# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): December 6, 2021**

# BOLT BIOTHERAPEUTICS, INC.

**(Exact name of Registrant as Specified in Its Charter)**

| **Delaware** | **001-39988** | **47-2804636** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| **900 Chesapeake Drive**<br>**Redwood City, California** | | **94063** |
|---|---|---|
| **(Address of Principal Executive Offices)** | | **(Zip Code)** |

**(650) 665-9295**
**(Registrant's Telephone Number, Including Area Code)**

**Not Applicable**
**(Former Name or Former Address, if Changed Since Last Report)**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| **Title of Each Class:** | **Trading Symbol(s):** | **Name of Exchange on Which Registered:** |
|---|---|---|
| **Common Stock, par value $0.00001 per share** | **"BOLT"** | **The Nasdaq Global Select Market** |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

**Item 7.01 Regulation FD Disclosure.**

On December 6, 2021, Bolt Biotherapeutics, Inc. (the "Company") announced the interim results of the Company's ongoing Phase 1/2 study of BDC-1001 as monotherapy in patients with HER2-expressing solid tumors. The Company issued a press release, which is filed as Exhibit 99.1 to this Current Report on Form 8-K. A poster of the interim results was also published on the European Society for Medical Oncology's website.

On December 6, 2021, the Company created a corporate slide presentation for use in meetings to discuss the interim BDC-1001 data with investors, analysts and others. The presentation is available through the Company's website and a copy is attached as Exhibit 99.2 to this Current Report on Form 8-K.

The information in this Item 7.01 of this Current Report on 8-K (including Exhibit 99.1 and Exhibit 99.2) is furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information shall not be deemed incorporated by reference into any other filing with the Securities and Exchange Commission made by the Company, whether made before or after today's date, regardless of any general incorporation language in such filing, except as shall be expressly set forth by specific references in such filing.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated December 6, 2021. |
| 99.2 | Corporate Slide Presentation dated December 6, 2021. |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Dated: December 6, 2021

**Bolt Biotherapeutics, Inc.**

By: /s/ William P. Quinn
William P. Quinn
Chief Financial Officer

**Bolt Biotherapeutics Reports Interim BDC-1001 Phase 1/2 Data Demonstrating a Safe and Well-tolerated Profile and Emerging Clinical Activity at the ESMO Immuno-Oncology Congress 2021**

Company to continue monotherapy dose-escalation and evaluate weekly dose regimen

Combination dose-escalation study of BDC-1001 with Opdivo® on target to initiate by year end 2021

Live conference call and webcast today at 8:00 a.m. ET/5:00 a.m. PT

REDWOOD CITY, Calif., Dec. 6, 2021 -- Bolt Biotherapeutics, Inc. (Nasdaq: BOLT), a clinical-stage biotechnology company pioneering a new class of immuno-oncology agents that combine the targeting precision of antibodies with the power of both the innate and adaptive immune systems, today announced the presentation of interim clinical data from the company's ongoing Phase 1/2 study of BDC-1001, the company's lead immune-stimulating antibody conjugate (ISAC) in a poster session at the European Society for Medical Oncology Immuno-Oncology (ESMO I-O) Congress 2021, being held virtually from Dec. 6-11, 2021. The lead author for the poster is Manish Sharma, M.D., START Midwest, with contributions from Ecaterina Dumbrava, M.D., MD Anderson Cancer Center, and other colleagues from the U.S. and South Korea.

The company reported data from 57 subjects participating in an ongoing Phase 1/2 study of BDC-1001, across 16 different types of HER2-expressing solid tumors. BDC-1001 demonstrated a favorable safety and tolerability profile at all evaluated doses and schedules, showing early signs of clinical activity with corresponding biomarker changes in the tumor microenvironment of post-treatment tumor biopsies. BDC-1001 is an immune-stimulating antibody conjugate (ISAC) comprising a HER2-targeting biosimilar of trastuzumab conjugated with a non-cleavable linker to an innovative TLR7/8 agonist.

"The favorable safety profile and early indications of clinical disease control in the BDC-1001 study are encouraging," said Dr. Sharma, Associate Director of Clinical Research at START Midwest. "There is a clear need for well tolerated, durable treatments in the fight against cancer and I'm excited to see if BDC-1001 can deliver on that potential as we explore higher drug exposure levels."

The poster presentation at ESMO I-O reported new safety, pharmacokinetic/pharmacodynamic, and efficacy results for the ongoing Phase 1 dose-escalation portion of the BDC-1001 monotherapy trial. Fifty-seven subjects have been treated at increasing dose levels up to 20 mg/kg every three weeks and 12 mg/kg every two weeks, and data from these subjects demonstrate that:

- BDC-1001 continues to have a favorable safety and tolerability profile with mild (grade 1/grade 2) infusion related reactions in some patients and no dose-limiting toxicities at dose levels up to 20 mg/kg every three weeks and 12 mg/kg every two weeks. There was no indication of cytokine release syndrome (CRS), and a maximum tolerated dose (MTD) has not been reached.
- Early signs of clinical activity are noted in 13 of 40 tumor evaluable subjects with one durable partial response maintained through 52 weeks and multiple subjects achieving stable disease for >12 weeks.

- The pharmacokinetic (PK) data demonstrate increasing peak drug levels with increasing dose, and linearity of PK above the 5 mg/kg dose level. Clinical PK modeling predicts that target exposure levels can be achieved with weekly dosing.
- Plasma and tissue biomarker results show increase in multiple biomarkers indicative of myeloid cell and TLR 7/8 activation that is consistent with BDC-1001's mechanism of action. Increasing drug exposure correlates with increases in plasma cytokines and corresponding biomarker changes in the tumor microenvironment of multiple post-treatment tumor biopsies, with intriguing signs of clinical disease control.

These encouraging data point to the need for increased drug exposure to optimize clinical benefit. The favorable safety profile of BDC-1001 allows for continued enrollment in the dose escalation portion of the study, and the Company's refined PK model based on data from more than 50 patients predicts that weekly administration will provide BDC-1001 exposures at or above the target exposure threshold. The data also support initiation of the combination therapy study with nivolumab (PD-1 inhibitor).

"Bolt Biotherapeutics is committed to agile clinical development based on data. In this Phase 1/2 study of BDC-1001, we have gained tremendous insight into the ability of this novel candidate to mobilize the patient's immune system in targeting the tumor and its microenvironment. The increases in myeloid cell infiltration and repolarization of macrophages we've seen in multiple post-treatment biopsies are provocative and consistent with our proposed mechanism of action," said Edith Perez, M.D., Chief Medical Officer of Bolt Biotherapeutics. "We look forward to exploring weekly dosing as we get closer to determining the recommended Phase 2 dose for BDC-1001 as monotherapy, and to initiating combination therapy with a checkpoint inhibitor."

**Presentation Details**

**Title:** Preliminary results from a phase 1/2 study of BDC-1001, a novel HER2 targeting TLR7/8 immune-stimulating antibody conjugate (ISAC), in patients (pts) with advanced HER2-expressing solid tumors
**Lead author:** Manish R. Sharma, M.D.
**Presentation Number:** 164P
**Timing:** On-demand access beginning Dec. 6 at 12:00 p.m. CET.

The poster presentation will be available on the ESMO I-O conference website and on Bolt's website.

**Conference Call and Webcast Details**

Bolt Biotherapeutics management will host a conference call for the investment community, in conjunction with the now virtual ESMO Immuno-Oncology Congress 2021, to discuss emerging clinical data and insights from the ongoing Phase 1/2 study today, Monday, December 6, 2021, at 8:00 a.m. ET/5 a.m. PT.

The conference call can be accessed by dialing +1 (833) 665-0609 within the U.S. or Canada or by dialing +1 (929) 517-0400 from international locations. The passcode for the call is 2633068. A live webcast, including slides, will be available on the Events & Presentations page of Bolt Biotherapeutic's website at www.boltbio.com. An archived replay can be accessed for 30 days following the webcast.

**About the Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) Platform**

ISACs are a new category of immunotherapy that combines the precision of antibody targeting with the strength of the innate and adaptive immune systems. Boltbody ISACs comprise three primary components: a tumor-targeting antibody, a non-cleavable linker, and a proprietary immune stimulant to activate the patient's innate immune system. By initially targeting a single marker on the surface of a patient's tumor cells, an ISAC can create a new immune response by activating and recruiting myeloid cells. The activated myeloid cells start a feed-forward loop by releasing cytokines and chemokines, chemical signals that attract other immune cells and lower the activation threshold for an immune response. This reprograms the tumor microenvironment and invokes an adaptive immune response that targets the tumor, with the goal of durable responses for patients with cancer.

**About Bolt Biotherapeutics, Inc.**
Bolt Biotherapeutics, Inc. is a clinical-stage biotechnology company pioneering a new class of immuno-oncology agents that combine the targeting precision of antibodies with the power of both the innate and adaptive immune systems. Bolt's proprietary Boltbody™ Immune-stimulating Antibody Conjugates (ISACs) are designed to target tumor cells for elimination by myeloid cells, which then activates the myeloid cells to recruit the adaptive immune system in the anti-tumor response. This leads to the conversion of immunologically "cold" tumors to "hot" tumors. Bolt's lead candidate, BDC-1001, is a Boltbody ISAC comprised of a HER2-targeting biosimilar of trastuzumab conjugated with a non-cleavable linker to one of Bolt's proprietary TLR7/8 agonists for the treatment of patients with HER2-expressing solid tumors. Bolt is also advancing BDC-2034, a Boltbody ISAC targeting CEA, and a pipeline of other immuno-oncology products.

**Forward-Looking Statements**

This press release contains forward-looking statements about us and our industry that involve substantial risks and uncertainties and are based on our beliefs and assumptions and on information currently available to us. All statements other than statements of historical facts contained in this press release, including statements regarding optimizing the dose and finding the recommended Phase 2 dose for BDC-1001 and the potential initiation of an additional combination dose escalation study by year-end, are forward-looking statements. In some cases, you can identify forward-looking statements because they contain words such as "anticipate," "believe," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "will," or "would," or the negative of these words or other similar terms or expressions. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Forward-looking statements represent our current beliefs, estimates and assumptions only as of the date of this press release and information contained in this press release should not be relied upon as representing our estimates as of any subsequent date. These statements, and related risks, uncertainties, factors and assumptions, include, but are not limited to the potential product candidates that we develop may not progress through clinical development or receive

required regulatory approvals within expected timelines or at all; clinical trials may not confirm any safety, potency or other product characteristics described or assumed in this press release; such product candidates may not be beneficial to patients or become commercialized. These risks are not exhaustive. Except as required by law, we assume no obligation to update these forward-looking statements, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future. Further information on factors that could cause actual results to differ materially from the results anticipated by our forward-looking statements is included in the reports we have filed or will file with the SEC, including our Annual Report on Form 10-K for the year ended December 31, 2020. These filings, when available, are available on the investor relations section of our website at investors.boltbio.com and on the SEC's website at www.sec.gov.

Opdivo® is a trademark of Bristol-Myers Squibb Company.

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Exhibit 99.2


# 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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# 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 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.

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.



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# BDC-1001 Dose Escalation Study Continues

| | |
|---|---|
| **Favorable Safety Profile** | • Recommended Phase 2 Dose (RP2D) not yet reached<br>• BDC-1001 has demonstrated favorable safety & tolerability to date<br>• 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<br>• Tumor microenvironment & plasma biomarker changes consistent with MOA<br>• No evidence of anti-drug antibody formation |
| **Early Signs of Clinical Disease Control** | • Early signs of disease control noted, even below target exposure level<br>• Disease control (SD or PR) noted in 13/40 evaluable subjects in multiple tumor types<br>• 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<br>• 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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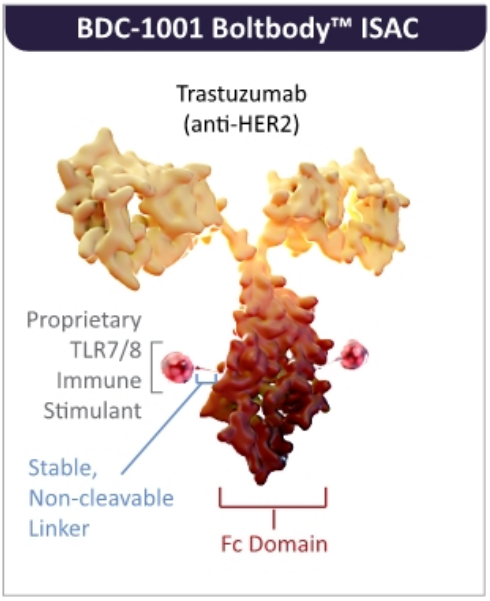
# Review of BDC-1001 Mechanism & Preclinical Data

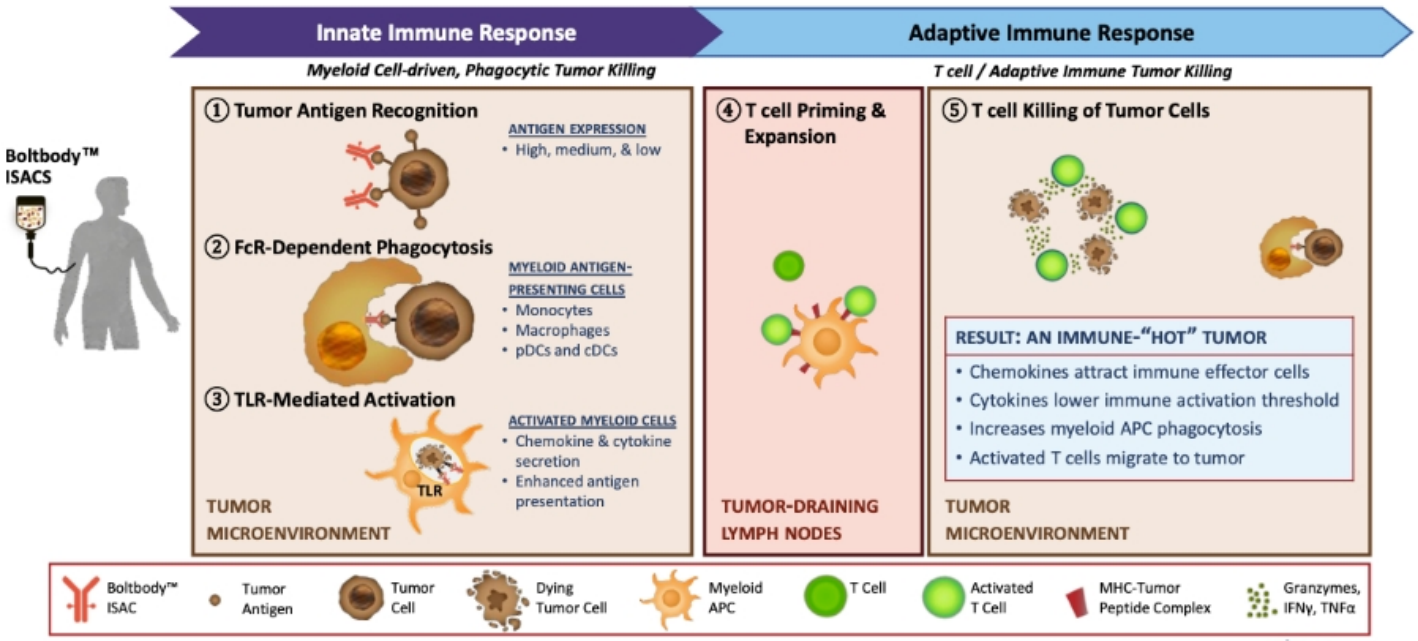
# BDC-1001: Key Features Combine to Deliver Unique MOA




**Key structural features:**

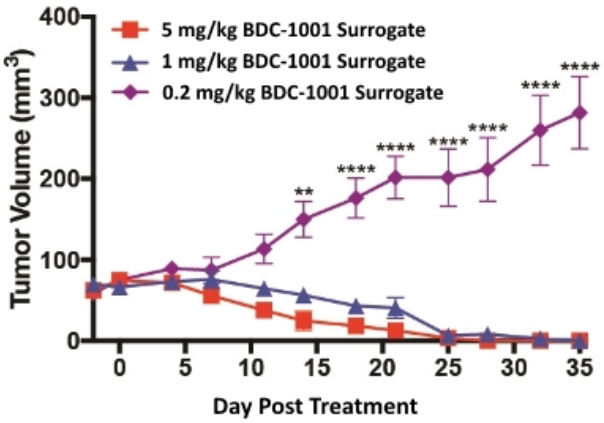
- Targeting: Trastuzumab (anti-HER2) biosimilar
- ADCP engagement via antibody Fc domain
- Stable, non-cleavable linker
- Proprietary TLR 7/8 immune stimulant

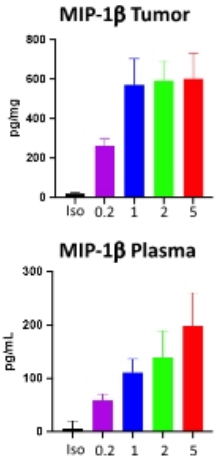
# Hallmarks of Boltbody™ ISAC Platform

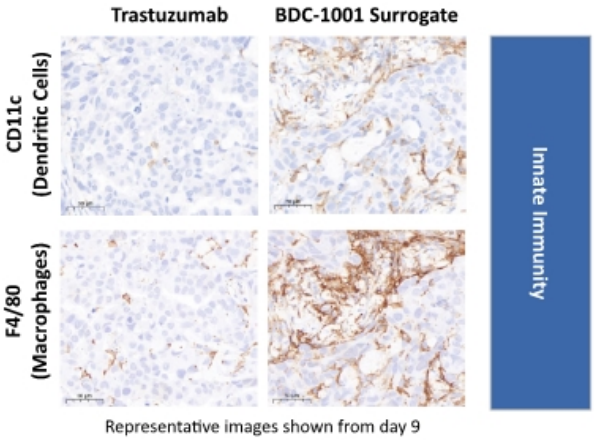


# BDC-1001 Surrogate Shows Dose-Dependent Efficacy and Pharmacodynamic Responses

## 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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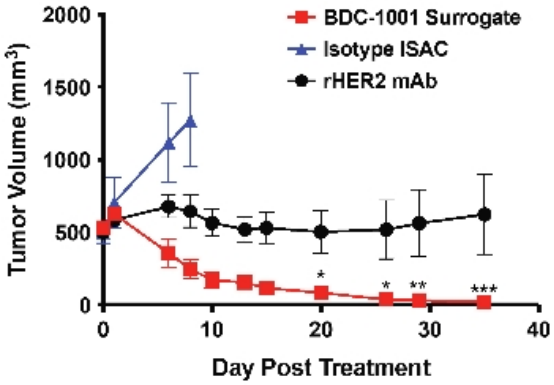
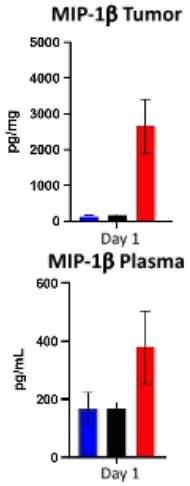
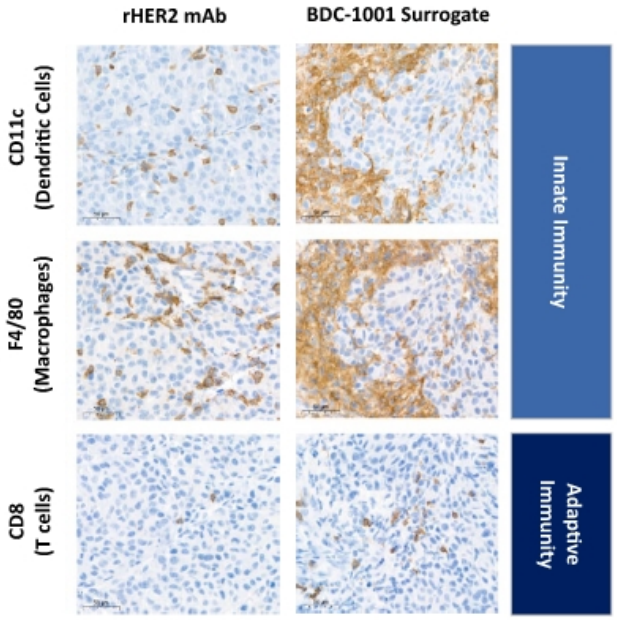
# BDC-1001 Surrogate Engages Innate and Adaptive Immune Responses

## 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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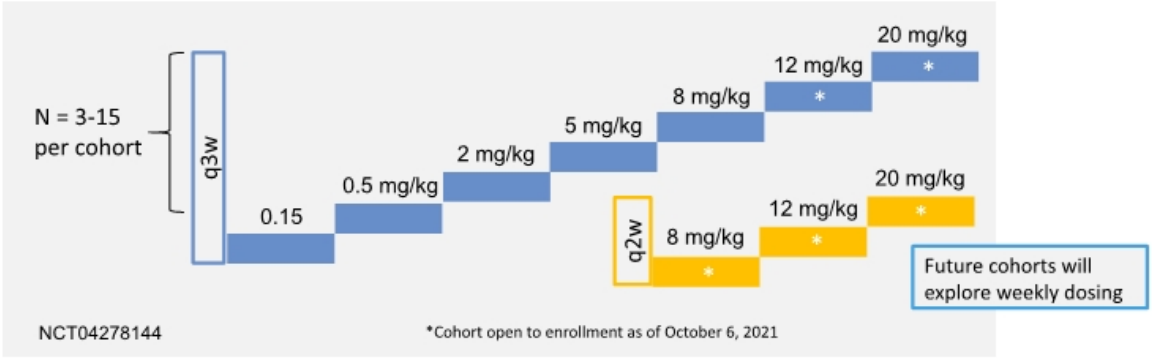
# BDC-1001 Interim Results

**Presented at**
**ESMO Immuno-Oncology 2021**

**December 2021**

# 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:<br>• HER2 IHC2+/3+ or<br>• HER2-amplified |



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

# 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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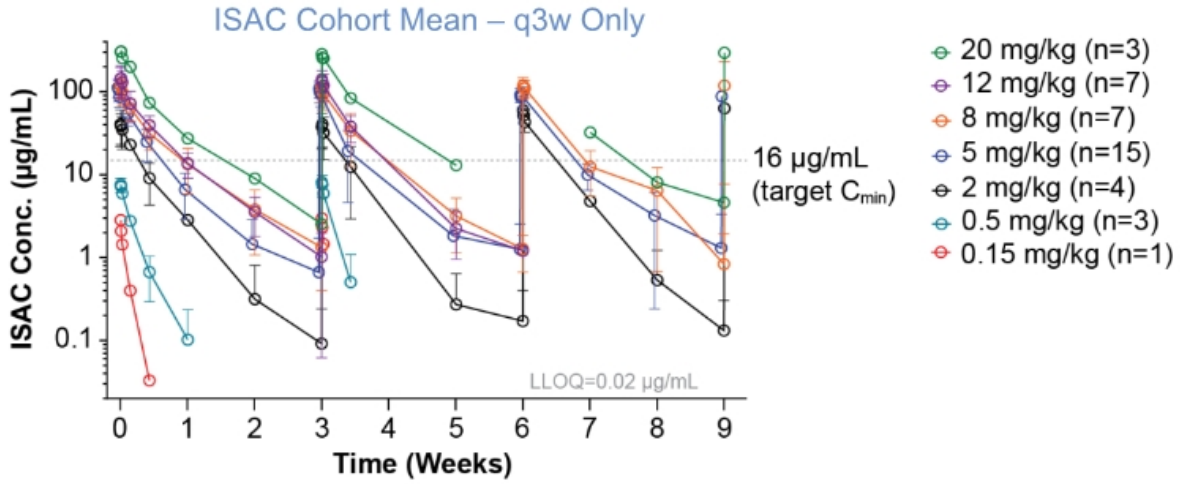
# BDC-1001 Overall Safety Summary

- 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



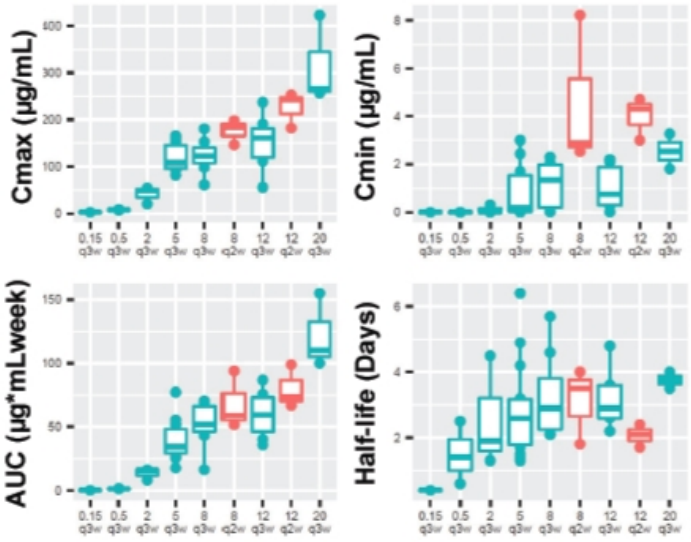

- No subjects (0/53) developed antibodies to BDC-1001 after treatment was initiated
  - 2/53 (3.8%) subjects were found to have pre-existing antibodies reactive to BDC-1001



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

# BDC-1001 PK Parameters Show Increase with Ascending Dose Levels

## PK Parameters vs Dose (mg/kg)




## 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

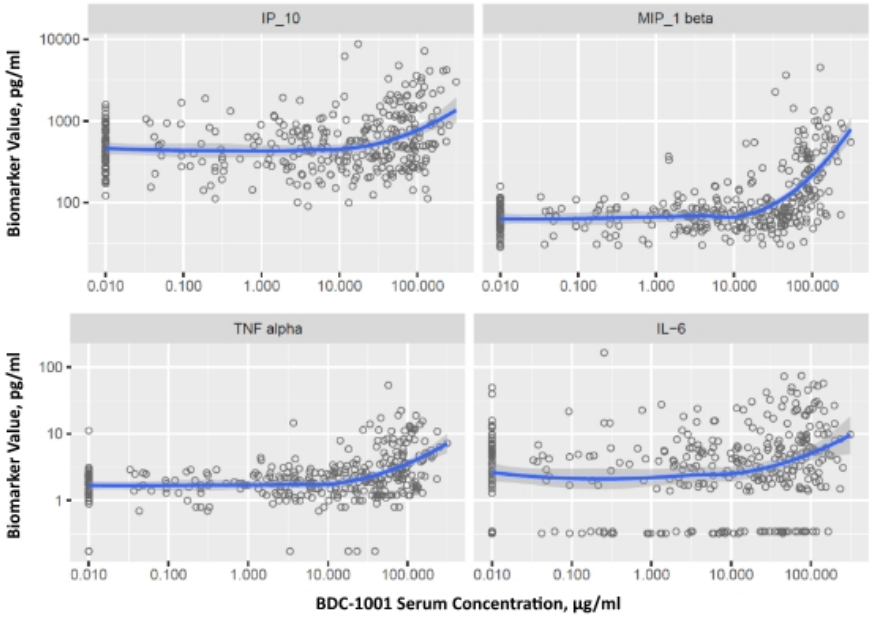
Sharma MR, et al., ESMO I-O Poster (2021); data as of October 6, 2021



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

BOLT BIOTHERAPEUTICS

## 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



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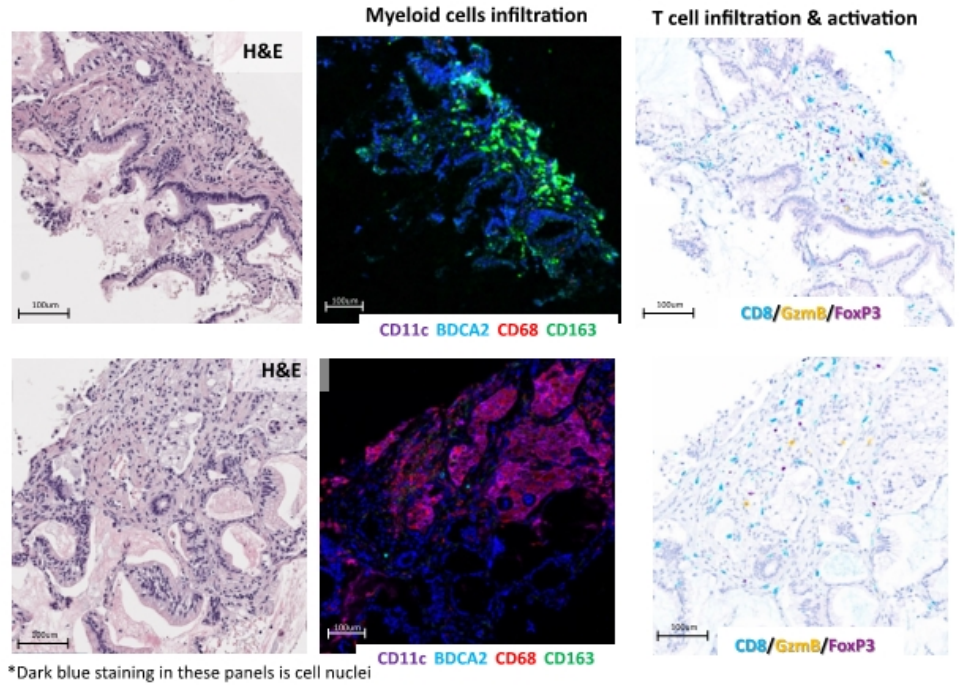
# Evidence of Activated Tumor Immunity in Paired Tissue Biopsies – Example 1

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




*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)



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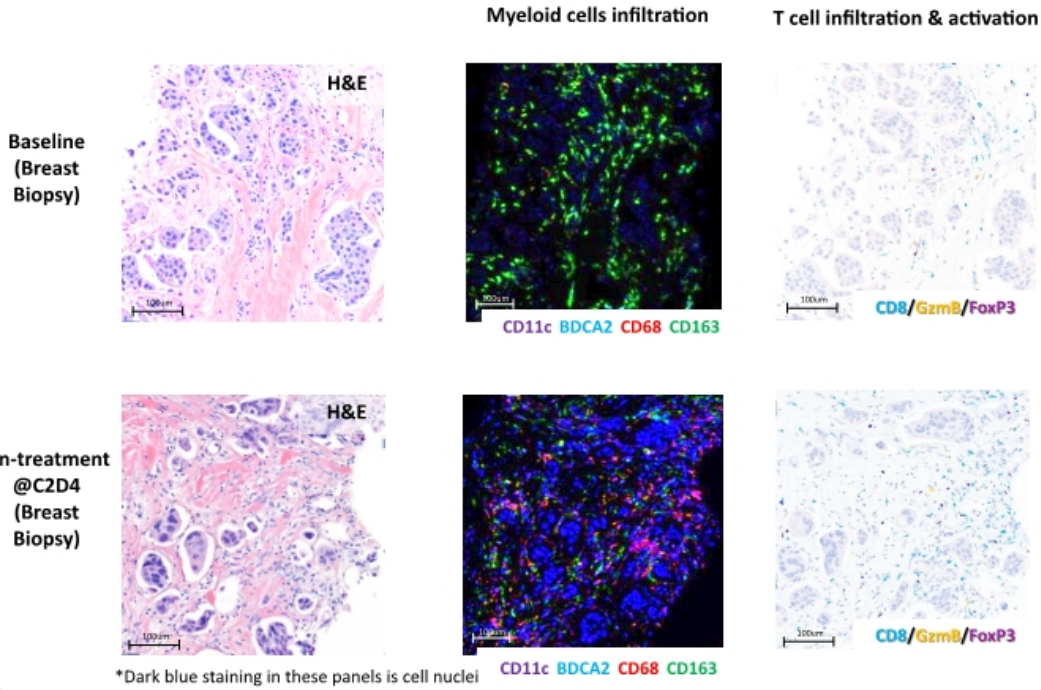
# Evidence of Activated Tumor Immunity in Paired Tissue Biopsies – Example 2

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




*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



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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



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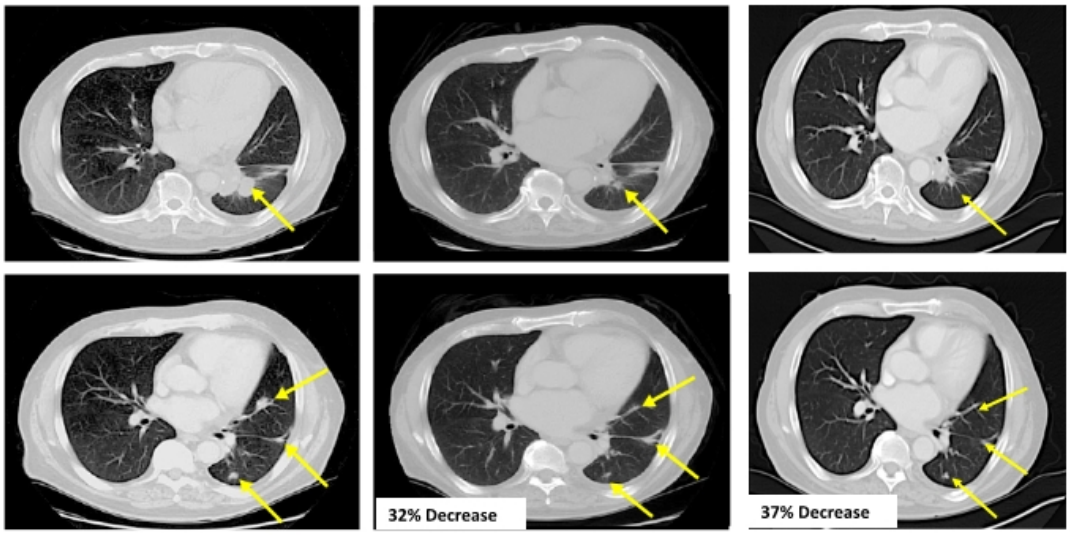
BOLT BIOTHERAPEUTICS

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

## Chest CT Scans




### 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**



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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


# Thank You