Purple Biotech Reports Positive New Preclinical Data Demonstrating Multi-Arm Anti-Tumor Activity Across Two CAPTN-3 Tri-Specific Antibodies at ESMO Immuno-Oncology Congress 2025

Data demonstrates the significant and sustained tumor regression achieved by the CAPTN-3 platform across two distinct tri-specific antibodies, IM1240 and IM1305, targeting different tumor antigens

Transcriptomic analysis across ~11,000 TCGA samples shows NKG2A expression is strongly associated with tumor expression of 5T4 or TROP2, supporting inclusion of the NKG2A arm in CAPTN-3 designs

NKG2A arm significantly contributes to IM1240 anti-cancer immune activity in PD1-resistant patient-derived explants

REHOVOT, Israel, Dec. 11, 2025 (GLOBE NEWSWIRE) -- Purple Biotech Ltd. (“Purple Biotech” or the “Company”) (NASDAQ/TASE: PPBT), a clinical-stage company developing first-in-class therapies that seek to overcome tumor immune evasion and drug resistance, today reported positive new preclinical data from its CAPTN-3 tri-specific antibody platform presented at the ESMO Immuno-Oncology (ESMO IO) Congress 2025. The data presented was generated in collaboration with the laboratory of Dr. Amir Horowitz of the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai.

These new preclinical data successfully demonstrates that two CAPTN-3 tri-specific antibodies, IM1240 (capped-CD3×5T4×NKG2A) and IM1305 (capped-CD3×TROP2×NKG2A), each achieve strong anti-tumor activity across different tumor antigens. IM1240 has also shown anti-tumor activity in models resistant to prior PD1 therapy. These results indicate that the CAPTN-3 architecture can generate potent multi-arm activity beyond a single target, supporting the platform’s potential applicability across a range of solid tumors. The CAPTN-3 platform is designed to unite three functional mechanisms—T-cell engagement and activation, enhanced by NKG2A-mediated innate

and adaptive immune activation, and tumor-antigen targeting—into a single tri-specific molecule intended to coordinate a synergistic immune response.

“Immune failure is one of the biggest obstacles in treating solid tumors, and CAPTN-3 was built to address that challenge,” said Gil Efron, Chief Executive Officer of Purple Biotech. “The data we presented at ESMO IO shows that IM1240 can activate an immune response even in tumors that no longer respond to PD-1 therapy, and that each component of the molecule contributes to its overall effect. At the same time, the introduction of IM1305 demonstrates how CAPTN-3 can be adapted to different tumor targets, underscoring the versatility and scalability of the platform. These findings support our development roadmap as we prepare for anticipated key milestones in 2026 and advance CAPTN-3 toward IND-enabling studies.”

“The NKG2A/HLA-E axis is emerging as a key post-treatment resistance mechanism, as previously shown by Dr. Horowitz of the Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai,” said Dr. Hadas Reuveni, VP Research and Development at Purple Biotech. “The added value of the aNKG2A arm in IM1240 design, shown both in vivo and in vitro through reactivation of suppressed immune cell subsets, is now further supported by enhanced anti-tumor activity in PD-1–resistant patient-derived explants from non-small cell lung cancer (NSCLC) and head and neck squamous cell carcinoma (HNSCC). These findings underscore the potential importance of the NKG2A arm in advanced and treatment-resistant disease.”

Key New Findings:

Lead Program IM1240: Anti-Tumor Activity in PD-1–Resistant Models

- The Company’s lead CAPTN-3 program, IM1240, demonstrated significant anti-tumor activity in three PD1–resistant ex-vivo models, including new results in HNSCC patient-derived biopsies. In these studies, IM1240 induced tumor cell apoptosis, with anti-tumor activity dependent on both CD3 and NKG2A arms.
- Similarly, IM1240’s immune-mediated anti-tumor activity in PD1-resistant NSCLC patient-derived explants was evidenced by a significant increase in IFNγ secretion.
- To discern IM1240’s selectivity, a transcriptomic analysis of ~11,000 TCGA (The Cancer Genome Atlas) human samples showed that NKG2A expression co-occurs with 5T4 in solid tissues, which provides rationale for inclusion of the αNKG2A arm unique to the CAPTN-3 platform.

Platform Versatility: New TROP2-Targeting Candidate IM1305

- The Company’s new TROP2-targeting candidate, IM1305, further validates the adaptability of the CAPTN-3 platform and demonstrated high-affinity binding to both TROP2 and NKG2A (EC_{50} ~2 nM).
- Potent PBMC-mediated tumor cell killing was observed at low concentrations (EC_{50} 1–5 pM) across multiple tumor types, including triple-negative breast, gastric, pancreatic, and head and neck cancers.

- Like IM1240, IM1305's anti-cancer activity and CD3 binding were fully restored after cap cleavage, a critical component of CAPTN-3's conditional activation design.

In humanized triple-negative breast cancer mouse models, IM1305 induced sustained tumor regression at low doses ($p < 0.0001$), reinforcing the platform's broad application potential. The poster will be accessible under the Publications section of the Purple Biotech website following the congress, or using the following link: https://purple-biotech.com/pipeline/#1Publications

About Purple Biotech

Purple Biotech Ltd. (NASDAQ/TASE: PPBT) is a clinical-stage company developing first-in-class therapies that seek to overcome tumor immune evasion and drug resistance. The Company's oncology pipeline includes CAPTN-3, CM24 and NT219. The Company is advancing CAPTN-3, a preclinical platform of conditionally activated tri-specific antibodies, which engage both T cells and NK cells to induce a strong, localized immune response within the tumor microenvironment. The cleavable capping technology confines the compound's therapeutic activity to the local tumor microenvironment, thereby potentially increasing the anticipated therapeutic window in patients. The third arm specifically targets the Tumor Associated Antigen (TAA). The technology presents a novel mechanism of action by unleashing both innate and adaptive immune systems to mount an optimal anti-tumoral immune response. IM1240 is the first tri-specific antibody in development that targets the 5T4 antigen, which is expressed in a variety of solid tumors and is associated with advanced disease, increased invasiveness, and poor clinical outcomes. IM1305 is the second tri-specific antibody from the platform in development and targets the TROP2 TAA. CM24 is a humanized monoclonal antibody that blocks CEACAM1, which supports tumor immune evasion and survival through multiple pathways. CEACAM1 on tumor cells, immune cells and neutrophil extracellular traps is a novel target for the treatment of multiple cancer indications. As proof of concept of these novel pathways, the Company completed a Phase 2 study for the treatment of pancreatic ductal adenocarcinoma (PDAC) with CM24 as a combination therapy with the anti-PD-1 checkpoint inhibitor nivolumab and chemotherapy, demonstrating clear and consistent improvement across all efficacy endpoints and the identification of two potential serum biomarkers and other potential tissue biomarkers. NT219 is a dual inhibitor, novel small molecule that simultaneously targets IRS1/2 and STAT3. A Phase 1 dose escalation study was concluded as a monotherapy and in combination with cetuximab, in which NT219 demonstrated anti-tumor activity in combination with cetuximab in second-line patients with recurrent and/or metastatic squamous cell carcinoma of the head and neck (R/M SCCHN). A Phase 2 study in collaboration with the University of Colorado, to treat R/M SCCHN patients with NT219 in combination with cetuximab or pembrolizumab was initiated. The Company's corporate headquarters are located in Rehovot, Israel. For more information, please visit https://purple-biotech.com

Forward-Looking Statements and Safe Harbor Statement

Certain statements in this press release that are forward-looking and not statements of historical fact are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include, but are not limited to, statements that are not statements of historical fact, and may be identified by words such as “believe”, “expect”, “intend”, “plan”, “may”, “should”, “could”, “might”, “seek”, “target”, “will”, “project”, “suggest”, “forecast”, “continue” or “anticipate” or their negatives or variations of these words or other comparable words or by the fact that these statements do not relate strictly to historical matters. You should not place undue reliance on these forward-looking statements, which are not guarantees of future performance. Forward-looking statements reflect our current views, expectations, beliefs or intentions with respect to future events, and are subject to a number of assumptions, involve known and unknown risks, many of which are beyond our control, as well as uncertainties and other factors that may cause our actual results, performance or achievements to be significantly different from any future results, performance or achievements expressed or implied by the forward-looking statements. Important factors that could cause or contribute to such differences include, among others, risks relating to: the plans, strategies and objectives of management for future operations; product development for NT219, CM24 and CAPTN-3; the process by which such early stage therapeutic candidates could potentially lead to an approved drug product is long and subject to highly significant risks, particularly with respect to a joint development collaboration; the fact that drug development and commercialization involves a lengthy and expensive process with uncertain outcomes; our ability to successfully develop and commercialize our pharmaceutical products; the expense, length, progress and results of any clinical trials; the impact of any changes in regulation and legislation that could affect the pharmaceutical industry; the difficulty in receiving the regulatory approvals necessary in order to commercialize our products; the difficulty of predicting actions of the U.S. Food and Drug Administration or any other applicable regulator of pharmaceutical products; the regulatory environment and changes in the health policies and regimes in the countries in which we operate; the uncertainty surrounding the actual market reception to our pharmaceutical products once cleared for marketing in a particular market; the introduction of competing products; patents obtained by competitors; dependence on the effectiveness of our patents and other protections for innovative products; our ability to obtain, maintain and defend issued patents; the commencement of any patent interference or infringement action against our patents, and our ability to prevail, obtain a favorable decision or recover damages in any such action; and the exposure to litigation, including patent litigation, and/or regulatory actions, and other factors that are discussed in our Annual Report on Form 20-F for the year ended December 31, 2024 and in our other filings with the U.S. Securities and Exchange Commission (“SEC”), including our cautionary discussion of risks and uncertainties under “Risk Factors” in our Registration Statements and Annual Reports. These are factors that we believe could cause our actual results to differ materially from expected results. Other factors besides those we have listed could also adversely affect us. Any forward-looking statement in this press release speaks only as of the date on which it is made. We disclaim any

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