BBOT Presents Preclinical Data Showing RAS:PI3Kα Breaker BBO-10203 Inhibits PI3Kα/AKT Signaling in HER2AMP Models at the AACR Annual Meeting 2026

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BBO-10203 physically and allosterically disrupts the interaction between RAS and PI3Kα, leading to signaling inhibition without inhibiting the kinase activity of PI3Kα and with no observed hyperglycemia

BBO-10203 displays strong in vivo combination effects with HER2 inhibitors tucatinib or trastuzumab in HER2^{AMP} models

Updated clinical data are expected in the second half of 2026

SOUTH SAN FRANCISCO, Calif., April 21, 2026 (GLOBE NEWSWIRE) -- BridgeBio Oncology Therapeutics, Inc. (“BBOT”) (Nasdaq: BBOT), a clinical-stage biopharmaceutical company focused on RAS-pathway malignancies, today presented new preclinical data in an oral presentation for BBO-10203, a first-in-class covalent small molecule RAS:PI3Kα breaker that selectively blocks the physical interaction between RAS and PI3Kα resulting in the inhibition of RAS-driven PI3Kα-AKT signaling in tumors with no observed hyperglycemia. The data were presented at the American Association for Cancer Research (AACR) Annual Meeting 2026.

"The interaction between RAS and PI3Kα plays a critical role in malignant cells,” said Pedro J. Beltran, PhD, Chief Scientific Officer of BBOT. “BBO-10203 physically disrupts the interaction between RAS and PI3Kα, leading to signaling inhibition and tumor regressions. Importantly, unlike competing approaches, no hyperglycemia has been observed to date. In addition, BBO-10203’s ability to block RAS-mediated activation of PI3Kα is independent of the mutational status of either *RAS* or *PI3Kα,* which may enable treatment of a broader patient population. These data suggest that non-canonical RAS proteins play a key role in PI3K*α* activation in HER2^{AMP} cell lines. Furthermore, BBO-10203 demonstrates strong *in vivo* combination activity with HER2-targeted therapies, including tucatinib and trastuzumab, in HER2 ^{AMP} models.”

Highlights from the oral presentation include:

- BBO-10203 physically and allosterically disrupts the interaction between RAS and PI3Kα, leading to signaling inhibition without inhibiting the kinase activity of PI3Kα
- BBO-10203 induces tumor regressions at 30 mg/kg QD and no hyperglycemia observed at 100 mg/kg QD
- BBO-10203 shows that PI3Kα activity in HER2^{AMP} cells is RAS-dependent
- RAS RBD mutations recapitulate the pAKT and viability effects of breaker activity in HER2^{AMP} cell lines
- Non-canonical RAS signaling appears to be the dominant driver of pAKT in HER2^{AMP} cell lines
- BBO-10203 displays strong *in vivo* combination effects with HER2 inhibitors tucatinib or trastuzumab in HER2^{AMP} models

The oral presentation is titled “*The RAS:PI3Kα breaker BBO-10203 inhibits PI3Kα/AKT activity in HER2^{AMP} models through non-canonical RAS signaling blockade*.” A copy of the presentation 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. Updated 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
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 related to 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; 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