

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

July 9, 2021

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.)

B900, Babraham Research Campus
Cambridge CB22 3AT
United Kingdom

(Address of principal executive offices)

Not Applicable

(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 July 9, 2021, BicycleTx Limited (“BTx”), a wholly-owned subsidiary of Bicycle Therapeutics plc (the “Company”), and Ionis Pharmaceuticals, Inc. (“Ionis”) entered into a collaboration and license agreement (the “Collaboration Agreement”). The parties entered into the Collaboration Agreement following the exercise on July 9, 2021 by Ionis of the exclusive option (the “Option”) granted by BTx to Ionis pursuant to an Evaluation and Option Agreement dated December 31, 2020, between the Company, BTx and Ionis (the “Option Agreement”). Pursuant to the Collaboration Agreement, BTx granted to Ionis a worldwide exclusive license under BTx’s relevant technology to research, develop, manufacture and commercialize products incorporating *Bicycle* peptides directed to the protein coded by the gene TFRC1 (transferrin receptor) (“TfR1 Bicycles”) intended for the delivery of oligonucleotide compounds directed to targets selected by Ionis for diagnostic, therapeutic, prophylactic and preventative uses in humans. Each party will be responsible for optimization of such TfR1 Bicycles and other research and discovery activities related to TfR1 Bicycles, and thereafter Ionis will be responsible for all future research, development, manufacture and commercialization activities. Bicycle has retained certain rights, including the right to use TfR1 Bicycles for all non-oligonucleotide therapeutic purposes.

Under the Collaboration Agreement, Ionis will make an upfront payment to BTx of \$31.0 million and will make an equity investment in the Company of \$11.0 million. Ionis also previously paid a \$3.0 million option fee under the Option Agreement to obtain the Option. On a collaboration target-by-collaboration target basis, Ionis will be required to make a payment to BTx of a low-single-digit million dollar amount upon acceptance of an investigational new drug application for the first product directed to such collaboration target (provided that Ionis will have a credit of a high single-digit million dollar amount to be applied towards the IND acceptance fee for four collaboration targets), and Ionis will be required to make milestone payments to BTx upon the achievement of specified development and regulatory milestones of up to a low double-digit million dollar amount per collaboration target. In addition, BTx is also eligible to receive up to a low double-digit million dollar amount in cumulative sales milestone payments. BTx is entitled to receive tiered royalty payments on net sales at percentages in the low single digits, subject to certain standard reductions and offsets. Royalties will be payable, on a product-by-product and country-by-country basis, until the latest of the expiration of specified licensed patents covering such product in such country, ten years from first commercial sale of such product in such country, or expiration of marketing exclusivity for such product in such country.

Either party may terminate the Collaboration Agreement for the uncured material breach of the other party or in the case of insolvency. Ionis may terminate the Collaboration Agreement for convenience on specified notice periods depending on the development stage of the applicable target, either in its entirety or on a target-by-target basis.

Share Purchase Agreement

Concurrently with the execution of the Collaboration Agreement on July 9, 2021, the Company entered into a share purchase agreement (the “Share Purchase Agreement”) with Ionis, pursuant to which Ionis will purchase 282,485 of the Company’s ordinary shares (the “Shares”) at a price per Share of \$38.94, for an aggregate purchase price of approximately \$11.0 million. The price per Share is equal to 1.3 times the volume weighted average price of one of the Company’s American Depositary Shares, each representing one ordinary share, for a twenty trading day period, starting with the opening of trading on the twentieth trading day prior to the date of Ionis’ exercise of its Option and ending with the close of trading on the trading day prior to the date of Ionis’ exercise of its Option.

Pursuant to the terms of the Share Purchase Agreement, Ionis has agreed not to, without the Company’s prior written consent and subject to certain conditions and exceptions, among other things, directly or indirectly acquire additional shares of the Company’s outstanding equity securities, seek or propose a tender or exchange offer, merger or other business combination involving the Company, solicit proxies or consents with respect to any matter, or undertake other specified actions related to the potential acquisition of additional equity interests in the Company (collectively, the “Standstill Restrictions”). The Standstill Restrictions will expire on the 18-month anniversary of the Share Purchase Agreement.

The Share Purchase Agreement also provides that, subject to limited exceptions, Ionis will hold and not sell any of the Shares until the earlier of (i) the first anniversary of the closing of the sale of the Shares under the Share Purchase Agreement (the “Closing Date”) and (ii) the termination of the Collaboration Agreement pursuant to its terms (provided, however, that in the event the termination of the Collaboration Agreement occurs less than six months after the Closing Date, Ionis shall hold and will not sell or otherwise enter into a transaction regarding the Shares until at least the date that is six months after the Closing Date).

The foregoing is only a brief description of the material terms of the Collaboration Agreement and the Share Purchase Agreement, does not purport to be a complete statement of the rights and obligations of the parties under these agreements and the transactions contemplated thereby, and is qualified in its entirety by the full text of such agreements, copies of which will be filed as exhibits to a subsequent filing by the Company with the Securities and Exchange Commission.

On July 13, 2021, the Company and Ionis 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.

Item 3.02. Unregistered Sales of Equity Securities

See the description set forth under Item 1.01 above with respect to the Share Purchase Agreement, which is incorporated into this Item 3.02 by reference. The Shares are being offered and sold to Ionis pursuant to the exemption from the registration requirements provided in Section 4(a)(2) of the Securities Act for transactions by an issuer not involving any public offering. Accordingly, the Shares have not been registered under the Securities Act and may not be offered or sold in the United States except pursuant to an effective registration statement or an applicable exemption from the registration requirements of the Securities Act.

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 Ionis, potential future regulatory filings and approvals of product candidates developed pursuant to the Collaboration Agreement, potential future payments that may become payable to the Company pursuant to the Collaboration Agreement and the completion of the sale of the Shares pursuant to the Share Purchase 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 presented by the ongoing COVID-19 pandemic; 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; risks and uncertainties related to customer closing conditions related to the Share Purchase Agreement 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” contained therein. 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 issued July 13, 2021

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: July 13, 2021

BICYCLE THERAPEUTICS PLC

By: /s/ Lee Kalowski

Name: Lee Kalowski

Title: Chief Financial Officer



Bicycle Therapeutics Enters Exclusive License and Collaboration Agreement with Ionis to Develop Targeted Oligonucleotide Therapeutics

- *Bicycle to receive a total of \$45 million upfront from Ionis and is eligible for development, regulatory and commercial milestone payments and royalties*
- *The agreement provides Ionis an exclusive license to Bicycles that bind with high specificity to the transferrin receptor without modifying natural function*
- *Bicycle retains rights to use transferrin binding bicycles to deliver all molecular payloads outside of oligonucleotides*

CAMBRIDGE, England, & BOSTON, MA; July 13, 2021 – 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 Ionis Pharmaceuticals has exercised its option and entered into an exclusive worldwide license and collaboration agreement for tissue-targeted delivery of oligonucleotide therapeutics using *Bicycles* with high affinity to the transferrin receptor (TfR1).

Ionis had an option for an exclusive license under the terms of a December 2020 evaluation and option agreement. The agreement granted Ionis the right to evaluate tissue-targeting TfR1 binding *Bicycles* as vehicles to deliver oligonucleotide therapeutics to specific organ systems and an option to obtain an exclusive license at the end of the evaluation period.

Bicycle receives a total of \$45 million upfront, which includes a license fee, an option fee, and an \$11 million equity investment. Bicycle is also eligible to receive development, regulatory and commercial milestone payments and royalties for each program developed under the collaboration.

“This agreement stems from a highly successful collaboration with Ionis that began earlier in the year, during which *Bicycles* were shown to selectively deliver oligonucleotide payloads into TfR1-expressing tissue,” said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. “These data build upon our own work, and that of our partners, which have shown *Bicycles* targeted to tumor antigens can rapidly and selectively deliver a variety of payloads into solid tumors. This tissue-targeting payload-delivery capability is facilitated by the unique nature of *Bicycles* that inherently enables the conjugation of a diverse range of molecular cargos without impacting the pharmacology of the target. We believe *Bicycles* have the potential to become the targeting technology of choice for the development of precision medicines.”

Bicycle has identified binders that it believes to be the first small molecules to target TfR1 with high specificity without modifying TfR1’s natural function. These binders present broad conjugation potential across multiple payloads, thereby resulting in the potential to treat diseases in multiple therapeutic areas, including those of the skeletal and cardiac muscles and of the central nervous system. Bicycle is currently also collaborating with the Dementia Discovery Fund (DDF) to advance potential TfR1 *Bicycles* for treating dementia.

Under the terms of the license and collaboration agreement, Ionis and Bicycle will collaborate to develop a pipeline of oligonucleotide therapeutic product candidates delivered using the tissue-targeting TfR1 *Bicycle* technology, while Bicycle retains the rights to use TfR1 *Bicycles* for all non-oligonucleotide therapeutic purposes, including within its existing collaboration with DDF targeting dementia.

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, and BT8009, a second-generation BTC targeting Nectin-4, a well-validated tumor antigen, 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 Centre for Drug Development of Cancer Research UK. 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 collaboration with Ionis; the development and potential commercialization of potential product candidates using Bicycle’s technology and under the license and collaboration agreement; the therapeutic potential for *Bicycles* in multiple applications; the potential of Bicycle’s platform to develop potential precision medicines; Bicycle’s continued collaboration with DDF; and the potential to receive milestone payments and royalties under the license and 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: risks to Bicycle’s and its collaboration partners’ abilities to meet anticipated deadlines and milestones presented by the ongoing COVID-19 pandemic; uncertainties inherent in the initiation and completion of preclinical studies and clinical trials and clinical development of Bicycle’s product candidates by Bicycle or its collaboration partners; the risk that Bicycle or its collaboration partners may not realize the intended benefits of Bicycle’s technology; availability and timing of results from preclinical studies and 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 studies and trials may be delayed and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; risks related to Bicycle’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, 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 6, 2021, 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 as a result of any new information, future events, changed circumstances or otherwise, except as otherwise required by law.

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