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Propanc Biopharma Highlights Differentiated Proenzyme Therapy PRP as a Potential Therapy of Choice Against RAS-Driven Cancers

Contrasting Science with Revolution Medicines and Erasca

MELBOURNE, Australia, Aug. 12, 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 provided a scientific comparison of its lead candidate PRP with the RAS-targeted approaches of Revolution Medicines, Inc. and Erasca, Inc. The Company articulates why PRP’s unique mechanism—promoting cancer cell differentiation, reversing epithelial-mesenchymal transition (EMT), and targeting cancer stem cells via pancreatic proenzymes—positions it as a potential long-term therapy of choice, particularly for aggressive, treatment-resistant cancers such as pancreatic ductal adenocarcinoma (PDAC).

“As we enter a world first clinical study for the use of our lead asset, PRP, as a novel way to combat PDAC but also aggressive, less differentiated tumor types often associated with a poor patient prognosis, we felt it was an important opportunity to highlight that we are entering a transformative phase for these killer diseases which is unprecedented,” said Mr. James Nathanielsz, Propanc’s Chief Executive Officer. “Recent advances by Revolution Medicines and Erasca Inc. are tremendously exciting, but further improvements can be made with complementary treatment modalities such as PRP that target the way cancer cells become malignant, invasive and spread. PRP is a novel therapy that targets these dangerous cells but leaves healthy cells intact. Therefore, it is not cytotoxic. It does not involve an inhibitory approach which often leads to drug resistance, but proteolysis (protein breakdown) is the basis for enforcing cancer cells to express certain pathways that induce differentiation so that they return to a normal state and die naturally. We expect to file a clinical trial application for the Phase 1b clinical study in advanced cancer patients in Q4 this year and are confident of replicating the successful peer reviewed, published results obtained in preclinical models and clinical observations from terminal patients treated at much lower doses for up to 18 months in a previous compassionate use study. We look forward to generating meaningful data demonstrating PRP as a long-term treatment option for metastatic cancer from solid tumors.”

Propanc's Science: Proenzyme-Driven Differentiation and Metastasis Suppression

PRP is a proprietary fixed-ratio combination of pancreatic proenzymes trypsinogen and chymotrypsinogen, administered once weekly by intravenous injection. Unlike cytotoxic agents or pathway inhibitors that directly kill dividing cells or block signaling, PRP activates upon administration to induce differentiation of malignant cells toward a more normal

phenotype (cellular characteristics).

Key effects include:

- Reversal of EMT, reducing invasive and stem-like properties of cancer cells.
- Suppression of metastasis, angiogenesis, and tumor microenvironment support (including effects on cancer-associated fibroblasts).
- Enhanced cell adhesion and promotion of natural cell death pathways.
- Favorable preclinical activity: >90%, mean tumor growth inhibition in orthotopic and patient-derived xenograft (PDX) models of advanced PDAC, marked reduction in metastatic burden (liver and peritoneum), and >2.5-fold extension of median overall survival versus controls ($p < 0.001$). PRP has also shown potential to resensitize chemo-resistant PDAC cells to standard agents such as gemcitabine/nab-paclitaxel at lower doses.

PRP holds FDA Orphan Drug Designation for pancreatic cancer. Limited prior compassionate-use experience with related proenzyme formulations showed signals of prolonged survival in advanced solid-tumor patients without severe treatment-related adverse events. The Company is advancing toward a Phase 1b first-in-human study in up to 40 – 45 patients with advanced solid tumors (focus on PDAC and other high-unmet-need indications), with GMP manufacturing and clinical partnerships progressing in 2026.

Revolution Medicines (RVMD): RAS(ON) Tri-Complex Inhibitors

RVMD develops a portfolio of RAS(ON) inhibitors that target the active, GTP-bound state of mutant (and in some cases wild-type) RAS proteins via a cyclophilin A tri-complex mechanism. Lead assets include daraxonrasib (RMC-6236), a multi-selective RAS(ON) inhibitor; allele-selective inhibitors such as zoldonrasib (RMC-9805, G12D-selective) and others targeting G12C and G12V; and emerging catalytic RAS(ON) approaches designed to stimulate GTP hydrolysis.

These agents block RAS-effector interactions, suppress downstream MAPK and other signaling, and have demonstrated robust preclinical and clinical activity, including statistically significant overall survival and progression-free survival benefits versus chemotherapy in previously treated metastatic PDAC (e.g., Phase 3 RASolute 302 data for daraxonrasib). They address a major oncogenic driver present in ~90%+ of PDAC, substantial fractions of NSCLC and colorectal cancer, and other RAS-addicted tumors. Limitations can include pathway reactivation/resistance mechanisms, on-target effects on wild-type RAS in normal tissues, and the need for continuous pathway suppression

Erasca (ERAS): RAS/MAPK Pathway Clamping and Direct RAS Targeting

Erasca focuses on the RAS/MAPK pathway with a modality-agnostic strategy. Key approaches include MAPKlamp (upstream SHP2 and downstream ERK inhibition to “clamp” signaling), direct RAS targeting via pan-RAS molecular glues such as ERAS-0015 (which forms a ternary complex with cyclophilin A and active RAS to block effector engagement), pan-KRAS inhibitors, and agents addressing escape routes (e.g., EGFR).

ERAS-0015 has shown early clinical signals of antitumor activity in RAS-mutant solid

tumors, including encouraging unconfirmed response rates in KRAS G12X NSCLC and PDAC cohorts, with pharmacodynamic evidence of target engagement (ctDNA reductions). The pipeline aims for broad coverage of RAS/MAPK alterations and resistance mechanisms. Like other targeted pathway inhibitors, challenges include incomplete pathway shutdown, adaptive resistance, and managing toxicity from multi-node inhibition.

Comparison and Contrast

Aspect	Propanc (PRP)	RVMD (RAS(ON) inhibitors)	Erasca (MAPKlamp / pan-RAS glues)
Primary Target	Cancer stem cells, EMT, differentiation	Active RAS(ON) proteins	RAS/MAPK nodes (SHP2, ERK, RAS itself)
Mechanism	Proenzyme-induced phenotypic reprogramming; metastasis suppression	Steric blockade of RAS-effector binding via tri-complex	Pathway clamping or molecular glue inhibition of RAS signaling
Breadth	Solid tumors broadly (stem-like/metastatic phenotype); not mutation-specific	RAS-mutant cancers (multi- or allele-selective)	RAS/MAPK-altered cancers
Toxicity Profile	Favorable in limited human experience; non-cytotoxic	Manageable but on-target pathway effects	Generally well-tolerated in early data; multi-node considerations
Resistance Risk	Targets upstream biology of aggressiveness rather than single pathway	Pathway reactivation / bypass possible	Escape routes actively addressed but still pathway-dependent
Administration	Once weekly IV	Oral (daily)	Oral
Stage	Preclinical/translational → Phase 1b FIH planned	Late-stage clinical / NDA pathway for some assets	Early-to-mid clinical

RVMD and Erasca represent important advances in directly targeting the long, “undruggable” RAS oncogene and its downstream pathway—addressing a core driver of many solid tumors. Their science is highly complementary to conventional chemotherapy and emerging combinations. However, both remain fundamentally pathway-centric: they suppress oncogenic signaling but do not inherently reverse the stem-like, mesenchymal, metastatic phenotype that drives recurrence and treatment failure, especially in PDAC and other aggressive cancers.

Propanc’s PRP operates at a different biological layer. By promoting differentiation and reversing EMT, it aims to reduce the reservoir of cancer stem cells responsible for resistance, dormancy, and dissemination. Preclinical data showing high tumor growth inhibition, metastatic burden reduction, survival extension, and potential chemo-sensitization support the hypothesis that PRP could serve as a backbone or sequential therapy—potentially enhancing durability when combined with RAS pathway inhibitors or used in maintenance settings where chronic, low-toxicity treatment is desirable.

Why PRP Could Prove the Therapy of Choice

For patients with advanced or high-risk solid tumors – particularly those with limited options

after progression on chemotherapy or targeted agents – PRP's profile offers several potential advantages:

1. Non-cytotoxic, a differentiation-based approach that may spare normal tissues while addressing the root drivers of metastasis and recurrence.
2. Broad applicability across solid tumors (80–90% of cancers) without requiring specific RAS mutations.
3. Favorable tolerability supporting long-term or intermittent use, critical for preventing relapse.
4. Synergy potential with existing standards of care and emerging RAS inhibitors (chemo-sensitization data already observed).
5. Orphan designation and focused development in PDAC, an indication with profound unmet need where both RVMD and Erasca are also active.

Propanc believes that while RAS(ON) and RAS/MAPK-targeted agents will transform outcomes for many patients by hitting the oncogenic switch, therapies that reprogram the malignant phenotype itself may ultimately deliver more durable control and improved quality of life. As PRP advances into the clinic, the Company looks forward to generating human data that will further clarify its role—potentially as a foundational, long-term option in the evolving treatment landscape for metastatic solid tumors.

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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