Bicycle Therapeutics Reports Fourth Quarter and Full Year 2020 Financial Results and Provides Corporate Update

March 11, 2021

- Significant progress achieved across pipeline of Bicycle® *Toxin Conjugates (BTCs™) and tumor targeted immune cell agonists (TICAs™)*

- Cash of $136.0 million at December 31, 2020 expected to provide financial runway through multiple clinical milestones

- First clinical trial site outside of the United States opened in ongoing Phase I/II trial of BT8009

CAMBRIDGE, England & BOSTON--(BUSINESS WIRE)--Mar. 11, 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 reported financial results for the fourth quarter and full year ended December 31, 2020 and discussed recent corporate updates.

"Bicycle has overcome the unprecedented challenges caused by the COVID-19 pandemic this past year, executing on our 2020 goals, including advancing multiple *Bicycle* Toxin Conjugates (BTCs) in the clinic and preparing our first tumor targeted immune cell agonist (TICA) for an expected clinical start later this year, while also thoughtfully strengthening our balance sheet," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We are encouraged by the progress of our pipeline and are looking forward to continuing the momentum in 2021. With our clinical data presented to date, we believe we are closer to actualizing a world where *Bicycles* offer a much-needed new treatment paradigm for people living with cancer and other serious diseases."

Fourth Quarter 2020 and Recent Highlights

- **Announced Publication of Preclinical Data of Tumor-targeted Immune Cell Agonizing Molecules (TICAs) in *the Journal for ImmunoTherapy of Cancer*.** The article, titled "Anticancer immunity induced by a synthetic tumor-targeted CD137 agonist," outlines the work Bicycle is undertaking to unlock a new method of cancer immunotherapy via small molecule agonism of TNF superfamily receptors.
- **Provided Oncology Pipeline Progress Update.** In January 2021**,** Bicycle announced progress updates for its wholly owned oncology pipeline:
    - **BT1718**: The Phase IIa portion of the Phase I/IIa trial of BT1718, a potential first-in-class BTC targeting a key tumor antigen MT1-MMP, is actively enrolling patients in the Phase I/IIa trial sponsored by Cancer Research UK's Center for Drug Development. Enrollment in the Phase IIa portion of the trial is ongoing at four clinical sites, with additional sites expected to begin enrolling patients during the first half of 2021. Patients are currently being enrolled into two solid tumor cohorts, one in squamous non-small cell lung cancer (NSCLC) and the other in an all-comers "basket" cohort. Following receipt of results from these first two cohorts, Cancer Research UK may initiate up to two additional cohorts.
    - **BT5528:** Enrollment in the company-sponsored Phase I/II trial of BT5528, a second-generation BTC targeting EphA2, a target for which prior antibody-based approaches have been unsuccessful**,** remains on track with additional sites expected to begin enrolling patients in 2021. BT5528 has been dosed up to 8.5mg/m2 weekly, which Bicycle believes, based on pre-clinical studies, is toward the top of the therapeutic range, with transient neutropenia observed at that dose. The dose-escalation of the Phase I/II trial remains ongoing. Bicycle observed preliminary signs of anti-tumor activity. Since implementation of an EphA2 immunohistochemistry (IHC) assay in 2020, as of January 14, 2021, two EphA2 selected patients have enrolled in the trial, one of whom was response evaluable: in a urothelial patient currently receiving 6.5mg/m^2 of BT5528 every other week, whose prior lines of therapies included both a PD-1 inhibitor and enfortumab vedotin, a 43% reduction in target lesions was observed at the first radiologic response assessment, constituting a partial response under RECIST version 1.1 criteria. Reductions in non-target lesions were also observed, and the patient remains enrolled in the trial.
    - **BT8009:** Early clinical data for BT8009, a second-generation Nectin-4-targeting BTC with a potentially differentiated profile as compared to a Nectin-4 targeting antibody-drug conjugate (ADC), supports a pharmacokinetic profile that is consistent with both preclinical predications and data as of January 14, 2021 from Bicycle's ongoing Phase I trial of BT5528, a BTC that utilizes the same linker and toxin payload. Patient enrollment in the Phase I portion of the Phase I/II clinical trial of BT8009 remains ongoing. The first clinical trial site outside of the United States opened in the first quarter of 2021.
    - **BT7480:** Bicycle continues to advance its novel TICAs and expects BT7480 to enter the clinic in the second half of this year. Bicycle has identified additional TICA candidates targeting natural killer (NK) cells through early immuno-oncology (I-O) discovery efforts and is moving these TICA candidates into lead optimization.

- **Presented Posters at the Society for Immunotherapy of Cancer's (SITC) 35 th Anniversary Annual Meeting.** In November 2020, Bicycle presented new data that demonstrated the potential generalizability of its TICA platform, with a Nectin-4/CD137 TICA and an EphA2/CD137 TICA exhibiting similar anti-tumor activity and immune modulation.
- **Continued to Strengthen the Balance Sheet in 2021.** In March 2021, the Company drew an additional $15.0 million available under its debt facility with Hercules Capital, Inc. and amended the loan and security agreement to extend the interest-only payment period until the second half of 2023, with the potential to further extend it into 2024, contingent on the satisfaction of performance milestones. In addition, gross proceeds from Bicycle's at-the-market (ATM) offering program during the first quarter of 2021 totaled $50.2 million as of March 10, 2021. Cash at December 31, 2020 does not include additional borrowings under the debt facility or gross proceeds from the ATM offering program received in the first quarter of 2021.

Financial Results

- Cash was $136.0 million as of December 31, 2020, compared to $92.1 million as of December 31, 2019. The increase in cash at December 31, 2020 was primarily due to net proceeds of $48.1 million received from the ATM offering program during 2020, $31.0 million received from Genentech under the strategic collaboration agreement, as well as $14.4 million in net proceeds received from the debt facility with Hercules Capital, Inc., offset by cash used in operating activities. Cash of $136.0 million at December 31, 2020 is expected to provide financial runway through multiple clinical milestones.
- Research and development expenses were $10.1 million for the three months ended December 31, 2020 and $33.1 million for the year ended December 31, 2020, compared to $6.6 million for the three months ended December 31, 2019 and $25.5 million for the year ended December 31, 2019. The increase in expense of $3.5 million for the three months ended December 31, 2020 as compared to the same period in the prior year was primarily due to increased clinical program expenses for BT5528 and BT8009, increased other unallocated discovery and platform related expenses due to the timing of development activities, and increased personnel-related expenses, including $0.3 million of incremental non-cash share-based compensation expense. The increase in expense of $7.6 million for the year ended December 31, 2020 as compared to the same period in the prior year was primarily due to increased clinical program expenses for BT5528 and BT8009, as well as increased TICA program development expenses and increased personnel-related expenses, including $1.3 million of incremental non-cash share-based compensation expense.
- General and administrative expenses were $10.9 million for the three months ended December 31, 2020 and $29.2 million for the year ended December 31, 2020, compared to $3.4 million for the three months ended December 31, 2019 and $14.6 million for the year ended December 31, 2019. The increase of $7.5 million for the three months ended December 31, 2020 and $14.6 million for the year ended December 31, 2020 as compared to the same period in the prior year was primarily due to an increase in professional fees and costs including costs due to operations as a public company, the settlement and license agreement with Pepscan entered into in November 2020, an unfavorable effect of foreign exchange rates and an increase in personnel-related costs, including $0.2 million and $2.1 million of incremental non-cash share-based compensation expense for the three months ended December 31, 2020 and for the year ended December 31, 2020, respectively.
- Net loss was $17.4 million, or $(0.83) basic and diluted net loss per share, for the three months ended December 31, 2020, and net loss was $51.0 million, or $(2.66) basic and diluted net loss per share for the year ended December 31, 2020, compared to net loss of $4.4 million, or $(0.25) basic and diluted net loss per share for three months ended December 31, 2019, and net loss of $30.6 million, or $(2.77) basic and diluted net loss per share for the year ended December 31, 2019.

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's lead product candidate, BT1718, a *Bicycle* Toxin Conjugate (BTC) that targets MT1-MMP, is being investigated in an ongoing Phase I/IIa clinical trial in collaboration with the Centre for Drug Development of Cancer Research UK. Bicycle is also evaluating BT5528, a second-generation BTC targeting EphA2, in a company-sponsored Phase I/II trial. BT8009 is a BTC targeting Nectin-4, a well-validated tumor antigen, and is also currently being evaluated a Company-sponsored Phase I/II trial. 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 and expansion of its pre-clinical and clinical pipelines; Bicycle's expected cash runway; anticipated enrollment in and progression of Bicycle's and its collaborators' clinical trials; the availability of data from clinical trials and preclinical studies; the therapeutic potential of Bicycle's product candidates; and Bicycle's ability to achieve planned milestones. 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 site initiation, clinical trial commencement, patient enrollment and follow-up, as well as to Bicycle's and its collaboration partners' abilities to meet other 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 may not realize the intended benefits of its 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 trials and studies 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 our actual results to differ from those contained in the forward-looking statements, are described in greater detail in the section entitled "Risk Factors" in our in our Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 5, 2020, 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 December 31,		Year Ended December 31,	
	2020	**2019**	**2020**	**2019**
Collaboration revenues	$ 3,848	$ 5,281	$ 10,390	$ 13,801
Operating expenses:				
Research and development	10,057	6,649	33,149	25,540
General and administrative	10,850	3,396	29,201	14,560
Total operating expenses	20,907	10,045	62,350	40,100
Loss from operations	(17,059)	(4,764)	(51,960)	(26,299)
Other income (expense):				
Interest income	8	220	683	814
Interest expense	(437)	—	(457)	—
Other expense, net	—	—	—	(5,377)
Total other income (expense), net	(429)	220	226	(4,563)
Net loss before income tax provision	(17,488)	(4,544)	(51,734)	(30,862)
Benefit from income taxes	(55)	(138)	(724)	(254)

Net loss	$ (17,433)	$ (4,406)	$ (51,010)	$ (30,608)
Net loss attributable to ordinary shareholders	$ (17,433)	$ (4,406)	$ (51,010)	$ (30,608)
Net loss per share attributable to ordinary shareholders, basic and diluted	$ (0.83)	$ (0.25)	$ (2.66)	$ (2.77)
Weighted average ordinary shares outstanding, basic and diluted	21,057,855	17,926,165	19,145,938	11,045,370

Balance Sheets Data

(In thousands)

(Unaudited)

	December 31, 2020	**December 31, 2019**
Cash	$ 135,990	$ 92,117
Working capital	132,594	95,325
Total assets	161,152	110,194
Shareholders' equity	95,460	93,198

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Investor and Media Contact:
Argot Partners
Maeve Conneighton
bicycle@argotpartners.com
+1-212-600-1902

Source: Bicycle Therapeutics plc