November 2, 2026

Propanc Biopharma Reports Preclinical Data with PRP & PRP plus TGF-β Inhibitor on TGF-β Pathway in Pancreatic Cancer

New Findings from Academic Collaboration Examine Tumor-Cell Behavior, TGF-B/SMAD Signaling & Stromal Responses; Australian Patent Application Filed for the Combination Approach

MELBOURNE, Australia, Nov. 02, 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 highlighted new preclinical findings evaluating its pancreatic proenzyme formulation (PRP) alone and in combination with galunisertib (GAL), a small-molecule inhibitor of transforming growth factor beta receptor I (TGF-βRI), in pancreatic ductal adenocarcinoma (PDAC) models. The Company has filed an Australian patent application relating to the combination approach.

The research was conducted in collaboration with investigators at the University of Jaén and the University of Granada in Spain. The study compared PRP, GAL and PRP plus GAL in wild-type BxPC-3 pancreatic cancer cells, gemcitabine-resistant BxPC-3 cells, normal-associated fibroblasts (NAFs) and cancer-associated fibroblasts (CAFs). Experiments assessed cell proliferation, colony formation, migration and invasion, together with molecular readouts associated with TGF-β signaling, epithelial–mesenchymal transition (EMT), extracellular-matrix (ECM) remodeling and fibroblast activation.

PDAC is characterized by complex interactions between malignant cells and the surrounding tumor microenvironment. TGF-β signaling can contribute to tumor-cell plasticity, EMT and stromal activation, although its effects depend on cellular context. The study investigated whether PRP could modulate these tumor- and stroma-associated processes and whether adding a TGF-β pathway inhibitor provided further effects.

"Our academic collaboration with the Universities of Jaén and Granada in Spain continues to provide strong scientific evidence and a rationale for the administration of PRP as a stand-alone therapy, but also as a combinatorial approach with inhibitor drugs that can successfully stop tumor growth and dissemination but can be limited due to resistance mechanisms developed over time as a result of alterations to the tumor microenvironment," said Mr. James Nathanielsz, Propanc's Chief Executive Officer. "PRP represents a new approach addressing these resistance mechanisms by inducing biological effects that alters the behavior of these malignant cells, rather than using the inhibitory approach. Our unique intellectual property portfolio continues to grow and strengthen as a result and is positioning the Company for long-term future growth, which our shareholders understand will come to fruition as future planned R&D milestones are achieved. Management believe these

milestones are near term as PRP (now called Company Candidate, PPC-001) enters the clinic. Further announcements are expected regarding current preparatory activities for our Phase 1b, First-In-Human study as we progress further."

Key preclinical findings:

- **Anti-proliferative activity in tumor models:** PRP reduced cell proliferation by approximately 50% in wild-type and gemcitabine-resistant BxPC-3 cells relative to untreated controls. PRP plus GAL reduced proliferation by 75% and 66%, respectively. The additional reduction versus PRP alone was significant in wild-type cells; in resistant cells, the further reduction was not statistically significant.
- **Reduced long-term colony-forming capacity:** PRP reduced colony formation by 59% in wild-type cells and 39% in gemcitabine-resistant cells. The combination reduced colony formation by 68% and 64%, respectively. The additional effect of the combination over PRP alone was significant in the resistant model, but not in the wild-type model.
- **Suppression of migration and invasion:** In wound-healing assays at 72 hours, wound closure was 21% with PRP in wild-type cells and 57% in resistant cells, compared with untreated controls. PRP plus GAL resulted in 19% and 30% wound closure, respectively; the combination significantly improved the result over PRP alone in resistant cells, but not in wild-type cells. In Matrigel invasion assays, PRP reduced invasion by 81% in wild-type cells and 47% in resistant cells. PRP plus GAL produced reductions of 89% and 80%, respectively.
- **Modulation of TGF-β/SMAD pathway-associated gene expression:** PRP significantly reduced SMAD2, SMAD3 and TGFBR1 transcript levels to 0.45-, 0.63- and 0.55-fold of control in wild-type cells, and to 0.42-, 0.36- and 0.23-fold in resistant cells, compared to control group. The combination produced further reductions in selected readouts, although the magnitude and statistical significance of the additional effects varied across models and markers.
- **Changes in EMT-associated markers:** PRP increased E-cadherin expression 5.29-fold in wild-type cells and 4.86-fold in resistant cells, while reducing Vimentin to 0.31- and 0.32-fold and Snail to 0.62- and 0.28-fold, respectively, relative to untreated controls. The combination produced additional changes in selected biomarkers, including stronger suppression of Snail in the resistant-cell model. These transcriptional findings are consistent with a shift towards a more epithelial gene-expression profile; they do not establish complete reversal of EMT.
- **Changes in genes are linked to tumor aggressiveness and cell survival:** In wild-type cells, PRP reduced MYC and SOX2 expressions to 0.27- and 0.54-fold of control, respectively, and increased the pro-apoptotic marker BAX 2.49-fold. In resistant cells, MYC and SOX2 fell to 0.11- and 0.22-fold, while BAX increased 2.74-fold. These are gene-expression results and can be interpreted as degree of apoptosis.
- **Differential responses in fibroblast populations:** PRP reduced CAF proliferation by up to 53% and CAF invasion by 85%, while its effect on NAF proliferation was modest and not statistically significant (approximately 22% reduction); NAF invasion was reduced by 19%. The gene-expression data showed a similar differential response. In CAFs, PRP reduced αSMA, FAPα and YAP1 expression to 0.56-, 0.27- and 0.58-fold

of untreated-control levels, respectively. It also reduced COL1A1, FN1, MMP9, IL6 and CXCL12 expressions to 0.65-, 0.42-, 0.49-, 0.25- and 0.54-fold of control, respectively. In NAFs, the corresponding reductions in COL1A1, FN1, MMP9, IL6 and CXCL12 expression were not statistically significant (0.81-, 0.86-, 0.76-, 0.75- and 0.81-fold of control, respectively); αSMA expression was 0.81-fold of control, YAP1 was 0.89-fold, and FAPα expression was undetectable. Overall, the pattern suggests a more pronounced effect on activated CAFs than on NAFs.

- **Combination effects and stromal selectivity:** Compared with PRP monotherapy, the addition of GAL enhanced the inhibition of selected CAF-associated functional and molecular features, although it also increased the impact on normal-associated fibroblasts. In proliferation assays PRP + GAL reduced CAF proliferation by 71%, compared with 53% with PRP alone, while inhibition in NAFs increased from a non-significant 22% with PRP to 55% with the combination. In clonogenic assays, the combination reduced colony formation by 78% in CAFs, compared with 69% with PRP alone; however, it also reduced NAF clonogenic capacity by 42%, whereas PRP largely preserved it. This additional reduction in NAF clonogenicity was significant (38.9% relative to PRP), while the additional reduction in CAFs was not significant (19.5%). Regarding migration, PRP + GAL limited wound closure in CAFs to 28% at 72 hours, compared with 35% with PRP alone, whereas NAF wound closure reached 100% under both treatment conditions. In Matrigel assays, the combination further reduced invasion in CAFs from 85% with PRP alone to 90%, while the reduction in NAF invasion increased from 19% to 32%. At the molecular level, PRP + GAL produced a slightly greater downregulation of CAF-associated genes than PRP alone, reducing COL1A1, FN1, MMP9, IL6 and CXCL12 expression to 0.40-, 0.32-, 0.29-, 0.16- and 0.32-fold of control levels, respectively, compared with 0.65-, 0.42-, 0.49-, 0.25- and 0.54-fold with PRP alone. The combination also reduced CAF activation markers αSMA and FAPα to 0.45- and 0.19-fold of control, respectively, compared with 0.46- and 0.30-fold with PRP. In NAFs, the combination reduced COL1A1, FN1, MMP9, IL6 and CXCL12 expressions to 0.63-, 0.85-, 0.56-, 0.68- and 0.80-fold of control, respectively, indicating broader effects than PRP monotherapy, for which these changes were modest and not statistically significant. Overall, PRP alone showed a more favorable stromal selectivity profile, whereas the addition of GAL enhanced suppression of several CAF-associated markers but also increased effects on NAF proliferation, clonogenicity and invasion.

What the findings mean

The addition of galunisertib enhanced the suppression of several CAF-associated markers, including genes involved in ECM remodeling and inflammatory signaling, and further reduced selected functional endpoints, particularly tumor-cell and CAF invasion. However, these additional effects were not uniform across all assays. Importantly, GAL-containing treatment also increased the suppression of several readouts in NAFs, including proliferation and clonogenic capacity. This distinction raises an important question: whether stronger inhibition of TGF-β associated signaling necessarily produces a more favorable overall response, or whether preserving the selectivity of the stromal response may be equally important. Within the conditions tested, PRP monotherapy showed a more favorable profile in terms of differential effects on CAFs and NAFs, whereas the combination produced broader stromal suppression at the expense of some of this apparent selectivity.

These findings do not establish that preserving NAF function improves clinical outcomes, but they support investigating stromal selectivity as an important parameter when evaluating future combination strategies.

In tumor cells, PRP also demonstrated activity across multiple functional and molecular endpoints in both wild-type and gemcitabine-resistant BxPC-3 models. These effects included reduced proliferation, colony-forming capacity, migration and invasion, together with changes in TGF-β/SMAD-associated signaling and EMT-related gene expression. Increased E-cadherin expression alongside reduced vimentin and Snail expression was consistent with a shift towards a more epithelial transcriptional profile, while changes in MYC, SOX2 and BAX suggested additional effects on genes associated with tumor-cell aggressiveness and apoptotic regulation. The combination with GAL enhanced selected responses, particularly invasion suppression in resistant tumor cells, although the magnitude of the additional benefit varied between models and experimental endpoints. These observations support further investigation of PRP as a potential modulator of aggressive tumor-cell phenotypes, including in a gemcitabine-resistant setting.

A central hypothesis emerging from this study is that PRP may offer a dual advantage: modulating aggressive tumor-cell characteristics while preferentially attenuating features of activated tumor-supportive stroma. TGF-β inhibition may reinforce some of these effects, but its broader impact on normal-associated fibroblasts suggests that the optimal therapeutic strategy may not simply be the one that produces the greatest overall suppression. Instead, the balance between tumor-directed activity, CAF modulation and preservation of normal stromal functions may be critical.

“These preclinical findings provide a rationale for continued investigation of PRP, both as a monotherapy and in combination with TGF-β pathway inhibition, in pancreatic cancer,” said Dr. Maria Belén Toledo, Lead Investigator at the University of Jaén. “They also identify stromal selectivity as a potentially valuable consideration in treatment development and suggest that therapeutic value of targeting the tumor microenvironment should be assessed not only by the extent of pathway suppression, but also by which cellular populations are affected and how this translates into tumor control. Further validation in more complex models will be conducted to confirm whether these effects can be reproduced and support a clinically meaningful therapeutic strategy.”

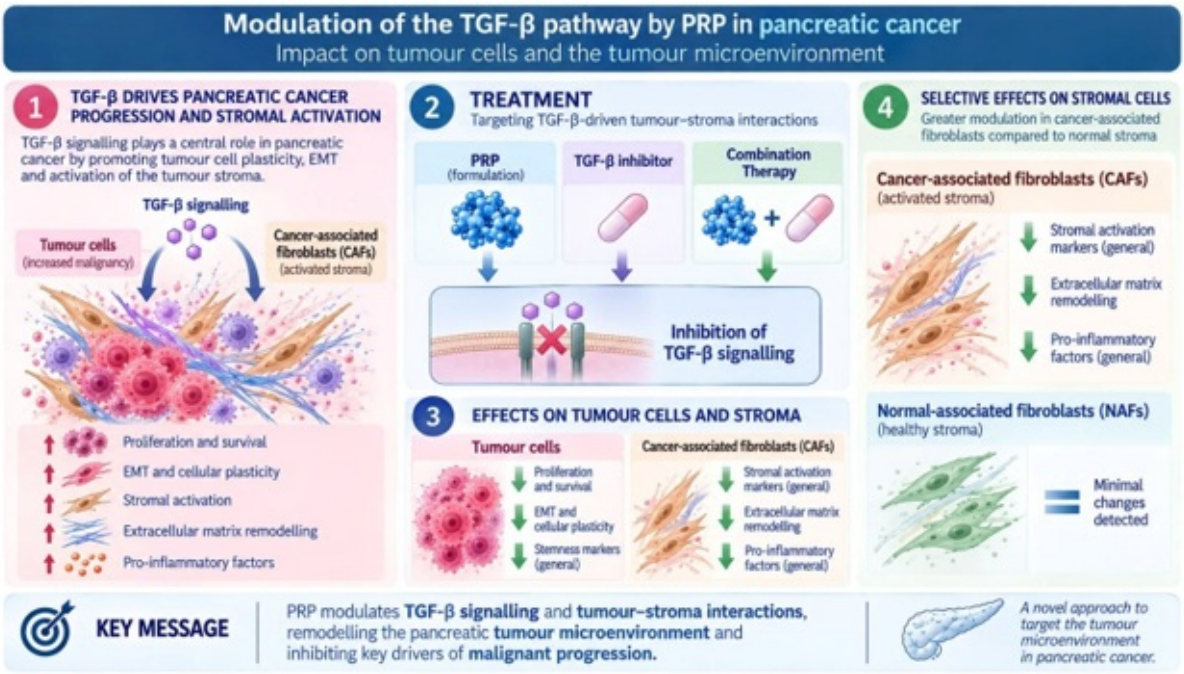


Illustration of the proposed effects of PRP and TGF-β pathway inhibition on tumor cells and the tumor microenvironment

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

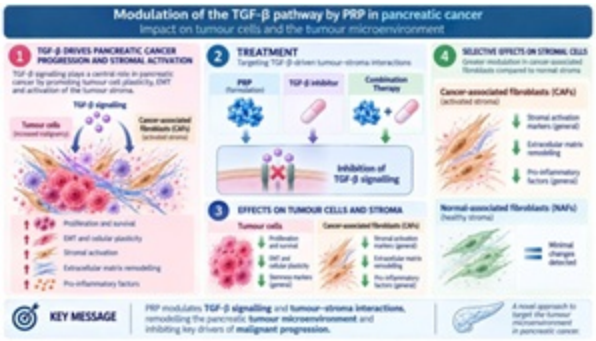
uncertainties related to market conditions, as well as those risks described under “Risk Factors” in the prospectus related to the proposed offering and those described in the Company’s filings with the SEC. The Company undertakes no obligation to revise or update information in this release to reflect events or circumstances in the future, even if new information becomes available.

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A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/6b88acd9-0745-449d-9f68-a061a7553c5d

Illustration of the proposed effects of PRP and TGF-β pathway inhibition on tumor cells and the tumor microenvironment



Modulation of the TGF-Beta Pathway by PRP in Pancreatic CancerImpact on Tumor Cells and the Tumor Microenvironment

Source: Propanc Biopharma, Inc.