Bicycle Therapeutics Selected to Participate in FDA Program to Expedite Commercial Manufacturing Readiness of BT8009 for Metastatic Bladder Cancer

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Program intended to facilitate CMC development for selected therapies with expedited clinical development timeframes to help patients get access sooner

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Oct. 19, 2023-- Bicycle Therapeutics (Nasdaq: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced that BT8009, the company's lead investigational therapy in development to treat metastatic bladder (urothelial) cancer, has been selected to participate in the Chemistry, Manufacturing and Controls (CMC) Development and Readiness Pilot (CDRP) Program recently launched by the U.S. Food and Drug Administration (FDA). BT8009 is one of up to nine products selected for the first year of the CDRP Program, which the FDA created to facilitate CMC development for therapies with expedited clinical development timeframes based on the anticipated clinical benefits of earlier patient access to the therapy. Through the CDRP Program, Bicycle Therapeutics plans to work closely with the FDA to facilitate CMC development and expedite commercial manufacturing readiness of BT8009.

"We are honored to participate in the inaugural cohort of the FDA's CDRP Program," said Mike Hannay, D.Sc., FRPharmS, senior vice president and head of CMC at Bicycle Therapeutics. "We look forward to working closely with the FDA to ensure the commercial manufacturing readiness for BT8009 keeps pace with its expedited clinical development. We welcome the guidance we will receive through more frequent and dedicated CMC discussions with the FDA, and in turn we hope the agency will become more familiar with our novel *Bicycle*® technology and its sophisticated manufacturing process."

"At Bicycle Therapeutics, we are pioneering an entirely new class of drugs with the goal of treating cancer and many other diseases. We believe BT8009 has the potential to be a transformative therapy for patients with metastatic bladder cancer, which is underscored by its selection for the FDA's CDRP Program in addition to its Fast Track designation and recently announced expedited development plan and registrational pathway," said CEO Kevin Lee, Ph.D. "On behalf of our entire team, I would like to thank the FDA for their continued collaboration as we work with urgency to develop and deliver this promising therapy to patients."

In September, Bicycle Therapeutics announced its plan to expedite development of BT8009 in metastatic bladder cancer following alignment with the FDA on the therapy's Phase 2/3 registrational trial, called Duravelo-2. The innovative trial design allows for the potential accelerated approval of BT8009 in untreated (first-line) and previously treated (second-line plus) metastatic bladder cancer. The company plans to initiate the Duravelo-2 trial in the first quarter of 2024.

About BT8009
BT8009 is an investigational *Bicycle* Toxin Conjugate (BTC™) targeting Nectin-4, a well-validated tumor antigen with elevated levels of expression in multiple tumor types, including bladder (urothelial) cancer. It is currently being evaluated in a Phase 1/2 clinical trial enrolling patients with Nectin-4 expressing advanced solid tumors. BT8009 will be evaluated in the Phase 2/3 Duravelo-2 trial, a global, multi-center, adaptive study designed to assess the safety and efficacy of the therapy for metastatic bladder cancer.

About Bicycle Therapeutics
Bicycle Therapeutics is a clinical-stage biopharmaceutical company developing a novel class of medicines, referred to as *Bicycles*, for diseases that are underserved by existing therapeutics. Bicycles are fully synthetic short peptides constrained with small molecule scaffolds to form two loops that stabilize their structural geometry. This constraint facilitates target binding with high affinity and selectivity, making *Bicycles* attractive candidates for drug development. The company is evaluating BT5528, a *Bicycle* Toxin Conjugate (BTC™) targeting EphA2; BT8009, a BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a *Bicycle* TICA™ targeting Nectin-4 and agonizing CD137, in company-sponsored Phase 1/2 trials. In addition, BT1718, a BTC that targets MT1-MMP, is being investigated in an ongoing Phase 1/2a clinical trial sponsored by the Cancer Research UK Centre for Drug Development. Bicycle Therapeutics is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Cambridge, Mass. For more information, visit bicycletherapeutics.com.

Forward Looking Statements
This press release may contain forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Forward-looking statements in this press release include, but are not limited to, statements regarding Bicycle Therapeutics' anticipated advancement of its product candidates, including the timing of initiation and design of the Duravelo-2 Phase 2/3 clinical trial and potential accelerated approval of BT8009; the anticipated progression of Bicycle Therapeutics' clinical trials; anticipated clinical and other benefits of Bicycle Therapeutics' participation in the CDRP Program, including potential earlier patient access to BT8009; the ability of the company to expedite commercial manufacturing readiness for BT8009 including ensuring that commercial manufacturing readiness for BT8009 keeps pace with its clinical development; and BT8009's potential to be a transformative therapy for patients with metastatic bladder cancer. Bicycle Therapeutics may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various factors, including: uncertainties inherent in the initiation, progress and completion of clinical trials and clinical development of Bicycle Therapeutics' product candidates; challenges or delays in the development and preparation of the commercial manufacturing readiness of BT8009; availability and timing of results from clinical trials; whether the

outcomes of preclinical studies will be predictive of clinical trial results; whether initial or interim results from a clinical trial will be predictive of the final results of the trial or the results of future trials; the risk that trials may have unsatisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle Therapeutics' product candidates; and other important factors, any of which could cause Bicycle Therapeutics' actual results to differ from those contained in the forward-looking statements, are described in greater detail in the section entitled "Risk Factors" in Bicycle Therapeutics' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 3, 2023, as well as in other filings Bicycle Therapeutics may make with the SEC in the future. Any forward-looking statements contained in this press release speak only as of the date hereof, and Bicycle Therapeutics expressly disclaims any obligation to update any forward-looking statements contained herein, whether because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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