



Proteomics International

LABORATORIES LTD

ASX Release

4 April 2017

ASX code: PIQ

Predictive diagnostic test for diabetic kidney disease: PromarkerD update

Proteomics International Laboratories Ltd (ASX: PIQ) (PILL), the leader in predictive diagnostics for diabetic kidney disease, presents a comprehensive update on commercialisation progress for its PromarkerD test.

- **PromarkerD rated the world's leading diagnostic test for diabetic kidney disease by global market research firm Frost & Sullivan**
- **First licensing income received**
- **Key patents secured and extended**
- **Clinical laboratory prototype manufacture on target for mid-2017**
- **First commercial sales are targeted for the end of 2017**
- **Validation study completed - announcement of results pending publication of the prior predictive development study**
- **Development study shows PromarkerD correctly predicts 95% of otherwise healthy diabetics who will develop chronic kidney disease**
- **Discussions continue with prospective diagnostic companies in the USA, China, Europe, Australia and Japan to secure licences for the commercialisation of PromarkerD**

About PromarkerD

PromarkerD is a predictive diagnostic test for diabetic kidney disease. In a clinical study PromarkerD correctly predicted 95% of otherwise healthy diabetics who went on to develop chronic kidney disease within four years. PromarkerD was last month rated the world's leading diagnostic test for diabetic kidney disease in the Frost & Sullivan report *Biomarkers Enabling Diabetes and Obesity Management*.

PromarkerD update: Summary of contents

1. Diabetes and kidney disease: Facts & figures
2. Requirements for market adoption: KOLs (Key Opinion Leaders)
3. Market size and intellectual property (IP) protection
4. Production pipeline: Manufacture and Licensing of the IVD (in vitro diagnostic) kit
5. Routes to market: pathology laboratories (IVD), LDT (Laboratory Developed Test) and CDx (Companion Diagnostic)
6. The PromarkerD online portal
7. PromarkerD: the test in detail
8. Next steps: Milestones and Timelines

PromarkerD update in detail

1. Diabetes and kidney disease: Facts & figures

- **1 in 3 adult diabetics, or 138 million people, have chronic kidney disease**
- **If unchecked, by 2040 the world is facing a potential dialysis bill of \$7.6 trillion per year on top of current dialysis costs**

According to the International Diabetes Federation, 415 million adults had diabetes in 2015. The US Center for Disease Control states that 1 in 3 adult diabetics have chronic kidney disease, that's 138 million people today.

Proteomics International Laboratories Ltd

ABN 78 169 979 971

Box 3008, Broadway, Nedlands, WA 6009, Australia

T: +61 8 9389 1992 | E: enquiries@proteomicsinternational.com | W: www.proteomicsinternational.com

Once detected, chronic kidney disease can be treated through medication and lifestyle changes to slow down the disease progression, and to prevent or delay the onset of kidney failure. However, the only treatment options for kidney failure are dialysis or a kidney transplant. There are no tests currently available to predict the clinical onset of diabetic kidney disease, with dialysis already costing more than \$100,000 per person per year.

The International Diabetes Federation further predicts the number of diabetics will rise to 642 million by 2040, which, if unchecked, will increase the number of adults with chronic kidney disease by 76 million to 214 million. That's a potential new dialysis bill of \$7.6 trillion per year.

PILL's commercialisation strategy for PromarkerD is to:

- engage with potential licensees whilst developing key components of the test kit
- strengthen its IP position alongside pursuit of Key Opinion Leader adoption of PromarkerD

2. Requirements for market adoption: KOLs (Key Opinion Leaders)

- **Peer-reviewed publications are essential to independently prove test results and achieve adoption by medical doctors and KOLs**
- **PILL's disruptive technology is first in class and required publication in a specialist journal**
- **Validation study completed but interpretation and announcement of results is pending publication of the prior predictive development study**

The medical community can be slow to embrace change and often a compelling case is required before new diagnostic tools are adopted. Academic publications and conference presentations are essential to achieve adoption of PromarkerD by medical doctors. This adoption will be led by KOLs in the field.

PILL's policy is to present its test results for rigorous peer-reviewed publication as a means of independently proving the findings. Without publication KOLs, including major diagnostics companies, are less likely to consider the results credible.

The Diabetic Kidney Disease (DKD) results achieved to date incorporate three areas: the Promarker™ platform technology, and three clinical studies 1) the *diagnostic* test, 2) the *predictive* test “development” clinical study, and 3) the *predictive* test follow-up “validation” clinical study.

1. Diagnostic study

A protein biomarker discovery workflow was applied to blood samples from patients at different stages of diabetic kidney disease. The protein biomarkers identified were statistically scrutinised against the current gold standard diagnostic tests for diabetic kidney disease on an analysis of 572 patients.

2. Predictive development study

The prognostic ability of the novel diagnostic protein biomarkers was assessed for predicting rapid eGFR (a measure of kidney function) decline in type 2 diabetes. A four year study was commenced with 576 patients enrolled in the study. Over the full duration of the study complete clinical and experimental data was collected from 345 patients.

3. Predictive validation study

The robustness of the models determined from the predictive development study are being assessed in an independent group of 500 patients over a four year period. Over the full duration of the study complete clinical and experimental data was collected from 447 patients.

The disruptive technology used by PILL is first in class and therefore the first data set required publication in a specialist proteomics journal (*EuPA Open Proteomics*) to describe both the technology platform and its basic application to diabetic kidney disease as a new *diagnostic* test. Importantly this foundation publication proved PromarkerD outperformed both current gold standard tests used for the *diagnosis* of patients already suffering from DKD. Note: The current diagnostic tests are called the albumin-creatinine ratio (ACR) and the estimated glomerula filtration rate (eGFR).

A second publication on the *predictive* test data from the development study has been submitted for review by the American Diabetes Association. The clinical study shows that PromarkerD can correctly predict 95% of otherwise healthy diabetics who go on to develop chronic kidney disease within four years. This peer-reviewed publication remains pending.

The time required for peer review is outside the control of PILL. This has delayed PILL's ability to finalise the interpretation of the data and release further results from its follow-up validation clinical study. In the interim PILL has presented its initial predictive test results at leading conferences hosted by the International Diabetes Federation, Australian Diabetes Society and Proteomics Society of India. This strategy will continue and further presentations will occur at international diabetes conferences during 2017 to continue to raise KOL awareness and acceptance of this first in class technology.

3. Market size and intellectual property (IP) protection

- **Patents granted in USA, Australia, Russia, Singapore, and China**
- **Once pending patents are granted, 304 million of the world's 415 million diabetics will be covered by PILL's patents**
- **Exclusive licence secured for new patent family:**
 - **provides immediate protection for PromarkerD in Europe**
 - **opens new markets for diagnosis of kidney damage by any cause**
- **"Promarker" successfully registered as a trademark in Australia, applications pending in other major jurisdictions.**

PILL's DKD patents are now granted in the USA, Australia, Russia, Singapore and China, covering a potential market size of 153 million adult diabetics (patent expiry 2031). Patents are pending in Brazil, Canada, Indonesia, India, Japan and Europe, which if granted will cover an additional 151 million diabetics. In total this represents 304 million of the world's estimated 415 million diabetic population.

In December 2016, prior to its first journal publication, PILL secured an exclusive licence to a family of allied patents for the diagnosis of kidney damage ("Method for the diagnosis of kidney damage in the early stages" European Patent no. EP1410039 and US Patent no. US 7,842,463 B2; "Method for predicting the progression of chronic kidney disease by measuring Apolipoprotein A-IV" European Patent no. EP1941274).

This licence 1) provides immediate protection for the PromarkerD test in Europe and 2) extends protection in the US from diabetic kidney disease alone to other forms of kidney disease. The licences have been secured for the lifetimes of the patents to 2025 and 2021 respectively.

Whilst diabetes is the leading and fastest-growing cause of kidney failure it accounts for only 44% of all such cases, according to the US National Center for Chronic Disease Prevention. Separately, kidney injury is an important measure of a patient's response to any drug treatment and hence is frequently measured as a safety marker in clinical trials. The acquired patents therefore permit exploration of the potential use of PromarkerD in two new and substantial markets: 1) prediction of any form of kidney disease, and 2) as an endpoint marker in clinical trials for *any* new drug.

Promarker™D

To strengthen the global IP position "Promarker" has been registered as a trademark in Australia and is pending in multiple other major jurisdictions. Promarker® trademark protection has the potential to extend the lifespan of future revenue streams beyond the expiry of PILL's patents.

4. Production pipeline: Manufacture and Licensing of the IVD (in vitro diagnostic) kit

- **First commercial sales of the IVD are targeted for the end of 2017**
- **First upfront licence and early access fees have been received for PromarkerD**
- **Puerto Rico is an entry point to the USA for diagnostic manufacturers**
- **Newsummit Biopharma have secured US\$200,000 to cover production work in China**
- **PILL is on track for development of its IVD prototype by mid-year**

Proteomics International Laboratories Ltd

ABN 78 169 979 971

Box 3008, Broadway, Nedlands, WA 6009, Australia

T: +61 8 9389 1992 | E: enquiries@proteomicsinternational.com | W: www.proteomicsinternational.com

First commercial sales of the IVD are targeted for the calendar year end in the Dominican Republic in Latin America as a result of PILL's first licensing deal. In this regard PILL is working closely with its licence partners Macrotech and Omics Global Solutions. The Dominican Republic has one of the most advanced healthcare systems in the Caribbean and this is coupled with the extensive market penetration of Macrotech as the country's exclusive provider of dialysis services.

The net present value of the Dominican Republic licensing deal is US\$1.5 million. Two payments have now been received for upfront licence and early access fees, with a milestone payment due upon first commercial sale and subsequent minimum annual royalties payable. Only 506,000 adults in Dominican Republic have diabetes representing 0.12% of the world's diabetics.

PILL is on track for development of its IVD prototype by Q1 FY18. Kit production will occur in the US Territory of Puerto Rico, which is used by a number of diagnostic manufacturers as an entry point to the USA. This strategic location offers a gateway to a future US roll-out of the test in accordance with FDA regulations.

Key reagents for the IVD kit are antibodies. These are being manufactured in Australia for worldwide use and in parallel in China specifically for the Chinese market. The latter is via an agreement with biopharmaceutical company Newsummit Biopharma (Shanghai) that provides for manufacture of the antibody components, development and validation of an IVD kit, and its registration with the Chinese Federal Drug Administration. Newsummit Biopharma has secured a Chinese Government grant of US\$200,000 to cover the costs of this development work, which is also targeting Q1 FY18 for delivery of its IVD prototype kit.

This dual approach enables the production of IVD kits tailored for their respective markets and which comply with the local regulations.

5. Routes to market: pathology laboratories IVD (In Vitro Diagnostic), LDT (Laboratory Developed Test) and CDx (Companion Diagnostic)

- **Discussions are on-going with diagnostic companies in the USA, China, Europe, Australia and Japan**
- **LDT could be brought to market in the USA and Europe in an accelerated timeframe**
- **21 drugs are in clinical trials for DKD – PromarkerD can act as a companion diagnostic test to identify patients for whom a drug will or will not work**

PILL is in discussion with pathology laboratories and diagnostic companies in Australia, Japan and the USA for the commercial use of PromarkerD as an IVD. These discussions are assisted by PILL's publication strategy.

PILL is also engaged with several entities in the USA and Europe for the roll-out of PromarkerD in specialist centres that form part of the growing number of laboratories targeting new technology platforms for diagnostics. Known as CLIA certified clinical laboratories, these facilities meet federal standards for performing patient testing for the diagnosis of disease, and offer an alternative route to market to traditional regulatory process.

An LDT could be brought to market in an accelerated timeframe as compared to the IVD, and would again attract upfront fees, milestone payments (e.g. at first sale) and royalties per test.

There are 21 drugs in clinical trials for DKD. This emphasises that the need for new therapeutic treatments for complications of diabetes has been recognised by the pharmaceutical industry. To reduce drug failure rates in clinical trials there is a growing requirement for a companion diagnostic test which can identify patients for whom the drug will or will not work. PILL is already in discussion with three companies for the potential use of PromarkerD as such a companion diagnostic and will continue to seek other opportunities through its KOL engagements.

6. The PromarkerD online portal

- **Web-based portal to analyse test results from pathology laboratories anywhere in the world**

Proteomics International Laboratories Ltd

ABN 78 169 979 971

Box 3008, Broadway, Nedlands, WA 6009, Australia

T: +61 8 9389 1992 | E: enquiries@proteomicsinternational.com | W: www.proteomicsinternational.com

A web-based portal is being designed that will analyse the results from patient samples collected and tested in a pathology laboratory anywhere in the world. This permits complete protection of the algorithm underpinning PromarkerD, which continues to be refined to optimise its performance under different clinical conditions.

7. PromarkerD: the test in detail

- **PromarkerD correctly predicts 95% of otherwise healthy diabetics who will develop chronic kidney disease**
- **False positives are less critical for PromarkerD because interventions to stop disease onset are non-invasive**
- **The power of the PromarkerD algorithm is that it can capture nearly all of those at risk of progressing towards dialysis**

PromarkerD measures the concentration of proteins that are found naturally circulating in the blood to predict kidney function decline in people with type 2 diabetes. PromarkerD can also detect those who already have diabetic kidney disease.

The simple endpoint from the predictive development study shows that PromarkerD can correctly predict 95% of otherwise healthy diabetics who go on to develop chronic kidney disease within four years. A primary clinical endpoint from the study determined a $\geq 30\%$ fall in eGFR (a measure of kidney function) over four years, and the statistical results showed that PromarkerD had Sensitivity 87%, Specificity 79%, and AUC 0.88.

High *sensitivity*, or true positive rate, is important for a diagnostic test in order to identify disease at the earliest stage. For DKD, a 'positive' test result can identify patients who need to make lifestyle choices or start a therapeutic intervention to prevent the onset of chronic kidney disease.

High *specificity* is normally important for a diagnostic test because it is associated with fewer false positives. This is less critical for PromarkerD because interventions to prevent the onset of DKD are non-invasive, unlike, for example, in cancer. A diabetes patient with a positive result will be monitored more closely. If it was a false positive it is likely this will be determined by follow-up tests that can compare the patient's own personalised baseline data to give a more accurate diagnosis.

Area Under the Curve (AUC) in a receiver operating characteristic curve, or ROC curve, is a graphical plot that illustrates the performance of a classifier system. The conventional interpretation of the clinical significance of the ROC curve AUC is: >0.7 acceptable discrimination; >0.8 excellent discrimination; > 0.9 outstanding discrimination.

The power of the PromarkerD algorithm is that it can be adjusted to provide optimal results to suit the clinical need, in this case to maximise sensitivity and capture nearly all of those at risk of progressing towards dialysis or kidney transplant.

8. Next steps: Milestones and Timelines

- **PILL continues to work closely with one of Australia's leading diabetologists**

Data from PILL's follow-up validation study on the DKD predictive test has been collected, but the interpretation of the results has been delayed as described above. Results from this independent study will be presented via KOL forums such as the American Diabetes Association, and released to ASX once the peer-review process has been completed in accordance with the Code of Best Practice for Reporting by Life Science Companies.

For these clinical studies PILL continues to work closely with the University of Western Australia Medical School and Fremantle Diabetes Study headed by one of Australia's leading diabetologists, Professor Tim Davis.

Milestone	2017			
	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dec
Key patents secured and extended	■			
Diagnostic test data published	■			
Independent market research report		■		
Predictive clinical study results published		■ ■		
Validation clinical study results announced		■ ■		
Prototype kit manufacture complete			■ ■	
First commercial sales targeted				■

PILL's philosophy is to maintain rigorous scientific standards whilst pursuing its commercial objective of bringing PromarkerD to market as soon as possible as described in the sections above. By identifying and treating people before clinical symptoms appear lives will be saved alongside billions of dollars in health costs, and by this process PromarkerD will become a flagship test for the new era of precision medicine.

ENDS

For further information please contact:

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

Susan Fitzpatrick-Napier [Media Contact]
 Digital Mantra Group
 T: +61 2 8218 2144
 E: team@dmgpr.com

Greg Wood [Corporate Advisor]
 Managing Director
 K S Capital
 T: +61 416 076 377
 E: g.wood@kscapital.com.au

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

PILL (ASX: PIQ) is a medical technology company focused on proteomics – the industrial scale study of the structure and function of proteins. In the last few years, proteins have become the drug class of choice for the pharmaceutical industry because of their intimate role in biological systems. Thus proteomics technology is now playing a key role in understanding disease, from finding new diagnostic biomarkers to determining drug targets, and discovering new biopharmaceutical drugs.

PILL is recognised as a global leader in the field of proteomics. It received the world's first ISO 17025 laboratory accreditation for proteomics services, and operates from state-of-the art facilities at the Harry Perkins Institute of Medical Research in Perth, Western Australia. The Company's business model uses its proprietary technology platform across three integrated areas, each massive growth markets:

- 1. Diagnostics:** Biomarkers of disease and personalised medicine - focus on diabetic kidney disease.
 By 2020 the biomarkers market is estimated to double in size to \$45.6 billion, and the personalised medicine market is forecast to be worth over \$149 billion.
- 2. Analytical services:** Specialist contract research fee-for-service model – focus on biosimilars QC.
 The global biosimilars market is expected to reach \$6.2 billion by 2020, almost trebling from its 2015 level, as it seeks to replicate the multiple billion dollar blockbuster drugs that are coming off patent.
- 3. Drug discovery:** Therapeutic peptide drug discovery - focus on painkillers and antibiotics.
 The global peptide therapeutics market is currently estimated to be worth \$18 billion and is expected to increase by over 10% per year during 2016-2025.

Proteomics International Laboratories Ltd

ABN 78 169 979 971

Box 3008, Broadway, Nedlands, WA 6009, Australia

T: +61 8 9389 1992 | E: enquiries@proteomicsinternational.com | W: www.proteomicsinternational.com