

# Transforming cancer care

## Jefferies London Healthcare Conference

15-17 November 2022

Andrew Newland & Ian Griffiths



# Legal disclaimer

---

This presentation has been prepared by ANGLE plc (the “Company”). By attending this presentation and/or reviewing the slides you agree to be bound by the following conditions.

The presentation slides which follow this notice and the oral presentation of which it forms part (together, the “Materials”) are personal to the recipient and have been prepared and issued by or on behalf of the Company. For the purposes of the remainder of this notice, the term Materials shall include the presentation, the question-and-answer session that follows the presentation, hard or electronic copies of this document and any other materials distributed at, or in connection with, the presentation. The recipient agrees to return all Materials held by it in relation to this presentation upon the Company’s request.

The information and opinions contained in this presentation have not been independently verified, are provided as at the date hereof and are subject to amendment, revision and completion without notice. No person is under any obligation to update or keep current the information contained in this presentation. No representation, warranty or undertaking, express or implied, is made by the Company, its advisers or representatives, or their respective officers, employees or agents as to, and no reliance should be placed on, the fairness, accuracy, completeness, correctness or reasonableness of the information or the opinions contained herein. The Company, its advisers or representatives, or their respective officers, employees and agents expressly disclaim any and all liability which may be based on this presentation and any errors therein or omissions therefrom.

This presentation does not constitute or form any part of, and should not be construed as, an offer to sell, or an invitation or solicitation or recommendation to purchase, or subscribe for or underwrite or otherwise acquire any securities in the Company in any jurisdiction and does not constitute or form part of a prospectus. No part of this presentation should form the basis of, or be relied on in connection with, or act as any inducement to enter into, any contract or commitment or investment decision whatsoever. The Company’s nominated adviser, Joh. Berenberg, Gossler & Co. KG (London branch) (“Berenberg”) has not approved this document for the purposes of section 21 of the Financial Services and Markets Act 2000 (“FSMA”) and accordingly it is a communication made only to persons who (a) fall within one or more of the exemptions from section 21 of FSMA contained in articles 19 and 49 of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (which includes persons who are authorised or exempt persons within the meaning of FSMA, certain other investment professionals, high net worth companies, unincorporated associations or partnerships and the trustees of high value trusts) and persons who are otherwise permitted by law to receive it and (b) are an “eligible counterparty” within the meaning of Article 24(2), (3) and (4) of Directive 2004/39/EC (“MiFID”) as implemented into national law of the relevant EEA state (together, the “Relevant Persons”). Any investment or investment activity to which this document relates is only available to the Relevant Persons. Persons of any other description, including those who do not have professional experience in matters relating to investments, should not rely on this document or act on its contents for any purpose whatsoever and should return it to Berenberg immediately.

This presentation should not be considered as the giving of investment advice by the Company or any of its shareholders, directors, officers, agents, employees or advisers. Each party to whom this document is made available must make its own independent assessment of the Company after making such investigations and taking such advice as may be deemed necessary. If you are in any doubt in relation to these matters, you should consult your stockbroker, bank manager, solicitor, accountant, taxation adviser or other independent financial adviser (where applicable, as authorised under FSMA).

This presentation contains certain statements that are neither reported financial results nor other historical information. These statements include information with respect to the Company’s financial condition, its results of operations and businesses, strategy, plans and objectives. Words such as “anticipates”, “expects”, “should”, “intends”, “plans”, “believes”, “outlook”, “seeks”, “estimates”, “targets”, “may”, “will”, “continue”, “project” and similar expressions, as well as statements in the future tense, identify forward-looking statements. These forward-looking statements are not guarantees of the Company’s future performance and are subject to assumptions, risks and uncertainties that could cause actual future results to differ materially from those expressed in or implied by such forward-looking statements. No statement in the Materials is intended to be nor may it be construed as a profit forecast. Many of these assumptions, risks and uncertainties relate to factors that are beyond the Company’s ability to control or estimate precisely and include, but are not limited to, the general economic climate and market conditions, as well as specific factors including the success of the Company’s and its subsidiaries’ (the “Group”) research and development and commercialisation strategies, the uncertainties related to regulatory clearance and the acceptance of the Group’s products by customers.

For further details regarding these and other assumptions, risks and uncertainties that may affect the Group, please read the Directors’ Report section including the “Principal risks and uncertainties” in the most recent Annual Report & Financial Statements of the Company. In addition, new factors emerge from time to time and the Company cannot assess the potential impact of any such factor on its activities or the extent to which any factor, or combination of factors, may cause actual future results to differ materially from those contained in any forward-looking statement. Except as may be required by law or regulation, the Company undertakes no obligation to update any of its forward-looking statements, which speak only as of the date of this document.

# ANGLE – Transforming cancer care

## National Cancer Institute United States:

An estimated 40% of men and women will be diagnosed with cancer during their lifetime

## Our Mission:

Enable personalized cancer care with a simple blood test to guide treatment, improving patient outcomes and reducing healthcare expenditure

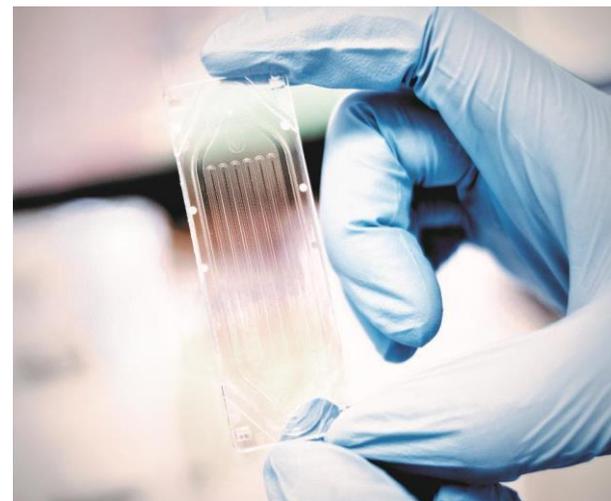
## Our Solution:

The Parsortix system

- **first and only FDA cleared product** for harvesting CTCs for subsequent analysis
- ANGLE believes it provides the **best sample** of a patient's cancer from a liquid biopsy
- enables effective, affordable, repeat testing of intact cells



Parsortix® instrument



Parsortix® cassette

# FDA clearance recognized as the gold standard

**First ever FDA clearance** for a device to harvest cancer cells from blood for subsequent analysis

- **enabling platform** for end users to develop clinical applications
- ahead of known competition with over six years of clinical development already completed
- initial focus on metastatic breast cancer with plan to extend into other cancer types

## INTENDED USE

The Parsortix<sup>®</sup> PCI system is an in vitro diagnostic device intended to enrich circulating tumor cells (CTCs) from peripheral blood collected in K<sub>2</sub>EDTA tubes from patients diagnosed with metastatic breast cancer. The system employs a microfluidic chamber (a Parsortix cell separation cassette) to capture cells of a certain size and deformability from the population of cells present in blood. The cells retained in the cassette are harvested by the Parsortix PCI system for use in subsequent downstream assays.

The end user is responsible for the validation of any downstream assay. The standalone device, as indicated, does not identify, enumerate or characterize CTCs and cannot be used to make any diagnostic/prognostic claims for CTCs, including monitoring indications or as an aid in any disease management and/or treatment decisions.

# Parsortix system could address flaws in standard of care



- **NCCN Guidelines recommend biopsies for all metastatic breast cancer patients (MBC)**
  - tissue biopsies from the primary tumor are out-of-date
  - up-to-date information is needed to select treatment for personalized care
  - only samples a single metastatic site at one time point
- **But half of all MBC patients do not have successful biopsies**
  - too ill for the surgery, tumor inaccessible and insufficient tissue
- There is a **critical need for an alternative approach** to guide care for these patients



**Dr Julie Lang**  
Cleveland Clinic Cancer Center

“In my team's research, we have demonstrated how **CTCs harvested by this system are a good surrogate for tissue biopsies of the metastatic site.** With this regulatory clearance we can now obtain repeat biopsies periodically to provide **up-to-date information to guide treatment decisions.**”

# Parsortix<sup>®</sup> system patent protected worldwide



- Stepped, microscale cell separators for fluid flow and cell separation
- Manufactured under ISO 13485:2016 quality control
- **Scalable business with third party manufacture**
- 26 granted patents: United States, Europe, China, Australia, Canada, Japan, Mexico with patent coverage to 2034
- Proprietary technology with copyright on software and designs, technical know-how, manufacturing and operating procedures, methods and processes

# Total addressable market > US \$100 billion p.a.



## All cancer liquid biopsy emerging multi-US\$ billion market: estimates

Cowen <sup>1</sup>	\$30-130 billion per annum
Frost & Sullivan <sup>2</sup>	>\$100 billion per annum
Guardant Health <sup>3</sup>	>\$80 billion per annum
Illumina (GRAIL) <sup>4</sup>	\$75 billion per annum
Bank of America <sup>5</sup>	\$45-70 billion per annum

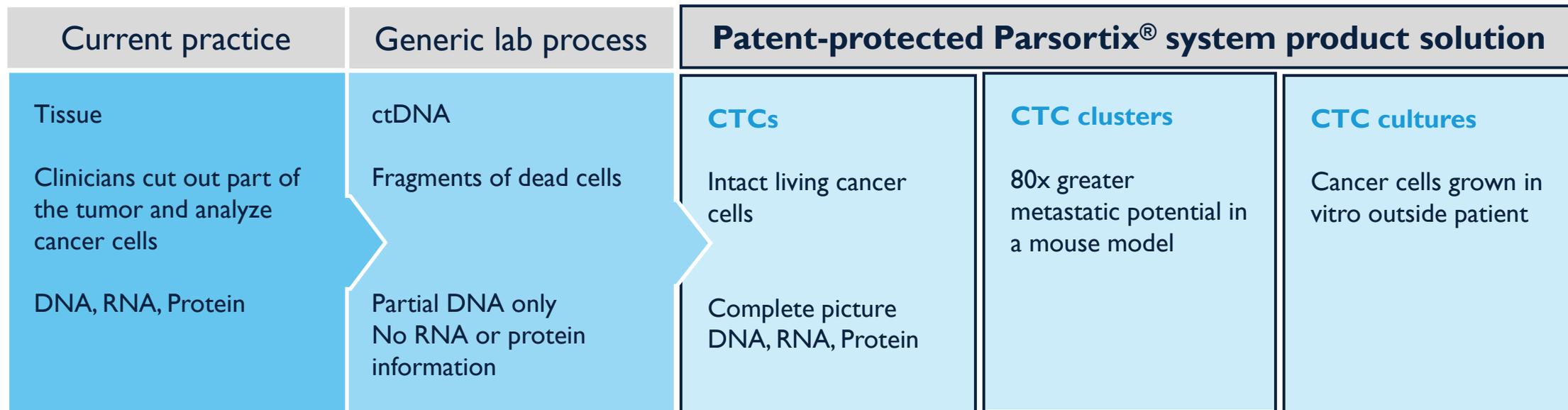


“The Parsortix system has a unique combination of features making it suitable for **routine clinical analysis** of patient blood samples.”

**Ged Brady**

Cancer Research UK Manchester Institute

# CTCs provide the complete picture for repeat biopsies



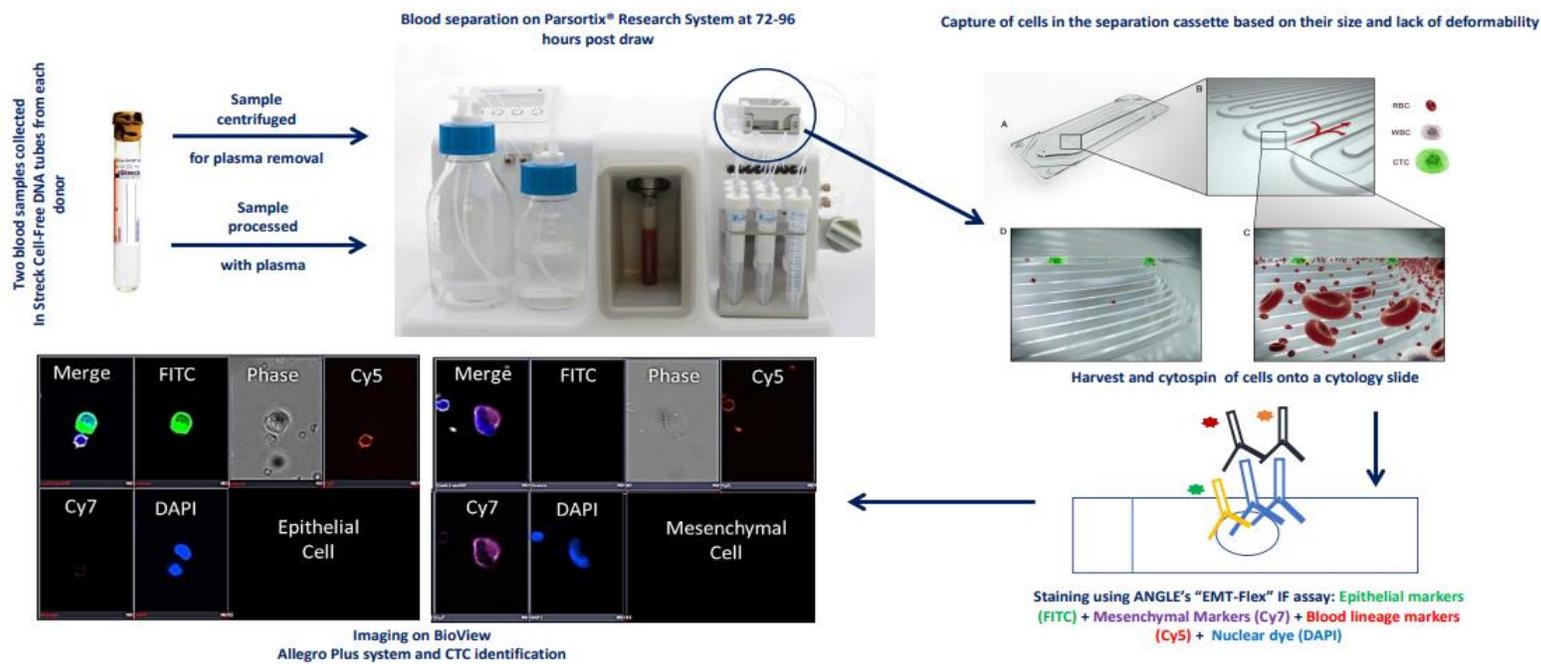
**Prof. Evi Lianidou**

Head of the Molecular Diagnostics Laboratory, National and Kapodistrian University of Athens

“**CTCs**, as living cells that are active in the metastatic process, can provide **prospective insight into a patient’s cancer**. In comparison, **ctDNA** derived mainly from dead and dying cells, provides important but **historical** information on patient disease. The genetic and phenotypic diversity observed in CTCs most likely mirrors that of the patient’s tumour and is reflective of cell evolution under treatment induced selective pressure.”

# CTCs and ctDNA analysis with a single blood draw

- **Poster presented at International Society for Liquid Biopsy Congress, Miami, October 2022**
- **No cancer cell / CTC loss** when pre-processing blood samples by centrifugation and plasma removal before Parsortix separation
- Workflow opens up possibility for clinical laboratories to **broaden the potential clinical utility of their assays, whilst limiting the overall blood requirement**



C	w Plasma	w/o Plasma
N	13	13
≥1 CTC (%)	39%	39%
CTC Range (in positive donors)	4-36	4-36
CTC mean (in positive donors)	17	14
CTC median (in positive donors)	13	10
Donor with ≥1 CTC Cluster (%)	39%	31%
N Cluster per donor (positive donors)	1-7	2-4
Range CTC per cluster	2-13	2-13

# Growing body of evidence Leveraged R&D strategy identifying new applications



- Translational research market **\$50 million p.a.**
- FDA clearance expected to help Parsortix become the CTC **system of choice**
- Installed base of **over 260** Parsortix systems in active use

## Parsortix samples processed

Current – >155,000 to 30 June 2022



Cumulative samples processed at 31 December



# Multi-pronged commercialisation strategy

## Business areas

- **Pharma services** clinical trials business and potential for CDx fully funded business model
- **Medtech partnership** seeking deals with downstream analysis companies to leverage sales channels and fund commercialisation
- **Product business** expanding existing research sales to clinical labs, setting up distributors to broaden sales effort

## Key commercialisation drivers

- **Regulatory clearance** FDA and CE mark in place
- **Clinical studies** run in real world conditions showing value of system, such as ovarian cancer study
- **Clinical laboratories** act as accelerators and demonstrators
- **Product development** to provide end-to-end solutions such as Pap staining
- **Reimbursement codes** with high priority to secure a code for Parsortix separation

# Differentiated pharma services offering

- **Customer base established and growing**
  - four customers secured to date, repeat business with two early customers
  - numerous others in discussion
  - anticipated to be the first significant revenue generator for ANGLE
- **Significant revenue and profitability potential**
  - each contract can be over US\$1 million
  - margins over 75%
  - each customer can offer numerous repeat contracts
  - only a small number of large-scale pharma customer relationships opens up a very large market
- **Assay development capability**
  - offers pharma bespoke services not possible otherwise
  - targeting the protein of action of the drug
  - cannot be achieved with ctDNA
  - longitudinal monitoring not possible with tissue biopsy
- **CRO out-source growth potential**



Memorial Sloan Kettering  
Cancer Center

## Howard I. Scher, MD Medical Oncologist

Head of the Biomarker Development Program; D. Wayne  
Calloway Chair in Urologic Oncology Prostate Cancer

Dr Scher identifies the presence or absence of CTCs as being the best biomarker to assess the effectiveness of a treatment. This **enables the early determination of whether a drug is efficacious for a particular patient** and might **speed up clinical trials and greatly reduce pharma costs**

<https://ascopost.com/videos/2019-genitourinary-cancers-symposium/howard-scher-on-circulating-tumor-cells-as-a-surrogate-endpoint-for-survival/>



# Pharma services – multi-US\$bn growth opportunity in multiple cancers



	Targeted cancer treatment			
Cancer type:	Breast cancer	Prostate cancer	Ovarian cancer	NSCLC
ANGLE supporting data:	26 publications 2 clinical trials	11 publications 2 planned clinical trials	3 publications 2 clinical trials	14 publications
Active industry sponsored trials: <i>Clinicaltrials.gov</i>	950 studies in c.247,000 patients	471 studies in c.100,000 patients	398 studies in c.72,000 patients	1,037 studies in c.215,000 patients
Actionable biomarkers:	BRCA1/2 HER2 ER PR CDK4/6 mTOR PIK3CA PD-L1 MSI MMR TMB NTRK	BRCA1/2 ATM CHEK2 PALB2 FANCA RAD51D CDK12 MSI MMR	BRCA1/2 MSI MMR TMB NTRK	ALK BRAF EGFR KRAS NTRK RET ROSI MET PD-L1 HER2
TAM:	>\$1.0bn	>\$410m	>\$260m	>\$850m

# FDA product clearance provides first mover advantage



## Post FDA clearance momentum

- **Enhanced** engagement post FDA with discussions initiated with two medtech companies, more than twenty biopharma companies and one Government body
- Outbound engagement increased with **direct marketing**
- Provides a strong indicator of potential future demand for commercial contracts
- Potential to become **the de facto industry standard** for the “best sample”
- Seeking to enable the entire industry



**Professor Dr. Naoto T. Ueno**  
MD Anderson Cancer Center

“Liquid biopsy to collect circulating live cancer cells is an **essential tool**. We anticipate that the Parsortix FDA clearance may help to develop novel biomarkers, therapeutic approaches and contribute to selecting the best treatment for metastatic breast cancer patients.”



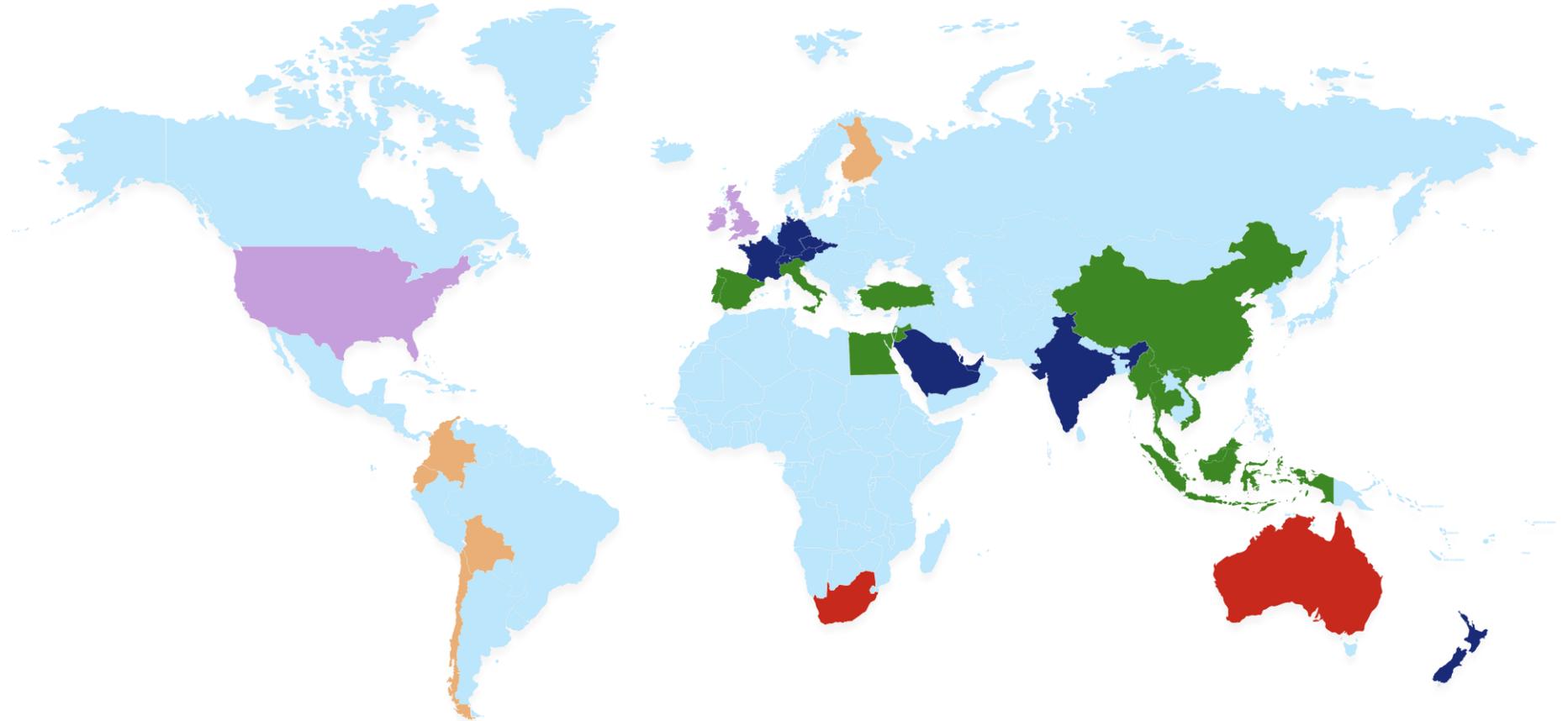
**Professor James M. Reuben**  
MD Anderson Cancer Center

“We look forward to the further development of CTC based assays that may bring **enormous benefits to patients with MBC as well as other cancers in the future.**”

# Sales and distribution network being established



- **Direct sales team** being expanded in United States and UK
- **Distribution partners** selected for other key territories based on:
  - local knowledge and language
  - exposure to oncology markets
  - compliance with quality systems
  - technical expertise and service capability



- Direct Salesforce
- Distributor Agreements in Place
- Active Discussion Ongoing
- Early Engagement
- Under Investigation

# Real world clinical validity study

## Ovarian cancer – *positive headline results*



“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

- **Excellent results in ovarian cancer with ROC-AUC 95.4%** based on molecular analysis of Parsortix harvest
- **Sensitivity 90%, Specificity 93%** maintaining best in class performance
- **50% or greater reduction in false positives** and false negatives
- **Strong clinical validation** in this difficult to diagnose setting
  - demonstrating ability to undertake complex molecular analysis of the Parsortix harvest
  - confirming its suitability for use in both hospital laboratories and central laboratories requiring sample shipping
- **Finalising detailed plans** for commercialisation of Parsortix Landscape<sup>+</sup> molecular assays

# Real world clinical validity study Prostate cancer in collaboration with Solaris Health



## Agreement signed with MidLantic Urology

- MidLantic Urology, affiliate of Solaris Health Partners
- >500 providers across 179 locations in 9 States with 729,000 patients p.a.
- Solaris Health to provide first route to market
- US TAM for clinical tests c. **US\$6.8 billion p.a.**



## Study design

- 100 patients scheduled to undergo prostate tissue biopsy
- Study will be conducted at 3 study sites in Pennsylvania over 9-month period
- Test to predict presence of clinically significant prostate cancer
- Headline results anticipated late 2023

“Preliminary data suggests that we may be able to create an **assay for the detection of clinically significant prostate cancer that has high specificity and sensitivity**. Moreover, the assay can be customized to operate in a wide spectrum of prostate cancer disease states, including pre-prostate biopsy, after a negative biopsy, active surveillance, after local failure, and in early and late metastatic disease states.”

**Dr Jose Moreno**, Principal Investigator, MidLantic Urology

# Products under development to drive adoption

---

- **Pap staining solution**
- **Portrait<sup>+</sup>** IF stained cells for epithelial, EMTing and mesenchymal cell identification
- **Portrait<sup>+</sup> PD-LI** assessing PD-LI status key target for immunotherapy
- **Portrait<sup>+</sup> DNA damage** assessing DNA damage on cells with application in drug trials for PARP inhibitors (assay development funded by customer)
- **Landscape<sup>+</sup> NGS** multiple collaborative projects in progress with aim of developing DNA and RNA targeted gene panels for molecular evaluation on CTCs



# ANGLE positioned for commercial growth

---

- FDA clearance a **major breakthrough** bringing global recognition
- **First mover advantage** in a very large market with high barriers to entry
- **ANGLE now in position to capitalise** with multiple corporate partnerships with leading medtech and pharma companies in discussion
- **First large-scale pharma services contract secured** and repeat business won
- **Multiple potential catalysts over next 12 - 18 months**



ANGLE

## **ANGLE plc**

ANGLE Europe Ltd  
10 Nugent Road  
Surrey Research Park  
Guildford GU2 7AF  
United Kingdom

ANGLE North America Inc  
5100 Campus Drive  
Suite 120  
Plymouth Meeting  
PA 19462  
USA

ANGLE Biosciences Inc  
50 Ronson Drive, Suite 105  
Toronto  
Ontario M9W 1B3  
Canada

[www.angleplc.com](http://www.angleplc.com)



# Additional information



ANGLE

# ANGLE – in numbers

- **8+ years** focused on development of the Parsortix system
- **May 2022** FDA product clearance
- **26** granted patents in all major markets with coverage to 2034
- **3** extensive patent families being progressed worldwide
- **70+** KOL peer-reviewed publications from **33+** cancer centers
- **230+** instruments in active use with **140,000+** samples processed
- **2** clinical labs (UK and US) recently established with **4** pharma customers already secured

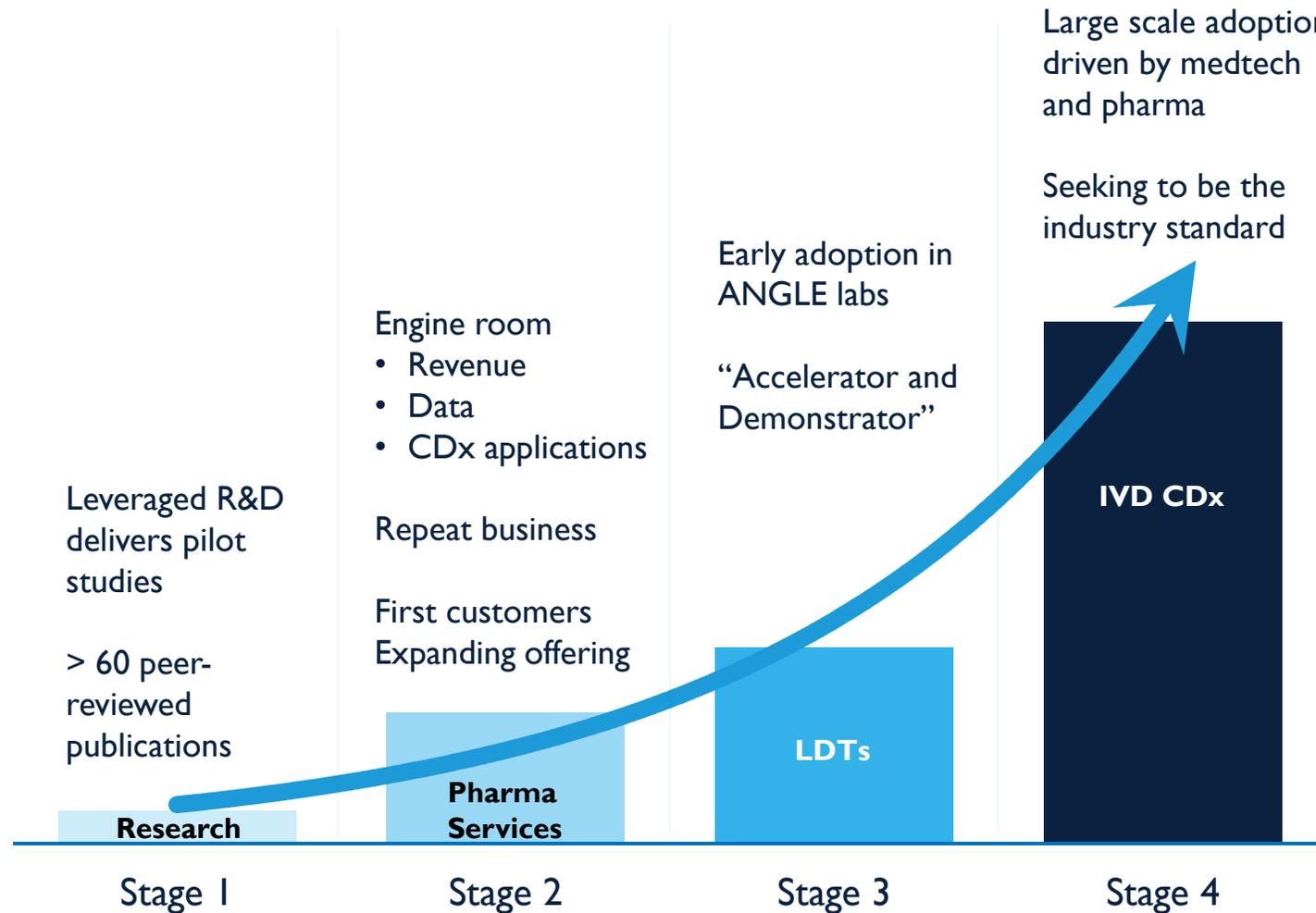


UK clinical services laboratory



US clinical services laboratory

# Targeting large-scale pharma, medtech and clinical laboratories to drive adoption world-wide

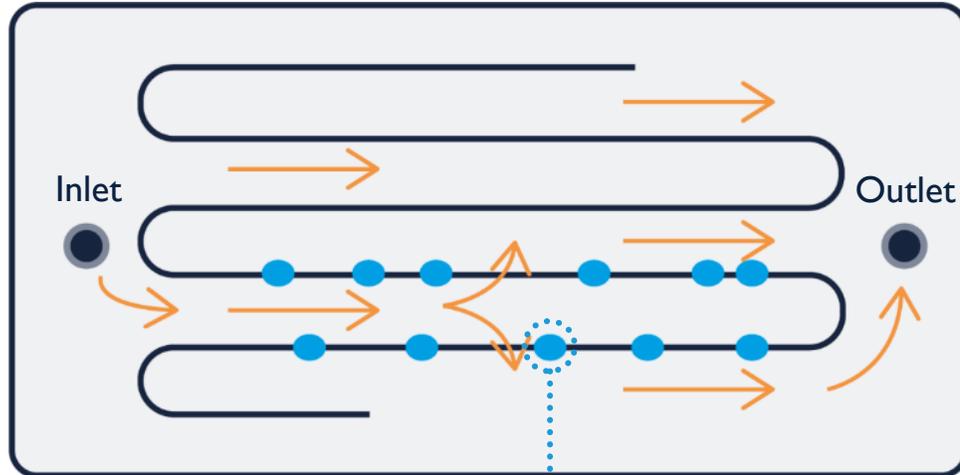


## Stages of Commercialization

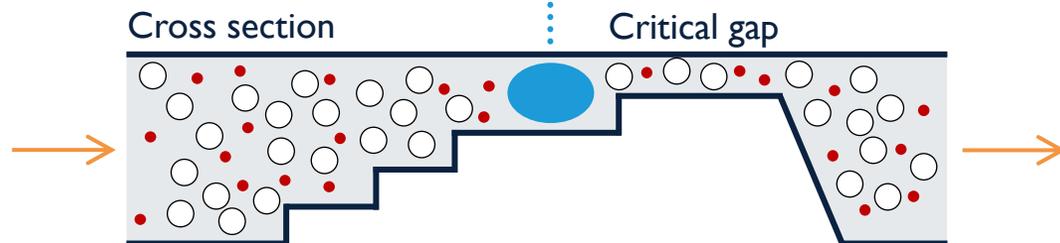
- **Stage 1:** Achieved
- **Stage 2:** Established and building
- **Stage 3:** Being established
- **Stage 4:** Developments driven by:
  - Stage 2 Pharma services
  - Stage 3 LDTs
  - Medtech partnership deals

# Parsortix system: capturing and harvesting living cancer cells

Plan view



**Patented multifold  
and separation step**



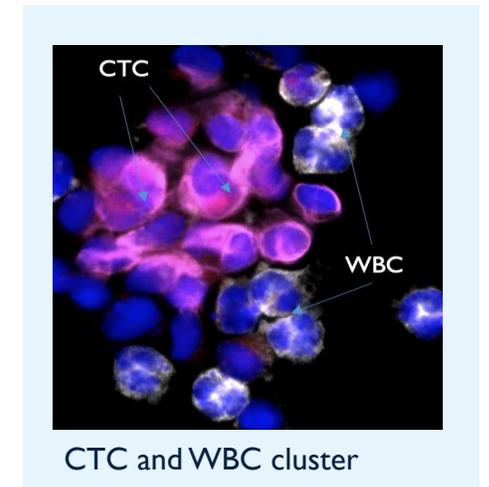
## Platform technology

The Parsortix system harvests **cancer cells from blood** based on their larger size and lack of deformability.

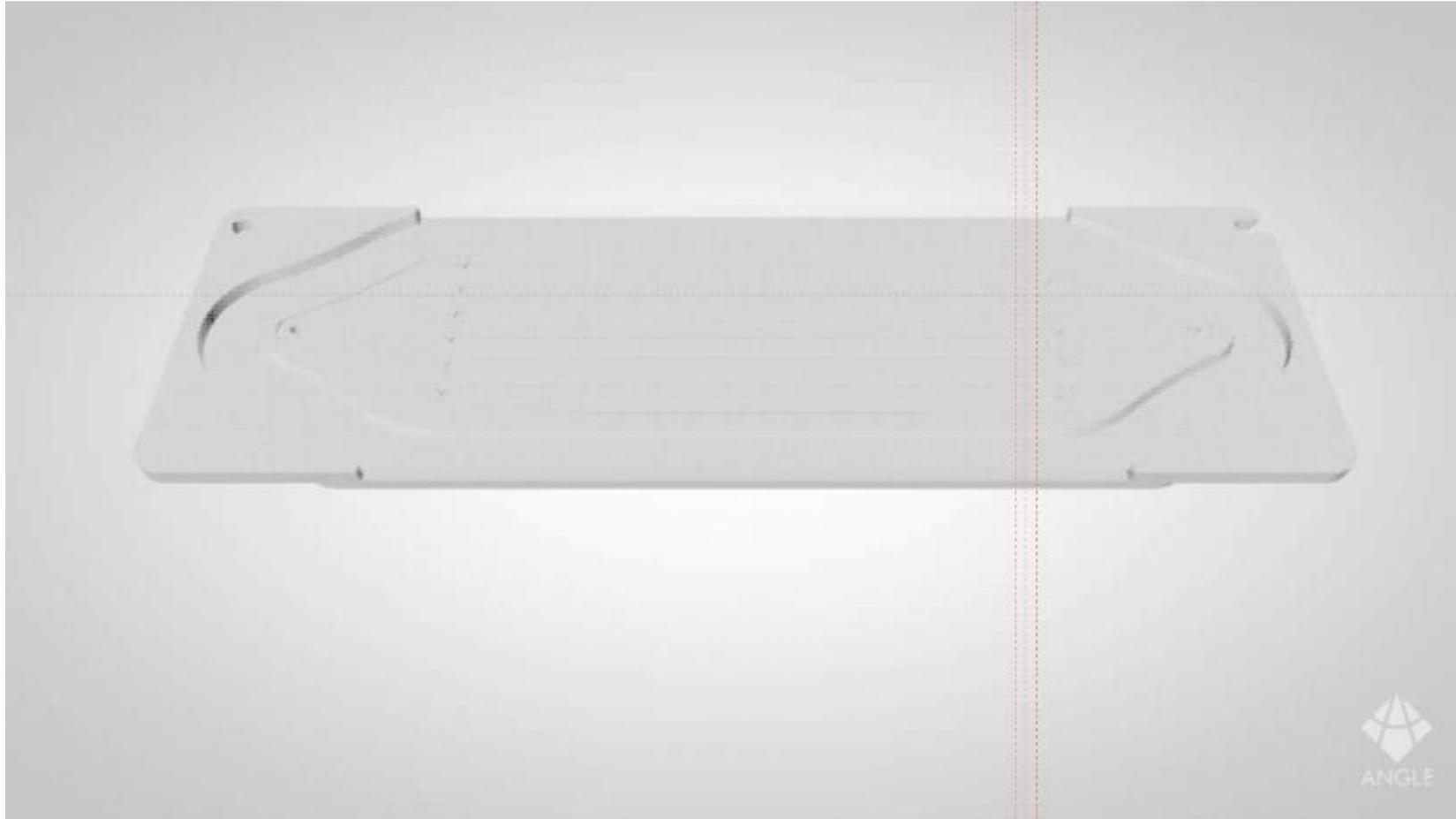
Other cells can be captured:

- **white blood cells** associated with the tumor microenvironment
- **megakaryocytes** (frequency may relate to cancer)
- **fetal cells** from maternal blood

- Captured CTCs
- White blood cells
- Red blood cells
- Blood flow

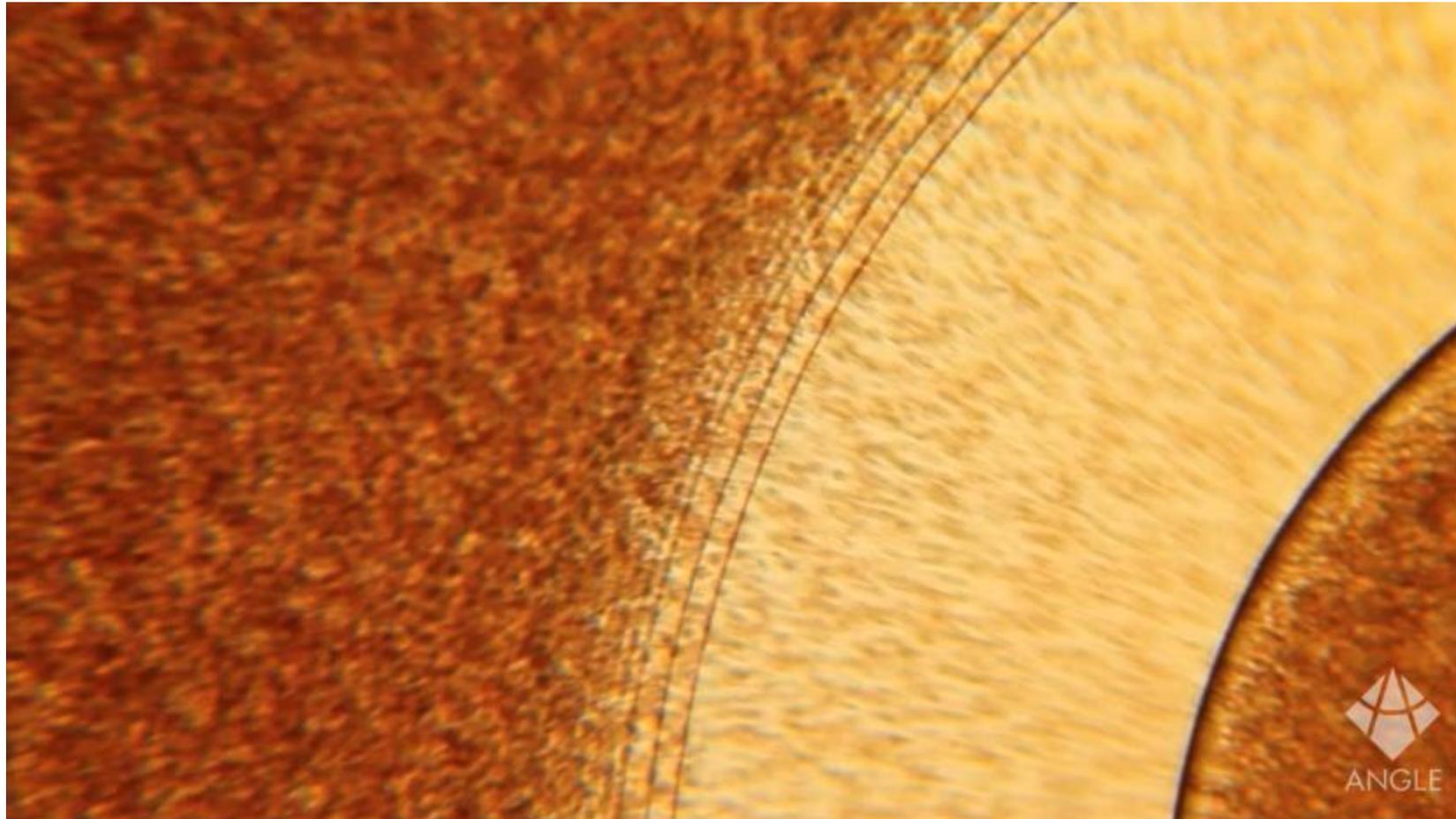


# Animation showing operation of Parsortix cassette



<https://www.youtube.com/watch?v=MJNkr8Ik2Nw>

# Patient blood flowing in Parsortix cassette



<https://www.youtube.com/watch?v=6mLcVloJ4Zk&t=6s>

# Benefits of Parsortix system CTC solution

Liquid biopsy denotes analysis of cancer material obtained from blood as opposed to tissue

Source	Solid tissue biopsy		Liquid biopsy	
	Primary tumor	Metastatic site	CTCs <sup>1</sup>	ctDNA <sup>2</sup>
Sample type	Intact cells	Intact cells	Intact cells	Fragmented DNA
Procedure	Invasive	Invasive	Non-invasive <sup>3</sup>	Non-invasive <sup>3</sup>
Sample accessibility	Not always accessible	Less accessible	<b>Accessible using Parsortix<sup>4</sup></b>	Accessible
Tumor 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 <sup>5</sup>	Difficult	Very difficult	Easy	Easy
Molecular analysis	DNA	Yes	Yes	Yes
	RNA	Yes	Yes	Difficult
	Protein	Yes	Yes	No
Live cells	Cell culture	Yes	Yes	No
	Xenograft	Yes	Yes	No
Standard of care	Proven	Proven	AR-V7 adopted in Prostate Cancer	Adopted for targeted treatment selection

1. CTCs (circulating tumor cells) are live cancer cells circulating in blood
2. ctDNA is cell-free circulating tumor fragments of DNA from dead cells, which may be found in the plasma component of blood
3. Tissue 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

# Parsortix - key competitive differentiation

Technology	Product Name	Company Name	Simple process	Low cost	Captures many types of cancer cells	Captures mesenchymal CTCs involved in metastasis	Easily harvests cells for downstream analysis	Harvest suitable for multiple downstream analyses	Cell viability (alive)	CTC Clusters	FDA approved	Product	Serviced lab
Microfluidic Step	Parsortix	ANGLE plc	✓	✓	✓	✓	✓	✓	✓	✓✓	✓	✓	✓
Antibody-based (capture)	CellSearch (only FDA authorised system)	Menarini	✗	✗	✓	✗	✗	✗	✗	✓	✓	✓	✗
	AdnaTest	QIAGEN											
	Target Selector	Biocept											
	TellDx	TellBio	✓✗	✗	✓✗	✓✗	✓✗	✓✗	✓✗	✓✗	✗	✓✗	✓✗
	CellCollector	GILUPI											
	IsoFlux	Fluxion Biosciences											
Antibody-based (identification)	LungLB	LungLifeAI	✓	✓	✗	✓	✓	✗	✗	✗	✗	✗	✓
Antibody-based (imaging)	Comprehensive Cancer Profiling	Epic Sciences	✓✗	✗	✗	✓	✗	✓	✗	✓	✗	✓✗	✓✗
	RareCyte Platform	RareCyte											
Membrane-based	ISET	Rarecells Diagnostics											
	CellSieve	Creatv MicroTech Inc	✓	✓	✓✗	✓	✓✗	✓	✓✗	✓	✗	✓	✗
	ScreenCell	ScreenCell											
Field flow fractionation	ClearCell FX1 System	Biolidics	✗	✓	✗	✓	✓	✓	✓	✓	✗	✓	✗

# NIH recognises proteome as critical for the future of precision medicine

- Cancer genome atlas has transformed the development of targeted treatment, however many patients who are matched to therapy based on their DNA do not respond. For example, only 13-36% of head and neck cancer patients respond to the EGFR inhibitor, Erbitux, despite genetic testing
- **Key information about the biology of the tumor is missing from looking at the genome alone.** The effect of mutations on the cell can only be understood fully by looking at protein expression; the proteome
- National Cancer Institute has invested heavily in programmes for the development of protein biomarkers to inform treatment and improve outcomes
- **“Understanding proteins is critically important when developing drugs, selecting treatments, and predicting treatment response. Integration of proteomic information is the next step in precision oncology”** *National Cancer Institute, 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.

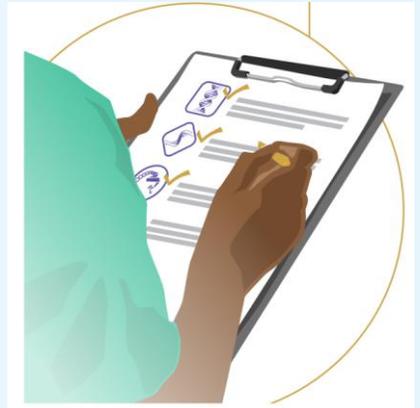
### Proteome

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.

**THE  
COMPLETE  
PICTURE**



Source: National Cancer Institute 2022 Annual Plan and Budget Proposal

# CTC clusters: breakthrough research using Parsortix system



- Dissociation of CTC clusters in mouse model **reduced metastatic spread of disease by 80x**
- CTC clusters **incorporate MDSCs** (immune suppressor cells) to avoid immune system
- Repeat testing with Parsortix system may enable a **new approach to cancer treatment**



**ETH** zürich

“CTC clusters are extraordinarily important mediators of breast cancer metastasis. The Parsortix state-of-the-art technology platform has played a key role in enabling us to isolate CTC clusters for investigation. We are now working on proof-of-concept clinical studies using Parsortix as a companion diagnostic.”

Dr Nicola Aceto, Associate Professor of Molecular Oncology at the Swiss Federal Institute of Technology (ETH) Zurich formerly University Hospital Basel, Switzerland



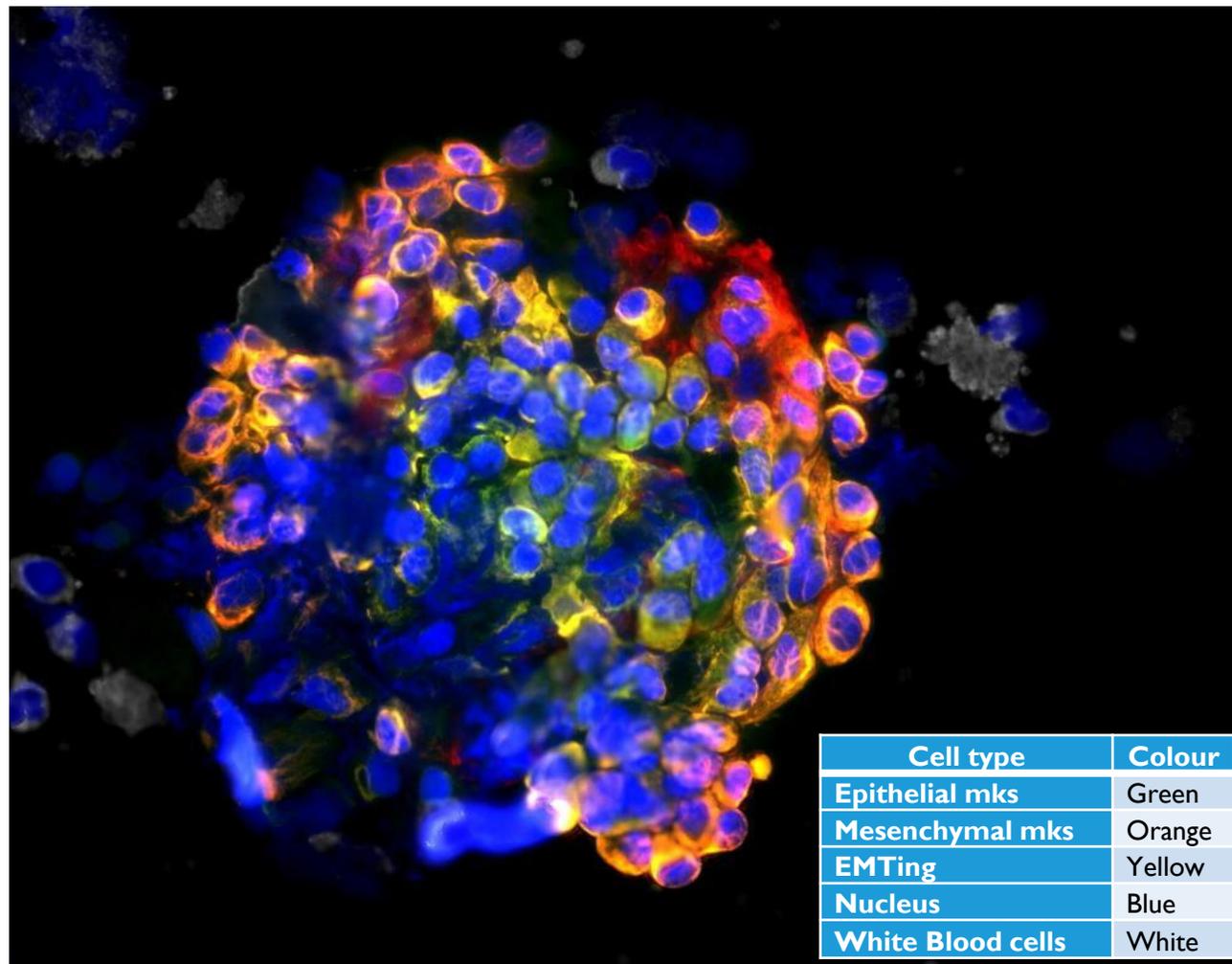
HOUSTON  
**Methodist**  
LEADING MEDICINE

“This opens up a whole new area of research with the prospect of stabilizing cancer progression to reduce its spread or metastasis. The Parsortix system state-of-the-art technology platform played a key role in enabling us to directly capture/isolate heterotypic CTC clusters from patients’ blood for downstream interrogation.”

Professor Dario Marchetti at the Biomarker Research Program, Houston Methodist Research Institute, Houston

# Circulating Tumor Cell (CTC) clusters

- Large CTC cluster of c.90 cells harvested from the peripheral blood of a metastatic breast cancer patient using ANGLE's Parsortix system
- Cluster comprises epithelial, mesenchymal and EMTing CTCs as well as white blood cells on the periphery
- Clusters are known to be 80x more metastatic than individual CTCs
- ANGLE's Parsortix system is the only CTC system demonstrated as being able to recover large scale CTC clusters for analysis

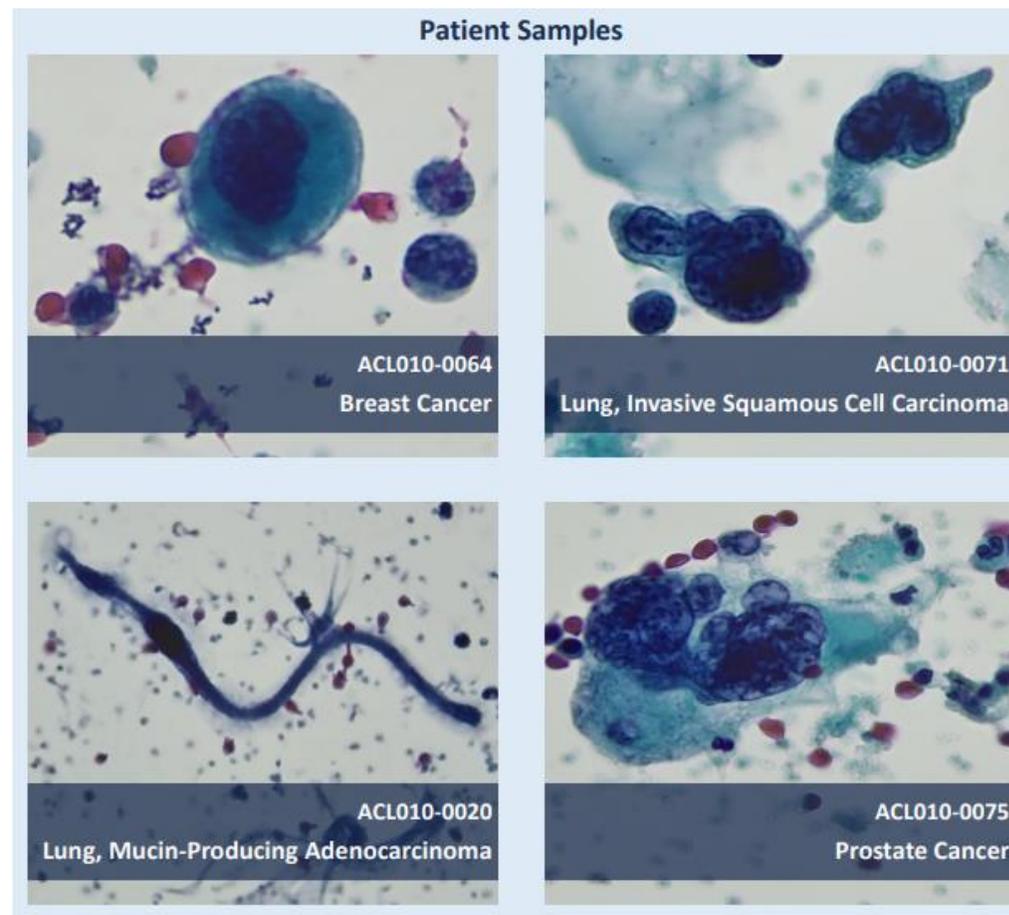


Sources: see <https://angleplc.com/library/publications/>

1. International Journal of Molecular Sciences, April 2019
2. Nature, February 2019
3. Cell, January 2019
4. British Journal of Cancer, August 2018

# Pap stain assay

- Simple, low cost CTC test designed to fit into existing pathology workflows
- **Utilises Pap staining process widely used for cervical smears**
- Test based on expertise of qualified cyto-technologist fast tracks potential use in clinical laboratories
- Presented at the 100th American Society for Clinical Pathology meeting and nominated as a finalist for a prestigious 'Blue Ribbon' Laboratory Management award
- Simple method to assess presence of cancer cells



# Uniformly positive results from key opinion leaders



MANCHESTER  
INSTITUTE



Universitätsklinikum  
Hamburg-Eppendorf

Barts  
Cancer Institute



- **Capture efficiency comparable to CellSearch when using spiked samples best suited for their system**
- Does not rely on antibody capture
- Applicable to a wide range of CTCs including mesenchymal CTCs
- Very high purity of harvested CTC's enabling molecular analysis

- **Effective for both epithelial and mesenchymal cells**
- CTC clusters can be captured as well as tumor cells
- Harvested cells are easily accessible and ready for molecular analysis
- Straight-forward to use with minimal user intervention

- **30x purer than a leading antibody-based system**
- Works well with prostate cancer
- Captures a high purity of CTCs
- CTC harvest well suited for downstream molecular analysis

- **Captured CTCs in twice as many patients as would be expected with CellSearch**
- High CTC capture in colorectal cancer
- Flexibility to handle varying blood sample volumes

- **Parsortix system results “sensational”**
- “Unprecedented sensitivity and specificity” in ovarian cancer
- Strong basis for clinical application in ovarian cancer

# First medtech collaboration under development with Abbott for HER-2 FISH application

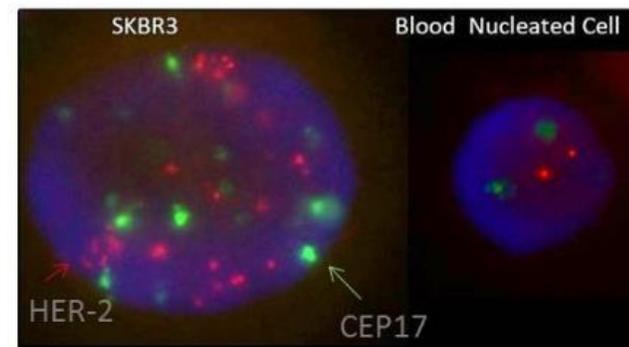


“Abbott is pleased to collaborate with ANGLE in this important evaluation of PathVysion in liquid biopsy specimens. The PathVysion HER-2 DNA FISH Probe kit is reliable and accurate in tissue biopsy samples and the Parsortix system may unlock the potential for PathVysion use in a simple blood test.”

**Kathryn B Becker, PhD**

Director, Licensing and Acquisitions

- Abbott is the **global leader for FISH testing** in solid tissue biopsies
  - FISH HER-2 to determine whether a patient should receive Herceptin (Trastuzumab)
  - about 1 in 5 breast cancer patients have a positive HER-2 result
  - HER-2 test market estimated to grow to c.\$627 million p.a. by 2031 (CAGR 6.5%)<sup>1</sup>
  - a patient’s HER-2 status **can change** and there is a need to assess HER-2 status at later points when a tissue biopsy is not feasible
- 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



SKBR3 cells enriched by the Parsortix system and hybridized using PathVysion HER-2 DNA Probe Kit

ANGLE's internal data

1. HER2 Breast Cancer Test Market Trends, 2021-2031. <https://www.transparencymarketresearch.com/her2-breast-cancer-test-market.html>

# Clinical management of MBC using the FDA cleared Parsortix system



USC Norris Comprehensive  
Cancer Center

“Successful validation of our approach in future clinical studies could **revolutionize clinical management of metastatic breast cancer and advance the promise of personalized cancer therapies**, ultimately positively changing the outcome for patients with metastatic disease.”

## Professor Julie E. Lang, MD, FACS

Chief, Breast Surgery and Co-Leader, Cleveland Clinic Breast Cancer Program  
Lerner Research Institute, formerly Norris Comprehensive Cancer Center,  
University of Southern California

## FDA clearance granted for metastatic breast cancer

‘Circulating Tumor Cell Transcriptomics as Biopsy Surrogates in Metastatic Breast Cancer’ published January 2022

- study first of its kind to directly compare molecular analysis of matched patient samples from an invasive metastatic tissue biopsy with Parsortix-harvested cells from a blood sample
- analysis using RNA-seq
- **high degree of concordance between CTCs** isolated using the Parsortix system **and metastatic tissue samples in clinically actionable genes**
- demonstrated how the Parsortix system could be utilized as a non-invasive, repeatable liquid biopsy to provide real time insight into MBC disease biology to inform targeted treatment selection

# US Ovarian cancer clinical tests c.US\$1.3 billion p.a.

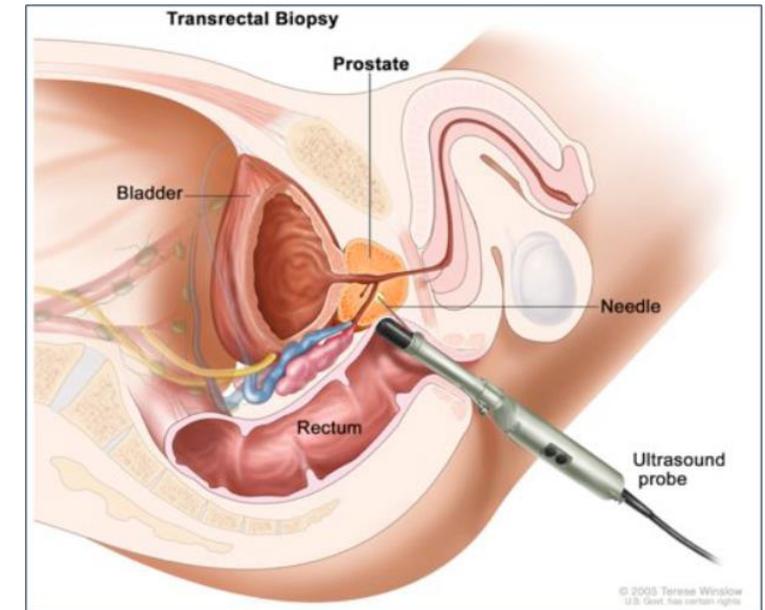
- 500,000 p.a. diagnosed with abnormal pelvic mass, c.200,000 surgery with c.20,000 ovarian cancer
- **Critical unmet medical need** to ensure suspected ovarian cancer patients referred to specialist
- Remission monitoring for 234,000 cancer survivors with **85% risk of recurrence**

Application	Reimbursement potential (US\$)	Number of patients p.a.	Number of tests per patient p.a.	Addressable market p.a.
1. Pelvic mass surgery triage	\$1,000	200,000	1	\$0.2bn
2. Watchful wait	\$1,000	300,000	2	\$0.6bn
3. Remission monitoring	\$1,000	234,000	2	\$0.5bn
		<b>734,000</b>		<b>\$1.3bn</b>

# Prostate cancer LDT – clinical studies initiated to address major unmet need



- **1 in 8 men will be diagnosed with prostate cancer**
  - in the United States alone, estimated 270,000 new cases (2022) and 3.2 million (2019) men living with prostate cancer
- **1 million prostate biopsies undertaken each year in United States**
  - despite advances in imaging, a tissue biopsy is required to establish diagnosis
  - 75% of biopsies are negative so unnecessary but miss 30%-40% of cancer cases
  - 25% of tissue biopsies diagnose prostate cancer (60% indolent, 40% aggressive)
- **Procedure has high incidence of complications**
  - 98% some side effects, 32% moderate and 1.4% major complications
  - post-biopsy sepsis occurs in 2-5% of cases with up to 25% of these admitted to ICU



*Liquid biopsy offers a unique opportunity to triage men with elevated PSA avoiding the need for invasive core tissue biopsy for the 90% of patients with benign or indolent disease*

# Non-invasive prostate biopsy

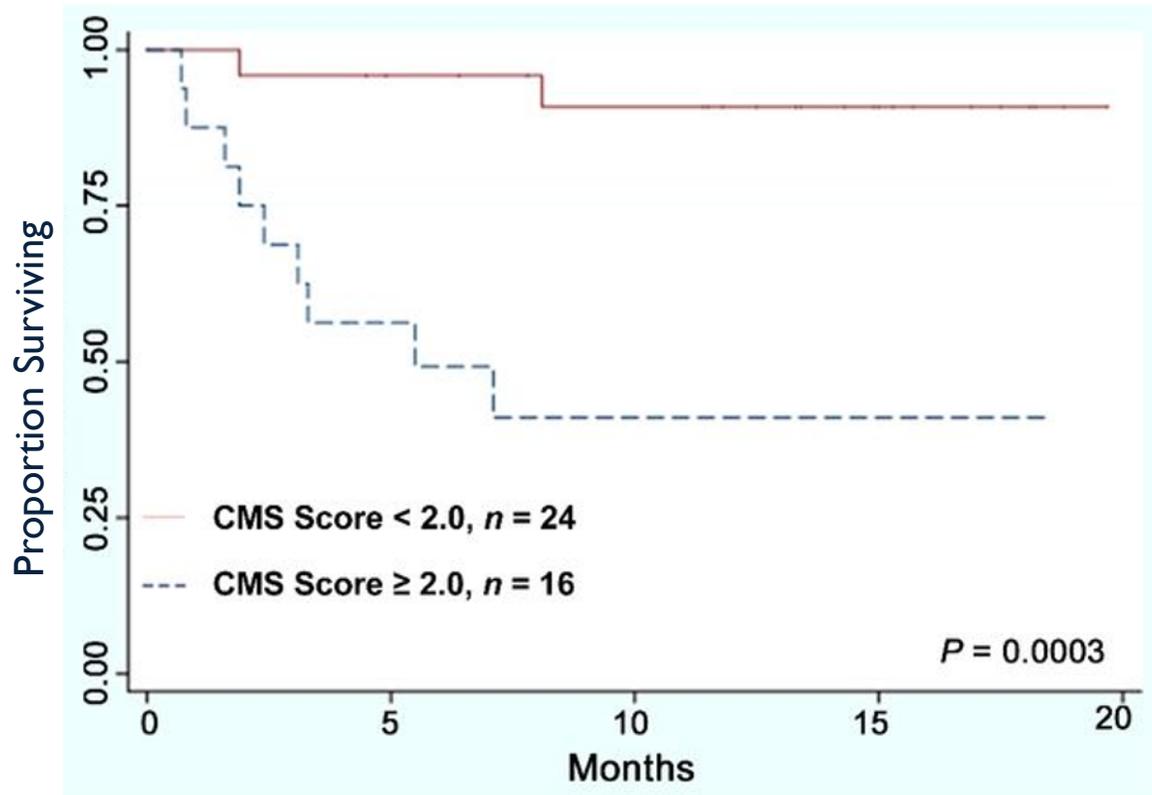


“The Parsortix system has shown the potential to **detect more severe cancer cases** thereby providing information which may enable clinicians to provide **different treatment for their patients**, potentially extending lives of those battling with cancer.”

**Professor Yong-Jie Lu, MBBS, MD, PhD**  
Molecular Oncology group leader at Barts Cancer Institute

- Barts Cancer Institute pilot studies
  - **CTC score plus PSA predicts clinically significant prostate cancer**
  - mesenchymal CTCs correlated with disease burden, tumor aggressiveness, and poorer survival
- **Simple blood test ahead of a standard tissue biopsy test to reduce unnecessary tissue biopsies**
  - **detect presence of prostate cancer**
  - **assess aggressiveness of disease**
  - patient risk stratification – differentiate between active surveillance (indolent) or intervention (aggressive)
- Blood cell discovery: cells identified as megakaryocytes linked to patient survival (40 patient study)
  - **option for worldwide exclusive licence over megakaryocyte IP**

# Prostate cancer aggressiveness – the key question



- Kaplan-Meier curve: 40 patient study
- **Patients classified as high risk using the Parsortix system 10x more likely to die than those classified as low risk**

**Source:**

Xu, L., et al. "The Novel Association of Circulating Tumor Cells and Circulating Megakaryocytes with Prostate Cancer Prognosis." *Clinical Cancer Research: an Official Journal of the American Association for Cancer Research* 23.17 (2017): 5112-5122.

# US prostate cancer clinical tests c.US\$6.8 billion p.a.

- 11 million men have a PSA test in the US each year – c.1.2 million will have an abnormal result
- Remission monitoring for c.2 million cancer survivors with **24%-48% risk of recurrence**

Application	Reimbursement potential (US\$)	Number of patients p.a. (US)	Number of tests per patient p.a.	Addressable market p.a.
1. High risk screening	\$1,000	1,220,000	1	\$1.2bn
2. Active surveillance	\$1,000	731,000	2	\$1.5bn
3. Therapeutic decision making	\$1,500	520,000	4	\$3.1bn
4. Residual disease monitoring	\$500	1,995,000	1	\$1.0bn
		<b>4,466,000</b>		<b>\$6.8bn</b>

# Growing burden of cancer in the United States

Selected solid tumor cancers (*Tested with Parsortix system = 89%)	Incidence	Mortality	Cancer survivors	Risk of Recurrence <sup>1</sup>
Breast*	287,850	43,250	3,771,795	30%
Lung*	236,740	130,180	576,924	27%
Prostate*	268,490	34,500	3,253,416	24-48%
Colorectum*	151,030	52,580	1,369,004	17%
Melanoma*	99,780	7,650	1,361,282	15-87%
Bladder*	81,180	17,100	712,644	50%
Kidney*	79,000	13,920	599,072	13-49%
Uterus*	65,950	12,550	822,388	13%
Pancreas*	62,210	49,830	89,248	36-46%
Oral Cavity and Pharynx	54,000	11,230	410,376	17-22%
Thyroid*	43,800	2,230	915,664	8-30%
Liver*	41,260	30,520	100,476	65%
Multiple myeloma*	34,470	12,640	159,787	100%
Stomach*	26,380	11,090	123,920	61%
Brain & CNS*	25,050	18,280	176,566	up to 100%
Ovary*	19,880	12,810	233,565	85%
Oesophagus*	20,640	16,410	49,084	50%
Cervix uteri*	14,100	4,280	295,381	35%
Small Intestine	11,790	1,960	75,828	17%
Testis*	9,910	460	283,792	13-50%
Anus	9,940	1,670	74,752	17%
Bone*	3,910	2,100	58,612	30-80%
<b>Total (All Cancers)</b>	<b>1,918,030</b>	<b>609,360</b>	<b>16,627,948</b>	

Source: National Cancer Institute – Cancer Stat Facts 1. Taken from published literature not limited to the US

- In 2022 an estimated 1.9 million new cases of cancer will be diagnosed. This is predicted to increase to 3 million per year by 2040
- Cancer is one of the leading causes of death. An estimated 609,000 people will die from cancer in 2022, corresponding to more than 1,600 deaths per day
- In 2019, there were an estimated 16.6 million cancer survivors, projected to increase to 26.1 million by 2040
- The AACR estimates that cancer care costs will exceed US\$245 billion by 2030

# Financial Results for six months ended 30 June 2022

	Six months ended 30 June 2022	Six months ended 30 June 2021
	£'000	£'000
<b>Statement of Comprehensive Income</b>		
Revenue	419	296
Cost of sales	(160)	(77)
Gross profit	259	219
Operating costs (net of grant income)	(10,625)	(8,881)
Tax credit and net finance costs	1,145	979
Loss for the period	(9,221)	(7,683)

	30 June 2022	31 December 2021
	£'000	£'000
<b>Statement of Financial Position</b>		
Trade and other receivables and R&D tax credit	7,715	5,779
Inventories	1,734	1,748
Cash	20,497	31,839
Property, plant and equipment and right-of-use assets	8,266	4,376
Intangible assets	3,590	3,573
<b>Total assets</b>	<b>41,802</b>	<b>47,315</b>

## Comments

- Revenue increased by 42%
- Gross margin at 62%
- Planned expenditure of £10.6 million
- Cash position of £20.5 million
- R&D tax credit due of £4.5 million
- Fundraise of £18.9 million (net) July 2022

# Board



**Non-executive Chairman  
Garth Selvey**

BSc in Physics and Electronic Engineering.  
36 years computer industry.  
Comino Group plc



**Chief Executive  
Andrew Newland**

MA Engineering from Cambridge, Chartered Accountant.  
Over 30 years building technology-based businesses;  
Over 20 years specialist medtech;  
12 years liquid biopsy



**Finance Director  
Ian Griffiths**

BSc Mathematics with Management Applications and Chartered Accountant.  
Technology commercialisation  
Over 30 years new technology based businesses;  
12 years liquid biopsy



**Non-executive director  
Jan Groen**

CEO Intravacc BV  
formerly CEO Novogenix, CEO MDxHealth, a genomic diagnostics company in prostate and bladder cancers.  
Previously President Agendia, co-founder of ViroClinics and DxOrange.  
Management positions at Quest Diagnostics, and Akzo-Nobel.  
PhD Medical Microbiology, BSc in Clinical Laboratory Studies



**Non-executive director  
Brian Howlett**

Lombard Medical Technologies PLC.  
Boston Scientific Ltd.  
Cobe Laboratories Inc.  
20 years pharmaceuticals  
Fisons plc

# Senior management 1/2



**Associate Commercial Director**  
**Ghada Abuali**

Ghada Abuali PhD in Cancer Research and MBA from Imperial College. Previously managed OEM sales in EMEA at QIAGEN, exceeding personal sales targets and responsible for a \$25 million budget. 5 years of commercial and business development experience was preceded by 10 years molecular diagnostic and postdoctoral experience.



**Head of R&D**  
**Anne-Sophie Pailhes-Jimenez**

Anne-Sophie has over 13 years of experience in cell biology and cancer research in the biotech and biopharma space. Previously, she worked at a biopharmaceutical company developing cancer immunotherapy solutions and as a senior scientist at the Gustave Roussy Institute in Paris, France where she gained a wealth of experience in oncology cellular biology.



**Head of Clinical Laboratories**  
**Madeline I. Repollet**

Madeline I. Repollet, PhD, has more than 30 years of clinical laboratory experience. Previously Head of Clinical Lab Operations and Services for Menarini Silicon Biosystems and Associate Director, Lab Operations for Janssen Dx, Madeline has managed clinical lab operations in the US and Europe and holds a B.S. in Biology, an M.S in QA/RA and a PhD in Health Care Administration.



**Director Manufacturing and Regulatory**  
**Martin Cooke**

Martin Cooke MEng degree in Electrical and Electronic Engineering. Chartered Engineer. 30 years product development/manufacturing experience. 8 years experience in liquid biopsy, medical device quality and regulatory systems. Previously global telecommunications responsible for product development and market introductions



**Clinical Studies Director**  
**Craig Miller**

Craig Miller BSc Biochemistry. Formerly VP Clinical Development Saladax Biomedical, Inc and Janssen R&D oncology biomarkers. Immunicon then Veridex (CellSearch) from 2001 to 2013 overseeing key clinical studies

# Senior management 2/2



**Vice President  
Commercial Operations  
Nick Claxton**

Nick Claxton has more than 35 years in the diagnostic and biotech industry. A biochemist within the NHS before joining the commercial world. Previous director roles in Becton Dickinson, Roche, LGC & Olympus as well as startups Epistem Genedrive and CCO at Premaitha.



**Business Development  
Director  
Michael O'Brien**

Michael O'Brien MA Engineering from Cambridge. MBA specialising in technology commercialisation. Sales and business development translational research. Previously environmental and cleantech development. 8 years in strategy and operations and work with Diageo on manufacturing and technology.



**Senior Group Leader –  
Product and Technology  
Development  
Stefan Peter**

Stefan holds a PhD in cell biology and proteomics from Sheffield University and a diploma in biotechnology. With expertise in biology and engineering he interlinks device development and biological assay development to ensure successful delivery of projects.



**Head of Investor Relations  
Andrew Holder**

Andrew Holder BSc. Chartered Accountant and Fellow of the CISI. 20 years healthcare sector investment experience. Previously portfolio manager in UK based wealth management business.



**Deputy Finance Director  
Sinéad Armstrong**

Sinéad Armstrong B.Comm, FCA is a chartered accountant with over 30 years' experience within finance functions including managing the day-to-day finance operations, high-level financial review, financial modelling and commercialisation support.

# Scientific Advisers I/2



**Dr Daniel Danila**

Associate attending physician at Memorial Hospital Cancer Center in New York researcher at Memorial Sloan Kettering Cancer Center. Principal investigator (PI) for “Circulating Tumor Cells as Biomarkers for Patients with Metastatic Prostate Cancer: Developing Assays for Androgen Receptor Signaling Pathway”



**Dr George Hvichia**

Inventor of the Parsortix technology trained in Bioengineering and is an expert in Microfluidics and Biochips. He has developed microdevices for industry and in academic settings



**Dr Joseph Khoury**

Professor of Pathology and Laboratory Medicine at The University of Texas MD Anderson Cancer Center, Houston. Director of the MD Anderson Institutional Immunohistochemistry Laboratory. Member of the College of American Pathologists. Incoming chair and Stokes-Shackleford professor at the Dept. of Pathology and Microbiology, University of Nebraska.



**Dr Adrian Newland**

Professor of Haematology at Barts Health NHS Trust and Queen Mary University of London. Chair, Diagnostics Assessment for National Institute for Health and Clinical Excellence (NICE) for new diagnostics. Member NICE Group for cancer drugs



**Dr James M Reuben**

Professor in the Department of Hemato-pathology, Division of Pathology/Lab Medicine at The University of Texas MD Anderson Cancer Center, Houston, Texas. Leading authority on circulating tumor cell subsets, including those with epithelial and mesenchymal phenotypes and their relevance to minimal residual disease in breast cancer and non-small cell lung cancer

# Scientific Advisers 2/2



**Mr Greg L Shaw**

Consultant Urological Surgeon at University College Hospital in London. Chief investigator for NIHR portfolio studies investigating 1) the effects on refinements to robotic surgery and 2) the use of drugs to prevent progression in men on active surveillance for prostate cancer respectively. Lead surgeon for the largest robotic surgery team in the UK at UCLH



**Dr Clive Stanway**

Former Chief Scientific Officer of CRUK's Cancer Research Technology. Expert in cancer drug discovery and key role in working closely with major pharmaceutical partners



**Dr Harold Swerdlow**

A freelance consultant. Formerly: Special Projects Lead at Oxford Nanoimaging. Head of NGS Technology Development at LGC Genomics. VP of Sequencing at the New York Genome Center. Head of Research and Development for the Wellcome Trust Sanger Institute. Expert in next-generation sequencing (NGS). Inventor of NGS at Solexa acquired by Illumina



**Dr Ashok Venkitaraman**

Director, Cancer Science Institute of Singapore, and Distinguished Professor of Medicine at the Yong Loo Lin School of Medicine. Senior Principal Investigator and Senior Adviser at the Agency for Science, Technology and Research (A\*STAR). Formerly Professor of Cancer Research at the University of Cambridge. Director of Medical Research Council's Cancer Cell Unit.