ASX Announcement

CLEO Strengthens FDA Submission Following Access to Globally Respected U.S. Biobank

Highlights

- **CLEO granted approval from U.S. National Cancer Institute to access blood samples from the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial**
- **PLCO biobank considered a 'gold standard resource' and is one of the largest and most influential U.S. longitudinal cancer studies conducted to date**
- **CLEO will use samples from PLCO biobank to:**
  - **Generate data to strengthen its FDA 510(k) submission for the Pre-Surgical Test**
  - **Accelerate development and commercialisation of its Screening Test**
- **Recruitment for U.S. clinical trials ongoing with completion anticipated Q4 CY2025.**

MELBOURNE, AUSTRALIA, 25th June 2025: Ovarian Cancer diagnostics company, **Cleo Diagnostics Limited** (**ASX:COV**) (**CLEO** or **the Company**) is pleased to announce it has received formal approval from the U.S. National Cancer Institute (**NCI**) to access blood samples held within the globally respected Prostate, Lung, Colorectal and Ovarian (**PLCO**) Cancer Screening Trial biobank. This represents a significant milestone that supports the Company's planned FDA 510(k) submission for its Ovarian Cancer Pre-Surgical Test.

Commenting on access to the PLCO biobank, Chief Executive Officer, Dr Richard Allman, said:

> *"Securing access to the PLCO biobank is a major milestone for CLEO, and another strong endorsement of the scientific merit behind our technology. The PLCO is a highly respected U.S.-based cancer screening study, and inclusion of data from this cohort will significantly strengthen the clinical evidence package supporting CLEO's FDA 510(k) submission.*
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> *Importantly, we are driving our commercial strategy forward which includes partnering with one of the world's largest biobanks. This adds to our recently announced partnership with University College London to access the UKCTOCS biobank. Together, these biobanks form a comprehensive, internationally representative intended-use population that CLEO will use to enhance the totality of its clinical evidence and substantially de-risk key regulatory milestones. Ultimately, this will help to fast-track our Screening Test development."*

Upcoming Clinical Studies to Validate CLEO's Technology

Following scientific review and endorsement by PLCO's Etiology and Early Marker Studies (**EEMS**) Steering Committee, CLEO will now initiate two pivotal studies using the high-quality, prospectively collected specimens.

- **Study 1:** Pre-Surgical Market – Evaluation of the ability for 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 (using longitudinal samples collected up to three years prior to diagnosis) in an asymptomatic average risk population.

CLEO's technology has consistently demonstrated superior performance in early studies, including 95% sensitivity and 95% specificity in distinguishing malignant from benign adnexal masses. In prior studies, CLEO's Pre-Surgical Test outperformed current standard-of-care tools, underscoring its potential to set a new benchmark in Ovarian Cancer diagnostics.

Significant Positive Impact on CLEO's FDA submission

These studies will generate supporting data for both clinical utility and regulatory progression, including CLEO's upcoming FDA 510(k) submission. **This data will strengthen the evidence package supporting CLEO's FDA submission, and significantly de-risks key regulatory milestones.**

Whilst CLEO's pivotal U.S. trials will provide the core evidence package, these additional studies can help to bolster the overall submission in multiple ways:

- Strengthens the totality of evidence using data from a US population, typically preferred by regulators;
- Pre-emptively addresses specific FDA questions that may arise prior to or during the submission review;
- Improves regulatory confidence;
- Helps to support labelling claims; and
- Enables a more efficient review process.

Crucially, CLEO's studies will now progress in a sample population that accurately reflects real-world Ovarian Cancer incidence. This is essential to generate meaningful, translatable performance metrics – critical for clinical adoption, payer reimbursement, and regulatory approval.

Strategic Biobank Partnerships to Strengthen Regulatory and Clinical Pathway

Together with CLEO's previously announced access to the United Kingdom Collaborative Trial of Ovarian Cancer Screening (**UKCTOCS**) biobank (*refer to ASX Announcement dated 28th April 2025*), the PLCO studies form a critical pillar of the Company's FDA regulatory strategy. These two globally respected biobanks provide CLEO access to complementary longitudinal datasets encompassing U.S. and U.K. populations. Leveraging these unique cohorts enhances the totality of clinical evidence to support CLEO's planned FDA 510(k) submission, and de-risks key regulatory and commercial milestones. Strategically, these agreements also advance CLEO's broader development pathway by enabling earlier assessment of test performance in asymptomatic populations, accelerating screening test development, and supporting future commercial claims.

About the PLCO Study

The PLCO Cancer Screening Trial is one of the largest and most influential longitudinal cancer studies conducted in the U.S. to date. Sponsored by the NCI, it enrolled over 155,000 participants and followed them for more than a decade. The PLCO biobank contains extensively annotated, rigorously collected biospecimens, offering a gold-standard resource for the development of early cancer detection technologies. Access to this cohort is highly competitive and reflects the quality, scientific credibility, and strategic importance of CLEO's diagnostic program.

This milestone marks a significant advancement in CLEO's clinical development journey, reinforcing the Company's commitment to improving early detection and outcomes in Ovarian Cancer.

U.S Clinical Trial Update

CLEO's pivotal FDA-enabling clinical trial continues to recruit patients in the U.S. Initial clinical trial recruitment has been focused on regional general practice clinics to satisfy patient diversity requirements in-line with FDA guidelines. The next and final phase of recruitment is targeting high-volume metropolitan surgical centres. Additional centres in the final stages of onboarding (with activation expected around July 2025) include the Beth Israel Deaconess Medical Centre / Dana Faber Cancer Institute, Rush University Medical Centre, Yale University Medical Centre, Duke University Medical Centre, Cleveland Clinic, Columbia University Medical Centre and University of Florida – Jacksonville. Together with existing recruitment sites, CLEO remains on track to meet its completion target of Q4 CY2025.

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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.