EDISON

Angle

Company update

Prostate cancer application gains momentum

Pharma & biotech

Today Angle has announced results from a prostate cancer research study carried out by its KOL partner Barts Cancer Institute (BCI). The final data are yet to be published, but headline results indicate that Parsortix can potentially perform as well as or better than current standard of care in terms of detecting early-stage prostate cancer and assessing its severity, and can do so with a simple blood test. While this will require further clinical studies, it represents a likely second clinical application, in which Parsortix can substantially affect the management of cancer patients.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
04/14	0.0	(2.0)	(2.4)	0.0	N/A	N/A
04/15	0.0	(3.6)	(7.5)	0.0	N/A	N/A
04/16e	0.3	(5.2)	(8.5)	0.0	N/A	N/A
04/17e	2.2	(3.2)	(5.1)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of intangibles, exceptional items and share-based payments.

New prostate cancer data from BCI

Close cooperation with key opinion leaders (KOLs) is at the heart of Angle's strategy in investigating the efficacy of the Parsortix cell separation system in diagnosing and treating various cancers. Angle's partner BCI presented latest data from its prostate cancer study at the 10th ISMRC International Symposium on Minimal Residual Cancer: Liquid Biopsy in Cancer Diagnostics and Treatment in Hamburg on 19-21 March. While the full results will be published in upcoming months, headline data suggest Parsortix potentially is as good as or better than current standard of care tests in detecting and assessing the aggressiveness of the prostate cancer and, importantly, can achieve this with a simple blood test as opposed to the current invasive solid biopsy procedures.

Parsortix potentially outperformed standard of care

During the study the researchers found that Parsortix detected circulating tumour cells (CTCs) in 100% of the metastatic prostate cancer patients. Parsortix was able to harvest CTCs even from men with the early stage of the disease, who were under active surveillance where it was deemed that an intervention was not necessary. There was a good correlation between the number of mesenchymal CTCs harvested by Parsortix and the Gleason scores (see page 2) suggesting that Parsortix may be able to provide the same or similar information as the biopsy in assessing the aggressiveness of the cancer. Finally, the results suggest that Parsortix may be able to indicate the metastatic or localised status of the disease with a higher level of accuracy than the Gleason score, which is the established method for determining the aggressiveness of the cancer, but requires an invasive solid biopsy.

Valuation: DCF-based valuation of £95m

The results are encouraging and we expect Angle will provide an update on the strategy for prostate cancer in the coming months, which may bring clarity about commercialisation. Once that is available, we will review our financial forecasts and the assumptions underlying our DCF-based valuation which, prior to adjustments for the new developments, is unchanged at £95m or 161p/share.

21 March 2016

Price	**70.5p**
Market cap	**£42m**

Net cash (£m) at 30 October 2015	5.8
Shares in issue	59.0m
Free float	89%
Code	AGL
Primary exchange	AIM
Secondary exchange	OTC QX

Share price performance

%	1m	3m	12m
Abs	23.7	3.7	(7.5)
Rel (local)	19.1	2.1	1.9

52-week high/low	104p	55p

Business description

Angle is a pure-play specialist diagnostics company. The proprietary Parsortix cell separation platform can be used for the detection and harvesting of very rare cells from a blood sample, including circulating tumour cells (CTCs). The resulting liquid biopsy enables the analysis of these cells for precision cancer care.

Next events

Results from KOL studies in other cancer indications	H216
Start of enrolment for ovarian cancer clinical trial	H116
FY16 results	July 2016

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Edison profile page

Prostate cancer – potential second application for Parsortix

Prostate cancer is unique in its high mortality due to complications caused by metastases combined with a high prevalence of non-metastasised disease that does not necessarily lead to death. Many prostate cancer patients have low-risk disease and are on "watchful waiting" and the disease may not necessarily progress to advanced cancer. For example, in contrast with lung cancer, which accounts for 14% of new cases annually, but 28% of cancer deaths in men; prostate cancer accounts for 26% of new cases but only 9% of deaths (American Cancer Society). Historically, often false positive screening and fear of incurable and unpredictable metastasis led to overtreatment of localised disease and avoidable harm to patients. Therefore, better prediction and knowledge of the biology of metastasis can improve care across the spectrum.[1]

Prostate cancer detection

Management of prostate cancer starts with screening, which is based on digital rectal exam and blood test for prostate-specific antigen (PSA), which so far has been the corner stone for the decision to refer patients to prostate biopsy. This is typically trans-rectal and in total can require up to 18 samples of tissues, which means 18 aspirations with a biopsy needle. Needless to say, a blood-based test is a much more convenient option. Overall, screening of prostate cancer is controversial to say the least. This is because PSA has low specificity and leads to large number of false positives, which results in a number of unnecessary biopsies. Indeed, estimates (cancer.gov) suggest that less than 10% of solid prostate biopsies indicate the need for treatment with around 80% showing a benign tumour. Over half of the identified malignant tumours require watchful waiting rather than treatment. On the other hand, solid prostate biopsy also poses challenges and may incorrectly draw conclusions relating to the aggressiveness of the disease.

Once a sample of prostate tissue has been obtained after the operation or biopsy, Gleason score is calculated based on the histological findings. It is one of the most established indicators of prognosis for prostate cancer patients. The Gleason score is composed of Gleason grades, which denote how abnormal the prostate cells look.

Where does the Parsortix system fit?

PSA lacks accuracy in reflecting disease burden and has low specificity, meaning that a lot of patients are unnecessarily referred to prostate biopsy. CTC analysis can fulfil the role of a biomarker by serving as an accurate, non-invasive measure of disease and can be followed throughout the course of the disease. In addition, the unreliability of PSA is a challenge in clinical trials, therefore a non-invasive biomarker could be well suited for use in clinical trials.

In many ways, CTC analysis is well suited to prostate cancer cases. However, to date, CTCs have been most extensively studied and qualified in advanced disease.[1] CellSearch is the only FDA-approved circulating tumour-cell (CTC) capturing device approved for enumeration of CTCs including an application in prostate cancer. It isolates CTCs using magnetic particles coated with antibodies that bind to a cell surface marker called anti-epithelial cell adhesion molecule (EpCAM). Once extracted, CTCs are enumerated, which has been proven to have prognostic value for progression-free survival and overall survival in patients with breast, colon, prostate and lung cancers.[2]

The data presented by the BCI indicate that Parsortix has the potential to be used much earlier in the disease. The exact process of metastasis is still unclear, but emerging data in this field point to epithelial

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1 B. Hu et al. Circulating Tumor Cells in Prostate Cancer. Cancers 2013, 5, 1676-1690; doi:10.3390/cancers 5041676

2 J. de Bono et al. Circulating Tumor Cells Predict Survival Benefit from Treatment in Metastatic Castration-Resistant Prostate Cancer. Clin Cancer Res 2008;14:6302-6309.

mesenchymal transition (EMT) being involved. EMT is the process in which malignant epithelial cells gain migratory and invasive properties.[1] Due to EMT circulating tumour cells may express fewer cell surface markers, like EpCAM. Therefore, antibody-based systems such as CellSearch limited to detecting epithelial markers could fail to detect spreading cancer. Parsortix uses a patented step-based microfluidic technology to capture CTCs on the basis of their size and compressibility, and therefore is not limited by cell marker bias. This puts Angle's Parsortix system in a strong competitive position.

The EMT circulating tumour cells were the cells analysed by BCI researchers using the Parsortix system to determine the aggressiveness of the disease. Since only headline results were released from the BCI study, it is premature to pinpoint the positioning of Parsortix in management of prostate cancer patients; however, two clear directions of use seem to be the detection of the cancer and the assessment of the aggressiveness, which impacts the interventional treatment. In particular the finding that Parsortix may be able to indicate the metastatic or localised status of the disease with a higher level of accuracy than the Gleason score looks to be striking, but will still need to be repeated in larger-scale trials.

Angle now intends to work with BCI and other cancer centres to conduct clinical studies to validate the use of the Parsortix system as a clinical application in the routine detection, assessment and treatment of prostate cancer patients. The company expects to take at least 18 months to complete the studies, while financial details remain undisclosed.

Prostate cancer could open multiple times larger market

We keep our valuation of Angle unchanged at £95m or 161p/share. Although we can see a substantial opportunity for Parsortix in prostate cancer, this application is still at an early stage, but today's news is clearly a positive step forward. We believe that Angle will provide more details about the development strategy in this direction in the upcoming months, which is when we will revisit the possibility of adding it to our model.

As a reminder, this is a second clinical application gaining momentum. The trial with Parsortix helping to triage women with ovarian masses before surgery is due to start in partnership with the Medical University of Vienna in H116 (our expectation). In addition, metastatic breast cancer is being investigated in the US as a part of Parsortix's FDA regulatory approval process.

In our valuation, we continue to include only the sales of the Parsortix system for use in research and clinical sales in ovarian mass triaging for operation. For comparison, we estimate c 600 thousand women underwent an operation due to adnexal masses globally. The prostate cancer population is substantially larger with c 220 thousand new cases in the US alone and over one million prostate biopsies per year in the US alone (cancer.gov). Based on the headline results from the BCI it is too early to exactly define the target population, but the finding that Parsortix correlates well with the Gleason score makes it potentially relevant for almost all stages of the disease and likely could be used repeatedly as a follow up. Currently there are c 2.9 million men living with some stage of the disease (American Cancer Society), which would represent an addressable population for Parsortix in the US alone.

Exhibit 1: DCF valuation

Key assumptions	NPV (£m)
Free cash flow model FY16-25e	17.9
Tapering growth free cash flows FY26-35e	36.3
Terminal value (2% growth rate assumed)	35.0
Total NPV	89.2
Net cash (Oct 30th 2015)	5.8
Valuation (£m)	95.0
Valuation/share (p)	161.2
Discount rate	10%
Tax rate	20%

Source: Edison Investment Research

Exhibit 2: Financial summary

£000s	2014	2015	2016e	2017e
Year end April	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	0	0	341	2,186
Cost of Sales	0	0	(102)	(648)
Gross Profit	0	0	238	1,537
Research and development	(900)	(1,600)	(3,080)	(2,458)
EBITDA	(1,994)	(3,452)	(5,093)	(3,059)
Operating Profit (before amort. and except.)	(2,051)	(3,563)	(5,256)	(3,254)
Intangible Amortisation	(99)	(204)	(358)	(378)
Share-based payments	(61)	(111)	(348)	(480)
Other	0	0	0	0
Operating Profit	(2,211)	(3,878)	(5,963)	(4,112)
Net Interest	13	9	33	15
Profit Before Tax (norm)	(2,038)	(3,554)	(5,223)	(3,239)
Profit Before Tax (FRS 3)	(2,198)	(3,869)	(5,929)	(4,097)
Tax	0	0	200	200
Discontinued operations	960	(18)		
Net Income (norm)	(1,078)	(3,572)	(5,023)	(3,039)
Net Income (FRS 3)	(1,238)	(3,887)	(5,729)	(3,897)
Average Number of Shares Outstanding (m)	45.1	47.6	59.1	59.3
EPS - normalised (p)	(2.39)	(7.50)	(8.50)	(5.12)
EPS - normalised and fully diluted (p)	(2.39)	(7.50)	(8.50)	(5.12)
EPS - (IFRS) (p)	(2.74)	(8.16)	(9.69)	(6.57)
Dividend per share (p)	0.0	0.0	0.0	0.0
Gross Margin (%)	N/A	N/A	70.0	70.3
EBITDA Margin (%)	N/A	N/A	N/A	N/A
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	N/A
BALANCE SHEET				
Fixed Assets	1,882	1,572	1,270	940
Intangible Assets	1,142	1,149	899	610
Tangible Assets	139	423	372	330
Investments	601	0	0	0
Current Assets	4,278	9,648	4,574	1,806
Stocks	52	197	196	250
Debtors	328	1,008	486	599
Cash	3,898	8,443	3,892	957
Other	0	0	0	0
Current Liabilities	(645)	(1,131)	(934)	(1,252)
Creditors	(645)	(1,131)	(934)	(1,252)
Short term borrowings	0	0	0	0
Long Term Liabilities	0	0	0	0
Long term borrowings	0	0	0	0
Other long term liabilities	0	0	0	0
Net Assets	5,515	10,089	4,911	1,494
CASH FLOW				
Operating Cash Flow	(1,899)	(3,413)	(4,533)	(2,908)
Net Interest	(4)	5	33	15
Tax	0	0	150	200
Capex	(83)	(325)	(112)	(153)
Acquisitions/disposals	4,326	126	0	0
Financing	(270)	8,152	0	0
Dividends	0	0	0	0
Net Cash Flow	2,070	4,545	(4,462)	(2,846)
Opening net debt/(cash)	(1,828)	(3,898)	(8,443)	(3,892)
HP finance leases initiated	0	0	0	0
Other	0	0	(89)	(89)
Closing net debt/(cash)	(3,898)	(8,443)	(3,892)	(957)

Source: Angle accounts, Edison Investment Research. Note: Historic reported revenues relate to the legacy business, which has now been divested. FY14 has been restated to exclude discontinued operations.

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