

# Investor Presentation

Building a powerful new future in cellular IO

April 2021

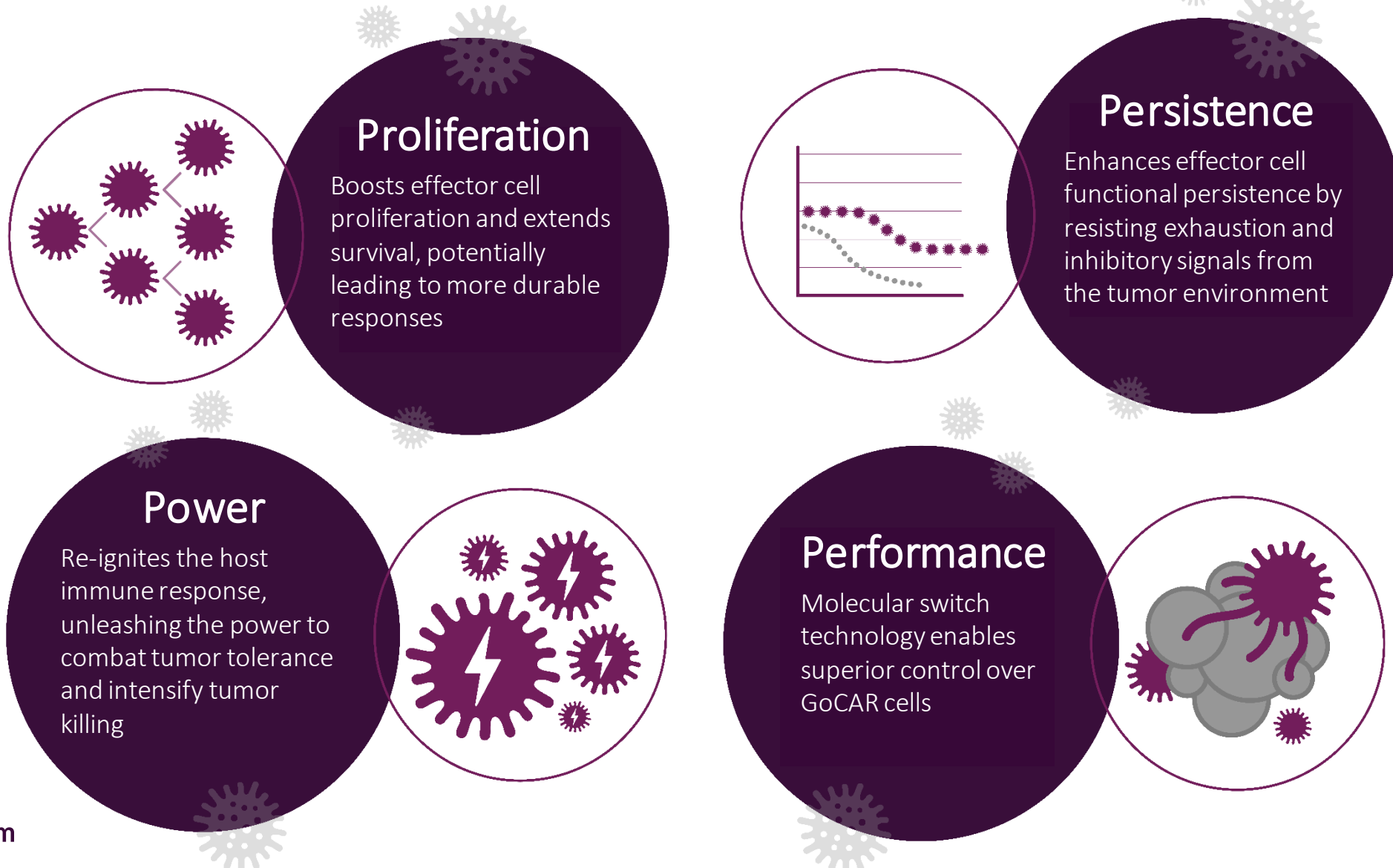
# Forward Looking Statement

This presentation contains estimates, projections and other forward-looking statements, concerning, among other things: our research and development activities relating to our GoCAR™ platform, 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; and our near-term restructuring plan, including focus of our clinical and research and development activities, reduction in employee headcount and reduction in cash utilization. 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, 2019 and our quarterly report on Form 10-Q for the period ended September 30, 2020.

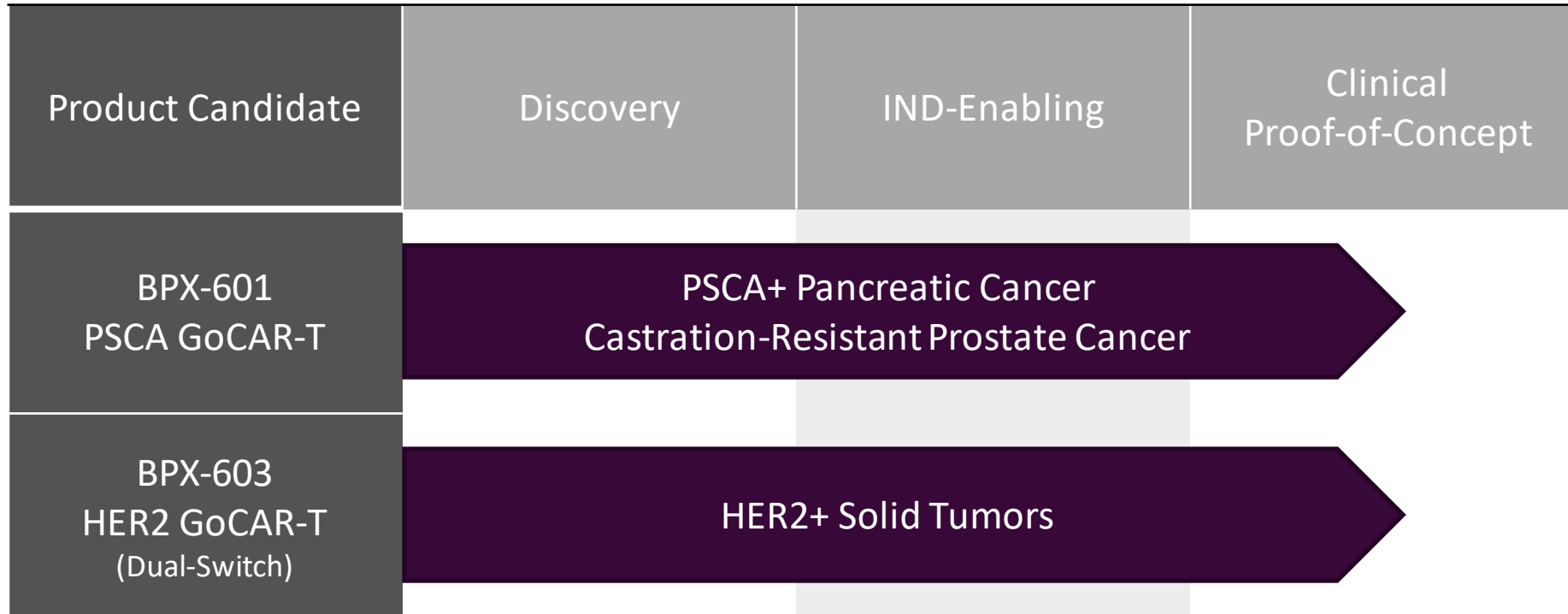
# Building a Powerful New Future in Cellular IO

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



# Product Pipeline

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

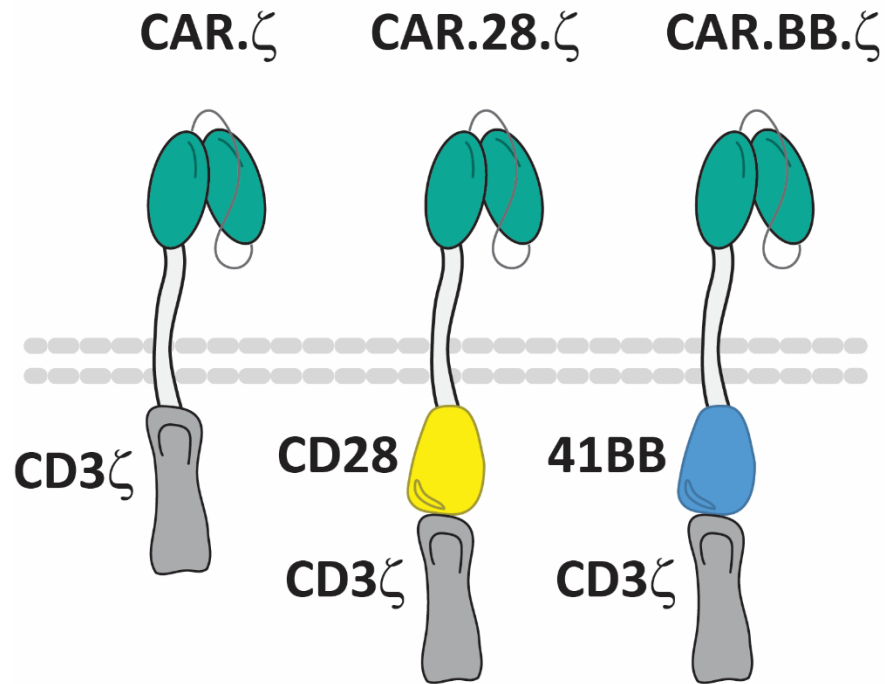




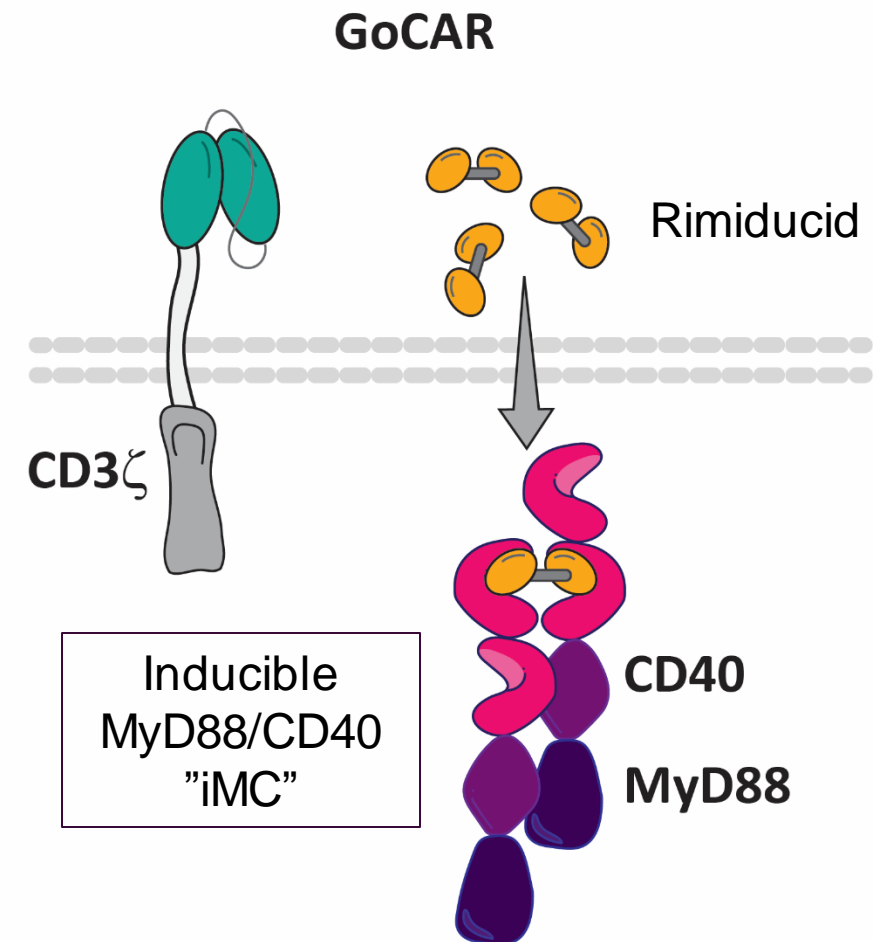
# Technology Overview

# GoCAR: Differentiated Technology Platform

## Current Generation CAR Technology



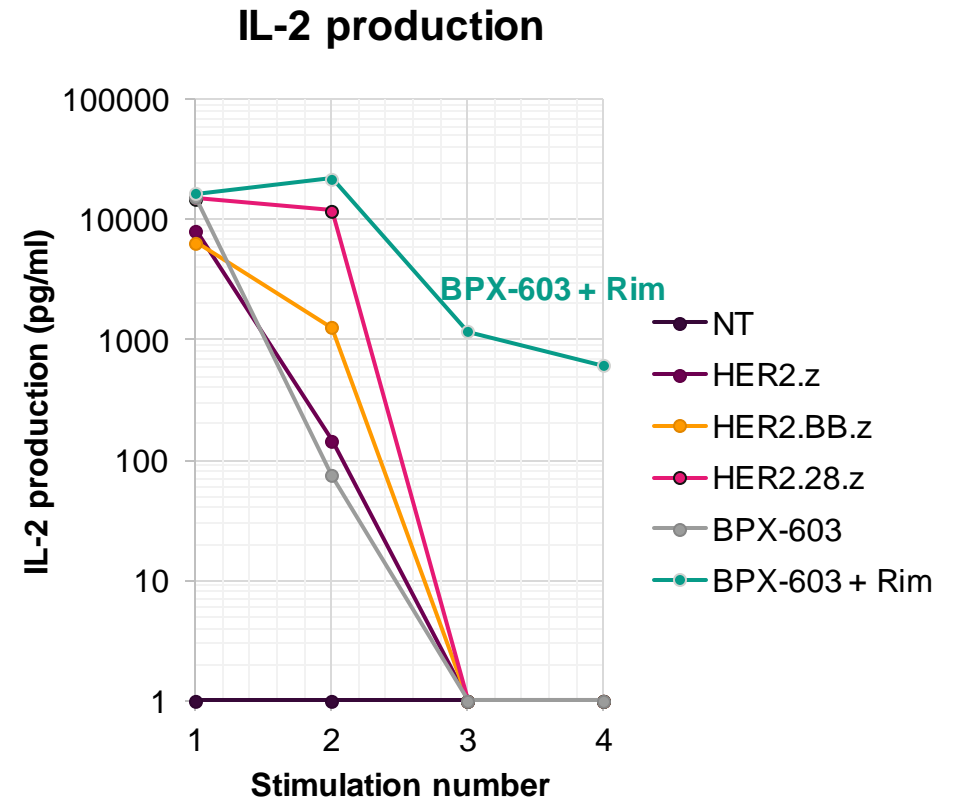
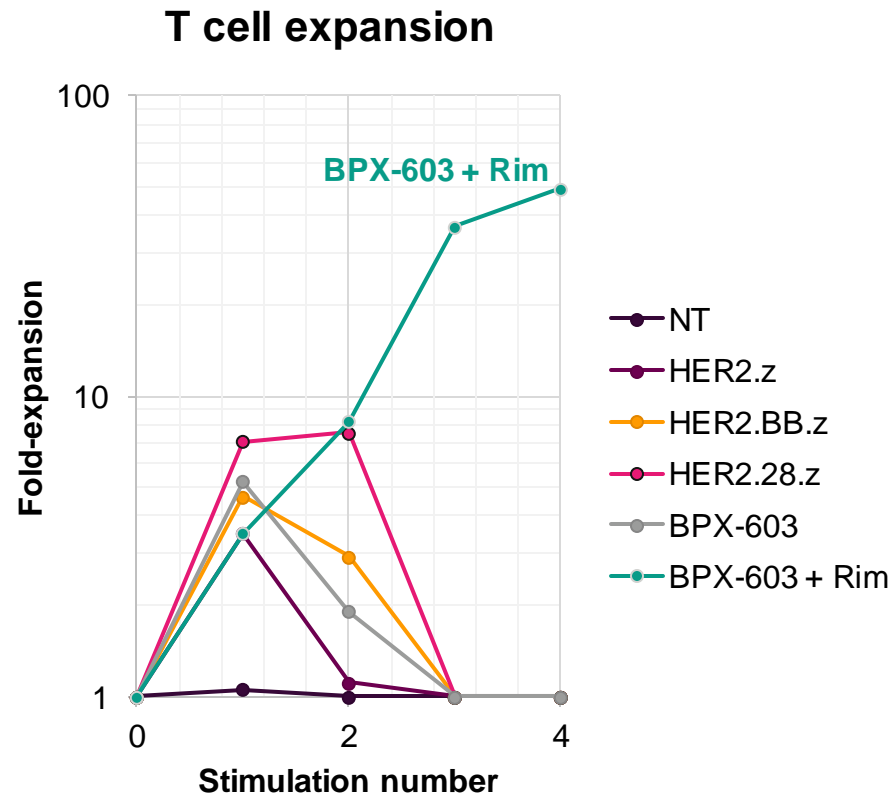
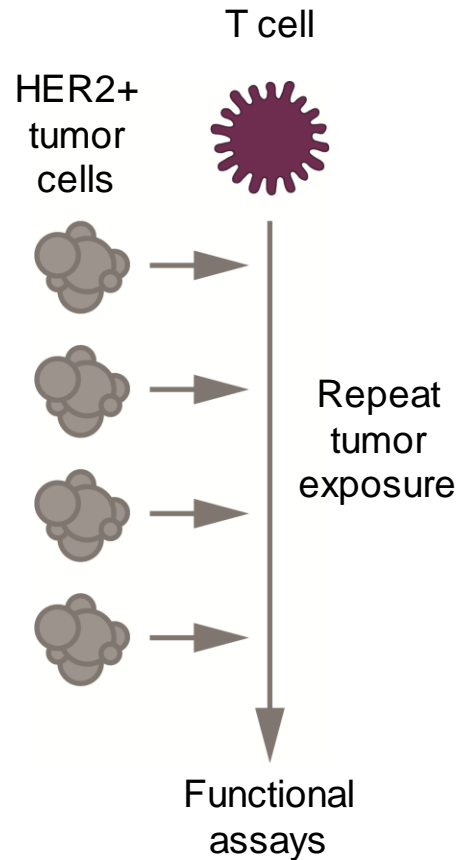
## Next Generation GoCAR Technology





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

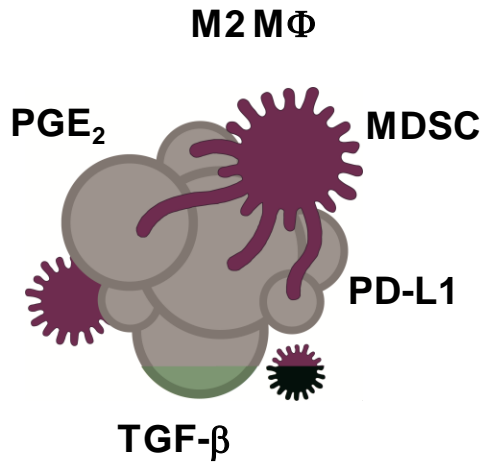
*iMC activation limits T cell dysfunction in repeat tumor stimulation exhaustion assay*



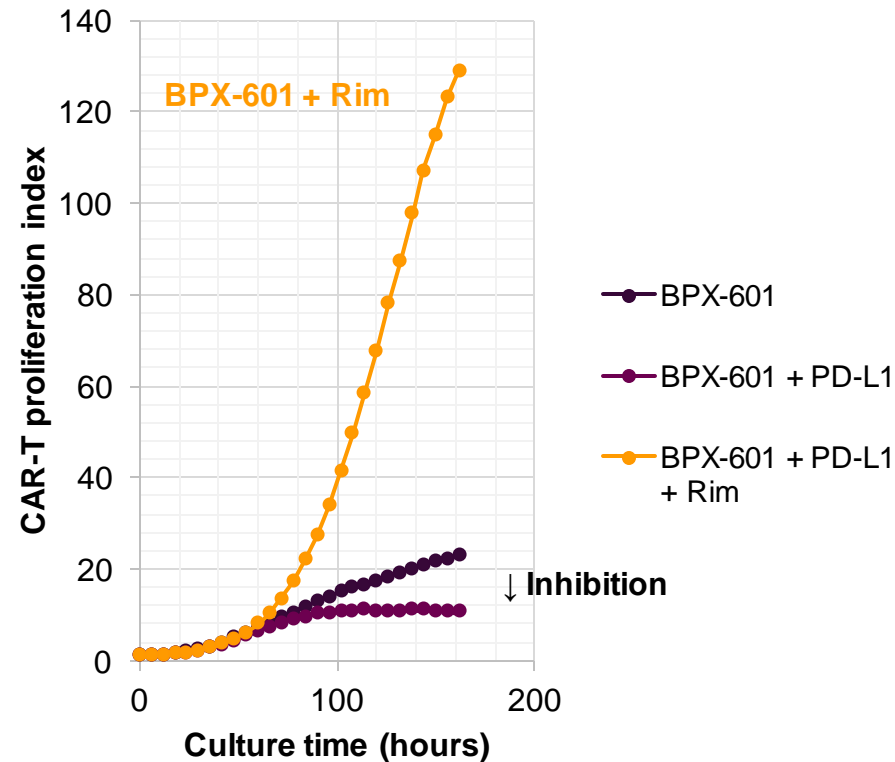
# GoCAR Persistence: Resistance to Immune Suppressive TME

*iMC overrides common inhibitory molecules in the tumor microenvironment*

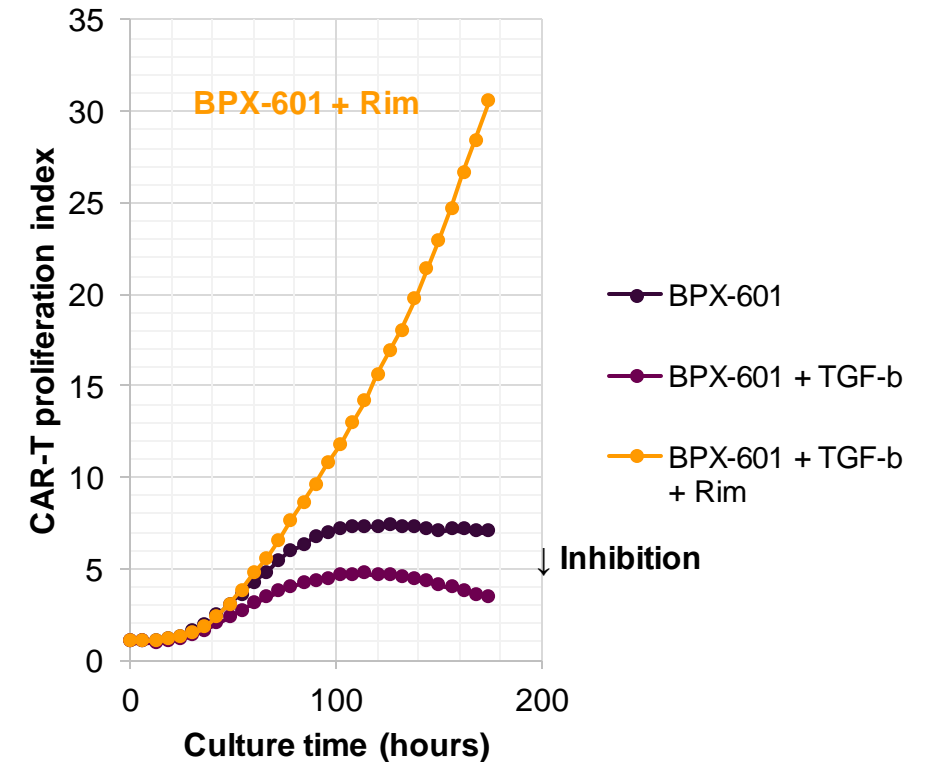
## Inhibitory TME



## PD-L1



## TGF-β



TME – tumor microenvironment





# BPX-601 PSCA GoCAR-T

# BPX-601 GoCAR-T Targets Solid Tumors Expressing PSCA

## Product Profile Summary

- Attractive first-in-class solid tumor CAR-T opportunity
- First-in-human experience with iMC

### Status Update

- FDA Clinical Hold removed January 28, 2021
- Dose escalation in previously treated mCRPC being initiated at 5m cells/kg followed by single-dose rimiducid

## Unmet Need

High unmet need in solid tumors expressing prostate stem cell antigen (PSCA)

	Annual Incidence (U.S.)	Annual Deaths (U.S.)	% Expressing PSCA
Prostate	165k	29k	75-90%
Pancreatic	55k	44k	~50%

Incidence and annual deaths: Noone AM, Howlader N, Krapcho M, Miller D, Brest A, Yu M, Ruhl J, Tatalovich Z, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2015, National Cancer Institute. Bethesda, MD, [https://seer.cancer.gov/csr/1975\\_2015/](https://seer.cancer.gov/csr/1975_2015/), based on November 2017 SEER data submission, posted to the SEER web site, April 2018.

PSCA expression: Argani et al, Cancer Res 2001; Reiter et al., PNAS 1998; Abate-Daga et al, HGT 2014; Data on file

# BPX-601: Phase 1 Trial

*Dose escalation in relapsed/refractory pancreatic cancer*

	Lead-in (Cohort 0)	Dose Escalation (Cohorts 3, 4, 5A)	Standard Conditioning (Cohort 5B)	Repeat Rimiducid (Cohort 5C)
Pancreatic Patient Population	2L to 6L	2L to 6L	2L	2L
BPX-601 Dose <i>x10<sup>6</sup> cells/kg @ Day 0</i>	1.25	1.25, 2.5, 5.0	5.0	5.0
Conditioning	Cytosan 1g/m <sup>2</sup> @ Day -3	Cytosan 1g/m <sup>2</sup> @ Day -3	Cytosan 0.5g/m <sup>2</sup> Fludarabine 30mg/m <sup>2</sup> @ Days -5, -4, -3	Cytosan 0.5g/m <sup>2</sup> Fludarabine 30mg/m <sup>2</sup> @ Days -5, -4, -3
Rimiducid Dose	None	Single dose Day 7	Single dose Day 7	<b>Weekly dosing starting at Day 7</b>

## Lead-In & Dose Escalation

Conservatively designed to evaluate safety

- Lead-in cohort with cells only
- Partial conditioning with Cytosan monotherapy
- Single dose of rimiducid to activate iMC

## Standard Conditioning Cohort (5B)

- Evaluated safety of standard Flu/Cy regimen with GoCAR-T
- Single dose of rimiducid to activate iMC

## Repeat Rimiducid Cohort (5C)

- First data using iMC repeatedly as designed

# BPX-601: Safety Reported Through Cohort 5C

*Updated based on data cut December 1, 2020\**

Patients, n (%)	Cohort 0 n = 3	Cohort 3 n = 3	Cohort 4 n = 3	Cohort 5A n = 4	Cohort 5B n = 5	Cohort 5C n = 5	All Patients n = 23
Any AE	3 (100)	3 (100)	3 (100)	4 (100)	5 (100)	5 (100)	23 (100)
Any SAE	1 (33)	1 (33)	0	3 (75)	4 (80)	4 (80)	13 (57)
AEs in >15% of all patients, n (%)							
Neutropenia	0	1 (33)	0	3 (75)	4 (80)	3 (60)	11 (48)
Febrile neutropenia	0	0	0	2 (50)	4 (80)	2 (40)	8 (35)
Leukopenia	0	0	0	1 (25)	3 (60)	3 (60)	7 (30)
Pyrexia	0	0	1 (33)	2 (50)	2 (40)	2 (40)	7 (30)
Fatigue	2 (67)	1 (33)	0	2 (50)	0	0	5 (22)
Anemia	0	0	0	1 (25)	2 (40)	2 (40)	5 (22)
Nausea	2 (67)	0	0	0	3 (60)	0	5 (22)
Hypotension	0	0	2 (67)	1 (25)	0	2 (40)	5 (22)
Blood bilirubin increased	0	0	0	1 (25)	2 (40)	2 (40)	5 (22)
Dysuria	0	0	0	0	4 (80)	0	4 (17)
Hematuria	0	0	0	0	3 (60)	1 (20)	4 (17)
Abdominal pain upper	0	1 (33)	0	1 (25)	1 (20)	1 (20)	4 (17)
Constipation	0	0	0	2 (50)	1 (20)	1 (20)	4 (17)
Vomiting	1 (33)	0	0	0	1 (20)	2 (40)	4 (17)
Back pain	1 (33)	1 (33)	0	2 (50)	0	0	4 (17)

- Adverse events (AEs) were generally consistent with cytotoxic chemotherapy or other cancer immunotherapies
- AEs related to BPX-601/rimiducid included:
  - One case of Grade 2 and one case of Grade 4 cytokine release syndrome (CRS)\*\*
  - One case of Grade 2 encephalopathy
  - Five cases of Grade 1-3 urologic toxicity, mitigated by prophylactic measures introduced in Cohort 5C

# BPX-601: Updated Efficacy Through Cohort 5C

*Updated based on data cut December 1, 2020\**

## Anti-tumor Activity in ITT Population

Patients, n (%)	Cohort 0 n = 3	Cohort 3 n = 3	Cohort 4 n = 3	Cohort 5A n = 4	Cohort 5B n = 5	Cohort 5C n = 5	Overall n = 23
Progressive Disease (PD), n	2	1	1	1	2	1	8
Stable Disease (SD), n	1	2	2	1	3	3	12
Partial Response (PR), n	0	0	0	0	0	0	0
Complete Response (CR), n	0	0	0	0	0	0	0
Disease Control Rate (CR+PR+SD), n(%)	1 (33)	2 (67)	2 (67)	1 (25)	3 (60)	3 (60)	12 (55)

ITT population defined as all patients who received BPX-601 and rimiducid and had at least one post-baseline disease evaluation.

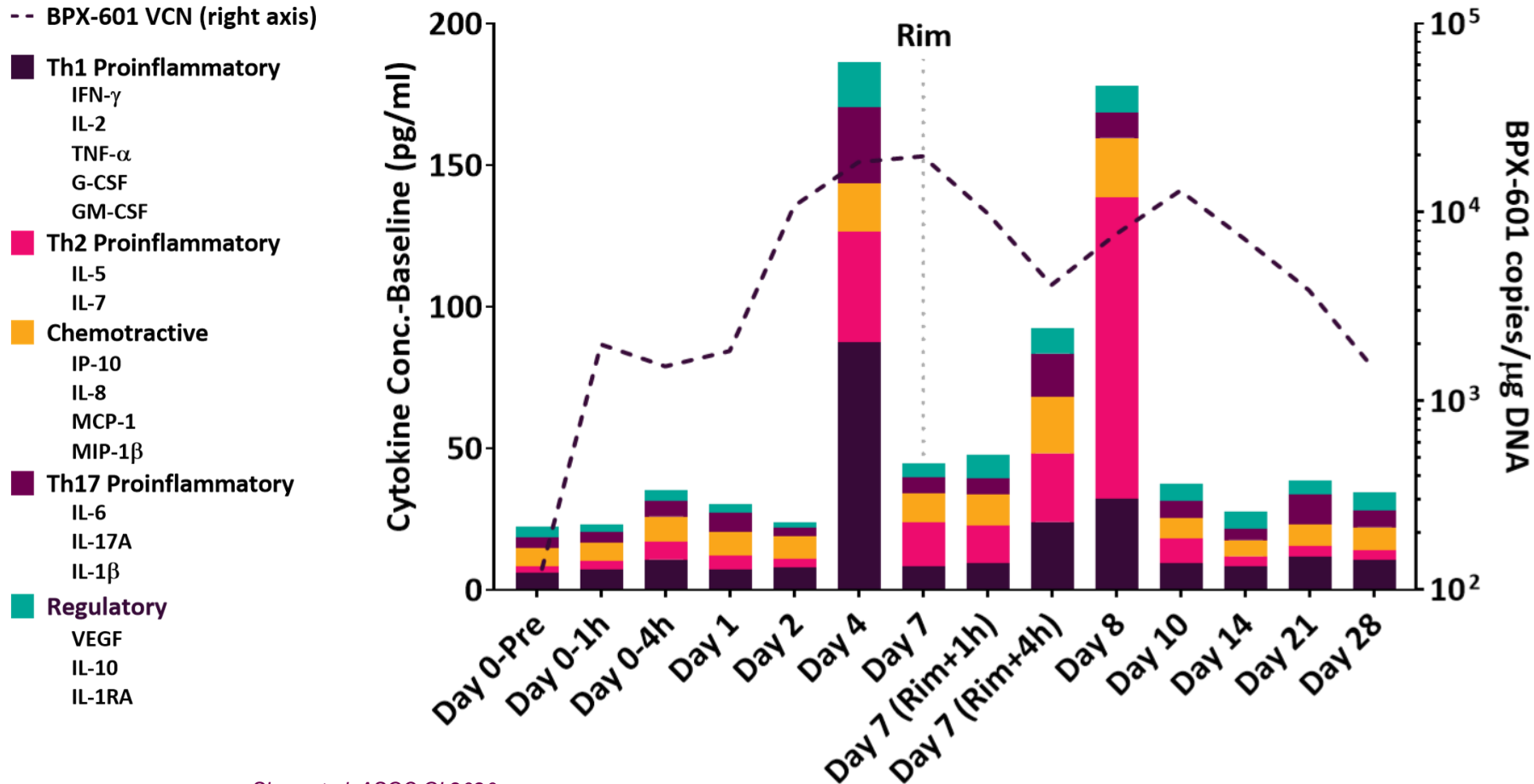
# Interim Biomarker Update: BPX-601 Cohort 5C

Evidence of repeat rimiducid-mediated CAR-T cell activation was observed

- Rimiducid administration was associated with increased serum cytokine levels, including IL-5, TNF- $\alpha$ , and IFN- $\gamma$
- Rimiducid treatment was also associated with increased expression of activation markers (e.g. CD25) on peripheral CD4+ and CD8+ T cells, indicative of systemic immune modulation via BPX-601 iMC activation
- In two evaluable subjects receiving >2 doses of rimiducid, repeat dosing was not shown to increase peak or AUC circulating BPX-601 cells relative to single-dose rimiducid
- Consistent with previous cohorts, rimiducid administration was associated with a transient decline followed by partial recovery in circulating BPX-601 cells

# BPX-601: GoCAR-T Increased Immunomodulatory Cytokines

*Infusion of BPX-601 and activation with rimiducid increased immunomodulatory cytokines*



Shaw et al, ASCO GI 2020

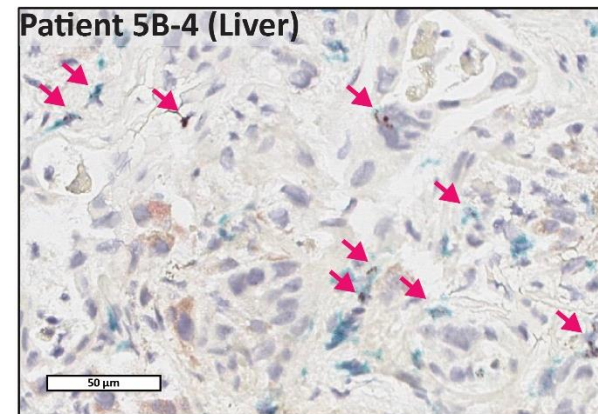
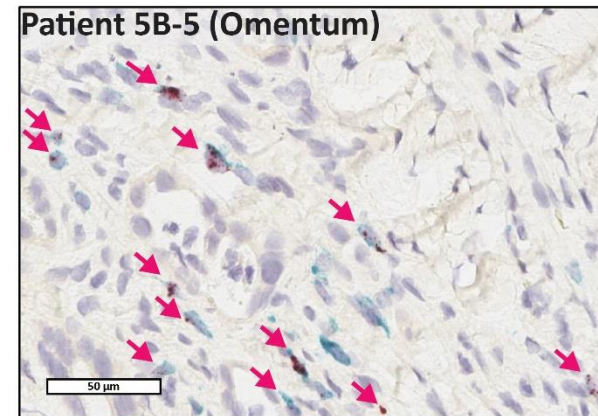
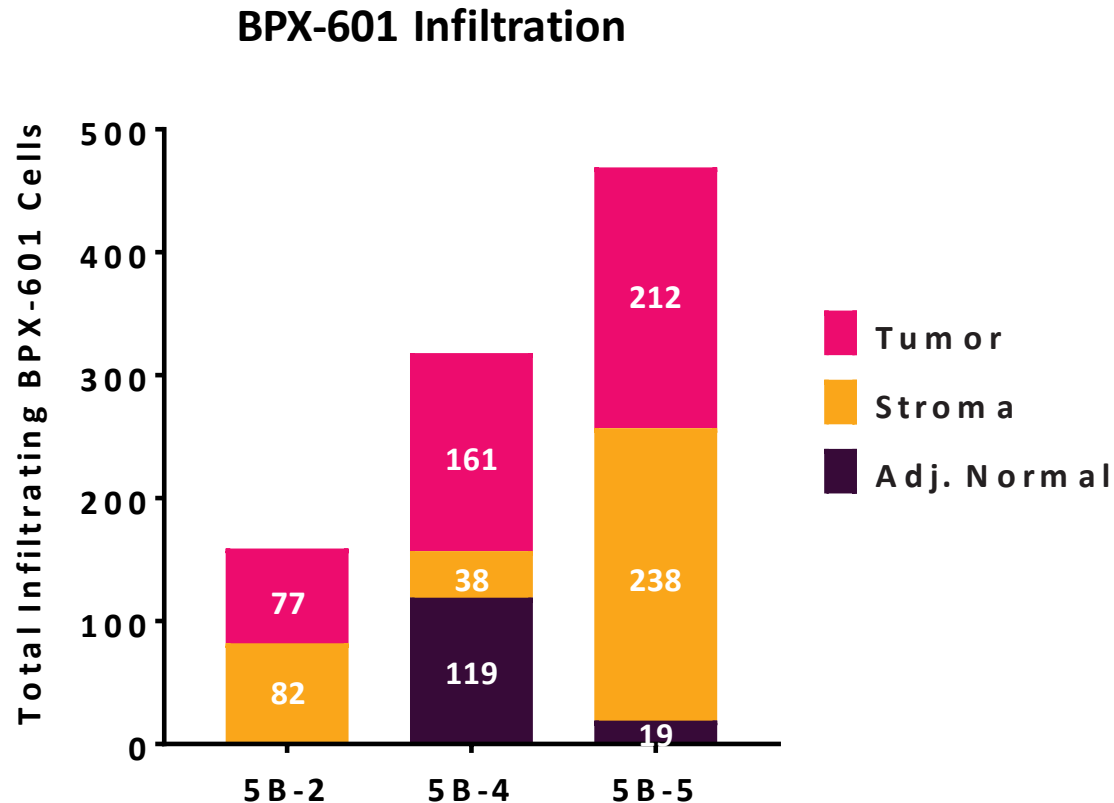
Stacked bars represent the summed mean fold-change in concentration of cytokines in each category in patients from Cohort 5B (n=5). Black dotted line represents the mean VCN for Cohort 5B. Gray dotted line represented rimiducid administration on Day 7. Conc., concentration; Rim, rimiducid.

- Increases in Th1 and Th2 cytokines were observed with:
- Administration of BPX-601 GoCAR-T cells
- GoCAR-T activation with rimiducid



# BPX-601: GoCAR-T Infiltrated Metastatic Pancreatic Tumors

*On-treatment biopsies taken from metastatic lesions show BPX-601 tumor infiltration*



CD3 = Blue; BPX-601 = Red, arrows

- Analysis of tumor metastases from patients showed:
  - Infiltration of BPX-601 GoCAR-T cells
  - BPX-601 effectively localized to tumor

Shaw et al, ASCO GI 2020

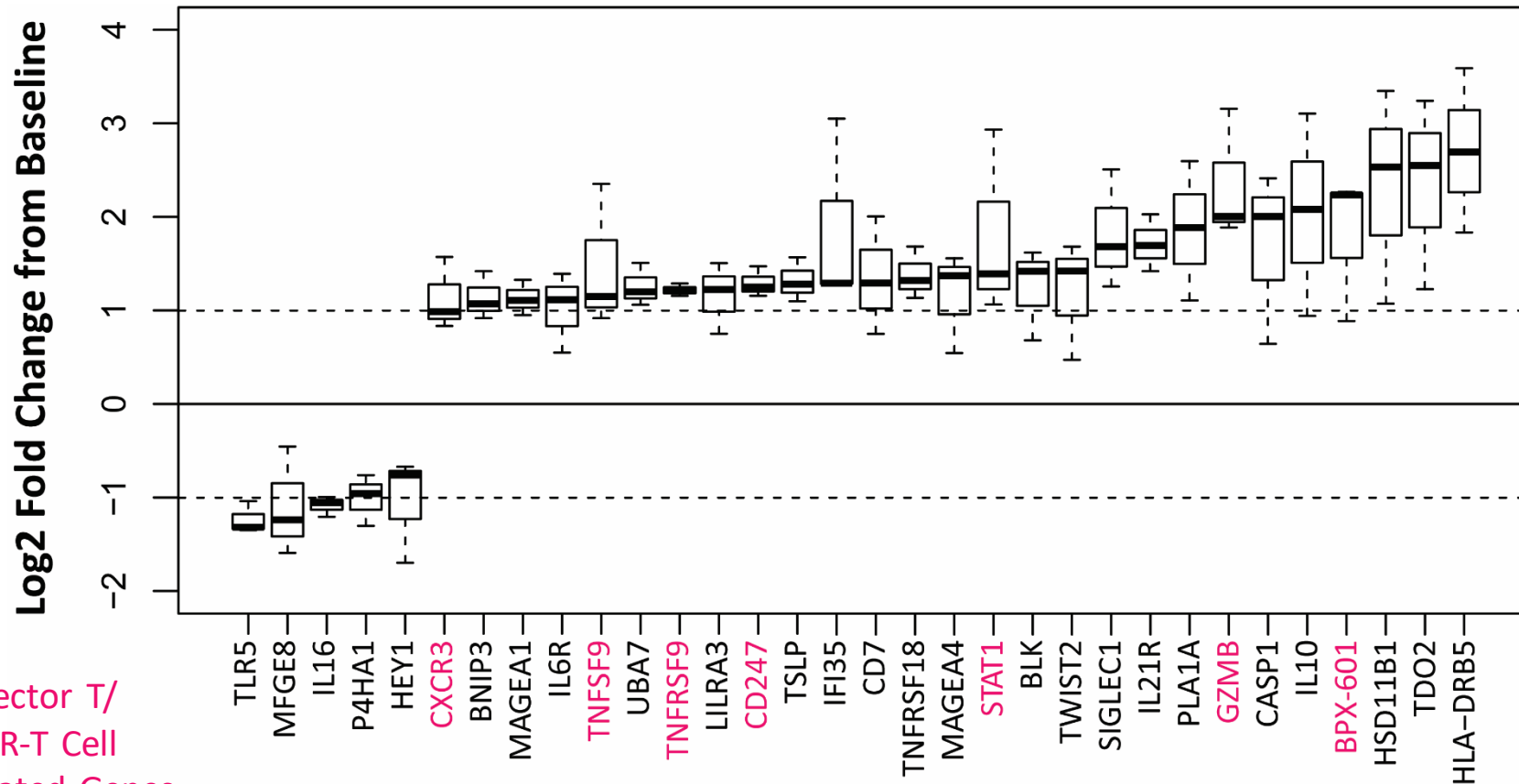
(Left) Stacked bars represent the total number of BPX-601 cells quantified in ISH stained tissue sections of available (n=3) biopsies from metastatic lesions of Cohort 5B patients. White numbers in bars indicate the number of BPX-601 cells measured within each ROI.

(Right) Representative images of CD3 (IHC) and BPX-601 (ISH) stained tissue sections of available (n=3) biopsies from metastatic lesions of Cohort 5B patients. Red arrows indicate BPX-601 GoCAR-T cells. Adj. normal, adjacent normal; ROI, region of interest.

# BPX-601: Modulation of Tumor Microenvironment

*Changes in gene expression consistent with productive T cell immune responses*

## Differentially Expressed Genes in Tumor Metastases After BPX-601 + Rim (Cohort 5B, n=3)



- Upregulation of T/CAR-T cell associated genes including:
  - GZMB—Target cell killing by cytotoxic T cells
  - CXCR3—Activated T cell trafficking
  - 41BB(TNFSF9)/41BBL(TNFRSF9)—T cell costimulation
  - CD3Z(CD247)—TCR Signaling
  - STAT1— Interferon signaling
  - BPX-601— Infiltrating GoCAR-T cells



# BPX-603 HER-2 GoCAR-T

# BPX-603 Dual Switch GoCAR-T Targeting HER2

## Product Profile 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

## Status Update

- Initial study sites activated; first patient enrolled

## Unmet Need

Indication	Incidence <sup>1</sup>	HER2 <sup>+</sup>	5-year OS (Stage IV) <sup>1</sup>
Gastric	28,000	10-30% <sup>3</sup>	<20%
Colorectal	145,000	10% <sup>4</sup>	<15%
Ovarian	22,000	20-30% <sup>5</sup>	<30%
Uterine/ Endometrial	61,000	50-80% <sup>6</sup>	14-69%
Glioblastoma	12,000	20-30% <sup>2</sup>	<20%
Breast	271,000	16% <sup>7</sup>	90%

<sup>1</sup>National Cancer Database, American Cancer Society, <https://www.cancer.org>, accessed 21 December 2018; <sup>2</sup>Liu et al., Cancer Res 2004; <sup>3</sup>Gravalos et al., Annals Oncol 2008; <sup>4</sup>Tu et al., Exp Ther Med 2018;

<sup>5</sup>Berchuck et al., Cancer Res 1990, Bartlett et al., Brit J Cancer 1996; <sup>6</sup>Grushko et al., Gynecologic Oncol 2008, (7) Cronin et al, Cancer Invest. 2010

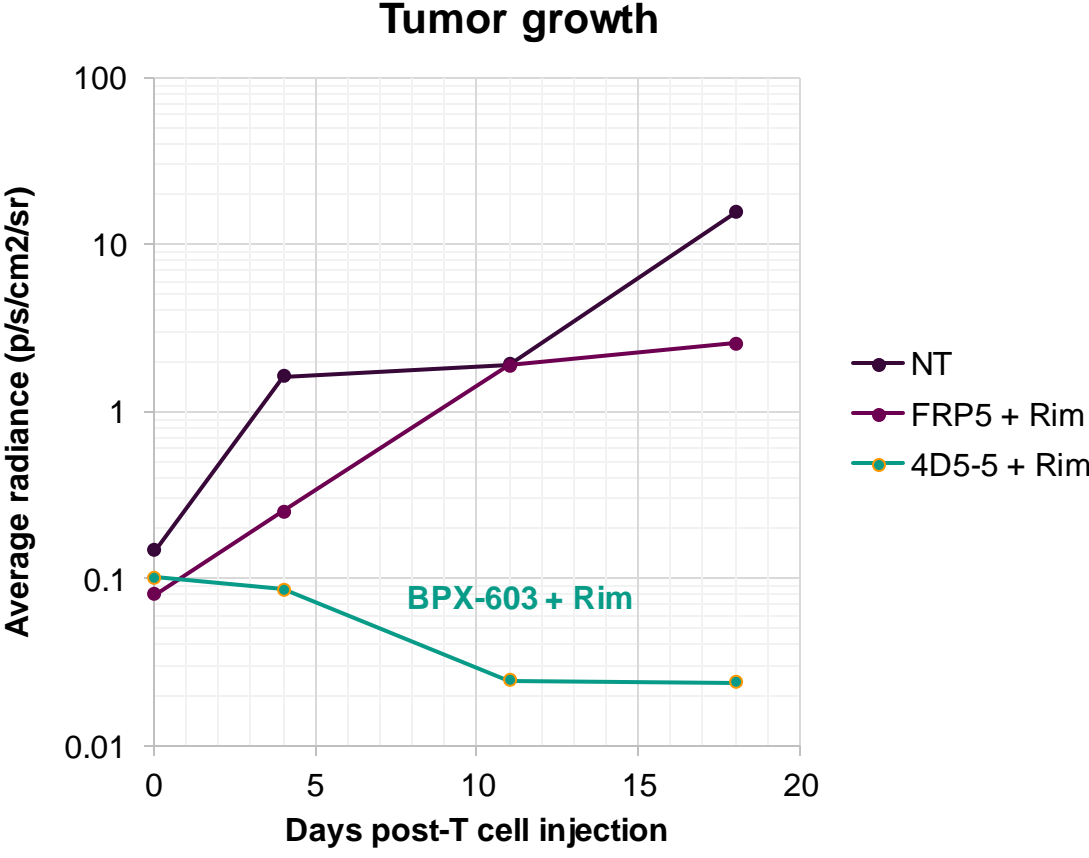
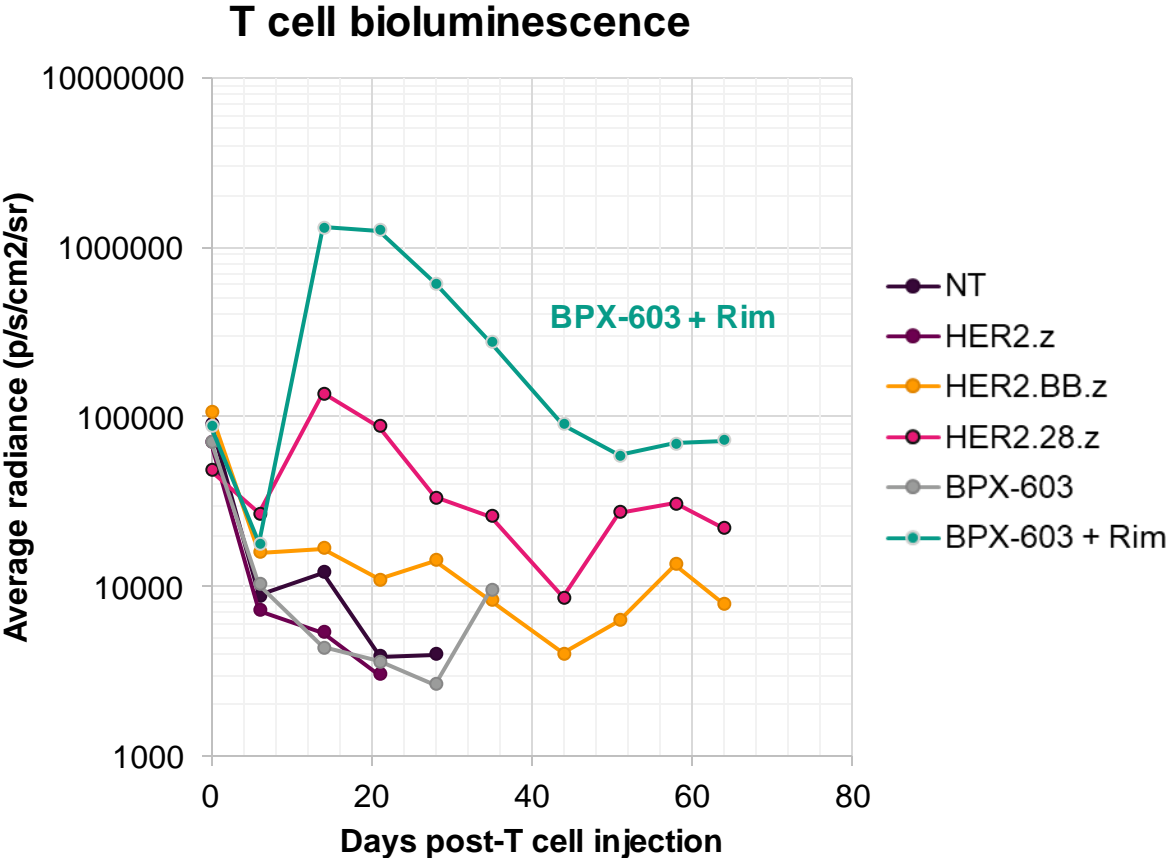
# Historical HER2 Studies: Modest Clinical Outcomes

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

# BPX-603: Compelling Preclinical Evidence

*iMC co-activation enhances cell proliferation  
relative to current CAR-T standards*

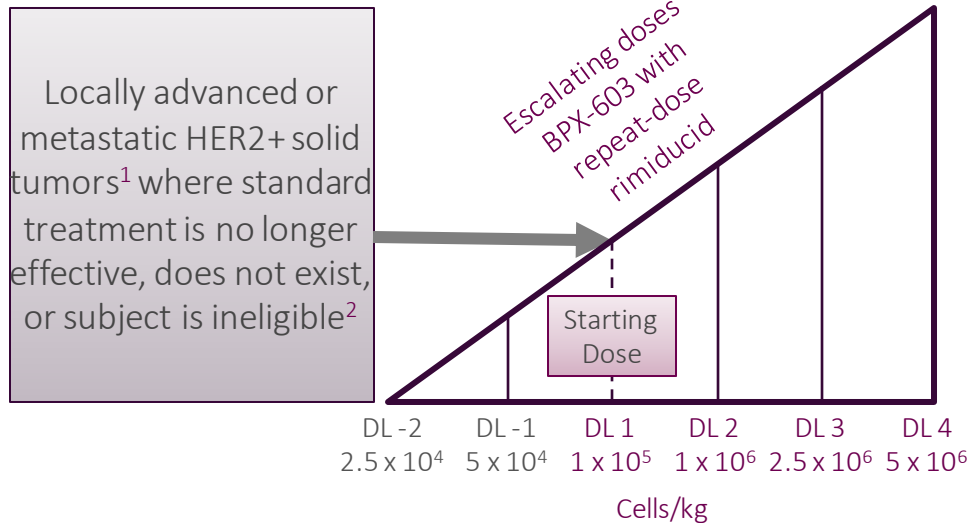
*Moderate affinity scFv enhances  
anti-tumor effect relative to low affinity FRP5*



# BPX-603 Phase 1/2 Trial Design

Two-Part Safety/Activity Study of HER2-Targeted Dual Switch GoCAR-T Cells in Previously Treated HER2+ Solid Tumors

## Phase 1: 3+3 Dose Escalation



- Sequential patient enrollment
  - ≥28 days for cohort 1
  - ≥14 days for subsequent cohorts
- First subject in each dose level receives cells only without rimiducid

## Phase 2: Multi-Arm Dose Expansion in Select Tumor Types

Cohort 1: Gastric

Cohort 2: Breast

If ≥1  
response

Cohort 3: Ovarian

Cohort 4: Colorectal

Cohort 5: GBM<sup>3</sup>

Cohort 6: Uterine/Endometrial

- Expansion cohorts 10 patients each
- Ability to expand each cohort based on clinical response

<sup>1</sup> GBM excluded from Phase 1

<sup>2</sup> Must include approved HER2-targeted therapy for breast/gastric cancers

<sup>3</sup> Subjects with GBM will be dosed at recommended dose for expansion (RDE) -1





# Summary

# Anticipated Key Program Goals & Milestones

	Goals & Milestones	Planned Timing
BPX-601	Phase 1 data update in mCRPC	1Q'22
BPX-603	Initial Phase 1 data	2H'21

# 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
- Screening for enrollment of a cohort in mCRPC underway
- Data update planned 1Q'22

### BPX-603

- Autologous Dual-Switch GoCAR-T targeting HER2 in HER2+ solid tumors
- Phase 1/2 trial initiated
- First data update planned 2H'2021

**Cash runway  
extends into 2Q'22**

- Cash balance of \$37.0M as of December 31, 2020