BridgeBio Oncology Therapeutics announces first patient dosed with BBO-8520 in the Ph. 1 ONKORAS-101 trial for KRASG12C NSCLC

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– The first patient has been dosed in the ONKORAS-101 trial for the study of BBO-8520 in adult subjects with $KRAS^{G12C}$ non-small cell lung cancer

– BBO-8520 is a first-in-class orally bioavailable and highly potent small molecule direct inhibitor of $KRAS^{G12C}$ that binds to the Switch II pocket in both the GTP-bound (ON) and GDP-bound (OFF) state conformations of $KRAS^{G12C}$

– BBO-8520 is expected to meaningfully improve outcomes for patients with $KRAS^{G12C}$ driven malignancies by providing optimal target coverage and addressing mechanisms of adaptive resistance to first generation $KRAS^{G12C}$ (OFF) state inhibitors

SOUTH SAN FRANCISCO, Calif. June 06, 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 in the ONKORAS-101 trial for its lead program, BBO-8520. BBO-8520 is a first-in-class orally bioavailable and highly potent small molecule direct inhibitor of $KRAS^{G12C}$ (ON) state. BBO-8520 binds covalently to the Switch II pocket in both the GTP-bound (ON) and GDP-bound (OFF) state conformations of $KRAS^{G12C}$, leading to rapid and sustained inhibition of $KRAS^{G12C}$ activity.

On dosing the first patient, Professor Benjamin Solomon, head of lung medical oncology at the Peter MacCallum Cancer Center, said, "We are excited to partner with BridgeBio Oncology Therapeutics to bring a transformative new therapy to patients. Non-small cell lung cancer is among the most prevalent malignancies globally and there is a significant need for new precision oncology medicines to improve outcomes for patients in the metastatic setting. BBO-8520 promises to have a substantial impact in improving outcomes and prognosis for this group of patients."

BBO-8520 was designed to inhibit the (ON) state to provide optimal target coverage and to address $KRAS^{G12C}$ amplification and receptor tyrosine kinase activation – the two key mechanisms of adaptive resistance to current (OFF) state inhibitors. BBO-8520 drives substantial tumor growth inhibition in multiple preclinical models, even after emergence of resistance to sotorasib, an FDA approved (OFF) state inhibitor of $KRAS^{G12C}$. BBO-8520's discovery was the result of a collaboration between the National Cancer Institute RAS Initiative at Frederick National Laboratory for Cancer Research, Lawrence Livermore National Laboratory, and BridgeBio Oncology Therapeutics.

The ONKORAS-101 study will enroll patients pre-treated with first generation $KRAS^{G12C}$ (OFF) inhibitors as well as patients with no prior $KRAS^{G12C}$ targeted therapy experience. The trial will enroll across the US, Australia, Canada, and the EU.

BridgeBio Oncology Therapeutics' CEO, Eli Wallace, PhD, added, "The initiation of the Phase 1 clinical trial of BBO-8520 represents an important advancement for BBOT, as we are now a clinical-stage organization. We are grateful for the opportunity to offer patients with $KRAS^{G12C}$-driven lung cancer a targeted therapy that is expected to provide a significant improvement over current standards of care."

About TheRas, Inc. d/b/a BridgeBio Oncology Therapeutics
BridgeBio Oncology Therapeutics 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, BridgeBio Oncology Therapeutics 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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