ANGLE Liquid Biopsy Sample to Answer
Presentation to Shares Investor Event
Andrew Newland and Ian Griffiths
28 November 2017
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Parsortix™ and Axela systems

- **Simple blood test for personalised cancer care**
- Proven performance with multiple Key Opinion Leaders
- **Emerging $ multi-billion market (Goldman Sachs $14bn in US alone by 2025)**
- Circulating tumor cell (CTC) solution with strong competitive differentiation
- **Product based solution with instruments and cassettes**
- Downstream analysis capability provides unique sample to answer solution
## Financial Results for the year ended 30 April 2017

<table>
<thead>
<tr>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Revenue</td>
<td>498</td>
<td>361</td>
</tr>
<tr>
<td>Cost of sales</td>
<td>(123)</td>
<td>(107)</td>
</tr>
<tr>
<td><strong>Gross profit</strong></td>
<td>376</td>
<td>254</td>
</tr>
<tr>
<td>Operating costs</td>
<td>(7,810)</td>
<td>(5,703)</td>
</tr>
<tr>
<td>Tax credit and other income</td>
<td>1,043</td>
<td>331</td>
</tr>
<tr>
<td><strong>Loss for the year</strong></td>
<td>(6,392)</td>
<td>(5,118)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statement of Financial Position</th>
<th>30Apr17</th>
<th>30Apr16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trade and other receivables and tax</td>
<td>1,975</td>
<td>798</td>
</tr>
<tr>
<td>Inventories</td>
<td>665</td>
<td>376</td>
</tr>
<tr>
<td>Cash</td>
<td>5,536</td>
<td>3,764</td>
</tr>
<tr>
<td>Property, plant and equipment</td>
<td>824</td>
<td>455</td>
</tr>
<tr>
<td>Intangible assets</td>
<td>1,918</td>
<td>1,346</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>10,918</td>
<td>6,739</td>
</tr>
</tbody>
</table>

### Comments
- Research use sales established and growing
- 75% gross margin
- Planned expenditure on clinical studies
- Cash position strengthened with £15m fundraise in November 2017
- Seeking a leading position in $ billion emerging market
Liquid biopsy improving healthcare and reducing costs: driving precision medicine

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

- Big pharma developing more selective drugs:
  - Colorectal cancer KRAS- Erbitux (Merck Serono)
  - Lung cancer EGFR+ Iressa (AstraZeneca)
  - Breast cancer HER2+ Herceptin (Genentech)
  - Non small cell lung cancer PDL1+ Keytruda (Merck)
  - Immunotherapies
Obtaining cancer cells for analysis

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, lung, brain, liver and bone cancers

- 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.

Over 90% of cancer deaths are caused by metastasis.
Animation showing Parsortix™ patented steps
Video showing blood flowing in Parsortix™ cassette
Parsortix™ system – the Complete Picture

- Intact CTCs not just ctDNA
  Compatible with existing downstream analysis techniques

- Parsortix™ system captures living cancer cells
  These cannot be present unless the patient has cancer

- Evidence-based driven by KOLs and clinical studies

- Patented product solution

- Scaleable business with third party manufacture
Axela patent protected downstream analysis solution

- **Ziplex® System**: medium-density microarray platform designed for routine and focused multiplex analysis of protein or RNA biomarkers

- Consumables: **Flow-thru TipChip®** containing gene expression/protein expression panels for common pathways or disease processes

- **HyCEAD chemistry** enables simultaneous measurement of 100s of genes while eliminating multiplex PCR constraints

- Software: embedded software for method creation, data gathering and data analysis

Axela products are well protected as the subject of multiple granted patents
## Benefits of Parsortix™ CTCs

<table>
<thead>
<tr>
<th>Source</th>
<th>Solid tissue biopsy</th>
<th>Liquid biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sample type</strong></td>
<td>Primary tumour</td>
<td>CTCs¹</td>
</tr>
<tr>
<td></td>
<td>Intact cells</td>
<td>Intact cells</td>
</tr>
<tr>
<td></td>
<td>Invasive</td>
<td>Non-invasive³</td>
</tr>
<tr>
<td></td>
<td>Not always accessible</td>
<td>Accessible using Parsortix⁴</td>
</tr>
<tr>
<td><strong>Procedure</strong></td>
<td>Varies</td>
<td>Accessible</td>
</tr>
<tr>
<td></td>
<td>Varies</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Varies</td>
<td>Lower</td>
</tr>
<tr>
<td><strong>Sample accessibility</strong></td>
<td>Varies – difficult</td>
<td>Shorter</td>
</tr>
<tr>
<td></td>
<td>Very difficult</td>
<td>Easy</td>
</tr>
<tr>
<td><strong>Patient recovery time</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test costs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Test turnaround time</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Repeatability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Molecular analysis</strong></td>
<td>DNA</td>
<td>CNA (cfDNA²)</td>
</tr>
<tr>
<td></td>
<td>RNA</td>
<td>Fragmented DNA</td>
</tr>
<tr>
<td></td>
<td>Protein</td>
<td>non-invasive³</td>
</tr>
<tr>
<td><strong>Live cells</strong></td>
<td>Cell culture</td>
<td>Accessible</td>
</tr>
<tr>
<td></td>
<td>Xenograft</td>
<td>None</td>
</tr>
<tr>
<td><strong>Standard of care</strong></td>
<td>Proven</td>
<td>Lower</td>
</tr>
<tr>
<td></td>
<td>Proven</td>
<td>Shorter</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Easy</td>
</tr>
<tr>
<td></td>
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</tbody>
</table>

1. CTCs are live cancer cells circulating in the blood known as circulating tumour cells
2. cfDNA also known as ctDNA is cell-free circulating fragments of DNA from dead cells, which may be found in the plasma component of the blood
3. Tissue obtained from simple peripheral blood test
4. Access to CTCs technically challenging given low number of CTCs present and historically has been very difficult. ANGLE’s Parsortix system has been specially designed to address this issue
Far-reaching market potential

Emerging $ multi-billion market (Goldman Sachs $14bn in US alone by 2025)

Evidence-based approach to prove performance with ovarian cancer, FDA breast cancer
Substantiating value as sample collection platform
Partnering strategy for widespread deployment
Clinical Applications

- Ovarian Cancer Triage
- Metastatic Breast Cancer
- Prostate Cancer
- Colorectal Cancer
- Head & Neck Cancer
- Lung Cancer
- Pancreatic Cancer

1a Research Discovery
1b Pilot Study
2 Verification Study
3 Validation Study

Platform Clearance
**Clinical application**

**Ovarian cancer clinical studies: 400 patients**

- 400 patient European (ANG-001) and United States (ANG-003) studies
  - Medical University of Vienna, Charité and Vivantes
  - University of Rochester Wilmot Cancer Center

- **Both studies report positive results**

- **Potential to significantly out-perform current clinical care** in discriminating malignant from benign
  - up to 95% sensitivity and nearly double specificity of CA125
  - provide valuable gene expression information on malignant cases

**£300 million p.a. market potential**

- **Moving to Optimisation and Validation Phase**
  - Optimisation (6 months) to improve performance still further
  - Validation studies (12-18 months) to support CE Mark and FDA clearance
  - Opportunities for accelerated commercialisation via commercial partnerships

- **750,000 women p.a. with abnormal pelvic mass in US alone**

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*Dr Richard Moore, Director of the Gynecologic Oncology Division, University of Rochester Medical Center Wilmot Cancer Institute*  
"The 200 patient ANG-003 clinical study shows that the Parsortix test has the ability to accurately discriminate malignant from benign pelvic masses prior to biopsy or surgery. The test also offers key additional benefits over existing practice through the gene expression information it provides, which may help to further guide choices for targeted therapy in women with ovarian cancer. Additionally, the test may allow separate identification of patients with low malignant potential and/or other cancer types using a non-invasive liquid biopsy test."
Regulatory clearance for clinical use

Breast cancer FDA clearance progress (400 patient study)

- **Potential to be first FDA cleared system for harvesting cancer cells from blood**

- **Seeking FDA clearance in metastatic breast cancer**
  - breadth of clearance to provide flexibility
  - base clearance to which specific clinical uses can be added
  - ovarian cancer and other cancer types to follow

- **Analytical studies in progress**
  - precision and reproducibility (internally and externally)
  - limits of quantification and detection
  - accuracy and linearity
  - potential interferents and carryover

- **FDA clearance will differentiate Parsortix in markets worldwide**

- **ANG-002 clinical study plan developed in consultation with several world-class US breast cancer centres**
  - designed to meet FDA regulatory requirements
  - 200 metastatic breast cancer patients and 200 age appropriate healthy volunteers

- **MD Anderson, #1 cancer centre in the US, contracted to lead ANGLE FDA clinical study**

- **Contractual negotiations with 6 major cancer centres in progress**

- **Results expected H1 2018**
Non-invasive metastatic breast cancer biopsy £1 billion p.a. market potential

- CTCs harvested and RNA-Seq analysis successful for 100% of patients

- **CTCs from Parsortix liquid biopsy had similar patterns of expression for 192 genes to the traditional biopsy of cancer cells from metastatic sites in all cases (21 patient study)**

- Wide range of metastatic sites
  Skin, pleural effusion (fluid around the lung), pericardial effusion (fluid around the heart), breast, cerebrospinal fluid (fluid found in brain and spine) and bone tissue

- **CTCs provide information on 66 different pathways that may be targeted by new or existing cancer drugs**

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

“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 Parsortix as from an invasive tissue biopsy and indeed may be advantageous over invasive tissue biopsies in regards to the diverse sites of metastatic disease ...”
Non-invasive prostate biopsy

Barts Cancer Institute pilot studies
- harvested CTCs in 100% of patients (52 patient study)
- number of mesenchymal CTCs showed good correlation to Gleason score (80 patient study)

Simple blood test before solid biopsy test
- detect presence of prostate cancer
- assess aggressiveness of disease
- patient risk stratification – differentiate between active surveillance (indolent) or intervention (aggressive)

Blood cell discovery with Parsortix: cells identified as megakaryocytes linked to patient survival (n=40)
- option for worldwide exclusive licence over megakaryocyte IP

New Parsortix CMS (combined EMTed CTC and megakaryocyte score) predicts overall survival: patients 10x more likely to die

Dr Yong-Jie Lu, Reader in Medical Oncology at Barts Cancer Institute
“The exciting part of this research is the potential for the Parsortix system to be used to assess the severity of the disease as well as to detect it. This meets a key medical need to avoid over-treatment as well as to ensure treatment is available for patients who need it.”
QIAGEN Co-marketing Agreement

✈ QIAGEN leading molecular testing company
  1. 500,000 customers and $1.3bn revenues
  2. NGS (next generation sequencing), PCR (polymerase chain reaction), single cell analysis products and bioinformatics capabilities

✈ Selected Parsortix after year long evaluation process identifying key benefits of Parsortix
  1) Epitope-independent: captures all relevant cells
  2) Cells harvested intact and alive
  3) Highly sensitive: works with almost all patients

✈ Opportunity to extend co-marketing to cover Axela platform

✈ Similar partnerships planned with other leading companies

Michael Kazinski, QIAGEN’s Senior Director Molecular Preanalytic Technologies

“ANGLE’s Parsortix system is a unique, epitope-independent CTC solution offering easy, automated processing of whole blood to harvest all types of CTCs, including the clinically relevant mesenchymal CTCs, for analysis. It complements very well with our AdnaTest CTC portfolio, now allowing for both phenotypic and molecular characterization of CTCs. The modular combination abilities of this system with QIAGEN’s liquid biopsy-based Sample to Insight offering, including AdnaTest, our targeted RNAseq and single cell solutions, along with our bioinformatics offering, will allow scientists and clinical researchers to significantly advance their research.”
Axela provides multiplex downstream analysis of nucleic acid and protein expression in an easy to use, automated platform for up to 100 genes simultaneously.

Axela platform can deliver results similar to NGS at the cost of qPCR:
- NGS covers a vast number of genes but is expensive (c. $500 to $1,000 per sample) and complex to perform
- qPCR is low cost (c. $20 to $100 dependent on # genes) but can only provide information on a small number of genes
- Axela potential to provide information on a large number of genes at low cost: meeting key requirements for cancer

Genomic Health’s Oncotype DX is a breast cancer gene panel (21 genes) based on solid tissue biopsy, which has a list price of $4,175 (FY16 test revenue $327m)

Combining Parsortix™ and Axela would offer the opportunity to develop similar cancer gene panels for liquid biopsy (simple blood test)

Together with Axela, ANGLE has the potential to access the entire liquid biopsy value chain with a cost of goods <$100 (Oncotype DX cost of goods $483)
Expected Newsflow

- Customers and KOLs working in 20 different cancer types
  - developing peer-reviewed publications, posters and presentations
  - 5 new peer-reviewed publications in process

- Multiple customer and KOL reports at recent ACTC Conference, Rhodes

- FDA studies patient enrolment

- Ovarian cancer study results published

- Ovarian cancer assay optimised

- FDA studies complete H1 2018

- Additional corporate partnership deals (medtech, pharma, CRO)
Parsortix™ patented system developing a world-leading position in emerging $ multi-billion liquid biopsy market

- Providing the **Complete Picture** (viable, intact CTCs for DNA, RNA, and protein analysis not just ctDNA)
  - Widespread adoption by leading cancer centres in Europe and the United States
- FDA study to support platform clearance for metastatic breast cancer with results expected H1 2018
- Ovarian cancer application successfully moved into optimisation / validation phase
- Co-marketing agreement with QIAGEN
- Acquisition strengthens market differentiation and captures more of value chain