BDC-1001 Interim Clinical Data

ESMO Immuno-Oncology 2021

December 2021

Today's Agenda

Randall Schatzman, Ph.D.
Chief Executive Officer

Introduction &
Closing Remarks

David Dornan, Ph.D.
Chief Scientific Officer

Review of BDC-1001
Mechanism & Preclinical Data

Edith A. Perez, M.D.
Chief Medical Officer

BDC-1001 Interim Results
Presented at
ESMO Immuno-Oncology 2021

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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 ability to achieve upcoming milestones for our product candidates and the success and results of our pipeline programs, 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 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, 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, 2020. 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.

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BDC-1001 Dose Escalation Study Continues

Favorable Safety Profile	• Recommended Phase 2 Dose (RP2D) not yet reached • BDC-1001 has demonstrated favorable safety & tolerability to date • No DLTs at dose levels up to 20 mg/kg q3w or 12 mg/kg q2w
PK/PD Insights Consistent with Mechanism	• Drug half-life shorter than expected: ~3 days • Tumor microenvironment & plasma biomarker changes consistent with MOA • No evidence of anti-drug antibody formation
Early Signs of Clinical Disease Control	• Early signs of disease control noted, even below target exposure level • Disease control (SD or PR) noted in 13/40 evaluable subjects in multiple tumor types • Durability: 6 patients with stable disease >12 weeks; PR maintained through 52 weeks
Dose Escalation Continues	• Data point to the need for increased drug exposure in patients to optimize benefit • Updated human PK model predicts achieving threshold exposure with weekly dosing

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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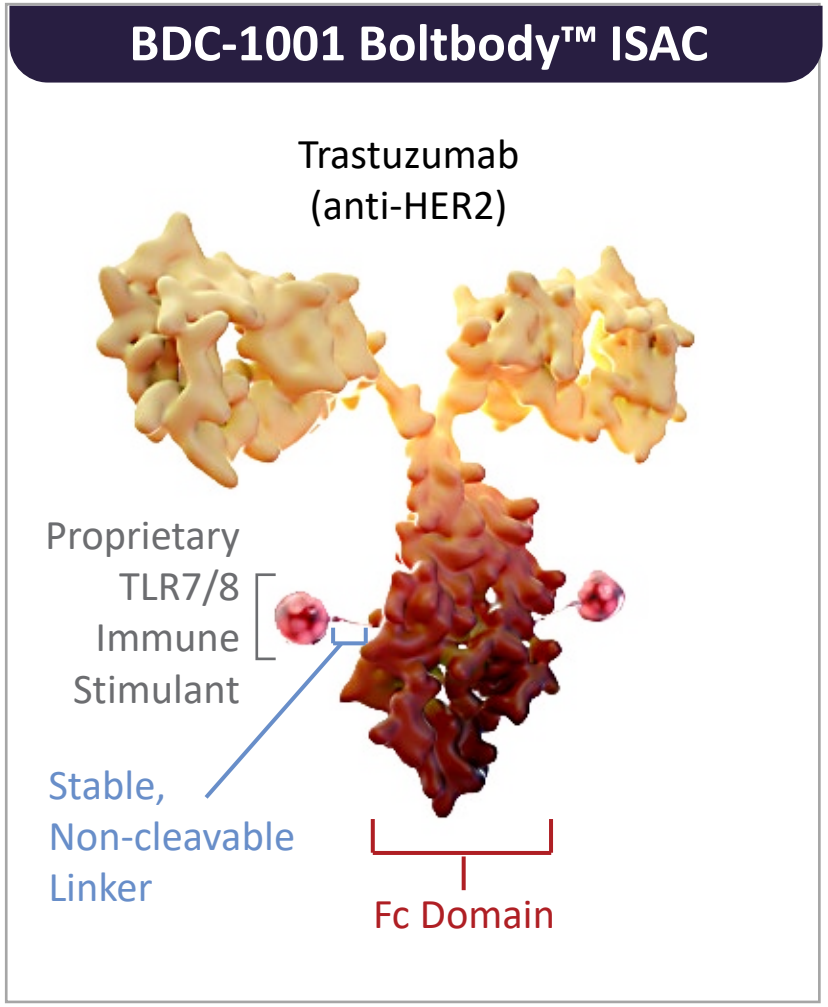
Review of BDC-1001 Mechanism & Preclinical Data

BDC-1001: Key Features Combine to Deliver Unique MOA



Key structural features:

- Targeting: Trastuzumab (anti-HER2) biosimilar
- ADCP engagement via antibody Fc domain
- Stable, non-cleavable linker
- Proprietary TLR 7/8 immune stimulant

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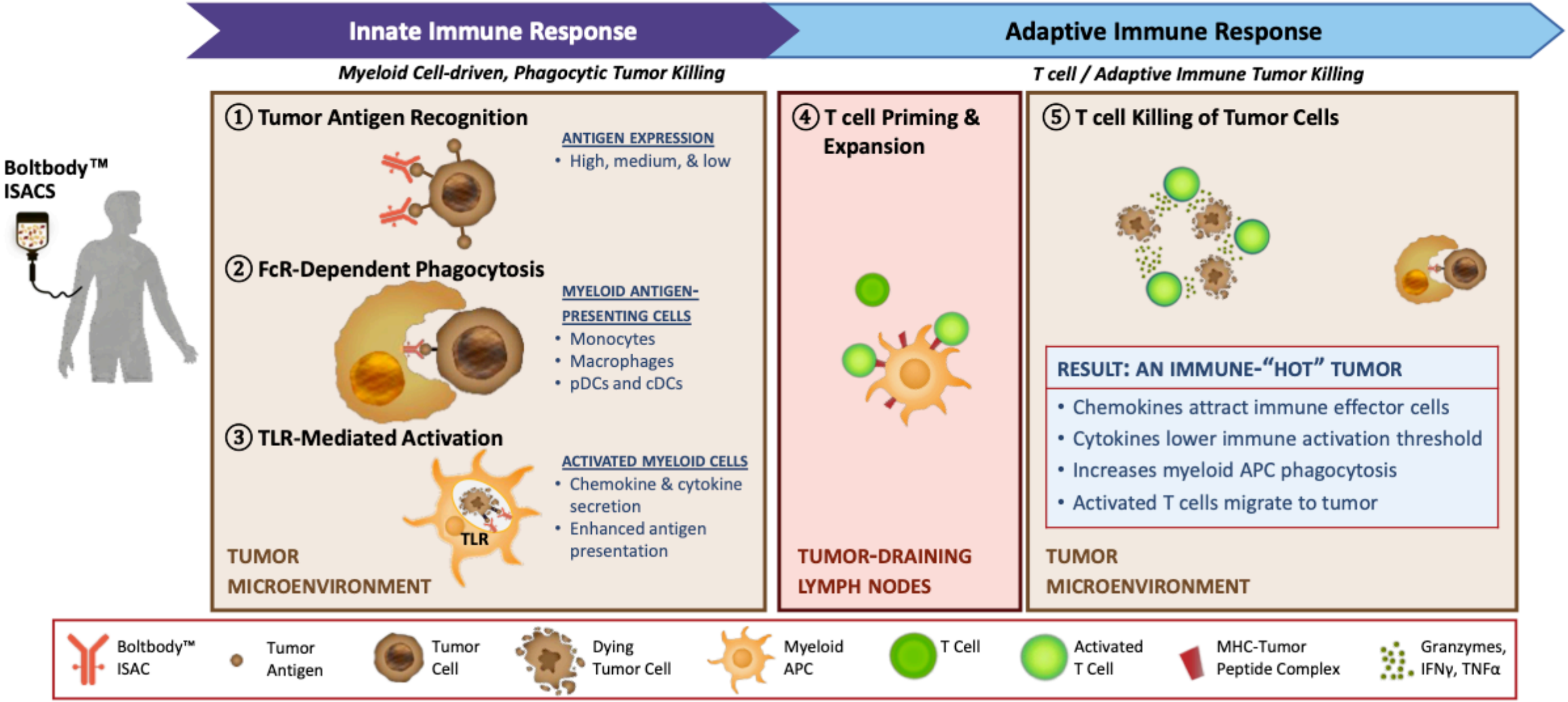
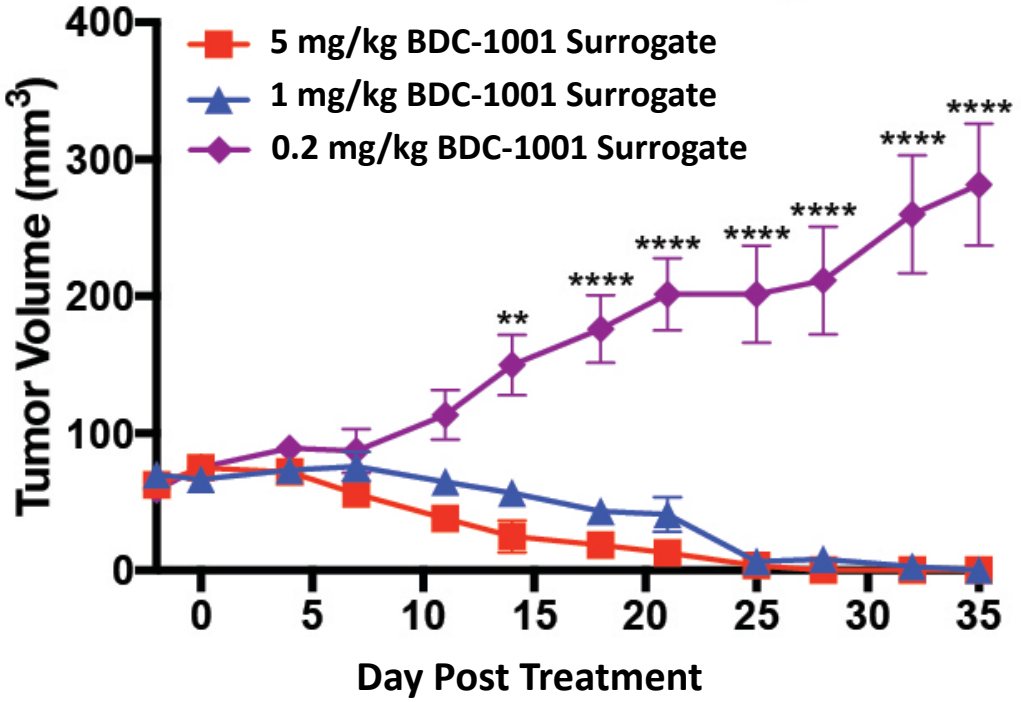
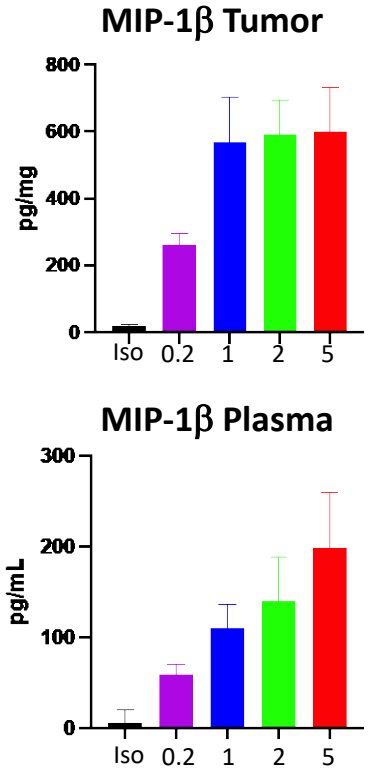
Hallmarks of Boltbody™ ISAC Platform

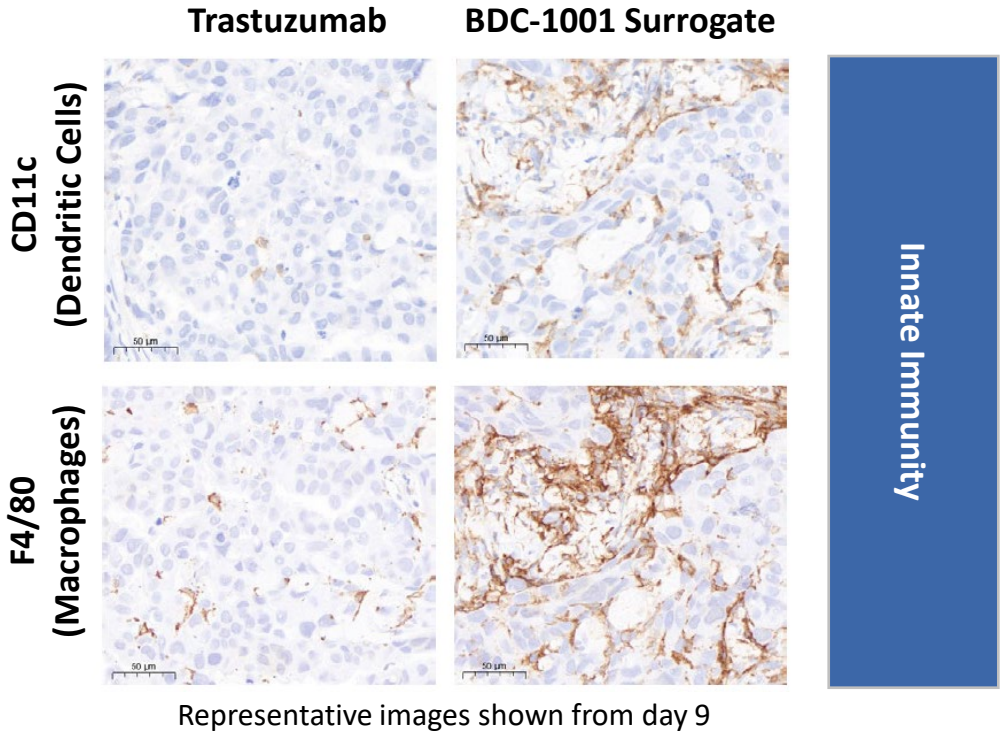


BDC-1001 Surrogate Shows Dose-Dependent Efficacy and Pharmacodynamic Responses

HCC1954 IHC3+ Xenograft Model (Functional Myeloid Cells Only)







Representative images shown from day 9

Efficacy:

Preclinical experiments indicate a minimal target serum concentration of **~16 μg/ml** at trough for optimal efficacy

Pharmacodynamic biomarkers:

- Increases in proinflammatory cytokines and chemokines in the tumor; modest increases in serum
- Recruitment of dendritic cells and macrophages to the tumor

SCID/Beige mice were dosed with BDC-1001 surrogate every 5 days through day 25 with cytokines and myeloid infiltration measured 24 hours or 9 days following the first dose, respectively. Representative figures are from independent experiments.

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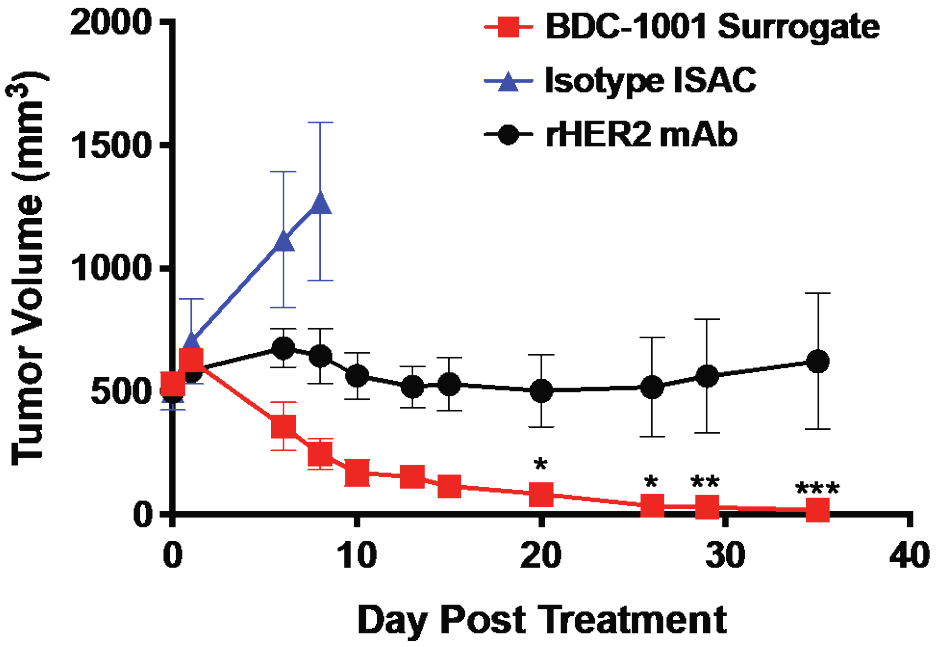
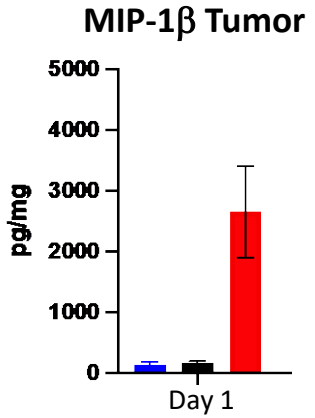
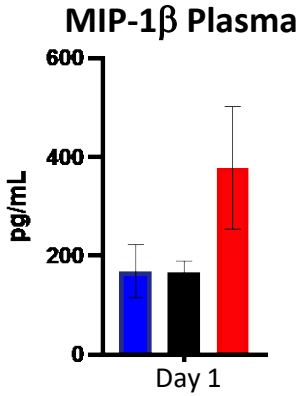
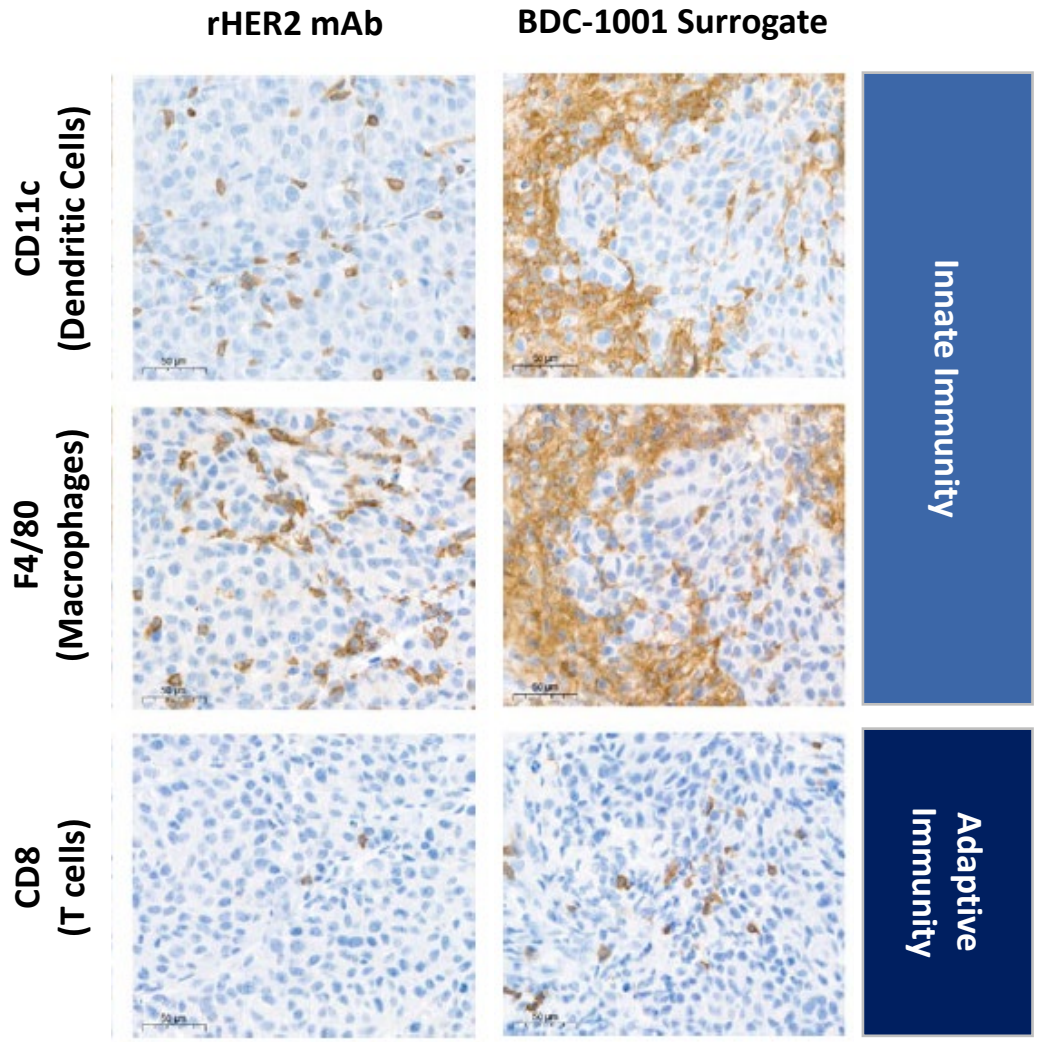
BDC-1001 Surrogate Engages Innate and Adaptive Immune Responses

MMC rHER2 Syngeneic Model (Fully Immune-Competent)









Representative images shown from day 6

Pharmacodynamic biomarkers:

- Increases in proinflammatory cytokines and chemokines in the tumor; modest elevation of serum cytokines and chemokines
- Recruitment of dendritic cells, macrophages & T cells to the tumor

FVB Erbb2 mice were dosed systemically with BDC-1001 surrogate on days 0 and 5 with cytokines and myeloid infiltration measured 24 hours or 6 days following the first dose, respectively. Representative figures are from independent experiments

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BDC-1001 Interim Results

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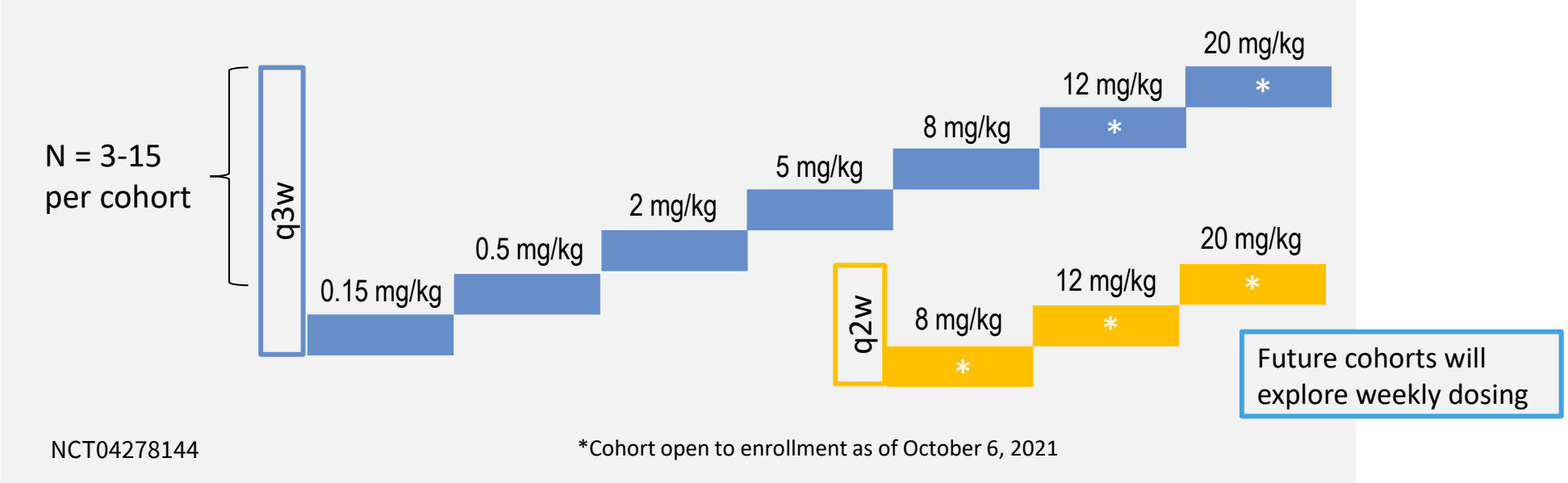
BDC-1001 Monotherapy Dose Escalation Design of Ongoing Phase 1/2



Primary Objectives	Safety and tolerability; recommended Phase 2 dose (RP2D) selection
Other Objectives	Pharmacokinetics, preliminary anti-tumor activity, plasma and tissue biomarkers to explore proof of mechanism
Key Eligibility	Any HER2-expressing solid cancer: • HER2 IHC2+/3+ or • HER2-amplified

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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BDC-1001 Ongoing Phase 1/2 Demographics and Baseline Characteristics

	All Subjects (N=57)
Median age, years (range)	64 (30, 84)
Sex, n (%)	
Female	33 (58)
Male	24 (42)
ECOG PS at baseline, n (%)	
0	17 (30)
1	40 (70)
Number of prior anti-cancer regimens, median (range)	4 (1, 11)
Subjects with prior anti-HER2 therapy (%)	45 (79)
HER2 categories, n (%)	
HER2 IHC3+	31 (54)
HER2 IHC2+	13 (23)
IHC2+ & ISH- or unknown	5
HER2 amplified* (ISH or NGS)	22 (39)
Tumor types, n (%)	
Gastroesophageal	18 (32)
Colorectal (CRC)	13 (23)
Breast	9 (16)
Endometrial	6 (10.5)
Cervix	2 (3.5)
Ovarian	2 (2.5)
Salivary duct	2 (3.5)
Other (Bladder, Biliary, Lung, Pancreas, Melanoma)	1 ea (9)

*Some subjects' tumors are both IHC 2+ or 3+ and NGS amplified

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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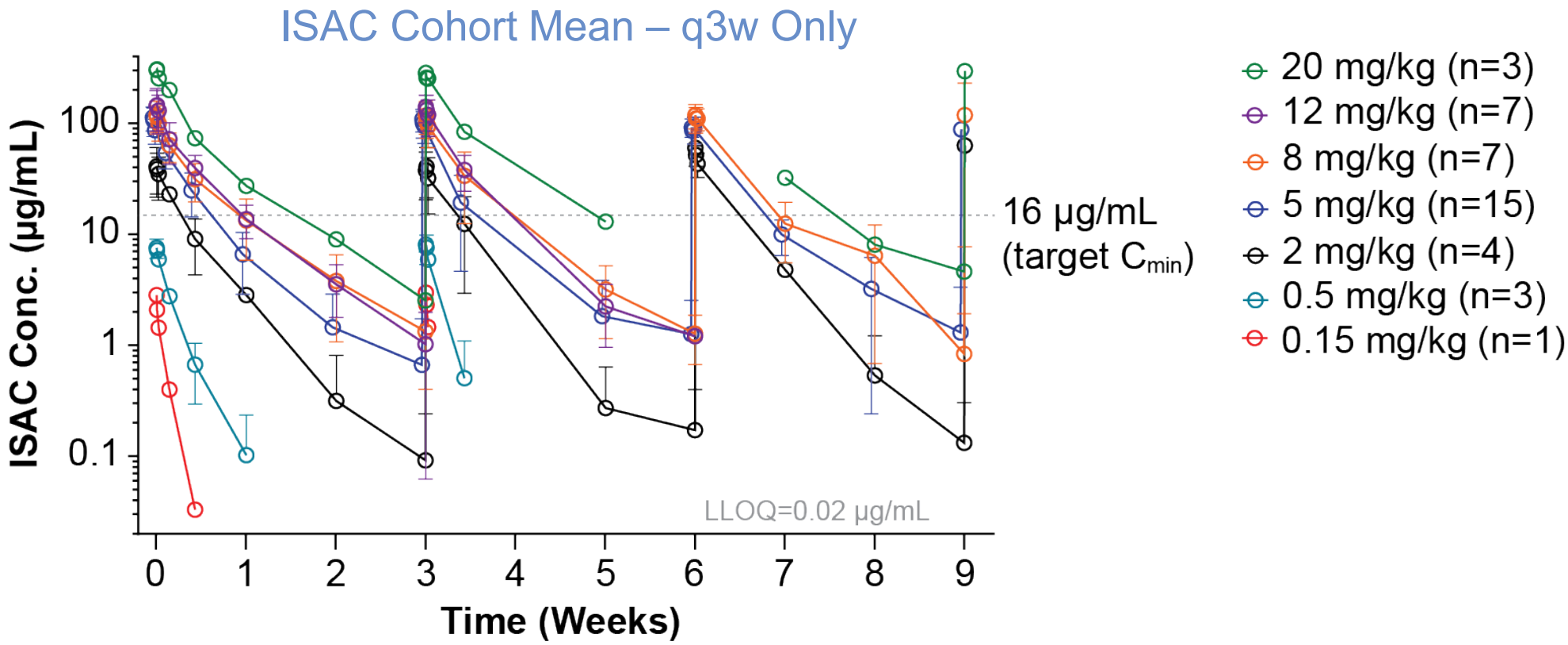
BDC-1001 Overall Safety Summary

- Consistent with BDC-1001's design, this agent has demonstrated good safety and tolerability at doses tested to date
  - No DLTs observed to date; MTD has not been reached at up to 20 mg/kg q3w or 12mg/kg q2w dose levels
- Two treatment-related SAEs, both of which led to treatment discontinuation
  - Asymptomatic Grade 3 ejection fraction decrease (>20%) after 4 cycles of therapy in an anti-HER2 therapy naïve subject with history of hypertension
  - Grade 4 bronchopulmonary hemorrhage in a subject who had a lung biopsy 5d prior to treatment
- Grade 1/2 infusion-related reactions (IRRs) occurred in 11 subjects starting at the 5mg/kg q3w cohort; none related to treatment discontinuation
  - Non-steroid pre-medication introduced at the 8 mg/kg dose level
- No AEs consistent with cytokine release syndrome (CRS) reported

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

BDC-1001 Demonstrates Rapid Clearance; No Evidence of Anti-drug Antibody (ADA) Formation



- No subjects (0/53) developed antibodies to BDC-1001 after treatment was initiated
  - 2/53 (3.8%) subjects were found to have pre-existing antibodies reactive to BDC-1001

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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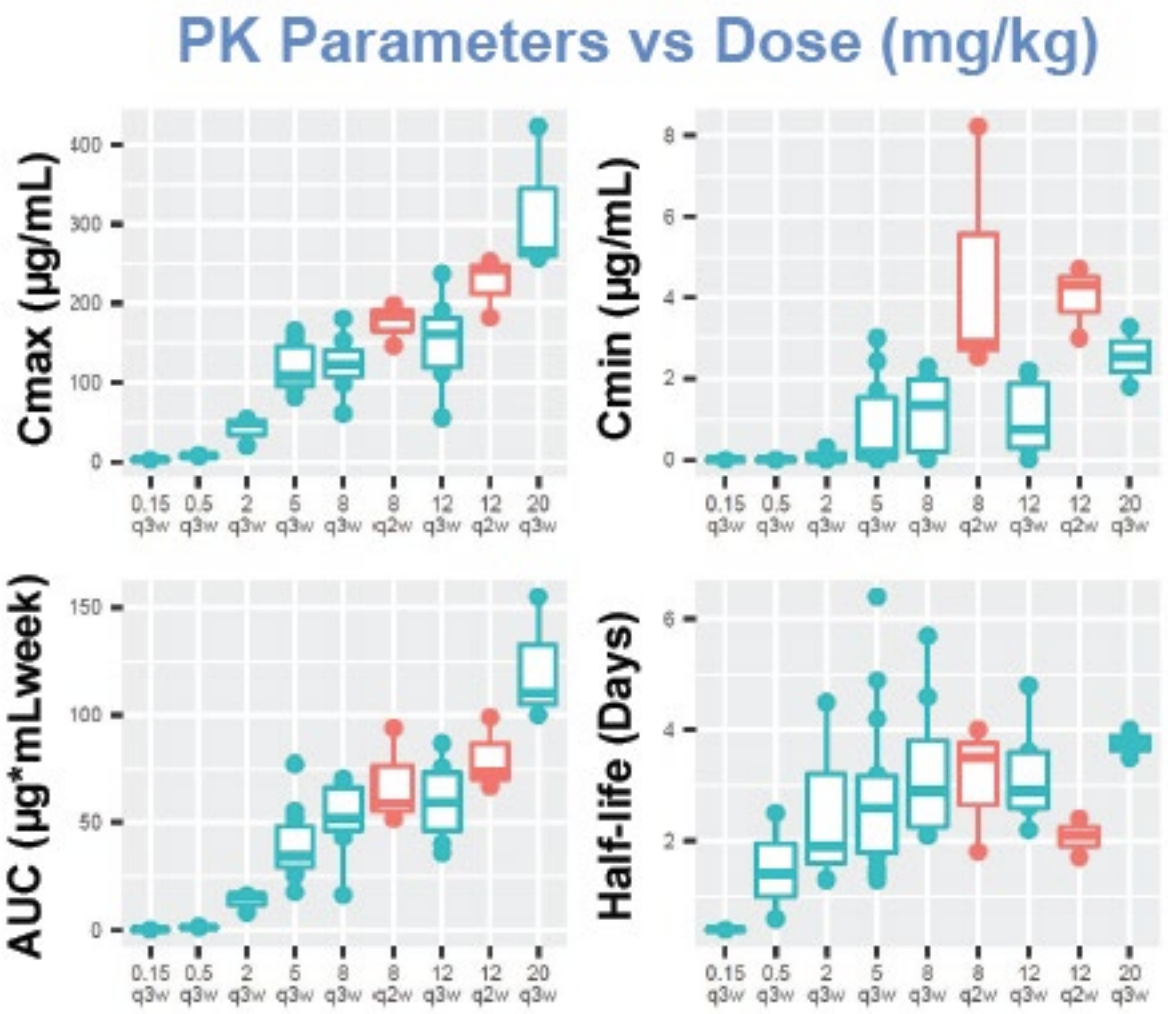
BDC-1001 PK Parameters Show Increase with Ascending Dose Levels



Summary of PK Data

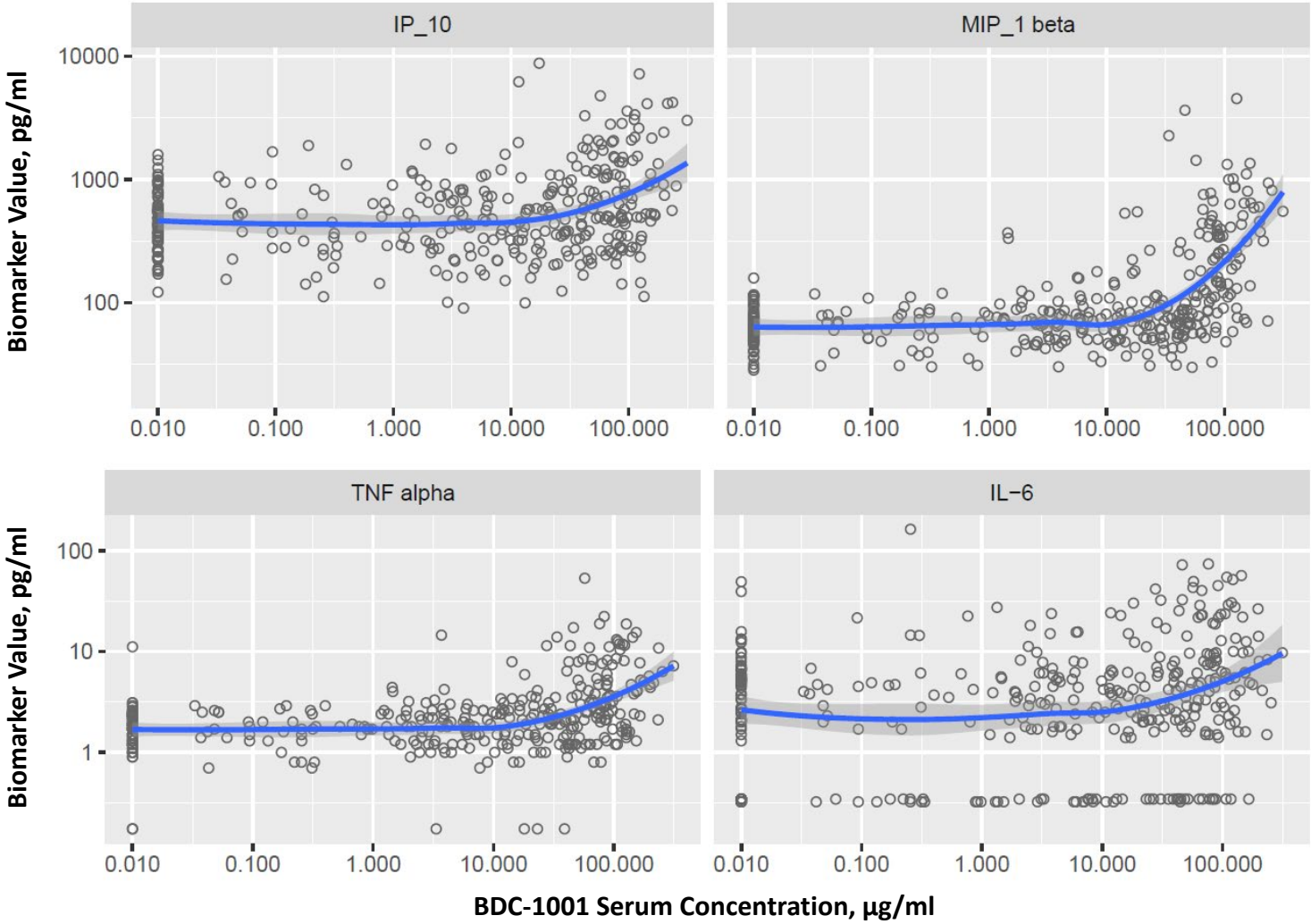
- Target C_{min} levels not yet achieved
  - (C_{min} of ~16 µg/ml for optimal efficacy)[1,3]
- Clinical PK modeling suggests that higher sustained trough levels >16 µg/mL can be achieved in humans via weekly dosing schedule
- Observed exposure levels to date are lower than those predicted based on NHP (non-human primate) modeling data; BDC-1001 does not follow the presumed allometric scaling regarding clearance
- C_{max} increases proportionally with dose

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

1. Ackerman SE, et al. *Nature Cancer*. 2021;2:18–33.
3. Bolt Biotherapeutics internal data.

Time-matched PK Concentration vs Plasma Biomarker Levels

Correlation Between Drug Concentration and Biomarker Levels



Increasing plasma cytokine/ chemokine levels were observed at higher drug concentration levels and have not reached a plateau

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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BDC-1001 Induces Changes in the Tumor Microenvironment Consistent with MOA as Seen in Paired Tissue Biopsies from Ongoing Clinical Trial

- Representative tissue biomarkers investigated with IHC:
  - Myeloid cell infiltration: CD11c, CD68, BDCA-2 (pDC), CD163 (M2s)
  - T cell infiltration and activation: CD8, Granzyme B
  - 22 paired samples to date: baseline + on-treatment at C2D4 (q3w) or C3D4 (q2w)
    - Twelve paired biopsies across dose levels have been analyzed for all markers
    - Analyses of additional samples are ongoing
    - Two representative paired biopsies are shown in the panels below

- Following BDC-1001 administration, the percentage of CD11c+ and CD68+ cells in the tumor trend higher in multiple samples, consistent with BDC-1001 inducing changes in the tumor microenvironment

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

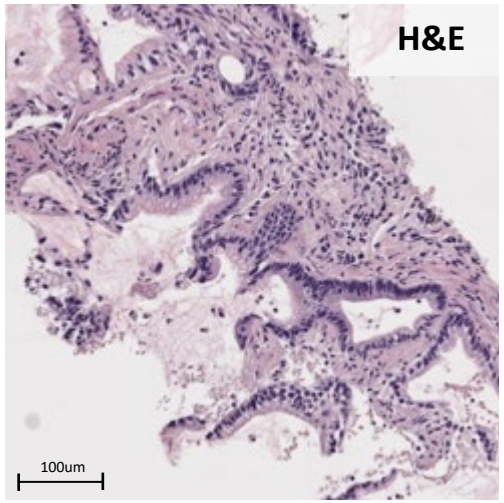
Evidence of Activated Tumor Immunity in Paired Tissue Biopsies – Example 1

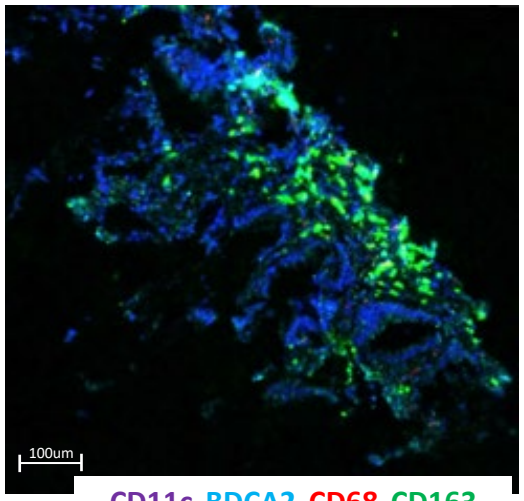
Clinical trial subject with cervical cancer on BDC-1001 5 mg/kg q3w

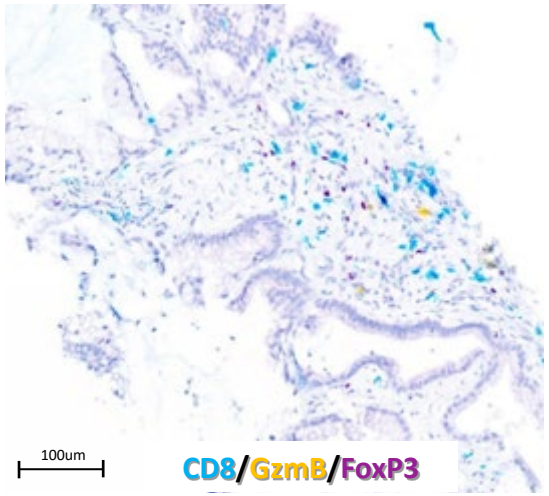
Myeloid cells infiltration

T cell infiltration & activation

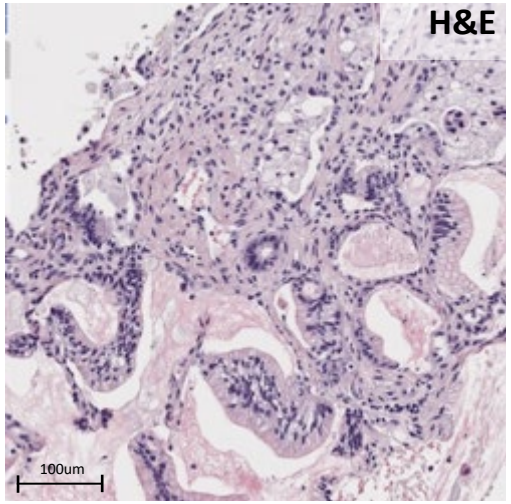
Baseline (Lung Biopsy)

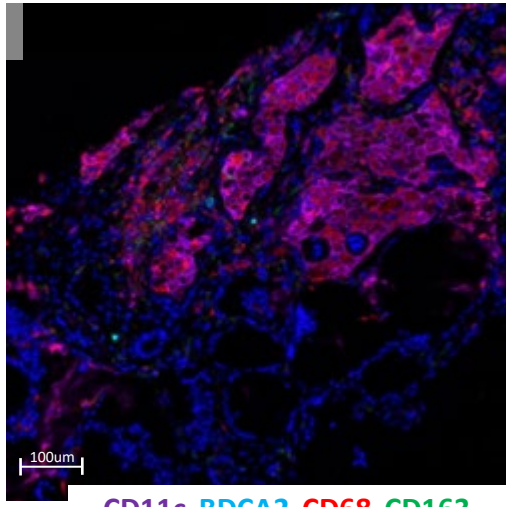


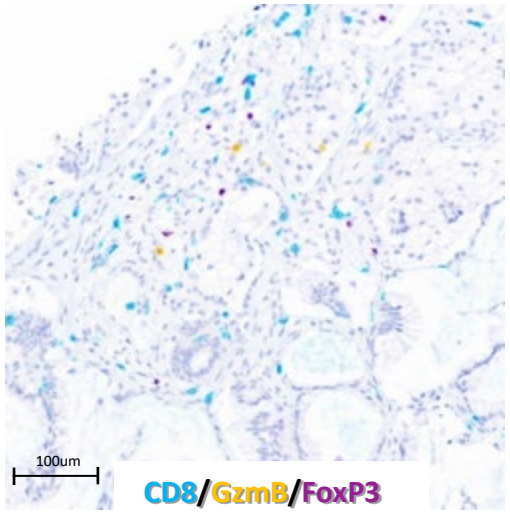




On-treatment @C2D4 (Lung Biopsy)







*Dark blue staining in these panels is cell nuclei

- 29-year-old female with recurrent metastatic endocervical cancer, HER2 amplified, MSS, PD-L1 negative
- Previously treated with surgical resection as well as multiple systemic regimens including cisplatin, carboplatin, paclitaxel, bevacizumab, ZW49
- On BDC-1001 5 mg/kg q3w with stable disease for 23+ weeks and ongoing

Key Changes:

- ~Four-fold increase in classic dendritic cell (cDC, CD11c+) and two-fold increase in plasmacytoid dendritic cell (pDC, BDCA2+) infiltration
- Six-fold increase in M1 (CD68+CD163-) and slight decrease in M2 (CD163+) macrophage infiltration
- Increase in dendritic cell (DC) infiltration and M1/M2 ratio on BDC-1001 treatment (vs baseline)

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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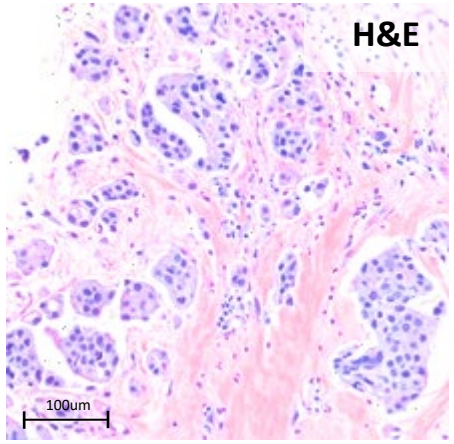
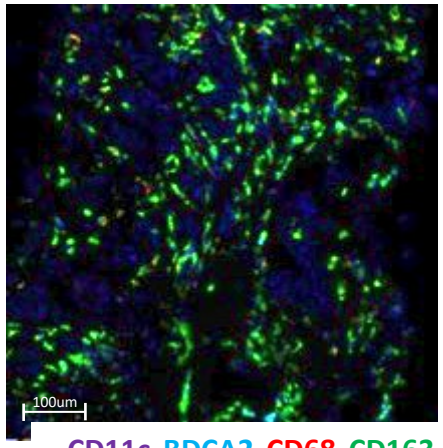
Evidence of Activated Tumor Immunity in Paired Tissue Biopsies – Example 2

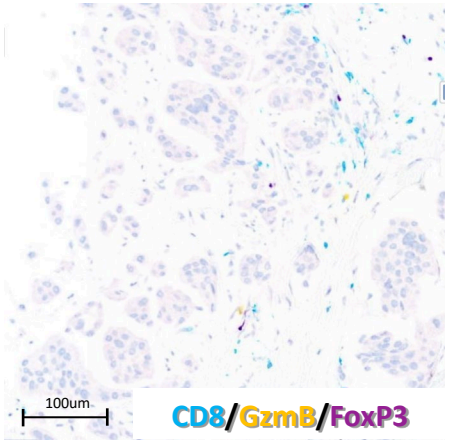
Clinical trial subject with breast cancer on BDC-1001 8 mg/kg q3w

Myeloid cells infiltration | **T cell infiltration & activation**

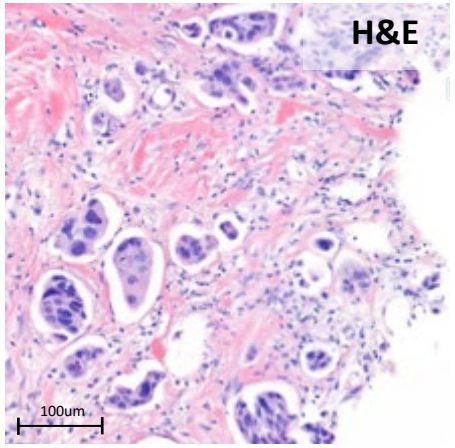
Baseline (Breast Biopsy)

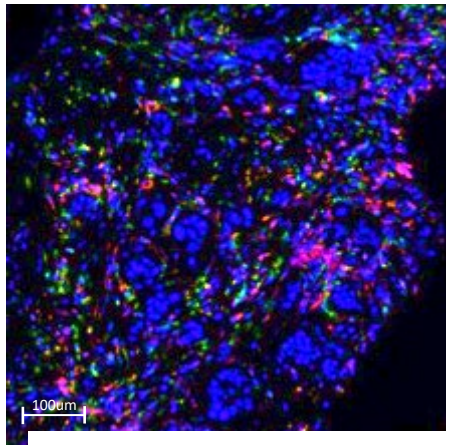


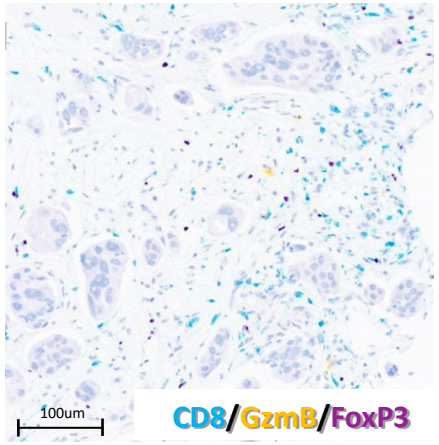




On-treatment @C2D4 (Breast Biopsy)







*Dark blue staining in these panels is cell nuclei

- 40-year-old female with metastatic HER2+ (IHC3+) breast cancer
- Previously treated with multiple anti-HER2 therapies, including Enhertu
- Stable disease on BDC-1001 as of week 12 scan and ongoing

Key Changes:

- Four-fold increase in cDC (CD11c+) infiltration
- Seven-fold increase in M1 (CD68+CD163-) and decrease in M2 (CD163+) macrophage infiltration
- Two-fold increase in CD8+ T cell infiltration and activation on BDC-1001 treatment (vs baseline)
- Observations suggest an overall increase in DC and T cell infiltration, increase in M1/M2 ratio

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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BDC-1001 Clinical Activity Seen in 13 of 40 Tumor-evaluable Subjects* Across Tumor Types and Dose Levels (2-20 mg/kg)

Tumor Response	Site of Primary Tumor	Duration of Disease Control (PR or SD) in Weeks	Cohort
Partial response (>36 weeks)	Colorectal	36§	5 mg/kg q3w
Long-term stable disease (>12 weeks)	Endometrial	24	2 mg/kg q3w
	Cervix	23+	5 mg/kg q3w
	Breast	15+	8 mg/kg q3w
	Melanoma	13+	8 mg/kg q3w
	Colorectal	19+	8 mg/kg q2w
	Colorectal	13+	8 mg/kg q2w
Stable disease at Week 6 scan	Gastro-esophageal	10+	12 mg/kg q3w
	Ovarian	6	20 mg/kg q3w
	Colorectal	6	2 mg/kg q3w
	Colorectal	6	5 mg/kg q3w
	Bile duct	6	8 mg/kg q3w
	Gastro-esophageal	7+	8 mg/kg q3w

*Defined as subjects with baseline and at least one post baseline tumor scan available as of the data cutoff date

§Patient continued with PR at 52 weeks without any subsequent therapies

+ Denotes subjects are still on treatment

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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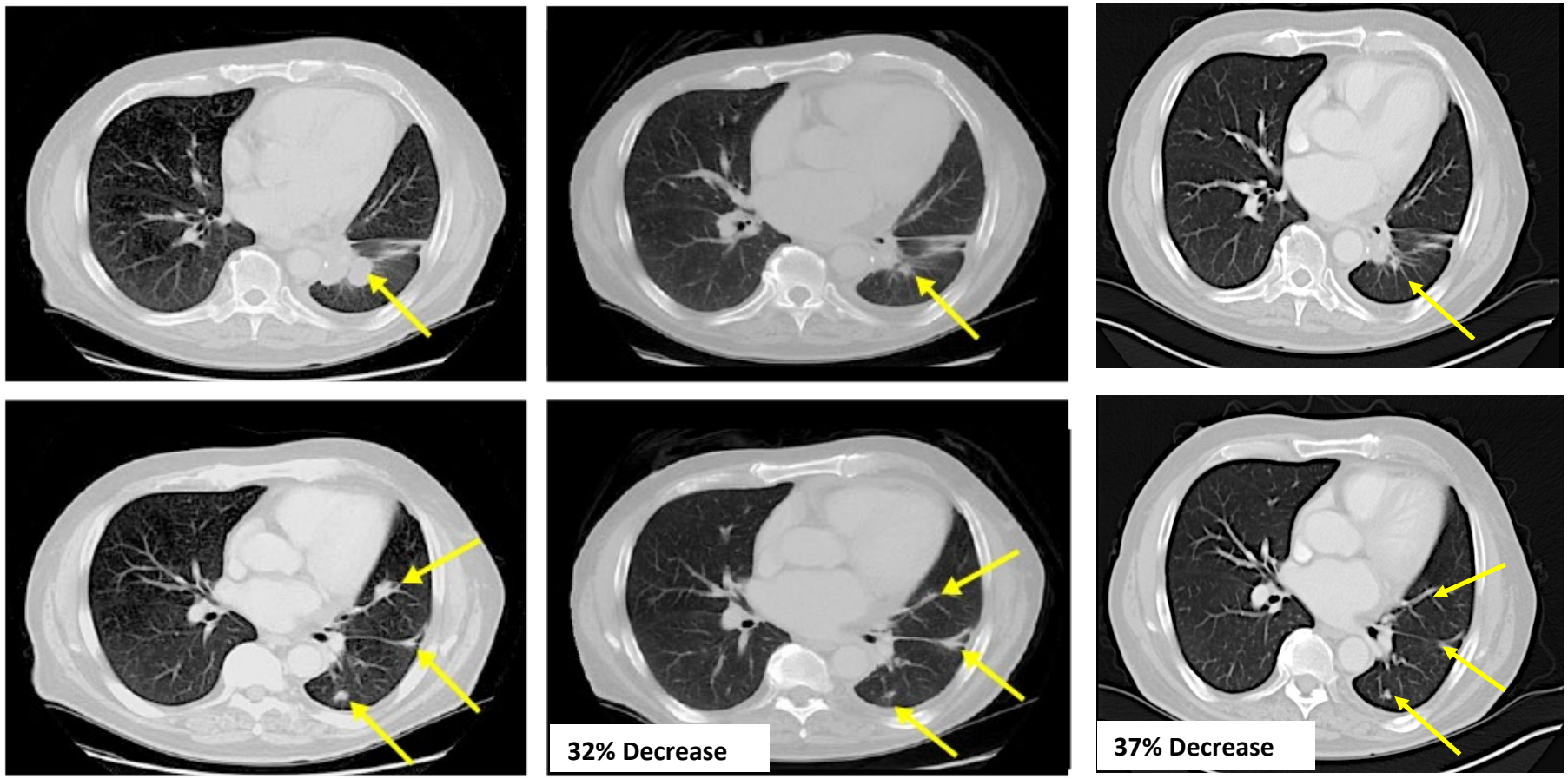
Subject with Metastatic CRC Confirmed PR at 36 Weeks, Maintained Through 52 Weeks

Chest CT Scans

Prior to BDC-1001 Treatment | **At 12 weeks** | **At 36 weeks**



66-year-old Male with Metastatic Adenocarcinoma of the Colon

- Tumor HER2+ (IHC3+, amplified; MSS, KRAS wt)
- Previous treatments include chemotherapy regimens +/- bevacizumab, anti-PD-1 and anti-LAG3 combination therapy
- BDC-1001 discontinued after 4 doses due to asymptomatic grade 3 decrease in LVEF, which has improved with follow up
- **Persistent PR with no anti-cancer therapy since 12 wks**

Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021

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Summary

Progress in Our Pioneering Journey

First-in-class Boltbody™ ISAC: BDC-1001

Broadly Enabling Platform Technology

Cash on Hand of $295.5 million[1] Achieves Key Milestones

Upcoming Milestones for BDC-1001

- 4Q21: Initiate dose-escalation combination trial with anti-PD-1
  - Opdivo® anti-PD1 antibody supplied by Bristol Myers Squibb
- 2022: Complete monotherapy dose escalation, determine RP2D
- 2022: Complete PD-1 combination dose escalation, determine RP2D
- 2022: Initiate monotherapy & combination Phase 2 dose expansion cohorts

Upcoming Milestones for BDC-2034

- 2022: File IND & Initiate Phase 1 clinical study

[1] Proforma Cash, cash equivalents, and marketable securities as of September 30, 2021: $290.5 million balance plus $5 million Innovent receivable

Opdivo® is a trademark of Bristol-Myers Squibb Company

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Thank You