Trinity Delta

ANGLE plc

Update

FDA approval awaited, LDT data expected H122

17 January 2022

ANGLE's updates reveal dialogue with FDA for Parsortix's approval for use in mBC (metastatic breast cancer) is continuing and constructive, first submissions for accreditation of UK and US clinical laboratories have been made, but development of the ovarian cancer LDT (Laboratory Developed Test) has been hampered by a delay to data read out from a key study (due to third-party supply issues) to H122. A new study comparing CTC harvest and downstream analysis against biopsies in mBC shows good correlation and indicates Parsortix use could materially benefit clinical diagnoses and treatments. The longer wait for FDA approval and first LDT roll-out prompt us to revisit our forecasts and valuation models. Our new valuation of £506m ($658m), or 215p/share compares to £581m ($755m), 248p/share previously.

Year-end: December 31	2019*	2020	2021E	2022E
Revenue (£m)	0.6	0.8	1.0	2.8
Adj. PBT (£m)	(9.1)	(13.8)	(20.4)	(22.0)
Net Income (£m)	(7.9)	(11.6)	(18.2)	(19.9)
Adj. EPS (p)	(4.7)	(6.7)	(7.7)	(8.4)
Cash (£m)	18.8	28.6	27.2	8.5
EBITDA (£m)	(8.4)	(12.3)	(19.8)	(20.5)

Source: Trinity Delta Note: Adjusted numbers exclude exceptionals * FY19 covers an eight-month period.

- **FDA dialogue is continuing and constructive** Submission of additional information requested by FDA under the De Novo regulatory pathway was completed in June 2021, with a constructive dialogue since. Parsortix's novelty means an inherently more uncertain process, with likely outcomes and timings unclear. Clearance would make it the first CTC (circulating tumour cells) harvesting system approved, and only the third product authorisation for any liquid biopsy. A timely peer-reviewed paper highlights the good correlation of CTC harvest and downstream analysis and secondary biopsies (in matched samples) in metastatic breast cancer. The study concludes Parsortix could provide valuable clinical insights and guide therapy.
- **Ovarian cancer data delay hampers LDT plans** Creation of market relevant LDTs (Laboratory Developed Tests) is, in our view, an important step in establishing attractive US reimbursement codes and confirming Parsortix's clinical benefit and commercial demand. The ovarian cancer LDT, to differentiate between a benign pelvic mass and a tumour requiring specialist treatment, is completing a final verification clinical trial. Due to COVID-19 related supply issues, processing of samples has been delayed, with headline results now expected in H122.
- **Accreditation of clinical laboratories in progress** First submissions for UKAS (UK) and CLIA (US) accreditation have been made, with the relevant processes underway. Provision of these CTC-harvest specific laboratory services, and of commercially pertinent LDTs, should act as important demonstrators of Parsortix's clinical utility and accelerators of market awareness, reimbursement codes, and adoption among the target customer base.
- **Valuation is £506m, or 215p a share** The revised timelines prompt us to revisit our forecasts and three-phase DCF model based of ANGLE, generating a new valuation of £506m, or 215p/share, which compares with £581m (248p/share) previously.

Price	121.0p
Market Cap	£284.5m
Enterprise Value	£244.6m
Shares in issue	235.1m
12 month range	60.0-143.9p
Free float	69.2%
Primary exchange	AIM
Other exchanges	OTC QX
Sector	Healthcare
Company Code	AGL
Corporate client	Yes

Company description

ANGLE is a specialist diagnostics company. Its proprietary Parsortix technology can capture and harvest very rare cells, including CTCs (circulating tumour cells), from a blood sample. FDA approval for its clinical use to guide precision cancer care will open up further multiple commercial opportunities.

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ANGLE: looking forward to a year of delivery

ANGLE has recently clarified the status and expected progress across the various elements in preparing its proprietary Parsortix liquid biopsy platform for widespread commercialisation. Results of the pivotal ovarian cancer study will now be available in H122 due to delays by a third-party supplier of key sample processing reagents. The Wilmot Cancer Center trial data is an essential element in creating the first of a series of in-house Laboratory Developed Tests (LDT) for the US market. Meanwhile, first submissions to establish CLIA and UKAS-accredited clinical laboratories have been made. An FDA approval decision on the regulatory package for De Novo Class II clearance for Parsortix use in CTC capture for subsequent downstream analysis in metastatic breast cancer (mBC) is pending, but dialogue with the agency continues to be constructive. A highly encouraging study, supporting the use of Parsortix enabled CTC analysis as surrogate markers for mBC, highlights the clinical relevance of the non-invasive liquid biopsy once approved. We have revisited our forecasts, detailed late; our DCF-based valuation is now £506m (215p/share), from £581m (248p/share).

Parsortix FDA approval dialogue continuing but key ovarian cancer LDT data delay to H122

ANGLE has issued a couple of updates, with the first covering progress with accreditation of its clinical laboratories and the timing of the ovarian cancer verification study results. The first submissions for UKAS (UK) and CLIA (US) accreditation have been made, and the CLIA process is underway pending results of the Wilmot Cancer Center ovarian cancer study. These results had been expected to be available before end-2021; however, delays to scheduled delivery of key reagents means the samples could not be processed as planned.

Ovarian cancer LDT should be truly innovative triage test

The 200-patient ovarian cancer study, at the University of Rochester Wilmot Cancer Center, is the critical element in supporting the development of the first of a series of in-house Laboratory Developed Tests (LDT) for the US market. The trial aims to demonstrate that a Parsortix based assay can accurately differentiate between a benign mass and ovarian cancer, allowing women with an abnormal pelvic mass to be triaged to the appropriate treatment option. The data are expected to show both high sensitivity (correctly detecting cancer) and high specificity (correctly detecting no cancer with a low false positive rate).

Results from verification study delayed due to reagent shortage

The revised timeline for data read out appears to be due to third-party supply chain issues attributable to COVID-related challenges. An unspecified key supplier was unable to deliver on schedule a number of reagents essential to the sample analysis. Management is closely monitoring the situation and now expects study headline results will be available during H122. Delays to timelines are unfortunate, but we recognise that where reagents are used for manufacturing COVID-19 tests, the market is particularly tight and delivery delays may be unavoidable.

LDTs are as important in the multi-faceted Parsortix adoption strategy as FDA approval

Understandably investor attention is more focussed on Parsortix's FDA approval, and it would certainly mark a defining moment in ANGLE's corporate development. However, this represents only one aspect of a multi-faceted approach to address the various opportunities that should drive growth across multiple revenue streams. Arguably, accredited laboratory facilities, coupled with pharma services and innovative in-house LDTs, are at least as important as FDA clearance. It is the laboratory services, and clinically relevant LDTs, that should act as important demonstrators of Parsortix's clinical utility and accelerators of market awareness, reimbursement codes, and adoption among the target customer base.

Dialogue with FDA is ongoing and constructive

FDA dialogue is continuing and constructive

Management has also provided a status update on the FDA approval process for use of Parsortix for CTC (circulating tumour cells) harvest and downstream analysis in metastatic breast cancer (mBC). An ongoing constructive dialogue with the FDA continues and a regulatory decision is awaited. As a reminder, the regulatory package for De Novo Class II clearance was submitted in September 2020 and a full response to FDA's Additional Information Request announced in early June 2021. With no predicate device to benchmark, the De Novo pathway is inherently more uncertain. FDA clearance would make Parsortix the first CTC harvesting system to be approved and only the third product authorisation for any form of liquid biopsy. We also note the documented COVID-19 related resource constraints at the FDA are still impacting normal activities and means timing of a decision remains unclear.

Newly published study confirms value of Parsortix in mBC diagnoses

Interestingly, the Parsortix CTC capture process has already been the subject of 54 peer reviewed publications from independent cancer centres, as well as numerous posters, articles, and presentations. These highlight the breadth of potential applications and demonstrate how harvesting viable CTCs can provide invaluable information about even remote tumours and guide treatments. With the FDA decision awaited, a timely study relating to mBC was published on January 9, 2022 (Circulating Tumor Cell Transcriptomics as Biopsy Surrogates in Metastatic Breast Cancer, Annals of Surgical Oncology 2022 Jan 9). This study highlights how mBC is responsible for virtually all breast cancer deaths and how the metastatic tumours are inherently different to the original primary tumour, hence typically requiring different treatment regimens. Usually, the metastatic tumours cannot be safely biopsied and so therapy is often sub-optimal.

High correlation between CTC analysis and tissue biopsies

The study evaluated 19 treatment-naïve mBC patients where tissue biopsies of the secondary cancer site were undertaken. These patients had peripheral blood draws (7.5ml) immediately prior to tissue biopsy that were used for CTC isolation using the Parsortix platform, providing 'matched samples' for analysis. The simplicity of the procedure meant the time from blood draw to CTC harvest did not exceed two hours. Whole Transcriptome RNA-Seq and Sanger Sequencing was performed on the CTCs using industry standardised workflows for 64 potentially clinically actionable target genes. The results showed a high degree of correlation between the tissue biopsy samples and CTCs. The study also evidenced the longitudinal monitoring of a tumour's evolving genetic status throughout treatment(s), which is not possible with tissue biopsy.

Conclusion supports routine use for Parsortix for mBC monitoring

The key finding was that "RNA-Seq of Parsortix-enriched CTCs could lead to minimally invasive, real-time diagnostic strategies for precision therapeutic decision making for mBC patients" and the "approach could serve as a surrogate liquid biopsy for potentially clinically actionable drug target gene expression and mutations, allowing longitudinal assessment of the evolution of a patient's cancer".

Addresses a clear and as yet unmet clinical need

The relevance of the study findings is connected to the difficulty of adhering to NCCN (National Comprehensive Cancer Network) treatment guidelines in mBC. These guidelines recommend a tissue biopsy of the secondary tumour site to guide further treatment selection, yet in over half of patients such a biopsy is not possible due to inaccessibility of the metastases or the patients themselves are too ill for such invasive procedures or insufficient tissue is recovered.

Valuation and Financials

Revisiting forecasts as expected timelines are clarified

We had previously highlighted that our forecasts are sensitive to the timing of FDA approval (assuming a positive recommendation), as well as progress with the development of key LDTs. Hence with delays confirmed, we take the opportunity to make a corresponding shift in the timings of our expected revenue streams.

The major changes reflect the shift in timings of revenues

Reviewing our expectations, we had factored in a revenue uplift in RUO (Research Use Only), TR (Translational Research), and Pharma Services once the FDA approval was received. This is the single largest element in our revised revenue forecast of c £1m, from £2.3m previously. In addition, we expect continued COVID-19 factors affecting demand, with RUO and TR impacted by reduced laboratory working time and lower grant/charitable donation funding. The more recent Pharma Services revenues are expected to still be relatively modest at this stage, but building given the profile of existing sold contracts and ramping up when clinical trial activities return to more normal levels.

Corresponding delay in expenditures mean little change at operating and cashflow level

As the new services gain traction, we anticipate that gross margins should be a little softer, given introductory pricing, and also expect the revised timings to shift significant elements of planned costs into subsequent years. This means operating costs should be correspondingly lower, with both operating losses and cash burn broadly in line with our prior expectations. We now forecast FY21 operating loss of £20.6m and a cash balance of £27.1m (vs a previous expectation of £20.4m and £27.3m respectively).

For FY22, again reflecting the timing shift, we now expect the revenue line to be c £2.8m, from £5.4m, and the operating loss and cash balance to be £22.0m and £8.5m, from £19.7m and £10.3m.

Our DCF model now values ANGLE at £506m, equivalent to 215p per share

Exhibit 1 shows our revised valuation, with our new expectations generating a valuation of £506m, equivalent to 215p per share. This compares to £581m, or 248p per share, previously. Whilst we are arguably being overly cautious, our model does leave scope for significant potential upside in our valuation as visibility increases with the execution of the commercialisation and partnering strategy.

Exhibit 1: Three-phase DCF valuation of ANGLE

Business line	NPV (£m)	NPV ($m)	rNPV (£m)	rNPV ($m)	rNPV/ share (p)	Notes
Research use	16.9	22.0	16.9	22.0	7.2	
Pharma services & LDTs	130.6	169.8	111.0	144.3	47.2	Includes priority LDT applications for PD-L1 and ovarian cancer triage. Overall 85% risk adjustment to reflect development and commercialisation risks.
Clinical Products	438.7	570.3	350.9	456.2	149.2	First meaningful sales FY23, following launch in FY22; 90% risk adjustment for mBC programme.
Operating costs	(13.1)	(17.0)	(13.1)	(17.0)	(5.6)	
Pro forma net cash	39.9	51.9	39.9	51.9	17.0	H121 net cash + £18.9m net funds raised in July 2021.
Total	**613.0**	**796.9**	**505.7**	**657.4**	**215.1**	

Source: Trinity Delta Note: 12.5% discount rate, 2.5% terminal growth rate, 20% tax rate, and $1.3/£ FX rate. mBC = metastatic breast cancer

Exhibit 2: Summary of financials

Year-end: Dec 31	£'000s	2018*	2019**	2020	2021E	2022E
INCOME STATEMENT						
Revenues		**628**	**581**	**762**	**1,043**	**2,823**
Cost of goods sold		(169)	(142)	(165)	(322)	(988)
Gross Profit		**459**	**439**	**597**	**721**	**1,835**
Operating expenses		(9,444)	(9,512)	(14,407)	(21,019)	(23,554)
Underlying operating profit		**(8,985)**	**(9,073)**	**(13,810)**	**(20,298)**	**(21,719)**
Share-based payments		(324)	(333)	0	(375)	(383)
Exceptionals		0	0	0	0	0
Other revenue/expenses		52	61	79	87	96
EBITDA		**(8,467)**	**(8,441)**	**(12,310)**	**(19,813)**	**(20,501)**
Operating Profit		**(9,257)**	**(9,345)**	**(13,731)**	**(20,586)**	**(22,006)**
Financing costs/income		8	(26)	(14)	(124)	(245)
Profit Before Taxes		**(9,249)**	**(9,371)**	**(13,745)**	**(20,710)**	**(22,251)**
Adj. PBT		**(8,977)**	**(9,099)**	**(13,824)**	**(20,422)**	**(21,964)**
Current tax income		1,387	1,482	2,139	2,474	2,350
Net Income		**(7,862)**	**(7,889)**	**(11,606)**	**(18,236)**	**(19,901)**
EPS (p)		**(8.2)**	**(4.8)**	**(6.5)**	**(7.8)**	**(8.5)**
Adj. EPS		**(8.0)**	**(4.7)**	**(6.7)**	**(7.7)**	**(8.4)**
DPS (p)		**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Average no. of shares (m)		95.5	163.7	178.0	234.2	235.1
BALANCE SHEET						
Current assets		**11,219**	**23,579**	**32,930**	**31,198**	**11,972**
Cash and short-term deposits		7,645	18,766	28,618	27,172	8,473
Trade and other receivables		828	627	1,443	858	619
Inventories		599	788	742	707	541
Other current assets		2,147	3,398	2,127	2,462	2,338
Non-current assets		**7,063**	**6,996**	**6,119**	**8,008**	**7,573**
Property, plant & equipment		1,475	1,508	1,176	2,648	1,839
Intangible assets		5,588	3,974	3,710	3,620	3,487
Other non-current assets		0	1,514	1,233	1,740	2,247
Current liabilities		**(2,398)**	**(2,777)**	**(3,777)**	**(2,772)**	**(2,628)**
Short-term debt		0	0	0	0	0
Trade payables		(2,398)	(2,425)	(3,343)	(2,474)	(2,585)
Other current liabilities		0	(352)	(434)	(298)	(43)
Non-current liabilities		**0**	**(1,201)**	**(928)**	**(928)**	**(928)**
Long-term debt		0	0	0	0	0
Other non-current liabilities		0	(1,201)	(928)	(928)	(928)
Equity		**15,884**	**26,597**	**34,344**	**35,507**	**15,989**
CASH FLOW STATEMENTS						
Operating cash flow		**(7,136)**	**(8,699)**	**(7,848)**	**(17,807)**	**(17,629)**
Profit before tax		(9,249)	(9,371)	(13,745)	(20,710)	(22,251)
Non-cash adjustments		1,074	1,498	2,268	1,273	2,132
Change in working capital		538	(767)	228	(385)	260
Interest paid		0	0	0	(124)	(245)
Taxes paid		501	(59)	3,401	2,139	2,474
Investing cash flow		**(5,466)**	**(15,564)**	**(1,966)**	**(2,156)**	**(563)**
CAPEX on tangible assets		(1,861)	(595)	(506)	(2,156)	(563)
Acquisitions/disposals		(3,613)	0	0	0	0
Other investing cash flows		8	(14,969)	(1,460)	0	0
Financing cash flow		**14,391**	**16,675**	**18,143**	**18,517**	**(507)**
Proceeds from equity		14,391	16,921	18,650	19,024	0
Increase in loans		0	0	0	0	0
Other financing cash flow		0	(246)	(507)	(507)	(507)
Net increase in cash		**1,789**	**(7,588)**	**8,329**	**(1,446)**	**(18,699)**
Cash at start of year		5,536	11,010	3,757	12,080	10,634
Cash at end of year		**7,321**	**18,766**	**28,618**	**27,172**	**8,473**
Net cash at end of year		**7,645**	**18,766**	**28,618**	**27,172**	**8,473**

Source: ANGLE, Trinity Delta. Note: Adjusted numbers exclude exceptionals. * FY18 relates to 12 month period ending 30 April 2018, ** FY19 relates to 8 month period ending 31 December 2019.

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Disclaimer

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