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

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ANGLE

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Creating a new future for personalised cancer care

- **FDA product clearance followed by**
  - product sales growing and distributor network building
  - breakthrough data achieved for combined DNA analysis
  - large pharma customer secured and repeat business from biopharma

- **Building in 2024 towards**
  - wider use in pharma clinical trials
  - clinical tests offered from ANGLE's laboratory to provide clinical data monitoring patients and supporting therapy selection
  - clinical data in prostate and ovarian cancer studies

- **Opportunity to play a key role in the US$100 billion liquid biopsy market**
  - over 90 peer-reviewed publications from >40 independent cancer centres

ANGLE – Transforming cancer care

Our Mission:

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

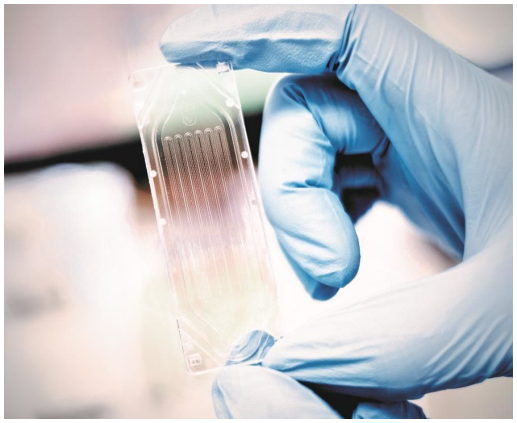
Our Solution:

The Parsortix system

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

Parsortix® instrument

Parsortix® cassette



INTENDED USE

The Parsortix® PC1 system is an in vitro diagnostic device intended to enrich circulating tumor cells (CTCs) from peripheral blood collected in K_2EDTA tubes from patients diagnosed with metastatic breast cancer. The system employs a microfluidic chamber (a Parsortix cell separation cassette) to capture cells of a certain size and deformability from the population of cells present in blood. The cells retained in the cassette are harvested by the Parsortix PC1 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.

Near term commercial milestones

- **Building services revenues**
  - Eisai secured as first large pharma customer. Other contract discussions in progress
  - Roll out of new assays (PD-L1, DDR, HER2 and DNA molecular)

- **Building product revenues**
  - Portrait+ product kit launched alongside instruments and cassettes
  - Distributors coming on line

- Breakthrough molecular results achieved with Illumina platform. **Work progressing on other molecular platforms** with large installed base

- Third-party molecular platforms (DNA and RNA) under investigation for analysis of banked **ovarian and prostate cancer** samples. Timing later in the year dependent on results

- **Clinical assays** (providing information about patient status) to be offered from ANGLE clinical laboratory **by year end**

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 personalised care
  – only samples a single metastatic site at one time point

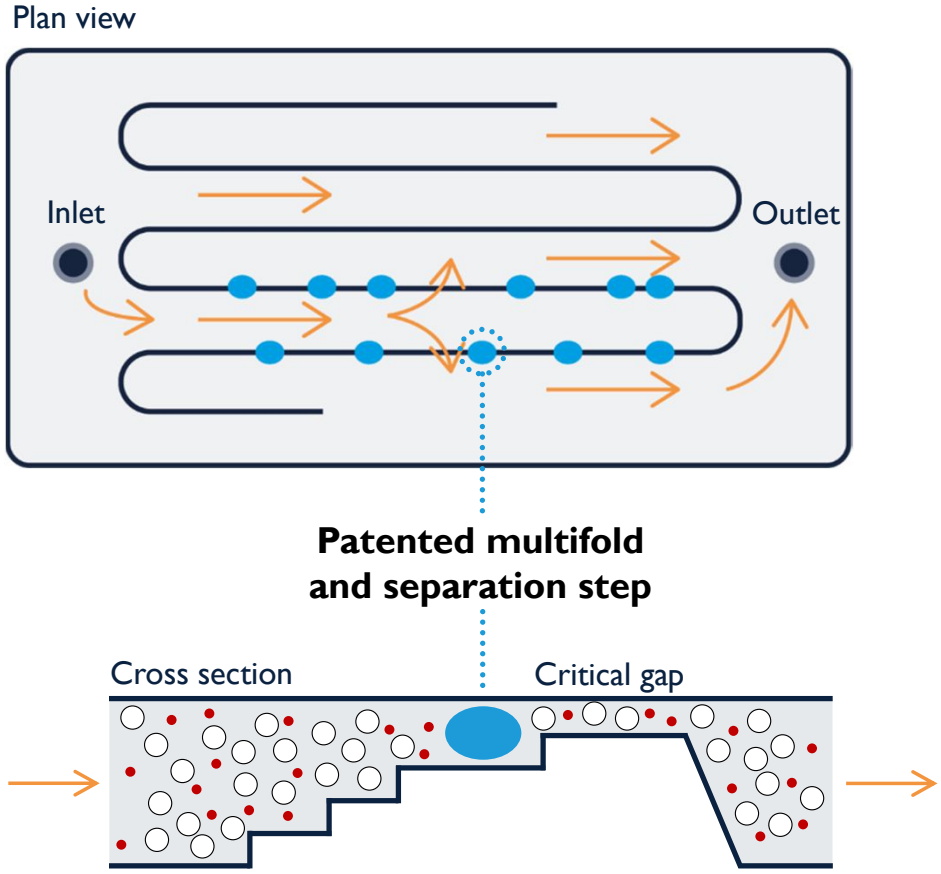
- **But half of all MBC patients do not have successful biopsies**
  – too ill for the surgery, tumor inaccessible and insufficient tissue

- 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 system: capturing and harvesting living cancer cells

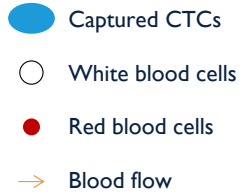


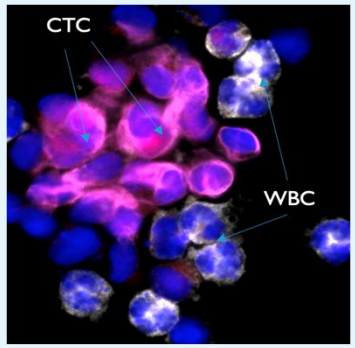
Platform technology

The Parsortix system harvests **cancer cells from blood** based on their larger size and lack of deformability. *CTC clusters including large CTC clusters are preferentially captured*

Other cells can be captured:

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



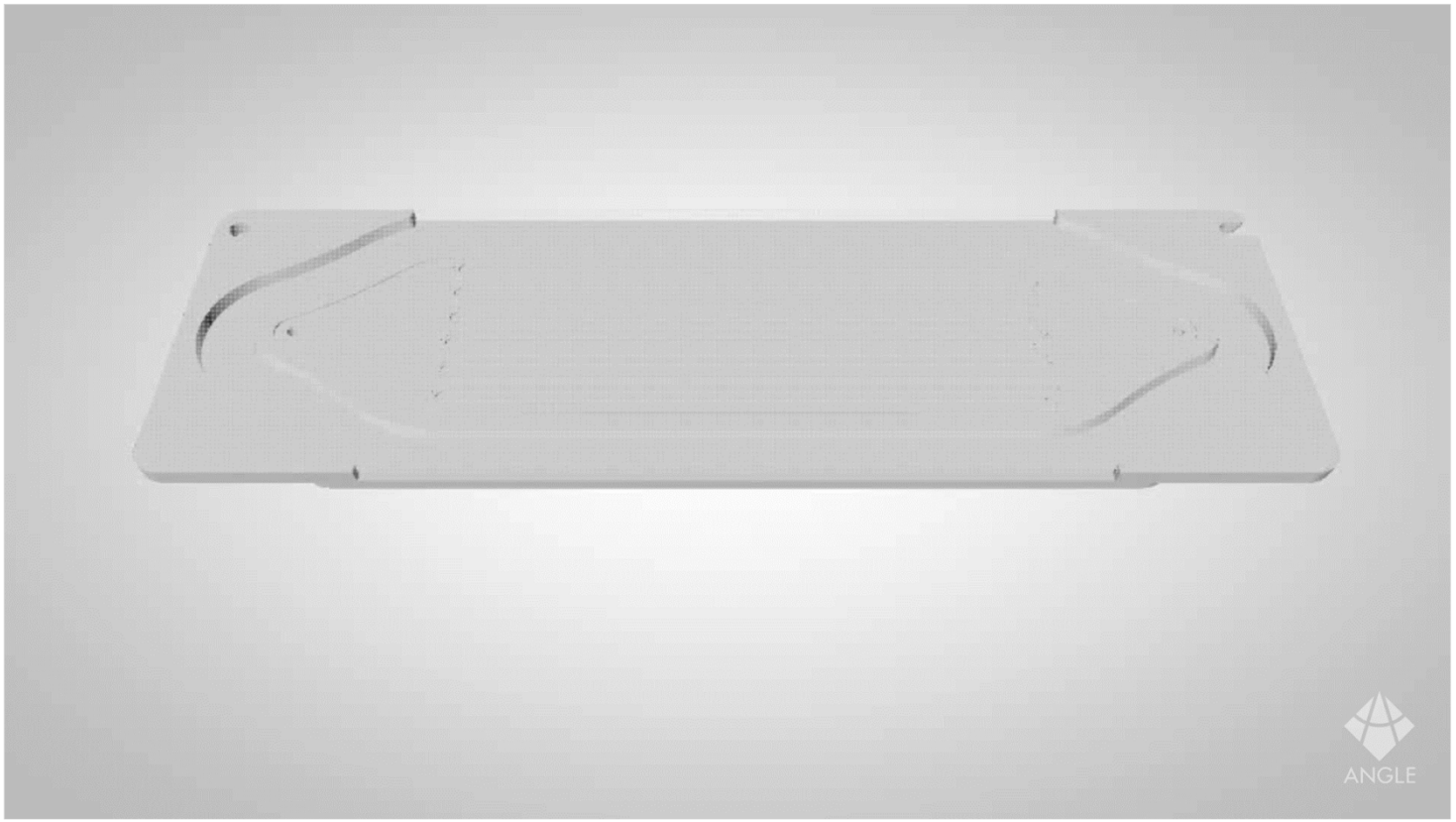


CTC and WBC cluster

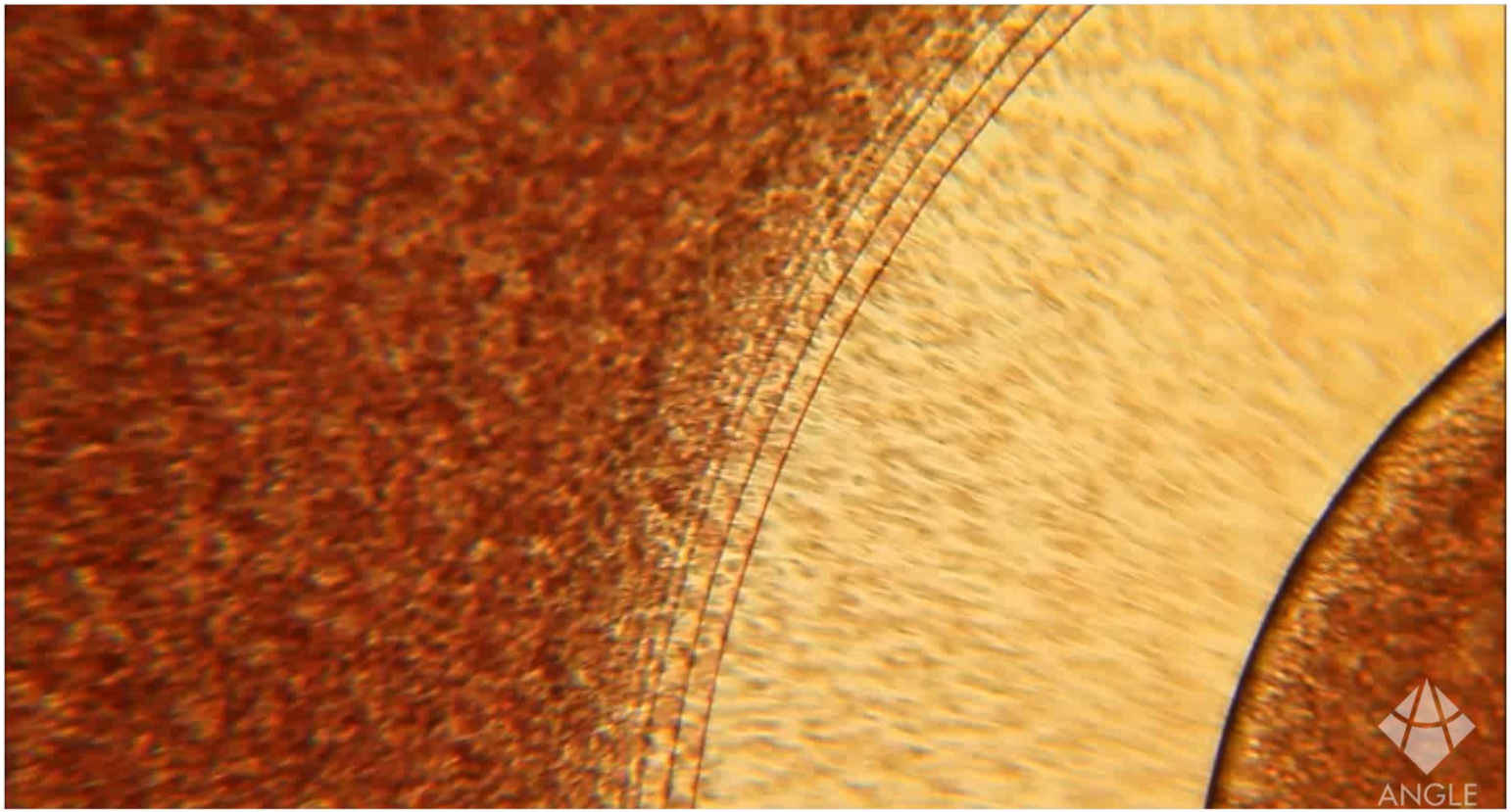
Parsortix® system patent protected worldwide

- Stepped, microscale cell separators for fluid flow and cell separation
- Manufactured under ISO 13485:2016 quality control
- **Scalable business with third-party manufacturers**
- 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

Animation showing operation of Parsortix cassette

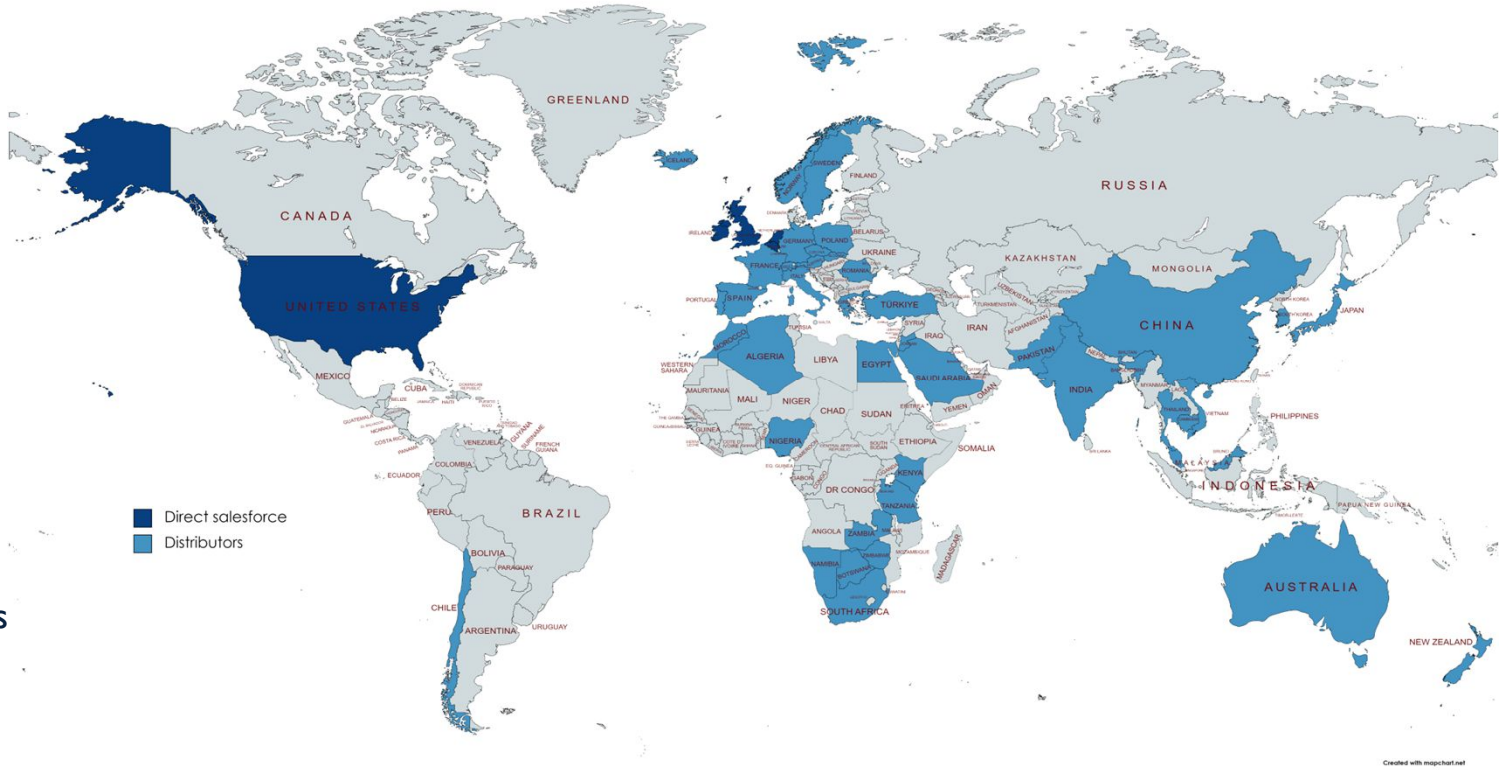


Patient blood flowing in Parsortix cassette



Products – international sales and distribution network

- **Continued expansion of commercial operations**
  - sales, logistics, product management, service and maintenance
- **Direct sales team**
  - US, UK, Ireland, Belgium and Netherlands
- **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



Services - differentiated pharma services offering

- **Customer base established and growing**
  - multiple customers, repeat business
  - new customers in 2024 and growing pipeline
- **Significant revenue and profitability potential**
  - potential for multi-US$ million contracts with margins >75%
  - each customer can offer numerous repeat contracts
  - only a small number of large-scale pharma customers needed
- **Assay development capability**
  - offers pharma bespoke services not possible otherwise
  - targeting the protein of action of the drug

Portrait+™ Powered by Parsortix®

Landscape+™ Powered by Parsortix®

Key differentiators

- Repeat testing **before, during and after** treatment
- Access to **live cancer cells**
- DNA, RNA, protein, cell morphology and CTC clusters
- CTCs feed into **existing techniques for analysing** tissue biopsy
- **CTC-DNA and ctDNA from the same blood sample**
- Sample stability for shipping
- CTC **centre of excellence**

Services – example customers and active projects

Global Japanese pharma company

- Revenues >£4 billion >10,000 employees
- >80 active oncology clinical trials >60,000 participants
- **HER2 targeting antibody-drug conjugate (ADC)** being co-developed by Eisai and Bliss Biopharmaceutical Co., Ltd as part of a US$ 2 billion deal
- ANGLE's HER2 assay to detect and assess HER2 low and HER2 + cancers

Cancer treatments targeting DNA Damage Response (DDR) pathways

- Bespoke assay development of DDR assay to measure DNA damage on CTCs
- Phase I study in advanced solid tumours (Breast, Ovarian, Prostate)

Immuno-oncology company developing targeted T cell enhancing therapeutics

- Portrait Flex assay to detect and phenotype CTCs and clusters
- Phase I prostate cancer study

Content – 'Portrait+' product kit for distribution

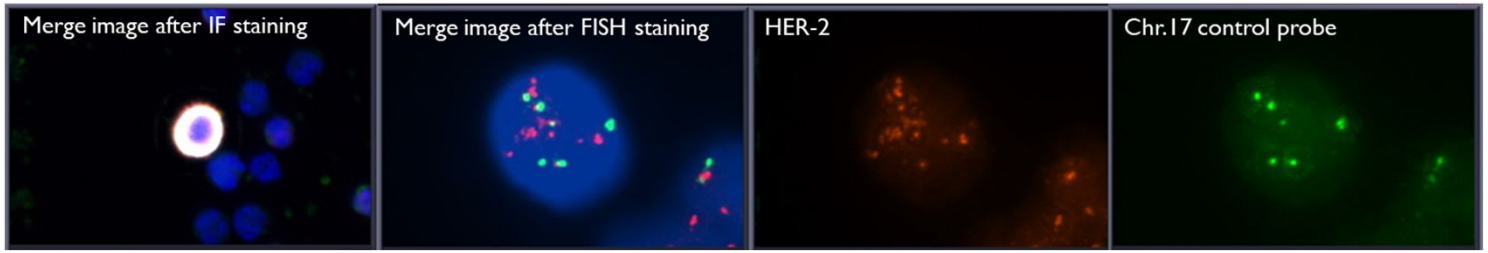
Antibody kit for robust and consistent imaging by Parsortix customers includes:

- Antibodies directly conjugated and mixed into a single vial:
  - Epithelial markers
  - Mesenchymal markers
  - Blood lineage markers
- Lyophilised for shipping, storage and improved stability

Content – HER2 assay kit in collaboration with BioView

- Breast cancer is highly heterogeneous and **HER2 status can change** over time
- **New antibody-drug conjugates** (ADCs) to treat patients with low HER2 status
- **Developing a product solution for a quantitative CTC based HER2 assay** that can monitor HER2 status over time
- 12-month development phase progressing well
- First phase generating **revenues of £1.2 million** for ANGLE

CTCs are enriched by the Parsortix system from 10 mL whole blood → Enriched cells are stained by IF for CTC detection and HER2 protein quantification → Slides are imaged, de-stained and processed for HER2 FISH analysis → Result: HER2 protein quantification and HER2 DNA amplification status



80.2%

predicted increase in global cases of breast cancer from 2020 to 2040

55%

of all breast cancer cases are HER2-low and could therefore be treated with ADCs like Enhertu

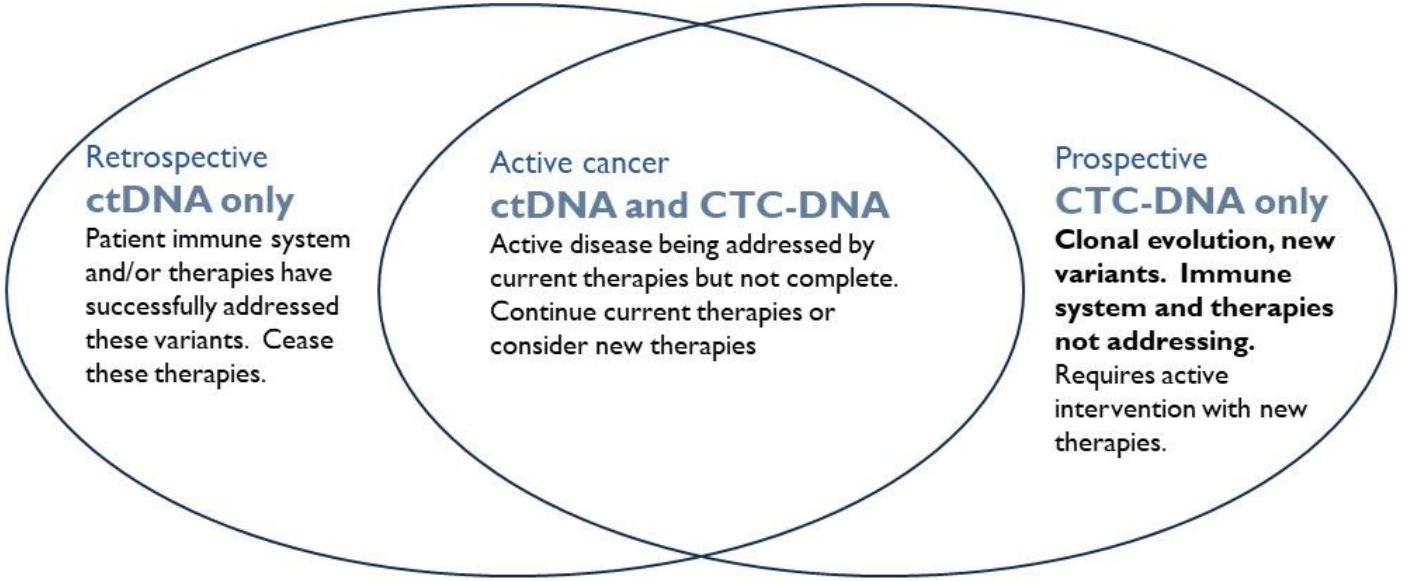
US$12.5bn

Global sales forecast for HER2 drugs in 2023

US$313.4m

Global value of HER2 diagnostics market in 2021.This is forecast to reach US$627.7 million by 2031

DNA sequencing of CTCs (living) and ctDNA (dead)



Hypothesis: Critical new information not currently available on how the cancer is progressing and which therapies may be effective

Cancer progression over time

ctDNA = DNA from circulating tumor fragments of dead cancer cells
CTC-DNA = DNA from living CTCs, cancer cells actively involved in cancer progression

Proof of concept on patient samples

DNA NGS Assay

High-multiplex Illumina NGS assay for DNA profiling

CTC-DNA and ctDNA extracted from blood samples of 47 patients with Breast, Lung, Ovarian or Prostate Cancer and profiled by NGS

- Overall good quality DNA extracted
- 100% DNA detection - all samples presented a signal, in both sample types

	Patients positive in CTCs	Patients positive in ctDNA	Patients with variants found in CTCs but not ctDNA
Breast	90%	60%	70%
Lung	90%	80%	70%
Ovarian	70%	50%	60%
Prostate	70%	70%	20%
Total	80%	65%	55%

CTC-DNA / ctDNA combined profiling: summary Illumina NGS

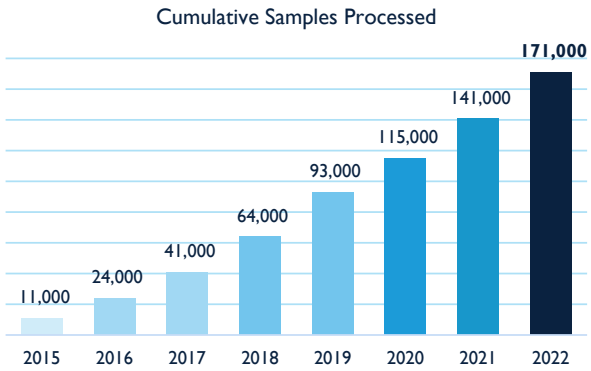
- Results from 47 cancer patients
- **High quality DNA** in all samples
- **Actionable DNA variants** found in CTCs not in ctDNA in 70% of breast and lung patients and 60% of ovarian cancer patients
- **Additional clinical data** obtained from the same blood tube **using Parsortix**

DNA variants found in CTCs with FDA cleared drugs for the variants in tissue or plasma including

- **PIK3CA** (E545K): Alpelisib (Piqray®) Novartis
- **EGFR** (T790M): Tagrisso (Osimertinib®) AstraZeneca
- **ESR1** (K303R): Elacestrant (Oserdu®) Menarini
- **MTOR** (T1977K): Everolimus (Afinitor®) Novartis
- **ERBB2** (R678Q): Trastuzumab, Pertuzumab, Neratinib, Afatinib marketed respectively by Astra Zeneca, Roche Genentech, Puma Biotechnology, and Boehringer Ingelheim

Strong body of evidence

- FDA clearance expected to help Parsortix become the CTC **system of choice**
- Installed base of **over 290** Parsortix systems in active use
- **Over 192,000** Parsortix samples processed to 30 June 2023



At 31 December 2023

Clinically actionable biomarkers including:

EGFR
BRAF
KRAS
PD-L1
HER2
TP53
AR
AR-V7
PIK3CA

# of publications by cancer type: top 5

Breast 36
Lung 25
Prostate 14
Melanoma 7
Head and neck 7

92 Peer-reviewed journal publications

81 published in high impact journals

41 independent centers in 14 countries

Complete picture DNA, RNA & proteins

2nd most published CTC system in last 5 years

14 studies demonstrating superiority to other methods

24 cancer types representing 89% of solid tumors

More than **3,800** patient samples processed

57 publications studying actionable biomarkers

Variety of downstream analysis techniques:

RT-qPCR
dPCR and ddPCR
RNAseq
Immunofluorescence
NGS/TGS
WGA, WES & WTA
Mass Spectrometry

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