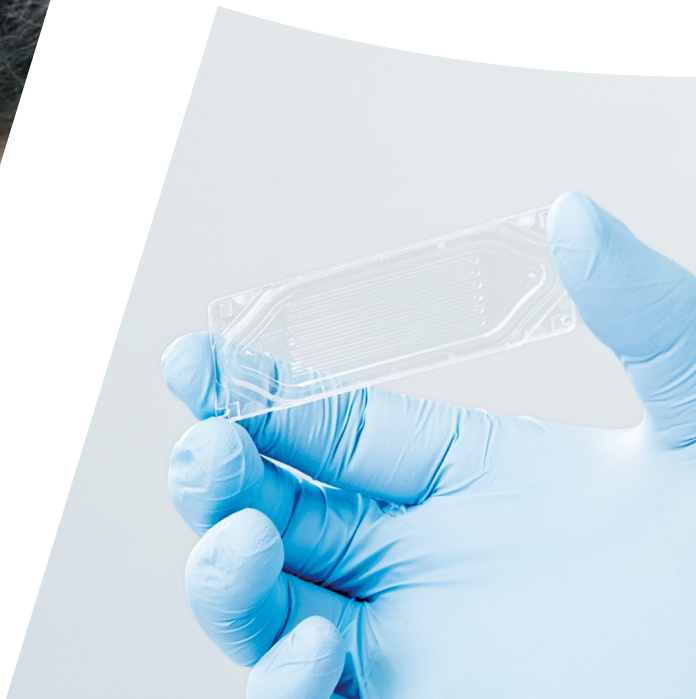
Transforming cancer care with a liquid biopsy based on a simple blood test

Annual Report and
Financial Statements
31 December 2021



ANGLE

WHO WE ARE

ANGLE plc

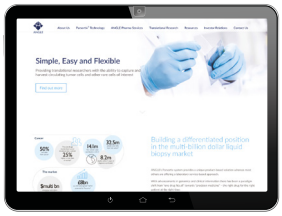
is a world-leading liquid biopsy company that has developed the revolutionary Parsortix® system for harvesting intact cancer cells (known as CTCs) from a patient's blood sample for subsequent analysis.

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

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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 impact of the COVID-19 pandemic, 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.

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 rapidly. This may cause a growth called a tumour.

How many people are affected?

In the US, cancer is responsible for 21% of all deaths and 9.3m Person-Years of Life Lost in 2018[1].

~40-50%

Of the population will be diagnosed with cancer in their lifetime[2,3]

50% increase

The number of annual cancer cases is increasing, and in the US has risen by 50% in the last two decades[2,5]

1.9m new cases

In the US in 2021, an estimated 1.9m new cases of cancer were diagnosed and 0.6m people died from the disease[2]
There are a further 16.3m people living with cancer[2]

1 https://seer.cancer.gov/csr/1975_2018/browse_csr.php
2 https://seer.cancer.gov/statfacts/html/all.html – USA (40%)
3 www.cancerresearchuk.org/about-cancer/what-is-cancer – UK (50%)
4 www.ncbi.nlm.nih.gov/pmc/articles/PMC3597235/
5 https://pubmed.ncbi.nlm.nih.gov/11577478/

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 tumour cells released into the blood circulation. When this happens, it is called **metastatic cancer**.

The process by which cancer cells spread to other parts of the body is called **metastasis**.

Why is metastasis so serious?

90%

Of cancer deaths are caused by metastasis[4]

The "stage" of cancer at diagnosis is extremely important to 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 just in one site then surgery or radiotherapy may be sufficient. If the cancer is "late" stage and has metastasised 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 stage at diagnosis and survival between cancer types. Some cancers have screening programmes or more obvious symptoms and can be detected earlier (e.g. breast, colorectal, cervical, skin) and others are mostly slow growing cancers which may remain early stage (e.g. prostate) and therefore have higher survival rates. Other cancers may have no obvious symptoms or are aggressive and often detected at a late stage once they have already spread (e.g. lung, ovarian, pancreatic) and therefore have lower survival rates.

What are the challenges to treatment?

During cancer treatment, particularly of secondary (metastatic) cancer, there are many challenges which can arise leaving both physicians and therefore patients with unanswered questions such as:

1. How do you know which drug will work most effectively?
2. How do you track whether drugs are working and continue to be effective?
3. How do you monitor patients in remission to assess any risk of the disease returning?

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 development of drug resistance
- Requires an **invasive** procedure and can cause adverse events
- **Poor tissue availability** due to inaccessibility of tumour (pancreatic, lung, brain, liver and bone cancers)
- Only samples **one site** and may not reflect tumour heterogeneity

AT A GLANCE

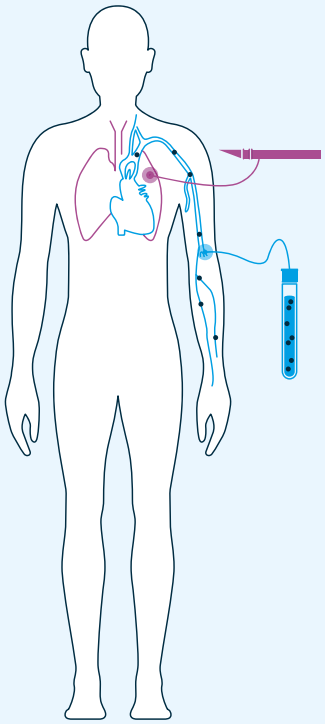
Liquid biopsy improving patient outcomes and reducing healthcare costs

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 only samples one site, and
3) the dynamic nature of the cancer response to treatment meaning the original biopsy information is rapidly out-of-date

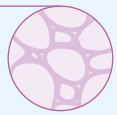
Obtaining cancer tissue for analysis



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	Not yet proven	Not yet proven

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

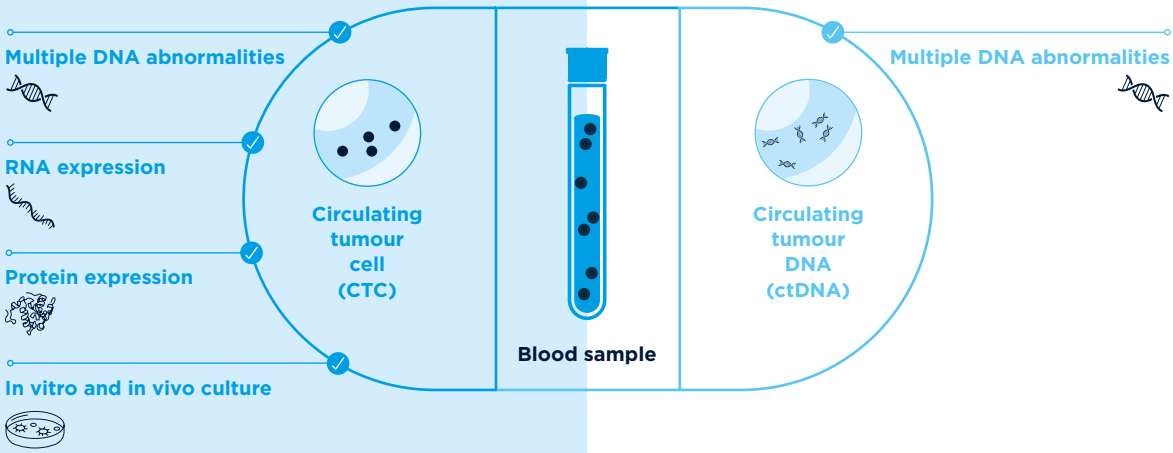
Circulating tumour cells (CTCs) and circulating tumour DNA (ctDNA) can be measured concurrently from a single blood draw to provide complementary information for clinical decision making. This includes early diagnosis, accurate prognosis, therapeutic target selection, spatiotemporal monitoring of metastasis, as well as monitoring response and resistance to treatment.

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 will 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.



The cancer genome atlas has revolutionised cancer diagnosis and treatment. Aided by this knowledge and advances in genomic sequencing technology, oncologists are increasingly selecting therapies based on the specific genomic abnormalities identified in a patient's tumour.

However, many patients who are matched to therapy based on their DNA 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 genome alone**. While the presence of mutations can be determined from sequencing a tumour's genome, the effect of mutations on protein function cannot be fully understood without interrogating the proteome, including the many modifications that occur to proteins in a tumour. Changes that normally occur in proteins after they are made (post-translational modifications) can affect how proteins function or how long they are present in a cell.

With sustained investments in proteogenomics research, doctors will, in the future, be able to assemble a more complete picture of a patient's tumor, one that informs diagnosis and treatment and improves outcomes.

NIH Annual Plan & Budget Proposal for Fiscal Year 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.

Molecular Diagnostics for Cancer Treatment: Expanding beyond the Genome published by the National Cancer Institute, August 2020

Liquid biopsy – helping healthcare systems meet the challenges of COVID-19

Across the globe, disruption to cancer services has slowed diagnoses, delayed treatment and hampered ongoing patient management. This has been driven by a multitude of factors, such as local and national lockdowns, patients' reluctance to attend in-person appointments for fear of contracting the virus, and reduced system capacity due to greater cleaning times, reprioritisation of services and reallocation of healthcare staff.

Diagnosis

Across Europe an **estimated 100 million screening tests did not happen**, and this huge drop-off is reflected in the reduced number of new cancer diagnoses. In Belgium and the Netherlands alone, the number of cancers diagnosed in the first lockdown of 2020 declined by 30–40%. Clinicians saw 1.5 million fewer patients with cancer in the first year of the pandemic, while urgent referrals were cut by up to a half[1].

Cancer treatment

In the UK, a report by the Institute for Public Policy Research (IPPR) think tank and the CF health consultancy suggests it could take more than a decade to clear the cancer treatment backlog. The pandemic led to a 37% drop in endoscopies, a 25% drop in MRI scans and a 10% drop in CT scans. The research also showed that during the height of the pandemic – March 2020 to February 2021 – 369,000 fewer people than expected were referred to a specialist with suspected cancer. There were also 187,000 fewer chemotherapy treatments and 15,000 fewer radiotherapy treatments[2].

Read more in our Corporate Responsibility Report on pages 36 to 43

Recurrence monitoring

The recommendations of the European Society for Medical Oncology for the management and treatment of cancer in the COVID-19 era have classified follow-up for most cancers, depending on risk of relapse, as either low or medium priority. This reprioritisation may have long-term implications for the detection of disease progression that may impact cancer outcomes. In addition, face-to-face appointments have been reduced, with routine services in many countries being switched to video/tele-consultations unless an in-person consultation is deemed essential. Although these changes have helped maintain continuity of care, they may be reducing opportunities for detecting symptoms of recurrence, undertaking advanced-care planning or coordinating palliative care[3].

1 Cancer care in a post-COVID environment, Pharmatimes, October 2021 https://www.pharmatimes.com/magazine/2021/september_2021/cancer_care_in_a_post-covid_environment

2 Cancer patients face perfect storm as covid piles pressure on the NHS – Guardian 22 October 2021 https://www.theguardian.com/society/2021/oct/22/cancer-patients-face-perfect-storm-as-covid-piles-pressure-on-nhs

3 https://www.nature.com/articles/s43018-020-0074-y

How can liquid biopsy support cancer care in a post-COVID-19 world?

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 are continuing to evolve to counter the substantial challenge of COVID-19. Ending delays and addressing backlogs – particularly cancer diagnosis and surgeries – will need to be an urgent priority moving forward.

The information provided by a liquid biopsy could help clinicians diagnose, monitor, and treat cancer more efficiently. Liquid biopsy is minimally invasive, can be undertaken safely in community clinics or in the home to provide patients with a rapid diagnosis and timely treatment with targeted therapies. Liquid biopsy may also help to safely monitor cancer patients in remission to provide early warning of recurrence. In the ongoing 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.

THE SOLUTION

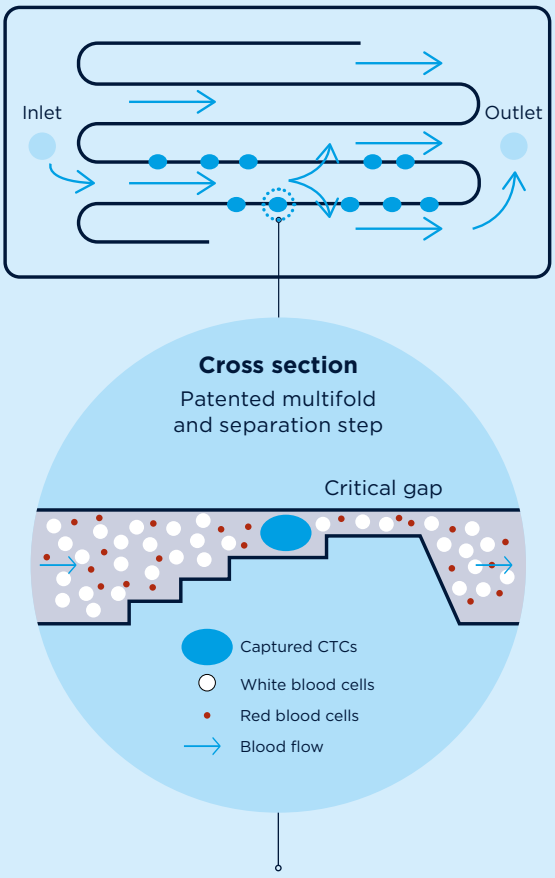
Parsortix system

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.

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 enable the **complete picture** of the cancer to be understood as they are viable, intact whole cells allowing DNA, RNA and protein analysis as well as culturing
- CTCs are **biologically specific** – 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
- 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 consequent better likelihood of success.

Competitive differentiation

Unlike many other CTC systems, the Parsortix system is applicable for **all solid tumour cancers**. The Parsortix system can be used without modification and to date has been shown to work with **24 different cancer types**.

Technology	Simple and flexible process	Low cost	Captures all types of cancer	Captures mesenchymal CTCs involved in metastasis	Easily harvest cells for analysis	High purity of harvest	Cell viability (alive)	CTC clusters
Parsortix microfluidic step	✓	✓	✓	✓	✓	✓	✓	✓
Antibody-based systems	×	×	×	×	×	×	×	×
Membrane-based systems	✓	✓	✓	✓	×	×	× ✓	×
Field Flow Fractionation systems	✓	✓	✓	✓	×	×	× ✓	×

"

CANCER RESEARCH UK

The Parsortix system has a unique combination of features making it suitable for routine clinical analysis of patient blood samples.

Ged Brady
Cancer Research UK Manchester Institute of Technology

HOW IT WORKS

Capture, harvest and analysis of CTCs

ANGLE owns both a CTC harvesting technology (the Parsortix® system) and a downstream molecular analysis technology (HyCEAD™) to interrogate the harvested CTCs.

ANGLE has well-differentiated patent-protected products. Both systems have proprietary consumables, which provide a "razor blade" approach to commercialisation.

ANGLE's proprietary technologies can be combined to provide automated, **sample-to-answer** solutions in both a centralised laboratory and point-of-use cartridge formats.

ANGLE has optimised the entire process, from blood collection and transportation to molecular diagnostic techniques, thereby minimising the risk of variability and allowing reliable, repeatable and scalable CTC analysis.

Automated process requiring minimum user intervention

1 Blood collection

Designed for a single 10 ml tube of blood.
No pre-processing required.

2 Automated blood processing

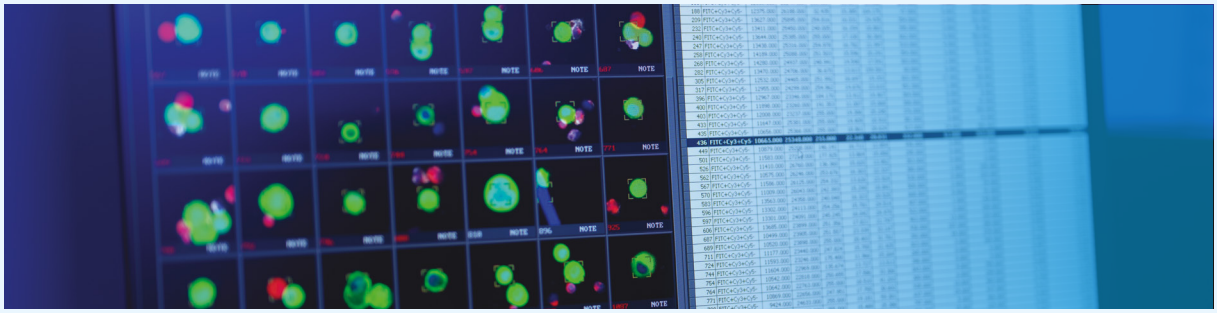
Blood is pumped through the cassette with minimal user input.

3 Cell capture in cassette

Proprietary single use cassette captures intact living cancer cells.

4 Cell harvest

CTCs can be harvested in <200µl buffer for multiple downstream analysis techniques.



Downstream analysis

5a 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:

- Cytopathology
- Immunofluorescence (IF)
- Fluorescent In Situ Hybridisation (FISH)
- Polymerase Chain Reaction (PCR)
- Next Generation Sequencing (NGS)
- RNA sequencing (RNA-seq)
- Whole Genome Amplification (WGA)
- Whole Exome Sequencing (WES)

5b Proprietary HyCEAD system

The HyCEAD system is a medium-density microarray platform designed for routine and focused multiplex analysis of DNA, RNA or protein biomarkers.

Advantages

Unlike expensive, high-density microarray systems that overwhelm researchers with large amounts of unnecessary data, the HyCEAD system uses a highly reproducible, lower density array to provide expression information on specific genetic or protein biomarker signatures. It uniquely combines three separate automated functions (hybridisation/protein binding, washing/labelling and imaging) into a single benchtop instrument providing researchers and laboratories with a highly flexible platform that is fast, simple to use and cost effective.

HyCEAD at a glance

- Benchtop laboratory platform
- DNA, RNA and protein biomarkers
- Low cost
- Highly multiplexed
- Rapid and sensitive capture of targets
- High variety of sample types

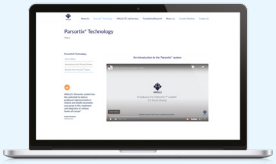
HyCEAD chemistry

>100

Enables simultaneous measurement of more than 100 genes in a single reaction

>500

Rapid content creation for new applications of more than 500 target genes to date



To watch our video visit:
www.angleplc.com/parsortix technology/introduction/

THE POTENTIAL

Seeking first ever FDA product clearance for a device to harvest cancer cells from metastatic breast cancer patient blood for subsequent analysis

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 competition.

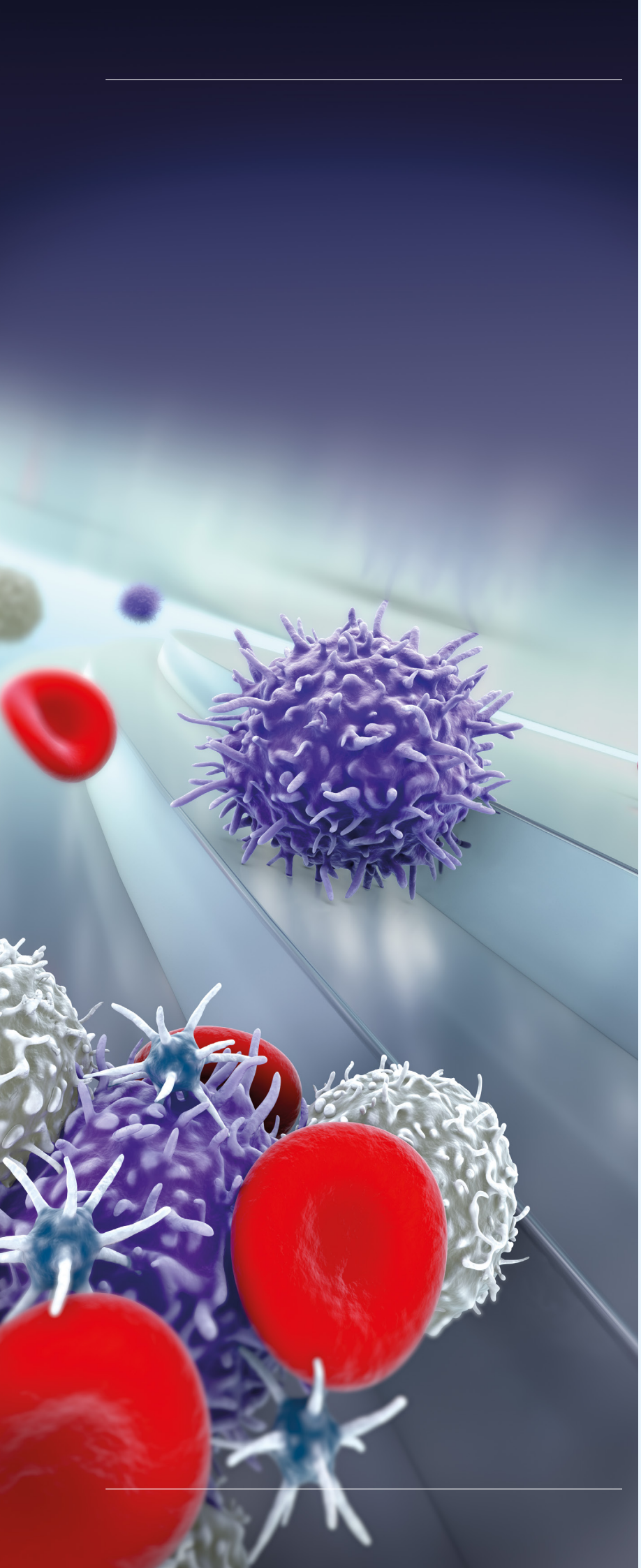
Read more on page 02

Read more on pages 06 and 07

Read more on pages 08 and 09

Read more on page 10

Read more on page 10



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MARKET OPPORTUNITY

A major opportunity in an emerging and growing global market

Market drivers

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

Key drivers of cancer diagnostics market
- Shift towards precision medicine drives need for companion diagnostics
- Health economics – reduced 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

40-50%
People will get cancer in their lifetime[2, 3]

47%
Estimated rise in global cancer cases within the next two decades[4]

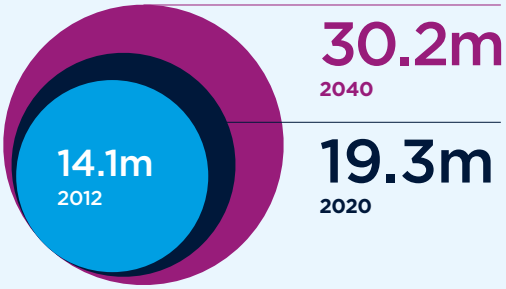
Growing market

Liquid biopsy: Emerging multi-US$ billion market
Cowen – up to $130 billion per annum (US only)

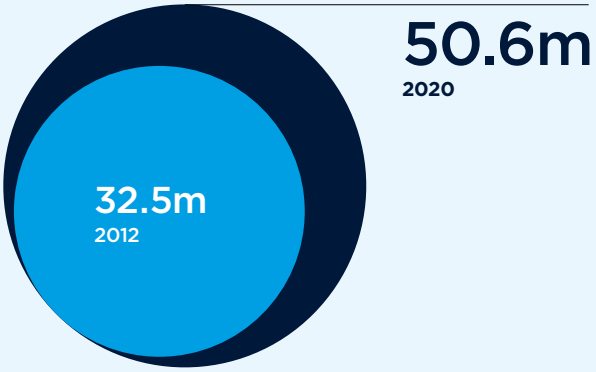
Frost & Sullivan – $100 billion per annum (US only)

Global burden of cancer[1]

New cancer incidence
(per annum)



Living with and after cancer



Deaths from cancer
(per annum)

1 International Agency for Research on Cancer (Globocan 2020)
2 www.cancer.gov/about-cancer/understanding/statistics – USA (40%)
3 www.cancerresearchuk.org/about-cancer/what-is-cancer – UK (50%)
4 Global cancer statistics, (Globocan 2020). Estimates of incidence and mortality worldwide for 36 cancers in 185 countries

ANGLE's focus

Current		Medium term		Longer term
Detection of cancer in high risk groups Ovarian pelvic mass Prostate pre-tissue biopsy screening	**Therapy selection** Breast HER-2 Abbott Prostate AR-V7 Qiagen Immunotherapy PD-L1/PD-1 inhibitors	**Assessing treatment** Assessing minimal residual disease	**Remission monitoring** Repeat testing to ensure CTCs not present	**Screening for early cancer** Need to assess aggressiveness and avoid false positives

FDA clearance would be a major validation opening up commercial pathway

Prospect of first ever FDA product clearance for harvesting cancer cells from metastatic breast cancer patient blood for analysis. Expected to accelerate sales and commercial partnerships.

- Existing **research use sales** to leading translational researchers will expand with new product development and sample-to-answer solutions.
- Growth in research use sales for **pharma** services in drug trials and potential for development of companion diagnostics.

US$27bn p.a. estimated US and European addressable market for potential Parsortix applications in breast, ovarian and prostate cancer.[1]

- **Service-led strategy** in LDTs (laboratory developed tests) market.
- **Product-led strategy** for clinical sales of Parsortix instruments and consumables direct to hospitals.

Research	Pharma	LDTs	Clinical products
Leveraged R&D model Proof-of-concept studies provide evidence and drive new applications	Large-scale research use sales for drug trials Biomarker discovery Companion diagnostics Culturing CTCs for drug testing	Laboratory developed tests in a service laboratory Accelerator and demonstrator Ovarian Metastatic breast Prostate	Product sales worldwide to hospitals and corporate partners Metastatic breast cancer Integration with existing cleared diagnostic assays e.g. • Abbott PathVysion • Qiagen AR-V7

Market accessible on multiple fronts with Parsortix product-based solution
Allows ANGLE to be both an equipment supplier and a diagnostic test provider

1 Company estimate

STRATEGY

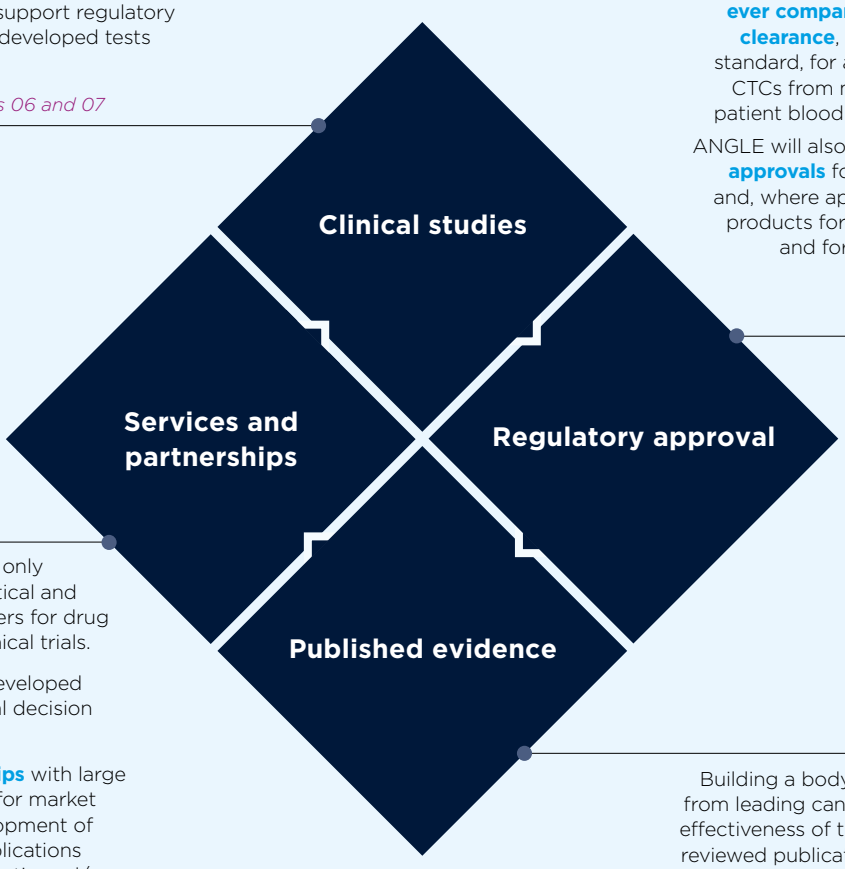
A clear path to success

ANGLE has a four-pronged strategy for achieving widespread adoption of its Parsortix system in the emerging multi-US$ billion liquid biopsy market.

Our strategy

Completion of rigorous large-scale **clinical studies** run by leading cancer centres, demonstrating the effectiveness of different applications of the system in cancer patient care to support regulatory approval of laboratory developed tests and products.

Read more on pages 06 and 07



ANGLE is seeking to become 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 analysis.

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

Read more on pages 08 and 09

Providing research use only services to pharmaceutical and biotechnology customers for drug research and use in clinical trials.

Providing laboratory developed tests for specific clinical decision making.

Establishing **partnerships** with large healthcare companies for market deployment and development of many other clinical applications incorporating the Parsortix and/or HyCEAD systems.

Read more on pages 12 to 15

Building a body of **published evidence** from leading cancer centres showing the effectiveness of the system through peer-reviewed publications, scientific data and clinical research evidence, highlighting a wide range of potential applications.

Read more on pages 10 and 11

Strong progress has been made in each of these areas

> **Delivering on our strategy has the potential to deliver significant financial returns for ANGLE's shareholders, profoundly improve the outcome for cancer patients, and reduce healthcare costs.**
>
> **Andrew D W Newland**
> Chief Executive

What we have achieved in the year

Building on previous achievements

Clinical studies – ovarian cancer

Patient enrolment completed and analysis in ANGLE's United States clinical laboratory initiated.

Short-term COVID-19 related supply chain constraints on reagents slowed progress towards the year-end but these were resolved in early 2022 and analysis is now in progress.

Successful results in two 200 US and European ovarian cancer patient studies. Lead study delivered **best in class 95.1% accuracy** in discriminating between benign and malignant pelvic masses, significantly out-performing standard of care.

Extensive optimisation of the HyCEAD molecular analysis platform successfully completed, demonstrating exceptionally high sensitivity.

Ovarian cancer clinical verification study established with leading US cancer centre. Pre-study phase completed successfully. 200 patient study initiated in August 2019 and clinical verification study patient enrolment progressed.

Regulatory approval – metastatic breast cancer

FDA Substantive Review continued as expected and Additional Information Request received with detailed and comprehensive response submitted by ANGLE in June 2021.

Ongoing dialogue and Q-Submission process with FDA.

Clinical studies enroling 600 subjects with four leading US cancer centres completed with positive result for primary and exploratory objectives. Analytical studies completed.

Full De Novo submission made to FDA. FDA Administrative review completed and Substantive Review in progress.

Published evidence – leveraged R&D model

Leading independent cancer centres have delivered a total of **54 peer-reviewed publications** as at 31 December 2021.

Since the year end there has been a further eight peer-reviewed publications.

29 independent cancer centres in 12 countries have published positive results on their use of the Parsortix system.

Total of 37 peer-reviewed publications from 26 independent cancer centres at 31 December 2020.

Services and partnerships

New clinical services laboratories opened ahead of schedule in the United States and UK.

First three biopharma customers onboarded, including CTC analysis in a large-scale phase III prostate cancer study and assay development work in the area of DNA damage repair.

Discussions ongoing with growing pipeline of potential customers which we expect to accelerate with FDA clearance.

Continued discussions with multiple potential corporate partners including Abbott (liquid biopsy solution for PathVysion), Philips and QIAGEN.

Significant preparatory work undertaken to establish ANGLE's own clinical laboratories in the United States and UK to support offer of laboratory developed tests into the clinical market and CTC analysis services into the pharma clinical trials market.

STRATEGIC AIMS IN ACTION

Clinical studies

Ovarian cancer clinical application – abnormal pelvic mass triage test

ANGLE's Parsortix system is being developed into a test to triage women having surgery for an abnormal pelvic mass to identify those with ovarian cancer using the HyCEAD system to analyse samples.

Extensive optimisation of the HyCEAD system and its combination with the Parsortix system was successfully completed.

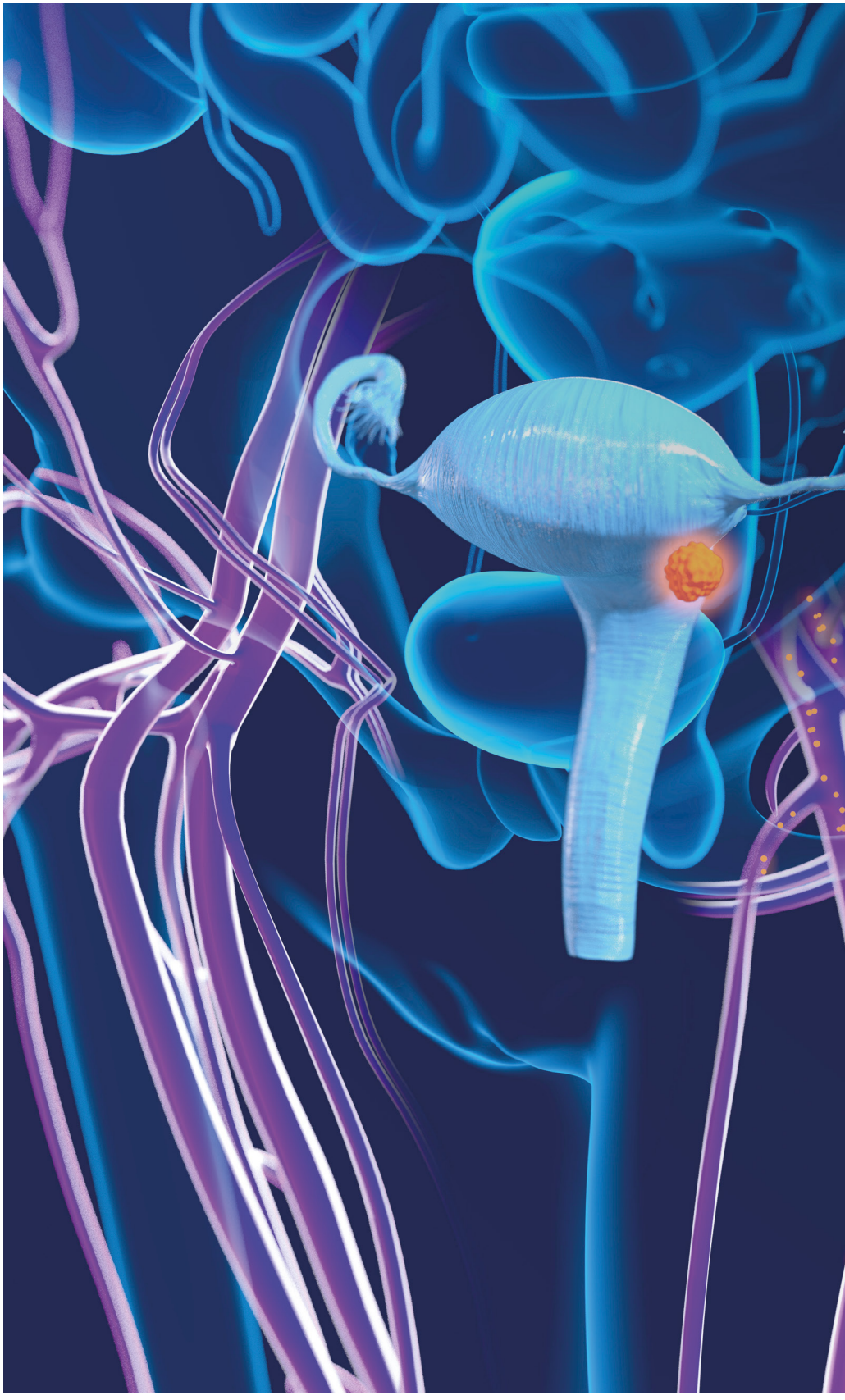
A detailed market review was completed to identify key user requirements for the test. Testing of the modified and further optimised platforms has been successfully completed and the performance of the improvements **confirmed in a pre-study**.

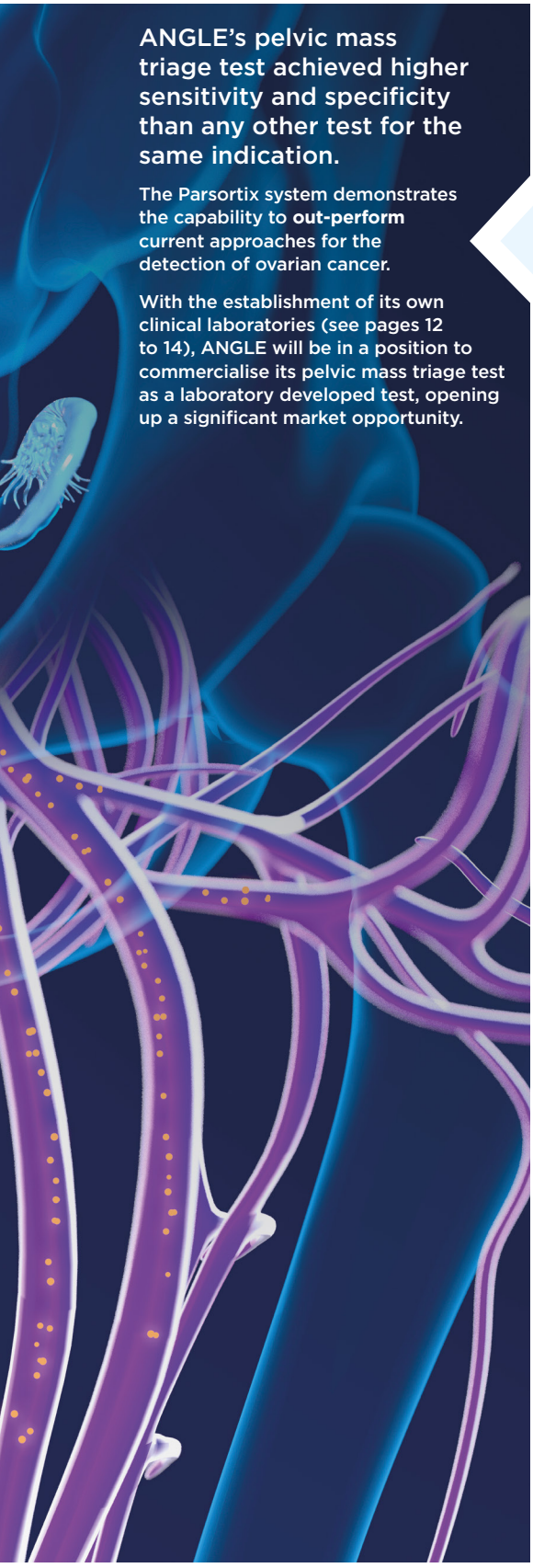
A 200 patient clinical verification study is in progress with the University of Rochester Medical Center Wilmot Cancer Institute. Patient enrolment was completed in April 2021.

Samples are being analysed in ANGLE's United States clinical laboratory.

Once the new performance data is available, ANGLE intends to establish this test as a laboratory developed test in-house and/or with third-party laboratories.

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





ANGLE's pelvic mass triage test achieved higher sensitivity and specificity than any other test for the same indication.

The Parsortix system demonstrates the capability to **out-perform** current approaches for the detection of ovarian cancer.

With the establishment of its own clinical laboratories (see pages 12 to 14), ANGLE will be in a position to commercialise its pelvic mass triage test as a laboratory developed test, opening up a significant market opportunity.

> **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

2x200
patient studies in Europe and the US completed and reported positively

95.1%
correct prediction of cancer with a best in class accuracy (area under the curve) 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 market 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 https://seer.cancer.gov/statfacts/html/ovary.html

STRATEGIC AIMS IN ACTION CONTINUED

Regulatory approval

Seeking FDA product clearance in metastatic breast cancer

Metastasis is responsible for the vast majority of breast cancer related deaths.

The FDA **clinical study** (Study) previously reported positive results that the Study had achieved its primary objective to demonstrate the ability of the Parsortix system to capture and harvest cancer cells from the blood of a significant proportion of metastatic breast cancer patients and that it had achieved secondary endpoints demonstrating that the cells harvested from patient blood could be interrogated using subsequent molecular analysis techniques.

A full De Novo FDA Submission was made in September 2020, comprising over 400 technical reports and documents based on over 15,000 samples run on the Parsortix system in the UK and at clinical sites in the US.

Following substantive review, FDA provided a written response in the form of an Additional Information Request (AIR). Some of the technical information requested necessitated some additional analytical studies. These additional studies, comprising a further 1,000 analytical samples, were completed and a full response to the AIR was announced in June 2021.

ANGLE is following a De Novo FDA process for the Parsortix system as there is no predicate device. Consequently, there is inherent uncertainty over the timing of the process and its ultimate success.

ANGLE believes that the capability 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. This approach has the potential to transform the treatment of metastatic breast cancer, providing patients with personalised cancer care through a non-invasive, repeat biopsy based on a simple blood test.

For more information on our work for breast cancer, go to our website at: **www.angleplc.com/translational-research/womens-health/breast-cancer/**

What is FDA?

FDA, the United States Food and Drug Administration, is the US agency responsible for the regulatory clearance process for medical devices (treating patients).

Why is it important?

FDA clearance allows a medical device **product** to be sold in the United States for the purpose of patient management. The FDA determines independently that the benefits of a product outweigh the potential risks and that the product 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 system for treating patients in the United States. It will also greatly facilitate sales into pharmaceutical drug trials directly and with contract research organisations.

ANGLE is seeking to become the first ever company to receive FDA Class II medical device clearance for a product for harvesting intact CTCs from metastatic breast cancer patient blood for subsequent analysis.

US regulatory clearance by FDA is considered the global standard for approval of medical devices and diagnostics. ANGLE believes that such clearance would provide ANGLE's Parsortix system with further competitive differentiation, which would **accelerate all forms of commercial adoption** of the system in both research and clinical settings.

ANGLE has committed significant resources in its effort to achieve FDA clearance in a sustained effort for over six years.

Four of the leading US cancer centres enrolled a total of **600 subjects** for the **clinical studies including approximately 300 metastatic breast cancer patients and 300 healthy volunteers**: The University of Texas MD Anderson Cancer Center, University of Rochester Medical Center Wilmot Cancer Institute, University of Southern California Norris Comprehensive Cancer Center, and Robert H Lurie Comprehensive Cancer Center Northwestern University. The global healthcare company **Abbott** joined the Study, enabling us to use its proprietary PathVysion HER-2 DNA FISH Probe Kits as one downstream analysis technique.

As a breast cancer surgeon, I am very enthusiastic about the potential of liquid biopsy. Our pilot data shows that potentially the same information can be obtained from a simple blood test using the Parsortix system as from an invasive tissue biopsy and indeed may be advantageous over invasive tissue biopsies in regards to the diverse sites of metastatic disease.

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

4
leading US cancer centres enrolled patients for FDA clinical studies

600
subject studies in the US completed and reported positively

US$3.9bn
p.a. estimated US market potential for the Parsortix system in metastatic breast cancer[1]

2.6m
women diagnosed globally with breast cancer in 2020[2]

7.8m
women living with and after breast cancer[2]

20-30%
of people initially diagnosed at early stages will develop metastatic breast cancer[3]

1 Company estimate – United States only
2 International Agency for Research on Cancer (Globocan 2020)
3 www.mbcn.org/incidence-and-incidence-rates/

STRATEGIC AIMS IN ACTION CONTINUED

Published evidence

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.

Leveraged R&D model achieving more

ANGLE's product-based approach means that we are able to deploy our system to leading cancer centres as 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 which shows the effectiveness of the system and is leading to new uses and applications for the Parsortix system as well as achieving **breakthrough research** in many areas due to the special attributes of the system. This is leading to an increasing number of peer-reviewed publications.

Further, ANGLE is not funding customer work, and indeed the sale of instruments and cassettes is generating revenues. We refer to this as a **leveraged R&D model**, because significantly more R&D work is being undertaken than if we had to pay for this ourselves.

29 independent cancer centres have published uniformly positive reports on their use of the Parsortix system. Using ANGLE's Parsortix system, leading independent cancer centres throughout Europe, North America and RoW 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.

New peer-reviewed publications

There were 54 peer-reviewed publications as at 31 December 2021 with 17 new publications announced during the year (see **https://angleplc.com/library/publications/**). Highlights of these publications included:

- Detection of **PD-L1** on CTCs in patients with **ovarian cancer** in research undertaken by Edith Cowan University in Perth. Hybrid-CTCs (expressing both epithelial and mesenchymal markers) harvested by the Parsortix system were found to be associated with PD-L1 expression. This study highlights the potential for the use of the Parsortix system to help in patient stratification for clinical trials utilising immunotherapy treatments.
- A study in **NSCLC** undertaken by the University of Athens utilising CTCs and ctDNA from a single sample in patients being treated with an immunotherapy. Identifying the differences between DNA methylation in ctDNA and CTCs in longitudinal studies could help guide therapy decisions and provide an important enhancement to monitoring patient response in cancer drug trials.
- A multi-centre trans-European study (CANCER-ID) undertaking proficiency testing of five CTC-processing systems. The Parsortix system performance was robust with mean cell capture rates of 71% (EpCAM high) and 67% (EpCAM low). In comparison, the FDA approved CellSearch was unable to enrich EpCAM low CTCs. The Parsortix system was comparable to CellSearch with respect to time required for sample processing, staining and cell identification and was considerably faster than RareCyte (2.5-3 hours vs. 36 hours).
- A study into a novel biomarker **Cyr61** in **breast cancer** by the University Medical Center, Hamburg-Eppendorf. Cyr61 was found to be a potential new CTC biomarker which could be used as an indicator of aggressive CTC subsets with increased metastatic potential. Cyr61 could also be a druggable target for a novel approach to metastasis prevention.
- A study in triple negative **breast cancer** by the IRCCS Istituto Nazionale dei Tumori, Milan, which demonstrated how ctDNA and CTCs can be used as complementary analytes and how the inclusion of CTCs in the analysis of disease progression was able to uncover therapeutically exploitable mutations including P13K, HER, Raf, platinum-resistance signalling, and regulation of immune response.
- Breakthrough research published by Washington University School of Medicine demonstrating the utility of the Parsortix system to isolate disseminated tumour cells from **breast cancer** patients. Bone metastasis is common in breast cancer, so the ability to isolate and characterise these cells could lead to the development of novel treatment strategies to prevent metastatic spread.

Since the year end there have been a **further eight peer-reviewed** publications. This includes breakthrough research by the University of Southern California in metastatic **breast cancer** demonstrating that longitudinal CTC monitoring could capture changes in mutational burden as the cancer evolves, including the development of resistance to anti-cancer therapies. This could help guide clinical decision making and treatment selection.

Installed base

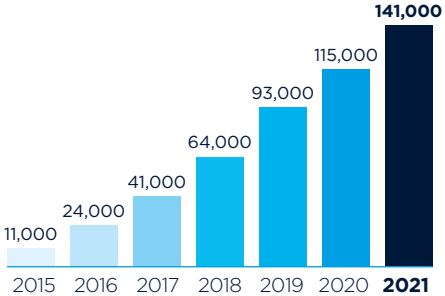
>230

Installed base of over 230 Parsortix systems in active use

- Translational research market **US$50 million p.a.**[1]
- FDA clearance expected to help Parsortix become the CTC **system of choice**

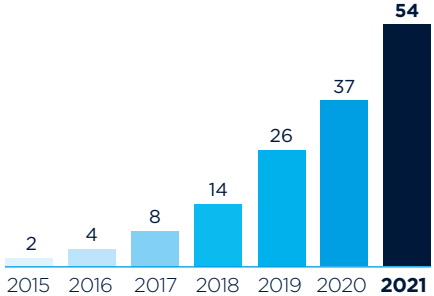
1 Company estimate

Parsortix samples processed



Cumulative samples processed at 31 December

Peer-reviewed publications



Cumulative publications at 31 December

The Parsortix system

Growing body of evidence

Leveraged R&D strategy identifying new applications

As at 31 December 2021

Some leading cancer centres we work with

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

STRATEGIC AIMS IN ACTION CONTINUED

Clinical laboratories and pharma services

ANGLE has established clinical laboratories in the UK and the United States (under its new "Onc-ADaPT Labs" brand) to accelerate commercialisation of the Parsortix system. The laboratories act as **accelerators and demonstrators**, and are offering CTC analysis services to pharmaceutical customers and will offer laboratory developed tests (LDTs) in the clinical market.

Parsortix®

Onc-ADaPT™ Labs
Part of the ANGLE Group

Portrait+™
Powered by Parsortix®

Landscape+™
Powered by Parsortix®

Pharma services

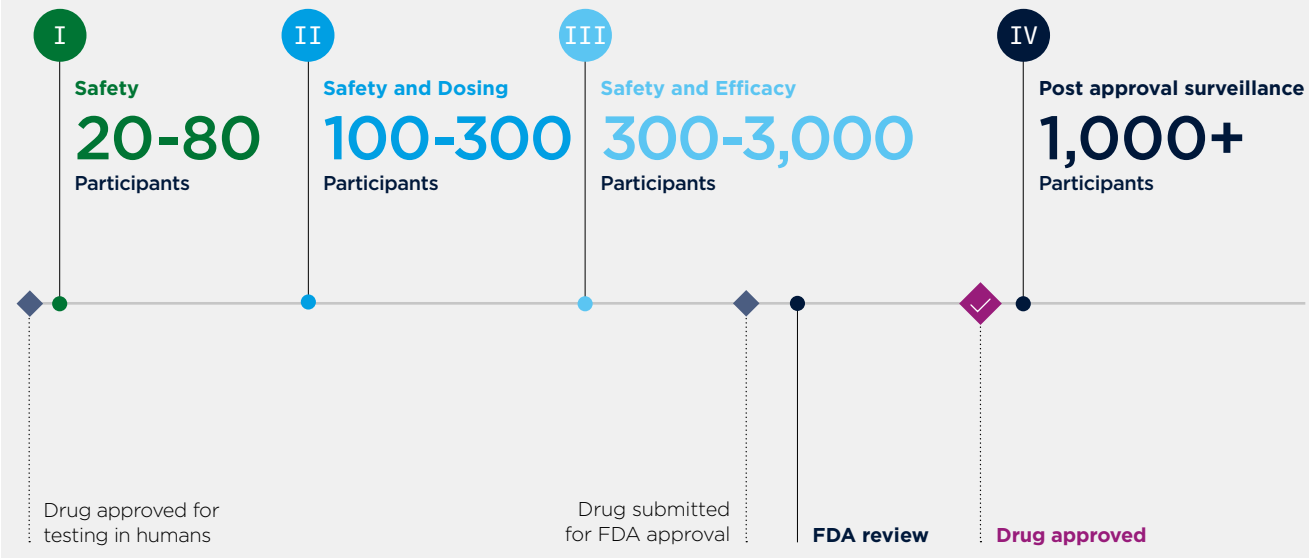
Liquid biopsies are moving towards routine clinical use, but in the meantime, they are already informing clinical trial outcomes and supporting drug discovery. A number of trials are already using CTCs as an exploratory endpoint. CTC presence and status are being used predominantly as a measure of response to treatment and may provide a much earlier measure 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 and 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 2,700 interventional PD-L1/PD-1 trials, in ~420,000 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 is now being utilised in a major global Phase III study in prostate cancer and in the development of bespoke assays for specific protein markers implicated in DNA damage repair, another 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 the Parsortix CTC analysis offering, as pharma clients can look at proteins on CTCs which directly align with the mode of action of the drug under investigation.

Clinical Trial Phases



PD-L1 as an immunotherapy biomarker

There are now several published studies demonstrating the use of the Parsortix system for enabling the molecular analysis of CTCs in solid tumours, including the investigation of PD-L1 (programmed death-ligand 1) expression, a key target for leading immunotherapy drugs.

ANGLE has made significant progress in developing a series of immunofluorescence (IF) imaging assays under the brand "Portrait⁺" including an assay for determination of PD-L1 expression levels in CTCs harvested by the Parsortix system (known as Portrait⁺ PD-L1). This work has been completed and ANGLE has a method for assessing the presence and number of PD-L1 positive and PD-L1 negative CTCs in patient blood samples. The Portrait⁺ PD-L1 assay is in the process of being fully validated in ANGLE's clinical laboratories before being offered to the biopharma services and clinical markets.

The newly developed in-house cell-based approach will enable use of the Parsortix system to assess PD-L1 status using two complementary techniques, molecular analysis (Landscape⁺) and cell imaging (Portrait⁺). We believe this is a powerful combination, which, together with the key advantages of the Parsortix system to capture both epithelial and mesenchymal CTCs (traditional antibody-based systems fail to capture the clinically relevant mesenchymal CTCs) and to capture CTC clusters, will provide significant benefits to the pharma services market (see page 14).

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

A significant number of PD-L1 inhibitors have been withdrawn from the market due to a failure to demonstrate overall survival benefit in patients. In December 2020, Bristol Myers Squibb announced the withdrawal of the immune checkpoint inhibitor Opdivo (nivolumab) from the US market for the treatment of patients with metastatic small cell lung cancer (SCLC). Merck announced in March 2021 that it would withdraw Keytruda (pembrolizumab) for the same indication. For the treatment of advanced bladder cancer AstraZeneca announced the withdrawal of Imfinzi (durvalumab) in February 2021 and Genentech announced the withdrawal of Tecentriq (atezolizumab) in March 2021. In April 2021 following a review, the FDA announced the withdrawal of Keytruda for gastric cancer and Opdivo for hepatocellular carcinoma.

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 CDx is urgently required in this space to optimise patient selection.

US$1.7bn

PD-L1 pharma services market value[1]

~US$31.5bn

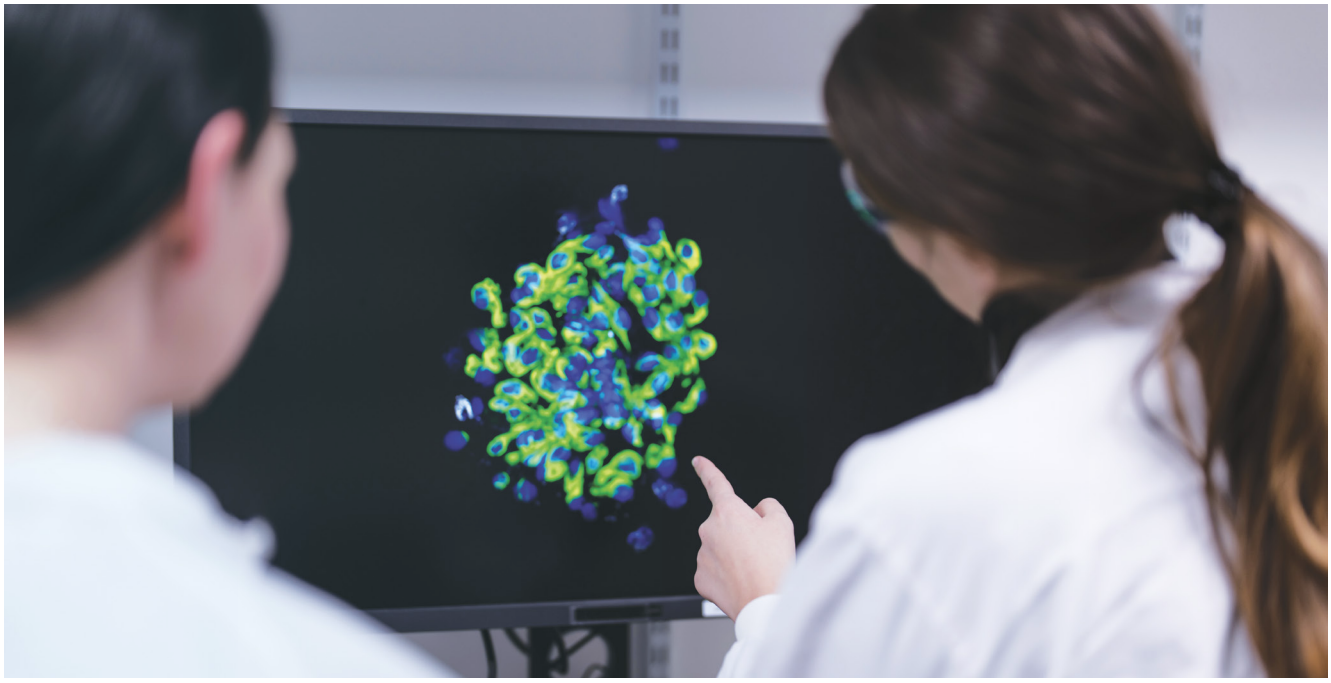
growing at >17% p.a.

Estimated spend on PD-L1 immunotherapy drugs in 2021[1]

1 Company estimate

STRATEGIC AIMS IN ACTION CONTINUED

Clinical laboratories and pharma services continued



Portrait+™ Powered by Parsortix®

Portrait+ EMT quantitative assay

In collaboration with a key pharma services customer, ANGLE is developing an IF based quantitative assay (Portrait+ EMT) to identify bespoke biomarkers on different subtypes of CTCs, including epithelial, mesenchymal and those undergoing Epithelial Mesenchymal Transition (EMT). The assay is being optimised and will be validated in the CLIA accredited United States laboratory as a pharma services offering.

What is Epithelial Mesenchymal Transition (EMT) and why is it important?

EMT is the transition of epithelial tumour cells to cells with a mesenchymal phenotype. EMT is important because it is involved in tumour progression, the development of metastasis and the development of drug resistance.

EMT is not complete in cancer cells, and tumour cells are in multiple transitional states and express mixed epithelial and mesenchymal genes. 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 EpCAM expression. 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.

ANGLE's clinical laboratories – initial focus on ovarian, EMT, PD-L1 and prostate cancer

ANGLE's United States laboratory has applied for CLIA accreditation, and both the United States and UK laboratories have applied for ISO accreditation, which will allow them to market LDTs to the medical community. Given the extensive clinical work already completed with the ovarian cancer pelvic mass triage assay, it is anticipated that this will be ANGLE's first LDT to market.

ANGLE is developing a pipeline of further assays to be launched as in-house LDTs or with partners, including tests for PD-L1 and EMT (see more above) and prostate cancer. ANGLE intends the laboratories will act as an "accelerator and demonstrator" for Parsortix clinical applications as an LDT will enable early progress with payers and receipt of reimbursement codes ahead of a FDA cleared product.

What is CLIA accreditation?

The Clinical Laboratory Improvement Amendments (CLIA) regulate laboratory testing and require all US clinical laboratories to be certified by the Center for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing.

CLIA

Services and partnerships

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

The Parsortix system is compatible with all existing downstream analysis techniques. In addition to the capture and harvest of CTCs the system can capture and harvest other rare cells such as foetal cells.

The HyCEAD system can be employed with many other sample types, not just CTCs, and in many other sectors, not just cancer. The priority has been on optimising this to work in the ovarian cancer pelvic mass triage test which involves a panel of genes. HyCEAD is being developed for other cancer panels, including breast and prostate, with potential partners.

Progressing partnerships with healthcare companies

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: medtech companies, pharma companies, contract research organisations and reference laboratories (laboratories offering clinical tests).

Abbott

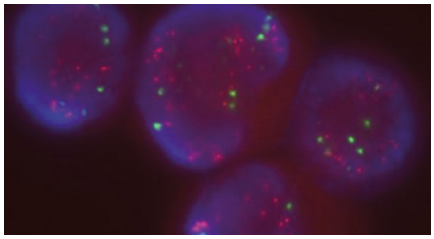
Abbott is the global market leader for HER-2 testing in solid tissue biopsies, a market estimated to be valued at US$313.4m in 2020 and to grow to US$627.7m by 2031. (**www.transparencymarketresearch.com**).

Abbott's proprietary PathVysion HER-2 DNA FISH Probe Kits were utilised in ANGLE's **FDA clinical study** for FISH (fluorescence in situ hybridization) analysis of circulating tumour cells. The process of analysis using FISH was **successful** and ANGLE is pursuing commercial discussions with Abbott.

There is now the potential for Abbott to offer a Parsortix-based product for HER-2 analysis from a routine blood test. Testing of CTCs for HER-2 could provide Abbott with a **repeat test** for HER-2 giving a 4x increase in use of their PathVysion test. Combining the Parsortix system and PathVysion could command much **higher reimbursement**, increasing margins as well as the potential for exclusivity in the repeat testing market.

Abbott is pleased to collaborate with ANGLE in this important evaluation of PathVysion in liquid biopsy specimens. The PathVysion HER-2 DNA FISH Probe Kit is reliable and accurate in tissue biopsy samples and the Parsortix system may unlock the potential for PathVysion use in a simple blood test.

Kathryn B Becker
Franchise Director Oncology and Companion Diagnostics, Abbott



Parsortix harvested HER-2 stained cells.

CHAIRMAN'S STATEMENT

Service laboratories established

> During the year, ANGLE moved into a new phase of commercialisation setting up clinical laboratories in the UK and United States and establishing a new pharma services business with initial contracts secured.

Garth R Selvey
Chairman

Following the De Novo Submission to FDA in September 2020, FDA's progress in reviewing ANGLE's submission was encouraging despite the well-publicised pressures on FDA resources due to the COVID-19 pandemic. ANGLE completed the additional analytical work required to provide a comprehensive response in June 2021 to the Additional Information Request from FDA.

ANGLE made excellent progress in establishing clinical laboratories in the UK and United States. They are being used as accelerators and demonstrators in support of the Company's product sales of Parsortix instruments and cassettes and to provide services to pharmaceutical and biotech customers running cancer drug trials. The laboratories are already offering pharma services and once accreditation is in place will be able to offer validated clinical tests. First submissions have been made in relation to CLIA and UKAS accreditation of the laboratories and, in the United States, a CLIA registration certificate was awarded post year end, an important step towards accreditation allowing samples to be processed for patient management.

Initial demand for pharma services has been encouraging and contracts are now in progress with five different customers, after two new customers were onboarded post year end. Discussions are ongoing with a number of other potential customers, and we are pleased with the level of interest being generated by the commercial teams in the UK and United States.

Patient enrolment for the Company's ovarian cancer assay clinical verification study was completed during the year but sample analysis was hindered by a shortage of key reagents due to COVID-19 related supply chain issues. These issues have been addressed and the required reagents have been received and are being validated before resuming sample analysis, with headline results anticipated mid-year. A laboratory developed test is scheduled for launch pending the results of the study and once the clinical laboratories have received accreditation.

In line with its strategy, ANGLE continues to explore potential new clinical applications for the Parsortix system and identify opportunities to develop additional assays for specific high-risk groups. To this end, ANGLE initiated discussions with a large-scale group of urology clinics in the United States and completed the design of a new study in prostate cancer, which is scheduled to start as soon as terms have been finalised.

Overview of Financial Results

Revenue of £1.0 million in the year (2020: £0.8 million) came mainly from research use sales of the Parsortix system with a small initial contribution from the newly established pharma services business. Research sales continued to be impacted by the COVID-19 pandemic but there was an encouraging improvement towards the end of the year as these pressures began to be alleviated. Importantly, both pharma services and research use product sales are expected to accelerate should the Company receive FDA clearance of the Parsortix system. ANGLE continued its investment in studies to develop and validate the clinical application and commercial use of the Parsortix system and to launch its new clinical laboratories and pharma services business, resulting in operating costs of £18.0 million (2020: £14.4 million) and a loss for the year of £15.0 million (2020: loss £11.6 million).

The cash and cash equivalents and short-term deposits combined balance was £31.8 million at 31 December 2021 (2020: £28.6 million) with R&D Tax Credits due at 31 December 2021 of £4.5 million (2020: £2.1 million).

FDA response awaited

ANGLE is seeking to become the first ever company to receive FDA product clearance for a medical device that harvests intact circulating tumour cells from the blood of metastatic breast cancer (MBC) patients for subsequent analysis. A full De Novo FDA Submission for its Parsortix PC1 system seeking FDA clearance for use with MBC patients was submitted in September 2020.

Following substantive review, FDA provided a written response in the form of an Additional Information Request (AIR). Receipt of an AIR was expected and is in line with typical De Novo clearance processes. Some of the technical information requested necessitated some targeted additional analytical studies. These studies did not require patient samples and were completed as planned and a comprehensive response to the AIR was announced in early June 2021. Regular and constructive dialogue with FDA continues and a regulatory response is awaited.

Clinical laboratories

ANGLE made excellent progress in establishing clinical laboratories in the UK and United States that will have the capability of offering validated clinical tests. The laboratories, in Guildford, UK and Plymouth Meeting, Pennsylvania, United States were completed ahead of schedule in Q1 2021 and are engaged in processing clinical samples. In line with the Company's strategy, the laboratories are being used as accelerators and demonstrators in support of the Company's established plan for product sales of Parsortix instruments and cassettes and to provide services to pharmaceutical and biotech customers running clinical trials.

Strategy

ANGLE has continued with its sustained focus on its four-pronged strategy for achieving widespread adoption of its Parsortix system in the emerging multi-US$ billion liquid biopsy market:

Clinical studies

Completion of rigorous large-scale clinical studies run by leading cancer centres, demonstrating the effectiveness of different applications of the system in cancer patient care

Regulatory approval

Securing regulatory approvals with the emphasis on FDA clearances as the de facto global gold standard. ANGLE is seeking to become the first ever company to gain FDA product clearance for a system which harvests circulating tumour cells (CTCs) from patient blood for subsequent analysis. ANGLE will look to build on the initial metastatic breast cancer clearance for specific clinical assays and, where appropriate, for additional cancer types, additional products and additional geographies through further regulatory submissions

Published evidence

Building a 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

Services and partnerships

Establishing a significant pharma services business and building partnerships with large healthcare companies for market deployment and development of multiple clinical applications utilising the Parsortix system, including our own laboratory developed tests from our clinical laboratories, once accredited, in the United States and the UK.

Read more about our strategy on pages 04 to 15

Operational Highlights

- US Food and Drug Administration (FDA) substantive review made good progress in the year with a comprehensive response made to FDA's Additional Information Request and continued constructive and supportive dialogue with the Agency throughout
- Clinical laboratories opened in the UK and United States and global pharma services business launched
  - » contracts in place with three pharma and biotech customers, with two new customers onboarded post year end
  - » discussions continue with multiple other potential customers, including large global pharma companies
  - » Clinical Laboratory Improvement Amendments (CLIA) and UKAS accreditation submissions initiated in the United States and UK and, post year end, CLIA Registration Certificate awarded to United States clinical laboratory
- Ovarian cancer clinical verification study with leading United States cancer centre nearing completion
  - » patient enrolment completed during the year but sample analysis was delayed due to COVID-19 related disruption to supplies of key reagents
- Prostate cancer study design completed and discussions progressed with a major group of United States urology clinics, with a view to partnering in studies and providing access to a significant patient base
- Over 26,000 samples processed during the year and a further 17 peer-reviewed publications from internationally recognised cancer centres with key developments in breast, ovarian, head and neck, non-small cell lung and prostate cancers

Outlook

- Regular constructive dialogue continues with FDA and a regulatory response is awaited
- Reagents required to complete the ovarian cancer study analysis have been received and are being validated so that analysis of ovarian samples can be resumed and headline results from the study are anticipated mid-year ahead of potential launch of the ovarian cancer test as ANGLE's first laboratory developed test (LDT)
- The pharma services business continues to build with a total of five independent customers onboarded. Deployment of the Parsortix system in the first contracts with these customers is progressing well and two early customers have already agreed additional contracts for further clinical trials

Processing of patient samples for clinical purposes (treating patients) requires the laboratories to be accredited under the appropriate local regulatory regimes. During the year, first submissions were made in relation to accreditation of the Company's United States and UK clinical laboratories respectively. Post year end, 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. Following CMS audit, including an inspection of the facilities and documentation on the validation of assays to be performed together with associated quality control procedures, a Certificate of Compliance will be issued. This will complete the accreditation process that permits the Laboratory to process samples for patient management from the majority of the United States, with a small number of States requiring additional procedures which will be progressed separately.

Global pharma services business

The Parsortix liquid biopsy has particular advantages in capturing intact cancer cells including mesenchymal cells and CTC clusters and provides an opportunity for longitudinal testing (before, during and after drug intervention) in a clinical setting, which is not possible with tissue biopsy. ANGLE believes that longitudinal monitoring of CTCs will prove highly attractive to the pharma industry looking for new insights in cancer drug trials.

CHAIRMAN'S STATEMENT CONTINUED

Despite lengthy initial sales processes (detailing the analysis capability, evidencing the laboratory quality systems, and agreeing the sampling handling and reporting requirements), ANGLE has already successfully secured pharma services contracts with five pharma and biotech companies including a Phase III prostate cancer trial for one customer and the development of bespoke immunofluorescence (IF) assays to detect specific target proteins for another.

The incorporation of bespoke assay development as a first phase in pharma services is a major development and is expected to significantly increase the attractiveness of the Parsortix CTC analysis offering, as pharma clients can look at proteins on CTCs which directly align with the mechanism of operation of their drug under investigation.

Once developed, the new assays will remain in the ownership of ANGLE and be added to ANGLE's menu of pre-developed tests that can be offered to other pharma customers. Pharma companies are commonly interested in investigating protein markers on actual cancer cells. These cannot be investigated using the alternative liquid biopsy approach ctDNA (fragments of dead cancer cells) since protein cannot be measured on ctDNA. Tissue biopsies provide cancer cells but cannot be used for longitudinal monitoring since only a single time point is usually possible with tissue biopsy. Consequently, pharma companies are unable to access this analysis without analysing CTCs.

The pharma services business continues to build with a total of five independent customers now onboarded. Deployment of the Parsortix system in the first contracts with these customers is progressing well and two early customers have already agreed additional contracts for further clinical trials.

Clinical applications

Patient enrolment for ANGLE's ovarian cancer clinical verification study, which is being undertaken by the University of Rochester Medical Center (URMC) Wilmot Cancer Institute, New York, USA was completed during the year. The study is designed to evaluate the use of ANGLE's combined Parsortix® and HyCEAD™ platforms as a simple blood test to detect the presence of ovarian cancer in women with an abnormal pelvic mass.

A positive outcome from the study will support ANGLE's plans to launch a clinical assay for the detection of ovarian cancer in women with an abnormal pelvic mass, with both high sensitivity (correctly detecting cancer) and high specificity (correctly detecting no cancer with a low false positive rate). Once the new performance data is available and, assuming positive results, ANGLE intends to establish this test as a laboratory developed test (LDT) in its accredited clinical laboratories. The test has the potential to significantly improve patient outcomes whilst also reducing overall healthcare costs.

While good progress was made in many areas of the study, towards the year end there were some third-party supply chain difficulties attributed to COVID-19 with a key supplier unable to deliver certain reagents as scheduled. Post year end, the reagents required to complete the ovarian cancer study analysis have been received and are being validated so that analysis of ovarian samples can be resumed and headline results from the study are anticipated mid-year.

Discussions regarding the initiation of a new study in prostate cancer with one of the largest groups of specialist urology clinics in the United States are well advanced and it is anticipated the study will start promptly once final terms for the collaboration have been agreed. ANGLE believes that compelling data from this study could form the basis for a further LDT to be offered from ANGLE's clinical laboratories and that the urology group concerned would provide the first route to market in the United States.

Building a body of published evidence

The Company continues to build momentum around the research use adoption of the Parsortix system by leading cancer research centres, in line with its strategy to drive independent third parties to use Parsortix for the development of new clinical applications.

Over 141,000 samples have been processed using the Parsortix system as at 31 December 2021, with some 26,000 samples in the year. There were 54 peer-reviewed publications as at 31 December 2021 with 17 new publications announced during 2021 (see https://angleplc.com/library/publications/).

- Western University and Lawson Health Research Institute, Ontario, Canada demonstrating the performance of the Parsortix system in a head-to-head comparison with the leading antibody-based CTC system
- CANCER-ID Consortium, the Europe-wide Public-Private-Partnership aimed at standardising protocols and driving wide adoption of liquid biopsy in clinical practice, establishing the performance and technical capabilities of five CTC isolation platforms, in which key advantages of the Parsortix system were identified
- National and Kapodistrian University of Athens, Greece, demonstrating the utility of the Parsortix system for minimally invasive, longitudinal monitoring of changes in CTC gene expression in non-small cell lung cancer patients with an EGFR mutation being treated with the tyrosine kinase inhibitor (TKI), Osimertinib (AstraZeneca's Tagrisso®)
- University Medical Centre Hamburg-Eppendorf, Germany, demonstrating the ability of the Parsortix system to harvest CTCs with a mesenchymal phenotype, which can be used to detect the metastatic biomarker cysteine-rich angiogenetic inducer 61 (Cyr61) in breast cancer patients
- Istituto Nazionale dei Tumori, Milan, Italy, utilising the Parsortix system together with whole genome sequencing to uncover therapeutic targets in patients with triple negative breast cancer
- University Hospital Ghent, Belgium, demonstrating the use of the Parsortix system in oesophageal cancer for the first time, consistently harvesting high-quality CTCs and validating a workstream that could enable targeted treatment in this hard-to-treat cancer
- Washington University, St Louis, Missouri, United States, supporting the potential use of the Parsortix system in the prevention of relapse of breast cancer patients in remission. The Parsortix system was successfully used to harvest cancer cells "hibernating" in the bone marrow
- National and Kapodistrian University of Athens, Greece, highlighting differences in EGFR mutations between ctDNA and CTCs in matched liquid biopsies from non-small cell lung cancer patients and supporting the view that CTCs can provide perspective insight into a patient's cancer, which may not be possible with ctDNA alone
- University Medical Centre Hamburg-Eppendorf, Germany, using the Parsortix system to successfully harvest CTCs for analysis from patients with brain metastasis, potentially enabling more personalised care where traditional tissue biopsy is not possible

- Institute of Oncology, Ljubljana, Slovenia, highlighting the ease of use and superior performance of the Parsortix system in harvesting CTCs from metastatic breast cancer patients compared to an alternative antibody-based approach
- University College London, UK, demonstrating the use of the Parsortix system to enable whole-genome sequencing of single CTCs from neuroendocrine neoplasms
- Medical University of Innsbruck, Austria, demonstrating the use of the Parsortix system to enable gene expression analysis of metastatic prostate cancer patients where longitudinal patient monitoring showed reduction in CTCs with patient drug response
- Health Research Institute of Santiago, Santiago de Compostela, Spain, demonstrating the use of the Parsortix system to assess PD-L1 status of CTCs in non-small cell lung cancer patients
- University of Birmingham, UK, exploring the use of the Parsortix system in harvesting CTCs for gene expression analysis, potentially providing markers of disease and prognosis in head and neck squamous cell carcinoma patients
- Medical University of Vienna, Austria, showing the Parsortix system as key in demonstrating RNA analysis of CTCs as a prognostic tool in non-small cell lung cancer patients. Multi-marker transcriptomic analysis of CTCs revealed multiple subtypes with different prognostic significance
- National and Kapodistrian University of Athens, Greece, supporting the analysis of CTCs captured using the Parsortix system, together with ctDNA, from serial liquid biopsies to provide information on disease progression and drug resistance in non-small cell lung cancer patients
- Edith Cowan University, Perth, Australia, using CTCs isolated with the Parsortix system to highlight the relationship between PD-L1 expression and epithelial to mesenchymal transition in ovarian cancer patients

Following the year end, there have been eight further publications, including the following of note:

- University of Southern California Norris Cancer Center, United States, a breakthrough study demonstrating, for the first time, concordance of a Parsortix liquid biopsy test with invasive tissue biopsy of the metastatic site and the potential for a Parsortix blood test to be used as an alternative to tissue biopsy in metastatic breast cancer
- IRCCS Istituto Nazionale dei Tumori, Milano, Italy, published their work in early-stage triple negative breast cancer, demonstrating how longitudinal monitoring of CTC's isolated by the Parsortix system can provide information on tumour evolution and identify actionable genes that could help determine future treatment options for patients with chemo-resistant disease
- Marlene and Stewart Greenebaum NCI Comprehensive Cancer Center, University of Maryland, Baltimore, United States, used the Parsortix system to isolate CTCs in a preclinical model of metastasis. The authors demonstrated how drug treatment with an approved therapeutic could significantly reduce the metastatic potential of CTCs. As metastasis is the leading cause of cancer deaths, drugs reducing or preventing metastatic spread could significantly improve patient survival
- University of Basel and University Hospital Basel, Switzerland, published ground-breaking research into the use of CRISPR to identify genes required for metastatic invasion of CTCs and CTC clusters isolated by the Parsortix system. The team were able to identify actionable gene pathways which could be targeted by novel or existing drugs to reduce metastatic spread

As at 31 December 2021, 29 separate cancer centres from around the world have published positive reports on their use of the Parsortix system. Using the Parsortix system, leading independent cancer centres across Europe, North America and elsewhere have undertaken research in 24 different cancer types.

Outlook

ANGLE gathered significant momentum in 2021 and this has carried through into the start of 2022. We look forward to a busy year ahead with the prospect of the first-ever FDA product clearance for a system to harvest cancer cells for subsequent analysis, laboratory accreditation in both the United States and the UK, major expansion of our pharma services business, clinical data in ovarian cancer and the initiation of a new study in prostate cancer as well as the deployment of our sample-to-answer solutions within our clinical laboratories and directly with customers.

Globally, operating costs are rising with inflationary pressures and some areas are experiencing supply chain constraints. In addition, there is considerable competition in the sector for talent and some cancer centres are facing a lack of availability of grant funding for cancer research. ANGLE is taking the necessary steps to address these challenges and does not anticipate any significant impact on its growth trajectory. The Company is strongly positioned in a large, fast growing market with a highly differentiated product that has the potential to improve cancer patient care and at the same time reduce healthcare costs and we expect to see the Company grow significantly as this product becomes widely adopted.

Clinical adoption of liquid biopsy solutions for cancer diagnosis is building in all major markets and drug developers are increasingly looking for new tools to improve clinical trial efficiency and support market acceptance for novel cancer treatments. The commercialisation of our unique liquid biopsy platform to support personalised cancer care is underway and we look forward to significant growth in the coming year and beyond.

Garth Selvey
Chairman
27 April 2022

BUSINESS STRATEGY

Sustained focus on delivering our strategy

> **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

ANGLE has been following a consistent strategy for several years to bring its Parsortix technology to market. This strategy is set out below.

Introduction

ANGLE is a world-leading liquid biopsy company commercialising a platform technology that can capture cells circulating in blood, such as 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 Parsortix 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. 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.

As well as cancer, the Parsortix technology has the potential for deployment with several other important cell types in the future, including for example foetal cells.

Cancer medical applications

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

- Each cancer patient may have different mutations from other patients with the same type of cancer
- Each cancer patient may have several different types of cancer cell mutation within a particular tumour
- Each patient's cancer may mutate and change over time.

In order to treat patients effectively, doctors need actionable information that will help them 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 in the long run.

There is therefore a crucial need for ongoing information as to the patient's cancer status. Initially, where the cancer tumour can be accessed, this is currently achieved through a solid tissue biopsy, for example through a breast cancer lumpectomy. The tissue excised is analysed and the oncologist makes a decision on therapy based on the analysis, 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 Herceptin or a similar drug but otherwise they will not.

The use of the solid tissue biopsy where it can be applied is effective and the current "gold standard" in treatment. However it is invasive, relatively costly and not suited to repeat testing compared with a blood test. Importantly it cannot always be used effectively 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 surgery.

Crucially, whether or not a solid tissue biopsy can be taken when the patient presents, biopsy of the primary tissue cannot be repeated at a later date when the tissue concerned has already been excised and is no longer there.

Primary cancers 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. If they can be harvested for analysis, the CTCs have the potential to provide, through a simple peripheral blood test as is routinely used in medical application, crucial medical information regarding the changing metastatic and 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 that individual patient at that particular time.

Economics of cancer patient treatment

Treatment of cancer patients can be very expensive. For example a single chemotherapy drug prescribed may cost US$10,000-US$100,000 for a course of treatment, depending on drug, method of administration and the number of treatments required. Newer immunotherapy drugs may cost c.US$170,000 for a course of treatment. Such drugs are prescribed because they are thought to be the best option available to treat patients, whilst in reality they will be beneficial to only a proportion, typically 13-50%, of patients.

In this situation, 50-87% of the drug cost may be wasted on patients who have no medical benefit from the treatment. Worse still these drugs are toxic and, regardless of whether they receive any benefit from the drug, patients will often experience severe side effects.

Furthermore, it is often the case that without specific information on the individual patient'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 an analysis that will enable a determination of which patients will benefit from which drug.

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 the National Institute for Health and Clinical Excellence (NICE) in the UK, and similar organisations elsewhere in the world, to ensure effective use of medical resources.

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 19.3 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 50.6 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.

Commercialisation

ANGLE has a clear strategy to commercialise its Parsortix technology.

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 is being prosecuted.

A great deal of work has been completed with the aim of ensuring the system is robust, operates reproducibly and can run patient samples efficiently. Following this the product was released for commercial launch with first sales registered in December 2015. Optimisation of the system is a continuous improvement process along with developing Standard Operating Procedures (SOP) for new applications and new product development to meet customer needs to ensure it operates effectively with existing medtech platforms for cell analysis. The system is well established with an installed base of more than 230 instruments in active use.

Successful evaluation of the system by major cancer research centres as Key Opinion Leaders (KOLs) for the market was achieved 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. Customers have also delivered ground-breaking research and identified new uses. This raises awareness of the Parsortix system through peer-reviewed publications and other published evidence as well as the cancer centres presenting at conferences.

Regulatory authorisation for the clinical use of the system in patient treatment in the European Union has already been achieved for a limited clearance and the process is ongoing with the FDA for the United States in metastatic breast cancer. Authorisation will also be sought in the UK and European Union for the same intended use as the FDA clearance. Additional authorisations will also be sought for specific clinical tests and clinical studies will be designed and run to provide the necessary data.

Widespread adoption of the Parsortix system in the clinical market crucially depends on ongoing work with KOLs and customers to:

- Undertake successful pilot studies demonstrating patient applications with clear medical utility (patient benefit)
- Select key medical applications with clear medical utility
- Undertake successful patient studies providing fully documented evidence of how the system should be used for particular patient applications in routine treatment
- Convert cancer centre support and peer-reviewed publications into widespread adoption of the Parsortix system in routine patient care.

Major areas of work currently in progress are described below.

Competitive differentiation

Major competitive differentiators of the system successfully demonstrated include:

- **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 the epithelial 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 so that they cannot be harvested for 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. Competing systems may have far more background white blood cell contamination thereby making analysis of target cells more difficult

BUSINESS STRATEGY CONTINUED

- **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, straightforward in training 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 CLIA (certified laboratory) approach where the customer has to send the patient sample for analysis at a remote laboratory and cannot process it near the patient.

Optimising the system and ongoing improvements

ANGLE continues to undertake work on the Parsortix system with the aim of ensuring that it is robust, operates reproducibly and can run patient samples efficiently.

ANGLE has successfully completed extensive work in key areas of functionality including:

- developing, testing and then automating the harvesting protocols to allow harvesting of cells from the Parsortix system for molecular analysis
- developing and refining protocols to reduce the level of background white blood cell contamination of the harvested cells. This enables the analysis of the harvested cells directly without the need for a separate single cell separation step, although this may still be useful in some applications

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

- developing interface protocols for the existing molecular analysis platforms deployed by some of the world's largest medtech companies
- investigating how best the Parsortix system can be used by major pharma companies for cancer drug development and as a "companion diagnostic" to determine the suitability and effectiveness of drugs for individual patients
- development of an in-house proprietary molecular analysis system HyCEAD, which allows multiplex gene expression for more than 100 genes simultaneously on a highly cost-effective basis
- enhancing automation and throughput in a next generation of the Parsortix system
- optimising the full process from blood collection and stability to cytological and molecular analyses in sample-to-answer solutions.

Secure regulatory authorisation

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.

ANGLE has secured a limited CE Mark authorisation for the use of the Parsortix system as an in vitro diagnostic device in the European Union in the treatment of patients.

ANGLE is working towards FDA Class II clearance for clinical use of the Parsortix system in the United States in metastatic breast cancer. The timing of FDA regulatory clearance is dependent on the FDA's review and responses to our submission. ANGLE is following a De Novo FDA process for the Parsortix system as there is no predicate device. Consequently, there is inherent uncertainty over the timing of the process and its ultimate success.

There are no FDA cleared systems for harvesting CTCs for analysis and only one system authorised for the capture and counting of CTCs, which is antibody-based. Securing FDA authorisation will be a key competitive differentiation of the Parsortix system.

Offer services through clinical laboratories

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.

They are being used to offer CTC analysis services to pharma and biotech customers for drug trials and, with accreditation, are able to offer validated clinical tests known as laboratory developed tests (LDTs) to support cancer patient management.

A growing number of drug trials are using CTC evaluation as a key biomarker to assess patient response as a proxy trial endpoint. CTC evaluation may provide a measure of response to treatment and may provide a much earlier measure 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 longitudinal monitoring of the patient response and condition during the trial through repeat measurements, 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 product approvals. 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.

Patient studies by Key Opinion Leaders to identify potential clinical applications

A critical element in progressing commercialisation of the Parsortix system is ensuring KOLs undertake successful patient 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 study in ovarian cancer demonstrated the potential to use the system to detect ovarian cancer in women having operations to surgically remove abnormal pelvic mass growths. This is now being developed as the Company's first clinical application 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. This application will save healthcare costs and improve patient outcomes by focusing resources appropriate to the patient condition. The clinical study programmes have been developed and are recruiting patients. This is described in more detail in the Chairman's Statement on pages 16 to 19.

The FDA clearance studies in metastatic breast cancer utilised cytological examination, RT-PCR, FISH and RNA-seq methods for analysing cancer cells.

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 has the potential to deliver significant financial returns for ANGLE's shareholders, profoundly improve the outcome for cancer patients, and reduce healthcare costs.

This report was approved by the Board of Directors on 27 April 2022 and is signed on its behalf by:

Andrew D W Newland
Chief Executive
27 April 2022

ANGLE's assay development team offers pharma the opportunity to develop a bespoke CTC assay investigating the pathways their drug is targeting.

Andrew D W Newland
Chief Executive

KEY PERFORMANCE INDICATORS

Strong progress against 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 (cash and cash equivalents and short-term deposits) at 31 December 2021 was £31.8 million (2020: £28.6 million). The Group is loss making while it invests in and develops the business and therefore carefully plans expenditure with rolling cash flow forecasts and tight financial control. Updated plans were put in place following the fundraise in June 2021 to deliver certain key milestones. The Group 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, avoiding long-term commitments as far as possible. Manufacturing of instruments and cassettes is outsourced and product can be ordered on relatively short lead times.
Clinical laboratories **Develop clinical laboratories** **Develop service offering** **Secure initial pharma services contracts**	Capital raising activities included funds to develop clinical laboratories in the UK and US for delivering pharma services and laboratory developed tests (LDTs). The focus in the year has been on developing these laboratories, fitting-out facilities, recruiting staff and implementing the necessary procedures and systems and commencing marketing. During the year the first three biopharma customers were 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, the HyCEAD system and new product development. 26 patents protecting the Parsortix system granted at the reporting date (2020: 26) in the United States, Europe, Australia, Canada, China, Japan, India and Mexico, extending patent coverage out to 2034. 9 patents protecting HyCEAD and Ziplex systems granted at the reporting date (2020: 11) in the United States, Europe, Canada, China and Japan, with an additional 16 in progress, extending patent coverage out to 2035.

KPI	Performance
Ovarian cancer clinical application: triaging abnormal pelvic mass **Progress patient enrolment and analysis of samples**	There have been two successful 200 patient studies for the detection of ovarian cancer in patients having surgery for abnormal pelvic masses and the optimisation of the ovarian assay combining the Parsortix system and HyCEAD has been completed. The optimised assay is now being tested in a new 200 patient study being run by the University of Rochester Medical Center Wilmot Cancer Institute (URMC). During the year, patient enrolment was completed and samples are now being analysed in the United States clinical laboratory ahead of the release of headline results in mid-2022.
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 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, easy to use and produces robust reproducible results. There were more than 230 Parsortix instruments in active use (in-house, KOLs, and customers) at the reporting date (2020: c.200). Over 141,000 blood separations have been performed on the system at the reporting date (2020: 115,000). 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 forms of analysis. To date the Parsortix system has been used successfully with 24 different types of cancer. Upgrades, enhancements and optimisation of the Parsortix and HyCEAD systems are ongoing to further enhance operational performance and product reliability and to develop additional utility and operating protocols based on customer and KOL feedback and in order to meet pharma services needs, for example, in blood sample stability.
Published evidence **Build the body of independent data**	Successful evaluations and studies with 29 independent cancer centres has led to a growing body of published evidence: • 54 publications in peer-reviewed journals as at 31 December 2021 (2020: 37) plus many posters

KEY PERFORMANCE INDICATORS CONTINUED

KPI	Performance
Regulatory authorisation **Progress FDA Submission and maintain quality control systems**	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 is pursuing FDA clearance (the gold standard) for the system for harvesting cancer cells from patient blood for analysis in the first instance for metastatic breast cancer patients. Clinical studies have been completed and reported positively. Four leading US cancer centres conducted the clinical studies included in our FDA Submission: • 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 Following the FDA De Novo Submission made in September 2020 FDA continued its substantive review. The Company subsequently received an Additional Information Request and the additional analytical work required was completed and submitted to FDA in early June 2021. The Company was notified by FDA that due to COVID-19 related impacts the review process would take longer than normal. 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. In addition, ANGLE Biosciences Inc., ANGLE's Toronto facility, secured ISO 13485:2016 certification (assessed by BSI North America) in March 2021.
Research use sales **Build product sales to leading translational researchers** **Secure initial pharma services contracts**	Product sales have been made to multiple customers in Europe, North America and elsewhere including existing KOLs, new research users, big pharma and immunotherapy companies comprising new instrument sales and repeat orders for cassettes and warranties. Revenues from products for the year were £0.9 million (2020: £0.8 million). The sales environment has remained challenging with customers experiencing ongoing COVID-19 impacts and a restricted grant environment. During the year, sales temporarily reduced due to the impact of COVID-19 with customer sites being closed. 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 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, with contracts extending into 2022. Revenues for the year were £0.1 million. In addition, ANGLE successfully completed the first phase of an assay development project in the field of DNA damage repair.

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 application in ovarian cancer	The Group is developing a clinical application in the triaging of abnormal pelvic masses. This is dependent on both successful harvesting of CTCs by the Parsortix system and identifying a set of RNA markers that can be detected by HyCEAD to discriminate between malignant ovarian cancer and other benign conditions. Clinical studies may be delayed due to slow or insufficient patient enrolment or may be temporarily ceased due to factors outside of our control. The COVID-19 pandemic did cause patient enrolment to stop for a period and subsequently resulted in slower patient enrolment. In addition, there has been some third-party supply chain difficulties attributed to COVID-19 with a key supplier unable to deliver certain reagents as scheduled. There can be no guarantee that the clinical application will be developed into a commercially viable product. Regulatory approval may be delayed or may not be obtained depending on the results of the studies. Data produced may not be sufficient to support roll-out of the application via a clinical service laboratory (CLIA Laboratory). 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 cancer) which have had thorough internal and third-party reviews, including the study lead and other experts. A significant amount of preparation, including additional R&D on the proposed RNA markers and study processes, has been undertaken to minimise the risks. The Group carefully selected this clinical application based on a set of key criteria including strong pilot study data, access to leading KOLs and access to patients. The Group assembles multiple study sites and partners where possible to achieve patient accrual rates in a timely fashion. The Group has undertaken independent market research to understand end user needs and ensure the studies produce the necessary data. The Group is taking 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 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, 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 simple, 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. The Group strengthened its competitive position through the acquisition of the HyCEAD technology as used in the ovarian cancer studies. This further differentiates the Group and enhances the ability of the Group to offer sample-to-answer solutions.

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 a new product and services in an emerging market and suitable clinical applications need to be identified, have successful clinical studies completed, achieve regulatory approvals and achieve market acceptance, and 2) the impact of the Group's FDA clearance to boost research use sales and in particular to pharma in drug trials is unknown. 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 suppliers and incurs costs in Euros and is exposed to Euro exchange rates which it is unable to control. Post-Brexit EU trading and human resource issues and the potential impact of further COVID-19 restrictions may have an effect on the Group operations. Exchange rates may be adversely affected. 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 (COVID-19, Ukraine-Russia conflict 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 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. 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 is building US and European sales to provide a natural hedge. The Group holds a modest 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 to 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 ongoing COVID-19 pandemic has impacted our supply chains. These events may 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.	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. We have established an ISO 13485:2016 manufacturing facility for the manufacture of reagents in our Toronto facility. Product manufacture is subject to good manufacturing practice and regulatory control and oversight. The Group also has product liability insurance.

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 will aim 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 application in ovarian 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. analytical studies for FDA clearance or 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 has 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. Staff can work remotely if required, although laboratory and engineering staff are limited in the amount of work they can undertake remotely. US and Canadian 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 clinical and analytical studies. 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 have and are being 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

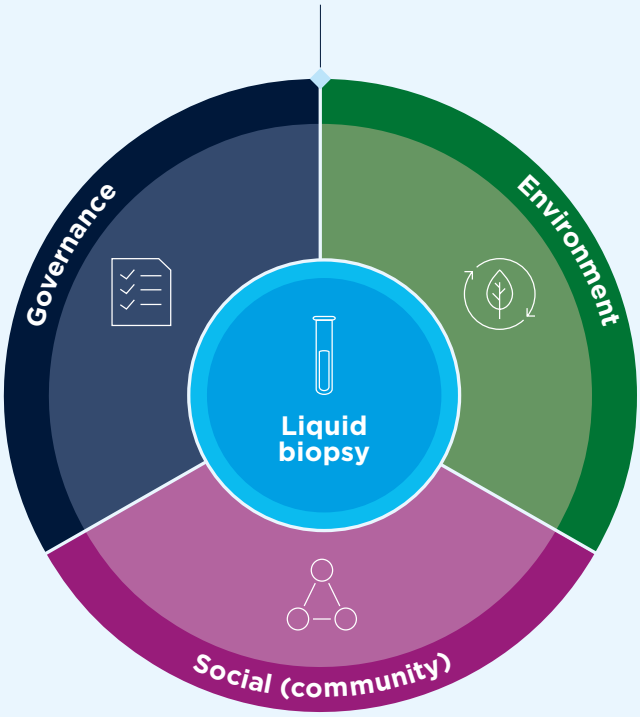
Risk	Description	Mitigation
Regulation and quality assurance	The Group operates in a highly regulated industry and needs to meet recognised quality assurance standards that are subject to third-party audit. The Group must comply with a broad range of regulations relating to the development, approval, 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 Europe (CE Mark) for the indicated clinical use. FDA regulatory clearance is in progress in the United States for the indicated clinical use. Authorisations will be sought in other territories in due course. The Group conducts its operations within ISO 13485:2016 quality system requirements in UK and Canada and continues to invest in its systems and people. The quality system is subject to annual Notified Body audit (BSI and BSI North America). 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 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 will replace the current 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. In March 2021, ANGLE Biosciences Inc. achieved ISO 13485:2016 quality system certification, which complements the ISO 13485:2016 quality system certification held since 2015 by ANGLE Europe Ltd. The current CE Mark regime for IVD devices is based upon a European Regulation which has been implemented 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 applied. We continue to monitor the development of, and transition to the relevant UKCA conformity assessment procedures being put in place by UK Government post-Brexit.

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 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 key suppliers in line with Quality System requirements and compliance 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.



2021 ESG Highlights

ANGLE sustainability and ESG reporting team established and associated work initiated

World Wide Generation appointed to provide tools and assistance with reporting

MS Teams introduced to strengthen communication and collaboration across the Group, reduce travel and facilitate work-from-home

Continuing to monitor government advice and modify practices to maintain a COVID-19 secure work environment, enabling ANGLE employees to work substantially as usual

ANGLE Biosciences Inc. achieved ISO 13485:2016 quality system certification

ANGLE believes that investing in culture and community and in 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

In 2021, ANGLE further responded to increasing investor demand for transparency and higher standards of sustainability reporting by engaging with World Wide Generation (WWG), the provider of a leading digital reporting tool for small and mediums sized companies.

The G17Eco Company Tracker platform will allow ANGLE to measure and monitor all its relevant social economic and environmental impacts, allow 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 has been 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 now 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.

Company Tracker is certified by:

UN GLOBAL COMPACT

SASB

GRI

CDP
DISCLOSURE INSIGHT ACTION

World Wide Generation is pleased to support ANGLE plc in its commitment to adopt best practices for its impact on society and the environment, and effectively report on its ESG impact.

WWG is an award-winning sustainability FinTech company that has developed G17Eco, a monitoring and marketplace technology platform. G17Eco uses ground-breaking 4iR (4th Industrial Revolution) technologies such as blockchain, designed to deliver trusted, comparable and timely impact data to empower all stakeholders with their sustainability reporting and decision making.

G17Eco has been developed with the support of over 300 experts, including our 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 new 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 and treated. Our Parsortix system captures circulating tumour cells (CTCs), which are shed from a tumour, and harvests them from peripheral blood for analysis. This is known as 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 different and highly complex and their cancer changes over time. Effective treatment requires personalised care.

The existing standard of care is a solid tissue biopsy, which is invasive, can have medical complications and uses a lot of healthcare resources – facilities, surgeon, anaesthetist, nurses etc with the associated high costs. Further, it is difficult to repeat, so risks missing the dynamic nature of cancer response, or 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 non-invasive and repeatable as well as reducing the costs and resources involved in cancer healthcare.

COVID-19 impact and response

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 and treatment. ANGLE believes that liquid biopsy could be a valuable tool in addressing what is becoming a secondary healthcare crisis due to 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 COVID-19. 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, monitor, and treat cancer more efficiently. Liquid biopsy is minimally invasive, can be undertaken safely in community clinics or in the home to provide patients with a rapid diagnosis and timely treatment with targeted therapies. Liquid biopsy may also help to safely monitor cancer patients in remission to provide early 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.

COVID-19 and ANGLE's response

From an internal perspective, ANGLE continued to follow Government guidance closely through 2021. Its work-from-home strategy remained in place wherever possible and ANGLE supported employees with the necessary resources and flexibility in working hours to allow for an effective and sustainable work-from-home experience. ANGLE continued to maintain regular communications using a variety of electronic media, notably management, project and team web conferencing supplemented by CEO video updates and Company-wide web conferences shared with the entire workforce. Early in the pandemic, ANGLE deployed its business continuity plan and created a dedicated COVID-19 response team that continuously reviewed its COVID-19 risk assessment and implemented any changes needed to respond to changing government guidelines and employee feedback. This included individual risk assessments to support vulnerable employees. This year, ANGLE strengthened its ability to collaborate across the company with the introduction of MS Teams.

Lessons for the future

ANGLE has learned from the challenges imposed by the COVID-19 pandemic and management believes that there have been some positive aspects that can be maintained in the future, in particular the greater collaborative mentality and cross-group endeavour that has been necessarily created. Employee Assistance Programmes, previously added to benefits remain in place to offer confidential support, counselling and advice. The impact on mental health has not gone unnoticed and ANGLE will continue to recognise and support global and local mental health awareness events as well as providing staff access to Company-funded counselling and advice where required. This year, ANGLE strengthened its mental health support and increased the number of trained Mental Health First Aiders across the organisation. Furthermore, the hybrid working approach established across ANGLE during the pandemic continues where practical and affords some flexibility in individuals' working arrangements and hence wellbeing, without compromising employee engagement or the achievement of corporate objectives.

CORPORATE RESPONSIBILITY REPORT CONTINUED

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 flexible working hours and part-time working 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 an effective placement programme 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. In 2021/22, for the first time, ANGLE supported a student taking advantage of the Erasmus exchange programme. In North America, two placements are offered annually within either the R&D or Administrative functions.

In the UK, from 2022, ANGLE will offer at least two apprenticeships (within the Finance and Human Resource teams), providing individuals the opportunity to combine practical training in a job with study.

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 Resource.

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 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, usually 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 ("Clear Review") to enable meaningful, regular performance management. This system is used to set, track and evaluate employee performance and development objectives.

ANGLE operates a Development Committee which meets twice yearly to consider career 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.

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.

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

ANGLE has also recently purchased an HR information system (PeopleHR). PeopleHR provides employees with increased transparency and ownership of their data and streamlined workflow processes, improving the overall employee experience.

In addition, the Clear Review platform provides a tool for bidirectional communication and feedback relating to professional (tied back to the organisational goals) and personal development goals and objectives of each employee.

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 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 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 Systems falls within the scope of ISO 13485:2016 and cover the design, manufacture, testing, storage, distribution, service of and the 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 Systems.

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 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 and BSI North America). 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 the quality 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 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.

ANGLE has recently further strengthened its health and safety arrangements with the appointment of new specialist health and safety advisors in both the UK and the US. ANGLE uses expert independent advisors to audit our operations to ensure compliance is ongoing and effective.

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 Guildford laboratory uses healthy volunteer blood donors to enable it to test multiple aspects of the Parsortix system and also to perform the analytical studies for its clinical applications. We are very grateful for the blood donors who are predominantly from the local vicinity. In 2022, ANGLE's facility in the US will also commence a blood donation programme and look forward to establishing a community presence in support of changing the way that cancer is diagnosed and treated.

The Group works with a number of 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 Guildford, Toronto and Philadelphia.

ANGLE recognises and supports relevant awareness days, such as the World Cancer Day in February 2022.

CORPORATE RESPONSIBILITY REPORT CONTINUED

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 53 to 60 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 for employees 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 that it needs to support 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 of their teams, but 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. ANGLE has, therefore, produced a Management Charter, which sets out the expectations of all employees in managerial roles.

ANGLE has recently developed a management training programme to include an introduction to the Management Charter and is rolling this out to new managers and supervisors.

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. In addition, ANGLE retains membership of the British In Vitro Diagnostics Association (BIVDA) and Regulatory Affairs Professionals Society (RAPS) in the UK.

Clinical trials programmes and standards

ANGLE engages in clinical studies designed to evaluate new and/or existing medical devices 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.

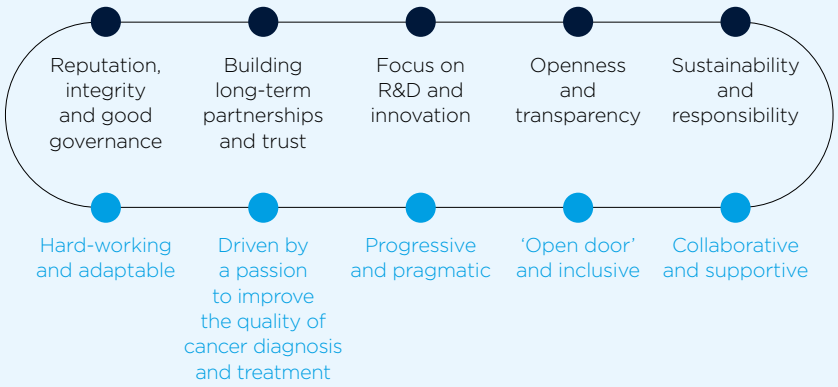
Project Teams are responsible for developing a regulatory strategy, developing and implementing an Investigational Plan (IP), monitoring the progress of ongoing studies, and fulfilling all reporting requirements required by applicable national and international regulations. The Project Team may outsource 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 and a copy of the Medical Licence of the site, Financial Disclosure Forms signed by the site Principal Investigator and all sub-investigators and 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.

Our values and our culture



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 must obtain local IRB/EC approval for the Protocol and Consent Form prior to enroling 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 written informed consent is obtained from all subjects participating in the study prior to any study procedures being done.

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 has 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.

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, and 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 size and deformability of CTCs with the instrument using pressure to harvest the cells rather than a chemical approach with the higher levels of antibody reagents and other chemicals used by many of our competitors.

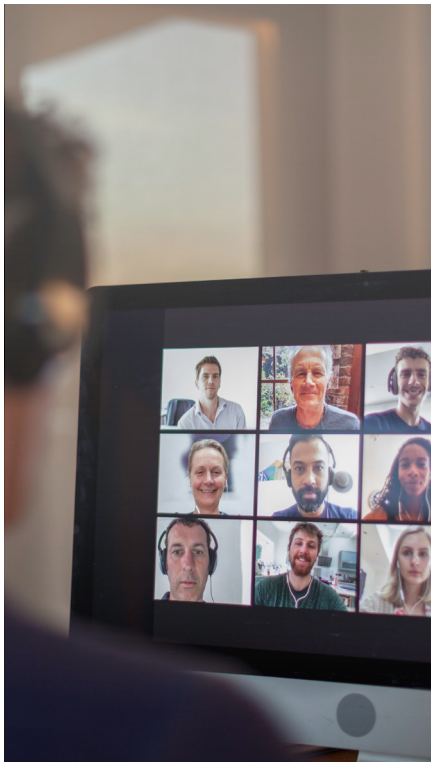
Energy management

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 two main sites with hydro-electricity in Toronto. The Group uses plumbed boiling water taps which are more energy efficient than kettles.

Travel

The Group seeks to restrict business travel to necessary business travel and promotes the use of video conferencing. 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, committed to improving transport and helping reduce emissions, within the UK, the Surrey Research Park has implemented an e-shuttle bus for rail commuters and many of the UK team take advantage of this scheme.

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 goods) 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

Substantial investment has continued in multiple areas of the business

> The Group is gearing up its commercialisation activities following a sustained period of development.
>
> The fundraise was well supported by new and existing shareholders.

Ian F Griffiths
Finance Director

Financial Highlights

£1.0 million at 70%
Research use revenues for the year of £1.0 million (2020: £0.8 million) at a gross profit margin of 70% (2020: 78%)

£18.0 million
Planned expenditure on Parsortix system of £18.0 million (2020: £14.4 million)

£15.0 million
Loss of £15.0 million (2020: loss £11.6 million)

£20.0 million
Fundraise of £20.0 million (£18.9 million net of expenses) in June 2021

£31.8 million
Cash and cash equivalents and short-term deposits combined balance at 31 December 2021 £31.8 million (2020: £28.6 million)

Introduction

The Group has continued to make substantial investment in the FDA analytical studies, the ovarian cancer pelvic mass triage clinical application studies, new 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 a successful fundraise in June 2021, ANGLE has made good progress across all these areas.

Consolidated Statement of Comprehensive Income

Revenues for the year were £1.0 million (2020: £0.8 million) with a gross profit margin of 70% (2020: 78%). Research use sales have been made to multiple customers of both Parsortix instruments (including an annually renewable service-based warranty) and cassettes (a one-time use consumable). As the installed base of instruments builds we are seeing recurring revenues from cassette sales and service-based warranty 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, COVID-19 related issues 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 three new contracts during the year both supporting drug trials and in assay development.

Planned investment in studies to develop and validate the clinical application and commercial use of the Parsortix system resulted in operating costs for the year of £18.0 million (2020: £14.4 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 £8.4 million (2020: £7.8 million) in research and development, in particular the FDA analytical studies, the ovarian cancer clinical application studies, in-house work and ongoing work with KOLs on pilot studies and other potential uses of the system as well as new product development, patent prosecution and new patent grants. The response Additional Information Response to our De Novo Submission to the FDA in September 2020 resulted in additional analytical studies being undertaken.

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

The Group made a loss before tax for the year of £17.4 million (2020: loss £13.7 million). The significant research and development expenditure resulted in research and development tax credits of £2.4 million for the year (2020: £2.1 million). The Group made a loss after tax of £15.0 million for the year (2020: £11.6 million) resulting in a basic and diluted loss per share attributable to owners of the parent of 6.67 pence for the year (2020: 6.52 pence).

Consolidated Statement of Financial Position

Intangible assets decreased in the year to £3.6 million (2020: £3.7 million). Intellectual property of £0.1 million (2020: £0.1 million) was capitalised during the year in accordance with IAS 38 Intangible Assets offset by amortisation and impairment costs.

Property, plant and equipment increased to £2.2 million (2020: £1.2 million) with the expansion of premises including the clinical laboratories and the addition of some key items of laboratory equipment offset by depreciation charges.

The right-of-use assets represented by our leased office and laboratory premises increased to £2.2 million (2020: £1.2 million) with the addition of new leases for the clinical laboratories of £1.5 million offset by depreciation and transfers to and from net investment in sublease.

Increasing inventories of £1.7 million (2020: £0.7 million) reflect 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 Brexit risk 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 decreased to £1.3 million (2020: £1.4 million). The current year balance includes £0.1 million (2020: £0.4 million) in respect of a Canadian COVID-19 relief subsidy (Canada Emergency Wage Subsidy) receivable.

The tax receivable balance of £4.5 million (2020: £2.1 million) reflects the fact that research and development expenditure is eligible for research and development tax credits. The current year receivable includes £2.1 million in relation to 2020.

The trade and other payables (current and non-current) balance of £4.6 million (2020: £3.3 million) includes an increased provision for employers' taxes on the theoretical gain on the exercise of unapproved share options and LTIP Options of £1.1 million (2020: £0.3 million) resulting from increased share option awards and share price appreciation, and a provision for bonus payments of £1.2 million (2020: £0.9 million).

Cash and short-term deposits

The Group ended the year with a cash and cash equivalents and short-term deposits combined balance of £31.8 million (2020: £28.6 million).

The Company completed a fundraise of £20.0 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, particularly in the United States and with a new specialist healthcare investor.

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, albeit ongoing COVID-19 related impacts do mean that certain activities have taken longer than expected. The immediate priorities are progressing the analysis of the clinical study data for our optimised ovarian cancer application to support the US and European launch of our first clinical application in ovarian cancer, building research use sales to translational researchers, undertaking key product development activities and developing capability and delivering our pharma services business from the service labs. There is a lot of effort going into building out the commercial team and plans.

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
27 April 2022

BOARD OF DIRECTORS

Experienced team delivering performance


1


2


3


4


5

Garth R Selvey
Chairman

1

Committee membership
A R N

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

2

Committee membership
N/A

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 12 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 12 years in the liquid biopsy space.

Committees key

- ◆ Chair of Committee
- ◇ Member of the Committee
- A Audit Committee
- R Remuneration Committee
- N Nomination Committee

Ian F Griffiths — 3

Finance Director

Committee membership
N/A

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 12 years in the liquid biopsy space.

Brian Howlett — 4

Non-executive Director and Senior Independent Director

Committee membership
◆ A ◇ R ◇ N

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 UK, Scandinavia and the Benelux markets within Fisons plc.

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

Dr. Jan Groen — 5

Non-executive Director

Committee membership
◇ A ◇ R ◇ N

Appointed
November 2018

Skills and experience
Dr. Jan Groen is currently the CEO and Chairman at Intravacc B.V. a contract development and manufacturing organisation for infectious disease and therapeutic vaccines in the Netherlands. Jan was previously the 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 Cergentis B.V. 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 lab-developed tests in Europe and the USA.

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 assistant 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 Signalling 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 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 a recognised expert in diagnostic pathology and has significant experience in the cytological and morphological analysis of cancer cells as well as molecular diagnostics and immunophenotyping. Dr. Khoury is a tenured Professor of Pathology and Laboratory Medicine at The University of Texas MD Anderson Cancer Center in Houston, Texas and is the Executive Director of the MD Anderson Cancer Network for the Division of Pathology and Laboratory Medicine. Dr. Khoury is also the Director of the MD Anderson Clinical Immunohistochemistry Laboratory. Additionally, Dr. Khoury is the incoming chair and Stokes-Shackleford professor at the Department of Pathology and Microbiology, University of Nebraska, Omaha, Nebraska.

Dr. Khoury is a leader in translational research focused on hematolymphoid neoplasia (a class of tumours that affect the blood, bone marrow, and organs of the immune system). Dr. Khoury has authored over 275 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 chairs the National Pathology Implementation Optimisation Delivery Group.

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. 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.

Mr Greg L Shaw

Skills and experience

Mr 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, Mr Shaw has published widely on prostate cancer and is currently an honorary Associate Professor at University College and Senior Lecturer at Queen Mary College of the University of London.

Mr 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. Mr Shaw is currently chief investigator for two NIHR portfolio studies investigating 1) the effects of refinements to robotic surgery and 2) the use of drugs to prevent progression in men on active surveillance for prostate cancer. Mr Shaw is lead surgeon for the largest robotic surgery team in the UK at UCLH. Mr 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. The annual research spend of Cancer Research UK is in the region of £375 million and Commercial Partnerships has annual revenues of approximately £50 million. Prior to becoming Chief Scientific Officer of Commercial Partnerships, Dr. Stanway established and led the drug discovery and biotherapeutic discovery activity within Cancer Research UK, which has been or is now 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 for an initial sepsis diagnostic offering and a future oncology test. Dr. Swerdlow is a leading expert in NGS and recently served as a consultant for both ONI (Oxford Nanoimaging a super-resolution microscopy company), and Nuclera Nucleics, a DNA synthesis start-up after being Head of NGS Technology Development at LGC Genomics. As VP of Sequencing at the New York Genome Center (NYGC) from 2014-2017, Dr. Swerdlow directed the Technology Innovation group and managed the production and clinical laboratory facilities (with about 30 Illumina DNA sequencers). Prior to NYGC, Dr. Swerdlow was Head of Research and Development for the Wellcome Trust Sanger Institute in Cambridge, UK (2008-2014). In that role, Dr. Swerdlow directed the R&D department and helped build the Sanger Institute's next-generation DNA-sequencing production facility into one of the world's largest. Previously, Dr. Swerdlow was the Chief Technology Officer of Dolomite Ltd., a leader in microfluidics and microfabrication. Prior to Dolomite, Dr. Swerdlow was an inventor of the core technology relating to NGS at Solexa Ltd., a company which he joined in 2000 when it had only three employees. From then until 2006, as Senior Director of Research, Dr. Swerdlow helped launch Solexa's first product, the Genome Analyzer DNA sequencing platform. At Solexa, Dr. Swerdlow was responsible for instrument engineering, integration of the next-generation DNA sequencing system and early applications work, along with assisting in the development of many of the system's biochemical components. Dr. Swerdlow was a key member of the Senior Management team that delivered Solexa's first genome sequence, an end-to-end proof-of-principle. Following its NASDAQ listing, Solexa was acquired by Illumina Inc. for US$600 million and 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 2021

The Directors present their audited Report and Financial Statements for the year ended 31 December 2021 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 45 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 45 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 24 and 26.

Results and dividends

The Consolidated Statement of Comprehensive Income for the year is set out on page 71.

The Group made a loss for the year of £15.0 million (2020: loss £11.6 million).

The Directors do not recommend the payment of a dividend for the year (2020: £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 £8.4 million (2020: £7.8 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 were:

I F Griffiths
J Groen
B Howlett
A D W Newland
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 62 to 64.

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 dated 7 March 2022:

Fund manager/shareholder	Number of shares	Holding
Conifer Management LLC	19,979,790	8.50%
Dermot Keane	12,777,088	5.43%
Morgan Stanley Investment Management	9,308,773	4.00%
Aegon Asset Management	8,979,293	3.82%
Chelverton Asset Management Limited	7,579,691	3.22%
Andrew D W Newland	7,054,686	3.00%

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 27 to 35.

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. They are also 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 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 2021

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), Brexit friction and residual COVID-19 impacts. 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 the 12-month period 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 auditor PricewaterhouseCoopers LLP, Chartered Accountants was appointed by the Board during the year and has indicated its 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 29 June 2022 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ. The Board is looking forward to once again welcoming shareholders to the Meeting in person. As has been the case in recent years, the Board is pleased to be able to continue to offer shareholders the opportunity to follow proceedings online via a live webcast. The Notice of Annual General Meeting is enclosed within this report on pages 105 to 109. The Company will continue to monitor the ongoing situation with regard to COVID-19 and any changes to the format of the AGM, including the ability for shareholders to attend in person, will be notified through a regulatory news service (RNS).

This report was approved by the Board of Directors on 27 April 2022 and is signed on its behalf by:

Andrew D W Newland
Chief Executive
27 April 2022

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 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, 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 45, 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 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 has continued with its sustained focus on its four-pronged strategy for achieving widespread adoption of its Parsortix system in the emerging multi-US$ billion liquid biopsy market:

1) Completion of rigorous large-scale clinical studies run by leading cancer centres, demonstrating the effectiveness of different applications of the system in cancer patient care
2) Securing regulatory approvals with the emphasis on FDA clearance as the de facto global gold standard. ANGLE is seeking to become the first ever company to gain FDA product clearance for a system which harvests circulating tumour cells from patient blood for subsequent analysis. ANGLE will look to build on the initial metastatic breast cancer clearance for specific clinical assays and, where appropriate, for additional cancer types, additional products and additional geographies through further regulatory submissions
3) Building a 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
4) Establishing a significant pharma services business and building partnerships with large healthcare companies for market deployment and development of multiple clinical applications utilising the Parsortix system, including our own laboratory developed tests from our clinical laboratories, once accredited, in the United States and the UK.

ANGLE's ultimate objective is the widespread adoption of the Parsortix system in the diagnosis, treatment and monitoring of cancer patients.

ANGLE is seeking to become the first ever company to receive FDA Class II clearance for a product for harvesting intact circulating tumour cells from patient blood for subsequent analysis. US regulatory clearance by the FDA is considered the global standard for approval of medical diagnostic systems and ANGLE believes that such clearance would provide ANGLE's Parsortix system with a further competitive differentiation, which would accelerate all forms of commercial adoption of the system in both research and clinical settings.

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.

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 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 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 Chairmen 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 virtual deal roadshow resulting in a successful fundraise in June 2021.

The Company employs a Head of Investor Relations to increase shareholder engagement and IR activities. The ongoing development of a Corporate Responsibility Report on pages 36 to 43 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 36 to 43 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. 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.

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.

17 peer-reviewed publications were issued in the year by KOLs and customers (2020: 11) taking the total to 54 publications as at 31 December 2021. A further eight publications have been issued since the year end. Due to COVID-19, conference attendance has predominately been of a virtual nature.

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 accreditation (Europe) and CE marking (IVDD) for the intended use. In addition, in March 2021, ANGLE Biosciences Inc., our Toronto, Canada facility, secured ISO 13485:2016 certification (assessed by BSI North America) and will also continue to receive annual compliance assessments by BSI under the terms of its certification. The scope of 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 and Canadian ISO 13485 certifications are independently maintained and enable 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 27 to 35.

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 judgements and estimates (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 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 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 both UK and Canada locations. 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 1) extensive cyber security training and infrastructure development to support hybrid working in line with COVID-19 restrictions; 2) continued implementation of COVID-19 secure working practices; 3) continued improvements in segregation of duties; 4) ongoing improvements to systems for supplier and equipment control within the quality system; 5) additional rollout of electronic forms, document signatures and signing authorities; 6) improvements to purchasing procedures and inbound/outbound goods inspections; 7) continued development of a new project management tool and dashboard reporting system across the Group and 8) significant improvements to trade compliance procedures to mitigate implications of Brexit on goods flows to the EU and adjustments to customs procedures in other territories.

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, two Non-executive and two Executive Directors. The QCA Code recommends there are at least two non-executive directors.

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 toward 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 lab-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 46 and 47.

There are currently no female or ethnic minority directors. 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 nevertheless 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 62) or represent a major shareholder, they receive no remuneration from the Company other than directors' fees and occasional consultancy fees (see page 62), 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.

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 46 and 47.

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 12 years in the liquid biopsy space.
- Ian Griffiths, Finance Director – over 30 years' experience in finance and technology-based businesses, and 12 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 lab-developed tests in Europe and the USA.
- Brian Howlett, Non-executive Director – extensive commercial operations experience of the medtech sector.

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.

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.

CORPORATE GOVERNANCE REPORT CONTINUED

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 36 to 43 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 regularly work at different offices in normal times, although the pandemic has resulted in virtual teams. 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 84% (2020: 87%) 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 47%:53% (2020: 43%:57%) Male:Female.
- Different nationalities, with 39 (2020: 35) 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. 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.

All Directors were re-elected by the shareholders at the AGM held on 30 October 2019 and accordingly all Directors are 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 Brian Howlett (Chairman of the Audit Committee), the Chairman Garth Selvey and the Non-executive Director Jan Groen. 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. 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.

Remuneration Committee
The members of the Committee are the Chairman Garth Selvey (Chairman of the Remuneration Committee) and the Non-executive Directors Brian Howlett and Jan Groen. 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 61 to 64 provides details of the Remuneration Policy and the Directors' Annual Remuneration.

Nomination Committee
The members of the Committee are the Chairman Garth Selvey (Chairman of the Nomination Committee) and the Non-executive Directors Brian Howlett and Jan Groen. 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.

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.

CORPORATE GOVERNANCE REPORT CONTINUED

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. Due to COVID-19 restrictions meetings have been held primarily 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 2021 is set out below:

	Garth Selvey	Brian Howlett	Jan Groen	Andrew Newland	Ian Griffiths
Board	12/12	12/12	12/12	12/12	11/12
Committee of the Board*	N/A	N/A	N/A	Yes	Yes
Audit	3/3	3/3	3/3	N/A	N/A
Remuneration	3/3	3/3	3/3	N/A	N/A
Nomination	0/0	0/0	0/0	N/A	N/A

* The Board appointed Andrew Newland and Ian Griffiths as a Committee of the Board of Directors in relation to three meetings 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 61 to 64 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 at 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	
	2021	2020
I F Griffiths	**1,203,832**	703,832
J Groen	**–**	–
B Howlett	**10,000**	10,000
A D W Newland	**7,054,686**	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	**2021 Total £'000**	2020 Total £'000
Chairman						
G R Selvey	25	–	–	–	**25**	25
Executive						
I F Griffiths	118	3	40	123	**284**	251
A D W Newland	242	10	–	194	**446**	392
Non-executive						
J Groen	25	–	–	–	**25**	25
B Howlett	25	–	–	–	**25**	25
Total	435	13	40	317	**805**	718

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

Performance bonuses were awarded in the current financial year under the terms of the Annual Bonus Plan. The Executives were deemed to have met the performance criteria in relation to a 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.

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 a 60% performance bonus, major factors of which were: submission to FDA for clearance of the Parsortix system, keeping the Group working effectively through the COVID-19 pandemic and a successful fundraise.

I F Griffiths sacrificed salary during the current year and in the prior year. 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 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 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 over the three-year performance period. 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

As at 20 December 2021 the share price target in relation to the 20% proportion vesting had been met. Under the discretion approved by the shareholders at the Annual General Meeting on 30 June 2021, reflecting COVID-19 related impacts, the performance period was extended to no later than 20 December 2022, and the holding period reduced accordingly such that the overall five-year period is unchanged. Other than this change in date, the overall performance is unchanged.

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 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 2021	Granted	Lapsed	Cancelled	Exercised	At 31 December 2021	Vested – capable of exercise	Exercise price (£)	Earliest exercise date	Expiry date
I F Griffiths	30/08/2011	466,019	–	–	–	(466,019)	**–**	Exercised	0.2575	Note (1)	29/08/2021
	18/11/2011	187,315	–	–	–	–	**187,315**	–	0.7550	Note (2)	17/11/2022
	05/11/2012	33,981	–	–	–	(33,981)	**–**	Exercised	0.2575	Note (1)	29/08/2021
	05/11/2012	312,685	–	–	–	–	**312,685**	–	0.7550	Note (2)	17/11/2022
	10/11/2014	500,000	–	–	–	–	**500,000**	–	0.8625	Note (3)	09/11/2024
	12/11/2015	46,980	–	–	–	–	**46,980**	46,980	0.1000	Note (4)	11/11/2025
	25/11/2016	500,000	–	–	–	–	**500,000**	500,000	0.6450	Note (5)	24/11/2026
		2,046,980	–	–	–	(500,000)	**1,546,980**	546,980			
A D W Newland	30/08/2011	603,334	–	–	–	(603,334)	**–**	Exercised	0.2575	Note (1)	29/08/2021
	18/11/2011	1,000,000	–	–	–	–	**1,000,000**	–	0.7550	Note (2)	17/11/2022
	05/11/2012	346,666	–	–	–	(346,666)	**–**	Exercised	0.2575	Note (1)	29/08/2021
	10/11/2014	1,000,000	–	–	–	–	**1,000,000**	–	0.8625	Note (3)	09/11/2024
	12/11/2015	73,826	–	–	–	(73,826)	**–**	Exercised	0.1000	Note (4)	11/11/2025
	25/11/2016	1,000,000	–	–	–	–	**1,000,000**	1,000,000	0.6450	Note (5)	24/11/2026
		4,023,826	–	–	–	(1,023,826)	**3,000,000**	1,000,000			

(1) Vesting is subject to a) a performance condition that the Company's share price together with any dividend payments has risen by at least 50% at some point from the market price on 30 August 2011, 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) the performance conditions that (i) the Company's share price must have increased to £2.00 at some point since the date of grant (this condition has not yet been met) 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).
(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 vested 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.

No share options were issued to Directors in the current year (2020: nil). No Directors' share options were forfeited, lapsed or cancelled in the current year (2020: nil). Certain share options were exercised in the current year (2020: nil). The expiry date of share options expiring on 17 November 2021 was extended to no later than 17 November 2022, under the discretion approved by the shareholders at the Annual General Meeting on 30 June 2021, reflecting COVID-19 related impacts. Other than this change in date, the performance conditions are unchanged.

Note 19 provides additional information on share options and LTIP Options.

Shareholder return

The market price of the Company's shares on 31 December 2021 was £1.19 and the range of market price during the year from 1 January until 31 December 2021 was between £0.48 (low) and £1.39 (high).

This report was approved by the Board of Directors on 27 April 2022 and is signed on its behalf by:

Garth Selvey
Remuneration Committee Chairman
27 April 2022

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 2021 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; 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, Consolidated and Company Statements of Cash Flows, Consolidated and Company Statements of Changes in Equity as at 31 December 2021; Consolidated Statement of Comprehensive Income 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 in Canada. The Group's head office is located in the UK where our work over the Group consolidation was performed.
- In total, locations where we performed audit work accounted for 96% of the Group loss before tax

Key audit matters

- For the year ended 31 December 2021, the Group used net cash in operating activities of £14.0 million and the Company generated net cash from operating activities of £35,000. Cash and cash equivalents and short-term deposits at 31 December 2021 were £31.8 million for the Group and £30.2 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 the 12 month period 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. (Group and Parent)
- The accounting treatment for share options can be complex and involves judgement and estimation. As shown in Note 19 to the Annual Report and Financial Statements, the Company has granted 5.8 million share options under the Company Share Option Plan (CSOP) and unapproved share option schemes as well as 3.0 million new share options under the Long-Term Incentive Plan (LTIP) in the year. The Directors have had to form a judgement to determine the appropriate valuation model to use for each share option scheme and estimate future volatilities as well as the likelihood of performance conditions being met. (Group and Parent)

Materiality

- Overall Group materiality: £868,000 (2020: £693,000) based on 5% of loss before tax
- Overall Company materiality: £937,000 (2020: £745,000) based on 1% of Total assets
- Performance materiality: £651,000 (2020: £520,000) (Group) and £702,750 (2020: £558,750) (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.

Treatment of expenditure on FDA clearance and the next generation Parsortix instrument, impairment assessment of goodwill, impairment assessment of intangibles subject to amortisation, expected credit loss on amounts due from Group undertakings and COVID-19, which were key audit matters last year, are no longer included because of these areas not being areas of the audit where the team spent significant amounts of time and effort to come to a conclusion. 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 Parent) For the year ended 31 December 2021, the Group used net cash in operating activities of £14.0 million and the Company used net cash in operations of £35,000. Cash and cash equivalents and short-term deposits at 31 December 2021 were £31.8 million for the Group and £30.2 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 the 12 month period 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.
Valuation of share-based payments (Group and Parent) The accounting treatment for share options can be complex and involves judgement. As shown in Note 19 to the Annual Report and Financial Statements, the Company has granted 5.8 million share options under the Company Share Option Plan (CSOP) and unapproved share option schemes as well as 3.0 million new share options under the Long-term Incentive Plan (LTIP) in the year. The Directors have had to form a judgement to determine the appropriate valuation model to use for each share option scheme as well as estimate future volatilities as well as the likelihood of performance conditions being met.	We obtained the Directors' calculations of the fair value of share options granted during the year. We assessed the valuation models used for each type of share option for appropriateness and engaged our specialist valuations team to assist in performing this work. We re-performed calculations to independently calculate the fair value of the share options in question. We assessed key inputs into the valuation models to ensure they were appropriate. From the procedures performed, we are satisfied that the Directors' valuation of share options granted during the year is materially correct.

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.

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	£868,000 (2020: £693,000)	£937,000 (2020: £745,000)
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 2021 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 £330,000 to £834,000. 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% (2020: 75%) of overall materiality, amounting to £651,000 (2020: £520,000) for the Group Financial Statements and £702,750 (2020: £558,750) 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 £43,400 (Group audit) (2020: £34,650) and £46,850 (Company audit) (2020: £37,250) 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 2021 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 legislation, 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 lack of governance over publications and regulatory announcements. 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.

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.

Other matter

In due course, as required by the Financial Conduct Authority Disclosure Guidance and Transparency Rule 4.1.14R, these Financial Statements will form part of the ESEF-prepared annual financial report filed on the National Storage Mechanism of the Financial Conduct Authority in accordance with the ESEF Regulatory Technical Standard ('ESEF RTS'). This Auditors' Report provides no assurance over whether the annual financial report will be prepared using the single electronic format specified in the ESEF RTS.

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

27 April 2022

CONSOLIDATED STATEMENT OF COMPREHENSIVE INCOME

For the year ended 31 December 2021

	Note	2021 £'000	2020 £'000
Revenue	2	**1,013**	762
Cost of sales	3	**(302)**	(165)
Gross profit		**711**	597
Other operating income		**41**	79
Operating costs	3	**(17,987)**	(14,407)
Operating profit/(loss)		**(17,235)**	(13,731)
Finance income	7	**29**	78
Finance costs	7	**(157)**	(92)
Profit/(loss) before tax		**(17,363)**	(13,745)
Tax (charge)/credit	8	**2,351**	2,139
Profit/(loss) for the year		**(15,012)**	(11,606)
Other comprehensive income/(loss)			
Items that may be subsequently reclassified to profit or loss:			
Exchange differences on translating foreign operations		**(175)**	562
Other comprehensive income/(loss)		**(175)**	562
Total comprehensive income/(loss) for the year		**(15,187)**	(11,044)
Earnings/(loss) per share attributable to owners of the parent	9		
Basic and Diluted (pence per share)		**(6.67)**	(6.52)

All activity arose from continuing operations.

CONSOLIDATED STATEMENT OF FINANCIAL POSITION

As at 31 December 2021

	Note	2021 £'000	2020 £'000
Assets			
Non-current assets			
Intangible assets	11	**3,573**	3,710
Property, plant and equipment	12	**2,172**	1,176
Right-of-use assets	13	**2,204**	1,233
Total non-current assets		**7,949**	6,119
Current assets			
Inventories	15	**1,748**	742
Trade and other receivables	16	**1,269**	1,443
Taxation		**4,510**	2,127
Short-term deposits		**–**	16,538
Cash and cash equivalents		**31,839**	12,080
Total current assets		**39,366**	32,930
Total assets		**47,315**	39,049
Non-current liabilities			
Lease liabilities	13	**(1,816)**	(928)
Trade and other payables	17	**(257)**	–
Total non-current liabilities		**(2,073)**	(928)
Current liabilities			
Lease liabilities	13	**(522)**	(434)
Trade and other payables	17	**(4,390)**	(3,343)
Total current liabilities		**(4,912)**	(3,777)
Total liabilities		**(6,985)**	(4,705)
Net assets		**40,330**	34,344
Equity			
Share capital	18	**23,514**	21,540
Share premium		**99,406**	81,532
Share-based payments reserve		**2,727**	1,745
Other reserve		**2,553**	2,553
Translation reserve		**(3,960)**	(3,785)
Accumulated losses		**(83,808)**	(69,139)
ESOT shares	20	**(102)**	(102)
Total equity		**40,330**	34,344

The Consolidated Financial Statements on pages 71 to 98 were approved by the Board of Directors and authorised for issue on 27 April 2022 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 2021

	2021 £'000	2020 £'000
Operating activities		
Profit/(loss) before tax	**(17,363)**	(13,745)
Adjustments for:		
Depreciation of property, plant and equipment	**701**	661
Depreciation and impairment of right-of-use assets	**532**	421
(Profit)/loss on disposal of property, plant and equipment	**4**	2
Amortisation and impairment of intangible assets	**254**	337
Share-based payments	**1,325**	268
Exchange differences	**(170)**	565
Net finance (income)/costs	**128**	14
Operating cash flows before movements in working capital	**(14,589)**	(11,477)
(Increase)/decrease in inventories	**(1,015)**	14
(Increase)/decrease in trade and other receivables	**204**	(658)
Increase/(decrease) in trade and other payables	**1,417**	872
Operating cash flows	**(13,983)**	(11,249)
Research and development tax credits received	**–**	3,410
Overseas tax payments	**(27)**	(9)
Net cash from/(used in) operating activities	**(14,010)**	(7,848)
Investing activities		
Purchase of property, plant and equipment	**(1,666)**	(412)
Purchase of intangible assets	**(122)**	(94)
Transfer (to)/from short-term deposits	**16,538**	(1,530)
Interest received	**24**	70
Net cash from/(used in) investing activities	**14,774**	(1,966)
Financing activities		
Net proceeds from issue of share capital – placing	**18,765**	18,627
Proceeds from issue of share capital – share option exercises	**925**	23
Principal elements of lease payments	**(614)**	(463)
Interest elements of lease payments	**(85)**	(44)
Net cash from/(used in) financing activities	**18,991**	18,143
Net increase/(decrease) in cash and cash equivalents	**19,755**	8,329
Cash and cash equivalents at 1 January	**12,080**	3,757
Effect of exchange rate fluctuations	**4**	(6)
Cash and cash equivalents at 31 December	**31,839**	12,080
Cash and cash equivalents	**31,839**	12,080
Short-term deposits	**–**	16,538
Cash and cash equivalents and short-term deposits at 31 December	**31,839**	28,618

CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2021

	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 2020	**17,277**	**67,272**	**1,518**	**2,553**	**(4,347)**	**(57,574)**	**(102)**	**26,597**
For the year to 31 December 2020								
Consolidated profit/(loss)						(11,606)		(11,606)
Other comprehensive income/(loss):								
Exchange differences on translating foreign operations					562			562
Total comprehensive income/(loss)					**562**	**(11,606)**		**(11,044)**
Issue of shares (net of costs)	4,263	14,260						18,523
Share-based payments			268					268
Released on exercise			(4)			4		–
Released on forfeiture			(37)			37		–
At 31 December 2020	**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 payments			1,325					1,325
Released on exercise			(295)			295		–
Released on forfeiture			(48)			48		–
At 31 December 2021	**23,514**	**99,406**	**2,727**	**2,553**	**(3,960)**	**(83,808)**	**(102)**	**40,330**

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 2021

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 2021 (including comparatives for year ended 31 December 2020). They have also been prepared in accordance with those parts of the Companies Act 2006 that apply to companies reporting under these standards.

The Financial Statements of the Parent Company have been prepared in accordance with IFRS and are presented on pages 99 to 104.

Accounting standards adopted in the year

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

Amendments to IFRS 7, IFRS 4 and IFRS 16	Interest Rate Benchmark Reform – Phase 2
Amendments to IFRS 4	Insurance contracts – deferral of IFRS 9

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 which have been issued by the IASB 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 – COVID-19 related rent concessions
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
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
IFRS 17	Insurance contracts – as amended in December 2021
Various	Narrow scope amendments to IFRS 3, IAS 16, IAS 17 and some annual Improvements on IFRS 1, IFRS 9, IAS 41 and IFRS 16

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 45. The principal risks and uncertainties are stated on pages 27 to 35. 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 Chairman's Statement provides information on the impact of COVID-19 on the business.

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), Brexit friction and residual COVID-19 impacts. 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 the 12-month period 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 2021

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 accounts 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 arise 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 volume 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.

Income 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.

Income from pharma services is recognised in the period in which the samples are reported 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 services (Note 1.7) includes the direct costs incurred in providing the service (time, travel and parts) and are reflected in costs of sales as they are incurred.

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 2021

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 is:

Brands and trademarks	Over the expected useful life of an actively used and/or marketed brand or trademark (10 years)
Critical supplier contracts and relationships, including exclusive agreements	Over the term of the agreement or the expected useful life of the relationship (1 to 3 years)
Customer contracts and relationships	Over the term of the contract or the expected useful life of the relationship (1 to 3 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 2021

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 liability represents 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 leases' 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 three 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 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 statement 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.

Short-term deposits

Short-term deposits in the statement of financial position comprise deposits with an original maturity of greater than three months and less than 12 months.

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 2021

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, assumptions and judgements 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 19)

In calculating the fair value of equity-settled share-based payments the Group uses options pricing models. The Directors are required to exercise their judgement in choosing an appropriate options pricing model 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. 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 year is an increase of £0.2 million (2020: £0.1 million) and a decrease of £0.2 million (2020: £0.1 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 and its HyCEAD multiplex analysis system. There are separate work streams on the Parsortix and HyCEAD systems however the HyCEAD system is used as the downstream analysis tool primarily in combination with Parsortix in the ovarian cancer clinical application. There is significant overlap of work between the teams involved in R&D and commercial activities and as a result the Directors believe that these activities are best 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 one significant customer (26%) who contributed 10% or more of Group revenues in the year (2020: no 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:

				2021				2020
	Product £'000	Product Service £'000	Pharma Service £'000	**Total £'000**	Product £'000	Product Service £'000	Pharma Service £'000	Total £'000
UK	33	6	49	**88**	30	6	–	36
Europe	563	42	97	**702**	490	80	–	570
North America – RoW	184	22	17	**223**	121	20	15	156
Total	780	70	163	**1,013**	641	106	15	762

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 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 £23,729 (2020: £nil) were subsequently invoiced.

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

Contract liabilities	**2021 £'000**	2020 £'000
At 1 January	**60**	54
Recognised in year, relating to amounts invoiced in prior years	**(34)**	(42)
Deferred at year end relating to amounts invoiced in the current year	**106**	48
At 31 December	**132**	60

The Group has applied the practical expedient to disclosure of performance obligations at the reporting date because all 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 2021

3 Costs

	2021 £'000	2020 £'000
Operating costs		
Employment costs (Note 5)	**9,907**	6,369
Depreciation of property, plant and equipment (Note 12)	**701**	661
Depreciation and impairment of right-of-use assets (Note 13)	**532**	421
Profit/(loss) on disposal of property, plant and equipment	**4**	2
Amortisation of intangible assets (Note 11)	**233**	282
Impairment of intangible assets (Note 11)	**21**	55
Operating lease costs – low value and short-term (Note 13)	**61**	56
Auditors' remuneration (see below)	**215**	220
Third-party research, development and clinical study costs	**2,911**	3,302
Patent and legal costs	**127**	152
Inventories used in research and development	**530**	357
Listed company costs	**594**	460
Foreign exchange	**(117)**	596
Other operating costs	**2,268**	1,474
Total operating costs	**17,987**	14,407
Cost of sales		
Inventories	**210**	136
Other	**92**	29
Total cost of sales	**302**	165
Total costs	**18,289**	14,572

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

Auditors' remuneration	2021 £'000	2020 £'000
Audit services		
Statutory audit of parent and consolidated financial statements	**205**	210
Statutory audit of subsidiaries	**10**	10
Total	**215**	220

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

	2021 £'000	2020 £'000
Aggregate emoluments for qualifying services	**765**	678
Employer pension contributions (Note 6)	**40**	40
Total per Directors' Remuneration Report (page 62)	**805**	718

LTIP Options were issued to Directors in the current and prior year. No Directors LTIP Options were forfeited, lapsed, cancelled or exercised in the current year (2020: nil). During the year, LTIP options issued on 20 December 2018 had their performance period extend by up to one year to 20 December 2022, to reflect COVID-19 related impacts. No share options were issued to Directors in the current year (2020: nil). Certain share options expiring in 2021 had their date of expiry extended by up to one year, to reflect COVID-19 related impacts. No Directors share options were forfeited, lapsed or cancelled in the current year (2020: nil). Certain share options were exercised in the current year (2020: nil). Disclosures relating to individual Directors' LTIP Options and Share Options are given in the Directors' Remuneration Report on pages 62 to 64.

4 Directors' emoluments continued

The above includes the following amounts paid in respect of the highest paid Director:

	2021 £'000	2020 £'000
Emoluments for qualifying services	**446**	392

Disclosures relating to individual Directors' emoluments are given in the Directors' Remuneration Report on pages 62 to 64.

5 Employment

Employment costs

The aggregate of employment costs of employees (including Directors) for the year was:

	2021 £'000	2020 £'000
Wages and salaries	**6,925**	5,293
Social security costs	**1,489**	643
Other pension costs (Note 6)	**168**	165
	8,582	6,101
Share-based payment charge (Note 19)	**1,325**	268
Total staff costs in operating costs (Note 3)	**9,907**	6,369

The key management personnel are the Directors and their remuneration is disclosed in Note 4 and within the Directors' Remuneration Report on pages 62 to 64.

Number of employees

The average monthly number of employees (including Directors) during the year was:

	2021 Number	2020 Number
Research and development, engineering, manufacturing, quality control and regulatory	**94**	75
Commercial and administrative	**34**	27
Total	**128**	102

6 Pension costs

The Group incurred UK pension contribution charges for the year as follows:

	2021 £'000	2020 £'000
Direct to personal pension plan schemes	**126**	131
ANGLE auto-enrolment pension scheme	**42**	34
Total	**168**	165

Contributions to pension scheme of were payable at the reporting date and are included in trade and other payables (Note 17) as follows:

	2021 £'000	2020 £'000
Direct to personal pension plan schemes	**25**	21
ANGLE auto-enrolment pension scheme	**10**	6
Total	**35**	27

One Director has received contributions under a defined contribution pension scheme (2020: one) – see Directors' Remuneration Report on page 62.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2021

7 Finance income and costs

	2021 £'000	2020 £'000
Finance income		
Interest on cash and cash equivalents and short-term deposits	**25**	71
Other interest	**4**	7
Total	**29**	78
Finance costs		
Lease liability finance charges (Note 13)	**(157)**	(92)
Total	**(157)**	(92)

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.

	2021 £'000	2020 £'000
Current tax:		
Research and development tax credit receivable for the current year	**(2,373)**	(2,126)
Prior year adjustment in respect of research and development tax credit	**22**	(13)
Deferred tax:		
Origination and reversal of timing differences	**–**	–
Tax charge/(credit)	**(2,351)**	(2,139)

	2021 £'000	2020 £'000
Profit/(loss) before tax	**(17,363)**	(13,745)
Corporation tax:		
Tax on profit/(loss) at 19.3% (2020: 19.0%)	**(3,355)**	(2,612)
Factors affecting charge:		
Disallowable expenses	**40**	33
Excess of depreciation (over)/under capital allowances	**(53)**	32
Enhanced research and development relief	**(1,051)**	(941)
Share-based payments	**(121)**	51
Unutilised losses carried forward	**2,190**	1,367
Other tax adjustments	**(23)**	(56)
Prior year adjustment	**22**	(13)
Tax charge/(credit)	**(2,351)**	(2,139)

The Group has accumulated losses available to carry forward against future trading profits of £54.2 million (2020 restated: £42.9 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% (2020 restated: 20.4%) is £13.5 million (2020 restated: £8.8 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.

The Group has restated the accumulated losses available to carry forward, the unrecognised deferred tax asset and the weighted average deferred tax rate for the year ended 31 December 2020 as shown above. Accumulated losses have been restated to £42.9 million from £51.4 million by excluding non-trading entities where losses are not expected to be utilised at any point in the future as well as correcting for a foreign exchange error. The weighted average deferred tax rate has been updated to 20.4% from 20.6% as a result of these changes. The unrecognised deferred tax asset is now shown as £8.8 million was incorrectly shown as £7.5 million in the prior year Financial Statements. The adjustment does not impact any financial statement line items and is purely an error in a disclosure.

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 £15.0 million (2020: £11.6 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 2021 and 2020 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.

	2021 £'000	2020 £'000
Profit/(loss) for the year attributable to owners of the parent	**(15,012)**	(11,606)

	Number of shares	Number of shares
Weighted average number of Ordinary shares	**225,186,639**	178,149,352
Weighted average number of ESOT shares	**(113,259)**	(113,259)
Weighted average number of Ordinary shares – basic	**225,073,380**	178,036,093
Effect of potential dilutive share options	**–**	–
Adjusted weighted average number of Ordinary shares – diluted	**225,073,380**	178,036,093
Earnings/(loss) per share attributable to owners of the parent		
Basic and Diluted (pence per share)	**(6.67)**	(6.52)

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 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 EU BV	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 structure is in the process of being further rationalised.

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.

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. Its registered address is Joop Geesinkweg 701, Rembrandt Kantoor, 1114 AB, Amsterdam-Duivendrecht, The 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 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 2021

11 Intangible assets

	Goodwill £'000	Acquired intangible assets £'000	Intellectual property £'000	Product development £'000	Total £'000
Cost					
At 1 January 2020	2,207	1,216	970	1,322	5,715
Additions	–	–	77	–	77
Exchange movements	–	(1)	(7)	(42)	(50)
At 31 December 2020	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**
Accumulated amortisation and impairment					
At 1 January 2020	–	327	299	1,115	1,741
Charge for the year	–	140	58	84	282
Impairment	–	–	55	–	55
Exchange movements	–	(1)	(5)	(40)	(46)
At 31 December 2020	–	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**
Net book value					
At 31 December 2021	**2,207**	**639**	**684**	**43**	**3,573**
At 31 December 2020	2,207	749	633	121	3,710

The goodwill arose on the acquisition of the assets of Axela Inc. on 1 November 2017. It represents the highly knowledgeable, skilled and specialised workforce, cost savings and operating synergies expected to result from having a larger R&D base in North America, the ability to access new markets, the advantages of the combination of the Parsortix system and HyCEAD technologies enabling sample-to-answer tests, capturing more of the value chain and competitive differentiation.

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 2021 stood at £279.8 million, and which after taking into account any possible costs of disposal exceeds the carrying amount of the CGU by a considerable margin.

Acquired intangible assets also relates 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 but also some modest amounts for customer contracts and relationships and critical supplier contracts and relationships. Identifiable intangible assets are amortised over their expected useful economic life. Acquired IP includes a carrying value of £0.6 million (2020: £0.7 million) in relation to Technology IP and has a remaining amortisation period of five years and ten months (2020: six years and ten months).

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 £0.7 million at 31 December 2021 (2020: £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 2020	320	112	2,760	156	3,348
Additions	171	37	74	27	309
Disposals	–	(12)	(124)	–	(136)
Transfers (to)/from inventories	–	–	(56)	–	(56)
Exchange movements	(1)	(1)	(15)	(3)	(20)
At 31 December 2020	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**
Accumulated depreciation					
At 1 January 2020	143	66	1,521	110	1,840
Charge for the year	131	33	466	31	661
Disposals	–	(12)	(122)	–	(134)
Transfers (to)/from inventories	–	–	(83)	–	(83)
Exchange movements	–	(1)	(11)	(3)	(15)
At 31 December 2020	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**
Net book value					
At 31 December 2021	**418**	**86**	**1,621**	**47**	**2,172**
At 31 December 2020	216	50	868	42	1,176

Laboratory equipment includes a carrying value of £0.2 million (2020: £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.

Capital commitments at 31 December 2021 amounted to £0.1 million (2020: £0.5 million).

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 2021

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**	**2021** **£'000**	2020 £'000
At 1 January	**1,233**	1,514
Additions	**1,478**	281
Transfer (to)/from net investment in sublease (Note 16)	**(16)**	(136)
Depreciation	**(532)**	(385)
Impairment	**–**	(36)
Exchange movements	**41**	(5)
At 31 December	**2,204**	1,233

The carrying amounts of lease liabilities and the movements during the year are shown below:

Lease liabilities	**2021** **£'000**	2020 £'000
At 1 January	**1,362**	1,553
Additions	**1,478**	281
Rent paid and payable	**(702)**	(556)
Accretion of interest (Note 7)	**157**	92
Exchange movements	**43**	(8)
At 31 December	**2,338**	1,362

	2021 **£'000**	2020 £'000
Non-current lease liability	**1,816**	928
Current lease liability	**522**	434
	2,338	1,362

The Group had total cash outflows for leases of £0.7 million for the year (2020: £0.5 million).

The Group added three leases in the year in respect of Clinical Laboratories in the UK and the United States. Of these additions £1.3 million relates to a ten-year lease with an 8% interest rate implicit in the lease.

The Group has two lease contracts that include extension and/or termination options. The Directors exercise significant judgement in determining whether these extension and termination options are reasonably certain to be exercised and agreed that it was reasonable to assume that these lease contracts would be extended beyond the termination option/notice 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 and/or termination options is to increase both the carrying value of the right-of-use assets and the non-current lease liability at the reporting date by £0.7 million (2020: £0.8 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 £61,148 (2020: £56,025).

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 2021	**626**	**473**	**1,048**	**814**
31 December 2020	434	387	495	134

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 17), overdraft facilities and finance leases. 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:

	2021 £'000	2020 £'000
Total equity attributable to owners of the parent	**40,330**	34,344
Total assets	**47,315**	39,049
Equity ratio	**85.2%**	88.0%

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 2021

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 £31.8 million (2020: £28.6 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 large 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 £0.3 million (2020: £0.3 million).

Interest rate risk

There is currently no interest rate risk on financial assets and liabilities.

Cash at bank of £31.8 million earns interest at fixed rates of between 0.01% and 0.15% (2020: £12.1 million, between 0.03% and 0.75%). Short-term deposits were £nil at the reporting date (2020: £16.5 million at 0.85%).

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 (2020: £nil was less than 12 months). Contractual maturities in respect of lease obligations are disclosed in Note 13 on page 90.

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 5% variation in currency exchange rates on the profit/(loss) for the year is as follows:

	2021 USD £'000	**2021 CAD £'000**	2020 USD £'000	2020 CAD £'000
Profit/(loss) – 5% strengthening	**(168)**	**(157)**	(133)	(134)
Profit/(loss) – 5% weakening	**185**	**174**	143	148

Hedging

The Group did not hedge its financial transactions in 2021 or 2020.

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:

	2021					2020				
	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	**62**	**93**	**143**	**–**	**298**	148	10	143	4	305
Short-term deposits	**–**	**–**	**–**	**–**	**–**	16,538	–	–	–	16,538
Cash and cash equivalents	**30,962**	**347**	**409**	**121**	**31,839**	10,948	793	247	92	12,080
Total	**31,024**	**440**	**552**	**121**	**32,137**	27,634	803	390	96	28,923
Financial liabilities										
Lease liabilities – non-current	**592**	**1,192**	**–**	**32**	**1,816**	673	83	–	172	928
Lease liabilities – current	**191**	**175**	**–**	**156**	**522**	199	43	–	192	434
Trade and other payables	**1,911**	**473**	**217**	**383**	**2,984**	1,842	431	30	312	2,615
Total	**2,694**	**1,840**	**217**	**571**	**5,322**	2,714	557	30	676	3,977

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

	2021 £'000	2020 £'000
Raw materials and work in progress	**762**	36
Finished goods	**986**	706
Total	**1,748**	742

16 Trade and other receivables

	2021 £'000	2020 £'000
Amounts receivable within one year		
Trade receivables	**202**	187
Other receivables	**405**	594
Net investment in sublease (see below)	**55**	85
Prepayments and contract assets	**607**	577
Total	**1,269**	1,443

Other receivables comprises recoverable taxes (VAT and HST) and a Canadian COVID-19 relief subsidy (Canada Emergency Wage Subsidy). 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 2021

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:	**2021 £'000**	2020 £'000
Not past due	**176**	179
0 – 30 days past due	**12**	3
30 – 60 days past due	**1**	2
> 60 days past due	**13**	3
Total	**202**	187

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.

During the 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. In August 2021, the Group accepted the surrender of a sublease, which had been entered into in the prior year, for the remaining life of the lease which expires in April 2022.

Net investment in sublease	**2021 £'000**	2020 £'000
At 1 January	**85**	–
Transfer from right-of-use assets (Note 13)	**71**	136
Transfer to right-of-use assets (Note 13)	**(55)**	–
Rental income received and receivable	**(51)**	(58)
Accretion of interest	**4**	7
Exchange movements	**1**	–
At 31 December	**55**	85

17 Trade and other payables

	2021 £'000	2020 £'000
Amounts payable after one year		
Other taxes and social security costs	**257**	–
Total	**257**	–

	2021 £'000	2020 £'000
Amounts payable within one year		
Trade payables	**1,124**	1,088
Other taxes and social security costs	**1,010**	395
Other payables	**35**	27
Accruals and contract liabilities	**2,221**	1,833
Total	**4,390**	3,343

Other taxes and social security costs include a provision for employers' taxes on the theoretical gain on the exercise of unapproved share options and LTIP Options, within one year of £0.9 million (2020: £0.3 million) and after more than one year of £0.3 million (2020: £nil). 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 bonuses (Note 22). 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.

18 Share capital

The share capital of the Company is shown below:

	2021 £'000	2020 £'000
Allotted, called up and fully paid		
235,143,050 (2020: 215,405,178) Ordinary shares of £0.10 each	**23,514**	21,540

The Company has one class of Ordinary shares which carry no right to fixed income.

The Company issued 17,241,380 new Ordinary shares with a nominal value of £0.10 at an issue price of £1.16 per share in a placing of shares realising gross proceeds of £20.0 million. Associated costs of £1.1 million were incurred. Shares were admitted to trading on AIM in July 2021.

The Company issued 2,496,492 new Ordinary shares with a nominal value of £0.10 at exercise prices between £0.10 to £0.8625 per share as a result of the exercise of share options by employees realising gross proceeds of £0.9 million. Shares were admitted to trading on AIM at various dates across the year.

19 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 £1.3 million (2020: £0.3 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.

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". Options granted may have a service condition and/or a non-market performance condition and/or a market performance condition (such as a target share price). If the performance conditions are not met, the options do not vest and will lapse at the date specified at the time of grant. In exceptional circumstances the performance date may be extended. Options are forfeited if the employee leaves the Group before the awards vest 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 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.

EMI Share Option Scheme and Unapproved Share Option Schemes

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. Share options are granted under a service condition and/or a non-market performance condition and/or a market performance condition. Options generally cease to be exercisable after ten years from the date of grant.

The movement in the number of employee share options is set out below:

	2021 Number of share Options #	2021 Weighted average exercise price (£)	2020 Number of share Options #	2020 Weighted average exercise price (£)
Outstanding at 1 January	**17,844,140**	**0.5467**	12,895,806	0.5517
During the year:				
Granted	**5,792,500**	**1.2473**	5,195,000	0.5357
Exercised	**(2,496,492)**	**0.3718**	(25,000)	0.6450
Forfeited/lapsed	**(281,669)**	**0.5128**	(221,666)	0.5705
Outstanding at 31 December	**20,858,479**	**0.7626**	17,844,140	0.5467
Capable of being exercised at 31 December	**8,182,645**	**0.5078**	5,600,808	0.4562

The options outstanding at 31 December 2021 had a weighted average remaining contractual life of seven years and nil months (2020: six years and three months).

The Company uses a Trinomial option pricing model as the basis to determine the fair value of the Company's share options.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2021

19 Share-based payments continued

The following assumptions are used in the model to determine the fair value of share options at the respective date of grant that are still outstanding at 31 December 2021:

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
18 November 2011	0.7550	0.7550	40.00%	0.62%	2.5	Nil	(1)	1,197,315
5 November 2012	0.7550	0.3750	40.00%	0.23%	2.0	Nil	(1)	312,685
11 December 2013	0.7300	0.7300	40.00%	0.97%	3.0	Nil	(2)	290,000
10 November 2014	0.8625	0.8625	40.00%	1.03%	3.0	Nil	(3)	20,000
10 November 2014	0.8625	0.8625	40.00%	1.53%	5.0	Nil	(4)	1,500,000
31 March 2015	0.8625	0.7850	40.00%	0.67%	3.0	Nil	(3)	330,000
12 November 2015	0.1000	0.7550	40.00%	0.68%	2.0	Nil	(5)	46,980
1 March 2016	0.5650	0.5650	40.00%	0.42%	3.0	Nil	(3)	150,000
25 November 2016	0.6450	0.6450	40.00%	0.30%	3.0	Nil	(3)	675,000
25 November 2016	0.6450	0.6450	40.00%	0.30%	3.0	Nil	(6)	1,500,000
1 November 2017	0.4000	0.4000	40.00%	0.57%	3.0	Nil	(7)	500,000
1 November 2017	0.4000	0.4000	40.00%	0.57%	3.0	Nil	(3)	450,000
16 November 2017	0.4025	0.4025	40.00%	0.55%	3.0	Nil	(3)	100,000
20 August 2018	0.4900	0.4900	40.00%	0.77%	3.0	Nil	(3)	100,000
20 December 2018	0.3850	0.3850	40.00%	0.75%	3.0	Nil	(3)	1,038,333
20 December 2018	0.3850	0.3850	40.00%	0.75%	3.0	Nil	(8)	2,000,000
21 May 2020	0.6150	0.6150	61.40%	(0.04)%	3.0	Nil	(3)	350,000
25 September 2020	0.5300	0.5300	57.60%	(0.12)%	3.0	Nil	(3)	3,005,666
25 September 2020	0.5300	0.5300	57.60%	(0.12)%	3.0	Nil	(9)	1,500,000
4 January 2021	0.4825	0.4825	55.54%	(0.12)%	3.0	Nil	(3)	250,000
10 May 2021	1.1100	1.1100	59.11%	0.11%	3.0	Nil	(3)	100,000
12 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(10)	2,306,623
12 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(11)	2,635,877
15 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(10)	250,000
15 November 2021	1.2850	1.2850	59.55%	0.52%	3.0	Nil	(12)	250,000
Total								**20,858,479**

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) the performance conditions that (i) the Company's share price must have increased to £2.00 at some point since the date of grant (this condition has not yet been met) 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).
(2) Vesting is subject to a) specific performance conditions for senior management (performance conditions have been met in relation to 100,000 of 200,000 share options) and b) a service condition with options vesting over a three-year period (this condition has been met).
(3) Vesting is subject to a service condition with options vesting over a period up to three years.
(4) 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).
(5) 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.
(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 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.
(7) 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.

19 Share-based payments continued

(8) 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.
(9) Vesting is subject to a) the Company achieving FDA clearance for its Parsortix system, and b) to a performance condition that the Company's share price has risen to at least £0.916 on 25 September 2023.
(10) Vesting is subject to a service condition with options vesting at three years.
(11) 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.
(12) 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 15 November 2024 and a service condition with options vesting at three years.

Once all performance and/or service conditions have been met the employee becomes unconditionally entitled to the options and they are capable of exercise. Based on these performance and/or service conditions a number of options have vested and become capable of exercise. 2,496,492 options were exercised in the year (2020: 25,000).

Long-Term Incentive Plan

The Company has a Long-Term Incentive Plan (LTIP) for Executive Directors. Disclosures for an award made on 12 November 2021 and for a modification to the 20 December 2018 award made on 12 November 2021 are set out in the Directors' Remuneration Report on pages 62 to 64 and below.

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 model to determine the fair value of LTIP Options at the respective date of grant that are still outstanding at 31 December 2021:

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
20 December 2018	0.0000	0.3850	45.04%	0.88%	5.0	Nil	2.063	3,000,000
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								**12,000,000**

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 is unchanged and effectively means the share price target could be met at any point in the extended period.

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 2021:

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
12 November 2021	0.0000	1.2850	50.60%	0.47%	2.1	Nil	2.063	3,000,000
Total								**6,000,000**

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2021

20 ESOT shares

	2021 £'000	2020 £'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 2021 the Trust held 113,259 shares (2020: 113,259 shares). The market value of these shares at 31 December 2021 was £134,778 (2020: £54,081). Shares purchased by the ANGLE ESOT are used to assist in meeting the obligations under employee remuneration schemes.

21 Guarantees and other financial commitments

The Group has a number of retainers with professional advisors which can be terminated on short notice periods.

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 2021 of up to £1.2 million over one year (2020: £2.2 million).

The Group signed a new ten year lease (with a five year break) for additional laboratory and office space in the UK in December 2021, for occupation in 2022. Lease payments of £0.3 million are payable within one year, £1.4 million are payable in two to five years.

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 short-term deposit account of £700,000 as security for a Bacstel-IP facility used in the normal course of business.

22 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 62 to 64 and below, none of the Directors had any interest at any time during the year ended 31 December 2021 in the share capital of the Company or its subsidiaries.

At the reporting date, £193,979 of remuneration (2020: £144,282) was due to Andrew Newland and £123,441 of remuneration (2020: £91,816) was due to Ian Griffiths.

Brian Howlett entered into a consultancy contract with effect from 7 January 2013 to provide specialist commercial advice outside of his normal Board responsibilities. Consultancy fees of £nil were paid in the year to Brian Howlett under this contract (2020: £nil).

SoBold Limited provides digital marketing services and website management to ANGLE with fees in the year of £35,250 (2020: £37,700) and a balance of £3,000 (2020: £6,220) 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 Business Development Director, Michael O'Brien.

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 2021

	Note	2021 £'000	2020 £'000
Assets			
Non-current assets			
Investment in subsidiaries	C3	**6,537**	5,212
Other receivables	C4	**56,962**	42,689
Total non-current assets		**63,499**	47,901
Current assets			
Other receivables	C4	**3**	35
Short-term deposits		**-**	15,822
Cash and cash equivalents		**30,210**	10,760
Total current assets		**30,213**	26,617
Total assets		**93,712**	74,518
Current liabilities			
Trade and other payables	C5	**-**	(155)
Total current liabilities		**-**	(155)
Total liabilities		**-**	(155)
Net assets		**93,712**	74,363
Equity			
Share capital	C6	**23,514**	21,540
Share premium		**99,406**	81,532
Share-based payments reserve		**2,704**	1,722
Accumulated losses		**(31,912)**	(30,431)
Equity attributable to owners		**93,712**	74,363

The Company's loss and total comprehensive loss for the year to 31 December 2021 were £1.8 million (2020: £1.2 million).

The Financial Statements on pages 99 to 104 were approved by the Board of Directors and authorised for issue on 27 April 2022 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 2021

	2021 £'000	2020 £'000
Operating activities		
Profit/(loss) before tax	**(1,824)**	(1,159)
Adjustments for:		
Impairment of loans	**1,824**	1,159
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 subsidiaries	**(16,097)**	(9,762)
Transfer (to)/from short-term deposits	**15,822**	(814)
Net cash from/(used in) investing activities	**(275)**	(10,576)
Financing activities		
Net proceeds from issue of share capital – placing	**18,765**	18,627
Proceeds from issue of share capital – share option exercises	**925**	23
Net cash from/(used in) financing activities	**19,690**	18,650
Net increase/(decrease) in cash and cash equivalents	**19,450**	8,074
Cash and cash equivalents at 1 January	**10,760**	2,686
Cash and cash equivalents at 31 December	**30,210**	10,760
Cash and cash equivalents	**30,210**	10,760
Short-term deposits	**–**	15,822
Cash and cash equivalents and short-term deposits at 31 December	**30,210**	26,582

COMPANY STATEMENT OF CHANGES IN EQUITY

For the year ended 31 December 2021

	Equity attributable to owners				
	Share capital £'000	Share premium £'000	Share-based payments reserve £'000	Accumulated losses £'000	Total equity £'000
At 1 January 2020	**17,277**	**67,272**	**1,495**	**(29,313)**	**56,731**
For the year to 31 December 2020					
Profit/(loss) for the year				(1,159)	(1,159)
Issue of shares (net of costs)	4,263	14,260			18,523
Share-based payments			268		268
Released on exercise			(4)	4	–
Released on forfeiture			(37)	37	–
At 31 December 2020	**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 payments			1,325	–	1,325
Released on exercise			(295)	295	–
Released on forfeiture			(48)	48	–
At 31 December 2021	**23,514**	**99,406**	**2,704**	**(31,912)**	**93,712**

NOTES TO THE COMPANY FINANCIAL STATEMENTS

For the year ended 31 December 2021

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 2021. They have also been prepared in accordance with those parts of the Companies Act 2006 that apply to companies reporting under these 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 75 to 98.

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

Accounting for intercompany loans

In accordance with IFRS 9 Financial Instruments, the Company is required to make an assessment of expected credit losses. Having considered the increased quantum of the loans and the reduced probability of credit losses expected to arise across a number of scenarios, an additional adjustment for expected credit loss of £1.8 million (2020: £1.2 million) was recognised in the year.

The calculation of the allowance for lifetime expected credit losses requires a significant degree of estimation and judgement, in particular in determining the probability weighted likely outcome for each scenario considered to determine the expected credit loss in each scenario. Should the outcomes vary, this could have a significant impact on the carrying value of the intercompany loans in following 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 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 £1.8 million (2020: £1.2 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 62 to 64.

Administrative expenses, including auditors' remuneration, are borne by other Group companies and are not recharged to the Company.

C3 Investment in subsidiaries

	2021 £'000	2020 £'000
Cost		
At 1 January	**5,212**	4,476
Share-based payments charge	**1,325**	268
Additions	**–**	468
At 31 December	**6,537**	5,212

Details of the Company's subsidiary undertakings at 31 December 2021 are shown in Note 10 to the Consolidated Financial Statements along with other interests held indirectly through subsidiary undertakings.

Additions in the prior year represent a direct holding of 9.47% in ANGLE North America Inc. (a 100% owned Group company). This was incorrectly represented as a holding by ANGLE Technology LLC since its acquisition in October 2018. Whilst the Group has a contractual right to transfer the holding between Group companies this transfer had not been affected. The adjustment identified had not been treated as a prior period adjustment on the basis of materiality.

C4 Other receivables

	2021 £'000	2020 £'000
Amounts receivable after one year		
Amounts due from Group undertakings		
Cost		
At 1 January	**75,267**	65,973
Additions/(repayments)	**16,097**	9,294
At 31 December	**91,364**	75,267
Provision		
At 1 January	**32,578**	31,419
Impairment charge	**1,824**	1,159
At 31 December	**34,402**	32,578
Net book value		
At 31 December	**56,962**	42,689

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.

	2021 £'000	2020 £'000
Amounts receivable within one year		
Other receivables	**3**	35

Other receivables comprise share capital receivable at 31 December 2021 (2020: recoverable VAT).

C5 Trade and other payables

	2021 £'000	2020 £'000
Amounts payable within one year		
Trade payables	**-**	151
Accruals	**-**	4
Total	**-**	155

Trade and other payables relate to professional fees associated with the fundraise.

C6 Share capital

The share capital of the Company is shown below:

	2021 £'000	2020 £'000
Allotted, called up and fully paid		
235,143,050 (2020: 215,405,178) Ordinary shares of £0.10 each	**23,514**	21,540

Details of the Company's share capital and changes in its issued share capital can be found in Note 18 to the Consolidated Financial Statements on page 95.

Details of the Company's share options schemes can be found in Note 19 to the Consolidated Financial Statements on pages 95 to 97.

NOTES TO THE COMPANY FINANCIAL STATEMENTS CONTINUED

For the year ended 31 December 2021

C7 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.

The Company provides financial support to its subsidiaries. Details of the Group's financial commitments are given in Note 21 to the Consolidated Financial Statements on page 98.

C8 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 22 to the Consolidated Financial Statements on page 98.

NOTICE OF ANNUAL GENERAL MEETING

Directors:
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)

Registered Office
10 Nugent Road
Surrey Research Park
Guildford
GU2 7AF

26 May 2022

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 29 June 2022 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 2021.
2. **Resolution 2** to approve the Directors' Remuneration Report for the year ended 31 December 2021 set out on pages 62 to 64 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 re-appoint as a Director Mr I F Griffiths who is retiring by rotation in accordance with Article 91 of the Company's Articles of Association and who, being eligible, is offering himself for re-election.
5. **Resolution 5** to re-appoint as a Director Dr. J Groen who is retiring by rotation in accordance with Article 91 of the Company's Articles of Association and who, being eligible, is offering himself for re-election.
6. **Resolution 6** to re-appoint as a Director Mr B Howlett who is retiring by rotation in accordance with Article 91 of the Company's Articles of Association and who, being eligible, is offering himself for re-election.
7. **Resolution 7** to re-appoint as a Director Mr A D W Newland who is retiring by rotation in accordance with Article 91 of the Company's Articles of Association and who, being eligible, is offering himself for re-election.
8. **Resolution 8** to re-appoint as a Director Mr G R Selvey who is retiring by rotation in accordance with Article 91 of the Company's Articles of Association and who, being eligible, is offering himself for re-election.
9. **Resolution 9** to grant the Directors authority to allot unissued shares in the capital of the Company up to an aggregate nominal amount of £7,838,324.

   Note: the Directors wish to renew their authorisations with respect to the allotment of new shares.
10. **Resolution 10** 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, 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.
11. **Resolution 11** to grant the Directors authority to purchase issued shares in the capital of the Company up to an aggregate nominal amount of £2,351,497.

    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 9, 10 and 11 will expire at the 2023 Annual General Meeting or, if earlier, 30 June 2023.

NOTICE OF ANNUAL GENERAL MEETING CONTINUED

Meeting arrangements

The Meeting of the Company will be held at 2:00 pm on Wednesday 29 June 2022 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ. The Board is looking forward to once again welcoming shareholders to the Meeting in person. As has been the case in recent years, the Board is pleased to be able to continue to offer shareholders the opportunity to follow proceedings online via a live webcast (joining instructions are provided below). 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. The Company will continue to monitor the ongoing situation with regard to COVID-19 and any changes to the format of the Meeting including the ability for shareholders to attend in person, will be notified through a regulatory news service (RNS).

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. Shareholders are invited to submit questions in advance of the Meeting, which the Board will aim to answer during the business update presentation. While it may not be possible to answer individual questions, questions will be grouped into key themes and we will endeavour to answer these during the presentation or as part of concluding matters. Questions should be submitted to **investor@angleplc.com** before 5:00pm on 28 June 2022.

Details of how to join the Meeting and the business update presentation via an electronic platform are provided on page 110.

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 IS HEREBY GIVEN that the nineteenth **ANNUAL GENERAL MEETING** (the **"Meeting"**) of ANGLE plc (**"the Company"**) will be held at 2:00 pm on Wednesday 29 June 2022 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 9 will be proposed as ordinary resolutions and resolutions numbered 10 and 11 will be proposed as special resolutions. Please refer to the notes to this Notice for details of how to watch the meeting online.

Ordinary Business

1. **TO** receive the Accounts of the Company for the year ended 31 December 2021, and the reports of the Directors and auditors thereon.
2. **TO** approve the Directors' Remuneration Report as set out on pages 62 to 64 of the Annual Report for the year ended 31 December 2021. 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 accounts are laid and to authorise the Directors to determine their remuneration.
4. **TO** re-appoint Mr I F Griffiths as a Director who, in accordance with the Articles of Association, is retiring at the Annual General Meeting and, being eligible, offers himself for re-election.
5. **TO** re-appoint Dr. J Groen as a Director who, in accordance with the Articles of Association, is retiring at the Annual General Meeting and, being eligible, offers himself for re-election.
6. **TO** re-appoint Mr B Howlett as a Director who, in accordance with the Articles of Association, is retiring at the Annual General Meeting and, being eligible, offers himself for re-election.
7. **TO** re-appoint Mr A D W Newland as a Director who, in accordance with the Articles of Association, is retiring at the Annual General Meeting and, being eligible, offers himself for re-election.
8. **TO** re-appoint Mr G R Selvey as a Director who, in accordance with the Articles of Association, is retiring at the Annual General Meeting and, being eligible, offers himself for re-election.

Special Business

9. **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 £7,838,324 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 30 June 2023 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.
10. **THAT**, subject to and conditional upon the passing of Resolution 9, 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 9 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) above) up to an aggregate nominal amount of £2,351,497.

    and the authority hereby conferred shall expire (unless previously renewed, varied or revoked by the Company in general meeting) on 30 June 2023 or at the conclusion of the next Annual General Meeting of the Company (whichever first occurs) EXCEPT that the Company may, before such expiry, make an offer or agreement which would or might require equity securities to be allotted after such expiry and the Directors may allot equity securities in pursuance of such offer or agreement as if the authority conferred hereby had not expired.

NOTICE OF ANNUAL GENERAL MEETING CONTINUED

11. **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 of £0.10 each in the capital of the Company 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 23,514,972 (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 of the Company 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) on 30 June 2023 or at the conclusion of the next Annual General Meeting of the Company (whichever first occurs) 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

By Order of the Board

Ian F Griffiths
Company Secretary

Dated 26 May 2022

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 proxy need not be a member of the Company. 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. The Company will continue to monitor the ongoing situation with regard to COVID-19 and any changes to the format of the Meeting, including the ability for Shareholders to attend in person, will be notified through a regulatory news service (RNS).

2. To be valid, an appointment of proxy must be registered with or returned to the Company's Registrars 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 registrars, 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 registrars, 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; or

    • 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 27 June 2022. 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 registrars no later than at least 48 hours before the time of the Meeting or any adjourned meeting.

Explanatory Notes:

Resolution 1: Report and Financial statements
The Directors are required to present to the Meeting the audited accounts and the reports of the Directors and the auditors for the year ended 31 December 2021.

Resolution 2: Directors' Remuneration Report
This resolution seeks approval of the Directors' Remuneration Report for the year ended 31 December 2021. The full text of the Directors' Remuneration Report is contained on pages 62 to 64 of the Company's Annual Report.

This is an advisory vote and no entitlement to remuneration for the year ended 31 December 2021 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 accounts 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.

Resolution 4 to Resolution 8: Re-appointment of Directors
Under Article 91 of the Articles of Association of the Company, each Director shall retire from office and will be eligible for re-appointment at the third Annual General Meeting after the meeting at which he was last re-appointed. Mr I F Griffiths, Dr. J Groen, Mr B Howlett, Mr A D W Newland and Mr G R Selvey were last re-appointed as Directors at the 2019 Annual General Meeting and, as such, are required to retire at this Annual General Meeting and, being eligible, offer themselves for re-election.

Resolution 9: 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 30 June 2023 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 9 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 £7,838,324 representing approximately one-third of the Company's nominal value of the issued share capital at the date of this notice.

Resolution 10: 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.

If passed Resolution 10 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 £2,351,497, representing approximately 10% of the Company's nominal value of the issued share capital at the date of this notice. This is proposed as a special resolution.

Resolution 11: Authority for market purchase
Resolution 11 will permit the Company to purchase up to 23,514,972 Ordinary shares of £0.10 each (representing approximately 10% of the 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 30 June 2023 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 29 June 2022.

The venue
The Meeting will be held at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ.

Attending the Meeting
The Meeting will be held in person at 2:00 pm on Wednesday 29 June 2022 at the Holiday Inn Guildford, Egerton Road, Guildford, GU2 7XZ. As has been the case in recent years, the Board is pleased to be able to continue to offer shareholders the opportunity to follow proceedings online via a live webcast (joining instructions are provided below). 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.

The Company will continue to monitor the ongoing situation with regard to COVID-19 and any changes to the format of the Meeting, including the ability for Shareholders to attend in person, will be notified through a regulatory news service (RNS).

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.

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.

Viewing the Meeting
The Meeting will be made available online to enable Shareholders to follow proceedings and shareholders can view the Meeting remotely. The Company will provide a business update presentation after the formalities of the Meeting are concluded.

A live webcast of the Meeting may be accessed via **https://www.investormeetcompany.com/angle-plc/register-investor**. Details of how to follow proceedings online can also be accessed via ANGLE's Investor Centre page, **https://angleplc.com/investor-relations**. Please register in advance and log on to the webcast approximately five minutes before 2:00pm on Wednesday 29 June 2022.

The Board remains keen to encourage engagement with our Shareholders. Shareholders are invited to submit questions in advance of the Meeting, which the Board will aim to answer during the business update presentation. While it may not be possible to answer individual questions, questions will be grouped into key themes and we will endeavour to answer these during the presentation or as part of concluding matters. Questions should be submitted to **investor@angleplc.com** before 5:00pm on 28 June 2022.

EXPLANATION OF FREQUENTLY USED TERMS

Term	Explanation
Analyte	The substance that is to be used 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–
AUC-ROC	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. Source: University of Cambridge MRC Unit
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
Biopsy	Process by which cancer cells are removed from the tumour for analysis
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
Capture	Process for capturing target cells from sample
Capture efficiency	Proportion of target cells captured
Carcinogen	Any substance that is directly involved in causing cancer
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
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
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 EC 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

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
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
Companion diagnostic	A medical device which provides information that is essential for the safe and effective use of a corresponding drug or biological product
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
CTC	Circulating tumour cell
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 3-dimensional views of tissues and organs
Cultured cells	Cultured cells grown in the laboratory from human-derived cells used for experimental work
Cytokeratin	Cytokeratins are a family of intracytoplasmic cytoskeleton proteins with members showing tissue specific expression
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
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
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
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-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

Term	Explanation
EMT	Epithelial-mesenchymal transition
Epitope	A part of a molecule to which an antibody will bind
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
Flow-Thru Chip®	A disposable consumable containing a highly uniform porous substrate on which up to 576 individual zones are printed with reagents that specifically bind to molecules of interest in the sample. Sample flowing through the 10 micron pores is forced into contact with the coated surface, providing very rapid and efficient capture of any targets present in solution that each assay is designed to measure
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
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
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
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 allow molecular analysis
Harvest efficiency	Proportion of target cells harvested
Harvest purity	The number of target cells (such as CTCs) in the harvest as a proportion of the WBC. The minimum purity from which downstream analysis is possible is 0.5%. Analysis of one target cell therefore requires no more than 200 WBC be in the harvest
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. In recent years the protein has become an important biomarker and target of therapy for ~ 30% of 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

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
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 Ziplex
Immunohistochemistry	A lab 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-cassette labelling or in-situ labelling	CTC labelling for cell identification undertaken inside the separation system
Indolent cancer	A type of low risk cancer that grows slowly
In vitro diagnostic (IVD)	An in vitro diagnostic is a method of performing a diagnostic test outside of a living body in an artificial environment, usually a laboratory
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.
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
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
Medtech	Med Tech, 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 detect the expression of thousands of genes at the same 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

Term	Explanation
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
mRNA	Messenger RNA used to direct the synthesis of proteins
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
NICE	Abbreviation for the National Institute for Health and Care Excellence
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 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
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 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-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
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

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
Pharma	Pharmaceutical companies collectively as a sector of industry
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
Pilot study	The initial study examining a new method or treatment
Plasma	Pale-yellow liquid component of blood obtained following removal of cells
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^{+TM}	ANGLE's proprietary 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
Radiotherapy	The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumours
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 again
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	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)

Term	Explanation
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 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
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 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
Tissue	Tissue is a group of cells that have similar structure and that function together as a unit
Transcriptome (whole)	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
Triage	The process of determining the priority of patients' treatments based on the severity of their condition
Tumor/Tumour	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) Tumor is the American English spelling and Tumour is the standard English spelling
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

EXPLANATION OF FREQUENTLY USED TERMS CONTINUED

Term	Explanation
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
Ziplex®	An automated hybridization array platform that combines chemiluminescence and Flow-Thru Chips for the detection of minute amounts of up to 500 nucleic acid or protein targets simultaneously

Primary source: **www.cancer.gov/publications/dictionaries/cancer-terms**

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