ASX Release
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A landmark in non-invasive Esophageal Cancer diagnosis - new PromarkerEso blood test clinical validation results published

- **First-in-class PromarkerEso blood test identifies esophageal adenocarcinoma with high accuracy**
- **Proteomics International's novel serum glycoprotein biomarker based test shows 91.4% sensitivity and 98.9% specificity in clinical validation study**
- **Esophageal adenocarcinoma is commonly caused by chronic acid reflux or GERD, a condition that is estimated to impact 10-20% of Western populations**
- **Results from a study of 259 participants across three independent cohorts published overnight in the peer-reviewed journal *Proteomes***
- **Current screening requires a specialist endoscopy procedure and the annual expenditure on treating esophageal cancer in the US is $2.9 billion**
- **Global health impact: currently 90% of esophageal adenocarcinoma cases go undetected - improved surveillance of at-risk patients using PromarkerEso could enable earlier diagnosis and significantly improve health outcomes**
- **Commercialisation of PromarkerEso in Australia is expected shortly, with other jurisdictions to follow**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ), a pioneer in precision diagnostics is pleased to announce the publication of clinical validation results in the journal *Proteomes* showing its PromarkerEso blood test can diagnose esophageal adenocarcinoma with high accuracy. This publication marks a significant milestone in the Company's efforts to advance non-invasive diagnostic solutions for this challenging disease.

Esophageal adenocarcinoma (EAC), the predominant form of esophageal cancer, is commonly caused by chronic acid reflux, also known as gastroesophageal reflux disease (GERD), and is often asymptomatic in its early stages. In Australia, the Royal Australian College of General Practitioners (RACGP) has reported that 11.6% of all GP clinic visits were for the management of gastric reflux[1] and it is estimated that 10-20% of Western populations have GERD[2].

For individuals living with GERD regular endoscopy surveillance is recommended to monitor for potential development of EAC. In the United States 6.1 million upper endoscopies are performed annually[3], however, these invasive procedures can be uncomfortable and costly for patients (US$2,750 in the United States[4]) and despite this surveillance up to 90% of EAC cases continue to go undetected[5]. As a result, many

[1] www.racgp.org.au/afp/2015/october/gastro-oesophageal-reflux-disease-gord-in-australia

[2] www.yalemedicine.org/conditions/gerd-gastroesophageal-reflux-disease

[3] Gastroenterology, 2019; doi: 10.1053/j.gastro.2018.08.063

[4] www.newchoicehealth.com/endoscopy/cost

[5] *Diseases of the Esophagus,* 2025, doi: 10.1093/dote/doaf038

diagnoses occur late, leading to poor prognosis and limited treatment options.

Proteomics International Managing Director Dr Richard Lipscombe said, "*The published results represent a major advancement in our mission to transform the lives of people living with chronic acid reflux. PromarkerEso has the potential to revolutionise how doctors manage the risk of esophageal cancer - offering a standard blood test that could reduce reliance on invasive procedures and improve early detection rates.*"

Esophageal cancer represents a critical global health challenge, ranking seventh in cancer-related mortality and eleventh in overall prevalence. The five-year survival rate for EAC is less than 20% with median survival time less than one year[6] and in the USA the cost of treating EAC totalled US$2.9 billion in 2018[7]. With the growing incidence of EAC, there is an urgent need for a more efficient, accurate, and patient-friendly diagnostic pathway.

The first-in-class PromarkerEso blood test provides a clear and simple 'traffic light' risk score - low, moderate, or high - indicating the likelihood of EAC for any patient, helping guide clinical decision-making. PromarkerEso is designed as a high-margin cost-effective test that is anticipated to garner significant interest, in particular in the USA, from end-users, clinicians and potential partners.

The results, derived from the analysis of 259 serum samples across three independent patient cohorts from Australia and the USA, validate the performance of the PromarkerEso test in detecting EAC. Proteomics International scientists, in collaboration with researchers from QIMR Berghofer Medical Research Institute, Flinders University and Emory University (Georgia, USA), compared cases of EAC with controls. The test delivered extremely strong diagnostic performance for disease detection, demonstrating 91.4% sensitivity and 98.9% specificity in a 147 person clinical validation study (AUC 0.98).

Professor Hugh Barr, MD, a world-renowned expert in esophageal cancer and Consultant General & Gastrointestinal Surgeon, Gloucestershire Hospitals NHS Foundation Trust, UK said, *"The early, prompt detection and precise risk assessment of esophageal adenocarcinoma will enable curative treatment for this disease. Advanced diagnostics, in particular PromarkerEso, are proving to be an important and effective way to transform the outcomes for our patients."*

The results, published overnight in *Proteomes*, a leading peer-reviewed journal for proteomics-based scientific advancements, build upon and extend earlier studies which demonstrated the potential of the test for diagnosing esophageal adenocarcinoma in different patient groups [ASX: 8 September 2023, 1 February 2024, 23 September 2024].

Next steps

- Commercialisation of PromarkerEso in Australia is expected shortly, with other jurisdictions to follow.
- The launch will leverage the Direct to Consumer (DTC) framework built for other Promarker tests, and in parallel target primary care (GP's) and patients at risk of EAC.
- Analytical methodology is being certified for use in a clinical environment under the ISO 15189 (clinical testing) pathway.
- Continuing to build awareness of the test with clinicians, key opinion leaders (KOL's) [ASX: 7 April] and advocacy groups in response to the growing incidence and awareness of GERD.

PromarkerEso is one of multiple assets in Proteomics International's pipeline of precision diagnostics and represents a substantial commercial opportunity in the public health market.

[6] Nature Reviews Gastroenterology & Hepatology, 2021, doi.org/10.1038/s41575-021-00419-3

[7] JAMA Netw Open, 2021;. doi:10.1001/jamanetworkopen.2021.27784

Summary of Study

Published in the journal *Proteomes* (advance article available online)[8].

> Titled: *"Clinical validation of a diagnostic test for esophageal adenocarcinoma based on a novel serum glycoprotein biomarker panel: PromarkerEso"*
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> Authors: J Sheahan[1], I Wang[1], P Galettis[1], D Watson[2], V Joshi[3], M Hill[4], R Lipscombe[1] S Bringans[1]
> [1] Proteomics International, Perth, WA; [2] Flinders University, Adelaide, SA; [3] Emory University, Atlanta, Georgia, United States; [4] QIMR Berghofer Medical Research Institute, Brisbane, Qld.

Aim: To clinically validate the performance of the PromarkerEso diagnostic test in patients with esophageal adenocarcinoma (EAC) against negative controls (NC) and healthy controls (HC).

Method: The PromarkerEso test measured the concentration of 4 glycoprotein biomarkers: alpha-1-antitrypsin, alpha-1-antichymotrypsin, complement C9, and plasma kallikrein, combined with a patient's age, sex and BMI using a logistic regression model. Glycoproteins were extracted from a standard blood sample using a lectin pull-down assay and their concentrations determined by mass spectrometry. The test output is the predicted probability score (from 0-100%) of the likelihood of EAC, with classification of samples into low-, moderate- and high-risk categories.

The test was developed by comparing N=48 EAC patients (confirmed positive by endoscopy) versus N=40 NC (confirmed negative by endoscopy) from the PROBE-NET Study, Australia (the 'development cohort'). Diagnostic performance of PromarkerEso was then assessed in two independent validation cohorts (N=10 EAC, N=14 NC [Ochsner Health System, USA] and N=58 EAC, N=89 HC [Victoria Cancer Biobank (VCB), Australia].

Results: The PromarkerEso test demonstrated excellent discrimination in diagnosing EAC when compared against negative controls and healthy population controls across all three patient cohorts:

Promarker®Eso performance: esophageal adenocarcinoma vs controls (number of patients vs controls)	AUC	Sensitivity (Sn)(%)	Specificity (Sp) (%)
Development cohort (N=48 EAC vs 40 NC)	0.91	97.9	87.5
Validation cohort 1 (N=10 EAC vs 14 NC)	0.82	100	85.7
Validation cohort 2 (N=58 EAC vs 89 HC)	0.98	91.4	98.9

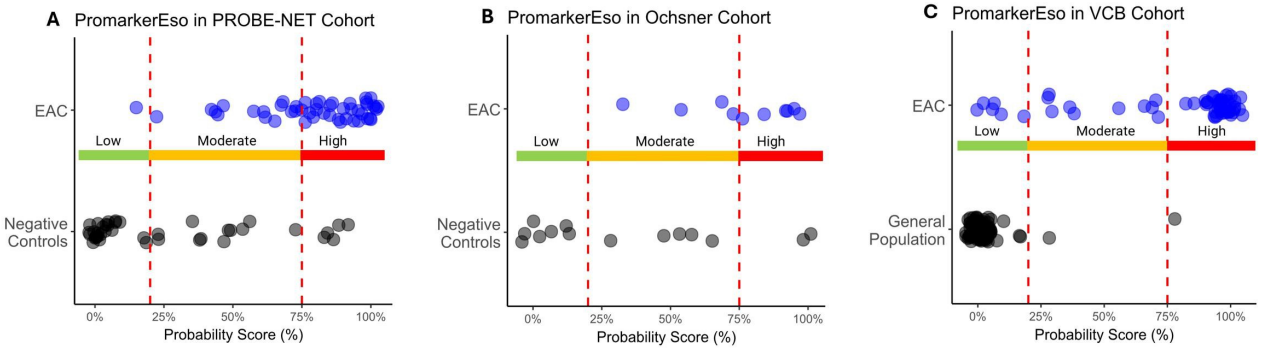

Figure: PromarkerEso distribution of esophageal adenocarcinoma (EAC) and control sample probability scores.
Results are classified into Low-, Moderate- and High-Risk categories: (A) development cohort (PROBE-NET), (B) validation cohort 1 (Ochsner), (C) validation cohort 2 (VCB).
Actual outcomes are represented as blue dots (EAC) and black dots (Negative Controls or General Population). Lower and upper cutoffs (20% and 75% respectively) are represented by the red dotted lines.

Conclusions:

- The PromarkerEso test provides highly accurate diagnosis of EAC versus negative and healthy controls via a novel combination of glycoprotein biomarkers.

[8] Proteomes: www.mdpi.com/2227-7382/13/2/23

- The traffic light risk category design of PromarkerEso enhances predictive accuracy while mitigating uncertainty in mid-range probability predictions, with elevated sensitivity and specificity at lower and upper cutoffs respectively.
- Future studies are required to assess the performance of PromarkerEso in different stages of cancer and applicability in broader demographic groups.
- This study highlights the potential of PromarkerEso as a tool to enhance the standard diagnostic framework for EAC, and a step towards improving patient care in this challenging disease.

Glossary

Sensitivity (Sn) (true positive rate)	The ability of a test to correctly identify those with the disease. E.g. sensitivity of 80% means that for every 100 people with disease, the test correctly diagnosed 80 with the condition.
Specificity (Sp) (true negative rate)	The ability of the test to correctly identify those without the disease. E.g. specificity of 75% means that for every 100 people without disease, a test correctly identifies 75 as not having the condition.
Negative Predictive Value (NPV)	The probability that people who get a negative test result truly do not have the disease. Also known as 'rule-out' rate, it is the probability that a negative test result is accurate.
Positive Predictive Value (PPV)	The probability that a patient with a positive (abnormal) test result actually has the disease.
Probability (P)	The *P* value, or calculated *probability*, that an observation is true. Most authors refer to statistically significant as $P < 0.05$ and statistically highly significant as $P < 0.001$ (less than one in a thousand chance of being wrong).
AUC	"Area Under the ROC Curve". A receiver operating characteristic curve, or ROC curve, is a graphical plot that illustrates the performance of a classifier system.
Interpreting AUC values	Conventionally the clinical significance of AUC is: > 0.7 acceptable discrimination > 0.8 excellent discrimination > 0.9 outstanding discrimination

For comparison, the statistical performance of the Prostate-Specific Antigen (PSA) diagnostic test (blood test measuring the concentration of the PSA protein) for the diagnosis of prostate cancer is[9]:

- Prostate cancer versus no cancer: AUC 0.68
- PSA cut-off threshold 3ng/ml: Sensitivity 32%, Specificity 87%

Authorised by the Board of Proteomics International Laboratories Ltd (ASX: PIQ).

ENDS

About Promarker®Eso

PromarkerEso is a first-in-class blood test that utilises biomarkers—'fingerprints' in the blood—to measure the risk of having EAC. The test that combines four key glycoproteins (alpha-1-antitrypsin, alpha-1-antichymotrypsin, complement C9, and plasma kallikrein) with patient clinical factors age, sex, and body mass index (BMI). These are analysed through a proprietary algorithm to generate an EAC risk score, classifying individuals as low-, moderate-, or high-risk for the disease. Patients identified as high risk of having EAC are recommended for an endoscopy. Promarker Eso has patents granted in Europe, China and Australia, with other territories pending.

About Proteomics International Laboratories (PILL) (www.proteomicsinternational.com)

Proteomics International (Perth, Western Australia) is a wholly owned subsidiary and trading name of PILL (ASX: PIQ), a medical technology company at the forefront of precision diagnostics and bio-analytical

[9] pubmed.ncbi.nlm.nih.gov/15998892/; JAMA. 2005 Jul 6;294(1):66-70; doi: 10.1001/jama.294.1.66

services. The Company specialises in the area of proteomics – the industrial scale study of the structure and function of proteins. Proteomics International's mission is to improve the quality of lives by the creation and application of innovative tools that enable the improved treatment of disease.

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