Bicycle Therapeutics and Orano Med Present Preclinical Bicycle® Radio-Conjugate Data at TIDES 2023

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CAMBRIDGE, England & BOSTON & PARIS--(BUSINESS WIRE)--May 11, 2023-- Bicycle Therapeutics plc (NASDAQ: BCYC) and Orano Med, two biotechnology companies respectively, announce pre-clinical results. Bicycle is pioneering a new and differentiated class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology and Orano Med is developing innovative radioligand therapies with lead-212 in oncology. The companies today announced co-authored preclinical results of Pb-BCY20603, a *Bicycle*® radio-conjugate (BRC™) that binds with high affinity to the tumor antigen MT1-MMP and carries a chelate of lead-212, a potent alpha particle emitting radioisotope. The results were presented at TIDES 2023 in San Diego, CA and can be accessed here.

"We are encouraged by the preclinical results that were presented at TIDES 2023 and are excited by the potent anti-tumor activity observed with this molecule," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "We estimate that on a dose per dose basis this prototype is over 1,000 times more potent than a comparator Bicycle toxin conjugate, demonstrating just how powerful targeted alpha therapy with lead-212 may be and providing further evidence that the unique properties of *Bicycles* make them a potentially powerful modality for precision guided delivery of radionuclide payloads."

Pb-BCY20603 showed tumor targeting in rodent tumor xenograft studies, with radioactivity levels of >45% Injected Dose (ID/g) 24 hours post injection. No body weight loss was seen in mice treated up to 30 µCi, and no significant changes were observed in hematology readout compared to vehicle treated mice. Pb-BCY20603 showed potent anti-tumor activity after a single dose of 5 µCi. Complete tumor regressions were seen after 3 dosing cycles of 10 µCi, given two weeks apart. Median survival was increased for each dosing group with 90% survival observed for the 3 cycles of 10 µCi, treatment at the end of the 100-day study. Importantly, the Bicycle displayed differentiated tumor penetration compared to a comparator antibody, highlighting an advantage of smaller molecules over larger biologics.

"The promising preclinical results of Pb-BCY20603 confirm the potential of targeted alpha therapies to open new perspectives for patients with difficult to treat cancers," said Julien Dodet, Chief Executive Officer of Orano Med. "We are convinced that alpha therapies, combined with innovative vectors such as Bicycle peptides, are the future of radiopharmaceutical therapies, providing an increased cytotoxic potential against cancer cells with limited toxicity to surrounding healthy cells. This reinforces Orano Med's commitment to make lead-212 based therapies available to the medical community and patients worldwide."

These data build on previously published studies demonstrating the precision-guided potential of *Bicycles*. Imaging data were also reported from two separate independent research groups. At the 2023 American Association for Cancer Research Annual Meeting, an independent team from Johns Hopkins published data from an EphA2 binding *Bicycle* in an orthotopic pancreatic cancer model (Sharma, et. al., *Non-invasive detection of pancreatic adenocarcinoma using Ga-88 labelled EphA2 targeting peptide*). In addition, a separate independent research team (Duan, et al., *Clinical Cancer Research,* 2023) demonstrated specific and sensitive imaging of a Nectin-4 targeted *Bicycle* observed in Nectin-4 positive metastases in human patients, despite the molecule not being optimized for this purpose. These data provide further evidence to support the ability of *Bicycles* to fully penetrate and bind to their targets deep into tumors providing additional confidence in the platform's potential clinical utility.

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.

About Orano Med

Orano Med is a clinical-stage biotechnology company which develops a new generation of targeted therapies against cancer using the unique properties of lead-212 (^{212}Pb), a rare alpha-emitting radioisotope and one of the more potent therapeutic payloads against cancer cells known as Targeted Alpha-Emitter Therapy (TAT). It relies on a simple concept: combining the ability of biological molecules to target cancer cells with the short-range cell-killing capabilities of alpha-emitting radioisotopes. Alpha decay results in irreparable double strand DNA breaks in cells adjacent only to area of alpha emission, which leads to an increased cytotoxic potential toward cancer cells while limiting toxicity to nearby healthy cells. As a result, alpha emitters are considered as the most powerful payloads to be found for targeted therapies. Orano Med develops several treatments using ^{212}Pb combined with various targeting agents. The company has ^{212}Pb manufacturing facilities, laboratories, and R&D centers in France and in the US and is currently investing to further expand its GMP-manufacturing capacities for ^{212}Pb radiolabeled pharmaceuticals in North America and Europe.

For more information, visit www.oranomed.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; and the therapeutic potential of the Bicycle platform in oncology and other indications. 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 the initiation, progress 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 or have unsatisfactory outcomes; potential adverse effects arising from the testing or use of Bicycle’s product candidates; the risk that the Company or its collaboration partners may not realize the intended benefits of its technology; 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 4, 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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