Bolt Biotherapeutics Presents Updated Preclinical Data for BDC-4182 and Key Learnings from Phase 1 Dose-Escalation Trial of BDC-1001 at SITC 39th Annual Meeting

November 7, 2024

BDC-4182 demonstrated compelling anti-tumor activity and an acceptable safety profile in preclinical studies

BDC-4182 outperformed cytotoxic claudin 18.2 ADCs in syngeneic model

Learnings from BDC-1001 data suggest Boltbody™ ISACs with enhanced immune activation could offer greater efficacy, warranting further testing

REDWOOD CITY, Calif., Nov. 07, 2024 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics (Nasdaq: BOLT), a clinical-stage biopharmaceutical company developing novel immunotherapies for the treatment of cancer, today presented updated preclinical data for BDC-4182, a next-generation Boltbody™ ISAC clinical candidate targeting claudin 18.2, and provided key learnings from its Phase 1 dose-escalation trial of BDC-1001 at the 39th Annual Meeting of the Society for Immunotherapy of Cancer (SITC), being held in Houston, Texas from November 6-10, 2024.

"We are encouraged by the preclinical BDC-4182 data presented at SITC. Most notably, our next-generation claudin 18.2 ISAC elicits better efficacy than claudin 18.2 ADCs in syngeneic tumor models and can eradicate tumors with low claudin 18.2 expression. We look forward to dosing our first patient in BDC-4182 in 2025," said Michael Alonso, Ph.D., Senior Vice President of Research. "Our key learnings from the Phase 1 BDC-1001 dose escalation trial that are being presented at SITC support our belief that next-generation Boltbody™ ISACs with enhanced immune activation will offer greater efficacy with the potential for durable responses."

BDC-4182 is a next-generation Boltbody™ ISAC clinical candidate targeting claudin 18.2, a clinically validated target in oncology with expression in gastric/gastroesophageal junction cancer, pancreatic cancer, and other tumor types. BDC-4182 has advanced into IND-enabling activities, supported by in vitro and in vivo experiments demonstrating potent anti-tumor activity in multiple preclinical models, with clinical trial initiation expected in 2025. In vivo assessment of anti-tumor activity was performed with a murine surrogate of BDC-4182 using xenograft and syngeneic tumor models with different levels of claudin 18.2 expression. The tolerability of BDC-4182 was also tested in non-human primates (NHPs). Key findings are summarized below.

- BDC-4182 demonstrated superior efficacy compared to cytotoxic claudin 18.2 ADCs
- BDC-4182 demonstrated anti-tumor activity in a wide range of tumor models and elicits immunological memory
- BDC-4182 has an acceptable safety profile in NHPs with findings consistent with TLR7/8 activation and claudin 18.2 targeting
- BDC-4182 toxicology profile may enable combinations with checkpoint inhibitors, chemotherapy and anti-angiogenesis agents used in first-line and second-line treatments

Key learnings from the Phase 1 dose escalation trial of BDC-1001 are summarized below.

- First-generation ISAC BDC-1001 demonstrated immunological activity in this first-in-human trial, particularly in patients with high HER2 antigen expression
- Greater immune activation was associated with clinical benefit
- Pharmacodynamic changes were observed in HER2 IHC3+ and HER2 IHC2+, with both the greatest increase and statistical significance in patients with HER2 IHC 3+ tumors
- Data supports the hypothesis that an ISAC with enhanced immune activation could offer greater efficacy, warranting further testing in next-generation ISACs

Details about the BDC-1001 oral presentation and the BDC-4182 poster presentation can be found on the SITC website. Additionally, copies of the presentations are available on the publications page of the Bolt Biotherapeutics website.

Title: Preclinical Activity of BDC-4182, a Claudin 18.2-Targeting ISAC with Enhanced Potency and an Encouraging Safety Profile
Presenter: Han Kim, Ph.D., Bolt Biotherapeutics
Session Date and Time: Saturday, November 9, 2024, 9:00 a.m. – 8:30 p.m. CT
Location: Exhibit Halls A B George R. Brown Convention Center
Abstract Number: 1052

Title: Key Learnings from BDC-1001 Phase 1 FIH Dose Escalation Trial Inform Next-generation ISACs
Presenter: Jason Ptacek, Ph.D., Bolt Biotherapeutics
Session Date and Time: Saturday, November 9, 2024, 5:15 p.m. – 6:35 p.m. CT

Location: George R. Brown Convention Center - Level 3 - Grand Ballroom C
Abstract Number: 30

About the Boltbody Immune-Stimulating Antibody Conjugate (ISAC) Program
Bolt Biotherapeutics' Boltbody™ ISAC platform harnesses the precision of antibodies with the power of the innate and adaptive immune system 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-3042, a first-in-class agonist antibody that activates macrophages by targeting Dectin-2, and BDC-4182, a next-generation Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) clinical candidate targeting claudin 18.2. BDC-3042 is currently in a Phase 1 dose escalation trial that includes patients with any of seven different solid tumor types. BDC-4182 is supported by strong *in vitro* and *in vivo* data demonstrating potent anti-tumor activity, and activities are underway to support the initiation of clinical trials in 2025. Bolt Biotherapeutics is also developing additional 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 potential initiation of clinical trials for BDC-4182, the anti-tumor potency, safety and tolerability, and characteristics of our product candidates, and the initiation of future clinical trials, 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, 2023. 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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