, Persistence and Cytokine Production

*BPX-601 cells detectable >200 days in mCRPC; consistent responsiveness to weekly rimiducid dosage*

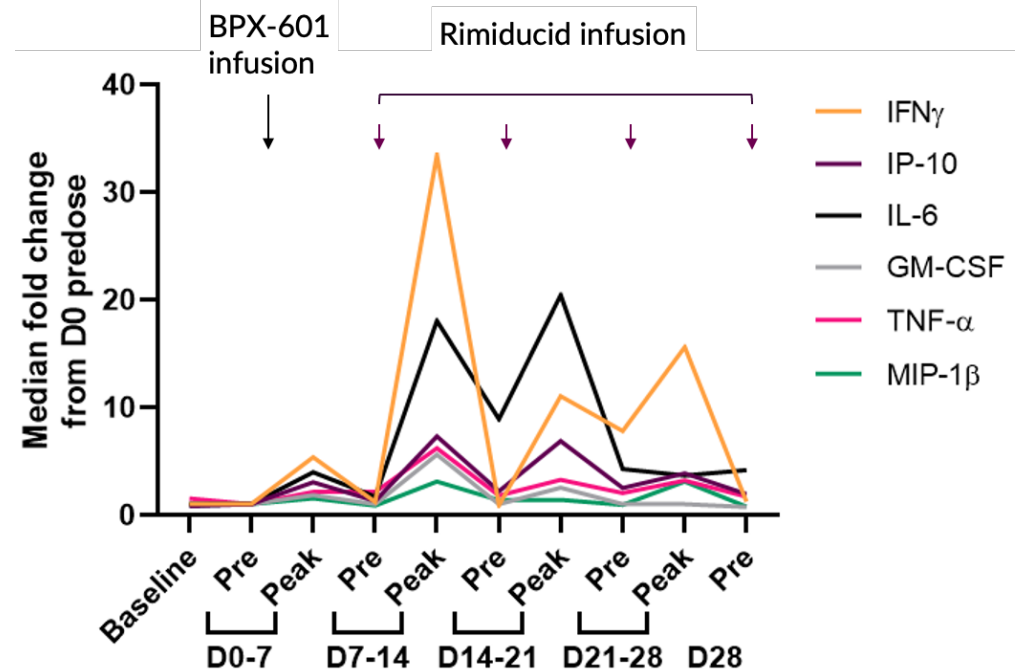
## BPX-601 cell pharmacokinetics in blood



Data shown is pre-rimiducid VCN value for each rimiducid dose. LOQ =  $10^1$   
VCN data obtained from whole blood (WB) or PBMCs; PBMC values normalized to WB.  
\* Death day 20 due to sepsis; received 1 dose of rimiducid; last VCN data on Day 15 shown

- Cell expansion generally consistent across patients
- Patient with GoCAR-T cells in peripheral blood > 200 days with stable disease by CT at 10 months

## Cytokine production



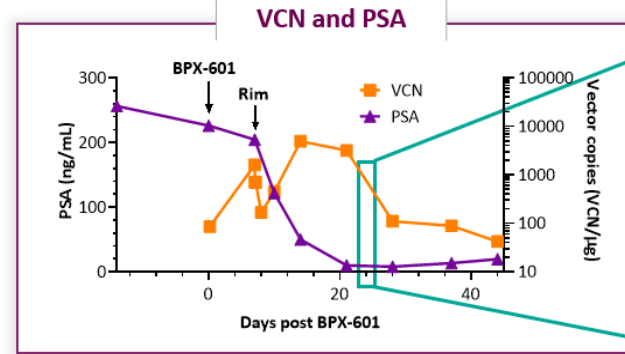
- Median weekly pro-inflammatory T cell cytokine production pre and post rim in DL2 Cohort (n=5)
- Serum levels rise and fall with repeated rim dosage

# Case #1: Confirmed PR Observed in mCRPC Patient

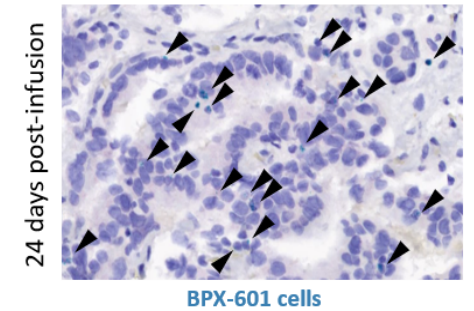
*Rapid and deep PSA response correlated to administration of BPX-601 and a single-dose of rimiducid*

68 y/o M with stage IV prostate adenocarcinoma diagnosed Aug 2019

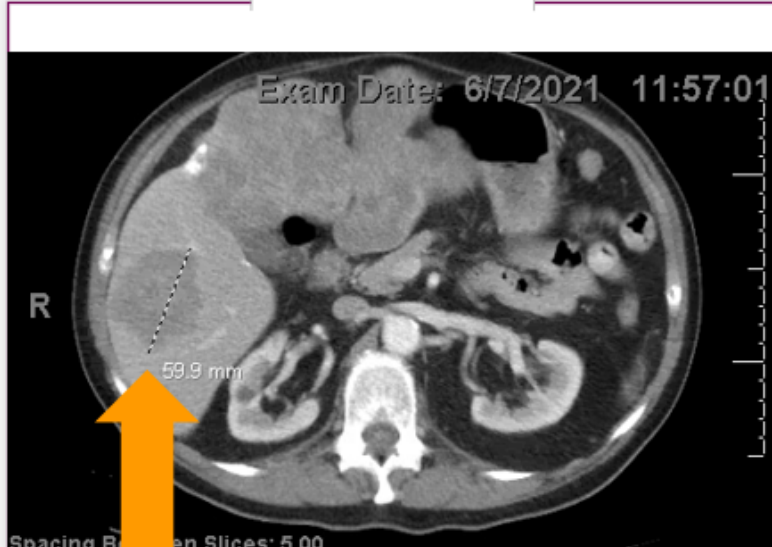
- Prior therapies included: Lupron, docetaxel, abiraterone/prednisone with docetaxel; investigational PSMA-targeted therapy with progressive disease
- ~ 50% reduction in sum of longest diameters of target lesions (liver); confirmed Day 71 with 60% reduction



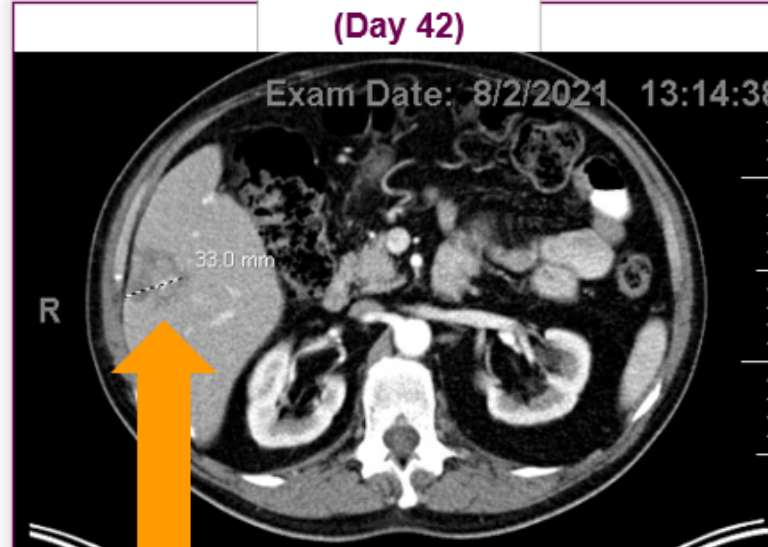
**BPX-601 cells infiltration in liver metastasis**



**Pre-Treatment**



**Post-Treatment  
(Day 42)**



- Treatment-free interval following BPX-601 and a single-dose of rimiducid was 4.5 months
- Patient was subsequently enrolled in a clinical trial with a PD-1/CTLA-4 bispecific + chemotherapy and continues on study



# Case #2: PSA90 Response Ongoing in Bone Only mCPRC

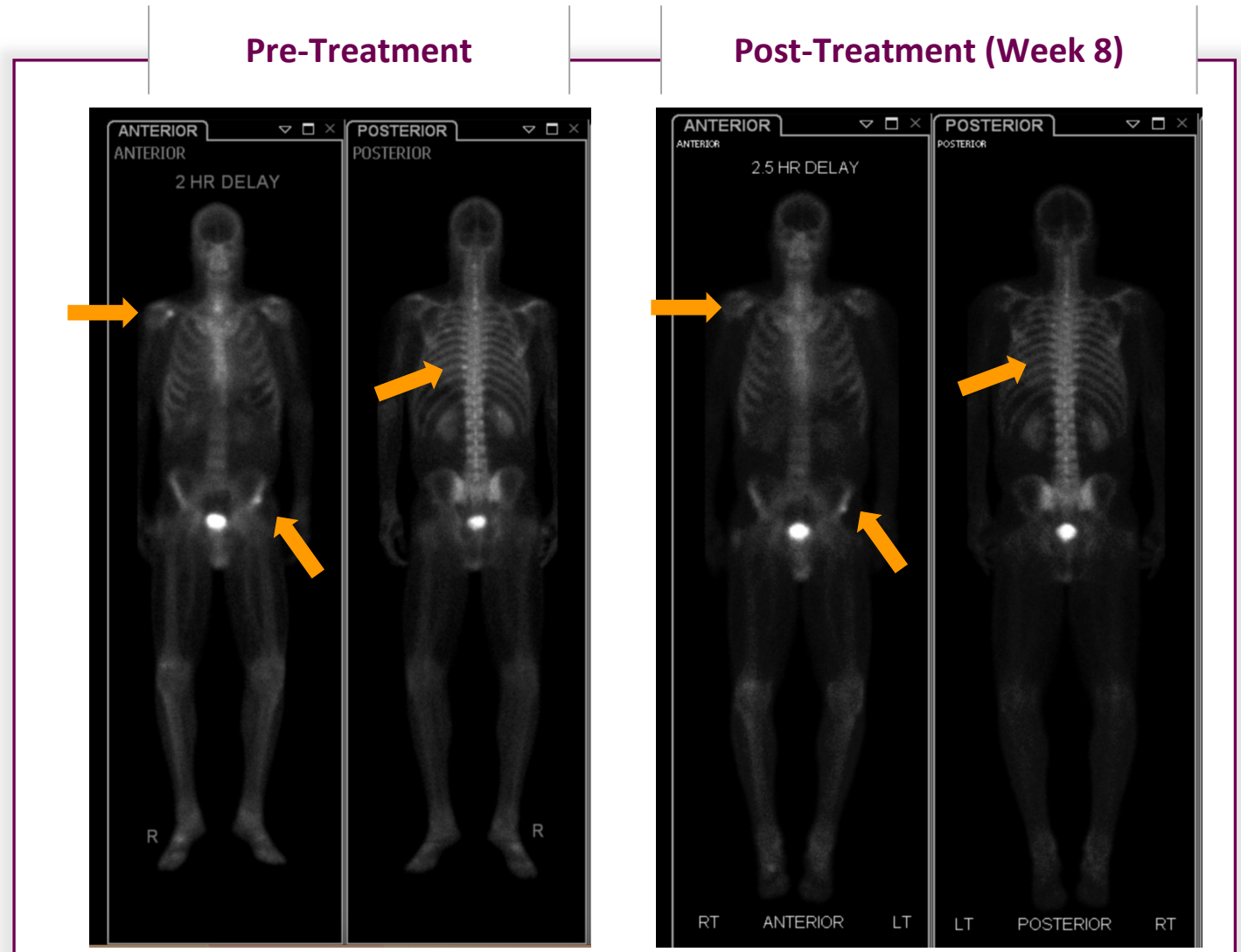
*Decreased enhancement in 3 of 4 Lesions on Week 8 Bone Scan*

59 y/o M with bone only mCPRC diagnosed Feb 2022

- Refractory to 6 prior lines of therapy, including multiple ADTs; prior to enrollment received cabazitaxel x 6 cycles

Study Timepoint	PSA ng/mL
Baseline	29.4
Day 28	1.1
Day 58	1.0
Day 86	1.2

- Patient continues weekly rimiducid with PSA90 response ongoing as of 15 Nov 22 (Day 86)



Additional lesion in L4th rib not easily noted here

Lesions R upper lateral scapula, posterior L 9<sup>th</sup> transverse and additional L4th rib no longer evident per radiology report

# BPX-601 mCRPC Conclusions

This interim update demonstrates encouraging preliminary efficacy of BPX-601 PSCA-directed GoCAR-T-cell product in combination with rimiducid in mCRPC

- BPX-601 with rimiducid induced biochemical and radiographic responses in heavily pretreated patients
  - Rapid declines in PSA (50% PSA50, 38% PSA90, n=8)
  - 33% RECIST response rate (n=6) and 50% of patients with bone-only disease (n=2) show improvement on bone scan
- Most common grade 3+ adverse events were myelosuppression due to lymphodepleting chemotherapy; grade 3+ CRS and ICANs were experienced by 2 (25%) and 1 (12.5%) patients respectively, which improved with standard of care treatment
- Consistent BPX-601 cell expansion observed in peripheral blood, with persistence over 200 days
- Pro-inflammatory T cell cytokine production in response to weekly rimiducid administration
- Evidence of BPX-601 cell infiltration in PSCA-positive tumor
- Dose escalation continues, with weekly rimiducid doses to  $\rightarrow 0.8 \rightarrow 1.6$  mg/kg and subsequently cell doses to  $\rightarrow 7.5 \rightarrow 10$  m cells/kg

# Comparative CAR-T Outcomes in mCPRC

	BPX-601 PSCA GoCAR-T <sup>1</sup> N=8		City of Hope PSCA CAR-T <sup>2</sup> (MB-105) N=12		P-PSMA-101 <sup>3</sup> N=14	
Baseline Demographics	Median (Min, Max)		Median (Min, Max)		Mean (Min, Max)	
Age (years)	67 (56, 75)		69 (42, 73)		70 (57, 79)	
Previous Regimens	6 (5, 9)		NR (≥1 Androgen Tx)		7 (3, 15)	
PSA						
PSA50 Response	4 (50%)		NR		5 (36%)	
PSA90 Response	3 (38%)		NR		1 (7%)*	
RECIST Objective Response <sup>‡</sup>	2/6 (33%)		0 (0%)		NR	
Bone Only PSA Response	1/2 (50%)		NR		NR <sup>‡</sup>	
TEAE	All Grades	Grade 3+	All Grades	Grade 3+	All Grades	Grade 3+
CRS	8 (100%)	2 (25%)	4 (33%)	0 (0%)	8 (57%)	2 (14%)
Neurotoxicity/ICANS	2 (25%)	1 (13%)	0 (0%)	0 (0%)	2 (14%)	1 (7%)
DLT	1 (Death due to sepsis)		2 (Cystitis)		1 (Death due to CRS/MAS)	

<sup>‡</sup> Objective response rate is defined as the proportion of subjects with a best overall response of PR or CR according to RECIST v1.1; includes 1 confirmed and 1 unconfirmed PR. \*Not reported; derived from waterfall.

<sup>‡</sup> Improvement in PSA and bone disease reported in one patient with both visceral and bone mets

FOR ILLUSTRATIVE PURPOSES ONLY: no head-to-head clinical trial has been conducted. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

1. Data on file. 2. J Clin Oncol 40, 2022 (suppl 6; abstr 91) and poster. 3. J Clin Oncol 40, 2022 (suppl 6; abstr 98) and poster. 4. J Clin Oncol 40, 2022 (40:6\_suppl, 94-94); Endpoint News (Jun 3, 2021)

Note<sup>4</sup>: Tmunity CART-PSMA-TGFβRDN program reported 1/13 (8%) PSA50 and PSA90 response, no Objective Response per RECIST; program terminated after two Grade 5 immune adverse events



# BPX-603 HER-2 Dual-Switch GoCAR-T

# BPX-603 Dual Switch GoCAR-T Targeting HER2

## Product Summary

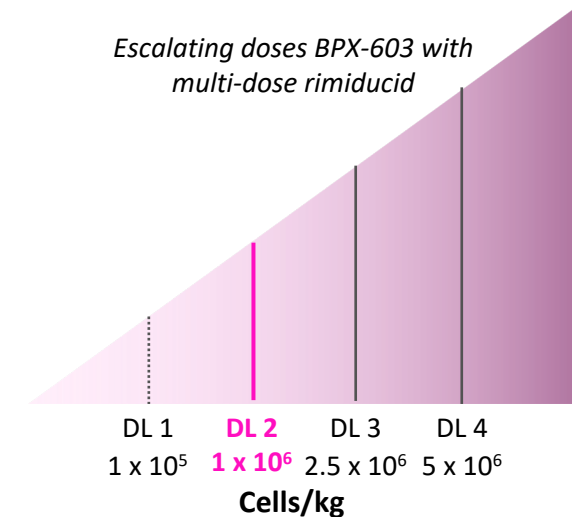
- HER2 is a validated tumor antigen expressed on numerous solid tumors with high unmet need
- BPX-603 designed to potentially address limitations of previous CAR-T efforts targeting HER2
  - Moderate affinity scFv to enhance target engagement and activity
  - MC signaling to increase cell proliferation & persistence, modulate the TME, and enhance host immunity
  - Bellicum switch technology designed to time and manage CAR-T activation and enable mitigation of acute toxicities

## Program Update

- Dose Level 1 cleared with no dose-limiting toxicity
- Cell dose escalation ongoing at DL 2

## Phase I: 3+3 Dose Escalation

Locally advanced or metastatic HER2+ solid tumors\* where standard treatment is no longer effective, does not exist, or subject is ineligible<sup>†</sup>



- Sequential patient enrollment
  - $\geq 28$  days for DL 1;  $\geq 14$  days thereafter
- First subject in each dose level receives cells only without rimiducid

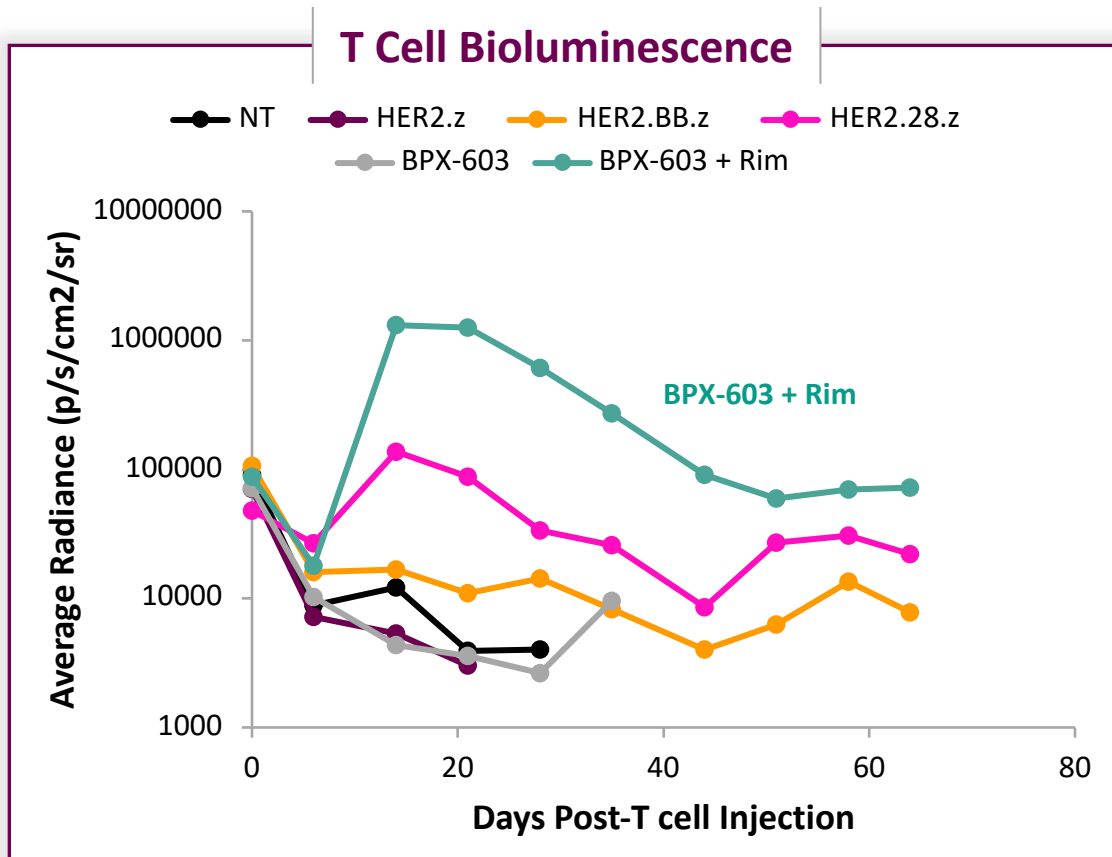
\*GBM excluded from Phase 1

# Historical HER2 CAR-T Studies: Modest Clinical Outcomes

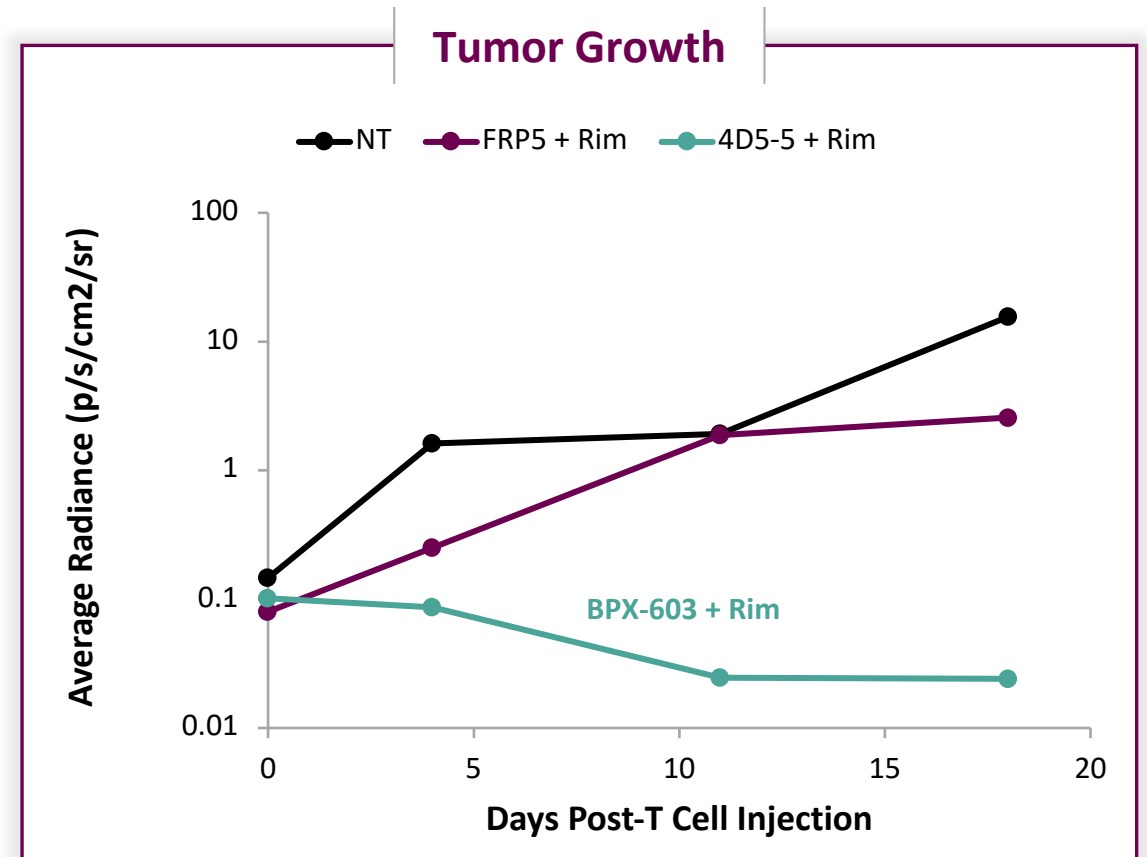
Study Properties	Morgan, 2010	Ahmed, 2015	Feng, 2017	Ahmed, 2017	Hegde, 2019
<b>Construct</b>	4D5-28-BB-z	FRP5-28-z	Her2-BB-z	FRP5-28-z	FRP5-28-z
<b>Indication(s)</b>	Metastatic colon	Sarcomas	CCA and PCa	GBM	Sarcomas
<b>Patient number</b>	1	19	11	17	10
<b>HER2 expression</b>	≥2+ (IHC)	≥1+ (IHC)	>50% positive	≥1+ (IHC)	≥1+ (IHC)
<b>CAR-T dose</b>	10 <sup>10</sup>	10 <sup>4</sup> - 10 <sup>8</sup>	10 <sup>6</sup>	10 <sup>6</sup> - 10 <sup>8</sup>	10 <sup>8</sup>
<b>CAR-T expansion</b>	NE	Negligible	>1,000 copies	Negligible	>10,000 copies
<b>Toxicity</b>	Lung reactivity	No DLTs	Mild AEs	Mild AEs	Mild AEs
<b>Outcome</b>	Grade 5 toxicity	1 PR	1 PR	1 PR	2 CR
<b>Total Responses: 2 CR, 3 PR, 5/58 (8.6% ORR)</b>					

# BPX-603: Compelling Preclinical Evidence

## iMC Co-Activation Enhances Cell Proliferation Relative to Current CAR-T Standards



## Moderate Affinity scFv Enhances Anti-tumor Effect Relative to Low Affinity FRP5







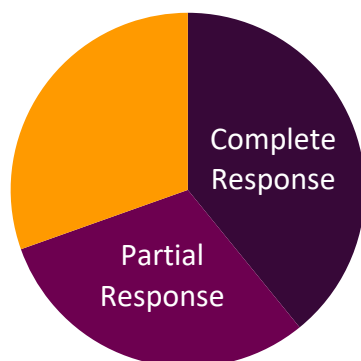
# Expanding the Use of CaspasIDe Through Licensing

# Clinical Experience with CaspaCIDE (iC9)

## Experience from Rivo-cel Program<sup>1</sup>

24 pediatric haplo-HSCT patients experienced advanced or steroid-refractory GvHD from iC9-containing allogeneic T cells and received rimiducid to trigger iC9

**70% Overall Response Rate\***  
(n=24)



**Four additional patients achieved CR by Day 30**

\*Evaluated at Day 7 post-rimiducid administration.

### Median Time to Response

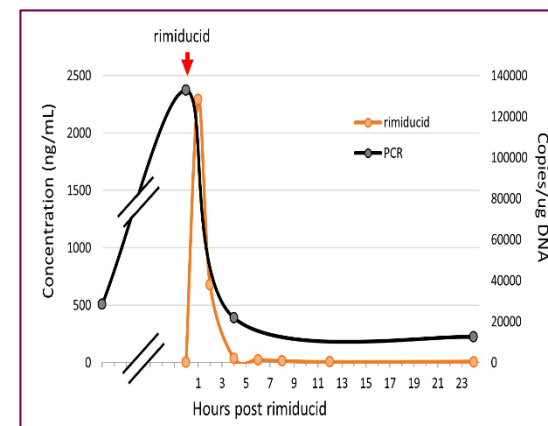
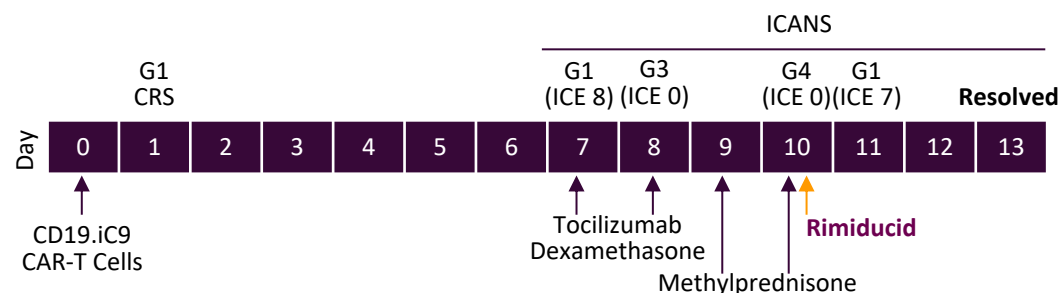
1 Day (Range 1–4 Days)

### Immunological Response

- All evaluable patients receiving rimiducid had reduction in circulating rivo-cel cells
- Majority of reduction observed within 4 hours

## CAR-T Case Report from University of North Carolina<sup>2</sup>

26-year-old female with relapsed B-ALL received CD19.iC9 CAR-T; received rimiducid to treat refractory ICANS



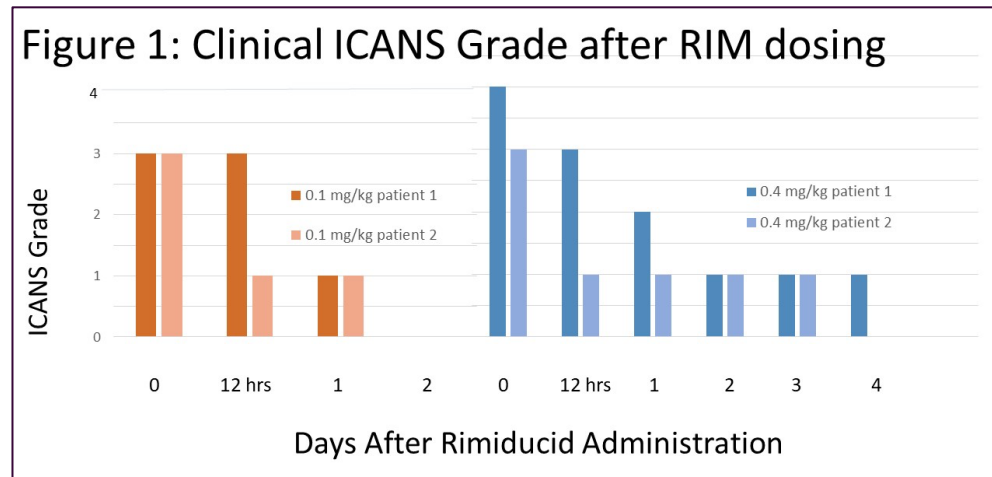
### Rapid Results After Rimiducid Administration

- >80% reduction in CAR-T transgene copies within 4 hours
- ICANs improvement to Grade 1 within 12 hours

# CaspaCIDE May Mitigate Severe CAR-T-Mediated Adverse Events

*Updated results from iC9 CAR.19 study presented at ASH 2022*

- Rimiducid use for management of severe, prolonged corticosteroid-refractory ICANS in patients with B-lymphoblastic leukemia (B-ALL) evaluated in an ongoing phase I/II study of iC9 CAR.19 cells IST at UNC-CH
- Clinical and pharmacodynamic courses of ICANS reported for four patients treated with rimiducid at two doses



- Grade 3-4 ICANS improved  $\geq 1$  grade within 24 hours and resolved within 2-5 days after administration of either 0.4mg/kg or 0.1mg/kg of rimiducid
- ddPCR for  $\Delta$ NGFR showed reduction in transcripts by  $>80\%$  in all patients at 4 hours after end of RIM infusion

- Rimiducid administration to these four patients with ICANS was associated with abrupt reduction of circulating iC9 CAR.19 cells and ICANS grade
- Doses of rimiducid as low as 0.01mg/kg are being explored to determine if toxicity may be mitigated without diminishing the therapeutic benefit of iC9 CAR.19 cells

# Expanding the Use of CaspaCIDE Through Licensing

## Summary

- CaspaCIDE is the most clinically-validated safety switch, offering the potential to improve the benefit/risk of cell therapies
- Bellicum has established option/license agreements with leading institutions for use of CaspaCIDE and rimiducid in cell therapies
  - Agreements currently cover nine CAR-T and CAR-NK programs with potential to add more over time
- Under these agreements, Bellicum is entitled to:
  - Sub-license execution fees upon out-license of program
  - % share of milestones and certain other sub-licensing revenue
  - Single digit % royalty on product net sales
- Agreements have generated over \$13m in revenue to date

## Current Agreements

- The University of Texas MD Anderson Cancer Center
- University of North Carolina Lineberger Comprehensive Cancer Center
- Massachusetts General Hospital Cancer Center
- Takeda Pharmaceutical\*

\* Rimiducid supply agreement for TAK-007, licensed CD19 CAR-NK from MDACC





# Summary

# Anticipated Key Program Goals & Milestones

Product Candidate	Goals & Milestones	Planned Timing
<b>BPX-601 PSCA GoCAR-T in mCRPC</b>	<ul style="list-style-type: none"><li>• Initial Phase 1 interim presentation</li><li>• Phase 1 data update</li></ul>	<div>✓</div> 1Q'2024
<b>BPX-603 HER2 GoCAR-T (Dual-Switch)</b>	<ul style="list-style-type: none"><li>• Program update</li><li>• Initial Phase 1 interim presentation</li></ul>	Mid-2023 1H'2024

# Investment Summary

*Building a next generation cell therapy pipeline around the GoCAR platform*

## GoCAR Platform

Differentiated co-activation domain (MyD88/CD40) and switch technology drive greater proliferation, persistence, power, and performance

### BPX-601

- Autologous GoCAR-T targeting PSCA
- Enrolling mCRPC patients in Phase 1/2 trial
- Biochemical and radiographic responses observed early in dose escalation
- Data update planned 1Q'2024

### BPX-603

- Autologous Dual-Switch GoCAR-T targeting HER2
- Enrolling HER2+ solid tumor patients in Phase 1/2 trial
- No DLTs observed in dose level 1
- Program update planned mid-2023; initial Phase 1 interim data presentation planned 1H'2024

### CaspaCDe Licensing

- Nine licensed programs to date
- Potential to expand use of switch technology

### Cash runway to mid-2023

- Cash balance of \$28.8M as of Sep 30, 2022