Twist Bioscience Internally-Discovered Single Domain Antibody TB202-3 Shows Potent Binding to Multiple Strains of SARS-CoV-2, Including Alpha, Beta, and Gamma Strains, in Preclinical Studies

September 23, 2021

– Results Published in *Science* –

– Blinded Analysis Conducted through COVID International Consortium –

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)--Sep. 23, 2021-- Twist Bioscience Corporation (Nasdaq: TWST) today reported that its internally-discovered antibody candidate TB202-3 (CoVIC-094), demonstrated potent binding to diverse SARS-CoV-2 variant mutations, including strains with the E484K, N501Y, D614G, Y453F and K417N mutations in pseudovirus assays, indicating this therapeutic antibody may be effective in treating many strains of COVID-19.

The Coronavirus Immunotherapy Consortium (CoVIC), an academic-industry, non-profit collaborative research effort, performed the blinded analysis, confirming that TB202-3 completely blocked SARS-CoV-2 spike protein from binding to human ACE2. The results were published in *Science* today

CoVIC used high-throughput surface plasmon resonance analysis and cryo-EM structural determination, sorting antibodies that react within the SARS-CoV-2 receptor binding domain (RBD) into 7 different “communities” (RBD-1 through RBD-7). Antibodies in the RBD-4 community bind to the outer face of the RBD and can do so in either the “up” or “down” RBD conformation. Monoclonal antibodies that target RBD-4 bind towards the outer edge of the receptor binding motif and can block binding to ACE2 on human cells, the entry point for the virus. Select properties of RBD-4 antibodies indicate they may have increased potency against the virus.

COVID-19 continues to evolve, spurring additional mutations and viral strains. TB202-3 binds to a majority of known mutations, with the exception of the L452R mutation present in the Delta and Epsilon variants. Twist developed a new VHH single domain antibody, TB339-031, with a similar structure and potency to TB202-3, which also binds and neutralizes the Delta and Epsilon variants, that is now advancing through late-stage discovery and validation testing.

SARS-CoV-2 is an RNA virus. Viruses survive by replicating in their target host, in the case of SARS-CoV-2 this is humans. During the replication process, there is often an error that results in the copying process, which is the definition of a mutation. Most of the time, mutations do not make a difference in the virus. Sometimes, however, a mutation makes the virus more transmissible or more deadly. Depending on the location of the mutation, it may reduce the efficacy of therapeutic antibodies that bind at the mutated location. Therapeutic antibodies that bind to the virus in a place that is not impacted by mutations can treat the widest range of COVID-19 variant strains successfully.

“Applying our proprietary drug discovery and optimization platform, we identified and advanced TB202-3 through preclinical studies and submitted this antibody to CoVIC for comprehensive testing in comparison to others,” said Emily M. Leproust, Ph.D., CEO and co-founder of Twist Bioscience. “With the continuous emergence of variant strains of SARS-CoV-2, antibodies that bind to regions away from the areas of frequent mutation will be critical to the ongoing global response. While broad-spectrum is a term used most often in relation to antibiotics, it applies here to Twist’s antibodies, as they show efficacy in neutralizing a wide range of SARS-CoV-2 variants.”

“These comprehensive results show that TB202-3 may be more resistant to receptor-driven selection pressure and Twist antibodies may work therapeutically against emerging SARS-CoV-2 variants,” continued Dr. Leproust. “In addition to binding location and neutralization efficacy, due to its small size, selectivity and preclinical efficacy, Twist antibodies may offer an advantage over traditional antibodies as they can be an integral component of a bispecific antibody or can be used with other antibodies. COVID-19 infection continues to spread throughout the world, and new therapeutic options will be required to treat emerging variants.”

Previous studies of TB202-3, a single domain VHH “nanobody”, demonstrated protection against weight loss, a key indicator of disease severity, at the lowest dose of 1 mg/kg in a preclinical hamster challenge model. Conducted at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), immunosuppressed animals were given 1, 5 or 10 mg/kg of each of the Twist antibodies and were assessed for weight loss. Animals treated with all doses of TB202-3 were protected against weight loss, whereas control animals lost a mean of 11.7% of their body weight. Validation and late-stage discovery studies continue for TB339-031.

About Twist Biopharma Antibodies

About 75 percent of the antibodies in the blood are IgGs. IgGs are made up of two heavy protein chains and two light protein chains that must pair together and cooperate to specifically recognize a target, in this case the Spike Protein on SARS-CoV-2. This specific targeting affords our immune systems “memory,” allowing it to selectively and precisely eliminate pathogenic threats.

Target recognition by VHH single domains, on the other hand, requires just a single domain found on heavy chain only antibody. With VHH-based antibodies able to exhibit pharmaceutically-relevant properties comparable to IgGs, they are a promising therapeutic with several advantages over their bulkier, more complex counterparts. The small size of VHH antibodies means they can squeeze into spaces and bind or block to parts of molecules that would otherwise be inaccessible to human IgG antibodies. They are also more thermally and chemically stable, making VHH-based therapeutics good candidates to address respiratory infections, administered by inhaler directly to the respiratory tract where the infection is concentrated. In addition, the small size simplifies manufacturing of VHH antibodies. In addition to SARS-CoV-2, Twist Biopharma discovers and

develops IgG and VHH antibodies to numerous different targets for partners and internal development.

About The Coronavirus Immunotherapy Consortium (CoVIC)

CoVIC is an academic-industry, non-profit collaborative research effort that brought together scientists from around the world and enabled them to share and evaluate candidate SARS-CoV-2 anti-S protein antibodies side-by-side in a blinded, multidisciplinary analysis. Together, they are identifying ideal therapeutic combinations, the assays that best predict efficacy, and the features that provide protection.

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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Legal Notice Regarding Forward-Looking Statements

This press release contains forward-looking statements. All statements other than statements of historical facts contained herein, including but not limited to TB202-3’s role as an important and viable candidate for clinical testing, its resistance to receptor driven selection pressure, its ability to work therapeutically against emerging SARS-CoV-2 variants and its advantage over traditional antibodies, 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. Such forward-looking statements involve known and unknown risks, uncertainties, and other important factors that may cause Twist’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 of the duration, extent and impact of the COVID-19 pandemic, including any reductions in demand for our products (or deferred or canceled orders) globally or in certain regions; 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 could make the products Twist is developing obsolete or non-competitive; uncertainties of the retention of a significant customer; supply chain and other disruptions caused by the COVID-19 pandemic or otherwise; risks of third party claims alleging infringement of patents and proprietary rights or seeking to invalidate Twist’s patents or proprietary rights; and the risk that Twist’s proprietary rights may be insufficient to protect its technologies. For a further 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’s business in general, see Twist’s risk factors set forth in Twist’s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2021 and subsequent filings with the SEC. In addition, many of the foregoing risks and uncertainties are, and could be, exacerbated by the COVID-19 pandemic and any worsening of global or regional business and economic environment as a result. We cannot at this time predict the extent of the impact of the COVID-19 pandemic and any resulting business or economic impact, but it could have a material adverse effect on our business, financial condition, results of operations and cash flows. 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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