# Bicycle Therapeutics Announces Expedited Development Plan for BT8009 in Metastatic Bladder Cancer

September 11, 2023

*Alignment with U.S. FDA on design of Phase 2/3 registrational trial, to be initiated in 1Q 2024*

*Innovative study design allows for potential accelerated approval in untreated (first-line) and previously treated (second-line plus) metastatic bladder cancer*

*Conference call and webcast today at 8 a.m. ET*

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Sep. 11, 2023-- Bicycle Therapeutics (Nasdaq: BCYC), a biotechnology company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced the company will proceed with its plan to expedite development of BT8009 for metastatic bladder (urothelial) cancer following recent discussions with the U.S. Food and Drug Administration (FDA). The company has aligned with the FDA on a Phase 2/3 registrational trial, called Duravelo-2, that has an innovative design allowing for potential accelerated approval in untreated (first-line) and previously treated (second-line plus) metastatic bladder cancer. The company plans to initiate the Duravelo-2 trial in the first quarter of 2024.

"We prepared a robust and innovative clinical development plan for BT8009, with the goal of getting this much-needed therapy to patients as quickly as possible. We are pleased to have reached alignment with the FDA on the registrational trial design, dose selection and clinical trial endpoints that could support potential accelerated approval in a broad metastatic bladder cancer population," said Santiago Arroyo, M.D., Ph.D., chief development officer at Bicycle Therapeutics. "In preparation for this positive outcome, we have put in place the clinical infrastructure that will allow us to start the registrational trial early next year."

The Phase 2/3 Duravelo-2 trial will assess BT8009 in untreated metastatic bladder cancer (Cohort 1) and previously treated metastatic bladder cancer (Cohort 2). In Cohort 1, two doses of BT8009 plus standard pembrolizumab regimen will be initially assessed. Following selection of the optimal dose, BT8009 plus pembrolizumab will be evaluated against chemotherapy. Potential accelerated approval will be determined by objective response rate (ORR), and progression-free survival (PFS) will be used to confirm clinical benefit.

In Cohort 2, two doses of BT8009 as monotherapy will be initially studied. Following selection of the optimal dose, an additional arm of BT8009 plus standard pembrolizumab regimen will be added. Potential accelerated approval for BT8009 monotherapy and in combination with pembrolizumab will be determined by ORR compared to historical control data. Discussions with the FDA about the design of the confirmatory trial for previously treated metastatic bladder cancer are ongoing.

"At Bicycle Therapeutics, we are committed to using our novel platform to develop precision targeted therapeutics and improve the lives of patients who are battling devastating diseases. This is why, in line with the philosophy of the FDA's Project FrontRunner and following the agency's recent draft guidance on accelerated approval of oncology therapeutics, we have initially focused on defining the regulatory path for BT8009 in untreated patients. We believe today's announcement is good news for patients, and we are greatly appreciative of the FDA for their collaboration and guidance," said Kevin Lee, Ph.D., chief executive officer of Bicycle Therapeutics. "As we look to the rest of 2023, we continue to make progress in our research and development programs and look forward to providing updates on BT8009, BT5528 and BT7480 later this year."

**Conference Call and Webcast Information**
Bicycle Therapeutics will host a conference call and webcast today, September 11, 2023, at 8 a.m. ET to review the BT8009 regulatory update. To access the call, please dial 1-833-816-1408 (U.S.) or +1 412-317-0501 (international) and ask to be joined into the Bicycle Therapeutics call. A live webcast and replay of the conference call will be available in the Investor section of the Bicycle website, bicycletherapeutics.com.

**About BT8009**
BT8009 is an investigational *Bicycle* Toxin Conjugate (BTC™) targeting Nectin-4, a well-validated tumor antigen with elevated levels of expression in multiple tumor types, including bladder (urothelial) cancer. It is currently being evaluated in a Phase 1/2 clinical trial enrolling patients with Nectin-4 expressing advanced solid tumors. BT8009 will be evaluated in the Phase 2/3 Duravelo-2 trial, a global, multi-center, adaptive study designed to assess the safety and efficacy of the therapy for metastatic bladder cancer.

**About Bicycle Therapeutics**
Bicycle Therapeutics 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. The company is evaluating BT5528, a *Bicycle* Toxin Conjugate (BTC™) targeting EphA2; BT8009, a BTC targeting Nectin-4, a well-validated tumor antigen; and BT7480, a *Bicycle* TICA™ targeting Nectin-4 and agonizing CD137, in company-sponsored Phase 1/2 trials. In addition, BT1718, a BTC that targets MT1-MMP, is being investigated in an ongoing Phase 1/2a clinical trial sponsored by the Cancer Research UK Centre for Drug Development. Bicycle Therapeutics is headquartered in Cambridge, UK, with many key functions and members of its leadership team located in Cambridge, Mass. 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 the timing of initiation and design of the Duravelo-2 Phase 2/3 clinical trial and potential accelerated approval of BT8009; the anticipated progression of Bicycle’s clinical trials; the availability of and timing of updates for clinical candidates BT8009, BT5528 and BT7480; and the therapeutic potential for *Bicycles* in bladder cancer and other oncologic indications. 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, progress and completion of clinical trials and clinical development of Bicycle’s product candidates; 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 have unsatisfactory outcomes; potential adverse effects arising from the testing or use 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, 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 August 3, 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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Source: Bicycle Therapeutics