BIOATLA CONDITIONALLY ACTIVE BIOLOGIC ANTIBODY DESIGN AND FUNCTIONALITY FOR CANCER TREATMENT DESCRIBED IN LEADING SCIENTIFIC JOURNAL PEER-REVIEWED PAPER

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BioAtla Scientists Discover Novel pH Mechanism Published in Proceedings of the National Academy of Sciences

SAN DIEGO, CA - February 22, 2021 - BioAtla, Inc., a global clinical-stage biotechnology company focused on the development of Conditionally Active Biologic (CAB) antibody therapeutics, today announced the publication by Proceedings of the National Academy of Sciences (PNAS) that describes the design and functionality of therapeutic antibody candidates utilizing BioAtla's proprietary CAB technology making them active only in the acidic tumor microenvironment while binding is reversibly inhibited in healthy tissue. This improved tumor targeting utilizes a newly discovered chemical switch system and is shown in animal models to provide for potent anti-tumor activity with markedly reduced toxicity to normal tissue, indicating a widened therapeutic index.

The peer reviewed paper, "Generating Tumor-selective Conditionally Active Biologic Anti-CTLA4 Antibodies Via Protein-associated Chemical Switches" by Hwai Wen Chang, Ph.D., Gerhard Frey, Ph.D., Haizhen Liu, Ph.D., Charles Xing, M.S., Lawrence Steinman, M.D., William J. Boyle, Ph.D., and Jay M. Short, Ph.D., describes the application of CAB technology in the context of the preclinical development of BioAtla's immuno-oncology based CAB-CTLA4 antibody candidates, as well as several CAB antibodies directed against other important oncology targets. "CAB antibodies utilize a newly discovered switch mechanism that allows them to be active only in the tumor microenvironment and not active under normal physiological conditions. CAB antibodies demonstrate reduced peripheral toxicity and therefore are expected to provide a wider therapeutic window compared to traditional antibodies currently available for cancer therapy, potentially enabling higher dosing and longer treatments for improved efficacy," stated co-inventor Jay M. Short, Ph.D., Chairman, Chief Executive Officer and co-founder of BioAtla, Inc.

The CAB technology capitalizes on the well-established Warburg Effect that through a glycolytic process leads to an acidic external tumor microenvironment. Extracellular pH levels in tumors have been measured to be as low as pH5.8 compared to the tightly controlled, alkaline, pH7.4 of blood, with even higher pH in healthy tissues. Glycolytic metabolism is also the basis of the established PET scanning technology for cancer detection for tumor types. CAB proteins have increased binding activity as the pH in the microenvironment becomes acidic, while being inactive in normal physiological environments. BioAtla scientists discovered a novel chemical switch mechanism involving physiological-occurring chemicals, such as bicarbonate and hydrogen sulfide. These molecules are negatively charged at physiological conditions and interact with positive charged areas on the protein surface. Under acidic conditions of the tumor microenvironment they are neutralized and released from the protein surface, uniquely allowing CAB antibodies to bind to their target and attack the tumor cell. BioAtla refers to this novel physiological mechanism, used for generating CABs, as Protein-associated Chemical Switch(es) or PaCS mechanism.

CAB antibodies belong to a novel class of tumor-selective therapeutics that do not require the addition of a protective group and irreversible enzymatic activation in the tumor that is used with prodrug designs. The CAB-CTLA4 candidates described in the paper showed substantially reduced binding at pH7.4 compared to binding at pH6.0, while the comparable Ipilimumab analogue (IpA) binding showed no dependence on pH, thereby leading IpA to bind and attack normal cells, which results in dangerous on-target off-tumor toxicity. In comparison, multiple CAB candidates demonstrated substantial binding differentials between pH6.0 and pH7.4 conditions ranging from 9-fold to over 175-fold by ELISA, which is expected to lead to an improved therapeutic index and the potential improved clinical risk benefit in future therapies. The ability to design CAB tumor target binding for a specific range of pH conditions demonstrates the flexibility provided by the PaCS mechanism and the CAB technologies. Selection of a CAB antibody candidate is based upon strong differential pH binding between tumor and normal cells that can lead to increased anti-tumor potency with reduced toxicity, while maintaining a low immunogenicity risk and efficient manufacturing characteristics.

In addition to the development of CAB-CTLA4 discussed in the paper, BioAtla has successfully generated several CAB antibodies against multiple targets including EpCAM, Her2, Nectin-4, and CD73. The proprietary technology has also successfully been used for the development of ADCs and T-cell engaging bispecific antibodies. The ability to design conditionally active therapeutics with stronger selectivity over narrower pH ranges using the PaCS mechanism offers the opportunity to greatly enhance both the safety and potency of future therapies for solid tumors.

Potential for additional therapeutic modalities and disease targets

It is expected from the studies described in the paper that there is a potential for other yet to be identified PaCS molecules in disease related microenvironments, whether controlled through pH, concentration, or other molecular characteristics (intra- or intermolecularly) for enhancing a drug's therapeutic index. Potential new therapeutic candidates addressing these opportunities are not limited to antibodies, but also include small molecules, encompassing lipids, sugars and nucleic acid-based agents or drugs. Further, it is expected that PaCS protein-chemical systems are important naturally occurring regulatory systems linked to a range of disease-related microenvironments, including cancer, inflammation and cellular senescence.

About BioAtla, Inc.

BioAtla is a global clinical-stage biotechnology company with operations in San Diego, California, and Beijing, China. Utilizing its proprietary Conditionally Active Biologics (CAB) technology, BioAtla develops novel monoclonal antibody and other protein therapeutic product candidates designed to have more selective targeting, greater efficacy, and more cost-efficient and predictable manufacturing than traditional antibodies. BioAtla has extensive and worldwide patent coverage for its CAB technology and products with more than 250 issued patents and more than 200 pending patent applications worldwide. Broad patent coverage in all major markets include methods of making, screening and manufacturing CAB product candidates in a wide range of formats and composition of matter coverage for specific products. BioAtla has two CAB programs currently in Phase 2 clinical testing in the United States, BA3011, a novel conditionally active AXL-targeted antibody-drug conjugate (CAB-AXL-ADC), and BA3021, a novel conditionally active ROR2-targeted antibody-drug conjugate (CAB-ROR2-ADC). BioAtla's investigational CAB CTLA-4 antibody, BA3071, is subject of a global co-development and collaboration agreement with BeiGene Ltd. for its development, manufacturing and commercialization. BA3071 is a

novel, CTLA-4 inhibitor that is designed to be conditionally activated in the tumor microenvironment in order to reduce systemic toxicity and potentially enable safer combinations with checkpoint inhibitors such as anti-PD-1 antibody.

Learn more at www.bioatla.com.

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