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A Breakthrough in Endometriosis Diagnosis - new PromarkerEndo blood test results published

- **Plasma protein biomarker panel identifies all stages of endometriosis with high accuracy**
- **Refined PromarkerEndo blood test able to distinguish healthy individuals and symptomatic cases from early stages of disease**
- **A prototype PromarkerEndo model achieved excellent diagnostic performance across earlier disease stages and a near perfect accuracy in distinguishing severe endometriosis from symptomatic controls**
- **Results from a study of 805 participant samples published in the prestigious medical journal *Human Reproduction***
- **The test has potential application in the context of fertility where there is approximately a three-fold increased incidence of endometriosis in otherwise healthy women undergoing fertility treatments**
- **Endometriosis affects one in nine women and girls and currently diagnosis typically takes an average of 7 years**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ), a pioneer in precision diagnostics is pleased to announce the publication of new results in the journal *Human Reproduction* showing its PromarkerEndo blood test can diagnose all stages of endometriosis with high accuracy.

Endometriosis, a chronic condition affecting millions of women worldwide, often takes an average of seven years to diagnose due to the reliance on invasive laparoscopy. The new study has identified a breakthrough: a novel panel of 10 plasma protein biomarkers that could revolutionise the diagnosis of this debilitating disease.

Proteomics International scientists, in collaboration with the Royal Women's Hospital and the University of Melbourne, analysed plasma samples from 805 participants across two independent clinical populations, comparing cases of endometriosis, general population controls, and symptomatic controls. Using advanced proteomics and statistical modelling, three diagnostic models were developed. The standout, Model 3, distinguished severe endometriosis from symptomatic controls with near-perfect accuracy (AUC: 0.997). It also showed excellent diagnostic performance across earlier disease stages (AUCs >0.85 for stages I–III).

The new results, published in the peer-reviewed journal *Human Reproduction*, build upon and extend earlier studies which demonstrated the potential of the test for diagnosing advanced stages of endometriosis in independent patient groups [ASX: 24 March 2023, 5 May 2024, 1 February 2024].

Proteomics International's Managing Director Dr Richard Lipscombe said, "*the integration of the PromarkerEndo blood test into clinical practice could streamline diagnosis, improve patient outcomes, and deepen the understanding of endometriosis. This advancement marks a significant step toward non-invasive, personalised care for a condition that has long been underserved by current medical approaches.*"

Professor Peter Rogers, Deputy Director of the Women's Gynaecology Research Centre, Research Director at the Royal Women's Hospital and the Professor of Women's Health Research in the Department of Obstetrics and Gynaecology at University of Melbourne said, *"this innovation seeks to address a critical need for a non-invasive, accurate diagnostic tool for early stages of endometriosis, that could help reduce delays in diagnosis and the associated health impacts. A blood test also has potential application in the context of fertility where endometriosis is associated with an increased risk of having difficulty becoming pregnant."*

Endometriosis is a common and painful disease that affects approximately one in nine women and girls, often starting in teenagers (see also PIQ Annual Report 2024). It occurs when tissue similar to the lining of the uterus grows in other parts of the body where it does not belong. Endometriosis severity is classified by the American Society for Reproductive Medicine as stage I/minimal, stage II/mild, stage III/moderate and stage IV/severe.

Currently, there is no simple way to test for endometriosis, which can cause pain and infertility, and costs Australia $9.7 billion each year[1]. The current gold standard for detection is an invasive laparoscopy followed by histopathology, a surgical procedure where a camera is inserted into the pelvis through a small cut in the abdominal wall and then a biopsy is taken for analysis.

The novel test uses biomarkers—protein 'fingerprints' in the blood—to screen for the painful condition. The PromarkerEndo diagnostic test targets potential early screening of patients to rule in or rule out the need for invasive surgery.

Next steps

The Company is pursuing multiple avenues to bring its novel blood test for endometriosis to the clinic with a target launch date of Q2 CY25 in Australia, with other jurisdictions to follow thereafter. Test status:

- Analytical methodology is being adapted for use in a clinical environment with target launch date for PromarkerEndo of Q2 CY25 in Australia.
- Diagnostic algorithm is being refined using 'traffic light' system to further improve test performance for clinical use.
- Development of the PromarkerEndo cloud-based software hub for reporting patient results has commenced.
- Clinical validation study on cohort of samples from the University of Oxford [ASX: 25 March 2024] is ongoing and subject to completion of the adapted method for clinical use.
- Discussions are advancing in key markets for licensing in women's health and fertility.
- Progressing direct-to-consumer/patient (DTC/P) by leveraging the Company's framework for its predictive test for diabetic kidney disease (PromarkerD) and diagnostic test for esophageal cancer (PromarkerEso), which are planned to launch Q1, CY25 in Australia.
- Continuing to build awareness of the test with clinicians, key opinion leaders (KOL's) and advocacy groups in response to the upsurge in demand for better diagnosis of endometriosis.
- Patents pending in all major jurisdictions.

[1] endometriosisaustralia.org/

Summary of Study

Published in the journal *Human Reproduction* (January 2025 issue; Advance article available online)[2].

Titled: *"Identification of plasma protein biomarkers for endometriosis and the development of statistical models for disease diagnosis."*

Authors: E Schoeman[1], S Bringans[1], K Peters[1], T Casey[1], C Andronis[1], K Chen[1], M Duong[1], J Girling[2], M Healey[2], B Boughton[2], D Ismail[1], J Ito[1], C Laming[1], H Lim[1], M Mead[1], M Raju[1], P Tan[1], R Lipscombe[1], S Holdsworth-Carson[2,3], P Rogers[2].
[1] Proteomics International, Perth, Australia; [2]University of Melbourne & Royal Women's Hospital, Melbourne, Australia; [3] Julia Argyrou Endometriosis Centre, Melbourne, Australia

Aim: To identify a plasma protein biomarker panel to accurately diagnose all stages of endometriosis.

Method: A proteomics discovery experiment (using N=56 samples) identified candidate biomarkers before a targeted mass spectrometry assay was developed and used to compare plasma samples from 464 endometriosis cases, 153 general population controls, and 132 symptomatic controls. Three multivariate models were developed: Model 1 (logistic regression) for endometriosis cases versus general population controls, Model 2 (logistic regression) for American Society for Reproductive Medicine (rASRM) stage II to IV (mild to severe) endometriosis cases versus symptomatic controls, and Model 3 (random forest) for stage IV (severe) endometriosis cases versus symptomatic controls.

Results: A panel of 10 protein biomarkers were identified across the three models which added significant value to clinical factors (age and BMI). Model 3 performed the best with an area under the receiver operating characteristic curve (AUC) of 0.997. Model 1 also demonstrated strong predictive performance with an AUC of 0.993, while Model 2 achieved an AUC of 0.729. Importantly for clinical use, Model 3 demonstrates strong performance for discriminating disease across all stages of endometriosis:

Symptomatic controls vs endometriosis stage (Model 3)	AUC	Sn (%)	Sp (%)
Stage I Endometriosis	0.852	87	72
Stage II Endometriosis	0.903	82	84
Stage III Endometriosis	0.908	91	84
Stage IV Endometriosis	0.997	98	96

Conclusions:

- This study represents an advancement toward precise non-invasive endometriosis diagnosis and personalised care, offering an earlier and simpler diagnosis of endometriosis compared to current standard of care.
- A blood test distinguishing healthy women from those with endometriosis has potential application in the context of fertility where there is approximately a three-fold increased incidence of endometriosis in otherwise healthy women undergoing fertility treatments.
- Further clinical validation of these biomarkers will fortify the robustness and reliability of this diagnostic tool and enable its integration into clinical practice, benefiting individuals affected by endometriosis and paving the way for improved patient care.

Glossary

Key terms used:

[2] Human Reproduction: doi.org/10.1093/humrep/deae278

Sensitivity (Sn) (true positive rate)	The ability of a test to correctly identify those with the disease. E.g. sensitivity of 90% means that for every 100 people with endometriosis, the test correctly diagnosed 90 with the condition.
Specificity (Sp) (true negative rate)	The ability of the test to correctly identify those without the disease. E.g. specificity of 85% means that for every 100 people with symptoms but no endometriosis, a test correctly identifies 85 as not having the condition.
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[3]:

- 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).

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About PromarkerEndo

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 blood test. It is a powerful alternative to genetic testing. PromarkerEndo is a diagnostic blood test for endometriosis, which could provide early screening to rule in or out the need for invasive surgery for women and girls presenting with symptoms of endometriosis. Endometriosis is a common and painful condition that affects one in nine women and girls, occurring when tissue similar to the lining of the uterus grows in other parts of the body where is does not belong. The current way to test for the condition is a surgical laparoscopy, with diagnosis taking an average of 7.5 years.

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.

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

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