Bicycle Therapeutics Reports Recent Business Progress and Third Quarter 2023 Financial Results and Announces Upcoming R&D Day

November 2, 2023

R&D Day on December 14 to provide clinical updates for BT8009, BT5528 and BT7480, and highlight broad capabilities of novel Bicycle® technology

Alignment with FDA on expedited development and design of Phase 2/3 registrational trial for BT8009 in metastatic bladder cancer, to be initiated in 1Q 2024

Selection of BT8009 for new FDA Chemistry, Manufacturing and Controls (CMC) Development and Readiness Pilot (CDRP) Program to facilitate expedited CMC development and commercial manufacturing readiness

Cash and cash equivalents of $572.1 million as of September 30, 2023, including approximately $215.1 million in net proceeds from July 2023 public offering

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Nov. 2, 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 third quarter ended September 30, 2023, and provided recent corporate updates.

"In the third quarter, we took important steps toward achieving our goal of quickly getting our novel therapies to those who need them. We are extremely pleased to have aligned with the FDA on an expedited clinical development plan and regulatory pathway for BT8009, our lead investigational therapy for metastatic bladder cancer, and that the agency selected BT8009 to be part of a new program that will help facilitate its expedited CMC development. Through close collaboration with the FDA, we will work to ensure BT8009's commercial manufacturing readiness keeps pace with its expedited clinical development timeframe," said Kevin Lee, Ph.D., CEO of Bicycle Therapeutics. "With a strengthened balance sheet through the proceeds of an upsized equity offering completed in July, we believe we are well-positioned to conduct our Phase 2/3 registrational trial, scheduled to begin in the first quarter of 2024, to support the potential accelerated approval of BT8009 in a broad metastatic bladder cancer population. Additionally, we continue to advance our research and development efforts across our pipeline, and we look forward to providing clinical updates on BT8009, BT5528 and BT7480 at our R&D Day next month."

Third Quarter 2023 and Recent Highlights

- **BT8009 Selected to Participate in U.S. Food and Drug Administration (FDA) Program to Expedite Commercial Manufacturing Readiness.** In October, Bicycle Therapeutics announced the FDA selected BT8009 to participate in the new Chemistry, Manufacturing and Controls (CMC) Development and Readiness Pilot (CDRP) Program, which was created to facilitate CMC development for therapies with expedited clinical development timeframes, based on the anticipated clinical benefits of earlier patient access to the therapy. BT8009 is one of up to nine products selected for the inaugural cohort of the CDRP Program.

- **Announced Expedited Clinical Development Plan and Regulatory Pathway for BT8009 in Metastatic (Urothelial) Bladder Cancer.** In September, Bicycle Therapeutics announced the company will proceed with its plan to expedite development of BT8009 for metastatic bladder cancer following recent discussions with the FDA. The company 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.
    - 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.

- **Raised Net Proceeds of $215.1 Million in Public Offering.** In July, Bicycle Therapeutics announced the closing of an underwritten public offering resulting in gross proceeds of approximately $230.0 million, including the full exercise of the underwriters' option to purchase additional shares. Net proceeds were approximately $215.1 million. In addition, the company also received net proceeds from Bicycle's at-the-market (ATM) offering program during the third quarter of 2023 totaling $19.4 million.

Pipeline updates planned at upcoming Research & Development (R&D) Day on December 14, 2023, in New York

Bicycle Therapeutics will provide updates from the company's Phase 1/2 clinical trials for BT8009, a Bicycle Toxin Conjugate (BTC™) targeting Nectin-4, a well-validated tumor antigen; BT5528, a BTC targeting EphA2; and BT7480, a Bicycle TICA™ targeting Nectin-4 and agonizing CD137. The company will also provide an overview of its novel *Bicycle*® technology, the broad capabilities of its drug discovery platform and potential future pipeline programs.

The R&D Day will begin at 8 a.m. ET on Thursday, December 14, 2023, and will conclude at approximately 12 p.m. ET. Analysts and investors who are interested in attending in person can RSVP to bicycle@argotpartners.com. A webcast of the event will be accessible from the Investor section of the company's website, www.bicycletherapeutics.com. A replay of the webcast will be archived and available following the event.

Financial Results

- Cash and cash equivalents were $572.1 million as of September 30, 2023, compared to $339.2 million as of December 31, 2022. The increase in cash and cash equivalents is primarily due to $215.1 million in net proceeds from the underwritten public offering in July 2023, $34.2 million of year-to-date net proceeds from our ATM offering program and $95.0 million received from our collaboration agreements with Novartis and Bayer, offset by cash used in operating activities.

- R&D expenses were $39.9 million for the three months ended September 30, 2023, compared to $22.8 million for the three months ended September 30, 2022. The increase in expense of $17.1 million was primarily due to increased clinical program expenses for BT8009 development and other discovery and platform-related activities, as well as increased personnel-related expenses, including incremental non-cash share-based compensation expense of $0.7 million.

- General and administrative expenses were $16.3 million for the three months ended September 30, 2023, compared to $10.0 million for the three months ended September 30, 2022. The increase of $6.3 million for the three months ended September 30, 2023, as compared to the same period in the prior year was primarily due to an increase in professional and consulting fees as well as an increase in personnel-related expenses, including incremental non-cash share-based compensation expense of $1.3 million.

- Net loss was $49.9 million, or $(1.26) basic and diluted net loss per share, for the three months ended September 30, 2023, compared to net loss of $28.3 million, or $(0.96) basic and diluted net loss per share, for three months ended September 30, 2022.

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 BT8009, a *Bicycle* Toxin Conjugate (BTC™) targeting Nectin-4, a well-validated tumor antigen; BT5528, a BTC targeting EphA2; 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 BT8009, BT5528 and BT7480; the anticipated progression of Bicycle's clinical trials, including the timing of initiation and design of the Duravelo-2 Phase 2/3 clinical trial and potential accelerated approval of BT8009; anticipated clinical and other benefits of Bicycle Therapeutics' participation in the CDRP Program, including potential earlier patient access to BT8009; the ability of the company to expedite CMC readiness for BT8009, including ensuring that commercial manufacturing readiness for BT8009 keeps pace with its clinical development; the availability of and timing of announcement of data from clinical trials and regulatory updates for clinical candidates, including the planned R&D Day on December 14, 2023; statements regarding Bicycle's collaborations with Bayer and Novartis; the discovery, development and potential commercialization of potential radiopharmaceutical or other product candidates using Bicycle's technology under the strategic collaboration agreements; BT8009's potential to be a transformative therapy for patients with metastatic bladder cancer; and the therapeutic potential for Bicycles in oncology and other applications. 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 or strategic collaborations; 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; challenges or delays in the development and preparation of the commercial manufacturing readiness of BT8009; 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.

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Collaboration revenues	$ 5,352	$ 3,040	$ 21,645	$ 11,278
Operating expenses:				
Research and development	39,868	22,752	111,799	56,890
General and administrative	16,281	10,047	45,557	38,830
Total operating expenses	56,149	32,799	157,356	95,720
Loss from operations	(50,797)	(29,759)	(135,711)	(84,442)
Other income (expense):				
Interest income	3,985	1,991	7,726	3,117
Interest expense	(814)	(817)	(2,443)	(2,518)
Total other income (expense), net	3,171	1,174	5,283	599
Net loss before income tax provision	(47,626)	(28,585)	(130,428)	(83,843)
Provision for (benefit from) income taxes	2,272	(238)	1,137	(1,104)
Net loss	$ (49,898)	$ (28,347)	$ (131,565)	$ (82,739)
Net loss per share, basic and diluted	$ (1.26)	$ (0.96)	$ (3.95)	$ (2.79)
Weighted average ordinary shares outstanding, basic and diluted	39,576,467	29,676,021	33,291,701	29,643,502

Balance Sheets Data
(In thousands)
(Unaudited)

	September 30, 2023	December 31, 2022
Cash and cash equivalents	$ 572,086	$ 339,154
Working capital	533,300	316,041
Total assets	638,683	410,609
Total shareholders' equity	416,022	270,783

View source version on businesswire.com: https://www.businesswire.com/news/home/20231102566789/en/

Investors:
Stephanie Yao
SVP, Investor Relations and Corporate Communications
ir@bicycletx.com
857-523-8544

Media:
Sarah Sutton
Argot Partners
media@bicycletx.com
212-600-1902

Source: Bicycle Therapeutics plc