Bicycle Therapeutics Announces First Patient Dosed in Phase I/II Trial of Bicycle® Toxin Conjugate BT8009 in Patients with Advanced Solid Tumors

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- BT8009 is the third program designed to explore the potential of Bicycles® *as next-generation tumor-targeting agents*

- BT8009 targets Nectin-4, a well-validated tumor antigen shown to be overexpressed in several common tumor types

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Sep. 10, 2020-- Bicycle Therapeutics plc (NASDAQ: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced the first patient has been dosed in the Phase I dose escalation portion of a company-sponsored Phase I/II trial of BT8009, a *Bicycle* Toxin Conjugate (BTC) targeting Nectin-4. BT8009 is a second-generation BTC, which uses a valine-citrulline cleavable linker and a cytotoxin MMAE payload. It targets Nectin-4, which is a well-validated tumor antigen. Overexpression of Nectin-4 has been observed in several common tumor types and is associated with poor disease prognosis. The Phase I/II trial of BT8009 will be conducted in patients with advanced solid tumors associated with Nectin-4 expression.

“BT8009 is one of a new class of tumor-targeting agents that we believe represent the next generation of treatments for solid tumors. With a molecular weight 50-100 times smaller than that of a typical antibody drug conjugate, or ADC, and the anticipated ability to fully penetrate tumors with precision, we believe *Bicycles*® may have significant advantages over antibody-based approaches to tumor antigen targeting, a hypothesis supported by results from our preclinical studies,” said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. “In preclinical head-to-head comparisons with an ADC targeting Nectin-4, BT8009 demonstrated superior anti-tumor activity, including complete regressions of very large and small tumors across multiple xenograft models. Given BT8009’s potential utility, we plan to pursue a clinical development path that could enable us to bring this novel therapy to patients efficiently.”

The Phase I/II multi-center, open-label trial will evaluate BT8009 administered once weekly. Enrollment is ongoing in the Phase I dose escalation of BT8009 given as a monotherapy, and the Company plans to evaluate BT8009 dosed in combination with an immune checkpoint inhibitor in future Phase I dose escalation cohorts. The Phase I portion of the trial is primarily designed to assess the safety and tolerability of BT8009, and to determine a recommended Phase II dose (RP2D). Following selection of an RP2D, Bicycle expects to initiate a Phase II dose expansion portion with the primary objective of evaluating the clinical activity of BT8009 in patients with Nectin-4-positive tumors.

About Bicycle Therapeutics

Bicycle Therapeutics (NASDAQ: BCYC) 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. Bicycle’s lead product candidate, BT1718, a *Bicycle* Toxin Conjugate (BTC) that targets MT1-MMP, is being investigated in an ongoing Phase IIa clinical trial in collaboration with the Centre for Drug Development of Cancer Research UK. Bicycle is also evaluating BT5528, a second-generation BTC targeting EphA2, in a Company-sponsored Phase I/II study. BT8009 is a BTC targeting Nectin-4, a well-validated tumor antigen, and is also currently being evaluated a Company-sponsored Phase I/II trial. Bicycle is headquartered in Cambridge, UK with many key functions and members of its leadership team located in Lexington, MA. 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 the clinical development of BT8009 or any of Bicycle’s other product candidates or programs; the expected design of Bicycle’s clinical trials, including the anticipated Phase II dose escalation portion of Bicycle’s clinical trial of BT8009; the safety, tolerability or efficacy of BT8009; and the potential benefits of BT5528 or any of Bicycle’s other product candidates. Bicycle 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: risks to site initiation, clinical trial commencement, patient enrollment and follow-up, as well as to Bicycle’s abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; uncertainties inherent in the initiation and completion of clinical trials and clinical development of Bicycle’s product candidates; availability and timing of results from clinical trials; 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 and studies may be delayed and may not have satisfactory outcomes; expectations for regulatory approvals to conduct trials or to market product; and other important factors, any of which could cause our 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’s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 5, 2020, as well as in other filings Bicycle 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 expressly disclaims any obligation to update any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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