Bicycle Therapeutics Announces Positive Topline Results from Oxurion's Phase I Trial Using a Novel Bicycle-based Plasma Kallikrein Inhibitor for the Treatment of Diabetic Macular Edema

July 1, 2019

Phase I results provide additional clinical activity data for *Bicycles*

CAMBRIDGE, U.K., & BOSTON--(BUSINESS WIRE)--Jul. 1, 2019-- Bicycle Therapeutics, a biotechnology company pioneering a new class of therapeutics based on its proprietary bicyclic peptide (*Bicycle*®) technology, today announced the successful completion of Oxurion's Phase I clinical trial evaluating the safety and tolerability of a single intravitreal injection of THR-149, a novel *Bicycle*-based plasma kallikrein (PKal) inhibitor, in patients with diabetic macular edema (DME). No dose-limiting toxicities or drug-related adverse events were reported. Activation of the PKal enzyme has been shown to increase retinal vascular permeability, microaneurysm and inflammation in DME.

This Phase I open-label, multi-center, non-randomized trial evaluated the safety of a single intravitreal injection of THR-149 at three ascending dose levels in 12 subjects with visual impairment due to center-involved DME. The study also investigated changes to patients' best corrected visual acuity (BCVA). A rapid onset of action was observed from Day 1, with an increasing average improvement in BCVA of up to 7.5 letters at Day 14. This activity was maintained with an average improvement in BCVA of 6.5 letters at Day 90 following a single injection of THR-149.

"These trial results represent additional human clinical data generated using *Bicycles*, a new therapeutic modality developed using our proprietary technology. It is impressive to see sustained activity out to 90 days in patients after a single injection, providing further support for the use of *Bicycles* in the ophthalmic setting. The safety and tolerability of THR-149 provides evidence of the clinical potential of this modality as we advance BT1718, our proprietary *Bicycle* Toxin Conjugate, which is currently in a Phase I/IIa clinical trial," said Kevin Lee, Ph.D., Chief Executive Officer of Bicycle Therapeutics. "Beyond our oncology programs, we are excited about the potential role that THR-149 may play for patients with DME. We look forward to building on our strong collaboration with Oxurion as the program moves into more advanced clinical development."

"With these favorable safety and tolerability results and initial data illustrating the long duration of action that can be obtained following a single injection of THR-149, we will continue our innovative, *Bicycle*-based approach to potential treatments for DME," said Patrik De Haes, M.D., Chief Executive Officer of Oxurion.

In 2013, Bicycle entered into a research collaboration and license agreement with Oxurion (Euronext: OXUR) related to the discovery and development of novel human plasma kallikrein inhibitors for use in ophthalmic indications.

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, is a *Bicycle* Toxin Conjugate being investigated in an ongoing Phase I/IIa clinical trial in collaboration with the Centre for Drug Development of Cancer Research UK. Bicycle is headquartered in Cambridge, U.K. with many key functions and members of its leadership team located in Lexington, MA. For more information, visit BicycleTherapeutics.com, connect with us on LinkedIn and follow us on Twitter at @Bicycle_tx.

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. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including statements regarding our collaboration with Oxurion; the therapeutic potential for Bicycles in ophthalmology and oncology; the discovery of potential product candidates using our technology; and the development of potential product candidates.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and other future conditions, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the risk that any one or more of our product candidates will not be successfully developed or commercialized, the risk of cessation or delay of any ongoing or planned clinical trials, the risk that the results of early clinical trials may not be predictive of the success of later clinical trials, the risk that we may not realize the intended benefits of our technology, and the risk that we may not maintain our collaboration with Oxurion or that we may not realize the intended benefits of this collaboration. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our final prospectus for our initial public offering filed with the Securities and Exchange Commission on May 23, 2019, as well as discussions of potential risks, uncertainties and other important factors in our subsequent filings with the Securities and Exchange Commission. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

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