Pioneering a liquid biopsy from a simple blood test with the aim of securing a leading position in the multi $ billion personalized cancer care market

Andrew Newland & Ian Griffiths
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Summary

- Increase in cancer incidence to 1 in 3 people set to drive a huge growth in market as personalized cancer care takes off
  - crucial medical need to be able to analyse individual patient’s cancer

- Parsortix patented circulating tumour cell (CTC) system harvests cancer cells from patient blood for analysis as a liquid biopsy

- Parsortix system established with strong, positive evaluations from leading cancer centers

- CE Mark for Europe in place. FDA authorisation in process for US
  - only one existing CTC system with FDA approval but that has limited application for counting cells and cannot harvest cells for analysis

- Major opportunities for commercial growth and collaboration
  - compatibility with existing major medtech analytical platforms (Roche, Illumina, Abbott, Life Technologies, Qiagen, Hologic, Agilent, Siemens Healthcare, bioMérieux etc)
  - key value generation for major pharma (development of new drugs, selection of patients for existing drugs, companion diagnostics)
US leads worldwide focus on personalized cancer care

“Personalized cancer care is the future of medicine. The faster we can develop cancer treatments that are tailored to the individual characteristics of each patient, the better we can concentrate interventions on those who will benefit the most from them and avoid the expense, side effects and emotional involvement on those who will not.”

“Each person is unique; each tumor is unique. This seemingly simple truth is the premise of personalized cancer therapy, a growing field based on analyzing these differences to find keys to unlock the mysteries of cancer.”

“A tumor contains a varied mix of cancer cells and the mix is constantly changing. This is known as tumor heterogeneity. The cells may have different sets of genes turned on and off — phenotypic heterogeneity — or have different numbers of genes and chromosomes — genetic heterogeneity.”

“Personalized treatment involves identifying characteristics of individual patients' tumors in order to determine their responsiveness to specific chemotherapy drugs. ... to determine which tumors are sensitive to a given drug and equally important, which tumors are resistant to specific drugs.”
Personalized cancer care

- Incidence of cancer growing. 1 in 3 people will suffer from cancer
  - 14 million new cases in 2012 up from 12.7 million cases in 2008
  - 8.2 million deaths up from 7.6 million

- Characteristic of cancer is that it continually evolves and mutates
  - Each patient’s cancer is different
  - The individual patient’s cancer changes over time

- Effective treatment requires personalized care
  - Understanding patient’s cancer
  - Selecting drugs that target their specific cancer
  - Advanced analytical techniques provide the key

- Healthcare economic pressures
  - Efficient and effective use of resources

- Major pharma are developing much more selective drugs
  - Colorectal cancer KRAS+ Cetuximab (Merck Serono)
  - Lung cancer EGFR+ Iressa (AstraZeneca)
  - Breast cancer HER2+ Herceptin (Genentech)
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 cancer
  - Lung cancer
  - Brain cancer

- Repeat tumour biopsy to see how the cancer may have changed is problematic as tissue not available for excision

**New approach: “liquid biopsy” harvest cancer cells from blood**

- Intense medical interest in liquid biopsy
- Non-invasive, repeatable, cost effective
- Challenge is only one CTC in one billion blood cells
The Parsortix system is a platform technology for harvesting rare cells from blood. In addition to cancer cells, other cells can be captured including fetal cells from maternal blood.
ANGLE’s patented Parsortix system

- **First Family** – Granted US Patent (expiry 8 November 2026) stepped, microscale cell separators for fluid flow and cell separation

- **Second Family** – Granted US Patent and patents pending worldwide (US expiry 2029) fetal cells and tumor cells specifically disclosed

- **Third Family** – Patents filed (20 years coverage) new capabilities
Parsortix cassette: captured cancer cells

Prostate cancer cells

Blood flow

- Lines are the Parsortix cell separation steps
- Two outer Steps (RHS) are 20µm apart. The inner steps are 10µm apart
- Large PC3 cells are shown captured on the outer steps

Colorectal cancer cells

Source: University of Surrey Oncology Dept

- CK20 – green
- CD45 – red
- Nuclear stain - blue
Positive evaluation. Key advantages:
- High level of capture (80-100%) and harvest (60-100%)
- Does not use antibody capture
- Exceptionally low WBC contamination
- Harvested cells can be analysed

Colorectal cancer patient validation
- High CTC capture rate
- Parsortix system demonstrated twice the sensitivity of currently accepted clinical practice for CTC capture

Cambridge Parsortix laboratory
- Bowel cancer including colorectal, pancreatic and oesophageal cancers
- New drug compounds
- Gene mutation analysis and next-generation sequencing (NGS)
Key opinion leaders Europe

- European leader in CTCs
- Successful six month evaluation
- Works with a wide range of cancers and all types of cancer cells
- Developing a liquid biopsy solution

- Specialising in ovarian cancer, which does not work with antibody systems
- Key player in Europe wide ovarian cancer group
- Testing RNA analysis with plans to move into drug trials
Key opinion leaders United States

- Professor Julie Lang, breast cancer surgeon
- American Society for Clinical Oncology guidelines
- Comparison of simple blood test using Parsortix with metastatic biopsy such as liver resection
- RNA and protein analysis including HER2 expression

- Professor Massimo Cristofanilli, acknowledged leader in CTCs since 2004
- "ANGLE’s Parsortix system offers the potential for two important advances. Firstly it captures all the relevant types of CTCs and secondly it provides an efficient means to harvest the cells for analysis"
Technical advantages of Parsortix over competing approaches

* Parsortix patented step system is simple, effective and affordable
  - Easy to use, automated, low user input

* Parsortix is a high performance, versatile system
  - Captures a high proportion of CTCs
  - Can be used with all solid tumour cancers (including breast, prostate, lung, colorectal, pancreatic, ovarian, cervical, brain)
  - Captured CTCs are intact, viable and undamaged
  - CTCs can be harvested (recovered from system) for analysis
  - Purity of CTCs very high (i.e. very low background contamination from white blood cells) allowing direct molecular analysis of harvested cells

* System does not use antibodies to capture cells
  - Antibody systems miss key target cells and do not work at all for some cancers
  - Antibody capture can compromise downstream molecular analysis
  - Antibody systems are complicated and expensive

* System does not use membranes to capture cells
  - Membrane systems can clog up and have high background contamination
  - CTCs cannot easily be harvested for analysis
Market advantages of Parsortix over competing approaches

- FDA submission in process
  - Potential to be the first FDA authorised CTC harvesting system

- In-house not CLIA (certified laboratory) remote service
  - Offer the hospitals a system that they can use in their own labs
  - Competitor systems without FDA approval can only offer a remote service
  - Parsortix in-house operation offers hospital customers a source of revenue

- Low production costs of machine and consumable
  - High margin potential
  - Cost competitive advantage
  - No costly antibodies

- Open source with wide application
  - All solid cancers and all applications
  - Designed to work with existing medtech platforms (not to compete with them)

- Compatible with cell-free DNA analysis
  - A single patient sample can be used for cell-free DNA and Parsortix CTC analysis
  - Parsortix RNA and protein analysis in addition to the DNA analysis of cell-free DNA
How ANGLE intends to secure its market position

- Focus on translational research with major US and international cancer centers (key opinion leaders)
- Go to market via commercial collaborations with major medtech and pharma companies
- Key opinion leader reporting on clinical applications supported by pilot studies
- Patient studies to support clinical applications
- FDA authorisation
- Roll out of sales
Summary

- Parsortix system harvests cancer cells from blood for analysis providing a liquid biopsy (simple blood test) and meets a major medical need:
  - Personalized cancer care
  - Early diagnosis, companion diagnostics and remission monitoring
  - Reduced costs

- Regulatory authorisation is in place in Europe and FDA is in process in United States

- ANGLE has established partnerships with world-leading cancer research groups to
  - Develop clinical applications
  - Undertake patient studies
  - Provide key opinion leader support

- Moving into commercialisation phase with partnerships with major medtech and pharma corporates planned

Parsortix system + regulatory authorisation + clinical application + patient data + key opinion leader = $bn market
“Personalized cancer care is the future of medicine. The faster we can develop cancer treatments that are tailored to the individual characteristics of each patient, the better we can concentrate interventions on those who will benefit the most from them and avoid the expense, side effects and emotional involvement on those who will not.”

“Personalised medicine is the most exciting change in cancer treatment since the invention of chemotherapy”
Professor Peter Johnson, Chief Clinician, Cancer Research UK

“The evaluation phase of our work is now successfully complete and we see great promise in the application of the Parsortix technology for harvesting CTCs for molecular analysis to enable personalised cancer care. We are now undertaking pilot studies using the Parsortix system in both colorectal cancer and pancreatic cancer.”
Deputy and Genomics Leader within the Clinical & Experimental Pharmacology group at Cancer Research UK Manchester Institute, Ged Brady

“This agreement will greatly facilitate the use of ANGLE’s Parsortix system in our research, and that of other colleagues in Cambridge. We foresee several exciting research avenues to test different applications of the Parsortix system in the diagnosis and personalised treatment of cancer.”
Medical Research Council Cancer Unit Director, Professor Ashok Venkitaraman
# Extensive clinical value in analysing CTCs

Potential Applications:

- Diagnosis
- Prognosis
- Mutational analysis and drug selection
- Drug development
- Treatment / drug effectiveness
- Remission monitoring

## Status

<table>
<thead>
<tr>
<th>Status</th>
<th>Pre-neoplastic Subclinical</th>
<th>Primary (-) CTCs and/or DTCs</th>
<th>Primary (+) CTCs and/or DTCs</th>
<th>Dormancy</th>
<th>Oligometastases</th>
<th>Systemic metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focus</td>
<td>Management of primary tumor</td>
<td>Prevention of metastasis</td>
<td>Prevention of metastasis</td>
<td>Treatment of metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Challenge</td>
<td>Early detection and prevention Identify high-risk patients</td>
<td>Prevent local and distant relapse Drug resistance of DTCs</td>
<td>Early detection of relapse Heterogeneity and drug resistance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New tools</td>
<td>Diagnostic markers</td>
<td>Prognostic markers</td>
<td>Profiling of primary tumor, metastases, CTCs and/or DTCs for accurate targeting Biomarkers and imaging technologies for disease monitoring Biomarkers for therapeutic efficacy</td>
<td></td>
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</tr>
</tbody>
</table>

## Possible treatment strategies

### Prophylactic treatment:
- Vaccination
- Surgery, radiotherapy (+) Systemic therapy
- Targeted therapy against driver oncogenes and their pathways tailored by genetic makeup of tumor cells
- Long-term adjuvant treatment (for high-risk patients):
  - Metronomic chemotherapy and anti-angiogenesis
  - Targeting common driver oncogenes and pathways
  - Immunotherapy
  - Targeting dormancy-related survival and CSC signaling and niche components
- Systemic therapy
- Immunotherapy
- Stroma-targeting treatments
- Palliative radiation and/or surgery
- Surgery stereotactic radiotherapy

### DTC and/or CTC survival pathways; stem cell features; tumor-stroma crosstalk and niche factors
- Activation of metastasis-suppressive signaling

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*Nature Medicine 11 November 2013: Tumor metastasis: moving new biological insights into the clinic*

*Liling Wan (Princeton University), Klaus Pantel (Hamburg University), Yibin Kang (Cancer Institute of New Jersey)*
Large growing market

Crucial drivers for diagnostics
- Early detection
- Targeted medication
- Reduced costs

Current molecular cancer testing market
(a subset of the Parsortix market)

<table>
<thead>
<tr>
<th>New cancer sufferers p.a.</th>
<th>Deaths p.a.</th>
<th>People alive who have had cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual (2012)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>1,824,701</td>
<td>1,589,925</td>
</tr>
<tr>
<td>Breast</td>
<td>1,676,633</td>
<td>521,907</td>
</tr>
<tr>
<td>Colorectum</td>
<td>1,360,602</td>
<td>693,933</td>
</tr>
<tr>
<td>Prostate</td>
<td>1,111,689</td>
<td>307,481</td>
</tr>
<tr>
<td>Cervix, uterus and ovary</td>
<td>1,085,948</td>
<td>493,749</td>
</tr>
<tr>
<td>Stomach</td>
<td>951,594</td>
<td>723,073</td>
</tr>
<tr>
<td>Blood</td>
<td>917,907</td>
<td>570,629</td>
</tr>
<tr>
<td>Liver</td>
<td>782,451</td>
<td>745,533</td>
</tr>
<tr>
<td>Other</td>
<td>4,378,624</td>
<td>2,555,345</td>
</tr>
<tr>
<td>Total</td>
<td><strong>14,090,149</strong></td>
<td><strong>8,201,575</strong></td>
</tr>
</tbody>
</table>

More than 1 in 3 people will get cancer

Growth in cancer worldwide
- Age
- Developing countries
- Smoking
- Obesity
- Lack of exercise
- Alcohol
- Other unknown


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Board and Senior Management

Non-executive Chairman, Garth Selvey BSc in Physics and Electronics Engineering. 36 years computer industry. Comino Group plc.

Chief Executive, Andrew Newland MA Engineering from Cambridge, Chartered Accountant. 25 years, building technology-based businesses 15 years specialist medtech

Finance Director, Ian Griffiths BSc Mathematics with Management Applications and Chartered Accountant. Technology commercialisation 20 years new technology based businesses

Non-executive director, Brian Howlett. Lombard Medical Technologies PLC. Boston Scientific Ltd. Cobe Laboratories Inc. 20 years pharmaceuticals Fisons plc

US Vice President, Peggy Robinson B.S., Biology / Medical Technology American Society of Clinical Pathologists Director of marketing for Johnson & Johnson company Veridex, responsible for CellSearch® Research Use

Chief Technology Officer, Dr Shane Booth PhD Biochemistry. Post doctoral experience Fred Hutchinson Cancer Center in Seattle. Sales, marketing and business development in laboratory equipment with Sartorius and Anderman

Business Development Director, Michael O’Brien MA Engineering from Cambridge. MBA specialising in technology commercialisation. 8 years in strategy and operations and work with Diageo on manufacturing and technology strategy

Head of Manufacturing and Regulatory, Martin Cooke MEng degree in Electrical and Electronic Engineering. Chartered Engineer. Previously product manager global telecommunications responsible for product development and market introductions
Scientific Advisers

Dr Harold Swerdlow, VP of Sequencing at the New York Genome Centre. Formerly, Head of Research and Development for the Wellcome Trust Sanger Institute, expert in next-generation sequencing (NGS). Inventor of NGS at Solexa acquired by Illumina

Dr Ashok Venkitaraman, Professor of Cancer Research at the University of Cambridge. Director of Medical Research Council’s Cancer Cell Unit. Joint Director of the Medical Research Council Hutchison Cancer Research Centre

Dr Adrian Newland, Professor of Haematology at Barts Health NHS Trust and Queen Mary University of London. Chair, Diagnostics Assessment for National Institute for Health and Clinical Excellence (NICE) for new diagnostics. Member NICE Group for cancer drugs

Dr Clive Stanway, Chief Scientific Officer of CRUK’s Cancer Research Technology. Expert in cancer drug discovery and key role in working closely with major pharmaceutical partners
### Financials year end 30 April (shown in GBP £’000)

<table>
<thead>
<tr>
<th>Statement of Comprehensive Income</th>
<th>2014</th>
<th>2013</th>
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<tbody>
<tr>
<td>Revenue</td>
<td>801</td>
<td>969</td>
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<tr>
<td>Investments portfolio gain</td>
<td>1,334</td>
<td>514</td>
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<tr>
<td></td>
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<tr>
<td>Operating costs</td>
<td>(3,485)</td>
<td>(2,556)</td>
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<tr>
<td>Other income</td>
<td>112</td>
<td>42</td>
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<tr>
<td>Loss before tax</td>
<td>(1,238)</td>
<td>(1,031)</td>
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<table>
<thead>
<tr>
<th>Statement of Financial Position</th>
<th>30Apr14</th>
<th>30Apr13</th>
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<tbody>
<tr>
<td>Investments</td>
<td>601</td>
<td>3,961</td>
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<tr>
<td>Trade and other receivables</td>
<td>328</td>
<td>454</td>
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<tr>
<td>Inventories</td>
<td>52</td>
<td>62</td>
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<tr>
<td>Cash</td>
<td>3,898</td>
<td>1,828</td>
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<tr>
<td>Property, plant and equipment</td>
<td>139</td>
<td>138</td>
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<tr>
<td>Intangible assets</td>
<td>1,142</td>
<td>1,080</td>
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<tr>
<td>Total assets</td>
<td>6,160</td>
<td>7,523</td>
</tr>
</tbody>
</table>

- Listed on London Stock Exchange AIM market; IPO 2004
- 45,243,059 issued shares trading at c. $1.15
- American Depositary Receipts with BNY Mellon trading on OTC-QX
- 1 ADR = 10 shares trading at c. $11.50
- Stock liquidity 90 day average volume c. $150,000 / day
Contact details

Andrew Newland
ANGLE plc
3 Frederick Sanger Road
The Surrey Research Park
Guildford GU2 7YD
United Kingdom

Tel: +44 1483 685830
Email: andrew.newland@ANGLEplc.com
Website: www.ANGLEplc.com

3711 Market Street
University Science Center 8th floor
Philadelphia PA 19104
USA

Tel: +1 (267) 265 6761