ASX Release
3 May 2023

ASX code: PIQ

Canagliflozin lowers PromarkerD diabetic kidney disease risk prediction scores

- **Research conducted with Janssen Research & Development looked at PromarkerD results of patients taking diabetes medication canagliflozin**
- **Study of over 2,000 participants found a significant reduction in the PromarkerD risk scores for developing diabetic kidney disease in those who took the medication compared to placebo**
- **Effect was greatest in participants predicted by PromarkerD to be at high-risk of a decline in kidney function at the start of the study**
- **Research published as a feature article in the peer-reviewed *Journal of Clinical Medicine***
- **Study shows the power of using PromarkerD as a Precision Medicine tool to assist in the treatment and prevention of diabetic kidney disease**

Proteomics International Laboratories Ltd (Proteomics International; ASX: PIQ) is pleased to announce results showing a significant reduction in the PromarkerD risk scores of patients with type 2 diabetes after taking the diabetes medicine canagliflozin, with the benefit greatest in patients identified as being at high-risk of diabetic kidney disease (DKD). The results were published yesterday as a feature article in the international peer-reviewed *Journal of Clinical Medicine*[1].

The study was conducted as part of a long-running collaboration between Proteomics International and Janssen Research & Development, LLC ("Janssen", the pharmaceutical arm of Johnson & Johnson) [ASX: 31 March 2020]. Researchers at the two companies examined the association between canagliflozin, an approved diabetes therapy with additional kidney and cardio protective benefits, and changes in PromarkerD scores in people with type 2 diabetes.

Proteomics International Managing Director Dr Richard Lipscombe said the publication demonstrates that gliflozin class drugs can lower PromarkerD risk scores, and have the potential to treat at-risk patients identified by the test. "*The findings illustrate the benefits of using PromarkerD testing - it's exciting that we can identify patients who are asymptomatic for diabetic kidney disease but still at high risk of developing the disease, and that canagliflozin significantly lowers their risk of developing diabetic kidney disease. It's an elegant example of using precision medicine to enable early intervention and slow or stop the onset of disease.*"

The research found the average PromarkerD risk score of patients taking canagliflozin dropped during the trial, while the average risk score of patients taking a placebo rose. The effect was greatest in participants who were identified by PromarkerD to be at high-risk of a decline in kidney function at the start of the study.

PromarkerD is a newly-developed blood test that can predict diabetic kidney disease before clinical symptoms appear, helping doctors make treatment decisions and improving outcomes for patients with type 2 diabetes.

Canagliflozin is an SGLT2-inhibitor drug used in the treatment of diabetes. It was the first diabetes medicine

[1] Peters (2023; doi.org/10.3390/jcm12093247

with an indication to slow the progression of diabetic kidney disease in patients with type 2 diabetes and DKD [FDA: 27 Sept 2019]. The gliflozin class of drugs is widely used to treat patients with type 2 diabetes[2].

The study examined blood samples from patients in Janssen's completed CANagliflozin cardioVascular Assessment Study (CANVAS)[3] clinical trial. The research team retrospectively measured PromarkerD scores in samples from 2,008 patients taken at the start of the trial and again three years later. Janssen provided the samples and Proteomics International tested them using PromarkerD. The publication follows an in depth joint analysis of the study results by the two research teams, and comprehensive peer review, and builds upon preliminary results first presented at the Australasian Diabetes Conference [ASX: 12 August 2021].

The Journal of Clinical Medicine is recognised as an influential journal in the field of general medicine, with feature papers considered to be of high importance and interest to the readership due to their novelty, originality, or potential impact on clinical practice or research. Feature papers are selected by the Editorial Board after recommendation by the journal's independent and external reviewers based on the quality and significance of the research presented in the article.

Publication Details: Journal of Clinical Medicine 2023, 12(9), 3247; doi.org/10.3390/jcm12093247

Title: Canagliflozin Attenuates PromarkerD Diabetic Kidney Disease Risk Prediction Scores

KE Peters [1], SD Bringans [1], RS O'Neill [1], TSC Lumbantobing [1], JKC Lui [1], TME Davis [2], MK Hansen [3] and RJ Lipscombe [1]

[1] Proteomics International, QEII Medical Centre, WA, Australia; [2] Medical School, The University of Western Australia, Fremantle Hospital, WA, Australia; [3] Janssen Research and Development, LLC, Spring House, PA 19477, USA.

Summary of Study

Aim: To examine whether the diabetes drug canagliflozin (an SGLT2-inhibitor) affected the PromarkerD risk score over a three-year follow-up period in participants with type 2 diabetes.

Method: Retrospective analysis was performed on 2,008 participants (N=629 placebo arm, N=1379 canagliflozin arm) from the completed multinational CANagliflozin cardioVas-cular Assessment Study (CANVAS), a randomized placebo-controlled trial, with preserved kidney function (baseline eGFR ≥ 60 mL/min/1.73 m2 with any uACR).

PromarkerD scores were calculated at baseline and Year 3 using the previously defined algorithm, and generalized estimating equations were used to assess the effect of canagliflozin versus placebo on PromarkerD scores during the 3-year follow-up period.

Results: After accounting for the known acute drop in eGFR following canagliflozin initiation, there was a significant treatment-by-time interaction ($p < 0.001$), whereby participants on canagliflozin had decreased mean PromarkerD scores from baseline to Year 3 (Δ score: −1.0%; $p = 0.039$), while the scores of those on placebo increased over the three-year period (Δ score: 6.4% ; $p < 0.001$). When stratified into PromarkerD risk categories, participants with high risk scores at baseline who were randomized to canagliflozin had significantly lower scores at Year 3 (Δ score: −5.6%; $p < 0.001$), while those on placebo retained high scores (Δ score: 4.5% ; $p = 0.035$) [See Figure].

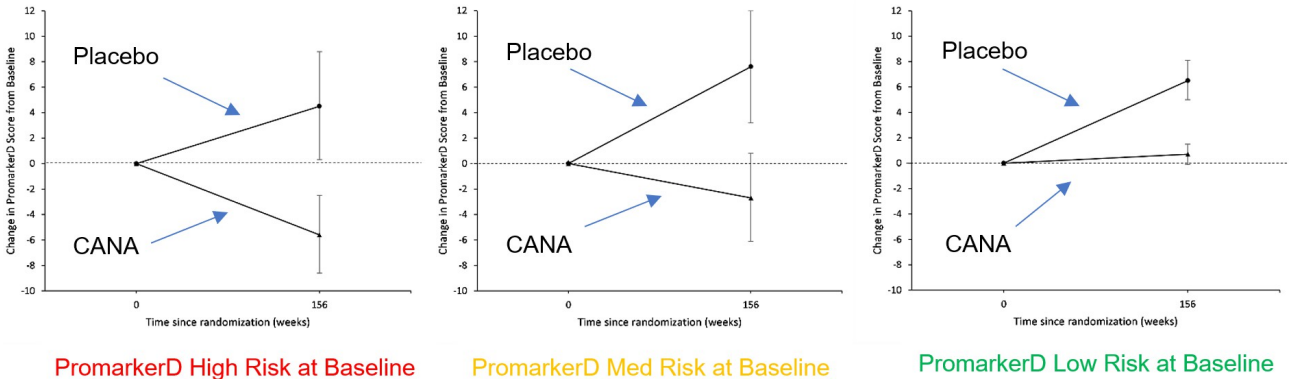

Figure: Change in PromarkerD score over time (with patients stratified by PromarkerD according to risk of developing DKD).

[2] doi: 10.31128/AJGP-05-20-5432

[3] clinicaltrials.gov/ct2/show/NCT01032629

Conclusions: Previous studies demonstrated that higher PromarkerD scores are significantly predictive of incident DKD in the next four years in community-based and clinical trial participants with type 2 diabetes.

- In the present study, canagliflozin significantly decreased mean PromarkerD scores compared to placebo over three years, with the effect greatest for those classified using PromarkerD as at high risk of a subsequent decline in kidney function at the outset.
- In contrast, PromarkerD scores for participants on placebo significantly increased during the three years.
- It follows that a decrease in PromarkerD scores is associated with a lower risk of future DKD, as well as longer term beneficial kidney and cardiovascular disease outcomes.

Patient risk stratification with PromarkerD allows a more informed approach to management of those at highest risk of developing DKD.

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 classifying individuals as high, medium or low risk of developing DKD. 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 available in the USA as a Laboratory Developed Test (LDT), is pending approval from the TGA in Australia, and 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