Bicycle Therapeutics Reports Third Quarter 2022 Financial Results and Provides Corporate Update

November 3, 2022

- Continued clinical progress across pipeline including BT5528 end of Phase I dose escalation update; completion of enrollment in BT5528 initial dose expansion cohorts expected in Q4

- BT8009 clinical update remains on-track for Q4

- Received $10 million option fee payment from Genentech this quarter triggered by exclusive strategic collaboration expansion option exercise in Q2

- Cash and cash equivalents of $361.5 million as of September 30, 2022; expected financial runway into 2025

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Nov. 3, 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 reported financial results for the third quarter ended September 30, 2022 and provided recent corporate updates.

"We are encouraged by the continued clinical progress across our pipeline," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "In the third quarter, we announced top-line results from the completed dose escalation portion of the Phase I/II trial in BT5528 and expect to complete enrollment in the initial expansion cohorts this quarter. In addition, clinical development of BT8009 remains on-track and we look forward to providing an update this quarter following completion of the dose escalation portion of the Phase I/II clinical trial. Finally, the dose escalation portion of our Phase I/II trial of BT7480 continues at a healthy pace and we expect to share clinical information in 2023."

"Recently, we added to our balance sheet through Genentech's second expansion of our immuno-oncology collaboration, resulting in a $10 million payment to us this quarter. We are pleased to have a strong balance sheet which helps support the advancement of our clinical oncology pipeline as well as our earlier discovery and development efforts and which we anticipate provides financial runway into 2025."

Third Quarter 2022 and Recent Highlights

- **Announced Top-Line Dose Escalation Results of Phase I Trial of BT5528.** In September, Bicycle announced top-line results from the Phase I dose escalation portion of its Phase I/II trial of BT5528, a *Bicycle*® Toxin Conjugate (BTC™) targeting EphA2, in patients with advanced solid tumors. Bicycle observed signs of anti-tumor activity in heavily pre-treated patients with EphA2-postive ovarian and urothelial cancers, demonstrating an overall response rate of 22% (including one complete response) and 67%, respectively. Previously, the company had established a recommended Phase II dose of 6.5mg/m^2 every other week. Low, or no, levels of incidence of neutrophil count decrease, peripheral neuropathy, skin rash and eye disorders were reported. Low-grade GI treatment-related events were those most commonly reported amongst the 15 patients at this dose. In addition, and in contrast to the toxicities observed with EphA2 antibody drug conjugates, Bicycle has observed no signs of treatment-related coagulopathy to date in any patient.

- **Enrollment of the Initial Cohorts of The Initial Expansion Cohorts of the BT5528 Phase I/II Trial Remains on Track to Complete This Quarter**. The company expects to provide an update on BT5528's clinical progress in 2023. In June 2022, Bicycle announced the dosing of the first patient in the Phase II dose expansion portion of the Phase I/II trial. The initial dose expansion enrollment plan includes urothelial (n=14) and ovarian (n=14) cancers as well as in a basket cohort of other solid tumors (n=28), including non-small cell lung, triple-negative breast, head and neck, and esophageal cancers.

- **Announced Publications Highlighting Preclinical Data from BT8009 in *Molecular Cancer Therapeutics* and the *Journal of Medicinal Chemistry.*** In September, Bicycle announced that an article titled "BT8009: a Nectin-4 targeting Bicycle® Toxin Conjugate for treatment of solid tumors" highlighting preclinical data from BT8009 was published in Molecular Cancer Therapeutics. In October, Bicycle announced an additional publication highlighting preclinical BT8009 data in the *Journal of Medicinal Chemistry*, titled "Discovery of BT8009: a Nectin-4 Targeting Bicycle® Toxin Conjugate for the Treatment of Cancer." Both articles are available at the publications section of the Bicycle website via this link.

- **Announced Expansion of Genentech Immuno-Oncology Collaboration.** In July 2022, Bicycle announced that Genentech exercised an option to initiate a new program, expanding the exclusive strategic collaboration agreement with Bicycle to discover, develop and commercialize novel *Bicycle*®-based immuno-oncology therapies. This expansion represented the second option exercised by Genentech under the terms of the original February 2020 agreement and triggered a $10 million payment to Bicycle, which was received in the third quarter of 2022.

Financial Results

- Cash and cash equivalents were $361.5 million as of September 30, 2022, compared to $438.7 million as of December 31,

2021. The decrease in cash is primarily due to cash used in operating activities.

- Research and development expenses were $22.8 million for the three months ended September 30, 2022, compared to $10.5 million for the three months ended September 30, 2021. The increase in expense of $12.2 million for the three months ended September 30, 2022 as compared to the same period in the prior year 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 $1.4 million of incremental non-cash share-based compensation expenses.

- General and administrative expenses were $10.0 million for the three months ended September 30, 2022, compared to $8.1 million for the three months ended September 30, 2021. The increase of $1.9 million for the three months ended September 30, 2022 as compared to the same period in the prior year was primarily due to an increase in personnel-related costs, including $1.3 million of incremental non-cash share-based compensation expense.

- Net loss was $28.3 million, or $(0.96) basic and diluted net loss per share, for the three months ended September 30, 2022, compared to net loss of $14.7 million, or $(0.59) basic and diluted net loss per share, for the three months ended September 30, 2021.

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, 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 BT5528, BT8009 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; the therapeutic potential for *Bicycles* in oncology and other applications; Bicycle’s plans to expand its discovery efforts and early development pipeline; 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: risks to clinical trial site initiation, patient enrollment and follow-up, as well as to Bicycle’s abilities to meet other anticipated deadlines and milestones, 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; 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 and may not have satisfactory 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 4, 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.

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,	
	2022	2021	2022	2021
Collaboration revenues	$ 3,040	$ 4,333	$ 11,278	$ 7,926
Operating expenses:				
Research and development	22,752	10,513	56,890	31,924
General and administrative	10,047	8,114	38,830	23,596

Total operating expenses	32,799	18,627	95,720	55,520
Loss from operations	(29,759)	(14,294)	(84,442)	(47,594)
Other income (expense):				
Interest income	1,991	24	3,117	61
Interest expense	(817)	(823)	(2,518)	(2,164)
Total other income (expense), net	1,174	(799)	599	(2,103)
Net loss before income tax provision	(28,585)	(15,093)	(83,843)	(49,697)
Benefit from income taxes	(238)	(415)	(1,104)	(915)
Net loss	$ (28,347)	$ (14,678)	$ (82,739)	$ (48,782)
Net loss per share, basic and diluted	$ (0.96)	$ (0.59)	$ (2.79)	$ (2.06)
Weighted average ordinary shares outstanding, basic and diluted	29,676,021	25,039,990	29,643,502	23,719,124

Balance Sheets Data
(In thousands)
(Unaudited)

	September 30, 2022	December 31, 2021
Cash and cash equivalents	$ 361,469	$ 438,680
Working capital	339,733	422,317
Total assets	417,148	479,792
Total shareholders' equity	289,474	346,254

View source version on businesswire.com: https://www.businesswire.com/news/home/20221103005134/en/

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