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Propanc Biopharma's Lead Asset PRP Reprograms Chemotherapy-Resistant Pancreatic Cancer Cells

New Preclinical Findings Identify Potential Strategy to Remodel Resistant Tumor State & Restore Therapeutic Vulnerability

MELBOURNE, Australia, Oct. 16, 2026 (GLOBE NEWSWIRE) -- Propanc Biopharma, Inc. (Nasdaq: PPCB) ("Propanc" or the "Company"), a biopharmaceutical company focused on developing novel treatments for chronic diseases including recurrent and metastatic cancer, today announced new preclinical research from an academic–industry collaboration from the Universities of Jaén and Granada, led by Dr. Maria Belén Toledo, has identified pancreatic proenzyme formulation, PRP, as a potential strategy for addressing chemotherapy resistance in pancreatic cancer.

Chemotherapy-resistant tumor cells can acquire adaptive cellular states that allow them to survive treatment and maintain aggressive characteristics. The study investigated whether PRP could remodel these resistant states and increase their vulnerability to subsequent chemotherapy. It combined functional cellular analyses with transcriptome-wide (i.e. RNA molecules within the cell) profiling in pancreatic cancer models with acquired chemotherapy resistance.

"These findings are highly significant as we progress PRP to a world-first, Phase 1b, First-In-Human study for advanced cancer patients with solid tumors in Q1 2027, because we envision PRP as a welcome addition to the treatment process, as a long term, metronomic therapy that minimizes threat of recurrence, whilst enabling patients to respond to standard treatment options where tumor resistance has become a critical, life threatening factor," said Mr. James Nathanielsz, Propanc's Chief Executive Officer. "Dr. Toledo's findings shows that PRP's targeted multiple effects reprograms pancreatic cancer cells through interconnected biological programs which alters chemoresistance, tumor cell plasticity and aggressive behavior. We are now in the unique position to investigate sequential combinatorial approaches that rely on inhibition of specific tumor pathways which are effective, but do not address tumor led resistance mechanisms."

A sequential strategy to remodel resistance

A defining feature of the experimental design was the treatment sequence. Chemoresistant (GR) cells were first exposed to PRP. Chemotherapy was then added to determine whether PRP pre-treatment had altered the resistant state and changed the subsequent response to chemotherapy.

GR CELLS → PRP PRE-TREATMENT → CHEMOTHERAPY → ASSESSMENT OF RESPONSE

According to Dr. Toledo, “This distinction is central to the study: PRP was used first as a resistance-modulating intervention, while chemotherapy was subsequently used as the challenge to test whether the cells had become more responsive and sensitive.”

Reprogramming the resistant cellular state

PRP induced coordinated changes across interconnected biological processes associated with chemoresistance, tumor cell plasticity and aggressive behavior. At a high level, these included:

- Tumor-cell plasticity and epithelial–mesenchymal transition (EMT)
- Drug-response and metabolic processes
- DNA replication and repair
- Cellular stress and survival programs
- Extracellular matrix organization
- Apoptotic susceptibility

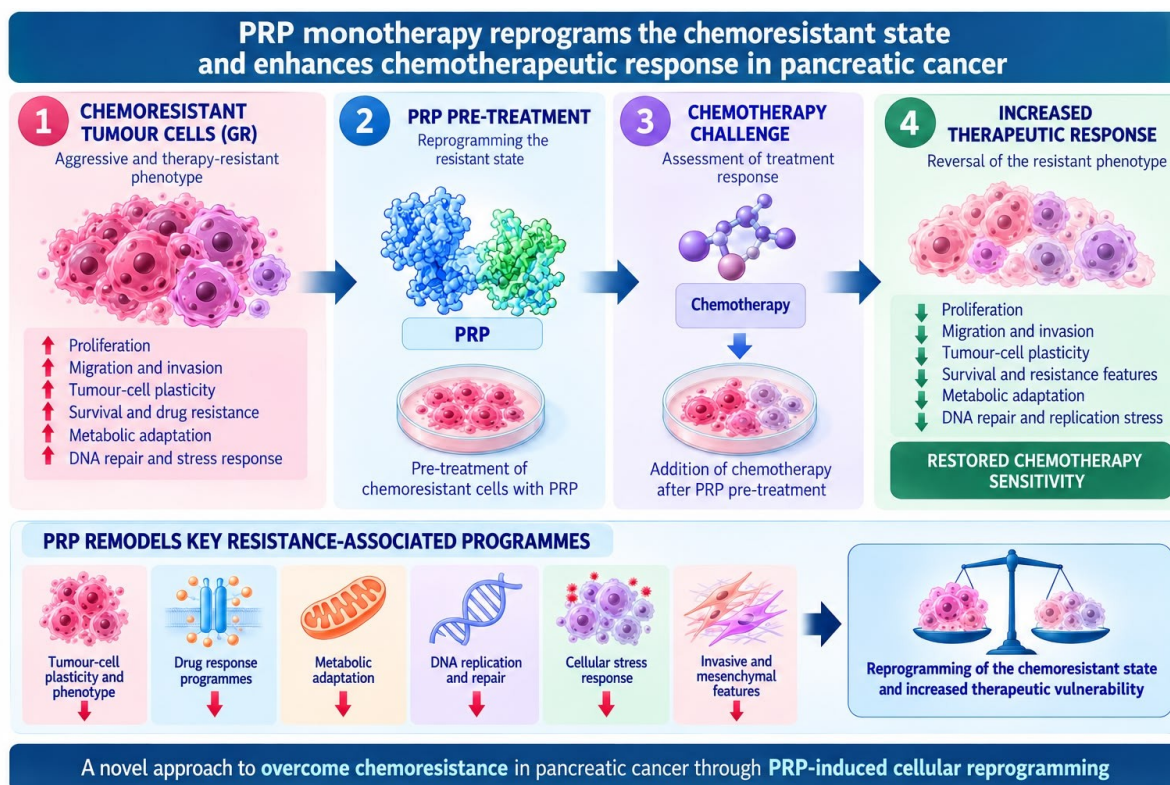
Importantly, PRP treatment alone produced changes consistent with partial restoration of features associated with chemotherapy sensitivity in resistant models. This supports the concept of PRP as a resistance-modulating intervention rather than simply a conventional cytotoxic agent.

Testing whether resistance can be overcome

Following PRP pre-treatment, chemotherapy was introduced to determine whether the resistant phenotype had been functionally weakened. The sequential PRP → chemotherapy strategy produced the strongest functional response in the study, supporting the hypothesis that remodeling the resistant state before chemotherapy can increase therapeutic vulnerability. The study evaluated complementary phenotypes including cellular growth, clonogenic capacity, migration, invasion and cell-death susceptibility.

A multimodal mechanism

Transcriptomic analyses revealed that PRP does not appear to act through a single resistance mechanism. Instead, the response involved coordinated remodeling of interconnected biological programs. The nature and magnitude of these changes differed between tumor models (WT and GR), highlighting the heterogeneity of chemotherapy resistance. Together, the data supports a systems-level interpretation in which PRP weakens adaptive programs sustaining the resistant state, creating a cellular context that is more vulnerable to subsequent chemotherapy.



Summary of Preclinical Findings

Observations	Results
Restoring Chemotherapy Sensitivity & Reducing Proliferation	- PRP monotherapy reduced cancer cell proliferation by 50% in wild-type (WT) and 54% in chemoresistant (GR) cells - Long-term clonogenic survival (colony formation capacity over 21 days) was suppressed by 59% in WT and 39% in GR cells following PRP pre-treatment
Suppressing Metastatic Behavior (Migration and Invasion)	- In 72-hour wound-healing migration assays, PRP monotherapy limited cell migration to 21% wound closure in WT and 57% in GR cells (compared to 100% closure in untreated controls) - Matrigel invasion assays demonstrated that PRP monotherapy reduced invasive capacity by 81% in WT and 47% in GR cells
Reversing Epithelial-Mesenchymal Transition (EMT) & Plasticity	- PRP treatment induced strong epithelial differentiation, significantly upregulating key epithelial markers E-cadherin (up to 5.29-fold in WT and 4.86-fold in GR cells) and EPCAM (up to 4.39-fold in WT) - Concurrently, PRP downregulated key mesenchymal drivers including Vimentin (reduced to ~0.31–0.32-fold of control) and Snail (reduced to 0.28–0.62-fold)

Inhibiting Canonical TGF-β/SMAD Signaling	- Quantitative RT-qPCR showed significant downregulation of SMAD2, SMAD3, and TGFBR1 gene expression (reduced to 0.23–0.42-fold in GR cells) - Protein-level immunofluorescence analysis confirmed that PRP monotherapy reduced nuclear translocation of SMAD2/3 by 81% in WT and 78% in GR cells
Inducing Apoptosis and Suppressing Oncogenic Stemness Drivers	- PRP shifted cells toward a pro-apoptotic state, increasing BAX expression (2.49-fold in WT and 2.74-fold in GR) while decreasing anti-apoptotic BCL2 (0.49-fold) - PRP upregulated cell cycle and stress response regulators CDKN1A (p21) (3.90 to 4.10-fold), ATM (2.88 to 3.34-fold), and TP53 (3.29 to 3.64-fold) - Key drivers of aggressiveness and cancer stemness, MYC and SOX2, were suppressed down to 0.11-fold and 0.22-fold in chemoresistant cells, respectively
Enhanced Synergistic Effect with TGF-β Inhibition (PRP + TGF-β inhibitor)	Combining PRP with a TGF-β inhibitor further amplified therapeutic response in chemoresistant cells, achieving 80% invasion inhibition, an 8.24-fold increase in E-cadherin, a 93% reduction in nuclear SMAD2/3 translocation, and a 4.42-fold induction of BAX

Future development

These findings provide a preclinical rationale for further investigation of PRP as a resistance-modulating strategy, including its potential use as a standalone intervention to remodel resistant tumor cells and as a sequential approach preceding chemotherapy.

Validation in clinically relevant models will be undertaken to determine whether this resistance-remodeling effect can translate into a therapeutic benefit, ultimately, in patients.

CHEMORESISTANCE → RESISTANCE REMODELLING → THERAPEUTIC VULNERABILITY

About Propanc Biopharma, Inc.

Propanc Biopharma, Inc. (Nasdaq: PPCB) is developing a novel approach to preventing cancer recurrence and metastasis by targeting and eradicating cancer stem cells through proenzyme activation. The Company's lead product candidate, PRP, is designed to address the underlying drivers of cancer proliferation and spread.

More information: www.propanc.com

Forward-Looking Statements

All statements in this press release that are not historical are forward-looking statements, including, among other things, statements relating to the Company's expectations regarding its market position and market opportunity, expectations and plans as to its product development, manufacturing and sales, and relations with its partners and investors, made in reliance upon the safe harbor provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements are not historical facts but rather are based on the Company's current expectations, estimates, and projections regarding its business, operations and other similar or related factors. Words such as "may," "will," "could," "would," "should," "anticipate," "predict," "potential," "continue," "expect," "intend," "plan," "project," "believe," "estimate," and other similar or related expressions are used to identify these forward-looking statements, although not all forward-looking statements contain these words. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and assumptions that are difficult or impossible to predict and, in some cases, beyond the Company's control. Forward-looking statements are not guarantees of future actions or performance. Actual results may differ materially from those in the forward-looking statements because of several factors, including, without limitation, risks and uncertainties related to market conditions, as well as those risks described under "Risk Factors" in the prospectus related to the proposed offering and those described in the Company's filings with the SEC. The Company undertakes no obligation to revise or update information in this release to reflect events or circumstances in the future, even if new information becomes available.

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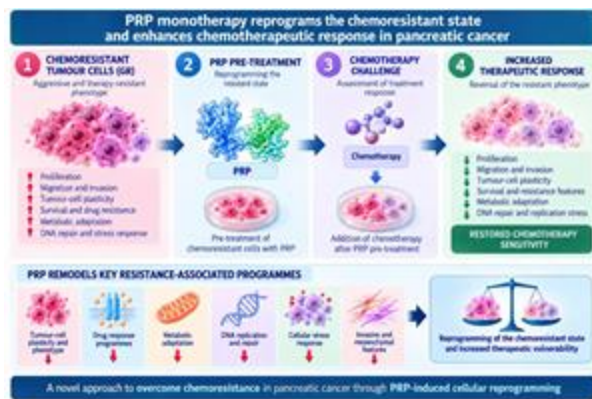
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A photo accompanying this announcement is available at

<https://www.globenewswire.com/NewsRoom/AttachmentNg/da1afeef-78de-4c02-a16a-7edcb0f4fc0d>



PRP Monotherapy Reprograms the Chemo-resistant State



PRP Monotherapy Reprograms the Chemo-resistant State and Enhances Chemotherapeutic Response in Pancreatic Cancer

Source: Propanc Biopharma, Inc.