

# Bicycle

## Bicycle Therapeutics Announces First Patient Dosed in Phase I Dose Escalation of BT5528 in Combination with Nivolumab

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*- Monotherapy Phase I dose escalation remains ongoing; BT5528 appears well-tolerated as dosing approaches clinically relevant levels*

*- BT5528 is the Company's first second-generation Bicycle® Toxin Conjugate and targets EphA2, a target for which antibody-based approaches have been unsuccessful*

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--May 5, 2020-- [Bicycle Therapeutics plc](https://www.bicycletherapeutics.com) (NASDAQ: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle®*) technology, today announced that the first patient has been dosed in a Phase I dose escalation of BT5528 in combination with nivolumab. The Phase I trial includes both a monotherapy arm as well as a combination arm. Per protocol, the monotherapy arm began first, with the first patient dosed in the fourth quarter of 2019, and dosing in both arms is now underway. In the monotherapy arm, doses administered to date appear well-tolerated as the escalation continues toward clinically relevant doses. BT5528 is a *Bicycle* Toxin Conjugate (BTC) that 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.

"We have been able to move the Phase I/II trial forward quickly by leveraging learnings from the ongoing clinical development of our first generation, pathfinder BTC, BT1718, which is sponsored by Cancer Research UK. We are very pleased with the progress we've made thus far in the BT5528 trial, which is intended to demonstrate the potential of *Bicycles* as a new therapeutic modality capable of addressing therapeutic needs that can't be reached by conventional treatment options," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "Doses of BT5528 administered to date continue to be well-tolerated, suggesting that BT5528 may circumvent limitations that have caused prior antibody drug conjugate, or ADC, approaches that target EphA2 to fail. Because we believe BTCs may result in improved safety and efficacy over ADCs, in part through more selective delivery of toxin to tumor, we similarly believe that our approach may improve on anti-tumor activity and immunologic effects observed for ADCs in combination with checkpoint inhibitors."

The Phase I/II multi-center, open-label trial of BT5528 is currently enrolling patients with advanced solid tumors in indications associated with EphA2 expression. The Phase I dose escalations of BT5528 as a monotherapy and in combination with nivolumab are primarily designed to assess safety and tolerability and to determine a recommended Phase II dose (RP2D). Following selection of an RP2D, we expect to initiate a Phase II dose expansion portion with the primary objective of evaluating the clinical activity of BT5528.

### 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](https://www.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; expectations for regulatory approvals to conduct trials or to market product; 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; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on March 10, 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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