BBOT Announces First Patient Dosed with BBO-11818, a PanKRAS Dual Inhibitor, in the Phase 1 KONQUER-101 Trial for Advanced Solid Tumors

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The first patient has been dosed with BBO-11818 in the KONQUER-101 first-in-human clinical study

BBO-11818 is an orally bioavailable small molecule panKRAS dual ("ON" and "OFF" states) inhibitor that directly binds to KRAS with picomolar affinity

BBO-11818 is expected to provide significant benefit to patients with tumors driven by these oncogenes by safely achieving optimal target inhibition

SOUTH SAN FRANCISCO, Calif. April 1, 2025 –(BUSINESS WIRE)- TheRas, Inc. d/b/a BridgeBio Oncology Therapeutics ("BBOT" or the "Company"), a clinical-stage biopharmaceutical company focused on RAS-pathway malignancies, today announced that the first patient has been dosed with BBO-11818 in the Phase 1 KONQUER-101 trial for advanced solid tumors. BBO-11818 is an orally bioavailable small molecule dual inhibitor that directly binds to both the "ON" and "OFF" states of KRAS. KONQUER-101 will enroll patients globally with certain KRAS mutations.

"The dosing of the first patient is a major milestone in assessing BBO-11818's potential benefit for patients with tumors driven by mutant KRAS," said Dr. Ignacio Garrido-Laguna, MD, PhD, Principal Investigator at Huntsman Cancer Institute at the University of Utah. "We are committed to bringing cutting-edge therapies to patients with advanced cancer in the Mountain Region. BBO-11818 has the potential to safely achieve optimal target inhibition and combine with other targeted therapies. We look forward to evaluating it in the KONQUER-101 trial."

BBO-11818 was designed to non-covalently bind both the inactive GDP-bound "OFF" and active GTP-bound "ON" forms of $KRAS^{G12D}$ and $KRAS^{G12V}$. In cellular assays, EC_{50} values for pERK inhibition in selected KRAS G12D and G12V-mutant cell lines range from sub-nanomolar to single-digit nanomolar potency. BBO-11818 is similarly effective in reducing cell viability in $KRAS^{G12D}$, $KRAS^{G12V}$, and $KRAS^{G12C}$-mutant cell lines. Further, NRAS and BRAF mutant cell lines show insensitivity to BBO-11818, and the molecule exhibits more than 500-fold selectivity for KRAS over H- and NRAS.

"There is a great need for new therapies that can safely treat patients with tumors driven by KRAS mutations, as the current standard of care lacks satisfactory options as monotherapy or to enable combinations of KRAS targeted therapies with other targeted agents," said Yong (Ben) Ben, MD, Chief Medical and Development Officer of BBOT. "BBO-11818 marks the third molecule entering the clinic for BBOT, further proving our capability to advance novel programs into the clinic. Of note, our portfolio is uniquely positioned to deliver the combination of MAPK (BBO-8520 and BBO-11818) and PI3Kα/AKT (BBO-10203) co-inhibition, with a therapeutic index. We hope this will bring unprecedented benefit to patients with RAS-driven cancers."

The discovery of BBO-11818 was the result of a collaboration between the RAS Initiative at Frederick National Laboratory, Lawrence Livermore National Laboratory, and BBOT.

About BBOT

BBOT is a clinical-stage biopharmaceutical company advancing a next-generation pipeline of novel small molecule therapeutics targeting RAS and PI3Kα malignancies. Initially formed as a subsidiary of BridgeBio Pharma, Inc. (Nasdaq: BBIO), BBOT has 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.

BBOT Contact:

Idan Elmelech
Senior Vice President, Strategy & Business Development
contact@bridgebiooncology.com
(650) 405-7021

Media Contact:

Jake Robison
Inizio Evoke Comms
Jake.robison@inizioevoke.com