

# Bicycle

## Bicycle Therapeutics Announces Continued Clinical Progress and Updates to Management Team

January 5, 2022

CAMBRIDGE, England, & BOSTON--(BUSINESS WIRE)--Jan. 5, 2022-- Bicycle Therapeutics plc (NASDAQ: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*<sup>®</sup>) technology, today announced continued progress in its ongoing Phase I/II clinical trials of BT8009, BT5528 and BT7480.

"Last quarter, we reported interim clinical results from ongoing trials of two of our *Bicycle* toxin conjugates, BT8009 and BT5528, demonstrating preliminary anti-tumor activity in two tumor types, and announced the first patient dosed in the Phase I clinical trial of BT7480, our first tumor-targeted immune cell agonist to enter the clinic. In our trial of BT8009, we are pleased to confirm the preliminary activity and see that these patients remain on trial. We look forward to presenting interim BT8009 Phase I results at a medical meeting and initiating the BT5528 expansion cohorts this year," said Kevin Lee, Ph.D., Chief Executive Officer. "We are also pleased with our progress advancing BT7480 in the ongoing Phase I clinical trial and look forward to sharing additional details regarding the potential for *Bicycles* beyond our toxin conjugates as we strive to become a leader in the development of targeted oncology therapeutics."

### ***Bicycle* Toxin Conjugates<sup>®</sup> (BTCs) BT8009 and BT5528**

In the ongoing Phase I portion of the Phase I/II clinical trial of BT8009, a second-generation BTC<sup>™</sup> targeting Nectin-4, four out of 11 patients were previously reported to have a partial response under Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, including one out of four (25%) in the 2.5mg/m<sup>2</sup> dose and three out of seven (43%) at the 5.0 mg/m<sup>2</sup> cohorts. All four patients previously reported as responders have since received at least one subsequent scan, and all have been confirmed as ongoing RECIST 1.1 responses. One patient in the 5.0 mg/m<sup>2</sup> cohort, who previously was reported to have a partial response with an 89% tumor reduction, has now received two subsequent scans, which each showed that total tumor volume has been reduced by 100%, constituting a confirmed complete response. All four patients previously reported to have a RECIST 1.1 clinical response remain on therapy. The tolerability profile of the 2.5mg/m<sup>2</sup> and 5.0 mg/m<sup>2</sup> cohorts remains consistent with that previously reported.

Dose escalation in the BT8009 Phase I trial remains ongoing, with patients currently being dosed at 7.5mg/m<sup>2</sup> weekly or every-other-week. Bicycle intends to present interim Phase I results from the ongoing clinical trial at a medical meeting this year.

The Phase I/II trial of BT5528, Bicycle's second-generation BTC targeting EphA2, is also ongoing, with plans remaining on track to initiate the expansion cohorts this year, with an expected recommended Phase II dose of 6.5mg/m<sup>2</sup> every-other-week.

### ***Bicycle* tumor-targeted immune cell agonist<sup>™</sup> *Bicycle* TICA<sup>™</sup>) BT7480**

Bicycle also initiated a Phase I clinical trial of BT7480, a novel, fully synthetic *Bicycle* TICA targeting Nectin-4 and agonizing CD137, in the fourth quarter of 2021, and dose escalation in that trial remains ongoing. BT7480 and other *Bicycle* TICAs, including a novel NK-cell-engaging molecule, were the subjects of four posters at SITC in November 2021.

### **Management Team Updates**

Bicycle is also announcing the expansion of and transition in its management team. Michael Skynner, Ph.D., the company's Chief Operating Officer (COO), has been appointed to the newly created position of Chief Technology Officer, effective January 3, 2022, to focus on leading and overseeing the growth of Bicycle's proprietary phage display discovery platform in oncology, as well as on creating innovative opportunities for the platform outside of oncology. Dr. Skynner joined the company in January 2016 as Vice President, Operations and Discovery and had served as COO since March 2018. Alistair Milnes, who has served as the company's Vice President, Human Resources and Communications since January 2021, has assumed the COO role. Mr. Milnes previously led human resources and communications at multinational energy and mineral companies. Both Dr. Skynner and Mr. Milnes are based in the United Kingdom.

"We are delighted to announce our recent management team appointments, with Mike Skynner becoming our new CTO and Alistair Milnes moving to the COO role. Mike has been an invaluable contributor to Bicycle's success to date and has led our platform discovery efforts since joining in early 2016. Following recent promising clinical progress, we believe it is time to focus on accelerating the growth of our proprietary oncology pipeline and on identifying innovative ways to potentially capitalize on our unique technology beyond our current therapeutic focus. I am confident that Mike can help us achieve these objectives." Dr. Lee added, "I am similarly enthusiastic about Alistair's appointment as COO and believe his operational experience and track record of successfully identifying, recruiting, and retaining key talent at large, multinational companies will be instrumental in helping guide Bicycle through our next phase of growth."

### **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<sup>™</sup>) targeting EphA2; BT8009, a second-generation BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a *Bicycle* TICA<sup>™</sup> 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 Lexington, MA. For more information, visit [bicycletherapeutics.com](http://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, development and potential commercialization of potential product candidates using Bicycle’s technology; Bicycle’s anticipated advancement of its product candidates, including BT5528, BT8009 and BT7480; the advancement of Bicycle’s product candidate pipeline; anticipated design of, initiation of expansion cohorts in and progression of Bicycle’s clinical trials; the availability of data from clinical trials; the therapeutic potential for *Bicycles* in oncology and other applications; and Bicycle’s ability to accelerate its product pipeline and identify potentially innovative applications of its technology beyond oncology. 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 clinical trial site initiation, patient enrollment and follow-up, as well as to Bicycle’s abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; uncertainties inherent in the initiation and completion of clinical trials and clinical development of Bicycle’s product candidates; the risk that Bicycle may not realize the intended benefits of its technology; availability and timing of results from 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 trials may be delayed and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; the risk that Bicycle may not be able to identify additional product candidates or additional applications of its technology; and other important factors, any of which could cause Bicycle’s actual results to differ from those contained in the forward-looking statements, are described in greater detail in the section entitled “Risk Factors” in Bicycle’s Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 4, 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 because of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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