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

Presentation at Proactive One2One Virtual Forum

Andrew Newland and Ian Griffiths
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Analysis of circulating tumor cells (CTCs) can revolutionise cancer care addressing flaws in patient care exposed by COVID-19
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“ANGLE’s mission is to enable personalised cancer care by providing the complete picture of the patient’s cancer from a simple blood test.

Product-based solution for simple, effective, affordable repeat testing of intact cells.”

Andrew Newland, Chief Executive
Parsortix liquid biopsy addresses flaws in standard of care

• **Existing approach: solid tissue biopsy**
  – clinicians cut out tumor and analyse the cancer cells
  – difficulty in accessing some tumors such as pancreatic, lung, brain, liver and bone cancers
  – repeat tissue biopsy problematic, expensive and can cause adverse reactions

• **NCCN Guidelines recommend tissue biopsies for metastatic breast cancer (MBC)**
  – tissue biopsies from the primary are out-of-date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

• **Half of all MBC patients do not have successful biopsies**
  – too ill for the surgery
  – tumor inaccessible
  – insufficient tissue

• **New approach: Parsortix liquid biopsy**
  – harvest intact cancer cells from blood
  – non-invasive, repeatable, real time, cost effective
  – can be COVID-secure with blood draw at patient’s home
Total addressable market > US $100 billion p.a.

“Successful validation of our approach in future clinical studies could revolutionize clinical management of metastatic breast cancer.”

Julie E. Lang, MD, FACS, Director, USC Breast Cancer Program, Associate Professor of Surgery, Norris Comprehensive Cancer Center, University of Southern California

<table>
<thead>
<tr>
<th>2018</th>
<th>2012</th>
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<tbody>
<tr>
<td>New cancer incidence (per annum)</td>
<td>18.1 million</td>
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<tr>
<td>Living with and after cancer</td>
<td>43.8 million</td>
</tr>
<tr>
<td>Deaths from cancer (per annum)</td>
<td>9.6 million</td>
</tr>
</tbody>
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1. Source: GLOBOCAN: Global burden of cancer

Liquid biopsy emerging multi US$ billion market: estimates

| Cowen² | Frost & Sullivan³ | Guardant Health⁴ | Grail (Illumina)⁵ |
| Up to ~$130 billion per annum | $100 billion per annum | $51 billion per annum | $75 billion per annum |

<table>
<thead>
<tr>
<th>Current focus</th>
<th>Therapy selection</th>
<th>Assessing treatment</th>
<th>Remission monitoring</th>
<th>Early screening for cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection of cancer in high risk groups</td>
<td>Breast HER-2 Abbott</td>
<td>Assessing minimal residual disease</td>
<td>Repeat testing to ensure CTCs not present</td>
<td>Need to assess aggressiveness and avoid false positives</td>
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<tr>
<td>Ovarian pelvic mass</td>
<td>Prostate AR-V7 Qiagen</td>
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<td>Active surveillance</td>
<td>Immunotherapy PD-L1</td>
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<td>Watchful waiting</td>
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CTCs provide the complete picture for repeat biopsies

**CTC cultures**
“Widely adopted, this approach has the potential to transform the way we treat cancer patients.”
Professor Massimo Cristofanilli
MD Associate Director; Translational Research, Robert H Lurie Comprehensive Cancer Center, Northwestern University, Chicago

**Analysis of CTCs is the closest proxy to tissue biopsy**

Over 90% of cancer deaths are caused by metastasis

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<table>
<thead>
<tr>
<th>Tissue</th>
<th>ctDNA</th>
<th>CTCs</th>
<th>CTC clusters</th>
<th>CTC cultures</th>
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</thead>
<tbody>
<tr>
<td>Clinicians cut out part of the tumor and analyse cancer cells</td>
<td>Fragments of dead cells</td>
<td>Harvest intact living cancer cells (CTCs)</td>
<td>80x greater metastatic potential in a mouse model</td>
<td>Growth of cancer outside patient</td>
</tr>
<tr>
<td>Invasive</td>
<td>Partial DNA picture</td>
<td>Complete picture of the cancer</td>
<td></td>
<td>Potential to test drugs outside patient</td>
</tr>
<tr>
<td>Not repeatable</td>
<td>No RNA or protein information</td>
<td>Non-invasive</td>
<td>Repeatable</td>
<td>Real-time</td>
</tr>
<tr>
<td>May be difficult to access</td>
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**Current practice**
DNA, RNA, Protein

**Generic lab process**
DNA only

**Patent-protected Parsortix® product solution**
DNA, RNA, Protein

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Over 90% of cancer deaths are caused by metastasis
Parsortix 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.

Other cells can be captured:
- **megakaryocytes** (frequency may relate to cancer)
- **fetal cells** from maternal blood

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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 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
Animation showing operation of Parsortix cassette
Patient blood flowing in Parsortix cassette
Growing body of evidence
Leveraged R&D strategy identifying new applications

• Translational research market US $50 million p.a.
• FDA clearance expected to help Parsortix become the CTC system of choice
• Installed base of c.200 Parsortix systems in active use

Parsortix samples processed

Cumulative samples processed at 31 December

4,000 12,000 25,000 42,000 67,000 96,000

Research use pricing

Instrument Cassette
Price $50,000 $100
Cost $15,600 $15
Margin 69% 85%

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

81% of research published in high impact journals*
including Cell (3) and Nature (1)

Enabling breakthrough research into:
1) CTC Clusters
2) Cancer Cell Culturing
3) Metastatic cancer including brain
4) Biomarkers for immunotherapy

Second most published CTC system (2017-2020) after CellSearch

Seven separate studies demonstrate Parsortix outperforms CellSearch

*Based on Impact Factor quartiles Q1 & Q2
Prospect of FDA clearance earliest Q2 CY21

- **Seeking first ever FDA clearance** for a device to harvest cancer cells from patient blood for subsequent analysis

- **Positive results from clinical and analytical studies with four leading US cancer centres participated**
  - University of Texas MD Anderson Cancer Center
  - University of Southern California Norris Cancer Center
  - University of Rochester Wilmot Cancer Center
  - Robert H Lurie Cancer Center Northwestern University

- FDA De Novo Submission for Class II clearance in metastatic breast cancer submitted 25 September 2020
  - over 15,000 samples
  - 400 reports and technical documents

- **Q-Submission process followed to de-risk process**

- Only the third product-based liquid biopsy FDA clearance and the first ever CTC harvesting for subsequent analysis

- **FDA clearance recognised as the gold standard globally and would be a major validation**
  - clinical use for breast cancer
  - pharma services
  - corporate partnerships
  - research use

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

Accredited clinical laboratories being established in US and UK as **accelerator and demonstrator**

- Pharma services and initial clinical services
- Offer new tests:
  - epithelial, EMTing, mesenchymal CTCs and clusters
  - ER/PR/HER2 application
  - PD-L1 immunotherapy
  - ovarian cancer test (pelvic mass assay)

**Accelerator for Parsortix LDT clinical applications**

- Enables early progress with payers and reimbursement codes ahead of FDA cleared product

**Demonstrator for Parsortix clinical applications**

- supporting product sales and corporate partnerships
Ovarian cancer pelvic mass triage test clinical study in progress

“The next generation ANGLE PMT 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

- 5-10% of women suffer from abnormal pelvic mass
- 295,000 women diagnosed globally with ovarian cancer in 2018
- Two 200 patient studies already completed with best in class results AUC >95% accuracy achieved. Potential for high sensitivity and high specificity
- Clinical verification 200 patient study in progress with the University of Rochester Wilmot Cancer Center
- Targeting completion of patient enrolment by Q2 CY21
- Establish the test as an LDT in an accredited clinical laboratory
Building on a leading position in the liquid biopsy market

- **Highly differentiated solution** for the emerging multi US$ billion liquid biopsy market
- **Prospect of FDA clearance earliest Q2 CY21** *
- **Ovarian cancer** clinical verification study expected to complete enrolment Q2 CY21
- **Growth planned** through sample-to-answer, pharma services and service laboratory
- **Expanding partnerships with medtech** (downstream analysis), pharma (companion diagnostics), CRO (drug trials), clinical laboratories (LDT)
- **Substantial body of peer-reviewed customer studies** showcasing breadth of utility

Leading cancer centres with original research and peer-reviewed publications using ANGLE’s Parsortix system (selection)

Corporate partnerships being developed

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