Bicycle Therapeutics Reports First Quarter 2023 Financial Results and Provides Corporate Update

May 4, 2023

- Continued progress across pipeline, including encouraging BT8009 Phase I dose escalation results presented in Q1'23

- Entered into a strategic collaboration with Novartis and expanded separate collaboration with the Division of Radiopharmaceutical Chemistry, German Cancer Research Center to develop Bicycle® Radio-Conjugates

- Cash position of $293.8 million at March 31, 2023 excludes $50 million upfront payment from Novartis, and is expected to provide financial runway into 2025

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--May 4, 2023-- 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 reported financial results for the first quarter ended March 31, 2023 and provided recent corporate updates.

"The beginning of 2023 has been impactful for Bicycle and our platform," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We reported encouraging Phase I dose escalation results from BT8009 that showed anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients and a median duration of response estimated to be 14 months in the 5 mg/m^2 cohort of patients with urothelial cancer. We look forward to providing further updates on BT8009 as well as on our other clinical-stage programs later this year."

"In addition, we entered into multiple research and development collaborations with organizations at the forefront of the development of radiopharmaceuticals to develop *Bicycle*® radio-conjugates (BRCs)," added Dr. Lee. "These collaborations provide further validation of our platform and enable us to advance a broad pipeline of partnered and wholly owned BRCs. This represents the third pillar of our oncology strategy beyond our Bicycle toxin conjugate (BTC™) and Bicycle tumor-targeted immune cell agonist® (Bicycle TICA™) programs. We are pleased with the progress we have made advancing our entire pipeline and expanding the potential applications of the Bicycle platform."

First Quarter 2023 and Recent Highlights

- **Announced Multiple Strategic Collaborations for Developing BRCs for Potential Oncology Targets**
  - **Strategic Collaboration with Novartis**. In March 2023, Bicycle announced a strategic collaboration with Novartis to collaborate on the discovery, development and commercialization of BRCs for multiple undisclosed oncology targets. Bicycle will utilize its proprietary phage platform to discover *Bicycles* to be developed into BRCs. Novartis will be responsible for and fund further development, manufacture and commercialization of the BRCs. Bicycle received a $50 million upfront payment in April 2023 and is eligible for development and commercial-based milestone payments totaling up to $1.7 billion. Bicycle will also be eligible to receive tiered royalties on Bicycle-based medicines commercialized by Novartis.
  - **Collaboration with the German Cancer Research Center.** In May 2023, Bicycle announced a collaboration with the German Cancer Research Center (DKFZ) to develop and discover BRCs for potential oncology targets. Bicycle and DKFZ have been collaborating on preclinical development of tumor targeting BRCs which have shown encouraging tumor uptake in preclinical studies. With this new alliance, the relationship has expanded to include a more continuous and purpose-driven commitment towards advancing wholly owned BRCs. Bicycle intends to commence initial testing of its wholly owned BRCs in patients by the end of 2024.
- **Presented Completed BT8009 Phase I Dose Escalation Results from Ongoing Phase I/II Study of BT8009 at the 2023 American Society for Clinical Oncology (ASCO) Genitourinary (GU) Cancers Symposium.** In February 2023, Bicycle presented monotherapy Phase I dose escalation results of the ongoing Phase I/II trial of BT8009, a novel BTC™ targeting Nectin-4, at the ASCO GU Cancers Symposium. BT8009 demonstrated anti-tumor activity in heavily pre-treated urothelial, lung and breast cancer patients with signs of differentiation compared to antibody-based approaches. Bicycle announced that it dosed its first patient in the Phase II expansion portion of the trial and established recommended Phase II doses of 5 mg/m^2 weekly and 7.5 mg/m^2 administered two-weeks on, one-week off over a 21-day cycle in November 2022. Enrollment in the clinical trial as well as discussions with the U.S. Food and Drug Administration (FDA) remain ongoing. The company expects to provide clinical and regulatory updates on BT8009 in 2023.
- **BT8009 Granted Fast Track Designation (FTD) by the FDA.** In January 2023, Bicycle announced that the FDA granted BT8009 FTD as a monotherapy for the treatment of adult patients with previously treated locally advanced or metastatic urothelial cancer.
- **Enhanced Leadership Team with Key Appointments**

- Bicycle appointed Santiago Arroyo M.D., Ph.D., as Chief Development Officer in March 2023. Dr. Arroyo brings to Bicycle over 20 years of biopharmaceutical industry experience, leading the clinical development of therapeutics across multiple disease areas. Dr. Arroyo will be responsible for overseeing all aspects of the pipeline as it continues to expand and advance and as Bicycle prepares to transition into late-stage clinical development.
- Bicycle promoted Jennifer Perry, Pharm.D., to Senior Vice President, Commercial. In this role, she will be responsible for establishing and growing the commercial organization.

Financial Results

- Cash and cash equivalents were $293.8 million as of March 31, 2023, compared to $339.2 million as of December 31, 2022. The decrease in cash is primarily due to cash used in operating activities. Cash at March 31, 2023 does not include the upfront payment from Novartis.

- Research and development expenses were $32.2 million for the three months ended March 31, 2023, compared to $14.3 million for the three months ended March 31, 2022. The increase in expense of $17.9 million was primarily due to increased clinical program expenses for BT5528 and BT8009, Bicycle TICA program development expenses, and other discovery and platform related expenses, as well as increased personnel-related expenses, including incremental non-cash share-based compensation expense of $2.2 million associated with equity grants issued in the three months ended March 31, 2023, offset by incremental UK research and development tax credit reimbursements.

- General and administrative expenses were $14.5 million for the three months ended March 31, 2023, compared to $17.0 million for the three months ended March 31, 2022. The decrease of $2.5 million for the three months ended March 31, 2023 as compared to the same period in the prior year was primarily due to a decrease in non-cash share-based compensation expense compared to the previous year.

- Net loss was $39.1 million, or $(1.30) basic and diluted net loss per share, for the three months ended March 31, 2023, compared to net loss of $27.6 million, or $(0.93) basic and diluted net loss per share, for three months ended March 31, 2022.

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 Cambridge, MA. 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, BT5528 and BT7480; the anticipated dosing in and progression of Bicycle’s clinical trials; the availability of and timing of announcement of data from clinical trials and regulatory updates for clinical candidates; statements regarding Bicycle’s collaborations with Novartis, and DKFZ; the discovery, development and potential commercialization of potential radiopharmaceutical or other product candidates using Bicycle’s technology under the strategic collaboration agreements; Bicycle’s intent to commence initial testing of its wholly owned BRCs in patients by the end of 2024; the therapeutic potential for Bicycles in oncology and other applications; and Bicycle’s expected financial runway. 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; 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 or have unsatisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; the risk that Bicycle’s projections regarding its expected financial runway are inaccurate or that its conduct of its business requires more cash than anticipated; 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) on February 28, 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.

Bicycle Therapeutics plc
Condensed Consolidated Statements of Operations and Comprehensive Loss
(In thousands, except share and per share data)

(Unaudited)

	Three Months Ended March 31,	
	2023	**2022**
Collaboration revenues	$ 4,896	$ 3,860
Operating expenses:		
Research and development	32,211	14,284
General and administrative	14,488	16,959
Total operating expenses	46,699	31,243
Loss from operations	(41,803)	(27,383)
Other income (expense):		
Interest income	2,929	218
Interest expense	(808)	(818)
Total other income (expense), net	2,121	(600)
Net loss before income tax provision	(39,682)	(27,983)
Benefit from income taxes	(618)	(419)
Net loss	$ (39,064)	$ (27,564)
Net loss per share, basic and diluted	$ (1.30)	$ (0.93)
Weighted average ordinary shares outstanding, basic and diluted	30,001,725	29,605,143

Balance Sheets Data
(In thousands)
(Unaudited)

	March 31, 2023	**December 31, 2022**
Cash and cash equivalents	$ 293,815	$ 339,154
Working capital	328,258	316,041
Total assets	428,801	410,609
Total shareholders' equity	243,163	270,783

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