EDISON

NetScientific

Development outlook

Progress continues

Pharma & biotech

NetScientific's healthcare portfolio progressed towards revenue generation during H117 with the soft launch of both Vortex and ProAxsis products into the research market. A series of value inflection points are expected in H217 and FY18 including Series A financings for all five holdings, the commercial ramp of ProAxsis's NEATstik following the recent CE mark approval, and targeting home health providers, payers, hospitals, and accountable care organisations to increase commercialisation of the Wanda platform. We value NetScientific at £57.3m or 83p per share.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/15	0.1	(11.3)	(24.4)	0.0	N/A	N/A
12/16	0.5	(12.3)	(20.6)	0.0	N/A	N/A
12/17e	1.4	(7.8)	(9.8)	0.0	N/A	N/A
12/18e	3.8	(11.8)	(14.1)	0.0	N/A	N/A

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

ProAxsis makes swift commercial progress

September 2017 proved to be a productive month for ProAxsis. It announced a series of commercial developments: it completed the development process for NEATstik, registered the product with a CE mark, partnered with an unnamed US biotech company to develop activity-based immunoassays for two essential respiratory proteases with ProteaseTag technology, and, lastly, named Diagenics Ltd as sales distributor of the ProteaseTag immunoassay kit for the UK and Ireland.

PDS partnered with Merck for PD-1 combo

In July, PDS announced that it had entered into a collaboration with Merck to use its PDS0101 cancer vaccine in combination with Keytruda (pembrolizumab) in its planned Phase II clinical trial in patients with refractory head and neck cancer driven by human papillomavirus. The trial is expected to start around YE17.

Vortex teams up with UCLA to test for PD-1/EGFR

Vortex has announced a collaboration with the University of Los Angeles to use its VTX-1 liquid biopsy system in two proof-of-concept trials in patients with non-small cell lung cancer (NSCLC). The first will use samples from 100 patients to examine their PD-1 expression status and if they are appropriate for checkpoint inhibitor therapy, and the second will similarly test if their tumours are driven by epidermal growth factor receptor (EGFR). The trials are expected to be complete by YE17.

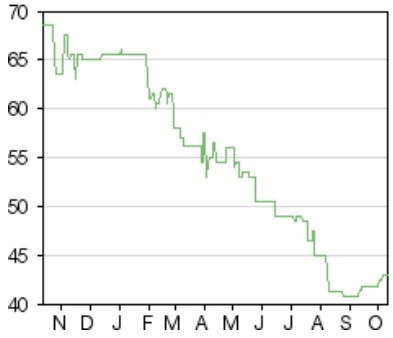
Valuation: Decreased to £57.3m or 83p per share

We have reduced our valuation £57.3m or 83p per share, from £68.4m or 99p per share, driven by delayed timelines across the portfolio, lower net cash (£11.1m) and an increased share count, partially offset by increasing the probability of success for ProAxsis from 10% to 15% and advancing our NPVs. We expect to update our valuations following the completion of Series A financings for Glycotest and PDS in H217 and Vortex and ProAxsis in H118.

11 October 2017

Price	**43.00p**
Market cap	**£29m**
	US$1.32/£
Net cash (£m) at 30 June 2017	11.1
Shares in issue	69.0m
Free float	56%
Code	NSCI
Primary exchange	AIM
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	5.5	(12.2)	(39.9)
Rel (local)	3.2	(14.5)	(44.0)
52-week high/low		68.50p	40.80p

Business description

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

Next events

Series A closure (Glycotest, PDS)	H217
Glycotest opening CLIA lab	H217
PDS and Merck Phase II initiation	H217-H118

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Investment summary

A portfolio of diverse technologies

NetScientific is a healthcare investment company with a portfolio of five major holdings, all in early stages of clinical validation. It is the majority shareholder for four of the companies. Vortex is developing a fluidics-based mechanism of isolating circulating tumour cells. Wanda is a digital health company launching a patient monitoring programme for heart failure and chronic obstructive pulmonary disease (COPD). ProAxsis is developing an at-home test for cystic fibrosis (CF), COPD exacerbations, and bronchiectasis. Glycotest is developing a test for hepatocellular carcinoma and PDS Biotechnology (the sole minority stake) is developing vaccines for HPV-driven cancers.

Valuation: £57.3m or 83p per share

Based on a risk-adjusted NPV analysis of each of the major holdings, we value NetScientific at £57.3m or 83p per share. We currently value Vortex as the highest value holding (£15.9m for NetScientific's share, £16.7m total valuation) because of the near-term commercial prospects in the research market (we estimate peak sales of £141m). We value the remaining investee shares in a range of £5m to £11m with 17% to 88% ownership. Valuations reflect the early stage of development across the board, with probabilities of success ranging from 5% to 15%.

Financials: £11.1m in cash; three Series A financings in 2018

NetScientific ended H117 with £11.1m in net cash and has announced expected Series A financing rounds for Glycotest and PDS in H217, Vortex and ProAxsis in H118, and Wanda in H218. Our model forecasts £77m is needed to bring the five companies to profitability, corresponding to £12m in additional financing for NetScientific's proportion of costs. We forecast slight decreases in combined R&D spending to £6.4m in 2017 (from £7.4m in 2016), partially associated with the movement of Wanda, Vortex and ProAxsis toward commercial activities and compounded by the delays in financing of these companies. We expect the parent company to become cash flow positive in 2020.

Sensitivities: Multiple early-stage programmes

NetScientific carries the risks associated with investing in early stage healthcare companies, and the individual portfolio companies can all be considered high risk. However, we expect the risk to the parent company to be mitigated by the portfolio approach and by potential exit strategies to realise value for investors and limit downstream risk. Wanda is the most commercially advanced company, with a product in the early stages of commercialisation. Wanda is also operating in a highly fractured space with low barriers to entry and significant competition. The other portfolio companies are all in the development stage and carry the associated clinical and regulatory risks. Vortex and Glycotest will likely need to seek pre-market approval (PMA), and will require both clinical validity and utility trials. Vortex is one of at least 37 companies developing technology to isolate circulating tumour cells. ProAxsis has a simpler pathway and may be able to seek a 510(k) approval, but we project low peak sales (£47m). Glycotest is entering a market that we expect to decline in incidence with increasing treatment of hepatitis C, but partially offset by increases in other liver disease such as non-alcoholic steatohepatitis. PDS Biotechnology has the high development costs and risk associated with therapeutic development, and cancer vaccines have historically underperformed in the clinic. All of the above risks are compounded by financing concerns, and these companies may not be able to raise sufficient capital. There have been delays to the financings for all the companies, although guidance now points to Series A financing rounds for Glycotest and PDS in H217, Vortex and ProAxsis in H118, and Wanda in H218.

A portfolio across healthcare

NetScientific is an investment company focused on early stage investing in healthcare companies across a range of different technologies. The company's main holdings include three diagnostics companies (Vortex, ProAxsis, Glycotest), a digital health company (Wanda), and a cancer therapeutic company (PDS Biotechnology) (Exhibit 1). NetScientific invests up to £20m and holds a majority in four companies.

The current model of the company follows a strategic change in direction away from seed-stage investing in 2015. François Martelet MD, a highly experienced biopharma professional, was appointed CEO in June 2015, along with additional appointments in the board and upper management. The company divested approximately half of the companies in the portfolio to focus on the four main companies, and in particular to accelerate the development programmes in Vortex and Wanda. To finance this, NetScientific issued 15.2m new shares at 120p in November 2015 raising £18.2m (gross) from new and existing shareholders. The company successfully completed an £8.1m offering (at 45p per share) in June 2017, resulting in approximately 18m new shares to offset the financing needs for the portfolio. The company retained a small number of seed investments (Exhibit 2), but these are beyond the scope of this report.

Exhibit 1: Core portfolio and material investment

Investment	Technology	% held	Founded	Status	Business advantage	Targets
Vortex	"Centrifuge-on-chip" cancer diagnostic using liquid biopsy from circulating tumour cells	95.0%	2012	VTX-1 instrument beta units prepared	Faster separation of viable cancer cells with high purity.	VTX-1 proof-of-concept trials for biomarkers with UCLA to be completed in Q417.
Wanda	Clinical decision support software to reduce hospitalisation risk. Initially focused on CHF	70.9%	2011	CHF and oncology deals signed Q116	Patient friendly interface. Highly scalable, predictive analytics.	Expand platform to cover additional chronic conditions. Strategic goal for 2017: build out a sales pipeline to target hospitals, payers, and ACOs.
ProAxsis	Protease-Tag diagnostic products for monitoring disease biomarkers; focus on CF and COPD	56.5%	2013	Lab tests launched; NEATstik in R&D	NEATstik home test detects neutrophil elastase with high reliability and specificity. Potential to reduce hospitalisation risk.	EU launch 2017 of in clinic and self-test NEATstik devices; develop activity-based immunoassays with US biotech; Series A financing in H217.
Glycotest	Liver cancer diagnostic test based on proprietary biomarkers and algorithms	87.5%	2012	HCC Panel developed, 208-pt clinical study completed	Outperforms current biomarker AFP test.	Clinical validation by Q417, CLIA lab opening Q417, Series A financing in China in H217, CLIA waiver H118, launch its HCC test in H218
PDS*	Therapeutic vaccine, clinical trials against HPV	17.4%	2006	Clinical	Low production cost; deals with Merck-Serono and MedImmune.	Phase II initiations; further licensing deals.

Source: NetScientific. Note: *Material investment. PoC = point-of-care; CHF = congestive heart failure; CF = cystic fibrosis; COPD = chronic obstructive pulmonary disease; ACOs = accountable care organisations; CLIA = Clinical Laboratory Improvement Amendments; AFP = alpha-fetoprotein; HCC = hepatocellular carcinoma.

Exhibit 2: Seed-stage investments

Investment	Technology	% held	Founded	Status	Business advantage	Targets
G-Tech	Electrical monitoring of GI function via wearable disposable patch	ND	2014	Early stage	Real-time diagnosis and monitoring of GI disease	Innovation needs to be linked to clinical outcomes
Longevity Biotech	Uses β amino acids scaffold to resist degradation in blood	ND	2014	Early stage	Longer half-life biosimilar therapeutics	Needs clinical equivalence and toxicology and safety
CytoVale	Microfluidics to measure >10 biophysical cell markers	2.15%	2014	Concept validation	Detects early stages of sepsis in white cells	Clinical validation and commercial test development
EpiBone	Customised bone grafts	ND	2015	Research	Grown from own stem cells	Clinical, economics
Neumitra	Real-time stress level measurement	ND	2015	Retail market	Neuma biowatch (embedded biomodules in jewellery)	Validation and marketing

Source: NetScientific. Note: Seed-stage investments sourced from Breakout Labs. ND = not disclosed.

NetScientific's strategy is to develop a balanced portfolio of digital health, diagnostics and therapeutics companies focused on chronic disease. The company intends to seek majority ownership in future portfolio investees, and to leverage its ability to recruit high-quality management to operate these companies independently. NetScientific has stated that the development of therapeutics companies is of high strategic importance. The goal is to structure a new therapeutics

company surrounding a therapeutic asset, as opposed to the acquisition of an existing entity. We predict that expansion of the portfolio will follow exits from the current investments. NetScientific aims to drive asset appreciation using external financings concurrent with investee inflection points such as clinical results. We do not expect NetScientific to invest during these subsequent rounds. We expect the company to exit pre-profits through a trade or public listing to limit its exposure to commercialisation risk.

Vortex: Isolating pristine cancer cells from the blood

Vortex BioSciences is a California-based spinout focused on cancer diagnostics. It has developed a novel 'liquid biopsy' system to capture rare circulating tumour cells (CTCs) from whole blood based on technology developed at the Department of Bioengineering at UCLA. The system includes a novel liquid biopsy automated instrument (VTX-1) and integrated microfluidic cartridge.

CTCs are an area of intense clinical research interest and technical development (see review in *Nature Reviews Cancer*) as they provide information about an individual's cancer, which can be used for prognostic, diagnostic and treatment stratification purposes. Rising CTC numbers are a known risk marker for cancer reoccurrence in diagnosed patients; therefore a combination of effective CTC isolation with sophisticated analysis could enable much better and earlier cancer diagnosis, monitoring and personalised cancer therapy. The initial focus is on the research market and the placing of instruments with strategic players. The VTX-1 system was introduced at the American Association for Cancer Research (AACR) conference in April 2016. The system received CE mark and FDA Class I registration and was soft-launched into the research market in the US and Europe in February 2017. Revenue from the research market is essential for the near-term cash flows for the company.

The Vortex technology, using microfluidics, isolates larger cells from whole blood. As CTCs tend to be much bigger than red blood cells and larger than most white immune cells, they are preferentially captured. Note that the method is not specifically selective for cancer. Key advantages include the rapid processing time (taking as little as one hour), collection efficiency (sensitivity) and purity of captured CTCs with limited white blood cell contamination (specificity). Most importantly, the captured CTCs are intact and undamaged and can be identified, analysed and enumerated using different methods. The Vortex technology is label-free, requiring no pre-treatment; hence, it can be used in a variety of applications including cancer diagnosis and monitoring, personalised medicine, drug development and cancer research. Two recent papers have highlighted the utility of the platform for western blotting and genotypic profiling. Moreover, because the cells remain viable during the process they can be further propagated via tissue culture.

In collaboration with UCLA, Vortex is investigating its VTX-1 liquid biopsy system in two proof-of-concept trials for PD-L1 and EGFR biomarkers. The aim of the first 100-patient trial is to determine whether CTCs isolated with VTX-1 can be evaluated for the PD-L1 biomarker for the purpose of identifying suitable patients for immunotherapy treatment, while the second study aims to target treatable patients by determining if EGFR mutations can be identified among 60 lung cancer patients using Vortex technology. The company aims to complete both trials by the end of the year.

Vortex is one of a number of companies with CTC detection systems in development (34 by management's estimates; Exhibit 3 shows a selection of those based on microfluidic isolation). A number are currently marketed for clinical use in Europe or for research use. CellSearch is the sole CTC system that is FDA approved, but its use is limited to enumeration in certain cancer types. In June 2016, the FDA approved the first ctDNA blood-based genetic test: Roche's cobas EGFR Mutation Test v2 as a blood-based companion diagnostic for Tarceva (erlotinib).

Vortex flags that liquid biopsy could represent a $22bn market opportunity (according to JP Morgan), excluding the research segment. Our estimates are more conservative: based on the rates for prostate specific antigen (PSA) testing, the most common current cancer blood test, and Vortex's pricing strategy (see below), we predict a market of approximately $13bn by 2031. Due to higher cost, the need for dedicated equipment and significantly lower throughput (each test requires an hour to perform on this platform) compared to the PSA test, as well as a high degree of competition, we expect initially low penetration (1%) of this market, but we expect this to expand (2% by 2030) as the company introduces more high throughput devices for clinical purposes. Regardless, this represents a significant growth opportunity for the company as its product pipeline expands from initial research use to downstream clinical applications, which will be addressed by next-generation instruments.

Three different generations are in the pipeline, but the timelines to commercialisation will depend on development progress and funding. We expect the company to have to perform clinical validity and utility trials in the US in order to support marketing claims regarding the efficacy of the test. We currently model this as approximately £5m in R&D spending before profitability in 2019 to support the clinical studies necessary to enter the diagnostic market. The company aims to complete this financing in either Series A or commercial partnership during H118 (it is in the process of placing VTX-1 systems with strategic players in order to assist them in considering a potential commercial partnership). The second-generation technology may be on the market in the next two to three years, and we expect the development of future platforms based on the technology to require additional research spending, and expect to update our valuation and estimates with the release of more details on these systems.

Exhibit 3: Selected microfluidics CTC detection technologies

Product (company)	Status	Notes
ClearCell FX System (Clearbridge Biomedics)	Marketed for research use only	Automated machine using the CTChip FR1 microfluidic chip to isolate CTCs on the basis of their size and inertia. Recovery >40% with spiked samples. Reports ultra-high purity and high throughput. Harvested CTCs are intact and viable. The system can be integrated with a number of downstream analysis technologies and culture of CTCs.
VTX-1 (Vortex Biosciences)	Marketed for research use only	Microfluidic chip to isolate CTCs on the basis of their size and other physical properties. Preliminary testing suggests >80% purity and high throughput. CTCs are viable and can be harvested for downstream analysis and culture.
Parsortix (Angle)	CE marked for clinical use	Microfluidic disposable cassette captures CTCs on the basis of their size and morphology. CTCs can be fixed and stained in situ or harvested for analysis or culture.
PREP100 (Celsee Diagnostics)	Marketed for research use only	Microfluidic system that isolates CTCs on the basis of size using tapered microchannels. The CTCs can then be stained or cultured directly in the isolation chamber to minimise contamination. 85% capture efficiency.

Source: Edison Investment Research, company websites. Note: Published data are limited on many systems.

Vortex's business model is akin to a razor/razor blade model whereby the instrument is sold at a small mark-up to cost, with profits made through the supply of the disposable microfluidic cartridges. Vortex's pricing strategy may evolve in the future, especially as more advanced systems enter the market, but indications are that each instrument will cost in the $125-150k range with a per-cartridge price of $250-350. We expect this pricing to ultimately be tempered by discounts, which we predict in the range of 30%.

Wanda: A monitoring solution for chronic disease

Wanda is a digital health company that has developed a software platform for the management of patients with chronic disease. The Wanda application is a recently patented, integrated solution to improve patient monitoring and provide behavioural modification and ultimately reduce hospitalisations. The company has developed applications to monitor patients for congestive heart failure (CHF) and COPD.

The Wanda application collects data from remote monitoring systems (RMS) and patient self-assessments on mobile devices to monitor disease progression and uses the company's

proprietary analytics to predict disease risk. The project resulted from 12 years of clinical research into chronic disease management at UCLA. The information gathered is automatically leveraged by the application to provide behavioural modifications to the patient, as well as to inform the patient's physician care team should intervention be necessary. The ultimate goal of the application is to reduce the number of hospitalisations by providing more timely feedback based on the patient's status.

Originally, Wanda was focused on marketing its patient monitoring platform to the home healthcare market. The key value proposition to these companies is that algorithmic patient monitoring can improve outcomes and reduce hospitalisations, thereby extending the value of these services. Wanda complements this market well because the platform is more easily integrated into the patients' routines due to persistent contact with healthcare professionals. Moreover, the monitoring solutions provided by Wanda closely mirror some of the responsibilities of the home healthcare provider. To this end, the company has signed contracts with three such networks (A to Z Home Health Care, 24Hr HomeCare, and Health Resource Solutions) and this market remains important to the company.

However, the company has stated it failed to gain significant traction in 2016 by targeting these providers and has since shifted its commercial plan earlier this year to target three additional players in the healthcare system with significant vested interests in patient outcomes including hospitals, payers, and accountable care organisations. Moreover, due to the nature of their businesses, there is the potential to attract significantly higher volumes through these channels and greater recurring revenue. Wanda has shifted its focus to sourcing contracts with these businesses. Although we see a higher barrier to entry into these markets, we believe that the metrics on outcomes gathered in the home healthcare market can be leveraged into larger contracts. A key strategic goal for 2017 is to build out a sales pipeline to target these markets, and Wanda's CTO Foad Dabiri was promoted to CEO to lead the transition, because of his experience in the digital health space. NetScientific anticipates a lower revenue projection for 2017 than previously suggested. Additionally, as part of the transition, Wanda has sold its equity in OncoVerse, its cancer patient monitor platform in development with Dignity Health. Its 35.9% stake was sold to BTG for £1.5m.

The Wanda platform is versatile and, hypothetically, can be employed to monitor a wide variety of chronic diseases. The first module developed for the platform was for the monitoring of patients with CHF. The software integrates the patient's medical record information with regular blood pressure and weight measurements gathered wirelessly from Bluetooth-enabled devices, as well as self-reported symptom assessments. The system was previously tested utilising a 1,500-person trial performed at UCLA. Wanda has developed a module for the prediction of complications associated with COPD, which comes bundled with the CHF module because of the comorbidity of these two diseases.

We model the combined CHF/COPD disease management market in the range of $4bn. Based on our understanding of the FDA guidance on mobile healthcare applications, we do not believe that Wanda will be classified as a device. However, we expect the company to engage in further clinical trials to support marketing claims to drive adoption in this area. We expect these clinical trials to be inexpensive compared, for instance, to therapeutics, and we have trimmed R&D spending in our model to around £4m before profitability in 2019, but a portion of this will be offset by near-term revenues. We expect the cost of the trials to be associated with device placements, support of physicians performing remote monitoring and the acquisition of medical records to support claims that Wanda reduces hospitalisations, but we expect a high degree of participation from healthcare providers given the low impact on their operations. Moreover, these trials will set up a footprint in participating institutions where Wanda is available, and could support market development. We

expect Wanda to require an additional investment of approximately £4m to commercialise the existing programmes.

The digital health market as a whole is poorly developed, with few to no market leaders, and is highly fragmented due to low barriers to entry. There are a large number of companies in the immediate space of Wanda, developing similar solutions for chronic disease management. This space (and the mobile med-tech space in general) is developing exceptionally quickly. These companies can be roughly sub-classified into different groups based on their approach, which include remote patient monitoring, data warehousing, analytics, remote care and behaviour modification. The Wanda combination of patient monitoring, analytics and behaviour modification is unique to our knowledge, but replicated in part in multiple instances.

ProAxsis: Point-of-care testing for respiratory disease

ProAxsis was founded in 2013 as a medical diagnostic spinout of Queen's University Belfast in Northern Ireland. ProAxsis has developed proprietary molecules, called Protease-Tags, which selectively bind to active proteases and can be used in a range of diagnostic and disease monitoring tools. The company produces a commercially available immunoassay for research use and has also developed a PoC test called NEATstik (Neutrophil Elastase Airways Test) for routine monitoring of neutrophil elastase (NE). Neutrophil elastase is involved in chronic respiratory diseases such as CF and COPD and is an established biomarker of infection and inflammation. NEATstik received a CE mark in September 2017 and is the first-to-market point-of-care NE test in the EU.

Active proteases ('molecular scissors') play a key role in many physiological processes and are considered important therapeutic targets, as well as being biomarkers of many diseases. They may be unregulated in diseases including cancer, heart disease, stroke, Alzheimer's disease, rheumatoid arthritis, multiple sclerosis, CF and COPD. Current assay systems for proteases utilise chromogenic or fluorogenic substrates, are often complex and may not be sufficiently specific to detect the active form of the enzyme. ProAxsis has developed novel and patented Protease-Tags to irreversibly inhibit/trap active proteases. Because they are designed to form a bridge to a solid support via covalent binding, they can be combined with established diagnostic technology platforms such as ELISA, lateral flow or multi-analyte biochips.

NEATstik is a lateral flow device for rapid, easy monitoring of NE levels in the clinic or home from sputum samples. One single-use test is sold for £18 and a box of 10 tests is sold for £150. NE activity in respiratory diseases is responsible for significant airway damage and is a strong predictor of lung function decline. Detecting increased NE levels earlier can reduce exacerbations and hospitalisation risk in patients with CF and COPD, and improve health outcomes.

ProAxsis's first Protease-Tag immunoassay kit was launched in August 2015 and was commercially available for research-only use, including academic labs and clinical research organisations involved in clinical trials. The kit measures active neutrophil elastase (NE), which is produced by white blood cells (neutrophils) in response to lung infections and is also a potential therapeutic target. Elastase destroys the elastic connective tissue that keeps the lungs supple, which results in permanent scarring. Clinical studies have shown that high neutrophil elastase levels are linked to deteriorating lung function (eg Sagel *et al* 2012).

Sales have been modest, although the company expects them to grow as further pharma company customers are secured. In order to increase sales potential, ProAxsis recently named Diagenics Ltd as sales distributor of its Protease-Tag immunoassay kit for the UK and Ireland. Beyond the NE kit, three further specific immunoassays are in development against different proteases targets, including those involved in pulmonary fibrosis, CF/COPD and acute respiratory distress syndrome.

In July 2017, ProAxsis was awarded a grant from Innovate UK to support continued development of its Protease-Tag technology. In addition, ProAxis announced a partnership with an unnamed US biotech company to develop activity-based immunoassays for two essential respiratory proteases using its Protease-ag technology in September 2017.

The chronic respiratory diseases CF and COPD are associated with frequent lung infections, irreversible tissue damage and lung function decline. There are 70,000 patients diagnosed with CF worldwide (30,000 patients in the US and Canada and c 40,000 elsewhere, mainly in Northern Europe) and 35.7 million patients with COPD in the US and EU. The treatment of lung diseases is estimated to cost the UK NHS £4.7bn a year and, according to NICE, "a reduction of 5% in COPD exacerbations would be expected to save the NHS £16 million per annum".

The target population for home testing is adult CF patients and moderate-severe COPD patients, 65% and 25% of whom, respectively, are 'natural sputum producers'. Even at a conservative price ($25 in the US, £15 in Europe), assuming a 40% share of CF patients (testing weekly) and a 20% share of COPD patients (testing monthly), ProAxsis estimates the European CF/COPD home test market could be around £16.5m. The US market would probably be twice this, giving an estimated US/EU market of c $70m, and these estimates are largely in line with our own. We expect the company to pursue a 510(k) submission in the US, which would additionally limit R&D spending. The company expects to complete a Series A financing in H217.

Glycotest: Improving the diagnosis of liver disease

Glycotest is a US-based company developing a non-invasive diagnostic and monitoring test for early-stage liver disease based on proprietary blood-based biomarker panels and algorithms. Its lead product (HCC Panel) is a biomarker panel for curable early-stage hepatocellular carcinoma (HCC), the most common form of primary liver cancer. Liver disease is a large and growing market and current surveillance tests under detect early-stage HCC. Glycotest's HCC Panel outperformed the alpha-fetoprotein (AFP) blood test, a commonly used screening test, in a 208-patient study. Using other biomarkers, Glycotest's approach could be extended to other liver diseases. Glycotest's commercialisation strategy in the US is to market HCC Panel as a laboratory service through a CLIA-accredited laboratory.

Glycotest was founded on technology developed at the Baruch S Blumberg Institute and Drexel University College of Medicine in Philadelphia. Diseased livers secrete a range of glycoproteins with fucose sugar modifications at abnormally high levels, and different diseases may have characteristically abnormal fucosylation patterns. Glycotest has licensed exclusive worldwide rights, with low royalties, to over 50 patented serum glycoprotein biomarkers that exhibit increased fucosylation in liver cancers. Glycotest also owns the rights to assay technology to quantify fucosylated glycoproteins using engineered lectins (sugar-binding molecules).

Glycotest has developed its proprietary HCC Panel test using six biomarkers that are elevated in HCC. The individual biomarkers have been evaluated in >800 patients and the HCC algorithm has been developed in thousands of patients. The technology can be extended to other liver diseases, using a different array of validated biomarkers. Glycotest is also developing tests for cholangiocarcinoma and intermediate-stage liver fibrosis-cirrhosis.

HCC is the third leading cause of cancer-related death worldwide and the fifth leading cause in the US, with an increasing incidence. Globally, there are c 500k deaths due to HCC per year. Cirrhosis is a scarring of the liver resulting from liver disease and 5-30% of patients with cirrhosis go on to develop HCC. The predominant risk factors for cirrhosis (and therefore HCC) are chronic hepatitis C infection (26% of cirrhosis), hepatitis B infection (15%), as well as non-viral factors such as alcohol consumption (21%) and non-alcoholic fatty liver disease (NAFLD; 18%). NAFLD is linked to

obesity (BMI >30) and is a growing problem affecting 30% of the US population. It can progress to non-alcoholic steatohepatitis (NASH), which has a 4-14% risk of cirrhosis. The prevalence of alcoholic steatohepatitis (ASH) is unknown, although it may be estimated from the prevalence of alcoholism (8% of the US population, one-third with ASH), which is still a major cause of liver disease in Western countries.

Based on AASLD guidelines of HCC risk (for hepatitis B/C, ASH and NASH), we estimate that two million diagnosed patients in the US would be eligible for liver cancer surveillance. However, we expect declining rates of hepatitis C virus (HCV) to reduce this number to 1.3 million by 2030. Assuming a 10% uptake, this gives a peak sales projection of over $150m in the US assuming two tests per year at a cost per test of $660 (Glycotest data) and a median 30% payer rebate. We note that the average cost of abdominal ultrasonography plus AFP test is around $500. Whether this higher cost/test pricing is achievable remains to be seen and will presumably hinge on the ability of HCC Panel to demonstrate cost-benefit in detecting early-stage HCC. However, growth drivers are likely to come from an increasingly obese population (increasing fatty liver disease and NASH), albeit offset by declining rates of hepatitis B virus (HBV) and HCV.

Glycotest will be able to offer the test as a laboratory service and will therefore not need FDA approval before marketing. However, the company will need to perform clinical utility trials demonstrating a change in treatment patterns to support the marketing claims and payer support for wider adoption. We predict an R&D cost of £6m before profitability in 2019. Glycotest is currently participating in a $10m Series A in China and it intends to use the financing to open a CLIA lab in H217. A CLIA waiver (expected in early to mid-2018) should enable the company to launch its HCC test in H218. The company also plans to expand its reach via overseas partnerships, particularly in regions that historically have a high rate of HBV and HCV such as Asia.

PDS Biotechnology: Cancer vaccines

PDS Biotechnology is a biopharmaceutical company focused on the development of novel cancer immunotherapies and vaccines for infectious diseases. PDS has seven planned oncology clinical programmes in collaboration with the US National Cancer Institute (NCI) and Merck throughout 2017-20. PDS's products are based on the company's proprietary and novel T-cell activating platform, Versamune. Successful clinical trials and regulatory decisions will be followed by sales and marketing of the products, which the company may choose to undertake on its own or with a suitable marketing partner. A licensing deal with Merck KGaA was signed in 2016; PDS is in discussions with other large pharma companies regarding clinical development partnerships.

Versamune is a nanoparticle antigen technology based on the use of synthetic positively charged (cationic) lipids. The Versamune platform overcomes a major hurdle in immunotherapy by enabling the unique cancer proteins (antigens) to enter the cytoplasm of the immune dendritic cells directly. This leads to effective priming of tumour-specific killer (CD8+) T-cells to recognise and attack the tumours, leading to tumour cell death. The unique lipid used in the Versamune platform acts as a potent immune activator, which induces proliferation and activation of the primed T-cells.

In contrast to other cancer vaccines, the Versamune-based products are able to reduce the population of certain immune-suppressor cells that could inactivate T-cells. The ability to induce high levels of potent killer T-cells (tumour attack) while simultaneously reducing the number of immune-suppressor cells (tumour defence) allows the product to overcome immune suppression leading to high anti-tumour efficiency.

The nature and potential advantages of the technology mean that PDS management sees Versamune-based products as having the ability to overcome significant shortcomings of existing immunotherapy approaches. Cancer vaccines have been sub-optimal in their ability to treat cancers

largely due to their inability to facilitate antigen cross-presentation via the MHC Class I pathway to killer T-cells, which is compounded by inability to overcome tumour immuno-suppression. Chimeric antigen receptor (CAR) T-cells and checkpoint inhibitors, due to their safety profiles, target the very late-stage/terminal cancer patients; hence there is a clear therapeutic gap with earlier-stage cancer patients who may be the most treatable by immunotherapy. However, for such subjects a safer immunotherapeutic approach is needed. The company's first therapeutic using this platform, PDS0101, indicated strong T-cell potency and safety in Phase I, which lends it to targeting early-stage cancer.

Phase II clinical trials for PDS0101 will be in (1) grade 2 and 3 cervical and anal neoplasia patients (AIN/CIN); (2) stage III cervical cancer patients; and (3) late-stage human papillomavirus (HPV)-positive head and neck cancer in combination with Merck's checkpoint inhibitor Keytruda (pembrolizumab). Note that AIN/CIN 2/3 are now termed high-grade squamous intraepithelial lesion (HSIL). This type of lesion (CIN 3) is cured surgically, so patients in the proposed study may be at risk of cervical cancer. Most studies establish a therapeutic effect in low-grade squamous intraepithelial lesion (LSIL) patients. In addition, PDS plans to initiate clinical programmes in prostate and ovarian cancers in 2018.

PDS management (based on commissioned independent market research) estimates a market for treatment of high-grade precancerous cervical, anal, vulvar and vaginal lesions of $1.1bn in the fifth year after launch. In addition, sales into metastatic anal, cervical and oropharyngeal cancer markets in the same geographies were estimated by PDS management at $180m, $430m and $330m, respectively. We expect R&D costs of approximately £42m total before profitability in 2022.

A significant number of cancer vaccine programmes have failed to progress in the clinic over the past decade. Most recently, Bavarian Nordic, a cancer immunotherapy/infectious disease vaccine company, announced the failure of its lead Phase III monotherapy cancer programme, Prostvac, for patients with metastatic castration-resistant prostate cancer. Therefore, we consider the risks associated with cancer vaccine programme development to be higher than for other therapeutics.

Given the high impact of checkpoint inhibitors and their capacity for significant synergies with other treatments, there have been an unprecedented number of combination studies initiated with these drugs. EvaluatePharma 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 head and neck cancer (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 4). We 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 4: 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

Sensitivities

The NetScientific investment strategy in early-stage companies carries the inherent risk associated with the ability of the investees to both develop products and source additional financing. At this point, however, the amount of capital paid in by NetScientific is £32.8m, and is outsized by the expected value of the investments even at our high-risk estimates. This positions NetScientific to be

able to make early exits, significantly improving the risk profile of the parent. It is unlikely given this model that NetScientific will have a position in any of the investees following commercialisation, but a thorough examination of the risks of the investees over the lifetime of the company gives insight into both current and exit value.

Wanda, Vortex and ProAxsis are the three portfolio companies with fully developed products while the remaining two companies are both in very early development stages with significant investment needed before any products can compete commercially. The company with the highest level of development-related risk is PDS, as it carries the associated risks of drug development.

The diagnostics companies (Vortex, ProAxis and Glycotest) may be able to market tests in the near term on a provisional basis via various mechanisms (CE mark, CLIA waiver, investigational use), but will require significant clinical testing before broader marketing approval. We expect the Vortex and Glycotest programmes to require PMA enabling clinical utility trials before they can fully realise their market potential.

Although the Vortex platform has strengths, there are a large number of other companies developing similar technology to isolate CTCs (37 companies by management's measure). In this highly fragmented market, the marginal differences between these technologies may be less important for ultimate success than commercial factors. Another limiting factor of the current system is the long processing time per sample (one hour) and lack of parallelism, which significantly limits throughput for the test, and will hinder adoption for more broad-based screening.

A significant limiting factor for the success of Glycotest is that the company's product is a test for HCC, and the incidence of this disease is closely linked with the prevalence of HCV. HCV is being cured at a dramatically increased rate due to new technology, which we predict will translate into a decline in HCC incidence, as well as a decline in the at-risk population targeted for surveillance.

There are a unique set of risks associated with the commercialisation of the Wanda platform, both in the currently available programmes and for other programmes that may become available for other diseases. This area of digital health (chronic disease management) is largely untested and the size of the addressable market is uncertain. We model the market for recurring services in CHF/COPD in the range of $4bn, but there is significant risk associated with the degree to which healthcare providers and payers will embrace this technology. Additionally, the low barrier to entry for the digital health market has resulted in a large number of competitors in the chronic disease management space. The company will need to establish a sizeable footprint quickly to forestall any future entrants into the CHF/COPD chronic disease management space.

PDS Biotechnology is the only therapeutic company in the portfolio, and carries the associated risks of drug development: high R&D costs, regulatory risk, etc. Historically, cancer vaccine companies have not been successful at development, and we view the company's lead programmes as very high risk. Moreover, incidence rates for HPV-related cancers have been steadily declining and may decline more quickly as the number of immunised individuals increases and the vaccines prevent infection from an increasing number of strains. Finally, cervical dysplasia, which is a large fraction of the company's potential market (approximately 900k patients per year), has effective surgical treatments.

Every portfolio company needs additional capital, with our projected R&D costs ranging from £2m (ProAxsis) to £42m (PDS). There is substantial risk that these companies will not be able to raise sufficient capital given the current fund-raising environment. There have already been significant delays in the expected financing schedule for these companies. Guidance now points to financing rounds for Glycotest and PDS in H217, Vortex and ProAxsis in H118, and Wanda in H218.

Valuation

We have reduced our valuation to £57.3m or 83p per share, from £68.4m or 99p per share. This change was driven by delays in development and our sales ramps to reflect the prolonged financing timelines for the portfolio companies. Moreover, our revenue expectations for Vortex and Wanda have been adjusted to reflect the lack of any sales in H117. We have delayed the expected date of profitability for Glycotest to 2020 due to lack of financing and PDS to 2022 due to the lack of clinical progress in 2017 to date. The reduction also reflects lower net cash (£11.1m down from £17.3m) and an increase in share count. This was partially offset by an increase in the probability of success for ProAxsis from 10% to 15% due to recent commercial progress including a CE mark, and by rolling forward our NPVs.

Although the potential market opportunity is large, we are only able to assess probability of success in the range of 5-15% due to the early stages of development of the portfolios. Each company is modelled on the basis of self-commercialisation at this point, as opposed to out-licensing of assets, as we believe this is more illustrative of the intrinsic value of the internal programmes at this early stage.

We are withholding a valuation of certain programmes from the various constituent companies, awaiting a clear pathway to market. We have not modelled ex-US launches of the Vortex and Glycotest diagnostics because we view the current planned pricing for both programmes to be prohibitive overseas. We will add these programmes in the event that the management for these companies expresses a viable overseas commercialisation strategy or partner. Although we believe that the ProAxsis Protease-Tags may have utility outside of CF and COPD, we are withholding valuation of these programmes until a clear clinical pathway is announced. Lastly, although we see potential for the Wanda platform for the management of other chronic diseases (besides CHF/COPD and cancer), we do not want to speculate as to the nature of these future programmes.

Exhibit 5: Valuation assumptions

Company	Assumptions
Vortex	Potential screening population based on PSA adherence individuals over the age of 50 (42m in the US). Low penetration expected due to competition. $250/test, $135k/machine. 80% gross margins. EU commercialisation not modelled due to high cost and reimbursement environment. £5m R&D before 2019.
Wanda	Currently includes only CHF/COPD programmes, $225 per placement and $60/per month, at 40% and 90% gross margins, respectively. £4m R&D before 2019, 20% selling costs. Very high risk due to unproven model and high competition.
ProAxis	Thin EU sales following CE mark until payer support and US approval in 2020. Market is CF and severe COPD sputum producers (880k US and EU). US price $20, EU price £7. Low rate (10%) of payer discounts. £2m R&D before 2020.
Glycotest	Addressable market is diagnosed HBV, HCV, and NASH with cirrhosis patients. 2.1m addressable patients declining to 1.3m by 2030. $620 per test. 70% gross margin. Only US launch included due to high cost of screening and EU reimbursement environment. £6m R&D before 2019.
PDS	Currently includes high-grade cervical dysplasia, cervical cancer, and head and neck cancer programmes. All three are expected to have declines in incidence. Cervical dysplasia market penetration expected to be low (max 1%) due to availability of effective alternatives. US price $25k, EU price £10k. 90% gross margin. £42m in predicted R&D costs before approval. Very high risk due to low success probability for cancer vaccines and early stage of development.

Source: Edison Investment Research

We assign our highest probability of success to Vortex at 15%. We view the technology behind the platform as robust, and the fact that it isolates cells without the need for affinity labels provides an added degree of versatility for downstream applications. This should prove to be a competitive advantage. That said, the main risks to the company are commercial, considering the highly fragmented landscape and the low adoption of CTC testing to date. If the company is able to establish a significant footprint (eg 10% penetration in the research market) or secures a favourable distribution agreement, this would correspond to a substantial reduction in downstream risks. Additionally, we may update our valuation to reflect the development and future commercialisation of next generation platforms, when the details of these systems are announced.

Exhibit 6: NetScientific valuation

Portfolio company	Probability of success	Profitability	Peak sales (£m)	Margin	rNPV (£m)	Ownership	Share value (£m)
Vortex	15.0%	2020	141	44%	16.7	95.0%	15.9
Wanda	5.0%	2019	331	52%	11.7	70.9%	8.3
ProAxsis	15.0%	2020	47	51%	11.1	56.5%	6.3
Glycotest	10.0%	2020	115	51%	12.3	87.5%	10.8
PDS	10.0%	2022	274	56%	28.6	17.4%	5.0
Total							46.2
Net cash and equivalents (H117) (£m)							11.1
Total firm value (£m)							57.3
Total shares (m)							69.0
Value per share (p)							83

Source: NetScientific reports, Edison Investment Research

Financials

NetScientific's H117 post-tax loss of £5.2m (H116: loss of £6.4m) reflects ongoing investment into a portfolio of pre-commercialisation and therefore currently loss-making companies. An investment of £3.0m was made into the development of fundamental technologies and products of the core portfolio companies. Wanda's move from development to commercialisation is reflected in the reduction in research and development expenditure in comparison to H116 (£3.7m). We forecast that NetScientific will invest additional capital in R&D during H217 as we expect Glycotest to complete its Series A this year, which should result in a concurrent increase in spending for that programme. Selling, general and admin costs for H117 were £3.0m, which includes a significant proportion of subsidiary management by NetScientific executives; the increase on H116 (£2.4) was driven by increased sales and marketing development at the portfolio level, in particular Vortex and Wanda.

NetScientific had cash on the balance sheet of £11.3m at 30 June 2017 (H116: £15.9m; FY16: £9.5m), which includes the £8.1m raised in the June 2017 private placement. The company reported a small amount of revenue (£164k) for H117, mainly attributed to sales made by Wanda to its associate OncoVerse. Additionally, NetScientific's operating income of £222k is from ProAxsis's research development tax credit (£154k) and Innovate UK grant income (£67k). We have reduced our projected revenue ramp for Vortex, Wanda and Glycotest to reflect slow existing sales and delayed financing timelines. This has reduced our expected 2017 revenue to £1.4m from £2.7m, and these reductions are carried forward. We have similarly reduced our expected operating loss in 2017 to £9.9m from £13.7m to reflect these operational delays.

We fully incorporate the financials of Vortex, Wanda, ProAxsis and Glycotest into our projections, and accounted for the difference in earnings due to minority interests. PDS, as the sole minority stake, is accounted for as an equity investment. The future financing needs of PDS attributable to NetScientific are recorded as the acquisition of additional equity.

All of the NetScientific portfolio companies will need additional financing before reaching profitability, and the company has announced expected Series A financing rounds for Glycotest and PDS in H217, Vortex and ProAxsis in H118, and Wanda in H218. Our model forecasts £77m needed before profitability for all five programmes. The degree of dilution of these assets and the proportional ownership by NetScientific will depend on the nature of these offerings, and we expect to update our forecasts at that time. In the interim, we have included £16m in illustrative debt (in 2018) on our balance sheet to reflect the additional financing requirement required by NetScientific (including minority interests). This is a reduction from our previous estimate of £24m due to the recent financing. After accounting for £4m in cash burn attributable to minority interests over the period, this corresponds to a net obligation of £12m.

Exhibit 7: Financial summary

£000s	2014	2015	2016	2017e	2018e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS					
Revenue	24	122	518	1,380	3,781
Cost of Sales	0	(6)	(255)	(291)	(868)
Gross Profit	24	116	263	1,089	2,914
Research and development	(3,098)	(7,256)	(7,443)	(6,439)	(7,197)
Selling, general & administrative	(3,212)	(4,260)	(5,001)	(4,396)	(5,928)
EBITDA	(6,352)	(11,530)	(12,570)	(10,123)	(10,426)
Operating Profit (before GW and except.)	(6,286)	(11,400)	(12,429)	(9,909)	(10,212)
Intangible Amortisation	0	0	0	0	0
Exceptionals/Other	(948)	(1,518)	(666)	0	0
Operating Profit	(7,234)	(12,918)	(13,095)	(9,909)	(10,212)
Net Interest	77	78	86	2,143	(1,587)
Other (change in fair value of warrants)	0	0	(49)	(46)	0
Profit Before Tax (norm)	(6,209)	(11,322)	(12,343)	(7,766)	(11,799)
Profit Before Tax (IFRS)	(7,157)	(12,840)	(13,058)	(7,812)	(11,799)
Tax	30	94	(18)	44	59
Deferred tax	0	0	0	0	0
Profit After Tax (norm)	(6,179)	(11,229)	(12,361)	(7,722)	(11,740)
Profit After Tax (IFRS)	(7,127)	(12,746)	(13,076)	(7,768)	(11,740)
Minority interest	702	1,905	1,881	1,909	1,984
Profit After Tax after minority interest (FRS 3)	(6,425)	(10,842)	(11,195)	(5,859)	(9,757)
Average Number of Shares Outstanding (m)	35.9	38.2	51.1	60.1	69.0
EPS - normalised (p)	(15)	(24)	(21)	(10)	(14)
EPS - IFRS (p)	(18)	(28)	(22)	(10)	(14)
Dividend per share (p)	0	0	0	0	0
BALANCE SHEET					
Fixed Assets	3,040	2,946	4,054	3,066	4,528
Intangible Assets	10	1	0	0	0
Tangible Assets	348	285	779	1,161	1,543
Other	2,681	2,660	3,275	1,905	2,985
Current Assets	17,720	23,799	11,034	10,627	13,943
Stocks	0	0	0	460	756
Debtors	853	560	1,578	1,119	378
Cash	16,867	23,239	9,456	9,048	12,809
Other	0	0	0	0	0
Current Liabilities	(1,324)	(2,206)	(2,172)	(2,152)	(2,581)
Creditors	(1,281)	(2,156)	(2,044)	(2,029)	(2,458)
Short term borrowings	(43)	(50)	(128)	(123)	(123)
Long Term Liabilities	(740)	0	(80)	(80)	(15,874)
Long term borrowings	(687)	0	(80)	(80)	(15,874)
Other long term liabilities	(53)	0	0	0	0
Net Assets	18,696	24,538	12,836	11,461	17
Minority Interest	(1,098)	(1,805)	(3,875)	(5,784)	(7,768)
Shareholder Equity	17,598	22,733	8,961	5,677	(7,751)
CASH FLOW					
Operating Cash Flow	(6,698)	(10,752)	(12,939)	(8,564)	(8,828)
Net Interest	67	38	43	(2)	(1,587)
Tax	19	83	112	44	59
Capex	(336)	(299)	(457)	(596)	(596)
Acquisitions/disposals	(2,181)	(144)	(1,261)	1,044	(1,080)
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)	9	(12,033)
Opening net debt/(cash)	(25,069)	(16,136)	(23,189)	(9,248)	(8,844)
HP finance leases initiated	0	0	0	0	0
Exchange rate movements	(140)	(212)	(603)	166	0
Other	218	92	1,098	(578)	0
Closing net debt/(cash)	(16,136)	(23,189)	(9,248)	(8,844)	3,188

Source: NetScientific reports, Edison Investment Research

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Management team

CEO: Dr François Martelet	Chairman: Sir Richard Sykes
François Martelet joined NetScientific in 2015. He was previously a senior advisor to the CEO at Stallergenes. Before this, he was CEO at Topotarget, and prior to that CEO of Avax Technologies. He has also held senior-level commercial positions at Merck, Novartis Pharma, Schering-Plough and Eli Lilly. François gained a doctorate in medicine and a master's degree in business from Dijon University, and holds a degree in legal medicine from R Descartes University School of Medicine, Paris. He is a graduate of the Advanced General Management Programme at INSEAD.	Sir Richard was CEO of GlaxoSmithKline from 1995 to 2000 and chairman until 2002. He was rector of Imperial College from 2000 to 2008. He has held a number of directorships since 2002 and became the chairman of NetScientific in 2013. He holds a BSc in microbiology from London University and a PhD in microbial metabolism from Bristol University.
CFO: Ian Postlethwaite	
Ian Postlethwaite was FD of Allergy Therapeutics from 2002 to 2016. He is a former director of Ellerman Investments, CEO of AFS, FD of several start-up technology companies and held senior finance positions with Ericsson and Philips Electronics. He is a qualified accountant and a fellow of the Association of Chartered Certified Accountants. Ian has a BSc (hons) in geological sciences from Aston University.	

Principal shareholders	(%)
Woodford Investment Management	45.0
Invesco Asset Management	19.8
Azima Trust	15.1
JO Hambro	8.5

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