ASX Release
8 September 2023

ASX code: PIQ

Proteomics' new oesophageal cancer test presented at global conference

- **Proteomics International's new Promarker*Eso* blood test shows strong discrimination of oesophageal cancer**
- **Test targets both oesophageal adenocarcinoma and patients with pre-malignant condition Barrett's oesophagus which affects 1-2% of adults and can arise from chronic acid reflux**
- **Advanced discrimination system correctly identified 89% of patients with oesophageal adenocarcinoma and 92% of patients without the disease**
- **Latest results presented tomorrow at the 19th ISDE World Congress for Esophageal Diseases in Toronto, Canada**
- **Oesophageal cancer is the 6th leading cause of cancer-related mortality, the 7th most common cancer globally and has a 20% five-year survival rate**
- **Current screening requires a specialist endoscopy procedure and the annual expenditure on treating oesophageal cancer in the US is $2.9 billion**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ) is pleased to announce its latest results for its novel blood test for oesophageal adenocarcinoma will be presented tomorrow at the 19th ISDE World Congress for Esophageal Diseases in Toronto, Canada, held 8-10 September 2023. The conference presentation builds upon earlier work which identified and validated a panel of glycoprotein biomarkers using 300 samples from two independent clinical cohorts [ASX: 27 September 2022].

Oesophageal adenocarcinoma is the most common form of oesophageal cancer with a five-year survival rate of approximately 20%. Oesophageal cancer and its pre-malignant condition Barrett's oesophagus can develop from chronic acid reflux. One in twenty cancer deaths worldwide in 2018 were attributed to oesophageal cancer[1].

Proteomics International Managing Director Dr Richard Lipscombe said the prototype test, named Promarker*Eso*, was now showing strong discrimination at early and late stages of the disease. "*We've refined our diagnostic models to correctly identify 89% of patients with oesophageal adenocarcinoma and 92% of patients without the disease. This means we could have a simple blood test to determine who would benefit from an endoscopy. We believe that such a test would garner significant clinical and commercial interest should it be further validated.*"

Screening for oesophageal adenocarcinoma currently requires a specialist endoscopy procedure that costs US$2,750 per patient in the United States[2], where the total expenditure on treating oesophageal cancer was

[1] Nature Reviews Gastroenterology & Hepatology, 2021, doi.org/10.1038/s41575-021-00419-3
[2] www.newchoicehealth.com/endoscopy

$2.9 billion in 2018[3]. This cancer represents an area of significant unmet medical need, and the Company believes there is large market potential for a simple diagnostic test.

The new results apply Proteomics International's 'traffic light' scoring system to categorise patients as green (low risk), amber (moderate risk) or red (high risk) for oesophageal adenocarcinoma. The results also suggest some individuals may have been misdiagnosed, although further work is required to confirm this.

Proteomics International's test uses biomarkers—protein 'fingerprints' in the blood—to diagnose both oesophageal adenocarcinoma and Barrett's oesophagus. An estimated 10-15% of patients with chronic acid reflux develop Barrett's oesophagus, a condition which is asymptomatic and affects 1-2% of Western populations[4]. People with Barrett's oesophagus are much more likely to get oesophageal adenocarcinoma, and are advised to get regular endoscopies to screen for oesophageal cancer [PIQ Annual Report 2022].

Engaging with Key Opinion Leaders (KOLs) who could guide early adoption of Promarker*Eso* is an important objective for the Company in attending the conference. These potential relationships would build upon Proteomics International's recent agreement to access 350 additional patient samples from the Victorian Cancer Biobank [ASX: 23 July 2023]. The cohort comprises blood samples from oesophageal and other selected cancer patients. These samples will be used for external validation of the accuracy of the Company's current prototype oesophageal cancer test, with results expected early next year.

Dr Lipscombe said the next steps in commercialising the Promarker*Eso* test are to:

- streamline the biomarker measurements to produce a test suitable for the US Laboratory Developed Test (LDT) pathway via CLIA certified clinical laboratories;
- confirm the clinical performance of the test in an additional independent patient cohort; and
- conduct formal Economic Health Benefit Modelling and Clinical Utility Studies to demonstrate how the new test could significantly change doctors' treatment decisions and improve outcomes for patients and healthcare systems.

The Company anticipates that these steps will be completed over the next 9 months.

International Society for Diseases of the Esophagus 19th World Congress 2023, Oral presentation OA05.04
[copy attached; summary below]

Titled: *A novel serum glycoprotein biomarker panel for screening of esophageal adenocarcinoma and surveillance of Barrett's esophagus*

Richard Lipscombe[1], Marisa Duong [1],Tammy Casey [1], Gareth Fernandez [1], Scott Bringans[1], Kirsten Peters [1], Michelle Hill[2], Pearl Tan [1], Lianzhi Chen [1]
[1] Proteomics International, Perth, WA, Australia;
[2] QIMR Berghofer Medical Research Institute, Brisbane, Qld, Australia

Summary of the Diagnostic Test Development and Validation Study

Method: To generate the diagnostic test Proteomics International's scientists analysed clinical samples from a development cohort of 249 people collected by the Progression of Barrett's Esophagus to Cancer Network (PROBE-NET, Australia). Patients were classified as having esophageal adenocarcinoma [EAC]; positive for Barrett's esophagus [BE+] and BE with low grade dysplasia; Barrett's esophagus with high grade dysplasia (severely abnormal cells) [BE-HGD]; negative controls. A series of statistical models were then built using protein biomarkers to attain optimal diagnostic performance in the development cohort. The performance of the statistical models was then tested in an independent validation cohort of 49 patient samples from the Ochsner Health System in New Orleans, United States.

Results:
Robust assay method for measuring the glycoprotein biomarkers developed (intraday CV = 9.3%; interday CV = 11.5%) suitable for use as a Laboratory Developed Test (LDT) via a specialist CLIA (US) certified clinical laboratory.

Panel of glycoprotein biomarkers confirmed that showed significant correlation with disease progression.

[3] JAMA Network Open, 2021, doi:10.1001/jamanetworkopen.2021.27784
[4] American Society for Gastrointestinal Endoscopy, www.asge.org

Diagnostic model for discriminating disease severity performed strongly in the validation cohort:

- For negative controls vs EAC: Area Under the Curve (AUC) 0.94, Sensitivity (Sn) 80%, Specificity (Sp) 93%.
- For negative controls vs EAC and BE-HGD: AUC 0.79, Sn 59%, Sp 93%.

Comment: these tests offer the potential to provide an early screening tool to minimise the requirements for an endoscopy.

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[5]:

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

Conclusions: A diagnostic test has been developed using novel serum glycoprotein biomarkers to provide a potential screening tool for both esophageal adenocarcinoma and Barrett's esophagus with high grade dysplasia.

In interpreting these results it is important to recognise that the total cohort size is 300 patients and the validation cohort is relatively small. Consequently, further work in additional patient samples is required to confirm the clinical accuracy of the Promarker*Eso* test.

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 oesophageal cancer, 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 with symptoms but no oesophageal cancer, 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. In other words, 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

Proteomics International is currently rolling-out PromarkerD, a simple blood test for predicting diabetic kidney disease. The Company also has advanced research programs targeting novel diagnostics for endometriosis, oxidative stress, asthma and COPD.

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

ENDS

About the Promarker™ Platform

Proteomics International's diagnostics development is made possible by the Company's proprietary biomarker discovery platform called Promarker, which searches for protein 'fingerprints' in a sample. This disruptive technology can identify proteins that distinguish between people who have a disease and people who do not, using only a simple blood test. It is a powerful alternative to genetic testing. The technology is so versatile it can be used to identify fingerprints from any biological source, from wheat seeds to human

[5] pubmed.ncbi.nlm.nih.gov/15998892/

serum. The Promarker platform was previously used to develop PromarkerD, a world-first predictive test for diabetic kidney disease, that is currently being commercialised. Other tests in development include for asthma & COPD, oesophageal cancer, diabetic retinopathy and oxidative stress.

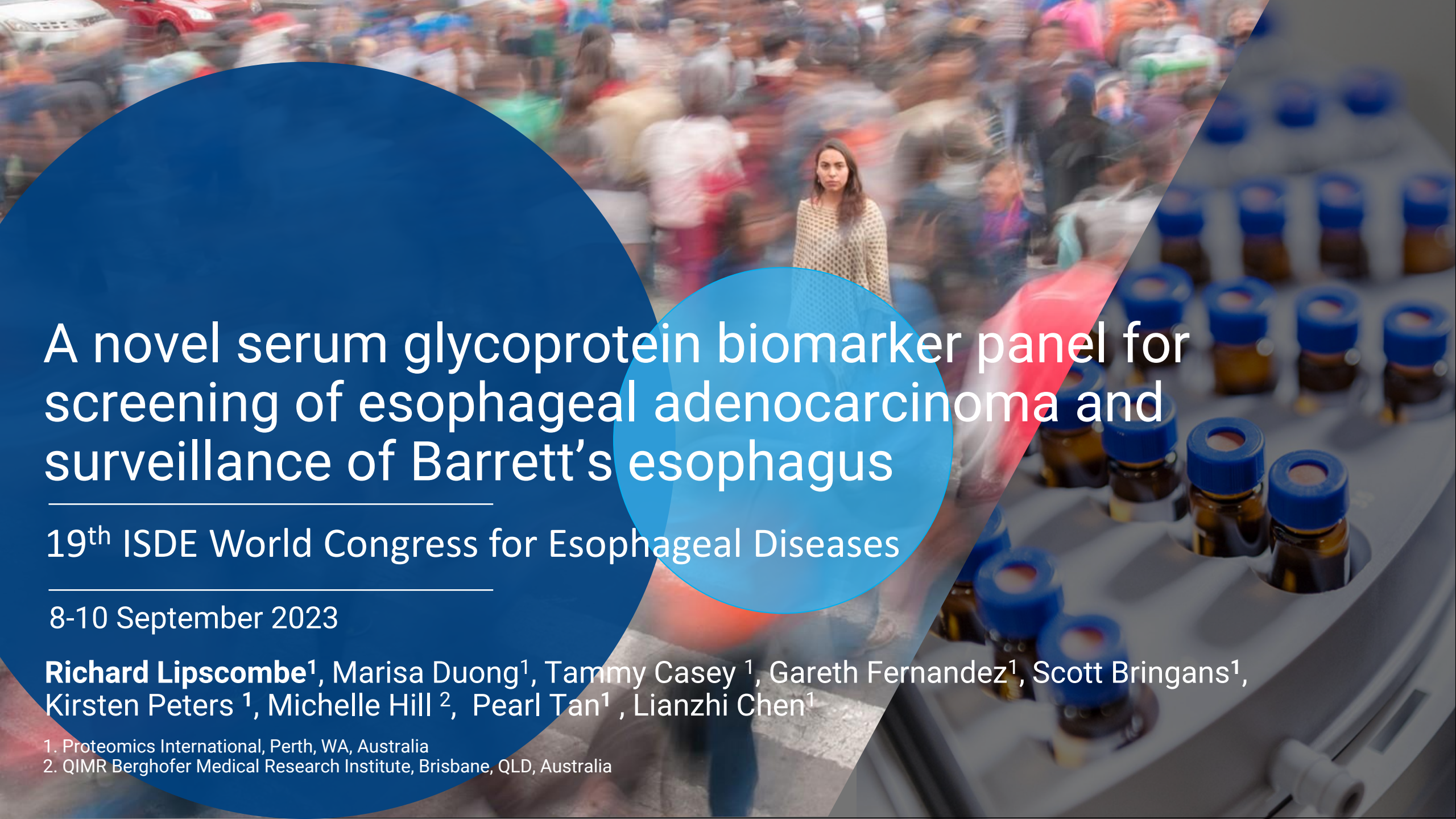
About Proteomics International Laboratories (PILL) (www.proteomicsinternational.com)
Proteomics International (Perth, Western Australia) is a wholly owned subsidiary and trading name of PILL (ASX: PIQ), a medical technology company at the forefront of predictive diagnostics and bio-analytical services. 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.

For further information please contact:

Dr Richard Lipscombe
Managing Director
Proteomics International Laboratories Ltd
T: +61 8 9389 1992
E: enquiries@proteomicsinternational.com

Dirk van Dissel
Investor Relations & Corporate Advisor
Candour Advisory
T: +61 408 326 367
E: dirk@candouradvisory.com.au

Kyle Moss
Corporate Advisor
Euroz Hartleys
T: +61 8 9488 1400
E: kmoss@eurozhartleys.com



A novel serum glycoprotein biomarker panel for screening of esophageal adenocarcinoma and surveillance of Barrett's esophagus

19th ISDE World Congress for Esophageal Diseases

8-10 September 2023

Richard Lipscombe[1], Marisa Duong[1], Tammy Casey [1], Gareth Fernandez[1], Scott Bringans[1], Kirsten Peters [1], Michelle Hill [2], Pearl Tan[1] , Lianzhi Chen[1]

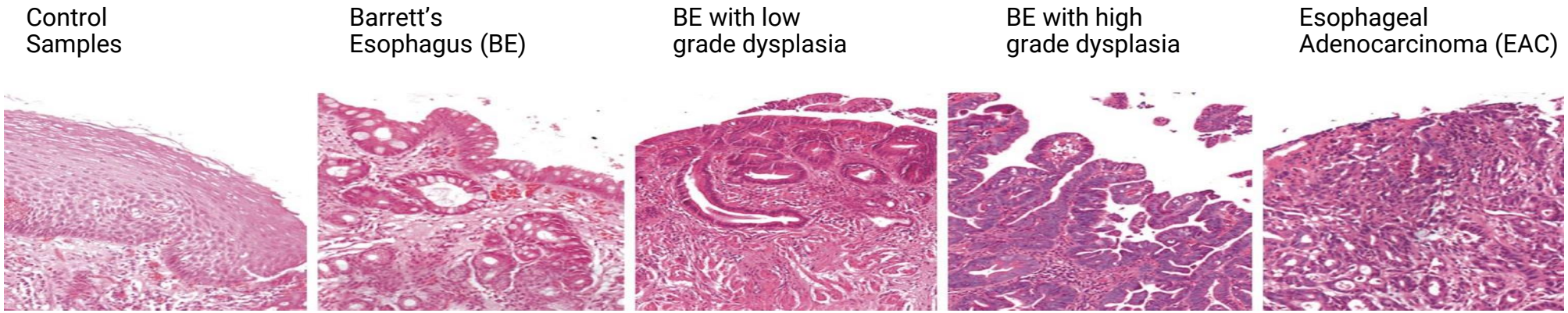
1. Proteomics International, Perth, WA, Australia
2. QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia

Disclosures

- The biomarker concentrations were measured by Proteomics International, and the risk scores were calculated using a proprietary algorithm
- This analysis used archived samples received via a collaboration with the QIMR Berghofer Medical Research Institute
- The study was funded by Proteomics International
- Presenter disclosures: Lipscombe is an employee and shareholder of Proteomics International Laboratories Ltd, which is the license owner of a patent covering the use of the biomarkers, consequently, Lipscombe may receive financial benefit from the commercial use of any test

Introduction

- The overall five-year survival rate for esophageal cancer is approximately 20%
- An estimated 10-15% of patients with chronic acid reflux develop Barrett's Esophagus (BE), which has estimated prevalence of 1-2%.
- Currently patients with BE usually undergo endoscopy-biopsy surveillance with the degree of dysplasia assessed by histology



Aim

- **To develop a simple blood test for the diagnosis of esophageal adenocarcinoma (EAC) and Barrett's Esophagus (BE)**
- **To validate diagnostics models to screen EAC and BE based on a panel of glycoprotein biomarkers**

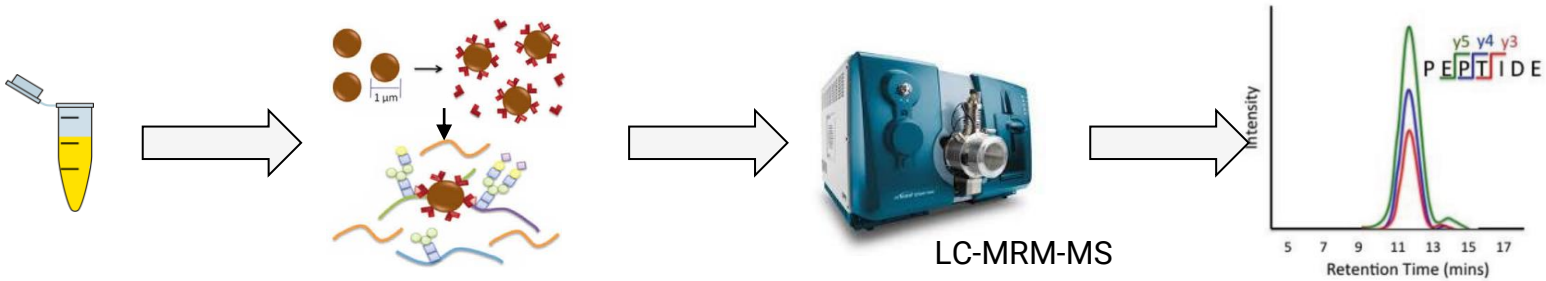
Study Design

- **Development cohort (N=249):** Participants from The Progression of Barrett's Esophagus to Cancer Network (PROBE-NET) study, Australia
- **Validation cohort (N=49):** Participants collected at Ochsner Healthy System, New Orleans, United

Group 1 - Controls Samples with normal endoscopy	Group 2 BE without/with low grade dysplasia	Group 3 BE with high grade dysplasia	Group 4 Esophageal Adenocarcinoma

Samples tested by endoscopy and biopsy

- Potential biomarkers analysed using a proteomics workflow, adapted for **glycoprotein** selection using a lectin magnetic bead array followed by targeted mass spectrometry (LC-MRM-MS)
- Multivariate regression performed



Serum | Bead-lectin capture | Analyse | Quantify

Robust
- Intraday CV is 9.3%
- Interday CV is 11.5%

Results - I

Development cohort (N=249)

- Five **glycoproteins** were found to show statistical correlation with disease state progression
- Three of these proteins remained significant after adjusting for patient age and sex

Validation cohort (N=49)

Controls versus EAC (Group 1 vs Group 4):

Model performance (N=24)	
Validation cohort:	
AUC (95% CI)	0.94 (0.85 – 1.00)
Sensitivity (%)	80%
Specificity (%)	93%
PPV(%)	89%
NPV(%)	87%

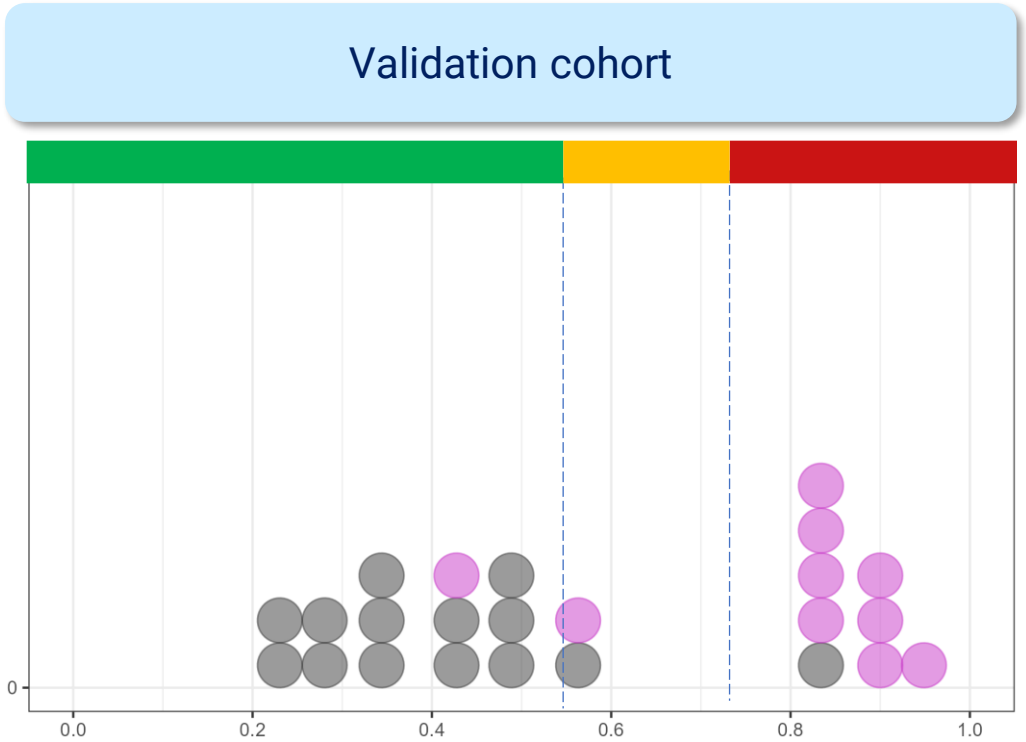
Controls versus BE-HGD & EAC (Group 1 vs Group 3+4):

Model performance (N=31)	
Validation cohort:	
AUC (95% CI)	0.79 (0.70 – 0.88)
Sensitivity (%)	59%
Specificity (%)	93%
PPV(%)	91%
NPV(%)	65%

Results - II

Controls versus EAC (Group 1 vs Group 4):

Frequency dot plot of Control and EAC



n = 14 controls

n = 10 EAC

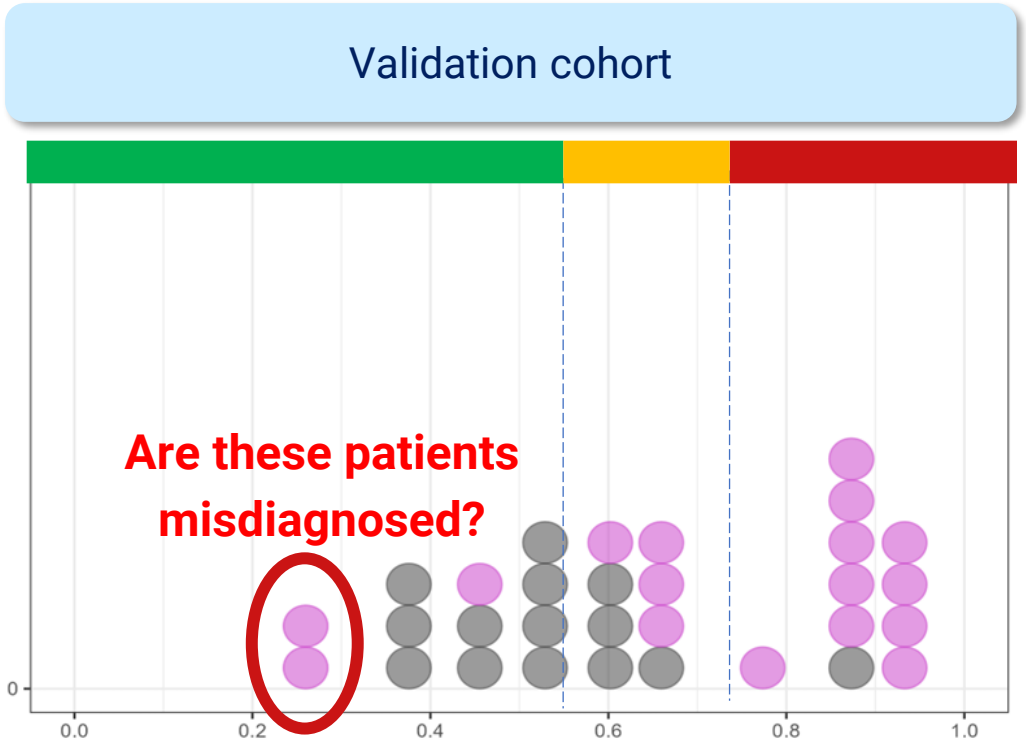
Classification	EAC	Controls	Accuracy
Red High probability	8	1	89%
Amber Moderate	1	1	
Green Low probability	1	12	92%

Traffic light system indicates if a patient is at risk of having EAC

Results - III

Controls versus BE-HGD & EAC (Group 1 vs Group 3+4):

Frequency dot plot of Control and BE-HGD & EAC



n = 14 controls

n = 17 BE-HGD & EAC

Classification	BE-HGD & EAC	Controls	Accuracy
Red High probability	10	1	91%
Amber Moderate	4	4	
Green Low probability	3	9	75%

Traffic light system indicates if a patient is at risk of having BE-HGD & EAC

Conclusions

- Panel of novel serum biomarkers (glycoproteins) were validated as showing significant correlation with esophageal adenocarcinoma and Barrett's esophagus with *high* grade dysplasia
- Diagnostic model developed as a potential simple screening tool for differentiating patients:
  - with EAC from negative controls
  - who required endoscopic surveillance (BE-HGD & EAC) from negative controls

- Further work required on larger cohorts to:
  - confirm diagnostic accuracy of test
  - establish a potential diagnostic tool to differentiate patients who require endoscopic surveillance (BE-HGD & EAC) from patients having BE with *low* grade/no dysplasia

Thank you!

Contact

E: biomarkers@proteomics.com.au

www.proteomics.com.au

Proteomics International

Esophageal Cancer PromarkerEso

Endometriosis PromarkerEndo

Diabetic Kidney Disease PromarkerD