

Bicycle

Bicycle Therapeutics Announces First Patient Dosed in Phase IIa Trial of Bicycle® Toxin Conjugate BT1718

September 2, 2020

- Two cohorts have been initiated: a squamous non-small cell lung cancer cohort and a solid tumor "basket" cohort; up to two additional cohorts may be added based on preliminary results

- Patients will be selected using prespecified tumor membrane H-scores for MT1-MMP expression

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Sep. 2, 2020-- [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 the first patient has been dosed in the Phase IIa expansion portion of the Phase I/IIa trial sponsored by Cancer Research UK, the world's leading cancer charity dedicated to saving lives through research. The trial is evaluating BT1718 in patients with MT1-MMP-positive squamous non-small cell lung cancer (NSCLC) and a basket of other MT1-MMP-positive solid tumors.

"With the Phase IIa expansion, we look forward to building on the encouraging data generated through the Phase I dose escalation, in which BT1718 appeared tolerable with manageable adverse events and preliminary signs of anti-tumor activity were observed," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "BT1718 is a *Bicycle* Toxin Conjugate, or BTC, that targets the antigen MT1-MMP, which was observed in our translational research to be highly expressed on the membrane of tumors of a squamous cell origin. Squamous NSCLC represents a key patient segment where there is a high unmet need for new treatment options, given the limitations of current therapies. We believe BT1718 represents a potential first-in-class therapy that could have significant potential in the treatment of squamous NSCLC, as well as more broadly across other MT1-MMP-expressing cancers with high unmet need."

BT1718 is a BTC targeting MT1-MMP and is comprised of a mono-hindered disulfide cleavable linker and a cytotoxic DM1 payload. The Phase IIa expansion will evaluate BT1718 administered once weekly at the recommended Phase II dose (RP2D) of 20 mg/m² in an MT1-MMP-positive squamous NSCLC cohort, as well as in an MT1-MMP-positive solid tumor "basket" cohort. For the first time in the Phase I/IIa trial, patients will be preselected based on levels of antigen expression in target lesions, as determined by the Company's proprietary clinical-grade MT1-MMP immunohistochemistry (IHC) assay. The primary objectives of the Phase IIa expansion portion are to evaluate the safety and tolerability profiles of BT1718. One of the secondary objectives is to assess anti-tumor response, as measured by RECIST criteria. The trial is sponsored by Cancer Research UK's Centre for Drug Development and will be conducted at sites in the UK.

Dr. Nigel Blackburn, Cancer Research UK's Director of Drug Development, said: "We're delighted to be sponsoring this Phase IIa trial of BT1718. Looking to the future, we believe BT1718 has the potential to create an entirely new treatment option for people with non-small cell lung cancer and other solid cancers whose therapeutic need is unaddressed by current medicines."

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.

About Cancer Research UK's Centre for Drug Development

Cancer Research UK has an impressive record of developing novel treatments for cancer. The Cancer Research UK Centre for Drug Development has been pioneering the development of new cancer treatments for 25 years, taking over 140 potential new anti-cancer agents into clinical trials in patients. It currently has a portfolio of 21 new anti-cancer agents in preclinical development, Phase I or early Phase II clinical trials. Six of these new agents have made it to market including temozolomide for brain cancer, abiraterone for prostate cancer and rucaparib for ovarian cancer. Two other drugs are in late development Phase III trials.

About Cancer Research UK

- Cancer Research UK is the world's leading cancer charity dedicated to saving lives through research.
- Cancer Research UK's pioneering work into the prevention, diagnosis and treatment of cancer has helped save millions of lives.
- Cancer Research UK has been at the heart of the progress that has already seen survival in the UK double in the last 40 years.
- Today, 2 in 4 people survive their cancer for at least 10 years. Cancer Research UK's ambition is to accelerate progress so that by 2034, 3 in 4 people will survive their cancer for at least 10 years.

- Cancer Research UK supports research into all aspects of cancer through the work of over 4,000 scientists, doctors and nurses.
- Together with its partners and supporters, Cancer Research UK's vision is to bring forward the day when all cancers are cured.

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 statements regarding the clinical development of BT1718 or any of Bicycle’s other product candidates or programs, the progression of Bicycle’s ongoing Phase I/IIa clinical trial of BT1718, the creation of additional cohorts of trial patients in the Phase IIa expansion of this clinical trial, the use of Bicycle’s MT1-MMP immunohistochemistry (IHC) assay to preselect patients, and the potential therapeutic potential of BT1718 and 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 clinical trials and clinical development of Bicycle’s product candidates; availability and timing of results from 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; 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; 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; 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 August 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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