



**BOLT**  
BIOTHERAPEUTICS

# Bolt Biotherapeutics

*Leveraging the immune system for a better way to treat cancer*

## BDC-1001 Overview

January 2024

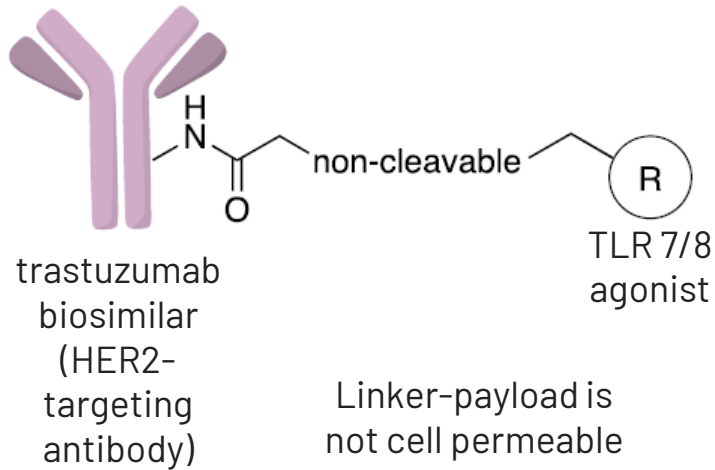
# Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding Bolt Biotherapeutics, Inc. (the "Company," "we," "us," or "our")'s future financial condition, ability to achieve upcoming milestones for our product candidates, the timing of our clinical trials, and the success and results of our pipeline programs and partnerships, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially," "predict," "should," "will" or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy, and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the success, cost and timing of our product development activities and clinical trials; our expectations about the timing of achieving regulatory approval and the cost of our development programs; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; our ability to fund our clinical programs and the sufficiency of our cash, cash equivalents, and marketable securities to fund operations through the achievement of key milestones; the commercialization of our product candidates, if approved; our plans to research, develop, and commercialize our product candidates; our ability to attract collaborators with development, regulatory and commercialization expertise; future agreements with third parties in connection with the commercialization of our product candidates; the success of our current collaborations with third parties, including our collaborations with Bristol-Myers Squibb Company, Roche, Innovent Biologics, Inc., Genmab A/S, and Toray Industries, Inc.; the achievement of milestone payments or any tiered royalties related to our collaborations; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; the rate and degree of market acceptance of our product candidates; and regulatory developments in the United States and foreign countries. These risks are not exhaustive. For a detailed discussion of the risk factors that could affect our actual results, please refer to the risk factors identified in our SEC reports, including, but not limited to our Annual Report on Form 10-K for the year ended December 31, 2022. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

# BDC-1001: First-in-Class HER2-Targeting Boltbody™ ISAC

## BDC-1001



## Clinical Proof of Concept in Evaluable HER2+ Tumors

- 29% monotherapy ORR at RP2D
- 29% ORR in combination with nivolumab at RP2D
- Evidence of innate & adaptive immune activation

## Tolerability & Safety Emerging as a Differentiator

- Well tolerated up to 20 mg/kg q1w, no maximum tolerated dose (MTD)
  - Well tolerated as monotherapy & in combination with nivolumab
- Only 7.6% of patients had Grade  $\geq$  3 TEAEs related to BDC-1001

## Status

- Phase 2 ongoing
  - HER2+ breast, colorectal, endometrial, & gastric cancers

Ackerman SE, et al. *Nature Cancer*. 2021;2(1):18-33.

Li B, et al. ASCO 2023. Abstract 2538

Li B, et al. *Ann Oncol*. 2023;34(suppl\_2):S458-S497 (ESMO, 2023)

ORR = overall response rate

RP2D = recommended Phase 2 dose

TEAE = treatment-emergent adverse event



# BDC-1001 Dose-Escalation Results

## Poster Presentations at ESMO and ASCO 2023

### Promising Clinical Efficacy at the recommended Phase 2 dose of 20 mg/kg q2w

- 29% ORR in evaluable patients with HER2+ tumors
  - 1 PR, 1 CR in monotherapy (n=7)
  - 2 PRs in combination with nivolumab (n=7)
- Disease control rate (PR or SD lasting  $\geq$  24 weeks) :
  - 43% (3/7) in monotherapy
  - 57% (4/7) in combination with nivolumab

### Well tolerated as both monotherapy and in combination

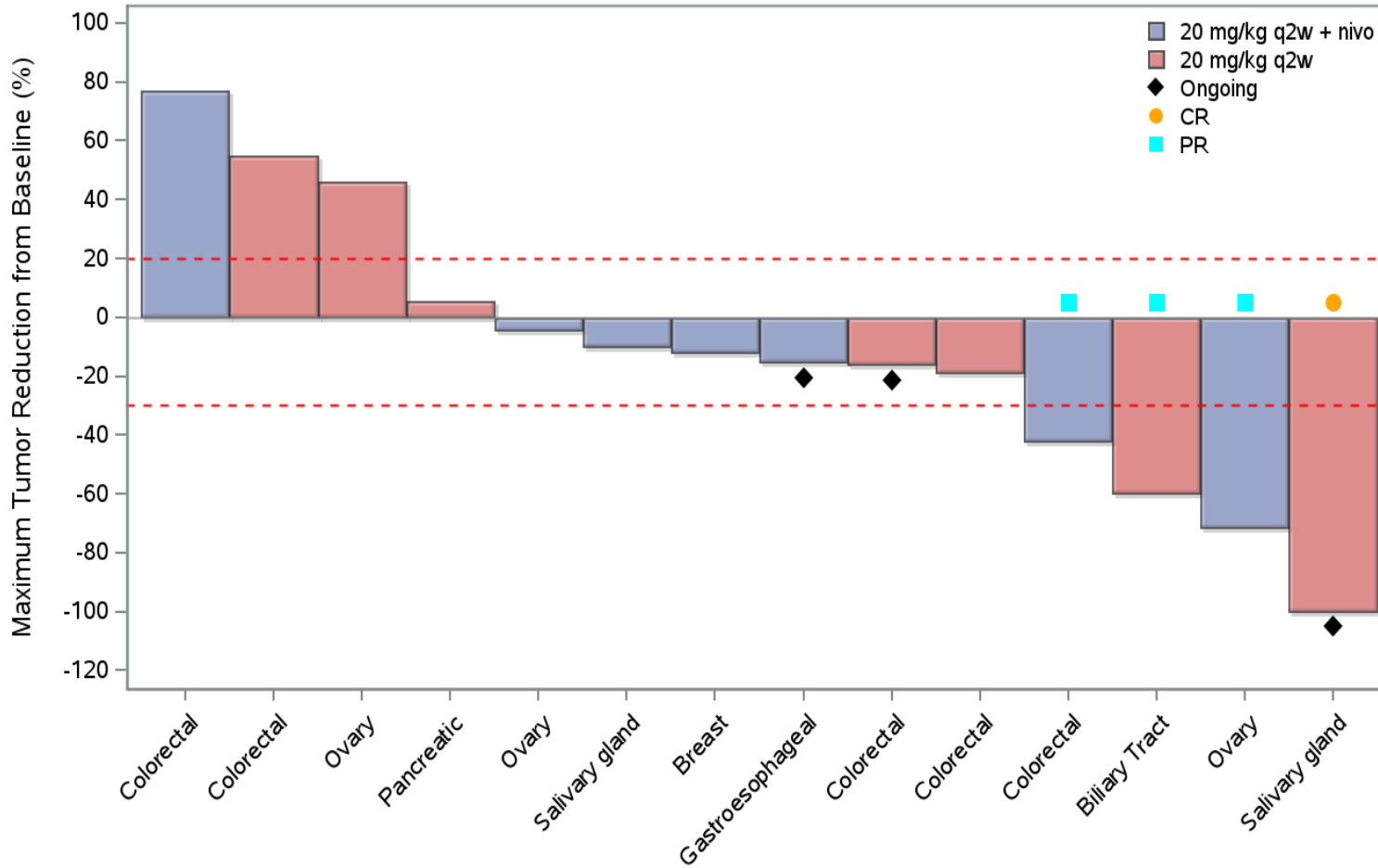
- Most frequent drug-related AEs were grade 1 or 2 infusion-related reactions (30%)
- 10 (8%) grade 3 or higher BDC-1001-related TEAEs
  - Only one was grade 4 and none were grade 5

### Plasma & tissue biomarkers support ISAC mechanism of action

- Increases in dendritic cells, macrophages, & CD8+ T cells
- Dose-dependent peak plasma increases for MIP-1 $\beta$  & IP-10

# 29% Overall Response Rate at 20mg/kg q2w in Evaluable HER2+ Tumors

## BDC-1001 Monotherapy and Combination with Nivolumab



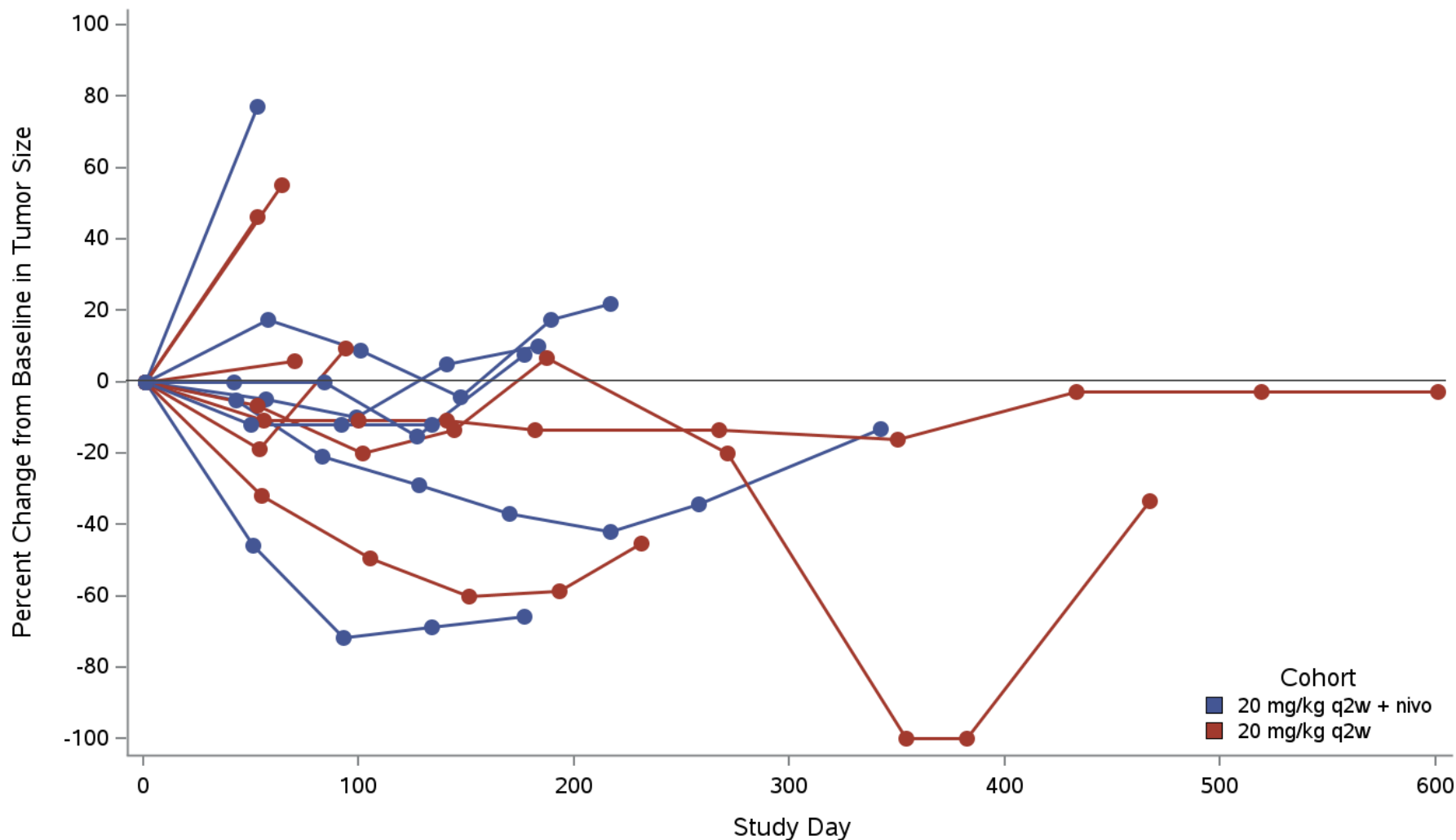
### Monotherapy (n=7)

- 29% achieved CR/PR
- 43% had disease control  $\geq 24$ w
- 57% achieved tumor shrinkage
  - Tumor types: biliary tract, colorectal, and salivary gland

### Combination with Nivolumab (n=7)

- 29% achieved PR
- 57% had disease control  $\geq 24$ w
- 86% achieved tumor shrinkage
  - Tumor types: breast, colorectal, gastroesophageal, ovary, and salivary gland

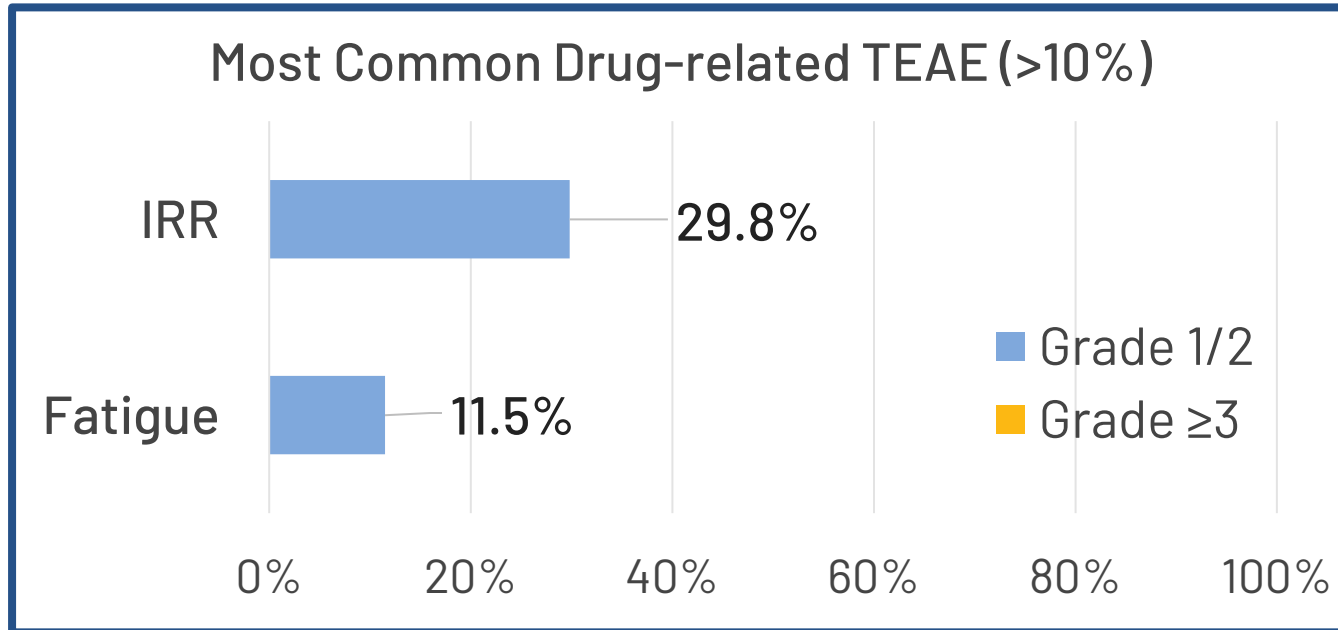
# Promising Duration of Response at 20mg/kg q2w in Evaluable HER2+ Tumors



3 patients have now received therapy for  $\geq 1$  yr

- 2 at 20 mg/kg q2w (RP2D)
- 1 at 5 mg/kg q3w

# BDC-1001 Dose Escalation Safety Summary



Not seen in any patients:

- Alopecia
- Interstitial lung disease (ILD)

10 patients (7.6%) had grade  $\geq 3$  BDC-1001-related TEAEs

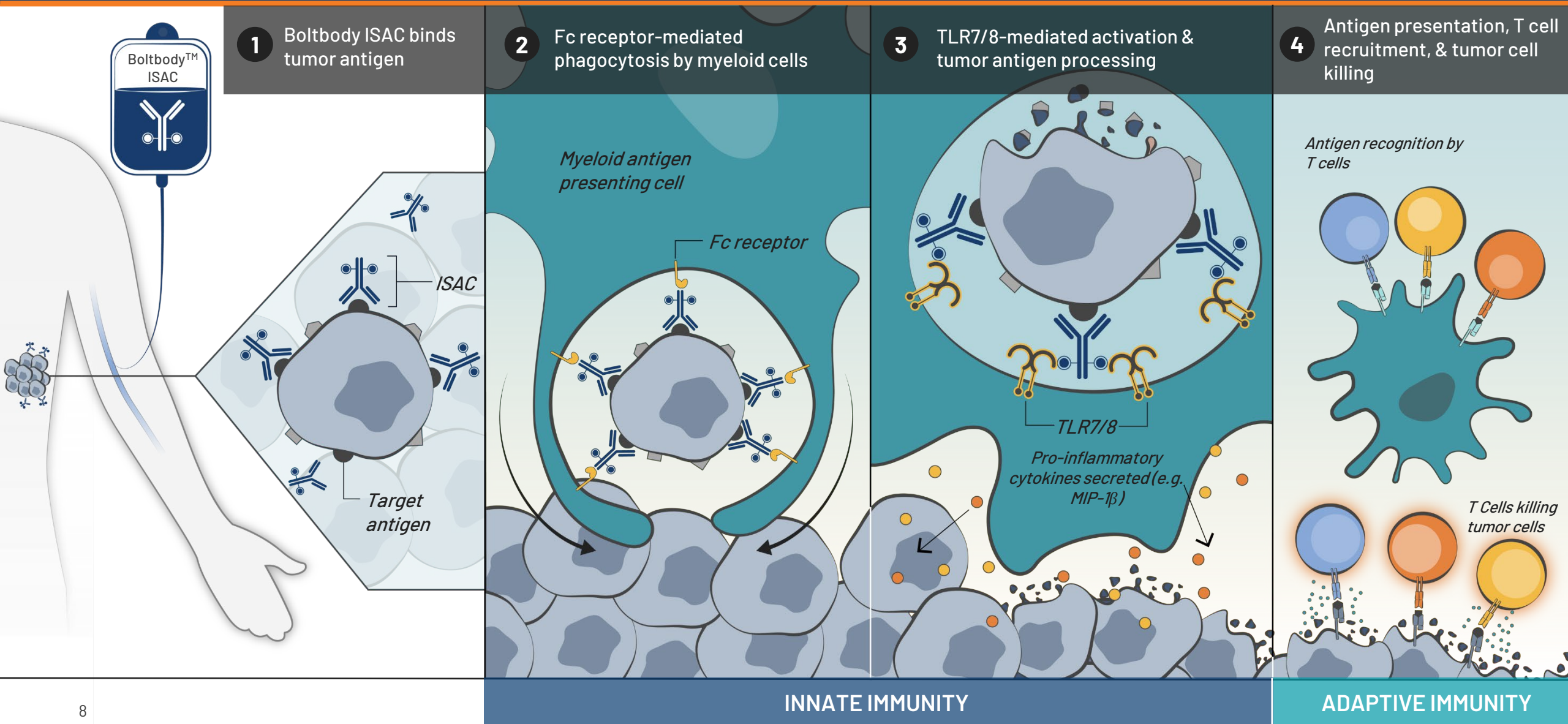
- 1 was grade 4 (post-lung biopsy epistaxis)

Grade 3 LVEF decreases seen in 5 patients (none at RP2D)

Well tolerated in combination with nivolumab



# BDC-1001 Boltbody™ ISAC Mechanism of Action

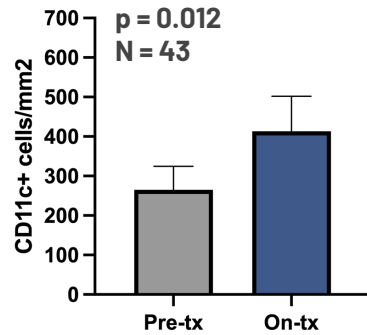




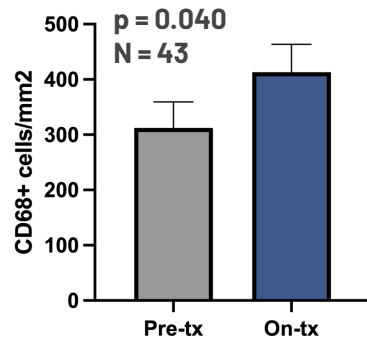
# BDC-1001 Drives Myeloid and T Cell Infiltration in HER2+ Tumors

## HER2+ Tumors (Enrollment data)

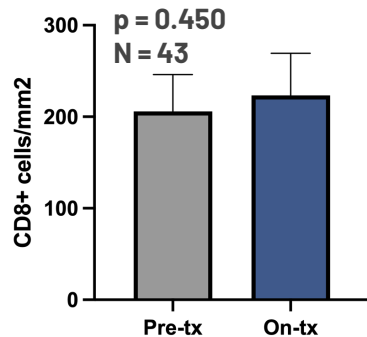
CD11c Density



CD68 Density

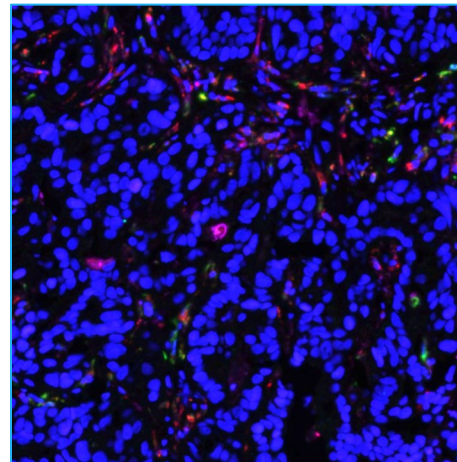


CD8 Density

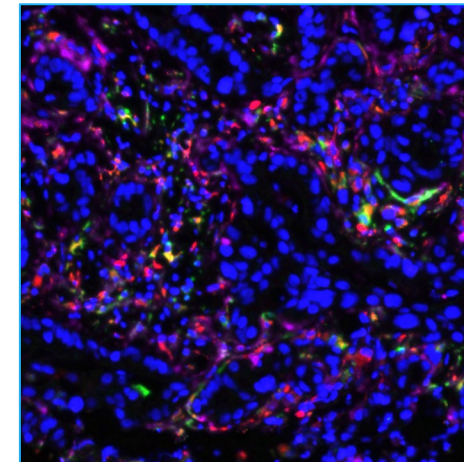


## Patient with Confirmed PR

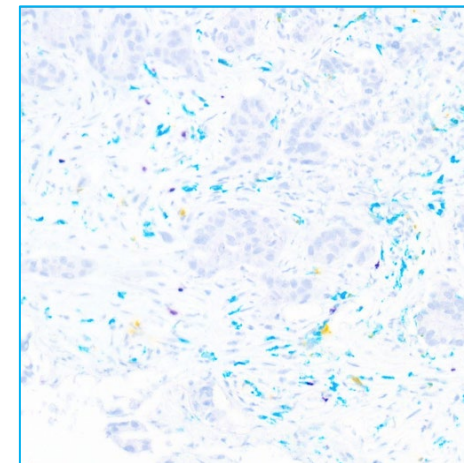
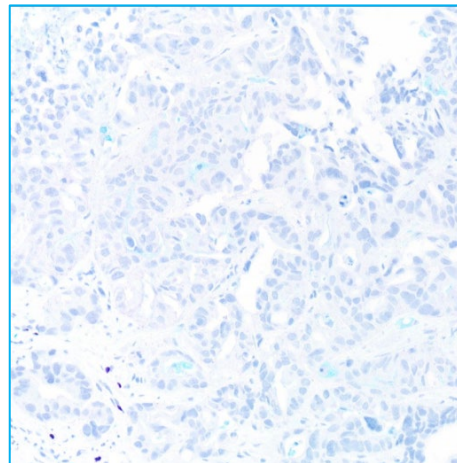
Pre-Treatment



On Treatment



BDCA2  
CD11c  
CD68  
CD163



CD8  
GzmB  
FoxP3

On-Treatment biopsies obtained ~4 weeks after 1<sup>st</sup> dose of BDC-1001

# BDC-1001 Phase 2 Clinical Program in Four HER2-Positive Tumor Types

## Phase 2 Dose Expansion

BDC-1001 monotherapy

Three distinct cohorts of HER2+ solid tumor types

Simon 2-stage design

Colorectal

Endometrial

Gastroesophageal

Additional cohorts in combination with PD-1 inhibitor nivolumab after demonstrating monotherapy activity

## Randomized Phase 2

BDC-1001 ± pertuzumab

Metastatic HER2+ breast cancer post-Enhertu<sup>®</sup>

Simon 2-stage design

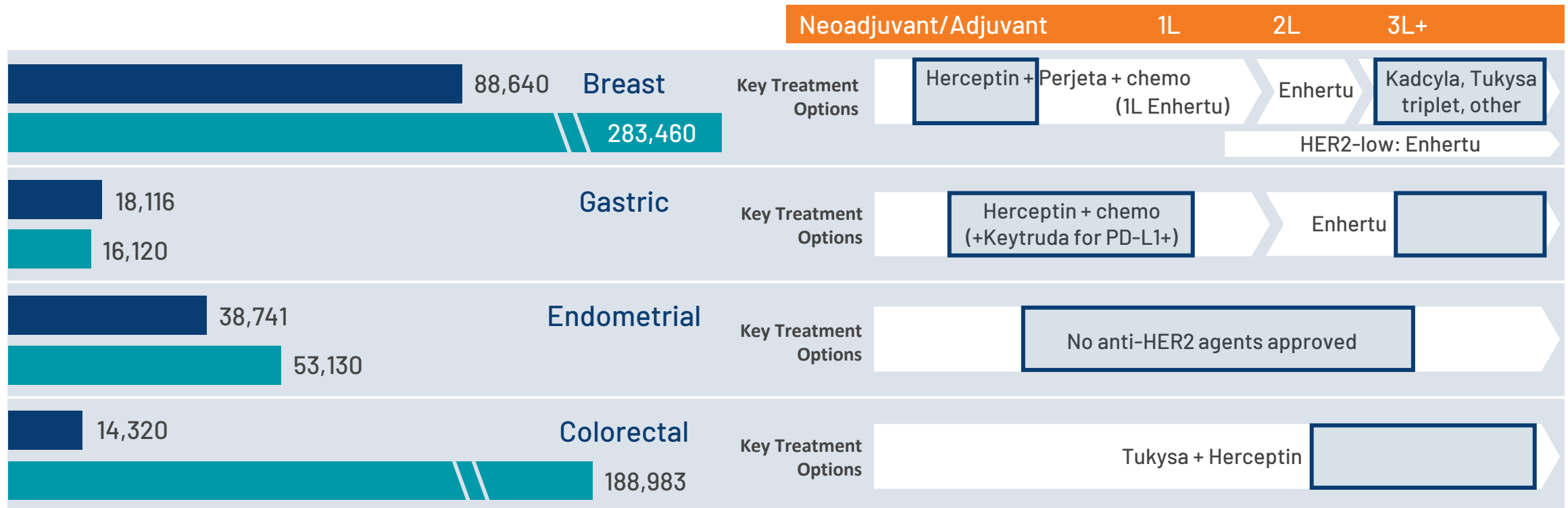
BDC-1001

BDC-1001 +  
Pertuzumab

## Clinical Supply Collaborations

- Bristol Myers Squibb supplying PD-1 checkpoint inhibitor nivolumab
- Roche supplying HER2-targeting antibody pertuzumab

# BDC-1001 Opportunities in the Dynamic HER2 Therapeutic Market



■ HER2+    
 ■ HER2-low    
  Opportunity

US + Top 5 EU incidence numbers based upon 2022 SEER/American Cancer Society(US) & 2020 European Cancer Information System.

HER2 segmentation based upon various scientific publications with HER2-low being IHC2+ unamplified & IHC1+ unamplified.



# Recommended phase 2 dose (RP2D) selection and pharmacodynamic data of the first-in-human immune-stimulating antibody conjugate (ISAC) BDC-1001 in patients with advanced HER2-expressing solid tumors

Bob T. Li,<sup>1</sup> Keun-Wook Lee,<sup>2</sup> Mark D. Pegram,<sup>3</sup> Manish R. Sharma,<sup>4</sup> Jeeyun Lee,<sup>5</sup> Alexander Spira,<sup>6</sup> Yoon-Koo Kang,<sup>7</sup> Kathleen Moore,<sup>8</sup> Drew Rasco,<sup>9</sup> Glenn J. Hanna,<sup>10</sup> Benjamin A. Weinberg,<sup>11</sup> Tai Yu,<sup>12</sup> Michael N. Alonso,<sup>12</sup> Jason Ptacek,<sup>12</sup> Ming Yin,<sup>12</sup> Coya Tapia,<sup>12</sup> Lu Xu,<sup>12</sup> Edith A. Perez,<sup>12</sup> Ecaterina E. Dumbrava<sup>13</sup>

1. Memorial Sloan Kettering Cancer Center, New York, NY, USA; 2. Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea; 3. Stanford University, Stanford, CA, USA; 4. START-Midwest, Grand Rapids, MI, USA; 5. Samsung Medical Center, Seoul, South Korea; 6. Virginia Cancer Specialists, US Oncology Research and NEXT Oncology Virginia, Fairfax, VA, USA; 7. Asan Medical Center, Seoul, South Korea; 8. Stephenson Cancer Center, Oklahoma City, OK, USA; 9. START, San Antonio, TX, USA; 10. Dana-Farber Cancer Institute, Boston, MA, USA; 11. Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; 12. Bolt Biotherapeutics, Redwood City, CA, USA; 13. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

**Presenting author: Bob T. Li, MD**

Memorial Sloan Kettering Cancer Center, New York, NY, USA

October 23, 2023

# Trial Overview and Data Update Since ASCO 2023<sup>1</sup>

## Phase 1 dose escalation results & RP2D selected

- 131 patients with 16 different HER2-expressing solid tumor types; 18 cohorts (doses: 0.5 – 20 mg/kg IV; schedules: q3w, q2w, q1w)
- BDC-1001 well tolerated up to 20 mg/kg q1w as monotherapy and in combination with nivolumab
- Clinical activity across all cohorts in a heterogenous, heavily pre-treated patient population: 1 CR, 5 PRs, 14 SDs ≥ 24 weeks
- BDC-1001 20 mg/kg q2w (as monotherapy or with nivolumab) selected as RP2D based on safety, clinical efficacy, and PK

## Safety for BDC-1001 Monotherapy and Combination with Nivolumab

	BDC-1001 Related-TEAEs Grade ≥ 3 n (%)	LVEF Decrease Grade ≥ 3 <sup>3</sup> n (%)	IRR n (%)
q3w <sup>2</sup> (N=52)	5 (9.6)	1 (1.9)	12 (23.1)
q2w (N=39)	1 (2.6)	1 (2.6)	11 (28.2)
q1w (N=40)	4 (10.0)	3 (7.5)	16 (40.0)
Total (N=131)	10 (7.6)	5 (3.8)	39 (29.8)

<sup>2</sup>q3w included monotherapy only; <sup>3</sup>Derived per CTCAE v5.0, Grade 3 is defined as 'Resting ejection fraction (EF) 39 - 20% OR ≥20% drop from baseline'. Grade 4 is defined as 'Resting ejection fraction (EF) <20%'.  
<sup>4</sup>Grade 4 is defined as 'Resting ejection fraction (EF) <20%'.

- Of 10 patients with grade ≥ 3 BDC-1001-related TEAEs, 1 grade 4
- 5 patients with grade ≥ 3 LVEF, all grade 3
- No grade ≥ 3 IRR was observed
- No increase in nivolumab toxicity in combination with BDC-1001
- Nivolumab did not increase toxicity of BDC-1001

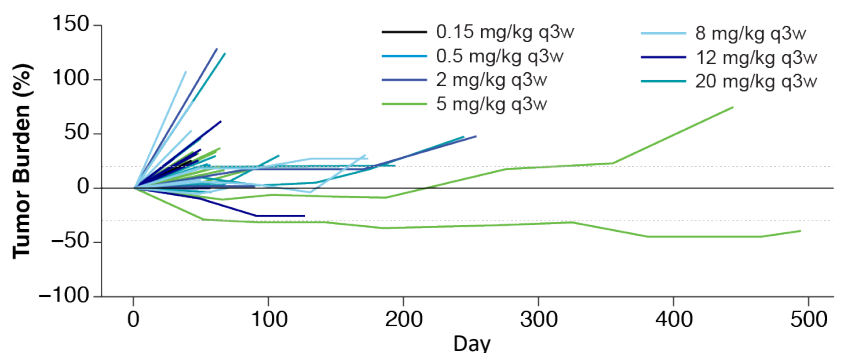
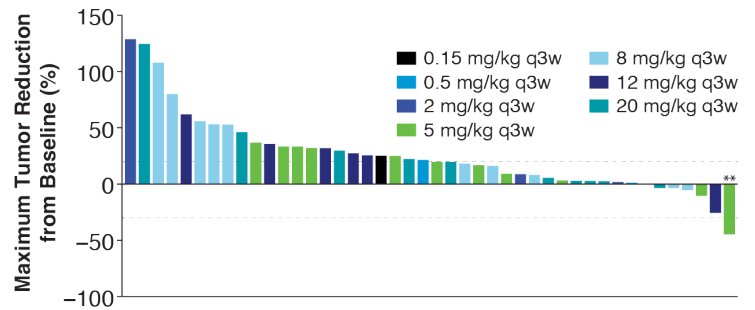
## PK and Biomarkers

- Median target serum exposure of at least 10 µg/mL reached at RP2D; BDC-1001 half-life is 4.8 days
- No clinically significant ADA formation observed (6.3% incidence with very low titers, without impact on PK)
- Dose-dependent increases of multiple plasma cytokines/chemokines, including low IL-6 levels observed
- Increases of myeloid and T cell infiltrations observed in paired tumor biopsies by IHC

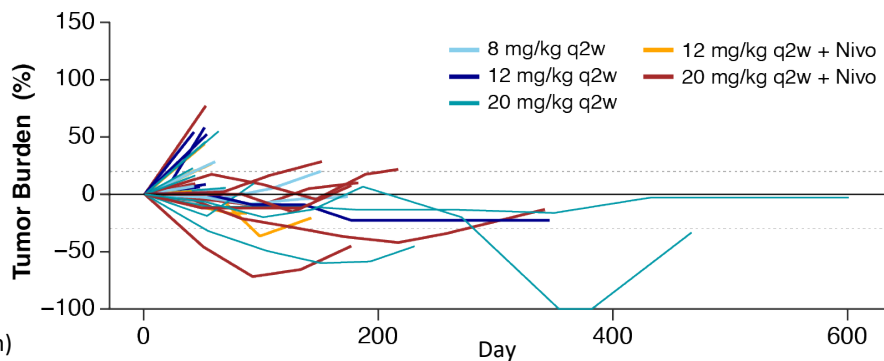
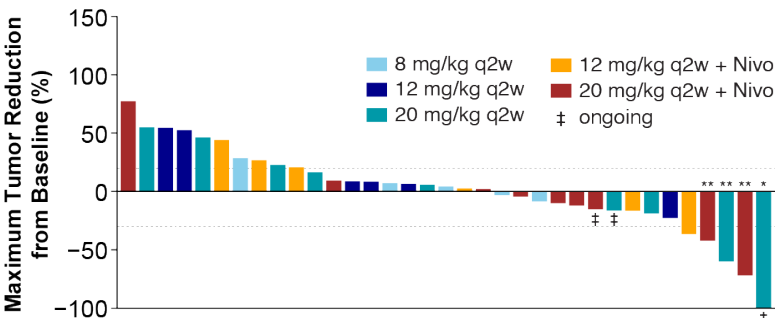
<sup>1</sup>Li B, et al. J Clin Oncol 41, 2023 (suppl 16; abstr 2538); ADA=anti-drug antibody, CR = complete response, IHC = immunohistochemistry, IRR = infusion related reaction, LVEF = left ventricular ejection fraction, PR = partial response, PK = pharmacokinetics, RP2D = recommended phase 2 dose, SD = stable disease, TEAE = treatment-emergent adverse event

# Improved BDC-1001 Efficacy Since ASCO:<sup>1</sup> 1 New CR, 2 Additional Long-Term SDs, and 3 Patients Have Now Received Therapy ≥ 1 Year

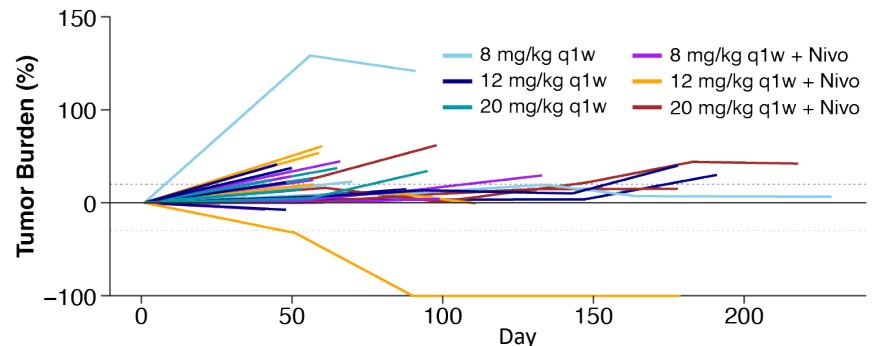
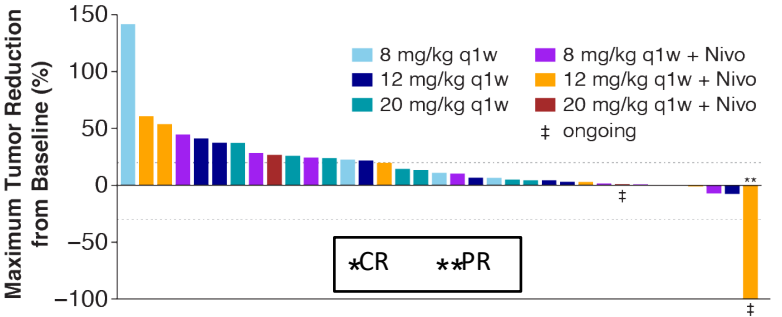
q3w (N = 44)<sup>2</sup>



q2w (N = 35)<sup>2</sup>



q1w (N = 35)<sup>2</sup>



## Efficacy at RP2D, 20 mg/kg q2w, in evaluable HER2+ tumors

- Monotherapy (n=7)
  - 1 CR, 1 PR (ORR = 29%)
  - 43% had disease control ≥24 weeks
  - 57% achieved tumor shrinkage
    - Tumor types: biliary tract, colorectal, salivary gland
- 2 patients received therapy for ≥1 year
- Combination with nivolumab (n=7)
  - 2 PRs (ORR = 29%)
  - 57% had disease control ≥24 weeks
  - 71% achieved tumor shrinkage
    - Tumor types: breast, colorectal, ovary, salivary gland

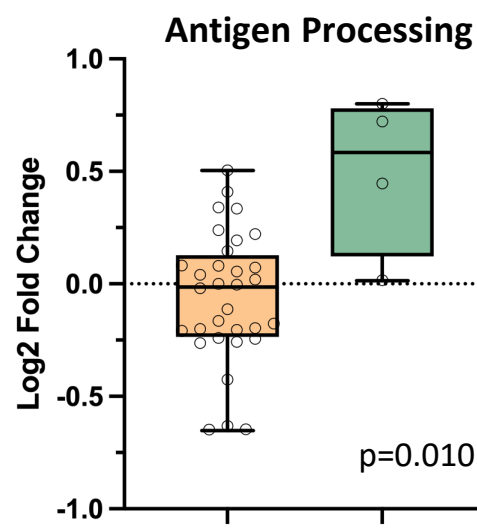
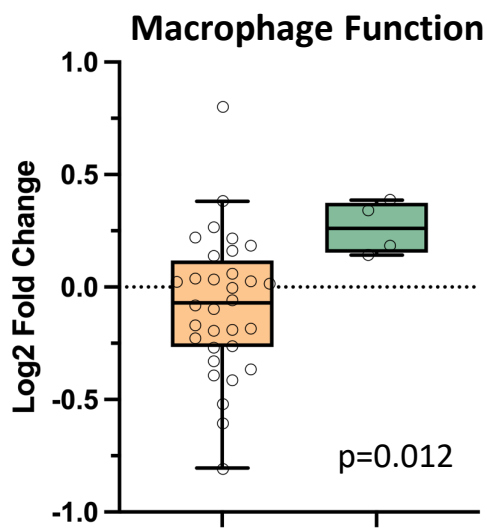
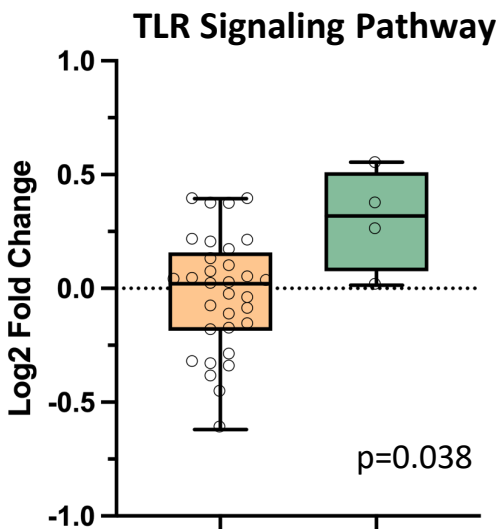
## Overall, 3 patients have now received therapy for ≥1 year

- 2 at 20 mg/kg q2w (RP2D)
- 1 at 5 mg/kg q3w

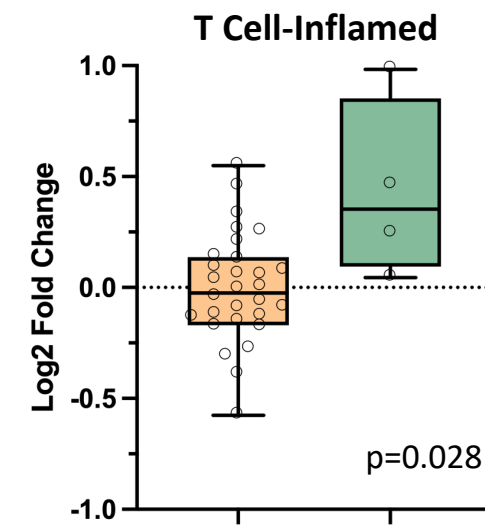


# BDC-1001 Upregulates TLR Signaling, Myeloid, and T Cell Pathways in Clinical Responders, Consistent with MOA

## Innate Immunity



## Adaptive Immunity



■ PR or SD ≥ 24 weeks (n=4)  
 ■ PD or SD < 24 weeks (n=32)

### Methods

- Matched tumor biopsies obtained at baseline and approximately 4 weeks
- Gene expression analyzed by RNAseq and displayed as fold change relative to baseline
- 37 patients had paired and evaluable gene expression data (q3w, q2w, q1w)
  - 1 patient missing response assessment

### Results

- Statistically significant<sup>1</sup> upregulation of TLR signaling pathway gene signature, innate immunity gene signatures, and T cell-inflamed phenotype<sup>2</sup> was observed in the 4 patients with clinical benefit

<sup>1</sup>MOA-driven evaluation of key signatures (Bolt Biotherapeutics; Nature Cancer 2021) assessed using Mann Whitney U test

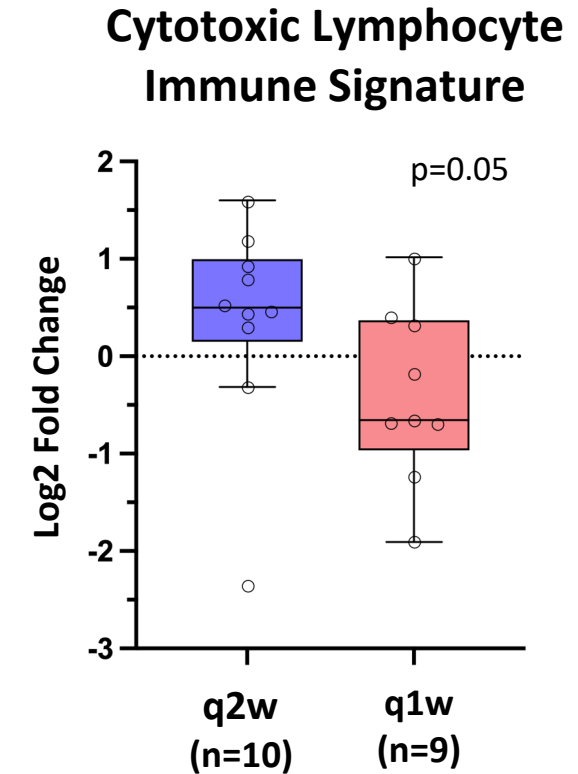
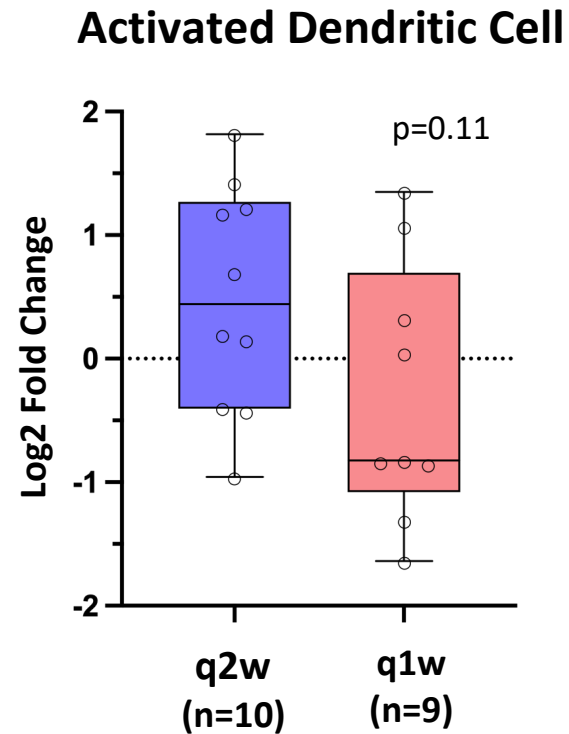
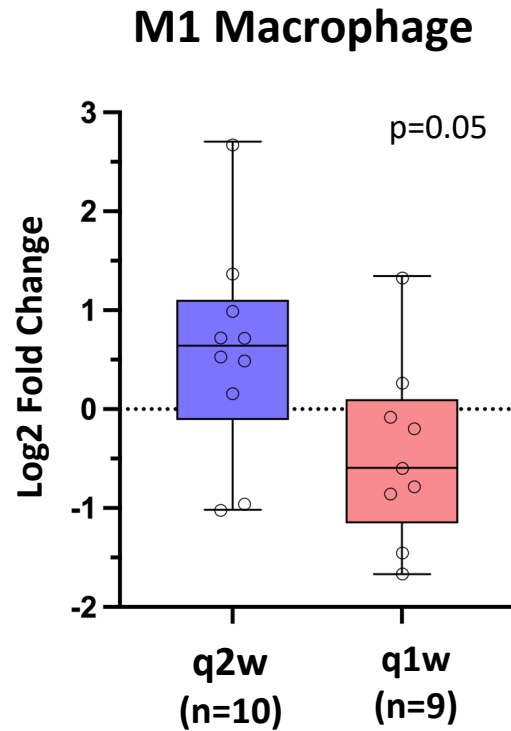
<sup>2</sup>TLR Signaling Pathway - KEGG database; Macrophage Function & Antigen Processing - NanoString; T Cell-Inflamed Signature - Ayers M 2017

Dose (mg/kg)	BDC-1001			BDC-1001 + Nivolumab	
	q3w	q2w	q1w	q2w	q1w
5*	5	0	0	0	0
8	3	1	0	0	1
12	5	1	3	3	0
20	5	1	5	4	0

\*1 patient missing response assessment



# Increases in Select Innate Immune and Adaptive Immune Signatures Were Observed in Patients in the q2w Cohorts, but Not in q1w Cohorts



Dose (mg/kg)	BDC-1001		BDC-1001 + Nivolumab	
	q2w	q1w	q2w	q1w
5	0	0	0	0
8	1	0	0	1
12	1	3	3	0
20	1	5	4	0

## Methods

- Gene expression data were generated by RNAseq
- 10 patients in q2w cohorts and 9 patients in q1w cohorts had paired and evaluable gene expression data

## Results

- Upregulation of select innate and adaptive immune signatures<sup>1</sup> were observed in q2w cohorts, but not q1w

<sup>1</sup>M1, activated DC and cytotoxic lymphocyte immune signatures – Jones WD 2020

# Summary and Next Steps from ESMO Presentation

## **BDC-1001, a novel ISAC targeting HER2, is well tolerated with encouraging clinical activity**

- Clinical activity across all cohorts (n=131): 1 CR, 5 PRs, and 14 SDs  $\geq$  24 weeks
- At RP2D, 20 mg/kg q2w (n=14<sup>1</sup>): 1 CR, 3 PRs (29% ORR), and 4 SDs  $\geq$  24 weeks
- No drug-related alopecia, interstitial lung disease, or grade  $\geq$ 3 infusion-related reaction

## **Gene expression analysis demonstrates**

- Upregulation of TLR signaling, myeloid, and T cell pathways in clinical responders, consistent with mechanism of action
- Increases in innate immune and adaptive immune signatures were observed in patients in the q2w cohorts, but not q1w

## **BDC-1001 is the first ISAC to advance to phase 2 trials**

- Dose expansion phase of BDC-1001 monotherapy and with nivolumab<sup>2</sup> in HER2+ colorectal, gastroesophageal, and endometrial cancers (NCT04278144)
- New trial of BDC-1001 monotherapy with or without pertuzumab<sup>3</sup> in HER2+ metastatic breast cancer following prior treatment with trastuzumab deruxtecan (NCT05954143)

<sup>1</sup>HER2+ evaluable, BDC-1001 as monotherapy and with nivolumab; <sup>2</sup>provided by BMS; <sup>3</sup>provided by Roche



## A Phase 1/2 Study of a First-in-Human Immune-Stimulating Antibody Conjugate (ISAC) BDC-1001 in Patients with Advanced HER2-Expressing Solid Tumors (NCT04278144)

Bob T. Li,<sup>1</sup> Mark D. Pegram,<sup>2</sup> Keun-Wook Lee,<sup>3</sup> Manish R. Sharma,<sup>4</sup> Jeeyun Lee,<sup>5</sup> Alexander Spira,<sup>6</sup> Glenn J. Hanna,<sup>7</sup> Yoon-Koo Kang,<sup>8</sup> Drew Rasco,<sup>9</sup> Kathleen Moore,<sup>10</sup> Benjamin A. Weinberg,<sup>11</sup> Michael N. Alonso,<sup>12</sup> Jason Ptacek,<sup>12</sup> Ming Yin,<sup>12</sup> Coya Tapia,<sup>12</sup> Lu Xu,<sup>12</sup> Edith A. Perez,<sup>12</sup> Ecaterina E. Dumbrava<sup>13</sup>

1. Memorial Sloan Kettering Cancer Center, New York, NY, USA; 2. Stanford University, Stanford, CA, USA; 3. Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seongnam, South Korea; 4. START-Midwest, Grand Rapids, MI, USA; 5. Samsung Medical Center, Seoul, South Korea; 6. Virginia Cancer Specialists, US Oncology Research and NEXT Oncology Virginia, Fairfax, VA, USA; 7. Dana-Farber Cancer Institute, Boston, MA, USA; 8. Asan Medical Center, Seoul, South Korea; 9. START, San Antonio, TX, USA; 10. Stephenson Cancer Center, Oklahoma City, OK, USA; 11. Georgetown Lombardi Comprehensive Cancer Center, Washington, DC, USA; 12. Bolt Biotherapeutics, Redwood City, CA, USA; 13. The University of Texas MD Anderson Cancer Center, Houston, TX, USA

# Eligibility & Objectives for Phase 1/2 Study (NCT04278144)

## Evaluating Single Agent BDC-1001 and BDC-1001 in Combination with Nivolumab

### Key Eligibility

- HER2-expressing solid tumors:
  - HER2 IHC3+ or gene amplified by ISH or NGS (HER2+)
  - HER2 IHC2+ and no gene amplification (HER2-low)
- Prior anti-HER2 and/or checkpoint inhibitor therapy allowed

### Primary Objectives

- Safety and tolerability; Recommended Phase 2 Dose (RP2D) selection

### Exploratory Objectives

- Pharmacokinetics, preliminary anti-tumor activity, plasma and tissue biomarkers to explore proof of mechanism

# Completed BDC-1001 Dose Escalation in HER2-Expressing Solid Tumors

## Monotherapy & Combination with PD-1 Inhibitor Nivolumab

	0.15 mg/kg n = 1	0.5 mg/kg n = 3	2 mg/kg n = 4	5 mg/kg n = 15	8 mg/kg n = 11	12 mg/kg n = 8	20 mg/kg n = 10
Monotherapy	q3w n = 52						
	q2w n = 22				8 mg/kg n = 5	12 mg/kg n = 8	20 mg/kg n = 9
	q1w n = 20				8 mg/kg n = 4	12 mg/kg n = 9	20 mg/kg n = 7
Combination	q2w n = 17					12 mg/kg n = 7	20 mg/kg n = 10
	q1w n = 20				8 mg/kg n = 10	12 mg/kg n = 6	20 mg/kg n = 4

# Demographics and Baseline Characteristics

Heterogenous and Heavily Pretreated Patient Population with 16 Different Tumor Types  
Majority of Patients Had HER2+ Tumors and Prior Anti-HER2 Therapy

	BDC-1001 Monotherapy				BDC-1001 + Nivolumab			All Patients
	q3w n = 52	q2w n = 22	q1w n = 20	Total n = 94	q2w n = 17	q1w n = 20	Total n = 37	Total n = 131
Median age, years (range)	64.0 (30, 84)	62.5 (42, 80)	63.0 (33, 85)	64.0 (30, 85)	65.0 (34, 71)	55.0 (31, 81)	57.0 (31, 81)	62.0 (30, 85)
Sex, n (%)								
Female	33 (63.5)	12 (54.5)	11 (55.0)	56 (59.6)	13 (76.5)	14 (70.0)	27 (73.0)	83 (63.4)
Male	19 (36.5)	10 (45.5)	9 (45.0)	38 (40.4)	4 (23.5)	6 (30.0)	10 (27.0)	48 (36.6)
ECOG								
0	16 (30.8)	5 (22.7)	8 (40.0)	29 (30.9)	7 (41.2)	10 (50.0)	17 (45.9)	46 (35.1)
1	36 (69.2)	17 (77.3)	12 (60.0)	65 (69.1)	10 (58.8)	10 (50.0)	20 (54.1)	85 (64.9)
Prior lines of systemic treatment, median (range)	4 (0, 12)	3 (1, 11)	4 (1, 9)	4 (0,12)	5 (1, 10)	5 (2, 13)	5 (1,13)	4 (0,13)
Prior anti-HER2 therapy, n (%)	43 (82.7)	8 (36.4)	11 (55.0)	62 (66.0)	12 (70.6)	16 (80.0)	28 (75.7)	90 (68.7)
Prior checkpoint inhibitor therapy, n (%)	16 (30.8)	5 (22.7)	8 (40.0)	29 (30.9)	4 (23.5)	5 (25.0)	9 (24.3)	38 (29.0)
HER2 categories from screening, n (%)								
HER2+ (IHC3+ or gene amplification)	51 (98.1)	18 (81.8)	16 (80.0)	85 (90.4)	15 (88.2)	18 (90.0)	33 (89.2)	118 (90.1)
HER2 low (IHC2+ and no gene amplification)	1 (1.9)	4 (18.2)	4 (20.0)	9 (9.6)	2 (11.8)	2 (10.0)	4 (10.8)	13 (9.9)
Tumor types, n (%)								
Colorectal	10 (19.2)	10 (45.5)	4 (20.0)	24 (25.5)	3 (17.6)	7 (35.0)	10 (27.0)	34 (26.0)
Gastroesophageal	16 (30.8)	4 (18.2)	4 (20.0)	24 (25.5)	2 (11.8)	2 (10.0)	4 (10.8)	28 (21.4)
Breast	9 (17.3)	1 (4.5)	5 (25.0)	15 (16.0)	2 (11.8)	8 (40.0)	10 (27.0)	25 (19.1)
Endometrial	6 (11.5)	0 (0.0)	1 (5.0)	7 (7.4)	2 (11.8)	1 (5.0)	3 (8.1)	10 (7.6)
Others*	11 (21.2)	7 (31.8)	6 (30.0)	24 (25.5)	8 (47.0)	2 (10.0)	10 (27.0)	34 (26.0)

\*Other tumor types include (monotherapy and combination combined): n=6 ovary, n=5 salivary gland, n=4 cervix, n=4 lung, n=4 pancreatic, n=2 biliary tract, n=2 skin, n=2 small intestine, and one each of head and neck, intestinal ampulla, liver, prostate, and urinary bladder.

Li B, et al. ASCO 2023. Abstract 2538



# Safety:

## BDC-1001 was Well Tolerated Up to 20 mg/kg q1w Monotherapy and in Combination with Nivolumab

- BDC-1001 has a wide therapeutic window, up to 20 mg/kg q1w with maximum-tolerated dose (MTD) not reached
  - One DLT of supraventricular tachycardia (grade 3) at 8 mg/kg BDC-1001 q1w in combination with nivolumab
  - One grade 4 and no grade 5 drug-related AEs
- Most frequent (29.0%) drug-related AEs were low grade (grade 1 and grade 2) infusion-related reactions (IRRs)
- One drug-related cytokine release syndrome (grade 1) at 12 mg/kg BDC-1001 q1w
- Left ventricular ejection fraction (LVEF) decrease
  - 6 patients with ejection fraction decrease (grade 2 [n=4], grade 3 [n=2])
    - 4 received BDC-1001 q1w
      - Monotherapy: 1 patient at 12 mg/kg, 2 at 20 mg/kg; combination: 1 at 8 mg/kg + nivolumab
    - 2 received BDC-1001 q3w or q2w
      - Monotherapy: 1 patient at 5 mg/kg q3w and 1 at 8 mg/kg q2w
- 2 patients discontinued therapy due to LVEF decrease
  - 5 mg/kg BDC-1001 q3w, 8 mg/kg BDC-1001 q2w



# BDC-1001 was Well Tolerated

## As Monotherapy and in Combination with Nivolumab

### Summary of Treatment-related TEAEs

	BDC-1001 Monotherapy				BDC-1001 + Nivolumab					
	Treatment-related TEAEs				BDC-1001 Treatment-related TEAEs			BDC-1001 + Nivolumab Treatment-related TEAEs		
	q3w n = 52	q2w n = 22	q1w n = 20	Total n = 94	q2w n = 17	q1w n = 20	Total n = 37	q2w n = 17	q1w n = 20	Total n = 37
All grades (%)	30 (57.7)	11 (50.0)	17 (85.0)	58 (61.7)	11 (64.7)	14 (70.0)	25 (67.6)	5 (29.4)	12 (60.0)	17 (45.9)
Grade ≥3 (%)	5 (9.6)	1 (4.5)	1 (5.0)	7 (7.4)	0	2 (10.0)	2 (5.4)	0	1 (5.0)	1 (2.7)
Serious adverse events (%)	3 (5.8)	0	0	3 (3.2)	1 (5.9)	1 (5.0)	2 (5.4)	0	1 (5.0)	1 (2.7)
Leading to treatment discontinuation	3 (5.8)	1 (4.5)	0	4 (4.3)	0	1 (5.0)	1 (2.7)	0	1 (5.0)	1 (2.7)
Leading to treatment interruption	5 (9.6)	2 (9.1)	2 (10.0)	9 (9.6)	1 (5.9)	1 (5.0)	2 (5.4)	0	1 (5.0)	1 (2.7)
Leading to death	0	0	0	0	0	0	0	0	0	0

Data cut-off: March 24, 2023

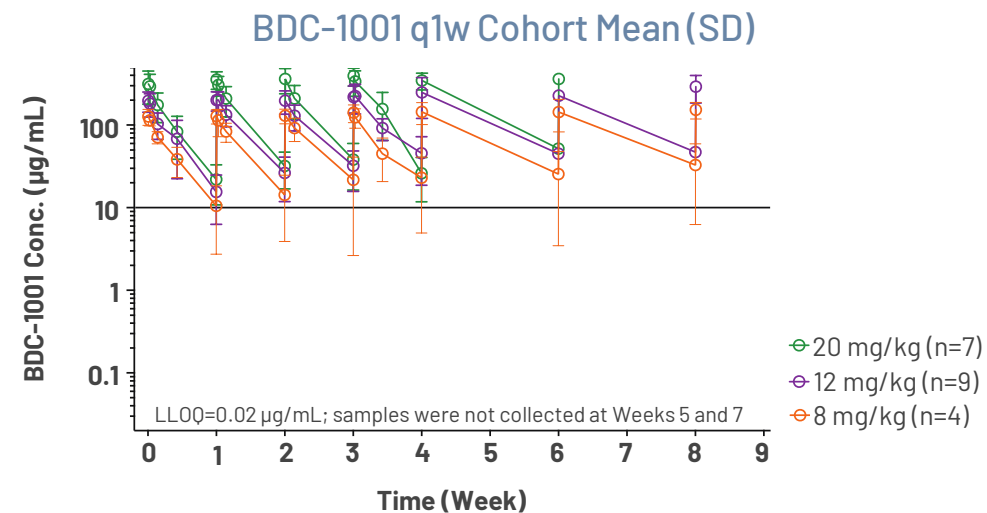
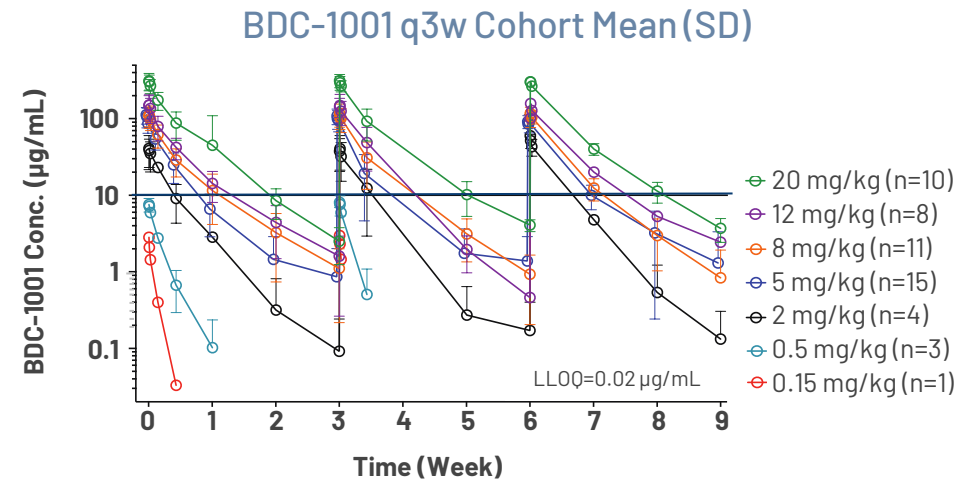
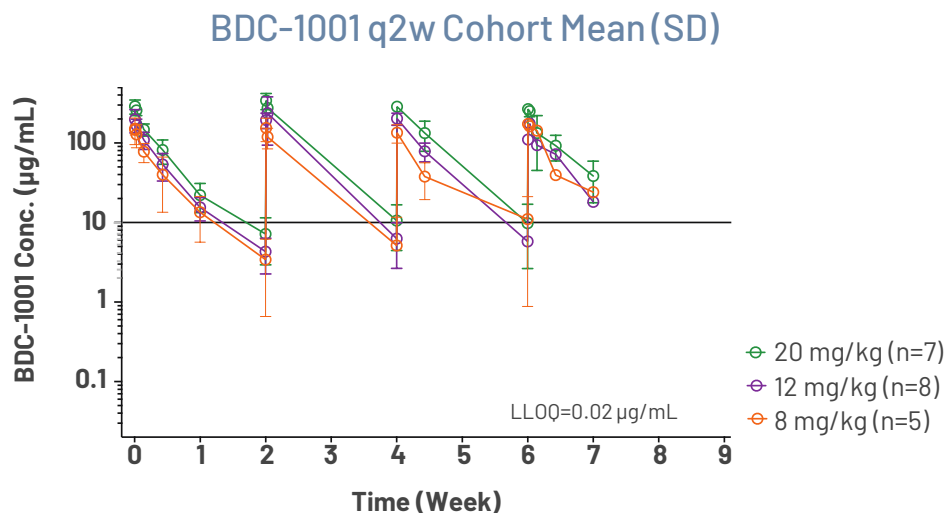
Safety graded by CTCAE v5; TEAE, treatment-emergent adverse event

Definition of treatment-related TEAEs = an AE considered as related to with unknown/missing relationship to study drug

# BDC-1001 Pharmacokinetics:

## Serum Target Exposure > 10µg/mL Achieved at RP2D of 20 mg/kg q2w

- Population mean clearance 1.6 L/day & terminal  $T_{1/2}$  of 4.3 days
  - Faster clearance at dose levels lower than 5 mg/kg exhibits TMDD (target-mediated drug disposition)
- 2-fold accumulation observed in median  $C_{min}$  with q2w & q1w dosing
  - At 20 mg/kg q2w,  $C_{min}$  increase from first dose to steady state: ~ 12 to 29 µg/mL
  - At 20 mg/kg q1w,  $C_{min}$  increase from first dose to steady state: ~ 34 to 68 µg/mL
  - Virtually no accumulation was observed with q3w dosing
- Presence of nivolumab did not impact PK of BDC-1001
- Low incidence of BDC-1001 ADA formation (4.2%) with no impact on PK, safety, or efficacy



# Efficacy:

## Most Clinically Meaningful Efficacy Observed at 20 mg/kg q2w (RP2D)

- Six patients had PRs
  - 3 colorectal, 1 ovarian, 1 biliary, 1 salivary
  - 4 at 20 mg/kg q2w (2 mono, 2 combo)
    - 3 were MSS (mono or combo) and 1 was MSI (mono)
  - 1 at 12 mg/kg q1w (combo) in MSS tumor
  - 1 at 5 mg/kg q3w (mono) in MSS tumor
- Twelve patients had SD  $\geq$  24 weeks
  - 4 colorectal, 1 melanoma, 1 endometrial, 2 gastric, 1 salivary gland, 2 cervical, 1 ovarian
  - 3 of 12 at 20 mg/kg q2w with colorectal, salivary gland, and ovarian cancer
- Tumor shrinkage observed in a variety of tumor types including biliary, breast, cervical, colorectal, endometrial, gastric, lung, salivary, skin (melanoma), and ovarian cancer

# Clinical Efficacy in All Patients with HER2+ Tumors Treated with 20 mg/kg q2w (RP2D) BDC-1001 Monotherapy or in Combination with Nivolumab

	BDC-1001 20 mg/kg (n = 7) 4 Tumor Types	BDC-1001 20 mg/kg + Nivolumab (n = 8)** 5 Tumor Types	All (n = 15) 7 Tumor Types
Response assessment, n (%)			
PR	2* (29%)	2 (25%)	4 (27%)
SD	3 (43%)	4 (50%)	7 (47%)
PD	2 (29%)	1 (13%)	3 (20%)
Not evaluable	0	1 (13%)	1 (7%)
Overall response rate, n (%)	2 (29%)	2 (25%)	4 (27%)
Disease control rate ≥ 6 weeks, n (%)	5 (71%)	6 (75%)	11 (73%)
Disease control rate ≥ 24 weeks, n (%)	3 (43%)	4 (50%)	7 (47%)
Tumor shrinkage, n (%)	4 (57%)	5 (63%)	9 (60%)

\*One PR confirmed post March 24, 2023 data cut-off; \*\*One non-evaluable patient included.  
4 HER2-low tumors (2 each from BDC-1001 monotherapy and in combination) are excluded.

Data cut-off: March 24, 2023

# Clinical Efficacy in All Patients with HER2+ Tumors was Greater with 20 mg/kg Compared to 12 mg/kg q2w

Data Fairly Comparable for BDC-1001 Monotherapy or in Combination with Nivolumab

	BDC-1001		BDC-1001 + Nivolumab	
	12 mg/kg (n = 7) 5 Tumor Types	20 mg/kg (n = 7) 4 Tumor Types	BDC-1001 12 mg/kg (n = 7) 6 Tumor Types	BDC-1001 20 mg/kg (n = 8)** 5 Tumor Types
Response assessment, n (%)				
PR	0	2* (29%)	0	2 (25%)
SD	1 (14%)	3 (43%)	2 (29%)	4 (50%)
PD	4 (57%)	2 (29%)	4 (57%)	1 (13%)
Not evaluable	2 (29%)	0	1 (14%)	1 (13%)
Overall response rate, n (%)	0	2 (29%)	0	2 (25%)
Disease control rate ≥ 6 weeks, n (%)	1 (14%)	5 (71%)	2 (29%)	6 (75%)
Disease control rate ≥ 24 weeks, n (%)	1 (14%)	3 (43%)	0	4 (50%)
Tumor shrinkage, n (%)	1 (14%)	4 (57%)	2 (29%)	5 (63%)

\* One PR confirmed post March 24, 2023 data cutoff; \*\*One non-evaluable patient included  
5 HER2-low tumors are excluded (1 at 12 mg/kg and 4 at 20 mg/kg)

Data cut-off: March 24, 2023

# BDC-1001 Clinical Activity: 6 PRs and 12 Long-lasting SDs (≥ 24 Weeks) Observed in 8 Tumor Types, Particularly in 20 mg/kg q2w Dose Cohorts

Best Response	Site of Primary Tumor, HER2 Status	Duration of Disease Control (PR or SD) in Wks	Prior Lines of Therapy	Prior Anti-HER2 Therapy	Prior Checkpoint Inhibitor	MSS/MSI	Dose Cohort
Partial Response	Colorectal, HER2+	84	4	No	Yes	MSS	5 mg/kg q3w
	<b>Biliary tract cancer, HER2+</b>	<b>36</b>	<b>2</b>	<b>No</b>	<b>No</b>	<b>MSS</b>	<b>20 mg/kg q2w</b>
	<b>Salivary gland, HER2+</b>	<b>48+</b>	<b>2</b>	<b>No</b>	<b>No</b>	<b>MSI</b>	<b>20 mg/kg q2w</b>
	<b>Ovarian cancer, HER2+</b>	<b>24</b>	<b>12</b>	<b>Yes</b>	<b>No</b>	<b>MSS</b>	<b>20 mg/kg q2w + nivolumab</b>
	<b>Colorectal cancer, HER2+</b>	<b>48</b>	<b>5</b>	<b>Yes</b>	<b>No</b>	<b>MSS</b>	<b>20 mg/kg q2w + nivolumab</b>
	Colorectal cancer, HER2+	12+	5	Yes	No	MSS	12 mg/kg q1w + nivolumab
Long lasting Stable Disease	Endometrial cancer, HER2+	36	3	Yes	No	No data	2 mg q3w
	Cervical cancer, HER2+	60	3	Yes	No	No data	5 mg/kg q3w
	Melanoma, HER2+	24	1	No	Yes	MSS	8 mg/kg q3w
	Colorectal, HER2+	36	11	Yes	No	MSS	20 mg/kg q3w
	Colorectal, HER2+	24+	2	No	No	MSS	8 mg/kg q2w
	Gastric cancer, HER2+	48+	2	Yes	No	No data	12 mg/kg q2w
	<b>Colorectal, HER2+</b>	<b>60+</b>	<b>2</b>	<b>No</b>	<b>No</b>	<b>MSI</b>	<b>20 mg/kg q2w</b>
	<b>Salivary gland cancer, HER2+</b>	<b>24</b>	<b>8</b>	<b>Yes</b>	<b>Yes</b>	<b>MSS</b>	<b>20 mg/kg q2w + nivolumab</b>
	<b>Ovarian cancer, HER2+</b>	<b>36</b>	<b>4</b>	<b>Yes</b>	<b>No</b>	<b>MSI</b>	<b>20 mg/kg q2w + nivolumab</b>
	Colorectal. HER2+	36	1	No	No	MSS	8 mg/kg q1w
	Cervical cancer, HER2+	24	5	Yes	Yes	MSS	12 mg/kg q1w
	Gastric cancer, HER2+	24	2	Yes	No	No data	12 mg/kg q1w

**Bold:** patients treated at RP2D

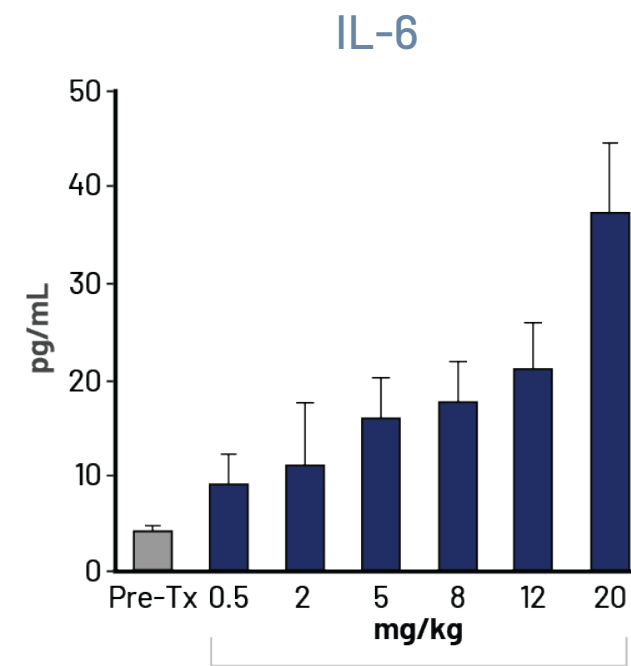
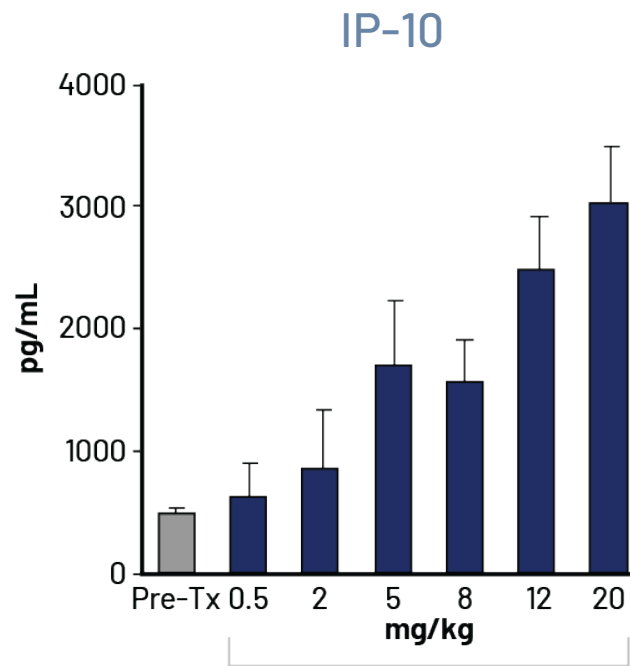
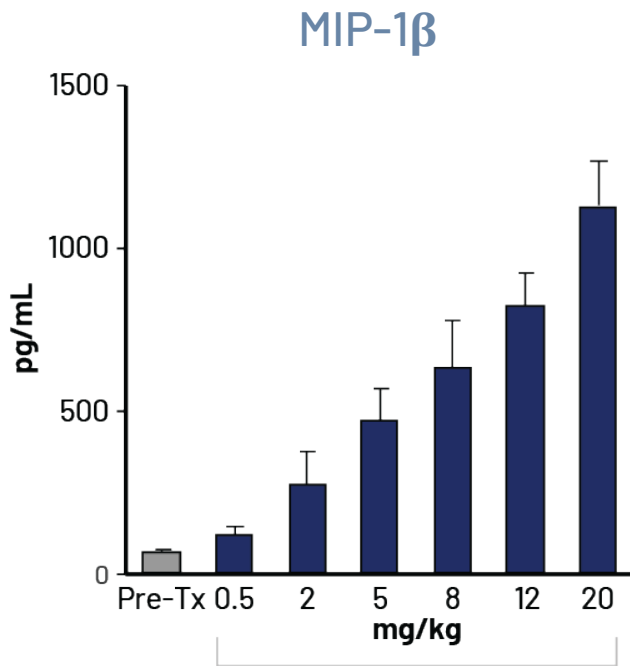
Data cut-off: March 24, 2023

# Increases in Plasma Myeloid Activation Markers Confirm MOA and Safety

## Peak Increases Seen at 4 Hours

- Plasma samples for cytokines and chemokines obtained from all patients
- Dose-dependent peak increases in Cycle 1 were observed in multiple cytokines and chemokines\*
  - Similar responses observed for MIP-1 $\alpha$ , IFN $\gamma$ , TNF $\alpha$  and eotaxin

Average IL-6 levels, a marker of inflammation, were low at all doses (< 50 pg/mL)

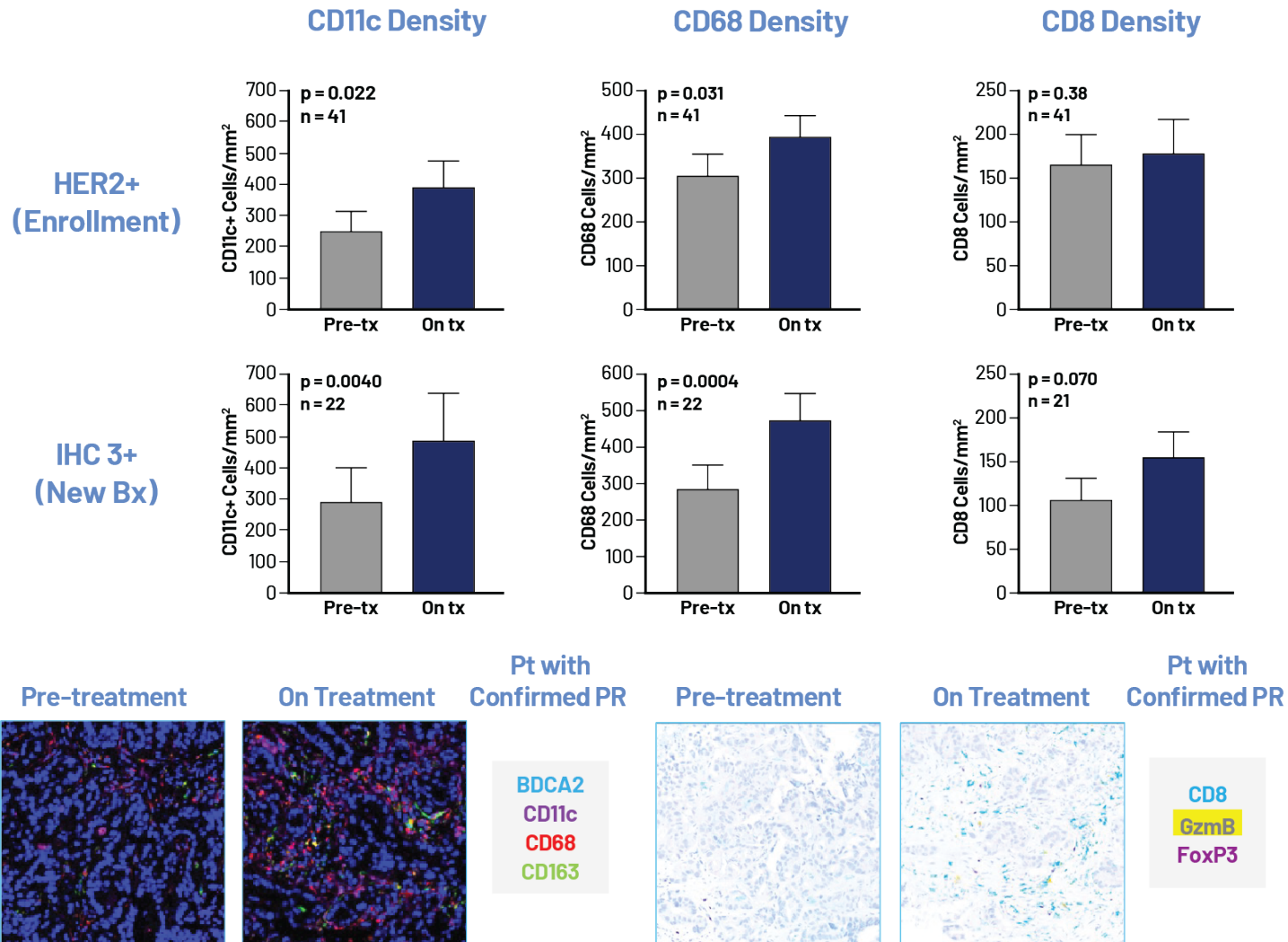


Data cut-off: March 24, 2023



# BDC-1001 Drives Myeloid and T Cell Infiltration in HER2+ Tumors

## Data from Paired Fresh Tumor Biopsies



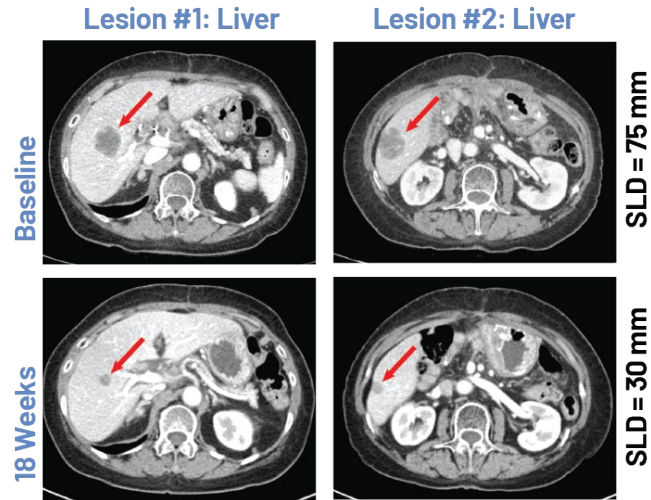
Data cut-off: March 24, 2023

# Biomarker Data Supports MOA with Increases in Myeloid and T Cells

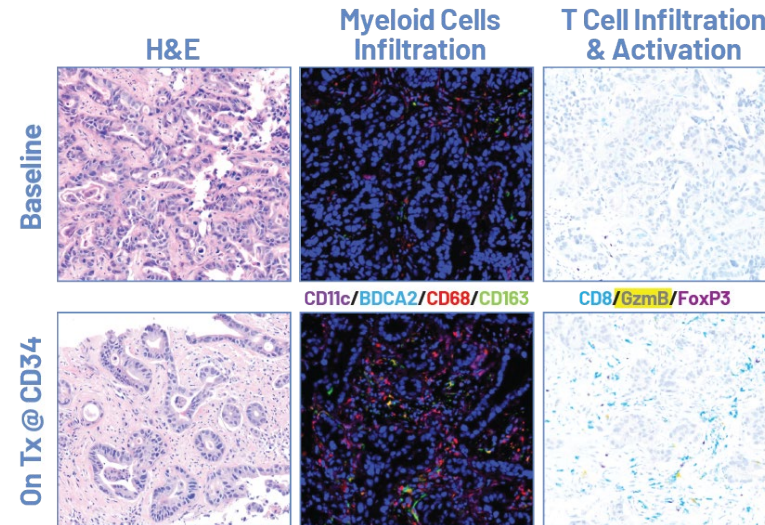
## CT Imaging & Fresh Matched Biopsies in Patient with PR

Patient with HER2+ by NGS, MSS biliary tract carcinoma  
 – No prior anti-HER2 or immunotherapy

Fresh matched (pre- and on-Tx) biomarker data



Maximum tumor reduction of target lesions was 60%



### Key observations:

- cDC (CD11c) increased by 16% and pDC (BDCA2) decreased by 70%
- 62% increase in M1 (CD68+CD163-) macrophage, 161% increased in monocyte-derived DCs (CD11c+CD163+), and 16% increase in cDC (CD11c+CD163-)
- 500% increase in CD8+ T cell infiltration and 400% increase in CD8+Granzyme B+ T cell activation

Data cut-off: March 24, 2023

# Conclusions from ASCO Presentation

Results demonstrate encouraging evidence of safety, anti-tumor efficacy, and biomarker changes consistent with MoA of ISAC technology

- BDC-1001 was well-tolerated at all doses and dosing frequencies up to 20 mg/kg q1w
  - In a heterogeneous (16 different tumor types in 18 cohorts) and heavily pretreated (median 4 prior lines of systemic treatment) patient population
- Target exposure established in preclinical models achieved at higher dose and increased frequency of administration
  - $C_{min}$  above 10  $\mu\text{g/mL}$  achieved at q2w and q1w schedules
  - Improved efficacy observed with q2w compared to q3w or q1w
- Clinical activity of BDC-1001 observed alone and in combination with nivolumab, particularly in 20 mg/kg q2w cohorts
- Pharmacodynamic responses in both plasma and tissue consistent with ISAC MOA
  - Responses of myeloid and T cell activation and infiltration not anticipated with trastuzumab treatment alone
- Selection of 20 mg/kg q2w as RP2D based on the totality of safety, efficacy, PK, and biomarkers
- Results support Phase 2 development of BDC-1001 as a single agent and in combination strategies



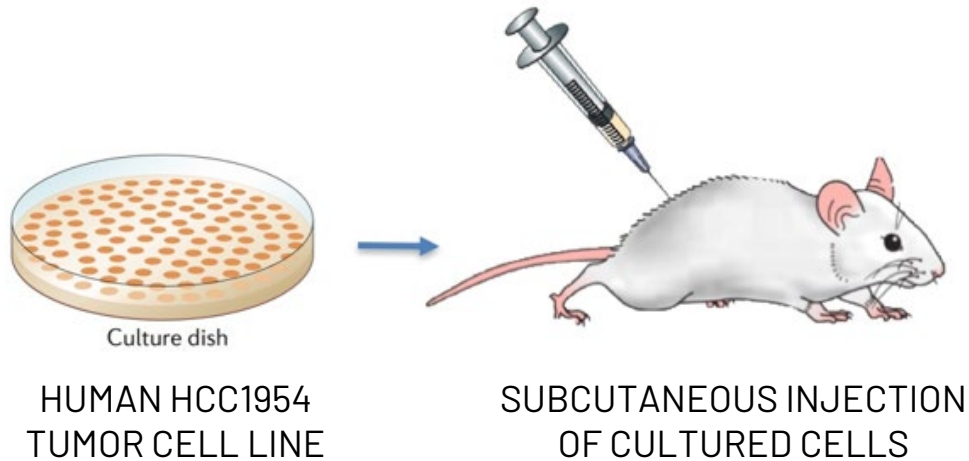
**BOLT**  
BIOTHERAPEUTICS

## BDC-1001 Preclinical Support

# ISACs Deliver Powerful Synergies

## Covalent Attachment of TLR7/8 Agonist Dramatically Improves Anti-tumor Efficacy

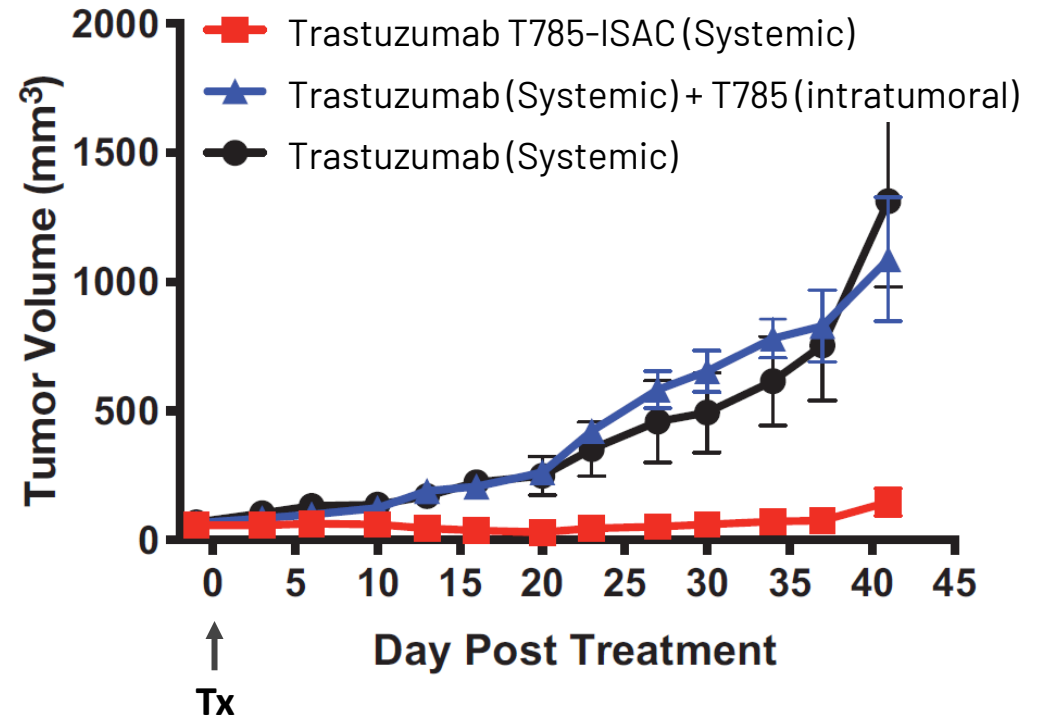
### HCC1954 Tumor Xenograft Model



- SCID/Beige lack T, B and functional NK cells, but retain a myeloid compartment
- Enables assessment of myeloid-mediated anti-tumor activity

Adapted from Creative Biolabs

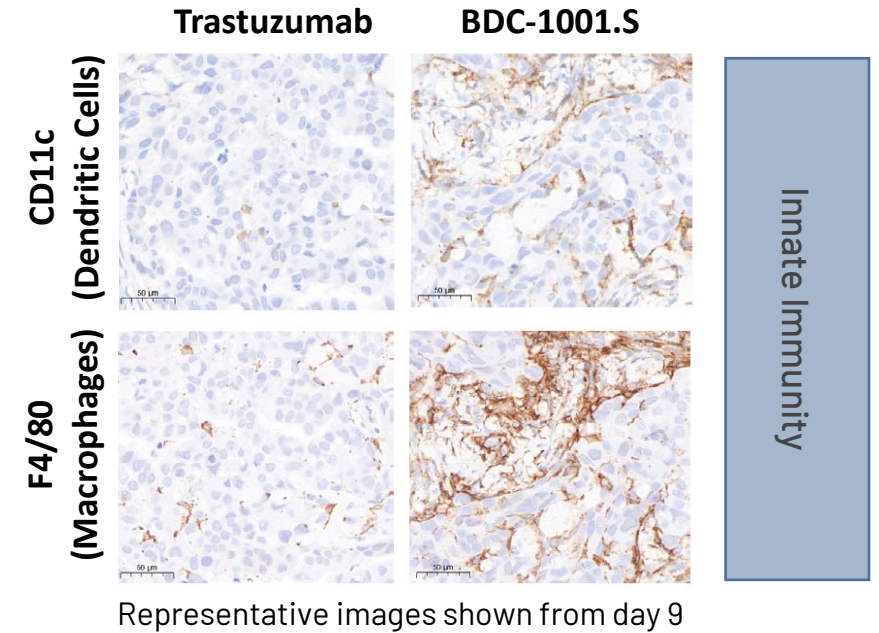
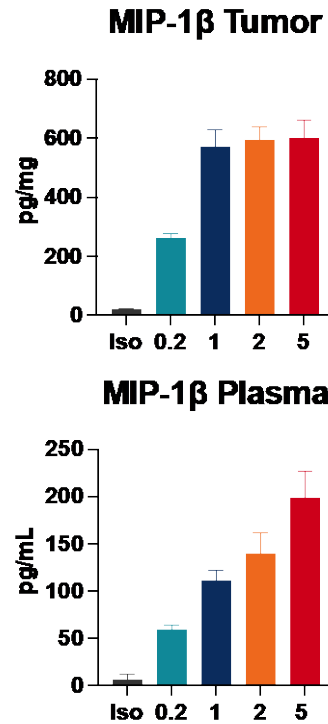
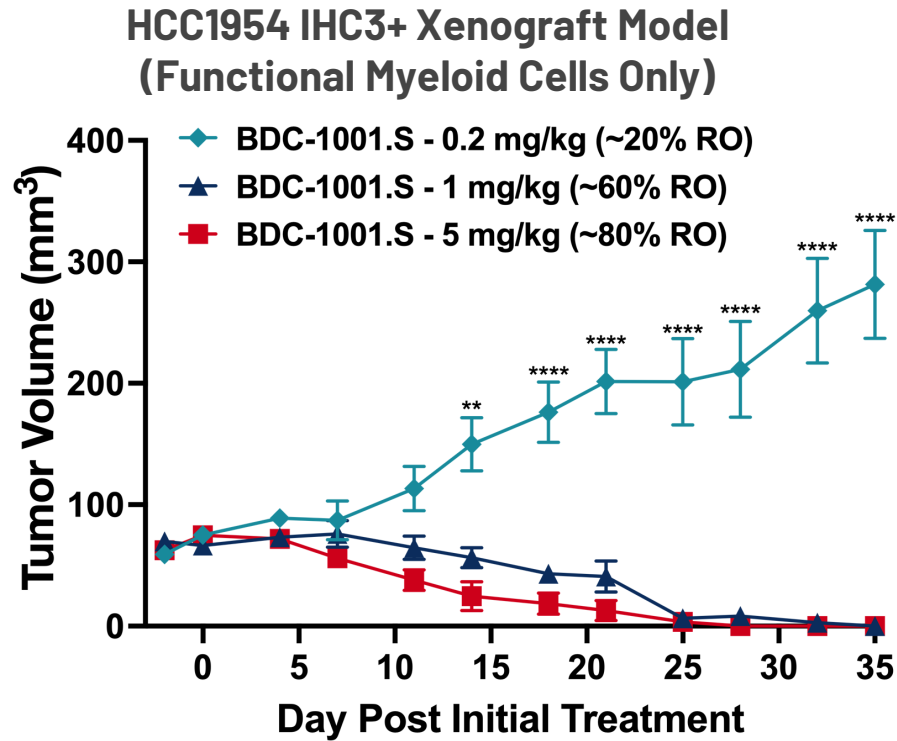
### Single ISAC Dose Mediates Tumor Regression





# BDC-1001 Exposure Hypothesis Emerged from Preclinical Data

## Targeting >10 µg/mL Trough Serum Concentration for Anti-tumor Activity



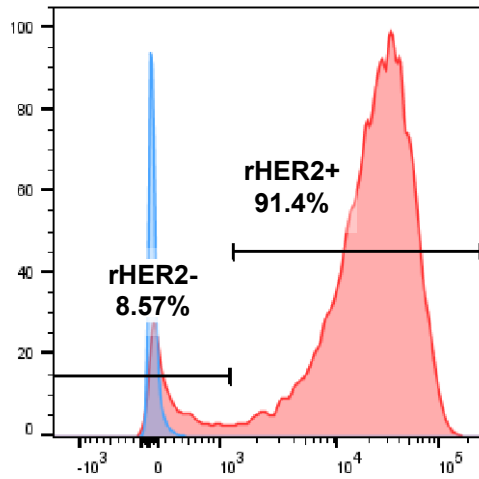
- Increases in proinflammatory cytokines & chemokines seen prior to tumor regression
- Levels of proinflammatory cytokines & chemokines in tumor much higher than serum
- Recruitment of dendritic cells & macrophages to tumor not seen with trastuzumab
- Anti-tumor activity requires sufficient target receptor occupancy, corresponding to a Cmin of >10 µg/mL

# Boltbody™ ISAC Induces Immune Memory that Extends to Tumors Lacking HER2

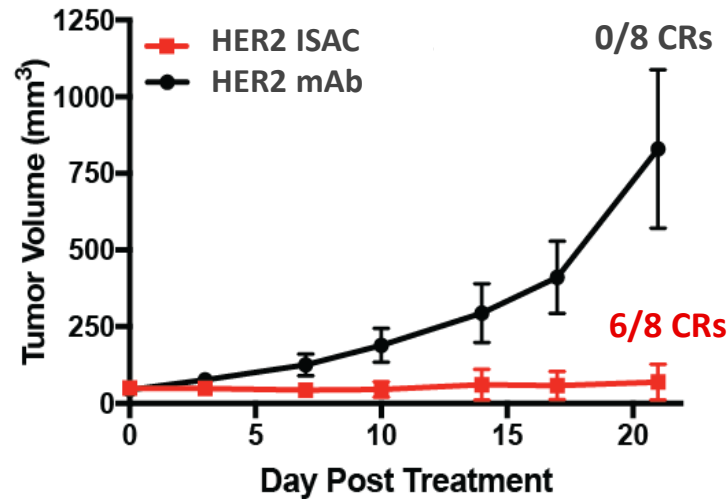
## Immunity Extends to Tumor Neoantigens through Epitope Spreading

### Heterogenous HER2+ Tumors 10% of Tumor Cells Lack HER2 Expression

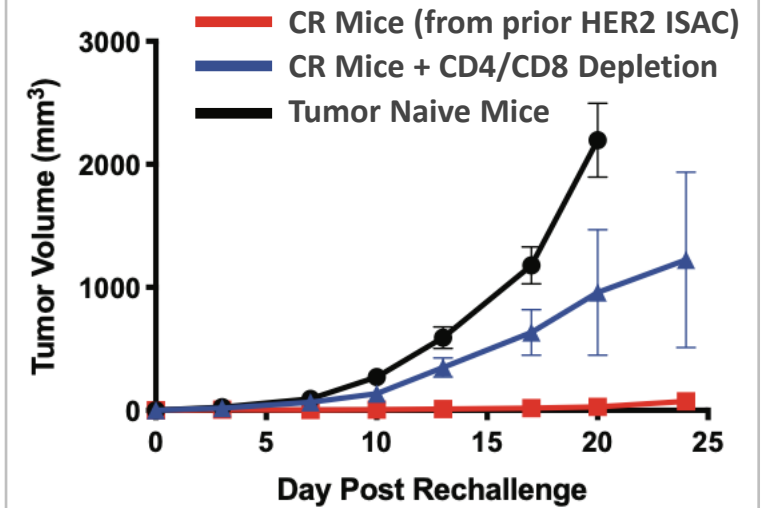
#### In Vivo rHER2 Expression



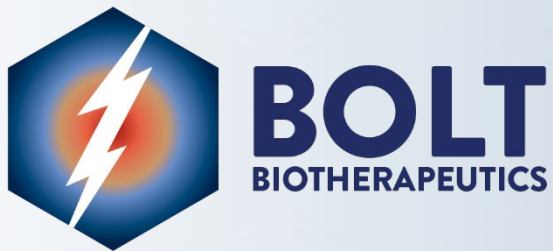
### Epitope Spreading with ISAC Clearance of Heterogenous Tumors in Mice



### Rechallenge with HER2<sup>neg</sup> CT26 Epitope Spreading Dependent on T Cells



## CT26-rHER2+ or CT26-rHER2<sup>neg</sup> Syngeneic Colorectal Cancer Models



## The combination of a trastuzumab ISAC and pertuzumab augments anti-tumor efficacy in multiple HER2+ tumor models relative to trastuzumab plus pertuzumab

Cecelia I. Pearson, Andrew Luo, Karla A. Henning, Anthony Lucas, David Omstead, Katelynn A. McEachin, Paul D. Ponath, Steven J. Chapin, Shelley E. Ackerman, Edith A. Perez, Han K. Kim, Michael N. Alonso

Bolt Biotherapeutics, Redwood City, CA



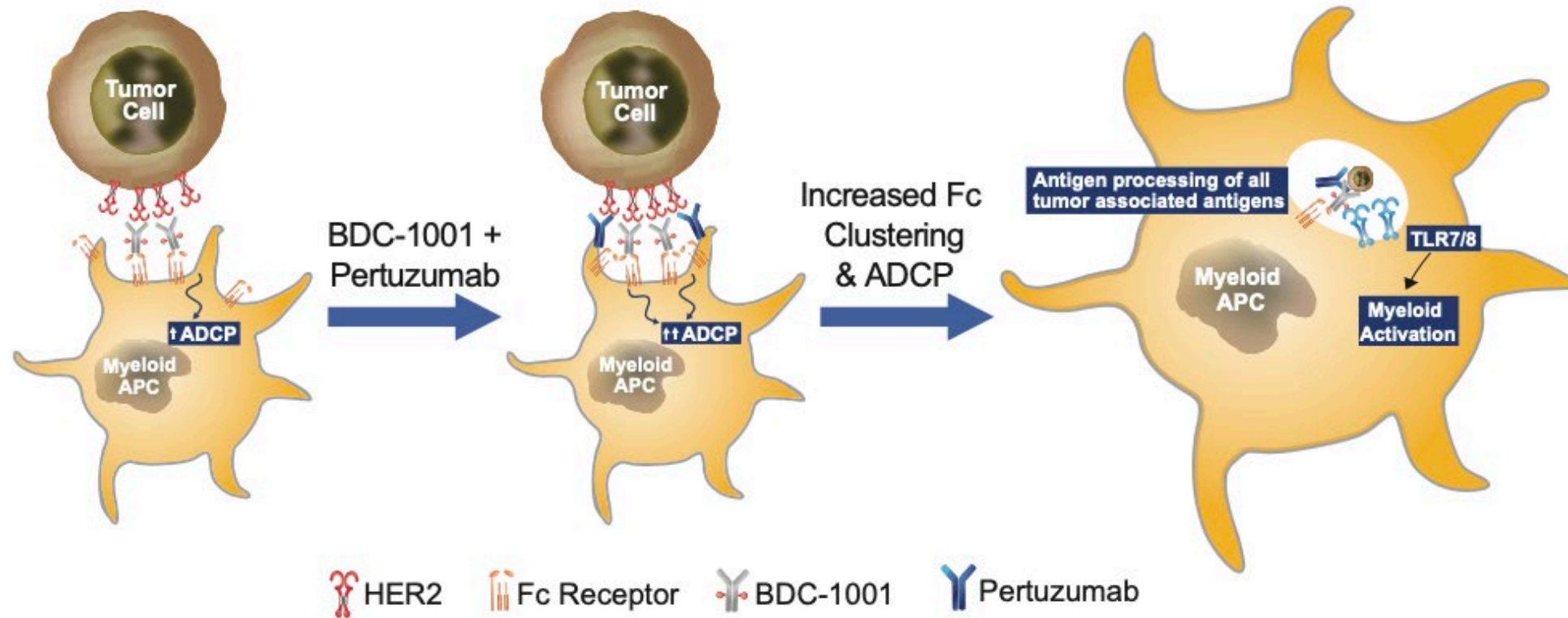
# Rationale for Combination of Pertuzumab with BDC-1001.S

- Combination of trastuzumab, pertuzumab, and chemotherapy is current standard of care for patients with HER2+ breast cancers
- Multiple mechanisms of action govern the activity of these two antibodies<sup>1</sup>
  - Direct binding to HER2 inhibits survival signals
  - Pertuzumab inhibits HER2 dimerization with HER3/EGFR
  - FcγR engagement drives antibody dependent cellular phagocytosis and cytotoxicity
  - Activation of the complement cascade induces complement dependent cytotoxicity
- The activity of BDC-1001.S is dependent on FcγR-mediated phagocytosis<sup>2</sup>
- Addition of pertuzumab to ISAC therapy may enhance anti-tumor efficacy by increasing Fc clustering and promoting phagocytosis

<sup>1</sup>Tsao et al. JCI Insight. 2022;7(6):e155636. <https://doi.org/10.1172/jci.insight.155636>.

<sup>2</sup>Ackerman et al. Nature Cancer 2021

# Proposed Mechanism of Action for Combination of Trastuzumab ISAC with Pertuzumab

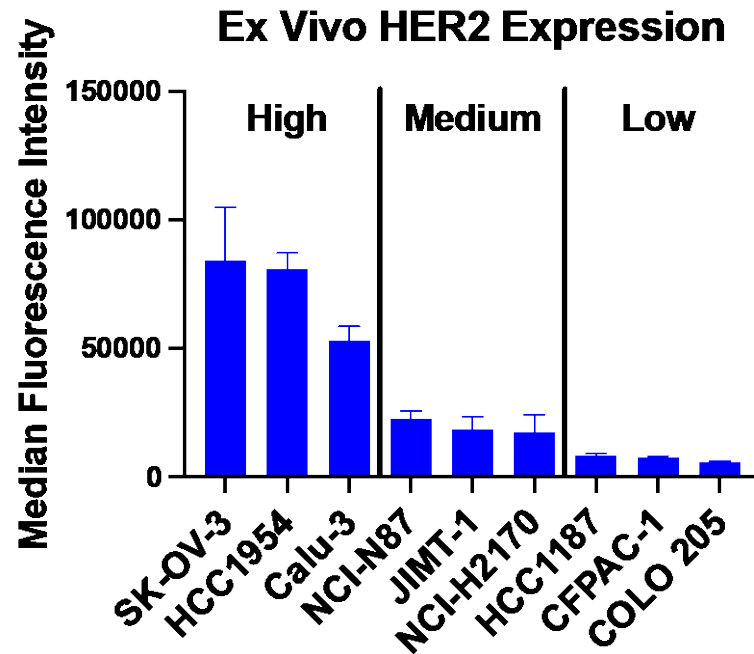


**Figure 1.** Combination of BDC-1001.S with Pertuzumab. ISACs mediate activation of myeloid APCs following binding of the targeted antigen and subsequent tumor engulfment via antibody-dependent cellular phagocytosis. Upon entering the myeloid cell, the ISAC mediates TLR7/8 activation. Addition of pertuzumab, which binds a distinct epitope of HER2, increases the number of bound antibodies to the tumor cell surface, increasing Fc clustering, which in turn increases Fc receptor-mediated phagocytosis. Schematic does not represent appropriate scale or binding dynamics.

# Selected Tumor Models Encompass HER2 High and Low Surface Expression








## 9 Different Tumor Models Investigated

Tumor Models	HER2 Status
HCC1954, SK-OV-3, Calu-3	HER2 <sup>High</sup>
JIMT-1, NCI-2170, NCI-N87	HER2 <sup>Medium</sup>
HCC1187, CFPAC-1, COLO 205	HER2 <sup>Low</sup>



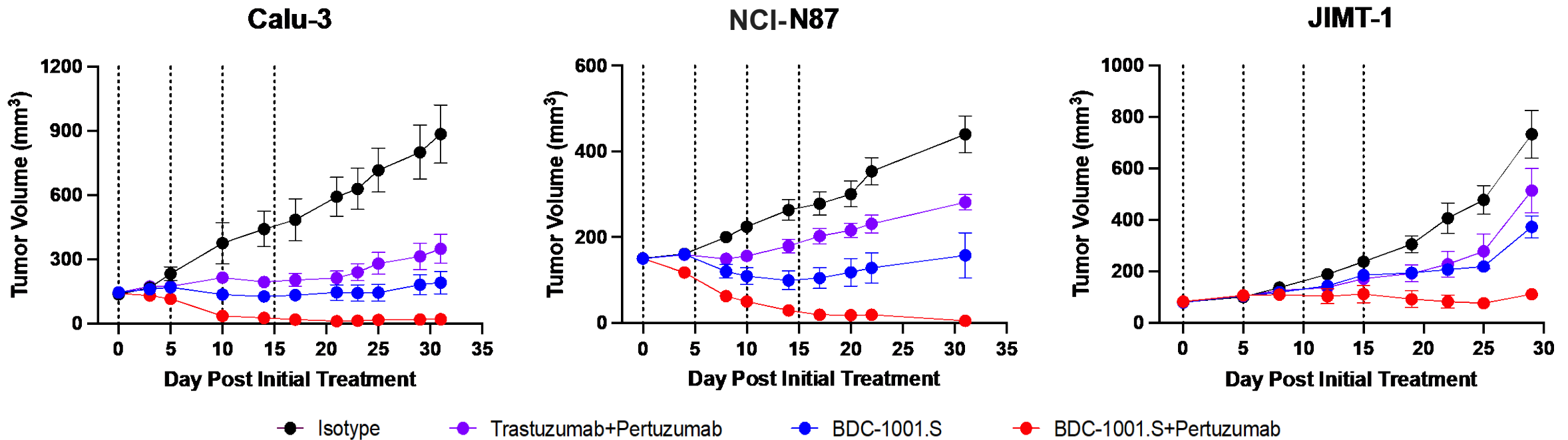
**Figure 2.** Surface expression of HER2 on the indicated tumors grown in SCID/beige mice was determined by flow cytometry. Upon reaching 100 mm<sup>3</sup>, tumors were isolated and dissociated to single cell suspensions to generate dissociated tumor cells (DTCs) (n=3-5 tumors per cell line). Cells were subsequently stained for tumor and immune cells using anti-HER2 antibody (clone 24D2) and anti-mouse CD45 antibody (clone 30F-11). HER2 expression on CD45<sup>-</sup> cells is expressed as median fluorescence intensity and is reported as mean with SEM (data are from one experiment and are representative of at least two experiments).

# Experimental Design: Efficacy of BDC-1001.S and Pertuzumab Combination

		Test Articles (with Dose Levels)			
		BDC-1001.S 1, 2, or 5 mg/kg	Trastuzumab 5 mg/kg	Pertuzumab 5 mg/kg	Isotype 5 or 10 mg/kg
Experimental Treatment Group	Isotype				
	BDC-1001.S Monotherapy				
	BDC-1001.S + Pertuzumab				
	Trastuzumab + Pertuzumab				

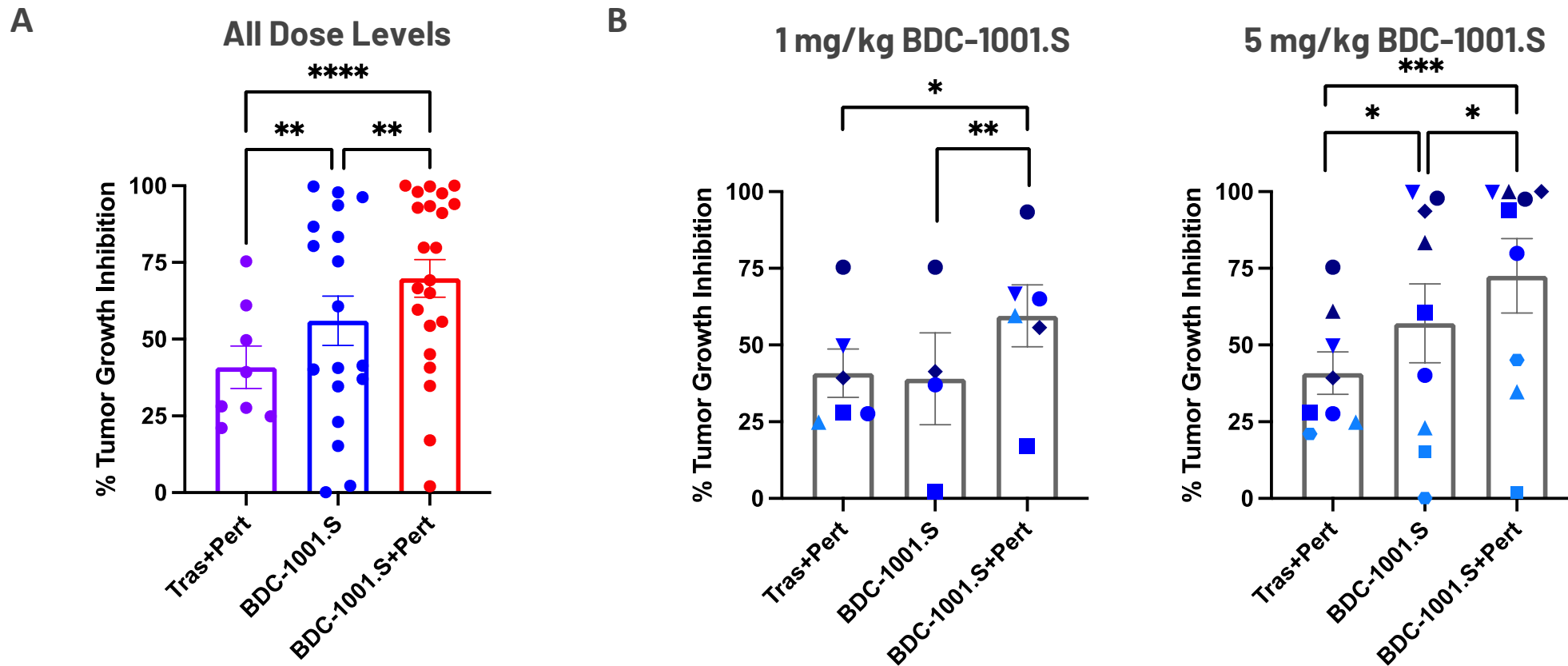
**Figure 3.** Tumor bearing SCID/beige mice (n=6 per group) were treated systemically with various doses of the indicated test articles q5dx4. Trastuzumab-T785 ISAC (BDC-1001.S) was administered at 1, 2 and/or 5 mg/kg, depending on the tumor model, with the isotype mAb administered at 10 mg/kg in the isotype group and 5 mg/kg in the BDC-1001.S monotherapy group. Percent Tumor Growth Inhibition (% TGI) was calculated relative to the Isotype group with the following formula:  $1 - (\text{AverageTV}_{\text{Treated}} / \text{AverageTV}_{\text{Control}}) * 100$ , where TV = tumor volume.

# Combination of BDC-1001.S and Pertuzumab Enhances In Vivo Anti-Tumor Efficacy



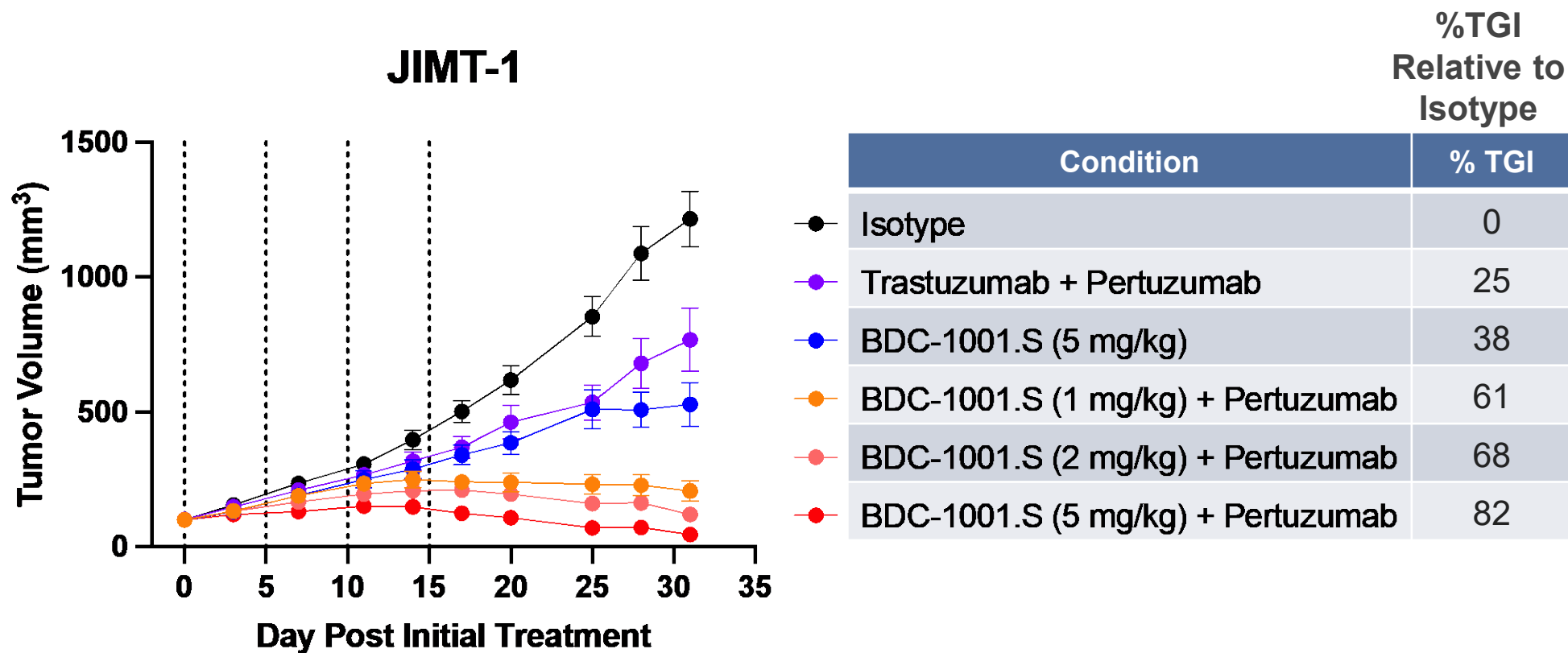
**Figure 4.** SCID/beige mice bearing the indicated HER2+ xenograft tumors (n=6 per group) were treated systemically with the indicated test articles q5dx4 (dashed lines). All test articles were dosed at 5 mg/kg, except in Calu-3 tumor-bearing mice, where BDC-1001.S and trastuzumab were dosed at 1 mg/kg. BDC-1001.S monotherapy was co-administered with an isotype control antibody. Data are shown as mean with SEM from one experiment and are representative of at least two experiments per tumor model.

# BDC-1001.S Combination with Pertuzumab Enhances Efficacy Across Multiple HER2-Expressing Models



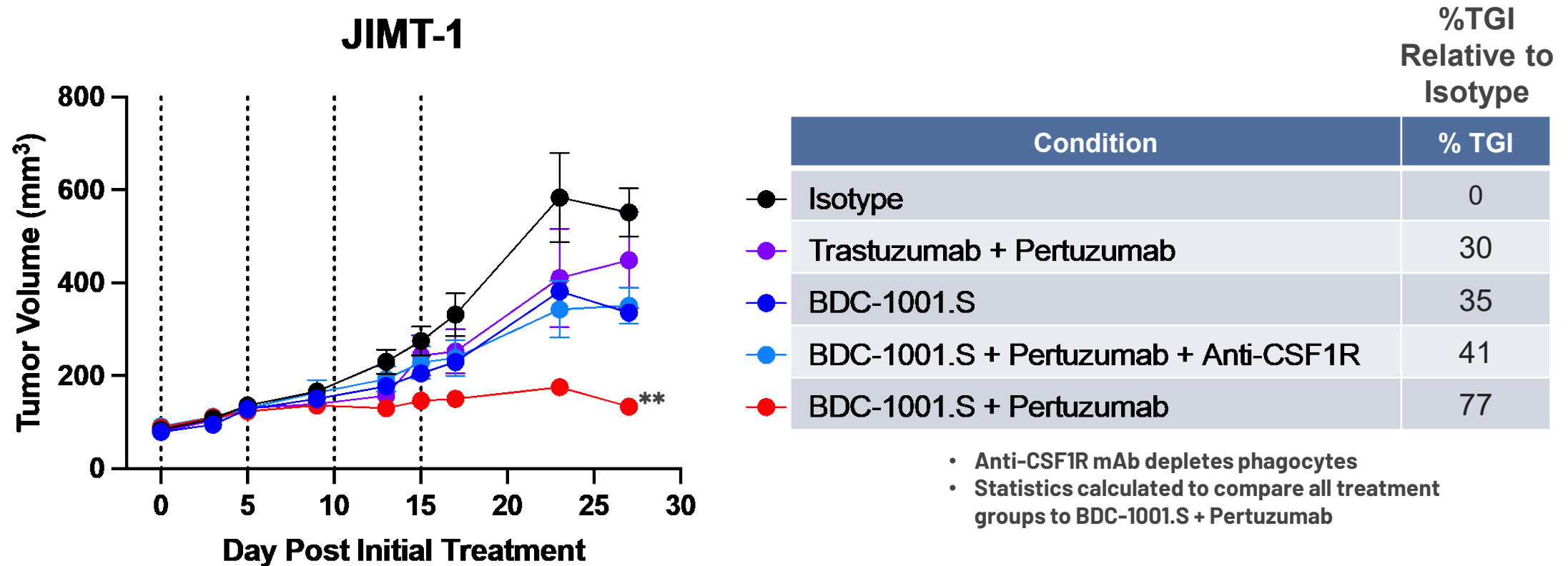
**Figure 5.** Tumor bearing SCID/beige mice (up to 9 different tumor models per condition, n=6 mice per group) were treated systemically with the following treatment conditions q5d<sub>x4</sub>: 5 mg/kg of BDC-1001.S with isotype antibody, 1, 2, or 5 mg/kg of BDC-1001.S with 5 m/kg pertuzumab, or with a combination of trastuzumab and pertuzumab at 5 mg/kg each. % TGI was calculated at Day 20-23 post-treatment relative to the isotype control (data not shown) using the following equation:  $1 - (\text{AverageTV}_{\text{treated}} / \text{AverageTV}_{\text{control}}) * 100$ . **A)** % TGI shown as aggregate data for all dose levels tested. \*, p<0.05; \*\*, p<0.01; \*\*\*, p<0.001; \*\*\*\*, p<0.0001 by two-way ANOVA. **B)** % TGI shown for the indicated conditions with BDC-1001.S administered at 1 or 5 mg/kg. \*, p<0.05; \*\*, p<0.01; \*\*\*, p<0.001 by paired t-test. Each symbol represents a unique tumor model, with red symbols: HER2<sup>High</sup>; blue symbols: HER2<sup>Medium</sup>; green symbols: HER2<sup>Low</sup>.

# BDC-1001.S Combination with Pertuzumab May Lower BDC-1001.S Dose Threshold for Efficacy



**Figure 6.** SCID/beige mice bearing JIMT-1 tumors (n=6 per group) were treated systemically with the indicated test articles q5dx4 (dashed lines). BDC-1001.S was administered at 1, 2 or 5 mg/kg in combination with 5 mg/kg pertuzumab. Pertuzumab and trastuzumab were each administered at 5 mg/kg, while the isotype was administered at 10 mg/kg. BDC-1001.S monotherapy was co-administered with an isotype control antibody. % TGI is calculated on Day 20 relative to isotype. Data are shown as mean with SEM from one experiment and are representative of three experiments.

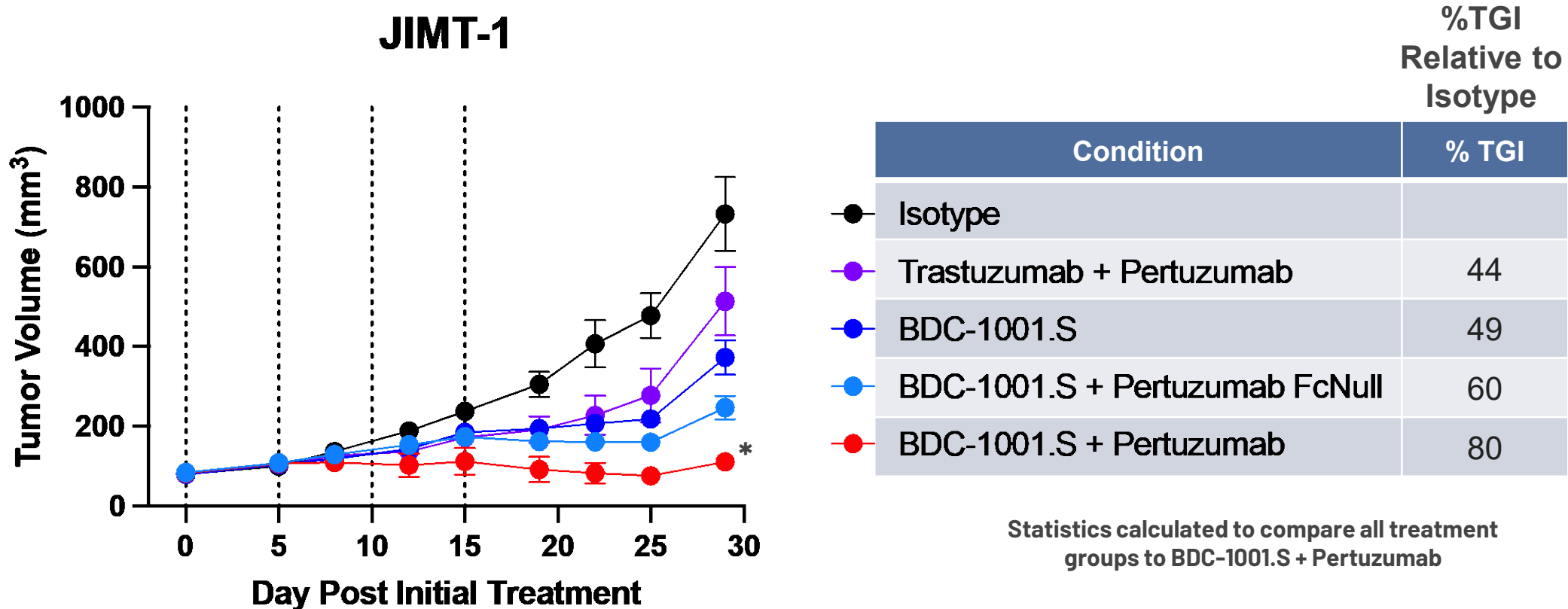
# Phagocytes Mediate Enhanced Efficacy in BDC-1001.S + Pertuzumab Combination



**Figure 7.** SCID/beige mice bearing JIMT-1 tumors were administered anti-CSF1R or IgG2a isotype antibody at 200 ug per mouse bi-weekly 2 weeks prior to treatment and continuing for the study duration to deplete phagocytes. >90% depletion of CD11c+F4/80+ phagocytes and ~50% depletion of Ly6C+ monocytes observed in the tumor at time of initial treatment. Mice were systemically treated with indicated test articles q5d x 4. BDC-1001.S was administered at 2 mg/kg while trastuzumab and pertuzumab were administered at 5 mg/kg and isotype was administered at 10 mg/kg. BDC-1001.S monotherapy was co-administered with an isotype control antibody at 5 mg/kg. % TGI is calculated on Day 23 relative to isotype. Data are shown as mean with SEM and are from one experiment. To compare all treatment groups to BDC-1001.S + Pertuzumab, statistics were determined by an ordinary two-way ANOVA across all time points with Dunnett’s multiple comparisons test. \*\*, p<0.01.



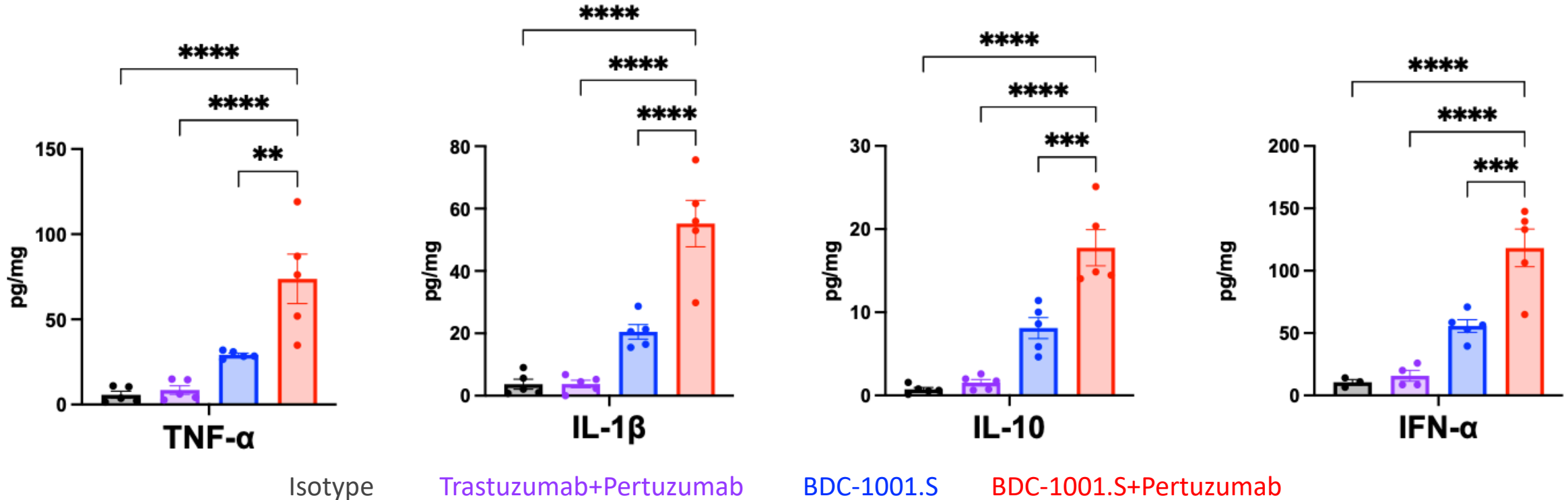
# Pertuzumab Fc-Effector Function is Required for Enhanced Anti-Tumor Activity



**Figure 8.** SCID/beige mice bearing JIMT-1 tumors (n=5 per group) were treated systemically with the indicated test articles q5dx4 at 5 mg/kg, except isotype which was administered at 10 mg/kg. Pertuzumab-FcNull is a variant of pertuzumab generated with a non-functional Fc region (mutations D265A and N297A). BDC-1001.S monotherapy was co-administered with an isotype control antibody at 5 mg/kg. % TGI is calculated on Day 22 relative to isotype. To compare all treatment groups to BDC-1001.S + Pertuzumab, statistics were determined by an ordinary two-way ANOVA across all time points with Dunnett's multiple comparisons test. \*, p<0.05. Data are shown as mean with SEM and are from one experiment.

# BDC-1001.S and Pertuzumab Combination Enhances Cytokine Secretion in Tumor

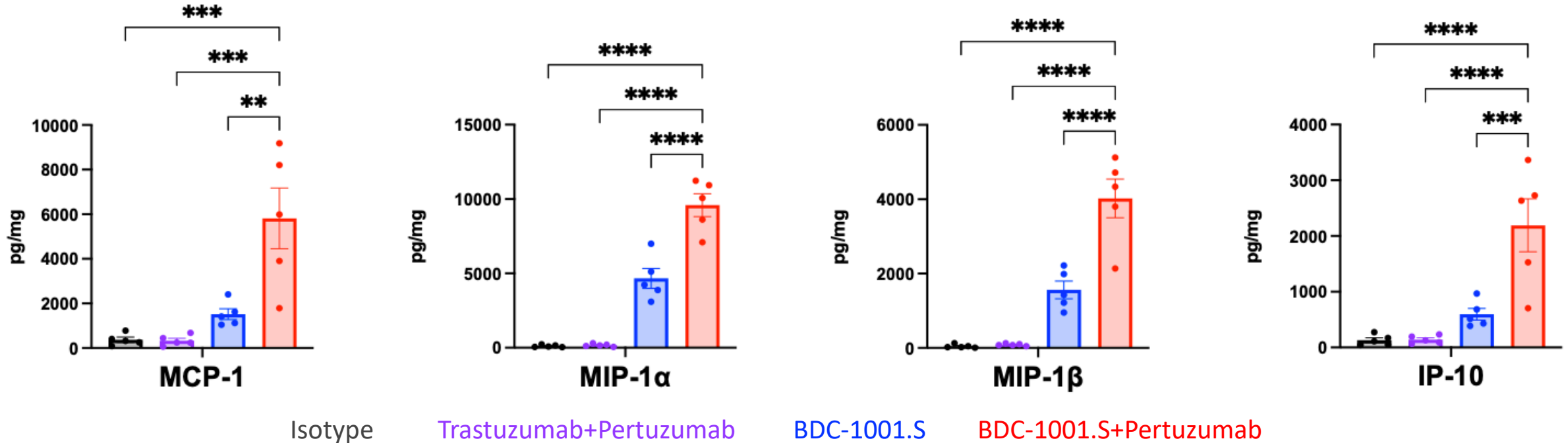
## Innate Immune Activation



**Figure 9.** SCID/beige mice bearing JIMT-1 tumors (n=5 per group) were treated systemically with the indicated test articles q5dx2 at 5 mg/kg, except isotype which was administered at 10 mg/kg. 24 hours after the second dose on Day 6, tumors were isolated and processed into protein lysates. Cytokine levels were measured by multiplex ELISA. Statistics were determined by one-way ANOVA relative to the BDC-1001.S+pertuzumab group; \* p<0.05; \*\* p<0.01; \*\*\* p<0.001; \*\*\*\* p<0.0001. Data are shown as mean with SEM and are from one experiment.

# BDC-1001.S and Pertuzumab Combination Enhances Chemokine Secretion in Tumor

## Myeloid Recruitment



**Figure 10.** SCID/beige bearing JIMT-1 tumors (n=5 per group) were treated systemically with the indicated test articles q5dx2 at 5 mg/kg, except isotype which was administered at 10 mg/kg. 24 hours after the second dose on Day 6, tumors were isolated and processed into protein lysates. Chemokine levels were measured by multiplex ELISA. Statistics were determined by one-way ANOVA relative to the BDC-1001.S+pertuzumab group; \* p<0.05; \*\* p<0.01; \*\*\* p<0.001; \*\*\*\* p<0.0001. Data are shown as mean with SEM and are from one experiment.

# Conclusions

- Combination of BDC-1001.S and pertuzumab significantly enhances anti-tumor efficacy in multiple HER2-expressing tumor models
- Addition of pertuzumab provides an additional source of “eat me” signals that likely enhances antibody-dependent cellular phagocytosis
- Anti-tumor efficacy was dependent on antibody-dependent cellular phagocytosis as depletion of phagocytes or the use of a pertuzumab variant lacking Fc effector function reduced efficacy
- This combination is being assessed in a multi-national randomized Phase 2 clinical trial with BDC-1001 and pertuzumab in patients with metastatic HER2+ breast cancer (NCT05954143) who have received prior treatment with Enhertu

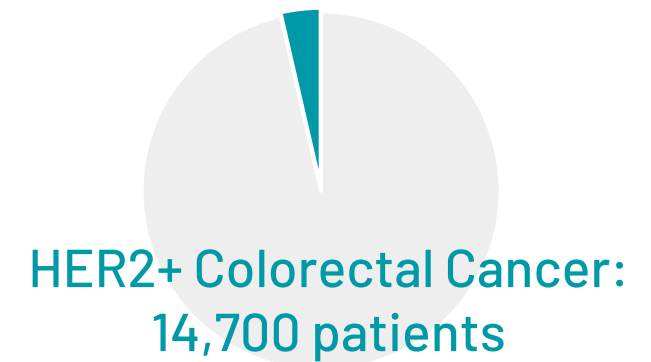
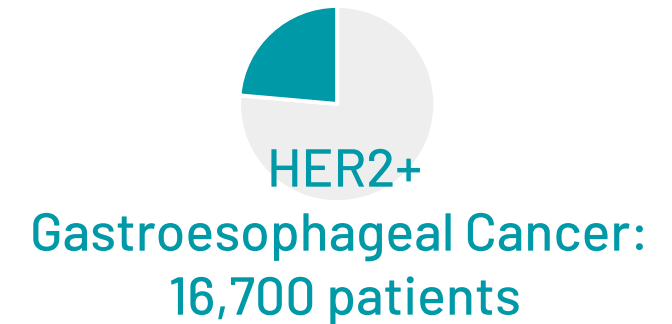
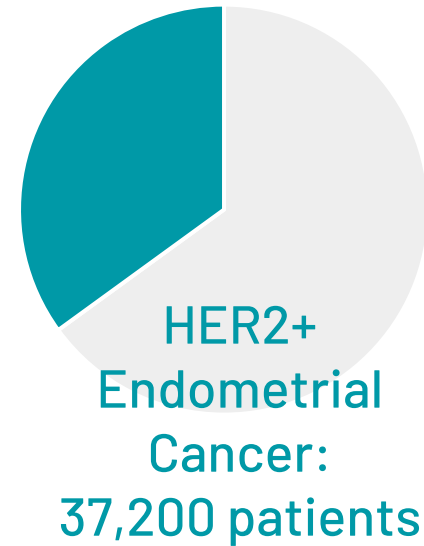
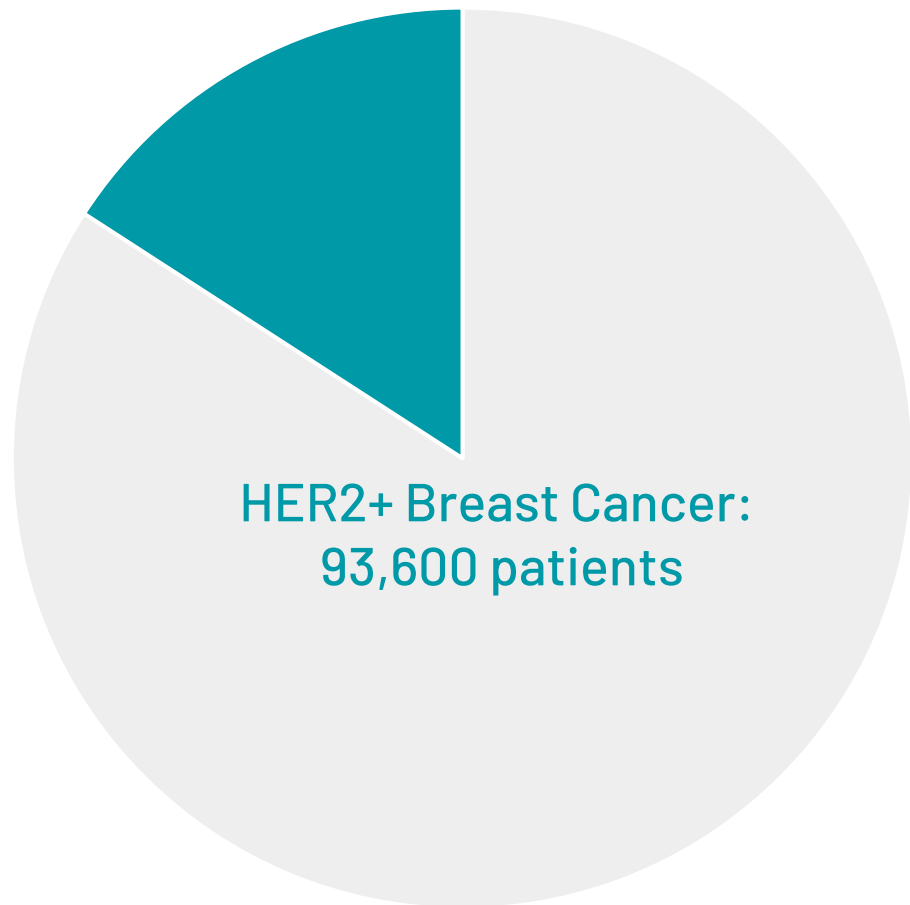


**BOLT**  
BIOTHERAPEUTICS

## BDC-1001 Commercial Considerations

# Significant Unmet Needs Exist for Patients with HER2-Positive Tumors

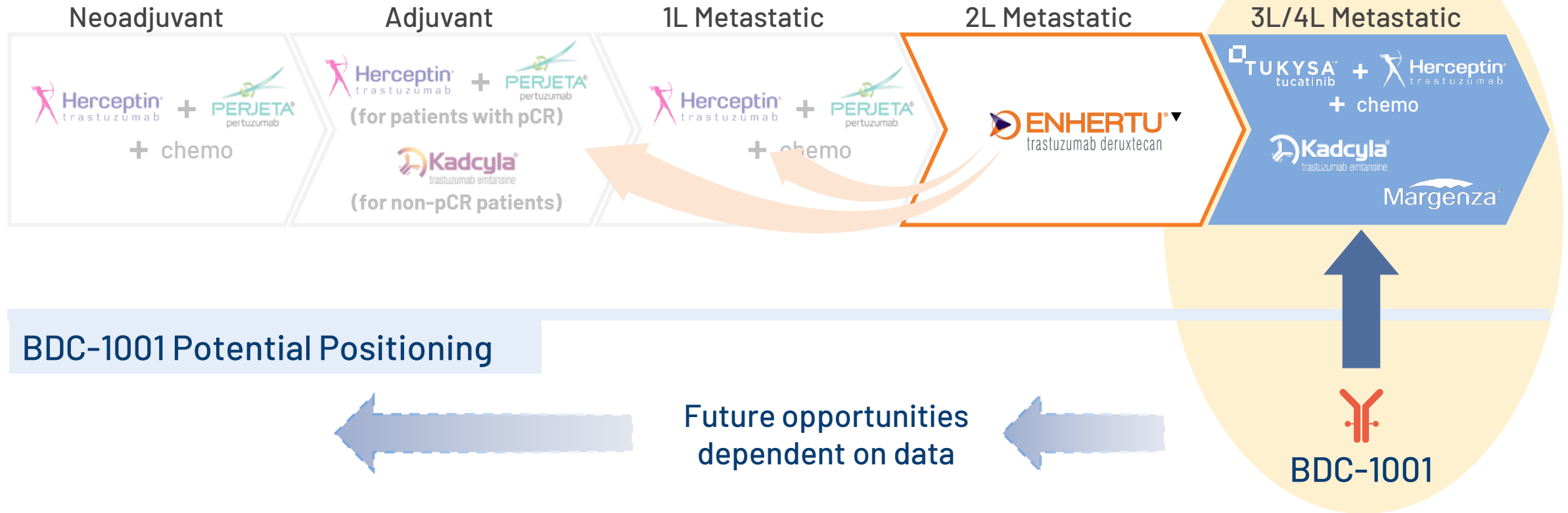
## Newly Diagnosed Patients in 2022



# BDC-1001: Initially Targeting Post-Enhertu® Opportunity, with Future Plans to Expand to Adjuvant/Neoadjuvant

HER2+ Breast Cancer

## HER2+ Breast Cancer (Standard of Care/Current Key Options)



# BDC-1001: Opportunity to be First HER2-Targeted Therapy in Endometrial Cancer

HER2+ Endometrial

## HER2+ Endometrial Cancer (Standard of Care/Current Key Options)

1L Metastatic

No anti-HER2 therapy approved  
(NCCN: Herceptin + chemo)

2L+ Metastatic

No anti-HER2 therapy approved.  
Re-treatment with Herceptin + chemo is the recommended option, specifically for serous carcinoma subtype

BDC-1001 Potential Positioning



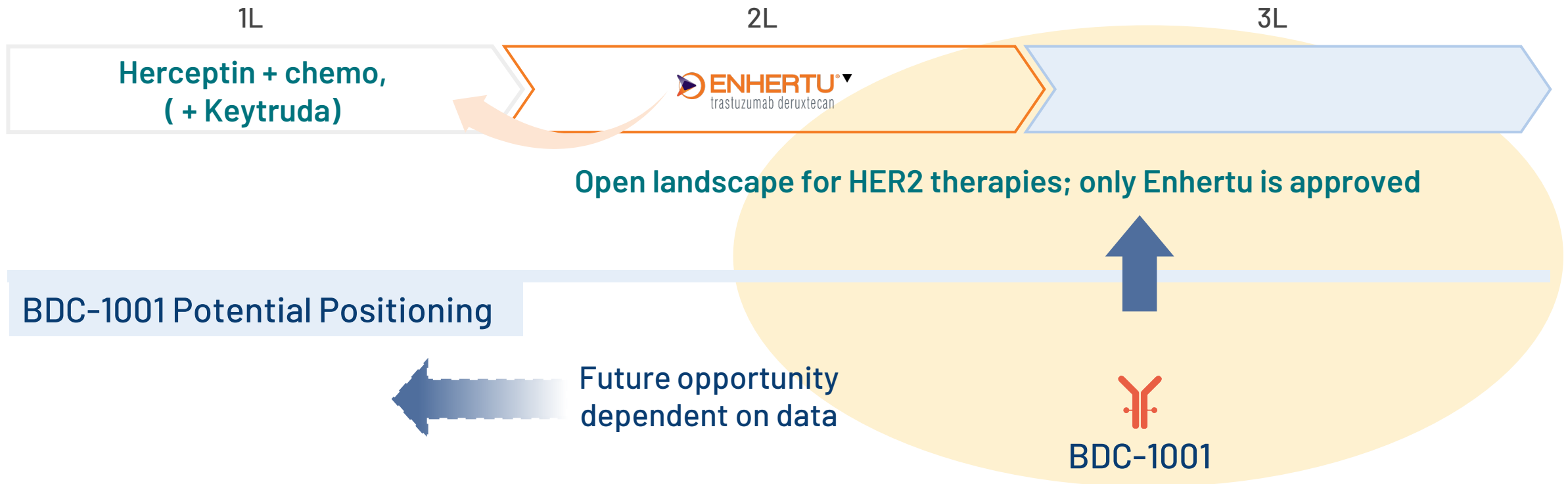
BDC-1001



# BDC-1001: Potential to Capitalize on Growing Role of Next-generation HER2 Therapies in Gastroesophageal Cancer

HER2+ Gastric

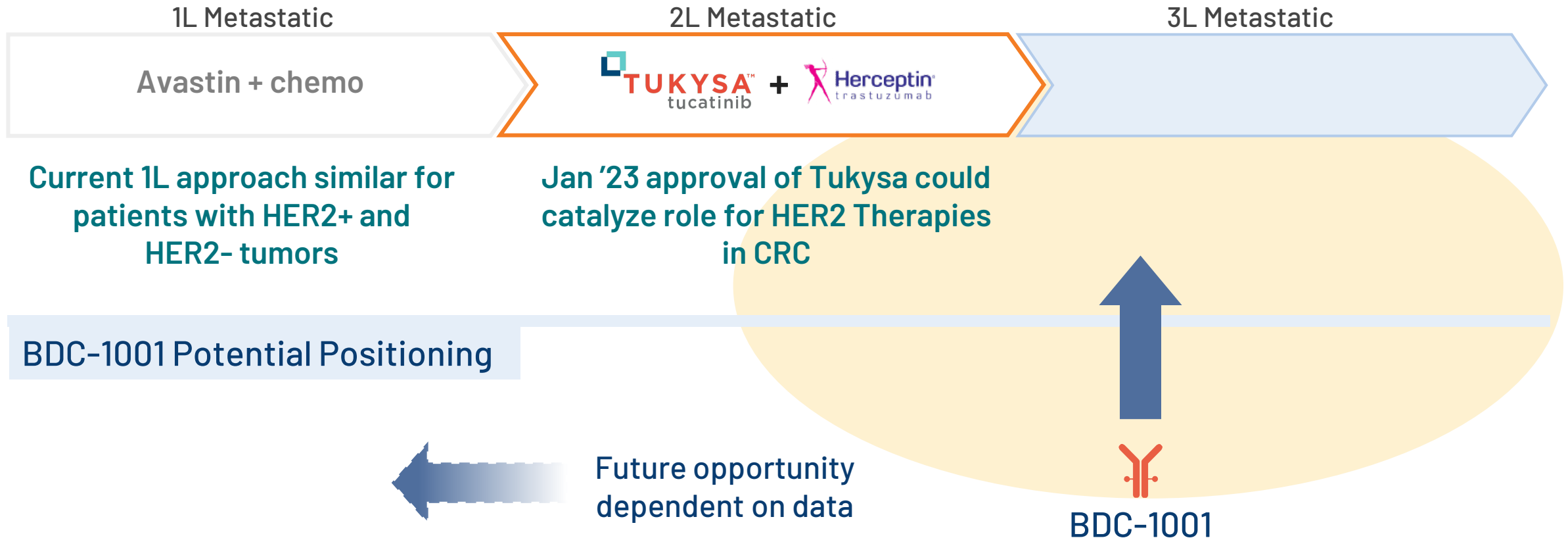
## HER2+ Gastroesophageal Cancer (Standard of Care/Current Key Options)



# BDC-1001: Capitalize on Emerging Opportunity for HER2 Therapies in CRC

HER2+ Colorectal

## HER2+ Colorectal Cancer (Standard of Care/Current Key Options)





**BOLT**  
BIOTHERAPEUTICS

Thank You