

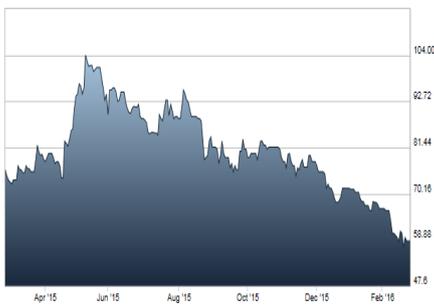
### Revolutionary new liquid biopsy approach to detecting cancer

#### Speculative Buy

Price: 58.50p

Sector: Biotech & Pharma

#### Share Price Performance



Source: London Stock Exchange

#### Key Data

Market:	London (AIM)
TIDM:	<a href="#">AGL.L</a>
1 Year Hi/Lo:	107.8p – 55.8p
Existing Shares:	58.97m
Market Cap:	£34.49m
ISIN:	GB0034330679
SEDOL:	3433067
Co. Website:	<a href="http://www.angleplc.com">www.angleplc.com</a>

#### Barry Gibb

Research Analyst

[barry.gibb@beaufortsecurities.com](mailto:barry.gibb@beaufortsecurities.com)

+44 020 7382 8422

#### Andy Senga

Junior Research Analyst

[Kazunaga.senga@beaufortsecurities.com](mailto:Kazunaga.senga@beaufortsecurities.com)

+44 020 7382 8407

Like most good ideas, this one is very simple. ANGLE's patented 'separation technology' makes possible a revolutionary new 'liquid biopsy' approach to conventional diagnostic methods which, in particular, have significant application in cancer detection. Using a competitively differentiated peripheral blood draw to harvest cancer cells, Parsortix is non-invasive, exceptionally accurate, easily repeatable and highly specific to each patient. Its product-based solution has potential addressable markets in the US alone estimated to be as large as US\$14bn by 2025. Already available for research use and collaboration projects, clinical application is where the giant opportunity for Parsortix will be found. The FDA, of course, is the world's hardest regulatory taskmaster, from whom seeking authorisation often takes much longer and is more expensive than first anticipated. Positive evaluations in lung, prostate and breast cancer during H2'2015, nevertheless support a very optimistic scenario for the product's future development.

- ANGLE is attempting to make a paradigm change by making it easier to isolate circulating tumour cells ('CTCs') from patient blood for a wide range of cancer indications. Clinical application progress to date by key-opinion-leaders of the international medical fraternity has produced highly successful patient studies, with minimal false outcomes while demonstrating overwhelming superiority to competing systems:
  1. *Medical University of Vienna – 100% specificity in primary epithelial ovarian cancer*
  2. *Barts Cancer institute – Harvested cancer cells from the blood of 100% of prostate cancer patients*
  3. *University of S. California – Obtained the same genetic information from a simple blood test as the invasive solid biopsy of the secondary cancer site in breast cancer*
  4. *Cancer Research UK & Christie Hospital – Harvested cancer cells from 100% of lung cancer patients*
- The medical world needs a new approach. Right now, the only route is for clinicians to carry out a solid tumour biopsy, by cutting out and analysing the cancer cells. This involves complex and costly invasive procedure, including mastectomy, lumpectomy, colorectal colonoscopy, prostatectomy etc., where repetition can be problematic or agitate the symptoms. The key USP in Parsortix's liquid biopsy approach is its ability to robustly capture and then harvest for analysis just a single CTC within 1bn blood cells.
- Very importantly, the US Patent Office has already granted Parsortix two US patents (along with China, Canada and Australia) on its separation technology and patents are pending in all major economic territories worldwide - so ANGLE has a prospective monopoly over its use.
- So what are the immediate challenges? These focus on gaining regulatory authorisation, while also challenging claims from emerging competitive technologies of their ability to deliver similar therapeutic outcome. The Parsortix system centres around the use of micro-fluidic technology in the form of a disposable cassette. FDA authorisation for its use as a general platform for detection and identification of cancer will require it to routinely and unchangingly deliver diagnostic results with minimum occurrence of false negatives and false positives. Proving such an outcome through extensive clinical trials will undoubtedly take time and incur costs. The Group's balance sheet presently holds cash sufficient to see it through to H1'2017; assuming further clinical progress is made with Parsortix's first selected indication, ovarian cancer, it should not be difficult to attract new funding, from either ordinary shareholders or commercial collaborators. That assumes, of course, that credible new competition does not suddenly complicate the competitive landscape. Recently, for example, there has been press from UCLA in relation to a saliva based cancer diagnostic. Unlike Parsortix, however, this is many years from market and is limited only to cancer detection for a small number of indications. By contrast, ANGLE's Parsortix system is already in the market, and works for a wide range of cancers, not just for detection but also for therapy selection.

**ANGLE plc - a commercially driven specialist medical diagnostic company**

ANGLE introduces pioneering products in cancer diagnostics and foetal health. Its lead product is the Parsortix cell separation system, which can capture very rare cells from blood. This includes circulating tumour cells in cancer patients' blood – even when there is less than one CTC in one billion healthy cells. The resulting liquid biopsy (simple blood test) enables the investigation of mutations in the patient's cancer for personalised cancer care. ANGLE has launched a product for the research market and has secured CE Mark regulatory approval for the clinical market in Europe. The FDA approval process is underway for the clinical market in the US.

**An urgent need Cancer Research**

UK's statistics suggest that men have a 45% likelihood of suffering cancer during their life. Women are only slightly lower at 41%. During treatment for the disease, particularly secondary (metastatic) disease, there are a number of challenges, including: How does the clinician know which drug will work most effectively on a patient? How does the clinician track whether drugs are in fact working and having a positive impact? How do clinicians monitor patients who are in remission to pick up any return of disease? The above treatment challenges can be complicated further with the fact that the form of the disease can evolve over time meaning that a drug that would not have been effective at one point, may at a later point turn out to be effective. In order to treat patients effectively, doctors need to deploy drugs that target the individual patient's cancer at that point in time. This approach is called 'personalised cancer care' and in recent years has become accepted worldwide as the most likely way to improve patient outcomes in the long run.

There is therefore a crucial need for ongoing information as to a patient's cancer status. Primary tumours will be completely removed if possible and hence repeat biopsy is not an option. Biopsy of secondary disease sites tends to be far more difficult, it is also both highly invasive and costly. Solid tumour cancers, such as breast cancer and prostate cancer, shed cancer cells into the patient's blood stream. CTCs are very rare, perhaps a single cell in one billion blood cells, and as a result are very difficult to isolate. They are however extremely valuable cells since they contain information on the type of disease – which has the potential to inform on 'personalised' care decisions and targeted drug therapies. Their presence and quantity has been shown to be indicative of patient prognosis. They are very likely to be the route by which primary (localised) tumours spread around the body so resulting in metastatic disease. The Parsortix system from ANGLE is able to capture and harvest CTCs from patient blood. This means that a simple peripheral blood test could be used to provide crucial medical information regarding the changing status of a patient's disease.

It is widely agreed that such a 'liquid biopsy' would have a profound impact in understanding the patient's current cancer status and ensuring the optimum treatment is deployed for that individual patient at that particular time. ANGLE's ultimate objective is the widespread adoption of the Parsortix system in the diagnosis and treatment of cancer patients. According to the World Health Organisation, there were an estimated 14 million new cancer cases worldwide in 2012, a marked rise on the 12.7 million cases in 2008. In 2012, there were an estimated 32.6 million people living with cancer (Source: [http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx)). The incidence of cancer continues to grow as a result of demographic, lifestyle and environmental factors and it is estimated that one in three people in the UK will get cancer during their lifetime. There are a wide range of potential applications for harvested CTCs including diagnosis, prognosis, mutational analysis and drug selection, drug development, assessment of treatment effectiveness, and remission monitoring. ANGLE's management estimate that this represents a potential global market for its Parsortix system worth in excess of £8 billion per annum. ANGLE's major focus is on the cancer market. There is also a substantial market available in non-invasive foetal diagnostics, harvesting foetal cells from the pregnant mother and analysing for Down's Syndrome and many other chromosomal and genetic conditions through a simple blood test.

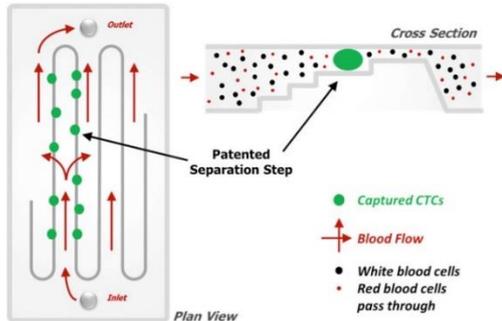
The Group has a clear strategy to commercialise its Parsortix technology. The cell capture and harvesting technology consists of a cell separation cassette together with an automated system to run blood samples through the cassette. There is extensive intellectual property protection around key elements of the system. Successful evaluation of the system by major cancer research centres has already been achieved and a major part of ANGLE's current efforts relate to further deployment with key opinion leaders in the field. Regulatory authorisation for the clinical use of the system in patient treatment in the EU has already been achieved and the process is ongoing with the FDA for the USA.

Widespread adoption of the Parsortix system in the clinical market crucially depends on ongoing work with key opinion leaders. Accordingly, ANGLE has completed numerous pilot studies assessing clinical applications for CTCs from which the most promising were selected. Beyond this the Group is planning to undertake larger patient studies providing fully documented evidence of how the system should be used for particular patient applications in routine treatment.

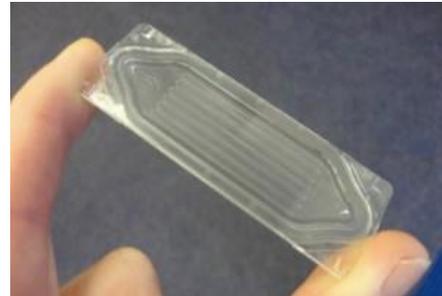
## How the Parsortix System Works

The Parsortix system from ANGLE uses a patented micro-fluidic technology in the form of a disposable cassette to capture and then harvest CTCs from blood. The cassette captures CTCs based on their less deformable nature and larger size compared to other blood components.

### Disposable Cassette



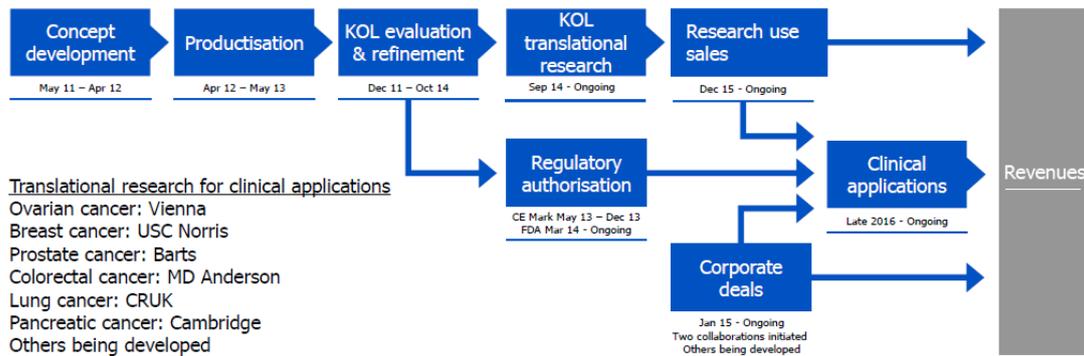
Source: Angle



Source: Angle

The disposable cassette is placed in a clamp, and the Parsortix system then automatically processes the patient sample. CTCs are caught on a step that criss-crosses the microscope slide sized cassette. Captured cells can be fixed and stained in the cassette to allow in-cassette identification and enumeration. Alternatively, they can be harvested from the system for analysis using established analytical systems. The system is available for research purposes globally. The Parsortix system is CE marked for use as an in-vitro diagnostic device in the EU and the Company is seeking FDA approval for clinical purposes in the US.

### Parsortix - Path to commercialisation



Source: Angle

## Strengths and Weaknesses

### Strengths

- ✓ Liquid biopsy market in the US alone estimated to be c.US\$14bn by 2025
- ✓ First research use sales have been secured
- ✓ Highly successful patient studies with minimal false positives or negatives
- ✓ International patents granted
- ✓ Experienced management team, Board of Directors and scientific advisers

### Weaknesses

- Additional financing requirements anticipated as it proceeds with multiple clinical applications
- Possible emergence of competitive technologies
- FDA approvals generally take longer and are more expensive than originally envisaged
- Possible legal cost of defending patent/intellectual property

Sources: Company website, Company RNS, Bloomberg, ProQuote, London Stock Exchange, Investee Companies' web sites, International Agency for Research on Cancer, World Health Organization

**Recommendations**

During the three months to end-January 2016, the number of stocks on which Beaufort Securities has published recommendations was 310, and the recommendations were as follows: Buy - 103; Speculative Buy - 194; Hold - 13; Sell - 0.

Full definitions of the recommendations used by Beaufort Securities in its publications and their respective meanings can be found on our website [here](#).

This report is published by Beaufort Securities ("Beaufort Securities"). Beaufort Securities is Authorised and Regulated by the Financial Conduct Authority and is a Member of the London Stock Exchange.

This research is non-independent and is classified as a Marketing Communication under FCA rules. As such it has not been prepared in accordance with legal requirements designed to promote independence of investment research and it is not subject to the prohibition on dealing ahead of the dissemination of investment research in COBS 12.2.5. However Beaufort Securities has adopted internal procedures which prohibit analysts from dealing ahead of non-independent research, except for legitimate market making and fulfilling clients' unsolicited orders.

**RELIANCE ON THIS NOTE FOR THE PURPOSE OF ENGAGING IN ANY INVESTMENT ACTIVITY MAY EXPOSE AN INDIVIDUAL TO A SIGNIFICANT RISK OF LOSING ALL OF THE FUNDS, PROPERTY OR OTHER ASSETS INVESTED OR OF INCURRING ADDITIONAL LIABILITY.**

By receiving this document, you will not be deemed a client or provided with the protections afforded to clients of Beaufort Securities. When distributing this document, Beaufort Securities is not acting for any recipient of this document and will not be responsible for providing advice to any recipient in relation to this document. Accordingly, Beaufort Securities will not be responsible to any recipient for providing the protections afforded to its clients.

Beaufort Securities may effect transactions in shares mentioned herein and may take proprietary trading positions in those shares, and may receive remuneration for the publication of its research and for other services. Beaufort Securities may be a shareholder in any of the companies mentioned in this report. Accordingly, this document may not be considered as objective or impartial. Additionally, information may be available to Beaufort Securities or the Group, which is not reflected in this material. The remuneration of the author of this report is not tied to the recommendations on any shares mentioned nor to the any transactions undertaken by Beaufort Securities or any affiliate company. Further information on Beaufort Securities' policy regarding potential conflicts of interest in the context of investment research and Beaufort Securities' policy on disclosure and conflicts in general are available on request.

Please refer to <http://www.beaufortsecurities.com/important-info>.

This document is not an offer to buy or sell any security or currency. This document does not provide individually tailored investment advice. It has been prepared without regard to the individual financial circumstances and objectives of persons who receive it. The appropriateness of a particular investment or currency will depend on an investor's individual circumstances and objectives. The investments and shares referred to in this document may not be suitable for all investors.

**Past performance is not a guarantee of future performance. Investments may go down in value as well as up and you may not get back the full amount invested. The listing requirements for securities listed on AIM or ISDX are less demanding and trading in them may be less liquid than main markets.**

This document is based on information Beaufort Securities has received from publicly available reports and industry sources. Beaufort Securities may not have verified all of this information with third parties. Neither Beaufort Securities nor its advisors, directors or employees can guarantee the accuracy, reasonableness or completeness of the information received from any sources consulted for this publication, and neither Beaufort Securities nor its advisors, directors or employees accepts any liability whatsoever (in negligence or otherwise) for any loss howsoever arising from any use of this document or its contents or otherwise arising in connection with this document (except in respect of wilful default and to the extent that any such liability cannot be excluded by the applicable law). This document is not to be relied upon and should not be used in substitution for the exercise of independent judgment.

This document includes certain statements, estimates, and projections with respect to the anticipated future performance of securities listed on stock exchanges and as to the market for these shares. Such statements, estimates, and projections are based on information that we consider reliable and may reflect various assumptions made concerning anticipated economic developments, which have not been independently verified and may or may not prove correct. No representation or warranty is made as to the accuracy of such statements, estimates, and projections or as to its fitness for the purpose intended and it should not be relied upon as such. Opinions expressed are our current opinions as of the date appearing on this material only and may change without notice. Other third parties may have issued other reports that are inconsistent with, and reach different conclusions from, the information presented in this report. Those reports reflect the different assumptions, views, and analytical methods of the analysts who prepared them. This report has not been disclosed to any of the companies mentioned herein prior to its publication.

The information contained in this document is confidential and is solely for use of those persons to whom it is addressed and may not be reproduced, further distributed to any other person or published, in whole or in part, for any purpose. Other persons who receive this document should not rely on it. Beaufort Securities, its directors, officers and employees may have positions in the securities mentioned herein.

© Beaufort Securities Ltd  
131 Finsbury Pavement, London EC2A 1NT

Company Name	Disclosure
Angle Plc	N/A

- In the past 12 months, Beaufort Securities Limited or its affiliates have had corporate finance mandates or managed or co-managed a public offering of the relevant issuer's securities or received compensation for Corporate Finance services from the relevant issuer.
- Beaufort Securities Limited expects to receive or intends to seek compensation for Corporate Finance Services from this company in the next six months.
- The investment analyst or a member of the investment analyst's household has a long position in the shares or derivatives of the relevant issuer.
- The investment analyst or a member of the investment analyst's household has a short position in the shares or derivatives of the relevant issuer.
- As of the month end immediately preceding the date of publication of this report, or the prior month end if publication is within 10 days following a month end, Beaufort Securities Limited and / or its affiliates beneficially owned 1% or more of any class of common equity securities of the relevant issuer.
- A senior executive or director of Beaufort Securities Limited or a member of his or her household is an officer, director or advisor, board member of the relevant issuer and / or one of his subsidiaries.
- Beaufort Securities Limited acts as corporate broker to the relevant issuer.

The investment analyst who is responsible for the preparation of this investment research is employed by Beaufort Securities Limited.