Bicycle Therapeutics Reports Recent Business Progress and Second Quarter 2024 Financial Results

August 6, 2024

Four abstracts containing data updates across clinical pipeline accepted for poster presentation at ESMO Congress 2024

Focused R&D pipeline on clinical programs and research areas that have the highest potential to maximize value creation

Streamlined leadership team to better align with strategic and pipeline priorities, and enhanced oncology expertise with formation of Clinical Advisory Board

Strengthened balance sheet with gross proceeds of approximately $555 million from May 2024 private investment in public equity (PIPE) financing

Cash and cash equivalents of $961.4 million as of June 30, 2024, expected to provide financial runway into 2H 2027

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Aug. 6, 2024-- Bicycle Therapeutics plc (NASDAQ: BCYC), a pharmaceutical company pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (Bicycle®) technology, today reported recent business progress and financial results for the second quarter ended June 30, 2024.

"In the second quarter, we continued to demonstrate the ongoing progress of our pipeline and highlight the emerging differentiated profiles of our Bicycle Toxin Conjugates® zelenectide pevedotin and BT5528 compared to antibody drug conjugates. As we enter the second half of the year, we look forward to sharing the first set of data updates from our clinical programs at the upcoming ESMO Congress," said Kevin Lee, Ph.D., CEO of Bicycle Therapeutics. "Additionally, I am honored to welcome renowned oncology experts from around the world to our Clinical Advisory Board. Their advice and counsel will be critical as we work to develop therapies that can help patients live longer and live well."

Dr. Lee continued: "Bicycle Therapeutics also significantly strengthened our balance sheet in the second quarter through the support of leading healthcare investors. Moreover, we have prioritized our pipeline and streamlined our leadership team to enable us to focus on the clinical programs and research areas that we believe have the highest potential for value creation and align with our strategy to support the long-term growth of our company."

Second Quarter 2024 and Recent Events

- **Four abstracts accepted for poster presentation at the European Society for Medical Oncology (ESMO) Congress 2024 being held September 13-17 in Barcelona.** Bicycle Therapeutics will present four abstracts containing updated clinical data for zelenectide pevedotin (formerly BT8009) in metastatic urothelial cancer (mUC), BT5528 in advanced solid tumors such as mUC and ovarian, and BT7480 in advanced solid tumors.

  In June, the company presented two abstracts at the 2024 American Society for Clinical Oncology (ASCO) Annual Meeting outlining clinical pharmacokinetics of Bicycle Toxin Conjugate® (BTC®) molecules zelenectide pevedotin and BT5528 compared to antibody drug conjugate enfortumab vedotin and evaluating the emerging safety profile of both BTC molecules, along with an overview of the company's ongoing Phase 2/3 Duravelo-2 registrational trial of zelenectide pevedotin in mUC.
- **Focused research and development (R&D) pipeline on clinical programs and research areas that the company believes have the highest potential to maximize value creation.** Activities include:
  - Prioritizing the clinical development of zelenectide pevedotin and BT5528 in multiple tumor types.
  - Focusing near-term research efforts on advancing the company's Bicycle Radionuclide Conjugate (BRC™) pipeline and the discovery of next-generation BTC molecules.
  - Except for BT7480, exploring innovative ways to continue development of the company's immuno-oncology portfolio, including Bicycle Tumor-targeted Immune Cell Agonist® (Bicycle TICA®) molecules, through collaboration.
- **Streamlined leadership team to better align with strategic and pipeline priorities.**
  - **Michael Skynner, Ph.D., chief technology officer**, has assumed leadership of Bicycle Therapeutics' discovery research team, and all discovery research activities will be consolidated and moved to the company's headquarters in Cambridge, UK.
  - **Jennifer Perry, Pharm.D., promoted to chief strategy officer and head of commercial**. Since joining Bicycle Therapeutics in August 2022, Ms. Perry has been instrumental in establishing and growing Bicycle Therapeutics' commercial organization. In this expanded role, she will oversee the company's corporate and end-to-end portfolio strategy while also fulfilling her existing commercial responsibilities. Ms. Perry has more than 20 years of experience in pharma and biotech, with 15 years in oncology. Her experience spans commercial and medical roles with a focus on go-to-market strategies for launching oncology medicines at GSK, Tesaro, TG Therapeutics and Pharmacyclics.

    - **Nick Keen, Ph.D., chief scientific officer**, is transitioning to an advisor role with the company as a distinguished fellow, where he will advise the company as needed. The company also hired **Eric Westin, M.D., former vice president of clinical development and translational sciences at ImmunoGen**, to an advisor role with the company as a distinguished fellow to help refine the company's translational and clinical strategy.
- **Formed new Clinical Advisory Board with distinguished global oncology experts to support the advancement of clinical oncology programs.** The company expects that the advisors will provide invaluable guidance and insights for the global clinical development of the company's clinical programs. Inaugural members include:
    - **Charles Swanton, M.D., Ph.D., FRS, FMedSci, FRCP,** is the chair of Bicycle Therapeutics' Clinical Advisory Board and Scientific Advisory Board. He leads the Cancer Evolution and Genome Instability Laboratory at the Francis Crick Institute in London. Dr. Swanton's research is focused on how tumors evolve over space and time, and he has authored over 250 papers developing an understanding of branching evolutionary histories of solid tumors, processes that drive cancer cell-to-cell variation and the impact of cancer diversity on effective immune surveillance and clinical outcome.
    - **Toni K. Choueiri, M.D.,** is the director of the Lank Center for Genitourinary (GU) Oncology at Dana-Farber Cancer Institute and the Jerome and Nancy Kohlberg Chair and Professor of Medicine at Harvard Medical School. Dr. Choueiri and colleagues have made seminal observations that have defined and evolved the treatment of kidney cancer and led to the approval of several therapies. He has over 800 PubMed-indexed publications and is the lead investigator of multiple national and international Phase 1-3 trials in GU cancers.
    - **Sherene Loi, MBBS (Hons), Ph.D., FRACP, FAHMS,** is a medical oncologist specialized in breast cancer treatment and a clinician scientist (lab head) with expertise in genomics, immunology and drug development at the Peter MacCallum Cancer Centre in Melbourne, Australia. She is recognized internationally as a leading clinician scientist whose work has led to new insights into the breast cancer immunology field as well as leading international clinical trials in breast cancer immunotherapy. Professor Loi has published over 330 research articles, co-chairs the International Breast Cancer Study Group and is the Inaugural National Breast Cancer Foundation of Australia Endowed Chair. In 2021, she received the Australian Prime Minister's Frank Fenner Prize for Life Scientist of the Year.
    - **Solange Peters, M.D., Ph.D.,** is full professor and chair of medical oncology and the chair of the thoracic malignancies program in the Department of Oncology at the University Hospital of Lausanne in Switzerland. She currently oversees teaching and patient care in thoracic malignancies at Lausanne University, and her main fields of interest include new biomarker discovery and validation in preclinical and clinical settings as well as cancer immunotherapy. She is the youngest president of ESMO, serving for an extended period of 2020-2022. Professor Peters has authored over 500 peer-reviewed manuscripts and book chapters and is associate editor of the *Annals of Oncology*, deputy editor of *Lung Cancer* and serves on the editorial board of several other oncology journals. She was the deputy editor of the *Journal of Thoracic Oncology* for 10 years.
- **Raised gross proceeds of $555 million in private investment in public equity (PIPE) financing.** The PIPE financing, with participation from leading healthcare investors, is expected to extend the company's financial runway into the second half of 2027. The company plans to use the net proceeds of $544.1 million to fund the continued development of its proprietary pipeline and for other R&D, as well as for general corporate purposes.
- **Repaid and voluntarily terminated outstanding debt with Hercules.** In July 2024, Bicycle Therapeutics announced the repayment of its loan with Hercules Capital, Inc., ahead of its 2025 maturity date, with total payments of $31.9 million, including accrued and unpaid interest, an end-of-term charge and an early repayment fee.

Second Quarter 2024 Financial Results

- Cash and cash equivalents were $961.4 million as of June 30, 2024, compared to $526.4 million as of December 31, 2023. The increase in cash and cash equivalents is primarily due to net proceeds from the PIPE financing and share option exercises, offset by cash used in operating activities.
- R&D expenses were $40.1 million for the three months ended June 30, 2024, compared to $39.7 million for the three months ended June 30, 2023. The increase in expense of $0.4 million was primarily due to increased clinical program expenses for zelenectide pevedotin development and increased personnel-related expenses, offset by decreased clinical program expenses for Bicycle TICA® molecule development, decreased discovery, platform and other expenses and incremental U.K. R&D tax credits.
- General and administrative expenses were $15.9 million for the three months ended June 30, 2024, compared to $14.8 million for the three months ended June 30, 2023. The increase of $1.1 million was primarily due to increased personnel-related costs.
- Net loss was $39.8 million, or $(0.77) basic and diluted net loss per share, for the three months ended June 30, 2024, compared to net loss of $42.6 million or $(1.41) basic and diluted net loss per share, for three months ended June 30, 2023.

About Bicycle Therapeutics

Bicycle Therapeutics is a clinical-stage pharmaceutical company developing a novel class of medicines, referred to as Bicycle® molecules, for

diseases that are underserved by existing therapeutics. Bicycle molecules 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 Bicycle molecules attractive candidates for drug development. The company is evaluating zelenectide pevedotin (formerly BT8009), a Bicycle® Toxin Conjugate (BTC®) targeting Nectin-4, a well-validated tumor antigen; BT5528, a BTC molecule targeting EphA2, a historically undruggable target; and BT7480, a Bicycle Tumor-Targeted Immune Cell Agonist® (Bicycle TICA®) targeting Nectin-4 and agonizing CD137, in company-sponsored clinical trials. Additionally, the company is developing Bicycle® Radio Conjugates (BRC™) for radiopharmaceutical use and, through various partnerships, is exploring the use of Bicycle® technology to develop therapies for diseases beyond oncology.

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 progress across its R&D pipeline and the advancement of its product candidates, including zelenectide pevedotin, BT5528 and BT7480; the anticipated progression of Bicycle’s clinical trials and the method and timing of announcement of data from clinical trials and program updates for clinical candidates; Bicycle’s beliefs regarding the clinical programs and research areas with the highest potential to maximize value creation and the company’s activities to focus on such programs and areas; the guidance and insights provided by the Clinical Advisory Board; the development of potential radiopharmaceutical or other product candidates using Bicycle’s technology through various partnerships; 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 research and development and 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 partnerships; timing of results from clinical trials; whether the outcomes of preclinical studies will be predictive of clinical trial results; the risk that trials may have unsatisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; the risk that Bicycle’s management have not focused the company’s activities on the clinical programs and research areas with the highest potential to maximize value creation; the risk that the Clinical Advisory Board does not provide guidance or insights or that such guidance turns out to be deficient; the risk that Bicycle’s projections regarding its expected cash 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 May 2, 2024, 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 June 30,		Six Months Ended June 30,	
	2024	2023	2024	2023
Collaboration revenues	$ 9,361	$ 11,397	$ 28,891	$ 16,293
Operating expenses:				
Research and development	40,059	39,720	74,923	71,931
General and administrative	15,949	14,788	32,331	29,276
Total operating expenses	56,008	54,508	107,254	101,207
Loss from operations	(46,647)	(43,111)	(78,363)	(84,914)
Other income (expense):				
Interest income	7,774	812	13,398	3,741
Interest expense	(824)	(821)	(1,645)	(1,629)
Total other income (expense), net	6,950	(9)	11,753	2,112
Net loss before income tax provision	(39,697)	(43,120)	(66,610)	(82,802)
Provision for (benefit from) income taxes	115	(517)	(235)	(1,135)
Net loss	$ (39,812)	$ (42,603)	$ (66,375)	$ (81,667)
Net loss per share, basic and diluted	$ (0.77)	$ (1.41)	$ (1.40)	$ (2.71)
Weighted average ordinary shares outstanding, basic and diluted	51,992,034	30,191,693	47,276,062	30,097,234

Condensed Consolidated Balance Sheets Data
(In thousands)
(Unaudited)

	June 30, 2024	December 31, 2023
Cash and cash equivalents	$ 961,364	$ 526,423
Working capital	958,645	492,331
Total assets	1,057,355	595,344
Total shareholders' equity	873,813	370,932

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