

Purple Biotech Reports Positive Final Results from Randomized Phase 2 Study of CM24 in Second Line Pancreatic Cancer

- *Final data demonstrate CM24 in combination with nivolumab and Na-IRI/5FU/LV chemotherapy clear and consistent improvement across all efficacy endpoints*
- *A biomarker enriched patient population analysis based on pretreatment ranges of serum CEACAM1 demonstrated significant improvement in the treatment arm over the control of 79% reduction in risk of death (HR 0.21, $P = 0.04$) with median OS improvement of 5.1 months and over 90% reduction in risk of progression or death (HR < 0.1, $P = 0.003$) with median PFS improvement of 2.9 months and improvement in the treatment arm over the control in ORR of 50% vs. 0%.*
- *Phase 2b clinical study is planned in multiple selected indications, potentially targeting patients based on biomarkers*

REHOVOT, Israel, Dec. 02, 2024 (GLOBE NEWSWIRE) -- [Purple Biotech Ltd.](#) ("Purple Biotech" or "the Company") (NASDAQ/TASE: PPBT), a clinical-stage company developing first-in-class therapies that overcome tumor immune evasion and drug resistance, today reported positive final results from the randomized Phase 2 study of its lead oncology drug, CM24, a humanized monoclonal antibody that blocks CEACAM1, in patients with pancreatic ductal adenocarcinoma (PDAC).

"We are very excited about the final data, demonstrating CM24's clear and consistent improvement across all efficacy endpoints evaluated in our randomized Phase 2 study," stated Purple Biotech CEO Gil Efron. "The enhanced results in patients with CEACAM1 and other serum markers gives us further optimism that a biomarker enriched patient population selection could further strengthen CM24's magnitude of efficacy, potentially positioning CM24 as a treatment for multiple CEACAM1-expressing malignancies in line with its mechanism of action."

Michael Cecchini, MD Associate Professor of Medicine at the Yale Cancer Center, a principal investigator in this study, commented, "The promising results in PDAC, along with the identification of a potential patient subgroup that may benefit from targeting CEACAM1 and NET serum levels, potentially position CM24 as an encouraging treatment option. As a clinician, it is inspiring to see data that suggest the potential for improved outcomes in patients with late-stage metastatic PDAC, who desperately need new and effective therapies. These findings support further investigation of CM24 in combination with a checkpoint inhibitor and standard-of-care chemotherapy to improve outcomes not only in PDAC but also in other challenging cancer types."

Summary of Data and Findings:

The Phase 2 study evaluated CM24, a novel first-in-class multi-functional anti-CEACAM1 antibody, in combination with Bristol Myers Squibb's immune checkpoint inhibitor nivolumab plus stand-of-care (SoC) chemotherapy in second-line metastatic PDAC patients versus SoC chemotherapy alone. CM24 is a humanized monoclonal antibody that blocks CEACAM1, a multi-faceted membrane glycoprotein that is one of the main proteins present on NETs, also acting as a pro-angiogenic and anti-apoptotic agent collectively promoting tumor invasiveness, metastasis and immune evasion.

The primary endpoint of the study is OS and the secondary endpoints include PFS, ORR and disease control rate (DCR). A Bayesian methodology was used to estimate the magnitude of effect of the experimental arm versus the SoC arm in each chemotherapy cohort; the study was not powered for hypothesis testing. A total of 63 patients were enrolled, across 18 centers in the U.S., Spain, and Israel in 2 parallel and independent randomized study cohorts (total of 2 arms per cohort). The experimental arms administered patients with CM24 plus nivolumab and a choice of one of two SoC chemotherapies for second-line PDAC, dependent on prior first line therapy regimen; either gemcitabine/nab-paclitaxel or liposomal irinotecan (Na-IRI)/5-fluorouracil (5-FU) and leucovorin (LV) (Na-IRI/5FU/LV), while the control arms administered either respective chemotherapy alone. CA19-9 as well as additional exploratory biomarkers were

also evaluated. Of the 63 patients enrolled, 32 were in the gemcitabine/nab-paclitaxel study (experimental and control) and 31 were in the NaI-IRI/5FU/LV study (experimental and control). The gemcitabine/nab-paclitaxel-based part of the study was impacted by informative censoring of the control arm that led to an imbalance between the control and experimental arms, rendering this part of the study unsuitable for analysis; this part of the study has no impact on the CM24+nivolumab+NaI-IRI/5FU/LV portion of the study.

The study's final efficacy results in the NaI-IRI/5FU/LV intent to treat (ITT) cohort population are summarized in the following table:

Metric	CM24 + Nivolumab + NaI/IRI/5FU/LV Arm (n = 16)	NaI/IRI/5FU/LV Arm (n = 15)
Hazard ratio for OS	0.81 (95% CI: 0.38-1.71)	
Median OS	7.92 months	5.55 months
6 months OS rate	53%	47%
Hazard Ratio for PFS	0.75 (95% CI: 0.35-1.61)	
Median PFS	3.9 months	2.0 months
3 months PFS rate	67%	47%
6 months PFS rate	17%	13%
ORR	25%	7%
DCR	63%	47%

A consistent and continuous decrease of CA19-9, a clinically validated PDAC biomarker, was observed in the experimental arm reaching a median percentage reduction from baseline of approximately 80% vs. an increase of 40% in the control arm.

Subgroup analysis of patients with a range of pretreatment serum CEACAM1 between 6,000 pg/mL and 15,000 pg/mL, resulted in statistically significant results as follows:

Metric	CM24 + Nivolumab + NaI/IRI/5FU/LV Arm (n = 4)	NaI/IRI/5FU/LV Arm (n = 7)
Hazard ratio for OS	0.21 (95% CI: 0.04-1.06)	
Median OS	9 months	3.9 months
Hazard ratio for PFS	< 0.1 (95% CI: 0-inf)	
Median PFS	4.7 months	1.8 months
ORR	50%	0%
DCR	100%	43%

An additional subgroup analysis of patients, which comprised 80% of the patients in the study cohort, with a range of pretreatment serum CEACAM1 between 6,000 pg/mL and 15,000 pg/mL together with patients with pretreatment serum Myeloperoxidase (MPO) levels of 200 ng/mL and 600 ng/mL, resulted in statistically significant results as follows:

Metric	CM24 + Nivolumab + NaI/IRI/5FU/LV Arm (n = 13)	NaI/IRI/5FU/LV Arm (n = 11)
Hazard ratio for OS	0.39 (95% CI: 0.16-0.98)	
Median OS	7.90 months	5.50 months
Hazard ratio for PFS	0.28 (95% CI: 0.11-0.73)	
Median PFS	4.1 months	1.9 months
ORR	31%	0%
DCR	69%	36%

Additional biomarkers analysis based on the patient pretreatment biopsies, demonstrated significant OS and PFS

benefit (HR 0.1, P=0.013 and HR 0.19, P=0.033, respectively) in patients with both high tumor CEACAM1 (> 100) and low Combined Positive Score (CPS) (< 1) (a measure of PD-L1 positive tumor cells) supporting the CM24/nivolumab combined treatment and its mechanistic rationale, and may open a new opportunity for patients who are not eligible for anti-PD1 therapy in various indications

The CM24+nivolumab+Nal/IRI/5FU/LV regimen was well tolerated, with the most frequent treatment emergent Grade 3 or higher adverse events being diarrhea (4 patients in the experimental arm vs. 1 patient in the control arm), fatigue (2 patients in the experimental arm vs. no patients in the control) and neutropenia (2 patients in the experimental arm vs. no patients in the control). Accordingly, no meaningful difference in safety and tolerability were observed between the experimental arm and SoC arm.

"The significant results in the subgroup based on certain range of serum CEACAM1 and MPO levels, that covered 80% of the patients in the Nal-IRI cohort, is encouraging. We believe that tumors with low CEACAM1 or NETs are less reliant on these targets whereas extremely high levels may suggest potential resistance to the treatment. Based on the emerging role of neutrophil extracellular traps (NETs) in cancer and the positive findings of our study in this selected population overlapping with CEACAM1 expression, we are planning a 3-arm Phase 2b study comparing either CM24 plus a PD1 inhibitor or CM24 monotherapy to SoC in multiple tumor types selected based on their NET and CEACAM1 expressions. This design will also investigate the contribution of parts in regard to the need for PD1 blockade on top of CM24. We plan to target patients with higher serum levels of CEACAM1 and MPO, as they are potentially more likely to benefit from CM24 treatment," stated Dr Michael Schickler, Head of Clinical and Regulatory Affairs.

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 CM24, NT219 and IM1240. CM24 is a humanized monoclonal antibody that blocks CEACAM1, that supports tumor immune evasion and survival through multiple pathways. CEACAM1 on tumor cells, immune cells and neutrophils extracellular traps is a novel target for the treatment of multiple cancer indications. As a proof of concept of these novel pathways, the Company is advancing CM24 as a combination therapy with anti-PD-1 checkpoint inhibitors in a Phase 2 study for the treatment of pancreatic ductal adenocarcinoma (PDAC). The Company has entered into a clinical collaboration agreement with Bristol Myers Squibb for the Phase 2 clinical trials to evaluate the combination of CM24 with the PD-1 inhibitor nivolumab in addition to chemotherapy. 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 SCCHN (R/N SCCHN). The Company is advancing CAPTN-3, a preclinical platform of conditionally-activated tri-specific antibody that engages 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, and thereby potentially increases 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 5T4 expressed in a variety of solid tumors and is correlated with advanced disease, increased invasiveness and poor clinical outcomes. 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", "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 IM1240; 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, 2023 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 which it is made. We disclaim any intention or obligation to publicly update or revise any forward-looking statement or other information contained herein, whether as a result of new information, future events or otherwise, except as required by applicable law. You are advised, however, to consult any additional disclosures we make in our reports to the SEC, which are available on the SEC's website, <https://www.sec.gov>.

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