

Bicycle

Bicycle Therapeutics Announces Presentations at the AACR Annual Meeting 2021

April 10, 2021

- BT7480 to be presented in a "New Drugs on the Horizon" session; on-track to enter the clinic in 2H'21

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Apr. 10, 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 for the first time, preclinical work describing the discovery of BT7480, a novel Nectin-4/CD137 tumor-targeted immune cell agonist (TICA™), will be presented virtually in a "New Drugs on the Horizon" session at the American Association for Cancer Research (AACR) Annual Meeting, taking place April 10-15, 2021. Additional work covering TICAs and *Bicycle* Toxin Conjugates® (BTCs), will also be covered in a late-breaking mini-symposium, as well as in five e-posters.

"Our TICA platform has made significant progress, and we are thrilled to present information about the discovery of BT7480, as well as preclinical data across multiple programs in our immuno-oncology pipeline," said Nicholas Keen, Ph.D., Chief Scientific Officer of Bicycle Therapeutics. "These presentations highlight the potential utility of *Bicycle*-based therapeutic candidates for treating multiple tumor types via diverse mechanisms as we pursue our goal of improving the treatment paradigm for patients with cancer."

Bicycle TICAs are potent, fully synthetic compounds that represent an immuno-oncology approach engineered to overcome the limitations of other immunomodulatory mechanisms. *Bicycles* are small, structurally constrained peptides discovered via phage display and optimized using structure-driven design and medicinal chemistry approaches. Bicycle has applied this disruptive technology by identifying CD137 *Bicycles* and chemically linking these to tumor antigen binding *Bicycles* to generate multifunctional molecules that induce tumor antigen-dependent, tumor-localized agonism of CD137. Bicycle expects BT7480 to enter the clinic in the second half of 2021.

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

Poster Title: Molecular-based enrichment strategy for Nectin-4 targeted *Bicycle* toxin conjugate BT8009

Abstract #: 391

Session, Date and Time: Biomarkers Predictive of Therapeutic Benefit, April 10, 8:30 AM

Poster Title: Nectin-4-dependent immune cell stimulation and anti-tumor efficacy by BT7480, a Nectin-4/CD137 *Bicycle*® tumor-targeted immune cell agonist (TICA™)

Poster #: 1728

Session, Date and Time: Immunomodulatory Agents and Interventions, April 10, 8:30 AM

Poster Title: Microinjection of Nectin-4/CD137 tumor-targeted immune cell agonist (TICA™) activates the local tumor microenvironment

Poster #: 1724

Session, Date and Time: Immunomodulatory Agents and Interventions, April 10, 8:30 AM

Poster Title: A multi tumor survey of Nectin-4 expression to guide BT8009 indication selection

Poster #: 1197

Session, Date and Time: Molecular Classification of Tumors for Diagnostics, Prognostics, and Therapeutic Outcomes, April 10, 8:30 AM

Poster Title: Rapid Accumulation of Cytotoxic Payload in Tumor Tissue Drives BT5528 Activity in Tumor Models

Poster #: 1319

Session, Date and Time: Novel Drug Delivery Systems, April 10, 8:30 AM

Presentation Title: BT7480, a novel Nectin-4 dependent agonist of the immune cell costimulatory receptor CD137

Session, Date and Time: New Drugs on the Horizon: Part 1, April 10, 1:30 – 3:15 OM, Channel 1

Presentation Title: Integrative surfaceome profiling identifies immunotherapeutic targets in osteosarcoma and preclinical testing of BT1769, an MT1-MMP-targeted *Bicycle*® toxin conjugate, in osteosarcoma by the Pediatric Preclinical Testing Consortium (PPTC)

Session, Date and Time: Late-Breaking Mini-symposium 2, April 12, 1:35 – 1:45 OM, Channel 7

The posters will be available on the Publications section of bicycletherapeutics.com following each session.

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. BT8009 is a BTC targeting Nectin-4, a well-validated tumor antigen, and is also currently being evaluated 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.

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 Bicycle’s anticipated initiation of a clinical trial of BT7480 and the therapeutic potential of Bicycle’s pre-clinical targets and 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 Bicycle’s and its collaboration partners’ abilities to meet 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 by Bicycle or its collaboration partners; the risk that Bicycle or its collaboration partners may not realize the intended benefits of Bicycle’s technology; availability and timing of results from preclinical studies and clinical trials; whether the outcomes of preclinical studies will be predictive of clinical trial results; 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 studies and trials may be delayed and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s 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 products; and other important factors, any of which could cause Bicycle’s actual results to differ from those contained in the forward-looking statements, and which 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 11, 2021, 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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