Bolt Biotherapeutics Enrolls First Patient in Phase 2 Clinical Study Evaluating BDC-1001 in Patients with HER2-Positive Breast Cancer Previously Treated with Enhertu®

December 5, 2023

- BDC-1001 is a Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) in Phase 2 development for HER2-positive breast, colorectal, endometrial, and gastroesophageal cancers
- Poster detailing trial design and rationale to be presented at the 2023 San Antonio Breast Cancer Symposium on Wednesday, December 6

REDWOOD CITY, Calif., Dec. 05, 2023 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics, Inc. (Nasdaq: BOLT), a clinical-stage biopharmaceutical company developing novel immunotherapies for the treatment of cancer, today announced that the first patient has been dosed in the Phase 2 clinical trial investigating BDC-1001, a HER2-targeting Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC), as a single agent and in combination with the HER2-targeting antibody pertuzumab.

The first patient was treated at City of Hope, one of the largest cancer research and treatment organizations in the United States, by Irene Kang, M.D., Medical Director, Women's Health Medical Oncology, and Assistant Professor, Department of Medical Oncology and Therapeutics Research at City of Hope's cancer center in Irvine, California.

"The dosing of the first patient in this trial is a significant achievement in our efforts to find new treatment options for patients with HER2-positive breast cancer that continues to progress after treatment," said Kang, a principal investigator on the study. "Despite the numerous HER2-targeted therapeutics approved for treating advanced or metastatic HER2-positive breast cancer, many patients ultimately have disease progression and new options for treating these individuals are urgently needed."

The addition of pertuzumab has been shown to improve anti-tumor efficacy in preclinical models. The trial will treat patients with HER2-positive metastatic breast cancer previously treated with trastuzumab deruxtecan (Enhertu®).

"Patients with HER2-positive breast cancer who progress after Enhertu have few therapeutic options," said Edith A. Perez, M.D., Chief Medical Officer of Bolt Biotherapeutics. "BDC-1001 has a unique mechanism of action compared to available agents, mobilizing the patient's immune system to fight cancer. This provides scientific and clinical rationale for this new study. This is also our first opportunity to clinically validate the compelling anti-tumor activity we saw preclinically when combining BDC-1001 surrogate with pertuzumab."

Bolt's BDC-1001 Phase 2 program includes this trial with BDC-1001 with or without pertuzumab in breast cancer, as well as another trial in three additional HER2-positive tumor types. Both trials utilize a Simon two-stage design. This multi-center, randomized, open-label Phase 2 trial will evaluate the efficacy, safety, tolerability, pharmacokinetics, and pharmacodynamics of BDC-1001 administered intravenously at 20 mg/kg every other week as a single agent and in combination with pertuzumab. Roche is providing pertuzumab in support of the trial. Please refer to clinicaltrials.gov [NCT05954143] for additional information.

A poster detailing the trial design and rationale will also be presented at the 2023 San Antonio Breast Cancer Symposium on Wednesday, December 6, 2023. Details for the poster presentation can be found below. Additionally, a copy of the poster will be available on the Publications page of the Bolt Therapeutics website at the start of the poster session.

Title: Phase 2 study of novel HER2-targeting, TLR7/8 immune-stimulating antibody conjugate (ISAC) BDC-1001 +/- pertuzumab in patients with HER2-positive metastatic breast cancer (MBC) previously treated with trastuzumab deruxtecan.
Poster Number: PO1-20-06
Poster Session: 1
Details: Wednesday, December 6, 2023, 12:00 p.m. – 2:00 p.m. CT

Preclinical research combining pertuzumab with a BDC-1001 surrogate demonstrated enhanced anti-tumor efficacy in multiple models and was originally reported in Ackerman SE, et al. Nat Cancer. 2021;2(1):18-33. A full dataset was presented at the 38th Annual Meeting of the Society for Immunotherapy of Cancer in San Diego in November (Pearson C, et al. SITC 2023. Abstract #821), demonstrating that the combination significantly enhanced anti-tumor efficacy in multiple HER2-expressing tumor models and providing a compelling mechanistic rationale for conducting a clinical trial to evaluate the potential benefit for patients. Pertuzumab, which binds a distinct HER2 epitope from the trastuzumab component of BDC-1001, may increase the amount of clustered Fc or "eat me signals" on the surface of the tumor. This is hypothesized to trigger enhanced antibody-dependent cellular phagocytosis, a key element of the BDC-1001 mechanism of action, resulting in further propagation of BDC-1001-driven immune activation and anti-tumor efficacy.

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 as described above.

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 is currently in Phase 2 clinical development following the successful completion of a Phase 1 dose-escalation trial that demonstrated tolerability and early clinical efficacy. BDC-3042, an agonist antibody targeting Dectin-2, is expected 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 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, the potential profile of BDC-1001, and the benefits of combining BDC-1001 with pertuzumab, 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.

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