Bicycle Therapeutics Announces Collaboration With the German Cancer Research Center, to Discover and Develop Wholly Owned Bicycle® Radio Conjugates for a Range of Oncology Targets

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CAMBRIDGE, England, & BOSTON--(BUSINESS WIRE)--May 4, 2023-- 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 it has entered into a collaboration with the German Cancer Research Center (DKFZ), to develop and discover *Bicycle*® radio conjugates (BRCs) for a range of oncology targets.

Founded in 1964, DKFZ is the largest biomedical research institution in Germany. It is a premier radioligand therapy organization that has a proven track record of supporting the development of such therapies and, together with the University of Heidelberg, was vital to the early development of Pluvicto™.

Bicycle and DKFZ have been collaborating on tumor targeting BRCs which in preclinical studies, have shown superior tumor uptake compared to antibody-based approaches. Results from the preclinical study were published in *Cancer Research* in February 2019 and can be accessed here. With this new alliance, the relationship has expanded to include a more continuous and purpose-driven commitment towards advancing candidates towards the clinic.

Professor Matthias Eder commented that he and his colleagues at DKFZ were excited to work with Bicycle to develop novel radiopharmaceutical therapies. “We have experience working with Bicycle scientists on radiochemistry projects and believe that the physicochemical properties of Bicycle’s constrained bi-cyclic peptides make them ideal ligands for targeted radioisotope delivery.”

“We believe the advancement of BRCs is a promising application of the Bicycle platform and represents the third leg within our core oncology focus. Building on the recent announcement of our collaboration with Novartis, we are excited to deepen our relationship with DKFZ, a leading radioligand research organization, to seek to accelerate the development of our wholly owned BRCs,” said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. “The goal of the collaboration is to develop a pipeline of wholly owned BRC compounds with the potential to become new treatment options for patients living with cancer.”

Dr. Lee continued, “We are thrilled to have now announced multiple collaborations in the radiopharmaceutical space this year, which we believe provides further validation of the Bicycle platform. Likewise, we remain encouraged by data generated to date from our wholly owned pipeline of Bicycle Toxin Conjugates® (BTCs) and Bicycle tumor-targeted immune cell agonists (Bicycle TICAs) which we believe demonstrates differentiation compared to antibody-based approaches and other modalities. We look forward to providing multiple updates this year as we advance BT8009, BT5528 and BT7480 in the clinic. In addition, we intend to commence initial testing of our own BRCs in patients by the end of 2024.”

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 is evaluating BT5528, a second-generation Bicycle Toxin Conjugate (BTC™) targeting EphA2; BT8009, a second-generation BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a Bicycle TICA™ targeting Nectin-4 and agonizing CD137, in company-sponsored Phase I/II trials. In addition, BT1718, a BTC that targets MT1-MMP, is being investigated in an ongoing Phase I/IIa clinical trial sponsored by the Cancer Research UK Centre for Drug Development. Bicycle is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Cambridge, MA. For more information, visit bicycletherapeutics.com.

About DKFZ

The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) with its more than 3,000 employees is the largest biomedical research institution in Germany. More than 1,300 scientists at the DKFZ investigate how cancer develops, identify cancer risk factors and search for new strategies to prevent people from developing cancer. They are developing new methods to diagnose tumors more precisely and treat cancer patients more successfully. The DKFZ's Cancer Information Service (KID) provides patients, interested citizens and experts with individual answers to all questions on cancer.

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 collaboration with DKFZ; the discovery and development of potential product candidates using Bicycle’s technology and under the collaboration agreement; the therapeutic potential for Bicycles in oncology; the provision of updates in relation to the clinical development of BT8009, BT5528 and BT7480; and the intention to commence initial testing of BRCs in patients by the end of 2024. 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 Bicycle may not realize the intended benefits of its technology or of the

collaboration agreement with DKFZ, including that Bicycle and DKFZ may not successfully identify and develop additional product candidates; the risk that Bicycle may not be able to maintain its collaboration with DKFZ and realize the benefits thereof; 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 February 28, 2023, 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 because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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