Bolt Biotherapeutics Presents New Preclinical Data on Three Pipeline Programs at Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 12, 2021

- Presentation of preclinical data supporting the selection of BDC-2034, an ISAC targeting CEA, as Bolt Biotherapeutics' second Boltbody™ ISAC development candidate
- Demonstration of the novel, multifunctional mechanism for an ISAC which combines PD-1/PD-L1 axis inhibition with TLR agonism
- Identification of novel agonist antibodies targeting Dectin-2, now revealed as Bolt Biotherapeutics' TAM1 target, designed to reprogram tumor-supportive macrophages into tumor-destructive macrophages

REDWOOD CITY, Calif., Nov. 12, 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 the company will be presenting posters with new data from three of its pipeline programs on Saturday, Nov. 13, at the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting, being held virtually and in person in Washington, D.C. from Nov. 10-14. Each presentation highlights the progress made in preclinical studies to demonstrate the potential for each pipeline candidate as a novel approach for the treatment for cancer.

"We are presenting new data for three of our pipeline programs that demonstrate the depth of our technology platform and the expertise of our team in modulating myeloid cell biology to develop promising therapeutic candidates," said David Dornan, Ph.D., Bolt Biotherapeutics' Chief Scientific Officer. "Repolarizing tumor-associated macrophages, or TAMs, to become tumor destructive via the novel target Dectin-2 is groundbreaking work that may be synergistic with our entire Boltbody ISAC portfolio. Our work targeting CEA and PD-L1 reinforces our commitment to develop therapeutics that could have promising activity against solid tumors where limited treatment options are available."

Highlights of the three poster presentations follow, and copies of the posters are available on the Bolt Biotherapeutics website.
Poster #784: "BDC-2034: Discovery of a CEA-targeting Immune-Stimulating Antibody Conjugate (ISAC) for Solid Tumors"
Presenter: William G. Mallet, Ph.D.
Details: Saturday, Nov. 13, 2021, 7:00 a.m. - 8:30 p.m. EST, Poster Hall

Key findings from the study:
CEA is a well-validated tumor antigen for the development of targeted therapies addressing multiple types of solid tumors, such as colon cancer, where new treatment options are urgently needed. Given the abundance of innate immune cells in CEA-expressing cancers, innate immune stimulation presents a promising therapeutic strategy. Applying Boltbody platform technology, Bolt Biotherapeutics scientists have developed a novel CEA-targeted ISAC, BDC-2034, to exploit over-expression of CEA in cancers. BDC-2034 is designed to trigger the innate immune system, leading to adaptive anti-tumor immunity and tumor destruction.

- BDC-2034 comprises a novel CEA-targeted, pro-phagocytic antibody conjugated to a proprietary TLR7/8 agonist payload. Both elements of this molecule are finetuned for selective immune activation in tumors.
- New data reported at SITC 2021 demonstrate both tumor cell clearance and innate immune activation in cellular and *in vivo* models of CEA-expressing cancers. Further, systemic administration in tumor-bearing animals results in tumor-selective immunity.
- Based on these data, Bolt Biotherapeutics designated BDC-2034 as a clinical candidate and is currently conducting IND-enabling studies with the expectation to initiate BDC-2034 clinical development in 2022.

Poster #782: "PD-L1-targeted ISAC combines myeloid cell activation, immune-checkpoint inhibition and ADCP to improve anti-tumor efficacy over anti-PD-L1 antibodies in preclinical models"
Presenter: Marcin Kowanetz, Ph.D.
Details: Saturday, Nov. 13, 2021, 7:00 a.m. - 8:30 p.m. EST, Poster Hall

Key findings from the study:
Bolt Biotherapeutics scientists are presenting for the first time preclinical data on a novel multifunctional PD-L1-targeted Boltbody ISAC that has demonstrated the potential to improve upon the efficacy of PD-L1/PD-1 inhibition, especially in tumor types that do not respond well to immune-checkpoint inhibition.

- Bolt Biotherapeutics' PD-L1 ISAC uniquely combines three mechanisms of action: the ADCP and myeloid cell activation of an ISAC, plus immune-checkpoint inhibition with the ability to act through PD-L1 expressed on both tumor and immune cells.
- Data presented at SITC 2021 demonstrate how PD-L1 ISAC induces robust, target-dependent activation of the immune system, including induction of immunological memory.
- Treatment with PD-L1 ISACs led to an effective anti-tumor response that was substantially improved over PD-L1 antibody blockage in preclinical models.

Poster #862: "Dectin-2, a novel target for tumor macrophage reprogramming in cancer immunotherapy"
Presenter: Justin A. Kenkel, Ph.D.
Details: Saturday, Nov. 13, 2021, 7:00 a.m. - 8:30 p.m. EST, Poster Hall

Key findings from the study:
For the first time, Bolt Biotherapeutics is presenting data providing preclinical validation of Dectin-2, formerly referred to as TAM1, as a novel target for cancer immunotherapy. Expressed by tumor-associated macrophages (TAMs), Dectin-2 is a pattern recognition receptor that stimulates proinflammatory cytokine production and antigen presentation to drive innate and adaptive immune responses.

- Findings reported at SITC 2021 demonstrate that agonism of Dectin-2 on TAMs elicits secretion of pro-inflammatory cytokines and chemokines capable of invoking productive anti-tumor immunity.
- In murine tumor models, Dectin-2 agonism mediates anti-tumor efficacy in a CD8 T cell-dependent manner and induces immunological memory against the tumor.
- Bolt Biotherapeutics scientists have generated Dectin-2 agonist antibodies that show the potential to reprogram tumor-supportive macrophages into tumor-destructive macrophages.

About the Boltbody™ Immune-Stimulating Antibody Conjugate (ISAC) Platform
ISACs are a new category of immunotherapy that combines the precision of antibody targeting with the strength of the innate and adaptive immune systems. Boltbody ISACs comprise three primary components: a tumor-targeting antibody, a non-cleavable linker, and a proprietary immune stimulant to activate the patient's innate immune system. By initially targeting a single marker on the surface of a patient's tumor cells, an ISAC can create a new immune response by activating and recruiting myeloid cells. The activated myeloid cells start a feed-forward loop by releasing cytokines and chemokines, chemical signals that attract other immune cells and lower the activation threshold for an immune response. This reprograms the tumor microenvironment and invokes an adaptive immune response that targets the tumor, with the goal of durable responses for patients with cancer.

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 Biotherapeutics' lead candidate, BDC-1001, is a Boltbody™ Immune-stimulating Antibody Conjugate (ISAC) comprising a HER2-targeting biosimilar of trastuzumab conjugated with a non-cleavable linker to one of the company's proprietary TLR7/8 agonists for the treatment of patients with HER2-expressing solid tumors. Bolt Biotherapeutics is also advancing BDC-2034, a Boltbody ISAC targeting CEA, and a pipeline of early-stage immuno-oncology products. To learn more about Bolt Biotherapeutics, please visit 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 success and results of our pipeline programs, our ability to synergize our pipeline programs with our Boltbody platform, our future results of operations, financial condition, business strategy and plans and objectives of management for future operations, 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," "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 SEC, including our Quarterly Report on Form 10-Q for the three months ended September 30, 2021. 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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