First Patient Enrolled in Phase I Program in STK11 Mutant Non-Small Cell Lung Cancer at Moffitt Cancer Center

MINNEAPOLIS, September 24, 2024 (GLOBE NEWSWIRE) -- Panbela Therapeutics, Inc. (OTCQB: PBLA), a clinical stage company developing disruptive therapeutics for the treatment of patients with urgent unmet medical needs, today announced the first patient enrolled in a Phase I dose escalation study to evaluate CPP-1X-S (eflornithine sachets) in STK11 mutant non-small cell lung cancer (NSCLC). The initial goal of the Phase I trial will be to determine the maximum tolerated dose of eflornithine in combination with the immune checkpoint inhibitor Keytruda, while evaluating efficacy and then moving into a Phase II efficacy trial. Data from the Phase I trial is expected by mid-2025, with a look to start the Phase II trial in 2024.

The trial entitled "Targeting ODC as an Immunotherapeutic Target in STK11 (LKB1) Pathway-Deficient NSCLC" is a Phase I/II trial where Phase I is a dose escalation study establishing the safety, toxicity and recommended Phase II dose of CPP-1X-S in combination with Keytruda in patients with STK11 mutant NSCLC at approximately one academic medical center in the United States. Detailed information on the trial can be located at https://clinicaltrials.gov/study/NCT06219174?term=DFMO&rank=4.

"Options for combining new agents with standard of care immunotherapy is critical to overcoming the reduced levels of anti-tumor T cells and immune evasion that is observed in STK11 mutant tumors," said Jhanelle Gray, M.D., Principal Investigator of the clinical trial, Chair of Moffitt's Department of Thoracic Oncology and Co-Leader of Moffitt's Molecular Medicine Program. "By working with Panbela, we are using CPP-1X-S to modulate polyamine levels and potentially restimulate the immune system, which may be a valuable therapeutic strategy to target these hard-to-treat tumors."

"With the recent approval of CPP-1X (DFMO) for neuroblastoma, the first oncology approval for a polyamine targeted therapy, we're really excited to have the first patient enrolled in the Phase I trial for CPP-1X-S led by Moffitt Cancer Center," said Jennifer K. Simpson, PhD, MSN, CRNP, President & Chief Executive Officer of Panbela. "Preclinical studies have shown that polyamine modulation has the potential to restimulate the immune system. This trial allows us to explore the potential of CPP-1X-S clinically in the STK11 mutant NSCLC population which historically have a poor response to checkpoint inhibitor therapy. Once the safety of CPP-1X-S in combination with Keytruda is established in this Phase I trial, the planned Phase II trial will determine the potential efficacy of combining polyamine targeted therapies with checkpoint inhibitors hopefully demonstrating the first clinical proof of concept of this unique approach. In

addition to the possibility of providing a better treatment option for this patient population, we are excited to evaluate the role of eflornithine and ivospemin as modulators of the immune system in combination with other immunotherapies such as CAR-T therapy for tumors where response rates have been low with immunotherapy."

About Panbela's Pipeline

The pipeline consists of assets currently in clinical trials with an initial focus on familial adenomatous polyposis (FAP), first-line metastatic pancreatic cancer, neoadjuvant pancreatic cancer, colorectal cancer prevention and ovarian cancer. The combined development programs have a steady cadence of anticipated catalysts with programs ranging from pre-clinical to registration studies.

Ivospemin (SBP-101)

Ivospemin is a proprietary polyamine analogue designed to induce polyamine metabolic inhibition (PMI) by exploiting an observed high affinity of the compound for pancreatic ductal adenocarcinoma and other tumors. It has shown signals of tumor growth inhibition in clinical studies of metastatic pancreatic cancer patients, demonstrating a median overall survival (OS) of 14.6 months and an objective response rate (ORR) of 48%, both exceeding what is typical for the standard of care of gemcitabine + nab-paclitaxel suggesting potential complementary activity with the existing FDA-approved standard chemotherapy regimen. In data evaluated from clinical studies to date, ivospemin has not shown exacerbation of bone marrow suppression and peripheral neuropathy, which can be chemotherapy-related adverse events. Serious visual adverse events have been evaluated and patients with a history of retinopathy or at risk of retinal detachment will be excluded from future SBP-101 studies. The safety data and PMI profile observed in the previous Panbela-sponsored clinical trials provide support for continued evaluation of ivospemin in the ASPIRE trial.

Flynpovi ™

Flynpovi is a combination of CPP-1X (eflornithine) and sulindac with a dual mechanism inhibiting polyamine synthesis and increasing polyamine export and catabolism. In a Phase III clinical trial in patients with sporadic large bowel polyps, the combination prevented > 90% subsequent pre-cancerous sporadic adenomas versus placebo. Focusing on FAP patients with lower gastrointestinal tract anatomy in the recent Phase III trial comparing Flynpovi to single agent eflornithine and single agent sulindac, FAP patients with lower GI anatomy (patients with an intact colon, retained rectum or surgical pouch), showed statistically significant benefit compared to both single agents ($p \leq 0.02$) in delaying surgical events in the lower GI for up to four years. The safety profile for Flynpovi did not significantly differ from the single agents and supports the continued evaluation of Flynpovi for FAP.

CPP-1X

CPP-1X (eflornithine) is being developed as a single agent tablet or high dose powder sachet for several indications including prevention of gastric cancer, treatment of neuroblastoma and

recent onset Type 1 diabetes. Preclinical studies as well as Phase I or Phase II investigator-initiated trials suggest that CPP-1X treatment may be well-tolerated and has potential activity.

About Panbela

Panbela Therapeutics, Inc. is a clinical-stage biopharmaceutical company developing disruptive therapeutics for patients with urgent unmet medical needs. Panbela's lead assets are Ivospemin (SBP-101) and Flynpovi. Further information can be found at **www.panbela.com.** Panbela's common stock is eligible for quotation on the OTCQB under the symbol "PBLA".

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements," including within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements can be identified by words such as: "anticipate," "believe," "can," "design," "expect," "focus," "intend," "looking forward," "may," "plan," "positioned," "potential," and "will." All statements other than statements of historical fact are statements that should be deemed forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations, and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. Our actual results and financial condition may differ materially and adversely from the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause our actual results and financial condition to differ materially from those indicated in the forward-looking statements include, among others, the following: (i) our ability to obtain additional capital, on acceptable terms or at all, required to implement our business plan; (ii) our lack of diversification and the corresponding risk of an investment in our Company and the corresponding risk of potential deterioration of our financial condition and results due to failure to diversify; (iii) our ability to obtain and maintain our listing on a national securities exchange; (iv) results, progress and success of our randomized Phase Ia/Ib and Phase II/III clinical trials; (v) our ability to demonstrate the safety and effectiveness of our product candidates: ivospemin (SBP-101), Flynpovi, and eflornithine (CPP-1X); (vi) potential delays or risks to the success of our randomized Phase II/III clinical trial resulting from a termination in our relationship with our CRO; (vii) our ability to obtain regulatory approvals for our product candidates, SBP-101, Flynpovi and CPP-1X in the United States, the European Union or other international markets; (viii) the market acceptance and level of future sales of our product candidates, SBP-101, Flynpovi and CPP-1X ; (ix) the cost and delays in product development that may result from changes in regulatory oversight applicable to our product candidates, SBP-101, Flynpovi and CPP-1X ; (x) the rate of progress in establishing reimbursement arrangements with third-party payors; (xi) the effect of competing technological and market developments; (xii) the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims; and (xiii) such other factors as discussed in Part I, Item 1A under the caption "Risk Factors" in our most recent Annual Report on Form 10-K , any additional risks

presented in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Any forward-looking statement made by us in this press release is based on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement or reasons why actual results would differ from those anticipated in any such forward-looking statement, whether written or oral, whether as a result of new information, future developments or otherwise.

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