



ANGLE

Liquid biopsy
Cells for precision medicine
January 2016



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Cancer Research UK: "One in two people born after 1960 in the UK will be diagnosed with some form of cancer during their lifetime."

- ❖ Each patient's cancer is different
 - ❖ Patient's cancer changes over time
 - ❖ Effective treatment requires personalised care
 - ❖ Reducing healthcare costs
- ❖ Major pharma developing more selective drugs
 - Colorectal cancer KRAS- Erbitux (Merck Serono)
 - Lung cancer EGFR+ Iressa (AstraZeneca)
 - Breast cancer HER2+ Herceptin (Genentech)



Existing approach: solid tumour biopsy

- ❖ Clinicians cut out part of the tumour and analyse the cancer cells
 - Breast cancer mastectomy or lumpectomy
 - Colorectal cancer colonoscopy tumour biopsy
 - Prostate cancer fine needle biopsy and prostatectomy
- ❖ Difficulty in accessing some tumours
 - Pancreatic cancer, Lung cancer, Brain cancer
- ❖ Repeat tumour biopsy problematic

New approach: liquid biopsy

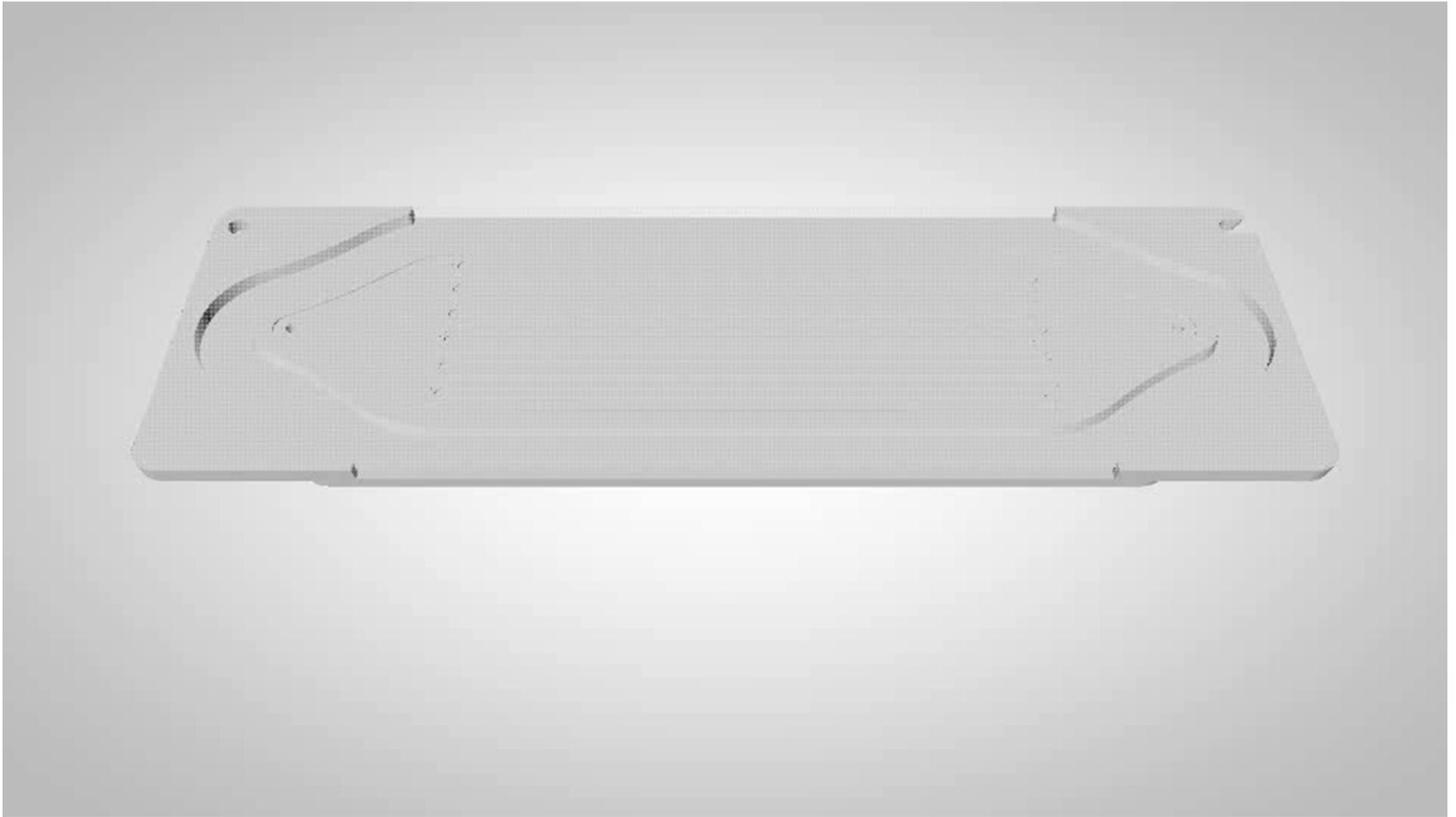
- ❖ Harvest intact cancer cells from blood
- ❖ Non-invasive, repeatable, real time, cost effective
- ❖ But only one CTC in one billion blood cells



Whole blood from a simple peripheral blood draw contains approximately one cancer cell per ml of blood. The cancer cells are circulating tumor cells shed by the primary tumour in the process of metastasis. The CTCs travel in the blood and if they take root in another organ are the cause of a secondary cancer at a new location.

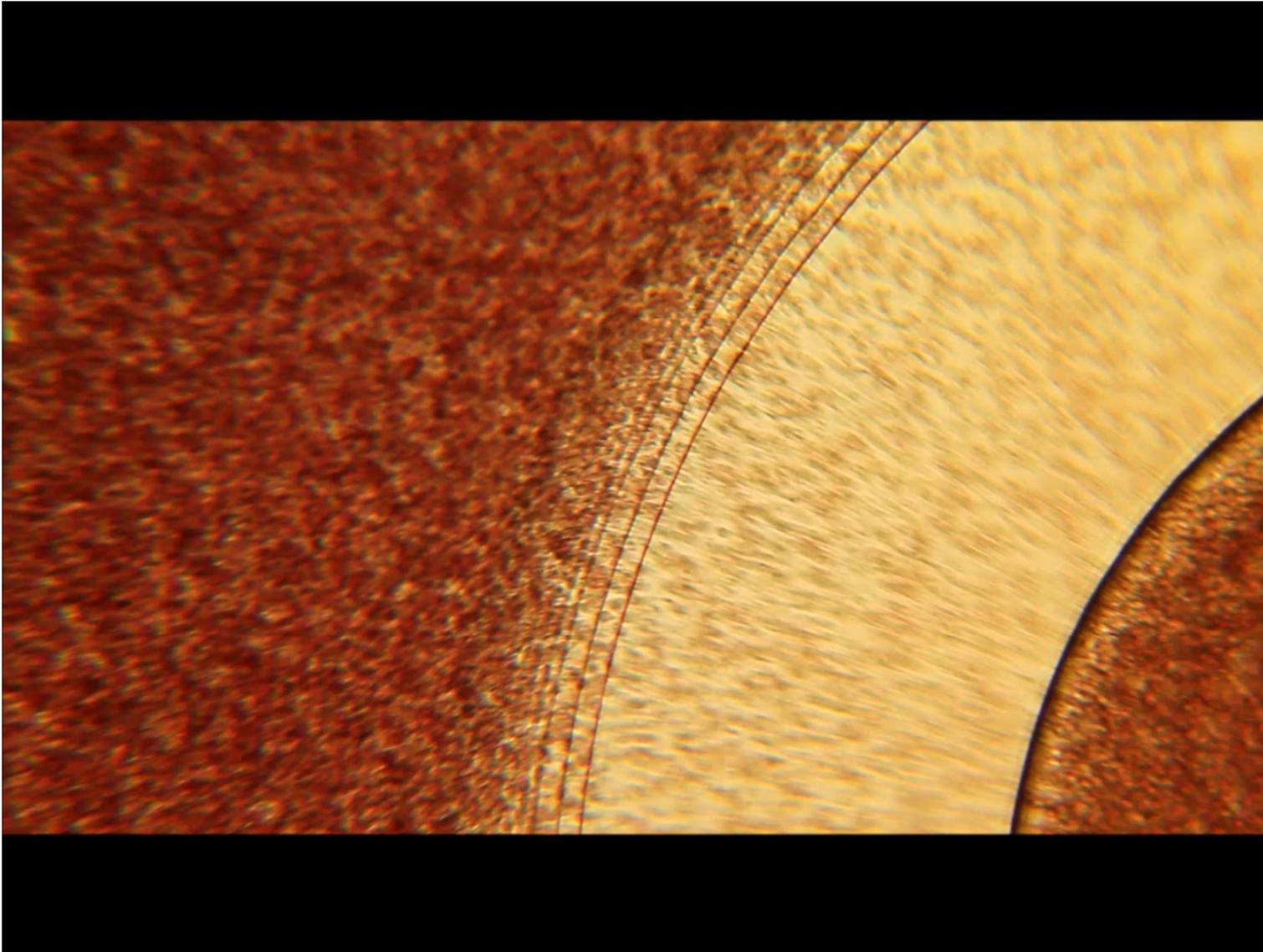


Animation showing Parsortix patented steps



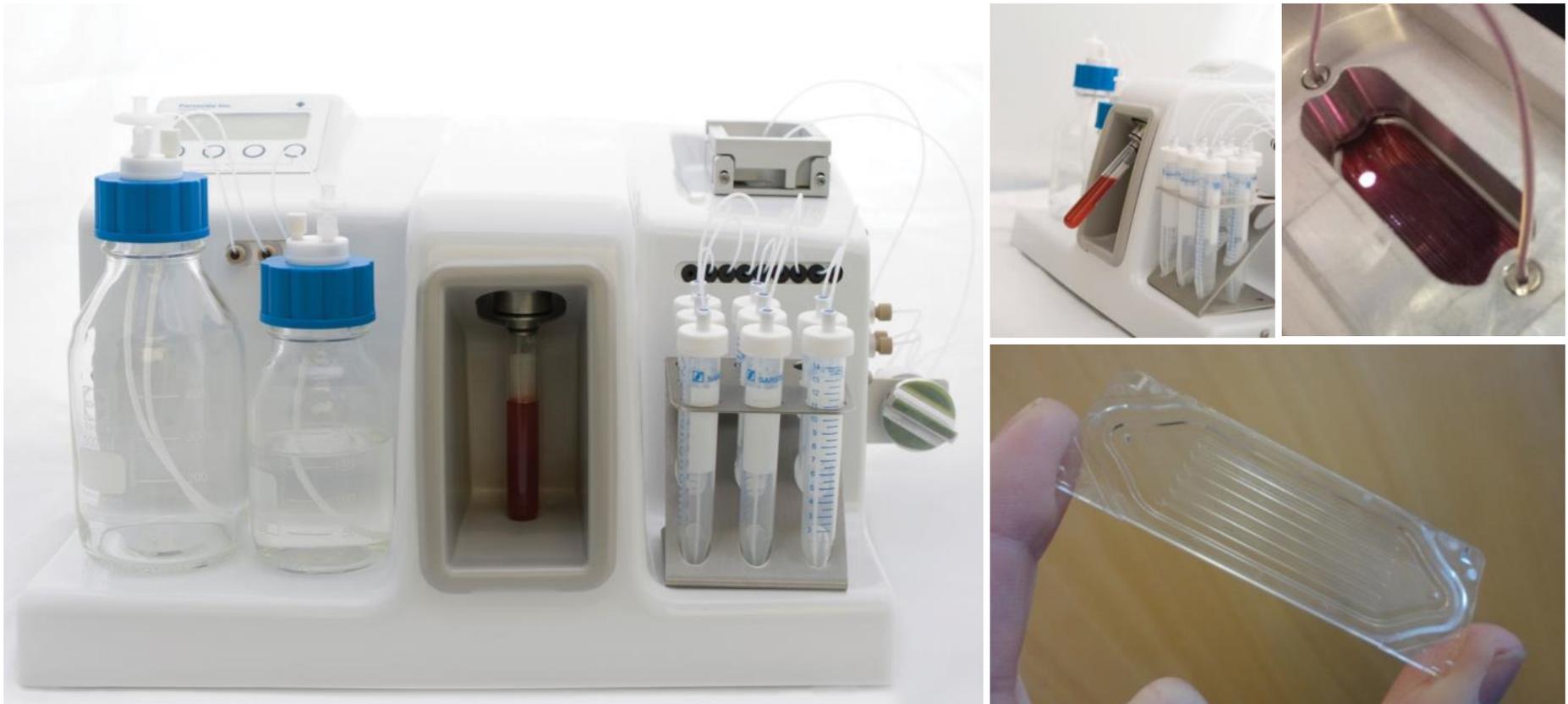


Video showing blood flowing in Parsortix cassette





ANGLE's patented Parsortix system



- ◆ Stepped, microscale cell separators for fluid flow and cell separation

- ◆ Two granted US Patents
- ◆ Granted patents in China, Canada and Australia

- ◆ Patents pending worldwide
- ◆ European patent expected later this financial year



Market size and drivers

- ❖ Total addressable market for liquid biopsy US\$ 14 billion in the United States market alone by 2025
- ❖ Four key market segments
 - Diagnostic screening
 - Therapeutic decision-making
 - Minimal residual disease
 - Post treatment monitoring
- ❖ Liquid biopsy comprises ctDNA and CTCs
 - “Whole cells (CTCs) offer the advantage of providing a clinician access to cellular morphology along with other genetic content such as RNA”
 - “CTCs are exceedingly rare ... and more difficult to isolate the ctDNA”

Source: The Goldman Sachs Group, Inc. Global Investment Research “Liquid Biopsy: Could a simple blood test revolutionize cancer care” Equity Research 6 October 2015

ANGLE is changing the paradigm by making it easy to isolate CTCs from patient blood for a wide range of cancers



Competitive differentiation in a \$ multi-billion market

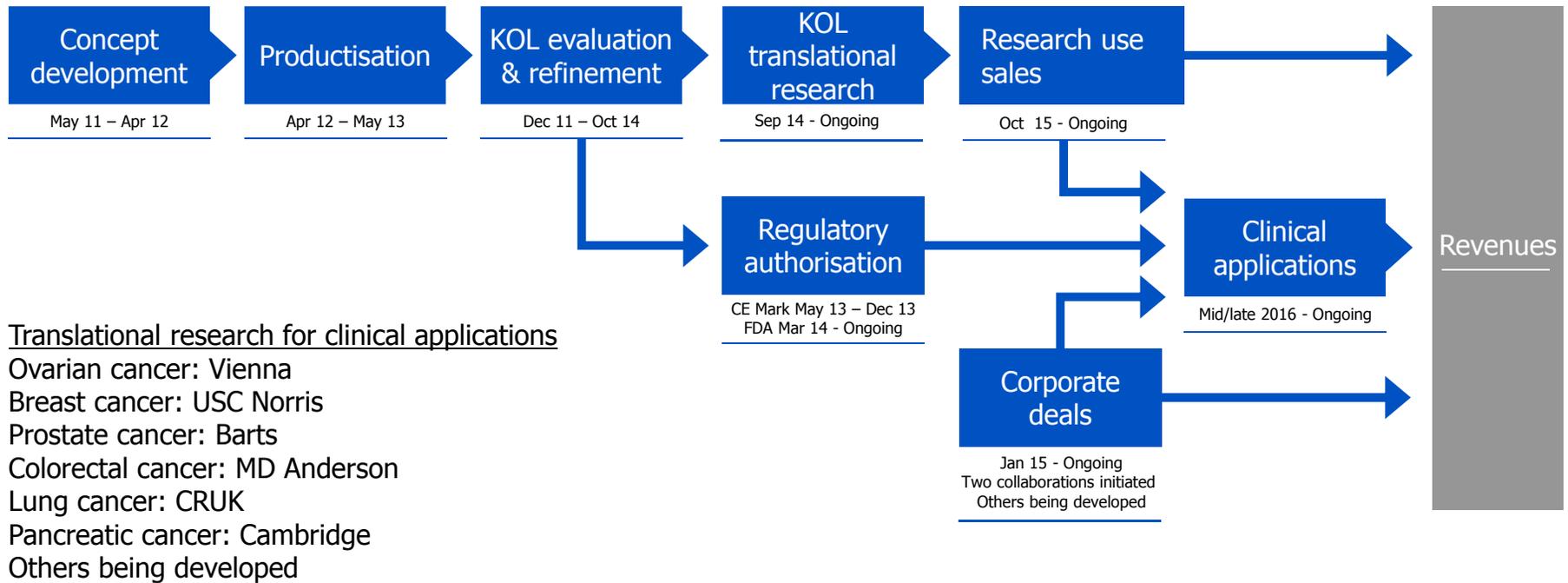
Technology	Name	Simple process	Low cost	Captures all types of cancer	Captures mesenchymal CTCs involved in metastasis	Able to easily harvest cells for analysis	High purity of harvested cells
Microfluidic step	Parsortix	✓	✓	✓	✓	✓	✓
Antibody-based system	CellSearch (only FDA authorised system)	✗	✗	✗	✗	✗	✗
	CTC iChip Magsweeper Cynvenio Biocept Isoflux Gilupi AdnaTest	✗	✗	✗	✗ ✓	✗ ✓	✗
Membrane-based	ISET Screencell CellSieve	✓	✓	✓	✓	✗	✗
Centrifugation	Dean Flow Fractionation	✓	✓	✓	✓	✗	✗
Cell-free DNA	Alternative process using plasma from blood	✓	✗	✓	✗	N/A ⁽¹⁾	✗

(1) Cell free DNA techniques can only analyse DNA, not RNA or proteins.

ANGLE is offering customers a Parsortix system for purchase comprising a desktop machine and a one-time use consumable. Many competitor systems are so complicated that they have to offer a CLIA (certified laboratory) solution where the customer sends them the sample and they operate the system and provide a result. This approach is commercially less attractive as it requires large in-house investment, is less scalable and deprives the clinical customer of much needed revenue in processing the samples.



Path to commercialisation





Research use sales to support drug trials and other research

- ❖ Following successful evaluations of the system by KOLs, ANGLE commenced research use sales in Q4 CY15 addressing a research use market of \$375m p.a.
- ❖ Secondary market providing establishment revenues, building market awareness and third party evidence to support clinical applications in multiple cancer types
- ❖ 750 addressable Phase II cancer drug trials p.a.
 - typically 100 patients two years 3 blood tests per patient
 - each trial potential to generate >\$150,000 revenue for ANGLE
- ❖ 120 addressable Phase III cancer drug trials p.a. initiated each year
 - typically 1,000 patients three years 5 blood tests per patient
 - each trial potential to generate >\$1m revenue for ANGLE
- ❖ Securing 5% of the Phase II and Phase III trials as customers offers potential Parsortix revenues of \$12m p.a.
- ❖ Cancer drug trials leading to a new drug may lead to the adoption of Parsortix as a companion diagnostic (CDx) for that drug

	Machine	Cassette
Price ¹	£40,000	£150
Cost	£12,000 ²	£17
Margin	70%	89%

1. High margins allow flexibility in pricing for competitive advantage
2. Includes maintenance, technical support, sales and distribution

- ❖ Sales of the Parsortix system for clinical use is the primary objective for commercialisation of the business
- ❖ Estimated clinical market available to ANGLE in excess of \$12 billion p.a.
- ❖ Requires both regulatory authorisation and patient data
- ❖ ANGLE has a comprehensive strategy to deliver clinical sales
 - regulatory authorisation
 - key opinion leaders
 - patient studies
 - corporate partnerships



- ❖ Multiple KOL studies in progress to investigate new clinical applications for the treatment of patients



Ovarian cancer: clinical application in development

Medical University of Vienna

- Highly successful patient study
 - 100% specificity in primary epithelial ovarian cancer (no false positives)
 - 78/80% sensitivity with 7 RNA markers
 - 100% sensitivity with 30 RNA markers
- Parsortix results “sensational”
 - best CTC alternative only 24.5% sensitivity

- Clinical application in triaging patients with abnormal pelvic mass
 - to identify those at high risk of ovarian cancer
 - in US, 200,000 women p.a. have surgery on abnormal pelvic masses c. 10% have cancer
 - Medicare reimbursement of \$516/test
- Clinical study over 18 months
- Ovarian sales potential >\$450m p.a.

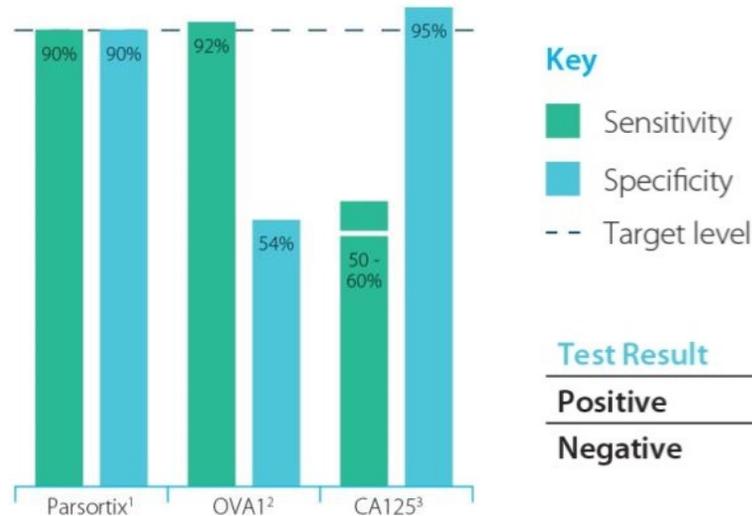
Parsortix effectiveness compared to other tests

Sensitivity

The test correctly identifies those with the disease (true positive). A low sensitivity means the test may miss many people who have cancer (false negative).

Specificity

The test correctly identifies those without the disease (true negative). A low specificity means patients are told they may have the disease when they do not (false positive).



	Cancer	No cancer
Test Result	Sensitivity	Specificity
Positive	True Positive	False Positive
Negative	False Negative	True Negative

1 Target for clinical studies
 2 Vermillion Inc
 3 Patient.co.uk / Fritsche HA, et al. (1998). CA-125 in ovarian cancer: advances and controversy. Clinical Chemistry. 44(7):1379-1380

Barts Cancer Institute

- ❖ CTCs harvested in 100% of patients (n=52)
- ❖ Barts study demonstrates Parsortix harvested cells are clinically relevant in prostate cancer
- ❖ Mesenchymal cells (involved in metastasis) as well as epithelial cells
- ❖ Clinically relevant cells harvested

- ❖ Barts researchers now investigating molecular biomarkers on the harvested cells to guide effective treatment

2. Different populations of CK+/Vimentin-/CD45-, CK+/Vimentin+/CD45-, and CK-/Vimentin+/CD45- cells were identified in clinical samples using 4-colour immunofluorescence (Figure 3).

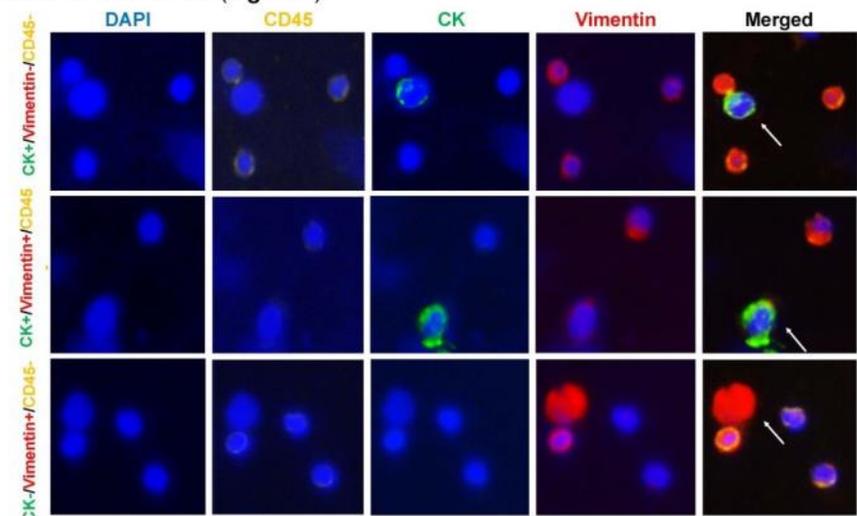
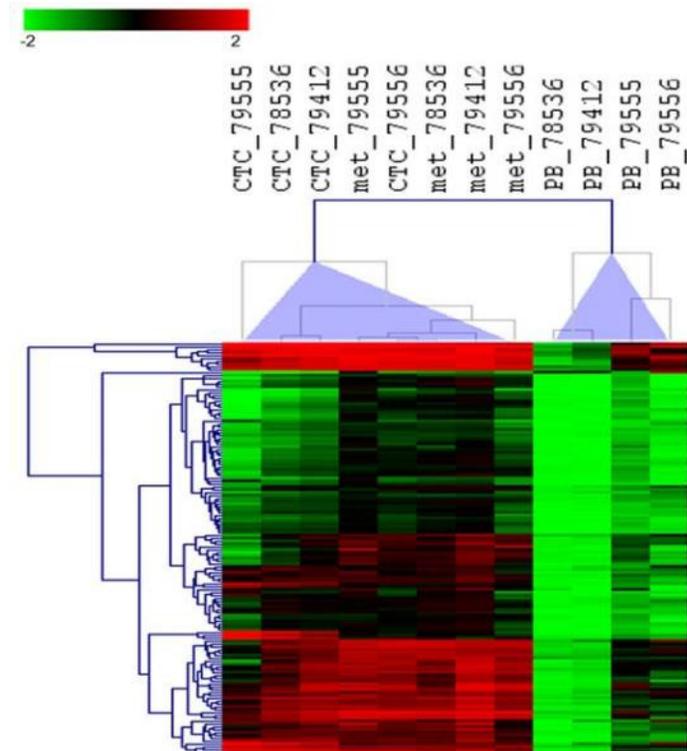


Figure 3. Representative images for different populations of detected cells in prostate cancer patients. The upper row: a CK+/Vimentin-/CD45- cell surrounded by CD45+ lymphocytes. The middle row: a CK+/Vimentin+/CD45- cell next to a CD45+ lymphocyte. The lower row: a CK-/Vimentin+/CD45- cell surrounded by CD45+ lymphocytes.

University of Southern California Norris Comprehensive Cancer Center

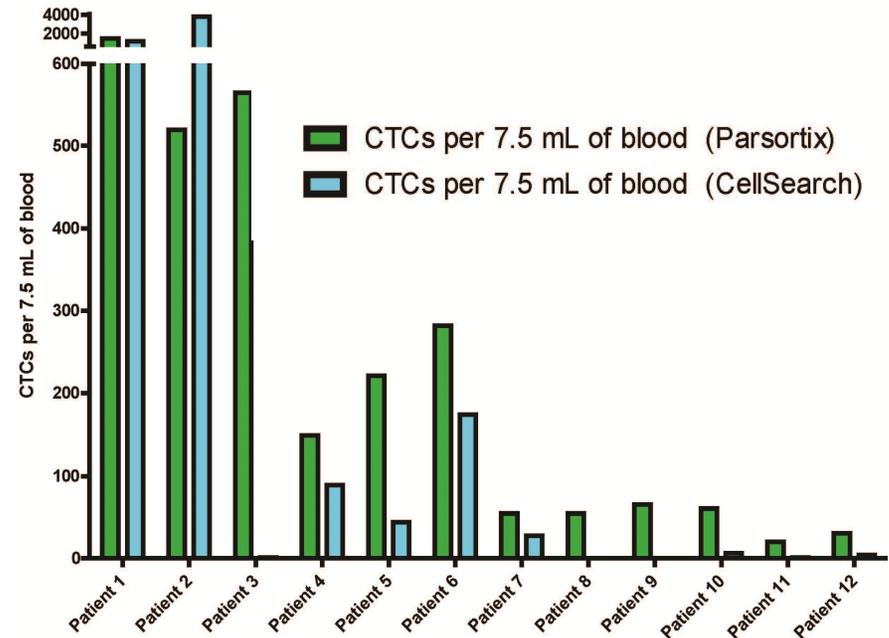
- ❖ CTCs harvested for RNA Seq analysis in 100% of patients
- ❖ CTCs from Parsortix liquid biopsy had similar patterns of gene expression to the traditional biopsy of cancer cells from metastatic sites in all cases (n=4)
- ❖ Parsortix liquid biopsy also provides additional clinical information beyond the biopsy of a single metastatic site
- ❖ Metastatic biopsies invasive, often requiring surgery, expensive and may delay treatment



Hierarchical two dimensional heat map of 214 genes differentially expressed in CTC and met vs peripheral blood.

Cancer Research UK Manchester Institute and Christie Hospital

- ❖ CTCs harvested 100% patients (n=12)
 - Parsortix harvested >5 cells from 100% of patients compared to 58% by leading competitive system
- ❖ Suitable for at least four days at room temperature
- ❖ Simple plug and play device
- ❖ Enables analysis of CTCs not detected by epitope dependent technologies
- ❖ Parsortix enables processing a single blood sample for both CTCs and cfDNA



Ged Brady, Cancer Research UK Manchester Institute

“The Parsortix system has a unique combination of features making it suitable for routine clinical analysis of patient blood samples. We have now incorporated the Parsortix workflow into multiple clinical trials and have been accumulating many hundreds of stored enriched samples that will be of immense value in our future CTC studies.”

Corporate collaborations with diagnostics companies



ANGLE's commercialisation strategy is to establish a series of partnerships with major medtech players such as Roche, Illumina, Abbott, Life Technologies, Qiagen, Hologic, Agilent, Siemens Healthcare, bioMérieux etc

- ❖ Cost-effective distribution channel
- ❖ Parsortix "open source" as a front end for existing analytical platforms deployed worldwide giving them new revenues

So far two commercial collaborations announced

- ❖ Diagnostics division of a large pharmaceutical company
 - combine Parsortix CTC harvesting platform with their single cell analysis system
 - Parsortix system may be sold as a source of patient samples for analysis using the Collaborator's analytical platform
- ❖ EKF Diagnostics Holdings plc
 - combine Parsortix CTC harvesting platform with EKF's PointMan™ DNA enrichment technology: liquid biopsy to identify genetic variation in the cancer
 - explore ways to offer the systems as a combined solution from blood to medical result

Parsortix patented system provides cells for precision medicine changing the paradigm in a \$ billion emerging market

- ❖ High performance in ovarian, prostate, breast and lung cancers
- ❖ Growing research use sales with a clear competitive advantage
- ❖ CE Mark authorised. FDA approval in process
- ❖ Ovarian cancer first clinical application in development

**Parsortix system + key opinion leader + patient data
+ regulatory authorisation + clinical application =
\$bn market**

~~MD Anderson
Cancer Center~~





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