

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

September 11, 2023

Date of Report (Date of earliest event reported)

Bicycle Therapeutics plc

(Exact name of registrant as specified in its charter)

England and Wales
(State or other jurisdiction
of incorporation)

001-38916
(Commission
File Number)

Not applicable
(IRS Employer
Identification No.)

**Blocks A & B, Portway Building,
Granta Park Great Abington, Cambridge
United Kingdom**
(Address of principal executive offices)

CB21 6GS
(Zip Code)

Registrant's telephone number, including area code: **+44 1223 261503**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.01 per share	n/a	The Nasdaq Stock Market LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.01 per share	BCYC	The Nasdaq Stock Market LLC

* Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 8.01 Other Events.

On September 11, 2023, Bicycle Therapeutics plc (the “Company”) issued a press release announcing that it will proceed with its development plan for BT8009 for advanced bladder cancer following recent discussions with the U.S. Food and Drug Administration. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated into this Item 8.01 by reference.

Also on September 11, 2023, the Company hosted a conference call to discuss the above-mentioned development plan for BT8009. A copy of the presentation used in the conference call can be accessed by visiting the “Presentation + Events” section at investors.bicyclerapeutics.com.

Item 9.01 Financial Statements and Exhibits

(a) Exhibits

99.1 [Press Release dated September 11, 2023](#)

104 Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 11, 2023

BICYCLE THERAPEUTICS PLC

By: /s/ Alethia Young

Name: Alethia Young

Title: Chief Financial Officer

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

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, UK, and BOSTON – September 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](https://www.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](https://www.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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