

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**FORM 8-K**

**CURRENT REPORT  
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**October 23, 2024**  
Date of Report (Date of earliest event reported)

**Bicycle Therapeutics plc**  
(Exact name of registrant as specified in its charter)

**England and Wales**  
(State or other jurisdiction  
of incorporation)

**001-38916**  
(Commission  
File Number)

**Not applicable**  
(IRS Employer  
Identification No.)

**Blocks A & B, Portway Building,  
Granta Park Great Abington, Cambridge  
United Kingdom**  
(Address of principal executive offices)

**CB21 6GS**  
(Zip Code)

Registrant's telephone number, including area code: **+44 1223 261503**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol (s)	Name of each exchange on which registered
Ordinary shares, nominal value £0.01 per share	n/a	The Nasdaq Stock Market LLC*
American Depositary Shares, each representing one ordinary share, nominal value £0.01 per share	BCYC	The Nasdaq Stock Market LLC

\* Not for trading, but only in connection with the listing of the American Depositary Shares on The Nasdaq Stock Market LLC.

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

**Item 8.01 Other Events.**

On October 23, 2024, Bicycle Therapeutics plc issued a press release announcing, among other news, the presentation at the European Association of Nuclear Medicine (EANM) 2024 Congress in Hamburg, Germany of the first human imaging data validating the potential of MT1-MMP as a novel target in the treatment of cancer, and an outline of the company's strategy to develop radiopharmaceuticals. A copy of the press release is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits**

(d) Exhibits

<b>Exhibit No.</b>	<b>Description</b>
<a href="#">99.1</a>	<a href="#">Press Release issued October 23, 2024</a>
104	Cover Page Interactive Data File (formatted in Inline XBRL)

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**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 23, 2024

**BICYCLE THERAPEUTICS PLC**

By: /s/ Alethia Young

Name: Alethia Young

Title: Chief Financial Officer

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**Bicycle Therapeutics Announces First Human Imaging Data from European Association of Nuclear Medicine 2024 Congress and Outlines Strategy for Leadership in Next-Generation Radiopharmaceuticals**

*First human imaging data validate the potential of MT1-MMP as a novel target in the treatment of cancer and demonstrate positive properties of Bicycle Radionuclide Conjugates (BRC®) for radiopharmaceutical use*

*Additional preclinical data demonstrate biodistribution of BRCs can be optimized to maintain high tumor uptake while significantly reducing kidney levels*

*Company strategy focuses on pursuing novel targets using a range of isotopes to develop radiopharmaceuticals with first-in-class potential*

*Bicycle to host conference call and webcast today at 8 a.m. ET*

CAMBRIDGE, England & BOSTON, October 23, 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 announced the presentation of the first human imaging data validating the potential of MT1-MMP as a novel target in the treatment of cancer and demonstrating the positive properties of Bicycle Radionuclide Conjugates (BRC®) for radiopharmaceutical use, as well as preclinical data demonstrating optimized BRC radioisotope delivery at the European Association of Nuclear Medicine (EANM) 2024 Congress in Hamburg, Germany.

“Since our founding, our goal at Bicycle Therapeutics has been to leverage the power of our platform in areas where we can have the most impact for patients. Over the years, we have built a robust pipeline of oncology therapies that includes targeted drug conjugates, immuno-oncology agents and now, radiopharmaceuticals,” said CEO Kevin Lee, Ph.D. “The exciting data presented at EANM underscore the potential of our Bicycle Radionuclide Conjugates to deliver a range of isotopes to novel cancer targets. Through our strategy of pursuing novel targets with first-in-class potential and selecting the isotope that best aligns with the target biology and indication, we have an opportunity to potentially broaden the use of radiopharmaceuticals to diagnose and treat cancer.”

In line with Bicycle Therapeutics’ radiopharmaceuticals strategy, the company selected tumor antigen EphA2 as its second BRC target and signed a letter of intent with leading isotope technology company Eckert & Ziegler to put in place an agreement to supply a range of radioisotopes and develop and manufacture BRC molecules. Bicycle Therapeutics, through its internal pipeline of wholly owned molecules and strategic collaborations with industry and academic leaders in the field, aims to be at the forefront of the development of next-generation radiopharmaceutical therapies. Bicycle® molecules have ideal properties for radioisotope delivery due to their low molecular weight, high selectivity and affinity for their intended target and rapid systemic clearance.

“The data presented at EANM demonstrate how our Bicycle® platform is a powerful tool for de novo identification of high-quality binders to important cancer targets. We believe the ability to optimize the biodistribution properties of our molecules, significantly reducing kidney retention while retaining rapid, selective uptake in tumors, position Bicycle Radionuclide Conjugates as a potentially best-in-class approach for targeted radionuclide therapy,” said Michael Skynner, Ph.D., chief technology officer of Bicycle Therapeutics. “MT1-MMP is the first target for radiopharmaceutical development that we are pursuing given its expression in many solid tumors such as non-small cell lung cancer, esophageal and triple negative breast cancer.”

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## EANM 2024 Congress Data Highlights

During an oral presentation, the German Cancer Consortium (DKTK) presented first human imaging data for a BRC targeting MT1-MMP. They focused on a case study in a 65-year-old male diagnosed with advanced pulmonary adenocarcinoma, the most common type of non-small cell lung cancer, in the lung and lymph nodes confirmed by endobronchial ultrasound (EBUS) biopsy. The patient received fluorine-18-labelled FDG-PET/CT imaging, and two weeks later received MT1-MMP PET/CT imaging up to one hour post injection of the gallium-68-labelled BRC tracer.

Both scans revealed multiple lymph node metastases and bone metastases in the sternum. MT1-MMP imaging demonstrated tracer uptake in the primary tumor in the lung and lymph node and bone metastases, consistent with FDG imaging. Additionally, the MT1-MMP BRC tracer showed renal excretion, with all other organs showing only negligible tracer uptake. Clear imaging contrast was also observed at early time points.

In an e-poster, Bicycle Therapeutics presented preclinical data demonstrating the suitability of Bicycle molecules to deliver indium to tumors *in vivo* due to their favorable properties, including specific tumor uptake, rapid tumor penetration and rapid renal elimination. Additionally, imaging showed how the biodistribution profile of BRCs can be optimized to maintain high tumor uptake and retention while significantly reducing kidney uptake and retention. These data build on the body of preclinical data the company has published in this area demonstrating the use of Bicycle molecules to effectively deliver various radioisotopes, such as lutetium and lead, to tumors.

Altogether, the data presented at EANM validate the potential of MT1-MMP as a novel target in the treatment of cancer, demonstrate the translatability of BRC preclinical data and highlight the potential of Bicycle molecules for targeted radionuclide therapy.

The e-poster, “Bicycle Radionuclide Conjugates for radioisotope delivery to solid tumors,” is available in the Publications section of the Bicycle Therapeutics website.

### Conference Call Details

Bicycle Therapeutics will host a conference call and webcast today, Oct. 23, at 8 a.m. ET to review the first human imaging data and outline the company’s radiopharmaceuticals strategy. To access the call, please dial 833-816-1408 (U.S.) or +1-412-317-0501 (international) and ask to join the Bicycle Therapeutics call. A live webcast and replay of the conference call will be accessible in the Investor section of the Company’s website at [www.bicycletherapeutics.com](http://www.bicycletherapeutics.com).

### About Bicycle Therapeutics

Bicycle Therapeutics is a clinical-stage pharmaceutical company developing a novel class of medicines, referred to as Bicycle<sup>®</sup> 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<sup>®</sup> Toxin Conjugate (BTC<sup>®</sup>) 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<sup>®</sup> (Bicycle TICA<sup>®</sup>) targeting Nectin-4 and agonizing CD137, in company-sponsored clinical trials. Additionally, the company is developing Bicycle Radionuclide Conjugates (BRC<sup>®</sup>) for radiopharmaceutical use and, through various partnerships, is exploring the use of Bicycle<sup>®</sup> technology to develop therapies for diseases beyond oncology.

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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 [www.bicycletherapeutics.com](http://www.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 validation of MT1-MMP as a target for the treatment of cancer, the suitability of BRCs for radiopharmaceutical use and the potential of this approach; Bicycle’s plans for an agreement with Eckert & Ziegler to develop, manufacture and supply a range of radioisotopes; Bicycle’s anticipated progress across its internal and partnered pipelines in radiopharmaceuticals, the translatability of Bicycle’s BRC preclinical data and the ability of the Bicycle platform to identify binders for cancer targets; Bicycle’s development across its R&D pipeline and the advancement of its product candidates, including zelenectide pevvedotin, BT5528 and BT7480; 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 research and development and in the initiation, progress and completion of preclinical studies and clinical trials and the identification and development of Bicycle’s potential and current product candidates; the risk that Bicycle may not realize the intended benefits of its platform, technology or partnerships; timing of results from preclinical studies and clinical trials; whether the outcomes of preclinical studies will be predictive of clinical trial results; the risk that preclinical studies and clinical 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; 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.

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