Bolt Biotherapeutics Presents Preclinical Results for Next-Generation Boltbody™ ISACs targeting CEA and PD-L1 at AACR Annual Meeting 2025

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CEA-targeted ISAC elicits complete responses in mice and is well-tolerated in NHPs

PD-L1 ISAC directly activates and reprograms PD-L1-expressing myeloid cells in the TME to drive complete responses and immunological memory

REDWOOD CITY, Calif., April 30, 2025 (GLOBE NEWSWIRE) -- Bolt Biotherapeutics (Nasdaq: BOLT), a clinical-stage biopharmaceutical company developing novel immunotherapies for the treatment of cancer, today announced preclinical results from its next-generation Boltbody™ ISACs targeting CEACAM5 and PD-L1 at the American Association for Cancer Research (AACR) Annual Meeting.

“We are encouraged by these early results from our next-generation Boltbody™ ISACs targeting CEA and PD-L1,” said Michael Alonso, Ph.D., Senior Vice President of Research. “There are currently no approved therapies targeting CEA, and our next-gen CEA ISAC induced complete and durable anti-tumor responses in mice and was well-tolerated in NHPs. Additionally, the preclinical results demonstrated that PD-L1 ISACs represent a compelling new approach to treat cancer, leveraging mechanisms that are distinct from and potentially complementary to conventional PD-1/PD-L1 blockade.”

CEA refers to a specific carcinoembryonic antigen cell adhesion molecule also known as CEACAM-5 that is commonly found in gastrointestinal cancers such as colorectal cancer. Bolt’s lead CEA-targeted ISAC comprises a novel, fully human antibody with high affinity and selectivity to CEA, and not to other members of the CEACAM family, conjugated to a proprietary next-generation TLR7/8 agonist via a non-cleavable linker. This ISAC drives enhanced phagocytosis of CEA-positive tumor cells and stimulates production of critical immune-activating cytokines including IL-12p70, IFNg, and TNFa. Key results with the next-gen CEA ISAC are below:

- Antigen-dependent induction of immune-stimulating cytokines in human, NHP and mouse effector cells
- Complete responses in CEA transgenic syngeneic model demonstrates robust efficacy
- Induction of immunological memory demonstrates potential for durable responses
- In a non-GLP NHP tox study, the next-generation CEA ISAC was well-tolerated with no significant drug-related adverse events observed up to 15 mg/kg, the highest tested dose

Bolt’s PD-L1 ISAC utilizes a novel human anti-PD-L1 antibody conjugated to a next-generation TLR7/8 agonist payload via a non-cleavable linker. This ISAC leverages a unique mechanism of action due to its ability to target both tumor and immune cells that express PD-L1. Key results are below:

- PD-L1 ISACs directly activate and reprogram PD-L1-expressing myeloid cells in the TME to promote innate and adaptive antitumor immunity
- PD-L1 ISACs elicit complete regressions and immunological memory in models that are resistant to PD-1/PD-L1 checkpoint inhibitor therapy
- Mechanistic studies indicate that PD-L1 expression by either tumor or immune cells is sufficient to drive antitumor efficacy
- Blockade of the PD-1/PD-L1 axis is not required for PD-L1 ISAC efficacy but may be a supportive mechanism and complementary combination strategy
- Favorable safety profile was demonstrated in non-GLP NHP toxicology studies supporting use in combination with SoC therapies & other agents

Details about the poster presentations can be found on the AACR website. Additionally, a copy of each poster is available on the Publications page of the Bolt Biotherapeutics website.

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 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 second quarter 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 future potential of our CEA ISAC in CEA-expressing cancers, the potential of our PD-L1 ISAC and the ability of our PD-L1 ISAC to complement PD-1 and PD-L1 inhibitors, 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, 2024. 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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