Preclinical Data Presented at the 2025 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics Support Potential of BBO-10203, a First-in-Class RAS:PI3Kα Breaker That Inhibits KRAS-Mutant Tumor Growth without Inducing Hyperglycemia

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- *Data demonstrate BBO-10203 blocks RAS-mediated activation of PI3Kα and strongly inhibits pAKT signaling in tumor cells without affecting glucose metabolism*
- *Robust monotherapy activity, as well as combination activity with BBOT's KRAS ^{G12C} ON/OFF inhibitor, BBO-8520, and panKRAS inhibitor, BBO-11818, was observed at well-tolerated dose levels in a panel of* KRAS*-mutant models*
- *The combination of a KRAS inhibitor with a PI3Kα pathway inhibitor may maximize the response rate and reduce the development of adaptive resistance mechanisms due to full inhibition of both MAPK and PI3Kα signaling*
- *BBOT-10203 is currently being evaluated in the Phase 1 BREAKER-101 trial for patients with HER2+ amplified or HR+/HER2- breast cancer, and* KRAS *mutant colorectal or non-small cell lung cancer with initial Phase 1 clinical data expected in the first half of 2026*

SOUTH SAN FRANCISCO, Calif., Oct. 25, 2025 (GLOBE NEWSWIRE) -- BridgeBio Oncology Therapeutics, Inc. ("BBOT") (Nasdaq: BBOT), a clinical-stage biopharmaceutical company focused on RAS-pathway malignancies, today announced new preclinical data showing BBO-10203 selectively and specifically blocks the physical interaction between RAS and PI3Kα, resulting in the inhibition of RAS-driven PI3Kα-AKT signaling in tumors without the risk of hyperglycemia. In addition, combination activity with BBOT's KRAS ^{G12C} ON/OFF inhibitor, BBO-8520, and panKRAS inhibitor, BBO-11818, was observed at well tolerated dose levels in a panel of *KRAS* mutant models. The data were presented at the 2025 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics.

"Aberrant activation of the PI3Kα pathway is among the most common oncogenic drivers across human cancers and leads to promotion of tumor growth, survival, and resistance to standard therapies," said Pedro Beltran, PhD, Chief Scientific Officer of BBOT. "Current PI3Kα inhibitors are hindered by dose-limiting toxicities like hyperglycemia, which restrict target coverage, limit the number of eligible patients, and shorten the duration of treatment – leaving a significant unmet medical need. We've designed BBO-10203 to break the interaction between RAS and PI3Kα and inhibit RAS-mediated activation of the PI3Kα pathway. These preclinical data demonstrate BBO-10203 can accomplish this in *in vivo* studies without affecting glucose metabolism and achieve robust anti-tumor activity both as a monotherapy and in combination with our KRAS inhibitors, BBO-8520 and BBO-11818."

These preclinical findings demonstrate BBO-10203 covalently binds PI3Kα on cysteine 242 in the RAS binding domain, breaking the protein-protein interaction between RAS and PI3Kα. Monotherapy results show achievement of complete cellular target engagement at low nanomolar concentrations and oral bioavailability with robust dose- and time-dependent inhibition of pAKT across diverse human cancer cell lines with *KRAS* mutations. Importantly, BBO-10203 does not induce hyperglycemia or hyperinsulinemia during an oral glucose tolerance test. In a panel of cell-line derived xenograft (CDX), patient-derived xenograft (PDX), and genetically engineered mouse (GEM) models, treatment with BBO-10203, both as a monotherapy and in combination with BBO-8520, BBOT's direct inhibitor of KRAS ^{G12C} in both the ON and OFF states, and with BBO-11818, the company's panKRAS inhibitor targeting mutant *KRAS* in both the ON and OFF states with strong potency against *KRAS*^{G12D} and *KRAS*^{G12V} mutants, show robust anti-tumor activity. Importantly, the combination of BBO-10203 + BBO-8520 and BBO-10203 + BBO-11818 induces deep tumor regressions through direct effects on tumor cell proliferation and apoptosis and are well-tolerated.

BBO-10203 is currently being evaluated in the Phase 1 BREAKER-101 trial for patients with HER2+ amplified or HR+/HER2- breast cancer, and *KRAS* mutant colorectal or non-small cell lung cancer as a monotherapy and in combination with standard of care treatment, and will be evaluated in combination with KRAS inhibitors.

"We are pleased to share these preclinical data on BBO-10203's potential as a RAS:PI3Kα breaker," said Eli Wallace, PhD, Chief Executive Officer of BBOT. "By breaking the interaction between RAS and PI3Kα while preserving normal insulin signaling, these results further support our belief that BBO-10203 represents a truly differentiated approach with significant biological and therapeutic potential. We continue to enroll patients in our Phase 1 BREAKER-101 trial and look forward to expanding into combination studies, including with our own KRAS inhibitors."

A copy of the poster titled "BBO-10203, a first-in-class, orally bioavailable, selective breaker of the RAS:PI3Kα interaction inhibits tumor growth alone and in combination with KRAS inhibitors in *KRAS* mutant models without inducing hyperglycemia" will be available on the "Publications" page of the BBOT website following the conference.

About BBO-10203
BBO-10203 is a first-in-class small molecule which breaks the protein-protein interaction between RAS and PI3Kα and inhibits RAS-mediated activation of the PI3Kα pathway. It selectively disrupts oncogenic RAS-PI3Kα signaling while sparing insulin-mediated glucose uptake, potentially maintaining efficacy with reduced risk of hyperglycemia or hyperinsulinemia. BBO-10203 is currently being evaluated in the Phase 1 BREAKER-101 trial for patients with locally advanced or metastatic HER2+ breast cancer, HR+/HER2- breast cancer, *KRAS* mutant colorectal cancer, and *KRAS* mutant non-small cell lung cancer. Initial Phase 1 clinical data are expected in the first half of 2026.

About BBOT
BBOT is a clinical-stage biopharmaceutical company advancing a next-generation pipeline of novel small molecule therapeutics targeting RAS and PI3Kα malignancies. BBOT has the goal of improving outcomes for patients with cancers driven by the two most prevalent oncogenes in human tumors. For more information, please visit **www.bbotx.com** and follow us on **LinkedIn**.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, as amended, and other federal securities laws. Any statements in this press release that are not historical facts may be deemed forward-looking statements, which generally are accompanied by words such as "believe," "may," "will," "estimate," "continue," "anticipate," "intend," "expect," "should," "would," "plan," "predict," "potential," "seem," "seek," "future," "outlook" and similar expressions that predict or indicate future events or trends. These statements are based on various assumptions, whether or not identified in this press release, and are the current expectations of BBOT's management and are not predictions of actual performance. Many actual events and circumstances are beyond the control of BBOT. These forward-looking statements are subject to a number of risks and uncertainties, including changes in domestic and foreign business, market, financial, political, and legal conditions; risks relating to the uncertainty of the projected financial information with respect to BBOT; risks related to the approval of BBOT's product candidates and the timing of expected regulatory and business milestones, including the progress of enrollment in clinical trials and availability of data from ongoing and planned clinical trials; the impact of competitive products; risks relating to BBOT's ability to obtain sufficient supply of materials; and those factors discussed in documents BBOT has filed or will file with the U.S. Securities and Exchange Commission.

In addition, forward-looking statements reflect BBOT's expectations, plans, or forecasts of future events and views as of the date of this press release and are qualified in their entirety by reference to the cautionary statements herein. BBOT anticipates that subsequent events and developments will cause BBOT's assessments to change. These forward-looking statements should not be relied upon as any guarantee, assurance, prediction or definitive statement of fact or probability or as representing BBOT's assessments as of any date subsequent to the date of this press release. Neither BBOT, nor any of its affiliates undertake any obligation to update these forward-looking statements, except as required by law.

BBOT Contacts:

Investor Contact:
Heather Armstrong, Head of Investor Relations
BBOT
Investors@BBOTx.com

Media Contact:
Jake Robison
Inizio Evoke Comms
Jake.robison@inizioevoke.com