BridgeBio Oncology Therapeutics (BBOT) Announces First Patient Dosed with First-in-Class BBO-10203, a RAS:PI3Kα Breaker, in the Phase 1 BREAKER-101 Trial for Advanced Solid Tumors

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The first patient has been dosed with BBO-10203 in the BREAKER-101 first in human clinical study

BBO-10203 is a first-in-class orally bioavailable small molecule with a novel mechanism that blocks the interaction between RAS and PI3Kα resulting in the inhibition of RAS-driven PI3Kα-AKT signaling in tumors

BBO-10203 is expected to offer clinically meaningful efficacy as well as safety to patients with RAS- and PI3Kα-driven malignancies

SOUTH SAN FRANCISCO, Calif., October 30, 2024 (BUSINESS WIRE) —TheRas, Inc. d/b/a BridgeBio Oncology Therapeutics ("BBOT" or the "Company"), a clinical-stage biopharmaceutical company focused on RAS-pathway malignancies, has announced that the first patient has been dosed with BBO-10203 in the BREAKER-101 trial. BBO-10203 is a first-in-class orally bioavailable RAS:PI3Kα breaker that blocks the interaction between RAS and PI3Kα to inhibit PI3Kα-AKT signaling in tumors, without directly inhibiting the catalytic activity of PI3Kα.

"I am thrilled to partner with BBOT to bring a potentially transformable new therapeutic to the clinic," said Dr. Minal Barve, Chief Medical Officer and Principal Investigator at Mary Crowley Cancer Research, Dallas, TX. "BBO-10203 represents a first-in-class drug with potential to address high unmet medical needs and change the landscape of cancer care. We look forward to evaluating BBO-10203 in the BREAKER-101 trial."

BBO-10203 was designed to bind covalently and selectively to the RAS-binding domain (RBD) of PI3Kα. This selective inhibition is agnostic to the mutational status of PI3Kα and RAS, and in preclinical models, results in complete inhibition of RAS-driven pAKT signal at single digit nanomolar concentration. Additionally, no hyperglycemia was observed in preclinical species treated with BBO-10203. The discovery of BBO-10203 was the result of a collaboration between the RAS Initiative at Frederick National Laboratory, Lawrence Livermore National Laboratory, and BBOT.

"BBO-10203 is a first-in-class program that inhibits the interaction of the two most mutated oncogenes in human cancer, and it will allow us to test, for the first time, the importance of RAS-coordinated activation of the MAPK and AKT signaling pathways," said Pedro Beltran, PhD, Chief Scientific Officer of BBOT. "The discovery of BBO-10203 was made possible by the dedicated collaboration between academic, national laboratory, and industry experts that synergized to advance medicines for patients suffering from cancer."

The BREAKER-101 trial will enroll patients globally with locally advanced or metastatic HER2-positive breast cancer, HR-positive/HER2-negative breast cancer, KRAS mutant advanced colorectal cancer, and KRAS mutant advanced non-small cell lung cancer.

"There is a tremendous opportunity to improve the standard of care in oncology by inhibiting oncogenic pAKT signaling without the metabolic side effects observed with kinase inhibitors, and the initiation of the Phase 1 study of BBO-10203 marks an important milestone in this regard," said Yong (Ben) Ben, MD, Chief Medical and Development Officer of BBOT. "The second IND within six months of establishing BBOT clearly demonstrates our team's capability in advancing our novel programs into the clinic. This novel mechanism and scientific rationale behind it will allow tremendous combination opportunities that optimally inhibit both pAKT and pERK – an approach we hope will bring unprecedented benefit to patients with RAS-driven cancers."

About TheRas, Inc. d/b/a BridgeBio Oncology Therapeutics (BBOT)
BridgeBio Oncology Therapeutics (BBOT) is a clinical-stage biopharmaceutical company advancing a next generation pipeline of novel small molecule therapeutics targeting RAS and PI3K malignancies. Initially formed as a subsidiary of BridgeBio, BBOT completed a $200M private financing with external investors in 2024 with the goal of improving outcomes for patients with cancers driven by the two most prevalent oncogenes in human tumors. For more information visit bbotx.com.

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