Bicycle Therapeutics Announces Interim BT8009 Phase I Clinical Trial Results at the 2022 AACR Annual Meeting

April 11, 2022

- 50% confirmed overall response rate, including one (13%) confirmed complete response in eight urothelial cancer patients dosed at 5.0mg/m^2 weekly

- Median duration of response not yet reached in the 2.5mg/m^2 and 5.0mg/m^2 weekly cohorts; four of five responders in these cohorts still on therapy after at least 24 weeks

- Tolerability profile maintained over time, with low incidence of skin, ocular and neurological toxicities showing potential for differentiation from antibody-based approaches

- Company to Host Conference Call Today at 8:30 a.m. ET

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Apr. 11, 2022-- 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 interim Phase I results from the Phase I/II trial of BT8009, a second-generation BTC™ targeting Nectin-4. The results were presented in an oral presentation on Sunday, April 10 at the 2022 American Association for Cancer Research Annual Meeting in New Orleans, LA.

“Since our initial BT8009 Phase I/II trial interim results last year, we are encouraged to see BT8009’s promising profile endure over time. Over the last six months, the preliminary anti-tumor findings have been confirmed, the initial responses have deepened and remained durable, and the tolerability profile remains unchanged,” said Dominic Smethurst, MRCP, Chief Medical Officer of Bicycle Therapeutics. “We believe BT8009 has the potential to offer clinically meaningful differentiation compared to currently available therapies and we look forward to advancing the program once the escalation phase is complete.”

“As previously hypothesized, we believe that the differentiated pharmacokinetic profile of BTCs has the potential to deliver improved outcomes for patients and it is pleasing to see these clinical data mature and with it, the promise for a potentially industry-leading product profile,” said Kevin Lee, Ph.D., Chief Executive Officer. “We look forward to providing additional updates on BT8009 as well as updates from our broad *Bicycle* oncology pipeline this year.”

As of March 7, 2022, thirty-seven patients have been dosed in the Phase I/II trial of BT8009. A total of twelve response evaluable urothelial cancer (UC) patients have been dosed in monotherapy cohorts of 2.5mg/m^2 and 5.0mg/m^2 weekly in the ongoing trial.

- **Four response evaluable UC patients were dosed at 2.5mg/m^2 weekly**. Among these four patients, one patient was observed to have tumor reductions constituting a confirmed partial response (PR) and two patients were observed to have stable disease (SD), reflecting a 25% overall response rate (ORR) and 75% disease control rate (DCR) in patients in this cohort.

- **Eight response evaluable UC patients were dosed at 5.0mg/m^2 weekly**. Among these eight patients, four patients were observed to have a confirmed complete response (CR) or PR, including one patient with a CR and three patients with a PR, and two patients with SD, reflecting a 50% ORR and a 75% DCR in UC patients for this cohort. Prior to enrollment, all patients in this cohort had previously received at least two prior lines of therapy, with a median of three.

- **The median duration of response has not yet been reached in either the 2.5 mg/m^2 or 5.0mg/m^2 cohort.** Four of the five responders have ongoing Response Evaluation Criteria in Solid Tumors (RECIST) tumor responses. As of the March 7, 2022 data cutoff date, all four of these patients have a treatment duration of at least 24 weeks and all four remain on therapy.

- **Tolerability profile remains consistent with earlier results from this trial.** No dose limiting toxicities have been observed in the 2.5mg/m^2 or the 5.0mg/m^2 cohorts, and with longer-term follow-up, incidence of skin and eye toxicity, neuropathy and hyperglycemia remains low.

- **Phase I dose escalation is ongoing.** Exploration of additional doses and frequencies continues, and Bicycle intends to provide further updates this year.

Conference Call Details

Bicycle Therapeutics will host a conference call and webcast today at 8:30 a.m. ET to review the data being presented. To access the call, please dial (800) 377-9118 (domestic) or (409) 937-8920 (international) and provide the Conference ID 2775710. A live webcast of the presentation will be available on the Investors & Media section of the Bicycle website, bicycletherapeutics.com.

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 Lexington, Massachusetts. 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 advancement of its product candidates, including BT8009, and participation in the AACR Annual Meeting. 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 intentions disclosed in these forward-looking statements as a result of various factors, including: Bicycle’s abilities to meet other anticipated deadlines 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; 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 1, 2022, 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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