BBOT Presents Preclinical Data Demonstrating Potential of BBO-11818 as a Potent panKRAS Inhibitor at the 2025 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

October 23, 2025

- *Data demonstrate potent suppression of MAPK signaling and viability in* KRAS *mutant cell lines, as well as anti-tumor activity across multiple* $KRAS^{G12D}$ *and* $KRAS^{G12V}$ *cell-derived xenograft (CDX) models*
- *BBO-11818's selectivity for KRAS demonstrated by its >1000-fold lower potency against NRAS, HRAS, and BRAF-mutant cell lines*
- *Efficacy of the combination with BBOT's RAS:PI3K α breaker, BBO-10203, is driven by a robust decrease in tumor cell proliferation and increase in apoptosis; combination benefit also observed with cetuximab and anti-PD-1 treatment*
- *BBO-11818 is currently being evaluated in the Phase 1 KONQUER-101 trial in patients with* KRAS *mutant pancreatic, non-small cell lung, and colorectal cancer with initial Phase 1 clinical data expected in the second half of 2026*

SOUTH SAN FRANCISCO, Calif., Oct. 23, 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 on BBO-11818 demonstrating its potential as a potent panKRAS inhibitor targeting mutant KRAS in both the ON (active GTP-bound) and OFF (inactive GDP-bound) states, with selectivity over HRAS and NRAS. The data were presented at the 2025 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics.

"*KRAS* is one of the most commonly mutated oncogenes in human cancers, and while current $KRAS^{G12C}$ inhibitors have shown promising clinical efficacy, they only address a subset of mutations, leaving many patients without effective options," said Pedro Beltran, PhD, Chief Scientific Officer of BBOT. "We've designed BBO-11818 as a potent panKRAS inhibitor with strong binding affinity for KRAS and broad selectivity over HRAS and NRAS with the goal of achieving high levels of KRAS inhibition in human tumors. The preclinical data presented on BBO-11818 demonstrate potent inhibition of MAPK signaling and viability in *KRAS* mutant cells, as well as anti-tumor activity across multiple $KRAS^{G12D}$ and $KRAS^{G12V}$ cell-derived xenograft (CDX) models."

In these preclinical findings, cell-based assays confirm BBO-11818 potently inhibits ERK phosphorylation and proliferation in *KRAS* mutant cell lines with single-digit nanomolar EC_{50} values observed. The selectivity of BBO-11818 for *KRAS* is demonstrated by its >1000-fold lower potency against *NRAS*, *HRAS*, and *BRAF*-mutant cell lines. Monotherapy results show strong anti-tumor responses, including favorable pharmacokinetics (PK) and oral bioavailability with dose- and time-dependent inhibition of pERK in *in vivo* pharmacodynamic (PD) studies, as well as regressions at well-tolerated doses in CDX models of *KRAS* mutant pancreatic, non-small cell lung, and colorectal cancer. Combination treatment with BBO-10203, BBOT's selective RAS:PI3K α breaker that blocks RAS-mediated activation of the PI3K-AKT pathway, and cetuximab, an approved anti-EGFR monoclonal antibody, demonstrated enhanced anti-tumor activity both *in vitro* and in CDX models. Importantly, the efficacy of the BBO-11818 + BB0-10203 combination is driven by a robust decrease in tumor cell proliferation and increase in apoptosis. BBO-11818 also showed a combination benefit with anti-PD-1 treatment resulting in complete tumor regressions in the $KRAS^{G12D}$ CT26 syngeneic tumor mouse model.

"We are pleased to share this updated preclinical data on BBO-11818, which further reinforces its clinical potential," said Eli Wallace, PhD, Chief Executive Officer of BBOT. "These results support further evaluation of BBO-11818 as a monotherapy and in combination as we continue to drive efforts to deliver meaningful value to patients and work towards fully unlocking the potential of RAS-focused therapies by optimizing target coverage."

A copy of the poster titled "BBO-11818: an orally bioavailable, highly potent and selective noncovalent pan-KRAS(ON) and (OFF) inhibitor with robust anti-tumor activity in KRAS-mutant preclinical models" will be available on the "Publications" page of the BBOT website following the conference.

About BBO-11818
BBO-11818 is a potent, selective, orally bioavailable non-covalent KRAS inhibitor with activity against multiple KRAS mutants, including $KRAS^{G12D}$ and $KRAS^{G12V}$ with high selectivity for KRAS over HRAS and NRAS. It targets KRAS in both the ON (active GTP-bound) and OFF (inactive GDP-bound) states, potently suppressing MAPK signaling and inhibiting cell proliferation in *KRAS* mutant cell lines. BBO-11818 is currently being evaluated in the Phase 1 KONQUER-101 trial in patients with *KRAS* mutant pancreatic, non-small cell lung, and colorectal cancer, $KRAS^{G12A}$, $KRAS^{G12C}$, $KRAS^{G12D}$, $KRAS^{G12S}$, or $KRAS^{G12V}$ mutations, or

KRAS amplification. Initial Phase 1 clinical data are expected in the second 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
Certain statements included in this press release that are not historical facts are forward-looking statements. Forward-looking statements 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 or that are not statements of historical matters. 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. These forward-looking statements are provided for illustrative purposes only and are not intended to serve as and must not be relied on by an investor as a guarantee, an assurance, a prediction, or a definitive statement of fact or probability. Actual events and circumstances are difficult or impossible to predict and may differ from assumptions. 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; failure to realize the anticipated benefits of the business combination; risks relating to any legal proceedings that may be instituted against BBOT following the closing of the business combination, 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 product candidates and commercial products; ability to obtain sufficient supply of materials; global economic and political conditions; the effects of competition on BBOT's future business; and those factors discussed in documents BBOT has filed or will file with the SEC. Additional risks related to BBOT's business include, but are not limited to: uncertainty regarding outcomes of BBOT's ongoing clinical trials, particularly as they relate to regulatory review and potential approval for its product candidates; risks associated with BBOT's efforts to commercialize its product candidates; BBOT's ability to maintain its existing agreements with third parties and to negotiate and enter into new definitive agreements on favorable terms, if at all; intellectual property-related claims; BBOT's ability to attract and retain qualified personnel; and BBOT's ability to source the raw materials for its product candidates.

If any of these risks materialize or BBOT's assumptions prove incorrect, actual results could differ materially from the results implied by these forward-looking statements. There may be additional risks that BBOT presently does not know or that BBOT currently believes are immaterial that could also cause actual results to differ from those contained in the forward-looking statements. 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 representing BBOT's assessments as of any date subsequent to the date of this press release. Accordingly, undue reliance should not be placed upon the forward-looking statements. Neither BBOT, nor any of its affiliates undertake any obligation to update these forward-looking statements, except as required by law.

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