



Bicycle Therapeutics Announces Publication of Article Highlighting Preclinical Data of Tumor-Targeted Immune Cell Agonists (TICAs™) in the Journal for ImmunoTherapy of Cancer

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CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Jan. 26, 2021-- [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 that an article highlighting preclinical studies of Bicycle's novel, fully synthetic *Bicycle* systemic immune cell agonists and tumor-targeted immune cell agonists (TICAs™) was published in the *Journal for ImmunoTherapy of Cancer (JITC)*. The article, titled "Anticancer immunity induced by a synthetic tumor-targeted CD137 agonist" is available online via this [link](#).

"The data published in *JITC* describe the application of Bicycle's unique technology to produce a new class of potential immuno-oncology therapies: tumor-targeted immune cell agonists, or TICAs," said Nicholas Keen, Ph.D., Chief Scientific Officer of Bicycle Therapeutics. "In contrast to immune checkpoint inhibitors, the use of antibodies as agonists of immune costimulatory receptors as cancer therapeutics has largely failed. Here we demonstrate the discovery of small, chemically synthetic *Bicycles* that bind to key co-stimulatory receptors and that can be coupled in a modular manner to tumor antigen binding *Bicycles* to produce tumor localized receptor agonism. We look forward to initiating a clinical trial for our lead TICA program, BT7480, this year."

The article outlines the work Bicycle is undertaking to unlock a new method of cancer immunotherapy via small molecule agonism of TNF superfamily receptors. In the studies, TICAs were evaluated in a suite of *in vitro* and *in vivo* assays to characterize the pharmacology and mechanism of action. Results showed that by linking a costimulatory receptor (e.g., CD137) targeting *Bicycle* to a tumor antigen (e.g., EphA2), targeting *Bicycle* potent agonists were created, which activated the costimulatory receptor selectively in the presence of tumor cells expressing that antigen. An EphA2/CD137 TICA efficiently co-stimulated human peripheral blood mononuclear cells *in vitro* in the presence of EphA2-expressing tumor cell lines, as measured by an increased secretion of interferon γ and interleukin-2. Treatment of C57/Bl6 mice (transgenic for the human CD137 extracellular domain, huCD137) bearing EphA2-expressing MC38 tumors resulted in increased infiltration of CD8+ T cells, the elimination of tumors, and generation of immunological memory. Tumor target-dependent CD137 agonism using TICAs afforded elimination of tumors in preclinical models using only intermittent dosing, suggesting the potential for a wide therapeutic index in humans.

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. 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 discovery and development of potential product candidates using Bicycle's technology; anticipated advancement of preclinical development efforts and initiation and progression of clinical trials; and the therapeutic potential for *Bicycles* in various disease applications. 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 and its collaboration partners' abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; 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 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; potential adverse effects arising from the testing or use of Bicycle's product candidates; expectations for regulatory approvals to conduct trials or to market products; 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 Annual Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 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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