

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 1, 2022

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	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 2.02. Results of Operations and Financial Condition

On March 1, 2022, Bicycle Therapeutics plc issued a press release announcing financial results for the fiscal quarter and the year ended December 31, 2021 and other business highlights. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 2.02 in this Current Report on Form 8-K (including Exhibit 99.1) shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”) or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Press Release issued March 1, 2022
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 1, 2022

BICYCLE THERAPEUTICS PLC

By: /s/ Lee Kalowski

Name: Lee Kalowski

Title: Chief Financial Officer



Bicycle Therapeutics Reports Fourth Quarter and Full Year 2021 Financial Results and Provides Corporate Update

- Continued clinical progress across pipeline of Bicycle Toxin Conjugates[®] (BTCs) and Bicycle tumor-targeted immune cell agonists (Bicycle TICAs)
 - Cash of \$438.7 million at December 31, 2021 expected to provide financial runway through 2024

CAMBRIDGE, England, & BOSTON, March 1, 2022 – 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, 2021, and provided recent corporate updates.

“We are encouraged by the progress we continue to make across our oncology pipeline,” said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. “As we previously reported, BT8009 and BT5528 have demonstrated anti-tumor activity in two tumor types, and we look forward to presenting interim results from our Phase I trial of BT8009 at a medical meeting and initiating the expansion cohorts in our clinical trial of BT5528 this year. We also are moving our *Bicycle* TICA[™] programs forward, including BT7480, which entered the clinic in the fourth quarter of 2021. Our plans to advance our clinical programs, as well as to expand our discovery efforts and early development pipeline, are on track and are supported by a strong balance sheet, with sufficient cash to fund these initiatives and support operations through 2024.”

Fourth Quarter 2021 and Recent Highlights

- **Announced Continued Progress in Ongoing Phase I/II Clinical Trials of BT8009, BT5528 and BT7480.** In January 2022, Bicycle announced progress updates for its wholly owned oncology pipeline, including BTCs BT8009 and BT5528 and *Bicycle* TICA BT7480. In the ongoing Phase I portion of the Phase I/II clinical trial of BT8009, a second-generation BTC[™] targeting Nectin-4, four out of 11 patients were previously reported to have a partial response under Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, including one out of four (25%) in the 2.5mg/m² dose and three out of seven (43%) at the 5.0 mg/m² cohorts. All four patients previously reported as responders have since received at least one subsequent scan, and all have been confirmed as ongoing RECIST 1.1 responses. One patient in the 5.0 mg/m² cohort, who previously was reported to have a partial response with an 89% tumor reduction, has now received two subsequent scans, which each showed that total tumor volume has been reduced by 100%, constituting a confirmed complete response.

The Phase I/II trial of BT5528, Bicycle’s second-generation BTC targeting EphA2, is also ongoing, with initiation of expansion cohorts planned for this year, with an expected recommended Phase II dose of 6.5mg/m² every-other-week.

Bicycle also initiated a Phase I clinical trial of BT7480, a novel, fully synthetic *Bicycle* TICA targeting Nectin-4 and agonizing CD137, in the fourth quarter of 2021, and dose escalation in that trial remains ongoing.

- **Announced Expansion of and Transition in Management Team.** In January 2022, Michael Skynner, Ph.D., previously the company's Chief Operating Officer (COO), was appointed to the newly created position of Chief Technology Officer, to focus on leading and overseeing the growth of Bicycle's proprietary phage display discovery platform in oncology, as well as on creating innovative opportunities for the platform outside of oncology. Dr. Skynner joined the company in January 2016 as Vice President, Operations and Discovery and had served as COO since March 2018. Alistair Milnes, who served as the company's Vice President, Human Resources and Communications since January 2021, has assumed the COO role. Mr. Milnes previously led human resources and communications at multinational energy and mineral companies. Both Dr. Skynner and Mr. Milnes are based in the United Kingdom.
- **Presented Preclinical BT7480 and BT7455 Data at the SITC 36th Annual Meeting.** In November 2021, Bicycle presented preclinical data for BT7480 and BT7455, an EphA2/CD137 *Bicycle* TICA. Results supported Bicycle's decision to initiate a Phase I/II clinical trial of BT7480 and its prioritization of potential indications to target. Additionally, Bicycle has developed a pharmacokinetic/pharmacodynamic (PK/PD) modelling framework intended to predict preclinical biomarker level and tumor growth inhibition in response to changes in the BT7480 dose and dosing schedule. Bicycle found that plasma and tumor drug concentration levels may be associated with tumor growth inhibition.

Financial Results

- Cash was \$438.7 million as of December 31, 2021, compared to \$136.0 million as of December 31, 2020. The net increase in cash is primarily due to financing activities during 2021, including net proceeds of \$188.4 million from a public offering of Bicycle's ADSs, net proceeds of \$102.6 million from Bicycle's at-the-market (ATM) offering program and net proceeds of \$15.0 million from Bicycle's debt facility with Hercules Capital, as well as \$45.0 million received from Ionis Pharmaceuticals under the 2021 collaboration and license agreement, and \$10.0 million received from Genentech for exercising an option to initiate an additional program under the 2020 collaboration agreement, offset by cash used for operating activities.
 - Research and development expenses were \$13.0 million for the three months ended December 31, 2021 and \$44.9 million for the year ended December 31, 2021, compared to \$10.1 million for the three months ended December 31, 2020 and \$33.1 million for the year ended December 31, 2020. The increase in expense of \$2.9 million for the three months ended December 31, 2021 as compared to the same period in the prior year was primarily due to increased *Bicycle* TICA clinical program spend and other discovery and platform related expenses, as well as increased personnel related expenses, including \$0.7 million of incremental non-cash share-based compensation expense. The increase in expense of \$11.7 million for the year ended December 31, 2021 as compared to the same period in the prior year was primarily due to increased clinical program expenses for BT8009, *Bicycle* TICA and other discovery and platform related expenses and increased personnel-related expenses, including \$2.4 million of incremental non-cash share-based compensation expense.
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- General and administrative expenses were \$8.8 million for the three months ended December 31, 2021 and \$32.4 million for the year ended December 31, 2021, compared to \$10.9 million for the three months ended December 31, 2020 and \$29.2 million for the year ended December 31, 2020. The decrease of \$2.1 million for the three months ended December 31, 2021 as compared to the same period in the prior year was primarily due to the settlement and license agreement with Pepscan Systems B.V. (“Pepscan”) entered into in November 2020, offset by increased costs to support operations as a public company and increased personnel-related costs, including \$0.7 million of incremental non-cash share-based compensation expense. The increase of \$3.2 million for the year ended December 31, 2021 as compared to the same period in the prior year was primarily due to increased personnel-related costs, including \$3.2 million of incremental non-cash share-based compensation expense and increased costs to support operations as a public company, offset by a decrease in professional and consulting costs, and the settlement and license agreement with Pepscan entered into in November 2020.
- Net loss was \$18.0 million, or \$(0.63) basic and diluted net loss per share, for the three months ended December 31, 2021, and net loss was \$66.8 million, or \$(2.67) basic and diluted net loss per share, for the year ended December 31, 2021, compared to net loss of \$17.4 million, or \$(0.83) basic and diluted net loss per share, for three months ended December 31, 2020, and net loss of \$51.0 million, or \$(2.66) basic and diluted net loss per share, for the year ended December 31, 2020.

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 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 anticipated advancement of its product candidates, including BT5528, BT8009 and BT7480; the anticipated design of, initiation of expansion cohorts in, dosing in and progression of Bicycle’s clinical trials; the availability of data from clinical trials; the therapeutic potential for *Bicycles* in oncology and other applications; Bicycle’s plans to expand its discovery efforts and early development pipeline; and Bicycle’s expected cash 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: risks to clinical trial site initiation, patient enrollment and follow-up, as well as to Bicycle’s abilities to meet other anticipated deadlines and milestones, presented by the ongoing COVID-19 pandemic; uncertainties inherent in the initiation 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 and may not have satisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; 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 November 4, 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 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
(In thousands, except share and per share data)
(Unaudited)

	Three Months Ended December 31,		Year Ended December 31,	
	2021	2020	2021	2020
Collaboration revenues	\$ 3,771	\$ 3,848	\$ 11,697	\$ 10,390
Operating expenses:				
Research and development	12,952	10,057	44,880	33,149
General and administrative	8,842	10,850	32,435	29,201
Total operating expenses	21,794	20,907	77,315	62,350
Loss from operations	(18,023)	(17,059)	(65,618)	(51,960)
Other income (expense):				
Interest income	58	8	120	683
Interest expense	(820)	(437)	(2,984)	(457)
Total other expense, net	(762)	(429)	(2,864)	226
Net loss before income tax provision	(18,785)	(17,488)	(68,482)	(51,734)
Benefit from income taxes	(748)	(55)	(1,663)	(724)
Net loss	\$ (18,037)	\$ (17,433)	\$ (66,819)	\$ (51,010)
Net loss per share, basic and diluted	\$ (0.63)	\$ (0.83)	\$ (2.67)	\$ (2.66)
Weighted average ordinary shares outstanding, basic and diluted	28,790,934	21,057,855	25,061,734	19,145,938

Balance Sheets Data
(In thousands)
(Unaudited)

	December 31, 2021	December 31, 2020
Cash	\$ 438,680	\$ 135,990
Working capital	422,317	132,594
Total assets	479,792	161,152
Shareholders' equity	346,254	95,460

Investors:

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