Bicycle Therapeutics Reports Fourth Quarter and Full Year 2022 Financial Results and Provides Corporate Update

February 28, 2023

- Significant progress across pipeline including advancing BT8009, BT5528, and BT7480 in ongoing clinical trials

- BT8009 granted Fast Track Designation by the U.S. Food and Drug Administration; completed Phase I results presented at ASCO GU Cancers Symposium

- Cash position of $339.2 million at December 31, 2022 expected to provide financial runway into 2025

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Feb. 28, 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 fourth quarter and full year ended December 31, 2022, and provided recent corporate updates.

"We have made continued clinical progress across our pipeline, including advancing BT8009 and BT5528 into the ongoing dose expansion cohorts and are encouraged by the progress of BT7480 in the ongoing dose escalation portion of its clinical trial," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We are pleased to have a balance sheet that has supported the advancement and expansion of our clinical portfolio, with an anticipated financial runway into 2025. We believe we are well-positioned ahead of multiple potential inflection points as we pursue our goal of demonstrating the true therapeutic potential of Bicycle Toxin Conjugates® and Bicycle tumor-targeted immune cell agonists."

Fourth Quarter 2022 and Recent Highlights

- **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 Bicycle Toxin Conjugate 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 had dosed its first patient in the Phase II expansion portion of the trial and established RP2Ds 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 remains ongoing. The company expects to provide an update on the program by the end of 2023.

- **BT8009 granted Fast Track Designation (FTD) by the U.S. Food and Drug Administration (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.

- **Presented Five Posters at the Society for Immunotherapy of Cancer's (SITC) 37 th Annual Meeting in November 2022.** Posters featured preclinical data from Bicycle tumor-targeted immune cell agonist® (Bicycle TICA™) programs.

- **Continue to Advance BT5528 and BT7480 in Clinical Trials**.
  - BT5528, a novel Bicycle Toxin Conjugate® targeting EphA2, continues in the dose expansion portion of the ongoing Phase I/II clinical trial. In September 2022, Bicycle announced results from the Phase I dose escalation portion of the ongoing Phase I/II trial in patients with advanced solid tumors. Bicycle observed anti-tumor activity in patients with EphA2-postive heavily pre-treated ovarian and urothelial cancers.
  - BT7480, a novel, fully synthetic Bicycle tumor-targeted immune cell agonist® (Bicycle TICA™) targeting Nectin-4 and agonizing CD137 is currently in the Phase I dose escalation portion of a company-sponsored Phase I/II trial. The company expects to provide an update later this year from the dose escalation portion of the trial.

Financial Results

- Cash and cash equivalents were $339.2 million as of December 31, 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 $24.7 million for the three months ended December 31, 2022 and $81.6 million for the year ended December 31, 2022, compared to $13.0 million for the three months ended December 31, 2021 and $44.9 million for the year ended December 31, 2021. The increase in expense of $11.8 million and $36.7 million for the three months and year ended December 31, 2022, respectively, 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 $1.3 million and $5.4 million for the three months and year ended December 31, 2022, respectively, offset by incremental UK research and development tax credit reimbursements.

- General and administrative expenses were $10.7 million for the three months ended December 31, 2022 and $49.5 million for the year ended December 31, 2022, compared to $8.8 million for the three months ended December 31, 2021 and $32.4 million for the year ended December 31, 2021. The increase of $1.8 million for the three months ended December 31, 2022 as compared to the same period in the prior year was primarily due an increase in personnel-related costs, including $1.2 million of incremental non-cash share-based compensation expense, offset by a decrease in professional- and consulting-related expenses. The increase of $17.1 million for the year ended December 31, 2022 as compared to the same period in the prior year was primarily due to an increase in personnel-related costs, including $9.3 million of incremental non-cash share-based compensation expense.

- Net loss was $30.0 million, or $(1.01) basic and diluted net loss per share, for the three months ended December 31, 2022, and net loss was $112.7 million, or $(3.80) basic and diluted net loss per share, for the year ended December 31, 2022, compared to net loss of $18.0 million, or $(0.63) basic and diluted net loss per share, for three months ended December 31, 2021, and net loss of $66.8 million, or $(2.67) basic and diluted net loss per share, for the year ended December 31, 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 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; 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 3, 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 December 31,		Year Ended December 31,	
	2022	2021	2022	2021
Collaboration revenues	$ 3,185	$ 3,771	$ 14,463	$ 11,697
Operating expenses:				
Research and development	24,719	12,952	81,609	44,880
General and administrative	10,677	8,842	49,507	32,435
Total operating expenses	35,396	21,794	131,116	77,315
Loss from operations	(32,211)	(18,023)	(116,653)	(65,618)

Other income (expense):				
Interest income	2,639	58	5,756	120
Interest expense	(826)	(820)	(3,344)	(2,984)
Total other income (expense), net	1,813	(762)	2,412	(2,864)
Net loss before income tax provision	(30,398)	(18,785)	(114,241)	(68,482)
Benefit from income taxes	(420)	(748)	(1,524)	(1,663)
Net loss	$ (29,978)	$ (18,037)	$ (112,717)	$ (66,819)
Net loss per share, basic and diluted	$ (1.01)	$ (0.63)	$ (3.80)	$ (2.67)
Weighted average ordinary shares outstanding, basic and diluted	29,711,570	28,790,934	29,660,659	25,061,734

Balance Sheet Data
(In thousands)
(Unaudited)

	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 339,154	$ 438,680
Working capital	316,041	422,317
Total assets	410,609	479,792
Total shareholders' equity	270,783	346,254

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