



Bicycle Therapeutics Announces First Patient Dosed in Phase I/II Trial of Bicycle® Toxin Conjugate BT5528 in Patients with Advanced Solid Tumors

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- BT5528 targets EphA2, an antigen believed to be overexpressed in tumor types with high unmet need and a target for which antibody-based approaches have been unsuccessful to date

- Phase I dose escalation has commenced in the U.S and will be conducted at sites in both the U.S. and UK

- BT5528 is the second Bicycle® Toxin Conjugate to enter clinical development

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Nov. 13, 2019-- [Bicycle Therapeutics plc](#) (NASDAQ: BCYC) a clinical-stage biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycles*®) technology, today announced that the first patient has been dosed in the Phase I dose escalation of its Phase I/II study of BT5528, a *Bicycle* Toxin Conjugate (BTC) targeting tumor antigen EphA2, in patients with advanced solid tumors associated with EphA2 expression. BT5528 is a second-generation BTC, which uses a valine-citrulline cleavable linker and a cytotoxin MMAE payload.

"The initiation of this trial is an important step for Bicycle as BT5528 is our first U.S. investigational new drug (IND), and this is the first clinical study to be sponsored by the Company," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "BT5528 is also the first of our second-generation BTCs to enter the clinic and has demonstrated promising anti-tumor activity and tolerability across a broad range of preclinical studies. Notably, unlike existing EphA2-targeting antibody drug conjugates, BT5528 did not show coagulopathy in preclinical studies, and the first clinical dose has been well tolerated. We are pleased to have achieved another milestone in progressing our pipeline based on our novel and differentiated *Bicycle* technology, which we believe could generate potential first-in-class treatment options for patients suffering from cancer and other serious diseases."

The Phase I/II multi-center, open-label trial will evaluate BT5528 administered once-weekly as a single agent and in combination with nivolumab. The Phase I portion is a dose escalation primarily designed to assess the safety and tolerability of BT5528 and to determine a recommended Phase II dose (RP2D). Following selection of an RP2D, a Phase II dose expansion portion will be initiated with the primary objective of evaluating the clinical activity of BT5528. The study will be conducted across sites in the U.S. and the UK.

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 I/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. 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 BT5528 or any of Bicycle's other product candidates or programs; the design of Bicycle's clinical trials; the safety, durability or efficacy of BT5528; 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: uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of Bicycle's product candidates; availability and timing of results from preclinical studies and 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; potential adverse effects arising from the testing or use of BT5528 or other product candidates; risks related to Bicycle's ability to maintain existing collaborations and realize the benefits thereof; 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, as described in greater detail in the section entitled "Risk Factors" in our Quarterly Report on Form 10-Q, filed with the Securities and Exchange Commission (SEC) on November 7, 2019, 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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