Twist Bioscience Publishes Data on VHH Single Domain Antibody Discovery Using New Methodology on Optofluidic Platform

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Demonstrates Ability to Generate Humanized PSMA-Specific VHH Single Domain Antibodies via Single B Cell Screening on the Beacon Platform

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Feb. 14, 2023-- Twist Bioscience Corporation (NASDAQ: TWST), a company enabling customers to succeed through its offering of high-quality synthetic DNA using its silicon platform, today published on the successful discovery of alpaca-derived VHH antibodies using a disruptive, function-forward *in vivo* discovery workflow developed by Abveris, also known as Twist Boston, on the Beacon optofluidic platform. The paper, titled "Alpaca Single B Cell Interrogation and Heavy-Chain-Only Antibody Discovery on an Optofluidic Platform," was published in BioRxiv.

"*In vivo* discovery approaches for VHH antibodies have been limited by the lack of methodologies available for camelid B cell interrogation to discover heavy-chain-only antibodies. Twist Boston developed highly sophisticated assay formats for use on the Beacon optofluidic platform, which can enable the enrichment and screening of alpaca B cells in a way that provides in-depth functional data from each cell," said Emily M. Leproust, Ph.D., CEO and co-founder of Twist Bioscience. "We are able to offer customers *in vivo* and library based VHH antibody discovery and optimization approaches, providing them with integrated solutions to identify VHH and other antibodies with improved characteristics, such as higher binding affinity and functional activity for difficult targets."

A VHH single domain antibody is the antigen binding domain from unique heavy-chain-only antibodies generated in camelids such as llamas and alpacas. Most antibodies contain two variable domains, the heavy and the light chains; however, camelids make antibodies containing just a heavy chain, from which the VHH single domain is derived. The small size of the VHH single domain antibodies allow them to access targets that traditional antibodies cannot, with tight binding affinities and high specificity. In addition, the lack of a paired light chain in VHH single domain antibodies simplifies downstream engineering, accelerating development timelines.

In this proof-of-concept study, custom enrichment, culture, detection, and sequencing methods were used to screen single B cells directly from immunized alpacas for target specificity and heavy-chain-only antibody secretion from alpacas immunized with two different targets, either human prostate specific membrane antigen (PSMA) or a second blinded target. B cells secreting target-specific heavy-chain-only antibodies were identified, exported, and sequenced.

PSMA-specific VHH hits were recombinantly expressed as VHH-Fc, purified, and characterized using label-free techniques. All but one VHH-Fc bound PSMA with a single-digit nanomolar affinity. Four VHH candidates were successfully humanized in silico using a rapid bulk humanization approach powered by machine learning. Next-generation repertoire sequencing of PBMCs harvested at longitudinal timepoints throughout immunization was also performed. This uncovered additional variants within the clonal lineages of the validated hits, some of which could potentially exhibit superior pharmacological properties.

This unique combination of repertoire sequencing and function-forward single B cell screening could be used for antibody optimization by leveraging Twist's library design platform to generate antigen-biased VHH single domain libraries to discover superior variants. In addition, functional validation of these optimized lead candidates could enable downstream development of high quality PSMA-specific VHH single domain antibodies for therapeutic or diagnostic purposes.

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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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, but not limited to, statements regarding the ability of the new methodology to be used for VHH single domain antibody optimization. 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 risks and uncertainties relating to COVID-19; the ability to attract new customers and retain and grow sales from existing customers; 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, including Abveris, and to achieve

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