Bolt Biotherapeutics Highlights Comprehensive Clinical Data from Phase 1 Dose-Escalation Trial of BDC-1001 as Monotherapy and in Combination with Nivolumab in HER2-Expressing Tumors at 2023 ASCO Annual Meeting

May 25, 2023

- Treatment with BDC-1001 at the recommended Phase 2 dose (RP2D) resulted in 29% objective response rate in evaluable patients with HER2-positive tumors, in both monotherapy and in combination with nivolumab
- 20 mg/kg dosed every other week (q2w) was selected as the RP2D
- BDC-1001 advancing to a focused Phase 2 clinical program in four HER2-positive tumor types: colorectal, endometrial, gastroesophageal, and breast

REDWOOD CITY, Calif., May 25, 2023 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics, Inc. (Nasdaq: BOLT) today announced the data from its Phase 1 dose-escalation clinical trial of BDC-1001 that will be presented in a poster session at the American Society of Clinical Oncology (ASCO) 2023 Annual Meeting, being held at McCormick Place in Chicago, Illinois and virtually from June 2-6, 2023.

BDC-1001 is an investigational Immune-Stimulating Antibody Conjugate (ISAC) in development for the treatment of patients with human epidermal growth factor receptor 2 (HER2)-expressing cancer. BDC-1001 comprises a HER2-targeting biosimilar of trastuzumab conjugated with a non-cleavable linker to a proprietary TLR7/8 agonist. The Phase 1 dose-escalation trial enrolled 131 patients with 16 different HER2-expressing solid tumor types across 18 dose levels in two arms, monotherapy and in combination with nivolumab. At enrollment, all patients entered in the study had evidence of tumor progression following prior standard of care treatments, and a majority of the patients were heavily pre-treated.

“BDC-1001 has demonstrated a favorable safety profile and encouraging efficacy including multiple objective responses and long-term stable disease, as well as biomarker evidence of immune activation that support our ISAC mechanism of action,” said Edith A. Perez, M.D., Chief Medical Officer of Bolt Biotherapeutics. “Furthermore, these data support the initiation of our Phase 2 clinical program in four HER2-positive tumor types this year.”

“BDC-1001 represents a promising new therapeutic modality in oncology,” said Bob T. Li, M.D., Ph.D., MPH, medical oncologist and principal investigator at Memorial Sloan Kettering Cancer Center (MSK). “The findings from the Phase 1 dose-escalation study demonstrate the potential of BDC-1001 to treat patients with HER2-expressing tumors and provide initial clinical validation of ISACs as a therapeutic approach. I look forward to presenting these data and engaging with the medical community during ASCO.”

Key findings from the recently completed BDC-1001 dose-escalation study are summarized below.

- The most clinically meaningful efficacy was observed at 20 mg/kg q2w, the dose level and frequency of administration selected as the RP2D for both monotherapy and combination therapy and which achieved the target drug exposure of >10 ug/ml. Four confirmed partial responses (PRs) were observed at the RP2D; two in the monotherapy arm in colorectal and biliary tract tumors, and two in the combination arm in colorectal and ovarian tumors. The response rate at the RP2D was 29% in evaluable patients with HER2-positive tumors, both in monotherapy (2/7, 29%) and in combination with nivolumab (2/7, 29%).
- At the RP2D, among evaluable patients with HER2-positive tumors, 43% (3/7) in the monotherapy arm and 57% (4/7) in combination experienced PRs or at least 24 weeks of disease control.
- The 20 mg/kg q2w dose level achieved the serum exposure target of more than 10 µg/mL throughout the dosing period. This dose level demonstrated the best efficacy, was well tolerated, and demonstrated evidence of pharmacodynamic changes, making it the clear choice for the RP2D.
- BDC-1001 was well tolerated through 20 mg/kg dosed weekly as both monotherapy and in combination with nivolumab. The most frequent drug-related AEs were grade 1 or 2 infusion-related reactions, which were observed in 29% of subjects. Grade 3 or higher treatment-related AEs were seen in nine subjects (6.9%), with only one grade 4 and no grade 5 drug-related AEs.
- Pharmacodynamic responses in both plasma and tissue were consistent with the mechanism of action for an ISAC. BDC-1001 treatment resulted in increases in dendritic cells, macrophages, and CD8+ T cells, as assessed in fresh biopsies. Dose-dependent peak plasma increases were observed for multiple cytokines and chemokines, including MIP-1β and IP-10. Levels of IL-6, a biomarker of inflammation, were low at all dose levels.

Bolt has initiated a Phase 2 program encompassing four HER2-positive solid tumor types. The original Phase 1/2 clinical trial will move into Phase 2

dose expansions in three separate cohorts evaluating colorectal, endometrial, and gastroesophageal cancers. Following demonstration of monotherapy anti-tumor activity in an indication, a separate cohort will be initiated to evaluate BDC-1001 in combination with nivolumab in that indication. In addition, a randomized two-arm Phase 2 clinical trial will investigate BDC-1001 as monotherapy and in combination with pertuzumab in patients with HER2-positive metastatic breast cancer whose disease has progressed following treatment with Enhertu®.

Details about the presentation can be found below and on the ASCO website. Additionally, a copy of the poster will be available on the Publications page of the Bolt Biotherapeutics website following the poster session.

- **Title:** 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
- **Presenter:** Bob Li, M.D., Ph.D., MPH, medical oncologist, and principal investigator at MSK
- **Abstract Presentation Number:** 2538
- **Poster Session:** Developmental Therapeutics—Immunotherapy
- **Details:** Saturday, June 3, 2023, 8:00 a.m. - 11:00 a.m. CDT

About the Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) Platform
Bolt Biotherapeutics' Boltbody ISAC platform harnesses the precision of antibodies with the power of the innate and adaptive immune system to reprogram the tumor microenvironment to generate a productive anti-cancer response. Each Boltbody ISAC candidate comprises a tumor-targeting antibody, a non-cleavable linker, and a proprietary immune stimulant. The antibody is designed to target one or more markers on the surface of a tumor cell and the immune stimulant is designed to recruit and activate myeloid cells. Activated myeloid cells initiate a positive feedback loop by releasing cytokines and chemokines, chemical signals that attract other immune cells and lower the activation threshold for an immune response. This increases the population of activated immune system cells in the tumor microenvironment and promotes a robust immune response, with the goal of generating durable therapeutic responses for patients with cancer.

About Bolt Biotherapeutics, Inc.
Bolt Biotherapeutics is a clinical-stage biopharmaceutical company developing novel immunotherapies for the treatment of cancer. Bolt Biotherapeutics' pipeline candidates are built on the Company's deep expertise in myeloid biology and cancer drug development. The Company's pipeline includes BDC-1001, a HER2-targeting Boltbody Immune-Stimulating Antibody Conjugate (ISAC), BDC-3042, a myeloid-modulating antibody, and multiple Boltbody ISAC collaboration programs. BDC-1001 has completed a Phase 1 dose-escalation study demonstrating tolerability and early clinical efficacy, and the Company plans to initiate Phase 2 studies in 2023. Bolt Biotherapeutics is advancing BDC-3042, an agonist antibody targeting Dectin-2, through IND-enabling activities and expects to initiate a Phase 1 trial in the second half of 2023. In preclinical development, BDC-3042 demonstrated the ability to convert tumor-supportive macrophages to tumor-destructive macrophages. Bolt Biotherapeutics is leveraging its ability to engineer and optimize novel applications of its Boltbody ISACs to develop multiple immuno-oncology candidates through strategic collaborations with leading biopharmaceutical companies. For more information, please visit https://www.boltbio.com/

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 the poster presentation at ASCO 2023, the advancement and success of our clinical trials and the expansion of our clinical trials across Europe, and the success of our collaborations 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," "on track," "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; and our ability to maintain our current collaborations and establish further collaborations. 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 Securities and Exchange Commission, including our Annual Report on Form 10-K for the year ended December 31, 2022. 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.

Dr. Li has provided uncompensated advisory board services to Bolt Biotherapeutics.

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