Parsortix Liquid Biopsy

Interim Results for the six months ended
31 October 2017

Andrew Newland and Ian Griffiths
31 January 2018
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Highlights

- **Positive clinical evidence from successful 400 patient Ovarian Cancer studies in Europe and US**
  - Acquisition of versatile Ziplex® downstream analysis system enables “sample to answer” solution with multiplex gene and protein expression

- **IRB approvals received for 400 patient Breast Cancer FDA Class II clearance clinical study with MD Anderson leading primary end point analysis**

- **Collaborations with two leading, global healthcare companies: QIAGEN and Philips**

- **Research use by world-leading cancer centres building with growing body of published evidence**
  - Breakthrough results in numerous areas including Prostate Cancer

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ANGLE’s Parsortix and Ziplex 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 tumour cell (CTC) solution with strong competitive differentiation
- Product based solution with instruments and cassettes
- Downstream analysis capability provides sample to answer solution

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Financial Highlights for the six months ended 31 October 2017

<table>
<thead>
<tr>
<th>Statement</th>
<th>2017</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement of Comprehensive Income</td>
<td>£'000</td>
<td>£'000</td>
</tr>
<tr>
<td>Revenue</td>
<td>188</td>
<td>219</td>
</tr>
<tr>
<td>Cost of sales</td>
<td>(54)</td>
<td>(43)</td>
</tr>
<tr>
<td>Gross profit</td>
<td>134</td>
<td>176</td>
</tr>
<tr>
<td>Operating costs</td>
<td>(4,245)</td>
<td>(3,088)</td>
</tr>
<tr>
<td>Other income</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>Loss before tax from continuing operations</td>
<td>(4,110)</td>
<td>(2,892)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Statement of Financial Position</th>
<th>31Oct17</th>
<th>30Apr17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trade and other receivables and R&amp;D tax credit</td>
<td>2,918</td>
<td>1,975</td>
</tr>
<tr>
<td>Inventories</td>
<td>854</td>
<td>665</td>
</tr>
<tr>
<td>Cash</td>
<td>4,281</td>
<td>5,536</td>
</tr>
<tr>
<td>Property, plant and equipment</td>
<td>849</td>
<td>824</td>
</tr>
<tr>
<td>Intangible assets</td>
<td>2,160</td>
<td>1,918</td>
</tr>
<tr>
<td>Total assets</td>
<td>11,062</td>
<td>10,918</td>
</tr>
</tbody>
</table>

Comments

- Research use sales established
  - >145 Parsortix instruments in active use
  - >39,000 blood separations have already been performed on the Parsortix system
- >70% gross margin
- Planned expenditure on clinical studies
- Cash position strengthened with £15m fundraise with majority of proceeds received post period end
- Leading institutional investors
  - Jupiter 14%
  - Legal & General 7%
  - Fidelity 6%
- Seeking a leading position in $ multi-billion emerging market
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
**Ziplex® high performance multiplex downstream analysis solution**

- **Ziplex® System**
  - Benchtop laboratory platform designed for routine and focused multiplex analysis of protein, DNA or RNA biomarkers
  - Sample to answer solution for distributed testing under development

- **HyCEAD chemistry**
  - Enables simultaneous measurement of 100’s of genes while eliminating multiplex PCR constraints
  - Rapid content creation for new applications, >500 target assays to date

- **Consumables**
  - Flow-thru TipChip® containing gene or protein expression panels for common pathways or disease processes
  - HyCEAD reagents and assay controls

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

- **Patented product solution**
### Benefits of Parsortix™ CTCs

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.

<table>
<thead>
<tr>
<th>Source</th>
<th>Solid tissue biopsy</th>
<th>Liquid biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Primary tumour</td>
<td>Metastatic site</td>
</tr>
<tr>
<td>Sample type</td>
<td>Intact cells</td>
<td>Intact cells</td>
</tr>
<tr>
<td>Procedure</td>
<td>Invasive</td>
<td>Invasive</td>
</tr>
<tr>
<td>Sample accessibility</td>
<td>Not always accessible</td>
<td>Less accessible</td>
</tr>
<tr>
<td>Patient recovery time</td>
<td>Varies</td>
<td>Longer</td>
</tr>
<tr>
<td>Test costs</td>
<td>Varies</td>
<td>Higher</td>
</tr>
<tr>
<td>Test turnaround time</td>
<td>Varies</td>
<td>Longer</td>
</tr>
<tr>
<td>Repeatability</td>
<td>Varies – difficult</td>
<td>Very difficult</td>
</tr>
<tr>
<td>Molecular analysis</td>
<td>DNA</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>RNA</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Protein</td>
<td>Yes</td>
</tr>
<tr>
<td>Live cells</td>
<td>Cell culture</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Xenograft</td>
<td>Yes</td>
</tr>
<tr>
<td>Standard of care</td>
<td>Proven</td>
<td>Proven</td>
</tr>
</tbody>
</table>

\(^{1}\) Access to CTCs through tissue biopsy is technically challenging given low number of CTCs present and historically has been very difficult.

\(^{2}\) Tissue obtained from simple peripheral blood test.

\(^{3}\) Access to CTCs using tissue biopsy is difficult.

\(^{4}\) 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)

ANGLE targets

Research use
- Screening trials

Clinical use
- Ovarian triage
- Prostate biopsy
- Metastatic breast

Tissue sample provision
- Platform feeding into existing molecular analysis systems for applications in all cancers in all segments “Parsortix inside”

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

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

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

**Ovarian studies completed: 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 reported 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**

- Ziplex worked very well with 65 genes in this study

- **Optimisation in progress to improve performance still further**

- Further studies (12-18 months) to support launch as a clinical assay

- Opportunities for accelerated commercialisation via commercial partnerships

- **750,000 women p.a. with abnormal pelvic mass in US market 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."
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 progressing well**
  - precision and reproducibility
  - limits of quantification and detection
  - accuracy and linearity
  - interferents and carryover
- **ISO13485 QMS system successfully approved for transition to new ISO13485:2016**
- **FDA clearance will differentiate Parsortix in markets worldwide**

- **ANG-002 clinical study commencing shortly**
  - 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, leading primary endpoint analysis** to confirm CTCs harvested for analysis
- **Secondary endpoints qPCR, FISH, RNA-Seq**
- **IRB approvals from MD Anderson and University of Rochester**
  - University of Southern California well advanced
- **Discussions with 3 other major cancer centres to participate in patient enrolment**
- **Studies expected to complete H2 CY18**
Non-invasive metastatic breast cancer biopsy  £1 billion p.a. market potential

- CTCs harvested and RNA-Seq analysis successful for 100% of patients (21 patient study)

- **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**

- 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

£3 billion p.a. market potential

**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 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

**New Parsortix CMS (combined EMTed CTC and megakaryocyte score) predicts overall survival: patients 10x more likely to die.** This may allow patients to receive stratified treatment

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**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.”
Co-marketing agreement with leading molecular testing company, QIAGEN

- QIAGEN leading molecular testing company
  - 500,000 customers and $1.3bn revenues
  - 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 Ziplex 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.”
Growing body of published evidence: recent breakthrough results

- 10 publications (30 April 2017: 4) and 19 posters (30 April 2017: 13)

- Barts Cancer Institute **megakaryocytes**: Parsortix CMS identifies patients 10x more likely to die

- University of Maryland **micro-tentacles** allows testing of drugs on living CTCs outside the patient

- University of Southern California **comparable gene expression** from blood as biopsy of metastatic site

- Heinrich Heine University Duesseldorf **cultured CTCs** to provide long term proliferation of cells

- Center for Women’s Health Tuebingen **harvested DTCs** responsible for relapse from bone marrow

- University of Hamburg, Medical University of Graz and Stockholm University detected **ARV7 transcripts** in prostate cancer linked to absence of response to Enzalutamide and Abiraterone

- Western University, Canada utilises Parsortix small volume adaptor in **mouse models**
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

- IRB approvals for FDA study to support platform clearance for metastatic breast cancer with studies expected to complete in H2 CY18

- Ovarian cancer application successfully completed 400 patient studies and in optimisation

- Collaboration agreements with QIAGEN and Philips

- Acquisition of Ziplex system provides unique potential for CTC sample to answer in liquid biopsy