Twist Bioscience Publishes Preclinical Data Detailing Discovery of Antibody Targeting Emerging Checkpoint Inhibitor

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TB206-001 shown to be a high-affinity, cross-reactive humanized antibody antagonist of $A_{2A}R$ with in vivo tumor suppressing activity

TB206-001 available for out-licensing

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Jun. 6, 2024-- Twist Bioscience Corporation (NASDAQ: TWST), a company enabling customers to succeed through its offering of high-quality synthetic DNA using its silicon platform, today announced the publication of a study detailing the discovery of TB206-001, a first-in-class antibody targeting adenosine A_{2A} receptor ($A_{2A}R$), a promising molecular target that could enhance cancer immunotherapy. The study titled, "Discovery of a potent, selective, and tumor-suppressing antibody antagonist of adenosine A2A receptor", was published in the journal PLOS ONE.

$A_{2A}R$ is an emerging immune checkpoint that plays a role in the immunosuppression of the tumor microenvironment. It is part of an important class of therapeutic targets, called G protein-coupled receptors (GPCRs), which are found on most immune cells and highly expressed in certain cancers. Tumors commonly produce excess adenosine, which activates A_{2A} receptors and suppresses immune cells. Blocking $A_{2A}R$ could alleviate the suppressive environment and restore tumor immunity. $A_{2A}R$ has been shown to play a role in various cancers including colorectal cancer, gastric cancer, lymph node metastasis, breast cancer and melanoma as well as in autoimmune diseases and Parkinson's.

"The majority of current therapies in clinical trials targeting $A_{2A}R$ are small molecules, as it has been traditionally difficult to discover antibodies that block GPCRs; however, antibodies have greater affinity for target molecules, do not cross into the central nervous system and could be dosed less frequently," said Emily M. Leproust, Ph.D., CEO and co-founder of Twist Bioscience. "With the right partner to take it forward, TB206-001, our Twist-discovered first-in-class antibody antagonist of $A_{2A}R$, could be developed as a powerful inhibitor to restore immune responses in immunosuppressive environments that allow cancer to grow."

In the study, the researchers immunized two different sets of animals with DNA encoding wildtype or mutant $hA_{2A}R$ (C144S, S334A, S338A) modified to minimize the impact of the receptor's natural signaling on its expression. Once the animals generated antibodies to the receptor, the researchers built immune and synthetic single-chain variable fragment (scFvs) phage display libraries from the immune repertoire. The libraries were subsequently screened against detergent solubilized $A_{2A}R$, and positive hits were reformatted into monoclonal antibodies for further testing. The result was TB206-001, which directly targets $A_{2A}R$ and activates immune cells. In preclinical studies, the antibody has shown high affinity and specific activity for $A_{2A}R$ over other adenosine receptors and shows tumor-suppressing activity in colon tumor-bearing HuCD34-NCG mice. Additional studies in animal models found that TB206-001 reduced tumor volume better than PD-1 inhibitors.

"There is still tremendous potential for immunotherapies either in combination with or in addition to those targeting PD-1 and CTLA-4," said Gregory Carven, Ph.D., one of the original inventors of Keytruda. "Using the ability to create large antibody libraries enabling discovery of novel and highly specific therapeutics, Twist has discovered an antibody that blocks $A_{2A}R$, a promising checkpoint target and demonstrated its activity in preclinical models. The antibody could be further developed as a standalone therapy, bispecific or combination therapy to bring potential therapeutic benefit to patients."

About Twist Bioscience Corporation

Twist Bioscience is a leading and rapidly growing synthetic biology and genomics company that has developed a disruptive DNA synthesis platform to industrialize the engineering of biology. The core of the platform is a proprietary technology that pioneers a new method of manufacturing synthetic DNA by "writing" DNA on a silicon chip. Twist is leveraging its unique technology to manufacture a broad range of synthetic DNA-based products, including synthetic genes, tools for next-generation sequencing (NGS) preparation, and antibody libraries for drug discovery and development. Twist is also pursuing longer-term opportunities in digital data storage in DNA and biologics drug discovery. Twist makes products for use across many industries including healthcare, industrial chemicals, agriculture and academic research.

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Twist Bioscience Legal Notice Regarding Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical facts contained herein are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including statements regarding the ability of TB206-001 to enhance cancer immunotherapy. Forward-looking statements involve known and unknown risks, uncertainties, and other important factors that may cause Twist Bioscience's actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the ability to achieve the expected benefits of Twist Bioscience's restructuring activities and reduced investments in DNA data storage; the ability to attract new customers and retain and grow sales from existing customers; the ability of Twist Bioscience to achieve sufficient revenue to achieve or maintain positive cash flow from operations or profitability in any given period will depend

heavily on the success of our existing products and the development and commercialization of additional products in the synthetic biology, biologic drug and data storage industries; risks and uncertainties of rapidly changing technologies and extensive competition in synthetic biology that could make the products Twist Bioscience is developing obsolete or non-competitive; uncertainties of the retention of significant customers; the ability of Twist Bioscience to successfully integrate acquired companies and to achieve expected benefits from acquisitions; supply chain and other disruptions; risks of third party claims alleging infringement of patents and proprietary rights or seeking to invalidate Twist Bioscience's patents or proprietary rights; and the risk that Twist Bioscience's proprietary rights may be insufficient to protect its technologies. For a description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Twist Bioscience's business in general, see Twist Bioscience's risk factors set forth in Twist Bioscience's Annual Report on Form 10-K filed with the SEC on November 21, 2023 and subsequent filings with the SEC. Any forward-looking statements contained in this press release speak only as of the date hereof, and Twist Bioscience specifically disclaims any obligation to update any forward-looking statement, whether as a result of new information, future events or otherwise.

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