EDISON

NetScientific

Clinical update

PDS collaborates with Merck

Pharma & biotech

One of NetScientific's portfolio companies, PDS Biotechnology (17.4% stake, 14.5% fully diluted), announced on 10 July 2017 that it has entered into a collaboration agreement with Merck to investigate the combination of the cancer vaccine PDS0101 with the PD-1 inhibitor Keytruda. PDS will be initiating a Phase IIb clinical study of the combination for the treatment of human papilloma virus-16 mediated forms of recurrent and metastatic head and neck cancer.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/15	0.1	(11.3)	(24)	0.0	N/A	N/A
12/16	0.5	(12.3)	(21)	0.0	N/A	N/A
12/17e	2.7	(14.1)	(18)	0.0	N/A	N/A
12/18e	11.6	(11.6)	(13)	0.0	N/A	N/A

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

A smart combo for next-gen immunotherapy

The premise of PD-1 inhibition is that it enables the body to leverage a natural T-cell mediated immune response against cancer cells. However, only 16% of patients with head and neck cancer respond to Keytruda, potentially because they lack natural targeting of T-cells to their cancer. PDS0101's ability to specifically sensitise T-cells to cancer antigens without significant toxicity therefore has the potential to unlock significant synergies with PD-1 inhibitors, such as Keytruda.

Lots of combos, not so many for head and neck

Given the high impact of checkpoint inhibitors and their capacity for significant synergies with other treatments, there has been an unprecedented number of combination studies initiated with these drugs: 783 according to Evaluate Pharma. However, only a fraction of these (less than 25) are sponsored by industry and are looking at recurrent head and neck cancer, and even fewer (less than 10) combine checkpoint inhibition with a cancer vaccine for the disease.

Newly capitalised with a £8.1m offering

NetScientific underwent a financing that combined an £8.1m offering (at 45p per share) in May 2017, resulting in the approximately 18m new shares. The proceeds from this offering substantially offset the financing needs for the portfolio, which we now estimate at £15.9m, although we expect this cash to be provided by outside investors in the portfolio companies.

Valuation: Changed to £68.4m or 99p per share

We have changed our valuation to £68.4m or 99p per share from £60.3m or 118p per share, based on increased cash and share counts following the offering. Otherwise, our model remains unchanged. We have not updated our valuation for PDS given the limited in-human data for the underlying technology, although we expect to update this in the future. The company announced that it intends to complete the Series A financing for Glycotest in H217 (delayed from H117).

13 July 2017

Price	**49.00p**
Market cap	**£34m**
	$1.29/£
Net cash (£m) at 31 December 2016 + offering	17.3
Shares in issue (est)	69.0m
Free float* *Company estimate	6.2%
Code	NSCI
Primary exchange	AIM
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	(3.0)	(13.3)	(31.0)
Rel (local)	(0.4)	(12.9)	(37.8)
52-week high/low		83.00p	48.50p

Business description

NetScientific is a transatlantic biomedical and healthcare technology group. Its portfolio of five core investments and one material investment is focused on three main sectors: digital heath (Wanda), diagnostics (Vortex, ProAxsis, Glycotest) and therapeutics (PDS Biotechnology).

Next events

Glycotest Series A	H217
NEATstik PoC launch	H217

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Edison profile page

Leveraging the immune system from multiple angles

On 10 July 2017, PDS announced that it had initiated a collaboration with Merck & Co to investigate the combination of its PDS0101 cancer vaccine technology with Merck's checkpoint inhibitor Keytruda (pembrolizumab) in a Phase IIb clinical trial for the treatment of recurrent or metastatic head and neck cancer (HNC). PDS0101 is a nanoparticle mediated cancer vaccine programme targeting human papilloma virus (HPV) mediated cancers, and the collaboration with Merck will target HNC as a result of HPV16 strain. HPV is a causative agent in approximately 25% of HNC, 90% of which are due to HPV16.[1] The national cancer institute estimates that there are approximately 11.2 new cases of HNC per 100,000 person-years, accounting for all causes and stages of the disease.

Scientific rationale

Keytruda is an inhibitor of programmed cell death 1 (PD-1) and its approval in 2014, along with other similar checkpoint inhibitors, has been lauded as a breakthrough in cancer treatment based on its ability to leverage the body's immune system to fight cancer. The immune system recognises cells with an aberrant biology either due to infectious disease or cancer through the interaction of cytotoxic T-cells (aka CD8+ cells) with the class I major histocompatibility complex (MHC-I) protein on the surface of the affected cell. MHC-I binds to foreign or mutated proteins in the cytoplasm of the cell and displays these antigens on the cell surface for identification by the immune system. The body is capable of routinely identifying and destroying very early stage cancer before it poses a health risk via this method.

However, cancers that progress develop some method of avoiding detection from the immune system. One method employed by many cancers is to express the ligand for PD-1 (PD-L1), which directs cytotoxic T-cells to ignore MHC-I antigens on these cells. By masking PD-1 on T-cells, Keytruda enables these T-cells to recognise MHC-I antigens and attack these cancer cells.

However, a limitation of checkpoint inhibitors is that the cancer cells must be expressing MHC-I antigens that have induced a cytotoxic T-cell response. Only 16% of patients with refractory head and neck squamous cell carcinoma respond to treatment with Keytruda, and these low response rates can potentially be explained by a lack of endogenous immune response in some cases. Therefore, there is tremendous potential to use checkpoint inhibitors in combination with cancer vaccines such as PDS0101, which can provide this targeting. PDS0101, in particular, is well chosen to be paired with checkpoint inhibition because it is specifically designed to induce a robust cytotoxic T-cell response (as opposed to an antibody or other immune response). PDS0101 directly introduces antigenic protein to the cytoplasm of cells, which is subsequently presented by MHC-I.

Competitive development landscape

Given the high potential for synergies between checkpoint inhibitors and cancer therapies, there has been an unprecedented number of combination studies of these agents. Evaluate Pharma reported in May 2017 that there were 783 ongoing combination studies employing PD-1 or PD-L1 inhibitors, 268 of which employed Keytruda. However, by our estimation from data available on clinicaltrials.gov, there are fewer than 60 industry-sponsored studies in HNC, and fewer than 25 are for recurrent forms of the disease. There are a relatively small number of clinical studies investigating the combination of Keytruda with cancer vaccines for this disease (Exhibit 1). We

1 Gillison ML, et al. (2000) Evidence for a Causal Association Between Human Papillomavirus and a Subset of Head and Neck Cancers. *J. Nat. Can. Inst.* 92, 709-720.

believe that the PDS technology is well positioned among this group given the straightforward mechanism of action and strong potentiation of cytotoxic T-cell responses.

Exhibit 1: Selected HNC vaccine/checkpoint combination studies

Drug	Company	Stage	Combination	Notes
PDS0101	PDS	Phase II	Keytruda	Nanoparticle HPV-16 antigen
TG4001	Transgene	Phase I/II	Bavencio	Viral HPV-16 antigen
Axalimogene filolisbac	Advaxis	Phase II	Imfinzi	Listeria vaccine

Source: Various

Valuation

We have not updated our model at this time except to account for the new estimated cash and share count following the May 2017 offering. £8.1m was raised via a public placement at 45p per share (and a small private placement of 45,700 shares). Our new valuation is £68.4m or 99p per share from £60.3m or 118p per share. Although we believe that PDS's newly announced collaboration with Merck has potential, we currently do not have sufficient patient data with the underlying technology to revise our probability of success, although we expect to update our assumptions upon the release of more information on the activity of this drug. NetScientific has a 17.4% interest in PDS, 14.5% on a fully diluted basis. Additionally, we expect to update our valuation once reports of sales for the recently launched products from Vortex, ProAxsis, and Glycotest are available.

Exhibit 2: NetScientific valuation

Development Program	Probability of success (%)	Profitability	Peak sales (£m)	Margin (%)	rNPV (£m)	Ownership	Share Value (£m)
Vortex	15.0%	2020	150	44%	18.0	95.0%	17.1
Wanda	5.0%	2019	352	52%	11.3	70.9%	8.0
ProAxsis	10.0%	2020	50	51%	8.6	56.5%	4.9
Glycotest	10.0%	2019	123	51%	16.4	87.5%	14.4
PDS	10.0%	2021	302	57%	38.7	17.4%	6.7
Total							51.0
Net cash and equivalents (YE16 + offering) (£m)							17.3
Total firm value (£m)							**68.4**
Total shares (m)							69.0
Value per share (p)							**99**

Source: NetScientific reports, Edison Investment Research

Financials

The recent raise of £8.1m supplements the £9.2m in net cash available at the end of 2016. This brings the total outstanding financing requirement for the constituent companies to £15.9m, which we include in our forecasts as illustrative debt, although we expect the financing to be from outside investment in these companies. For instance, NetScientific stated that it expects Glycotest to complete its Series A in H217 (a delay from previous reports of H117). Otherwise, our financial projections remain unchanged.

Exhibit 3: Financial summary

£'000s	2014	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	24	122	518	2,682	11,630
Cost of Sales	0	(6)	(255)	(656)	(4,130)
Gross Profit	24	116	263	2,025	7,500
Research and development	(3,098)	(7,256)	(7,443)	(9,677)	(10,081)
Selling, general & administrative	(3,212)	(4,260)	(5,001)	(6,063)	(7,397)
EBITDA	(6,352)	(11,530)	(12,570)	(13,856)	(10,119)
Operating Profit (before GW and except.)	(6,286)	(11,400)	(12,429)	(13,715)	(9,978)
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	(948)	(1,518)	(666)	0	0
Operating Profit	(7,234)	(12,918)	(13,095)	(13,715)	(9,978)
Net Interest	77	78	86	(400)	(1,600)
Other (change in fair value of warrants)	0	0	(49)	0	0
Profit Before Tax (norm)	(6,209)	(11,322)	(12,343)	(14,115)	(11,578)
Profit Before Tax (IFRS)	(7,157)	(12,840)	(13,058)	(14,115)	(11,578)
Tax	30	94	(18)	71	58
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(6,179)	(11,229)	(12,361)	(14,044)	(11,520)
Profit After Tax (IFRS)	(7,127)	(12,746)	(13,076)	(14,044)	(11,520)
Minority interest	702	1,905	1,881	3,216	2,596
Profit After Tax after minority interest (FRS 3)	(6,425)	(10,842)	(11,195)	(10,828)	(8,924)
Average Number of Shares Outstanding (m)	35.9	38.2	51.1	60.1	69.0
EPS - normalised (p)	(15)	(24)	(21)	(18)	(13)
EPS - IFRS (p)	(18)	(28)	(22)	(18)	(13)
Dividend per share (p)	0	0	0	0	0
BALANCE SHEET					
Fixed Assets	3,040	2,946	4,054	5,063	7,029
Intangible Assets	10	1	0	0	0
Tangible Assets	348	285	779	638	497
Other	2,681	2,660	3,275	4,425	6,532
Current Assets	17,720	23,799	11,034	21,060	8,268
Stocks	0	0	0	894	2,326
Debtors	853	560	1,578	268	1,163
Cash	16,867	23,239	9,456	19,897	4,779
Other	0	0	0	0	0
Current Liabilities	(1,324)	(2,206)	(2,172)	(2,947)	(3,273)
Creditors	(1,281)	(2,156)	(2,044)	(2,947)	(3,273)
Short term borrowings	(43)	(50)	(128)	0	0
Long Term Liabilities	(740)	0	(80)	(15,997)	(15,997)
Long term borrowings	(687)	0	(80)	(15,997)	(15,997)
Other long term liabilities	(53)	0	0	0	0
Net Assets	18,696	24,538	12,836	7,178	(3,972)
Minority Interest	(1,098)	(1,805)	(3,875)	(7,091)	(9,686)
Shareholder Equity	17,598	22,733	8,961	88	(13,659)
CASH FLOW					
Operating Cash Flow	(6,698)	(10,752)	(12,939)	(11,952)	(11,469)
Net Interest	67	38	43	(400)	(1,600)
Tax	19	83	112	71	58
Capex	(336)	(299)	(457)	0	0
Acquisitions/disposals	(2,181)	(144)	(1,261)	(1,150)	(2,108)
Financing	0	18,208	0	8,083	0
Dividends	0	0	0	0	0
Other	119	39	66	0	0
Net Cash Flow	(9,010)	7,172	(14,436)	(5,348)	(15,119)
Opening net debt/(cash)	(25,069)	(16,136)	(23,189)	(9,248)	(3,900)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	(140)	(212)	(603)	0	0
Other	218	92	1,098	0	0
Closing net debt/(cash)	(16,136)	(23,189)	(9,248)	(3,900)	11,219

Source: NetScientific reports, Edison Investment Research

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