Bolt Biotherapeutics Announces AACR 2021 Presentation of Boltbody™ Platform Mechanism of Action and Clinical Properties of Lead ISAC, BDC-1001

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Bolt's first-in-class clinical candidate, BDC-1001, is a novel HER2-targeting, TLR 7/8 immune-stimulating antibody conjugate (ISAC) currently in an ongoing Phase 1/2 first-in-human study

REDWOOD CITY, Calif., April 10, 2021 (GLOBE NEWSWIRE) -- 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 that an online oral presentation with live Q&A and a Trial in Progress poster presentation for lead agent BDC-1001 are being presented at the American Association for Cancer Research (AACR) Annual Meeting 2021 being held virtually from April 10-15th.

The oral presentation explores immunosuppression mediated by various cells in the tumor microenvironment (TME), as well as the tumor-supportive nature of antigen presenting cells (APCs) in the TME in preclinical models. Reawakening these immunosuppressed APCs may result in a productive and durable anti-tumor immune response. Bolt is utilizing its Boltbody™ platform to create immune-stimulating antibody conjugates (ISACs), such as BDC-1001, that invoke this mechanism and provided complete tumor regression in preclinical tumor models.

"In murine models we have seen efficacy in a variety of tumors that are immunologically cold and well-established. Furthermore, consistent with our proposed mechanism of action for ISACs, we see evidence of increased myeloid and T cell infiltration in the tumor microenvironment mediated by BDC-1001 surrogate ISACs," said David Dornan, Ph.D., Chief Scientific Officer at Bolt Biotherapeutics. "We're excited to share our rationale for selecting the linker-payload for BDC-1001 to optimize anti-tumor activity while minimizing the potential for the formation of anti-drug antibodies."

BDC-1001 is comprised of a tumor antigen-targeting monoclonal antibody (mAb), a trastuzumab biosimilar and an immune-stimulating agent (a TLR7/8 agonist) conjugated to each other with a non-cleavable linker. In a series of preclinical studies with BDC-1001, Bolt demonstrated the mechanism of action for their HER2-targeted ISAC. BDC-1001 surrogate was able to eliminate established, treatment-resistant tumors through the engagement of both innate and adaptive immunity. There were no adverse findings in toxicology studies of BDC-1001.

A Trial in Progress poster is also being presented by Manish R. Sharma, M.D. of START Midwest, a principal investigator in Bolt's ongoing BDC-1001 Phase 1/2 trial. The poster details the design of the study: a four-part study with two dose-escalation parts and two dose-expansion parts. The study is evaluating BDC-1001 administered intravenously with or without an immune checkpoint inhibitor targeting PD-1 in up to 390 patients with HER2-expressing or HER2-amplified advanced or metastatic solid tumors. The dose escalation parts will evaluate sequential doses of BDC-1001 as a monotherapy or in combination with a PD-1 checkpoint inhibitor in a 3+3 design, with the ability to backfill up to an additional 12 patients in each dose cohort. The dose expansion parts will evaluate the recommended Phase 2 dose as monotherapy or in combination with a PD-1 checkpoint inhibitor in four cohorts of patients.

The primary objective of the dose escalation portion of the study is to assess safety as measured by the incidence of adverse events and serious adverse events; dose-limiting toxicities within the 3+3 design; and potential immune-related toxicities and determine the recommended phase 2 dose. Secondary objectives will evaluate pharmacokinetic parameters and pharmacodynamic biomarkers in tumor tissue and in peripheral blood associated with drug exposure. These exploratory studies will help reinforce the ISAC mechanism of action in humans and seek to identify biomarkers associated with BDC-1001 biological activity with or without an immune checkpoint inhibitor.

In January, Bolt presented a preliminary clinical update on the first 20 patients that showed early signs of clinical activity, including stable disease in several patients and a confirmed partial response by RECIST, and acceptable safety with all 20 patients completing their dose-limiting toxicity (DLT) evaluation period without DLTs or drug-related serious adverse events. Treatment-emergent adverse events deemed to be related to BDC-1001 have been mild or moderate in severity, including mild infusion-related reactions without interruption to dosing. Bolt expects to provide an update on the trial sometime in the second half of 2021.

About Bolt Biotherapeutics' Immune Stimulating Antibody Conjugate (ISAC) Platform Technology
The Boltbody™ ISAC platform technology harnesses the ability of innate immune agonists to convert cold tumors into immunologically hot tumors, thereby illuminating tumors to the immune system and allowing them to be invaded by tumor killing cells. Boltbody ISACs have demonstrated the ability to eliminate tumors following systemic administration as monotherapy in preclinical models and have also led to the development of immunological memory, which is predicted to translate into more durable clinical responses for patients.

About the Ongoing BDC-1001 Phase 1/2 Study in Patients with HER2-Expressing Solid Tumors
The Phase 1/2, multi-center, open-label study is evaluating the safety, pharmacokinetics, pharmacodynamics and proof of mechanism of BDC-1001 in patients with HER2-expressing solid tumors. The first portion of the study includes a monotherapy dose-escalation phase in which cohorts of patients will receive ascending intravenous doses of BDC-1001 to determine the maximum tolerated dose and/or the recommended dose to advance into expansion cohorts and Phase 2 based on safety and tolerability. The second portion of the study is a dose expansion phase in which patients will receive BDC-1001 monotherapy to further evaluate the safety, tolerability and clinical antitumor activity of the recommended Phase 2 dose. Please

refer to www.clinicaltrials.gov NCT04278144 for additional clinical trial information.

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) approach uses immunostimulants to engage and activate myeloid cells that directly kill tumor cells. 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 to one of Bolt's proprietary TLR7/8 agonists for the treatment of patients with HER2-expressing solid tumors. Bolt is also advancing additional Boltbody ISAC product candidates targeting CEA and PD-L1.

For more information, 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 our clinical trials, the timing of enrollment for our Phase 1/2 trial for BDC-1001 for the treatment of patients with HER2-expressing solid tumors, the potential of BDC-1001's anti-tumor activity while minimizing the formation of anti-drug antibodies, the potential that APCs may result in a productive and durable anti-tumor immune response, and the prediction that Boltbody ISACs may translate into more durable clinical responses for patients. 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 Securities and Exchange Commission, 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.

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