Bolt Biotherapeutics Announces Positive Topline Data from BDC-1001 Phase 1 Dose-Escalation Trial in HER2-Expressing Tumors, Supporting Advancement to Phase 2 Clinical Studies

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- BDC-1001 elicited objective clinical responses, including multiple PRs and long-term stable disease, across a diverse set of solid tumor types in monotherapy and in combination with nivolumab
- Data support selection of a recommended Phase 2 dose and advancement into Phase 2 studies in breast, colorectal, endometrial, and gastroesophageal cancers
- Entered into a new collaboration with Roche, as part of further BDC-1001 Phase 2 program expansion, supplying pertuzumab (Perjeta®) to evaluate in combination with BDC-1001

REDWOOD CITY, Calif., March 29, 2023 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics, Inc. (Nasdaq: BOLT), a clinical-stage biopharmaceutical company pioneering novel immuno-oncology therapeutics for the treatment of cancer, today reported positive topline data from the company's recently completed dose-escalation study of BDC-1001 in HER2-expressing solid tumors that support advancing into two Phase 2 studies. BDC-1001 is an investigational Immune-Stimulating Antibody Conjugate (ISAC) in development for the treatment of patients with HER2-expressing cancer. Data will be presented at an upcoming medical meeting.

Topline findings from this trial indicate that BDC-1001 was well tolerated at all dose levels and schedules evaluated, both as monotherapy and in combination with nivolumab. Target drug exposure levels were achieved at or near the recommended Phase 2 dose (RP2D) by more frequent administration including every other week (q2w) and weekly (q1w) administration schedules. Anti-tumor activity was observed in the form of multiple partial responses (PRs), tumor shrinkage, and long-term stable disease at or near the RP2D across multiple HER2-expressing solid tumor types in monotherapy and in combination with nivolumab. Moreover, biomarker data demonstrate that corresponding clinical and safety data are related to the ISAC mechanism. These data support the selection of a RP2D and advancement to Phase 2 studies.

"We are enthusiastic to be taking the next step in investigating the therapeutic promise of BDC-1001. In the study, we not only achieved target exposure levels for BDC-1001, but at those levels we saw promising signs of clinical activity as a single agent and in combination with nivolumab," said Edith A. Perez, M.D., Chief Medical Officer of Bolt Biotherapeutics. "We look forward to sharing full data at an upcoming major medical conference, and to initiating a focused Phase 2 program working with a diverse group of investigators in the U.S. and internationally. I'd like to express my gratitude to all the patients and investigators who are participating in our trial and to the incredible team at Bolt for their hard work and dedication."

"While we have made remarkable progress in developing new treatments for patients with HER2-expressing cancers, there remains an urgent need for innovation," said Bob T. Li, M.D., Ph.D., MPH, medical oncologist, and principal investigator at Memorial Sloan Kettering Cancer Center (MSK). "In this international dose-escalation trial, BDC-1001 leveraged a novel mechanism of HER2-targeted immune stimulating antibody conjugate and demonstrated encouraging evidence of efficacy and manageable safety, providing hope of a potential new treatment option for patients with HER2-expressing tumors."

Bolt Biotherapeutics' Phase 1 dose-escalation trial enrolled more than 100 patients with 16 different HER2-expressing solid tumor types. 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.

New Agreement with Roche Supporting Phase 2 Study
Bolt Biotherapeutics also announced today that it has entered into a clinical supply agreement with Roche to evaluate pertuzumab (Perjeta®) in combination with BDC-1001. Through a supply agreement, Roche will provide pertuzumab in support of a Phase 2 metastatic breast cancer trial.

Preclinical research combining pertuzumab with a BDC-1001-surrogate demonstrated enhanced anti-tumor efficacy in multiple models and a compelling mechanistic rationale for conducting a clinical trial to evaluate a potential impact on 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 appears 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.

BDC-1001 Phase 2 Clinical Program
Bolt's Phase 2 clinical plan includes two distinct studies, each using a Simon two-stage design. These studies will build upon Bolt's existing clinical sites and clinical trial centers of excellence in the U.S. and South Korea, expanding into multiple countries in Europe, and include:

- Phase 2 dose expansions of the current Phase 1/2 trial will initially focus on investigating BDC-1001 as a monotherapy, given the positive single-agent clinical data seen in the Phase 1 trial, enrolling HER2-positive colorectal, endometrial, and gastroesophageal cancer patients. Combination arms with nivolumab are expected to initiate in each indication following

demonstration of monotherapy anti-tumor activity. Bristol Myers Squibb, Bolt's clinical collaborator for this study, will continue to supply nivolumab at no cost for such expansion cohorts.
- Initiation of a two-cohort Phase 2 clinical trial exploring BDC-1001 as monotherapy and BDC-1001 in combination with pertuzumab in patients with HER2-positive metastatic breast cancer who have developed tumor progression following treatment with Enhertu.

About the Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) Platform
Bolt Biotherapeutics' Boltbody ISAC platform unites 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 advancement and success of our clinical trials and the expansion of our clinical trials across Europe, the success of our collaborations and the ability of our clinical collaboration partners to supply nivolumab and pertuzumab (Perjeta®), and the application of our ISAC platform 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.

Perjeta® is a trademark of Roche
Dr. Li has provided uncompensated advisory board services to Bolt Biotherapeutics.

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