EVOLUTION CAPITAL

COV | INITIATION REPORT | HEALTHCARE

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Precision in Ovarian Cancer Triage

Cleo Diagnostics Ltd

Cleo Diagnostics ('COV', 'Cleo') is an Australian diagnostics company which has developed a blood-based multi-marker test to more accurately triage women with a suspected ovarian mass. Upon FDA approval (expected late 2026), we see a clear opportunity for Cleo to slot into the existing diagnostic pathway as the objective adjunct to transvaginal ultrasound (together with CA-125 biomarker blood test, the existing standard-of-care), reducing unnecessary surgery and facilitating appropriate specialist intervention in ovarian cancer.

Critical Unmet Need

Ovarian cancer is the deadliest gynaecological malignancy largely because it is usually found late. Current standard-of-care tools – CA-125 (blood biomarker test) and transvaginal ultrasound (TVU) – are poor at separating benign from malignant masses; around 90% of women taken to theatre for a "suspicious" adnexal mass are ultimately found to have benign disease, driving avoidable morbidity, inefficient use of gyn-onc capacity, and >US$1bn of largely wasted spend each year. CleoDx is designed specifically to fix this diagnostic bottleneck by providing a pre-surgical malignancy risk score to guide referral and operative planning.

Accurate & Reliable Proprietary Technology

CleoDx measures five analytes – active and total CXCL10, CA-125, HE4 and IL-6 – and feeds them into a proprietary algorithm to generate a single "risk of malignancy" index. The inclusion of CXCL10 activity (active vs total) is unique and proprietary. In retrospective validation (n=334), CleoDx delivered 95% sensitivity and 95% specificity and correctly identified ~80% of early-stage cancers, materially outperforming predicate commercially available tests ROMA and OVA1. When combined with TVU it has shown positive predictive value above 90% in specialist cohorts and strong ability to "rescue" cases where CA-125 is falsely normal or falsely elevated. Together, this data gives the test a high degree of technical credibility and directly address the weaknesses of the current standard of care.

Defined Commercial Strategy

The initial commercial focus is US pre-surgical triage. Of ~3.4m US women who present annually with a suspected adnexal mass, around 2m proceed to further imaging and/or biomarker testing and ~370k undergo surgery. At a benchmark price in line with existing multivariate assays (~US$1,000), this triage segment alone represents an addressable market of ~US$2bn p.a. We view recurrence monitoring and screening as logical follow-on indications and genuine sources of upside, but do not underwrite them in our base case.

Outlook & Valuation

Cleo is targeting FDA 510(k) clearance, supported by an ongoing ~500-patient prospective US pivotal study with results expected early 2026, and large-scale biobank work to validate performance across broader populations and use-cases. Our DCF values only US pre-surgical triage, assumes peak penetration of 15% of the ~2m women who undergo further investigation (~300k tests/year), a long-term ASP of US$1,000 and a 35% revenue share to Cleo. Applying a 15% WACC and a blended probability of success of 51% (regulatory and commercial) yields a risk-adjusted fair value of A$1.03 per share, implying meaningful upside from current levels.

Recommendation	**Spec BUY**
Fair Valuation	**$1.03**
Share Price	**$0.69**
TSR	**49%**

Company Profile

Market Cap	$88.7M
Enterprise Value	$82.2M
SOI (diluted)	~145.3M
Free Float	77%
ADV (3-month)	$152k
52-Week Range	$0.31 - $0.73

Price Performance

%	1M	3M	12M
Absolute	68.3%	100.0%	97.1%
ASX/S&P200	-3.1%	-1.4%	1.7%

Company Overview

Cleo Diagnostics is an Australian medical technology company developing CleoDx, a next-generation blood-based multi-marker test designed to more accurately triage women with suspected ovarian masses. The test combines CA-125, HE4, IL-6 and a proprietary active-to-total CXCL10 ratio to deliver markedly higher sensitivity and specificity than current standard-of-care tools, aiming to reduce unnecessary surgeries and improve early cancer detection. Cleo is progressing a ~500-patient US pivotal study ahead of a planned 510(k) submission, targeting commercial launch into the ~2 million-patient US triage market.

Analyst

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Financial Summary

VALUATION DETAILS	
Share Price (A$)	$0.69
Market Cap (A$m)	88.7
Enterprise Value (A$m)	82.2
Fair Value/Share (A$)	$1.03

FINANCIAL STATEMENTS (A$m)	FY25	FY26E	FY27E	FY28E	FY29E
Income Statement					
Revenue	1.18	0.86	1.05	1.77	2.57
EBITDA	-3.94	-5.64	-6.45	-5.82	-5.74
EBIT	-4.00	-6.03	-6.45	-5.82	-5.74
Net Income	-4.00	-5.77	-6.06	-5.69	-5.09
Balance Sheet					
Cash & Cash Equivalents	6.46	9.68	3.31	16.28	11.17
Inventory	0.00	0.00	0.00	0.06	0.08
Receivables	0.07	1.52	1.52	1.61	1.76
Other Assets	0.45	0.41	0.01	0.01	0.01
Total Assets	6.98	11.60	4.84	17.97	13.02
Total Debt	0.00	0.00	0.00	0.00	0.00
Other Liabilities	1.10	1.75	1.44	1.46	1.59
Total Liabilities	1.10	1.75	1.44	1.46	1.59
Shareholders' Equity	5.83	9.47	3.40	16.51	11.43
Cash Flow Statement					
Net Income	-4.00	-5.77	-6.06	-5.69	-5.09
Add: D&A	0.06	0.39	0.00	0.00	0.00
Less: NCWC	0.60	-0.81	-0.31	-0.13	-0.03
Cash Flow from Operations	-2.90	-6.18	-6.37	-5.82	-5.12
Cash Flow from Investing	-0.01	0.00	0.00	0.00	0.00
Equity Raised (net)	0.00	9.40	0.00	18.80	0.00
Less: Dividends Paid	0.00	0.00	0.00	0.00	0.00
Cash Flow from Financing	0.00	9.40	0.00	18.80	0.00
Unlevered Free Cash Flow	-2.91	-6.44	-6.76	-5.95	-5.77

PER SHARE DATA	FY25	FY26E	FY27E	FY28E	FY29E
Diluted SOI (m)	145.3	161.3	160.0	160.0	160.0
Normalised EPS (A$)	-0.03	-0.04	-0.04	-0.04	-0.03
DPS (A$)	0.00	0.00	0.00	0.00	0.00
Payout	0%	0%	0%	0%	0%
Franking	0%	0%	0%	0%	0%

RATIOS	FY25	FY26E	FY27E	FY28E	FY29E
Liquidity					
Current Ratio	19.41	5.94	6.42	3.37	12.33
Quick Ratio	5.93	6.41	3.36	12.28	8.11
Solvency					
Debt to Equity	0.19	0.18	0.42	0.09	0.14
Equity to Assets	0.84	0.84	0.70	0.92	0.88
Profitability					
ROA	-47.6%	-63.6%	-75.5%	-49.9%	-32.8%
ROE	-52.5%	-75.4%	-94.2%	-57.2%	-36.4%
EBITDA Margin	-612.1%	-332.4%	-651.8%	-614.3%	-328.5%
NPAT Margin	-337.5%	-667.1%	-577.4%	-321.0%	-197.8%
Growth					
TTV	N/A	N/A	N/A	N/A	210.5%
Revenue	N/A	N/A	N/A	N/A	210.5%
EBITDA	-7.2%	-43.1%	-14.5%	9.7%	1.5%
Underlying NPAT	-6.4%	-44.2%	-5.1%	6.1%	10.7%
EPS	-2.9%	20.9%	0.3%	-5.8%	-10.7%
Valuation					
P/E	-33.1	-27.4	-27.3	-29.0	-32.4
EV/Sales	N/A	N/A	N/A	205.5	101.0
EV/EBITDA	-32.0	-26.3	-25.1	-25.5	-26.8
Dividend Yield	0.0%	0.0%	0.0%	0.0%	0.0%

Investment Thesis

Pillar 1: Addressing the Critical Bottleneck in Ovarian Cancer Diagnosis
Ovarian cancer remains the deadliest gynaecological malignancy, primarily due to late diagnosis. The critical diagnostic challenge occurs when an ovarian or adnexal mass is suspected. Current standard-of-care tools – the CA-125 blood test and transvaginal ultrasound – are unreliable at distinguishing between benign and malignant masses. This diagnostic ambiguity leads to a systemic failure: approximately 90% of women undergoing surgery for a suspected mass are ultimately found to have benign disease. This results in significant patient morbidity, inefficient use of specialist resources, and a substantial financial burden on the healthcare system. Cleo Diagnostics has developed a technology poised to reform this pathway by providing accurate, pre-surgical triage.

Pillar 2: Differentiated Technology
CleoDx is a novel, multi-biomarker blood test designed to accurately assess malignancy risk early in the triage process. The test integrates traditional markers (CA-125, HE4) with a proprietary measurement of the CXCL10 chemokine (specifically the ratio of active vs. total forms), providing a unique biological signal of malignancy that incumbents miss. The clinical data generated to date is compelling. In retrospective validation studies (n=334), CleoDx demonstrated 95% sensitivity and 95% specificity. This significantly outperforms existing FDA-cleared tests like OVA1 (high sensitivity but poor specificity) and ROMA. Crucially, CleoDx correctly identified 80% of early-stage cancers in validation cohorts, compared to roughly 50% with conventional approaches, highlighting its potential to enable earlier intervention. This technological differentiation is evidenced in 3 published peer-reviewed articles.

Pillar 3: Clear Regulatory Pathway and Substantial Market Opportunity
Cleo is prioritizing the US market and pursuing FDA clearance via the 510(k) pathway, leveraging existing predicates. We anticipate a potential submission in 2026 and a commercial launch in 2027. Opting for FDA clearance rather than the Lab Developed Test (LDT) route creates a higher regulatory barrier to entry and provides a clearer path to broad reimbursement and guideline inclusion. The initial addressable market – pre-surgical triage in the US – is significant. Approximately 2 million women undergo diagnostic investigation for adnexal masses annually. At a benchmark price of US$1,000 per test (consistent with existing multivariate assays), this represents a $2 billion TAM.

Pillar 4: A Platform Technology with Significant Unmodelled Upside
The pre-surgical triage test is the first application of Cleo's biomarker platform. The technology holds significant potential for expansion into high-value adjacent markets. The next logical step is recurrence monitoring for ovarian cancer survivors. Further down the line, the test could be applied to high-risk screening. Cleo is already validating its markers on large biobank cohorts to explore these future applications.

Pillar 5: Undervaluation Presents Compelling Entry Point
Our risk-adjusted valuation of $1.03 per share is based on a conservative DCF model that includes several downside protections:

- Modelling of solely the US pre-surgical trial program (no ROW, Recurrence/Screening).
- We assume peak penetration of only 15% of the 2 million annual investigation volume (in-line with the circa 370,000 ovarian/adnexal mass surgeries performed in the US per annum), following a gradual s-curve adoption with very low initial sales.
- We apply a 51% probability of success (PoS) factor accounting for hurdles to success – regulatory approval (85%), and commercial traction (60%).

We believe the combination of a superior diagnostic addressing a clear clinical need, a defined path to market, and substantial blue-sky potential not captured in our base case presents a compelling investment opportunity. We think the market is still over-discounting reimbursement risk and under-appreciating the weight of peer-reviewed data.

Figure 1: Expected Catalyst table.

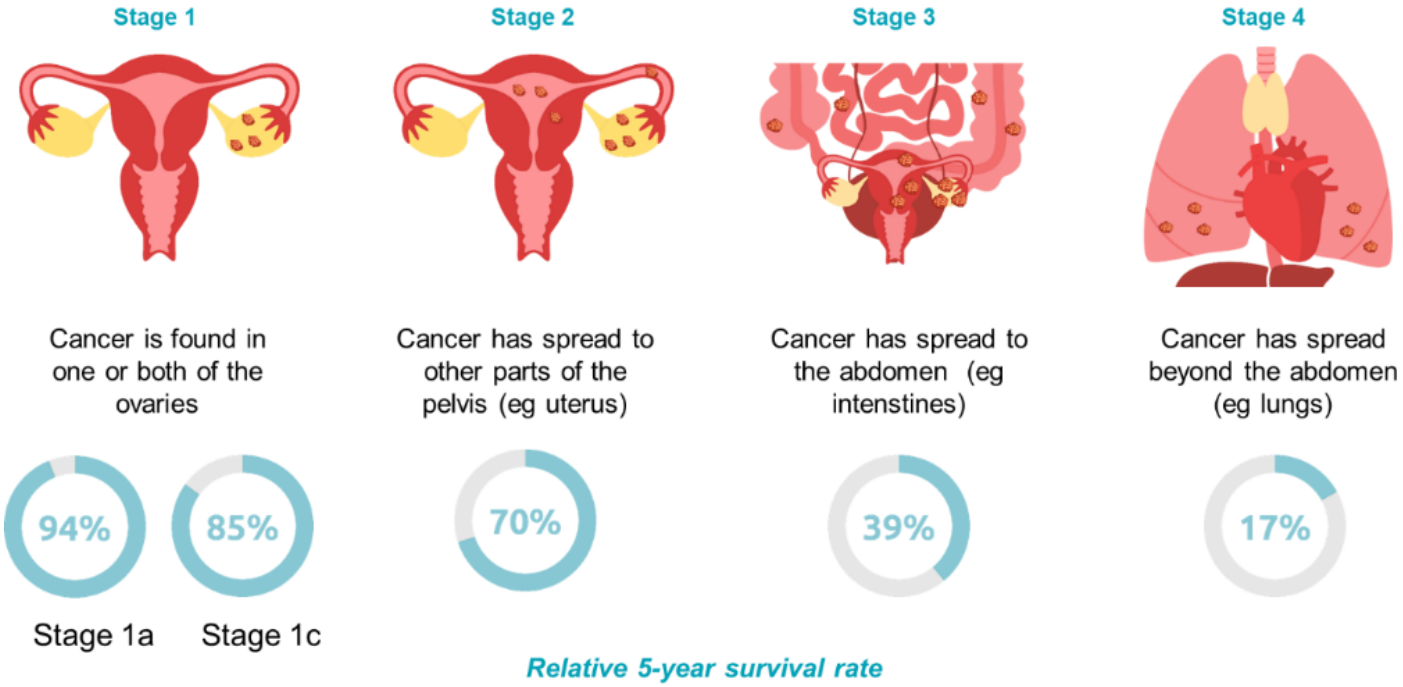
Estimated Timing	Event / Catalyst	Impact & Significance
Late CY2025	US health-economic analysis and market study completed	Quantifies cost savings from avoiding benign surgeries and confirms ~2.0m-patient US pre-surgical triage TAM; strengthens reimbursement story and supports our TAM assumptions.
H2 CY2025	Completion of US Prospective Pivotal Study Recruitment	High Impact. Cleo is aiming to recruit ~500 patients for its prospective US trial by the end of 2025. Completing enrolment on schedule is a critical de-risking event, confirming clinical interest and keeping the FDA submission timeline on track.
H1 CY2026	Top-Line Results from Prospective Pivotal Study	Critical Impact. This is the most significant near-term valuation catalyst. The data must replicate the high sensitivity (95%) and specificity (95%) seen in retrospective studies. Positive results will form the core of the FDA submission and validating the clinical utility argument for payers.
Mid-Late CY2026	FDA 510(k) Submission	High Impact. Submission of the 510(k) dossier marks the transition from clinical validation to regulatory review. It demonstrates that the data package is complete and substantially equivalent to predicates like OVA1.
H2 CY2026	Execution of US Commercial Distribution Agreement	Medium-High Impact. We anticipate Cleo will sign an exclusive distribution agreement with a top-tier national reference lab/pathology network ahead of launch. The identity of the partner (e.g., Quest, LabCorp equivalent) and deal terms (revenue share) will be key for modelling commercial reach.
Late CY2026 / Early CY2027	FDA 510(k) Clearance	Critical Impact. Regulatory clearance is the "green light" for US commercialisation. It removes the primary regulatory overhang and allows the company to legally market the test for pre-surgical triage.
Early CY2027	US Commercial Launch (First Commercial Sales)	High Impact. The official market entry. Initial sales volume will likely be low, but this validates the operational supply chain and the partner's readiness.
CY2027	Publication of Health Economic & Utility Data	Medium Impact. Post-launch, Cleo needs to publish data showing the test reduces unnecessary surgeries to support reimbursement discussions. Positive health economic outcomes will drive payer coverage decisions.
CY2027	Securing of CPT/PLA Codes & Initial Payer Coverage	High Impact. Obtaining a dedicated PLA code or successfully billing via existing codes (like 81503), along with initial coverage determinations from private payers or Medicare, is essential for moving from clinical availability to revenue generation.
2028+	Potential TGA Submission / Australian Launch	Low-Medium Impact. While the US is the priority, an Australian launch (via MSAC application and TGA approval) represents an incremental revenue stream and validates the technology in the home market.
2028+	Clinical Guideline Inclusion (NCCN / ACOG)	Long-Term Strategic Impact. Inclusion in guidelines is the "holy grail" for diagnostics, driving standard-of-care adoption. While this may take longer, early engagement or mention in bulletins would be a strong positive signal.

Clinical Unmet Need

Epidemiology

Ovarian cancer remains one of the most lethal malignancies in women, largely due to late detection. Only about 20% of cases are caught at an early (localized) stage – when 5-year survival exceeds 90% – whereas overall 5-year survival is below 50%. In the United States, an estimated 20,890 women will be diagnosed with ovarian cancer in 2025, resulting in 12,730 deaths. In Australia, roughly 1,786 women were diagnosed in 2023 and ~1,050 died of the disease. Ovarian cancer accounts for only ~1% of female cancers but is the fifth-leading cause of cancer-related death among women, making it the deadliest gynaecologic cancer. Attempts at broad early screening using existing technologies have failed to reduce mortality and large trials showed no mortality benefit: The Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) was a large randomized controlled trial designed and sponsored by the National Cancer Institute and aimed to determine the effects of screening on cancer-related mortality in men and women aged 55-74. Among women in the general US population, simultaneous screening with CA-125 and transvaginal ultrasound compared with usual care did not reduce ovarian cancer mortality. Routine screening is therefore no recommended/required for average-risk women with the current technology available. Most cases present with advanced disease.

Figure 2: Ovarian Cancer Staging and Outcomes. Illustration of disease spread and the corresponding sharp decline in 5-year survival rates. Source: Cleo Diagnostics.



Current Diagnostic Workflow

When an ovarian/adnexal mass is detected (often via pelvic exam or incidentally on imaging), the standard approach is a transvaginal ultrasound (TVU) and a CA-125 blood test. Ultrasound assesses morphology of the ovarian mass, and CA-125 is a tumour marker often elevated in ovarian cancer. However, these tools are insufficient to reliably distinguish benign from malignant masses. CA-125 has well-known limitations: many benign gynaecologic conditions (endometriosis, fibroids, pelvic inflammatory disease, etc.) can elevate CA-125 and cause false positives, reducing specificity.

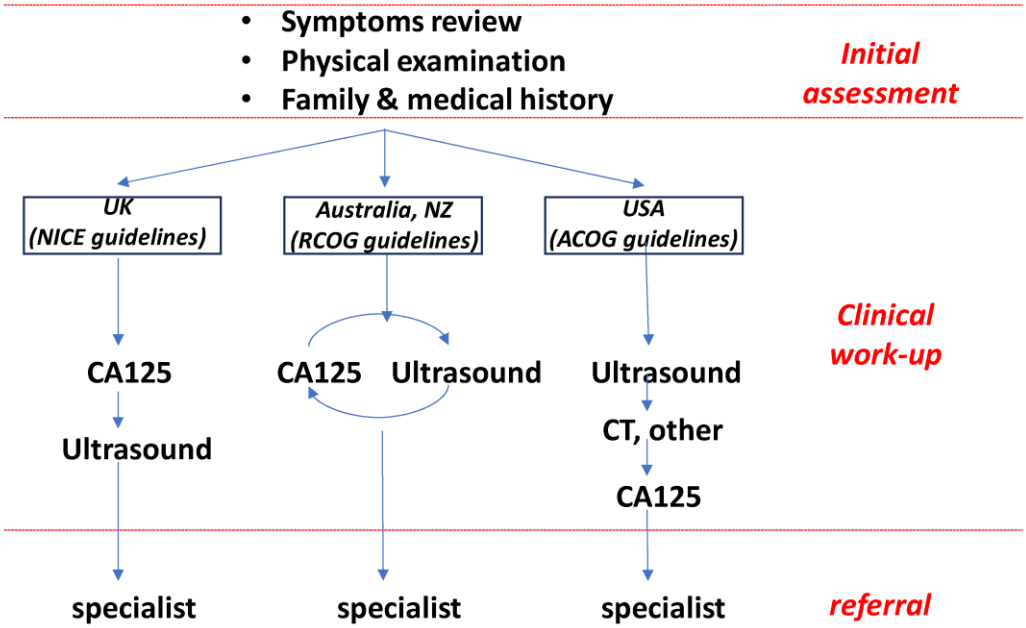
At the same time, a large fraction of early-stage ovarian cancers do not raise CA-125 levels, limiting sensitivity. Ultrasound provides anatomical detail and can characterize cysts or solid masses, but many tumours have indeterminate ultrasound features – imaging alone cannot definitively tell cancer vs. benign except in extreme cases. Ovarian masses are rarely biopsied pre-op due to peritoneal-spill risk; suspected cancer

typically proceeds directly to definitive surgery or neoadjuvant chemo. As a result, clinicians often err on the side of caution and refer patients to surgery even with equivocal results.

Up to ~90% of women taken for exploratory surgery due to a "suspicious" ovarian mass are ultimately found to have benign disease, meaning a very large number of invasive surgeries are done on non-cancerous lesions. This is the crux of the issue in the current diagnostic workflow. Conversely, some malignant tumours are initially missed or not flagged as high-risk (e.g. if CA-125 is normal), leading to delayed specialist referral – fewer than half of ovarian cancer patients nationally receive their first surgery from a gynaecologic oncologist, despite evidence that specialist care improves outcomes.

This underscores a critical unmet need for better diagnostic triage tools: clinicians need more accurate, objective tests to determine which adnexal masses are likely cancerous (warranting immediate referral to a gyn-oncologist and optimal surgical planning) and which are likely benign (where surgery could be minimal or avoided). Cleo Diagnostics aims to fill this gap with a more reliable pre-surgical diagnostic test.

Figure 3: Disease Progression and Prognosis. Visual summary of ovarian cancer staging and the corresponding sharp decline in 5-year survival rates from >90% in early stages to <20% in advanced metastatic disease. Source: Stephens et al., *Diagnostics* 2024, *14*, 671.



Typical clinical workflow for diagnosis and referral of patients with adnexal mass. Dependent on geographical region and guidelines adopted patients experience a different workflow. However, all commence with an assessment of symptoms, physical examination, medical and familial history. In the United Kingdom CA-125 testing is performed prior to ultrasound; in Australia/NZ both are typically performed; and in the US ultrasound is generally performed before biomarker testing. In all cases the information is used to provide the ultimate surgical referral.

Health Economic Burden of Unnecessary Surgeries

Each year in the US, circa 370,000 women undergo surgery for a benign adnexal mass. These "unnecessary" or non-malignant surgeries represent a significant financial burden for payers (Medicare, Medicaid, and private insurers). Uninsured patients face total bills on the order of $7,000 to $15,000 (or more) for ovarian cyst or mass removal (hospital charges plus surgeon fees). Even with insurance, payers reimburse substantial amounts – e.g. bundled cash prices of about $10k per case are reported, and Medicare's average allowed amount for an outpatient hysterectomy with ovary removal is around $1,100 to $1,800 (significantly below typical private insurance payments). Multiplying per-case costs by the ~370,000 benign surgeries annually suggest well over $1 billion in aggregate spending each year on surgeries that ultimately prove unnecessary.

Beyond the immediate procedure cost, downstream expenses add to the payer burden. Nearly all such surgeries involve general anaesthesia and hospital facility use, often including inpatient stays, particularly for open surgeries or if cancer is suspected. A laparotomy (open removal of an ovarian mass) usually requires 2+ days of hospitalization for recovery, increasing the cost. Even laparoscopic procedures can incur overnight observation abd later hospital visits if complications arise. Importantly, complication rates range from ~3% up to 15% for surgeries on benign ovarian tumours.[1] These complications – such as infections, bleeding, surgical injuries, or venous thromboembolism – often trigger extra treatment costs, ED visits, or readmissions. Payers also indirectly bear the cost of inefficient specialist utilization: many surgeries are referred to gynaecologic oncologists (given the cancer concern), a high-cost specialist resource that might have been avoided with better pre-op diagnostics. Overall, unnecessary adnexal surgeries create a multi-factorial economic burden: procedure reimbursements, hospital stay costs, management of complications, and wasted specialist consultations all accrue with little health benefit when the disease is benign.

System/Provider Perspective: Resource Utilisation & Opportunity Costs

From the health system and provider standpoint, avoiding unnecessary ovarian surgeries is crucial for operational efficiency and quality of care. Operating room (OR) resources are significant: each benign mass surgery consumes valuable OR time, staff, and equipment that could serve other critical cases. Studies estimate OR time costs about $36-$37 per minute in US hospitals when accounting for direct and indirect expenses.[2] Typical operative time for laparoscopic oophorectomy is 60-80 minutes[3], meaning each potentially avoidable surgery ties up an OR for 1-2 hours, incurring substantial overhead.

Moreover, these cases often require highly trained personnel. If there is any suspicion of malignancy, gynaecologic oncologists are involved or perform the surgery. However, when 9 out of 10 cases turn out benign, it implies that gynaecologic oncologists and specialized surgical teams are frequently being occupied by non-malignant cases – an opportunity cost. Those specialists and OR slots could have been allocated to other surgeries or to true gynaecologic cancer patients who need timely care.

Unnecessary surgeries can also impact provider performance metrics and workload. Hospitals are increasingly measured on value-based care and outcome metrics. Avoidable surgeries expose patients to risk without benefit, which can reflect poorly in quality metrics (for example, higher complication or readmission rates for benign disease). By reducing unwarranted operations, providers can improve throughput and allocate operating rooms, hospital beds, and specialist consults more effectively. It also mitigates the risk of malpractice or reputational harm that could arise if a patient suffers a major complication from a surgery that hindsight shows was unnecessary. In sum, from a system perspective each avoided surgery saves scarce surgical resources and allows care teams (especially gynaecologic oncologists) to concentrate on cases with clear therapeutic benefit.

[1] Yoeli-Bik, R., Longman, R.E., Wroblewski, K., Weigert, M., Abramowicz, J.S. and Lengyel, E. (2023). Diagnostic Performance of Ultrasonography-Based Risk Models in Differentiating Between Benign and Malignant Ovarian Tumors in a US Cohort. *JAMA Network Open*, [online] 6(7), p.e2323289. doi:https://doi.org/10.1001/jamanetworkopen.2023.23289.

[2] Childers, C.P. and Maggard-Gibbons, M. (2018). Understanding Costs of Care in the Operating Room. *JAMA Surgery*, 153(4), p.e176233. doi:https://doi.org/10.1001/jamasurg.2017.6233.

[3] Quinlan, D.J., Townsend, D.E. and Johnson, G.H. (1997). Safe and cost-effective laparoscopic removal of adnexal masses. *The Journal of the American Association of Gynecologic Laparoscopists*, 4(2), pp.215–218. doi:https://doi.org/10.1016/s1074-3804(97)80012-6.

CleoDx: A Novel Multi-Marker Ovarian Cancer Test

CleoDx is a blood-based test designed to accurately assess the malignancy risk of an ovarian mass before a patient undergoes surgery. It is a multi-biomarker panel measuring five analytes from a patient's blood sample: the chemokine CXCL10 in both its active form and total form (Cleo measures the ratio of biologically active CXCL10, based on research that ovarian tumours produce an inactive CXCL10 variant), plus traditional markers CA-125 and HE4, and an inflammatory cytokine IL-6. These markers are integrated via a proprietary algorithm to produce a single "Risk of Malignancy" score (on a 1–10 scale) for the adnexal mass. The test is intended to be simple for clinicians: a routine blood draw yields a quantitative risk score. A high score would prompt urgent referral to a gynaecologic oncologist for proper surgical management, whereas a low score could support a more conservative approach or watchful waiting for a likely benign tumour. In essence, CleoDx's value proposition is to outperform the crude CA-125 + ultrasound assessment with a more robust, multi-factor diagnostic, thereby reducing unnecessary surgeries and improving referral of true cancers.

Figure 4: Sample render of CleoDx test box. Source: Cleo Diagnostics.

Test Process

The CleoDx process is designed to integrate seamlessly into existing clinical workflows:

i. **Test Order:** The treating physician orders the CleoDx test for a patient with a suspected adnexal or ovarian mass.

ii. **Sample Collection:** A blood sample is drawn and serum is separated for analysis.

iii. **Sample Processing:** The clinical laboratory receives the sample and loads it, together with CleoDx reagents, onto a compatible automated laboratory analysis platform.

iv. **Assay Run:** The lab scientist runs the protocol to measure levels of active and total CXCL10, IL-6, HE4 and CA-125.

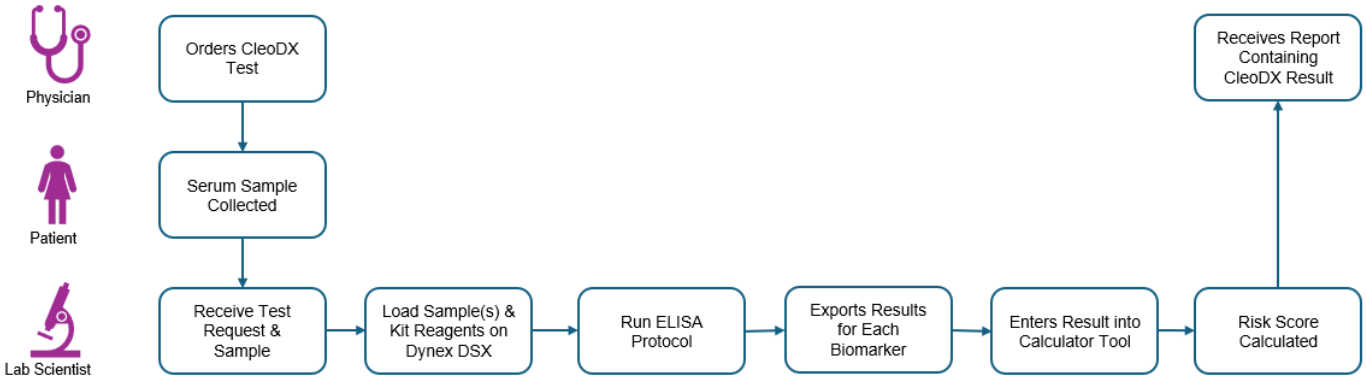
v. **Data Export:** Results for each biomarker are exported and entered into Cleo's proprietary calculator tool.

vi. **Risk Calculation:** The algorithm integrates biomarker values to generate a quantitative "Risk of Malignancy" score.

vii. **Report Delivery:** The final CleoDx report summarising the malignancy risk and interpretation guidance is securely transmitted back to the ordering physician, who uses the result to inform surgical referral and management decisions.

This streamlined, seven-step workflow allows CleoDx to deliver an actionable risk score within routine laboratory operations, providing clinicians with a clear, objective assessment before surgery.

Figure 5: Operational Workflow. Overview of the sample journey from patient collection to result delivery, utilizing standard laboratory infrastructure and Cleo's proprietary algorithm. Source: Cleo Diagnostics.



Why CXCL10 Matters

C-X-C motif chemokine liganSDd 10 (CXCL10) is a small cytokine (chemokine) with key roles in immune cell trafficking and inflammation. In ovarian cancer, CXCL10 has emerged as a relevant biomarker and immune mediator in the tumour microenvironment. High CXCL10 expression within the tumour is strongly associated with a more inflamed tumour microenvironment. Multiple studies (independent of Cleo) have identified CXCL10 as a robust positive prognostic marker in ovarian cancer: patients whose tumours have elevated CXCL10 tend to show prolonged overall survival and enriched tumour-infiltrating lymphocytes (TILs).[4,5] For example, one large study in high-grade serous ovarian cancer (HGSC) found that cases with high CXCL10 had roughly double the median overall survival compared to low-CXCL10 tumours, with confirmation in an independent cohort.

The key is that CleoDx quantifies active and total CXCL10 and uses their ratio alongside CA-125, HE4 and IL-6. Ovarian tumours can generate N-terminally truncated, inactive CXCL10 proteoforms that blunt immune trafficking; the active/total ratio therefore carries malignancy signal that is largely invisible to single-analyte tests. Prior work shows CXCL10 activity improves discrimination and, when combined with CA-125, materially lifts AUC versus CA-125 alone.

Tumour Microenvironment Role

Biologically, CXCL10 acts as a chemoattractant for cytotoxic and helper T cells in the ovarian tumour microenvironment. Studies support a causal anti-tumour role: in preclinical models, increasing CXCL10 levels led to reduced ovarian tumour burden and ascites (abnormal accumulations of fluid in the abdominal cavity), likely by enhancing immune cell recruitment and inhibiting pro-tumour factors.[6] For instance, an HGSC mouse model with CXCL10 over-expression showed decreased tumour growth, lower ascites accumulation, and reduced angiogenic cytokines, along with increased CD8^+ T cell infiltration and cancer cell apoptosis. Conversely, CXCL10 knockdown accelerated disease progression and increased ascites in the same model.

[4] Bronger, H., Singer, J., Windmüller, C., Reuning, U., Zech, D., Delbridge, C., Dorn, J., Kiechle, M., Schmalfeldt, B., Schmitt, M. and Avril, S. (2016). CXCL9 and CXCL10 predict survival and are regulated by cyclooxygenase inhibition in advanced serous ovarian cancer. *British Journal of Cancer*, [online] 115(5), pp.553–563. doi:https://doi.org/10.1038/bjc.2016.172.

[5] Jin, J., Li, Y., Muluh, T.A., Zhi, L. and Zhao, Q. (2021). Identification of CXCL10-Relevant Tumor Microenvironment Characterization and Clinical Outcome in Ovarian Cancer. *Frontiers in Genetics*, 12. doi:https://doi.org/10.3389/fgene.2021.678747.

[6] K Au, K., Peterson, N., Truesdell, P., Reid-Schachter, G., Khalaj, K., Ren, R., Francis, J.-A., Graham, C.H., Craig, A.W. and Koti, M. (2017). CXCL10 alters the tumour immune microenvironment and disease progression in a syngeneic murine model of high-grade serous ovarian cancer. *Gynecologic oncology*, [online] 145(3), pp.436–445. doi:https://doi.org/10.1016/j.ygyno.2017.03.007.

Collectively, CXCL10 appears to promote an immune-responsive, tumour-suppressive microenvironment in ovarian cancer, making it an attractive marker of tumour microenvironment status and patient prognosis.

Diagnostic/Prognostic Developments

Ovarian tumour cells and immune cells secrete CXCL10 that can be detected in ascites or blood. CXCL10 (and related chemokines) are significantly elevated in ovarian cancer tissues compared to normal ovarian tissues.[7] However, the diagnostic use of CXCL10 is complicated by the existence of active vs inactive forms. A study co-authored by Andrew Stephens (Cleo CSO) introduced an "Active Ratio Test (ART)" to distinguish biologically active CXCL10 proteoforms in patient samples. In a cohort of 275 women, this CXCL10 activity assay effectively discriminated malignant ovarian cancer from benign conditions (area under curve 0.86) and, when combined with CA-125 levels, greatly improved diagnostic accuracy (AUC ~0.95).[8] This underscores CXCL10's significance not only as a prognostic tumour microenvironment marker, but also as a potential diagnostic adjunct.

How CleoDx Addresses the Clinical Gap

By combining multiple complementary biomarkers, Cleo's test tackles the shortcomings of single markers. CA-125 alone misses many early cancers and is often elevated by benign conditions; HE4 (human epididymis protein 4) is another tumour marker that can improve specificity, and IL-6 adds a gauge of tumour-driven inflammation. Notably, Cleo's inclusion of CXCL10 active vs total is unique – research by Cleo's founders showed that ovarian cancer can inactivate CXCL10 (an immune-related chemokine), so measuring the fraction of active CXCL10 provides a signal of malignancy.

This multi-marker approach is designed to catch cancers that CA-125 would overlook (e.g. tumours that secrete little CA-125 but have other marker signals) while filtering out many benign cases that would have triggered false alarms (e.g. benign cysts can elevate CA-125, but likely not the full Cleo panel). In theory, the CleoDx test should improve sensitivity without sacrificing specificity, hitting the sweet spot needed for triage. Initial positioning is pre-surgical triage of ultrasound-positive adnexal masses, used in conjunction with TVU and other findings.

Reported Performance

Distinguishing Benign from Malignant

Early results are compelling. In a retrospective validation published in *Cancers* (Nov 2023), Cleo's multi-marker panel was tested on n=334 plasma samples from women with known benign or malignant ovarian pathology. The CleoDx algorithm achieved 95% sensitivity and 95% specificity for distinguishing malignant vs. benign disease.[9]

This is a markedly high accuracy. By comparison, standard CA-125/ultrasound workflows have been reported to have positive predictive value (PPV) in the 60-70% range at best. Cleo's panel also correctly identified 80% of early-stage (Stage I–II) ovarian cancers in that cohort, whereas conventional approaches typically catch only ~50% of early cases (many early cancers don't raise CA-125). These results suggest the CleoDx test could dramatically improve pre-surgical risk stratification.

[7] Li, W., Ma, J.-A., Sheng, X. and Xiao, C. (2021). Screening of CXC chemokines in the microenvironment of ovarian cancer and the biological function of CXCL10. *World Journal of Surgical Oncology*, 19(1). doi:https://doi.org/10.1186/s12957-021-02440-x.

[8] Kang, S.-W., Rainczuk, A., Oehler, M.K., Jobling, T.W., Plebanski, M. and Stephens, A.N. (2021). Active Ratio Test (ART) as a Novel Diagnostic for Ovarian Cancer. *Diagnostics*, 11(6), p.1048. doi:https://doi.org/10.3390/diagnostics11061048.

[9] Stephens, A.N., Hobbs, S.J., Kang, S.-W., Maree Bilandzic, Rainczuk, A., Oehler, M.K., Jobling, T.W., Plebanski, M. and Allman, R. (2023). A Novel Predictive Multi-Marker Test for the Pre-Surgical Identification of Ovarian Cancer. *Cancers*, 15(21), pp.5267–5267. doi:https://doi.org/10.3390/cancers15215267.

Figure 6: Diagnostic Performance of the Multi-Marker Panel vs. Competitors. Comparison of diagnostic accuracy (ROC curves) and score distribution (violin plots). Source: Stephens et al., *Cancers* 2023, *15*, 5267.

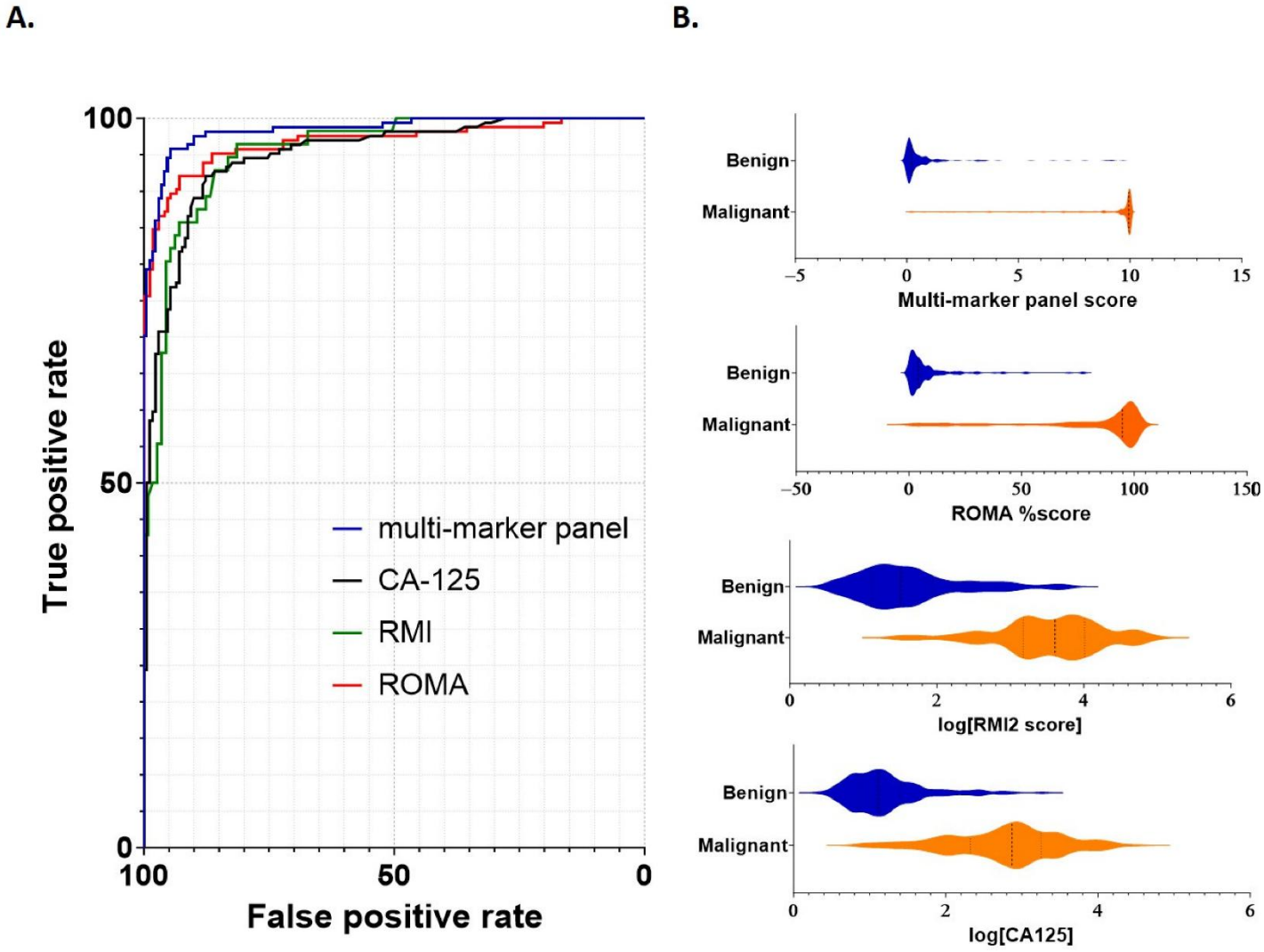


Figure A: This figure displays Receiver Operating Characteristic (ROC) curves, which are used to evaluate the accuracy of a diagnostic test. A perfect test would have a curve that goes straight up the y-axis and then across the x-axis, enclosing the top-left corner of the plot. The y-axis shows the true positive rate and x-axis is false positive rate. The plot compares four tests: CleoDx (multi-marker panel), CA-125, RMI, and ROMA. The blue line, representing the CleoDx panel, is consistently closer to the top-left corner than the other curves. This indicates that at any given false positive rate, the CleoDx panel has a higher true positive rate, making it a more accurate and reliable diagnostic tool. **Figure B:** This figure uses violin plots to show the distribution of test scores for patients with benign (non-cancerous) versus malignant (cancerous) conditions. The width of the "violin" at any given point represents the frequency of that score. Each of the four plots corresponds to one of the tests from Figure A. The blue violins show the score distributions for benign cases, while the orange violins show the distributions for malignant cases. In all four plots, the scores for malignant cases are, on average, higher than for benign cases. However, the degree of overlap between the blue and orange violins varies. A smaller overlap indicates that the test is better at distinguishing between benign and malignant conditions. The CleoDx score plot at the top shows a clearer separation between the benign and malignant distributions compared to the other tests.

Where CA-125 is Misleading

A follow-up study published Mar 2024 in *Diagnostics* focused on scenarios where CA-125 is misleading – either falsely reassuring or falsely alarming. It showed that using the CleoDx multi-marker index could 'rescue' cases that CA-125 misses: for patients whose CA-125 was in normal range despite having cancer, Cleo's test correctly identified malignancy in a significant portion (improving detection by an estimated 71% in those low-CA-125 cancer cases).[10] Conversely, among patients with very high CA-125 due to benign conditions, Cleo's test was able to correctly reclassify up to 90% as benign, avoiding unnecessary surgical referrals. This demonstrates net reclassification

[10] Stephens, A.N., Hobbs, S.J., Kang, S.-W., Oehler, M.K., Jobling, T.W. and Allman, R. (2024). ReClassification of Patients with Ambiguous CA-125 for Optimised Pre-Surgical Triage. *Diagnostics*, 14(7), pp.671–671. doi:https://doi.org/10.3390/diagnostics14070671.

improvement: CleoDx adds value on both ends – catching cancers that a CA-125-based rule would overlook and ruling out cancer in many patients that CA-125 alone would have flagged as high-risk.

In Combination with TVU

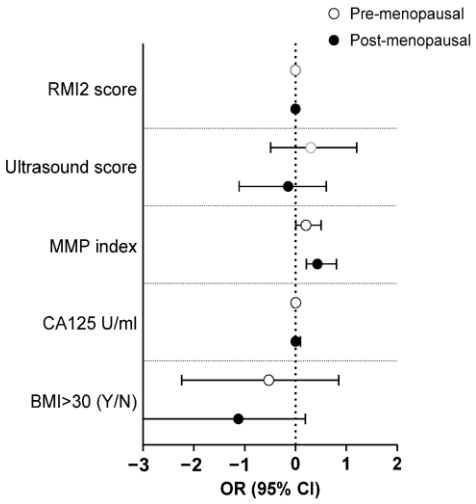
Most recently, Cleo reported results incorporating ultrasound findings alongside the blood test. In a *Cancers* (May 2024) publication, the combination of Cleo's multi-marker score with transvaginal ultrasound achieved a positive predictive value (PPV) of 92.9% for malignancy, far higher than the ~66% PPV when using standard CA-125 plus ultrasound assessment.[11] In practical terms, this means that if Cleo's test says a mass is high-risk and ultrasound is concerning, over 92% of those cases truly have cancer (vs ~66% with current methods). Importantly, 90% of early-stage cancers in the study could be correctly triaged by using CleoDx + ultrasound, compared to only ~50% caught by the conventional CA-125 + ultrasound approach.

Figure 7: Classification Accuracy and Risk Factors. Evaluation of the CleoDX multi-marker model's performance. The test achieved >95% overall accuracy (A) and demonstrated superior predictive value compared to standard clinical variables like CA-125 and ultrasound score (B). Source: Stephens et al., *Cancers* 2024, *16*, 2048.

A. Classification Table

		Predicted Benign (n=)	Predicted Malignant (n=)	Total (n=)	% Correctly classified	Positive predictive power (%)	Negative predictive power (%)
Pre-menopausal	Observed Benign (n=)	56	1	57	98.3%	96.6%	87.5%
	Observed Malignant (n=)	2	7	9	77.8%		
	Total (n=)	58	8	66	95.5%		
Post-menopausal	Observed Benign (n=)	53	3	56	94.6%	94.6%	93.6%
	Observed Malignant (n=)	3	44	47	93.6%		
	Total (n=)	56	47	103	94.2%		
Combined	Observed Benign (n=)	108	5	113	95.6%	97.3%	91.4%
	Observed Malignant (n=)	3	53	56	94.6%		
	Total (n=)	111	58	169	95.3%		

B. Odds ratios



A. Classification table. The single logistic-regression model achieves ~95% accuracy in separating benign from malignant adnexal masses, with similar performance in pre-menopausal and post-menopausal subgroups. Note the study treats benign as 'positive' and malignant as 'negative'. The model's PPV is very high – 96.6% pre-menopause and 94.6% post-menopause – while NPV is 87.5% pre-menopause and 93.6% post-menopause. Combined across all patients PPV is 97.3% and NPV is 91.5%. Clinically, this means the model is very reliable at both 'ruling in' and 'ruling out' cancer. **B. Odds-ratio plot.** The multi marker panel (MMP) index is the only variable with a statistically significant association with malignancy in both subgroups (pre-menopausal OR ~1.61; post-menopausal OR ~2.71; 95% CIs exclude 1), whereas RMI2, ultrasound score, CA-125, and BMI>30 are not significant in this already high-risk, specialist-triaged cohort. This underscores that the MMP index drives most of the model's discriminatory power, consistent with the high accuracy/NPV reported above.

[11] Stephens, A.N., Hobbs, S.J., Kang, S.-W., Oehler, M.K., Jobling, T.W. and Allman, R. (2024b). Utility of a Multi-Marker Panel with Ultrasound for Enhanced Classification of Adnexal Mass. *Cancers*, 16(11), pp.2048–2048. doi:https://doi.org/10.3390/cancers16112048.

Figure 8: Performance Metrics by Modality. Summary of sensitivity, specificity, and predictive values for Ultrasound, RMI2, and CleoDx. The data demonstrates that adding Cleo's biomarkers to ultrasound yields the most robust diagnostic accuracy. Source: Stephens et al., *Cancers* 2024, *16*, 2048.

Predictor	Published Cut-Off	Menopausal Status	n=	AUC (95%CI)	Sensitivity %	Specificity %	PPV %	NPV %
Ultrasound	1 or 4	combined	169	0.77 (0.70–0.85)	63.2%	87.1%	76.8%	77.9%
		pre	66	0.87 (0.74–10.0)	50.0%	98.0%	88.9%	86.0%
		post	103	0.72 (0.62–0.82)	67.3%	76.5%	74.5%	69.6%
RMI2 score	≥200	combined	169	0.95 (0.93–0.98)	90.2%	85.2%	66.1%	96.5%
		pre	66	0.98 (0.94–1.00)	85.7%	94.9%	66.7%	98.2%
		post	103	0.94 (0.89–0.98)	88.9%	77.6%	68.1%	92.9%
MMP index	≥3.648	combined	169	0.99 (0.98–1.00)	91.1%	95.6%	91.1%	95.6%
		pre	66	0.97 (0.94–1.00)	85.7%	94.9%	66.7%	98.2%
		post	103	0.99 (0.97–1.00)	92.0%	98.1%	97.9%	92.9%
MMP Index + Ultrasound	n/a	combined	169	0.98 (0.97–1.00)	91.2%	96.4%	92.9%	95.6%
		pre	66	0.97 (0.93–1.00)	85.7%	94.9%	66.7%	98.2%
		post	103	0.99 (0.97–1.00)	92.0%	98.1%	97.9%	92.9%

Results Table. Across 169 women, the CleoDx MMP index delivers the best overall discrimination between benign and malignant adnexal masses. In the combined cohort, MMP shows AUC 0.99, sensitivity 91.1%, specificity 95.6%, PPV 91.1%, NPV 95.6%; pairing MMP with ultrasound gives a small incremental gain in specificity (96.4%) with essentially unchanged sensitivity (91.2%). Both approaches clearly outperform RMI2 (AUC 0.95; 90.2%/85.2% sens/spec) and ultrasound alone (AUC 0.77; 63.2%/87.1%). The key takeaway is that CleoDx, alone or with ultrasound, provides the strongest, most balanced accuracy.

This indicates the Cleo test can enable much earlier intervention. Though, given the proportion of malignancy is less in reality (10% vs 33%), PPV will be notably lower. To illustrate the real potential impact: assuming ~370,000 women undergo surgery for adnexal masses in the US each year, using a 95% sensitive and 95% specific test could prevent an estimated ~318k unnecessary surgeries (benign cases spared), while still catching ~35k true cancers, though it might miss a small number (~1.9k) that would need follow-up. The improvement in efficiency would be dramatic: currently only ~10% of surgeries for suspected ovarian cancer find cancer, but with Cleo's triage, up to ~68% (the Positive Predictive Value) of those surgeries would be for actual malignancies (i.e. two-thirds yield, as only high-risk test positives go to surgery). the Negative Predictive Value (NPV) is an extremely high 99.4%. Therefore, the test is exceptionally reliable for ruling out cancer with a negative result, but a positive result requires definitive follow-up diagnostics to confirm the disease due to the significant chance of it being a false alarm.

Figure 9: Hypothetical Clinical Impact (US Annual Cohort). Contingency table illustrating the potential performance of CleoDx across the estimated 370,000 annual US adnexal mass surgeries.

	Test Positive	Test Negative	Total
Malignant	35,150 (True Positives)	1,850 (False Negatives)	37,000
Benign	16,650 (False Positives)	316,350 (True Negatives)	333,000
Total	51,800	318,200	370,000

In summary, CleoDx's published data show far superior performance to the status quo, suggesting it can both increase the cancer detection rate (especially early cancers) and decrease the intervention rate on benign tumours.

Development Status

Cleo Diagnostics is in the final clinical development phase for this test. The technology originated from research at the Hudson Institute of Medical Research (Melbourne) as part of a flagship ovarian cancer biomarker program. To strengthen clinical proof, prospective trials are underway: Cleo has initiated a prospective clinical trial in the US aiming to enrol ~500 women with ovarian/adnexal masses, where the CleoDx risk score will be compared head-to-head with standard CA-125 and ultrasound.

This real-world study will provide data on how the test performs in practice before surgery. Management has stated they expect recruitment to finish by the end of calendar year 2025.

Biobank Partnerships

Additionally, Cleo has formed collaborations to validate the assay on large biobank cohorts: for example, they are accessing samples from the US NCI's PLCO trial (one of the largest ovarian cancer screening trials) and 2,000 samples from the UKCTOCS trial (the world's largest ovarian screening study). Testing CleoDx on these thousands of archived samples (with known outcomes) could demonstrate the test's robustness across diverse populations and even explore its ability to detect cancer in a screening setting. These steps – prospective trials and big-cohort validations – are critical for building the case to clinicians, regulators, and payers. It's worth noting that Cleo's current focus is not general population screening but rather improving diagnosis in symptomatic women or those with a detected mass (the immediate market). However, if the test proves extremely sensitive, it could eventually open doors to high-risk or early-detection applications down the line.

Regulatory & Commercial Pathway

US FDA Clearance Pursuit

In the US, Cleo will pursue and FDA clearance via a 510(k) submission, leveraging the fact that there is a predicate (OVA1) already cleared for the intended use of triaging adnexal masses prior to surgery. Those predicates have FDA-cleared labelling indicating they are to be used in conjunction with other clinical and imaging findings (such as TVU) to assess cancer risk in women with pelvic masses who haven't been referred to an oncologist (explicitly not standalone cancer diagnostics). Cleo's test likely will mirror that intended use. By demonstrating "substantial equivalence" in safety and effectiveness to an existing test like OVA1, Cleo can use the 510(k) pathway rather than the more onerous De Novo and PMA routes. This is a well-trodden path for multivariate index assays. Cleo is currently generating the clinical data needed and is guiding for a possible FDA submission by mid-late 2026. Given that timeline, a US launch (clearance and commercialization) might occur in early 2027.

Requirements for Australia

On the Australian front, Cleo would need approval from the Therapeutic Goods Administration (TGA). This would likely involve obtaining inclusion on the Australian Register of Therapeutic Goods (ARTG) for the test as an IVD device. Typically, if the product has FDA clearance and a strong evidence dossier, TGA approval can follow, but the company has indicated the US is the primary focus and Australian regulatory steps will likely come after the US milestone.

Commercially, Cleo may choose to offer the test through its own CLIA laboratory (as many diagnostic startups do in the US initially) or partner with labs, but ultimately broad adoption will require insurance reimbursement and possibly integration into guidelines. Cleo has already begun market access initiatives, such as engaging a US industry partner (HcFocus) for reimbursement strategy and starting physician outreach in Australia to build awareness. In sum, the roadmap involves building clinical evidence (ongoing), achieving FDA clearance (target 2026/27), and securing reimbursement and guideline inclusion to drive adoption.

TAM Analysis: Market Opportunity

Primary Addressable Market: US, Pre-Surgical

Cleo's immediate addressable market is the population of women being evaluated for a suspected adnexal mass pre-surgery. Epidemiological and health insurer data obtained by Norstella indicates that circa 3.4 million US women present with a suspected ovarian/adnexal mass per annum. Of these, an average of circa 2 million women proceed to further diagnostic investigation through radiological imaging and/or biomarker testing (such as CA125). This 2-million-person cohort represents the pre-surgical triage market opportunity for CleoDx.

Each year in the US, approximately 370,000 women undergo surgery for a pelvic/adnexal mass, yet only around 10% of those surgeries result in a cancer diagnosis. In other words, roughly 9 out of 10 surgeries for suspected ovarian neoplasm turn out to be benign – a huge inefficiency and cost burden. This 9:1 ratio (which comes from consensus data and recent hospital statistics) implies a large pool of patients who could benefit from better triage. If CleoDx were used on all women heading to surgery for an ovarian mass, that's ~370k tests per year in the US at an assumed price similar to existing tests ($800–$1000 range), the TAM would be on the order of $300 million per year. This is a niche but significant market in the diagnostics space.

Pricing Signals & Reimbursement Dynamics

The pricing of ovarian cancer diagnostic tests in the US is largely informed by existing products and the Clinical Lab Fee Schedule (CLFS) set by Medicare. As a benchmark, OVA1 (the closest analogue to Cleo's test) has a CMS reimbursement rate of about US$897 (CPT code 81503, Multivariate Index Assay). This rate was established after OVA1 demonstrated its value and was adjusted based on market data; it's been in this range since 2018 and confirmed through 2024 for Medicare.

Similarly, Aspira's newer OvaWatch test (a monitoring tool for benign masses) was recently priced by Medicare at the same $897 level (by crosswalk to OVA1). These suggest that high-complexity ovarian risk assays are valued around $800-$900 by payers. Another data point: Avantect (ClearNote Health's cfDNA early detection test) just received a PLA code (0507U) and CMS proposed a reimbursement of $1,160. Avantect Ovarian is more expansive (genomic sequencing-based), but the fact that Medicare is willing to pay >$1k for an ovarian cancer blood test in a high-risk context is encouraging for pricing. In short, Cleo can reasonably target a price in the high hundreds of dollars per test, justified by the significant clinical benefit (avoiding surgeries and catching cancers early).

Reimbursement Requires Coverage

Historically, payer coverage for ovarian mass diagnostic tests has been mixed. OVA1 obtained an NTAP (New Technology Add-On Payment) code and is on the CLFS, but local Medicare Administrative Contractors (MACs) vary in their coverage policies. Some MACs in the past issued non-coverage or limited coverage for multi-marker ovarian tests, citing insufficient evidence or concerns about clinical utility. Over time, as more data emerged (and with guideline support from ACOG and others), coverage has improved, but it's by no means universal.

Private insurers likewise often label such tests as "investigational" until there is robust outcomes data. To overcome this, Cleo will need to demonstrate that use of its test changes patient management and improves outcomes (e.g., fewer unnecessary surgeries, more cancers handled by specialists, potential cost savings). Health economic studies and inclusion in clinical guidelines (like NCCN, ACOG bulletins) will be pivotal. On that front, OVA1's journey is instructive: it eventually gained an ACOG recommendation and an SGO (Society of Gynaecologic Oncology) statement, which helped drive coverage. Cleo has already published peer-reviewed studies – these will form the evidence dossier to approach payers. The company's engagement of a US

reimbursement consultancy (HcFocus) is a proactive step toward securing billing codes and positive coverage decisions.

In terms of coding, if CleoDx is launched via a single central lab (Cleo's own lab), they could pursue a PLA (Proprietary Laboratory Analysis) code like Avantect did, which would uniquely identify the test. Alternatively, if they partner or sell kits broadly, a traditional CPT code (possibly even piggybacking on the existing 81503 if deemed similar enough, or obtaining a new code) could be used. There is also the approach of billing the individual components (CA-125, HE4, etc., plus perhaps an algorithm charge), though that is less straightforward. Notably, ROMA is often billed by laboratories using the component codes for CA-125 (CPT 86304) and HE4 (CPT 86305), since those are existing reimbursable tests. Cleo's panel adds markers that are not routine (CXCL10, IL-6 in this context), so a bundled code is more likely. Payors will scrutinise the test's clinical utility: 'does it lead to better outcomes or cost savings?' Cleo will likely emphasize the potential to spare costly surgeries and improve oncologist referral rates, which could be very persuasive if backed by trial data.

Australian Market

Australia represents a secondary but noteworthy market for Cleo. The ovarian cancer incidence is much smaller (approximately 1,700–1,800 new cases per year), which hich by the same ~9:1 ratio suggests around 15,000–16,000 surgeries for adnexal masses per year in Australia. So, the volume is an order of magnitude less than the US, and the healthcare system is different – a mix of public and private, with the national Medicare system playing a big role in test reimbursement. One immediate hurdle in Australia is that HE4 (a key component of ROMA) is not reimbursed by the public Medicare (MBS) – this has limited the use of ROMA in Australian practice. CA-125 is reimbursed (MBS item 66650) and widely used, but any new multi-marker test like CleoDx would require government evaluation. In Australia, new tests typically need to go through the MSAC (Medical Services Advisory Committee) process to get an MBS item number and funding for use in public system. This can be a lengthy health technology assessment focusing on cost-effectiveness.

Cleo will likely pursue this after generating strong clinical data and (if possible) after a US. approval which would lend credibility. The pricing in Australia might differ; often tests are cheaper than US. list price, and lab reimbursement may be handled via Medicare agreements. As of now, there's no direct Australian competitor test widely in use (doctors rely on CA-125, ultrasound, and risk algorithms like RMI). This means Cleo could potentially capture the market if it proves its worth, but it will have to convince not just clinicians but also payers. The upside in Australia is that if the test gets MBS-funded, adoption in the public hospital system could be broad (since doctors would have no cost barrier to order it). Cleo's initial market priority is clearly the US., but eventually an MSAC submission in Australia perhaps around 2027–28, aligning with post-FDA clearance could unlock an incremental few million dollars of TAM annually (e.g. 16k tests * A$500 reimbursed = ~$8M). In addition, success in Australia could open doors in other markets in Asia-Pacific or Europe, but those are beyond the current scope.

Beyond Pre-Surgical Triage

High-Risk Screening Market

To be pursued post commercialisation for pre-surgical triage, Cleo has a broader market: if an ovarian blood test is proven extremely accurate, one could envision screening high-risk women or even general population in the future. Large trials (UKCTOCS, PLCO) of screening with CA-125 and ultrasound did not reduce mortality, which has made regulators very cautious. However, Cleo's partnerships to test their markers in those trial biobank samples indicate they are exploring whether their panel might detect cancer earlier than CA-125 did. The incidence of ovarian cancer in average-risk women is only ~11–12 per 100,000 per year, so any screening test must have extremely high specificity to avoid too many false positives. Cleo's reported 95% specificity is promising, but even

at 95% specificity, a population screening would flag many false positives given the rarity of disease.

Therefore, the most likely extension market is high-risk women (e.g. BRCA mutation carriers, or those with family history). For now, the company is appropriately not positioning for general screening, and guidelines actively advise against routine screening in asymptomatic women. But if Cleo's test can detect a good fraction of early-stage cancers (as current data suggests), it may in time target the high-risk surveillance niche, like how Avantect is positioned. That could expand TAM significantly, though it would require separate regulatory and clinical endeavours. Investors should monitor any developments on this front, but the core valuation driver remains the pre-surgical triage market.

Recurrence Market

Most women treated for epithelial ovarian cancer (EOC) face a meaningful risk of relapse – roughly 70% overall, rising to 70-90% in stage III and 90–95% in stage IV disease. As a result, long-term surveillance is routine after completion of first-line therapy. In the US, an estimated ~244k women are living with ovarian cancer and a substantial subset of this population subset cycle through follow-up clinics each year, creating a large, recurring testing opportunity. Current surveillance relies on interval history/physical, CA-125 (when it was elevated at diagnosis), and selectively ordered imaging; practice varies by centre, and guidelines emphasize shared decision-making around biomarkers and imaging intensity.

A high-NPV, multi-marker rule-out test like CleoDx could (i) extend intervals between scans and clinic visits when negative; (ii) prioritize imaging or specialty review when positive; and (iii) offer surveillance utility to women without a trackable CA-125 at baseline. Evidence also suggests HE4 may signal recurrence earlier than CA-125 in some cohorts, supporting the rationale for multi-analyte monitoring; both CA-125 and HE4 are already widely used/cleared for monitoring rather than screening. Cleo's distinctive biology (active/total CXCL10 ratio plus CA-125, HE4, IL-6) positions it to improve specificity over single-marker approaches while retaining sensitivity. Prospective data will be required to demonstrate clinical utility (e.g., fewer unnecessary CTs, fewer unplanned visits, preserved QoL) rather than earlier chemotherapy alone.

Determining an addressable volume requires assumptions:

- Population under surveillance: 40-60% of the ~244k prevalent US EOC population are in post-treatment follow-up in any given year, giving us ~100k-150k women.

- Visit frequency: typical schedules translate to 2-3 surveillance touchpoints/year in years 1-5 post-therapy.

These inputs imply a wide range of ~200k-450k potential surveillance tests per annum in the US at steady state. At parity pricing to triage assays (say US$1,000/test), the recurrence use case represents a meaningful opportunity that is not included in our base-case DCF but can be unlocked with outcomes-focused evidence and a label expansion.

Competitive Landscape

Multi-Factor Risk Algorithms

Aspira Women's Health

Aspira's OVA1 was the first FDA-cleared multivariate blood test for ovarian mass assessment. It measures a panel of 5 serum proteins (including CA-125, but also transthyretin, apolipoprotein A1, β2-microglobulin, and transferrin) and uses a proprietary algorithm to stratify risk. In clinical studies, OVA1 demonstrated very high sensitivity (approximately 97%) but at the expense of low specificity (~55%). In one head-to-head trial, OVA1 detected essentially all ovarian cancers in the cohort, but because of

its low specificity it also flagged nearly half of benign cases as "high risk". This means many false positives, roughly only 1 in 2 surgeries recommended by OVA1, would actually find cancer.

To address this, Aspira developed Overa (a second-generation test with a refined biomarker panel). Overa achieved improved specificity (reported around 69-75% in validation) while maintaining high sensitivity (~90%). Aspira now offers OVA1*plus*, a reflex protocol where a sample is first run on OVA1, and if high-risk, a confirmatory Overa is done. This combination aims to balance sensitivity and specificity. OVA1 has gained some clinical acceptance: ACOG (American College of Obstetricians and Gynaecologists) gives it a Level B recommendation for evaluating masses, and it's included in NCCN guidelines as an option. However, uptake in practice has been modest. Aspira has struggled with reimbursement and physician inertia: for context, they performed about 24,000 OVA1/OvaWatch tests in 2024, which is only a small fraction of the ~230k annual potential cases.

Key limitations of OVA1/Overa include the need to ship samples to Aspira's lab (turnaround time), the moderate false-positive rate even with Overa, and historical lack of broad insurance coverage (some insurers deemed it experimental for years). By comparison, CleoDx is claiming far higher specificity at 95% while still catching 95% of ovarian cancers, which, if borne out in practice, would be a major improvement over OVA1's performance. Cleo will, however, face the same challenges of convincing conservative clinical practice to change – Aspira's experience underlines that having an FDA-cleared test is only step one, and generating real-world utility data and gaining payer support is crucial for adoption.

ROMA™

ROMA (Risk of Ovarian Malignancy Algorithm) combines HE4 and CA-125 levels, plus menopausal status, to categorize a pelvic mass as high or low risk for cancer. It was developed in academia and later cleared by FDA (2011) as an aid in triage. Many laboratories can run ROMA since it just requires the two biomarker assays (HE4 and CA-125 are available tests) and a calculation. In terms of accuracy, ROMA generally shows intermediate performance: in the same study mentioned above, ROMA had about 87% sensitivity and 83% specificity for ovarian cancer. So, ROMA misses more cancers than OVA1 (it's less sensitive), but it also produces far fewer false alarms (much higher specificity).

Limitations of ROMA include its reliance on HE4 (which, as noted, isn't universally used; e.g. it lacks reimbursement in some countries like Australia), and the fact that some ovarian tumor subtypes (e.g. mucinous carcinomas) may not elevate HE4. Also, ROMA is typically used only after a mass is identified – like other triage tests, it's not for screening. In practice, the uptake of ROMA has been variable; some centers use it routinely, while others stick to traditional Risk of Malignancy Indices (RMI, which incorporate ultrasound scores and CA-125). ROMA's existence as a predicate is actually a benefit to Cleo: it paved a regulatory pathway and showed that multi-marker algorithms can gain acceptance. CleoDx's panel essentially extends the concept (adding CXCL10 and IL-6, etc.). If Cleo can demonstrate clear superiority over ROMA (e.g. higher combined sensitivity & specificity), it can position itself as a next-generation algorithm.

According to Cleo's published data, their test did outperform ROMA's predictive power in head-to-head comparison. For instance, Cleo's PPV and NPV were reported as better than ROMA's, independent of menopausal status. The challenge will be convincing clinicians to switch: ROMA is relatively easy/cheap if labs already run HE4, whereas Cleo's test will be new and presumably cost more. But given ROMA still yields ~15% false negatives and false positives each, there is room for improvement.

Avantect Ovarian by ClearNote Health

Avantect represents a different technological approach – it's a blood test analyzing cell-free DNA (cfDNA) with epigenomic methods for early cancer detection. ClearNote Health launched Avantect Ovarian as a lab-developed test aimed at women at high risk

for ovarian cancer (e.g. BRCA1/2 mutation carriers, those with strong family history or prior breast cancer). It is not positioned specifically as a triage test for adnexal masses, but rather as an adjunct screening tool for high-risk, asymptomatic patients – essentially trying to find ovarian cancer earlier in those predisposed. Avantect uses next-gen sequencing to detect tumor-associated patterns in cfDNA, including 5-hydroxymethylcytosine (5hmC) markers, copy number variants, and fragment size differences. In its validation (a case-control study), Avantect achieved 78.2% sensitivity and 94.0% specificity for ovarian cancer detection. This included some early-stage cancers; the company reported >60% sensitivity for stage I-II disease with the test. However, Avantect is not yet FDA-approved; it's offered under CLIA/CAP lab certification and thus cannot be marketed as a definitive "diagnostic" – it's to be used alongside other assessments.

ClearNote recently secured an AMA CPT PLA code 0507U for Avantect and a preliminary CMS pricing of $1,160, effective 2025. This underscores that payers see it as a high-complexity test deserving substantial reimbursement. In terms of competition with Cleo: Avantect and CleoDx differ in use-case. Cleo is targeting women who already have an adnexal mass and need to know if it's cancer – essentially downstream in the diagnostic pathway. Avantect is targeting women who do not have a diagnosed mass, to catch cancer signal early (upstream, possibly even before imaging). Thus, they could complement more than directly compete. A high-risk patient might get Avantect periodically, and if positive or if a mass is seen, Cleo's test could be used to evaluate that mass. That said, from an investor perspective, both are blood tests vying to become standard of care in ovarian cancer detection, so there is overlap in mindshare and budgets. Avantect's strengths are its non-invasive nature and high specificity, but its sensitivity (~78%) is well below Cleo's reported 95%. Also, Avantect's current label is limited to high-risk patients, whereas Cleo's test is for any woman with a pelvic mass.

Comparative Summary

We can boil the comparison down to sensitivity vs specificity trade-offs. CA-125 alone might catch ~78% of ovarian cancers at ~78% specificity (varies by cohort), which is not great. ROMA improves that to ~85% sens, 80% spec in many studies. OVA1 pushes sensitivity to ~97% but with only ~55% spec, meaning lots of false positives, whereas Overa/OVA1Plus try to raise spec into the ~70% range while keeping sens ~90%. CleoDx, should it deliver 95% specificity and sensitivity in practice, would facilitate a material step change in diagnostic capability.

Avantect excels in specificity (94%) and is unique for screening context, but its moderate sensitivity means it could miss ~1 in 5 cancers, particularly some early ones. It's also not intended for the same point in patient management as CleoDx.

From a commercial standpoint, OVA1 (Aspira) is the incumbent but has struggled to penetrate the market fully; ROMA is available but not dominantly used; and newer entrants like Avantect are carving out a niche in high-risk patients. Cleo's key differentiators will be: (i) its high accuracy demonstrated in peer-reviewed studies (if confirmed prospectively); (ii) its focus on a clear clinical decision point (pre-surgical triage, where there's an obvious need and cost savings to be had); and (iii) the fact that it's protein-based and potentially easier to run widely than an NGS-based test. Cleo's challenges will mirror what competitors faced – convincing obstetrician-gynaecologists and gynaecologic oncologists to trust a new test over or alongside long-standing practices (ultrasound, CA-125, clinical judgment) and getting insurers on board so that physicians can order the test without burdening patients with cost.

Overall, Cleo Diagnostics enters the landscape with a strong value proposition: a test that could drastically improve the triage of ovarian masses, reduce unnecessary surgeries and facilitate earlier specialist intervention for cancer patients. The clinical need is undeniable, and the initial data are highly encouraging. Success will depend on converting that evidence into regulatory approvals, guideline endorsements, and real-world adoption in the face of incumbents like OVA1/Overa and algorithms like ROMA. If

CleoDx delivers on its promise, it has the potential to become the new standard for ovarian cancer risk assessment – a significant win for women's health and a meaningful commercial opportunity in a space that has seen limited innovation for decades.

Valuation

Commercialisation Model

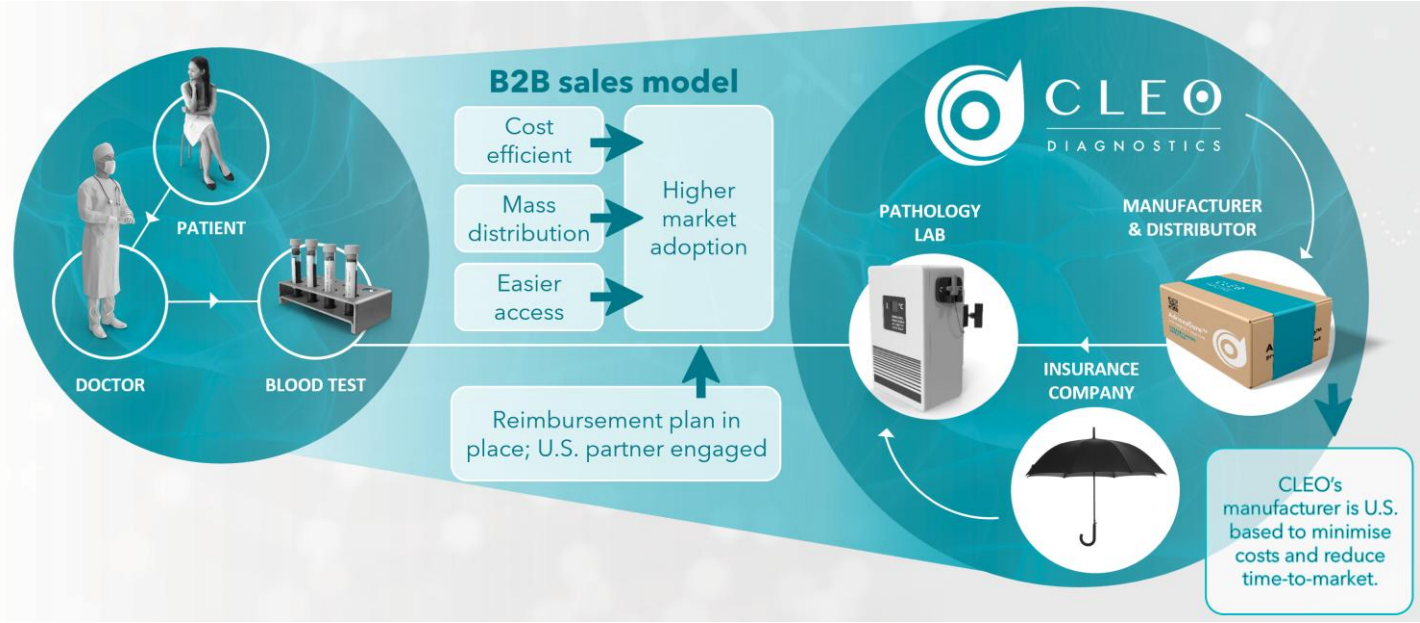
We expect Cleo to commercialise CleoDx in the US via an exclusive distribution agreement with a top-tier national reference laboratory/pathology network. Cleo would retain responsibility for manufacturing (in-house and/or via CMO), algorithm IP and updates, supply chain, QA/QC, and medical education; the partner will handle CLIA validations, lab operations, payer contracting and billing, and field sales into OB-GYN and gyn-oncology channels. Economics are modelled as a revenue-share: Cleo receives 35% of net cash collections per test; the distributor retains 65% for lab processing, sales and market access.

Key Assumed Terms

- Timing: Agreement executed in 2H CY2026, ahead of an initial CY2027 US launch, allowing time for CLIA validation, payer pilots and site onboarding.
- Territory & Scope: US-exclusive with a term encompassing the entirety of the modelled forecast period.
- Partner profile: A top-5 national lab with established OB-GYN/gyn-onc coverage and broad payer relationships, multi-state footprint anchored in California, Texas, Florida, New York and Pennsylvania to match Cleo's initial rollout focus.
- Economics: Cleo receives 35% of net collected test revenue; kits and critical reagents are manufactured/supplied by Cleo, with cost of goods borne by Cleo. Price governance via a floor ASP and annual minimum-volume commitments; shared co-marketing/medical-education budgets.
- Operating Responsibilities: Cleo responsible for manufacturing/CMO oversight, supply planning, QA/QC, algorithm stewardship and software, MSL/KOL programs, and training. Distributor responsible for
- Regulatory pathway: 510(k)-cleared kit/service once FDA clearance is obtained; unified CleoDx co-branding.

This structure lowers execution risk and SG&A intensity while preserving control over core technology and manufacturing.

Figure 10: Commercial Model. We expect the company to operate a B2B sales model targeting pathology laboratories, supported by US-based manufacturing to minimize costs. Source: Corporate Presentation. June 2025.



Revenue Model

New Medical technologies typically see slow initial uptake, then rapid growth, and finally a plateau as the market saturates. A logistic S-curve captures this pattern by constraining growth to a maximum *L* (the total addressable market) and modelling the inflection from early adopters to mainstream use. This is appropriate for COV's ovarian cancer test, which will require physician education, clinical guideline inclusion, and payer coverage before it achieves widespread adoption.

We avoid simple linear ramps or piecewise growth assumptions. A linear model might overestimate early sales (since it doesn't account for the initial hesitation and proof-gathering period) or overshoot the TAM, while an exponential curve might overstate growth in later years. The logistic S-curve is preferred here because it naturally limits uptake to the estimated TAM of ~2 million tests/year and reflects the real-world adoption hurdles.

- **Market Potential (L = 300k tests/year):** This cap is 15% of the estimated US annual addressable volume for COV's ovarian cancer triage test, being 2 million tests/year. It aligns with epidemiological data and current practice patterns, and we use it as the asymptotic ceiling L. At full penetration (100% adoption of triage testing), revenue would equal 2m tests x ASP. In fact, at an illustrative ~$900 price, that's an annual market of ~$1.8 billion.

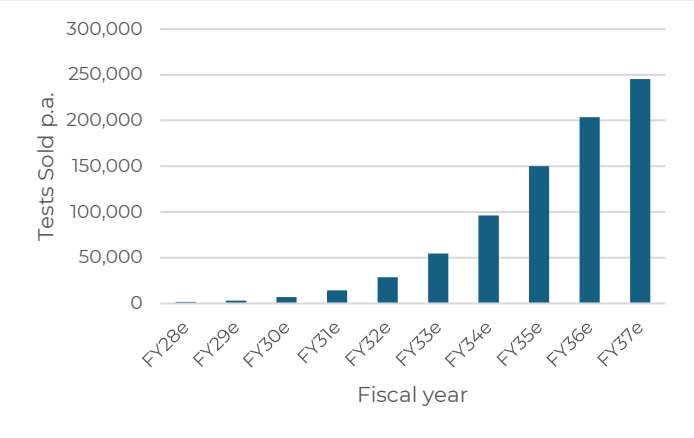
- **Growth Rate (k = 0.75):** The logistic coefficient k controls how steeply adoption accelerates after the early phase. A value of 0.75 reflects moderate adoption speed – slower than a "viral" consumer tech product, but reasonable for a medical innovation that must overcome clinical inertia and reimbursement hurdles. This choice of k causes adoption to be relatively cautious in the initial years (e.g. only a few percent of TAM in the first year) before picking up momentum around mid-decade.

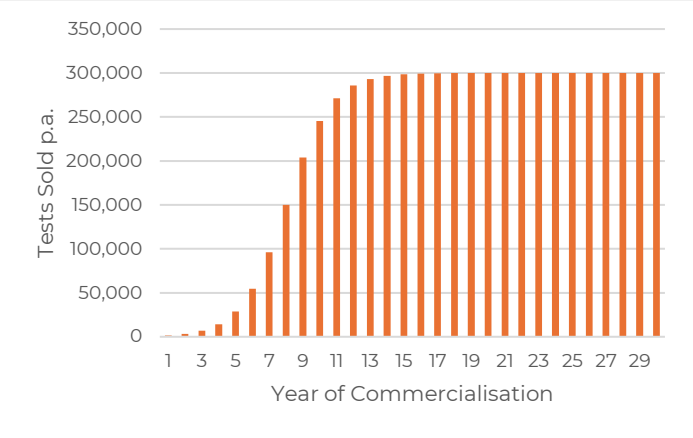
- **Inflection point (t_0 = 8):** The inflection point (50% of L=300k test/year) in our model occurs at t_0 = 8 (Year 8 of sales, ~FY2035), meaning we assume it takes about 5–6 years post-launch for COV's test to really hit mainstream usage. This aligns with a plausible timeline: regulatory approval by 2026/27, initial roll-out in 2028, then roughly 7 years of growing clinical acceptance to reach ~150k tests/year around 2035. After that, the curve naturally plateaus, approaching ~80%+ of TAM by the end of our 10-year forecast. In sum, k and t_0 are chosen so

that by year 10 the model nearly saturates the Market Potential assumption, which is ambitious but achievable if COV's test becomes standard-of-care.

- **Average Selling Price (ASP = $1,000):** We assume COV realizes about $1,000 per test on average. This figure is grounded in current pricing benchmarks for multi-marker ovarian cancer tests. Notably, in 2024 Medicare set a reimbursement rate of ~$897 for Aspira's OvaWatch (an LDT intended for indeterminate pelvic masses). Moreover, a new cfDNA methylation test for ovarian cancer (Avantect) secured a PLA code with a 2025 Clinical Lab Fee Schedule price of $1,160. Those reference points suggest that a $1,000 price is a suitable baseline for a high-performance triage assay in this space. $1,000 also allows room for rebates or payer discounts off a higher list price. In our model, this ASP is held roughly steady (in real terms) – appropriate if we assume a mix of Medicare and private pay rates and some pricing power offset by volume-based discounts.

Figure 11: Forecast Sales Trajectory. (Left) Evolution Capital's base-case forecast for CleoDx test volumes (FY28e-FY37e), showing the initial ramp-up phase following projected US commercial launch. (Right) Illustrative logistic S-curve model used to project long-term adoption. This theoretical curve demonstrates the assumed adoption lifecycle over a hypothetical 30-year period, where sales accelerate after an initial education phase before plateauing as the market saturates.





With these inputs, the S-curve revenue model produces a gradual sales ramp beginning in FY2028. Year 1 volume is only ~1.5k tests (a few percent of the TAM, consistent with limited initial launch scope), equating to ~$1.6 million in TTV. By Year 5, the model projects a much larger share of L (circa 10%, equating to around 29k tests), and by Year 10 the annual sales approach the L ceiling (~245k+ tests, ~$245m TTV). This trajectory is reasonable given the need to accumulate clinical evidence and drive adoption. It also reflects that COV is focusing only on US sales in our model, which is a conservative stance (any upside from ex-US markets or expansion into broader screening use is excluded from the base case).

Figure 12: Revenue & Cost Build-Up. Detailed breakdown of projected sales volumes, revenue generation (based on US$1,000 ASP and 35% revenue share), and associated cost structures (COGS, R&D, SG&A) used to drive the DCF valuation.

	FY28e	FY29e	FY30e	FY31e	FY32e	FY33e	FY34e	FY35e	FY36e	FY37e
US - Pre-surgical Triage										
Year (t)	1	2	3	4	5	6	7	8	9	10
Tests Sold (units)	1,566	3,296	6,893	14,228	28,605	54,728	96,246	150,000	203,754	245,272
% of 10y market potential	0.52%	1.10%	2.30%	4.74%	9.53%	18.24%	32.08%	50.00%	67.92%	81.76%
ASP (USD)	$1,000	$1,000	$1,000	$1,000	$1,000	$1,000	$1,000	$1,000	$1,000	$1,000
Total Transaction Value (USD M)	1.6	3.3	6.9	14.2	28.6	54.7	96.2	150.0	203.8	245.3
Cleo Revenue (AUD M)	0.7	1.5	3.2	6.6	13.2	25.3	44.4	69.2	94.0	113.2
COGS & Inventory										
Base Test Mfg Cost (USD)	$40.00	$40.00	$40.00	$40.00	$40.00	$40.00	$40.00	$40.00	$40.00	$40.00
Target DIO (days)	150	100	80	80	80	80	80	80	80	80
COGS (AUD M)	-0.1	-0.2	-0.4	-0.9	-1.8	-3.4	-5.9	-9.2	-12.5	-15.1
Target Inventory (units)	990	1,389	2,324	4,798	9,645	18,454	32,454	50,580	68,705	82,705
Kits to Manufacture	3,000	4,000	8,000	16,000	34,000	63,000	111,000	168,000	222,000	259,000
End Inventory	1,434	2,138	3,245	5,017	10,412	18,684	33,438	51,438	69,684	83,412
DIO (days)	217	129	93	69	64	63	64	67	71	74
Operating Expenses										
R&D Expense (AUD M)	-3.5	-3.6	-3.7	-3.8	-3.9	-4.1	-4.2	-4.3	-4.4	-4.6
SG&A Expense (AUD M)	-4.0	-4.5	-4.5	-4.5	-4.5	-4.5	-5.0	-6.0	-7.0	-8.0

Key DCF Assumptions

Sales Scope – US Only Sales Modelled

We deliberately limit the revenue model to US sales only, not factoring in any ex-US revenue. This is a conservative modelling choice meant to focus on COV's primary target market and avoid speculative assumptions about international expansion. While markets like Europe or Australia could be pursued later, those would involve separate regulatory processes (CE mark, TGA, etc.) and possibly partners – too many uncertainties to include at this stage. By excluding non-US sales, we ensure the valuation isn't over-inflated by unproven expansion plans. Any upside from international markets or broader uses (e.g. general ovarian cancer screening, if ever recommended) would be pure upside to our model. In effect, our DCF values only the US triage-test opportunity, which is the core investment thesis.

Cleo's initial US commercial rollout will concentrate resources in California, Texas, Florida, New York, and Pennsylvania – states with dense KOL footprints (NCI-designated and other high-volume gyn-onc centres) and large hospital-managed ovarian cancer populations. The approach will anchor each state with leading KOL sites, use MSL-led education and data-driven pathways to cascade adoption across affiliated OB-GYNs and community hospitals, and align payer pilots/HEOR dossiers with hospital value-analysis processes. Field teams, logistics, and payer engagement will be clustered around these hubs to maximise early case capture and visibility, creating a repeatable template for subsequent state-by-state expansion.

Margins & Expenses

We have made several cost assumptions to project profitability, based on COV's current financials and typical industry patterns:

- **COGS:** In the base case we model Cleo as an inventory-bearing kit business from launch, with COGS driven primarily by the cost of producing and supplying CleoDx kits to the distributor. Accordingly, purchases of inventory/raw materials begin in FY27 to build launch stock ahead of the FY28 first commercial sales; these pre-launch cash outflows appear in working capital (increase in inventory, partly offset by payables) and are then expensed through COGS as tests are sold. What is being bought included in COGS is the inventoriable kit bill-of-materials and manufacturing services: proprietary and commercial reagents (antibody pairs and assay components for CXCL10 active/total, CA-125, HE4, IL-6), calibrators/controls, plates/tubes/labels/packaging, contract manufacturing and kitting fees (assembly, filling, labelling), QA/QC release testing, and freight-in. Non-inventoriable COGS are limited to minor items (e.g., outbound logistics and handling not capitalized).

- **R&D Spending:** COV is still in a R&D-intensive phase, developing and validating its test. In FY25, the Company's total R&D expense was roughly A$2.9 million. We expect this to climb to A$3m for FY26 and A$4m for FY27. Thereafter, we expect tie R&D to climb steadily as more investment is placed in development of CleoDx for the Recurrence and Screening markets.

Probability of Success (PoS) Adjustment

Regulatory risk for the 510(k) pathway is relatively low compared to new drug approval, for example. Historically, about 85% of 510(k) submissions are eventually found substantially equivalent and granted clearance by the FDA. But even with this, commercial success is not guaranteed. COV faces significant challenges in achieving widespread clinical adoption and reimbursement for CleoDx. Key risk factors include:

- **Insurance Coverage & Reimbursement:** Securing broad payer reimbursement can be difficult for new diagnostics. Medicare Administrative Contractors (MACs) have, in some cases, denied coverage for multi-marker ovarian cancer tests, and insurers typically demand extensive evidence of clinical utility before paying for a test. Without coverage, test uptake will be limited, as patients or hospitals may be unwilling to pay out-of-pocket. COV will need to convince payers that CleoDx improves patient outcomes (e.g. by avoiding unnecessary surgeries) to obtain favourable coverage policies.

- **Guideline Acceptance & Workflow Integration:** Gaining inclusion in clinical practice guidelines and routine workflows is a lengthy process. To date, adoption of predicate tests has remained modest. For example, Aspira's FDA-cleared OVA1/Overa and OvaWatch tests – which similarly assess malignancy risk in adnexal masses – were used only ~24,300 times in 2024, a fraction of the ~231,000 annual surgeries for ovarian masses. This low uptake is attributed to mixed guideline enthusiasm (lukewarm endorsements by medical societies), variable payer coverage, and practical frictions (e.g. the need for send-out testing and result turnaround time). In short, even an effective test can struggle to change entrenched clinical practices.

The company is taking steps – ongoing clinical trials to demonstrate outcome benefits, health economic studies, and likely engaging key opinion leaders – but there is no certainty these will translate into rapid market penetration. We therefore assign a moderate probability of commercial success to CleoDx.

Therefore, to risk-adjust the DCF-derived valuation, we multiply the above probabilities: Regulatory PoS ~85% x Commercial PoS ~60% = **Combined PoS 51%.**

Discount Rate

Conventional CAPM yields a WACC that is far too low for a circa $50m market capitalisation, pre-revenue medical technology company as beta (3yr, weekly return vs ASX Small Ordinaries index) is x. Standard Damodaran methodology involves a building a bottom-up beta: median of unlevered peer betas. Cost of equity = risk-free rate + $\beta_{bottom\ up}$ x EMRP + Size Premium + Illiquidity Premium. R_f 4.3%; β 1.2; EMRP 6%; Size Premium 3%; Illiquidity Premium 1% yields WACC of circa 15%.

Final Valuation

The present value of unlevered free cash flows from FY26e to FY37e (12-year build-out) amounts to $53.4 million. Applying a perpetuity growth model with 4% long-term growth rate to the terminal year UFCF of $111.78 million, we yield a terminal value of $1.1bn, with present value of $265.9m. Together, this results in an enterprise value of $319.3m. Assuming FY25 actual cash of $6.46m, our unrisked equity value is $325.7m, yielding a $2.02/share unrisked fair value. Factoring in our PoS of 51%, risked fair value equals $1.03/share.

Enterprise Value	(A$M)
PV of Explicit FCFs	53.36
PV of Terminal Value	265.92
Enterprise Value	319.28

Equity Value	
Enterprise Value	319.28
Add: Cash (FY25a)	6.46
Less: Debt	0.00
Equity Value	325.74

Per Share Value	
Equity Value (A$M)	325.74
Diluted SOI (end FY25)	161.25
Value per share (A$) Unrisked)	2.02
Value per share (A$) (Risked)	**1.03**

Sensitivity Analysis

our risked fair val./sh is highly sensitive to many key assumptions due to the significant weighting of near-term losses to the enterprise value calculation: near-term losses are discounted far less than the later-stage profits (profitability is not expected until FY32). Pricing and distribution deal economics also have a significant sway.

	WACC					
	$0.78	13%	14%	15%	16%	17%
PoS	30%	0.84	0.71	0.61	0.51	0.44
	40%	1.13	0.94	0.81	0.68	0.58
	51%	1.43	1.20	1.03	0.86	0.74
	60%	1.69	1.41	1.21	1.02	0.87
	70%	1.97	1.65	1.41	1.18	1.02

Sensitivity to Discounting Factors

The unrisked fair value per share is highly sensitive to both the probability of success and the discount rate. The valuation has a strong positive correlation with the PoS, as increasing it from 30% to 70% (at 15% WACC) more than doubles the value from $0.61 to $1.41. Conversely, the value is highly sensitive and negatively correlated with WACC; an increase in WACC from 13% to 17% (at 51% PoS) cuts the valuation in half from $1.43 to $0.74. This is due to the lower discounting of near-term losses, and higher discounting of later-term profits in the modelling.

	L					
	$0.78	200k	250k	300k	350k	400k
k	0.65	0.60	0.81	1.01	1.22	1.43
	0.70	0.60	0.81	1.02	1.23	1.44
	0.75	0.61	0.82	1.03	1.24	1.45
	0.80	0.62	0.83	1.04	1.25	1.46
	0.85	0.62	0.83	1.05	1.26	1.47

Sensitivity to Adoption

This table shows that the valuation is sensitive to the assumed market potential (L, or total tests per year) but almost completely insensitive to the adoption speed coefficient (k). For example, holding the adoption speed (k) at 0.75, increasing the market potential (L) from 200k to 400k tests more than doubles the value from $0.61 to $1.45. In contrast, changing k from 0.65 to 0.85 (at L=300k) only changes the value from $1.01 to $1.05, indicating that the total size of the market is a far more significant driver than the exact steepness of the S-curve.

	L					
	$0.78	200k	250k	300k	350k	400k
t0	6	0.92	1.20	1.49	1.78	2.07
	7	0.77	1.02	1.27	1.52	1.78
	8	0.61	0.82	1.03	1.24	1.45
	9	0.43	0.59	0.75	0.92	1.08
	10	0.23	0.35	0.46	0.58	0.69

Sensitivity to Adoption

Similar to the previous table, the valuation is strongly and positively correlated with the market potential (L). However, this table introduces the inflection point (t0), or the timing of peak adoption, which is also a critical driver. The valuation is highly sensitive and inversely related to t0; delaying the inflection point from year 6 to year 10 (at L=300k) causes the value to plummet from $1.49 to $0.46. This demonstrates that delays in market penetration severely erode the present value of future cash flows.

	ASP					
	$0.78	800	900	1,000	1,100	1,200
Rev Sh.	20%	0.35	0.44	0.54	0.64	0.74
	25%	0.54	0.66	0.79	0.91	1.03
	30%	0.74	0.88	1.03	1.18	1.32
	35%	0.93	1.10	1.27	1.45	1.62
	40%	1.13	1.32	1.52	1.71	1.91

Sensitivity to Pricing & Economics

The valuation is exceptionally sensitive to the fundamental unit economics of the business. Both the Average Selling Price (ASP) and the revenue share retained by Cleo have a powerful, positive, and direct impact on the share value. Increasing the revenue share from 20% to 40% (at $1,000 ASP) causes the value to more than triple from $0.35 to $113. Likewise, increasing the ASP from $800 to $1,200 (at 30% Rev Sh.) almost doubles the value from $0.74 to $1.32, highlighting that these two inputs are among the most powerful levers in the model.

Corporate Items

We expect Cleo to fund the next phase of its growth primarily via further equity raisings as it progresses through US pivotal clinical development, regulatory submission and initial commercialisation. In our model we assume a total of approximately A$30m of new equity raised at today's market price over FY26-FY28, which we see as sufficient to support ongoing R&D (including recurrence/screening work), biobank validation, inventory build and working capital for US launch. While this is dilutive, it is explicitly captured in our forecasts and DCF, and on our numbers still supports a risk-adjusted fair value of A$1.03 per share.

Key Risks

Funding and Financial Risks

Cleo Diagnostics is a pre-revenue company with significant ongoing capital requirements. We forecast negative cash flows for several years as the company funds clinical trials, regulatory processes, and commercial launch activities. Cleo will likely require multiple future capital raises before reaching profitability (not expected until FY32). Failure to secure necessary funding on favourable terms could lead to shareholder dilution or significant delays in the commercialisation timeline.

Clinical Validation Risk

The compelling performance metrics reported for CleoDx (95% sensitivity and 95% specificity) are currently based on retrospective validation studies. There is a risk that the ongoing prospective clinical trials may not replicate this high level of accuracy in a real-world setting. Any significant decrease in observed sensitivity or specificity in prospective data could negatively impact regulatory submissions, payer negotiations, and clinician confidence in the test.

Regulatory Risk

The company is pursuing FDA clearance via the 510(k) pathway, targeting a submission in mid-late 2026. This pathway requires demonstrating 'substantial equivalence' to existing predicate tests (e.g., OVA1, ROMA). If the FDA determines that the clinical data is insufficient or that the test is not substantially equivalent, Cleo may face delays, requirements for additional trials, or the need for a more stringent approval pathway, postponing the anticipated US launch.

Reimbursement and Market Access

Securing adequate reimbursement from Medicare (CMS) and private insurers is critical to commercial success. Payer coverage for multi-marker ovarian diagnostic tests has historically been mixed, with insurers often requiring extensive evidence of clinical utility and health economic benefits. If Cleo cannot secure favourable coverage decisions or achieve its target pricing (modelled at US$900), market penetration will be severely limited.

Commercial Adoption and Clinical Inertia

Even with regulatory approval and reimbursement, achieving widespread clinical adoption is a significant hurdle. Gynaecologists may be slow to change entrenched diagnostic workflows that rely heavily on CA-125 and ultrasound. As evidenced by the modest uptake of existing FDA-cleared tests like OVA1, Cleo must generate compelling real-world utility data and secure inclusion in key clinical guidelines (e.g., NCCN, ACOG) to drive a change in the standard of care.

Competition

The market for ovarian cancer diagnostics includes established competitors and emerging technologies. Cleo must displace incumbents such as Aspira's OVA1/Overa and the widely available ROMA algorithm, which benefit from existing clinician familiarity and guideline inclusion. Furthermore, new entrants utilizing different modalities, such as cfDNA analysis (e.g., ClearNote Health's Avantect), could shift the competitive landscape.

Intellectual Property

Cleo's competitive advantage relies on its proprietary algorithm and the novel use of the CXCL10 biomarker (measuring the ratio of active vs total forms). The long-term value proposition is dependent on the strength and defensibility of the intellectual property protecting this technology. Any successful challenges to Cleo's patents, or the development of alternative methods that circumvent the IP, could erode the company's market position and pricing power.

Appendix

SWOT Analysis

Strengths (Internal)	Weaknesses (Internal)
Superior Accuracy: CleoDx demonstrates 95% sensitivity and 95% specificity, significantly outperforming current standards (CA-125 + Ultrasound) and predicate tests like OVA1. **Novel IP:** The test uses a proprietary ratio of active vs. total CXCL10, a unique biomarker not used by competitors, providing strong defensibility. **Early Detection Capability:** The test correctly identifies ~80% of early-stage cancers compared to ~50% for standard methods, addressing a critical clinical gap. **Published Data:** Proven ability to correctly reclassify benign cases that have high CA-125 (false positives) and detect cancers with normal CA-125 (false negatives).	**Pre-Revenue Status:** The company is currently pre-revenue with negative cash flows and will require ongoing capital to fund trials and operations until launch. **Single-Product Dependency:** Initial commercial success is entirely dependent on the pre-surgical triage test; failure here would jeopardize the entire valuation. **Adoption Inertia:** Clinical practice is conservative; displacing the entrenched CA-125/ultrasound workflow will require significant effort in education and behavioural change.
Opportunities (External)	**(Threats (External)**
Significant US TAM: The initial pre-surgical triage market alone represents a ~$2 billion opportunity (~2 million tests/year). **Pipeline Expansion:** Validation work is already underway for recurrence monitoring and high-risk screening, which represent large, unmodelled upside. **Guideline Inclusion:** Securing ACOG or NCCN guideline inclusion would drive standard-of-care adoption and force payer coverage. **International Markets:** Potential for future expansion into Australia (via MSAC) and Europe, which are not currently factored into the base valuation.	**Regulatory Delays:** FDA 510(k) clearance is not guaranteed; failure to demonstrate substantial equivalence could delay launch or require more costly trials. **Reimbursement Risk:** Payers may classify the test as "investigational" or deny coverage without long-term health economic data, limiting revenue. **Competitive Landscape:** Incumbents like Aspira (OVA1) and new entrants like ClearNote Health (Avantect) are vying for similar market share and clinician trust. **Dilution Risk:** Future capital raises required to reach profitability (expected FY32) could dilute existing shareholders.

Board & Management

Adrien Wing – Non-Executive Chairman

Mr. Wing is a CPA-qualified corporate executive with over 25 years of experience, specializing in ASX-listed small-cap companies. He has a strong track record in corporate structuring and capital markets, having successfully led numerous initial public offerings (IPOs) and reverse takeovers across a variety of industries and jurisdictions.

Dr. Richard Allman – Executive Director & CEO

Dr. Allman serves as CEO and brings extensive experience in research leadership, innovation management, and intellectual property strategy. With a PhD in Microbiology from the University of Wales, his expertise covers oncology and diagnostics, where he has successfully guided complex product development programs from discovery to commercialisation.

Dr. Andrew Stephens – Executive Director & CSO
Dr. Stephens is a career research scientist with a PhD in Molecular Biology from Monash University. He is the inventor of Cleo's core technology. He holds numerous patents in the cancer diagnostic and therapeutic space and has authored over 60 academic publications, underpinning the scientific validity of the Company's platform.

Lucinda Nolan – NED
Ms. Nolan is a highly experienced executive who previously served as CEO of the Ovarian Cancer Research Foundation (OCRF) and as the first female CEO of the Country Fire Authority (CFA). She brings significant leadership and governance experience, having also served as Deputy Commissioner of Victoria Police, and is an alumna of the Harvard University Advanced Management Programme.

Prof. Tom Jobling – Executive Director & Medical Advisor
Professor Jobling is a distinguished gynaecological oncologist with over 30 years of clinical experience treating ovarian cancer. He currently serves as the Head of Gynaecological Oncology at Monash Health and is a co-founder and former Chairman of the Ovarian Cancer Research Foundation (OCRF), providing critical clinical insight to the Company.

Shareholders

Ranking	Shareholder Name	Shareholding	Percentage Held
1	Adrien Wing	14,250,000	11.09
2	Richard Vom	9,125,000	7.1
3	Hudson Institute Investment Holdings Pty Ltd	7,189,140	5.59
4	Natalie Patterson	3,000,000	2.33
5	Zen Innovations Pty Ltd	3,000,000	2.33
6	Clinton Carey	2,125,000	1.65
7	Hardy Road Investments Pty. Ltd.	2,120,000	1.65
8	Anthony Hall	2,000,000	1.56
9	Eduardo Vom	2,000,000	1.56
10	Dc & Pc Holdings Pty Ltd	1,700,000	1.32
11	Patrick Gowans	1,500,000	1.17
12	Richard Alman	1,500,000	1.17
13	Carl Charalambous	1,365,000	1.06
14	Apnea Holdings Pty Ltd	1,300,000	1.01
15	Thomas Jobling	1,250,000	0.97
16	Brett Wing	1,200,000	0.93
17	Kevin Wellisch	1,125,000	0.88
18	Syzygy Holdings Pty Ltd	1,050,000	0.82
19	Andrew Stephens	500,000	0.39

Source: Iress.

Evolution Capital Ratings System

Recommendation Structure	• **Buy:** The stock is expected to generate a total return of >10% over a 12-month horizon. For stocks classified as 'Speculative', a total return of >30% is expected. • **Hold:** The stock is expected to generate a total return between -10% and +10% over a 12-month horizon. • **Sell:** The stock is expected to generate a total return of <-10% over a 12-month horizon.
Risk Qualifier	• **Speculative ('Spec'):** This qualifier is applied to stocks that bear significantly above-average risk. These can be pre-cash flow companies with nil or prospective operations, companies with only forecast cash flows, and/or those with a stressed balance sheet. Investments in these stocks may carry a high level of capital risk and the potential for material loss.
Other Ratings	• **Under Review (UR):** The rating and price target have been temporarily suppressed due to market events or other short-term reasons to allow the analyst to more fully consider their view. • **Suspended (S):** Coverage of the stock has been suspended due to market events or other reasons that make coverage impracticable. The previous rating and price target should no longer be relied upon. • **Not Covered (NC):** Evolution Capital does not cover this company and provides no investment view.

Expected total return represents the upside or downside differential between the current share price and the price target, plus the expected next 12-month dividend yield for the company. Price targets are based on a 12-month time frame.

Disclaimer & Disclosures

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