BBOT Announces Late-Breaking Preclinical Data on BBO-10203, a First-in-Class RAS:PI3Kα Breaker, at the San Antonio Breast Cancer Symposium (SABCS)

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- *Preclinical data demonstrate BBO-10203 blocks RAS-mediated activation of PI3Kα, strongly inhibits pAKT signaling in tumor cells without inducing hyperglycemia, and shows robust anti-tumor activity both as monotherapy and in combination with standard of care therapies in mutant or wild-type PIK3CA breast cancer models*
- *BBOT will also present a trial in progress poster on BREAKER-101, a Phase 1 clinical trial evaluating BBO-10203 in 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 with initial Phase 1 data expected in the first half of 2026*

SOUTH SAN FRANCISCO, Calif., Dec. 10, 2025 (GLOBE NEWSWIRE) -- BridgeBio Oncology Therapeutics, Inc. (“BBOT”) (Nasdaq: BBOT), a clinical-stage biopharmaceutical company focused on RAS-pathway malignancies, today announced late-breaking preclinical data on BBO-10203, a first-in-class covalent small molecule RAS:PI3Kα breaker that selectively and specifically blocks the physical interaction between RAS and PI3Kα resulting in the inhibition of RAS-driven PI3Kα-AKT signaling in tumors without inducing hyperglycemia. The data is being presented today at the San Antonio Breast Cancer Symposium (SABCS). BBOT will also present a trial in progress poster on the Phase 1 BREAKER-101 trial in 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 on Friday, December 12.

“PIK3CA mutations are common, particularly in HR+/HER2- and HER2+ advanced breast cancer,” said Andreas Varkaris, MD, PhD, Attending Physician and Investigator at Massachusetts General Hospital and an investigator in the BREAKER-101 study. “Historically, we have treated these patients with successive generations of PI3K inhibitors, which have their limitations. We now look forward to a new generation of inhibitors, such as BBO-10203, that can more selectively target the mutant enzyme without affecting normal cells, potentially enabling us to treat more patients. Importantly, by improving selectivity and tolerability, these next-generation agents may also allow for combinations with other targeted therapies, something that was challenging in the past due to toxicity.”

“Although PI3Kα inhibitors have provided an important treatment option for HR+/HER2- and HER2+ breast cancer with PI3Kα mutations, their use is often limited by dose-dependent hyperglycemia and reduced treatment duration,” said Pedro Beltran, PhD, Chief Scientific Officer of BBOT. “Our preclinical work shows that BBO-10203 offers a differentiated mechanism by disrupting the RAS–PI3Kα interaction rather than inhibiting PI3Kα’s kinase activity. Because RAS-dependent activation drives tumor growth but not glucose regulation, this approach enables broad pathway inhibition without the risk of hyperglycemia. BBO-10203 also shows strong monotherapy and combination activity, underscoring its potential to extend treatment responses alongside standard-of-care therapies.”

Late Breaking Preclinical Data Highlights

- Preclinical findings demonstrate BBO-10203 covalently binds PI3Kα on cysteine 242 in the RAS binding domain, which prevents the interaction of PI3Kα and RAS.
- Oral administration of BBO-10203 resulted in robust PK, dose- and time-dependent inhibition of pAKT, and efficacy.
- BBO-10203 did not induce hyperglycemia or hyperinsulinemia in an oral glucose tolerance test.
- BBO-10203 showed activity alone and in combination with fulvestrant or ribociclib in ER+ HER2- breast cancer models with either a PIK3CA helical or kinase domain mutations.
- Similar efficacy was observed with BBO-10203 or STX-478 (LY4064809), a PIK3CA mutant-selective inhibitor, in an ER+ HER2- breast cancer model with a PIK3CA kinase domain mutation.
- BBO-10203 also showed activity alone and in combination with ribociclib in an ER+ HER2- breast cancer model with wild-type PIK3CA.

Trial in Progress Poster

BREAKER-101 (NCT06625775) is a first-in-human, multicenter, open-label, Phase 1a/1b study evaluating the safety, tolerability, pharmacokinetics, and preliminary antitumor activity of BBO-10203 as monotherapy and in combination with trastuzumab, fulvestrant ± ribociclib, or FOLFOX + bevacizumab in 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. The study includes a dose escalation phase as well as an expansion phase. Key endpoints include safety and tolerability, anti-tumor activity, and

pharmacokinetics. Intracranial activity of BBO-10203 will also be evaluated as an exploratory endpoint. The study is currently enrolling patients in the United States and Australia, and initial Phase 1 clinical data are expected in the first half of 2026.

A copy of the posters titled “BBO-10203, a first-in-class breaker of the RAS:PI3Kα interaction, inhibits tumor growth alone and in combination with fulvestrant or ribociclib in breast cancer models without inducing hyperglycemia” and “BREAKER-101: a phase 1a/1b open-label study evaluating the safety, tolerability, pharmacokinetics, and efficacy of BBO-10203 in patients with advanced solid tumors” will be available on the “ Publications” page of the BBOT website following the conference.

About BBO-10203
BBO-10203 is an orally bioavailable small molecule with a novel mechanism of action designed to inhibit the physical interaction between RAS and PI3Kα, inhibiting RAS-driven PI3Kα-AKT signaling in tumors. BBO-10203 binds directly and covalently to the RAS-binding domain of PI3Kα, preventing its activation by KRAS, HRAS and NRAS, reducing downstream signaling and tumor growth. It is a protein-protein inhibitor and not a kinase inhibitor, enabling inhibition of RAS-driven PI3Kα-AKT signaling in tumors without the risk of hyperglycemia. Importantly, BBO-10203’s ability to block RAS activation of PI3Kα is agnostic to the mutational status of either *RAS* or *PI3Kα*. In addition to a potentially differentiated safety profile, BBO-10203 could be combined with direct KRAS inhibitors, such as BBO-8520 and BBO-11818, or drugs that target HER2 or ER receptors. BBO-10203 is being evaluated in the Phase 1 BREAKER-101 trial (NCT06625775) 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 its affiliates undertake any obligation to update these forward-looking statements, except as required by law.

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