ASX Release
18 October 2021

ASX code: PIQ

Clinical utility study demonstrates benefit of PromarkerD testing - evidence to support payor reimbursement

- **New study shows the PromarkerD predictive test for diabetic kidney disease significantly impacts clinical management decisions for patients with type 2 diabetes**
- **PromarkerD test results changed physicians' prescribing and monitoring decisions and were more important to doctors than current standard-of-care tests**
- **Clinical utility study to add to the weight of evidence supporting a US reimbursement code application for PromarkerD**
- **Results significant to patients, clinicians and healthcare systems presented today at the Academy of Managed Care Pharmacy (AMCP) Nexus conference 2021 in Denver, USA**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ) is pleased to announce the results of a clinical utility study demonstrating the PromarkerD predictive test for diabetic kidney disease (DKD) can help inform doctors' treatment decisions and improve clinical outcomes for patients with type 2 diabetes.

The US-based web survey of 400 primary care physicians and endocrinologists found the PromarkerD test significantly impacted physicians' prescribing and monitoring decisions. The results from the conjoint analysis showed that PromarkerD tests were more important to physicians than the current standard-of-care tests—estimated glomerular filtration rate (eGFR) and albumin-to-creatinine ratio (ACR). Compared with no PromarkerD test results, a PromarkerD result showing a patient at high-risk of developing DKD was also associated with significantly higher odds of increasing monitoring frequency of a patient (odds ratio [OR]: 2.56), prescribing SGLT2 inhibitors (OR: 1.98), replacing ibuprofen (OR: 1.78), and increasing ACE inhibitors dose (OR: 1.48).

More than three-quarters of physicians reported they were very or extremely likely to use PromarkerD in the future. The results will be presented today at AMCP Nexus, a managed-care pharmacy conference in Denver, USA[1] in association with Boston Healthcare Associates and specialist US endocrinologists.

PromarkerD is a simple blood test for diabetic kidney disease that can predict future kidney function decline in patients with type 2 diabetes and no existing DKD. The biomarker-based test can predict a decline in renal function up to four years in advance.

Senior author of the study Dr Alexander Turchin, an endocrinologist at Boston's Brigham and Women's Hospital, said the physicians were asked to assess 42 real-life scenarios for patients with type 2 diabetes.

"*When presented with moderate or high-risk PromarkerD results, physicians were more likely to implement renoprotective changes—such as increasing monitoring frequency, prescribing SGLT2*

[1] https://2021.amcpnexus.org

inhibitors or replacing ibuprofen—than if they did not have the PromarkerD test results. These changes can help avoid end-stage interventions such as dialysis and kidney transplant."

"In contrast, w*hen presented with low-risk PromarkerD results, the likelihood of aggressive treatment and health care resource utilisation reduced*."

Proteomics International's managing director Dr Richard Lipscombe said, "*The findings demonstrate PromarkerD's appeal to clinicians and payors in the management of diabetes. This study shows PromarkerD offers a cost-effective, personalised approach to improving patient outcomes. It allows earlier targeted treatment of those patients at highest risk of diabetic kidney disease, while avoiding unnecessary interventions for people at low risk.*"

AMCP Nexus is an in-person conference attended by US insurance companies and payors, and runs 18-21 October 2021. The results are being presented as a scientific poster (*see attached copy*) titled:

***Evaluation of the Clinical Utility of PromarkerD In-Vitro Test in Predicting Diabetic Kidney Disease and Rapid Renal Decline*.**

Proteomics International is also exhibiting a trade booth at the event showcasing PromarkerD.

The conference forms part of the Company's ongoing engagement with Key Opinion Leaders (KOL's) and industry representatives and follows Proteomics International's recent attendance at the virtual 57th European Association for the Study of Diabetes Annual Meeting (EASD 2021), from 28 September to 1 October[2]. The event is the largest diabetes conference in Europe, and attracted more than 14,000 delegates from 136 countries.

US Reimbursement Code

This clinical utility study demonstrating the beneficial impact of PromarkerD testing on patient treatment decisions by physicians provides the second of two essential components for the Company's dossier to support an application for a US reimbursement code. This study, together with the previous studies showing the economic health benefit of PromarkerD testing (and presented at the world's leading conference for health economics, Virtual ISPOR 2021 in May, and at the world's largest diabetes conference, the American Diabetes Association's 81st Scientific Sessions, in June) [ASX: 2 July] provide strong evidence for the adoption of PromarkerD testing internationally.

The economic health benefit study demonstrated the potential cost savings to the US Healthcare system if PromarkerD was adopted, compared to the current standard of care. That study found that instigating PromarkerD testing produced savings primarily from slowing the progression of DKD, and delaying or preventing dialysis and kidney transplants, against the costs associated with increased testing and the use of preventative medications.

The clinical utility study and the economic health benefit study will support the Company's application for a reimbursement code, which will facilitate the reimbursement of the PromarkerD test by insurance companies and other payors in the US. This is important because it means that the cost of the test may be covered by insurers or other payors, instead of the patient.

New reimbursement codes are approved quarterly by the American Medical Association (AMA) and its Current Procedural Terminology (CPT) Editorial Panel, and follow assessment of the economic health benefit and clinical utility of a new test. A CPT Proprietary Laboratory Analyses (PLA) code uniquely identifies a test for the laboratory and the payors. The Company will seek a unique code for PromarkerD once the test is available in the US, and prior to such granting intends to follow standard procedure and use a miscellaneous reimbursement code.

Proteomics International is in ongoing discussions with potential US laboratory partners to provide PromarkerD to diabetes patients. There are approximately 31 million at-risk diabetes patients in the US[3] where DKD is the 16th leading cause of death accounting for 40,000 deaths per year[4].

2 www.proteomics.com.au/promarkerd-at-easd

3 International Diabetes Federation 2019

4 The State of US Health, 1990-2016

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

ENDS

About PromarkerD (www.PromarkerD.com)
Diabetic kidney disease (DKD) is a serious complication arising from diabetes which if unchecked can lead to dialysis or kidney transplant. PromarkerD is a prognostic test that can predict future kidney function decline in patients with type 2 diabetes and no existing DKD. The patented PromarkerD test system uses a simple blood test to detect a unique 'fingerprint' of the early onset of the disease by measuring three serum protein biomarkers, combined with three routinely available conventional clinical variables (age, HDL-cholesterol and estimated glomerular filtration rate (eGFR)). A cloud based algorithm integrates the results into a patient risk report. In clinical studies published in leading journals PromarkerD correctly predicted up to 86% of otherwise healthy diabetics who went on to develop diabetic kidney disease within four years. The PromarkerD test is CE Mark registered in the European Union.

Further information is available through the PromarkerD web portal.

To visit the PromarkerD virtual booth please see: www.PromarkerD.com/product

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

Evaluation of the Clinical Utility of PromarkerD In-Vitro Test in Predicting Diabetic Kidney Disease and Rapid Renal Decline

Fusfeld L[1], Murphy JT[1], Yoon YJ[1], Kam LY[2], Peters KE[2], Tan PL[2], Morrison JC[3], Shanik M[4,5], Turchin A[6]

[1]Boston Healthcare Associates, Boston, MA, USA, [2]Proteomics International, Perth, WA, Australia, [3]Proteomics International, Boston, MA, USA,
[4]Stony Brook University Medical Center, Stony Brook, NY, USA, [5]Endocrine Associates of Long Island, PC, Smithtown, NY, USA, [6]Brigham and Women's Hospital, Boston, MA, USA

E: info@promarkerd.com
W: www.promarkerd.com, www.proteomics.com.au

Presented at the AMCP Nexus
October 18-21, 2021

Background

- Diabetic kidney disease (DKD) develops in 1 in 3 people with type 2 diabetes (T2D)[1] and is the leading cause of end-stage renal disease (ESRD), associated with increased morbidity and mortality.[2,3]
- DKD and ESRD impose economic burdens and lower quality of life, costing the US Medicare system $50 billion annually.[4]
- Existing standard-of-care tests for detecting DKD are the estimated glomerular filtration rate (eGFR) blood test and the urinary albumin-to-creatinine ratio (ACR). Despite the well established KDIGO (Kidney Disease Improving Global Outcomes) guidelines,[5] currently 80% of at-risk patients do not receive adequate testing.[6]
- Early identification of patients at risk of developing DKD or rapid renal decline is imperative for selecting appropriate patient interventions and treatment,[7] however, both the eGFR and ACR tests have limited accuracy in predicting the risk of developing DKD.[8]
- PromarkerD is an innovative protein biomarker-based blood test that can predict future renal function decline within the next 4 years in people with T2D, including in those with no existing DKD.

Aim

- To evaluate the impact of PromarkerD on clinical treatment decisions for T2D patients.

Methods

- A conjoint analysis was used to infer the importance of PromarkerD and other patient attributes on physician decision-making via a web-based survey administered to a convenience sample of 400 primary care physicians (PCPs) and endocrinologists.
- 42 hypothetical patient profiles were generated, with varying levels of the following attributes: PromarkerD result (low-, moderate-, or high-risk), albuminuria (as measured by ACR), eGFR, blood pressure (BP), glycemic control (HbA1c), and age (Table 1).
- A web-based survey asked each physician to make monitoring and treatment selection/dosing decisions for eight randomly selected profiles.
- Respondents were shown a blinded description of PromarkerD (which was described throughout the survey as "Test X").

Table 1. Detailed attributes and levels

Attributes and Levels				
Attribute	**Level 1**	**Level 2**	**Level 3**	**Level 4**
PromarkerD result	No test	Low risk	Moderate risk	High risk
Albuminuria	15 mcg/mg (mildly increased)	165 mcg/mg (moderately increased)	500 mcg/mg (severely increased)	N/A
eGFR	110 ml/min/1.73m^2 (normal)	75 ml/min/1.73m^2 (mildly decreased)	45 ml/min/1.73m^2 (moderately decreased)	N/A
Blood pressure (BP)	120/70 mmHg	135/90 mmHg	150/95 mmHg	N/A
Glycemic control (HbA1c)	6.3%	7.5%	8.4%	N/A
Age	48 years	66 years	83 years	N/A

N/A = not applicable

- For each patient, physicians indicated with their decision-making outcomes about monitoring frequency (increase/decrease/same), treatment selection (Sodium-Glucose Cotransporter-2 [SGLT2] inhibitors, renotoxic medication), and dosing (ACE inhibitors) (Table 2).

Methods

Table 2. Detailed decision-making outcomes

Outcomes	
Outcome	**Operationalisation (Single select for each outcome)**
Monitoring frequency of risk factors (albuminuria, eGFR, blood pressure, and HbA1c)	Increase, decrease, or maintain standard monitoring frequency*
Prescribe SGLT2 inhibitors	Yes or no
Replace ibuprofen	Yes or no
Increase lisinopril dose to 20mg per day	Yes or no

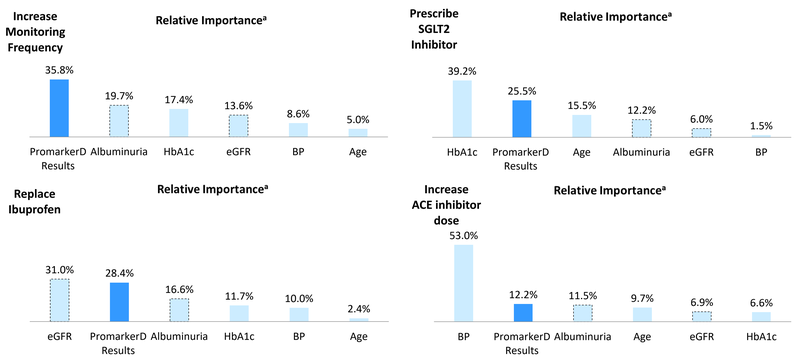
*In the analysis, the categories "decrease monitoring frequency" and "maintain standard monitoring frequency" of the monitoring frequency outcome variable were combined due to sparse data, as "decrease monitoring frequency" was selected as an option for only 5% of the patient profiles. Consequently, this monitoring outcome was analyzed as a binary variable (increase in monitoring frequency versus no increase in monitoring frequency).

- Data analysis was conducted with Sawtooth Software (Conjoint Value Analysis Module, version 3). A multivariable logit model for each outcome was used to analyze the impact of PromarkerD and other patient attributes on physician decision-making.
- Additionally, the survey included questions about current management of T2D patients and physicians' expected use of PromarkerD.

Results

- Four hundred physicians (203 PCPs; 197 endocrinologists) completed the survey.
- Sixty-three percent of endocrinologists (124/197) and 67% of PCPs (136/203) acknowledged the difficulty of using current tools to predict the progression of DKD, and 44% of endocrinologists (87/197) and 46% of PCPs (93/203) indicated predicting the onset of DKD in the near future for T2D patients is a challenge.
- Seventy-eight percent of physicians reported they are very or extremely likely to use PromarkerD.
- The conjoint analysis indicated that the PromarkerD test result was the most important attribute for the decision to increase the frequency of risk factor monitoring (Figure 1).
- PromarkerD was second to HbA1c for the decision to prescribe SGLT2 inhibitors with a DKD indication, second to eGFR for replacing ibuprofen with a non-nephrotoxic medication, and second to blood pressure (BP) for increasing the dose of lisinopril (ACE inhibitor) (Figure 1).

Figure 1. The relative importance of each attribute in influencing measured outcomes

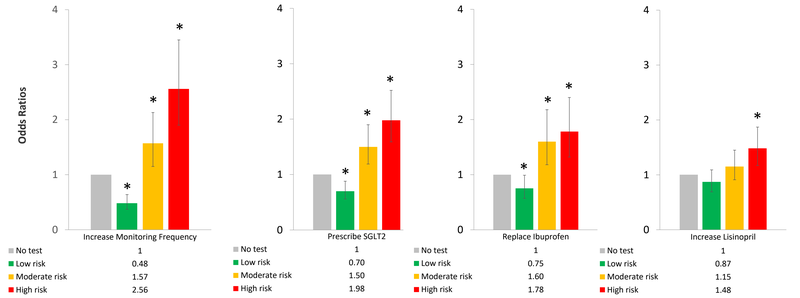


[a] While attribute importance values sum to 100% across attributes for each outcome assessed, percentages listed may not add to 100% as a result of rounding.

Results

- Compared with no PromarkerD test results, a high-risk PromarkerD result was associated with significantly higher odds of increasing monitoring frequency (odds ratio [OR]: 2.56, 95% confidence interval: 1.90-3.45), prescribing SGLT2 inhibitors (OR: 1.98 [1.56-2.52]), replacing ibuprofen (OR: 1.78 [1.32-2.40]), and increasing ACE inhibitors dose (OR: 1.48 [1.17-1.87]) (Figure 2).
- Compared with no PromarkerD test results, a moderate-risk PromarkerD result was also associated with significantly higher odds of increasing monitoring frequency (OR: 1.57 [1.15-2.13]), prescribing SGLT2 inhibitors (OR: 1.50 [1.19-1.90]), and replacing ibuprofen (OR: 1.60 [1.18-2.18]) (Figure 2).
- Compared with no PromarkerD test results, a low-risk PromarkerD result was associated with significantly lower odds of increasing monitoring frequency (OR: 0.48 [0.37-0.64]), prescribing SGLT2s (OR: 0.70 [0.56-0.88]), and replacing ibuprofen (OR: 0.75 [0.57-0.99]) (Figure 2).

Figure 2. Impact of PromarkerD test results on physician decision-making [a]



[a] Vertical lines represent the 95% confidence interval for the odds ratio estimates.
* Significant at α=0.05, compared to no PromarkerD test results.
"No test" was the reference level.

Conclusions

- The study suggests implementing PromarkerD testing would significantly impact physicians' prescribing and monitoring decisions for T2D patients.
- PromarkerD results were relatively more important to physicians than the current standard-of-care tests, eGFR and ACR (albuminuria) for three of four outcomes.
- PromarkerD could help inform T2D management decisions, with physicians viewing moderate- and high-risk PromarkerD results as expected to increase the likelihood of renoprotective changes in management of T2D patients at risk of DKD or rapid renal decline compared with no test results, while low-risk results were expected to lower the likelihood of aggressive treatment and health care resource utilization.
- Physician data from this study indicate PromarkerD could provide clinical utility in the management of DKD in patients with T2D and offer a cost-effective personalized approach to improving patient outcomes by earlier targeted treatment of those patients at highest risk of DKD.

References

1. US CDC. Chronic Kidney Disease in the United States, 2021. https://www.cdc.gov/kidneydisease/pdf/Chronic-Kidney-Disease-in-the-US-2021-h.pdf
2. Afkarian M, et al. Clinical manifestations of kidney disease among US adults with diabetes, 1988-2014. *JAMA - J Am Med Assoc.* 2016;316(6):602-610.
3. Chen Y, et al. Diabetic kidney disease: challenges, advances, and opportunities. *Kidney Dis.* 2020;6(4):215-225.
4. NIDDK United States Renal Data System 2020 Annual Data Report. https://adr.usrds.org/2020.
5. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl.* 2013;3: 1-150
6. Alfego D, et al. Chronic kidney disease testing among at-risk adults in the U.S. remains low: real world evidence from a national laboratory database. *Diabetes Care.* 2021; Aug 5, Online ahead of print.
7. Tuttle KR, et al. Diabetic kidney disease: a report from an ADA Consensus Conference. *Diabetes Care.* 2014;37(10):2864-2883.
8. Braun LA, et al. High burden and unmet patient needs in chronic kidney disease. *Int J Nephrol Renovasc Dis.* 2012;5:151-163.