Transforming cancer care with the first FDA cleared medical device for the capture and harvest of circulating tumor cells

Annual Report and Financial Statements
31 December 2022

ANGLE

WHO WE ARE

ANGLE plc is a world-leading liquid biopsy company that has developed the revolutionary Parsortix® PC1 Clinical System, the first ever FDA cleared* platform for harvesting CTCs (intact cancer cells) from a metastatic breast cancer patient's blood for subsequent analysis.

By enabling repeat liquid biopsies to assess cancer status, **ANGLE's** Parsortix® system has the potential to deliver profound improvements in clinical and health economic outcomes in the diagnosis and treatment of cancer.

Our purpose
To revolutionise cancer diagnosis and treatment

Mission
To enable personalised cancer care by providing intact cancer cells as the **best sample** for a complete picture of the patient's cancer from a simple blood test

Vision
To make precision medicine a reality

Visit our website for more information at:
www.angleplc.com

@parsortix

ANGLEplc

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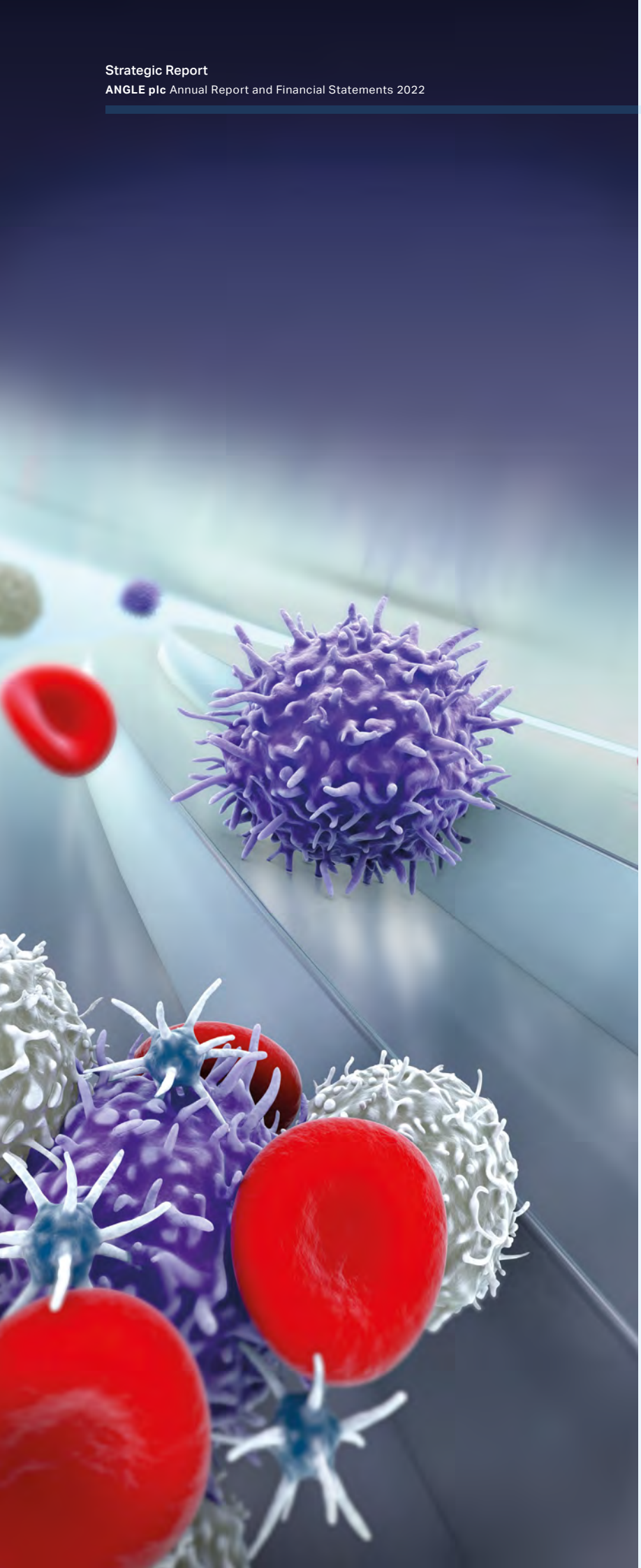
The Annual Report and Financial Statements may contain forward-looking statements. These statements reflect the Board's current view, are subject to a number of material risks and uncertainties and could change in the future. Factors that could cause or contribute to such changes include, but are not limited to, the general economic climate and market conditions, as well as specific factors including the success of the Group's research and development activities, commercialisation strategies, the uncertainties related to clinical study outcomes and regulatory clearance, obtaining reimbursement and payor coverage, acceptance into national guidelines and the acceptance of the Group's products by customers.

* Any reference to regulatory authorisations such as FDA clearance, CE marking or UK MHRA registration of the Parsortix® PC1 Clinical System shall be read in conjunction with the full intended use of the product:

The Parsortix® PC1 Clinical System is an in vitro diagnostic device intended to enrich circulating tumor cells (CTCs) from peripheral blood collected in K2EDTA tubes from patients diagnosed with metastatic breast cancer. The system employs a microfluidic chamber (a Parsortix cell separation cassette) to capture cells of a certain size and deformability from the population of cells present in blood. The cells retained in the cassette are harvested by the Parsortix PC1 Clinical System for use in subsequent downstream assays. The end user is responsible for the validation of any downstream assay. The standalone device, as indicated, does not identify, enumerate or characterize CTCs and cannot be used to make any diagnostic/prognostic claims for CTCs, including monitoring indications or as an aid in any disease management and/or treatment decisions.

Any other product or services offered are for research use only and not for use in diagnostic procedures.



OVERVIEW

ANGLE plc content highlights

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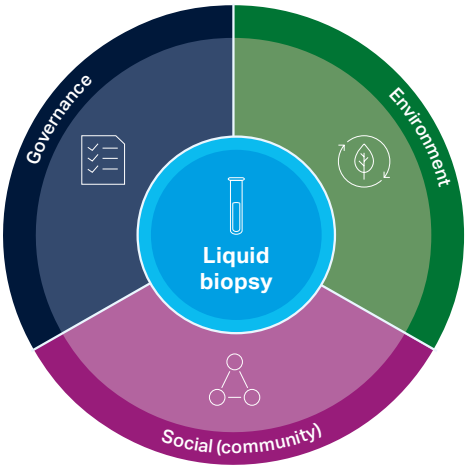
Chairman's Statement

Hear from our Chairman on how the ground-breaking FDA product clearance for the Parsortix PC1 Clinical System in metastatic breast cancer heralds a new era for personalised cancer care.

The Group promotes a values-based corporate culture.

ISO 15189* (quality) accreditation received in the year.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.



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Corporate Responsibility Report

Read more on how ANGLE is committed to adopting best practice with respect to its impact on society and the environment.

Read more on ***pages 42 to 49***

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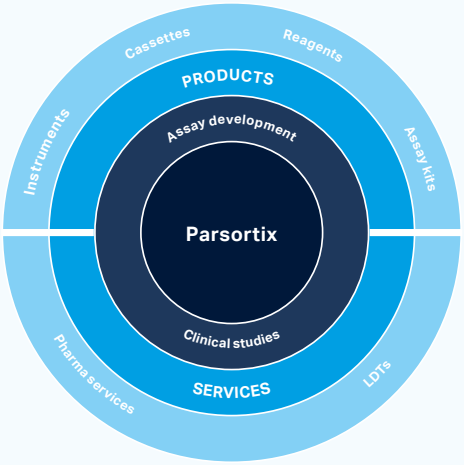
Financial Statements

Read more in the Financial Review on ***pages 50 and 51***



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Strategy

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Corporate Governance Report

The Board is committed to high standards of corporate governance and adheres to the QCA Corporate Governance Code.

Read more on ***pages 59 to 66***

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Learn more about cancer, liquid biopsy, CTCs and the Parsortix system

CHAIRMAN'S STATEMENT

ANGLE is focusing on the most immediate commercial opportunities

// 2022 was a breakthrough year for ANGLE with the world's first ever FDA product clearance for a system to harvest CTCs, intact living cancer cells, from metastatic breast cancer patient blood for subsequent analysis.

Garth R Selvey
Chairman

Operational Highlights

Products

- FDA De Novo clearance received for the Parsortix® PC1 Clinical System for its intended use with metastatic breast cancer (MBC) patients
  - first ever FDA product clearance to harvest intact cancer cells from a patient blood sample for subsequent user-validated analysis
  - multiple global distribution agreements secured to support commercial roll-out

Pharma services

- Increased pharma industry engagement post FDA clearance
  - repeat contract, worth up to $1.2 million, from large-scale pharma customer
  - assay development contract successfully delivers DNA Damage Repair (DDR) assay
  - ISO 15189 accreditation received for the United States laboratory

Clinical uses

- Ovarian cancer
  - excellent headline results from ovarian study with ROC-AUC 95.4%
  - results demonstrate clinical validity employing molecular analysis of cancer cells captured using the Parsortix system in a difficult to diagnose real-world setting
- Prostate cancer
  - partnership established with Solaris Health, a major United States urology group, to evaluate the Parsortix system in prostate cancer
  - clinical study now underway and expected to complete during 2023

The ground-breaking FDA product clearance for the Parsortix PC1 Clinical System in metastatic breast cancer heralds a new era for personalised cancer care. Large-scale medtech and pharma companies now have an FDA cleared platform on which to develop new diagnostic solutions for personalised cancer care and ANGLE is now moving to commercial roll-out of the system.

I am pleased to welcome two new Non-executive Directors to the Board, who joined in January 2023. Juliet Thompson, who brings specialist knowledge in the areas of financing, strategy and corporate governance, and Dr. Joe Eid, who brings extensive experience of biomarkers in oncology and a wide pharma industry network.

Overview of Financial Results

Revenue of £1.0 million in the year (2021: £1.0 million) came mainly from research use sales of the Parsortix system with an initial contribution from the newly established pharma services business.

ANGLE continued substantial investment in studies to develop and validate the clinical application and commercial use of the Parsortix system and to expand its commercial team ahead of anticipated customer demand, resulting in operating costs for the year of £24.8 million (2021: £18.0 million) and a loss for the year of £21.7 million (2021: loss £15.0 million).

In July 2022, ANGLE moved rapidly post FDA clearance to complete a capital raise of £20.1 million (£18.9 million net of expenses) to support the Company's commercialisation plans through to mid-2024. The orderly wind down of the site in Toronto, Canada, and resultant streamlining of the Company's operations in the second half of 2022 further increases the cash runway into H2 2024, leaving ANGLE in a strong position to deliver on planned objectives and milestones.

The Company is tightly controlling its cash resources and, post year end, the decision was taken not to pay cash bonuses in relation to 2022 despite strong performance against agreed objectives during the year. Instead share options and LTIP Options were granted with a three-year vesting period and a further two-year holding period for Executive Directors. Share price performance conditions were set for senior management and Executive Directors, which must be met as a precondition if options are to be exercised.

// ANGLE's vision is to secure widespread adoption of the Parsortix system by providing CTCs as the "best sample" for analysis.

Commercial strategy

ANGLE's vision is to secure widespread adoption of the Parsortix system by providing CTCs as the "best sample" for analysis in the emerging multi-US$ billion liquid biopsy oncology market. To drive commercialisation, ANGLE has established both a product business and a services business.

Both business areas are supported by a growing body of scientific evidence and clinical studies from leading cancer centres in published peer-reviewed journals.

Outlook

2022 was a breakthrough year for ANGLE, with both FDA clearance and the growing level of scientific evidence increasing the pipeline of opportunities for both our product and pharma services businesses. The Company is engaging with some of the largest pharma companies, medtech companies and clinical laboratories globally, with the capacity to drive Parsortix adoption through multiple clinical validation, specific regulatory approvals and acceptance by clinical service payers.

ANGLE is focusing on the most immediate commercial opportunities and has the resources in place to deliver on its strategic and commercial plans. The current year has started well with several new customers and orders confirmed and revenues are up strongly in Q1 2023 year-on-year.

Garth Selvey
Chairman
20 April 2023

2023 Progress and Outlook

- 2023 product and services revenues both progressing well with unaudited Q1 2023 revenue strongly ahead year-on-year
- Pharma services business growing well with new customers, such as Crescendo Biologics, and a growing pipeline of opportunities under discussion
- Strong repeat pharma services business model being demonstrated with existing customers signing additional contracts
- Prostate cancer pilot study enrolment on track for headline data around the end of 2023
- Corporate deal signed with BioView for development of a HER2 breast cancer test, to deliver revenues of c. £1.2 million in the initial phase, and with the prospect of adding other large corporate partners in due course
- Encouraging initial results from third-party molecular tests on the Parsortix CTC harvests opening the potential for high value molecular tests in the future for pharma services and clinical use
- Shortly after the year end, two new Non-executive Directors were appointed strengthening the Board for the next phase of the Company's development
- Current pipeline of commercial opportunities supports management's confidence in delivering strong growth in 2023 and beyond

CHIEF EXECUTIVE'S STATEMENT

Focus on commercial execution

// ANGLE's ultimate objective is to transform cancer diagnosis, treatment and monitoring, enabling personalised medicine for all cancer patients.

Andrew D W Newland
Chief Executive

Commercial strategy

ANGLE's vision is to secure widespread adoption of the Parsortix technology by providing CTCs as the "best sample" for analysis in the emerging multi-US$ billion liquid biopsy market. To drive commercialisation, ANGLE has established both a product business and a services business with differing regulatory pathways, routes to market and near and longer-term revenue potential.

1. Product business area

ANGLE has developed the Parsortix system including instruments and one-time use cassettes that can be sold to third-party laboratories for their use in research, pharmaceutical development or clinical use. To enable customers to carry out downstream analysis of the Parsortix harvest, ANGLE will also offer assay kits for cell imaging, use protocols and data packets for molecular platforms and algorithms for clinical interpretation of results.

2. Services business area

ANGLE has established clinical laboratories in the UK and United States as accelerators and demonstrators that have the capability and required quality systems to process patient samples and offer validated clinical tests using the Parsortix system. The laboratories, in Guildford, UK and Plymouth Meeting, Pennsylvania, United States, are being used to provide services to pharma and biotech customers running clinical trials (pharma services) and will be able to offer laboratory developed tests (LDTs) for patient management as a first step towards product roll out of tests.

Both business areas are supported by a growing body of published evidence from leading cancer centres showing the utility of the system through peer-reviewed publications, scientific data and clinical research evidence, highlighting a wide range of potential applications.

This includes breakthrough research such as that published in June 2022 by the Molecular Oncology Laboratory at the Swiss Federal Institute of Technology in Zurich, Switzerland. The study revealed the link between cancer metastasis and the circadian rhythm, demonstrating that the spread of breast cancer accelerates during sleep. The research was published in the high-impact journal Nature and provides novel insights and potential targets for drug discovery.

Read more on ***pages 15 to 29***

Parsortix products

On 25 May 2022, FDA granted a De Novo Class II classification for the Parsortix PC1 Clinical System for use in harvesting CTCs, intact living cancer cells, from metastatic breast cancer (MBC) patient blood for subsequent analysis. This means that an entirely new medical device classification has been granted by FDA for the Parsortix PC1 Clinical System. De Novo clearance is extremely challenging and costly and consequently is rare and the Parsortix clearance is the first such medical device classification for a new instrument in oncology for many years.

With a view to driving longer-term product revenues, during the year ANGLE expanded its commercial operations team, including product management, logistics, service and maintenance, and, following the FDA clearance and CE marking, has successfully established agreements to build an international network of oncology focused distribution partners. This network covers territories in Europe, including Germany, Austria, Czech Republic, Switzerland, Spain and France, the Middle East, China, India and New Zealand, with other geographies in discussion. These partners will provide valuable sales, implementation and ongoing service and maintenance support in their chosen markets.

// The ground-breaking FDA product clearance for the Parsortix PC1 Clinical System in metastatic breast cancer heralds a new era for personalised cancer care.

Parsortix assay development

To support adoption of its technology by adding "content", ANGLE has been developing a suite of imaging assays (branded Portrait+) and molecular assays (branded Landscape+) to analyse the cancer cells harvested by the Parsortix system. These assays are designed to build a menu for ANGLE's pharma services business and to be sold as products for third-party customers through the growing distribution network for use with the Parsortix system.

ANGLE has made good progress in the in-house development of a pipeline of new products, including a sample-to-answer Portrait+ imaging solution for the identification of epithelial and mesenchymal CTCs as well as CTCs in the process of epithelial mesenchymal transition (EMT). A Portrait+ PD-L1 assay is also in progress, enabling quantitative identification of this key target protein for immunotherapy on CTCs harvested using the Parsortix system.

The decision has been taken to focus development of the downstream molecular assays (Landscape+) on third-party platforms which have greatly improved in sensitivity and reduced in cost in recent years and offer an installed base of molecular products, which can be leveraged for new Parsortix applications.

Early results for evaluations of third-party systems have been highly encouraging and offer the prospect of combining the Parsortix harvest with platforms that are already widely adopted with a global installed base and where there are targeted sequencing panels already validated and commercially available for a wide range of solid tumour types.

Pharma services

The pharma services business utilising the Parsortix system offers the potential for substantial revenues in the large cancer drug trials market where ANGLE is clearly differentiated. The FDA clearance has helped open doors to pharma and the pipeline of potential pharma services customers has expanded significantly. There is a growing number of potential new customers and projects in discussion, including major pharma companies. In addition, ANGLE anticipates a high level of repeat business opportunities with existing customers and, during the year, announced it had secured an additional multi-year contract, worth up to US$1.2 million, with its first large-scale pharma services customer.

ANGLE made excellent progress during the year with its first bespoke assay development customer. Following validation in ANGLE's clinical laboratories, the customer expects to employ the assays in clinical studies starting in 2023. The assays identify two target proteins on CTCs that are implicated in DNA Damage Repair (DDR), γ-H2AX and pKAP1. This is an area of focus for drug companies developing PARP inhibitors for a range of solid tumours and the assays will be added to our "menu" of pre-developed tests that can be offered to other customers. Initial interest in these assays, which were introduced at an industry event in early 2023, has been very encouraging.

To support its pharma services business, ANGLE has been seeking regulatory accreditation of its Parsortix clinical laboratories in the United States and UK. ISO 15189 accreditation was received for the United States laboratory towards the end of the year and is expected for the UK laboratory in due course. This is an important achievement and demonstrates that ANGLE's clinical laboratories maintain globally recognised quality standards meeting all the requirements of major pharma customers. This is a key element as pharma services customers require evidence that the laboratories are stable, robust, compliant, and subject to periodic external inspections by recognised organisations.

ANGLE believes that longitudinal monitoring of CTCs is a highly attractive proposition for the pharma industry looking for new insights in cancer drug trials and that prospects are very positive for the growth of this business. ANGLE has initiated its roll out of assays with the EMT and DDR assays being offered to pharma services customers from the clinical laboratories.

Clinical services

ANGLE intends that its Parsortix clinical laboratories will also offer a limited number of laboratory developed tests (LDTs) to physicians for patient management. These tests will act as "accelerators" of clinical commercialisation and also as "demonstrators" of clinical utility to support the product strategy. They will be the first step towards product roll-out of tests.

Processing of patient samples for clinical purposes requires the laboratories to be accredited under the appropriate local regulatory regimes. In March 2022, the Centers for Medicare and Medicaid Services (CMS) issued a Certificate of Registration, under the CLIA process, to the Company's United States clinical laboratory. This is a key step towards achieving CLIA accreditation of the laboratory. The process will be completed once the first LDTs are being offered from the laboratories, which is a requirement.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

CHIEF EXECUTIVE'S STATEMENT CONTINUED

Parsortix clinical studies

ANGLE is conducting clinical studies in selected high-risk patient groups. Successful studies demonstrate the value of CTC analysis by providing evidence of their predictive power. Successful results will also provide the data required to support the launch of LDTs from ANGLE's own clinical laboratories as accelerators and demonstrators (see above). Once published, results could also encourage third-party laboratories to offer these tests from their own accredited laboratories, enabling the sale of instruments and consumables.

Ovarian cancer

ANGLE has utilised Parsortix to investigate the diagnosis of ovarian cancer in women with an abnormal pelvic mass. Headline results for the clinical validity study were announced during the year demonstrating exceptional performance with ROC-AUC (accuracy) of 95.4%. This was in line with the Company's earlier clinical study and achieved the Company's objective of best in class results with both sensitivity and specificity of 90% or greater. This result far out-performed standard of care for the detection of ovarian cancer demonstrating the value of the Parsortix system for real-world clinical decision-making and the clinical relevance of investigating CTCs.

Following these excellent results, ANGLE has carefully considered the most appropriate commercial route for this test. With a view to maximising commercial potential and recognising the improvement in sensitivity and reduction in costs of other molecular systems with an established installed base, the Landscape+ Ovarian assay will now be optimised utilising a third-party molecular analysis platform. Validation of the optimised assay can be undertaken utilising patient samples stored from the already completed studies. The major advantage of this approach is it will leverage the third-party installed base providing them with "content" and will allow a larger scale product-based commercialisation strategy for ovarian cancer, substantially increasing market potential and the rate of adoption.

Prostate cancer

During the year, ANGLE announced it had signed a master clinical study agreement with Solaris Health Holdings, LLC (Solaris) and joinder agreements with MidLantic Urology LLC, to collaborate and conduct clinical studies in prostate cancer and as a potential route to market in the United States.

MidLantic Urology, an affiliate of Solaris, is one of the largest providers of specialist urology services in the United States with more than 70 physicians operating from 47 dedicated urology centres across the state of Pennsylvania. The Solaris Health network encompasses more than 500 clinical urology providers across 179 locations and nine States with more than 729,000 unique patients annually.

Together with MidLantic Urology, ANGLE has initiated a clinical study aimed at investigating the use of the Parsortix system for the detection of prostate cancer and prediction of its severity in patients who present with an elevated prostate specific antigen (PSA) level and/or abnormal digital rectal exam.

This study is initially enrolling 100 men scheduled to undergo a prostate tissue biopsy at a minimum of three study sites. Blood samples collected by MidLantic Urology are being shipped to ANGLE's United States clinical laboratory for processing by the Parsortix system to harvest and analyse CTCs and associated immune cells. The Parsortix harvests will be evaluated by both imaging and molecular analysis to assess the potential to predict the presence of clinically significant prostate cancer prior to tissue biopsy and to assess potential correlation with established disease severity scores (e.g. the Gleason score) in those patients found to have prostate cancer. Patient enrolment for the pilot study is on track and ANGLE expects headline results around the year end.

Solaris is planned to be ANGLE's first route to market for this test, offering the established test to their extensive patient base and opening up a significant market opportunity for ANGLE.

Parsortix corporate partnerships

Addressing a large and complex healthcare market with a new technology requires significant resources and ANGLE is seeking long-term corporate partnerships on a case-by-case basis to assist in accelerating market access and maximising commercial potential across its business lines. The partnership with Solaris in prostate cancer signed during the year provides an example of this approach, fast-tracking clinical studies and providing a valuable first route to market with a substantial patient base.

The agreement with BioView to develop a CTC HER2 assay for breast cancer using a combination of ANGLE's FDA cleared Parsortix® PC1 Clinical System and BioView's automated microscopy systems and software to detect and assess the HER2 expression and/or gene amplification in CTCs is another significant development. The changing market dynamics of the HER2 breast cancer marketplace, with the introduction of new drugs targeting low HER2 expression, have provided ANGLE and BioView with a major commercial opportunity to develop a quantitative CTC-based HER2 assay, to assess HER2 protein expression and/or gene amplification levels by analysing fluorescence intensities.

This would be the only product-based solution on the market for this purpose, leveraging both companies' previous FDA product clearances. Unlike current standard of care tests developed for use on FFPE tissue, a CTC HER2 assay could be used for longitudinal monitoring of HER2 status throughout disease progression, thereby ensuring the patient is targeted for the most appropriate treatment at every stage. The development phase is estimated to take around a year to complete and will generate revenue of c. £1.2 million.

Given the significant third-party interest in a new assay for quantitative HER2 analysis based on CTCs, the agreement allows for the inclusion of third parties in this project and its funding at the commercialisation stage after the initial development work is complete. ANGLE continues to discuss strategic routes to market with potential corporate partners.

As described above, following a review of third-party molecular systems, ANGLE has focused its resources on evaluating the performance of Parsortix samples in combination with multiple third-party downstream DNA and RNA sequencing technologies. Initial results from these evaluations have been highly encouraging and ANGLE believes this will open the door to partnering discussions with these technology providers, who are keen to add "content" to their product menus.

Summary

Despite very challenging macro conditions outside the Company's control, ANGLE is making strong progress building both its products and services businesses. Harvesting intact living cancer cells for analysis, ANGLE's FDA cleared Parsortix PC1 Clinical System is differentiated from all other approaches to liquid biopsy and offers the prospect of cost-effective, non-invasive repeat testing for cancer patients.

ANGLE is now well on the way to getting this approach adopted by pharma in the cancer drug trials process and is building the data to drive adoption in the diagnosis and treatment of cancer patients to improve patient outcomes and reduce healthcare costs.

Andrew D W Newland
Chief Executive
20 April 2023

// ANGLE has established both a product business and a services business with differing regulatory pathways, routes to market and near and longer-term revenue potential. ANGLE is now well on the way to getting this approach adopted by pharma in the cancer drug trials process and is building the data to drive adoption in the diagnosis and treatment of cancer patients to improve patient outcomes and reduce healthcare costs.

BUSINESS STRATEGY

Following a sustained period of focus on product development and successful FDA clearance, ANGLE has now moved into the commercialisation phase.

Introduction

ANGLE is a world-leading liquid biopsy company commercialising a platform technology that can capture and harvest cancer cells circulating in the blood even when they are as rare in number as one cancer cell in one billion blood cells.

ANGLE's cell separation technology is called the Parsortix® system and is the subject of granted patents in the United States, Europe, China, Australia, Canada, India, Japan and Mexico. Three extensive families of patents are being progressed worldwide with protection out to 2034. The system is based on a microfluidic device that captures CTCs, intact living cancer cells, based on a combination of their larger size and reduced compressibility.

The analysis of CTCs, intact living cancer cells, harvested from patient blood with ANGLE's Parsortix system has the potential to deliver profound improvements in clinical and health economic outcomes in the treatment and diagnosis of various forms of cancer.

Cancer medical applications

The treatment of cancer is highly problematic, primarily because of the heterogeneity of cancer in multiple dimensions:

1. **Inter-patient variability:** patients with the same type of cancer have different mutations present in their cancer cells and therefore require different targeted treatment
2. **Intra-patient variability:** even within a single tumour, cells contain different mutations. This means that not all cells in a tumour respond the same way to a drug
3. **Clonal evolution:** each patient's cancer mutates and changes over time often in response to treatment selection pressure.

To treat patients effectively, doctors need actionable information that will help them to deploy drugs that target the individual patient's cancer at that point in time. This approach is called precision medicine and in recent years has become accepted worldwide as the most likely way to improve patient outcomes.

There is therefore a crucial need for ongoing information into the patient's cancer. Currently, if the tumour is accessible, then this is achieved through a solid tissue biopsy, for example through a core tissue biopsy or a fine needle aspiration procedure. Based on the biomarkers identified the oncologist can make an informed decision on targeted treatment. For example, in breast cancer if the patient is HER2 positive (human epidermal growth receptor 2, a protein which, if positive, promotes the growth of cancer cells) they may receive trastuzumub or a similar drug but if negative they will not.

The use of the solid tissue biopsy where available is the current "gold standard" in guiding treatment. However, it is invasive, relatively costly and not suited to repeat longitudinal testing. Importantly it cannot always be used in difficult to access tumours, such as brain, pancreatic and lung cancers where insufficient tissue may be obtained for analysis or the patient is too ill for the biopsy to be undertaken.

Crucially repeat biopsy of the primary tissue cannot often be undertaken at a later date as the tissue concerned has already been excised and is no longer present.

Primary tumours shed cancer cells into the patient's bloodstream. These cells circulate in the blood and are known as circulating tumour cells or CTCs. The CTCs can then land in another part of the body and initiate a secondary cancer. Harvest and analysis of CTCs has the potential to provide, through a simple peripheral blood test, crucial insight into the changing mutational status of the patient's disease.

It is widely agreed that a non-invasive liquid biopsy that could harvest CTCs for analysis on a repeat basis would have a profound impact in understanding the patient's current cancer status and evolution and ensuring the optimum treatment is deployed for each individual patient at that timepoint.

// The global credibility associated with FDA clearance cannot be overestimated.

Economics of cancer patient treatment

Treatment of cancer patients can be very expensive. For example, a single chemotherapy drug may cost US$10,000 to US$100,000 for a course of treatment, depending on the drug, method of administration and the number of treatment cycles required. Newer immunotherapy drugs, such as Immune Checkpoint Inhibitors (ICIs), may cost c. US$170,000 for a complete year of treatment. Although the clinical development of ICI therapy has brought about a new era of anti-tumour therapy, with sustained responses and significant survival advantages, most patients do not benefit with studies reporting a 13-50% response rate.

In this situation, 50-87% of the drug cost may be wasted on patients who have no medical benefit from the treatment but, irrespective of treatment response, experience severe and sometimes long-lasting adverse side effects.

Furthermore, it is often the case that, without specific up-to-date information on the individual's cancer, a cocktail of drugs is prescribed where the doctors know that several will be ineffective for that patient, but they do not know which ones.

ANGLE's aim is to demonstrate the Parsortix system's capability to harvest CTCs for analysis that will enable a determination of which patients will benefit from which drug at any point during their treatment pathway.

This will not only improve patient treatment and reduce unnecessary side effects but dramatically reduce overall patient treatment costs allowing more efficient and effective deployment of medical resources. This approach will support the efforts of governments across the world dealing with aging populations and an unsustainable healthcare cost burden.

Market size

ANGLE's ultimate objective is the widespread adoption of the Parsortix system in the diagnosis, treatment and monitoring of cancer patients. According to the World Health Organization, there were an estimated 18.1 million new cancer cases worldwide in 2020, a marked rise on the 14.1 million cases in 2012. In 2020, there were an estimated 10.0 million deaths from cancer (2012: 8.2 million) and an estimated 44.1 million people living with and after cancer (2012: 32.5 million). (Source: International Agency for Research on Cancer – Globocan 2020).

The incidence of cancer continues to grow as a result of demographic, lifestyle and environmental factors and it is estimated that one in two people in the UK will get cancer during their lifetime. (Source: CRUK).

There is a wide range of potential applications for harvested CTCs including diagnosis, prognosis, mutational analysis and drug selection, drug development, assessment of treatment effectiveness, and remission monitoring. Frost & Sullivan and Cowen have estimated that the liquid biopsy market will be worth $100 billion and up to $130 billion per annum respectively in the United States alone.

Competitive differentiation

The ability to harvest cancer cells from patient blood (CTCs) opens up a wide range of possibilities for protein, DNA, RNA and morphological analysis of cancer not currently possible with existing analytes. ANGLE's CTC system is the only system with an FDA product clearance for harvesting CTCs from blood for subsequent analysis. It is differentiated from other CTC approaches on multiple levels including:

- **Epitope independence with no requirement** for the use of an antibody to capture cells. The Parsortix system has key advantages over antibody-based systems that rely on the expression of a cell surface protein (such as EpCAM) including:
  - the system is able to capture CTCs that have undergone epithelial to mesenchymal transition during the process of metastasis and are no longer EpCAM positive
  - the system is able to capture CTCs in cancer types, such as ovarian cancer, which only have weak or no EpCAM expression
  - the system is versatile and may be used for other cell types such as foetal cells
  - the harvest is clean and does not contain immuno-magnetic beads or other additives needed for the antibody-based cell capture systems, which may compromise analysis of the cells
- **Easy harvest of cells from the system for molecular analysis**, unlike many other systems where cells may be captured but can get stuck in the separation system preventing further analysis
- **Low level of background white blood cell contamination** thereby allowing either single cell analysis or direct analysis of the harvested cells containing both the CTCs and a low number of white blood cells. Some competing systems may have more background white blood cell contamination thereby making analysis of target cells more difficult
- **Simplicity and cost effectiveness** so that both the one-time use consumable, the Parsortix cassette, and the automated instrument that runs the blood through the cassette are simple, easy to use and cost competitive
- **The Parsortix system is easily deployed at customer sites** in stark contrast to many competing systems which, as a result of their size and complexity, need expert operators and have difficulty in securing regulatory authorisation and may be forced to rely solely on a services approach, where the customer has to send the patient sample for analysis at a remote certified laboratory (e.g. a CLIA accredited laboratory) and cannot therefore process the sample near the patient.

Optimising the system and ongoing improvements

The Parsortix system is robust, operates reproducibly and can run patient samples efficiently. Work continues on optimising downstream applications to analyse the cells harvested by the Parsortix system.

BUSINESS STRATEGY CONTINUED

Commercialisation

ANGLE has a clear strategy to commercialise its Parsortix technology, offering a combination of both products and services. Whilst ANGLE's ultimate goal is the adoption of the Parsortix system for clinical use worldwide, services to both the pharmaceutical industry and the clinical community for patient management in specific settings offer a route to nearer-term revenues as well as demonstrating the utility of the system.

Products

The cell capture and harvesting technology has been developed together with an automated instrument to run blood samples through the cell separation cassette and extensive intellectual property protection of the system has been prosecuted.

A great deal of work has been completed to ensure that the system is robust, operates reproducibly and can run patient samples efficiently. The Parsortix system is well established with an installed base of more than 260 instruments in active use. The focus is now on the development of downstream analysis processes utilising established laboratory techniques and third-party platforms to analyse the cancer cells harvested by the Parsortix system to address clinical questions.

Successful evaluation of the system by major cancer research centres as Key Opinion Leaders (KOLs) for the market has been ongoing and has led to good adoption amongst leading translational researchers. ANGLE continues to work with a select number of KOLs to develop 1) new uses of the system 2) new clinical applications 3) proof that the system works with different types of cancer and 4) proof that CTCs harvested by the system can be analysed using multiple methods. Customers have also delivered ground-breaking research and furthered the understanding of the metastatic process. This raises awareness of the Parsortix system through peer-reviewed publications and other published evidence as well as the cancer centres presenting at conferences.

Capitalising on FDA product clearance

In order to be able to sell the Parsortix system for use in treating patients in the clinical market, it is necessary to secure regulatory authorisation for the clinical use of the system in patient treatment in each geographic region.

In May 2022, FDA, the US regulator, granted a De Novo Class II classification for the Parsortix PC1 Clinical System for clinical use in harvesting CTCs, intact living cancer cells, from metastatic breast cancer patient blood for subsequent user validated analysis.

This ground-breaking FDA clearance is the first ever FDA product clearance to harvest CTCs, intact living cancer cells, from patient blood for subsequent analysis, giving ANGLE first mover advantage for intact cell analysis in the global liquid biopsy market. FDA clearance is considered the gold standard for medical devices and the global credibility associated with this achievement cannot be overestimated.

ANGLE has since secured a CE mark and MHRA registration for the use of the Parsortix PC1 Clinical System as an in vitro diagnostic device in the European Union and United Kingdom for the same intended use.

Additional product authorisations may be sought for specific clinical tests and clinical studies would be designed and run to provide the necessary data to support these regulatory applications.

Establishing a global distribution network

Distribution channels are now being established in multiple territories around the world through agreements with experienced oncology focused partners.

These partners have been carefully selected for their knowledge of their local markets, access to leading cancer centres and ability to offer ongoing service support and product maintenance.

In addition, ANGLE intends to strengthen the product offering to end customers by launching selected assay kits for immunofluorescent analysis of CTCs (e.g. EMT and PD-L1 etc) as well as protocols and operating instructions for automating the harvesting of cells from the Parsortix system for molecular analysis using a variety of third-party platforms including PCR, digital PCR and Next Generation Sequencing.

Product reimbursement

Widespread adoption will also depend on the ability for clinicians to receive reimbursement from payors for diagnostic work undertaken using the Parsortix system to process blood samples and/or for downstream assays performed on the cancer cells harvested using the system. Work has commenced to pursue reimbursement in various territories and plans are being developed to leverage applications where the patient will pay for services. This is a complex environment globally and can take time and considerable investment to achieve.

Development of downstream assays

To support both adoption of the Parsortix system by third-party laboratories and to build a menu to offer to pharma services customers, ANGLE is developing and launching sample-to-answer assays which will allow researchers and clinicians to answer key clinical questions.

The main areas of work that are currently taking place include:

- Developing assays for immunofluorescent staining of CTCs (marking their presence), CTC subtypes (epithelial, mesenchymal and those undergoing epithelial to mesenchymal transition – EMT), as well as for specific biomarkers.
- Developing assays and interface protocols using existing molecular analysis platforms deployed by some of the world's largest medtech companies including DNA digital PCR assays (such as EGFR, PIK3CA etc) and RNA digital PCR assays, DNA NGS assays and RNA NGS assays based on a variety of cancer panels.
- Exploring "companion diagnostic" opportunities with pharma companies to determine the suitability and effectiveness of drugs for individual patients or for rapid measurement of treatment response in clinical studies.

// The focus is now on the development of downstream analysis processes utilising established laboratory techniques and third-party platforms to analyse the cancer cells harvested by the Parsortix system to address clinical questions.

Services

ANGLE has established clinical laboratories in the UK and United States to provide a global service capability. These laboratories are intended to act as accelerators and demonstrators to support ANGLE's product-led strategy.

With ISO 15189* accreditation in place, they are being used to offer CTC analysis services to pharma and biotech customers for drug trials and, with additional accreditation, will be able to offer validated clinical tests known as laboratory developed tests (LDTs) to support cancer patient management.

A growing number of clinical studies are using CTC evaluation as a key biomarker to assess patient response as an outcome measure. CTC evaluation may provide a measure of response to treatment and may provide a much earlier indicator of treatment resistance, when compared to radiological measures (e.g. CT and MRI scans). A key advantage of CTCs when compared to tissue biopsy is the ability to undertake repeat longitudinal monitoring of patient response and cancer status during the study, for example before, during and after treatment. There is also the potential for remission monitoring and long-term follow up.

Pharma services utilising the clinical laboratories presents a large-scale commercial opportunity that can be accessed ahead of specific FDA or EMA product clearance for clinical diagnostic use. With CLIA accreditation, ANGLE can offer LDTs from its own laboratories for patient management, again ahead of FDA product clearance. The clinical laboratory service approach is an established business model for many diagnostic companies. In addition, it enables early progress with payers and reimbursement codes ahead of FDA cleared product. The adoption of clinical laboratories alongside ANGLE's core product-based strategy is intended to accelerate commercialisation and revenue generation.

Clinical studies to demonstrate clinical applications

A critical element in progressing commercialisation of the Parsortix system is ensuring KOLs undertake successful clinical studies to demonstrate patient applications with clear medical utility. This involves working closely with KOLs to encourage and support, with both human and financial resources, their investigative work using the Parsortix system.

The first such KOL to report was the Medical University of Vienna, whose pilot study in ovarian cancer demonstrated the potential to use the system to detect ovarian cancer in women having surgery to remove abnormal pelvic mass growths. This has been further developed as a clinical application through three separate 200-patient studies with the objective of a simple blood test to determine which patients are likely to have ovarian cancer (approximately 10%) and which are likely to have benign growths. Headline results from a clinical verification study with the University of Rochester Medical Center, Wilmott Cancer Institute, USA were announced in June 2022 and demonstrated best in class performance. ANGLE now intends to develop the test on a third-party molecular platform to maximise the commercial opportunity.

ANGLE has also commenced prostate cancer studies in partnership with MidLantic Urology, an affiliate of Solaris Health which is one of the largest specialist urology networks operating in the US. The studies build on encouraging pilot work done by KOLs at Barts Cancer Institute, and, if successful, will allow ANGLE to offer a test to identify the presence and clinical significance of prostate cancer in men prior to tissue biopsy or surgery. The agreement with Solaris Health, which gives access to a large patient base, also provides a template for future partnerships focused on high-risk patient groups.

These applications will save healthcare costs and improve patient outcomes by focusing resources appropriate to the patient condition and are described in more detail in the Chairman's Statement on pages 04 and 05 and the Chief Executive's Statement on pages 06 to 09.

Summary

ANGLE has a well-differentiated patent-protected product addressing a large developing medical market with a clear strategy to secure a substantial market share.

Effective execution of the strategy, which is now in the commercial stage, has the potential to deliver significant financial returns for ANGLE's shareholders. In addition, we have the opportunity to profoundly improve the current standard of care and outcome for cancer patients, and significantly reduce healthcare costs.

This report was approved by the Board of Directors on 20 April 2023 and is signed on its behalf by:

Andrew D W Newland
Chief Executive
20 April 2023

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

MARKET OPPORTUNITY

A major opportunity in an emerging and growing global market

Market drivers

Key drivers of cancer diagnostics market

- Shift towards precision medicine drives need for companion diagnostics
- Health economics – reduce costs
- Early detection (screening)
- Therapy selection, treatment monitoring and remission monitoring

Precision medicine

With advancements in genomics and clinical information, a **paradigm shift has begun** from "one drug fits all" towards **precision medicine – the right drug for the right patient at the right time.**

Key drivers

- Each patient's cancer is different
- Each patient's cancer changes over time
- Effective treatment requires personalised care

Key drivers of cancer incidence

- Increasing average life span
- Smoking, poor diet, obesity and alcohol
- Overexposure to sun
- Lack of exercise
- Exposure to carcinogens
- Infections and HIV
- Hormones
- Inherited gene mutations

Projected increase in cancer incidence

47%

Estimated rise in global cancer cases within the next two decades[1]

28.9m

Estimated annual cancer cases by 2040[1]

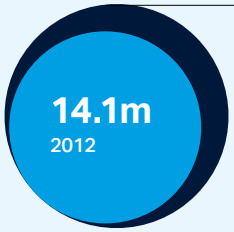
Growing market

Liquid biopsy: Emerging multi-US$ billion market

Cowen – up to $130 billion per annum (US only)

Frost & Sullivan – $100 billion per annum (US only)

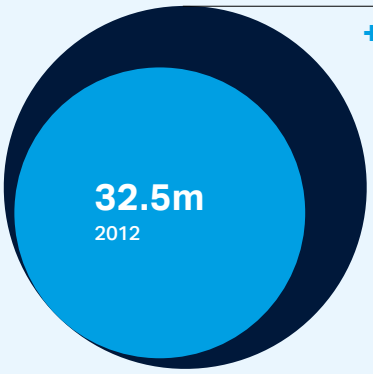
Global burden of cancer[1]
New cancer cases (per annum)



+28%

18.1m
2020

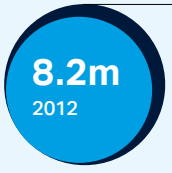
Living with and after cancer



+36%

44.1m
2020

Deaths from cancer
(per annum)



+22%

10.0m
2020

1 International Agency for Research on Cancer (Globocan 2020).

▸ STRATEGY

A clear path to market

Our strategy

ANGLE has identified key steps to support widespread adoption of its Parsortix system in the emerging multi-US$ billion liquid biopsy market.

Capitalise on FDA product clearance
ANGLE is the first ever company to gain FDA product clearance, the de facto global gold standard, for a system which harvests CTCs from metastatic breast cancer patient blood for subsequent, user-validated analysis.

ANGLE will also seek further regulatory approvals for specific clinical assays for additional products, cancer types and geographies.

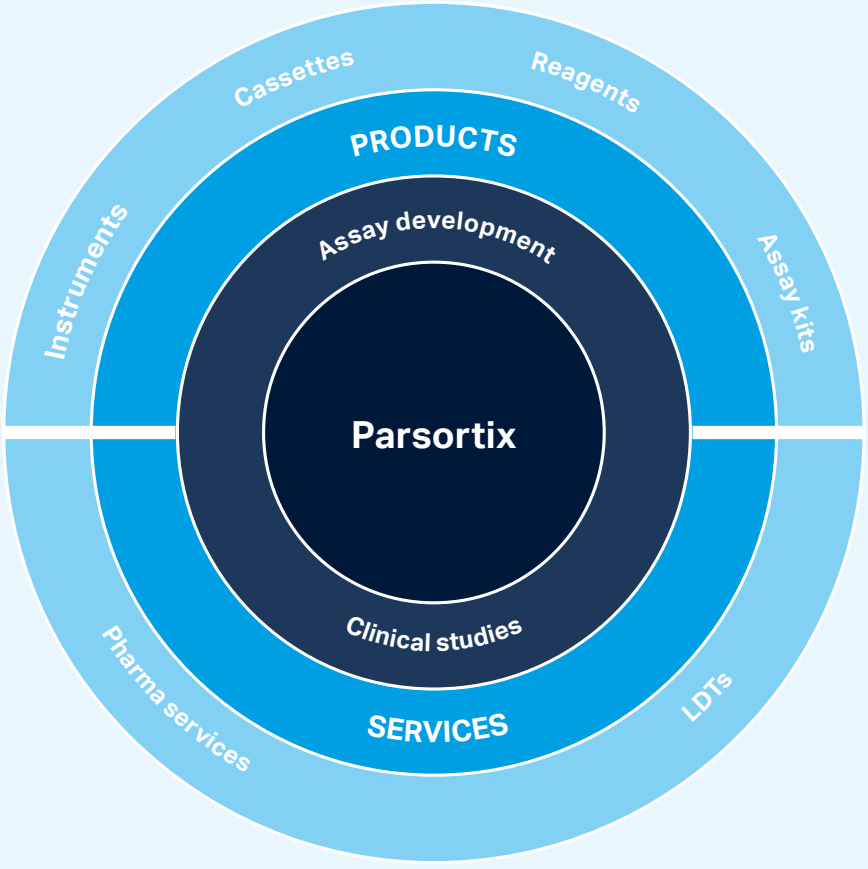
*Read more on **pages 12 and 16***

Develop downstream assays
Developing state-of-the-art assays for use in ANGLE's GCLP accredited clinical laboratories provides biopharma and CROs with robust validated assays to support drug development.

*Read more on **pages 20 to 23***

Clinical studies
Completion of rigorous large-scale clinical studies run by leading cancer centres, to demonstrate the effectiveness of different applications of the system to support regulatory approval of LDTs and products.

*Read more on **pages 24 to 27***



Build a global distribution network
Distribution channels to extend geographical reach.

*Read more on **page 17***

Partnerships
Establishing partnerships with large healthcare companies for market deployment and development of clinical applications incorporating the Parsortix system.

*Read more on **page 19***

STRATEGIC AIMS IN ACTION

Products

FDA cleared instrument

On 25 May 2022, FDA granted a De Novo Class II classification request for the **Parsortix PC1 Clinical System** for the capture and harvest of CTCs from metastatic breast cancer (MBC) patient blood for subsequent analysis. This provides gold-standard validation of the system. Regulatory approval for additional cancer types and different applications/Intended Use may be applied for. With the Parsortix PC1 Clinical System acting as a predicate device, such applications should be possible down the more streamlined 510(k) pathway.

Read more on ***pages 128 and 129***

Our journey to clearance

Dialogue with FDA	Study planning & design	Analytical & clinical studies	Q-sub process completed	**De Novo submission made**	Substantive review	Additional Information Request & Response	**Classification request granted**
2015	**2016**	**2017**	**Jan 20**	**Sep 20**	**Oct 20**	**Jun 21**	**May 22**

Note: COVID-19 delays extended timelines for ANGLE analytical studies & FDA review.

Portrait+™ Powered by Parsortix®

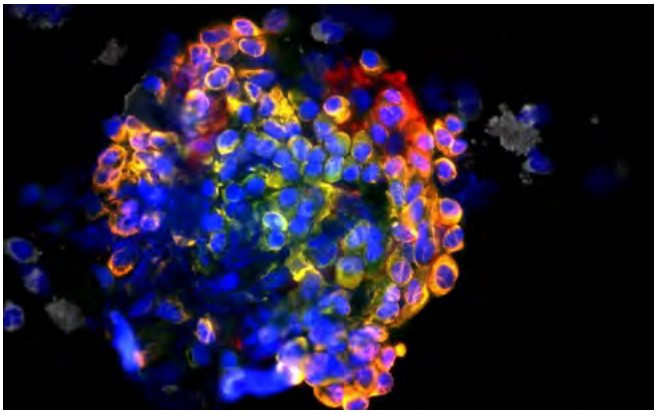
EMT IF assay

ANGLE has developed an immunofluoresence (IF) based quantitative assay (Portrait Flex) to identify bespoke biomarkers on different subtypes of CTCs, including epithelial, mesenchymal and those undergoing epithelial to mesenchymal transition (EMT). The assay is being optimised and will be validated in the ISO 15189* accredited United States laboratory as a pharma services offering.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

What is epithelial to mesenchymal transition (EMT) and why is it important?

Read more on ***pages 123 and 125***



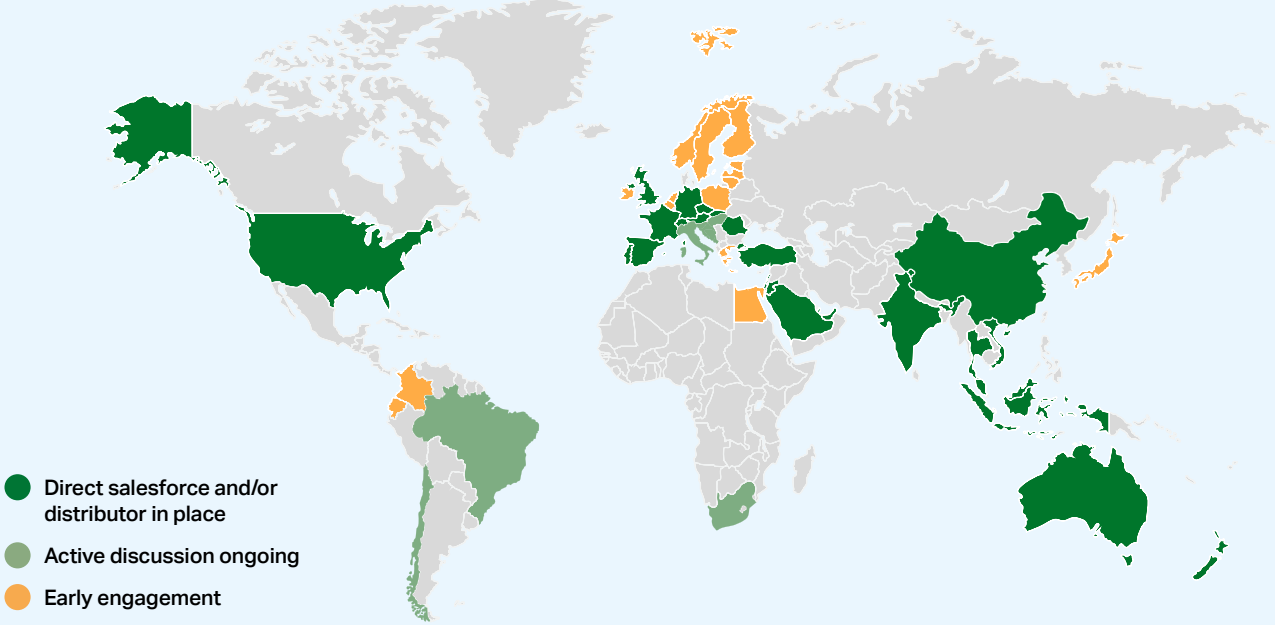
Cell type	Colour
Epithelial	Green
Mesenchymal	Orange
EMT	Yellow
Nucleus	Blue
White blood cells	White

Global distribution network

With a view to driving longer-term product revenues, ANGLE has expanded its commercial operations team, including product management, logistics and service and maintenance.

In addition, ANGLE has successfully established agreements to build an international network of oncology focused distribution partners in **Europe** (including France, Spain, Portugal, Italy, Germany, Austria, Switzerland, Czech Republic, Slovakia, Romania and Türkiye), **the Middle East** (including Saudi Arabia, UAE, Qatar, Jordan, Israel and India), **the Far East** (including China, Singapore, Thailand, Vietnam and Malaysia) and **Australasia** (Australia and New Zealand).

Additional geographies are in discussion. These partners will provide local sales and marketing capabilities and ongoing service and maintenance support in their jurisdictions. We expect product sales to build gradually with expansion being stimulated over time by downstream assays, clinical utility and local reimbursement.



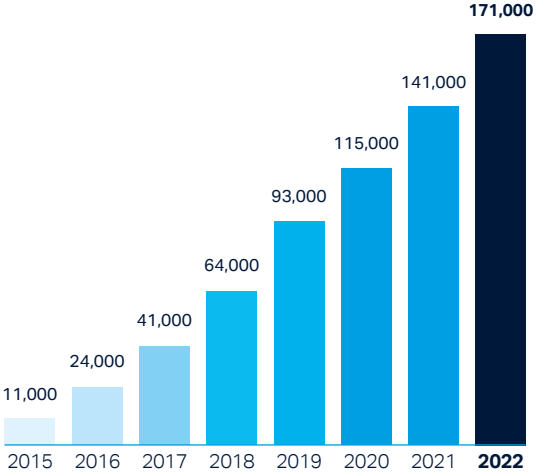
With FDA clearance and CE Mark in place, commercial roll-out is now underway with a network of sales partners being established. This will open distribution channels for Parsortix instruments and consumables globally. In addition to sales these partners all provide invaluable market access and ongoing service and maintenance support in their jurisdictions.

// **Since we announced the FDA clearance, there has been a considerable global interest in working with CTCs. The requirement to have a presence, not only for sales and marketing, but for customer technical support, has resulted in us establishing a genuine global footprint through partnered distributors. We are proud to have formed close relationships with our commercial partners which will ignite more interest at local levels.**

Andrew D W Newland
CEO

>260
Installed base of Parsortix instruments

Cumulative samples processed



▸ **STRATEGIC AIMS IN ACTION** CONTINUED

Services

ANGLE obtains ISO 15189* accreditation in US clinical laboratory

ANGLE's US laboratory has received ISO 15189* accreditation from the International Organization for Standardization (ISO), demonstrating quality and competence recognised globally.

This accreditation confirms that ANGLE's laboratory quality system is stable, robust and compliant with external inspections and audits from regulating authorities.

This achievement is a key milestone in the provision of services to biopharma customers and Clinical Research Organisations (CROs).

* The ANGLE US laboratory ISO 15189 accreditation scope is specific for the CTC Pap Stain Assay.

Pharma services

Liquid biopsies are moving towards routine clinical use, but in the meantime, they are already informing clinical trial outcomes and supporting drug discovery. A number of trials are already using CTCs as an exploratory endpoint. CTC presence and status are being used predominantly as a measure of treatment response and may provide a much earlier indicator of treatment resistance, when compared to radiological measures (e.g. CT and MRI).

A key advantage of CTCs when compared to tissue biopsy is longitudinal monitoring; the ability to provide access to tumour cells throughout the study duration (i.e. at baseline before, during and after drug intervention, remission monitoring and long-term follow-up) which is not possible with tissue biopsy.

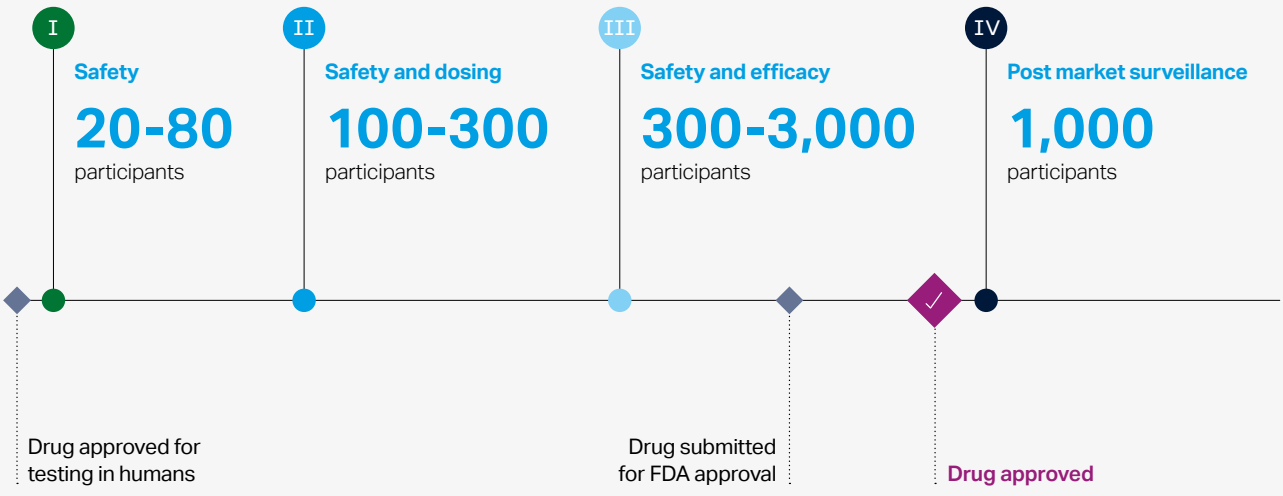
Harvesting intact CTCs and CTC clusters with the Parsortix system for downstream analysis in a robust and scalable sample-to-answer solution is proving highly attractive to pharmaceutical and biotech industry partners. As an example, there are over 2,800 interventional PD-L1/PD-1 trials, in ~430,000 patients currently in progress. In these studies, assessment of PD-L1 status on CTCs from patient blood samples may have a major bearing on whether the trial is successful.

Future clinical studies will be targets for adoption of the Parsortix system and ANGLE has developed a service capability to process samples on a commercial scale to support these trials. ANGLE has already attracted three significant biopharma customers and the Parsortix system has been utilised in the development of bespoke assays for specific protein markers implicated in DNA damage repair, a key area of focus for new drug discovery. The incorporation of bespoke assay development as a first phase in pharma services is a major development and expected to significantly increase the attractiveness of Parsortix based CTC analysis, as biopharma clients can look at proteins on CTCs which directly align with the mode of action of the drug under investigation.

Parsortix®

Onc-ADaPT™ Labs
Part of the ANGLE Group

Clinical trial phases



Strategic partnerships

ANGLE's strategy is to partner with large-scale companies for market deployment and the development of multiple clinical applications incorporating our system and assays.

Large-scale deployment of the Parsortix system across numerous cancer types and application areas requires ANGLE to partner with large, global healthcare companies to take advantage of their distribution and sales channels, and economic resources. Discussions are ongoing with companies in relevant fields including medtech, pharma, Contract Research Organisations, and reference laboratories (laboratories offering clinical tests).

ANGLE has, for example, already collaborated with Abbott, the global market leader for HER2 testing in solid tissue biopsies. Abbott's proprietary PathVysion HER2 DNA FISH Probe Kits were successfully utilised in ANGLE's FDA clinical study for FISH (fluorescence in situ hybridisation) analysis of CTCs. Following FDA clearance, there is now the potential for Abbott to offer a Parsortix-based CTC test for HER2 analysis from a routine blood test. Testing CTCs for HER2 could provide Abbott with a repeat, longitudinal test for HER2 resulting in an estimated 4x increase in the use of PathVysion HER2 test. Combining the Parsortix system and PathVysion could also command higher reimbursement, increasing margins.

It is recognised that breast cancer can be highly heterogeneous[1] and that HER2 status can change over time[2]. As such, the binary positive or negative result provided by current HER2 FISH testing represents a rather "black and white" view of patients and their likely response to HER2 targeted treatment. Results from a recent study have revealed that patients categorised with HER2-low breast cancer (and defined as HER2-negative by FISH), can in fact benefit from new HER2 targeted antibody-drug conjugates, which have previously been reserved for HER2-high expressing (and hence deemed positive) cancer patients[3].

This suggests a shift is needed in how HER2 expression is classified, with a move away from a binary result to one which more accurately reflects and recognises the levels of HER2 expression in the spatiotemporal tumour environment[1]. Recent FDA approval of the use of Daiichi-Sankyo/AstraZeneca's antibody-drug conjugate, Enhertu, in HER2-low breast cancer patients[4] reinforces the need to accurately quantify HER2 expression in this disease, to ensure all patients have the opportunity to benefit from potentially life-changing treatment.

HER2-low breast cancer accounts for 55% of all breast cancer cases whereas HER2-high (or positive) cancer accounts for just 25% of cases[1,5]. The expanded use of Enhertu to include HER2-low patients has analysts predicting up to a US$3 billion annual increase in sales value[5]. Because of market expansion into HER2-low patients, there will likely be a desire by medtech and pharma for quantitative HER2 detection assays to enable accurate stratification of patient populations.

This has provided ANGLE with an opportunity to commence the development of a CTC-based HER2 immunofluorescence (IF) assay to assess HER2 protein expression levels by analysing fluorescence intensity. Unlike current standard of care tests developed for use on FFPE tissue, an IF CTC HER2 assay could be used for longitudinal monitoring of HER2 status throughout disease progression, thereby ensuring the patient is targeted for the most appropriate treatment at every stage. As a result, whilst ANGLE continues to progress discussions with Abbott, commercial opportunities have increased across the HER2 testing market and discussions with additional potential partners are anticipated.

1. Marchiò, C. et al. Semin. Cancer Biol. 72, 123–135 (2021).
2. Niikura, N. et al. Annals of Oncology, 27, 480-487 (2016).
3. Modi, S. et al. N. Engl. J. Med. 387, 9–20 (2022).
4. www.mskcc.org/news-releases/asco-2022-practice-changing-findings-identify-her2-low-targetable-subset-breast-cancer-redefining-treatment-more-60-percent-her2-negative-metastatic-breast-cancer-patients.
5. www.pharmaphorum.com/news/enhertu-gets-breakthrough-tag-in-her2-low-breast-cancer.

▸ STRATEGIC AIMS IN ACTION CONTINUED

Assay development: imaging solutions

Immunofluorescence assays: DNA Damage Repair

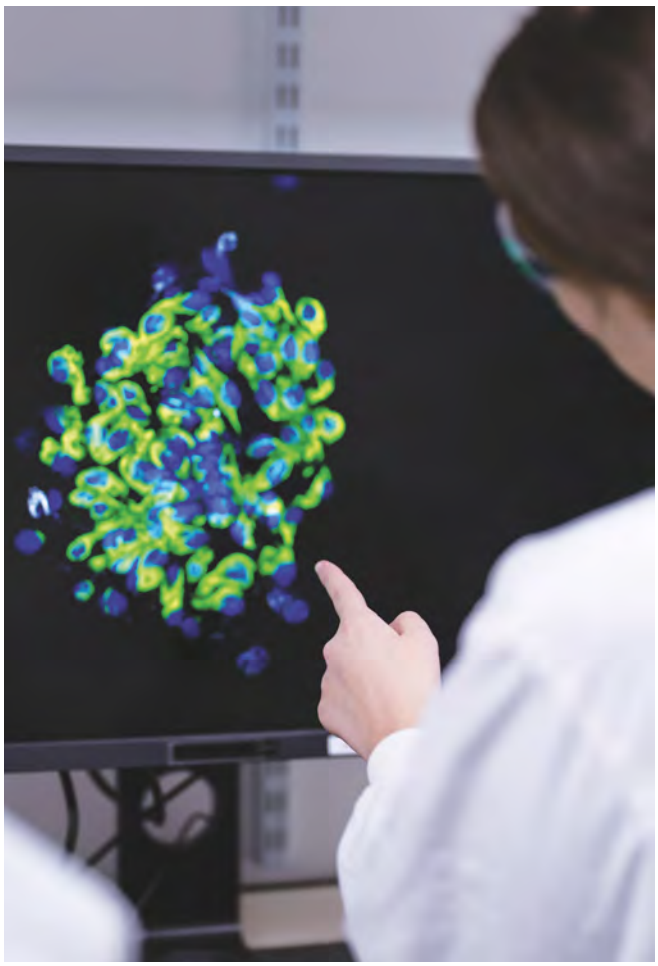
γH2AX and pKAP1 immunofluorescence assays – highly sensitive and specific for DNA Damage Repair

ANGLE has developed DNA Damage Repair (DDR) immunofluorescence assays for two biomarkers, gamma H2AX (γH2AX) and phospho-KAP1 (pKAP1). These are commercially available to biopharma customers though our ISO 15189* accredited laboratory in the US and clinical laboratory in the UK. The combination of ANGLE's Parsortix system with our downstream γH2AX and pKAP1 assays enables detection of these biomarkers in all types of circulating tumour cells (CTCs). These assays are available for use in clinical studies.

An increase in γH2AX positive CTCs can be seen after a single dose[1]

γH2AX expression in CTCs can be utilised to rapidly assess the pharmacodynamic effects and treatment response to chemotherapeutic agents when given either alone or in combination with DDR/PARP inhibitors. The emerging importance and utility of DDR inhibitors in combination with immune checkpoint inhibitor therapies further broadens the utility of γH2AX and pKAP1 assays as indicators of DNA damage and clinical effectiveness.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.



What are γH2AX and pKAP1 and why are they important?

Tumour progression is strongly correlated with defects in the DDR pathway which result in uncontrolled cell proliferation.

γH2AX acts as a critical and early sensor to DNA damage, responsible for the activation of DDR pathways. This marker is reliable, sensitive and specific, and has become the gold standard for visualising DNA damage via immunofluorescence.

Similarly, pKAP1 acts as a sensor to DNA damage, and the expression of pKAP1 is a biomarker for cancer diagnosis, prognosis and disease monitoring.

Monitoring γH2AX and pKAP1 in CTCs can allow the assessment of DNA damage and the effectiveness of treatment.

US$3.5bn
estimated global market value of DDR therapeutics in 2020[2]

US$24.8bn
estimated global market value of DDR therapeutics by 2030 with a CAGR of 21.3%[2]

123,000
patients currently enrolled in active DDR clinical studies[3]

105
DDR drugs in development[3]

1 Wang, L. H. et al. Clin Cancer Res.16(3),1073-1084 (2010).
2 www.researchandmarkets.com/reports/5141852/global-dna-damage-response-drugs-market-focus-on.
3 www.clinicaltrials.gov.

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Immunofluorescence assays: PD-L1

PD-L1 assay for patient selection and treatment response to Immune Checkpoint Inhibitors

Because CTCs are live, intact cancer cells, PD-L1 expression can be measured on CTCs as an alternative to tissue biopsy. Eight independent peer-reviewed publications in 373 patients report on the assessment of PD-L1 on CTCs isolated using the Parsortix system. These studies report on CTC PD-L1 status across four cancer types – lung, breast, ovarian, and head and neck cancer. In addition to patient selection, studies suggest that an increase in PD-L1 positive CTCs could have the potential to predict resistance to PD-L1/PD-1 inhibitor treatment[1].

ANGLE has developed a GCLP quantitative immunofluorescence assay as part of its Portrait assays for determination of PD-L1 expression levels. The Portrait PD-L1 assay is in the process of being fully validated in ANGLE's clinical laboratories and will be available to biopharma and clinical markets in Q2, 2024.

The newly developed in-house cell-based approach will enable use of the Parsortix system for the assessment of PD-L1 status on CTCs with the key advantage that the Parsortix system can capture both epithelial and mesenchymal CTCs (missed by traditional antibody-based CTC systems). This will provide significant benefit to the pharma services market.

Read more on ***page 18***

What is PD-L1?

PD-L1 is a protein expressed on the cell membrane that acts as a "brake" to keep the body's immune response under control. PD-L1 may be found on some types of normal cells but is often found in higher levels on cancer cells. When PD-L1 binds to another protein called PD-1 (a protein found on white blood cells), it stops the white blood cells from killing the PD-L1-containing cells, including cancer cells. Targeted anticancer drugs called Immune Checkpoint Inhibitors (ICIs) bind to PD-L1 and block its binding to PD-1. This releases the "brakes" on the immune system and leaves white blood cells free to kill cancer cells.

Patients who have PD-L1 positive CTCs may be indicated for treatment with an ICI inhibitor.

Why does industry need a companion diagnostic (CDx) for PD-L1 inhibitors?

A significant number of PD-L1/PD-1 inhibitors have been withdrawn from the US market due to a failure to demonstrate overall survival benefit in patients. In the 24 months from December 2020 to December 2022, there have been eight FDA products withdrawn for a given indication. The most recent of these was the withdrawal of Tecentriq (atezolizumab) by Genentech for the treatment of bladder cancer in December 2022.

Overall response rate to PD-L1/PD-1 inhibitors is low (20-40%) with significant and sometimes long-term side effects associated with their use. As such a CDx to support better patient selection is a significant unmet need.

Failing in late-stage clinical development or post-approval in Phase IV is costly and time-consuming for the pharmaceutical and biotech industry. As such, a robust PD-L1 biomarker is urgently required in this space to optimise clinical study design and patient selection.

US$1.7bn
PD-L1 pharma services market value[2]

US$31.4bn
spend on PD-L1 immunotherapy drugs in 2021 growing at 5-year CAGR of 27%

~430,000
patients currently enrolled on an active PD- L1/PD-1 clinical study[3]

US$175,000
average ICI treatment cost per patient per year[2]

1 www.pubmed.ncbi.nlm.nih.gov/31212989/.
2 Company estimate.
3 www.clinicaltrials.gov.

▸ **STRATEGIC AIMS IN ACTION** CONTINUED

Assay development: molecular solutions

Molecular diagnostics are a collection of techniques used to analyse biological markers and are seen as the future of cancer diagnostic testing by providing comprehensive genomic (DNA) and transcriptomic (RNA) information. Highly sensitive and specific PCR tests on smaller arrays of genes are driving the existing market. However, with costs continuing to fall, Next Generation Sequencing (NGS), which can analyse the complete genome or transcriptome, is becoming increasingly attractive and accessible for routine patient care.

The Parsortix system is compatible with multiple downstream molecular techniques

ANGLE is developing a variety of molecular assays, including:

1. **Landscape DNA digital PCR assay –** detection of mutations (e.g. EGFR, KRAS and PIK3CA) in CellDNA (i.e. DNA from CTCs) and ctDNA
2. **Landscape RNA digital PCR assay –** gene expression analysis for CTC detection (development of panels for prostate and ovarian cancer)
3. **Landscape DNA NGS assay –** sequencing of both CellDNA (i.e. DNA from CTCs) and ctDNA
4. **Landscape RNA NGS assay –** sequencing of CellRNA (i.e. RNA from CTCs)

The assays under development utilise commercially available third-party cancer gene panels and commonly used instrumentation (e.g. QIAcuity digital PCR, Illumina sequencing platforms etc).

Assay development has been designed so that the output from the Parsortix system (i.e. CTCs) can be analysed using existing laboratory instruments. This enables the Parsortix system and associated Landscape assays to be easily incorporated into the workflow of any laboratory already performing dPCR and/or NGS.

ANGLE can benefit from the existing installed base of these dPCR and NGS instruments. For example, QIAGEN have over 1,000 QIAcuity dPCR instruments installed across the globe[1], and as of early 2022 Illumina have 20,000 sequencers in laboratories globally[2].

The Landscape assays will be offered as both a product (ready to assemble protocols for use with a Parsortix sample) and as a service from our ISO 15189* accredited clinical laboratory in the US. The ISO 15189* accreditation demonstrates that ANGLE's clinical laboratories maintain globally recognised standards and provides evidence for pharma services customers that the laboratories are stable, robust, compliant and subject to periodic external inspections by recognised organisations.

For more information on US clinical laboratory ISO 15189* accreditation see page 18.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

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Next Generation Sequencing

Next Generation Sequencing (NGS) is a massively parallel sequencing technology that offers ultra-high throughput, scalability and speed. NGS is able to generate a huge amount of data at low cost and has become a standard tool for many applications in basic and advanced research, as well as in clinical practice[3].

The estimated market value for NGS in 2021 was US$10.3 billion and is projected to reach US$24 billion by 2026[2]. Continuous technological innovations in sequencers coupled with the wide-scale adoption of NGS technologies (due to its lower price and high efficiency) are the some of the factors driving the growth of the NGS market[4].

The National Human Genome Research Institute (NHGRI), which is part of the NIH, has tracked the cost of sequencing over a 20-year period from September 2001 to August 2021. The cost to generate a high-quality whole genome sequence was almost US$6,000 in late 2014 and had fallen to less than US$600 by August 2021[5]. Since then Illumina Inc., a major player in the NGS field, have claimed they can sequence a whole genome for US$200 with their newest sequencing instrument[6].

In May 2022, Californian biotech Ultima Genomics announced that its UG 100 platform was capable of **sequencing an entire human genome for just US$100**, a landmark moment in the history of the field. The announcement was particularly remarkable because few had previously heard of the company, a relative unknown in an industry long dominated by global giant Illumina which controls about 80% of the world's sequencing market [7].

NIH reported sequencing cost per genome (USD)

ANGLE's Landscape DNA NGS assays and Landscape RNA NGS assays will leverage NGS to capitalise on this increasingly accurate and cost-effective method of molecular analysis.

1 https://s28.q4cdn.com/125951340/files/doc_financials/2022/q3/2022-07-11-Press-release_QIAGEN-Q3-2022-RESULTS_EN_FINAL.pdf
2 www.illumina.com/company/news-center/press-releases/press-release-details.html?newsid=e3ad6d4e-fcbe-4a0d-ac1d-5a3996d1bfd8.
3 Athanasopoulou, K. et al. Life Basel Switz. 12, 30 (2021).
4 www.marketsandmarkets.com/Market-Reports/next-generation-sequencing-ngs-technologies-market-546.html.
5 www.genome.gov/about-genomics/fact-sheets/DNASequencing-Costs-Data.
6 Illumina Aims to Push Genetics Beyond the Lab With $200 Genome. Bloomberg.com (2022).
7 www.leaps.org/genome.

▸ **STRATEGIC AIMS IN ACTION** CONTINUED

Clinical validity studies: ovarian cancer

Ovarian cancer clinical application – abnormal pelvic mass triage test

In September 2022, ANGLE announced positive results from an ovarian cancer clinical verification study, demonstrating that the Parsortix system can be used to determine if a woman is at risk of a malignant pelvic mass. This marks another significant milestone for ANGLE, confirming the clinical validity of the assay.

This 200-patient study was performed with the University of Rochester Medical Center Wilmot Cancer Institute. Samples were analysed in ANGLE's United States clinical laboratory.

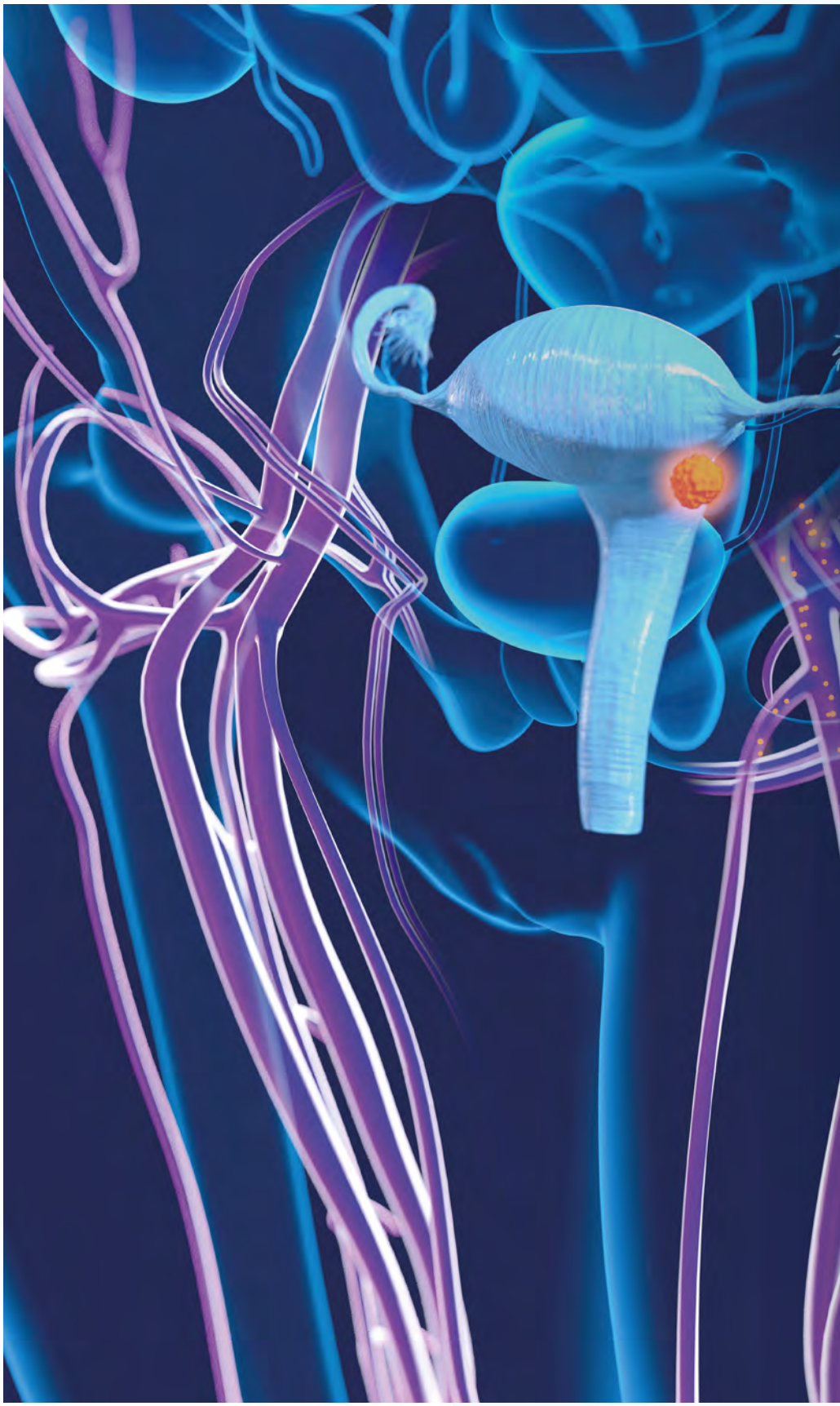
CTCs were evaluated using ANGLE's ovarian assay to determine the expression levels of 164 different gene transcripts. Analysis of the data produced an algorithm for the prediction of the risk of malignancy that combines the physician's initial cancer risk assessment (benign vs. malignant), the patient's age, and the RNA expression levels of 23 critical genes.

The **performance** of the Parsortix ovarian assay in this study was **AUC 95.4%. This is in line with the high level of accuracy** demonstrated in our earlier 200-patient multi-centre study reported in 2018 (AUC 95.1%) and achieved ANGLE's objective of **best in class** results with both sensitivity and specificity **exceeding 90%.**

The clinical results demonstrate ANGLE's capability to undertake **complex molecular analysis** of the Parsortix harvest and confirms the system's suitability for use in both hospital laboratories and centralised laboratories (where samples can be shipped).

Following these excellent results, ANGLE is finalising detailed plans for porting the assay to its landscape platform. The Landscape ovarian assay will utilise a third-party molecular platform in combination with the gene panel optimised in the clinical verification study to deliver an accurate and cost-effective assay to market.

The test has the potential to significantly improve patient outcomes whilst at the same time reduce overall healthcare costs.



// The next generation ANGLE pelvic mass triage test has the ability to out-perform current clinical practice in accurately discriminating malignant from benign pelvic masses prior to biopsy or surgery. The improved accuracy of the test results in a high level of sensitivity as well as a substantial reduction in false positives.

Dr. Richard Moore
Director of the Gynecologic Oncology Division, University of Rochester Medical Center Wilmot Cancer Institute

3x200
patient studies in Europe and the US completed and reported positively

95.4%
correct prediction of cancer with a best in class accuracy (AUC) for the predictive assay

US$1.7bn
p.a. estimated US market potential for the Parsortix system in ovarian cancer[1]

5-10%
of women will develop a pelvic mass requiring surgery at some point in their lives[2]

>200,000
women p.a. have pelvic mass surgery in the US alone[1]

314,000
women diagnosed with ovarian cancer globally in 2020[3]

c.60%
of women are only diagnosed when their cancer has already metastasised[4]

93% at stage I
30% at stage IV
US 5-year survival rates by stage at time of diagnosis[4]

1 Company estimate – United States only.
2 www.contemporaryobgyn.net/view/pelvic-mass-workup.
3 International Agency for Research on Cancer (Globocan 2020).
4 www.seer.cancer.gov/statfacts/html/ovary.html.

▸ **STRATEGIC AIMS IN ACTION** CONTINUED

Clinical studies: prostate cancer

Prostate cancer clinical study in partnership with MidLantic Urology

In May 2022, ANGLE formalised a partnership with a major specialist clinical service provider, MidLantic Urology, to initiate ANGLE's first clinical study in prostate cancer.

The purpose of the study is to evaluate whether ANGLE's novel liquid biopsy assay, in combination with current standard of care (PSA levels, patient history and physical examination), can reduce the over-detection of indolent prostate cancer whilst identifying aggressive disease. This could improve patient stratification and avoid over-diagnosis and treatment.

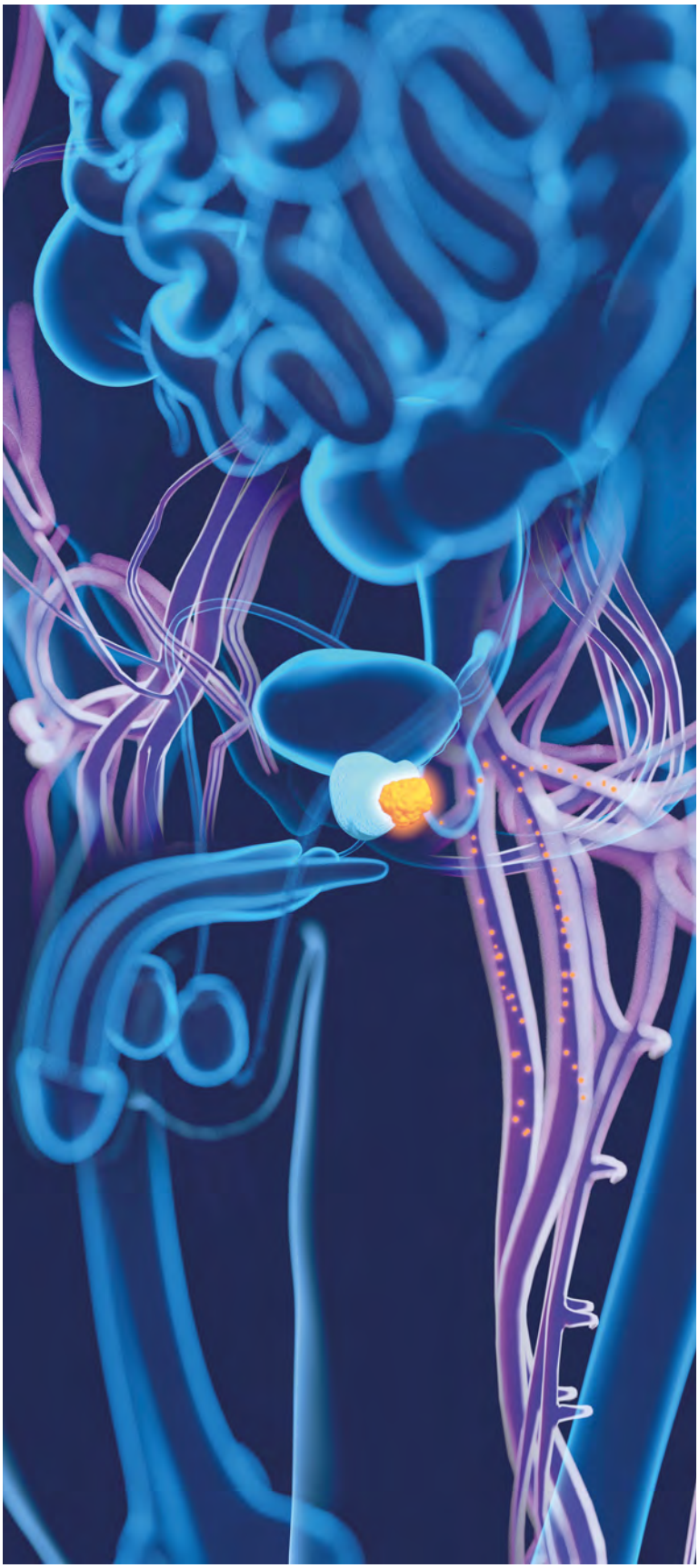
The study, known as **'DOMINO'**, is based on the highly successful pilot studies conducted independently by Barts Cancer Institute (Queen Mary University London). DOMINO will enroll 100 men with either an elevated blood PSA or an abnormal rectal exam, who are scheduled to undergo a prostate tissue biopsy.

Blood samples collected by MidLantic Urology will be shipped to ANGLE's US clinical laboratory for processing by the Parsortix system and harvested CTCs, and associated immune cells, will be analysed using a combination of imaging and molecular assays. Patients will be followed-up to determine if the presence and/or number of these rare cells can identify patients with clinically significant prostate cancer prior to tissue biopsy.

The first patients were enrolled into this study in January 2023, with headline results expected later in 2023. Compelling data from the DOMINO study could form the basis of a LDT which ANGLE would offer from its clinical laboratories in the US and the UK.

MidLantic Urology, an affiliate of Solaris Health Partners (Solaris), is one of the largest providers of specialist urology services in the US. The Solaris Health network encompasses more than 500 clinical urology providers across 179 locations and nine states treating ~730,000 unique patients annually.

Solaris could be ANGLE's first route to market for this test, offering the established test to their extensive patient base.



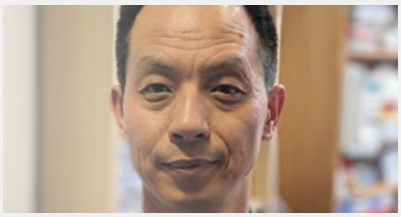
ANGLE's prostate test offers a **unique opportunity to triage men** with an elevated PSA **avoiding the need for invasive core tissue biopsy** for the 90% of patients with benign or indolent disease.

A simple blood test will reduce unnecessary tissue biopsies to:

1. detect the presence of prostate cancer;
2. assess the aggressiveness of disease; and
3. differentiate between patients requiring active surveillance (indolent disease) or surgical intervention (aggressive disease).

// **The Parsortix system has shown the potential to detect more severe cancer cases, where the patient is likely to die sooner, thereby providing information which may enable clinicians to provide different treatment for their patients, potentially extending the lives of those battling with cancer.**

Dr. Yong-Jie Lu
Professor in Molecular Oncology at Barts Cancer Institute



The US Preventive Services Task Force recommends that all men between the ages of 55-69 years be offered annual prostate screening using the blood-based PSA assay.

U.S. Preventive Services TASK FORCE

Under this programme an estimated 11 million men were screened with 1.5 million men returning an abnormal result. This led to ~1 million prostate tissue biopsy procedures with a high incidence of complications:

- 98% report some side effects, 32% report moderate complications and 1.4% report major complications; and
- post-biopsy sepsis occurs in 2-5% of cases with up to 25% of these admitted to an intensive care unit.

1 in 8
men will be diagnosed with prostate cancer in their lifetime[1]

11 million
men between the age of 55 and 69 undergo prostate cancer screening in the US each year[2]

US$6.8 billion
estimated annual US market potential for the Parsortix system in prostate cancer[3]

1.5 million
men in the US have an abnormal PSA result and require further investigation[4]

270,000
men in the US were diagnosed with prostate cancer in 2022[5]

3.3 million
men living with prostate cancer (active or in remission) in the US with a 24-48% chance of recurrence[5]

1 www.prostatecanceruk.org/prostate-information/about-prostate-cancer.
2 https://progressreport.cancer.gov/detection/prostate_cancer.
3 Company estimate.
4 www.academic.oup.com/jnci/article/97/15/1132/2521305.
5 https://seer.cancer.gov/statfacts/html/prost.html.

▸ **STRATEGIC AIMS IN ACTION** CONTINUED

Translational research

The medical devices industry is evidence led, and in addition to the clinical studies and regulatory studies described previously, peer-reviewed publications are a key performance metric.

ANGLE's product-based approach means that we are able to deploy our system to leading cancer centres for use by key opinion leaders and research customers. ANGLE's **unique approach** to capturing and harvesting CTCs is enabling translational researchers to undertake a wide range of research leading to new uses and applications for the Parsortix system as well as achieving **breakthrough research** in many areas. This is leading to an increasing number of peer-reviewed publications.

34 independent cancer centres have published uniformly positive reports on their use of the Parsortix system. Using ANGLE's Parsortix system, leading cancer centres throughout Europe, North America and the rest of the world have undertaken research in **24 different cancer types.**

This deployment of the Parsortix system for translational research now means that the system is widely presented and discussed at leading cancer conferences around the world.

22 peer-reviewed journal articles published in 2022

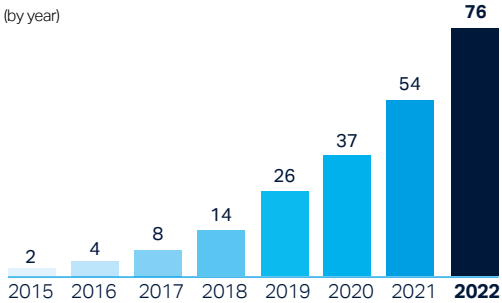
There were 76 peer-reviewed publications as of 31 December 2022 with 22 new publications announced during the year (see **www.angleplc.com/library/publications/**). Highlights of these publications included:

- The Parsortix system was employed to isolate and enumerate CTCs and cancer associated macrophage-like cells (CAMLs) from **pancreatic ductal adenocarcinoma (PDAC)** patient blood. The study outlined the potential value of CTCs and CAMLs as markers of prognosis and disease monitoring and identified CAMLs as **a novel biomarker for a disease** with tragic survival rates and unmet clinical needs.
- A multi-centre study undertaken with the University of Texas MD Anderson Cancer Center utilised the Parsortix system to enrich CTCs in 207 **metastatic breast cancer (MBC)** patients. The study performed multiple downstream analytical techniques including cytology, real-time quantitative reverse transcriptome PCR (qRT-PCR), RNA sequencing and fluorescence in situ hybridisation (FISH). This research highlighted the **successful use of the Parsortix system** in tandem with well-known downstream analytical techniques and commercially available reagents. **This research supported the De Novo Class II FDA clearance**.
- A study undertaken in partnership with the Wilmot Cancer Institute showcased the utility of the Parsortix system for cancer detection in 183 **women with a pelvic mass**. CTCs were subject to multiplexed gene expression analysis combined with serum protein biomarker analysis to form a predictive algorithm, which successfully and accurately detected malignancy more effectively than serum biomarkers alone. **The algorithm was also able to accurately identify early and late stage ovarian cancer**. ANGLE intends to establish this test as a Landscape ovarian assay which will be made available as an LDT.
- A study into **head and neck squamous cell carcinoma (HNSCC)** undertaken at the University of Birmingham characterised the epithelial-mesenchymal transition (EMT) status of CTCs. CTCs were identified in 65% of patients and 77% of positive samples were undergoing EMT. The study showed that **EMT status was almost exclusively associated with advanced disease** and that CTC EMT status was independent to that of tumour tissue, highlighting the clinical utility of the system.
- A study in advanced **non-small cell lung cancer (NSCLC) and sarcoma** patients by the Fondazione IRCCS Instituto Nazionale dei Tumori, Milan, demonstrated that the Parsortix system could **successfully isolate CTCs from frozen blood samples.** The research shows retrospective analysis and sample sharing potential. CTCs were assessed for single cell retrieval for whole genome sequencing and the **assessment of druggable mutations** by digital PCR, showcasing huge potential for the system.
- In a study using CRISPR engineered **metastatic breast cancer** models, the Molecular Oncology Laboratory at the Swiss Federal Institute of Technology, Zurich isolated **CTCs and CTC clusters**, which were then sequenced to characterise metastasis related genes. **The study identified druggable targets which could be utilised for drug discovery.**
- A study by the Istituto Nazionale dei Tumori, Italy, in patients with hard to treat **triple negative breast cancer,** reported that CTCs isolated and harvested using the Parsortix system could be analysed using whole genome and targeted sequencing methods. This enabled changes in the patient's cancer to be **tracked over time**, identifying the **development of treatment induced drug resistance and the emergence of new druggable targets that could guide treatment selection.**

US$50 million p.a.
Translational research market[1]

22
Record number of Parsortix publications in 2022

Cumulative Parsortix system publications



1 Company estimate.

The Parsortix system

A growing body of evidence

As of 31 December 2022

Some of our professional research partners

Robert H. Lurie Comprehensive Cancer Center of Northwestern University
Barts Cancer Institute
Fraunhofer ITEM
University of Basel
hhu Heinrich Heine Universität Düsseldorf
Universitätsklinikum Hamburg-Eppendorf
MD Anderson Cancer Network
Medical University of Vienna
ECU Edith Cowan University Australia
University of Rochester
Cancer Research UK Manchester Institute
Houston Methodist Leading Medicine
Hellenic Republic National and Kapodistrian University of Athens
USC Norris Comprehensive Cancer Center
Fondazione IRCCS Istituto Nazionale dei Tumori

KEY PERFORMANCE INDICATORS

Strong progress against most key milestones

The Group measures its performance according to a range of key performance indicators (KPIs). The main KPIs and details of performance against them are as follows:

KPI	Performance
Cash position **Manage cash and expenditure to deliver the strategy**	The cash position at 31 December 2022 was £31.9 million (2021: £31.8 million). The Group is loss making while it invests in and develops the business and therefore diligently plans expenditure with rolling cash flow forecasts and tight financial control. Updated plans were put in place following the fundraise in July 2022 to deliver key milestones. A decision was made in the second half of the year to close the Canadian operations in Toronto, leading to some one-off costs recognised in 2022 but thereafter delivering significant cash savings and extending the cash runway into H2-2024. The Group also has a high level of discretionary expenditure given the nature of its activities. The Group utilises a collaborative cost sharing leveraged R&D model approach with key opinion leaders (KOLs) and an outsourced approach with third-party suppliers, in particular for the manufacturing of instruments and cassettes, thereby enabling a flexible and scalable approach while avoiding the associated capital and operation expenses necessary for such facilities.
Clinical laboratories **Develop clinical laboratories** **Develop service offering** **Secure initial pharma services contracts**	Capital raising activities included funds to continue the build out of the capacity and capability of clinical laboratories in the UK and US for delivering pharma services and laboratory developed tests (LDTs). The focus in the year has been on completing the development of these laboratories, fitting-out facilities, recruiting and training staff, implementing the necessary procedures and systems and commencing marketing. The US laboratory has achieved ISO 15189* accreditation and both laboratories are processing clinical samples and validating assays for use internally and by customers. Four biopharma customers have now been onboarded – see research use sales below.
Intellectual property **Increase the depth and breadth of IP**	Intellectual property strengthened with new patent filings increasing the breadth and duration of patent coverage and the range of medical applications covered. Patent applications are being progressed worldwide associated with the core Parsortix system and new product development. 26 patents protecting the Parsortix system granted at the reporting date (2021: 26) in the United States, Europe, Australia, Canada, China, Japan, India and Mexico, extending patent coverage out to 2034.
Ovarian cancer clinical application: triaging abnormal pelvic mass **Headline results reported** **Transfer to third-party downstream analysis systems**	There have been two successful 200-patient studies for the detection of ovarian cancer in patients undergoing surgery for an abnormal pelvic mass. The optimisation of the ovarian assay combining the Parsortix system and HyCEAD was completed. The optimised assay was tested in a new 200-patient study run by the University of Rochester Medical Center Wilmot Cancer Institute (URMC). The headline results were reported in June 2022 demonstrating best in class performance with 95.4% accuracy. Given significant improvements in sensitivity, specificity, throughput and cost, a commercial decision was taken to leverage globally adopted third-party systems for downstream molecular analysis, rather than the in-house HyCEAD platform. The ovarian assay is now being evaluated using these systems before proceeding with commercial launch as a laboratory developed test.

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

KPI	Performance
Prostate cancer clinical application: presence and severity prior to tissue biopsy **Partnership signed with Solaris Health**	In May 2022, ANGLE signed an agreement with MidLantic Urology, an affiliate of Solaris Health, to conduct clinical studies in prostate cancer. There is a major unmet need for a pre-screening tool ahead of invasive tissue biopsy as an aid to assessing prostate cancer presence and aggressiveness to guide treatment choices. Together with MidLantic Urology, ANGLE has designed a 100-patient study to evaluate Parsortix based imaging and molecular assays in this setting. Headline results from this study are expected around the end of 2023, subject to successful participant enrolment which is outside ANGLE's control. Compelling data could form the basis for a laboratory developed test which ANGLE would offer from its clinical laboratories in the US and the UK. Solaris Health is one of the largest urology groups in the US and offers a potential route to market with a substantial and established patient base.
Product development **Deliver ongoing upgrades, enhancements and optimisation of our systems**	The Parsortix cell capture and harvesting technology has been developed and comprises an automated instrument to run blood samples through the separation cassette, a single use consumable. Extensive product development and system optimisation has been successfully completed to address the operational requirements of a wide range of KOLs and customers. Product development work has been completed to develop, test, optimise, characterise and document key operating protocols enabling customers to undertake analysis in a specific area of interest. The Parsortix system has been demonstrated to be reliable and easy to use and produces robust reproducible results. There are more than 260 Parsortix instruments in active use (in-house, KOLs and customers) at the reporting date (2021: c.230). Over 171,000 blood separations have been performed on the system at the reporting date (2021: 141,000). This experimental data provides a broad body of evidence that demonstrates the system's potential to be applicable to a wide range of cancer types and multiple methods of downstream analysis. To date the Parsortix system has been used successfully with 24 different types of cancer. Upgrades, enhancements and optimisation of the Parsortix system are ongoing to further enhance operational performance, product reliability and to develop additional utility and operating protocols, based on customer and KOL feedback, and to meet pharma services' needs, for example, in blood sample stability.

KEY PERFORMANCE INDICATORS CONTINUED

KPI	Performance
Published evidence **Build the body of independent data**	Successful evaluations and studies with 34 independent cancer centres have led to a growing body of published evidence: • 76 publications in peer-reviewed journals as at 31 December 2022 (2021: 54) plus many posters
Regulatory authorisation **Breakthrough FDA clearance achieved**	Regulatory authorisation is a requirement before the Parsortix system can be sold for use in the clinical diagnostics market (where results obtained are used for the purposes of patient management). ANGLE successfully achieved FDA clearance (the gold standard) for the Parsortix PC1 Clinical System for harvesting CTCs, intact living cancer cells, from patient blood for user validated analysis in metastatic breast cancer patients. CE marking and MHRA registration of the Parsortix PC1 Clinical System in the European Union and United Kingdom respectively were received for the same intended use. Four leading US cancer centres conducted the FDA clinical studies: • The University of Texas MD Anderson Cancer Center • University of Rochester Medical Center Wilmot Cancer Institute • University of Southern California Norris Comprehensive Cancer Center • Robert H Lurie Comprehensive Cancer Center Northwestern University ANGLE Europe Ltd maintains its Quality Control system to ISO 13485:2016 and has a BSI certificate of registration certifying its compliance with this standard and is subject to and continues to receive annual compliance audits by BSI. Work is ongoing to prepare for 21CFR820 compliance in support of FDA clearance.
Research use sales **Build product sales to leading translational researchers** **Build distributor network** **Secure additional pharma services contracts** **Pipeline building but new customer adoption slower than expected**	Product sales have been made to multiple customers in Europe, North America and certain other countries including existing KOLs, new research users, big pharma and immunotherapy companies comprising new instrument sales and repeat orders for cassettes and support and maintenance contracts. The sales environment has remained challenging with customers experiencing continued post COVID-19 impacts and a restricted grant funding environment. Revenues from products for the year were £0.7 million (2021: £0.8 million). ANGLE has entered into agreements with oncology focused distribution partners in multiple geographies. These partners all provide valuable sales, implementation and ongoing service and maintenance support. Sales are expected to build gradually as downstream assays are developed, clinical validity studies are completed, and reimbursement codes are secured. Following the establishment of clinical laboratories in the United States and the UK in 2021, ANGLE secured its first customers for its newly launched pharma services business. Initial contracts provided for sales of up to £1.0 million over a multi-year period, generated through the combined use of the Parsortix system with imaging analysis to process samples in a global Phase III study in prostate cancer and two smaller Phase I studies. Although sample delivery issues and slower than expected patient recruitment impacted revenue recognition in 2022, the same customer subsequently signed a contract for a new study to begin in 2023 (up to a further £1.0 million over a multi-year period). In addition, ANGLE successfully completed an assay development project in the field of DNA Damage Repair for another customer who expects to take the assay into clinical studies in 2023. Onboarding of new customers was slower than expected during the year, reflecting an adverse funding environment for biopharma and an uncertain macroeconomic outlook, although the pipeline of potential customers is building strongly following the FDA clearance. Revenues for the year were £0.3 million (2021: £0.2 million).

PRINCIPAL RISKS AND UNCERTAINTIES

Managing risks

The nature of medical diagnostics development and the early stage and scale of our operations means there are a number of risks and uncertainties.

The Directors maintain a risk register and have summarised the principal risks and uncertainties that could have a material impact on the Group. These are set out in the table below, along with mitigation strategies.

Risk	Description	Mitigation
Clinical applications (ovarian cancer, prostate cancer)	The Group is developing a clinical application for the triage of women presenting with an abnormal pelvic mass. This is dependent on both a successful harvest of CTCs by the Parsortix system and identifying a set of RNA markers that can discriminate between malignant ovarian cancer and other benign conditions. The Group achieved best in class results from a clinical verification study using its in-house HyCEAD molecular sequencing platform for the downstream analysis. The assay is now being transferred to commercially available third-party systems as they have improved in sensitivity and reduced in cost and this approach will support the widest commercial adoption. There can be no guarantee that this transfer will ultimately be successful. The Group has also initiated studies in prostate cancer in partnership with a leading group of urology clinics in the United States to identify the presence of prostate cancer and its clinical significance prior to tissue biopsy or surgery. The studies include an imaging assay and a molecular assay using a third-party platform. The development and commercialisation of clinical applications is subject to a variety of risks including those set out below. Clinical studies may be delayed due to slow or insufficient patient enrolment or may be temporarily ceased due to factors outside our control. Data produced may not be sufficient to support roll out of the clinical application. There can be no guarantee that clinical applications will be developed into commercially viable laboratory tests or regulated devices. Appropriate third-party payer reimbursement codes may be delayed or may not be obtained thereby limiting commercial uptake of the application. Vested and competing interests may impede market acceptance for either a laboratory developed test or a regulated device.	The Group employs an experienced clinical studies director, who has developed detailed clinical study programmes (including prior experience in CTCs and ovarian and prostate cancer) which have had thorough internal and third-party reviews, including by the study lead and other experts. A significant amount of preparation, including additional R&D on proposed biomarkers and study processes, is undertaken to minimise the risks. The Group carefully selects clinical applications based on a set of key criteria including strong pilot study data, access to leading KOLs and access to patients. In relation to ovarian cancer, data from the successful clinical verification study gives the Group confidence that the RNA markers and algorithms selected can be used to produce similar results using a third-party molecular sequencing platform. The Group assembles multiple study sites and partners where possible to achieve patient enrolment rates in a timely fashion. The Group undertakes independent market research to understand end user needs and ensure the studies produce the necessary data. In order to mitigate ongoing global supply chain issues, the Group holds higher levels of inventory, reagents and consumables than it normally would, however, certain reagents either cannot be ordered until their precise make-up is known and/or have a short shelf-life. The Group takes independent advice on reimbursement codes and commercialisation strategy.

PRINCIPAL RISKS AND UNCERTAINTIES CONTINUED

Risk	Description	Mitigation
Competitive position	There are numerous competitive groups seeking to develop alternative cancer diagnostic products in direct competition (other CTC technologies) and indirect competition (other liquid biopsy methods, for example, ctDNA analysis). It is possible at any time that a competing technology which out-performs Parsortix may enter the market. Some competitors have greater resources which may allow them to deploy commercial tactics which restrict the Group.	The Group manages its product development and IP position, accelerates product launch and monitors customer needs and competitors internally, with its Scientific Advisory Board (SAB), through its relationships with key opinion leaders (KOLs), customers and prospective customers, and through attendance at conferences. The Directors believe that the patented Parsortix technology has the potential to be more effective and affordable than competing technologies. The Group has developed a low-cost affordable solution, which puts it in a strong position for pricing, and it is antibody independent allowing for a range of cancers to be analysed that other CTC systems may not be able to handle. Liquid biopsy CTCs may be the closest solution to a conventional solid tissue biopsy allowing all types of cellular and molecular analyses to be undertaken and is therefore differentiated from a liquid biopsy ctDNA analysis.

Risk	Description	Mitigation
Financial	The Group is investing significantly in R&D, clinical studies, FDA/regulatory studies, product development, clinical laboratories and product marketing and consequently is loss making and utilising cash reserves to support operational activities. The commencement of material revenues is difficult to predict as 1) the Group is launching new products and services in an emerging market and suitable clinical applications need to be identified, have successful clinical studies completed, achieve regulatory clearance and achieve market acceptance, and 2) the impact of the Group's FDA clearance to boost research use sales and in particular to be employed in pharma drug trials is still in the early stages. Operating losses are anticipated to continue for some time. In the event that new funds are required there can be no guarantee that these will be available on acceptable terms, at the quantum required, or at all, which could affect the ability to commercialise the technology and may require operations to be scaled back, delayed or even affect the ability to continue as a going concern. The Group incurs significant costs in US and Canadian Dollars and is exposed to US and Canadian Dollar exchange rates which it is unable to control. The Group also has critical European and US suppliers and incurs costs in Euros and US Dollars and is exposed to Euro and US Dollar exchange rates which it is unable to control. Post-Brexit EU trading and human resource issues and the ongoing impact of earlier COVID-19 restrictions may have an effect on the Group's operations. With the UK status as a "Third Country", the movement of goods between ANGLE and European customers and within ANGLE's European supply chain may be adversely affected.	The Board undertakes careful planning, management of expenditure and rolling cash flow forecasting, has a strong focus on milestone and performance delivery and avoids long-term supplier contracts where it can. The Group seeks to maintain a reasonable cash balance to mitigate against the need to raise funding in potentially adverse market conditions (macroeconomic factors such as high interest rates, market correction etc). Discretionary and/or non-mission critical expenditure can be deferred or reduced where necessary to conserve cash until the environment is more certain. The Group may utilise Government support schemes where appropriate. The research use market offers the potential for earlier revenues than the clinical market and sales have been initiated in this area with leading translational researchers and to pharma/biotech customers. The development of a laboratory service-based offer to the pharma/biotech sector providing CTC capture and analysis services that support the use of CTC derived information in drug development studies, pre-clinical and clinical drug trials is an important aspect. The Group is developing and launching multiple sample-to-answer assays to support this offering. The Group is working with KOLs, SAB members and specialist consultants to identify suitable clinical applications which offer significant revenue potential either as a laboratory developed test or FDA cleared product. Clinical applications need to meet key criteria and the Group is progressing its clinical application in ovarian cancer and potential clinical application in prostate cancer. The Board maintains close shareholder relations, high standards of corporate governance and explores different sources of funding including potential partners. The Group has successfully raised funds on several occasions in the past. The Group monitors its currency exposures on an ongoing basis. The Group has closed down its Canadian operations which both reduces cash burn and mitigates any adverse exchange rate movements. The Group is building US and European sales to provide a natural hedge. The Group holds a modest parts and finished goods inventory, held in multiple locations to help mitigate any COVID-19 and Brexit related supply chain problems. The Group established a Dutch subsidiary to facilitate EU sales and mitigate post-Brexit trading issues. The Group is considering establishing a European logistics centre to overcome ongoing friction in exporting to and the servicing of equipment in the EU. Details of the Group's financial risk objectives and policies are disclosed in Note 14 of the Financial Statements.

PRINCIPAL RISKS AND UNCERTAINTIES CONTINUED

Risk	Description	Mitigation
Intellectual property	The Group's success depends in part on its intellectual property (IP) in order that it can stop others from exploiting its inventions. There is a risk that patent pending applications will not be issued. It is possible that competitors may infringe this IP or otherwise challenge its validity, which may result in uncertainty, litigation costs and/or loss of earnings.	The Group invests significantly in its IP, employs experienced patent agents and protects its IP with confidentiality agreements, patents and patent applications in order to reduce the risks over their validity and enforceability. The Group has also undertaken freedom-to-operate searches. The Group had 26 granted patents protecting the Parsortix system at the reporting date in the USA, Europe, Australia, Canada, China, India, Japan and Mexico, with others in progress, extending patent coverage out to 2034.
Manufacturing	As precision equipment, it is extremely important that manufacturing is of a consistent and extremely high quality to ensure that instruments and cassettes operate as specified and produce consistent results and meet the necessary manufacturing tolerances specified. Product lead times need to be appropriate for timely delivery whilst maintaining product quality. The Group is dependent on three key single source suppliers. Problems at outsourced manufacturers and their suppliers could lead to disruption in supplies, delays, product inconsistency and product failure. The Group has also established a flexible, small volume pilot manufacturing facility in the UK to support the roll out of sample-to-answer imaging and molecular assays to the Group clinical service laboratories and early adopter customers. This provides high levels of operational flexibility whilst maintaining quality system standards. However, the Group remains exposed to global supply chain issues in relation to highly application specific reagents and materials. The COVID-19 pandemic impacted our supply chains. These events may still result in increased lead times, product costs, duties and taxes and may require a reconfiguration of supply chains with associated knock-on time and cost impacts. Certain products were being manufactured at the Group's Toronto facility which has now been closed. Although the manufacturing is being transferred to the UK, manufacturing problems could lead to these products not being available when required for use in R&D or for customers as elements of planned product kits.	The Group has outsourced manufacturing to specialist organisations that can manufacture the separation cassettes at the required tolerances, can assemble instruments and have capacity for scale-up of production. Investment has been made in specialist moulding tools and validated processes to help achieve the highest standards. Key suppliers are ISO 13485:2016 certified and subject to ongoing audit by the Group. Where possible, designs use standard components and any components on long lead times are held in inventory. Designs are subject to continuous improvement to help eliminate issues as they arise. To manage the risk of loss or disruption of supply (e.g. from COVID-19 and Brexit), "safety" inventory levels have been established, (held at multiple locations) of critical components and also finished product, thereby enabling the Group to continue to supply for a finite period whilst manufacturing capability and/or supply lines are restored. Dual sourcing of product from key suppliers is actively being pursued but it is unlikely that this will be fully achievable in the short term. Third-party and on-site product manufacture is subject to good manufacturing practice and Group regulatory control and oversight. The Group also has product liability insurance. Products and product parts previously manufactured in Toronto have been transferred to the UK operations including using a key third-party supplier. Significant effort was put into achieving an orderly handover of processes and procedures and ensuring there was a level of inventory to provide cover while the new UK manufacturing capability is developed, tested and brought into production.

Risk	Description	Mitigation
Market acceptance	Success depends on both clinical and health economic acceptance of the Group's products. Studies are required to demonstrate the utility of clinical applications and there is a risk that the data may be weak, inconclusive or negative. The medical diagnostics market is conservative by nature, CTC systems are an emerging technology, customers may be slow to adopt new products, vested interests may impede market penetration and products may not achieve commercial success. The Group may not be able to sell its products profitably if reimbursement by third-party payers is limited or unavailable. The Group may be subject to price limits on reimbursement of products which are outside its control, negatively impacting revenues.	Although relatively modest, the research use sales market to leading translational researchers is a good market in its own right and will help generate additional data on utility, new uses and clinical applications as well as generating peer-reviewed publications. The Group undertakes in-house R&D and works with partners and KOLs to act as reference customers, to obtain data relating to clinical applications and the efficacy, safety and quality of the product. It monitors industry developments and customer needs through its interaction with customers and prospects, attendance at conferences and through the Group Scientific Advisory Board and KOLs. The Group has a laboratory service-based offer for research use sales to the pharmaceutical sector providing CTC capture and analysis services that supports the use of CTC derived information in drug development studies, pre-clinical and clinical drug trials. This aims to promote the wider use of the Parsortix system and associated technology in the development of drugs and treatment protocols, which may ultimately lead to the establishment of the Parsortix system as a companion diagnostic for particular therapies in the oncology space. Clinical studies are set up to generate clinical data and analysis for accurate and complete submissions to secure regulatory approvals. Health economic studies, advocacy and other activities will be undertaken at the appropriate time. The Group is working with KOLs and SAB members including specialist consultants to identify suitable clinical applications which offer significant revenue potential either as a laboratory developed test or FDA (or other regulatory body cleared) IVD product. Clinical applications need to meet key criteria and the Group is progressing its clinical applications in ovarian and prostate cancer.

PRINCIPAL RISKS AND UNCERTAINTIES CONTINUED

Risk	Description	Mitigation
Operational	In order for the Group to operate effectively the infrastructure needs to be robust, efficient and scalable. Unexpected events (such as COVID-19) could disrupt the business by affecting a key facility or critical equipment or donor or patient enrolment which could lead to an inability to undertake development work (e.g. clinical studies with partners). Cyber-crime is increasing in sophistication, consequences and incidence, with risks including virus and malware infection, unauthorised access and fraud.	The Group has a disaster recovery and business continuity plan to ensure a rapid response in an effective and managed way to a variety of situations. This plan was deployed in the COVID-19 pandemic due to its impact across the entire operations of the business and allowed a rapid and effective response, ensuring a practical level of continuity of Group operations, despite ongoing restrictions across the world. Business critical systems are cloud-based facilitating remote working and back-up mechanisms are also regularly tested. Staff have laptops and ongoing IT training. Certain staff can work remotely if required. Laboratory and engineering staff are limited in the amount of work they can undertake remotely, however, split-shift working was adopted during COVID-19 to facilitate social distancing. US facilities have emergency back-up power to protect against loss of valuable samples and reagents. Critical equipment has service and maintenance contracts. The Group uses expert IT firms to ensure it operates with appropriate cyber defences. There is daily offsite back-up for rapid recovery from a problem. The back-up is regularly tested.

Risk	Description	Mitigation
Pandemic/ epidemic	Exposure to a pandemic, such as COVID-19, or an epidemic that directly or indirectly leads to disruption of the Group's operations in particular to laboratory-based operations and delays to clinical studies.	The Group has a disaster recovery and business continuity plan that enables the rapid establishment and deployment of a Leadership Team (LT) to assess and manage disruptions to operations and task sub-teams with specific actions. It is the LT's responsibility to ensure the Group complies with all laws and guidance issued by Governments at any time. This may result in the Group's offices and/or laboratories being temporarily closed or operated on a restricted basis. It is the LT's responsibility to ensure management practices keep staff safe and healthy and produce updated or new procedures as required. Staff are transitioned where appropriate to working from home and with unnecessary travel avoided. Staff unable to work from home are transitioned where appropriate to split-shift working to assist social distancing and with the use of PPE, hygiene and enhanced procedures as appropriate to manage the work environment. The LT reviews the impact of Government Laws and Guidelines and how they impact Group activities. While the Group may be able to mitigate certain aspects of any Government Laws and Guidelines by enhancing or introducing new procedures, in certain situations studies may need to be temporarily paused in order to meet such Government Laws and Guidelines and can only be restarted once the Government Laws and Guidelines are updated and relaxed. This may include restrictions on the collection of patient samples needed for clinical studies and/or healthy volunteer blood samples needed for analytical studies. The LT also reviews customer needs in the context of the pandemic. Ways of working were adapted to provide virtual support to customers. The existing customer base is predominantly leading translational researchers based at hospitals and universities and consequently Government Laws and Guidelines may result in their operations temporarily being ceased, which means evaluations and ongoing research work may also be paused and sales reduced significantly until Government Laws and Guidelines are eased. The LT reviews supply chain requirements. Close contact is maintained with key suppliers to ensure they are able to provide services and goods in a relatively normal fashion, although noting they may have to modify their ways of working. The Group already holds significant levels of certain critical inventories to mitigate any potential supply chain problems and to date has not experienced any significant supply chain issues with the exception of one event in relation to the delayed delivery of reagents for the ovarian cancer study. Other supplies may be ordered to ensure the Group has a buffer stock and can continue operations.

PRINCIPAL RISKS AND UNCERTAINTIES CONTINUED

Risk	Description	Mitigation
Regulation and quality assurance	The Group operates in a highly regulated industry and needs to meet recognised quality assurance standards that are subject to third-party audit. The Group must comply with a broad range of regulations relating to the development, approval, manufacturing and marketing of its products and is subject to regulatory inspection. There is a risk that a regulatory audit will find problems that could have severe consequences on the Group's ability to sell products in the relevant country, lead to a loss of marketing authorisation, a loss of reputation, a loss of customers, recall or remediation costs as well as enforcement action and sanctions from a regulator. Major success with the cancer diagnostic product (and other products) will require regulatory authorisation for clinical use from various regulatory authorities which will require data from studies relating to the efficacy, safety and effectiveness of the product. Regulatory regimes are complex and dynamic and it can be difficult to predict their exact requirements, so authorisations may be delayed and alterations to the regulations may also result in delays. If it proves difficult to achieve authorisations, major revenues may be delayed or without authorisation may not be achievable.	Regulatory authorisation has been achieved in the United States (FDA), Europe (CE mark) and the UK (MHRA) for the indicated clinical use. Authorisations in other territories are being investigated in partnership with distributors and will be sought in due course. The Group conducts its manufacturing operations within ISO 13485:2016 quality management systems in the UK and continues to invest in its systems and people. The quality system is subject to annual Notified Body audit (BSI). The Group uses external specialist resources (regulatory, design, manufacturing etc) as required to achieve business objectives. The Group employs an experienced clinical studies director to design and develop clinical study programmes that will meet international regulatory requirements and adhere to ICH GCP Guidelines as appropriate. The Group is currently responding to significant changes in the European regulatory environment driven by the release of the ISO 13485:2016 standard to which we have already transitioned and the new In Vitro Diagnostic Device Regulation (IVDR), which replaced the previous IVD Directive in 2022. The Group is confident that compliance with the new IVDR requirements can be successfully achieved in line with the certified transition period. The United States clinical laboratory has received ISO 15189* accreditation, and this has been applied for by the UK laboratory. This is particularly relevant for pharma services customers that require evidence that the laboratories are stable, robust, compliant, and subject to periodic external inspections by recognised organisations. The current CE mark regime for IVD devices is based upon a European Regulation. This has not been implemented yet in the UK. How this regulation will evolve beyond current UK law and what the impact on the Group will be is not clear at this time. The Group's UK based Notified Body BSI has put in place contingency measures such that European IVDR compliance certificates and Quality System certificates can continue to be issued from within Europe and hence CE mark can be applied. We continue to monitor the development of and transition to the relevant UKCA conformity assessment procedures being put in place by the UK Government post-Brexit.

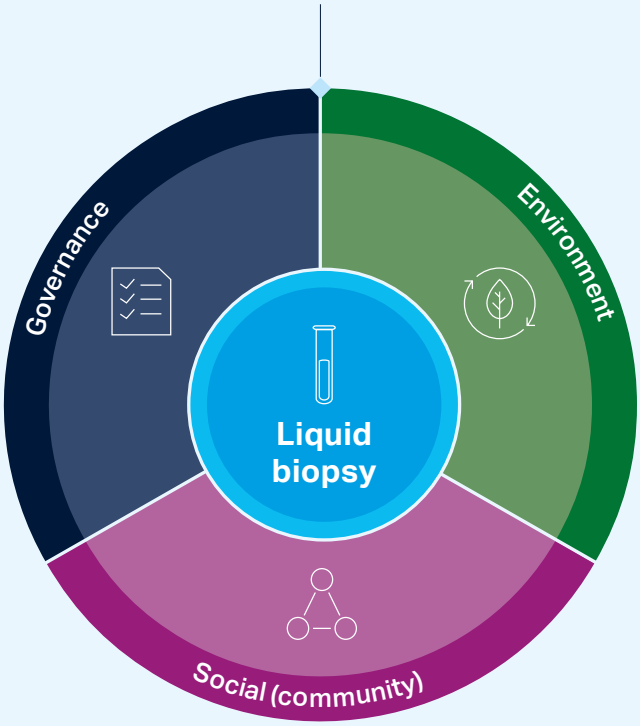
* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

Risk	Description	Mitigation
Research and development	The Group undertakes significant research and development activity with the aim of launching improved and new products and services, but there remain considerable technical risks, which may result in delays, increased costs or ultimately failure.	The Group uses skilled staff and third-party experts in various fields from science and product design to engineering and manufacturing. There is good knowledge and experience within the Group and third-party experts in place with established relationships. The nature of medical devices means that although development can be challenging, there should generally be a technical solution, provided sufficient resources and expertise are applied to the problem. As developments and enhancements are generally to existing products there is somewhat less risk than developing a completely new product.
Staff, key suppliers and key partners	The Group's future success is dependent on its management team and staff and there is the risk of loss of key personnel. With complex and critical development projects, alignment of business and project objectives, good project planning and clear staff focus are required. The Group also outsources certain aspects of product development, regulatory advice and manufacturing and is heavily dependent on these key suppliers. The Group is also heavily dependent on its clinical study partners who are responsible for patient and subject enrolment and on occasion core laboratory work.	The Group manages staff requirements closely, invests in skills development and new staff and has staff incentive schemes for retention and motivation. Using our competency framework, staff are assessed regularly to ensure they develop and maintain the skills needed for high performance. Individual competencies and skills are aligned with business objectives and requirements and personal development goals. Suppliers, clinical study partners and KOLs are carefully chosen and actively managed. Written agreements are in place for all staff and key suppliers in line with local laws and are reviewed and updated on a regular basis. Quality System requirements and compliance are assured through regular auditing. Work with collaborators is controlled using contracts and clinical study protocols where appropriate. Clinical study protocols are generally subject to institutional scientific and ethics approval prior to study commencement.

CORPORATE RESPONSIBILITY REPORT

Sustainability and ESG strategy overview

ANGLE is committed to adopting best practice with respect to its impact on society and the environment.



2022 ESG Highlights

Ongoing work with World Wide Generation to develop reporting framework and agree goals, capture information and monitor

New mental health awareness program and access to trained mental health first aiders introduced

Ongoing commitment to flexible working, training and development, student placements and apprenticeships

Post market surveillance infrastructure established following FDA clearance and CE-IVD marking

ISO 15189* (quality) accreditation received for the United States laboratory

* The ANGLE US laboratory ISO 15189 accreditation is specific for the CTC Pap Stain Assay.

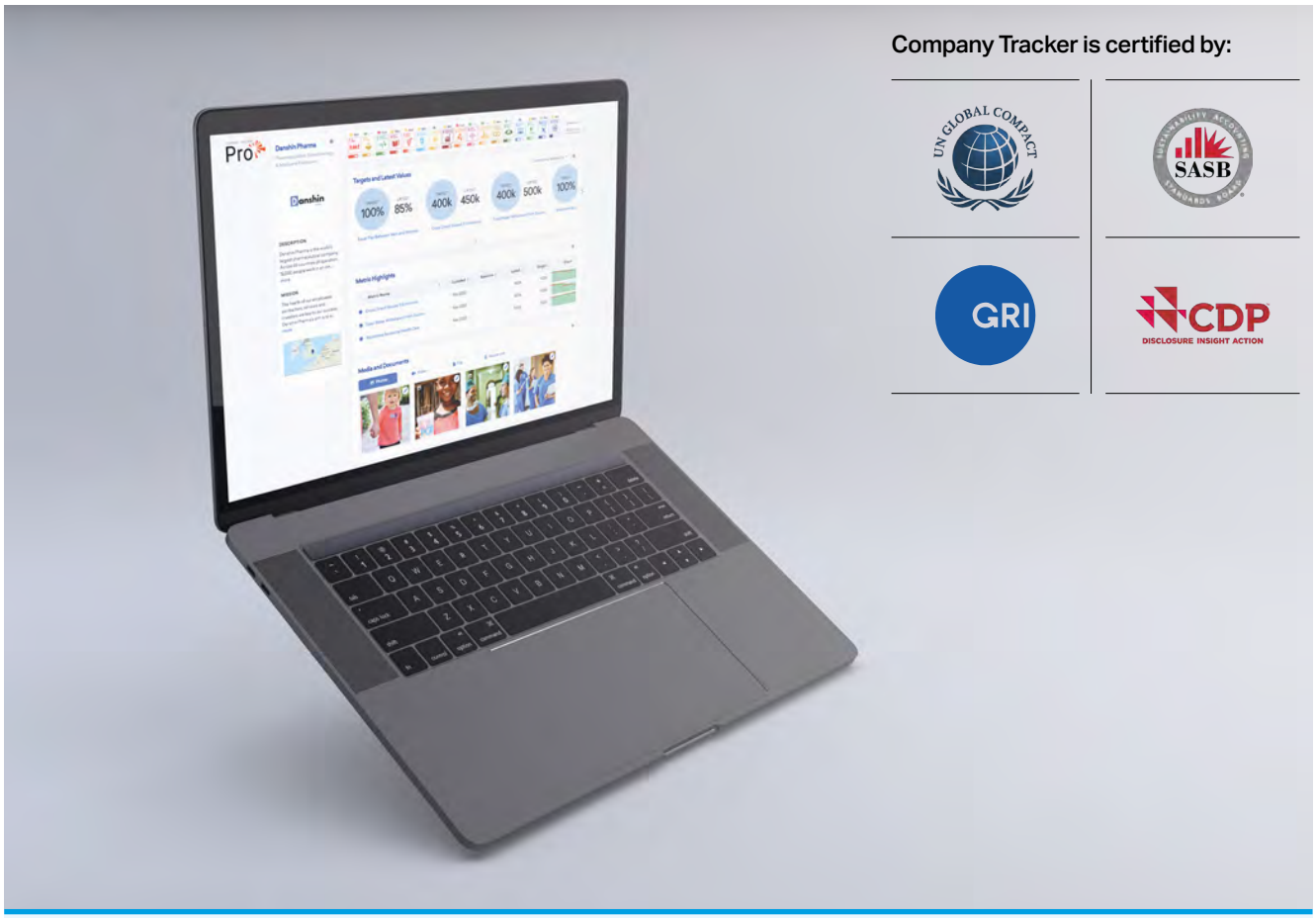
ANGLE believes that investing in culture and community and making a positive impact on the environment will help the Group meet its business, financial and commercial objectives. ANGLE encourages diversity and inclusion and aims to support all employees to reach their full potential. ANGLE also aims to minimise its impact on the planet through its energy use, resource and material requirements, waste recovery and transportation. ANGLE views these efforts not as additional costs but as investments towards a sustainable future. Further, ANGLE is committed to good corporate governance and operational excellence, going above and beyond the requirements of the regulatory environment in which it operates.

WORLD WIDE GENERATION G17Eco

Sustainability reporting and the WWG G17Eco platform

ANGLE continues to work with World Wide Generation (WWG), the provider of a leading digital reporting tool for small and medium sized companies on its sustainability reporting requirements. The G17Eco Company Tracker platform allows ANGLE to measure and monitor all its relevant social, economic and environmental impacts, allows benchmarking against key policies, standards and frameworks and maps directly to the UN Sustainable Development Goals.

With a view to enabling the collection of reliable and consistent data on ANGLE's performance, an ANGLE team was assembled with contributors from across functions (e.g. finance, human resources, R&D, manufacturing, clinical laboratories) and across each of ANGLE's geographic locations. The team is in the process of identifying the relevant standards and frameworks and building its initial database of key metrics and data. Once complete, the Company will be in a position to set targets for future performance and develop the required internal policies and procedures to capture the necessary data and move towards meeting those targets. ANGLE's sustainability reporting will evolve as this work progresses.



WWG has developed G17Eco, a monitoring and marketplace technology platform.

G17Eco has been developed with the support of over 300 experts, including its own Standards Council comprised of the world's leading academic institutions and sustainability experts. The Standards Council delivers the harmonisation and mapping of thousands of metrics from standards, policies and frameworks, making sustainability reporting literally and acronymically S.I.M.P.L.E. (Strategic, Interconnected, Meaningful, Purposeful, Long-term and Educative).

Within G17Eco, WWG has created several apps, namely Company Tracker, Portfolio Tracker and World Tracker, allowing all stakeholders to map, monitor, measure, manage and market their sustainability impact in a trusted, comparable and timely way.

Company Tracker is certified by the UN Global Compact (UNGC), Sustainability Accounting Standards Board (SASB), Global Reporting Initiative (GRI) and CDP (formerly the Carbon Disclosure Project) and covers all sustainability areas. Contributions are also measured against the 17 Sustainable Development Goals (SDGs).

Company Tracker enables users to report to key standards and frameworks, bring greater real-time transparency to their sustainability performance and report across multiple sites and countries.

www.g17.eco
www.worldwidegeneration.co

CORPORATE RESPONSIBILITY REPORT CONTINUED

Liquid biopsy

Access to healthcare and the role of liquid biopsy

As one of its 17 Sustainable Development Goals, the United Nations describes "ensuring healthy lives and well-being at all ages as essential to sustainable development". The UN goes on to set a number of targets to achieve this goal, including a one-third reduction in non-communicable diseases by 2030, including cancer. In addition, the UN places diagnosis, early warning and risk reduction at the heart of its ambition to make healthcare more accessible and affordable for all countries.

This target is similarly reflected in the UK's NHS Long-Term Plan which sets out ambitions in cancer care. These include that:

- by 2028, the proportion of cancers diagnosed at stages 1 and 2 will rise from 50% to 75% of cancer patients
- genomic testing will be offered to all cancer patients
- all cancer patients will have access to personalised care and targeted treatment
- after treatment, patients will have rapid access to clinical support where they are worried that their cancer may have recurred.

ANGLE's stated mission is to change the way that cancer is diagnosed, treated and monitored. Our Parsortix system enables the capture and harvest of circulating tumour cells (CTCs), which are cells shed from a tumour into the peripheral blood, for analysis. This is known as a liquid biopsy, and its use has enormous potential throughout the patient care continuum to improve outcomes and reduce healthcare costs.

Cancer has a major negative social impact – an estimated one in two people born after 1960 in the UK will be diagnosed with cancer during their lifetime. Each patient's cancer is unique, highly complex and changes over time. Effective treatment requires personalised care that evolves with the cancer.

The existing standard of care for obtaining tumour material for evaluation is a solid tissue biopsy, which is invasive, can result in medical complications, and uses a lot of healthcare resources – facilities, surgeon, anaesthetist, nurses etc, with the associated high costs. Further, it is difficult and generally impossible to perform repeat solid tissue biopsies, which risks treatment decisions being made on historical information missing the dynamic nature of cancer treatment response, or the development of resistance to treatment.

ANGLE believes its Parsortix liquid biopsy system has the potential to significantly improve care for cancer patients, as it is minimally-invasive and repeatable, and reduces the costs and resources involved in cancer care.

COVID-19 and cancer – the big picture

Whilst the Government enforced lockdowns resulted in positive environmental effects (working from home more, less business travel etc), there has been a notable negative impact on cancer diagnosis, treatment and disease monitoring with a growing backlog of diagnostics and treatment. ANGLE believes that liquid biopsy could be a valuable tool in addressing what has become a secondary healthcare crisis following the global pandemic. Cancer is the leading cause of death in most developed nations, responsible for an estimated 10 million deaths per year globally. As such, cancer diagnosis and care remain a priority and services will need to rapidly evolve to counter the substantial challenge of the current and any future pandemic. Ending delays and addressing backlogs, particularly cancer surgeries and diagnostic tests, will need to be an urgent priority moving forward.

The information provided by liquid biopsy could help clinicians diagnose, treat and monitor cancer more efficiently. Liquid biopsy is minimally invasive, can be undertaken safely in community clinics or in the home, and can provide patients and physicians with real-time results, leading to more timely diagnoses and better-informed, dynamic treatment decisions with targeted therapies. Liquid biopsy may also help to safely monitor cancer patients in remission to provide earlier warning of potential recurrence. In a future pandemic, the benefit of these features cannot be overstated. The adverse impact of COVID-19 on cancer care has shown that it is essential to have a diagnostic tool which is quick, easy and alleviates the burden of conducting hospital-based surgical tissue biopsies.

Social (community)

Human capital

ANGLE understands that long-term growth and business performance depends on the talent, skills and passion of its employees. The Directors therefore aim to create a work environment that appeals to, empowers and involves all employees at every level of the organisation.

Finding and keeping the best people

In order to attract and retain the best talent, ANGLE offers competitive and comprehensive salary and benefits packages. Salaries are reviewed annually, and key roles are benchmarked externally. Benefits plans are also reviewed regularly to determine comprehensiveness and external competitiveness.

ANGLE offers hybrid, flexible and part-time working arrangements to employees to accommodate individuals' needs and commitments outside the workplace. This is reflected in the fact that some 10% of staff are employed on a part-time basis and a significant proportion of staff who are able to balance working with caring for young children.

The Group works with universities to support science and operates placement programmes in both the UK and North America. In the UK, ANGLE offers placements to up to six undergraduate students each year, typically within the R&D and Engineering teams. ANGLE has also supported a student taking advantage of the Erasmus exchange programme and currently sponsors PhD studentships at two UK universities. In North America, two placements have been offered annually within either the R&D or Administrative functions.

In 2022, ANGLE offered five apprenticeships (within the Finance and Human Resource teams), providing individuals the opportunity to obtain practical experience. The Group also acted as host for multiple work placement opportunities for school age individuals.

Training and development

The Group places a high priority on training and development throughout the organisation and from the start of a career at ANGLE. There is a comprehensive induction process in place to ensure that new employees are quickly integrated and operating with the Group's quality standards. This includes scheduled catch-up sessions between the new joiner and their supervisor and the new joiner and Human Resources.

Thereafter, employees and managers are encouraged to identify and discuss individual training and competency needs during regular one-to-one review meetings in support of Company quality objectives. A training and competency needs analysis is embedded into the performance management and quality management system processes with various forms of training available to meet the differing needs of employees and their job functions. In addition, ANGLE always seeks to promote staff internally, maximising the potential for career progression and development.

Performance management

Employees and managers are encouraged to meet regularly, at a minimum monthly, to discuss performance feedback. Formal annual reviews are undertaken following the Company's financial year end. As a key tool in that process, ANGLE uses a performance management software system to enable meaningful, regular performance management. This system is used to set, track and evaluate employee performance and development objectives.

ANGLE operates a Career Development Committee which meets twice yearly to consider development opportunities and promotions across the organisation.

Diversity and equal opportunity

The Group recognises the diversity and potential that different people can bring to their work and is committed to equal opportunities in the provision of services and in employment. ANGLE strives to allow all its people to develop as fully as possible in accordance with their individual aspirations and abilities. In all aspects of employment, including recruitment, pay, training and promotion, ANGLE avoids discrimination or harassment of any kind and specifically on the grounds of race, colour, nationality, ethnic or national origin, religion, gender, marital status, sexual orientation, medical condition including progressive illness, age and disability.

The Directors believe that, in addition to the over-arching responsibility of the Group and its management, all employees must take individual responsibility for promoting an environment that provides equality of opportunity for all. ANGLE asks all its people to embrace its policy of equal opportunities as their own and to take personal responsibility for making the workplace one that is free of discrimination. Where discrimination is found to have taken place, ANGLE will take strong action to address this. Discrimination of any nature, direct or indirect, will be regarded as misconduct, will be treated as a disciplinary matter and may lead to dismissal. Similarly, victimisation of anyone who has made a complaint will not be tolerated.

Mental health awareness

ANGLE recognises the importance of the mental health of our employees. We recognise and support global and local mental health awareness events as well as providing staff access to Company-funded counselling and advice. Our mental health support is internally strengthened through providing our employees with access to a number of trained mental health first aiders throughout the organisation. We added to the number of trained mental health first aiders during 2022 and introduced Wellness Rooms at two of our sites. These rooms provide a relaxing space to employees to have a private conversation, pray or simply take time out.

Communication and feedback

ANGLE ensures that appropriate emphasis is given to the practice of good communications and that time is allocated to it. Communications are encouraged on a two-way basis both through a consultative process and by encouraging feedback through all levels of the management chain. Managers are aware of their obligation to communicate to those with whom they work and staff managing activities have responsibilities to communicate relevant information to other staff involved with these activities.

Every available means, including the appropriate use of information technology, is used for the dissemination of relevant, accurate and prompt organisational and operational information.

CORPORATE RESPONSIBILITY REPORT CONTINUED

Social (community) continued

All employee calls are scheduled regularly (targeted every other month) to include a CEO business update, project spotlights from across the organisation and a social/team building element. As described below, ANGLE has adopted MS Teams and this platform is used to hold these calls and share content.

ANGLE uses various platforms to increase communication and feedback including the Clear Review platform for performance management, PeopleHR for management of employee data, MS Teams for communications, and monday.com to assist with project management. The technologies are used to increase transparency and ownership and to streamline workflow processes, improving the overall employee experience.

Product quality

ANGLE is committed to providing quality in vitro diagnostic devices and accessories for the capture, harvest and analysis of cells present in blood based on their larger size and deformability, fulfilling the market and regulatory requirements to meet the needs of the customer and for the benefit of the patient. The quality of medical devices as a minimum will conform to the In Vitro Diagnostic Directive 98/79/EC (transitioning to In Vitro Diagnostic Regulation EU 2017/746), FDA GMP 21 CFR 820 and other requirements as applicable to the countries in which the device or service is intended to be offered for sale.

The Group will commit to encouraging staff to identify non-conformities and inefficiencies with the intent of creating and operating systems which cause zero harm to the patient. It is the policy of the Group to have a commitment to quality, with all quality procedures being maintained to ISO 13485:2016 +A11:2021 reflecting the current state of the art and Post Market Surveillance findings. This policy is regularly reviewed and notified to all employees to ensure that it is understood, implemented and maintained.

ANGLE's Quality Management System falls within the scopes of ISO 13485:2016 +A11:2021 and covers the design, development, manufacture, testing, storage, distribution, service and sale of in vitro diagnostic devices, associated equipment and consumables for the capture and harvest of cells present in blood. There are no exclusions within the Quality Management System. Customer requirements, national standards, directives, external documents and regulatory and statutory requirements are all considered as inputs to our Quality Management System.

Certain activities are outsourced or subcontracted to third-party manufacturers, including the design, development and manufacture of mechanical, electrical and software components. In this instance, the third-party's procedures are used if compliant with ISO 13485:2016 +A11:2021 and certified by a suitable Notified Body with appropriate scope.

ANGLE's Quality Management System is subject to inspection audits by an external Notified Body (BSI). A complete annual programme of internal audits is also established. ANGLE's Quality Manager is responsible for addressing any corrective or preventative actions required.

Key Performance Indicators (KPIs) are established and performance data is analysed to ensure that ANGLE's Quality Management System remains effective. Issues arising are investigated in accordance with ISO 13485:2016 CAPA and Defect Reporting Procedures. CAPA process requires evidence of effective completion and all information is captured in our Quality Management System records and confirmed through internal and external audits.

Health and safety

The Directors are committed to ensuring high standards of health and safety for employees, visitors and the general public. The Group complies with all applicable laws and regulations wherever it operates and holds all the licences necessary to operate its business. Each location has a joint health and safety committee made up of both employee and management representation.

Last year, ANGLE further strengthened its health and safety arrangements with the appointment of specialist health and safety advisors in both the UK and the US. ANGLE uses independent expert advisors to audit our operations to ensure compliance is ongoing and effective and, in 2022, employed a full-time resource dedicated to health and safety matters.

Health and safety: a shared responsibility

As the employer, ANGLE is ultimately responsible for employee health and safety and takes every reasonable precaution for the protection of workers in the workplace but believes all employees share a responsibility, and should work together, to reduce the risk of injury and occupational disease. ANGLE makes every effort to provide a safe, healthy work environment. The employer and all supervisors and employees are dedicated to reducing the risk of injury.

Supervisors are held accountable for the health and safety of workers under their supervision. Supervisors are subject to various duties in the workplace, including the duty to ensure that machinery and equipment are safe and that employees work in compliance with established safe work practices and procedures.

ANGLE requires that every employee must protect his or her own health and safety by working in compliance with the law and with safe work practices and procedures established by the employer. Employees will receive information, training and competent supervision in their specific work tasks to protect their health and safety. It is in the best interest of all parties to consider health and safety in every activity. Commitment to health and safety must form an integral part of this organisation from the executives to the employees.

Zero tolerance of workplace violence and harassment

ANGLE is committed to the prevention of workplace violence and harassment and to protecting the health and safety of our employees in the workplace. We will take whatever steps are reasonable to protect employees from workplace violence and harassment. At ANGLE there is zero tolerance for workplace violence or harassment of any kind, including towards or from customers, clients, supervisors, employees, blood donors or members of the public.

ANGLE has a process to report and investigate complaints of workplace violence or harassment. All complaints and investigations will be dealt with in a fair, respectful and timely manner. We will take all reasonable precautions to protect workers from all sources of work-related harassment. Supervisors are responsible to support a respectful workplace by reinforcing a zero-tolerance violence and harassment policy and providing information and training to employees.

All ANGLE employees are encouraged to work together to support a safe, healthy and respectful workplace.

Community, charity and outreach

The ANGLE R&D laboratory and clinical laboratories in both the UK and the US use healthy volunteer blood donors to enable the testing and control of multiple aspects of the Parsortix system, to perform analytical studies for its clinical applications, and in support of changing the way that cancer is diagnosed and treated. We are very grateful to all of the blood donors who voluntarily participate in our approved blood collection programs.

The Group works with various charitable organisations, such as Cancer Research UK, and has donated products and funded medical research in pursuit of our mission. We have also worked with each of the local universities near our facilities. In 2022, ANGLE closed its operations in Toronto and as such was able to make notable donations of office equipment and supplies, and laboratory equipment and supplies to the local community and to two Toronto universities.

ANGLE recognises and supports relevant awareness days, such as the World Cancer Day, World Cancer Research Days, World Mental Health Day and Mental Health Awareness Week.

Governance

Governance and business ethics

Leadership from the Board of Directors

The Board is committed to high standards of corporate governance and adheres to the Quoted Companies Alliance (QCA) Corporate Governance Code for small and mid-size quoted companies (the "QCA Code").

Section 172 statement

The Corporate Governance Report on pages 59 to 66 and this Corporate Responsibility Report set out how the Board has approached its duty under Section 172 of the Companies Act, which is summarised below, in order to meet these requirements. Specifically, it refers the reader to QCA Principle 1 (Strategy and business model), Principle 2 (Meeting shareholder needs), Principle 3 (Manage our responsibilities to wider stakeholders) and, in particular within this report, the sections headed 'Human capital' and 'Health and safety' and the section headed 'Environmental stewardship' for the impact of the Group's operations on the community and environment. The Corporate Governance Report can also be found on the Company's website **www.angleplc.com.**

In accordance with Section 172 of the Companies Act 2006, the Directors recognise the importance of our wider stakeholders to the sustainability of our business. The Directors behave and carry out their activities to promote the long-term success of the Group for the benefit of the Company's shareholders, employees, partners, customers, suppliers and other stakeholders such as regulatory authorities. The Group engages with stakeholders to reflect their insights and views when making decisions on strategy, delivering operational effectiveness, driving initiatives and delivering outcomes.

The culture and values promoted by the Directors create a focus across the Group on observing and maintaining high standards of regulatory compliance, quality control and business conduct whilst promoting the long-term success of the Group.

Management charter

ANGLE recognises the importance of supporting its employees as they take on additional responsibility, and nowhere is this truer than in their roles as managers. Managers not only help to deliver success through the organisation and support for their teams, but they also shape the culture of the Group through their behaviour and leadership style. As ANGLE grows it is striving to ensure that its values are upheld and its collaborative, supportive and inclusive culture continues to develop.

The fundamental leadership competencies ANGLE collectively values are represented in the ANGLE Competency Model, which among other things serves to unite our management team in the areas of strategic thinking and managing and developing others. New managers are trained on the significance of these competencies when they originally assume a leadership role and these competencies are embedded in various management processes such as training, 1-1 feedback, annual reviews and career development.

Responsible marketing

ANGLE is required to have systems in place to ensure it meets medical device regulatory standards for the accurate marketing of function and performance of in vitro diagnostic (IVD) and research use only (RUO) products in territories in which ANGLE operates. At the moment, this is primarily the requirements of the IVDD and IVDR in Europe, MDR 2002 in the UK and 21CFR 801, 809, 820, 830 and 1010 in the USA. The ANGLE clinical laboratories are working towards securing appropriate clinical laboratory accreditations to enable the processing of human samples for diagnostic testing. This includes Clinical Laboratory Improvement Amendments (CLIA) certification in the USA and MHRA registration in the UK. In addition, ANGLE retains membership of the British In Vitro Diagnostics Association (BIVDA) and Regulatory Affairs Professionals Society (RAPS) in the UK.

CORPORATE RESPONSIBILITY REPORT CONTINUED

Governance continued

Clinical trials programmes and standards

ANGLE engages in clinical studies designed to evaluate new and/or existing medical devices and in vitro diagnostics for new uses and is responsible for complying with applicable national and international ethics, medical device and IVD regulations and requirements (e.g. the Food and Drug Administration (FDA), Code of Federal Regulations (CFR), European Union Medical Device and IVD Regulations, Institutional Review Boards (IRB) / Ethics Committees (EC), International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) etc) and for ensuring that all responsibilities are properly assigned.

Project teams are responsible for developing a regulatory strategy, developing and implementing an Investigational Plan (IP), monitoring the progress of ongoing studies, and fulfilling all reporting requirements required by applicable national and international regulations. The project team may outsource one or more of these activities to external organisations (e.g. independent contractors, Contract Research Organisations (CROs) or other vendors). ANGLE must ensure these external entities are properly selected and have the proper training, experience and resources to adequately conduct the outsourced activities. ANGLE remains the ultimate authority and is responsible for all aspects in the conduct of regulated activities and ensures clinical studies are carried out in accordance with the IP and applicable regulations.

Standard Operating Procedures (SOPs) are in place for all clinical trial activities and all sites are trained in those SOPs prior to study initiation via Study Initiation Visits and maintenance of training records.

ANGLE's clinical study procedures require each site Principal Investigator and all sub-investigators to provide a current CV, a copy of their Medical or Nursing Licence, a signed Financial Disclosure Form, and a Duly completed Duties and Signature Log (a.k.a. Delegation of Authority Log).

Any ANGLE sponsored study investigator is responsible for ensuring that the study is performed in accordance with the protocol, current ICH guidance E6(R2) on Good Clinical Practice (GCP), and applicable regulatory and institution-specific requirements.

GCP is an international ethical and scientific quality standard for designing, conducting, recording and reporting studies that involve the participation of human subjects.

Compliance with this standard provides public assurance that the rights, safety and well-being of study subjects are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the study data are credible.

The site's Responsible Investigator (in collaboration with ANGLE) must obtain local IRB/EC approval for the Protocol and Consent Form prior to enrolling subjects in the study and must obtain IRB/EC approval for any amendments to the protocol as necessary.

The site's Responsible Investigator must ensure that voluntary informed consent is obtained from all subjects participating in the study prior to any study procedures being performed.

The site's Responsible Investigator must ensure that subjects are enrolled according to the Inclusion/Exclusion criteria and that all information on Informed Consent Forms, Sample Logs, and data captured on appropriate Case Report Forms (CRFs) and/or in an electronic Data Capture Service (eDCS) is complete and accurate.

It is the responsibility of the site's investigators and study coordinators to ensure that, to the best of their knowledge, all subject information is complete and accurate.

Informed consent

As part of the requirement to perform studies in line with ICH GCP guidelines, all subjects enrolled in any ANGLE sponsored study must have provided informed consent to participate.

Each subject must give written informed consent according to local requirements after the nature and any participation risks of the study have been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the sponsor and by the reviewing IRB and be in a language that the patients can read and understand. The informed consent should be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory and/or country specific requirements, and institutional policies.

Furthermore, our pharma services agreements include the requirement for clients to provide assurances that samples have been ethically provided in line with ICH and other applicable regulations prior to the commencement of sample processing.

Our Values

Integrity

- Meeting commitments and earning trust

Customer Focus

- The ability to identify, assess, understand and meet customer/ stakeholder needs
- Passionate about meeting or exceeding customer/stakeholder needs

Collaboration and Inclusion

- Building effective, beneficial and enduring relationships, internally and externally
- Engaging positively with diverse views and cultures

Shared Excellence

- Driving to do things better, striving for and setting new standards of performance
- Being constantly curious, fostering and rewarding innovation

Our Culture

- Hard-working and adaptable
- Driven by a passion to improve the quality of cancer diagnosis and treatment
- Progressive and pragmatic
- Open door and inclusive
- Collaborative and supportive

Environmental

Environmental stewardship

As a technology-based Group with most staff in a small number of locations, ANGLE believes its environmental footprint is small and climate related risks are low. Nevertheless, ANGLE views protection of the environment as a core priority. Our landlords also take their sustainability responsibilities seriously. For example, information can be found on our head office location at **www.surrey.ac.uk/sustainability/estates-and-operations.**

Waste management

Our landlords offer waste management services and seek to divert landfill and recycle as much as possible. The Group undertakes some additional recycling with specialist suppliers associated with old electrical equipment, coffee pods etc and uses specialist hazardous waste disposal experts for laboratory waste. The Group uses plumbed water coolers which reduces the consumption of plastic bottles.

Our Parsortix system uses a microfluidic cassette that takes advantage of the larger size and deformability of CTCs with the instrument using pressure to harvest the cells rather than a chemical approach thereby avoiding the higher levels of antibody reagents and other chemicals used by many of our competitors.

In our clinical studies, the insulated containers and gel wraps used for the shipment of blood samples from the clinical sites to our laboratory facilities are recycled and reused.

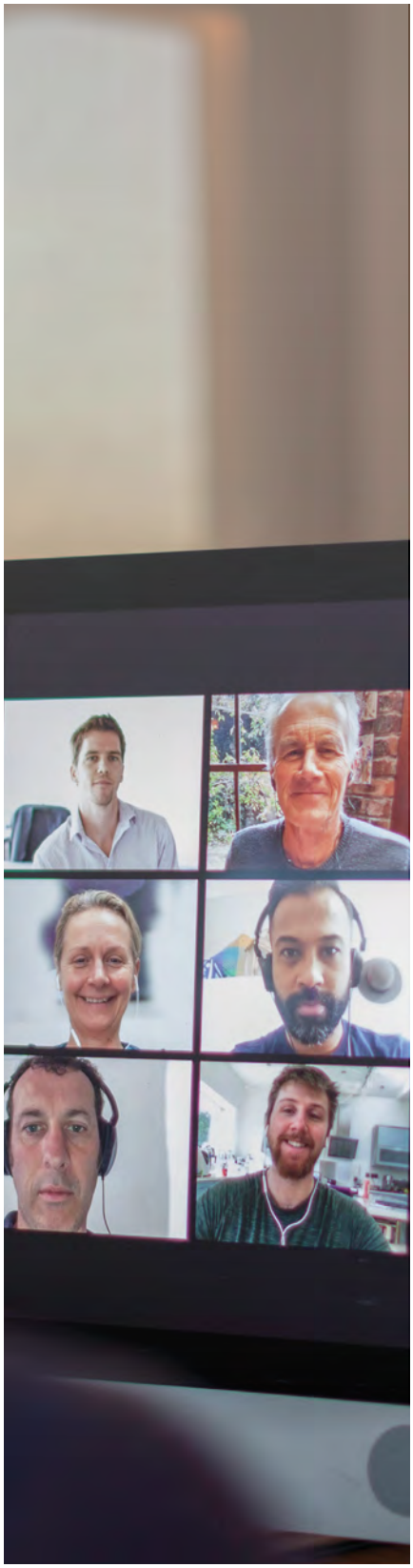
Energy management

All of our offices now use LED lights with a programme of updates to tungsten and some halogen lighting since 2016. As well as providing a better working environment for staff, this is forecast to produce a 64% reduction in our consumption of energy for lighting purposes. We also use lighting sensors so that lights are automatically turned off for areas not in use. We have installed energy saving internet enabled thermostats and use programmed heating controls seeking to optimise temperatures dependent on whether people are present. We aim to buy higher rated energy efficient equipment for our laboratories. We use 100% renewable energy at our main site. The Group uses plumbed boiling water taps which are more energy efficient than kettles.

Travel

The Group seeks to restrict business travel to only necessary business travel and promotes the use of video conferencing where possible/practical. The Group promotes home and flexible working where feasible to reduce overall travel and travel during rush hour. Several of our employees are carpooling and we also promote the use of the cycle-to-work scheme. Furthermore, the Surrey Research Park is committed to improving transport and helping reduce emissions within the UK and has an e-shuttle bus for rail commuters which is used by many of the Group's UK team.

Parsortix system-based tests have the potential to significantly reduce patient travel and the consumption of healthcare resources. Blood can be drawn locally by a phlebotomist and shipped (with other laboratory specimens) rather than an individual having to drive to a clinic for a tissue biopsy. A negative liquid biopsy result, such as with our ovarian cancer pelvic mass triage test, may allow local surgery with a simplified procedure rather than having to travel to a major cancer centre for surgery.



FINANCIAL REVIEW

Carefully executing our strategy in challenging market conditions

// The Group is developing its commercialisation activities to exploit a world first FDA clearance and its excellent ovarian cancer results.

Ian F Griffiths
Finance Director

Financial Highlights

£1.0 million
Research use revenues for the year of £1.0 million (2021: £1.0 million) at a gross profit margin of 59% (2021: 70%)

£24.8 million
Planned expenditure on Parsortix system of £24.8 million (2021: £18.0 million)

£21.7 million
Loss of £21.7 million (2021: loss £15.0 million)

£20.1 million
Fundraise of £20.1 million (£18.9 million net of expenses) in July 2022

£31.9 million
Cash and cash equivalents balance at 31 December 2022 of £31.9 million (2021: £31.8 million)

Introduction

The Group has continued to make substantial investment in various studies, new services and product development, the new clinical laboratories and sales and marketing for research use sales to advance and drive the development and adoption of the Parsortix cell separation system. Following receipt of FDA clearance in May 2022 and a successful fundraise in July 2022, ANGLE has made good progress across all these areas although revenues are taking time to develop reflecting the later than expected FDA clearance and adverse markets making customers more cautious. The wider economic and market headwinds resulted in the Group carefully reviewing its costs and plans and the need to streamline operations in order to increase the cash runway. This, along with proposed changes to the UK R&D Tax credit scheme making research and development in Canada 50% more expensive, led to the decision to close the Group's Canadian operations and centralise all in-house research and development in the UK. The results reflect the impact of the closure of the Canadian operations together with the need to expand some of the UK facilities.

Consolidated Statement of Comprehensive Income

Revenues for the year were flat at £1.0 million (2021: £1.0 million) with a gross profit margin of 59% (2021: 70%) with certain sales delayed for reasons outside the Group's control that are now expected in 2023. Research use sales have been made to multiple customers of both Parsortix instruments (including an annually renewable support and maintenance contract) and cassettes (a one-time use consumable). As the installed base of instruments builds, we are seeing recurring revenues from cassette sales and support and maintenance contract renewals increase. The sales pipeline is developing in the research use market and our sales team continues to focus on supporting customers as they evaluate the Parsortix system in their laboratory procedures. However, evaluations have taken longer to close than expected, generally because of limitations in downstream analytical techniques outside the Parsortix system and the grant funding environment for our research customers remains very challenging. Research use sales for services from our new laboratories have also been made to pharma customers with some new contracts during the year both supporting drug trials and in assay development. This is a new area for the business, and we have offered some introductory pricing to initial customers as well as taking a cost-sharing approach on assay development activities so that we can retain the assay and add this to our menu of offerings. As a consequence, this area of the business is operating with lower margins while we go through this establishment phase.

Planned investment in building capacity, capability and studies to develop and validate the clinical application and commercial use of the Parsortix system resulted in operating costs for the year of £24.8 million (2021: £18.0 million). Expenditure was also made on Intangible assets (including patents) and Property, plant and equipment and this is discussed in the Consolidated Statement of Financial Position section below.

This planned expenditure includes investment of £10.8 million (2021: £8.4 million) in research and development, in particular clinical studies, assay and product development and ongoing work with KOLs on pilot studies and other potential uses of the system as well as patent prosecution and new patent grants.

Expenditure includes sales and marketing costs associated with product promotion and attendance at conferences for marketing purposes. Corporate costs including costs associated with being a listed company were in line with plans.

Following an impairment review arising from the closure of the Canadian operations, Acquired intangible assets and Intellectual property were impaired by £0.8 million. Other non-cash costs include a share-based payment charge of £4.4 million (2021: £1.3 million) offset by a foreign exchange credit for unrealised gains on the retranslation of Group balances of £2.1 million (2021: £0.2 million gain).

The Group made a loss before tax for the year of £24.4 million (2021: loss £17.4 million). The significant research and development expenditure resulted in research and development tax credits of £2.8 million for the year (2021: £2.4 million). The Group made a loss after tax of £21.7 million for the year (2021: £15.0 million) resulting in a basic and diluted loss per share attributable to owners of the parent of 8.79 pence for the year (2021: 6.67 pence).

Consolidated Statement of Financial Position

Intangible assets decreased in the year to £2.8 million (2021: £3.6 million) reflecting the impairment of £0.8 million arising from the closure of the Canadian operations described above. Intellectual property costs in relation to patents and trademarks of £0.2 million (2021: £0.1 million) were capitalised during the year in accordance with IAS 38 Intangible Assets.

Property, plant and equipment increased to £3.5 million (2021: £2.2 million) with the expansion and fit-out of premises including the core research and development facilities and the clinical laboratories and the addition of key items of laboratory equipment offset by depreciation charges.

The right-of-use assets represented by our leased office and laboratory premises increased to £5.0 million (2021: £2.2 million) with the addition of new leases for the research and development and clinical laboratories of £3.6 million offset by depreciation and impairment.

Increased inventories of £2.1 million (2021: £1.7 million) reflects building inventory levels for research use sales and sales prospects where systems are placed out for an initial evaluation period prior to sale, increased inventory required for studies (in-house, KOLs and clinical study sites) and as a post-Brexit and COVID-19 supply chain issues mitigation strategy. As the Group relies on a number of single-source key suppliers, higher levels are maintained than would otherwise be the case.

The trade and other receivables balance increased to £1.8 million (2021: £1.3 million). The year-on-year increase includes increases of £0.1 million for trade receivables, VAT/GST recoverable, accrued income and deposits on leasehold premises respectively.

The tax receivable balance of £2.9 million (2021: £4.5 million) reflects the fact that research and development expenditure is eligible for research and development tax credits. The prior year receivable includes tax credits receivable in relation to 2021 and 2020.

The trade and other payables (current and non-current) balance of £4.0 million (2021: £4.6 million) includes an accrual of £0.3 million (2021: £nil) for statutory severance costs associated with the closure of the Canadian operations, a reduction in bonus accrual with no bonus declared for FY2022 (2021: £1.2 million), a reduced provision for employers' taxes on the theoretical gain on the exercise of unapproved share options and LTIP Options of £0.5 million (2021: £1.1 million) resulting from prior share option awards and a lower share price.

As described in the introduction, the Company closed its operations in Toronto, Canada in an orderly wind down. The closure was substantially completed by the reporting date but there remained various costs associated with redundancy pay and support, completing tax returns, other compliance matters and formal company dissolution. A provision of £0.6 million has been made for the estimated remaining costs to complete the winding down of the Canadian operations.

Cash

The Group ended the year with cash and cash equivalents of £31.9 million (2021: £31.8 million).

The Company completed a fundraise of £20.1 million (£18.9 million net of expenses) during the year. The Company was pleased with the continued support from our major institutional investors and existing and new investors.

The fundraise, orderly wind down of the site in Toronto, Canada, and resultant streamlining of the Company's operations increased the cash runway into H2 2024, leaving ANGLE in a strong position to deliver on planned objectives and milestones.

Summary

The Group is carefully executing its strategy so that business activities are in line with the available and anticipated cash resources. Good progress has been made against key milestones, in particular securing the world's first FDA product clearance for a system to harvest CTCs, intact living cancer cells, and the ovarian cancer study delivering best in class results. The later than expected FDA clearance and adverse market related impacts do mean that certain activities have taken longer than expected and we have not yet seen the revenues develop although the pipeline is building strongly. The immediate priorities are building research use sales to pharma customers and translational researchers, undertaking key service and product development activities and developing capability. There is a lot of effort going into building out the commercial team and plans and post FDA clearance we now have a number of distributors signed up.

The Directors have a reasonable expectation that the Group has adequate resources to continue in business for the foreseeable future as detailed in Note 1.4 to the Financial Statements.

On behalf of the Board

Ian F Griffiths
Finance Director
20 April 2023

BOARD OF DIRECTORS

Experienced Board overseeing implementation

Garth R Selvey
Chairman

Appointed
September 2006

Skills and experience
Garth Selvey has a BSc in Physics and Electronic Engineering from the University of Manchester and has spent over 36 years in the computer industry in technical, product, sales and marketing roles.

He became Managing Director of TIS Applications Ltd in 1984 and a main board Director of TIS Ltd prior to its acquisition by Misys in 1989. He organised the management buyout of the social housing division of Misys and became Group Chief Executive of Comino Group plc when it floated on AIM in 1997. Comino moved to a full listing in 1999 where he remained until its successful public sale to Civica plc in February 2006.

Garth joined ANGLE as a Non-executive Director in September 2006 and became Chairman in September 2007.

Brings to the Board
Extensive experience of the listed sector and leading companies.

Andrew D W Newland
Chief Executive

Appointed
March 2004

Skills and experience
Andrew Newland is Chief Executive of ANGLE plc. He has an MA in Engineering Science from the University of Cambridge and is a qualified Chartered Accountant. He has over 20 years of medical diagnostics experience and has specialised in the liquid biopsy space for the last 13 years.

He has led the development of technology-based businesses based on strong intellectual property for over 30 years and for the last 20 years he has been Chairman or on the Board of several specialist medical technology companies. After working with the engineering conglomerate TI plc, he worked for KPMG from 1982 to 1994; from 1985 to 1987 he was based in the US as a manager providing corporate finance and business advice to high technology firms in the area around Route 128, Boston, Massachusetts. During this time, he led KPMG's involvement in the IPO of the medical technology company Cardio Data Inc. From 1987 to 1994 he worked for KPMG in the UK with responsibility for establishing KPMG's UK and European High Technology Practices and High Technology Consulting Group.

Andrew founded ANGLE in 1994. In 1999, Andrew led the team that founded the medical diagnostic company Acolyte Biomedica. Acolyte was the first ever spin-out of the Defence Science and Technology Laboratory (Dstl) Porton Down, which specialised in rapid diagnosis of MRSA, the 'hospital super-bug'. Andrew chaired the company for several years and successfully led the company through three major rounds of venture capital investment. Andrew also founded Provexis, the first ever spin-out of Rowett Institute, Europe's leading nutrition research institute. Andrew chaired the Board of Provexis, a specialist nutraceutical company with a heart-health product, through to its successful flotation in 2005.

Brings to the Board
Over 30 years' experience of setting up, leading and building technology-based businesses, over 20 years leading specialist medtech businesses, and 13 years in the liquid biopsy space.

Ian F Griffiths
Finance Director

Appointed
March 2004

Skills and experience
Ian Griffiths is the Finance Director of ANGLE plc. He has specialised in technology commercialisation for over 30 years and is an expert on the development and growth of new technology-based businesses. Ian has a BSc in Mathematics with Management Applications from Brunel University and is qualified as a chartered accountant. For seven years he worked for KPMG, initially in accountancy with a special work focus, then in management consulting within KPMG's High Technology Consulting Group where he specialised in financial modelling, business planning, corporate finance, market development and strategy work.

Ian joined ANGLE in 1995. As well as leading the finance function at ANGLE plc, he has been closely involved with the development and delivery of the former UK, US and Middle East Consulting and Management services businesses and in developing new Ventures, both third-party and ANGLE's own. Ian has been heavily involved in the start-up phase and also the ongoing development of ANGLE's own ventures by working closely with management on business plans, financial and operational management, fundraising and commercial aspects, including both medical and physical sciences companies. Ian led the financial aspects of ANGLE plc listing on the Alternative Investment Market.

Brings to the Board
Over 30 years' experience in finance and technology-based businesses, and 13 years in the liquid biopsy space.

Committees key

- ◆ Chair of Committee
- ◇ Member of the Committee

- A Audit Committee
- R Remuneration Committee
- N Nomination Committee

Dr. Joseph E Eid
Non-executive Director

4

Appointed
January 2023

Skills and experience
Dr. Joseph Eid is a qualified physician, board certified in medical oncology, haematology and internal medicine. He is a highly experienced pharmaceutical industry executive with over 25 years of proven expertise in people and portfolio management, planning, designing and executing Phase I to IV clinical trials and building and managing clinical and medical affairs teams and strategies.

He has successfully designed and implemented clinical development, medical affairs and life cycle management plans for pharmaceutical products including cytotoxic agents, monoclonal antibodies, immuno-oncology agents, antibody-drug conjugates and CAR-T Cell therapies. His previous experience includes senior positions in clinical development and medical affairs at Bristol Myers Squibb, Merck & Co. and Hoffman-La Roche. Whilst at Merck, Joe led the global Keytruda® (pembrolizumab, MK-3475) first-in-human strategy, including oversight of the clinical, regulatory and manufacturing planning and execution and development of the PD-L1 biomarker strategy on tissue biopsy, which led to a first-in-class anti-PD-1 BLA filing and approval in the US.

Brings to the Board
Valuable knowledge and experience in oncology drug development and the use of biomarkers in the clinical trials process and as companion diagnostics.

Brian Howlett
Non-executive Director and Senior Independent Director

5

Appointed
January 2013

Skills and experience
Brian Howlett has a wealth of international experience as a medtech leader which he is currently applying in a Non-executive/ Chairman capacity for neuro-endovascular company Oxford Endovascular Ltd, and medical device coating and surface modification company Accentus Medical Ltd, as well as ANGLE plc. Brian was formerly CEO of Lombard Medical Technologies PLC, an AIM listed company specialising in stents for abdominal aortic aneurysms, from 2005 to 2009.

During his tenure significant capital was raised to fund the development of operations to commercialise the Aorfix stent graft towards regulatory approvals and growing revenues in the EU, USA, Russia and Brazil.

Corporate experience includes six years as UK Country Leader of Boston Scientific Ltd, between 1999 and 2005, during which time major medical devices such as the TAXUS drug eluting stent were launched driving sales and profits to the point where the UK and Ireland subsidiary became one of the leading revenue contributors to the corporation's European operations. Between 1987 and 1999, Brian was Managing Director of the UK sales and manufacturing subsidiary of Cobe Laboratories Inc. In addition, Brian spent almost 20 years in the pharmaceutical industry, gaining strong sales and marketing experience through a number of senior management positions in the UK, Scandinavia and Benelux markets within Fisons plc.

Brings to the Board
Extensive commercial operations experience of the medtech sector.

Dr. Jan Groen
Non-executive Director

6

Appointed
November 2018

Skills and experience
Dr. Jan Groen is currently the CEO and Chairman of the board at Intravacc B.V., a contract development and manufacturing organisation for infectious disease and therapeutic vaccines in the Netherlands. Jan was previously the President and CEO of MDxHealth, a Euronext listed genomic diagnostics company that improves the lives of patients by reducing diagnostic ambiguity in urological cancers. MDxHealth's genomic tests are setting new standards in prostate and bladder cancer diagnosis, where they have helped over 100,000 patients avoid unnecessary diagnostic procedures.

Jan's career spans over 25 years in clinical diagnostics and life science global markets. Jan was previously the President and COO of Agendia, responsible for their United States and European diagnostic operations, respectively. Jan is co-founder of Viroclinics and DxOrange and has held numerous management and scientific positions at Focus Diagnostics, a subsidiary of Quest Diagnostics, the Erasmus Medical Center, and Akzo-Nobel. Jan has had board mandates in several diagnostic companies. Currently he is the Chairman at Pictura Bio Limited in the UK and serves on the board of Novigenix SA in Switzerland and SPL Medical in the Netherlands.

Jan holds a PhD degree in Medical Microbiology from the Erasmus University Rotterdam, a BSc in Clinical Laboratory Studies and has published more than 125 papers in international scientific journals in the field of clinical diagnostics.

Brings to the Board
Expertise in new product development, including development and successful commercialisation of CE marked and FDA cleared diagnostic products and laboratory developed tests in Europe and the USA.

Juliet Thompson
Non-executive Director

7

Appointed
January 2023

Skills and experience
Juliet Thompson has over 30 years of finance, banking and board experience with significant focus on the healthcare sector. Juliet is a proven FTSE 250 non-executive and audit chair, and a former investment banker who has spent her career advising life science companies. She played a leading role in setting up Code Securities, which was quickly acquired by Nomura (becoming Nomura Code) but remained independent. At Nomura Code, Juliet was advising companies on their financing and strategic options. She worked on over 50 transactions including IPOs, secondary offerings, private placements and M&A. As Nomura Code was devolved, she joined Stifel with a team from Nomura Code to head up the life sciences team. Since leaving the City, Juliet has built a diverse portfolio; she currently chairs the Audit Committee of Indivior PLC (FTSE 250) and Novacyt, both listed companies and is also a Non-Executive Director of Organox, a private company spun out of Oxford University. She previously served on the Board of Vectura plc (FTSE 250) as well as GI Dynamics, a Boston-based medical device company. She holds a BSc in Economics from the University of Bristol and is a Chartered Accountant holding an ACA from the Association of Chartered Certified Accountants.

Juliet replaced Brian Howlett as Chair of the Audit Committee in January 2023.

Brings to the Board
Over 20 years' experience in advising listed healthcare companies in UK and Europe as an investment banker.

SCIENTIFIC ADVISORY BOARD

Wealth of experience and expertise

The Scientific Advisory Board (SAB) is comprised of a group of individuals that have significant scientific technical backgrounds in medical devices, diagnostics and other areas related to ANGLE's products. SAB members provide strategic input, insight and expertise in the blood and cancer fields and also advise the Company on technical aspects in relation to platform development, product development and clinical studies as well as providing broader industry input.

Dr. Daniel Danila

Skills and experience
Dr. Daniel Danila is an associate attending physician at Memorial Hospital Cancer Center in New York. Dr. Danila also serves as an associate professor of medicine with the Weill Cornell Medical College. Dr. Danila's primary research focuses on prostate cancer. Specifically, Dr. Danila is exploring a hypothesis that molecular profiling of CTCs can be used to assess biological determinants of the growth of prostate cancer tumors.

Dr. Danila served as the principal investigator (PI) for "Circulating Tumor Cells as Biomarkers for Patients with Metastatic Prostate Cancer: Developing Assays for Androgen Receptor Signaling Pathway," which focused on analysing CTCs from patients with metastatic prostate cancer for molecular biomarkers predictive of tumour sensitivity to targeted treatments. Funding for the research was provided by the Department of Defense Congressionally Directed Medical Research Programs, Prostate Cancer Research Program, Physician Research Training Award. Dr. Danila received his MD from Carol Davila University of Medicine and Pharmacy in Bucharest, Romania and was a research fellow, intern and resident at Massachusetts General Hospital prior to joining Memorial Sloan Kettering Cancer Center in 2005.

Brings to the SAB expertise in –
development and adoption of CTCs as predictive biomarkers to help clinicians select appropriate treatments, prostate cancer and wide network of contacts in the field.

Dr. George Hvichia

Skills and experience
Dr. George Hvichia is the original inventor of the core Parsortix technology and played a lead role in ANGLE's Parsortix patents. Dr. Hvichia is an expert in microfluidic technology related to cell and particle separation and platform integration. Dr. Hvichia was the first person to recognise the combined principle of separation by size and deformability of rare cells in fluids, such as blood, and that microfluidic devices could be used to achieve this, even though manufacturing at the necessary tolerances was not possible at the time. This core technology yields low cost, efficient, single use and scalable micro-devices for use in the fields of Liquid Biopsy and Precision Medicine.

Dr. Hvichia played a lead role in advancing the Parsortix technology by working in the laboratory and introducing multiple solutions and innovations. Dr. Hvichia also focused on collecting and analysing data from the microfluidic cassette, instrument and assay development process, resulting in ANGLE's first peer-reviewed publication in the International Journal of Cancer (IJC) in January 2016. This publication made the prestigious list of 10 most popular cancer publications in recent years, presented at World Cancer Congress 2018 by renowned publisher Wiley and the International Journal of Cancer.

Brings to the SAB expertise in –
microfluidics and biochips with ongoing thoughts and advice on development of the Parsortix system.

Dr. Joseph Khoury

Skills and experience
Dr. Joseph Khoury is the Stokes-Shackleford professor at the Department of Pathology and Microbiology, University of Nebraska, Omaha, Nebraska. Dr. Khoury is an expert in diagnostic pathology and has significant experience in the cytological and morphological analysis of cancer cells as well as molecular diagnostics, immunophenotyping, and other advanced diagnostic laboratory techniques.

Dr. Khoury is internationally recognised as a leader in translational research focused on haematolymphoid neoplasia, a class of tumours that affect the blood, bone marrow and organs of the immune system. He has authored over 300 publications, many in prestigious peer-review scientific and medical journals, two textbooks and several book chapters. He has trained numerous clinical and research fellows. Dr. Khoury is an active member of the College of American Pathologists and has lectured extensively at various institutions and conferences globally.

Brings to the SAB expertise in – diagnostic pathology and cytological and morphological analysis of cancer cells.

Prof. Adrian Newland

Skills and experience
Prof. Adrian Newland (who is not related to ANGLE's Chief Executive) is Professor of Haematology at Barts Health NHS Trust and Queen Mary University of London. Prof. Newland was also Director of Pathology for the Trust and Clinical Director of the North East London Cancer Network until 2018. Prof. Newland was President of the Royal College of Pathologists from 2005 to 2008 and the International Society of Hematology from 2014 to 2016. Prof. Newland chaired the National Blood Transfusion Committee and was pathology lead for NHS London. Prof. Newland was National Clinical Advisor in Pathology to NHS Improvement and Clinical Advisor to the Transforming Cancer Service Team in London. He chaired the National Pathology Implementation Optimisation Delivery Group until 2020.

Prof. Newland was previously chair of the Diagnostic Assessment Programme for the National Institute for Health and Clinical Excellence (NICE) and of the NICE Sifting Group for cancer drugs. Prof. Newland has been a member of the Scientific Advisory Panel of the Institute of Cancer Research from 1995 until 2003 and Chair of the London Cancer New Drugs Group since 2002. Prof. Newland was a member of the National Chemotherapy Implementation Group until 2018 and a member of the Expert Reference Group on Cancer Care in London, the National Cancer Outcomes Advisory Group and the Human Genome Strategy Group. Prof. Newland is co-chair of the WHO Strategic Advisory Group of Experts for In-Vitro Diagnostic Devices (SAGE-IVD) and recently completed the five-year review of the WHO Cancer programme. He is currently a non-executive director of the UK Accreditation Service and chairs their Healthcare Forum.

Brings to the SAB expertise in –
haematology, pathology, cancer diagnostics, accreditation and NICE.

Dr. James M. Reuben

Skills and experience
Dr. James Reuben is Professor in the Department of Hematopathology, Division of Pathology/Lab Medicine at The University of Texas MD Anderson Cancer Center, Houston, Texas. Dr. Reuben is a leading authority and has conducted significant research on circulating tumour cell subsets, including those with epithelial and mesenchymal phenotypes and their clinical relevance to minimal residual disease in breast cancer and non-small cell lung cancer.

Some related publications include "Circulating tumor cells, disease progression, and survival in metastatic breast cancer" in the New England Journal of Medicine; "Circulating tumor cells are associated with increased risk of venous thromboembolism in metastatic breast cancer patients" in the British Journal of Cancer; and "Circulating tumor cells in metastatic inflammatory breast cancer" published in the Annals of Oncology. Dr. Reuben received his PhD in immunology from McGill University in Montreal, Canada and his MBA from University of Houston, Houston, Texas. Dr. Reuben completed his research fellowship in the Department of Experimental Therapeutics at The University of Texas MD Anderson Cancer Center with Evan M. Hersh, MD and Emil J Freireich, MD, as mentors.

Brings to the SAB expertise in – knowledge and understanding of CTCs, breast cancer and wide network of contacts in the field.

Prof. Greg L Shaw

Skills and experience

Prof. Greg Shaw is a Consultant Urological Surgeon at University College Hospital in London and is a clinical academic with a strong interest in prostate cancer diagnostics and treatment. Having completed an M.D. in prostate cancer at the University of London investigating circulating tumour cells in prostate cancer, and subsequently completed four years as a lecturer at the University of Cambridge, Prof. Shaw has published widely on prostate cancer and is Professor of Urology at University College London.

Prof. Shaw leads several research programmes focused on current weaknesses in the way prostate cancer is treated and is interested in exploring the role novel biomarkers may play in advancing practice in these areas. Prof. Shaw is currently chief investigator for several NIHR portfolio studies investigating prostate cancer. Prof Shaw has performed over a thousand robotic radical prostatectomies and is lead surgeon for the largest robotic surgery team in the UK at UCLH. Prof. Shaw is known for his innovative approach and commitment to quality assurance.

Brings to the SAB expertise in – prostate cancer diagnostics and treatment.

Dr. Clive Stanway

Skills and experience

Dr. Clive Stanway is currently an independent drug discovery and development advisor to several companies including acting as a non-executive director for CytoSeek Ltd and Atelerix Ltd. Amongst others, he advises Cumulus Oncology Ltd and Arais Biotech AG. Also, he serves as a non-executive director of Babraham Research Campus Ltd.

Dr. Stanway was until 2018 Chief Scientific Officer of Cancer Research UK's Commercial Partnerships which is responsible for the development and commercialisation of research innovations. Dr. Stanway is an expert in cancer drug discovery and a key part of his former role was working closely with major pharmaceutical partners. Dr. Stanway has extensive knowledge and experience of cancer research, detailed understanding of the drug discovery and development process, and worldwide contacts with major pharma development groups.

Dr. Stanway was engaged in raising the scientific profile of Commercial Partnerships with the pharmaceutical industry; his efforts have led to several significant partnerships and alliances. Dr. Stanway has also driven internal Commercial Partnerships projects addressing cancer immunomodulation bringing together different technologies and expertise leading to a compound progressing towards a Phase 1 trial. During this time, the annual research spend of Cancer Research UK was in the region of £375 million and Commercial Partnerships had annual revenues of approximately £50 million. Prior to becoming Chief Scientific Officer of Commercial Partnerships, Dr. Stanway established and led a drug discovery and biotherapeutic discovery unit within Cancer Research UK, which has been partnered with AstraZeneca, FORMA Therapeutics, BMS, Artios, Ono Pharmaceutical and Merck KGaA.

Brings to the SAB expertise in – cancer drug discovery and development and major pharma networks.

Dr. Harold Swerdlow

Skills and experience

Dr. Harold Swerdlow is currently a freelance consultant. He was previously Senior Director of NGS R&D at DNA Electronics (DNAe) in London. His role there involved managing Next Generation Sequencing (NGS) technology and product development. Dr. Swerdlow is a leading expert in NGS and recently served as a consultant for ONI (Oxford Nanoimaging, a super-resolution microscopy company), Nuclera Nucleics (a DNA synthesis start-up) and LGC Genomics. He was VP of Sequencing at the New York Genome Center (NYGC) from 2014-17, Head of Research and Development for the Wellcome Trust Sanger Institute in Cambridge, UK (2008-2014) and Chief Technology Officer for Dolomite Ltd. (microfluidics and microfabrication). Prior to Dolomite, from 2000-2006, Dr. Swerdlow was Senior Director of Research at Solexa Ltd., and a key inventor of their innovative NGS technology. Subsequently acquired by Illumina, Solexa's technology became the core of Illumina's world-leading NGS products.

Brings to the SAB expertise in –
Next Generation Sequencing, genomics, operational management and system integration.

Prof. Ashok Venkitaraman

Skills and experience

Prof. Ashok Venkitaraman is the Director, Cancer Science Institute of Singapore, and Distinguished Professor of Medicine at the Yong Loo Lin School of Medicine, National University of Singapore. He also holds appointments as Senior Principal Investigator and Senior Adviser at the Agency for Science, Technology and Research (A*STAR).

Prof. Venkitaraman's research has contributed fundamentally to our understanding of how cancer is suppressed by genes that maintain the integrity of DNA in the human genome. His laboratory first discovered that mutations in the breast and ovarian cancer gene, BRCA2, provoke genome instability leading to carcinogenesis. In his current roles, Prof. Venkitaraman aims to achieve a deeper understanding of the steps that underlie carcinogenesis to find new strategies to intercept cancer development before the disease reaches an advanced and hard-to-treat stage. To help translate such fundamental insights to clinical practice, Prof. Venkitaraman has worked with colleagues from many different disciplines to develop new approaches for the discovery and early development of next-generation medicines. He has developed new technology platforms for therapeutics discovery that have led to serial Cambridge University spin-out companies like PhoreMost.

In his previous roles, Prof. Venkitaraman held the Ursula Zoellner Professorship of Cancer Research at the University of Cambridge from 1998-2020, where he was Director of the Medical Research Council's Cancer Unit and Joint Director of the Medical Research Council/Hutchison Research Centre from 2006-2019. Prof. Venkitaraman was elected a Fellow of the Academy of Medical Sciences, London, in 2001, and a member of the European Molecular Biology Organization (EMBO) European Academy, Heidelberg, in 2004.

Brings to the SAB expertise in – cancer cell biology and personalised cancer care.

DIRECTORS' REPORT

For the year ended 31 December 2022

The Directors present their audited Annual Report and Financial Statements for the year ended 31 December 2022 for ANGLE plc (the "Company") and its subsidiaries (the "Group" or "ANGLE"). ANGLE plc, Company registration number 04985171, is a public limited company limited by shares, incorporated and domiciled in the United Kingdom and quoted on the London Stock Exchange Alternative Investment Market (AIM). ANGLE plc also has a Level 1 American Depository Receipt (ADR) program that trades on the Over-The-Counter (OTC) market in the United States.

Principal activities

The principal activity of the Company is that of a holding company. The Group's principal trading activity is undertaken in relation to the development and commercialisation of the Parsortix cell separation system, with deployment in liquid biopsy – non-invasive cancer diagnostics.

Review of the business and future developments

The Strategic Report (including the Chairman's Statement and the Financial Review) on pages 02 to 51 reports on the Group's performance during the past financial year and its prospects.

The information that fulfils the requirements of the Business Review is contained within the Strategic Report (including the Chairman's Statement and the Financial Review) on pages 02 to 51 and is incorporated into this report by reference.

Key Performance Indicators (KPIs)

The Group's main KPIs and details of performance against them are set out on pages 30 to 32.

Results and dividends

The Consolidated Statement of Comprehensive Income for the year is set out on page 77.

The Group made a loss for the year of £21.7 million (2021: loss £15.0 million).

The Directors do not recommend the payment of a dividend for the year (2021: £nil). The Board periodically reviews the Company's dividend policy in the context of its financial position.

Research and development

Total expenditure on research and development in the year including both third-party research and development costs and own staff costs amounted to £10.8 million (2021: £8.4 million).

Directors and their interests

The Directors of the Company who were in office during the year and up to the date of approval of the Financial Statements, unless otherwise stated, were:

J E Eid	Appointed 19 January 2023
I F Griffiths	
J Groen	
B Howlett	
A D W Newland	
J Thompson	Appointed 5 January 2023
G R Selvey	

The Directors' interests, including beneficial interests, in the Ordinary shares and share options of the Company are shown in the Directors' Remuneration Report on pages 68 to 70.

Directors' and Officers' liability insurance

As permitted by the Companies Act 2006, the Directors and Officers of the Company and its subsidiaries are indemnified under the Group's Directors' and Officers' liability insurance in respect of proceedings which might be brought by a third party. The cover was in place for the duration of the reporting year and is in place at the date of approval of these Financial Statements. No cover is provided in respect of any fraudulent or dishonest acts.

Significant shareholdings

The following fund managers and shareholders had an interest in 3% or more of the Company's Ordinary share capital, according to the Argus Vickers share register analysis 3 February 2023 as updated by subsequent TR-1 announcements and the LINK share register at 14 April 2023:

Fund manager/shareholder	Number of shares	Holding
Conifer Management LLC	19,979,790	7.67%
Global Frontier Investments LLC	13,868,946	5.32%
Baillie Gifford & Co	13,686,737	5.25%
Dermot Keane	12,777,088	4.90%

Risk management

Details of the Group's financial risk management objectives and policies are disclosed in Note 14 to the Financial Statements, along with further information on the Group's use of financial instruments.

Principal Risks and Uncertainties

The Directors consider that the Group is exposed to a number of risks and uncertainties which it seeks to mitigate, and the principal ones are set out on pages 33 to 41.

Directors' responsibilities

The Directors are responsible for preparing the Strategic Report, Directors' Report and the Financial Statements in accordance with applicable law and regulations.

Company law requires the Directors to prepare Financial Statements for each financial year. Under that law the Directors have prepared Group and Company Financial Statements in accordance with UK-adopted international accounting standards.

Under company law the Directors must not approve the Financial Statements unless they are satisfied that they give a true and fair view of the state of affairs of the Group and the Company and of the profit or loss of the Group for that year.

In preparing the Group and Company Financial Statements, the Directors are required to:

- select suitable accounting policies and then apply them consistently;
- state whether applicable UK-adopted international accounting standards have been followed, subject to any material departures disclosed and explained in the Financial Statements;
- make judgements and accounting estimates that are reasonable and prudent; and
- prepare the Financial Statements on the going concern basis unless it is inappropriate to presume that the Group and the Company will continue in business.

The Directors are responsible for safeguarding the assets of the Group and the Company and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

The Directors are also responsible for keeping adequate accounting records that are sufficient to show and explain the Group's and the Company's transactions and disclose with reasonable accuracy at any time the financial position of the Group and Company and enable them to ensure that the Financial Statements comply with the Companies Act 2006.

The Directors are responsible for the maintenance and integrity of the corporate and financial information included on the ANGLE plc website. The Group's website is intended to meet the legal requirements for the United Kingdom. Legislation in the United Kingdom governing the preparation and dissemination of financial information may differ from legislation in other jurisdictions.

DIRECTORS' REPORT CONTINUED

For the year ended 31 December 2022

Directors' confirmations

The Directors who held office as at the date of approval of this Directors' Report confirm that, so far as they are each aware, there is no relevant audit information of which the Company's auditors are unaware, and each Director has taken all the steps that they ought to have taken as a Director to make themselves aware of any relevant audit information and to establish that the Company's auditors are aware of that information.

Going concern

The Directors have considered the uncertainties, risks and potential impact on the business associated with potential negative trading scenarios, market and geopolitical uncertainty (Ukraine-Russian conflict). Discretionary expenditure within the business provides flexibility to scale back operations to address adverse events if required. Mitigation measures to reduce costs could be taken if needed and other potential sources of funding exist such as grants, exclusivity and/or milestone payments for corporate partnerships being developed and equity proceeds.

The Directors have prepared and reviewed the financial projections for a period in excess of 12 months from the date of approval of these Financial Statements with discretionary expenditure carefully controlled in line with available resources, as certain projects may be deferred until additional resources are available. Based on the level of existing cash and expected R&D tax credits, the projected income and expenditure (the quantum and timing of some of which is at the Group's discretion) and other potential sources of funding, the Directors have a reasonable expectation that the Company and Group have adequate resources to continue in business for the foreseeable future. Accordingly, the going concern basis has been used in preparing the Financial Statements. Note 1.4 provides additional information.

Independent auditors

The auditors PricewaterhouseCoopers LLP, Chartered Accountants, were appointed by the Board during the year and have indicated their willingness to continue in office.

Annual General Meeting

The Annual General Meeting (AGM) of the Company will be held at 2:00 pm on Wednesday 28 June 2023 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ. The Board is looking forward to welcoming shareholders to the AGM in person. The Notice of Annual General Meeting is enclosed within this report on pages 112 to 117.

This report was approved by the Board of Directors on 20 April 2023 and is signed on its behalf by:

Andrew D W Newland
Chief Executive
20 April 2023

CORPORATE GOVERNANCE REPORT

Corporate Governance

The Company's shares trade on the Alternative Investment Market (AIM) of the London Stock Exchange.

The Board is committed to high standards of corporate governance and adheres to the Quoted Companies Alliance (QCA) Corporate Governance Code for small and mid-size quoted companies (the QCA Code).

The Board has voluntarily applied the QCA Code since 2014, with elements of the UK Corporate Governance Code prior to that. From 28 September 2018, AIM companies are required to comply or explain against a recognised corporate governance code. The QCA Code was revised in April 2018 (QCA Code 2018) and sets out ten broad principles of corporate governance, states what are considered to be appropriate corporate governance arrangements for growing companies and requires companies to provide an explanation about how they are meeting the principles through certain prescribed disclosures.

The Board has considered how each principle of the QCA Code 2018 is applied and provides below an explanation of the approach taken in relation to each and how they support the Company's medium to long-term success.

In accordance with Section 172 of the Companies Act 2006, as described on page 60, the Board recognises the importance of our stakeholders to our business. The Board has thought carefully about how to formalise its consideration of the impact of its decisions on key stakeholders and how it applies the S172 duties under the Companies Act 2006, in particular as it relates to QCA Principles 2 and 3.

Chairman's Statement

As Chairman of the ANGLE plc (ANGLE) Board, it is my responsibility to ensure that the Board is performing its role effectively and has the capacity, ability, structure and support to enable it to continue to do so.

We believe that a sound and well understood governance structure is essential to maintain the integrity of the Group in all its actions, to enhance performance and to impact positively on our shareholders, staff, customers, suppliers and other stakeholders.

ANGLE applies the QCA Code 2018 as the benchmark for measuring our adherence to good governance principles. These principles provide us with a clear framework for assessing our performance as a Board and as a Company, and the report below shows how we apply the Code's ten guiding principles in practice and also incorporate Section 172 of the Companies Act 2006.

Strategy and business model (QCA Principle 1)

The Group's strategy and business model is explained within the Strategic Report on pages 02 to 51 and is summarised below.

ANGLE is a world-leading liquid biopsy company commercialising a platform technology that can capture cells circulating in blood, such as CTCs, intact living cancer cells, even when they are as rare in number as one cell in one billion blood cells, and harvest the cells for analysis.

ANGLE's cell separation technology is called the Parsortix system and is the subject of granted patents in multiple jurisdictions. The system is based on a microfluidic device that captures cells based on a combination of their size and compressibility.

The analysis of the cells that can be harvested from patient blood with ANGLE's Parsortix system has the potential to deliver profound improvements in clinical and health economic outcomes in the treatment and diagnosis of various forms of cancer.

ANGLE's vision is to secure widespread adoption of the Parsortix technology by providing CTCs as the "best sample" for analysis in the emerging multi-US$ billion liquid biopsy market. To drive commercialisation, ANGLE has established both a product business and a services business with differing regulatory pathways, routes to market and near and longer-term revenue potential.

1. Product business area

ANGLE has developed the Parsortix system including instruments and one-time use cassettes that can be sold to third-party laboratories for their use in research, pharmaceutical development or clinical use. To enable customers to carry out downstream analysis of the Parsortix harvest, ANGLE will also offer assay kits for cell imaging, use protocols and data packets for molecular platforms and algorithms for clinical interpretation of results.

2. Services business area

ANGLE has established clinical laboratories in the UK and United States as accelerators and demonstrators that have the capability and required quality systems to process patient samples and offer validated clinical tests using the Parsortix system. The laboratories, in Guildford, UK and Plymouth Meeting, Pennsylvania, United States, are being used to provide services to pharma and biotech customers running clinical trials (pharma services) and will be able to offer laboratory developed tests (LDTs) for patient management as a first step towards product roll out of tests.

Both business areas are supported by a growing body of published evidence from leading cancer centres showing the utility of the system through peer-reviewed publications, scientific data and clinical research evidence, highlighting a wide range of potential applications.

CORPORATE GOVERNANCE REPORT CONTINUED

Meeting shareholder needs (QCA Principle 2)

The Company seeks to maintain and enhance good relations with its shareholders and analysts. The Company employs a Head of Investor Relations to increase shareholder engagement and IR activities. The Group's Interim and Annual Reports are supplemented by regular published updates to investors on commercial progress. All investors have access to up-to-date information on the Group via its website, **www.angleplc.com**, which has an investor relations section providing contact details for investor relations queries, details on the Company's share price, share price graphs and share trading activity. The Company also distributes Group announcements electronically. Shareholders and other interested parties wishing to receive announcements via email are invited to sign up to the "Email Alert" facility in the Investor Relations, Regulatory News section on the Company's website.

The Directors seek to build on a mutual understanding of objectives between the Company and its shareholders, especially considering the specialist and medium-term nature of the business. Institutional shareholders, private client brokers and analysts are in contact with the Directors and Head of Investor Relations through a regular programme of briefing presentations and meetings to discuss issues and give feedback, primarily following the announcement of the interim and preliminary results, but also throughout the year as required. The Board also uses and receives formal feedback through the Company's joint stockbrokers, financial public relations advisor and other advisors. Investor forums and presentation seminars and shows provide other channels of communication to shareholders, analysts and potential investors. Individual shareholders are welcome to and regularly make contact with the Company via email or telephone.

All shareholders are encouraged to make use of the Company's Annual General Meeting (AGM) to vote on resolutions (see Principle 10) and to raise any questions regarding the strategy, management, operations and corporate governance of the Group. The Chairs of the Audit, Remuneration and Nomination Committees are available to answer any questions from shareholders at the AGM.

Berenberg and Jefferies act as joint brokers to the Company, to further improve the quality and quantity of investor relations activities.

Along with the usual presentations and webinars the Company held a number of virtual non-deal roadshows in the year and a hybrid deal roadshow resulting in a successful fundraise in June 2022.

The ongoing development of a Corporate Responsibility Report on pages 42 to 49 is in response to shareholder requests to better understand how the Group deals with sustainability and environmental, social and governance (ESG) issues.

Manage our responsibilities to wider stakeholders (QCA Principle 3)

The Board recognises its prime responsibility under UK corporate law is to promote the success of the Group for the benefit of its members as a whole. We conduct business in an ethical way and take seriously our responsibilities to our wider stakeholders including employees, clinical study partners, contractors, key opinion leaders, trading partners, research and laboratory customers, suppliers and regulatory authorities. The Corporate Responsibility Report on pages 42 to 49 provides more details and Principle 8 also talks about our values-based corporate culture.

Employees

We recognise that our employees are a core fundamental component to our success. We hold regular all-employee meetings to discuss business progress and provide updates on initiatives. These meetings also include opportunities for staff to present on ongoing projects. One of the goals of these meetings is to ensure that staff feel valued and engaged with the wider Group.

ANGLE provides training and development programmes, inclusive and interactive appraisal systems, merit-based promotions, flexible and family-friendly employee policies and a range of employee and family benefits. Woven throughout all initiatives and programmes is a philosophy which promotes an open culture for discussion and honest feedback. (See "Our Values and Our Culture" on page 48 of the Corporate Responsibility Report). Employees are encouraged to be creative and offer ideas across the Group. Group-wide competitions have been held to encourage creativity and camaraderie.

The Company places importance on the development of internal candidates for management roles and utilises a combination of competency and development plans to progress this. The Company has a Management Charter which formalises the ANGLE culture and clarifies our expectations to and from staff and puts in place a structure to ensure we achieve it. This has delivered a number of ongoing initiatives across the Group including a refined structured promotions process, a coaching programme to support managers and a New Manager training course. Regular one-to-one support is being provided to all managers with teams working from home.

Towards the end of 2022, the Company made the decision to embark on an orderly wind down of its Canadian operations which had been primarily developing a downstream analysis technology for use in combination with the Parsortix system. This decision was made in the light of proposed changes to R&D tax credit conditions by UK HMRC which would significantly increase the costs of operating in Canada, together with the backdrop of a challenging capital market environment and the improved performance of alternative downstream analysis techniques. The Directors concluded that closure of the Canadian operations was in the best interests of the Company and its shareholders. Regrettably, this resulted in the Company needing to make its Canadian staff redundant.

Contractors and suppliers

ANGLE operates a high standard of quality management to ensure we comply with the appropriate regulations in the various territories in which we operate. The Group uses external specialists where needed in relation to areas such as the quality systems and health and safety.

The complex nature of our products and product development process means that close working relationships with a number of key suppliers are essential to ensure we receive the highest quality products and services. An ISO 13485:2016 quality system is mandatory for key suppliers. This involves senior staff clearly communicating requirements and working closely with suppliers to develop appropriate products and services. We ensure there are clear processes for change control to avoid issues and clear billing arrangements and we aim to pay suppliers based on the terms agreed. As a result, we receive high quality goods delivered on time and to specification. It puts us in a position to negotiate discounts, for example, bulk discounts on cassettes through frame orders.

Key opinion leaders, customers and clinical study partners
We work closely with key opinion leaders (KOLs) and customers who have access to patient samples, who provide feedback on their use of the system, including problems encountered, development needs such as new processes and workflows and working with different downstream analysis systems. Our success, competitive advantage and reputation are dependent on understanding these needs and providing solutions. The relationships are managed by key account managers. KOLs, customers and the Group regularly present at scientific conferences. We have a leveraged R&D model driving an increased number of peer-reviewed publications enabled by the Parsortix system in order to be at the forefront of CTC research and clinical adoption. We contract with leading cancer centres to run clinical studies on our behalf as they have access to the necessary patient blood samples and subsequent outcome data.

22 peer-reviewed publications were issued in the year by KOLs and customers (2021: 17) taking the total to 76 publications as at 31 December 2022 (2021: 54). A further three publications have been issued since the year end. While conference attendance was predominantly of a virtual nature during COVID-19 we are increasingly returning to physical attendance with the associated networking benefits.

Regulatory authorities
We operate in a highly regulated area of business. National governments and regulators (Competent Authorities) implement highly structured product certification regimes to national, supra-national and international standards. Such certifications are necessary by law to manufacture and market devices for research and clinical use.

Notified Bodies are designated by Competent Authorities to perform assessments to agreed standards. ANGLE is subject to those assessments where appropriate to the products manufactured and marketed by the Company.

We employ consultants with high levels of regulatory knowledge, experience and contacts to ensure our working knowledge is comprehensive, up to date and appropriate to our needs. Guidance documents and training are identified to enable us to keep up to date with regulatory developments across different regulatory bodies and different standards domains.

Through engagement, we ensure that we understand the regulatory landscape so that we can identify and comply with all applicable product standards in all relevant territories. We engage with regulatory authorities, through telephone, email and face-to-face meetings, to ensure we obtain their views, understand the regulations and their impact on our work plans and submissions.

During the year, we maintained ISO 13485:2016+A11:2021 accreditation (Europe) and secured FDA De Novo classification and CE marking (IVDD) for the Parsortix PC1 Clinical System for the stated intended use. The scope of quality system certification for the site includes the design, development, manufacture, sale, distribution, installation and service of instruments and test methods, consumables and reagents for cellular and molecular diagnostics. The UK ISO 13485 certification is independently maintained and enables the businesses to pursue a wide range of medical device development and manufacturing activities in line with the Company's strategic objectives.

Risk management (QCA Principle 4)
The Board is responsible for identifying the major business risks faced by the Group and for determining the appropriate course of action and systems to manage and mitigate those risks.

The nature of medical diagnostics development and the early stage and scale of our operations means there are a number of risks and uncertainties. The Directors maintain a risk register and have summarised the principal risks and uncertainties that could have a material impact on the Group. The Principal Risks and Uncertainties are reported on pages 33 to 41.

The Board monitors the key areas such as clinical applications, competitive position, financial, intellectual property, manufacturing, market acceptance, operational, regulation and quality assurance, research and development, staff, key suppliers and key partners. An ongoing assessment is made of their potential impact and mitigation strategies and actions. New potentially material risks which arise between reviews are added to the risk register, discussed at Board level as they arise and followed up by the Board as appropriate.

The Audit Committee has adopted formal terms of reference (see Principle 9) and considers financial reporting, corporate governance and internal controls. Its review of financial reporting includes discussion of major accounting issues, policies and compliance with UK-adopted international accounting standards, the law (Companies Act 2006), review of key management estimates and judgements (Note 1.22 Critical accounting estimates and judgements), review and update of the risk register, risk identification and assessment and risk management and mitigation activities and going concern assumptions.

Internal control systems are designed to meet the particular needs of the Group and the risks to which it is exposed. The system of internal control is designed to manage the risk of failure to achieve business objectives, rather than to eliminate it, and by its nature can only provide reasonable but not absolute assurance against material misstatement or loss.

A quarterly review process exists to ensure early identification of new accounting issues arising from the introduction of new areas of business and/or the adoption of new or amended accounting standards. The process will ensure the impacts are assessed, advice or training is obtained if required and policies (new or revised) are agreed and documented on a timely basis.

An internal financial audit function is not considered necessary or practical due to the size of the Group and the close day-to-day control exercised by the Executive Directors and senior management. The Board will continue to monitor the requirement to have an internal audit function.

CORPORATE GOVERNANCE REPORT CONTINUED

The key procedures that the Directors have established with a view to providing an effective system of internal control are as follows:

Management structure
The Board has overall responsibility for the Group and focuses on the overall Group strategy (see Principle 1) and the interests of shareholders (see Principles 2 and 10). There is a schedule of matters specifically reserved for decision by the Board (see Principle 9). The Board has an organisational structure with clearly defined responsibilities and lines of accountability and each Executive Director has been given responsibility for specific aspects of the Group's affairs (see Principles 5 and 9). Internal financial risks are controlled through authorisation procedures/levels and segregation of accounting duties. Delegation of Authority processes are regularly reviewed and updated.

Quality and integrity of personnel
The integrity and competence of personnel are ensured through high recruitment standards and subsequent training. We assess employee competence at all levels, identify development requirements and provide training and development support, aligned with business and personal objectives. High-quality, motivated personnel are seen as an essential part of the control environment.

Budgets and reporting
Each year the Board approves the annual budget which includes an assessment of key risk areas. Performance is monitored and relevant action taken throughout the year through regular reporting to the Board of variances from the budget and preparation of updated forecasts for the year together with information on the key risk areas.

Investment and divestment appraisal
All material investment and divestment decisions require appraisal, review and approval by the Board.

Internal controls
The Board reviews the effectiveness of the Group's systems of internal controls and has a process for the continuous identification, evaluation and management of the significant risks the Group faces. Assessment considers the external environment, the territories in which the Group operates, the industry in which the Group operates including applicable regulations and standards, the internal environment and non-financial risks such as operational and legal risks. The risks identified are ranked based on significance and likelihood of occurrence. The Board reviews the controls in place to mitigate those risks and improvements are made where required. The Group conducts its operations in accordance with the ISO 13485:2016+A11:2021 quality management system standard and continues to invest in its systems and people in light of Group strategy and risk assessment to ensure the appropriate operational controls and measures are in place and working effectively. The quality system is subject to annual Notified Body audit (BSI) in the UK. The Group uses external specialist resources (regulatory, design, manufacturing etc) as required. Day-to-day responsibility for the implementation of effective internal control and risk monitoring rests with senior management.

Metrics and quality objectives continue to be actively implemented and monitored as part of a continual improvement programme. A number of incremental improvements have been made in the year driven by planned internal quality system auditing and risk assessment and other larger improvements have been identified and are being progressed. Improvements have included:

A. A globally aligned P2P process which allows greater visibility over supplier performance such as delivery times, fulfilment accuracy, price variances etc and provides further controls over use of approved suppliers etc.

- Standardisation of internal NPD project budgeting, reporting and approval processes on both a detailed stage-by-stage and broader life-cycle basis, providing detailed and consistent project analysis from which to make more informed business decisions at critical time points.
- A new budgeting process and reporting dashboard developed and deployed with a focus on business ownership and accountability.
- New processes for the management of inventory items and the flow of actuals and corresponding charging to departments/projects.
- The introduction of standards for internal processes to improve visibility of the full cost of studies and development projects.
- Extensive process mapping in preparation for an ERP Discovery phase has resulted in formalisation of sub-processes allowing consistent delivery and identification of efficiency improvements in key areas.
- Recruitment of specialist employees (Health & Safety Officer, Trade Compliance Controller etc) to bring expertise in-house to minimise exposure to risks in day-to-day business.
- Introduction of a new HRIS system to facilitate HR management and support recruitment processes.
- Continued cyber security training and IT improvements including Duo Security, a two-factor authentication service.
- Procedure and technical documentation updates to support product roll out in territories across the world as our Distributor base expands.
- Transition of ANGLE's product risk management system to meet the requirements of the updated risk management standard: ISO14971:2019.

Maintain a well-functioning Board (QCA Principle 5)

The Board of Directors is led by the Chairman, has overall responsibility for strategy (see Principle 1) and is responsible to shareholders for the governance of ANGLE plc and for the effective operation and management of the Group. Its aim is to provide leadership and control in order to ensure the growth and development of a successful business, while representing the interests of the Company's shareholders (see Principles 2 and 10).

Composition
The Board comprises the Chairman, four Non-executive and two Executive Directors. The QCA Code recommends there are at least two non-executive directors. Two Non-executive Directors were added to the Board in January 2023.

Different Directors hold the roles of Chairman and Chief Executive and there is a clear division of responsibilities between them. The Chairman is responsible for corporate governance, for overseeing the running of the Board, ensuring that no individual or group dominates the Board's decision making and ensuring that the Non-executive Directors are properly briefed on matters. The Chief Executive has responsibility for implementing the strategy of the Board and managing the day-to-day business activities of the Group through his management of the Executive Directors and senior managers. The Finance Director also acts as the Company Secretary as the size and nature of the business activities do not justify a dedicated person or a need to outsource the activity; in this role he supports the Chairman directly on governance matters as well as dealing with legal and regulatory compliance.

The Board's composition is geared towards the Group's current stage of development and priorities and will be refreshed as appropriate. The skill set of the Board therefore includes experience in non-executive director/chairman/CEO roles, listed companies, investor relations, fundraising, medical diagnostics, technology development, product development and commercialisation, operating clinical laboratories and laboratory developed tests, CE mark and FDA cleared product approvals and reimbursement. Individual Directors possess a wide variety of skills and experience, and biographical details of the Directors are set out on pages 52 and 53.

The Board currently has one female Director and one ethnic minority Director. The Board is confident both that the opportunities in the Company are not excluded or limited by any diversity issues (including gender) and that the Board contains the necessary mix of experience, skills and other personal qualities and capabilities necessary to deliver its strategy. This area will continue to be monitored.

Independence
The Chairman and Non-executive Directors are considered by the Board to be independent of management and free of any relationship which could materially interfere with the exercise of their independent judgement. They do not have a significant shareholding (see page 57) or represent a major shareholder, they receive no remuneration from the Company other than Directors' fees and occasional consultancy fees (see page 68), they have no day-to-day involvement in running the business and have never been employees of the Company, they have no personal financial and/or material interest in any other matters to be decided, such as contracts, and they have no conflicts of interests arising from cross-directorships or advisory roles. Each Board meeting starts with a declaration of Directors' interest to identify potential or actual conflicts of interest. The Board considers that the Non-executive Directors are of sufficient calibre to bring the strength of independence to the Board. The Board has nominated Brian Howlett as Senior Independent Director. Issues can also be raised directly through the normal channels of the Chairman, Chief Executive and Finance Director and where necessary the Non-executive Directors can be approached directly.

The Chairman joined the Board in September 2006 and became Chairman in September 2007. The Chairman was independent at the time of his appointment and under the previous QCA Code he counted as an independent director. The Board considers that the Chairman's long-standing knowledge and detailed experience of the business are extremely valuable and that the length of tenure does not affect his independence of judgement. The Nomination Committee, which has appointed a new Chair during 2022, considers this matter directly and as part of its succession planning discussions.

Committees of the Board
The Board maintains Audit, Remuneration and Nomination Committees. All Committees operate with written terms of reference (see Principle 9).

Ensure Directors have necessary, up-to-date skills (QCA Principle 6)
Individual Directors possess a wide variety of skills and experience.

Detailed biographical information on the individual Directors are set out on pages 52 and 53.

The key skills they bring to the Board are:

- Garth Selvey, Chairman – extensive experience of the listed sector and leading companies.
- Andrew Newland, Chief Executive – over 30 years' experience in setting up, leading and building technology-based businesses, over 20 years leading specialist medtech businesses, and 13 years in the liquid biopsy space.
- Ian Griffiths, Finance Director – over 30 years' experience in finance and technology-based businesses, and 13 years in the liquid biopsy space.
- Jan Groen, Non-executive Director – expertise in new product development, including development and successful commercialisation of CE marked and FDA cleared diagnostic products and laboratory developed tests in Europe and the USA.
- Brian Howlett, Non-executive Director – extensive commercial operations experience of the medtech sector.
- Juliet Thompson, Non-executive Director – over 20 years in advising listed healthcare companies in UK and Europe as an investment banker.
- Joseph Eid, Non-executive Director – valuable knowledge and experience in oncology drug development and the use of biomarkers in the clinical trials process and as companion diagnostics.

The Non-executive Directors also serve on other boards in the medical diagnostics sector which gives a broad range of skills, capabilities and experience. All Directors are able to take training and/or independent professional advice in the furtherance of their duties if necessary. Directors keep their skill set up to date through attending industry events, seminars and research. The Executive Directors will typically undertake specific training during the year. All Directors also have access to the Company's Nominated Advisor, legal advisors, financial advisors and other independent professional advisors as required. Professional advisors provide briefings and update notes on necessary legislation from time to time.

CORPORATE GOVERNANCE REPORT CONTINUED

No individual Director or Committee of the Board received any external advice in relation to their Board duties in the year.

There is an induction process for new Directors including briefing by the Nominated Advisor and the Company.

Evaluate Board performance (QCA Principle 7)

The Company supports the concept of an effective Board leading and controlling the Company. The Chairman discusses and deals with any concerns with an individual Director, or the Board as a whole, on Board performance as they arise. Additionally, the Board undertakes a periodic formal evaluation of its performance, its Directors and its Committees, the last one being undertaken in 2021. The review, led by the Chairman, involves each Board member providing feedback and comments on the others and where necessary specific actions are identified to improve certain areas.

The evaluation criteria take into account the Financial Reporting Council's guidance on board effectiveness. The criteria against which board, committee and individual effectiveness is considered comprise the board structure (composition, constitution, diversity and succession planning – see Principle 5), the dynamics and functioning of the board (annual board meeting schedule, quality of information, interactions and communications with the executive directors and senior management team, cohesiveness and the quality of participation in board meetings), the board's role in strategy and the financial reporting process. Evaluation procedures are evolving to ensure they are relevant to the Group's stage of development and Board dynamics. Due to the experience and size of the Board and the size of the Company, the Board does not consider it necessary to have evaluations facilitated by an external consultant but will keep this under review.

Promote a values-based corporate culture (QCA Principle 8)

The Board places emphasis on its values-based corporate culture and ethical behaviour which are crucial to the Group's reputation in the highly regulated field in which it operates. The Corporate Responsibility Report on pages 42 to 49 provides more details and Principle 3 also talks about our responsibilities to wider stakeholders. The Group's success depends on maintaining a supportive, innovative and can-do culture when working with suppliers and customers.

The Group manages a highly regarded quality management system which has a very strong influence on culture. The Group's competency framework sets values-based expectations at all levels in terms of the way we communicate and behave towards each other and external stakeholders. Our competency framework links to our performance management system and, in turn, to our rewards strategy.

The Group operates a flat structure with all staff having the ability to discuss matters with Directors and senior managers. The management teams meet regularly to promote communications and teamwork. The majority of projects take a team-based approach. Staff participate through virtual teams as well as regular office visits. Recruitment practices are heavily focused on recruiting people with similarly strong values. We have expanded our HR team to ensure a consistently open and ethical approach to recruitment, management and employee communication throughout our offices.

The Group has established a Management Charter which formalises and clarifies expectations that managers at all levels take responsibility for supporting and promoting an ethical values-based culture. Senior managers are coached in the development and maintenance of an open and ethical culture. This Charter forms the basis of our management development programme and is part of management objectives.

The Group has taken further steps to promote a supportive culture. These include improving healthcare benefits, training mental health first aiders, subscription for employees to Employee Assistance Programmes (e.g. Thrive: Mental Wellbeing app) and team building events.

The highly skilled and diverse nature of the Group influences culture which, at the most recent review, is characterised by:

- Qualifications, with 81% (2021: 84%) of staff having higher education qualifications including Degrees, Masters and Doctorates as well as Chartered Accountants and MBAs, with the majority of staff having multiple qualifications.
- Gender split, with 49%:51% (2021: 47%:53%) Male:Female.
- Different nationalities, with 35 (2021: 39) different countries represented.

Maintain fit for purpose governance structures (QCA Principle 9)

Roles and responsibilities

Chairman: the Chairman is responsible for the leadership of the Board and ensuring the effective running and management of the Board. He is also responsible for the Board's oversight of the Company's affairs, which includes ensuring that the Directors receive accurate, timely and clear information, ensuring the effective contribution of the Non-executive Directors and implementing effective communication with shareholders.

Chief Executive Officer: the Chief Executive Officer is responsible for the day-to-day management and the executive leadership of the business. His other responsibilities include the progress and development of objectives for the Company, managing the Company's risk exposure, implementing the decisions of the Board and ensuring effective communication with shareholders and regulatory bodies.

Non-executive Directors' independence

The Board considers the Non-executive Directors to be sufficiently independent to provide appropriate oversight and scrutiny (see Principle 5).

Service contracts and letters of appointment

The two Executive Directors Andrew Newland and Ian Griffiths have service contracts with the Company dated 9 March 2004 and effective from 17 March 2004, as amended from time to time. The contracts are not set for a specific term but include a rolling twelve-month notice period by the Company or the individual. In the event of a change in control, the Executives have the right to terminate their employment without the requirement to work their notice period.

The Chairman Garth Selvey has a letter of appointment dated and effective from 7 September 2006. The Non-executive Director Brian Howlett has a letter of appointment dated and effective from 7 January 2013. The Non-executive Director Dr. Jan Groen has a letter of appointment dated and effective from 1 November 2018. The Non-executive Director Juliet Thompson has a letter of appointment dated and effective from 5 January 2023. The Non-executive Director Dr. Joseph Eid has a letter of appointment dated and effective from 19 January 2023. These letters are issued in place of service contracts. These appointments are not set for a specific term and are terminable at will without notice by either party.

Re-election and election of Directors
In accordance with the Company's Articles of Association, Directors are subject to re-election every three years, and newly appointed Directors are subject to election at the first Annual General Meeting (AGM) after their appointment.

Juliet Thompson and Joe Eid were appointed in January 2023 and will be seeking election this year. All other Directors were re-elected by the shareholders at the AGM held on 29 June 2022 and accordingly will not be seeking re-election at the AGM this year.

Committees of the Board
The Board maintains Audit, Remuneration and Nomination Committees. All Committees operate with written terms of reference, the details of which can be found on the website. Their minutes are circulated for review and consideration by the full Board of Directors, supplemented by oral reports on matters of particular significance from the Committee Chairmen at Board meetings.

Audit Committee
The members of the Committee are the Non-executive Director Juliet Thompson (Chair of the Audit Committee from appointment in 2023), the Non-executive Director Brian Howlett (former Chairman of the Audit Committee) and the Non-executive Director Jan Groen. Further to Joe Eid's appointment in 2023, it was agreed that the Chairman Garth Selvey and Non-executive Director Joe Eid will attend as observers. The Audit Committee meets at least twice a year to review the interim and annual financial statements before they are submitted to the Board. The external auditors, Finance Director and Chief Executive may attend by invitation. Provision is made to meet with the auditors at least once a year without any Executive Director present.

The Committee has adopted formal terms of reference and considers financial reporting, corporate governance and internal controls. Its review of financial reporting includes discussion of major accounting issues, policies and compliance with UK-adopted international accounting standards, the law (Companies Act 2006), review of key management judgements and estimates, review and update of the risk register, risk assessment and risk management activities and going concern assumptions. Risks have been described in more detail in QCA Principle 4 and the Principal Risks and Uncertainties are reported on pages 33 to 41. Note 1.22 describes the critical accounting estimates and judgements. The Committee also reviews the scope and results of the external audit and the independence and objectivity of the auditors and makes recommendations to the Board on issues surrounding their remuneration, rotation of partners/staff, appointment, resignation or removal. The Audit Committee also considers and determines relevant action in respect of any control issues raised by the auditors. The Audit Committee is also responsible for monitoring the provision of non-audit services provided by the Group's auditors and assesses the likely impact on the auditors' independence and objectivity when considering an award of any material contract for additional services. The fees in respect of audit and non-audit services are disclosed in Note 3. A new ethical standard for auditors came into force with effect from 15 March 2020 which restricts the non-audit services that auditors can provide, and the Company has developed a policy in relation to this.

Remuneration Committee
The members of the Committee are the Chairman Garth Selvey (Chairman of the Remuneration Committee) and the Non-executive Directors Brian Howlett, Jan Groen, Juliet Thompson and Joe Eid. The Remuneration Committee meets as required. The Chief Executive and Finance Director may attend by invitation but are not present when matters affecting their own remuneration arrangements are considered.

The Committee has adopted formal terms of reference and the Committee reviews and sets the remuneration and terms and conditions of employment of the Executive Directors and senior management. It also agrees a policy for the salaries of all staff and is responsible for the development of the Company's remuneration scheme. The decisions of the Committee are formally ratified by the Board.

The Company is not required by either the AIM Listing Rules or the Companies Act to produce a remuneration report but provides the information in the Annual Report and Financial Statements as recommended by the QCA because of its commitment to maintaining high standards of corporate governance. The Company's Remuneration Policy is the responsibility of the Remuneration Committee. The Remuneration Policy, in so far as it relates to the Directors, is subject to an advisory vote by Shareholders every three years and was last approved at the 2021 Annual General Meeting (AGM). The Directors' Annual Remuneration Report is subject to an advisory vote by Shareholders at each AGM.

The Remuneration Report on pages 67 to 70 provides details of the Remuneration Policy and the Directors' Annual Remuneration.

Nomination Committee
The members of the Committee are the Non-executive Director Jan Groen (Chairman of the Nomination Committee, appointed during 2022), the Chairman Garth Selvey (former Chairman of the Nomination Committee) and the Non-executive Directors Brian Howlett, Juliet Thompson and Joe Eid. The Nomination Committee meets as required. The Chief Executive and Finance Director may attend by invitation.

The Committee has adopted formal terms of reference and is responsible for reviewing the structure, size and composition of the Board, planning for succession and for identifying and recommending to the Board suitable candidates for both executive and non-executive Board appointments.

Information
Management supplies the Board and/or Committees with appropriate and timely information, including a business update and management accounts so that trading performance can be regularly reviewed.

CORPORATE GOVERNANCE REPORT CONTINUED

Matters reserved for the Board
The Board has a schedule of matters specifically reserved to it for decision, including the review and approval of:

- Group policy and long-term plans and strategy for the profitable development of the business;
- interim and annual Financial Statements;
- major investments and divestments;
- other significant financing matters such as fundraising, material contracts including clinical studies and product development, acquisitions and capital item purchases;
- management accounts, cash flow forecasts, annual budgets and amendments; and
- senior executive remuneration and appointments.

Share dealing code
The Company has adopted and operates a share dealing code governing the share dealings of the Directors and applicable employees to ensure compliance with the AIM Rules.

Commitment
Directors are required to allocate sufficient time to the Company to discharge their responsibilities effectively. The Chairman is required to commit approximately 3 to 5 days per month. Non-executive Directors are required to commit approximately 2 to 4 days per month. Executive Directors work full-time.

Directors' attendance
The Board has at least eight main Board meetings per year with additional special meetings as required. Meetings have been held as a mixture of face-to-face and by video conference. Certain Directors may be appointed as a Committee of the Board of Directors. Directors' attendance at Board and Committee meetings during the year ended 31 December 2022 is set out below:

	Garth Selvey	Brian Howlett	Jan Groen	Andrew Newland	Ian Griffiths
Board	11/13	13/13	13/13	13/13	13/13
Committee of the Board*	N/A	N/A	N/A	Yes	Yes
Audit	3/3	3/3	3/3	N/A	N/A
Remuneration	4/4	4/4	4/4	N/A	N/A
Nomination	5/5	5/5	5/5	N/A	N/A

* The Board appointed Andrew Newland and Ian Griffiths as a Committee of the Board of Directors in relation to one meeting associated with the fundraise and multiple meetings associated with employee option exercises during the year.

Scoring represents individual Directors' attendance for those meetings when they were members of the Board or Committee.

In addition, the Board has other non-Board meetings to discuss strategy, certain meetings with advisors and key business areas with the senior management team.

Communicate governance and performance with shareholders (QCA Principle 10)
The Board communicates regularly with shareholders providing updates on Group performance to shareholders via interim and annual financial reports, trading updates, investor presentations and a regular news flow of significant developments for the Group (see Principle 2). The website includes historical financial statements and governance related material.

The members and role of the Remuneration Committee are described in QCA Principle 9. The Remuneration Report on pages 67 to 70 describes the Remuneration Policy for the Group as well as detailing the Directors' remuneration for the year. Discussions are held with significant shareholders ahead of any significant changes in Remuneration Policy and Shareholders are able to make an advisory vote annually on the Directors' Remuneration Report and every three years on the Remuneration Policy.

The Annual General Meeting presents an opportunity for shareholders to vote on the various resolutions proposed.

REMUNERATION REPORT

The Company is not required by either the AIM Listing Rules or the Companies Act to produce a separate directors' remuneration policy and report although AIM companies are required to report and disclose certain information on directors' pay under AIM Rule 19 and pursuant to s412 of the Companies Act 2006. The Company has provided the information below as recommended by the QCA because of its commitment to maintaining high standards of corporate governance. The Company's Remuneration Policy is the responsibility of the Remuneration Committee.

Remuneration Policy

The Company's aim is to attract, retain and incentivise the Executive Directors, senior management and staff in a manner consistent with the goals of good corporate governance. In setting the Company's Remuneration Policy, the Remuneration Committee considers a number of factors including the basic salary, benefits and incentives available to Executive Directors, senior management and staff of comparable companies and for new senior recruits based on executive search specialist advice. The Company's remuneration packages awarded to Executive Directors and senior management are intended to be competitive, include a significant proportion of performance related remuneration and align employees' with shareholders' interests.

The Remuneration Policy was approved as an advisory vote by Shareholders at the 2021 Annual General Meeting (AGM) and remains effective for three years.

Basic salary and benefits

Salary levels are reviewed annually. The Committee believes that basic salary and benefits should be competitive in the relevant employment market and reflect individual responsibilities and performance. Medical health insurance, life cover, income replacement and pension benefits are also provided to employees once they have met eligibility criteria. Executive Directors and senior management are eligible for employer pension contributions on the same basis as eligible staff in the relevant jurisdiction. Basic salary may be taken in part as a pension payment. Basic salary and pension are considered together as a "Combined Figure".

Annual Bonus Plan

The Annual Bonus Plan allows a bonus payment of up to 50% of the Combined Figure upon the achievement of defined targets relating to business progress and up to a further 50% in the case of exceptional achievement. The Remuneration Committee has the discretion to settle an element of any bonus in the form of share options, "Bonus Options", exercisable at par value and not subject to performance conditions.

Share option schemes

The Company has an Enterprise Management Incentive (EMI) Scheme, a Company Share Option Plan (CSOP) and Unapproved Share Option Schemes as a means of encouraging ownership and aligning the interests of staff and external shareholders. Reflecting the need to attract, incentivise, reward and retain high calibre staff to deliver the business strategy, the Remuneration Committee has established a limit for the Company's share option schemes of up to 16% of the issued and to be issued share capital from time to time.

Long-Term Incentive Plan

The Company has a Long-Term Incentive Plan (LTIP) as a means of further encouraging ownership and aligning the interests of senior management and shareholders to achieve key strategic goals and build long-term value. The Company's Non-executive Directors are not eligible to participate in the LTIP. The LTIP provides for awards of options to acquire shares for nil consideration subject to performance conditions, "LTIP Options". Performance conditions, targets and weightings will be set by the Remuneration Committee at the time of an award to ensure they are stretching and aligned with the Company's strategy to build shareholder value. Details in respect of each award will be disclosed in an RNS at the time of award and also in the subsequent Annual Report and Financial Statements. LTIP Options have a performance and holding period of not less than five years, with a minimum performance period of three years and an additional holding period. Awards vest only to the extent that the performance conditions and targets have been met by the end of the relevant performance period and will be capable of sale once the holding period is completed. The LTIP contains normal "good leaver", "bad leaver" and change of control provisions. Malus and clawback provisions will apply under certain circumstances. Awards will be made from within the overall 16% limit described in Share options above.

Discretionary incentives

The Group may operate with discretionary incentives either in addition to or instead of the incentives described above in any particular year, dependent on the needs of the business.

Non-pensionable

None of the awards under the Annual Bonus Plan, Share Option Schemes, Long-Term Incentive Plan or discretionary incentives are pensionable.

Non-executive Directors

Non-executive Directors receive a fixed fee for their services. The remuneration of the Non-executive Directors is determined by the Board as a whole within the overall limits stipulated in the Articles of Association. Non-executive Directors are not eligible to participate in any of the Company's incentive schemes.

REMUNERATION REPORT CONTINUED

Directors' Remuneration Report

Directors' interests – shares

The Directors' interests, including beneficial interests, in the Ordinary shares of the Company were as stated below:

	Number of Ordinary shares of £0.10 each	
	2022	2021
I F Griffiths	**1,241,332**	1,203,832
J Groen	**–**	–
B Howlett	**10,000**	10,000
A D W Newland	**7,179,686**	7,054,686
G R Selvey	**50,000**	50,000

Directors' emoluments

The aggregate remuneration received by Directors who served during the year was as follows:

	Salary/Fees £'000	Benefits £'000	Pension £'000	Bonus £'000	**2022 Total £'000**	2021 Total £'000
Chairman						
G R Selvey	27	–	–	–	**27**	25
Executive						
I F Griffiths	161	3	–	–	**164**	284
A D W Newland	253	11	–	–	**264**	446
Non-executive						
J Groen	27	–	–	–	**27**	25
B Howlett	27	–	–	–	**27**	25
Total	495	14	–	–	**509**	805

During the year the Non-executive Director fees were increased to more closely reflect market rates and practice. The Chairman has voluntarily waived £20,000 of his fees.

Benefits include amounts in respect of private medical insurance and taxation advice.

Performance bonuses were not awarded in the current financial year under the terms of the Annual Bonus Plan due to the potential impact and associated uncertainties of the ongoing adverse macroeconomic and stock market conditions and the desire of the Company to conserve cash. This is notwithstanding the fact the Executives were deemed to have met the performance criteria in relation to a proportion of the performance bonus, major factors of which were: receipt of FDA De Novo clearance of the Parsortix system, a successful fundraise, delivering best in class ovarian cancer results and further developing the ANGLE clinical laboratories and pharma services business.

Performance bonuses were awarded in the prior financial year under the terms of the Annual Bonus Plan. The Executives were deemed to have met the performance criteria in relation to an 80% performance bonus, major factors of which were: response to FDA Additional Information Request for clearance of the Parsortix system, keeping the Group working effectively through the COVID-19 pandemic, a successful fundraise and establishing the ANGLE clinical laboratories and establishing the new pharma services business.

In the prior year, I F Griffiths sacrificed salary and the Company elected to make contributions to his personal pension.

Directors' interests – options

The Directors' interests in LTIP Options and share options over the Ordinary shares of the Company were as stated below.

LTIP Options

A Long-Term Incentive Plan (LTIP) was established in 2018. The intention of the LTIP is to reward tangible increases in shareholder value. Subject to the rules of the LTIP, awards will vest only to the extent that the performance conditions have been met at the end of the performance period and the underlying shares may only be traded once the holding period is completed.

Award #1 – 20 December 2018
The Remuneration Committee approved a grant of nil-cost options to Executive Directors on 20 December 2018, as amended by shareholders at the Annual General Meeting on 30 June 2021 to extend the performance period by one year due to COVID-19 related impacts, over a maximum of 6,000,000 Ordinary shares of £0.10. The LTIP Options have performance conditions as set out below, a performance period of four years and an additional holding period of one year.

The performance conditions for the LTIP Options relate to the compound annual growth rate (CAGR) of the share price over three years. The mid-market share price on 20 December 2018 was £0.385 per Ordinary share. As different levels of performance are achieved the number of shares that vest increases up to a maximum, as set out below:

Share price CAGR	Multiple of share price (at 3 years)	Proportion vesting	Andrew Newland Number	Ian Griffiths Number	Total Number
< 40%	< 2.70	0%	0	0	0
> 40%	> 2.70	20%	720,000	480,000	1,200,000
> 55%	> 3.70	50%	1,800,000	1,200,000	3,000,000
> 75%	> 5.40	100%	3,600,000	2,400,000	6,000,000
Vested as at 31 December 2022			**1,800,000**	**1,200,000**	**3,000,000**

As at 20 December 2022 the share price target in relation to the proportion vesting of 50% had been met and therefore 3,000,000 LTIP options have vested and are now within the holding period to 20 December 2023. The remaining 50% or 3,000,000 LTIP options have been forfeited.

Award #2 – 25 September 2020
The Remuneration Committee approved a grant of nil-cost options to Executive Directors on 25 September 2020 over a maximum of 3,000,000 Ordinary shares of £0.10. The LTIP Options have performance conditions as set out below, a performance period of three years and an additional holding period of two years.

The performance conditions for the LTIP Options relate to i) the Company achieving FDA clearance for its Parsortix system (this condition has been met) and ii) the compound annual growth rate (CAGR) of the share price over the three-year performance period. The mid-market share price on 25 September 2020 was £0.53 per Ordinary share. As different levels of performance are achieved the number of shares that vest increases up to a maximum, as set out below:

Share price CAGR	Multiple of share price (at 3 years)	Proportion vesting	Andrew Newland Number	Ian Griffiths Number	Total Number
< 20%	< 1.70	0%	0	0	0
> 20%	> 1.70	20%	360,000	240,000	600,000
> 35%	> 2.50	50%	900,000	600,000	1,500,000
> 50%	> 3.40	100%	1,800,000	1,200,000	3,000,000

Award #3 – 12 November 2021
The Remuneration Committee approved a grant of nil-cost options to Executive Directors on 12 November 2021 over a maximum of 3,000,000 Ordinary shares of £0.10. The LTIP Options have performance conditions as set out below, a performance period of three years and an additional holding period of two years.

The performance conditions for the LTIP Options relate to the compound annual growth rate (CAGR) of the share price being met at some point over the three-year performance period. The mid-market share price on 12 November 2021 was £1.285 per Ordinary share. As different levels of performance are achieved the number of shares that vest increases up to a maximum, as set out below:

Share price CAGR	Multiple of share price (3 years)	Proportion vesting	Andrew Newland Number	Ian Griffiths Number	Total Number
< 20%	< 1.73	0%	0	0	0
> 20%	> 1.73	20%	360,000	240,000	600,000
> 25%	> 1.95	50%	900,000	600,000	1,500,000
> 30%	> 2.20	100%	1,800,000	1,200,000	3,000,000

REMUNERATION REPORT CONTINUED

Share options

Name	Date of grant	At 1 January 2022	Granted	Lapsed	Cancelled	Exercised	**At 31 December 2022**	Vested – capable of exercise	Exercise price (£)	Earliest exercise date	Expiry date
I F Griffiths	18/11/2011	187,315	–	(187,315)	–	–	**–**	–	0.7550	Note (1)	17/11/2022
	05/11/2012	312,685	–	(312,685)	–	–	**–**	–	0.7550	Note (1)	17/11/2022
	10/11/2014	500,000	–	–	–	–	**500,000**	–	0.8625	Note (2)	09/11/2024
	12/11/2015	46,980	–	–	–	–	**46,980**	46,980	0.1000	Note (3)	11/11/2025
	25/11/2016	500,000	–	–	–	–	**500,000**	500,000	0.6450	Note (4)	24/11/2026
		1,546,980	–	(500,000)	–	–	**1,046,980**	546,980			
A D W Newland	18/11/2011	1,000,000	–	(1,000,000)	–	–	**–**	–	0.7550	Note (1)	17/11/2022
	10/11/2014	1,000,000	–	–	–	–	**1,000,000**	–	0.8625	Note (2)	09/11/2024
	25/11/2016	1,000,000	–	–	–	–	**1,000,000**	1,000,000	0.6450	Note (4)	24/11/2026
		3,000,000	–	(1,000,000)	–	–	**2,000,000**	1,000,000			

(1) Vesting is subject to a) the performance conditions that (i) the Company's share price must have increased to £2.00 at some point since the date of grant and (ii) the Parsortix separation device must have been demonstrated to successfully capture circulating tumour cells from cancer patient blood (this condition has been met), and b) a service condition with options vesting over a three-year period (this condition has been met). The £2.00 share price target performance condition was not met by the expiry date and these options therefore lapsed in the year.

(2) Vesting is subject to the performance conditions that a) the Company's share price must have increased to £2.00, £2.25, £2.50 and £2.75 at some point since the date of grant for each quarter of the allocation (this condition has not yet been met) and b) a time/event condition with options vesting after five years or on the sale of the Parsortix business, whichever is earliest (this condition has been met).

(3) Options were granted as Bonus Options in accordance with the Remuneration Committee's discretion to settle an element of the Annual Bonus in the form of share options. The Bonus Options vested immediately and are exercisable at par value.

(4) Vesting is subject to a) a performance condition that the Company's share price has risen by at least 100% at some point from the market price on 25 November 2016, and b) a service condition with options vesting over a three-year period. These conditions have been met and the options are fully vested and capable of exercise.

No share options were issued to Directors in the current year (2021: nil). No Directors' share options were forfeited or cancelled in the current year (2021: nil). 1,500,000 share options lapsed in the current year (2021: nil). No share options were exercised in the current year (2021: 1,523,826).

Note 20 provides additional information on share options and LTIP Options.

Shareholder return

The market price of the Company's shares on 31 December 2022 was £0.505 and the range of market price during the year from 1 January until 31 December 2022 was between £0.45 (low) and £1.64 (high).

This report was approved by the Board of Directors on 20 April 2023 and is signed on its behalf by:

Garth Selvey
Remuneration Committee Chairman
20 April 2023

INDEPENDENT AUDITORS' REPORT

To the Members of ANGLE plc

Report on the audit of the Financial Statements

Opinion

In our opinion, ANGLE plc's Group Financial Statements and Company Financial Statements (the "Financial Statements"):

- give a true and fair view of the state of the Group's and of the Company's affairs as at 31 December 2022 and of the Group's loss and the Group's and Company's cash flows for the year then ended;
- have been properly prepared in accordance with UK-adopted international accounting standards as applied in accordance with the provisions of the Companies Act 2006; and
- have been prepared in accordance with the requirements of the Companies Act 2006.

We have audited the Financial Statements, included within the Annual Report and Financial Statements (the "Annual Report"), which comprise: Consolidated and Company Statements of Financial Position as at 31 December 2022; Consolidated Statement of Comprehensive Income, Consolidated and Company Statements of Cash Flows and Consolidated and Company Statements of Changes in Equity for the year then ended; and the notes to the Financial Statements, which include a description of the significant accounting policies.

Basis for opinion

We conducted our audit in accordance with International Standards on Auditing (UK) ("ISAs (UK)") and applicable law. Our responsibilities under ISAs (UK) are further described in the Auditors' responsibilities for the audit of the Financial Statements section of our report. We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

Independence

We remained independent of the Group in accordance with the ethical requirements that are relevant to our audit of the Financial Statements in the UK, which includes the FRC's Ethical Standard, as applicable to listed entities, and we have fulfilled our other ethical responsibilities in accordance with these requirements.

Our audit approach

Overview

Audit scope

- The ANGLE Group's finance function is in the UK. The Group also operates in the US and Canada. It was announced on 18 October 2022 that the Canadian operations would be closed with formal company dissolution anticipated in 2023.
- The Group's head office is located in the UK where our work over the Group consolidation was performed.

Key audit matters

- Going concern (Group and Company)
- Expected credit loss on amounts due from Group undertakings (Company)

Materiality

- Overall Group materiality: £1,222,000 (2021: £868,000) based on 5% of loss before tax.
- Overall Company materiality: £1,041,000 (2021: £937,000) based on 1% of total assets.
- Performance materiality: £917,000 (2021: £651,000) (Group) and £781,000 (2021: £702,750) (Company).

The scope of our audit

As part of designing our audit, we determined materiality and assessed the risks of material misstatement in the Financial Statements.

INDEPENDENT AUDITORS' REPORT CONTINUED

To the Members of ANGLE plc

Our audit approach continued

Key audit matters

Key audit matters are those matters that, in the auditors' professional judgement, were of most significance in the audit of the Financial Statements of the current period and include the most significant assessed risks of material misstatement (whether or not due to fraud) identified by the auditors, including those which had the greatest effect on: the overall audit strategy; the allocation of resources in the audit; and directing the efforts of the engagement team. These matters, and any comments we make on the results of our procedures thereon, were addressed in the context of our audit of the Financial Statements as a whole, and in forming our opinion thereon, and we do not provide a separate opinion on these matters.

This is not a complete list of all risks identified by our audit.

Expected credit loss on amounts due from Group undertakings is a new key audit matter this year. Valuation of share-based payments, which was a key audit matter last year, is no longer included because the Company did not grant any new share options during the year. Otherwise, the key audit matters below are consistent with last year.

Key audit matter	How our audit addressed the key audit matter
Going concern (Group and Company) For the year ended 31 December 2022, the Group used net cash in operating activities of £16.1 million and the Company generated net cash from operating activities of £nil. Cash and cash equivalents as at 31 December 2022 were £31.9 million for the Group and £30.8 million for the Company. As stated in Note 1.4 to the Annual Report and Financial Statements, the Directors have prepared and reviewed the financial projections for a period in excess of 12 months from the date of approval of these Financial Statements with discretionary expenditure carefully controlled in line with available resources, as certain projects may be deferred until additional resources are available. Based on the level of existing cash and expected R&D tax credits, the projected income and expenditure (the quantum and timing of some of which is at the Group's discretion) and other potential sources of funding, the Directors have a reasonable expectation that the Company and Group have adequate resources to continue in business for the foreseeable future. Accordingly, the going concern basis has been used in preparing the Financial Statements.	For our audit response and conclusions in respect of going concern, see the 'Conclusions relating to going concern' section below.
Expected credit loss on amounts due from Group undertakings (Company) Companies adopting IFRS 9 in their stand-alone Financial Statements are required to calculate expected credit losses on all financial assets, including intercompany loans within the scope of IFRS 9. The Directors have calculated an expected credit loss on the amounts due from Group undertakings by assigning probabilities of recovery to various repayment scenarios as discussed in Note C1.3. The impairment charge for the year totals £13.1 million and the provision as at 31 December 2022 totals £47.5 million.	We obtained the Directors' calculation, tested the mathematical accuracy and assessed the probabilities assigned to each scenario including understanding the movements from prior year and challenging the probabilities assigned to the various scenarios. From the procedures performed, we found that the Directors' expected credit loss provision is supportable and that the disclosures within the Company Financial Statements are appropriate.

How we tailored the audit scope
We tailored the scope of our audit to ensure that we performed enough work to be able to give an opinion on the Financial Statements as a whole, taking into account the structure of the Group and the Company, the accounting processes and controls, and the industry in which they operate.

In establishing the overall approach to the Group audit, we assessed the audit significance of each entity in the Group by reference to both its financial significance and other indicators of audit risk, such as the complexity of operations and the degree of estimation and judgement in the financial results.

Following this assessment, we determined that we needed to focus our audit work on ANGLE Europe Limited and ANGLE Biosciences Inc. Through discussions with the Group finance team, we obtained an understanding of the operational activities of these entities, and appropriately determined the audit risks for each entity based on the size of individual financial statement line items and the judgements/ estimates made by the Directors. This, together with additional procedures performed at the Group level over the consolidation process, gave us the evidence we needed for our opinion on the Financial Statements as a whole.

The financially significant components for the audit were ANGLE Europe Limited and ANGLE Biosciences Inc. as these were the only two components that contributed more than 15% to the loss before tax. We also performed audit work on ANGLE plc for cash and cash equivalents and total equity and for ANGLE North America Inc. we audited payroll costs, right-of-use assets, property, plant and equipment and lease liabilities in order to ensure we had sufficient coverage over these financial statement line items from a Group perspective. We also performed analytical procedures on certain out of scope entities.

All work was done by the Group audit team and no component auditors were involved in the audit.

The impact of climate risk on our audit
As part of our audit we made enquiries of management to understand the extent of the potential impact of climate risk on the Group's and Company's Financial Statements, and we remained alert when performing our audit procedures for any indicators of the impact of climate risk. Our procedures did not identify any material impact as a result of climate risk on the Group's and Company's Financial Statements.

Materiality
The scope of our audit was influenced by our application of materiality. We set certain quantitative thresholds for materiality. These, together with qualitative considerations, helped us to determine the scope of our audit and the nature, timing and extent of our audit procedures on the individual financial statement line items and disclosures and in evaluating the effect of misstatements, both individually and in aggregate, on the Financial Statements as a whole.

Based on our professional judgement, we determined materiality for the Financial Statements as a whole as follows:

	Financial Statements – Group	Financial Statements – Company
Overall materiality	£1,222,000 (2021: £868,000)	£1,041,000 (2021: £937,000)
How we determined it	5% of loss before tax	1% of total assets
Rationale for benchmark applied	Whilst the Group has generated revenue in the year ended 31 December 2022 it is still loss making for the year. Given this and based on the benchmarks used in the Annual Report, we believe that loss before tax is the primary measure used by the shareholders in assessing the financial performance of the Group, and is a generally accepted auditing benchmark.	The entity fulfils the role of the holding company within the Group. The entity's main function in the Group has historically been the raising of funds through equity issues to fund the Group's development activities and manage the Group's cash reserves. As such, we believe that total assets is the most appropriate measure to assess the financial position of the Company, and is a generally accepted auditing benchmark.

For each component in the scope of our Group audit, we allocated a materiality that is less than our overall Group materiality. The range of materiality allocated across components was between £470,000 and £1,155,000. Certain components were audited to a local statutory audit materiality that was also less than our overall Group materiality.

We use performance materiality to reduce to an appropriately low level the probability that the aggregate of uncorrected and undetected misstatements exceeds overall materiality. Specifically, we use performance materiality in determining the scope of our audit and the nature and extent of our testing of account balances, classes of transactions and disclosures, for example in determining sample sizes. Our performance materiality was 75% (2021: 75%) of overall materiality, amounting to £917,000 (2021: £651,000) for the Group Financial Statements and £781,000 (2021: £702,750) for the Company Financial Statements.

In determining the performance materiality, we considered a number of factors - the history of misstatements, risk assessment and aggregation risk and the effectiveness of controls - and concluded that an amount at the upper end of our normal range was appropriate.

We agreed with those charged with governance that we would report to them misstatements identified during our audit above £61,100 (Group audit) (2021: £43,400) and £52,050 (Company audit) (2021: £46,850) as well as misstatements below those amounts that, in our view, warranted reporting for qualitative reasons.

INDEPENDENT AUDITORS' REPORT CONTINUED

To the Members of ANGLE plc

Conclusions relating to going concern

Our evaluation of the Directors' assessment of the Group's and the Company's ability to continue to adopt the going concern basis of accounting included:

- Testing the mathematical integrity of the cash flow forecasts and assessing management's historical forecasting accuracy.
- Assessing the completeness and accuracy of costs included within the cash flow forecasts based on historical expenditure and committed future costs.
- Assessing the reasonableness of assumptions within the base case model around sales growth, based on our understanding of the business and by comparing against historical results.
- Evaluating a scenario with discretionary expenditure carefully controlled in line with available resources under which certain projects may be deferred until additional resources are available. We evaluated the levers available to the Directors in order to conserve cash, considering the timing of when such decisions would have to be made in order to have the desired effect on the cash run rate of the business. This scenario showed that based on the level of existing cash and expected R&D tax credits, the projected income and expenditure (the quantum and timing of some of which is at the Group's discretion) and other potential sources of funding, the Directors have a reasonable expectation that the Company and Group have adequate resources to continue in business for the foreseeable future.

Based on the work we have performed, we have not identified any material uncertainties relating to events or conditions that, individually or collectively, may cast significant doubt on the Group's and the Company's ability to continue as a going concern for a period of at least twelve months from when the Financial Statements are authorised for issue.

In auditing the Financial Statements, we have concluded that the Directors' use of the going concern basis of accounting in the preparation of the Financial Statements is appropriate.

However, because not all future events or conditions can be predicted, this conclusion is not a guarantee as to the Group's and the Company's ability to continue as a going concern.

Our responsibilities and the responsibilities of the Directors with respect to going concern are described in the relevant sections of this report.

Reporting on other information

The other information comprises all of the information in the Annual Report other than the Financial Statements and our Auditors' Report thereon. The Directors are responsible for the other information. Our opinion on the Financial Statements does not cover the other information and, accordingly, we do not express an audit opinion or, except to the extent otherwise explicitly stated in this report, any form of assurance thereon.

In connection with our audit of the Financial Statements, our responsibility is to read the other information and, in doing so, consider whether the other information is materially inconsistent with the Financial Statements or our knowledge obtained in the audit, or otherwise appears to be materially misstated. If we identify an apparent material inconsistency or material misstatement, we are required to perform procedures to conclude whether there is a material misstatement of the Financial Statements or a material misstatement of the other information. If, based on the work we have performed, we conclude that there is a material misstatement of this other information, we are required to report that fact. We have nothing to report based on these responsibilities.

With respect to the Strategic Report and Directors' Report, we also considered whether the disclosures required by the UK Companies Act 2006 have been included.

Based on our work undertaken in the course of the audit, the Companies Act 2006 requires us also to report certain opinions and matters as described below.

Strategic Report and Directors' Report

In our opinion, based on the work undertaken in the course of the audit, the information given in the Strategic Report and Directors' Report for the year ended 31 December 2022 is consistent with the Financial Statements and has been prepared in accordance with applicable legal requirements.

In light of the knowledge and understanding of the Group and Company and their environment obtained in the course of the audit, we did not identify any material misstatements in the Strategic Report and Directors' Report.

Responsibilities for the Financial Statements and the audit

Responsibilities of the Directors for the Financial Statements

As explained more fully in the Directors' responsibilities, the Directors are responsible for the preparation of the Financial Statements in accordance with the applicable framework and for being satisfied that they give a true and fair view. The Directors are also responsible for such internal control as they determine is necessary to enable the preparation of Financial Statements that are free from material misstatement, whether due to fraud or error.

In preparing the Financial Statements, the Directors are responsible for assessing the Group's and the Company's ability to continue as a going concern, disclosing, as applicable, matters related to going concern and using the going concern basis of accounting unless the Directors either intend to liquidate the Group or the Company or to cease operations, or have no realistic alternative but to do so.

Auditors' responsibilities for the audit of the Financial Statements

Our objectives are to obtain reasonable assurance about whether the Financial Statements as a whole are free from material misstatement, whether due to fraud or error, and to issue an auditors' report that includes our opinion. Reasonable assurance is a high level of assurance, but is not a guarantee that an audit conducted in accordance with ISAs (UK) will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these Financial Statements.

Irregularities, including fraud, are instances of non-compliance with laws and regulations. We design procedures in line with our responsibilities, outlined above, to detect material misstatements in respect of irregularities, including fraud. The extent to which our procedures are capable of detecting irregularities, including fraud, is detailed below.

Based on our understanding of the Group and industry, we identified that the principal risks of non-compliance with laws and regulations related to Companies Act 2006 and tax regulation, and we considered the extent to which non-compliance might have a material effect on the Financial Statements. We evaluated management's incentives and opportunities for fraudulent manipulation of the Financial Statements (including the risk of override of controls), and determined that the principal risks were related to posting inappropriate journal entries to increase revenue and misappropriation of cash. We have also identified a risk of manipulation of publications and regulatory announcements, in particular after the FDA clearance of the Parsortix system in May 2022 and prior to the July 2022 fundraise, given any announcements around this time may have a significant impact on share price and thus management compensation for example via the LTIP. Audit procedures performed by the engagement team included:

- Discussions with the Directors, including considerations of known or suspected instances of fraud or non-compliance with laws and regulations as well as review of Board and other Committee minutes.
- Performing detailed testing over compliance with tax legislation including evaluating the Group's transfer pricing arrangements and auditing R&D tax credits.
- Evaluation of management's controls designed to prevent and detect irregularities.
- Identifying and testing journal entries, in particular any journal entries that credit cash or credit revenues where the offsetting entry was to an unexpected account based on the normal flow of transactions for these financial statement line items.
- Assessing the governance process around publications and review and approval of a sample of publications on the Company's website after the FDA clearance of the Parsortix system in May 2022 and prior to the July 2022 fundraise.

There are inherent limitations in the audit procedures described above. We are less likely to become aware of instances of non-compliance with laws and regulations that are not closely related to events and transactions reflected in the Financial Statements. Also, the risk of not detecting a material misstatement due to fraud is higher than the risk of not detecting one resulting from error, as fraud may involve deliberate concealment by, for example, forgery or intentional misrepresentations, or through collusion.

Our audit testing might include testing complete populations of certain transactions and balances, possibly using data auditing techniques. However, it typically involves selecting a limited number of items for testing, rather than testing complete populations. We will often seek to target particular items for testing based on their size or risk characteristics. In other cases, we will use audit sampling to enable us to draw a conclusion about the population from which the sample is selected.

A further description of our responsibilities for the audit of the Financial Statements is located on the FRC's website at: **www.frc.org.uk/auditorsresponsibilities**. This description forms part of our auditors' report.

Use of this report

This report, including the opinions, has been prepared for and only for the Company's members as a body in accordance with Chapter 3 of Part 16 of the Companies Act 2006 and for no other purpose. We do not, in giving these opinions, accept or assume responsibility for any other purpose or to any other person to whom this report is shown or into whose hands it may come save where expressly agreed by our prior consent in writing.

INDEPENDENT AUDITORS' REPORT CONTINUED

To the Members of ANGLE plc

Other required reporting

Companies Act 2006 exception reporting

Under the Companies Act 2006 we are required to report to you if, in our opinion:

- we have not obtained all the information and explanations we require for our audit; or
- adequate accounting records have not been kept by the Company, or returns adequate for our audit have not been received from branches not visited by us; or
- certain disclosures of Directors' remuneration specified by law are not made; or
- the Company Financial Statements are not in agreement with the accounting records and returns.

We have no exceptions to report arising from this responsibility.

David Farmer (Senior Statutory Auditor)
for and on behalf of PricewaterhouseCoopers LLP
Chartered Accountants and Statutory Auditors
Reading
20 April 2023

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME

For the year ended 31 December 2022

	Note	**2022 £'000**	2021 £'000
Revenue	2	**1,041**	1,013
Cost of sales	3	**(428)**	(302)
Gross profit		**613**	711
Other operating income		**1**	41
Operating costs	3	**(24,821)**	(17,987)
Operating profit/(loss)		**(24,207)**	(17,235)
Finance income	7	**136**	29
Finance costs	7	**(368)**	(157)
Profit/(loss) before tax		**(24,439)**	(17,363)
Tax (charge)/credit	8	**2,753**	2,351
Profit/(loss) for the year		**(21,686)**	(15,012)
Other comprehensive income/(loss)			
Items that may be subsequently reclassified to profit or loss:			
Exchange differences on translating foreign operations		**(2,023)**	(175)
Other comprehensive income/(loss)		**(2,023)**	(175)
Total comprehensive income/(loss) for the year		**(23,709)**	(15,187)
Earnings/(loss) per share attributable to owners of the parent	9		
Basic and Diluted (pence per share)		**(8.79)**	(6.67)

All activity arose from continuing operations.

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

As at 31 December 2022

	Note	2022 £'000	2021 £'000
Assets			
Non-current assets			
Intangible assets	11	**2,764**	3,573
Property, plant and equipment	12	**3,505**	2,172
Right-of-use assets	13	**4,971**	2,204
Total non-current assets		**11,240**	7,949
Current assets			
Inventories	15	**2,059**	1,748
Trade and other receivables	16	**1,797**	1,269
Taxation		**2,876**	4,510
Cash and cash equivalents		**31,896**	31,839
Total current assets		**38,628**	39,366
Total assets		**49,868**	47,315
Non-current liabilities			
Lease liabilities	13	**(4,339)**	(1,816
Provisions	17	**(157)**	–
Trade and other payables	18	**(59)**	(257)
Total non-current liabilities		**(4,555)**	(2,073)
Current liabilities			
Lease liabilities	13	**(662)**	(522)
Provisions	17	**(610)**	–
Trade and other payables	18	**(3,978)**	(4,390)
Total current liabilities		**(5,250)**	(4,912)
Total liabilities		**(9,805)**	(6,985)
Net assets		**40,063**	40,330
Equity			
Share capital	19	**26,058**	23,514
Share premium		**115,918**	99,406
Share-based payments reserve		**5,321**	2,727
Other reserve		**2,553**	2,553
Translation reserve		**(5,983)**	(3,960)
Accumulated losses		**(103,702)**	(83,808)
ESOT shares	21	**(102)**	(102)
Total equity		**40,063**	40,330

The Consolidated Financial Statements on pages 77 to 105 were approved by the Board of Directors and authorised for issue on 20 April 2023 and signed on its behalf by:

Ian F Griffiths
Director

Andrew D W Newland
Director

CONSOLIDATED STATEMENT OF CASH FLOWS

For the year ended 31 December 2022

	2022 £'000	2021 £'000
Operating activities		
Profit/(loss) before tax	**(24,439)**	(17,363)
Adjustments for:		
Depreciation and impairment of property, plant and equipment	**920**	701
Depreciation and impairment of right-of-use assets	**940**	532
(Profit)/loss on disposal of property, plant and equipment	**172**	4
Amortisation and impairment of intangible assets	**978**	254
Share-based payment charge	**4,386**	1,325
Exchange differences	**(2,072)**	(170)
Net finance (income)/costs	**232**	128
Operating cash flows before movements in working capital	**(18,883)**	(14,589)
(Increase)/decrease in inventories	**(580)**	(1,015)
(Increase)/decrease in trade and other receivables	**(650)**	204
Increase/(decrease) in trade and other payables	**(978)**	1,417
Increase/(decrease) in provisions	**594**	–
Operating cash flows	**(20,497)**	(13,983)
Research and development tax credits received	**4,506**	–
Overseas tax payments	**(59)**	(27)
Net cash from/(used in) operating activities	**(16,050)**	(14,010)
Investing activities		
Purchase of property, plant and equipment	**(1,718)**	(1,666)
Purchase of intangible assets	**(169)**	(122)
Transfer (to)/from short-term deposits	**–**	16,538
Interest received	**136**	24
Net cash from/(used in) investing activities	**(1,751)**	14,774
Financing activities		
Net proceeds from issue of share capital – placing	**18,922**	18,765
Proceeds from issue of share capital – share option exercises	**123**	925
Principal elements of lease payments	**(814)**	(614)
Interest elements of lease payments	**(135)**	(85)
Net cash from/(used in) financing activities	**18,096**	18,991
Net increase/(decrease) in cash and cash equivalents	**295**	19,755
Cash and cash equivalents at 1 January	**31,839**	12,080
Effect of exchange rate fluctuations	**(238)**	4
Cash and cash equivalents at 31 December	**31,896**	31,839

CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2022

	Equity attributable to owners of the parent							
	Share capital £'000	Share premium £'000	Share-based payments reserve £'000	Other reserve £'000	Translation reserve £'000	Accumulated losses £'000	ESOT shares £'000	Total equity £'000
At 1 January 2021	**21,540**	**81,532**	**1,745**	**2,553**	**(3,785)**	**(69,139)**	**(102)**	**34,344**
For the year to 31 December 2021								
Consolidated profit/(loss)						(15,012)		(15,012)
Other comprehensive income/(loss):								
Exchange differences on translating foreign operations					(175)			(175)
Total comprehensive income/(loss)					(175)	(15,012)		(15,187)
Issue of shares (net of costs)	1,974	17,874						19,848
Share-based payment charge			1,325					1,325
Released on exercise			(295)			295		–
Released on forfeiture/lapse			(48)			48		–
At 31 December 2021	**23,514**	**99,406**	**2,727**	**2,553**	**(3,960)**	**(83,808)**	**(102)**	**40,330**
For the year to 31 December 2022								
Consolidated profit/(loss)						(21,686)		(21,686)
Other comprehensive income/(loss):								
Exchange differences on translating foreign operations					(2,023)			(2,023)
Total comprehensive income/(loss)					(2,023)	(21,686)		(23,709)
Issue of shares (net of costs)	2,544	16,512						19,056
Share-based payment charge			4,386					4,386
Released on exercise			(43)			43		–
Released on forfeiture/lapse			(1,749)			1,749		–
At 31 December 2022	**26,058**	**115,918**	**5,321**	**2,553**	**(5,983)**	**(103,702)**	**(102)**	**40,063**

Share premium
Represents amounts subscribed for share capital in excess of nominal value, net of directly attributable share issue costs.

Share-based payments reserve
The share-based payments reserve is used for the corresponding entry to the share-based payments charged through a) the Consolidated Statement of Comprehensive Income for employee incentive arrangements relating to ANGLE plc equity and b) the Consolidated Statement of Financial Position for acquired intangible assets in investments comprising intellectual property (IP). Transfers are made from this reserve to accumulated losses as the related share options are exercised, forfeited, lapse or expire.

Other reserve
The other reserve is a merger reserve arising from the acquisition of the former holding company.

Translation reserve
The translation reserve comprises cumulative exchange differences arising on consolidation from the translation of the Financial Statements of international operations. Under IFRS this is separated from accumulated losses.

ESOT shares
This reserve relates to shares held by the ANGLE Employee Share Ownership Trust (ESOT) and may be used to assist in meeting the obligations under employee remuneration schemes.

Accumulated losses
Represents cumulative profit and loss net of distribution to owners.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

For the year ended 31 December 2022

1 Accounting policies

1.1 Basis of preparation

The Financial Statements of the Group have been prepared in accordance with UK-adopted international accounting standards for the year ended 31 December 2022 (including comparatives for the year ended 31 December 2021). They have also been prepared in accordance with those parts of the Companies Act 2006 that apply to companies reporting under those standards.

The basis of preparation of the Financial Statements of the Parent Company is set out in Note C1.1 and the Financial Statements are presented on pages 106 to 111.

Accounting standards adopted in the year

The following standards relevant to the Group have been amended or implemented during the year:

Various	Narrow scope amendments to IFRS 3, IAS 16, IAS 37 and some Annual Improvements 2018-2020

The Consolidated Financial Statements have been prepared in accordance with these changes where relevant. Their adoption has not had a material impact on the Consolidated Financial Statements. Apart from these changes, the accounting policies set out in the Notes have been applied consistently to both reporting years presented in these Consolidated Financial Statements.

Accounting standards issued but not yet effective

The following pronouncements have been issued by the IASB and are effective for annual years beginning on or after 1 January 2022. The Directors have not yet assessed the impact of the adoption of these Standards and Interpretations for future years.

Amendments to IFRS 16	Leases – Lease Liability in a Sale and Leaseback
Amendments to IFRS 17 and IFRS 4	Insurance contracts – deferral of IFRS 9
Amendments to IAS 1	Presentation of financial statements – on classification of liabilities
Amendments to IAS 1	Presentation of financial statements – on non-current liabilities with covenants
Various	Narrow scope amendments to IAS 1, Practice statement 2 and IAS 8
Amendments to IAS 12	Deferred tax related to assets and liabilities arising from a single transaction
Amendments to IAS 8	Accounting policies, Changes in Accounting Estimates and Errors: Definition of Accounting Estimates
IFRS 17	Insurance contracts – as amended in December 2021

1.2 Accounting convention

These Financial Statements have been prepared under the historical cost convention. The basis of consolidation is set out in Note 1.5.

1.3 Presentation of Financial Statements

The financial information, in the form of the primary statements contained in this report, is presented in accordance with International Accounting Standard (IAS) 1 Presentation of Financial Statements. The Group has reviewed the items disclosed separately on the face of the Statement of Comprehensive Income and the components of financial performance considered by management to be significant, or for which separate disclosure would assist, both in a better understanding of financial performance and in making projections of future results. This has been done taking into account the materiality, nature and function of components of income and expense.

1.4 Going concern

The Financial Statements have been prepared on a going concern basis which assumes that the Group will be able to continue its operations for the foreseeable future.

The Group's business activities, together with the factors likely to affect its future development, performance and financial position, are set out in the Chairman's Statement and Strategic Report on pages 02 to 51. The principal risks and uncertainties are stated on pages 33 to 41. In addition, Note 14 to the Financial Statements includes details of the Group's exposure to capital risk, liquidity risk, credit risk, interest rate risk and foreign currency risk.

The Directors have considered the uncertainties, risks and potential impact on the business associated with potential negative trading scenarios, market and geopolitical uncertainty (Ukraine-Russia conflict). Discretionary expenditure within the business provides flexibility to scale back operations to address adverse events if required. Mitigation measures to reduce costs could be taken if needed and other potential sources of funding exist such as grants, exclusivity and/or milestone payments for corporate partnerships being developed and equity proceeds.

The Directors have prepared and reviewed the financial projections for a period in excess of 12 months from the date of approval of these Financial Statements with discretionary expenditure carefully controlled in line with available resources, as certain projects may be deferred until additional resources are available. Based on the level of existing cash and expected R&D tax credits, the projected income and expenditure (the quantum and timing of some of which is at the Group's discretion) and other potential sources of funding, the Directors have a reasonable expectation that the Company and Group have adequate resources to continue in business for the foreseeable future. Accordingly, the going concern basis has been used in preparing the Financial Statements.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

1 Accounting policies continued

1.5 Basis of consolidation

The Consolidated Financial Statements incorporate the Financial Statements of the Company and its subsidiaries.

Subsidiary undertakings

Subsidiary undertakings are entities controlled by the Group, generally as a result of owning a shareholding of more than half of the voting rights. The Group controls an entity when it is exposed to, or has rights to, variable returns from its involvement with the entity and has the ability to affect those returns through its power over the entity.

Subsidiary undertakings are consolidated on the basis of the acquisition method of accounting. Under this method of accounting the results of subsidiaries sold or acquired are included in the consolidated statement of comprehensive income up to or from the date control passes. Subsidiary undertakings' accounting policies are amended where necessary to ensure consistency with the policies adopted by the Group.

Intra-group transactions and balances are eliminated fully on consolidation and the consolidated financial statements reflect external transactions only.

1.6 Business combinations

Acquisitions of businesses are accounted for using the acquisition method. The consideration for each acquisition is measured at the aggregate of the fair values (at the date of exchange) of identifiable assets, liabilities incurred or assumed, and equity instruments issued by the Group in exchange for control of the acquired entity. Identifiable assets are recognised if the asset is separable or arises from contractual or other legal rights and its fair value can be measured reliably. The excess of the cost of acquisition over the fair value of the Group's share of the identifiable net assets, including intangible assets, is recorded as goodwill. If the cost of acquisition is less than the fair value of the net assets acquired the difference is recognised directly in the income statement as a bargain purchase. Acquisition-related costs are charged to the statement of comprehensive income as incurred.

Where a business combination is achieved in stages, the Group's previously held interests in the acquired entity are re-measured to fair value at the acquisition date (i.e. the date at which the Group attains control) and the resulting gain or loss, if any, is taken through the statement of comprehensive income.

1.7 Revenue

Revenue for the sale of instruments, cassettes and reagents "products" and instrument hire, fee-for-service, support and maintenance "services" is measured at the fair value of the consideration received or receivable for the sale of products and services net of sales taxes, rebates and discounts and excludes intercompany sales.

Revenue for the delivery of pharma services and assay development is recognised only when the performance obligations are satisfied. Customer contracts clearly identify key events or milestones against which performance can be measured.

Where contracts contain multiple deliverables, and the value of each deliverable can be determined with reasonable certainty, then the transaction price, assessed against a standard price list, will be allocated to each performance obligation based on the expected cost of each item.

Sale of products

Revenue from the sale of products is recognised when control over the products has transferred to the customer. This is usually when a Group company has delivered products to the customer, the customer has accepted delivery of the products and collection of the related receivables is reasonably assured.

A small number of customers may request Bill and Hold arrangements, where the Group holds the goods sold to the customer on their behalf until the customer is ready to receive them. Revenue is only recognised on a bill and hold basis when a formal contract is in place, the goods are on hand and are separately identified as belonging to the customer and are unable to be redirected to an alternative customer, are ready for delivery, and the customer has acknowledged formal acceptance of the bill and hold transaction.

Sale of services

Revenue from services provided is recognised over the period during which the service has been performed.

Revenue from support and maintenance is recognised in the period in which the related chargeable costs are incurred and when the service is completed or where applicable on a straight-line basis over the period of the contract to match the benefits to the customer.

Revenue from pharma services is recognised in the period in which the processed sample results are reported or the harvested sample is delivered to the customer or in the case of assay development when the defined Work Package has been completed and accepted by the customer.

Contract liabilities

Advance payments received from customers are credited to contract liabilities and the related revenue is released to the consolidated statement of comprehensive income in accordance with the recognition criteria described above.

1 Accounting policies continued

1.8 Cost of sales

Cost of sales for products (Note 1.7) includes the direct costs incurred in manufacturing and bringing products to sale in the market (shipping, installation, training and evaluation).

Cost of sales for support and maintenance services (Note 1.7) includes the direct costs incurred in providing the service (time, travel and parts) and are reflected in costs of sales in line with recognised revenues.

Cost of sales for pharma services and assay development (Note 1.7) includes the direct costs incurred in providing the service (time and consumables) and are reflected in costs of sales in line with recognised revenues.

1.9 Other operating income – grants

Grant income is disclosed as Other operating income on the face of the consolidated statement of comprehensive income.

Grant income receivable or received in respect of revenue expenditure is released to the statement of comprehensive income as the related expenditure is incurred when there is a reasonable assurance that the grant money will be received, and any conditions attached to it have been fulfilled. Grant income receivable is held on the statement of financial position as contract assets and grant income received in advance of expenditure is held on the statement of financial position as contract liabilities.

Grant income receivable or received in respect of capital expenditure is recognised as contract liabilities in the statement of financial position and is released to the statement of comprehensive income on a straight-line basis over the expected useful life of the related assets.

1.10 Employee benefits

Share-based payments

IFRS 2 Share-based Payment has been applied to all share-based payments.

Share-based incentive arrangements which allow Group employees to acquire shares of the Company may be provided to employees, subject to certain criteria. The fair value of options granted is recognised as a cost of employment within operating costs with a corresponding increase in equity. Share options granted are valued at the date of grant using an appropriate option pricing model and taking into account the terms and conditions upon which they were granted. Market related performance conditions are taken into account in calculating the fair value, while service conditions and non-market related performance conditions are excluded from the fair value calculation, although the latter are included in initial estimates about the number of instruments that are expected to vest. The fair value is charged to operating costs over the vesting period of the award, which is the period over which all the specified vesting conditions are to be satisfied. Options are fully vested and capable of exercise when the employee becomes unconditionally entitled to the options. The annual charge is modified to take account of revised estimates about the number of instruments that are expected to vest, for example, options granted to employees who leave the Group during the performance or service condition vesting period and forfeit their rights to the share options and in the case of non-market related performance conditions, where it becomes unlikely they will vest. A modification to an award that is beneficial to an employee will result in an increased charge, as determined at the modification date using an appropriate option pricing model and inputs, and is recognised over the remaining vesting period. A change to market related performance conditions results in a change in the fair value of the instruments granted. A change in service conditions and non-market related performance conditions results in a revision to the estimated number of instruments that will vest.

For options granted to employees under unapproved share-based payment compensation schemes, including the Long-Term Incentive Plan, to the extent that the share price at the reporting date is greater than the exercise price then a provision is made for any employer's National Insurance Contributions or equivalent. Share option agreements in the UK and Canada include a tax indemnity that allows employer's National Insurance Contributions, or equivalent, to be recovered from the Optionholder and where this is likely to be applied a receivable for such taxes is also recorded, otherwise a charge is made to the statement of comprehensive income.

Pension obligations

Pension costs are charged against profits as they fall due and represent the amount of contributions payable to the Group's defined contribution pension scheme or employee personal pension schemes on an individual basis. The Group has no further payment obligations once the contributions have been paid.

Compensated absences

A liability for short-term compensated absences, such as vacation, is recognised for the amount the Group may be required to pay as a result of the unused entitlement that has accumulated at the reporting date.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

1 Accounting policies continued

1.11 Taxes

Tax on the profit or loss for the year comprises current and deferred tax.

Current tax is the expected tax payable on the taxable income for the year, using tax rates (and laws) that have been enacted or substantively enacted at the reporting date, and any adjustment to tax payable in respect of previous years.

The Group undertakes research and development activities. In the UK these activities qualify for tax relief and result in tax credits.

Deferred tax is provided for in full on all temporary differences resulting from the carrying value of an asset or liability and its tax base, except where they arise from the initial recognition of goodwill or from the initial recognition of an asset or liability that at the date of initial recognition does not affect accounting or taxable profit or loss on a transaction that is not a business combination. Deferred tax is determined using tax rates (and laws) that have been enacted or substantively enacted at the reporting date and are expected to apply when the related deferred tax liability is settled or deferred tax asset realised.

Deferred tax liabilities are recognised on any increase in the fair value of investments to the extent that substantial shareholdings relief or unutilised losses may be unavailable. Deferred tax assets are only recognised to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilised.

IAS 12 Income Taxes requires the separate disclosure of deferred tax assets and liabilities on the statement of financial position. If there is a legally enforceable right to offset current tax assets and liabilities, and they relate to taxes levied by the same tax authority, and the Group intends to settle current tax liabilities and assets on a net basis, or their tax assets and liabilities will be realised simultaneously, then deferred tax assets and liabilities are offset.

Deferred tax is provided on temporary differences arising on investments in subsidiaries, except where the timing of the reversal of the temporary difference can be controlled and it is probable that the temporary difference will not reverse in the foreseeable future.

1.12 Intangible assets

Intellectual property (IP)

IP assets (comprising patents, know-how, copyright and licences) are recognised as a purchase at cost or where acquired by the Group as a result of a business combination are initially recognised at fair value (Note 1.6 – in accordance with IFRS 3 Business Combinations), and are capitalised.

Internally generated IP costs are written off as incurred except where IAS 38 Intangible Assets criteria, as described in research and development below, would require such costs to be capitalised.

The Group's view is that capitalised IP assets have a finite useful life and to that extent they should be amortised over their respective unexpired periods with provision made for impairment when required. Capitalised IP assets are not amortised until the Group is generating an economic return from the underlying asset. Amortisation is calculated using the straight-line method to allocate the costs of IP over their estimated useful economic lives. Estimated useful economic life is based on remaining patent life or specific terms of licences or agreements, or in the absence of any observable date, ten years. The amortisation period applied to these assets, when originally assessed, ranges from 8.5 to 19 years. Amortisation is included within operating costs.

Computer software

Under IAS 38 Intangible Assets, acquired computer software should be capitalised as an intangible asset unless it is an integral part of the related hardware (such as the operating system) where it remains as an item of property, plant and equipment.

Internally developed computer software will be capitalised in accordance with the research and development accounting policy. If the software is developed for in-house use the capitalised amount is reclassified from research and development to computer software.

Amortisation is calculated using the straight-line method to allocate the cost of the software over its estimated useful economic life and is included within operating costs. The useful economic life is estimated at three years, unless there are specific circumstances that dictate this should be for a shorter or longer period.

Research and development

Research expenditure is written off as incurred.

Development expenditure is written off as incurred, except where the Directors are satisfied that a new or significantly improved product or process results and other relevant IAS 38 Intangible Assets criteria are met as to the technical, commercial and financial viability of individual projects that would require such costs to be capitalised. In such cases, the identifiable directly attributable expenditure is capitalised and amortised.

The Group's view is that capitalised assets have a finite useful life and to that extent they should be amortised over their respective unexpired periods with provision made for impairment when required. Assets capitalised are not amortised until the associated product is available for use or sale. Amortisation is calculated using the straight-line method to allocate the costs of development over the estimated useful economic lives. Estimated useful economic life is assessed by reference to the remaining patent life and may be adjusted after taking into consideration product and market characteristics such as fundamental building blocks and product life cycle specific to the category of expenditure. The amortisation period applied to these different categories when originally assessed ranges from 5.0 to 13.5 years. Amortisation is included within operating costs.

1 Accounting policies continued
1.12 Intangible assets continued

Other acquired intangible assets

Other intangible assets acquired by the Group as a result of a business combination that are separable or arise from contractual or other legal rights and can be reliably measured are initially recognised at fair value (Note 1.6 – in accordance with IFRS 3 Business Combinations) and are capitalised.

The Group's view is that these acquired intangible assets have a finite useful life and to that extent they should be amortised over their respective unexpired periods with provision made for impairment when required. Acquired intangible assets are not amortised until the Group is generating an economic return from the underlying intangible asset. Amortisation is calculated using the straight-line method to allocate the costs over their estimated useful economic lives. Estimated useful economic life is based on specific terms of contracts and agreements. Amortisation is included within operating costs. The acquired intangible assets that may be recognised and the amortisation period applied are:

Brands and trademarks	Over the expected useful life of an actively used and/or marketed brand or trademark (10 years)
Technology*	Over the remaining life of the key patents or the expected useful life (10 years)

* Technology includes patents, licensed IP, copyright on software and designs, developed and in-process products, completed and in-process research and development, documented trade secrets such as technical know-how, manufacturing and operating procedures, methods and processes.

Impairment of intangible assets excluding goodwill

The Group is required to review, at least annually, whether there are indications (events or changes in circumstances) that intangible assets have suffered impairment and that the carrying amount may exceed the recoverable amount. If there are indications of impairment then an impairment review is undertaken.

An impairment loss is recognised within operating costs for the amount by which the carrying amount in the cash-generating units (CGUs) exceeds its recoverable amount. The impairment loss is allocated to reduce the assets of the CGUs on a pro-rata basis. The recoverable amount is the higher of the asset's fair value less costs to sell and the value-in-use. In the event that an intangible asset will no longer be used, for example, when a patent is abandoned, the balance of unamortised expenditure is written off. Where intangible assets have suffered an impairment, they are reviewed for possible reversal of the impairment at each reporting date.

Impairment reviews require the estimation of the recoverable amount based on value-in-use calculations. Intangible assets relate typically to in-process development and patents and require broader assumptions than for developed technology. Key assumptions taken into consideration relate to technological, market and financial risks and include the chance of product launch taking into account the stage of development of the asset, the scale of milestone and royalty payments, overall market opportunities, market size and competitor activity, revenue projections, estimated useful lives of assets (such as patents), contractual relationships and discount and terminal value rates to determine present values of cash flows.

Goodwill

Goodwill arising in a business combination is recognised as an intangible asset at the date of acquisition and represents the excess of the cost of a business combination over the Group's interest in the fair value of the identifiable assets, liabilities and contingent liabilities including those intangible assets identified under IFRS 3 Business Combinations. After initial recognition, goodwill is stated at cost less any accumulated impairment losses.

Goodwill is deemed to have an indefinite useful life and is not amortised but is reviewed for impairment annually or more frequently if events or changes in circumstances indicate a potential impairment. Goodwill arising on a business combination is allocated to the associated CGUs expected to benefit from the acquisition and any synergies of the combination. This is then assessed against the estimation of the recoverable amount based on fair value less costs to sell calculations of the CGUs for impairment. Where the recoverable amount of the CGUs is less than the carrying amount, including goodwill, an impairment loss is recognised in operating costs. The impairment loss is allocated first to reduce the carrying amount of any goodwill allocated to the CGUs and then to assets of the CGUs on a pro-rata basis. An impairment loss recognised for goodwill is not reversed in a subsequent period.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

1 Accounting policies continued

1.13 Property, plant and equipment

Property, plant and equipment is stated at historical cost less accumulated depreciation or impairment value. Cost includes the original purchase price and expenditure that is directly attributable to the acquisition of the items to bring the asset to its working condition. Assets acquired through a business combination are initially recognised at their fair value. Depreciation is provided at rates calculated to write off the cost less estimated residual value of each asset over its expected useful economic life. Assets held under finance leases, if any, are depreciated over their expected useful economic life on the same basis as owned assets, or where shorter the lease term. Assets are reviewed for impairment when events or changes in circumstances indicate that the carrying amount may not be recoverable.

The following rates are used:

Computer equipment	33.33%	Straight-line
Fixtures, fittings and equipment	20.00% – 33.33%	Straight-line
Laboratory equipment	20.00% – 50.00%	Straight-line
Moulds and tooling	Utilisation basis	Volume
Leasehold improvements	Term of the lease	Straight-line

1.14 Leases

At the inception of a contract the Group assesses whether the contract is, or contains, a lease. A lease is defined as a contract that conveys the right to use an underlying asset for a period of time in exchange for consideration. The Group applies a single recognition and measurement approach for all leases, except for short-term leases and leases of low-value assets. The lease liabilities represent the Group's obligation to make lease payments and the right-of-use asset representing the right to use the underlying asset.

In respect of short-term leases and leases of low-value assets, the Group has elected to recognise the payments as an expense in the statement of comprehensive income on a straight-line basis over the lease term.

Right-of-use assets

The Group recognises right-of-use assets at the commencement date of the lease (the date the underlying asset is available for use). The right-of-use asset is measured at cost, which is made up of the initial lease liability, any direct costs incurred, and lease payments made at or before the commencement date net of any lease incentives received.

The Group depreciates right-of-use assets on a straight-line basis over the shorter of the lease term and the estimated useful lives of the assets over the term of the lease.

The right-of-use assets are also subject to impairment and are adjusted for any re-measurement of lease liabilities.

Lease liabilities

At the commencement date of the lease, the Group recognises lease liabilities measured at the present value of lease payments, unpaid at the date, to be made over the lease term.

In calculating the present value of lease payments, the Group uses the interest rate implicit in the lease, or the lease's incremental borrowing rate at the lease commencement date where the interest rate implicit in the lease is not readily determinable. After the commencement date, the amount of lease liabilities is increased to reflect the accretion of interest and reduced for the lease payments made. In addition, the carrying amount of lease liabilities is re-measured if there is a modification, a change in the lease term, a change in the lease payments (e.g. changes to future payments resulting from a change in an index or rate used to determine such lease payments) or a change in the assessment of an option to purchase the underlying asset.

Right-of-use assets and lease liabilities are separately identified as line items on the statement of financial position.

Short-term leases and leases of low-value assets

The Group applies the short-term lease recognition exemption to its short-term leases of property and equipment (i.e. leases that have a 12 month or less lease term from date of commencement and do not contain a purchase option). The Group also applies the lease of low-value assets recognition exemption to leases of office and laboratory equipment that are considered low value. Lease payments relating to short-term leases and leases of low-value assets are recognised as expense on a straight-line basis over the lease term.

Net investment in sublease

The Group classifies a sublease as a finance lease or an operating lease by reference to the head lease. Net investment in a sublease is created initially by derecognising the right-of-use asset and recognising a receivable equal to the amount of lease payments receivable discounted by the interest rate implicit in the lease.

1 Accounting policies continued

1.15 Instruments loaned to customers

In order to support the development of the sales platform and use of the Parsortix system in the clinical market, the Parsortix instruments may be placed on long-term loan with leading cancer research centres (key opinion leaders) so that they can provide valuable feedback on the operation of the instruments and suggest new uses and protocols, act as reference customers, identify clinical applications and provide clinical data. Where these instruments are expected to be placed for a period longer than six months, the instruments are transferred at book value to property, plant and equipment and depreciated over five years. Where instruments are placed on a short-term loan for a customer evaluation and it is expected that the instrument will be sold at the end of the loan period, the instruments are included within inventories.

1.16 Inventories

Inventories comprises finished goods (instruments, cassettes and production parts) that are available for sale and use internally or with partners, raw materials and work in progress. Inventories are initially recognised at cost and subsequently held at the lower of cost and net realisable value. Cost includes materials and direct labour. Cost is based on standard cost the basis of which is the last price paid in combination with the most frequent purchase price where there are stepped price points and is updated annually. Inventories acquired through business combinations are initially recognised at their fair value.

Net realisable value is the estimated selling price, less all estimated costs of completion and costs to be incurred in marketing, selling and distribution. Provision is made, if necessary, for any costs of modifications required to bring the asset to a working condition due to new standards and/or regulations, or for slow-moving or obsolete inventory. If net realisable value is lower than the carrying amount, a write down provision is recognised within operating costs for the amount by which the carrying amount exceeds its net realisable value.

Inventories of finished goods used for research and development projects are initially recognised at cost, as all inventories are held together and available for sale, and subsequently charged to research and development expenditure as they are used.

1.17 Employee Share Ownership Trust

The Group has an Employee Share Ownership Trust (ESOT) to assist with meeting the obligations under share option and other employee remuneration schemes. The ESOT is consolidated as if it is a subsidiary and accounted for as Treasury (own) shares. Shares in ANGLE plc held by the ESOT are stated at weighted average purchase cost and presented in the statement of financial position as a deduction from equity under the heading of ESOT shares. Gain or loss is not recognised on the purchase or sale of ESOT shares and consideration paid or received is recognised directly in equity. Finance and administration costs relating to the ESOT are charged to operating costs as incurred.

1.18 Foreign currency

The Consolidated Financial Statements are presented in Pounds Sterling, which is the Company's functional and presentational currency. The Group determines the functional currency of each entity and items included in the Financial Statements of each entity are measured using that functional currency. The functional currencies of the Group's operations are Pounds Sterling, US Dollars, Euros and Canadian Dollars.

Transactions denominated in foreign currencies are recorded at the rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are translated at the rates of exchange ruling at the reporting date.

Non-monetary assets and liabilities denominated in foreign currencies and held at cost use the exchange rate at the date of the initial transactions. Non-monetary assets and liabilities denominated in foreign currencies and held at fair value use the exchange rate at the date that the fair value was determined.

Profits and losses on both the individual transactions during the year and monetary assets and liabilities are dealt with in the statement of comprehensive income.

On consolidation, the statements of comprehensive income of the foreign subsidiaries are translated at the average exchange rates for the year and the statements of financial position at the exchange rates at the reporting date. The exchange differences arising as a result of translating statements of comprehensive income at average rates and restating opening net assets at closing rates are taken to the translation reserve. On disposal of a foreign operation, the cumulative amount recognised in the translation reserve relating to that particular foreign operation is recognised in the statement of comprehensive income.

1.19 Financial instruments

Financial assets and liabilities are recognised in the statement of financial position when the Group becomes a party to the contractual provisions of the instrument.

Cash and cash equivalents

Cash and cash equivalents in the statement of financial position comprise cash at bank and in hand and short-term deposits with an original maturity of three months or less.

Bank loans, loan notes and borrowings

All loans and borrowings are initially recognised at the fair value of the consideration received net of issue costs associated with the borrowings. After initial recognition, these are subsequently measured at amortised cost.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

1 Accounting policies continued

1.19 Financial instruments continued

Other assets

Assets, other than those specifically accounted for under a separate policy, include trade and other receivables and are recognised at amortised cost. Receivables may be impaired by means of a provision, to take into account any difficulties in recovering the outstanding amounts. Provisions for impairment are determined by comparing the carrying value and the likely realisable value, which is defined as the present value of the estimated recoverable amounts.

For trade receivables, expected credit losses are measured by applying an expected loss rate to the gross carrying amount. The expected loss rate comprises the risk of a default occurring and the expected cash flows on default based on the ageing of the receivable. The risk of a default occurring always takes into consideration all possible default events over the expected life of those receivables (the lifetime expected credit losses). Different provision rates and periods are used based on groupings of historic credit loss experience by product type, customer type and location.

Other liabilities

Liabilities, other than those specifically accounted for under a separate policy, include trade and other payables and are stated based on their amortised cost at the amounts which are considered to be payable in respect of goods or services received up to the reporting date.

1.20 Provisions

Provisions are recognised when the Group has a present obligation of uncertain timing or amount as a result of past events, and it is probable that the Group will be required to settle that obligation and a reliable estimate of the obligation can be made. The provisions are measured at the Directors' best estimate of the amount to settle the obligation at the reporting date and are discounted back to present value if the effect is material. Changes in provisions are recognised in the statement of comprehensive income for the reporting year.

1.21 Operating segments

The Group determines and presents operating segments based on the reporting information that is provided to the Board of Directors to allow it to make operating decisions. The Board of Directors is responsible for all significant decisions and collectively is the Chief Operating Decision-Making (CODM) body as defined by IFRS 8 Operating Segments.

An operating segment is a component of the Group that engages in business activities from which it may earn income and incur expenses, including income and expenses that relate to transactions with any of the Group's other components. An operating segment's results are reviewed regularly by the Board of Directors to make decisions about resources to be allocated to the segment and assess its performance.

1.22 Critical accounting estimates and judgements

The preparation of the Financial Statements requires the use of estimates, assumptions and judgements that affect the reported amounts of assets and liabilities at the date of the Financial Statements and the reported amounts of revenues and expenses during the reporting year. Although these estimates, assumptions and judgements are based on the Directors' best knowledge of the amounts, events or actions, and are believed to be reasonable, actual results ultimately may differ from those estimates.

The estimates that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities are described below.

Share-based payments (Notes 1.10 and 20)

In calculating the fair value of equity-settled share-based payments the Group uses option pricing models. The Directors are required to exercise their judgement in choosing appropriate option pricing models and determining input parameters that may have a material effect on the fair value calculated. These key input parameters are expected volatility, expected life of the options and the number of options expected to vest. No awards were made in the year. In the prior year a sensitivity analysis was performed on the impact of a +/-10% variation in the expected volatility used in the share-based payment models. The impact on the share-based payment charge in the prior year was an increase of £0.2 million and a decrease of £0.2 million respectively.

2 Operating segment and revenue analysis

Operating segment

The Group's principal trading activity is undertaken in relation to the commercialisation of its Parsortix cell separation system. All operating activities are shown as one operating segment. All significant decisions are made by the Board of Directors with implementation of those decisions on a Group-wide basis. The Group manages all overseas R&D and commercial activities from the UK.

Segmental analysis is not considered necessary for one operating segment, as the segment information is substantially in the form of and on the same basis as the Group's IFRS information.

Revenue analysis

The Group revenues are to the research use market and involve a mix of customers located in various territories. These are early-stage revenues with a modest customer base.

Significant customers

The Group had two significant customers who contributed 10% or more of Group revenues in the year (2021: one customer contributing more than 10% of revenues).

Analysis of revenue from contracts with customers

The Group derives revenues from the sale of products and services in the following geographical regions:

	2022				2021			
	Product £'000	Product services £'000	Pharma services £'000	**Total £'000**	Product £'000	Product services £'000	Pharma services £'000	Total £'000
UK	96	6	119	**221**	33	6	49	88
Europe	374	92	–	**466**	563	42	97	702
North America – RoW	124	14	216	**354**	184	22	17	223
Total	594	112	335	**1,041**	780	70	163	1,013

All of the revenues are recognised in line with the Group's accounting policy (Note 1.7) and have been generated from contracts with customers.

Assets and liabilities related to contracts with customers

Services in-progress but not yet invoiced result in a contract asset and products and services paid for in advance but not yet delivered result in a contract liability and are recognised in line with the Group's accounting policy (Note 1.7). At the point where completed work is invoiced the contract asset is derecognised and a corresponding receivable is recognised.

Contract assets at the reporting date of £67,759 (2021: £23,729).

Sales of instruments include a service-based support and maintenance contract which is renewable annually. Revenue associated with the unexpired support and maintenance contract period and service is deferred at the reporting date.

Contract liabilities	**2022 £'000**	2021 £'000
At 1 January	**132**	60
Recognised in year, relating to amounts invoiced in prior years	**(115)**	(34)
Deferred at year end relating to amounts invoiced in the current year	**233**	106
At 31 December	**250**	132

The Group has applied the practical expedient to disclosure of performance obligations at the reporting date because all significant contracts with customers for product related services have an expected duration of one year or less at the reporting date.

The standard credit period allowed for trade receivables is 30 days, although this may be extended such that invoices become payable after completion of a key milestone.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

3 Costs

	2022 £'000	2021 £'000
Operating costs		
Employment costs (Note 5)	**13,998**	9,907
Depreciation and impairment of property, plant and equipment (Note 12)	**920**	701
Depreciation and impairment of right-of-use assets (Note 13)	**940**	532
Profit/(loss) on disposal of property, plant and equipment	**172**	4
Amortisation of intangible assets (Note 11)	**191**	233
Impairment of intangible assets (Note 11)	**787**	21
Operating lease costs – low-value and short-term (Note 13)	**34**	61
Auditors' remuneration (see below)	**230**	215
Third-party research, development and clinical study costs	**4,039**	2,911
Patent and legal costs	**327**	127
Inventories used in research and development	**449**	530
Listed company costs	**610**	594
Foreign exchange	**(2,060)**	(117)
Other operating costs	**4,184**	2,268
Total operating costs	**24,821**	17,987
Cost of sales		
Inventories	**180**	210
Other	**248**	92
Total cost of sales	**428**	302
Total costs	**25,249**	18,289

Third-party research and development costs include the cost of clinical studies (patient enrolment, CRO fees, core laboratory work etc), key opinion leader research agreements, instrument design, scientific advisory board fees and laboratory supplies.

Costs associated with the closure of the Canadian operations of £2.1 million are included within operating costs, including £0.7 million of compensation costs, £1.0 million impairment charges in respect of intangible assets, property plant and equipment and right-of-use assets, and £0.4 million in respect of professional fees and other closure costs including logistics. See Note 17 for additional detail.

Auditors' remuneration	2022 £'000	2021 £'000
Audit services		
Statutory audit of parent and consolidated financial statements	**186**	175
Statutory audit of subsidiaries	**44**	40
Total	**230**	215

The Group has taken advantage of the exemption from audit for certain subsidiary undertakings. Audit work is still required on the exempt subsidiaries to support the Group audit opinion and these costs are included with the "Statutory audit of parent and consolidated financial statements".

4 Directors' emoluments

	2022 £'000	2021 £'000
Aggregate emoluments for qualifying services	**509**	765
Employer pension contributions (Note 6)	**–**	40
Total per Directors' Remuneration Report (page 68)	**509**	805

No LTIP Options were granted to Directors in the year (2021: 3,000,000). 3,000,000 LTIP Options were forfeited in the year (2021: nil) as a result of not meeting the highest-level performance condition. No LTIP Options were lapsed, cancelled or exercised in the year (2021: nil). No share options were granted to Directors in the year (2021: nil). 1,500,000 share options lapsed in the year (2021: nil). No Directors' share options were forfeited or cancelled in the year (2021: nil). No share options were exercised in the year (2021: 1,523,826). Disclosures relating to individual Directors' LTIP Options and share options are given in the Directors' Remuneration Report on pages 68 to 70.

4 Directors' emoluments continued

The above includes the following amounts paid in respect of the highest paid Director:

	2022 £'000	2021 £'000
Emoluments for qualifying services	**264**	446

Disclosures relating to individual Directors' emoluments are given in the Directors' Remuneration Report on pages 68 to 70.

5 Employment

Employment costs

The aggregate of employment costs of employees (including Directors) for the year was:

	2022 £'000	2021 £'000
Wages and salaries	**9,280**	6,925
Social security costs	**159**	1,489
Other pension costs (Note 6)	**173**	168
	9,612	8,582
Share-based payment charge (Note 20)	**4,386**	1,325
Total staff costs in operating costs (Note 3)	**13,998**	9,907

The key management personnel are the Directors and their remuneration is disclosed in Note 4 and within the Directors' Remuneration Report on pages 68 to 70.

Number of employees

The average monthly number of employees (including Directors) during the year was:

	2022 Number	2021 Number
Research and development, engineering, manufacturing, quality control and regulatory	**121**	94
Commercial and administrative	**49**	34
Total	**170**	128

6 Pension costs

The Group incurred UK pension contribution charges for the year as follows:

	2022 £'000	2021 £'000
Direct to personal pension plan schemes	**108**	126
ANGLE auto-enrolment pension scheme	**65**	42
Total	**173**	168

Contributions to pension schemes were payable at the reporting date and are included in trade and other payables (Note 18) as follows:

	2022 £'000	2021 £'000
Direct to personal pension plan schemes	**36**	25
ANGLE auto-enrolment pension scheme	**15**	10
Total	**51**	35

No Director has received contributions under a defined contribution pension scheme (2021: one) – see Directors' Remuneration Report on page 68.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

7 Finance income and costs

	2022 £'000	2021 £'000
Finance income		
Interest on cash and cash equivalents	**128**	25
Other interest	**8**	4
Total	**136**	29
Finance costs		
Lease liabilities finance charges (Note 13)	**(354)**	(157)
Provision for dilapidations finance charges (Note 17)	**(14)**	–
Total	**(368)**	(157)

8 Tax

The Group undertakes research and development activities. In the UK these activities qualify for tax relief resulting in research and development tax credits.

	2022 £'000	2021 £'000
Current tax:		
Research and development tax credit receivable for the current year	**(2,791)**	(2,373)
Prior year adjustment in respect of research and development tax credit	**38**	22
Deferred tax:		
Origination and reversal of timing differences	**–**	–
Tax charge/(credit)	**(2,753)**	(2,351)

	2022 £'000	2021 £'000
Profit/(loss) before tax	**(24,439)**	(17,363)
Corporation tax:		
Tax on profit/(loss) at 19.1% (2021: 19.3%)	**(4,655)**	(3,355)
Factors affecting charge:		
Disallowable expenses	**68**	40
Excess of depreciation (over)/under capital allowances	**(114)**	(53)
Enhanced research and development relief	**(1,281)**	(1,051)
Share-based payments	**814**	(121)
Unutilised losses carried forward	**2,274**	2,190
Other tax adjustments	**103**	(23)
Prior year adjustment	**38**	22
Tax charge/(credit)	**(2,753)**	(2,351)

The Group has accumulated losses available to carry forward against future trading profits of £70.1 million (2021: £54.2 million). No deferred tax asset has been recognised in respect of tax losses since it is uncertain at the reporting date as to when future profits will be available against which the unused tax losses can be utilised. The estimated value of the deferred tax asset not recognised, measured at a weighted average rate of 25.0% (2021: 25.0%), is £17.6 million (2021: £13.5 million). An increase in the main rate of Corporation Tax from 19.0% to 25.0% was announced and included in Finance Bill 2021. This will come into effect from 1 April 2023.

9 Earnings/(loss) per share attributable to owners of the parent

The basic and diluted earnings/(loss) per share is calculated by dividing the after tax loss for the year attributable to the owners of the parent of £21.7 million (2021: £15.0 million) by the weighted average number of shares in the year.

In accordance with IAS 33 Earnings per Share, 1) the "basic" weighted average number of Ordinary shares calculation excludes shares held by the Employee Share Ownership Trust (ESOT) as these are treated as treasury shares and 2) the "diluted" weighted average number of Ordinary shares calculation considers potentially dilutive Ordinary shares from instruments that could be converted. Share options are potentially dilutive where the exercise price is less than the average market price during the year. Due to the losses in 2022 and 2021 share options are non-dilutive for those years as adding them would have the effect of reducing the loss per share and therefore the diluted loss per share is equal to the basic loss per share.

	2022 £'000	2021 £'000
Profit/(loss) for the year attributable to owners of the parent	**(21,686)**	(15,012)

	Number of shares	Number of shares
Weighted average number of Ordinary shares	**246,692,903**	225,186,639
Weighted average number of ESOT shares	**(113,259)**	(113,259)
Weighted average number of Ordinary shares – basic	**246,579,644**	225,073,380
Effect of potential dilutive share options	**–**	–
Adjusted weighted average number of Ordinary shares – diluted	**246,579,644**	225,073,380
Earnings/(loss) per share attributable to owners of the parent		
Basic and Diluted (pence per share)	**(8.79)**	(6.67)

10 Investments

The Company has investments in the following subsidiaries:

Company name	Principal activity	Class of share held	Holding %
ANGLE Biosciences Incorporated[1]	Medical diagnostics	Common	100
ANGLE Europe Limited[1]	Medical diagnostics	Ordinary	100
ANGLE EU BV	Medical diagnostics	Ordinary	100
ANGLE North America Incorporated[2]	Medical diagnostics	Common & Preferred	100
ANGLE Technology Limited[1]	Medical diagnostics	Ordinary	100
ANGLE Technology Ventures Limited	Medical diagnostics	Ordinary	100
ANGLE Partnerships Limited[1]	Dormant	Ordinary	100
ANGLE Technology Licensing Limited	Dormant	Ordinary	100
ANGLE Technology LLC	Dormant	Membership units	100
ANGLE Technology Ventures LLC	Dormant	Membership units	100

(1) Subsidiary held directly.
(2) Direct holding in subsidiary of 9.47%.

The Group has taken advantage of the exemption from audit in accordance with section 479A of the Companies Act 2006 for ANGLE Technology Limited and ANGLE Technology Ventures Limited.

ANGLE Biosciences Incorporated is incorporated and registered in British Columbia, Canada. Its registered address is 725 Granville Street, Suite 400, Vancouver, British Columbia, V7Y 1G5, Canada. On 18 October 2022, the Company announced the decision to close the facilities in Toronto, Canada in an orderly wind down. The closure was substantially completed by the reporting date and all operating activity ceased. Formal company dissolution is anticipated in 2023.

ANGLE Europe Limited, ANGLE Technology Limited, ANGLE Technology Ventures Limited, ANGLE Partnerships Limited and ANGLE Technology Licensing Limited are incorporated and registered in the United Kingdom. Their registered address is 10 Nugent Road, Surrey Research Park, Guildford, Surrey, GU2 7AF, UK.

ANGLE EU BV is incorporated in the Netherlands as a vehicle to overcome Brexit issues and facilitate the fulfilment of EU wide product sales. Its registered address is Joop Geesinkweg 701, Rembrandt Kantoor, 1114 AB, Amsterdam-Duivendrecht, Netherlands.

ANGLE North America Incorporated, ANGLE Technology LLC and ANGLE Technology Ventures LLC are registered in the United States. ANGLE North America Incorporated's registered address is 5100 Campus Drive, Suite 120, Plymouth Meeting, PA 19462, USA. ANGLE Technology LLC and ANGLE Technology Ventures LLC's registered address is Rees Broome, PC, 1900 Gallows Road STE 700, Tysons Corner, VA 22182, USA.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

11 Intangible assets

	Goodwill £'000	Acquired intangible assets £'000	Intellectual property £'000	Product development £'000	Total £'000
Cost					
At 1 January 2021	2,207	1,215	1,040	1,280	5,742
Additions	–	–	117	–	117
Exchange movements	–	2	2	13	17
At 31 December 2021	2,207	1,217	1,159	1,293	5,876
Additions	–	–	155	–	155
Disposals	–	–	–	(9)	(9)
Exchange movements	–	5	27	156	188
At 31 December 2022	**2,207**	**1,222**	**1,341**	**1,440**	**6,210**
Accumulated amortisation and impairment					
At 1 January 2021	–	466	407	1,159	2,032
Charge for the year	–	110	45	78	233
Impairment	–	–	21	–	21
Exchange movements	–	2	2	13	17
At 31 December 2021	–	578	475	1,250	2,303
Charge for the year	–	110	68	13	191
Disposals	–	–	–	(9)	(9)
Impairment	–	531	256	–	787
Exchange movements	–	3	19	152	174
At 31 December 2022	**–**	**1,222**	**818**	**1,406**	**3,446**
Net book value					
At 31 December 2022	**2,207**	**–**	**523**	**34**	**2,764**
At 31 December 2021	2,207	639	684	43	3,573

Goodwill is deemed to have an indefinite useful life, is carried initially at fair value and is reviewed for impairment annually or more frequently if events or changes in circumstances indicate a potential impairment.

Goodwill acquired in a business combination is allocated at acquisition to the cash-generating units (CGUs) that are expected to benefit from that business combination. The goodwill has been allocated to the combined Group as a single CGU for the purposes of the impairment review, since this is the lowest level within the entity at which management monitors goodwill and the related cash flows are primarily generated from a combined existing and acquired technology product offering. The whole Group is expected to benefit from the business combination.

The carrying amount of goodwill has been assessed by reference to the fair value less costs to sell of the single CGU, which comprises the combined Group. The fair value of the Group can be estimated by reference to the market capitalisation of ANGLE plc, which at 31 December 2022 stood at £131.6 million, and exceeds the carrying amount of the CGU by £129.4 million less any costs of disposal.

Acquired intangible assets relate to the acquisition of the assets of Axela Inc. and comprises the fair value of the identifiable intangible assets arising at the date of acquisition. This comprises mainly the technology which was being amortised over its expected useful economic life with a remaining amortisation period of four years and ten months (2021: five years and ten months). The closure of the Canadian facility resulted in an impairment assessment and subsequent review. Due to the uncertainty surrounding the future development of the HyCEAD technology, the acquired IP has been impaired in full.

11 Intangible assets continued

Product development relates to internally generated intangible assets that were capitalised in accordance with IAS 38 Intangible Assets (Note 1.12). A negligible amount relating to Computer software has been combined in the total. Capitalised product development costs are directly attributable costs comprising cost of materials, specialist contractor costs, labour and overheads. Product development costs are amortised over their estimated useful lives commencing when the related new product is in commercial production. Development costs not meeting the IAS 38 criteria for capitalisation continue to be expensed through the statement of comprehensive income as incurred.

IAS 38 criteria are reviewed at the end of each accounting year. Internally generated intangible assets had a carrying value of £0.6 million at 31 December 2022 (2021: £0.7 million).

The carrying value of intangible assets excluding goodwill is reviewed for indications of impairment whenever events or changes in circumstances indicate that the carrying value may exceed the recoverable amount. No indications of impairment have been identified.

Amortisation and impairment charges are charged to operating costs in the consolidated statement of comprehensive income.

12 Property, plant and equipment

	Leasehold improvements £'000	Computer equipment £'000	Laboratory equipment and tooling £'000	Fixtures, fittings and equipment £'000	Total £'000
Cost					
At 1 January 2021	490	136	2,639	180	3,445
Additions	388	75	1,143	32	1,638
Disposals	–	(12)	(48)	–	(60)
Transfers (to)/from inventories	–	–	12	–	12
Exchange movements	4	1	20	1	26
At 31 December 2021	882	200	3,766	213	5,061
Additions	1,077	132	733	68	2,010
Disposals	(68)	(74)	(361)	(39)	(542)
Transfers (to)/from inventories	–	–	133	–	133
Exchange movements	34	8	141	14	197
At 31 December 2022	**1,925**	**266**	**4,412**	**256**	**6,859**
Accumulated depreciation					
At 1 January 2021	274	86	1,771	138	2,269
Charge for the year	189	39	446	27	701
Disposals	–	(12)	(44)	–	(56)
Transfers (to)/from inventories	–	–	(43)	–	(43)
Exchange movements	1	1	15	1	18
At 31 December 2021	464	114	2,145	166	2,889
Charge for the year	188	63	643	26	920
Disposals	(46)	(50)	(235)	(39)	(370)
Transfers (to)/from inventories	–	–	(137)	–	(137)
Exchange movements	5	4	32	11	52
At 31 December 2022	**611**	**131**	**2,448**	**164**	**3,354**
Net book value					
At 31 December 2022	**1,314**	**135**	**1,964**	**92**	**3,505**
At 31 December 2021	418	86	1,621	47	2,172

Laboratory equipment includes a carrying value of £0.3 million (2021: £0.2 million) in relation to Parsortix instruments being used in-house and on long-term loan to key opinion leaders, including instruments for the ongoing clinical studies. Tooling includes amounts in relation to moulds for the productionisation of cassettes, enabling higher volume production, lower pricing and compliance with medical device manufacturing quality requirements.

Depreciation charges are charged to operating costs in the consolidated statement of comprehensive income.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

13 Leases

The Group has lease contracts for office accommodation and specialist laboratories. These lease contracts generally have lease terms between 3 and 10 years, with earlier break clauses in some cases. The Group's obligations under its leases are secured by the lessor's title.

The carrying amounts of right-of-use assets recognised and the movements during the year are shown below:

Right-of-use assets **Laboratory and office premises**	**2022** **£'000**	2021 £'000
At 1 January	**2,204**	1,233
Additions	**3,575**	1,478
Transfer (to)/from net investment in sublease (Note 16)	**–**	(16)
Depreciation	**(896)**	(532)
Impairment	**(44)**	–
Exchange movements	**132**	41
At 31 December	**4,971**	2,204

The carrying amounts of lease liabilities and the movements during the year are shown below:

Lease liabilities **Laboratory and office premises**	**2022** **£'000**	2021 £'000
At 1 January	**2,338**	1,362
Additions	**3,508**	1,478
Rent paid and payable	**(1,259)**	(702)
Transfer to provision for dilapidations (Note 17)	**(90)**	–
Accretion of interest (Note 7)	**354**	157
Exchange movements	**150**	43
At 31 December	**5,001**	2,338

	2022 **£'000**	2021 £'000
Non-current lease liabilities	**4,339**	1,816
Current lease liabilities	**662**	522
Total	**5,001**	2,338

The Group had total cash outflows for leases of £1.1 million for the year (2021: £0.7 million).

The Group added three leases in the year with the addition of new premises in the UK and the United States. Of these additions £2.5 million relates to a new ten-year lease (with a five-year break clause) at a 6.7% implied interest rate.

The Group has one lease contract that includes a break-clause, with option to extend. The Directors exercise judgement in determining whether this option is reasonably certain to be exercised and agreed that it was reasonable to assume it would be extended beyond the break-clause option period due to significant fit-out and renovations to create specialist laboratories and the prohibitive cost of finding equivalent alternative accommodation. The impact of including the extension option is to increase both the carrying value of the right-of-use assets and the non-current lease liabilities at the reporting date by £1.0 million (2021: £0.7 million).

The Group also holds certain leases with lease terms of 12 months or less and leases of low-value office equipment. The Group applies the 'short-term lease' and 'lease of low-value assets' recognition exemptions for these leases. Payments made under such leases are expensed on a straight-line basis and the expense recorded in the year relating to such leases was £33,774 (2021: £61,148).

Maturity analysis of the undiscounted lease payments:

	Within 1 year £'000	1 to 2 years £'000	2 to 5 years £'000	More than 5 years £'000
31 December 2022	**1,015**	**908**	**2,469**	**2,335**
31 December 2021	626	473	1,048	814

14 Financial risk management

Overview

The Group is exposed, through its normal operations, to a number of financial risks, the most significant of which are credit, liquidity and investment (market) risks.

The Group's financial instruments comprise cash, trade and other receivables and trade and other payables which arise directly from its operations, and from time to time short-term bank deposits, overdrafts and finance leases.

It is the Group's policy that no trading in financial derivatives shall be undertaken.

Financial assets

Financial assets of the Group comprise cash at bank and in hand as well as short-term bank deposits and trade and other receivables (Note 16). It is the Group's policy to place surplus cash resources on deposit at both floating and fixed term deposit rates of interest with the objective of maintaining a balance between accessibility of funds and competitive rates of return.

Financial liabilities

Financial liabilities of the Group in the normal course of business comprise trade and other payables (Note 18), provisions (Note 17) and lease liabilities (Note 13). It is the Group's policy to use various financial instruments with floating and fixed rates of interest with the objective of maintaining a balance between continuity of funding, matching the liability with the use of the asset and finding flexible funding options for a reasonable charge.

The Group currently does not utilise overdraft facilities or finance leases. The Group has no long-term borrowings or undrawn committed borrowing facilities. The Group is currently not exposed to any interest rate risk on its financial liabilities.

Capital risk management

The capital structure of the Group comprises cash and cash equivalents, short-term deposits and total equity. The Group's objectives when managing capital are to:

- safeguard the Group's ability to continue as a going concern;
- have available the necessary financial resources to allow the Group to meet milestones and deliver benefits from its operational activities; and
- optimise the return to investors based on the level of risk undertaken.

As part of achieving these objectives, the Group identifies the principal financial risk exposures to be foreign currency risk, credit risk and liquidity risk. The Group's approach to these risks is outlined below.

In order to maintain or adjust the capital structure the Group may issue new shares.

The Group's capital and equity ratios are shown in the table below:

	2022 £'000	2021 £'000
Total equity attributable to owners of the parent	**40,063**	40,330
Total assets	**49,868**	47,315
Equity ratio	**80.3%**	85.2%

Liquidity risk

The principal risk to which the Group is exposed is liquidity risk, which is that the Group will not be able to meet its financial obligations as they fall due. The Group seeks to manage liquidity through planning, forecasting, careful cash management and managing the operational risk.

The nature of the Group's activities means it finances its operations through earnings and the issue of new shares to investors. The principal cash requirements are in relation to funding operations and meeting working capital requirements.

The Company may also find it difficult to raise additional capital to develop its business depending on progress with meeting milestones and/or market conditions.

Sensitivity analysis examining a small percentage increase and decrease in liquidity is of limited use and accordingly no analysis has been shown.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

14 Financial risk management continued

Credit risk

The Group's credit risk is attributable to its cash and cash equivalents, short-term deposits and trade receivables.

The Group's risk on cash and cash equivalents and short-term deposits is limited as funds are held in banks with credit ratings of A-1 and above (S&P). The maximum exposure to cash and cash equivalents and short-term deposits is £31.9 million (2021: £31.8 million).

The risk for trade receivables is that a customer fails to pay for goods or services received and the Group suffers a financial loss. The Group's objective with respect to credit risk is to minimise the risk of default by customers. The customer base is primarily academic institutions and pharmaceutical businesses. The exposure is managed centrally, and Group policy is to use judgement and past experience to assess the credit quality of each customer and where appropriate seek full or part-payment in advance.

The Group has applied the IFRS 9 Financial Instruments simplified approach to measuring expected credit losses, and the expected credit loss rates are based on historical experience that the risk of loss is low. On this basis any credit loss provision would be negligible, and no provision has been made.

The maximum exposure to trade and other receivables is £0.7 million (2021: £0.3 million).

Interest rate risk

There is currently no interest rate risk on financial assets and liabilities.

Cash at bank of £31.9 million earns interest at fixed rates of between 0.20% and 1.10% (2021: £31.8 million, between 0.01% and 0.15%).

There is currently no interest rate risk on financial liabilities as the Group has no interest-bearing loans or borrowings.

All amounts, excluding lease liabilities, have maturity dates of less than 12 months (2021: £nil maturity greater was less than 12 months). Contractual maturities in respect of lease obligations are disclosed in Note 13 on page 96.

Foreign currency risk

The Group has overseas subsidiaries whose income and expenses are primarily denominated in US Dollars (USD) and Canadian Dollars (CAD). As a result the Consolidated Financial Statements will be affected by movements in the USD:Sterling and CAD:Sterling exchange rates.

The majority of the Group's operating revenues and expenses are in Sterling, Euros, USD and CAD. Sales are priced in Sterling, Euros and USD although the Group may have a limited amount of revenues denominated in other currencies. The Group monitors its currency exposures on an ongoing basis and is building US and European sales which provide a natural hedge for USD and Euro expenditure. Excess exposure, if any, may be managed for all significant foreign currencies using forward currency contracts or currency swaps.

Sensitivity analysis

The impact of a 10% variation in currency exchange rates on the profit/(loss) for the year is as follows:

Profit/(loss) – realised gains/(losses)	**2022 USD £'000**	**2022 CAD £'000**	2021 USD £'000	2021 CAD £'000
Profit/(loss) – 10% strengthening	**(274)**	**(480)**	(320)	(292)
Profit/(loss) – 10% weakening	**280**	**587**	391	357

Profit/(loss) – unrealised gains/(losses)	**£'000**	**£'000**	£'000	£'000
Profit/(loss) – 10% strengthening	**2,091**	**(85)**	1,706	2
Profit/(loss) – 10% weakening	**(1,918)**	**104**	(2,085)	(3)

The Company provides a centralised treasury function to trading subsidiaries through ANGLE Technology Limited. The amounts due from Group undertakings are held on the books of the subsidiary undertakings as loans denominated in Sterling. Under IFRS 9 these loans are retranslated at the rate of exchange at the reporting date giving rise to an unrealised exchange gain or loss.

Hedging

The Group did not hedge its financial transactions in 2022 or 2021.

14 Financial risk management continued

Currency profile

The Group's financial assets and financial liabilities which are stated at amortised cost have the following currency profile:

	2022					2021				
	Sterling £'000	**USD £'000**	**Euro £'000**	**CAD £'000**	**Total £'000**	Sterling £'000	USD £'000	Euro £'000	CAD £'000	Total £'000
Financial assets										
Trade and other receivables	**254**	**185**	**255**	**–**	**694**	62	93	143	–	298
Cash and cash equivalents	**31,579**	**167**	**88**	**62**	**31,896**	30,962	347	409	121	31,839
Total	**31,833**	**352**	**343**	**62**	**32,590**	31,024	440	552	121	32,137
Financial liabilities										
Non-current										
Lease liabilities	**2,644**	**1,695**	**–**	**–**	**4,339**	592	1,192	–	32	1,816
Provisions	**157**	**–**	**–**	**–**	**157**	–	–	–	–	–
Current										
Lease liabilities	**511**	**151**	**–**	**–**	**662**	191	175	–	156	522
Provisions	**–**	**16**	**–**	**594**	**610**	–	–	–	–	–
Trade and other payables	**1,735**	**434**	**141**	**238**	**2,548**	1,911	473	217	383	2,984
Total	**5,047**	**2,296**	**141**	**832**	**8,316**	2,694	1,840	217	571	5,322

Fair values of financial assets and liabilities

The Directors believe that the fair value and the book value of financial assets and financial liabilities are not materially different. Trade payables and receivables have a remaining life of less than one year so their value on the consolidated statement of financial position is considered to be a fair approximation of fair value.

15 Inventories

	2022 £'000	2021 £'000
Raw materials and work in progress	**167**	762
Finished goods	**1,892**	986
Total	**2,059**	1,748

16 Trade and other receivables

	2022 £'000	2021 £'000
Amounts receivable within one year		
Trade receivables	**317**	202
Other receivables	**491**	405
Net investment in sublease (see below)	**27**	55
Prepayments and contract assets	**962**	607
Total	**1,797**	1,269

Other receivables comprises recoverable taxes (VAT and HST). Contract assets include amounts for services in progress but not yet invoiced (Note 2).

All trade and other receivable accounts are short-term. The Directors consider the carrying amount of trade and other receivables to approximate their fair value and that all the above financial assets are of good credit quality and no changes have been experienced since initial recognition. Receivables are unsecured and interest free, unless past their due date when interest may be charged.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

16 Trade and other receivables continued

The Group has applied the IFRS 9 Financial Instruments simplified approach to measuring expected credit losses, and the expected credit loss rates are based on historical experience that the risk of loss is low. On this basis any credit loss provision would be negligible, and no provision has been made.

Age profile of trade receivables:	**2022 £'000**	2021 £'000
Not past due	**208**	176
0 – 30 days past due	**47**	12
30 – 60 days past due	**58**	1
> 60 days past due	**4**	13
Total	**317**	202

The standard credit period allowed for trade receivables is 30 days, although this may be extended such that invoices become payable after completion of a key milestone.

In the prior year, the Group entered into a sublease arrangement in respect of a right-of-use asset. The sublease is for the remaining life of the lease which expires in December 2023.

Net investment in sublease	**2022 £'000**	2021 £'000
At 1 January	**55**	85
Transfer from right-of-use assets (Note 13)	**–**	71
Transfer to right-of-use assets (Note 13)	**–**	(55)
Rental income received and receivable	**(35)**	(51)
Accretion of interest	**2**	4
Exchange movements	**5**	1
At 31 December	**27**	55

17 Provisions

	2022 £'000	2021 £'000
Non-current		
Provision for dilapidations	**157**	–
Total	**157**	–

	2022 £'000	2021 £'000
Current		
Provision for closure costs	**594**	–
Provision for dilapidations	**16**	–
Total	**610**	–

On 18 October 2022, the Company announced the decision to close the facilities in Toronto, Canada in an orderly wind down. This decision was taken in light of the increasing costs of operating in Canada due to proposed changes in the UK R&D Tax credit rules which effectively made overseas R&D costs 50% higher. The closure was substantially completed by the reporting date but there remained various costs associated with redundancy pay and support, completing tax returns, other compliance matters and formal company dissolution. A provision has been made for the estimated remaining costs to complete the winding down of Canadian operations.

A provision for dilapidations in respect of right-of-use leasehold property of £0.1 million was included within the lease liability balances at 31 December 2021. This has been reclassified from leases (Note 13) to provisions in the current reporting period.

17 Provisions continued

Movement in provisions

	Closure costs £'000	Dilapidations £'000	**2022 Total £'000**	2021 Total £'000
At 1 January	–	–	**–**	–
Transfer from lease liabilities (Note 13)	–	90	**90**	–
Additions	603	67	**670**	–
Accretion of interest (Note 7)	–	14	**14**	–
Exchange movements	(9)	2	**(7)**	–
At 31 December	594	173	**767**	–

18 Trade and other payables

	2022 £'000	2021 £'000
Amounts payable after one year		
Other taxes and social security costs	**59**	257
Total	**59**	257

	2022 £'000	2021 £'000
Amounts payable within one year		
Trade payables	**1,495**	1,124
Other taxes and social security costs	**658**	1,010
Other payables	**51**	35
Accruals and contract liabilities	**1,774**	2,221
Total	**3,978**	4,390

Other taxes and social security costs include a provision for employers' taxes on the theoretical gain on the exercise on unapproved share options and LTIP Options, within one year of £0.4 million (2021: £0.8 million) and after more than one year of £0.1 million (2021: £0.3 million). The theoretical gain uses an estimated employers' tax rate multiplied by a number determined by 1) the share price at the reporting date less the exercise price, to the extent this is greater than the exercise price 2) pro-rata vesting over the vesting period and 3) assumes any performance and service conditions will be met and options vest.

Accruals include amounts for professional fees, vacation, salary and severance costs of the Canadian operation, and in the prior year for employee bonuses (Note 23). Contract liabilities include amounts for pre-billed revenues (Note 2).

Except as disclosed above, trade and other payables are short-term. The Directors consider that the carrying value of trade and other payables are a reasonable approximation of fair value. The contractual maturity of all the amounts above are within one year of the reporting date.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

19 Share capital

The share capital of the Company is shown below:

	2022 £'000	2021 £'000
Allotted, called up and fully paid		
260,580,547 (2021: 235,143,050) Ordinary shares of £0.10 each	**26,058**	23,514

The Company has one class of Ordinary shares which carry no right to fixed income.

The Company issued 25,162,500 new Ordinary shares with a nominal value of £0.10 at an issue price of £0.80 per share in a placing of shares realising gross proceeds of £20.1 million. Associated costs of £1.2 million were incurred. Shares were admitted to trading on AIM in July 2022.

The Company issued 274,997 new Ordinary shares with a nominal value of £0.10 at exercise prices between £0.385 to £0.530 per share following the exercise of share options by employees, realising gross proceeds of £0.1 million. Shares were admitted to trading on AIM at various dates across the year.

20 Share-based payments

The key disclosures that enable the user of the Financial Statements to understand the nature and extent of share-based payment charges through the statement of comprehensive income in relation to ANGLE plc shares are detailed below.

The share-based payment charge for the Company Employee Share Option Schemes and Long-Term Incentive Plan (LTIP) was £4.4 million (2021: £1.3 million).

Company – Share Option Schemes

The Company operates Share Option Schemes as a means of encouraging ownership and aligning interests of staff and external shareholders. The Company also operates an LTIP for Executive Directors. These are a key part of the remuneration package and granted at the discretion of the Remuneration Committee taking into account the need to motivate, retain and recruit high calibre executives and staff.

The Company has an Enterprise Management Incentive (EMI) Share Option Scheme, a Company Share Option Plan (CSOP) and Unapproved Share Option Schemes for the United Kingdom, Canada and the United States. Each scheme is governed by a specific set of rules and administered by the Directors of the Company. Options are generally granted at the market price of the shares on the date of grant, except for "Bonus Options" and "LTIP Options". Share options are granted under a service condition and/or a non-market performance condition and/or a market performance condition (such as a target share price). Options generally cease to be exercisable after ten years from the date of grant.

To the extent these conditions are met the share options vest and become capable of exercise. To the extent these conditions are not met then the share options are forfeited or lapse. In exceptional circumstances the performance date may be extended. Options are forfeited if the employee leaves the Group unless the conditions under which they leave are such that they are considered to be a "good leaver"; in this case some or all of their vested options may remain exercisable for a limited period of time, subject to any performance condition having been met. Options lapse if they are not exercised by the date they cease to be exercisable. LTIP Options also have an additional holding period of up to two years such that the minimum performance and holding period is five years.

The movement in the number of employee share options is set out below:

	2022 Number of share options #	2022 Weighted average exercise price (£)	2021 Number of share options #	2021 Weighted average exercise price (£)
Outstanding at 1 January	**20,858,479**	**0.7626**	17,844,140	0.5467
During the year:				
Granted	**–**	**–**	5,792,500	1.2473
Exercised	**(274,997)**	**0.4865**	(2,496,492)	0.3718
Forfeited/lapsed	**(3,425,335)**	**1.0143**	(281,669)	0.5128
Outstanding at 31 December	**17,158,147**	**0.7168**	20,858,479	0.7626
Capable of being exercised at 31 December	**9,177,646**	**0.5165**	8,182,645	0.5078

The options outstanding at 31 December 2022 had a weighted average remaining contractual life of six years and three months (2021: seven years and nil months).

20 Share-based payments continued

The Company uses a Trinomial option pricing model as the basis to determine the fair value of the Company's share options. The following assumptions are used in the option pricing model to determine the fair value of share options at the respective date of grant that are still outstanding at 31 December 2022:

Date of grant	Exercise price (£)	Share price at date of grant (£)	Expected volatility	Risk free interest rate	Expected life of option (years)	Expected dividends	Vesting conditions	Outstanding share options
11 December 2013	0.7300	0.7300	40.00%	0.97%	3.0	Nil	(1)	290,000
10 November 2014	0.8625	0.8625	40.00%	1.03%	3.0	Nil	(2)	20,000
10 November 2014	0.8625	0.8625	40.00%	1.53%	5.0	Nil	(3)	1,500,000
31 March 2015	0.8625	0.7850	40.00%	0.67%	3.0	Nil	(2)	330,000
12 November 2015	0.1000	0.7550	40.00%	0.68%	2.0	Nil	(4)	46,980
1 March 2016	0.5650	0.5650	40.00%	0.42%	3.0	Nil	(2)	150,000
25 November 2016	0.6450	0.6450	40.00%	0.30%	3.0	Nil	(2)	675,000
25 November 2016	0.6450	0.6450	40.00%	0.30%	3.0	Nil	(5)	1,500,000
1 November 2017	0.4000	0.4000	40.00%	0.57%	3.0	Nil	(6)	500,000
1 November 2017	0.4000	0.4000	40.00%	0.57%	3.0	Nil	(2)	450,000
16 November 2017	0.4025	0.4025	40.00%	0.55%	3.0	Nil	(2)	100,000
20 December 2018	0.3850	0.3850	40.00%	0.75%	3.0	Nil	(2)	983,333
20 December 2018	0.3850	0.3850	40.00%	0.75%	3.0	Nil	(7)	2,000,000
21 May 2020	0.6150	0.6150	61.40%	(0.04)%	3.0	Nil	(2)	350,000
25 September 2020	0.5300	0.5300	57.60%	(0.12)%	3.0	Nil	(2)	2,717,334
25 September 2020	0.5300	0.5300	57.60%	(0.12)%	3.0	Nil	(8)	1,500,000
4 January 2021	0.4825	0.4825	55.54%	(0.12)%	3.0	Nil	(2)	250,000
10 May 2021	1.1100	1.1100	59.11%	0.11%	3.0	Nil	(2)	100,000
12 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(9)	1,295,500
12 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(10)	2,400,000
Total								**17,158,147**

Expected volatility was derived from observation of the historic volatility of the Company's shares for the commensurate period since 2020. Prior to this, expected volatility was derived from observation of the volatility of quoted shares in similar sectors to the Company and observation of the historic volatility of the Company's shares, adjusted for any unusual historic events and expected changes to future volatility. The expected life used in the model is based on management's best estimate taking into account the effects of non-transferability, exercise restrictions, behavioural conditions and expected future events.

The share options issued were subject to both performance and service (employment) conditions:

(1) Vesting is subject to a) specific performance conditions for senior management and b) a service condition with options vesting over a three-year period. These conditions have been met and the options are fully vested and capable of exercise.

(2) Vesting is subject to a service condition with options vesting over a period up to three years.

(3) Vesting is subject to the performance conditions that a) the Company's share price must have increased to £2.00, £2.25, £2.50 and £2.75 at some point since the date of grant for each quarter of the allocation (this condition has not yet been met) and b) a time/event condition with options vesting after five years or on the sale of the Parsortix business, whichever is earliest (this condition has been met).

(4) Options were granted as Bonus Options in accordance with the Remuneration Committee's discretion to settle an element of the Annual Bonus in the form of share options. The Bonus Options vest immediately and are exercisable at par value.

(5) Vesting is subject to a) a performance condition that the Company's share price has risen by at least 100% at some point from the market price on 25 November 2016 and b) a service condition with options vesting over a three-year period. These conditions have been met and the options are fully vested and capable of exercise.

(6) Vesting is subject to a) a performance condition that the Company's share price has risen by at least 100% at some point from the market price on 1 November 2017 and b) a service condition with options vesting over a three-year period. These conditions have been met and the options are fully vested and capable of exercise.

(7) Vesting is subject to a performance condition that the Company's share price has risen to at least £1.056 on 21 December 2021. This condition has been met and the options are fully vested and capable of exercise.

(8) Vesting is subject to a) the Company achieving FDA clearance for its Parsortix system (this condition has been met) and b) a performance condition that the Company's share price has risen to at least £0.916 on 25 September 2023.

(9) Vesting is subject to a service condition with options vesting at three years.

(10) Vesting is subject to a performance condition that the Company's share price has risen to at least £2.220 at some point during the period to 12 November 2024 and a service condition with options vesting at three years.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

20 Share-based payments continued

Long-Term Incentive Plan

The Company has a Long-Term Incentive Plan (LTIP) for Executive Directors. Disclosures are set out in the Directors' Remuneration Report on pages 68 to 70 and below. LTIP Options are subject to share price performance targets and to the extent these targets are met within the performance period then LTIP Options vest although remain subject to an additional holding period. To the extent these targets are not met then the LTIP Options are forfeited. LTIP Options cease to be exercisable after ten years from the date of grant.

The movement in the number of LTIP Options is set out below:

	2022 Number of LTIP Options #	2021 Number of LTIP Options #
Outstanding at 1 January	**12,000,000**	9,000,000
During the year:		
Granted	**–**	3,000,000
Forfeited	**(3,000,000)**	–
Outstanding at 31 December	**9,000,000**	12,000,000
Vested at 31 December	**3,000,000**	1,200,000

The LTIP Options outstanding at 31 December 2022 had a weighted average remaining contractual life of seven years and six months (2021: eight years and two months).

The Company uses a Monte Carlo simulation option pricing model as the basis to determine the fair value of the Company's LTIP Options. The following assumptions are used in the option pricing model to determine the fair value of LTIP Options at the respective date of grant that are still outstanding at 31 December 2022:

Date of grant	Exercise price (£)	Share price at date of grant (£)	Expected volatility	Risk free interest rate	Expected life of option (years)	Expected dividends	Barrier (performance condition) (£)	Outstanding LTIP Options
20 December 2018	0.0000	0.3850	45.04%	0.88%	5.0	Nil	1.056	1,200,000
20 December 2018	0.0000	0.3850	45.04%	0.88%	5.0	Nil	1.434	1,800,000
25 September 2020	0.0000	0.5300	53.46%	(0.09)%	5.0	Nil	0.916	600,000
25 September 2020	0.0000	0.5300	53.46%	(0.09)%	5.0	Nil	1.304	900,000
25 September 2020	0.0000	0.5300	53.46%	(0.09)%	5.0	Nil	1.789	1,500,000
12 November 2021	0.0000	1.2850	56.20%	0.62%	5.0	Nil	2.220	600,000
12 November 2021	0.0000	1.2850	56.20%	0.62%	5.0	Nil	2.510	900,000
12 November 2021	0.0000	1.2850	56.20%	0.62%	5.0	Nil	2.823	1,500,000
Total								**9,000,000**

Expected volatility was derived from observation of the historic volatility of the Company's shares for the commensurate period. The expected life used in the model is based on management's best estimate taking into account the effects of non-transferability, exercise restrictions, behavioural conditions and expected future events. The barrier reflects the share price targets that must be met for a proportion of the award to vest.

Under the discretion approved by the shareholders at the Annual General Meeting on 30 June 2021, reflecting COVID-19 related impacts, the performance period for the LTIP Options issued on 20 December 2018 was extended from 20 December 2021 to no later than 20 December 2022, and the holding period reduced accordingly such that the overall five-year period is unchanged. Other than the change in date, the overall performance condition is unchanged and effectively means the share price target could be met at any point in the extended period.

20 Share-based payments continued

Long-Term Incentive Plan continued

The modification required an assessment of the fair value of the equity instruments originally granted measured immediately before and after the modification. The difference between these two fair values is the incremental fair value and this has been calculated at £3.1 million and is expensed over the remaining vesting period of the options. The following assumptions are used in the model to determine the fair value of LTIP Options at the date of modification that are still outstanding at 31 December 2022:

Date of modification	Exercise price (£)	Share price at date of modification (£)	Expected volatility	Risk free interest rate	Expected life of option (years)	Expected dividends	Barrier (performance condition) (£)	Outstanding LTIP Options
12 November 2021	0.0000	1.2850	50.60%	0.47%	2.1	Nil	1.056	1,200,000
12 November 2021	0.0000	1.2850	50.60%	0.47%	2.1	Nil	1.434	1,800,000
Total								**3,000,000**

21 ESOT shares

	2022 £'000	2021 £'000
At 31 December	**102**	102

Employee Share Ownership Trust (ESOT) shares are ANGLE plc shares held by the ANGLE Employee Trust. At 31 December 2022 the Trust held 113,259 shares (2021: 113,259 shares). The market value of these shares at 31 December 2022 was £57,196 (2021: £134,778). Shares purchased by the ANGLE ESOT are used to assist in meeting the obligations under employee remuneration schemes.

22 Guarantees and other financial commitments

The Group has a number of retainers with professional advisors which can be terminated on short notice periods.

In December 2020, the Group entered into a guaranty agreement in favour of the landlord, who absorbed significant bespoke fit-out costs, for the clinical laboratory in Plymouth Meeting, Pennsylvania, USA in respect of obligations under the lease, initially for $800,000 and then reducing by $80,000 per annum from the date of occupation. The guaranty was increased by a further US$244,800 in April 2022 to cover bespoke fit-out costs to be absorbed by the landlord for additional premises. The additional guaranty reduces by US$27,200 per annum. The total guaranty value at 31 December 2022 was US$964,800 (2021: US$800,000).

During the year, the Group entered into certain commitments in relation to the development of the Parsortix cancer diagnostic product, building inventory and the new clinical laboratories. In aggregate these gave rise to financial commitments at 31 December 2022 of up to £2.8 million over one year (2021: £1.2 million).

The Group has taken advantage of the exemption from audit in accordance with section 479A of the Companies Act 2006 for ANGLE Technology Limited and ANGLE Technology Ventures Limited. ANGLE plc has provided a statutory guarantee over these subsidiaries' liabilities in accordance with section 479C of the Companies Act 2006.

Other than these, the Group has no contractual commitments to provide financial support to its investments.

NatWest Bank (the Group's UK commercial bankers) have placed a charge over a 35-day notice account of £700,000 as security for a Bacstel-IP facility used in the normal course of business.

23 Related party transactions

Transactions between subsidiaries within the Group are not disclosed as they are eliminated on consolidation.

Directors' interests – related party interests and transactions

Apart from the interests disclosed in the Directors' Remuneration Report on pages 68 to 70 and below, none of the Directors had any interest at any time during the year ended 31 December 2022 in the share capital of the Company or its subsidiaries.

At the reporting date, £nil of remuneration (2021: £193,979) was due to Andrew Newland and £nil of remuneration (2021: £123,441) was due to Ian Griffiths.

Brian Howlett entered into a consultancy contract with effect from 7 January 2013 to provide specialist commercial advice outside his normal Board responsibilities. Consultancy fees of £nil were paid in the year to Brian Howlett under this contract (2021: £nil).

SoBold Limited provides digital marketing services and website development and management to ANGLE with fees in the year of £77,209 (2021: £35,250) and a balance of £3,000 (2021: £3,000) due at the reporting date. Andrew Newland's son is the managing director and a main shareholder of SoBold Limited. The relationship is managed by VP Commercial Operations, Nick Claxton.

No other Director had a material interest in a contract, other than a service contract, with the Company or its subsidiaries, or investments during the year.

COMPANY STATEMENT OF FINANCIAL POSITION

As at 31 December 2022

	Note	2022 £'000	2021 £'000
Assets			
Non-current assets			
Investment in subsidiaries	C3	**10,923**	6,537
Other receivables	C4	**62,356**	56,962
Total non-current assets		**73,279**	63,499
Current assets			
Other receivables	C4	**14**	3
Cash and cash equivalents		**30,812**	30,210
Total current assets		**30,826**	30,213
Total assets		**104,105**	93,712
Net assets		**104,105**	93,712
Equity			
Share capital	C5	**26,058**	23,514
Share premium		**115,918**	99,406
Share-based payments reserve		**5,298**	2,704
Accumulated losses		**(43,169)**	(31,912)
Equity attributable to owners		**104,105**	93,712

The Company's loss and total comprehensive loss for the year to 31 December 2022 were £13.0 million (2021: £1.8 million).

The Financial Statements on pages 106 to 111 were approved by the Board of Directors and authorised for issue on 20 April 2023 and signed
on its behalf by:

Ian F Griffiths
Director

Andrew D W Newland
Director

Registered No. 04985171

COMPANY STATEMENT OF CASH FLOWS

For the year ended 31 December 2022

	2022 £'000	2021 £'000
Operating activities		
Profit/(loss) before tax	**(13,049)**	(1,824)
Adjustments for:		
Impairment of loans	**13,049**	1,824
Operating cash flows before movements in working capital	**–**	–
(Increase)/decrease in trade and other receivables	**–**	35
Net cash from/(used in) operating activities	**–**	35
Investing activities		
Loans (to)/from subsidiaries	**(18,443)**	(16,097)
Transfer (to)/from short-term deposits	**–**	15,822
Net cash from/(used in) investing activities	**(18,443)**	(275)
Financing activities		
Net proceeds from issue of share capital – placing	**18,922**	18,765
Proceeds from issue of share capital – share option exercises	**123**	925
Net cash from/(used in) financing activities	**19,045**	19,690
Net increase/(decrease) in cash and cash equivalents	**602**	19,450
Cash and cash equivalents at 1 January	**30,210**	10,760
Cash and cash equivalents at 31 December	**30,812**	30,210

COMPANY STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2022

	Equity attributable to owners				
	Share capital £'000	Share premium £'000	Share-based payments reserve £'000	Accumulated losses £'000	Total equity £'000
At 1 January 2021	**21,540**	**81,532**	**1,722**	**(30,431)**	**74,363**
For the year to 31 December 2021					
Profit/(loss) for the year				(1,824)	(1,824)
Issue of shares (net of costs)	1,974	17,874			19,848
Share-based payment charge			1,325		1,325
Released on exercise			(295)	295	–
Released on forfeiture/lapse			(48)	48	–
At 31 December 2021	**23,514**	**99,406**	**2,704**	**(31,912)**	**93,712**
For the year to 31 December 2022					
Profit/(loss) for the year				(13,049)	(13,049)
Issue of shares (net of costs)	2,544	16,512			19,056
Share-based payment charge			4,386		4,386
Released on exercise			(43)	43	–
Released on forfeiture/lapse			(1,749)	1,749	–
At 31 December 2022	**26,058**	**115,918**	**5,298**	**(43,169)**	**104,105**

NOTES TO THE COMPANY FINANCIAL STATEMENTS

For the year ended 31 December 2022

C1 Accounting policies

C1.1 Basis of preparation

The Parent Company Financial Statements have been prepared in accordance with UK-adopted international accounting standards for the year ended 31 December 2022. They have also been prepared in accordance with those parts of the Companies Act 2006 that apply to companies reporting under those standards.

The accounting policies of the Company which have been applied consistently throughout the year are the same as those of the Group and are presented on pages 81 to 88.

C1.2 Presentation of Financial Statements

The financial information, in the form of the primary statements contained in this report, is presented in accordance with International Accounting Standard (IAS) 1 Presentation of Financial Statements.

C1.3 Judgements and key sources of estimation uncertainty

The preparation of the Financial Statements requires the use of estimates, assumptions and judgements that affect the reported amounts of assets and liabilities at the date of the Financial Statements and the reported amounts of revenues and expenses during the reporting year. Although these estimates, assumptions and judgements are based on the Directors' best knowledge of the amounts, events or actions, and are believed to be reasonable, actual results ultimately may differ from those estimates.

The estimates that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities are described below.

Accounting for intercompany loans (Note C4)

In accordance with IFRS 9 Financial Instruments, the Company is required to make an assessment of expected credit losses on intercompany loans. Having considered the increased quantum of the intercompany loans and the probability of credit losses expected to arise across a number of repayment scenarios, an adjustment to provisions for expected credit losses of £13.0 million (2021: £1.8 million) was recognised in the year.

The calculation of the provision for lifetime expected credit losses requires a significant degree of estimation, in particular in determining the probability weighted likely outcome for each repayment scenario considered to determine the expected credit loss in each scenario. Input parameters have included significant positive factors, for example, with regard to the FDA product clearance and excellent results from the ovarian cancer study, as well as significant negative factors, for example, an adverse market for growth companies which may affect access to capital to develop the Company as well as our customer base. Should the outcomes vary, this could have a significant impact on the carrying value of the intercompany loans in future years.

C1.4 Investments

Investments in subsidiaries are stated at cost plus capital contribution to the subsidiary in respect of share-based payments, less any provision for impairment. The Company considers the recoverability of intercompany loans and investments on an annual basis. Where there is an indication that the carrying value exceeds the recoverable amount an impairment review will be undertaken and a provision for impairment made when considered necessary. An impairment loss is recognised in the profit and loss in the statement of comprehensive income.

C2 Total comprehensive income

As permitted by Section 408 of the Companies Act 2006, the Parent Company's Statement of Comprehensive Income has not been included in these Financial Statements. The total comprehensive loss for the year was £13.0 million (2021: £1.8 million).

The only employees of the Company are the Directors; the remuneration of the Directors is borne by Group subsidiary undertakings. Full details of their remuneration can be found in the Directors' Remuneration Report on pages 68 to 70.

Administrative expenses, including auditors' remuneration, are borne by other Group companies and are not recharged to the Company.

C3 Investment in subsidiaries

	2022 £'000	2021 £'000
Cost		
At 1 January	**6,537**	5,212
Share-based payment charge	**4,386**	1,325
At 31 December	**10,923**	6,537

Details of the Company's subsidiary undertakings at 31 December 2022 are shown in Note 10 to the Consolidated Financial Statements along with other interests held indirectly through subsidiary undertakings.

NOTES TO THE COMPANY FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2022

C4 Other receivables

	2022 £'000	2021 £'000
Amounts receivable after one year		
Amounts due from Group undertakings		
Cost		
At 1 January	**91,364**	75,267
Additions/(repayments)	**18,443**	16,097
At 31 December	**109,807**	91,364
Provision		
At 1 January	**34,402**	32,578
Impairment charge	**13,049**	1,824
At 31 December	**47,451**	34,402
Net book value		
At 31 December	**62,356**	56,962

The Company provides a centralised treasury function to trading subsidiaries through ANGLE Technology Limited. The amounts due from Group undertakings are interest free, unsecured and have no fixed date of repayment. Amounts due from Group undertakings are due on demand but are not expected to be recovered within 12 months.

Having considered the increased quantum of the intercompany loans and the probability of credit losses expected to arise across a number of repayment scenarios, an adjustment to provisions for expected credit losses of £13.0 million (2021: £1.8 million) was recognised in the year. Input parameters for the year have included significant positive factors, for example, with regard to the FDA product clearance and excellent results from the ovarian cancer study, as well as significant negative factors, in particular an adverse market for growth companies which may affect access to capital to develop the Company as well as the ability of our customer base to progress studies and purchase our products and services. Overall, the Directors believe that the negative factors outweigh the positive factors for the year (2021: positive factors outweigh the negative factors) and there is a corresponding increase in the provision. Outcomes may be different and this could have a significant impact on the carrying value of the intercompany loans in future years.

	2022 £'000	2021 £'000
Amounts receivable within one year		
Other receivables	**14**	3

Other receivables comprise share capital receivable.

C5 Share capital

The share capital of the Company is shown below:

	2022 £'000	2021 £'000
Allotted, called up and fully paid		
260,580,547 (2021: 235,143,050) Ordinary shares of £0.10 each	**26,058**	23,514

Details of the Company's share capital and changes in its issued share capital can be found in Note 19 to the Consolidated Financial Statements on page 102.

Details of the Company's share options schemes can be found in Note 20 to the Consolidated Financial Statements on pages 102 to 105.

C6 Guarantees and other financial commitments

In December 2020 the Company entered into a guaranty agreement in favour of the landlord, who absorbed significant bespoke fit-out costs, for the clinical laboratory in Plymouth Meeting, Pennsylvania, USA in respect of obligations under the lease, initially for $800,000 and then reducing by $80,000 per annum from the date of occupation. The guaranty was increased by a further US$244,800 in April 2022 to cover bespoke fit-out costs to be absorbed by the landlord for additional premises. The additional guaranty reduces by US$27,200 per annum. The total guaranty value at 31 December 2022 was US$964,800 (2021: US$800,000).

The Company provides financial support to its subsidiaries. Details of the Group's financial commitments are given in Note 22 to the Consolidated Financial Statements on page 105.

C7 Related party transactions

Group transactions and balances

Details of balances owed by ANGLE Technology Limited are given in Note C4 above.

Directors' interests – related party interests and transactions

Details are given in Note 23 to the Consolidated Financial Statements on page 105.

NOTICE OF ANNUAL GENERAL MEETING

Directors:
J E Eid (Non-executive Director)
I F Griffiths (Finance Director)
J Groen (Non-executive Director)
B Howlett (Non-executive Director)
A D W Newland (Chief Executive)
G R Selvey (Chairman)
J Thompson (Non-executive Director)

Registered Office
10 Nugent Road
Surrey Research Park
Guildford
GU2 7AF

12 May 2023

Dear Shareholder

Annual General Meeting

You will find included with this document a Notice convening the Annual General Meeting (the "Meeting") of ANGLE plc for 2:00 pm on Wednesday 28 June 2023 at which the following resolutions will be proposed:

1. **Resolution 1** to receive the Annual Report and Financial Statements of the Company for the year ended 31 December 2022.
2. **Resolution 2** to approve the Directors' Remuneration Report for the year ended 31 December 2022 set out on pages 68 to 70 of the Annual Report.

   Note: this is an advisory vote only.
3. **Resolution 3** to re-appoint the auditors of the Company, PricewaterhouseCoopers LLP, and authorise the Directors to determine their level of remuneration.
4. **Resolution 4** to appoint as a Director Dr. J E Eid who was appointed as a Director of the Company since the 2022 Annual General Meeting, who is retiring in accordance with Article 96 of the Company's Articles of Association and who, being eligible, is offering himself for election.
5. **Resolution 5** to appoint as a Director Ms J Thompson who was appointed as a Director of the Company since the 2022 Annual General Meeting, who is retiring in accordance with Article 96 of the Company's Articles of Association and who, being eligible, is offering herself for election.
6. **Resolution 6** to grant the Directors authority to allot unissued shares in the capital of the Company up to an aggregate nominal amount of £8,686,018.

   Note: the Directors wish to renew their authorisations with respect to the allotment of new shares.
7. **Resolutions 7 and 8** to disapply statutory pre-emption rights.

   Note: the Directors wish to renew their authorisations for the disapplication of the statutory pre-emption rights in respect of the allotment of new shares pursuant to rights issues or otherwise for cash and for financing a transaction which the Directors determine to be an acquisition or other capital investment, as detailed in the Notice of Annual General Meeting, to enable the Directors to take advantage of opportunities as they arise without the need for further Shareholder approval. The resolutions proposed are in line with the most recent Statement of Principles on Disapplying Pre-emption Rights published by the Pre-Emption Group in November 2022 (the "PEG Statement of Principles 2022") and in line with the guidance issued by the Investment Association.
8. **Resolution 9** to grant the Directors authority to purchase issued shares in the capital of the Company up to an aggregate nominal amount of £2,605,806.

   Note: whilst the Directors have no present intention of purchasing the Company's shares, the Directors are seeking authorisation as they wish to have the flexibility to do so if this was generally in the best interests of the Shareholders and (except in the case of purchases intended to satisfy obligations under share schemes) the expected effect of the purchase would be to increase earnings per share of the remaining shares.

The authorities requested in items 6, 7, 8 and 9 will expire at the 2024 Annual General Meeting or, if earlier, 15 months from the date of the passing of the resolution.

Meeting arrangements

The Meeting will be held at 2:00 pm on Wednesday 28 June 2023 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ. Please note that only those shareholders or their nominated proxies who attend in person will be deemed to be present at the Meeting and will be entitled to speak and vote at the Meeting. If you are unable to attend the Meeting in person, you are strongly encouraged to vote in advance by appointing the Chairman or another duly nominated person as your proxy (instructions are provided below). Questions are invited to be submitted before the Meeting.

Business update presentation

The Board remains keen to encourage engagement with Shareholders. The Company will provide a business update presentation after the formalities of the Meeting are concluded.

Action to be taken

Shareholders should register their Proxy Vote either online at **www.signalshares.com** or through CREST as outlined in the Notes to the Notice of Annual General Meeting as soon as possible, but in any event no later than 48 hours before the time fixed for the Meeting. Shares held in uncertificated form (i.e. in CREST) may be voted through the CREST Proxy Voting Service in accordance with the procedures set out in the CREST Manual.

Recommendation

Your Directors consider the resolutions to be proposed at the Annual General Meeting to be in the best interests of the Company and its Shareholders. Accordingly, the Directors unanimously recommend Shareholders to vote in favour of all the resolutions to be proposed at the Annual General Meeting.

Yours faithfully

Garth Selvey
Chairman

(Company number 04985171)

NOTICE OF ANNUAL GENERAL MEETING CONTINUED

NOTICE IS HEREBY GIVEN that the **ANNUAL GENERAL MEETING** (the "**Meeting**") of ANGLE plc ("**the Company**") will be held at 2:00 pm on Wednesday 28 June 2023 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ for the purpose of considering and, if thought fit, passing the following resolutions of which the resolutions numbered 1 through 6 will be proposed as ordinary resolutions and resolutions numbered 7 through 9 will be proposed as special resolutions.

Ordinary Business

1. **TO** receive the Financial Statements of the Company for the year ended 31 December 2022, and the reports of the Directors and auditors thereon.
2. **TO** approve the Directors' Remuneration Report as set out on pages 68 to 70 of the Annual Report for the year ended 31 December 2022. Note: this is an advisory vote only.
3. **TO** re-appoint PricewaterhouseCoopers LLP as auditors of the Company to hold office from the conclusion of this Meeting until the conclusion of the next Annual General Meeting of the Company at which Financial Statements are laid and to authorise the Directors to determine their remuneration.
4. **TO** appoint Dr. J E Eid as a Director, who was appointed as a Director of the Company since the 2022 Annual General Meeting.
5. **TO** appoint Ms J Thompson as a Director, who was appointed as a Director of the Company since the 2022 Annual General Meeting.

Special Business

6. **THAT**, for the purposes of section 551 of the Companies Act 2006 ("**the Act**"), the Directors be and they are hereby generally and unconditionally authorised to exercise all powers of the Company to allot shares in the Company, or grant rights to subscribe for or convert any security into shares in the Company, up to an aggregate nominal amount of £8,686,018 PROVIDED that this authority shall expire (unless previously renewed, varied or revoked by the Company in general meeting) at the earlier of the conclusion of the next Annual General Meeting of the Company or on the date falling 15 months after the passing of this resolution EXCEPT that the Company may, before such expiry, make an offer or agreement which would or might require shares to be allotted or the granting of rights to subscribe for, or convert any security into, shares in the Company after such expiry and the Directors may allot shares and grant rights to subscribe for, or convert any security into, shares in the Company in pursuance of any such offer or agreement as if the authority conferred hereby had not expired. This authority shall replace any existing like authority which is hereby revoked with immediate effect but without prejudice to any allotment of shares or grant of rights already made, offered or agreed to be made pursuant to such authorities.
7. **THAT**, subject to and conditional upon the passing of Resolution 6, the Directors be and they are hereby generally empowered, in addition to all existing authorities, pursuant to section 570 of the Act to allot equity securities (within the meaning of section 560 of the Act) for cash pursuant to the authority conferred by Resolution 6 above as if section 561 of the Act did not apply to any such allotment, provided that this power shall be limited to:

   (a) the allotment of equity securities in connection with an offer of equity securities open for acceptance for a period fixed by the Directors to holders of equity securities on the register of members of the Company on a date fixed by the Directors in proportion (as nearly as may be practicable) to their respective holdings of such securities or in accordance with the rights attached thereto but SUBJECT to such exclusions, variations or other arrangements as the Directors may deem necessary or expedient to deal with:

      i. fractional entitlements;

      ii. directions from any holders of shares to deal in some other manner with their respective entitlements;

      iii. legal or practical problems arising in any overseas territory;

      iv. the requirements of any regulatory body or stock exchange; or

      v. otherwise howsoever;

   (b) the allotment of equity securities (otherwise than pursuant to sub-paragraph (a) of this resolution 7) up to an aggregate nominal amount of £2,605,806; and

   (c) the allotment of equity securities or sale of treasury shares (otherwise than under paragraph (a) or paragraph (b) of this Resolution 7 up to a nominal amount equal to 20% of any allotment of equity securities or sale of treasury shares from time to time under paragraph (b) of this Resolution 7, such authority to be used only for the purposes of making a follow-on offer which the Board of the Company determines to be of a kind contemplated by paragraph 3 of Section 2B of the PEG Statement of Principles 2022 prior to the date of this notice.

   such authority to expire at the end of the next AGM of the Company or, if earlier, at the close of business on the date falling 15 months after the passing of this resolution but, in each case, prior to its expiry the Company may make offers, and enter into agreements, which would, or might require equity securities to be allotted (and treasury shares to be sold) after the authority expires and the Board may allot equity securities (and sell treasury shares) under any such offer or agreement as if the authority had not expired.

8. **THAT**, if Resolution 6 is passed, the Board be authorised in addition to any authority granted under Resolution 7 to allot equity securities (as defined in the Act) for cash under the authority given by that Resolution 6 and/or to sell ordinary shares of £0.10 each in the capital of the Company ("Ordinary Shares") held by the Company as treasury shares for cash as if section 561 of the Act did not apply to any such allotment or sale, such authority to be limited to:

   (a) the allotment of equity securities or sale of treasury shares up to a nominal amount of £2,605,806, such authority to be used only for the purposes of financing (or refinancing, if the authority is to be used within 12 months after the original transaction) a transaction which the Board of the Company determines to be either an acquisition or a specified capital investment of a kind contemplated by the PEG Statement of Principles 2022 prior to the date of this notice; and

   (b) the allotment of equity securities or sale of treasury shares (otherwise than under paragraph (a) of this Resolution 8) up to a nominal amount equal to 20% of any allotment of equity securities or sale of treasury shares from time to time under paragraph (a) of this Resolution 8, such authority to be used only for the purposes of making a follow-on offer which the Board of the Company determines to be of a kind contemplated by paragraph 3 of Section 2B of the PEG Statement of Principles 2022 prior to the date of this notice,

   such authority to expire at the end of the next AGM of the Company or, if earlier, on the date falling 15 months after the passing of this resolution but, in each case, prior to its expiry the Company may make offers, and enter into agreements, which would, or might, require equity securities to be allotted (and treasury shares to be sold) after the authority expires and the Board may allot equity securities (and sell treasury shares) under any such offer or agreement as if the authority had not expired.

9. **THAT**, the Company be and is hereby generally and unconditionally authorised for the purposes of section 701 of the Act to make market purchases (within the meaning of section 693(4) of the Act) of Ordinary Shares on such terms and in such manner as the Directors may from time to time determine, provided that:

   (a) the maximum number of Ordinary Shares that may be purchased is 26,058,055 (representing approximately 10% of the Company's issued share capital at the date of this notice);

   (b) the minimum price (exclusive of expenses) which may be paid for each Ordinary Share is £0.10;

   (c) the maximum price (exclusive of expenses) which may be paid for each Ordinary Share is an amount equal to 105% of the average of the middle market quotations of an Ordinary Share taken from the London Stock Exchange Daily Official List for the five business days immediately preceding the day on which the Ordinary Share is contracted to be purchased,

   and the authority hereby conferred shall expire (unless previously renewed, varied or revoked by the Company in general meeting) at the end of the next AGM of the Company or, if earlier, at the close of business on the date falling 15 months after the passing of this resolution EXCEPT that the Company may, before such expiry, enter into one or more contracts to purchase Ordinary Shares under which such purchases may be completed or executed wholly or partly after the expiry of this authority and may make a purchase of Ordinary Shares in pursuance of any such contract or contracts.

Registered Office
10 Nugent Road
Surrey Research Park
Guildford
GU2 7AF

Dated 12 May 2023

By Order of the Board

Ian F Griffiths
Company Secretary

NOTICE OF ANNUAL GENERAL MEETING CONTINUED

Notes:

1. Under the Articles of Association of the Company, a member of the Company entitled to attend and vote at the Annual General Meeting may appoint one or more proxies to vote instead of him. A shareholder may appoint more than one proxy in relation to the Meeting provided that each proxy is appointed to exercise the rights attached to a different ordinary share or ordinary shares held by that shareholder. A proxy need not be a shareholder of the Company.

2. To be valid, an appointment of proxy must be registered with or returned to the Company's Registrar at least 48 hours before the time of the Meeting or any adjourned meeting by one of the following methods:

   - by logging on to **www.signalshares.com** and following the instructions;
   - you may request a hard copy Form of Proxy directly from the Registrar, Link Group, on Tel: 0371 664 0300. Calls are charged at the standard geographic rate and will vary by provider. Calls outside the United Kingdom will be charged at the applicable international rate. Link Group are open between 09:00 and 17:30, Monday to Friday excluding public holidays in England and Wales. The Form of Proxy in hard copy duly executed, together with the power of attorney or other authority (if any) under which it is signed (or a notarially certified copy of such power or authority) must be deposited at the Company's Registrar, Link Group, PXS1, Central Square, 29 Wellington Street, Leeds, LS1 4DL. If a hard copy Form of Proxy is used to appoint more than one proxy, the Form of Proxy should be photocopied and completed for each proxy holder and the proxy holder's name should be written on the Form of Proxy together with the number of shares in relation to which the proxy is authorised to act. The box on the Form of Proxy must also be ticked to indicate that the proxy instruction is one of multiple instructions being given;
   - if you are an institutional investor, you may also be able to appoint a proxy electronically via the Proxymity platform, a process which has been agreed by the Company and approved by the Registrar. For further information regarding Proxymity, please go to **www.proxymity.io**. Your proxy must be lodged by 2pm on Monday 26 June 2023 in order to be considered valid or, if the meeting is adjourned, by the time which is 48 hours before the time of the adjourned meeting. Before you can appoint a proxy via this process you will need to have agreed to Proxymity's associated terms and conditions. It is important that you read these carefully as you will be bound by them, and they will govern the electronic appointment of your proxy. An electronic proxy appointment via the Proxymity platform may be revoked completely by sending an authenticated message via the platform instructing the removal of your proxy vote;
   - in the case of CREST members, by utilising the CREST electronic proxy appointment service in accordance with the procedures set out in Note 4 of this document.

3. Pursuant to regulation 41 of the Uncertificated Securities Regulations 2001, the Company has specified that, to be entitled to vote at the Meeting (and for the purpose of determining the number of votes they may cast), members must be entered on the Company's register of members at close of business on 26 June 2023. Changes to entries on the relevant register of securities after that time shall be disregarded in determining the rights of any person to vote at the Meeting.

4. To appoint a proxy or to give or amend an instruction to a previously appointed proxy via the CREST system, the CREST message must be received by the issuer's agent RA10 by at least 48 hours before the time of the Meeting or any adjourned meeting. For this purpose, the time of receipt will be taken to be the time (as determined by the timestamp applied to the message by the CREST Applications Host) from which the issuer's agent is able to retrieve the message. After this time any change of instructions to a proxy appointed through CREST should be communicated to the proxy by other means. EUI does not make available special procedures in CREST for any particular messages, therefore normal system timings and limitations will apply in relation to the input of CREST proxy instructions. CREST Personal Members or other CREST sponsored members, and those CREST Members who have appointed voting service provider(s) should contact their CREST sponsor or voting service provider(s) for assistance with appointing proxies via CREST. For further information on CREST procedures, limitations and system timings please refer to the CREST Manual. We may treat as invalid a proxy appointment sent by CREST in the circumstances set out in Regulations 35(5) (a) of the Uncertificated Securities Regulations 2001. In any case your Proxy Vote must be received by the Company's Registrar no later than at least 48 hours before the time of the Meeting or any adjourned meeting.

5. Any corporation which is a member can appoint one or more corporate representatives who may exercise on its behalf all of its powers as a member provided that they do not do so in relation to the same shares.

6. A corporation must execute the Form of Proxy under the hand of a duly authorised officer or attorney. The power of attorney or authority (if any) should be returned with the Form of Proxy.

7. In the case of joint holders, where more than one of the joint holders purports to appoint a proxy, only the appointment submitted by the most senior holder will be accepted. Seniority is determined by the order in which the names of the joint holders appear in the Company's register of members in respect of the joint holding (the first-named being the most senior).

8. If a shareholder submits more than one valid proxy appointment, the appointment received last before the latest time for the receipt of proxies will take precedence. If the Company is unable to determine which appointment was received last, none of them will be treated as valid in respect of that share.

9. To be entitled to attend and vote at the AGM (and for the purpose of the determination by the Company of the votes they may cast), shareholders must be registered in the register of members of the Company at 6.00 p.m. on 26 June 2023 (or, in the event of any adjournment, not less than 48 hours before the time of the adjourned meeting (excluding any part of a day that is not a working day)). Changes to the register of members after the relevant deadline shall be disregarded in determining the rights of any person to attend and vote at the meeting.

10. As at 12 May 2023, being the last practicable day prior to the date of this Notice of AGM, the Company's issued share capital consisted of 260,580,547 Ordinary Shares. Each Ordinary Share carries the right to one vote at a general meeting of the Company and, therefore, the total number of voting rights in the Company as at 12 May 2023 is 260,580,547.

Explanatory Notes:

Resolution 1: Report and Financial statements
The Directors are required to present to the Meeting the audited Financial Statements and the reports of the Directors and the auditors for the year ended 31 December 2022.

Resolution 2: Directors' Remuneration Report
This resolution seeks approval of the Directors' Remuneration Report for the year ended 31 December 2022. The full text of the Directors' Remuneration Report is contained on pages 68 to 70 of the Company's Annual Report.

This is an advisory vote and no entitlement to remuneration for the year ended 31 December 2022 is conditional on the resolution being passed.

Resolution 3: Re-appointment of auditors
The Company is required to appoint auditors at each general meeting at which Financial Statements are laid before the Company, to hold office until the end of the next such meeting. This resolution proposes the appointment and, in accordance with standard practice, gives authority to the Directors to determine the remuneration to be paid to the auditors.

Resolutions 4 and 5: Appointment of Directors
Under article 96 of the Articles of Association of the Company, a Director appointed since the previous Annual General Meeting shall hold office only until the next Annual General Meeting when he/she shall retire from office and will be eligible for appointment at the Annual General Meeting. Dr. J E Eid and Ms J Thompson were appointed since the 2022 Annual General Meeting and, as such, are required to retire at this Annual General Meeting and, being eligible, offer themselves for election.

Resolution 6: Directors' authority to allot shares
Section 551 of the Act provides that the directors of a company may not allot shares (or grant rights to subscribe for shares or to convert any security into shares) in a company unless they have been given prior authorisation for the proposed allotment by ordinary resolution of the company's shareholders or by the Articles of Association of a company.

Accordingly, this resolution seeks to grant a new authority under section 551 of the Act to authorise the Directors to allot shares in the Company or grant rights to subscribe for, or convert any securities into, shares of the Company and will expire on the date falling 15 months after the passing of this resolution or at the conclusion of the next Annual General Meeting of the Company following the passing of this resolution, whichever occurs first.

If passed, Resolution 6 would give the Directors authority to allot shares or grant rights to subscribe for, or convert any security into, shares in the Company up to a maximum nominal value of £8,686,018 representing approximately one-third of the Company's nominal value of the issued share capital at the date of this notice.

Resolutions 7 and 8: Disapplication of pre-emption rights
Under section 561(1) of the Act, if the Directors wish to allot any of the unissued shares or grant rights over shares for cash (other than pursuant to an employee share scheme) they must in the first instance offer them to existing shareholders in proportion to their holdings. There may be occasions, however, when the Directors will need the flexibility to finance business opportunities by the issue of shares without a pre-emptive offer to existing Shareholders. This cannot be done under the Act unless the Shareholders have first waived their pre-emption rights. The resolutions proposed are in line with the PEG Statement of Principles 2022 and in line with the guidance issued by the Investment Association.

If passed, Resolution 7 empowers the Directors to allot equity securities for cash other than in accordance with the statutory pre-emption rights in respect of (i) rights issues and similar offerings, where difficulties arise in offering shares to certain overseas Shareholders, and in relation to fractional entitlements and certain other technical matters and (ii) generally in respect of Ordinary Shares up to a maximum nominal value of £2,605,806, representing approximately 10% of the Company's nominal value of the issued share capital as at the date of this notice, together with authority for up to a maximum nominal value of £521,161, representing approximately 2% of the Company's issued ordinary share capital as at the date of this notice, to be used only for the purposes of a follow-on offer which the Directors determine to be of a kind contemplated by paragraph 3 of section 2B of the PEG Statement of Principles 2022. This is proposed as a special resolution.

If passed, Resolution 8 empowers the Directors to make allotments for cash, in respect of a further maximum nominal value of £2,605,806, representing approximately 10% of the Company's issued ordinary share capital as at the date of this notice, provided that this power may be used only for the purposes of financing (or refinancing, if the authority is to be used within six months of the original transaction) a transaction which the Directors determine to be an acquisition or other capital investment of a kind contemplated by the PEG Statement of Principles 2022, together with authority for up to maximum nominal value of £521,161, representing approximately 2% of the Company's issued ordinary share capital as at the date of this notice, to be used only for the purposes of a follow-on offer which the Directors determine to be of a kind contemplated by paragraph 3 of section 2B of the PEG Statement of Principles 2022. This is proposed as a special resolution.

The Directors intend to adhere to the guidelines set out in the PEG Statement of Principles 2022, and not to allot shares for cash on a non pre-emptive basis pursuant to the authority in Resolution 7 or Resolution 8 in excess of an amount equal to 10% of the Company's issued ordinary share capital (excluding treasury shares) in any one-year period, whether or not in connection with an acquisition or specified capital investment, in each case other than in connection with an acquisition or specified capital investment which is announced contemporaneously with the allotment or which has taken place in the preceding six-month period and is disclosed in the announcement of the allotment.

These authorities will expire on the date falling 15 months after the passing of the resolutions or, if sooner, the conclusion of the next AGM of the Company after the passing of the resolutions. The exception to this is that the Directors may allot equity securities after the authorities have expired in connection with an offer or agreement made or entered into before the authorities expired.

Resolution 9: Authority for market purchase
If passed, Resolution 9 will permit the Company to purchase up to 26,058,055 Ordinary Shares (representing approximately 10% of the Ordinary Shares in issue as at the date of this notice) through the market subject to the pricing limits set out in the resolution and shall expire (unless previously renewed, varied or revoked by the Company in general meeting) on the date falling 15 months after the passing of this resolution or at the conclusion of the next Annual General Meeting of the Company (whichever first occurs). This is proposed as a special resolution.

GENERAL INFORMATION FOR SHAREHOLDERS

In respect of the Annual General Meeting

Time of the Meeting

The Meeting will start promptly at 2:00 pm on Wednesday 28 June 2023.

The venue

The Meeting will be held in person at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ.

Shareholders are asked to exercise their votes by submitting their proxy as set out in the Notice of Meeting above. All Shareholders are strongly recommended to vote electronically at **www.signalshares.com** as your vote will automatically be counted.

Travel details

Directions to the venue can be found at **https://www.ihg.com/holidayinn/hotels/gb/en/guildford/guisu/hoteldetail/directions**

There is easy access to the venue from the A3 and there is a large secure car park. Please note you need to register your car for free parking.

The nearest railway station is Guildford, and the venue is located approximately five minutes taxi ride or ten minutes bus ride from the railway station. The bus stop is situated at the end of the hotel driveway.

Introducing the Parsortix PC1 Clinical System

THE CHALLENGE

Cancer: a significant and growing problem

What is cancer?

Cancer is a disease in which abnormal cells divide without control and can invade nearby tissues.

Cancer starts when genetic changes make one cell or a few cells begin to grow and multiply, unchecked by normal restraints. This may cause a growth called a tumour that can have dangerous consequences for organs in the body.

How many people are affected?

1 in 2

people will be diagnosed with cancer in their lifetime[2,3]

50% growth

The number of annual cancer cases is increasing, and in the US has risen by 50% in the last two decades[2,4]

18m new cases

Globally, 18 million people were diagnosed with cancer and 10 million people died from the disease in 2020[1]. There are a further 44 million people living with cancer[1]

1 www.gco.iarc.fr/today/home.
2 www.seer.cancer.gov/statfacts/html/all.html – USA (40%).
3 www.cancerresearchuk.org/about-cancer/what-is-cancer – UK (50%).
4 www.pubmed.ncbi.nlm.nih.gov/11577478/.
5 www.ncbi.nlm.nih.gov/pmc/articles/PMC3597235/.

How cancer spreads

The main reason that cancer is so serious is its ability to spread in the body. Cancer cells can spread locally by moving into nearby tissue or spread regionally, to nearby lymph nodes, tissues or organs. It can also spread to distant parts of the body from circulating tumour cells (CTCs) released into the blood. When this happens, it is called **metastatic cancer**.

The process by which cancer cells spread to other parts of the body is called **metastasis**[5].

Why is metastasis so serious?

90%

of cancer deaths are caused by metastasis[5]

The "stage" of cancer at diagnosis is extremely important for predicting patient survival. Cancer staging is a way of describing the size of a cancer and how far it has spread into the surrounding tissues or other sites in the body (metastasis). Staging is important in helping determine treatment. If the cancer is "early" stage and found in only one place in the body then surgery or radiotherapy may be sufficient. If the cancer is "late" stage and has metastasised to many places in the body, then treatment is needed that also circulates throughout the whole body such as chemotherapy, hormone therapy or targeted cancer drugs.

Once cancer spreads it can be hard to control and whilst some types of metastatic cancer can be driven into remission with treatment, most cannot. There is significant variation in the likely stage at diagnosis between different cancer types. Some cancer types have no obvious symptoms or are fast growing and as a result patients are often diagnosed at a late stage, once the cancer has already spread. These include lung, ovarian and pancreatic cancer.

Why is treating cancer so challenging?

During cancer treatment there are many challenges to optimal patient management:

1 **How do you know which drug will work most effectively?**
Mutations in cancer cells vary from patient to patient with the same cancer type so the same drug isn't effective for all patients.

2 **How do you track whether drugs are working and continue to be effective?**
A single tumour contains cancer cells with many different mutations – this is known as heterogenity. This means that a drug may only be effective against part of the tumour.

3 **How do you monitor patients in the long-term?**
Over time cancer cells evolve and can change in response to treatment selection pressure. Continual monitoring is needed to deliver targeted treatment.

Tissue biopsy shortcomings

The standard diagnostic test for cancer is to undertake a **solid tissue biopsy**. This approach has many shortcomings compared to a **liquid biopsy**:

Expensive to perform and requires a lot of hospital resources.

Patients experience a longer **recovery** time which may **delay** treatment.

Difficult to repeat so unable to track the changes in the cancer over time and the development of drug resistance.

Requires an **invasive** procedure and can cause adverse events.

Poor tissue availability due to inaccessibility of the tumour (pancreatic, lung, brain, liver and bone cancers).

Only samples **one site** and may not reflect tumour heterogeneity.

AT A GLANCE

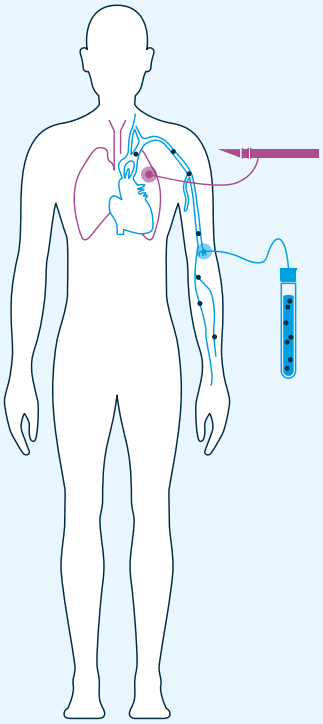
Liquid biopsy improving patient outcomes and reducing healthcare costs

The Parsortix system captures circulating tumour cells (CTCs) which cause cancer metastasis and harvests them for analysis.

Tissue biopsy is the current standard of care but has many shortcomings and is challenged by:

1) the frequent lack of tissue availability (too ill for surgery, tumour inaccessible, insufficient tissue);
2) tumour heterogeneity as it only samples one site; and
3) the dynamic nature of the cancer response to treatment meaning the original biopsy information is rapidly outdated.

Obtaining cancer tissue for analysis



Solid tissue biopsy

Tumour tissue is cut out from the cancer site through an **invasive** procedure

Tissue samples
Tissue is specially prepared so sections can be examined – usually formalin-fixed paraffin-embedded (FFPE) samples

Liquid biopsy

Cancer cells or cell fragments are obtained from **a simple blood test.** Non-invasive, repeatable, real-time, cost effective

CTCs
Living intact cancer cells shed from a tumour into the bloodstream which can cause metastasis

Circulating tumour DNA (ctDNA)
DNA from **fragments of dead cells** shed into the bloodstream can contain cancer-related mutations

Benefits of Parsortix CTC solution

		Solid tissue biopsy		Liquid biopsy	
Source		**Primary tumour**	**Metastatic site**	**CTCs[1]**	**ctDNA[2]**
Sample type		Intact cells	Intact cells	Intact cells	Fragmented DNA
Procedure		Invasive	Invasive	Non-invasive[3]	Non-invasive[3]
Sample accessibility		Not always accessible	Less accessible	**Accessible using Parsortix[4]**	Accessible
Tumour heterogeneity		Site of biopsy sampling	Site of biopsy sampling	Multi-site sampling	Multi-site sampling
Patient recovery time		Varies	Longer	None	None
Test costs		Varies	Higher	Lower	Lower
Test turnaround time		Varies	Longer	Shorter	Shorter
Longitudinal monitoring[5]		Difficult	Very difficult	Easy	Easy
Molecular analysis	DNA	Yes	Yes	Yes	Yes
	RNA	Yes	Yes	Yes	Difficult
	Protein	Yes	Yes	Yes	No
Live cells	Cell culture	Yes	Yes	Yes	No
	Xenograft	Yes	Yes	Yes	No
Standard of care		Proven	Proven	Adopted in prostate cancer for AR-V7	Adopted for targeted treatment selection

1 CTCs (circulating tumour cells) are live cancer cells circulating in the blood.
2 ctDNA is cell-free circulating tumour fragments of DNA from dead cells, which may be found in the plasma component of the blood.
3 Sample obtained from simple peripheral blood draw.
4 Access to CTCs from blood is technically challenging given the low number of CTCs present and historically has been very difficult. ANGLE's Parsortix system has been specially designed to address this issue.
5 Solid tissue biopsy information is a one-time snapshot and rapidly becomes outdated and does not reflect response to treatment and current mutational status. Liquid biopsy information is dynamic as tests can be repeated to provide real time information to monitor changes over time.

▸ WHICH SAMPLE?

CTCs provide the complete picture

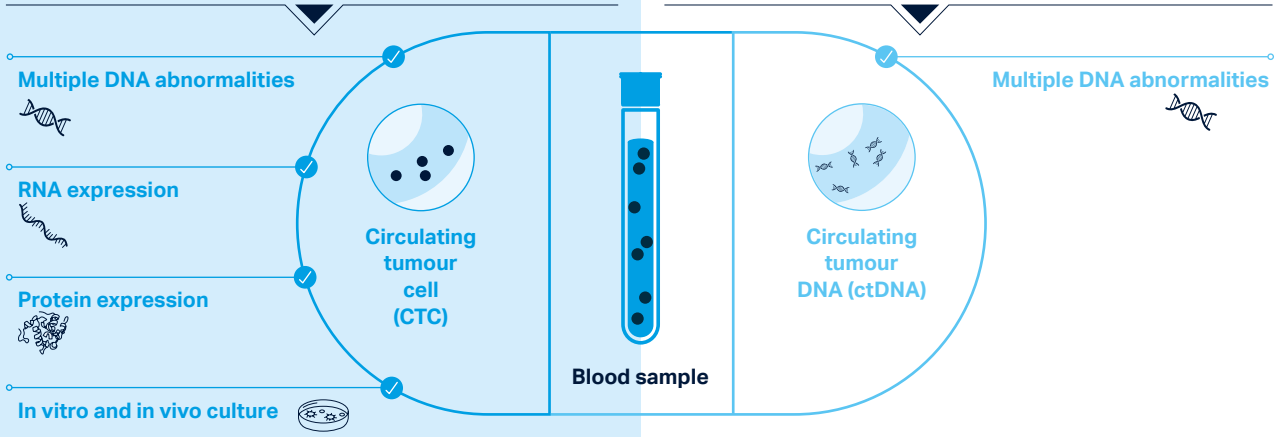
Circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) can be measured concurrently from a single blood draw to provide complementary information about a patient's disease. Liquid biopsy has the potential to advance current standard of care throughout the patient treatment pathway.

CTCs Complete DNA, RNA and proteins

CTCs are living cells that cause metastasis and are often also resistant to drug therapy. Identifying and targeting these cells may improve patient outcomes.

ctDNA DNA fragments only

ctDNA is derived from dead cells and provides little insight into how the cancer might develop in the future, e.g. emerging drug resistance.



"CTCs, as living cells that are active in the metastatic process, can provide prospective insight into a patient's cancer. In comparison, ctDNA derived from dead and dying cells provides important but historical information on patient disease. The genetic and phenotypic diversity in CTCs most likely mirrors that of the patient's tumour and is reflective of cell evolution."

Prof. Evi Lianidou, Head of the Molecular Diagnostics Laboratory, National and Kapodistrian University of Athens

With advances in genomic sequencing oncologists are increasingly able to select therapies based on the specific DNA mutations identified in a patient's tumour. However, many patients fail to respond to targeted treatment or do not have a sustained response.

That may be, in part, because **key information about the biology of the tumour is missing from looking at the DNA alone.** While the presence of mutations can be determined from DNA, the effect of mutations on protein function cannot be fully understood without analysing gene expression (RNA) or the proteome. Understanding protein expression is critical for drug development, treatment selection and predicting treatment response.

With sustained investment in proteogenomic research, doctors will be able to get a complete picture of a patient's tumour, to inform diagnosis and treatment which will improve outcomes[1].

The study of CTCs allows complete DNA, RNA and protein expression analysis for genomic, transcriptomic and proteomic research.

1 NIH Budget Report 2022.

What is the genome, transcriptome and proteome?

Genome

Between

20,000-25,000 genes

Genes are units of DNA that code for proteins. Abnormalities in certain genes can result in cancer development and growth.

Transcriptome

Approximately

100,000 transcripts

To make proteins, genes must first be transcribed into messenger RNA (mRNA). Different sections of a gene can either be included or excluded from the mRNA transcript, producing multiple different transcripts from a single gene that result in related but different proteins.

Proteome

Estimated more than

1,000,000 proteins

After mRNA transcripts are translated into proteins, proteins undergo modifications that affect their activity and how long they are present in a cell. Protein abundance, diversity and function could hold the key to understanding why targeted therapies may not always work as expected.

Clinical utility of CTCs

To find out more watch:
www.medpagetoday.com/meetingcoverage/sabcsvideopearls/102475

CTC based liquid biopsies enable minimally invasive, longitudinal monitoring of cancer for the entirety of the patient care pathway.

CTCs can provide complementary information alongside current standard of care for clinical decision making. This includes:

1. **Diagnosis and accurate prognosis:**
   - CTCs have been isolated and enumerated as a prognostic biomarker in multiple cancers[1,2].
   - Gene expression analysis of CTCs has been shown to **accurately** differentiate between early and late-stage cancer, providing a more **effective predictor of disease** as compared to gold standard biomarkers alone[3].
   - CTCs and cancer associated macrophage-like cells (CAMLs) are markers for disease **prognosis**[4,5] and **disease monitoring** after surgery, to aid patient management[5].
2. **Therapeutic target selection:**
   - CTCs contain intact whole cancer genomes and transcriptomes, and can offer **complementary** information alongside ctDNA[1,6]. This information can provide clinical targets for **drug selection** in multiple cancers[1]. These targets have been shown to mirror matched metastatic tissue biopsy[7].
   - Molecular analysis of CTCs has shown clinical relevance, providing additional information to **guide treatment decisions**[1] **and** identify **targets for drug selection** such as HER2[4].
3. **Monitoring treatment response and resistance:**
   - CTCs have been analysed to study mutations and **changes in mutations** to **track tumour evolution** throughout the treatment process[8]. This is relevant for studying treatment response and treatment resistance. This allows a real-time view of cancer status to inform **current and future drug selection.**
4. **Spatiotemporal monitoring of metastasis:**
   - CTCs are responsible for **metastasis**, and therefore provide information on the **metastatic process**[8]. As a result, CTCs are more representative of cancer **heterogeneity** than single tissue samples and provide up-to-date clinical information.
   - Analysis of CTCs has shown high levels of epithelial to mesenchymal transition (EMT). EMT is a key transition step in cancer cells associated with **progression, metastasis, resistance to treatment and relapse**[9]. This status has been reported to be almost **exclusively** associated with advanced disease and was **independent of the EMT status of matched tissue** biopsy[9].
   - Monitoring EMT status in CTCs has been reported as a **marker of cancer metastasis**[10].
5. **Disease relapse:**
   - CTCs have the potential to **detect** minimal residual disease (MRD) **prior to standard of care**[11-13].
   - In some cases ctDNA and CTCs have been shown to **predict relapse earlier** than imaging and more accurately than serum markers[14].
   - CTCs have been reported to identify patient groups at **high risk of relapse** that may benefit from systemic therapy[15].
   - The presence of specific markers on CTCs has been reported to independently predict an increased risk of **disease relapse, death and potential immune response**[16].
   - CTC analysis during relapse has shed light on treatment **resistance** and the **metastatic process**[8] to inform **current and future drug selection.**

Diagnosis and early assessment	Early-stage cancer	Advanced-stage cancer	Post treatment
Patient timeline			
High risk screening	First line treatment	Disease progression	Disease remission
CTC analysis in the patient assessment stage can predict: • Risk of cancer presence • Prognosis • Overall survival • Risk of death	**CTC analysis in early-stage cancer can:** • Identify novel biomarkers • Inform targeted drug selection • Monitor treatment response and early prediction of drug resistance	**CTC analysis in advanced-stage cancer can:** • Confirm diagnosis of metastatic cancer • Inform targeted drug selection • Monitor treatment response and drug resistance • Identify new/changing drug targets as the tumour evolves	**CTC analysis post treatment can:** • Identify MRD before current standard of care/imaging • Identify risk of relapse

1 Ortolan, E. et al. ESMO Open **6**, (2021).
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THE SOLUTION

Parsortix system

The Parsortix system from ANGLE uses a patented microfluidic technology in the form of a single use cassette to capture and then harvest circulating tumour cells (CTCs) from blood.

The cassette captures CTCs based on their less deformable nature and larger size compared to other blood cells.

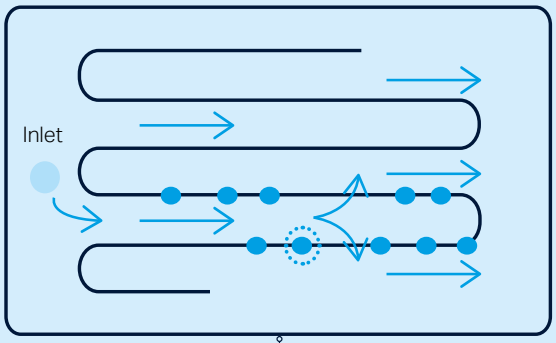
// The Parsortix system has a unique combination of features making it suitable for routine clinical analysis of patient blood samples.

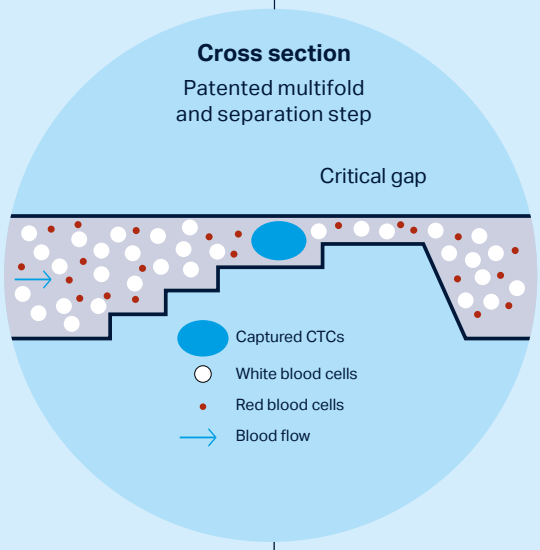
Prof. Ged Brady
Cancer Research UK Manchester Institute of Technology

CANCER RESEARCH UK

A closer look at the cassette

CTCs are caught on a step that "folds over" in a microscope slide sized cassette.





Able to capture one CTC in a billion blood cells.

CTCs provide the best sample

A simple peripheral blood test can be used to provide crucial medical information regarding a patient's disease.

- CTCs are living cells from a patient's tumour, carrying large amounts of up-to-date information as the tumour changes and mutates. These intact whole cells enable the **complete picture** of the cancer to be understood as they allow DNA, RNA and protein analysis.
- CTCs are **biologically specific and can provide a prospective view of a patient's cancer** – they cannot be present unless the patient has cancer.
- By **analysing** CTCs you can identify the characteristics of the cancer to better determine which drugs will be more effective.
- By looking at the **number** of CTCs and how this changes over time, you can predict survival rates for patients and monitor how well the treatment is progressing.
- Clusters of CTCs isolated by the Parsortix system have been shown to have an 80 times increase in metastatic potential compared to single CTCs.
- A simple blood test **monitoring** the levels of CTCs for patients in remission may act as an early warning system of a relapse, well ahead of symptoms, allowing earlier treatment with consequently a better likelihood of success.

Competitive differentiation

Unlike some other CTC systems, we believe the Parsortix system is applicable for all solid tumour cancers and has been exemplified in **24 different cancer types.**

The Parsortix system can identify all CTC subpopulations, including epithelial or mesenchymal cells or those undergoing epithelial to mesenchymal transition (EMT).

EMT is important because it is involved in tumour progression, the development of drug resistance and metastasis.

EMT is not complete in cancer cells, and tumour cells are in multiple transitional states and express mixed epithelial and mesenchymal markers. Such hybrid cells in partial EMT can move collectively as clusters and can be more aggressive than cells with a distinct phenotype.

EMT results in a loss of expression of the epithelial marker, EpCAM. **As a result, up to 50% of CTCs are missed by EpCAM dependent CTC enrichment systems.**

It is important to identify all CTC subpopulations given their different prognostic significance with respect to clinical outcomes and treatment response.

Technology	Simple and flexible process	Low cost	Captures CTCs from all types of solid cancers investigated	Captures mesenchymal CTCs involved in metastasis	Easily harvests cells for analysis	Cell viability (alive)	Captures CTC clusters
Parsortix microfluidic step	✓	✓	✓	✓	✓	✓	✓
Antibody-based systems	×	×	×	×	×	×	×
Membrane-based systems	✓	✓	✓	✓	×	✓	×
Field Flow Fractionation systems	✓	✓	✓	✓	×	× ✓	×

HOW IT WORKS

Capture, harvest and analysis of CTCs

The Parsortix® System is a next generation liquid biopsy technology. Starting from a simple blood draw, which is non-invasive and can be repeated as often as needed, the system isolates and harvests CTCs, intact cancer cells, providing a real-time sample for subsequent analyses using widely adopted laboratory techniques.

Unlike ctDNA, which is limited to DNA analysis and is the focus for most of the liquid biopsy industry, a full range of analyses (DNA, RNA and protein) can be undertaken with CTCs, giving a potential alternative to a tissue biopsy and providing the best sample for analysis.

Automated process requiring minimum user intervention

1 Blood collection

Designed for a single 10ml tube of blood. No pre-processing required.

2 Automated blood processing

Blood is pumped through the cassette with minimal user input.

3 Cell capture in cassette

Proprietary single use cassette captures CTCs, intact living cancer cells.

4 Cell harvest

CTCs can be harvested in <200µl buffer for multiple downstream analysis techniques.

5 Downstream analysis

Widely available techniques

The cells harvested by the Parsortix system can be analysed using existing techniques already established for tissue biopsy and cell analysis including:

Imaging assays
- Cytopathology
- Immunofluorescence (IF)

Molecular assays
- Fluorescent In Situ Hybridisation (FISH)
- Polymerase Chain Reaction (PCR)
- Next Generation Sequencing (NGS) and Third Generation Sequencing (TGS)
- RNA sequencing (RNA-seq)
- Whole Genome Amplification (WGA)
- Whole Exome Sequencing (WES)

Imaging assays

Portrait+™
Powered by Parsortix®

ANGLE is developing numerous assays for immunofluorescent staining of CTCs (marking their presence), CTC subtypes (epithelial, mesenchymal and those undergoing epithelial to mesenchymal transition – EMT), as well as for specific biomarkers.

These include:
- Portrait Flex: for EMT CTC detection
- Portrait PD-L1: for EMT and PD-L1 detection on CTCs
- Portrait gamma H2AX (γH2AX): for DNA damage assessment
- Portrait phospho-KAP1 (pKAP1): for DNA damage assessment
- Quantitative HER2 IF assay
- Custom assays and panels including EMT staining with an open channel

Read more on ***page 20***

Molecular assays

Landscape+™
Powered by Parsortix®

ANGLE is developing numerous assays for the molecular analysis of CTCs.

These include:
- Landscape DNA digital PCR assay (such as EGFR, KRAS and PIK3CA)
- Landscape RNA digital PCR assay
- Landscape DNA NGS assay
- Landscape RNA NGS assay
- Custom assays and panels

Planned assays include:
- Single cell picking workflow
- MassArray panel
- FISH HER2 assay
- Pan-cancer panel

Read more on ***page 22***

To watch our video visit:
www.angleplc.com/parsortix technology/introduction/

FDA CLEARANCE

ANGLE achieves world first with FDA De Novo product clearance towards a new era of personalised cancer care

In May 2022, the FDA granted ground-breaking product clearance (De Novo Class II) for the Parsortix PC1 Clinical System to harvest CTCs, intact cancer cells, from metastatic breast cancer (MBC) patient blood for subsequent, user-validated analysis. This rare gold standard for medical device clearance involved rigorous assessment of the platform's performance proving robust evidence of its capabilities.

ANGLE followed a FDA De Novo process for the Parsortix PC1 Clinical System as there is no predicate device. This FDA clearance is the first ever product clearance to harvest CTCs, intact cancer cells, from a patient blood sample for subsequent analysis and offers the prospect of a new era of personalised cancer care.

FDA product clearance, which is the global gold standard for medical devices, gives ANGLE a first mover advantage for intact cell analysis in the global liquid biopsy market, which is estimated to grow to over US$100 billion per annum in the United States alone[1]. Securing this clearance is the culmination of a sustained effort by the Company over six years, utilising unique technology developed, owned and patent protected by ANGLE.

ANGLE believes that the ability to harvest CTCs provides the best sample of the patient's metastatic breast cancer, offering the potential for a wide range of downstream analyses using established techniques and an existing installed base of downstream instruments. This approach has the potential to transform treatment decisions for cancer patients as it provides the opportunity for repeat non-invasive liquid biopsies based on a simple blood test to assess cancer status.

For more information on our work involving breast cancer, go to our website at: **www.angleplc.com/parsortix-pc1-clinical-system/**

4
leading US cancer centres enrolled patients for FDA clinical studies

600
subjects recruited into US clinical studies supporting the De Novo application

US$3.9bn
p.a. estimated US market potential for the Parsortix system in metastatic breast cancer[2]

2.3m
women diagnosed globally with breast cancer in 2020[3]

7.8m
women living with and after breast cancer[3]

20-30%
of people initially diagnosed at early stages will develop metastatic breast cancer[4]

FDA U.S. FOOD & DRUG ADMINISTRATION

What is FDA?
The United States Food and Drug Administration (FDA) is the US federal agency responsible for the regulatory clearance of medical devices used for the diagnosis or treatment of patients.

Why is it important?
FDA clearance allows a medical device to be sold in the United States for the purpose of patient management. The FDA determines independently that the benefits of a device outweigh the potential risks and that the device is safe and effective when used in accordance with the intended use statement.

What are the benefits?
Securing FDA clearance will allow ANGLE to sell the Parsortix PC1 Clinical System for its intended use in the United States. It will also facilitate sales into pharmaceutical drug studies and with Contract Research Organisations.

1 Cowen 2020, Liquid Biopsy: Early Detection of a Huge Investment Opportunity.
2 Company estimate – United States only.
3 International Agency for Research on Cancer (Globocan 2020).
4 www.mbcn.org/incidence-and-incidence-rates/.

FDA studies supported by leading US cancer centres

My lab's overarching interest is to develop assays that will serve as companion diagnostics to assist clinicians who treat cancer patients (MBC and non-small cell lung cancer) with therapies such as immune checkpoint inhibitors and targeted agents. Therefore, we have devoted considerable effort to developing multiple cellular assays utilizing CTCs which offer a minimally invasive approach to monitor a patient's cancer and their response to these therapies. Data from our trial with Parsortix showed the system was able to effectively capture a single cancer cell in a blood sample for analysis. **We look forward to the further development of CTC based assays that may bring enormous benefits to patients with MBC as well as other cancers in the future.**

Dr. James, M. Reuben
Professor, Department of Hematopathology, Division of Pathology/Lab Medicine, The University of Texas MD Anderson Cancer Center and co-principal investigator of the trial

In my team's research, we have demonstrated how circulating tumor cells harvested by this system are a good surrogate for tissue biopsies of the metastatic site. **With this regulatory clearance we can now obtain repeat biopsies periodically to provide up-to-date information to guide treatment decisions, improving care and minimising invasive procedures for these patients.**

Julie E. Lang
Chief of Breast Surgery, Cleveland Clinic. Formerly Director, USC Breast Cancer Program, Associate Professor of Surgery, Norris Comprehensive Cancer Center, University of Southern California

MBC is a heterogenous disease that requires targeted and biological therapies and diagnostic monitoring of the natural molecular evolution of the disease to be able to longitudinally identify and implement the most effective treatment and measure its benefit. I believe that the Parsortix® PC1 system provides the ideal technology for such purpose allowing point of care diagnostic capabilities that capture the complexity of the ever-changing molecular landscape of MBC. In fact, **I envision that the clinical application of the Parsortix® PC1 system can result in an unprecedented opportunity to perform a real-time molecular diagnostic assessment of enriched CTCs with comprehensive molecular information on both protein expression and genomic abnormalities driving the disease.**

Dr. Massimo Cristofanilli
Chief, Breast Medical Oncology and Associate Director of Precision Medicine, Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine, Formerly Associate Director of Translational Research and Precision Medicine at Northwestern University

Liquid biopsy to collect circulating live cancer cells is an essential tool that we need to make advancements in understanding the biology of metastatic breast cancer. We anticipate that this announcement may help to develop novel biomarkers, therapeutic approaches and **contribute to selecting the best treatment for metastatic breast cancer patients.**

Dr. Naoto T. Ueno
Director, University of Hawaii Cancer Center. Formerly Professor, Department of Breast Medical Oncology, Chief of Section of Translational Breast Cancer Research, The University of Texas MD Anderson Cancer Centre

As a leading translational research team, we have a long association with the team at ANGLE and are delighted to have played a key role in their clinical studies in an effort to bring the Parsortix system into clinical use. **Real-time analysis of live circulating tumor cells offers the potential to transform patient care by enabling actionable information that can guide treatment decisions** in heterogeneous and dynamic cancers such as MBC. FDA clearance is a major advance in cancer care and we look forward to bringing this benefit to MBC patients as well as continuing to support further research into the advantages of CTC analysis using the Parsortix system.

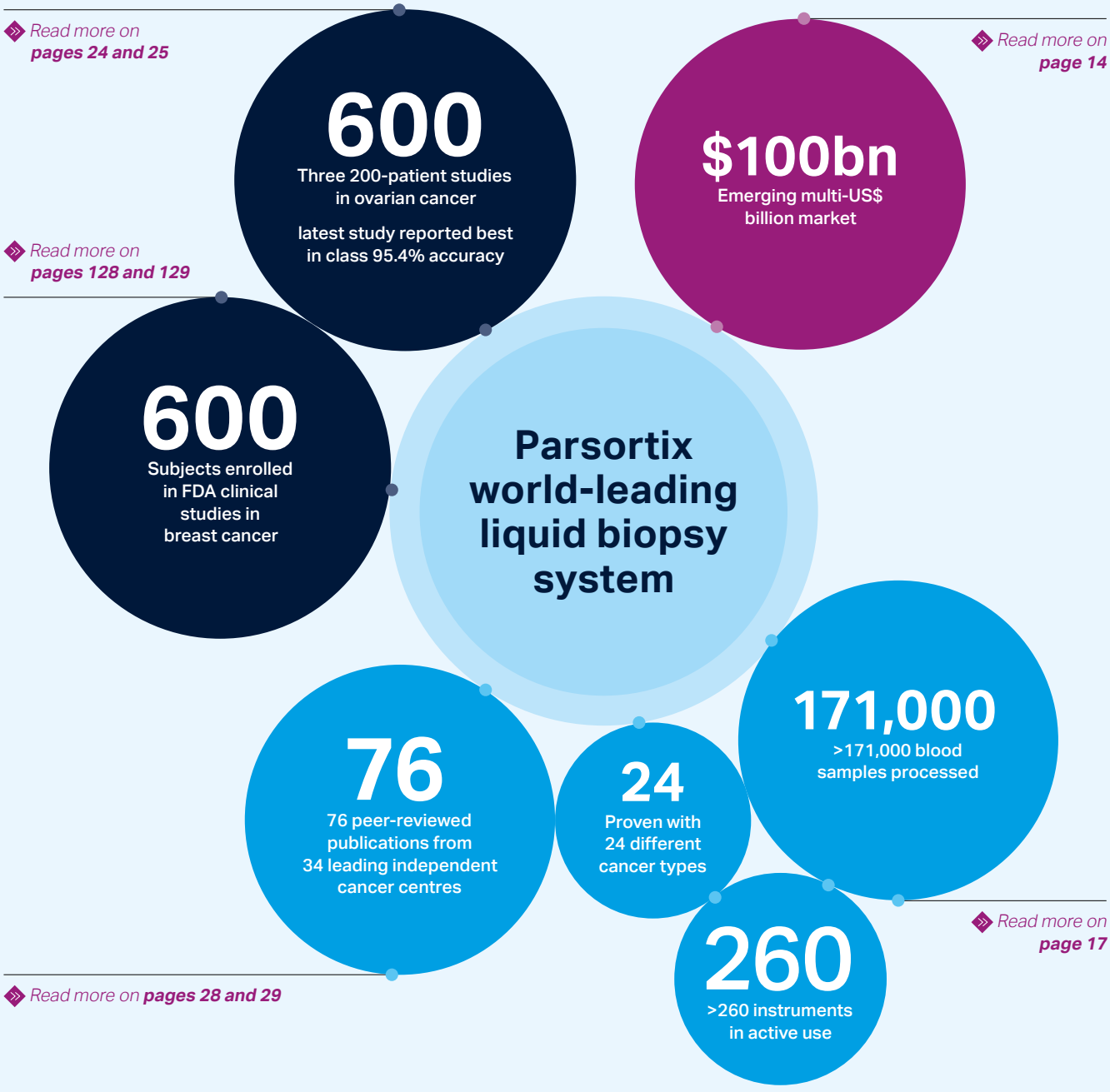
Dr. Richard Moore
Director of Gynecologic Oncology Division, University of Rochester Medical Center, Wilmot Cancer Institute

THE POTENTIAL

Transforming cancer care with a liquid biopsy based on a simple blood test

Following FDA clearance, ANGLE is focused on commercialising its liquid biopsy system which has the potential to transform cancer diagnosis and treatment.

Unique patented microfluidic approach, strongly differentiated from the competition.



EXPLANATION OF FREQUENTLY USED TERMS

Term	Explanation
Analyte	The substance that is being investigated, identified or measured in the analysis/test/assay
Antibody	A protein made by white blood cells in response to an antigen (a toxin or foreign substance). Each antibody can bind to only one specific antigen. The purpose of this binding is to help destroy the antigen
Antigen	Proteins that can be used as markers in laboratory tests to identify cancerous and normal tissues or cells
AR-V7	The androgen receptor (AR) has been proposed as a mechanism of therapeutic resistance to AR signalling (ARS) inhibitors. Androgen receptor variant 7 (AR-V7) participates in regulating prostate cancer cell proliferation and gene expression and is correlated with drug resistance. Patients with low-risk disease should receive taxanes if they are AR-V7+ or ARS inhibitors if they are AR-V7–
Assay	A laboratory test to find and measure the amount of a specific substance
AUC-RO	The area under the curve (AUC) for a receiver operating characteristic (ROC) plot, a plot of 1-specificity on the x-axis vs. the sensitivity on the y-axis at each possible threshold for a test's results, is a measure of a diagnostic test's accuracy. The accuracy of the test depends on how well the test separates the two groups being compared into those with the outcome (sensitivity) and those without the outcome (specificity) in question. An AUC of 1 (100%) represents a perfect test while an AUC of 0.5 (50%) represents a worthless test. The traditional academic classification system for AUC-ROCs is 90% to 100% = excellent; 80% to 90% = good; 70% to 80% = fair; 60% to 70% = poor; 50% to 60% = fail. Reference for further information: div-class-title-understanding-receiver-operating-characteristic-roc-curves-div.pdf (cambridge.org)
Baseline	An initial measurement of a condition taken at an early timepoint used for comparison over time
Benign	Not cancerous. Benign tumours may grow larger but do not spread to other parts of the body. Also called non-malignant
Biomarker	A biological molecule found in blood, other body fluids or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how a disease is developing or how well the body responds to a treatment for a disease or condition. Also called molecular marker and signature molecule
Biopharma	Biopharmaceutical companies collectively as a sector of industry
Biopsy	Process by which cancer cells are removed from the tumour for analysis
CAGR	Compound Annual Growth Rate. A measure of revenue growth that has been compounded over time
Cancer	A term for diseases in which abnormal cells divide without control and can invade nearby tissues. Cancer cells can also spread to other parts of the body through the blood and lymph systems
Cancer associated macrophage-like cells (CAMLs)	Specialised white blood cells found in the peripheral blood which are associated with the presence of solid tumours
Capture	Process for capturing target cells from a sample
Capture efficiency	Proportion of target cells captured
Carcinogen	Any substance that is directly involved in causing cancer
Cassette	ANGLE's patent protected microfluidic consumable that captures CTCs
CD45	The CD45 antibody recognises the human CD45 antigen, also known as the leukocyte common antigen. WBC are CD45+ whereas CTCs are CD45-. Staining with CD45 often used as a negative confirmation that CTCs are not WBC
CD47	Is known as integrin associated protein found on the surface on many cells in the body. The protein tells immune cells not to destroy a cell, helping the protection of cells and also the detection of aging or diseased cells. It is overexpressed in many types of cancer allowing the cells to avoid death
CDx	Companion diagnostic
Cell(s)	In biology, the smallest unit that can live on its own and that makes up all living organisms and the tissues of the body. The human body has more than 30 trillion cells
Cell culture	See cultured cells
Cell-free DNA	Genomic DNA found in the plasma
Cell labelling	Technique involving the staining of target cells with fluorescent and/or chromogenic markers for cell identification
Cell lines	Cultured cells

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
CE mark	Regulatory authorisation for the marketing and sale of products for clinical use in the European Union. The CE marking is the manufacturer's declaration, following appropriate assessment by a CE Notified Body, that the product meets the requirements of the applicable CE directives
Chemotherapy	The treatment of cancer by chemicals (drugs). In cancer care the term usually means treatment with drugs that destroy cancer cells or stop them from growing
Circulating tumour cell	Cancer cell that has detached from a tumour and is circulating in the patient's blood
Circulating tumour DNA	Circulating tumour DNA (ctDNA) is tumour-derived fragmented DNA in the bloodstream that has been released by dead/dying tumour cells
CLIA Laboratory	The Clinical Laboratory Improvement Amendments (CLIA) of 1988 are federal regulatory standards that apply to all clinical laboratory testing performed on humans in the United States (with the exception of clinical trials and basic research). A clinical laboratory is defined by CLIA as any facility which performs laboratory testing on specimens obtained from humans for the purpose of providing information for health assessment and for the diagnosis, prevention or treatment of disease
Clinical application	Use in treating patients
Clinical samples	Patient samples usually blood
Clinical study	A type of research study that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis or treatment of a disease
Clinical use	Use in treating patients
Clinician	A healthcare professional/doctor
Companion diagnostic (CDx)	A medical device which provides information that is essential for the safe and effective use of a corresponding drug or biological product. Also abbreviated as CDx
Comprehensive genomic information	Information gained from profiling large amounts of patient genes including relevant cancer biomarkers and gene alterations to guide the patient pathway
Contract Research Organisation (CRO)	A company hired by another company or research centre to take over certain parts of running a clinical trial. The company may design, manage and monitor the trial, and analyse the results. Also abbreviated as CRO
Copy number alterations	Changes to chromosome structure that result in a loss or gain in copies of sections of DNA
CRISPR	Clustered regularly interspaced short palindromic repeats, a segment of short repeats that can be used as a gene editing tool
CT	Computerised tomography, a form of diagnostic imaging that combines a series of X-rays
CTC(s)	Circulating tumour cell(s)
CTC clusters	Groups of more than two CTCs that travel together in the bloodstream
CTC labelling	CTCs are often labelled with three markers and are formally identified as CTCs if they are CK+, CD45-, DAPI+
ctDNA or cfDNA	Abbreviation for circulating tumour DNA also known as cell-free DNA
CT scan	A procedure that uses a computer linked to an x-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles and are used to create three-dimensional views of tissues and organs
Cultured cells	Cultured cells grown in the laboratory from human-derived cells used for experimental work
Cytokeratin (CK)	Cytokeratins are a family of intracytoplasmic cytoskeleton proteins with members showing tissue specific expression
Cytopathology	A branch of pathology involving the study and diagnosis of disease at a cellular level
CK	Cytokeratin
CK+	A cell positive for the presence of cytokeratin protein or mRNA with the presence of distinct cytokeratins often used to identify epithelial cells
Cytopathological	A branch of pathology that studies and diagnoses diseases at the cellular level, generally used on samples of free cells or tissue fragments
DAPI	A nuclear stain that is often used to identify the nucleus in a cell
DDR	DNA Damage Repair. A group of cellular restoration processes in response to DNA damage
De Novo	An FDA clearance marketing pathway to classify novel medical devices – see FDA De Novo below

Term	Explanation
DEPArray™	A commercial single cell isolation system
Diagnosis	The process of identifying a disease, condition or injury from its signs and symptoms. A health history, physical examination and tests, such as blood tests, imaging tests and biopsies, may be used to help make a diagnosis
Diagnostic Leukapheresis (DLA)	Removal of the blood to collect specific blood cells such as leukocytes. The remaining blood is then returned to the body
Diagnostic test	A type of test used to help diagnose a disease or condition
Digital PCR	A third generation of PCR that enables absolute quantification through partitioning the reaction
DNA	Deoxyribonucleic acid (DNA) is the molecule that encodes the genetic instructions used in the development and functioning of all known living organisms and many viruses
DNA damage	A change in DNA structure that can cause cellular injury, or negatively impact cell function/activity
DOMINO	A prostate cancer pre-biopsy study run by ANGLE and MidLantic Urology
Downstream technologies	Technologies used to undertake molecular analysis of harvested cells after the separation has taken place
EGFR	The epidermal growth factor receptor – a signalling molecule which is typically present on the cell surface and can control cell activity including cell proliferation. Mutations in EGFR or deregulation have been associated with a number of cancers including ~30% of all epithelial cancers
Enrichment	Generic term for concentrating target cells or molecules in a starting heterogeneous mixture
Enumeration	To determine the number of; count
EpCAM	The Epithelial Cell Adhesion Molecule (EpCAM) protein is found spanning the membrane that surrounds epithelial cells, where it is involved in cell adhesion
EpCAM+ cells	Cells that express EpCAM. CTCs can be either EpCAM+ or EpCAM-
Epithelial cells	Cells that line the surfaces and cavities of the body
Epithelial to mesenchymal transition	Process by which epithelial cells lose their cell polarity and cell-cell adhesion, and gain migratory and invasive properties to become mesenchymal cells. EMT is thought to occur as part of the initiation of metastasis and is often responsible for cancer progression
EMT	Epithelial to mesenchymal transition
Epitope	A part of a molecule to which an antibody will bind
Exploratory endpoint	An endpoint is a targeted outcome of a clinical trial. Exploratory endpoints are to explore new hypotheses
FDA	U.S. Food and Drug Administration responsible for authorised medical products in the United States
FDA Class II Device	Medical devices with an intended use that is considered medium or moderate risk. For non-exempt devices the FDA require a pre-market clearance or approval to be issued before a company can legally market their device. The company will be required to have general medical device quality system controls in place as well as device specific special controls (which may include device labelling and design control processes and documentation)
FDA 510(k)	A 510(k) is a premarket submission made to the FDA to demonstrate that the device to be marketed is at least as safe and effective, that is, substantially equivalent, to a legally marketed device that is not subject to Premarket Approval. Submitters must compare their device to one or more similar legally marketed devices and make and support their substantial equivalency claims
FDA De Novo	The De Novo process provides a pathway to classify novel medical devices for which general controls alone, or general and special controls, provide reasonable assurance of safety and effectiveness for the intended use, but for which there is no legally marketed predicate device (therefore the FDA 510(k) route does not apply). Devices that are classified into class I or class II through a De Novo classification request may be marketed and used as predicates for future premarket (510(k)) submissions
Fluorescence In-Situ Hybridization (FISH)	A laboratory technique for detecting and locating a specific DNA sequence on genes or chromosome in tissue and cells. The technique relies on exposing genes or chromosomes to a small DNA sequence called a probe that has a fluorescent molecule attached to it. The probe sequence binds to its corresponding sequence on the genes or chromosome and they light up when viewed under a microscope with a special light
Formalin-fixed paraffin-embedded (FFPE)	A form of preservation and preparation for solid tissue biopsy specimens that allows sample evaluation

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
Gamma-H2AX or γH2AX	A sensitive marker for DNA damage. Specifically, for double-stranded DNA breaks. This can be used to assess treatment
GCLP	Good Clinical Laboratory Practice
Gene expression	The process by which a gene gets turned on in a cell to make RNA and proteins. Gene expression may be measured by looking at the RNA or the protein made from the RNA
Genome	Genetic material of an organism. The genome includes both protein coding and non-coding sequences
Genotyping	Process of determining differences in the genetic make-up (genotype) by examining the DNA sequence
Genomic abnormalities	Changes or rearrangements within the genome that drive disease
Gleason score	A system of assessing how aggressive prostate cancer tissue is based on how it looks under a microscope. Gleason scores range from 2 to 10 and indicate how aggressive and fast-growing the cancer is. A low Gleason score means the cancer tissue is similar to normal prostate tissue and the tumour is less likely to spread; a high Gleason score means the cancer tissue is very different from normal prostate tissue and the tumour is more likely to spread
Global market value	The amount a product or service is worth in a global market
Gynaecological cancer	Cancer of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus and vagina
Harvest	Process for recovering captured cells from the separation system to enable imaging and molecular analysis
Harvest efficiency	Proportion of target cells harvested
Harvest purity	The proportion of target cells (such as CTCs) in the harvest as a proportion of the WBC or other blood cells
HER2	A member of the epidermal growth factor receptor (EGFR/ERBB) family. Amplification or overexpression of HER2 has been shown to play an important role in the development and progression of certain aggressive types of breast cancer. The protein has become an important biomarker and target of therapy for breast cancer patients
Heterogeneity	A word that signifies diversity
Histopathology	The study of diseased cells and tissues using a microscope
HNV	Healthy normal volunteer
HT29	Cultured colorectal cancer cell line
HyCEAD™	Hybrid Capture, Enrichment, Amplification and Detection A sample preparation method for capturing targeted nucleic acid sequences (RNA or DNA) directly from biological samples without the need for extraction, introducing universal priming sequences into copies of those specific sequence regions, and permitting amplification of all targets simultaneously in a single PCR reaction for direct detection on a Ziplex instrument
Immune check inhibitors (ICI)	A type of immunotherapy that blocks immune checkpoints – key regulators of the immune system. See PD-L1/PD-1
Immune system	A complex network of cells, tissues and organs that help the body fight infections and disease
Immunofluorescence	A technique used to determine the location of an antigen or antibody labelled with a fluorescent dye
Immunohistochemistry	A laboratory test that uses antibodies to test for certain antigens (markers) in a sample of tissue. Immunohistochemistry is used to help diagnose diseases, such as cancer. It may also be used to help tell the difference between different types of cancer
Immunostain	A general term that applies to any use of an antibody-based method to detect a specific protein or antigen in a sample
Immunotherapy	Treatment that stimulates the body's immune system to fight cancer
In vitro diagnostic (IVD)	An in vitro diagnostic is a method of performing a diagnostic test outside a living body in an artificial environment, usually a laboratory
In-cassette labelling or in-situ labelling	CTC labelling for cell identification undertaken inside the separation system
Inhibitor	An agent that slows down or interferes with a process or activity
Indolent cancer	A type of low-risk cancer that grows slowly

Term	Explanation
Installed base	Number of units installed and being used by customers, KOLs and the Company
ISO 15189	An international standard for medical laboratories. Laboratory accreditation helps laboratories develop quality management systems, assesses their competence and ensures they are functioning in line with industry and legal standards
Invasive procedure	A medical procedure that invades (enters) the body, usually by cutting or puncturing the skin
Key opinion leader	Key opinion leaders (KOLs) are research centres and/or physicians who influence their peers' medical practice
KRAS	A signalling molecule frequently mutated in the development of many cancers
Laboratory developed test (LDT)	A laboratory developed test (LDT) is a type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory.
Landscape+™	ANGLE's proprietary molecular assay providing pharma services and clinicians with a sample-to-answer solution
Leukocytes	White blood cells
Liquid biopsy	Term used for the process of obtaining cancer cells (or cell-free DNA) from a blood sample. Unlike solid biopsy, liquid biopsy is non-invasive and repeatable
Localised	Describes disease that is limited to a certain part of the body. For example, localised cancer is usually found only in the tissue or organ where it began and has not spread to nearby lymph nodes or to other parts of the body. Some localised cancers can be completely removed by surgery
Longitudinal	Repeat sampling or observations at different points in time
Lymphocyte	A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue. A lymphocyte is a type of white blood cell
Lysis	The breaking down of a cell, often by viral, enzymatic, or osmotic mechanisms that compromise its integrity
Malignant	Cancerous. Malignant cells form part of the tumour, and can invade and destroy nearby tissue and spread to other parts of the body
Marker	A diagnostic indication that disease may develop or is already present. A chemical substance produced by a cancer and used to monitor the progress of the disease. These chemicals are usually measured by a blood test
Mass spectrometry	A tool for measuring the mass-to-charge ratio of one of more molecules present in a sample
MBC	Metastatic breast cancer
Medtech	Medtech, or medical technology, is a broad discipline. It is defined as a field that accounts for technologies i.e. devices to the healthcare systems for diagnosis, patient care, treatment and improvement of a person's health
meEGFR	Arginine methylation of the epidermal growth factor receptor
Megakaryocyte	A large bone marrow cell with a lobulated nucleus responsible for the production of blood thrombocytes (platelets), which are necessary for normal blood clotting
Mesenchymal CTCs	CTCs generally lacking epithelial markers with mesenchymal features
Metastasis	Spread of a cancer from one site to another
Microfluidic device	An instrument that uses very small amounts of fluid on a microchip to do certain laboratory tests. A microfluidic device may use body fluids or solutions containing cells or cell parts to diagnose diseases
Microarray	A microarray is a laboratory tool used to analyse large numbers of genes or proteins at one time
Microtentacles	Microtubule-based membrane protusions in detached cancer cells
Molecular analysis	Analysis of DNA, RNA and protein often used to determine the mutational status of a patient
Molecular evolution	The study of evolutionary change at a molecular level
Morphology	The study of the form and structure of cells
Mouse model	The use of special strains of mice to study a human disease or condition, and how to prevent and treat it
MRI	Magnetic resonance imaging, a form of diagnostic imaging that uses strong magnetic fields as well as radio waves
mRNA	Messenger RNA used to direct the synthesis of proteins

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
Mutation	A gene mutation is a permanent change in the DNA sequence that makes up a gene. Gene mutations can be inherited from a parent or can happen during a person's lifetime. Mutations passed from parent to child are called hereditary or germline mutations. Mutations that happen during a person's life, known as somatic mutations, can be caused by environmental factors such as ultraviolet radiation from the sun. Or they can occur if a mistake is made as DNA copies itself during cell division
Mutational analysis	Testing for the presence of a specific mutation or set of mutations
Next Generation Sequencing (NGS)	Also known as high-throughput sequencing, is the catch-all term used to describe a number of different modern sequencing technologies including: Illumina (Solexa) sequencing. Roche 454 sequencing. ThermoFisher Ion torrent: Proton/PGM sequencing. It is a method by which the bases of DNA and RNA can be determined, which is used in biological research and to obtain clinically relevant information
NHGRI	The National Human Genome Research Institute
NICE	National Institute for Health and Care Excellence
NIH	National Institute of Health
Non-invasive	In medicine, it describes a procedure that does not require inserting an instrument through the skin or into a body opening. Although a needle is inserted to draw blood, liquid biopsies are referred to as non-invasive or minimally-invasive as they do not require surgery
NSCLC	Non-Small Cell Lung Cancer
Off-chip labelling	CTC labelling for cell identification of harvested cells undertaken outside the separation system
Oncologist	A doctor who has special training in diagnosing and treating cancer and may also specialise in certain cancers or techniques
Oncology	A branch of medicine that specialises in the diagnosis and treatment of cancer. It includes medical oncology (the use of chemotherapy, hormone therapy and other drugs to treat cancer), radiation oncology (the use of radiation therapy to treat cancer) and surgical oncology (the use of surgery and other procedures to treat cancer)
Paired samples	Two related samples often used to compare different systems
PARP	Poly (ADP- ribose) polymerase. An enzyme involved in many functions of the cell including the repair of DNA
Parsortix® PC1 Clinical System	The name of the FDA cleared Parsortix system developed and used by ANGLE to capture and harvest metastatic breast cancer CTCs for subsequent, user validated analyses, comprising the automated instrument to run blood samples through the microfluidic cassette and all the associated operating procedures and protocols
Parsortix® system	The name of the core technologies developed and used by ANGLE to capture and harvest CTCs comprising the automated instrument to run blood samples through the microfluidic cassette and all the associated operating procedures and protocols
Pathologist	A doctor who has special training in identifying diseases by studying cells and tissues under a microscope
PathVysion	The name of the Abbott Molecular test kit. The PathVysion HER-2 DNA Probe Kit II (PathVysion Kit II) is designed to detect amplification of the HER-2/neu gene via FISH in formalin-fixed, paraffin-embedded human breast and gastric cancer tissue specimens. The PathVysion HER-2 DNA Probe Kit II is one of the first examples of what is recognized as genomic disease management, or personalized medicine. This means that the test helps enable the accurate assessment of a patient's HER-2 status at the DNA level with a high degree of accuracy and helps guide doctors to make the most appropriate therapy decisions based on the patient's own genetic profile
Patient care pathway	Refers to all stages of a patient's experiences in the management of their disease
Patient study	A type of research study, on a smaller scale than a clinical study, that tests how well new medical approaches work in people. These studies test new methods of screening, prevention, diagnosis or treatment of a disease
PCR	See Polymerase Chain Reaction
PD-1	Programmed Death 1 Receptor. A receptor for PD-L1, a key component in programmed death signalling
PD-L1	Programmed Death-Ligand 1 (PD-L1) is the principal ligand of programmed death 1 (PD-1), a coinhibitory receptor that can be constitutively expressed or induced in myeloid, lymphoid, normal epithelial cells and in cancer

Term	Explanation
Peer-reviewed publications	A publication that contains original articles that have been written by scientists and evaluated for technical and scientific quality and correctness by other experts in the same field
Pelvic mass	A general term for any growth or tumour on the ovary or in the pelvis. A pelvic mass can be cystic (cystadenoma), solid (fibroma) or both (dermoid). A pelvic mass can be benign or malignant
Peripheral blood	Blood circulating throughout the body
Personalised cancer care	Treating a patient individually based on their personal data often including mutational and disease status
Pharma	Pharmaceutical companies collectively as a sector of industry
Pharmacodynamics	The study of the biochemical, physiologic and molecular effects of a drug on the body
Phenotype	A phenotype is the composite of an organism's observable characteristics or traits, such as its morphology, development, biochemical or physiological properties, behaviour and products of behaviour. A phenotype results from the expression of an organism's genes as well as the influence of environmental factors and the interactions between the two
PIK3CA	A gene that makes one of the proteins in an enzyme called PI3K, which is involved in many cell functions
Pilot study	The initial study examining a new method or treatment
Plasma	Pale-yellow liquid component of blood obtained following removal of cells
pKAP1	Phospho-KA1. A protein involved in response to DNA damage
Polymerase Chain Reaction (PCR)	A laboratory technique used to amplify DNA sequences. The method involves using short DNA sequences called primers to select the portion of the genome to be amplified. The temperature of the sample is repeatedly raised and lowered to help a DNA replication enzyme copy the target DNA sequence. The technique can produce a billion copies of the target sequence in just a few hours
Portrait+™	ANGLE's proprietary imaging assay providing pharma services and clinicians with a sample-to-answer solution
Precision medicine	The customisation of healthcare – with medical decisions, practices and/or products being tailored to the individual patient. In this model, diagnostic testing is often employed for selecting appropriate and optimal therapies based on the context of a patient's genetic content or other molecular or cellular analysis
Pre-labelled cell lines	Cells which are labelled often with a fluorescent label to facilitate identification during analysis or enrichment
Prognosis	The likely outcome or course of a disease; the chance of recovery or recurrence
Prostate-Specific Antigen (PSA)	A protein made by the prostate gland and found in the blood. PSA blood levels may be higher than normal in men who have prostate cancer, benign prostatic hyperplasia (BPH), or infection or inflammation of the prostate gland
Proteogenomics	The study of how information about the DNA in a cell or organism relates to the proteins made by that cell or organism. This includes understanding how genes control when proteins get made and what changes occur to proteins after they are made that may switch them on and off. Proteogenomics may help researchers learn more about which proteins are involved in certain diseases, such as cancer, and may also be used to help develop new drugs that block these proteins
Proteome	The complete set of proteins made by an organism. Proteins are made in different amounts and at different times, depending on how they work, when they are needed, and how they interact with other proteins inside cells
Protocol	A detailed plan of a scientific or medical experiment, treatment or procedure. In clinical studies, it states what the study will do, how it will be done and why it is being done. It explains how many people will be in the study, who is eligible to take part in it, what study drugs or other interventions will be given, what tests will be done and how often, and what information will be collected
PSA	See Prostate-Specific Antigen
Purity	The relative absence of extraneous matter in a sample
Q-Submission	The FDA's Pre-Submission Program which allows medical device and IVD manufacturers to discuss specific aspects of the regulatory process and requirements with FDA experts
Quantitative assay	An assay which gives an accurate and exact numeric measure of the substance being investigated
Radiotherapy	The use of high-energy radiation from x-rays, gamma rays, neutrons, protons and other sources to kill cancer cells and shrink tumours
Real-time analysis	An assessment providing the most up-to-date and accurate representation of the patient's disease status

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
Recurrence	Cancer that has recurred, usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body
Regulatory authorisation	The authorisation by the appropriate regulatory body for a specific territory that allows an in vitro diagnostic product to be sold for clinical use in that territory
Relapse	When an illness that has seemed to be getting better, or to have been cured, comes back or gets worse
Remission	If a cancer is in remission, there is no sign of it in examinations or tests. Generally, the longer the remission, the less likely it is that the patient will relapse
Research Use Only (RUO)	Sales can be made to certain organisations of in vitro diagnostic products without the need for regulatory authorisation provided they are labelled as Research Use Only (RUO) or Investigational Use Only (IUO)
RNA	Ribonucleic acid performs multiple vital roles in the coding, decoding, regulation and expression of genes. Together with DNA, RNA comprises the nucleic acids, which, along with proteins, constitute the three major macromolecules essential for all known forms of life
RNA-Sequencing (RNA-seq)	Also called whole transcriptome shotgun sequencing (WTSS), uses Next Generation Sequencing (NGS) to reveal the presence and quantity of RNA in a biological sample at a given moment in time
Screening	Checking for disease when there are no symptoms. Since screening may find diseases at an early stage, there may be a better chance of curing the disease
Sensitivity	Refers to the percentage of people who test positive for a specific disease or condition among people who actually have the disease or condition
Separation	Term used for processing of a sample through the Parsortix system
Single cell analysis	Extraction/picking of a single target cell from the harvest for analysis
Solid biopsy	Standard process for surgically excising (cutting out) cells from a solid tumour when that tumour is accessible
Spatiotemporal metastasis monitoring	To monitor the physical spread/growth of cancer metastasis over time
Specificity	Refers to the percentage of people who test negative for a specific disease or condition among a group of people who do not have the disease or condition
Spiked cell experiments	Experiments where cultured cells are added (spiked) to HNV blood to assess the capture and harvest efficiency of the system
Stage	The extent of a cancer in the body. Staging is usually based on the size of the tumour, whether lymph nodes contain cancer and whether the cancer has spread from the original site to other parts of the body
Standard of care	The current treatment that is accepted by medical experts as the most effective treatment of a disease and is widely used by healthcare professionals. Also known as best practice, standard medical care and standard therapy
Standard Operating Procedure (SOP)	Written instructions for doing a specific task in a certain way. In clinical trials, Standard Operating Procedures are set up to store records, collect data, screen and enrol subjects and submit Institutional Review Board (IRB) applications and renewals
Subsequent analysis	The downstream assessment (via imaging or molecular analysis) of CTCs
Therapeutics	A branch of medicine that deals with the treatment of disease
Tissue	Tissue is a group of cells that have similar structure and that function together as a unit
Transcriptome	The transcriptome is the set of all messenger RNA molecules in one cell or a population of cells
Translational research	A term used to describe the process by which the results of research done in the laboratory are used to develop new ways to diagnose and treat disease
Treatment resistance	The failure of a disease or disorder to respond positively or significantly to treatment
Triage	The process of determining the priority of patients' treatments based on the severity of their condition
Triple negative breast cancer	A subtype of breast cancer that refers to the fact that the cancer cells do not have estrogen or progesterone receptors and also do not make (or make too much) of the protein HER2. This cancer type grows and spreads faster than other cancer types and has fewer treatment options
Tumour/Tumor	An abnormal mass of tissue that results when cells divide more than they should or do not die when they should. Tumours may be benign (not cancer) or malignant (cancer) Tumour is the standard English spelling. Tumor is the standard American English spelling

Term	Explanation
Tumour evolution	Cancer cells acquire genotypic and phenotypic changes over the course of disease as a result of treatment exposure and/or environmental changes
Tumour heterogeneity	Describes the observation that different tumour cells can show distinct morphological and phenotypic profiles, including cellular morphology, gene expression, metabolism, motility, proliferation and metastatic potential. This phenomenon occurs both between tumours (inter-tumour heterogeneity) and within tumours (intra-tumour heterogeneity) The heterogeneity of cancer cells introduces significant challenges in designing effective treatment strategies
Tumour marker	A substance found in tissue, blood or other body fluids that may be a sign of cancer or certain benign (non-cancerous) conditions. Most tumour markers are made by both normal cells and cancer cells, but they are made in larger amounts by cancer cells. A tumour marker may help to diagnose cancer, plan treatment or determine how well treatment is working or if the patient has relapsed Examples of tumour markers include CA-125 (in ovarian cancer), CA 15-3 (in breast cancer), CEA (in colon cancer) and PSA (in prostate cancer)
WBC	White blood cells
Whole Exome Sequencing (WES)	A genomic technique for sequencing all of the protein-coding regions of genes in a genome (known as the exome). It consists of two steps: the first step is to select only the subset of DNA that encodes proteins. These regions are known as exons – humans have about 180,000 exons, constituting about 1% of the human genome, or approximately 30 million base pairs. The second step is to sequence the exonic DNA using any high-throughput DNA sequencing technology
Whole Genome Amplification (WGA)	A PCR technique that is used to produce large quantities of DNA from a small amount of starting material. Unlike conventional PCR, WGA is aimed at amplifying the entire genome of an organism rather than a specific region. It can then be sequenced using WGS
Whole Genome Sequencing (WGS)	A method that is used to learn the exact order of all of the building blocks (nucleotides) that make up a person's genome (complete set of DNA). WGS is used to find changes that may cause diseases, such as cancer
Whole Transcriptome Amplification (WTA)	A method used to amplify the entire transcriptome from RNA isolated from cells or tissues prior to RNA sequencing. RNA sequencing has enabled high-throughput gene expression profiling to provide insight into the functional link between genotype and phenotype. This has enabled profiling of gene expression in cancer
Xenograft	The transplant of an organ, tissue or cells to an individual of another species. A common example used in cancer biology is a mouse model (mouse xenograft)

Primary source: www.cancer.gov/publications/dictionaries/cancer-terms.

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