ASX Announcement

CLEO to Fast Track Development of Ovarian Cancer Test

Highlights

- **CLEO signs Collaboration Agreement with University College London (UCL) to accelerate test development, securing access to ~2,000 high-quality blood samples**
- **Samples sourced from UKCTOCS, the world's largest Ovarian Cancer screening trial, to strengthen CLEO's clinical validation program**
- **Collaboration with UCL and renowned Ovarian Cancer expert, Professor Usha Menon, will evaluate CLEO's technology in two clinical studies focussed on the pre-surgical and screening markets**
- **The initiative with UCL forms part of CLEO's broader commercial strategy to deliver its Ovarian Cancer detection technology to the global screening market.**

MELBOURNE, AUSTRALIA, 28th April 2025: Ovarian Cancer diagnostics company, **Cleo Diagnostics Limited** (**ASX:COV**) (**CLEO**, or the **Company**) is pleased to announce that it has entered into a Collaboration Agreement with University College London (**UCL**) to access over 2,000 samples from the United Kingdom Collaborative Trial of Ovarian Cancer Screening (**UKCTOCS**), the world's largest Ovarian Cancer screening trial.

Major Step Forward for CLEO's Pre-Surgical and Screening Test Development Program

CLEO will use the samples to advance its Ovarian Cancer diagnostic and screening programs. Access to the collection is prioritised based on the potential impact, scientific merit, and alignment with UKCTOCS objectives. In this context, CLEO's granted access demonstrates confidence in the Company's potential to disrupt the Ovarian Cancer diagnosis landscape. This is particularly significant considering a key finding of UKCTOCS was that current Ovarian Cancer screening tests did not reduce the number of deaths and cannot be recommended in the general population – creating a significant opportunity for CLEO to solidify its position on the global stage.

Data collected using CLEO's test will be independently analysed in partnership with UCL, providing unbiased validation of CLEO's Ovarian Cancer technology.

Commenting on the UCL partnership, CLEO Chief Executive Officer, Dr Richard Allman, said:

> *"The opportunity to collaborate with UCL and be granted access to the UKCTOCS biobank is an extraordinary endorsement of our technology and its potential impact. This biobank is one of the most prestigious and rigorously protected Ovarian Cancer resources in the world, and not all applicants are granted access. To be selected reinforces the credibility and potential of our technology to become a globally adopted screening test.*

This collaboration will also support and progress CLEO's staged execution strategy. Integrating UKCTOCS samples into our clinical studies will help to fast-track our development and regulatory pathways – in particular validation of our pre-surgical test, as well as advancing our longer-term goal to deliver an effective screening tool for early Ovarian Cancer detection."

World-leading gynaecological oncology expert, Professor Usha Menon added:

"The UKCTOCS sample collection is a vital and irreplaceable asset for advancing Ovarian Cancer research. The performance data and evidence behind CLEO's technology are very encouraging, and we are excited to work with CLEO to assess how its tests can potentially be used in detection and screening strategies to reduce mortality from the disease."

Upcoming Clinical Studies to Evaluate CLEO's Technology

As part of the Collaboration Agreement, CLEO will use samples and data from the UKCTOCS biobank to conduct the following two clinical studies:

- **Study 1:** Pre-Surgical Market – Evaluation of the ability of CLEO's pre-surgical test to correctly discriminate a benign from malignant adnexal mass in a prospectively collected cohort; and
- **Study 2:** Screening Market – Evaluation of CLEO's technology to improve diagnostic lead time in an asymptomatic average risk population.

With respect to Study 1 focusing on the pre-surgical market, patients will be selected from women identified within the screen arms of the UKCTOCS multicentre trial who underwent surgery for adnexal lesions or persistent abnormality on transvaginal ultrasound (**TVU**) and subsequently received a post-surgical diagnosis or were found to have no ovarian cancer during follow-up. The CLEO pre-surgical test will be used to measure blood analytes in blinded samples and calculate a score indicating the risk of malignancy. This score will then be retrospectively correlated with diagnosis (benign versus malignant) as the primary endpoint. Secondary objectives will include subgroup analysis by histotype and stage.

With respect to Study 2 focusing on the screening market, cases (all clinically diagnosed) will be selected from women identified within the non-screening arm of the UKCTOCS multicentre trial. Single serum samples will be obtained from cases donated up to 3 years prior to cancer diagnosis. Controls will be selected from women for whom no ovarian cancer was detected during follow-up in the trial.

All serum samples will be evaluated using the CLEO test to generate a risk score. The primary endpoint will be to establish diagnostic lead time using the CLEO test relative to CA-125 as a first-line test. These data will be used to determine whether earlier identification of malignant disease is possible using the CLEO test. Secondary objectives will include subgroup analysis of invasive epithelial Ovarian Cancer, as well as high grade serous Ovarian Cancer and non-high grade serous Ovarian Cancer.

Following the execution of the Collaboration Agreement, CLEO is arranging for the dispatch of the first batch of samples, with the commencement of the trial to commence shortly thereafter. The clinical studies will continue to run alongside CLEO's ongoing clinical trials.

The potential outcomes for CLEO from this Collaboration Agreement are extensive:

- Demonstrate the superior performance of CLEO's proprietary technology by its ability to correctly discriminate a benign from malignant adnexal mass
- Evaluate the ability of the CLEO's technology to provide an early indication of malignancy by benchmarking it against the gold standards of CA-125 and transvaginal ultrasound

- Highlight the potential of CLEO's technology to be used for national screening
- Provide highly credible endorsement through the independent review and partnership with UKCTOCS
- Support initial market access in the U.S. and open opportunities to access other markets outside the U.S.
- Assist in establishing the revenue and logistics platform for CLEO to achieve long term success
- Improve and/or speed up market adoption
- Truncate the timeframe of the Company's strategy to deliver its Ovarian Cancer technology to all patient markets, with global population screening being the pinnacle
- Solidify CLEO's position on the global stage as the leading Ovarian Cancer detection technology.

Accelerated Development and Commercialisation of CLEO's Ovarian Cancer Tests

CLEO has developed a simple blood test for the accurate and early diagnosis of Ovarian Cancer based on the novel patented CXCL10 biomarker, which is produced early and at high levels by ovarian cancers but is largely absent in non-malignant disease. CLEO's pre-surgical test can discriminate malignant from benign gynaecological disease in patients with an adnexal mass. Initial testing, performed retrospectively in a 334 patient Australian cohort, demonstrated a 95% sensitivity and 95% specificity for differentiation of adnexal masses. This finding was largely independent of menopausal status, and a significant improvement over the use of CA-125 alone. Importantly, the blood test identified up to 90% of early-stage malignancies when combined with transvaginal ultrasound score[1], a significant advancement over current clinical practice.

The Company is progressing trials in the U.S. in-order to submit a 510(k) application with the Food and Drug Administration (**FDA**) with a blood test for the evaluation of Ovarian Cancer in women prior to surgery. Following this, CLEO intends to bring two additional tests to market, namely the recurrence test and screening test – with its screening test being the pinnacle. Access to the UKCTOCS samples will greatly assist in fast-tracking CLEO's development and regulatory pathways as the data can be integrated into its clinical studies, leading to substantial time and cost savings for the Company.

About the UKCTOCS Trial

Background

The UK Collaborative Trial of Ovarian Cancer Screening is a multi-centre randomised controlled trial conducted by the Medical Research Council (**MRC)** Clinical Trials Unit at UCL that evaluated whether it would be possible to save lives using population screening to detect Ovarian Cancer earlier. The trial involved over 200,000 postmenopausal women aged 50-74 in the UK, who donated their data and over 500,000 samples for secondary studies. UKCTOCS ran for more than 20 years, and is estimated to have cost around £30 million. Funding was provided by the MRC, National Institute for Health and Care Research (**NIHR**), Cancer Research UK, and The Eve Appeal (charity funding).

UKCTOCS Longitudinal Women's Cohort (**UKLWC**) is the bioresource created as a result of the UKCTOCS, and there are several principles governing its access for use in secondary studies. Access to the collection is governed by a rigorous review process, ensuring only projects with strong scientific merit and high potential for significant clinical impact can secure access.

Objectives

In the UK, Ovarian Cancer causes more deaths than all the other gynaecological cancers combined. Majority of patients present with advanced disease, which is associated with poor survival. In contrast, five-year survival rates for women diagnosed with Stage I Ovarian Cancer are over 90%, suggesting that early detection through screening is likely to improve outcomes.

[1] DOI: 10.3390/cancers16112048: Utility of a Multi-Marker Panel with Ultrasound for Enhanced Classification of Adnexal Mass - PubMed

The UKCTOCS trial ultimately concluded that current Ovarian Cancer screening measures cannot be recommended in the general population. In addition to the following:

- Current gold-standard tests comprising CA-125 and ultrasound was not suitable for screening average-risk women
- Annual multimodal screening (**MMS**) using the CA-125 blood test and Risk of Ovarian Cancer Algorithm (**ROCA**) and second line transvaginal ultrasound resulted in a 10% reduction in late-stage diagnoses, but this did not translate into a reduction in deaths due to Ovarian Cancer
- Due to the lack of mortality reduction, routine Ovarian Cancer screening for asymptomatic average risk women using current testing technologies is not recommended
- Research using large-scale valuable data and samples collected prior to cancer diagnosis in one of the largest trial biobanks may help refine future detection methods to identify better screening strategies.

Given the emergence of novel diagnostic tests, UCL is looking to leverage the bioresource established during UKCTOCS to find and assess Ovarian Cancer screening technologies that can detect the disease early enough to reduce the impact on mortality.

-ENDS-

This ASX announcement was authorised for release on behalf of the Cleo Diagnostics Ltd Board.

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About Cleo Diagnostics Ltd ASX:COV

CLEO aims to bring to market a simple blood test for the accurate and early diagnosis of ovarian cancer based on the novel patented CXCL10 biomarker, which is produced early and at high levels by ovarian cancers but is largely absent in non-malignant disease. The test aims to distinguish benign from malignant growths in a standard format that will be readily compatible with existing equipment used by diagnostic laboratories worldwide.

The platform is backed by over 10 years of scientific Research & Development at the Hudson Institute of Medical Research, with two clinical studies conducted with over 500 patients. Pursuant to a licence agreement with the Hudson Institute of Medical Research, CLEO has a worldwide exclusive licence to commercialise the intellectual property which underpins its operations and the ovarian cancer tests.

The clinical unmet worldwide need is urgent. An accurate and early detection blood test could shift survivability for ovarian cancer significantly as seen with other cancers. CLEO is advancing the availability of its simple blood test, under a modular execution strategy which is designed to eventually address all ovarian cancer detection markets with specific tests including surgical triage, recurrence, high risk, and early-stage screening.