ASX Announcement
2 August 2023

BCAL Diagnostics announces breakthrough results - a major step towards commercialisation of BCAL's breast cancer diagnostic test

Highlights

- **Breakthrough results from Precion US study**
- **Results are transformational in path to commercialisation of BCAL test**
- **Sensitivity of 90% and a specificity of 85.5%**
- **First sales expected H2 CY2024**
- **Precion result enables blood samples to be analysed in many commercial laboratories worldwide fast-tracking market access and penetration**

BCAL Diagnostics Limited ("BCAL" or "the Company")(ASX: BDX) has received breakthrough results from a clinical study it sponsored with Precion Inc. in North Carolina, US ("Precion").

The analysis undertaken achieved an **impressive sensitivity of 90%** and a **specificity of 85.5%**. These results were consistent with the findings of earlier studies conducted in Australia using a different mass spectrometry platform. This validation shows strong potential performance with a balance of sensitivity (ability to detect true positive samples) and specificity (ability to detect true negative samples).

The replication of these results is a major breakthrough in the path to commercialisation of the BCAL test. These results enhance the confidence of the Company that the BCAL blood-based test for detecting breast cancer will be available for commercial sales, in conjunction with mammograms, in the second half of calendar 2024.

The results mean that the BCAL test should readily be capable of being replicated not only in BCAL's dedicated laboratory in Australia but, more importantly, will enable blood samples to be analyzed (using the BCAL test) in commercial laboratories throughout the world. This will fast-track BCAL's access and penetration into existing and new markets globally.

The Board and executive management of BCAL consider these results to be a very significant development and vindication of the efforts of the BCAL team over the past 10 years, particularly since BCAL listed on the ASX in 2021.

Jayne Shaw, Executive Chair of BCAL commented "*These results are a major step towards making our test broadly available to patients and clinicians. We will continue to work closely with leading scientists and doctors as our science team further optimises the test to make it more cost-effective when it is launched as a patient friendly blood test for detecting breast cancer".*

Scientific and technical information of the test results obtained by Precion are set out in Appendix A to this announcement.

Investor Webinar Details

BCAL will be hosting an investor webinar on Tuesday 8 August 2023 at 11am to update shareholders and provide further information on the Precion results and implications for the BCAL test.

The call will be hosted by Jayne Shaw, Founder & Managing Director, Dr John Hurrell, Chief Executive Officer and Dr Amani Batarseh, Chief Scientific Officer.

Webinar details Date:	Tuesday 8 August 2023
Time:	11:00am - 12:00pm (AEST)
To register:	Register here
Dial in details:	Will be provided to you upon registration

Participants will be able to submit questions during the webinar via a written Q&A facility displayed at the bottom of the webinar screen or can submit them in advance to bhall@bcaldiagnostics.com.

This announcement has been approved by the BCAL Board.

ENDS

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About BCAL Diagnostics

BCAL Diagnostics Limited is an Australian screening and diagnostic company committed to the early, accurate diagnosis of breast cancer, and therefore early intervention and improved outcomes for women. Over the past decade BCAL has developed a non-invasive blood test for the detection of breast cancer, The test is initially designed to complement current imaging technologies, such as the mammogram, with the aim of becoming a monitoring and screening tool suitable for women of all ages and backgrounds in any location. With more than two million new cases of breast cancer diagnosed globally each year, a substantial opportunity exists for BCAL to improve patient outcomes. BCAL has partnered with Precion Inc. to optimise protocols and procedures for the clinical studies required for regulatory approvals across several jurisdictions, commercialisation and market entry points.

Founded in 2010, BCAL is headquartered in Sydney and listed on the Australian Securities Exchange (ASX: BDX). For more information: https://www.bcaldiagnostics.com/

About Precion Inc

Precion applies mass spectrometry technology to develop and provide targeted metabolite panels for profiling various chronic disease conditions and associated health areas for clinical research. Precion offers development of diagnostics and precision medicine assay formats for downstream applications. Precion's testing services for commercial and research customers provide data for various sample types and project objectives. Precion offers a range of targeted panels and custom developed panels for partners with specific clinical objectives. For more information: https://www.precion.com/

APPENDIX A – Explanation of the test results obtained by Precion

Precion was contracted by BCAL to develop the analytical assay for the plasma lipids BCAL had previously identified as the signature indicative of breast cancer in its discovery research conducted in Sydney. The Precion assay method is a progression from the approach formerly used by BCAL for research purposes and is designed as the method to be used when the BCAL test is released for commercial use

The analytical assay was designed for a Triple Quadrupole Mass Spectrometer, a widely available analytical instrument in clinical laboratories across Australia, the US, and Europe. Following assay development, Precion Inc. independently conducted the study using plasma from prospectively collected blood samples from 390 breast cancer patients in the early stages of the disease and 266 healthy control subjects, all provided by and previously analysed by BCAL. All participants gave their consent, and strict protocols were followed during sample collection. The breast cancer patients were confirmed through biopsies and were treatment naïve at the time of blood collection. Importantly, all participants had no previous history of cancer.

Dr Klaus-Peter Adam, Chief Technology Officer, Precion Inc. explains, *"Precion developed a quantitative plasma based assay for breast cancer screening. Using a liquid chromatography-tandem mass spectrometry (LC-MS/MS) method, the assay is fully quantitative and follows the typical clinical assay design. The assay uses authentic reference standards for each of the key lipid biomarkers identified earlier by BCAL in the lipidomics discovery phase. Clinical plasma samples*

from 656 breast cancer patients and healthy control subjects were analysed using this quantitative assay. Data analysis using enhanced Machine Learning techniques by OmniOmics.ai, a Sydney based leading statistical analysis company, showed the performance of the test in distinguishing between breast cancer or non breast cancer is remarkably similar to previous results obtained from BCAL's discovery platform. This clearly shows the robust nature and transferability of the BCAL breast cancer signature, since we utilised a different mass spectrometry platform and sample processing method."

The breakdown of the types of cancer and the stage of the disease used in this study is shown in the following table.

	Stage 0	Stage I	Stage II	Total
Healthy Controls				266
IDC		124	167	291
ILC		20	28	48
DCIS	51			51
Total				656
IDC	Invasive Ductal Carcinoma			
ILC	Infiltrative Lobular Carcinoma			
DCIS	Ductal Carcinoma in Situ			

The 5-year survival rate for Stage 1 (early) breast cancer is, on average, 100% and Stage 2 is 95%. For locally advanced cancers (known as Stage 3) the survival rate is 81%, while the 5-year survival rate for Stage 4 (metastatic breast cancer) is significantly lower at 32%. - National Breast Cancer Foundation

The study involved analysing each patient sample using the analytical method developed by Precion Inc., allowing them to calculate the concentration of 48 lipids. These lipids were carefully selected from previous lipid analysis carried out by BCAL scientists in Sydney. They included lipids from the previously identified 20-lipid signature shown to be associated with breast cancer, along with other lipids that have been found to be altered in breast cancer patients in the previous studies.

Using advanced machine learning techniques, the data analysis achieved an **impressive sensitivity of 90%** and a **specificity of 85.5%** through internal Leave-One-Out Cross Validation (LOOCV) with 24 of the measured lipids. These results were consistent with the findings of earlier studies conducted in Sydney using a different mass spectrometry platform.

Moreover, Precion Inc. utilised reference lipid standards from commercial sources as well as in-house and custom synthesis to validate the identity of the lipids present in the breast cancer signature. They also employed deuterated lipid standards, where some hydrogen atoms in the lipid molecules were replaced with a heavy isotope of hydrogen called deuterium. These deuterated lipid standards, with distinct masses in the mass spectrometer compared to their biological counterparts in plasma, were added to the samples as internal standards. This approach enables more accurate quantification and reduces variability in the assay, surpassing the conventional practice of using one or two unlabeled lipid standards per lipid class.

The successful confirmation of lipid identity and the use of deuterated internal and reference standards are essential steps towards the potential regulatory approval of the BCAL breast cancer test. This study marks a significant milestone in the path towards commercialising the BCAL test. Currently, BCAL researchers are working on further analysis to optimise the number of lipids in the breast cancer signature, with the goal of making the test more cost-effective when it is launched as a patient friendly blood test for detecting breast cancer.

Dr John Hurrell, CEO, BCAL confirmed *"this study shows the robustness of the BCAL breast cancer plasma lipid signature and the transferability of the test between laboratories and instrument types. The initial BCAL research was conducted with high sensitivity research instrumentation while the Precion results were obtained with instrumentation and procedures in routine use in clinical laboratories. This is a major step towards making our test broadly available to patients and clinicians."*.