September 16, 2026

Propanc Biopharma Positions PRP's EMT-Reversal Mechanism as a Complementary Backbone to Emerging RAS Inhibitors from Revolution Medicines, Inc. and Erasca, Inc.

New Preclinical PDAC Data for PRP Show >90% Tumor-Growth Inhibition & >2.5-Fold Survival Benefit; Company Highlights How Reversing Epithelial-Mesenchymal Transition May Deepen & Extend Responses to RAS(ON) & Pan-RAS Therapies

MELBOURNE, Australia, Sept. 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 issued a comparative analysis of its lead candidate PRP against recently reported clinical datasets from leading RAS-targeted programs, including Revolution Medicines' daraxonrasib (RASONQUE™; RMC-6236) and Erasca's pan-RAS molecular glue ERAS-0015.

The analysis is intended to clarify two distinct layers of tumor biology. RAS inhibitors block oncogenic RAS signaling and have produced practice-changing clinical results in RAS-mutant pancreatic ductal adenocarcinoma (PDAC) and encouraging activity in RAS-mutant non-small cell lung cancer (NSCLC). PRP, a proprietary fixed-ratio combination of the pancreatic proenzymes, trypsinogen and chymotrypsinogen, does not inhibit RAS. Instead, it promotes differentiation of malignant cells toward a more normal phenotype, reverses epithelial-mesenchymal transition (EMT), depletes cancer stem cells (CSCs), and remodels the fibrotic tumor microenvironment (TME).

Propanc believes these mechanisms address residual drivers of resistance, dormancy, and metastasis that can persist after RAS pathway blockade – creating a scientific rationale for combination or sequential use with RAS inhibitors.

A Landmark Moment for RAS-Targeted Therapy

RAS mutations drive approximately 90% of PDAC and roughly 30% of NSCLC. For decades the target was considered undruggable. That landscape has shifted rapidly.

Revolution Medicines – daraxonrasib: In the randomized Phase 3 RASolute 302 trial in previously treated metastatic PDAC, oral once-daily daraxonrasib produced median overall survival (OS) of 13.2 months versus 6.6–6.7 months with investigator's-choice

chemotherapy (hazard ratio 0.40; $p < 0.0001$), median progression-free survival (PFS) of 7.3 months versus 3.5 months, and an objective response rate (ORR) of approximately 33% versus 12%. The U.S. Food and Drug Administration approved daraxonrasib in August 2026 for pretreated metastatic pancreatic adenocarcinoma. In previously treated RAS-mutant NSCLC, a Phase 1/2 study published in The New England Journal of Medicine reported ORRs of 31–37% across evaluated dose bands; in a docetaxel-naïve subgroup treated at 160–220 mg, confirmed ORR was 42%, disease-control rate 89%, median PFS 8.3 months, and median OS 16.0 months.

Erasca – ERAS-0015: Preliminary Phase 1 monotherapy data from the U.S. AURORAS-1 and China JYP0015M101 trials showed unconfirmed overall response rates (uORR) of 62% in second-line or later KRAS G12X NSCLC at pharmacologically active doses of 16–32 mg once daily, and 75% in the post-checkpoint-inhibitor / platinum 2/3L NSCLC subset. In second-line KRAS G12X PDAC, uORR was 40% at 16–32 mg and 42% at recommended expansion doses of 24–32 mg; a July 2026 update reported a 57% uORR at 8 weeks at the 32 mg recommended expansion dose in 2L+ KRAS G12X PDAC. The program has been generally well tolerated to date, with mostly low-grade treatment-related adverse events and no dose-limiting toxicities reported at disclosed cutoffs. Erasca has described ERAS-0015 as a potentially best-in-class pan-RAS molecular glue and has outlined registration-enabling plans in pancreatic and lung cancers.

These datasets validate RAS as a therapeutically tractable node. They also leave an open clinical question: how to convert high response rates and doubled survival into durable, metastasis-free outcomes when residual mesenchymal and stem-like cells remain.

PRP Preclinical Profile in Advanced PDAC

In orthotopic and patient-derived xenograft (PDX) models of advanced PDAC, three-times-weekly intravenous PRP achieved:

- Greater than 90%, mean, tumor-growth inhibition versus vehicle controls ($p < 0.001$).
- Marked reduction in metastatic burden in liver and peritoneum.
- Significant TME remodeling, including decreased cancer-associated fibroblast (CAF) activity, reduced fibrosis, and suppression of EMT markers.
- Re-sensitization of chemo-resistant PDAC cells to gemcitabine/nab-paclitaxel, supporting lower chemotherapy doses with improved efficacy.
- Median overall survival extension of more than 2.5-fold versus controls.

These findings are built on previously reported >85% tumor-growth inhibition, peer-reviewed work on PRP’s effects on PDAC fibroblasts and CSCs, and limited prior compassionate-use experience with related proenzyme formulations that showed signals of prolonged survival and a favorable safety profile with no severe treatment-related adverse events. PRP holds FDA Orphan Drug Designation for pancreatic cancer and is not restricted to a specific RAS genotype.

Important context: PRP efficacy cited here is preclinical. Daraxonrasib and ERAS-0015 data are from human clinical trials. Cross-modality numerical comparisons are directional only and are not head-to-head results.

Comparative Snapshot

Attribute	PRP (PPCB)	Daraxonrasib	ERAS-0015
Modality	IV proenzyme combo (trypsinogen + chymotrypsinogen, 1:6)	Oral RAS(ON) multi-selective inhibitor	Oral pan-RAS molecular glue
Primary node	Differentiation / EMT reversal / CSCs / TME	Oncogenic RAS(ON) signaling	Pan-RAS (KRAS G12X and related)
Evidence stage	Preclinical PDAC + limited compassionate use; Phase 1b planned Feb 2027	Phase 3 PDAC (approved Aug 2026); Phase 1/2 NSCLC in NEJM	Phase 1 dose-escalation / expansion; registration path outlined
PDAC activity	>90% TGI; >2.5× median OS in models; metastasis and fibrosis reduced	Ph3 2L: mOS 13.2 vs 6.6–6.7 mo; mPFS 7.3 vs 3.5 mo; ORR ~33% vs ~12%	Ph1 2L KRAS G12X: uORR 40–42%; 57% uORR8wk at 32 mg RDE (2L+)
NSCLC activity	Not a primary disclosed indication to date	Ph1/2 RAS-mutant: ORR 31–37%; docetaxel-naïve subset ORR 42%, mOS 16 mo	Ph1 2L+ KRAS G12X: uORR 62%; post-ICI/platinum 2/3L uORR 75%
Genotype limit	Not RAS-mutation restricted	RAS-mutant tumors (multi-selective, non-G12C-only)	RAS / KRAS G12X enriched populations
Resistance biology addressed	EMT, CSCs, CAFs, fibrosis, metastasis, chemo-re-sensitization	Oncogene-addicted proliferation; adaptive MAPK reactivation remains a known class issue	RAS output; combinations (e.g., anti-EGFR) being explored

Sources: Company disclosures & peer-reviewed or conference reports for September 2026. Figures are not from a single comparative trial.

How Reversal of EMT Occurs — and Why It Matters After RAS Blockade

EMT is a developmental program co-opted by carcinomas. When it is activated, epithelial tumor cells lose polarity and adhesion, acquire a mesenchymal, invasive, and stem-like state, and become more resistant to apoptosis, chemotherapy, and targeted agents. In PDAC, EMT is tightly coupled to TGF-β signaling, a dense desmoplastic stroma, CAF activation, and a CSC reservoir that seeds metastasis and late relapse.

Oncogenic RAS feeds this program. KRAS signaling promotes MAPK- and PI3K-dependent transcriptional networks that stabilize EMT transcription factors, loosen cell–cell junctions, and maintain stemness. RAS inhibitors can collapse that upstream drive and produce rapid tumor shrinkage. They do not, by themselves, reliably extinguish cells that have already completed EMT or that reside in a fibrotic niche that limits drug penetration and immune access. Those residual populations are a leading hypothesized source of acquired resistance to RAS-targeted drugs.

PRP acts at a different biological layer:

- **Proenzyme activation and PAR signaling:** After intravenous administration, trypsinogen and chymotrypsinogen are activated and engage proteinase-activated receptors (PAR-1 and PAR-2), which are frequently overexpressed on tumor cells. This cascade is associated with reduced TGF-β pathway output — a master inducer of EMT in late-stage cancer.
- **Restoration of an epithelial phenotype:** Peer-reviewed studies show PRP increases epithelial adhesion proteins such as E-cadherin and β-catenin and decreases EMT transcription factors. Cells become less motile, more adherent, and more differentiated — the operational definition of EMT reversal (sometimes described as mesenchymal-to-epithelial transition, or MET).
- **Depletion of cancer stem cells:** In pancreatic CSC models, PRP reduced ALDH-high cells and surface markers CD44, CD326, and CXCR4; suppressed primary and secondary sphere formation; down-regulated CSC and metastasis gene programs; and impaired tumor engraftment in vivo.
- **TME and fibroblast remodeling:** PRP decreased CAF activity and fibrosis in PDAC models. A less desmoplastic stroma can improve drug delivery and reduce TGF-β-driven conversion of non-stem tumor cells into CSCs — a problem that pathway inhibitors alone do not solve.
- **Chemo- and pathway-sensitization:** By pushing cells out of a mesenchymal, drug-tolerant state, PRP resensitized chemo-resistant PDAC cells to gemcitabine/nab-paclitaxel at lower doses. The same logic applies to RAS inhibitors: a smaller mesenchymal reservoir should theoretically reduce the probability of adaptive escape.

In short, RAS inhibitors turn the oncogenic engine off. PRP is designed to convert the remaining cells back toward a less dangerous epithelial identity and to dismantle the niche that protects them. The two approaches are biologically orthogonal.

Strategic Implication for RAS Inhibitor Developers

For companies such as Revolution Medicines and Erasca, durability — not only response rate — will define long-term competitive position as multiple RAS agents enter the same PDAC and NSCLC populations. Three practical implications follow from the EMT-reversal thesis:

- **Combination potential:** A RAS inhibitor plus an EMT-reversing, CSC-targeting agent could pair rapid cytoreduction with suppression of the cells most likely to seed resistance. PRP's non-cytotoxic differentiation mechanism and historically benign compassionate-use safety profile make it a candidate for add-on or maintenance designs that RAS companies are already exploring with chemotherapy, anti-EGFR antibodies, and RAS-doublet regimens (for example, zoldonrasib plus daraxonrasib).
- **Post-progression and maintenance use:** When tumors adapt to RAS blockade, mesenchymal drift and fibrotic remodeling are common escape routes. An agent that reverses EMT and reduces CAFs could be sequenced after RAS-inhibitor response to lock in epithelial differentiation and limit metastatic outgrowth.

- **Broader eligible population:** PRP is not genotype restricted. In mixed RAS-mutant / RAS-wild-type settings, or in tumors that lose RAS dependence after therapy, a differentiation backbone could extend benefit beyond the label of any single RAS agent.

Propanc is not announcing a partnership with Revolution Medicines or Erasca. The Company is putting the mechanistic case on record as it advances PRP into first-in-human development and as the RAS field looks beyond first-generation survival gains.

Clinical Path

Propanc plans to initiate a multicenter, open-label Phase 1b first-in-human study of PRP in February 2027 in up to 50 patients with advanced solid tumors, including pancreatic, ovarian, and refractory prostate cancers, at sites in Australia. The two-part design will use Bayesian optimal interval dose escalation with backfill, followed by tumor-specific expansion. PRP is planned as a weekly intravenous infusion on Days 1, 8, 15, and 22 of each 28-day cycle. GMP manufacture, pharmacokinetics assay validation, and ethics submissions are advancing in parallel.

“RAS inhibitors have rewritten what is possible in pancreatic and RAS-mutant lung cancer. That is a genuine inflection point for patients,” said James Nathanielsz, Propanc’s Chief Executive Officer. “Our thesis is that turning RAS off is necessary but may not be sufficient. The cells that survive RAS blockade are often the mesenchymal, stem-like cells that PRP differentiate and disarm. If that biology holds in the clinic, PRP could help RAS-focused companies convert high response rates into longer, cleaner remissions.”

“EMT is the program that lets a carcinoma leave home, hide, and return,” said Dr. Ralf Brandt, Propanc’s Research & Development Director. “PRP does not compete with daraxonrasib or ERAS-0015 at the GTPase. It reverses the downstream identity change those tumors used to resist almost every class of drug. That is why we see suppression of EMT markers, loss of CSC phenotypes, less fibrosis, fewer metastases, and more than a two-and-a-half-fold survival extension in PDAC models. Those are the exact liabilities a RAS inhibitor leaves on the table.”

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.

Company:
Propanc Biopharma, Inc.
James Nathanielsz

+61-3-9882-0780

info@propanc.com

Investor Contact:

irteam@propanc.com

Source: Propanc Biopharma, Inc.