Bolt Biotherapeutics Presents Updated Clinical Data from Phase 1 Dose-Escalation Trial of BDC-1001 as Monotherapy and in Combination with Nivolumab in HER2-Expressing Tumors at ESMO 2023 Congress

October 23, 2023

- Updated safety data supports the selection of 20 mg/kg q2w as the recommended Phase 2 dose (RP2D)
- Improved efficacy with one partial response (PR) improving to a complete response (CR), two additional patients with long-term stable disease (SD), and three patients who have now received therapy for ≥ 1 year
- BDC-1001 continues to be well tolerated

REDWOOD CITY, Calif., Oct. 23, 2023 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics (Nasdaq: BOLT), a clinical-stage biopharmaceutical company developing novel immunotherapies for the treatment of cancer, today presented updated data from its Phase 1 dose-escalation trial of BDC-1001 at the European Society for Medical Oncology (ESMO) 2023 Congress, being held in Madrid, Spain and virtually from October 20-24, 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)-positive 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.

“The encouraging updated Phase 1 dose escalation data of BDC-1001 that was presented at ESMO further support the initiation of our Phase 2 dose-expansion clinical trial in patients with HER2-positive colorectal, breast, endometrial and gastric cancers,” said Edith A. Perez, M.D., Chief Medical Officer of Bolt Therapeutics. “We look forward to presenting initial data from the Phase 2 dose-expansion trial in 2024.”

“The updated data from the Phase 1 dose-escalation study continue to provide clinical validation of ISACs as a potential therapeutic approach using BDC-1001 to treat patients with HER2-expressing tumors,” said Bob T. Li., M.D., Ph.D., MPH, medical oncologist, and principal investigator at Memorial Sloan Kettering Cancer Center (MSK).

Key findings from the updated Phase 1 BDC-1001 dose escalation study are summarized below.

- Improved BDC-1001 efficacy was observed since the data presented at ASCO in June 2023 with one new CR, two additional long-term SDs, and three patients who received therapy for at least one year.
- At the RP2D, one CR was observed in the monotherapy arm in a patient with salivary gland cancer and three PRs were observed at the RP2D; one in the monotherapy arm in a patient with biliary tract cancer and two in the combination arm in patients with colorectal and ovarian cancer. 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 the combination arm experienced at least 24 weeks of disease control, and 57% (4/7) in the monotherapy arm and 71% (5/7) in the combination arm achieved tumor shrinkage.
- BDC-1001 continues to be well tolerated at all dose levels and schedules as both monotherapy and in combination with nivolumab with no increase in toxicity in combination with BDC-1001. The most frequent drug-related treatment-emergent adverse events (TEAEs) were grade 1 or 2 infusion-related reactions, which were observed in 29.8% of subjects. Grade 3 or higher treatment-related TEAEs were seen in ten subjects (7.6%), 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. Statistically significant upregulation of TLR signaling pathway gene signature, innate immunity gene signatures and T cell inflamed phenotype was observed in the four patients with clinical benefit. Increases in innate immunity signatures was observed in patients in the q2w cohorts, but not q1w.
- The once-weekly dosing cohorts experienced higher rates of adverse events versus every-two-week (q2w) dosing, including: grade 3 or higher BDC-1001-related TEAEs (10.0% versus 2.6%), grade 3 or higher LVEF decreases (7.5% versus 2.6%), and infusion-related reactions (40.0% versus 28.2%), providing further support for the selection of 20 mg/kg q2w as the RP2D.

Details about the presentation can be found below and on the ESMO website. Additionally, a copy of the presentation is available on the Publications page of the Bolt Therapeutics website.

- **Title:** Recommended phase 2 dose (RP2D) selection and pharmacodynamic (PD) data of the first-in-human immune-stimulating antibody conjugate (ISAC) BDC-1001 in patients (pts) with advanced HER2-expressing solid tumors
- **Presenter:** Bob Li, M.D., Ph.D., MPH, medical oncologist, and principal investigator at MSK
- **Presentation number:** 657MO
- **Presentation session:** Developmental therapeutics
- **Details:** Monday, October 23, 2023, 10:30 a.m. – 12:00 p.m. EDT

About BDC-1001

Bolt Biotherapeutics' lead program, BDC-1001, is a human epidermal growth factor receptor 2 (HER2) ISAC comprising a HER2-targeting biosimilar of trastuzumab conjugated with a non-cleavable linker to a proprietary TLR7/8 agonist. Following the successful completion of the BDC-1001 dose-escalation trial for the treatment of patients with HER2-expressing solid tumors, Bolt is now conducting two Phase 2 clinical trials in the U.S., Europe, and South Korea: NCT04278144 for patients with colorectal, endometrial, and gastroesophageal cancers and NCT05954143 for patients with breast cancer.

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 leveraging the immune system for a better way to treat cancer. The company is developing novel immunotherapies using an approach that teaches the immune system to recognize and kill cancer in a way that is immediately personalized to each patient. Its pipeline candidates are built on the Company's deep expertise in myeloid biology and cancer drug development and include BDC-1001, a HER2-targeting Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) being evaluated in a Phase 2 trial, and BDC-3042, a myeloid-modulating agonist antibody targeting Dectin-2, being evaluated in a Phase 1 trial. Bolt Biotherapeutics is also developing multiple Boltbody™ ISACs in 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 advancement and success of our clinical trials and any potential future patent term extensions or adjustments, 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; and 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 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.

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