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

March 27, 2023
Date of Report (Date of earliest event reported)

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

England and Wales	**001-38916**	**Not applicable**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

Blocks A & B, Portway Building, Granta Park Great Abington, Cambridge United Kingdom	**CB21 6GS**
(Address of principal executive offices)	(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 1.01 Entry into a Material Definitive Agreement.

Collaboration and License Agreement

On March 27, 2023, BicycleTx, Limited. (the "Company") and Novartis Pharma AG ("Novartis") entered into a collaboration and license agreement (the "Collaboration Agreement"), pursuant to which the parties will perform research and discovery activities under a mutually agreed upon research plan during a research term of up to a specified number of years per target program to generate compounds incorporating optimized *Bicycle* constructs directed to two specified targets, under the oversight of a joint steering committee. For each collaboration program, Novartis may elect, at its sole discretion, to progress compounds arising from activities under the research programs into further preclinical development of potential products directed to the target of such collaboration program. On a target-by-target basis, if Novartis elects to progress development candidates directed to such target into further clinical development, Novartis will be required to use commercially reasonable efforts to develop and seek regulatory approval in certain major markets for products directed to the applicable target. During the term of the Collaboration Agreement, Company will be exclusive to Novartis with respect to bicycles directed (as their primary mechanism of action) to targets included within the collaboration, and with respect to any compounds arising from the activities under the research program and directed to such selected targets.

Novartis will make an upfront payment to the Company of $50 million. During the research term, upon achievement of a specified discovery milestone for the first target program, Novartis will make a one-time payment to Company in the low single digit millions. On a target-by-target basis, if Novartis elects to progress one or more candidate compounds into further development, Novartis will be required to pay a candidate selection fee for the first such compound progressed by Novartis that incorporates a radionuclide, and for the first such compound that does not incorporate a radionuclide, in each case in the mid-teen millions. On a target program-by-target program basis, if Novartis successfully conducts clinical development achieves regulatory approval for compounds arising from the collaboration, Novartis will be required to pay to Company development and regulatory/first commercial sale milestones of up to $210 million for each of the first radionuclide product and non-radionuclide product directed to the applicable target to achieve such milestones, or $840 million in the aggregate if Novartis successfully develops both a radionuclide and a non-radionuclide product in each of the target programs. In addition, if Novartis successfully commercializes products arising from the collaboration, Novartis will be required to pay to Company, on a product-by-product basis, tiered royalties on net sales of products by Novartis, its affiliates or sublicensees at percentages ranging from the high single digits to the very low double digits, subject to standard reductions and offsets in certain circumstances, and a royalty floor. Royalties will be payable under the Collaboration Agreement on a product-by-product and country-by-country basis, commencing on the first commercial sale of each product, until the latest of (a) the expiration of the last valid claim of certain patents licensed by Company to Novartis, (b) a specified number of years following first commercial sale of such product, and (c) expiration of all data and regulatory exclusivity for such product in the applicable country. Novartis will also owe Company tiered sales milestones based on the achievement of specified levels of net sales of such products totaling up to $200 million in the aggregate per product, or $800 million in the aggregate if Novartis successfully commercializes both a radionuclide and a non-radionuclide product in each of the target programs.

The Collaboration Agreement will remain in force on a product-by-product and country-by-country basis, unless earlier terminated by either party, until the expiration of the obligation for Novartis to make royalty payments to Company for such product in such country, and will terminate in its entirety on the expiration of all such royalty terms in all countries. Either party may terminate the agreement upon 60 days' written notice for the other party's uncured material breach, or upon the other party's insolvency. In addition, Novartis may terminate the Collaboration Agreement (i) in its entirety or on a product-by-product or target-by-target basis for any reason upon 90 days' written notice to Company, and (ii) on a target-by-target basis on 30 days' written notice if Novartis determines that a safety or regulatory issue exists which would have a material adverse effect on the development, manufacture, or commercialization of any product with respect to a given target.

On March 28, 2023, the Company and Novartis issued a joint press release announcing the transactions described above. A copy of the press release is attached to this report as Exhibit 99.1.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as “may,” “will,” “expect,” “plan,” “anticipate,” “estimate,” “intend,” “potential” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These forward-looking statements are based on the Company’s expectations and assumptions as of the date of this Current Report. Each of these forward-looking statements involves risks and uncertainties. Actual results may differ materially from these forward-looking statements. Forward-looking statements contained in this Current Report include statements regarding the Company’s collaboration with Novartis, potential future regulatory filings and approvals of product candidates developed pursuant to the Collaboration Agreement, and potential future payments that may be become payable to the Company pursuant to the Collaboration Agreement. Many factors may cause differences between current expectations and actual results, including risks to the Company’s and its collaboration partners’ abilities to meet anticipated deadlines and milestones; uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of product candidates by the Company’s collaboration partners; the risk that the Company or its collaboration partners may not realize the intended benefits of its technology; risks related to the Company’s ability to maintain existing collaborations and realize the benefits thereof; expectations for regulatory approvals to conduct trials or to market products and other important factors. Other factors that may cause actual results to differ from those expressed or implied in the forward-looking statements in this Current Report are discussed in the Company’s filings with the Securities and Exchange Commission, including the section titled “Risk Factors” in the Company’s Annual Report on From 10-K filed with the Securities and Exchange Commission (the “SEC”) on February 28, 2023, as well as other filings the Company may make with the SEC in the future. Except as required by law, the Company assumes no obligation to update any forward-looking statements contained herein to reflect any change in expectations, even as new information becomes available.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release dated March 28, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: March 28, 2023

BICYCLE THERAPEUTICS PLC

By: /s/ Lee Kalowski
Name: Lee Kalowski
Title: Chief Financial Officer

Exhibit 99.1

Bicycle Therapeutics Announces a Strategic Collaboration with Novartis to Discover, Develop and Commercialize Bicycle® Radio-Conjugates

- *Bicycle and Novartis will collaborate on the discovery and development of multiple targeted radioligand therapies in oncology*
- *Bicycle will receive a $50 million upfront payment as well as potential milestones and tiered commercial royalties*

CAMBRIDGE, England, & BOSTON, March 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 announced that it has entered into a strategic collaboration agreement with Novartis to develop, manufacture and commercialize *Bicycle*® radio-conjugates (BRCs) for multiple agreed upon oncology targets.

"This collaboration builds on the groundbreaking clinical work we have been doing in the toxin conjugate field and provides new and additional validation for this unique technology," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We look forward to working closely with Novartis to pioneer the discovery and development of potential new cutting-edge radiopharmaceutical cancer treatments based on *Bicycles.* We believe the properties of *Bicycles* make them well suited for the development of precision guided radiopharmaceuticals and represents the next leg in the application of our proprietary discovery platform in oncology."

Under the terms of the agreement, Bicycle will utilize its proprietary phage platform to discover *Bicycles* to be developed into BRCs. Novartis will be responsible for further development, manufacture and commercialization of the BRCs. Novartis will fund all pre-clinical and clinical development and commercialization activities. Bicycle will receive a $50 million upfront payment and is eligible for development and commercial-based milestone payments totaling up to $1.7 billion. Bicycle will also be eligible to receive tiered royalties on *Bicycle*-based medicines commercialized by Novartis.

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 collaboration with Novartis; the discovery, development and potential commercialization of potential radiopharmaceutical or other product candidates using Bicycle’s technology under the strategic collaboration agreement; the therapeutic potential for Bicycles in oncology and other applications; and the potential to receive milestone payments under the strategic collaboration agreement. 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: the risk that Bicycle may not realize the intended benefits of its technology or of the collaboration agreement with Novartis, including that Bicycle and Novartis may not successfully identify, develop and commercialize additional product candidates; the risk that Bicycle may not be able to maintain its collaboration with Novartis and realize the benefits thereof; 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-K filed with the Securities and Exchange Commission (SEC) on February 28, 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.

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