

Bicycle

Bicycle Therapeutics Presents New Translational Data for BT5528 and Preclinical Data for Tumor-targeted Immune Cell Agonists at AACR Virtual Annual Meeting II

June 22, 2020

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Jun. 22, 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 new translational data for BT5528 and preclinical data for tumor-targeted immune cell agonists (TICAs[™]) will be presented during poster sessions at the American Association for Cancer Research (AACR) Virtual Annual Meeting II on June 22-24, 2020.

"The translational and preclinical data we are presenting at AACR further inform the potential utility *Bicycle*-based therapeutic candidates have as a new modality that could shift the treatment paradigm for cancer, among other serious diseases," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "Our fit-for-purpose immunohistochemistry, or IHC, assay was developed for use in the BT5528 Phase I/II trial and is designed to help us maximize our chances of success in the clinic by guiding tumor type selection and patient enrollment criteria. Additionally, the preclinical data we continue to generate for our TICA molecules remains very encouraging, especially as we look to initiate clinical studies of BT7480 next year."

New translational data for BT5528, a second-generation *Bicycle* Toxin Conjugate (BTC) that targets EphA2, describe the development of Bicycle's proprietary IHC assay. This assay will be used to support patient selection and assess EphA2 expression levels in tumor samples collected in the ongoing Phase I/II trial of BT5528. EphA2 is a well-known tumor antigen shown to be overexpressed in a range of difficult to treat solid tumor types. While many independent EphA2 IHC assays have been reported, Bicycle's is the first to specifically detect the extracellular domain of EphA2 and to score its expression at both the tumor cytoplasm and tumor membrane, which is where BT5528 binds.

Bicycle TICAs are potent, fully synthetic compounds that represent an immuno-oncology approach engineered to overcome the limitations of other immunomodulatory mechanisms. At AACR, the Company will present new preclinical data for BT7480, a TICA targeting Nectin-4 and agonizing CD137 (4-1BB), indicating that anti-tumor responses in a syngeneic mouse model can be achieved with an intermittent dosing regimen, which suggests that continuous target coverage may be unnecessary for efficacy. Additional PK/PD and safety data for BT7480 from *in vivo* mouse and non-human primate models demonstrate potent, target-dependent anti-tumor activity. At dose levels tested, BT7480 has been shown to be well-tolerated in preclinical species, with no signs of toxicity issues associated with other immuno-oncology agonist therapies. IND-enabling activities for BT7480 are ongoing.

New preclinical data for EphA2/CD137 TICAs similarly indicate highly target dependent CD137 agonism, most notably in a syngeneic mouse model that showed robust antitumor activity. Complete responder animals in this model were subsequently re-challenged with the same tumor cell implantation and no tumor growth was observed, implying development of immunogenic memory. In further PK/PD experiments, intermittent plasma exposure of an EphA2/CD137 TICA produced robust anti-tumor activity, again implying continuous target coverage is not required for efficacy. Earlier this year, Bicycle selected BT7455, an EphA2/CD137 TICA, as another *Bicycle*-based immuno-oncology candidate to advance into clinical studies.

Details on Bicycle's poster presentations at AACR are as follows:

Session Title: Molecular Classification of Tumors for Diagnostics, Prognostics, and Therapeutic Outcomes 2

Session Category: Experimental and Molecular Therapeutics

Poster Title: A survey of EphA2 expression by immunohistochemistry (IHC) in tumor tissue microarrays (TMAs) to support BT5528 indication selection

Abstract #: 3302

Session Title: Immunomodulatory Agents and Interventions 2

Session Category: Immunology

Poster Title: BT7480, a novel fully synthetic tumor-targeted immune cell agonist (TICA[™]) induces tumor localized 4-1BB agonism

Abstract #: 5241

Session Title: Immunomodulatory Agents and Interventions 3

Session Category: Immunology

Poster Title: A fully synthetic EphA2/4-1BB tumor-targeted immune cell agonist (TICA[™]) induces tumor localized 4-1BB agonism

Abstract #: 4613

The posters are available on the Publications section of [bicycletherapeutics.com](https://www.bicycletherapeutics.com).

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 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](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 therapeutic potential of our product candidates; the ability of our proprietary IHC assay to support patient selection and assess EphA2 expression levels in tumor samples in the ongoing Phase I/II trial of BT5528; anticipated advancement of preclinical development efforts and initiation and progression of clinical trials; possible dosing regimens; ; and the safety, tolerability or efficacy of our 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: the risk that we may not realize the intended benefits of our technology uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of our product candidates; availability and timing of results from preclinical studies and clinical trials; whether the outcomes of preclinical studies will be predictive of clinical trial results; 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 clinical trial commencement, patient enrollment and follow-up, as well as to our 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 our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 7, 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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