EDISON

Proteome Sciences

Data, deal and results

Data-driven progress

Pharma & biotech

Proteome Sciences signed its first major biomarker service contract in September. This followed on from the data from the 1,148-patient Alzheimer's disease (AD) study, which could lead to a blood-based AD diagnostic test being developed. Data published this year on the SysQuant assay highlighted its potential as a drug development and diagnostic tool. These data are expected to lead to more service contracts and licensing agreements in the medium to long term. We therefore raise our valuation to £194m, although in the short term we are lowering our estimates as it has taken longer than anticipated to sign major service contracts.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
12/12	1.2	(5.2)	(2.2)	0.0	N/A	N/A
12/13	2.1	(3.6)	(1.6)	0.0	N/A	N/A
12/14e	1.7	(4.2)	(1.7)	0.0	N/A	N/A
12/15e	2.3	(4.0)	(1.6)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding intangible amortisation, exceptional items and share-based payments. Note: Forecasts exclude any revenue from licensing deals.

AD data leads to first major service contract

A paper in *Alzheimer's & Dementia* in July showed that a panel of 10 blood-based protein biomarkers was able to identify patients with mild cognitive impairment who would develop AD within a year with a sensitivity of 85% and specificity of 88%. Proteome Sciences subsequently signed a $2m contract with a subsidiary of TauRx Therapeutics to analyse blood samples from a Phase III AD study. We expect other similar contracts to be signed.

Potential of SysQuant becomes more apparent

Proteome Sciences' SysQuant assay has considerable potential, as it provides detailed information of the overall state of a cell and its activity. This is supported by the data in scientific papers from pancreatic cancer and AD studies, which indicated that the assay could be used to facilitate drug discovery and function as a diagnostic tool for physicians, across various therapeutic fields.

CK1d takes another step closer to being partnered

No adverse results were found during additional preclinical toxicology testing of products from the CK1d programme in AD, Proteome Sciences' sole drug discovery project. This helps to de-risk the programme and should facilitate the partnering of the asset, which has already been shown to improve cognition in an animal model.

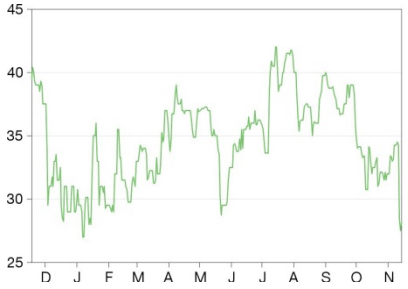
Valuation: DCF valuation of £194m (90p per share)

We have raised our valuation by £47m to £194m, because of the data with the AD biomarker panel and SysQuant. However, it is taking longer than expected for major biomarker service contracts to be signed, so we have reduced our numbers in line with the revised guidance, and our estimates exclude any upfront payments from potential licensing deals for AD biomarkers or the CK1d programmes.

17 November 2014

Price	**28.25p**
Market cap	**£60m**
Net debt (£m) at 30 June 2014	4.1
Shares in issue	214.1m
Free float	67%
Code	PRM
Primary exchange	AIM
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(16.9)	(25.2)	(29.4)
Rel (local)	(20.5)	(24.8)	(29.5)
52-week high/low		42p	27p

Business description

Proteome Sciences is a protein biomarker contract research organisation. It has a broad patent portfolio covering isobaric mass tagging in mass spectrometry and biomarkers for various neurological and oncology indications.

Next events

Potential licensing deals	H115
FY14 results	May 2015

Analysts

Dr Mick Cooper	+44 (0)20 3077 5734
Christian Glennie	+44 (0)20 3077 5727

healthcare@edisongroup.com

Edison profile page

Update: Data-driven progress

It has taken longer than forecast for Proteome Sciences' services to be adopted, but the first major contract for its PS Biomarker Services division shows that they are gaining important commercial traction. The $2m contract is with Genting TauRx Diagnostic (GTD), a subsidiary of TauRx Therapeutics, to analyse blood samples from patients in a Phase III trial in AD. This was announced after the publication of data from a 1,148-patient trial, which showed that a panel of 10 of Proteome Sciences' blood-based biomarkers was able to identify with 87% accuracy the patients with mild cognitive disorder who would develop AD within a year. Proteome Sciences has also further developed its SysQuant test, which has great potential in assisting oncology drug development and helping cancer patients receive the correct treatment, based on data presented in April.

We are more cautious about the rate of revenue growth for Proteome Sciences as it appears to be taking longer to convert pilot projects into large commercial programmes, such as the one with GTD. However, the value of its proprietary biomarkers and assays, particularly in AD, is becoming more apparent, which raises the likelihood of biomarker licensing deals; consequently, we have increased our valuation by £47m to £194m. There is additional upside from its only drug discovery programme (CK1d for AD), which could be out-licensed during the next 12 months.

Alzheimer's disease biomarker potential made clear

Proteome Sciences has an extensive portfolio of biomarkers across various areas, including oncology, stroke, liver toxicology and dermatology, which have been identified using its proprietary mass spectrometry technology (tandem mass tagging [TMT], a form of isobaric mass tagging). However, its most valuable proprietary biomarkers are in the field of AD. It is becoming increasingly apparent that the early diagnosis of AD is important to be able to treat the disease, and that the test ideally needs to be a blood-based test, given the large number of people diagnosed with AD each year. In collaboration with its partners at King's College London, Proteome Sciences has developed a panel of 10 biomarkers, which could address this issue.

In July, a paper in the journal *Alzheimer's & Dementia*[1] indicated that the panel of 10 plasma-based biomarkers could be used to identify patients for clinical trials in AD in the first instance, before becoming an AD diagnostic test for people with mild cognitive impairment (MCI). Of the 1,148 people in the study, 169 patients had MCI that did not convert into AD within a year and 51 had MCI that converted. Analysis of blood samples from 75% of these patients was used to identify the optimum panel of a priori specified biomarkers, and the resulting panel was subsequently tested on the other 25% of MCI patients (n=55). When the 10-biomarker panel for MCI patients expected to develop AD within one year was tested on the 55 remaining patients, it was found to have a sensitivity of 85%, specificity of 88% and accuracy of 87%.

These data confirm the potential of Proteome Sciences' AD biomarkers, and have already laid the platform for the £2m contract with GTD. Proteome Sciences' PS Biomarker Services division will analyse the proteins found in the blood from c 1,000 patients taking part in TauRx's Phase III trial in mild AD with LMTX (TRx0237, which inhibits the aggregation of microtubule-associated protein Tau), to construct biomarker panels for the detection of AD and monitor treatment efficacy. Proteome Sciences will receive upfront and milestone payments totalling £2m and will then be eligible for a share of any commercialisation rights from companion diagnostic tests.

[1] Hye et al (2014); Plasma proteins predict conversion to dementia from prodromal disease; Alzheimer's & Dementia; 1-9.

We believe it is likely that other companies developing treatments for AD will look to use PS Biomarker Services to assist them with their clinical trials. The key challenge with clinical trials in this indication is identifying a relatively homogeneous population of patients with mild/prodromal AD. The main method used currently is the MMSE (mini-mental state examination), which detects cognitive impairment, but cannot identify those patients likely to progress from MCI to AD in a short period of time. This is a particular issue for drug development companies, because as few as 10% of MCI patients might develop AD over the next 12 months, meaning that an AD drug might fail a clinical trial as it was being tested in people with very slow progressing AD, where any benefit would only be seen after a number of years.

Proteome Sciences' AD biomarker panel also has the potential to become a standard test for patients with signs of cognitive impairment to see if they are likely to develop AD. Initially, it might be used as a screening tool for patients likely to develop AD before using other more established assays that are more costly and can be more invasive, such as cerebral spinal fluid (CSF) analysis, MRI or PET scans. However, in time it could be the main test used to identify AD patients so that they receive the most appropriate therapy as quickly as possible.

The data on the AD biomarker panel could also lead to the biomarkers being licensed to companies for use in diagnostic tests. It is possible that a test based on the panel could be launched within the next two years, in Europe under a CE mark and in the US as a laboratory-developed test performed in CLIA-certified labs. Initially, the use of the panel could be limited until there is additional validation of its utility. This process is already underway, with Proteome Sciences involved with various collaborations (eg AddNeuroMed, and Alzheimer's Research UK) to gain more data on its AD panel.

The potential value of Proteome Sciences' AD biomarkers is indicated by Eli Lilly acquiring Avid Radiopharmaceuticals in December 2010 for $300m and up to $500m in milestones to obtain control of the amyloid-plaque imaging agent Florbetapir, even though its use requires a PET scan. Proteome Sciences' biomarkers have much greater potential than Florbetapir, as a special instrumentation like a PET scanner would not be needed and the company has indicated that the biomarker tests could be priced at a level (c $400 per test) that would allow the broad use of Proteome Sciences' biomarkers. We currently estimate that biomarkers using Proteome Sciences' panel will generate peak sales of $850m, but this could be much greater if the tests become standard methods of diagnosing and monitoring AD.

SysQuant: Shining a light on cell activity

SysQuant assay is the other key asset developed by Proteome Sciences and could become a key workflow during drug discovery, clinical trials and in helping physicians to decide the most appropriate treatment for patients. SysQuant has particular potential in oncology, but can also be used in many other therapeutic fields, including CNS diseases.

During FY14, Proteome Sciences has quadrupled the capabilities of the SysQuant test, so that it can assess the state of over 22,000 different phosphorylation sites in a single experiment. A cell's activity is often modulated by adding or removing a phosphate group from certain positions on specific proteins. Therefore, Proteome Sciences can gain valuable insights into the metabolism or disease state of a cell by using SysQuant to identify the proteins that are phosphorylated and those that are not.

The ability of SysQuant to provide such detailed information about what is occurring in a cell means it could be used:

- to support drug discovery programmes, including identifying potential targets, by providing new insights into the underlying causes of diseases;

- to monitor the effect of a drug on cells/tissues in preclinical and clinical studies. This could provide a better understanding of a drug's efficacy and safety profile, including allowing companies to gain an early indication of a drug's activity in clinical trials or use adaptive clinical trial designs; and
- to identify patients likely to respond to a therapy or combination of treatments. This could improve the likelihood of success in clinical trials and enable the prescription of more appropriate therapies.

The importance of phosphorylation pathways is well known in cancer, where various kinases (enzymes that add phosphate groups to proteins) are often drug targets, eg sunitinib (Sutent) is a tyrosine kinase inhibitor. So this is an area where pharmaceutical companies will probably be most interested in assessing SysQuant, especially as a paper published in the journal PLOS ONE[2] in March presented data on tumour and non-tumour pancreatic cancer, highlighting its utility. SysQuant identified 635 changes in phosphorylation patterns in the tumour tissue for proteins, some of which are involved with cell migration and the formation of focal adhesions. The study also concluded that SysQuant analysis could be used to help oncologists select the best combination of treatments for their patients.

The ability of SysQuant to analyse the many different phosphorylation pathways at the same time is key to its utility. The various pathways interact with each other and cancer cells often have mutations that affect more than one of them. So by using SysQuant, it should be possible to select the optimum therapy, as stated in the PLOS ONE paper. This could be of particular use in patients who are not responding to treatment, which is why the introduction of the Saatchi Bill in the UK could lead to demand for SysQuant. The Bill, which we expect to come into law in 2015, will allow doctors to treat patients with any experimental medicine, but this will require the careful characterisation of a patient's disease by a product such as SysQuant.

Changes in phosphorylation patterns are equally important in many other diseases. A poster presented at the Alzheimer's Association International Conference (AAIC) showed that SysQuant was able to observe the phosphorylation patterns of proteins in tissue from an animal model for degenerative diseases and measure the impact of treatment with a kinase inhibitor and identified novel modes of action for their compounds targeting CK1d in the tau pathway. SysQuant could therefore eventually be used throughout drug development and beyond, across many disease areas.

CK1d inhibitor set for out-licensing

Proteome Sciences has no intention of becoming a drug development company and only initiated a drug discovery project to demonstrate the strength and capabilities of its mass spectrometry technology platforms. However, its one drug development programme, CK1d inhibitors, could be an important value driver for the company.

Proteome Sciences identified CK1d (casein kinase 1 delta) as a protein that is expressed at higher levels in AD brain tissue and appears to play an important role in the progression of AD. From this finding, the company identified specific inhibitors of CK1d from compound libraries, optimised the initial molecules and conducted initial preclinical studies with the assistance of CROs. The CK1d inhibitors (PS110 and PS278-05) have so far been shown to improve cognition in AD animal models and have been shown to have a favourable safety profile in preclinical toxicology studies (including Ames and Cyp tests).

The company now plans to out-license the programme and let a partner take full responsibility for the development and commercialisation of the programme. The latest data reported in September

[2] Britton et al (2014); Quantification of pancreatic cancer proteome and phosphorylome: indicates molecular events likely contributing to cancer and activity of drug targets; PLOS ONE 9(3): e90948.

(the Ames and Cyp test results) should help de-risk the programme from the perspective of a possible licensee and facilitate a deal. There also appears to be a growing interest in the field of AD following the political initiatives in the UK and US. The most recent deal for an early-stage AD asset was for the co-development of AstraZeneca's BACE inhibitor AZD3293 (a Phase I study completed) with Lilly in September, in which Lilly acquired 50% of the programme rights for up to $500m in development and regulatory milestones ($50m due in H115), with all costs and revenues to be shared equally. The terms of any deal for Proteome Sciences will probably be smaller in biodollar terms as the CK1d programme is at an earlier stage of development and Proteome Sciences is not looking to enter into a co-development deal. However, this recent deal highlights that the company could partner the Ck1d programme on very favourable terms.

Valuation

We have raised our valuation of Proteome Sciences from £147m to £194m or 90p per share based on a sum-of-the-parts DCF valuation (Exhibit 1). The increase results from the data and progress with its AD biomarkers and SysQuant, although it has taken longer than expected for major contracts to be signed (see below). There is also additional upside from the CK1d programme, which is not included in our valuation due to its early stage, and uncertainty regarding the timing of any deal or the potential terms.

Exhibit 1: Summary of DCF valuation

Value driver	Value (£m)	Value per share (p)	Notes
TMT sales	21.4	10	Based on Proteome Sciences revenues from TMT increasing from c £0.5m in FY13 to £4.6m in FY17. All revenues treated as royalties.
PS Biomarker services	23.3	11	Based on PS Biomarker Services revenues increasing from c £1m in FY12 to £2.7m in FY17 (4x £500k biomarker services contracts and 2.8k x £250 biomarker assays); gross margin: 85%, likelihood of success: 80%.
Alzheimer's disease biomarkers*	110.4	47	Cost per test: $750; market penetration 10%; peak sales: $760m; launch date: 2017; likelihood of success: 60%; royalty: 10%.
Stroke biomarkers*	59.0	28	Cost per test: $750; market penetration 10%; peak sales: $495m; launch date: 2015; likelihood of success: 40%; royalty: 10%.
SysQuant/Cancer biomarkers*	63.0	29	Cost per test: $6,400; market penetration of breast and lung cancer markets: 10%; peak sales: $580m; launch date: 2017; likelihood of success: 60%; royalty: 10%.
Grants and licence fees	0.5	0	
Admin	(52.4)	(25)	
Tax	(21.0)	(10)	Tax paid from 2018 at 10% tax rate.
Capex	(0.7)	(0)	
Net cash	(4.1)	(2)	Net cash at H114.
Total	193.7	90	

Source: Edison Investment Research. Note: WACC of 12.5% is used, peak sales of biomarkers at five years after launch. *The value of potential royalties for Proteome Sciences' biomarkers from diagnostic tests.

The main changes to our valuation are:

- a reduction in the value of the PS Biomarker Services business from £42m to £23m because it has taken longer than expected for pilot programmes to be converted into significant commercial contracts;
- an increase in the value of the AD biomarkers from £47m to £110m after increasing the likelihood of success from 30% to 60% because of the data published in the *Alzheimer's & Dementia* paper and the contract with GTD; and
- an increase in the value of SysQuant/cancer biomarkers from £25.2m to £63m after increasing the likelihood of success from 30% to 60% because of the data presented in the *PLOS ONE* paper.

The next catalysts for the shares are expected to be potential licensing agreements for biomarkers or CK1d, the announcement of major PS Biomarker Service contracts or licensing deals for its AD or stroke biomarkers.

Financials

Proteome Sciences' sales from licences/sales/services were essentially flat at £0.71m during H114 (£0.75 in H113) and overall sales including grant income were £0.78m during the period (£0.89 in H113). There is no further breakdown of the sales, but H113 sales had probably included an upfront payment for the second agreement with Thermo Fisher Scientific, a £2.1m contract signed in June 2013. Proteome Sciences also reported that the sales of the TMT reagents by Thermo Fisher Scientific increased by 98% in H114. So, despite the apparent lack of revenue growth in H114, we still believe the company is maintaining its momentum, and this view is supported by the $2.0m AD biomarker contract signed with GTD in September.

Proteome Sciences maintained its tight control on expenses in H114 so that admin expenses only increased by 5.3% to £2.46m, although the company has significantly increased its commercialisation activities. This resulted in the net loss for the period increasing by £0.18m to £1.84m.

We have reviewed our estimates as indicated in Exhibit 2, taking into account the H114 results and the fact that it has taken longer than we had anticipated for pilot programmes with PS Biomarker Services to be converted into major contracts similar to the one with GTD. Our new numbers are in line with the company's revised financial guidance. It is not unusual for contracts to take a long time to negotiate with large pharma companies. We therefore remain confident that large PS Biomarker Services will be signed in due course, because of the strength of Proteome Sciences' mass spectrometry technology platform and broad biomarker portfolio; however, we believe it is prudent to be more conservative about the rate at which we expect Proteome Sciences to grow. It is important to note that our estimates do not include potential licensing deals for biomarkers or its CK1d drug discovery programme.

Proteome Sciences had a gross cash position of £3.5m at H114 (net debt of £4.1m), including the equity issue of £5m in February 2014. With our more conservative estimates, this should allow the company to operate into H215 without raising additional capital. However, the cash runway could be significantly extended by the formation of licensing agreements for its biomarkers and/or CK1d programme with potentially significant upfront and milestone payments.

Exhibit 2: Summary of changes to estimates

	Sales (£m)			PBT (£m)			EPS (p)		
	Old	New	% chg.	Old	New	% chg.	Old	New	% chg.
2014e	5.7	1.7	(69.3)	0.7	(4.2)	N/A	0.1	(1.7)	N/A
2015e	8.3	2.3	(72.5)	1.3	(4.0)	N/A	0.9	(1.6)	N/A

Source: Edison Investment Research

Exhibit 3: Financial summary

£000s	2011	2012	2013	2014e	2015e	2016e
Year end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	1,021	1,153	2,137	1,736	2,291	3,572
Cost of Sales	(257)	(385)	(593)	(561)	(626)	(1,010)
Gross Profit	764	767	1,544	1,176	1,666	2,562
EBITDA	(4,136)	(4,838)	(3,205)	(3,624)	(3,506)	(2,931)
Operating Profit (before GW and except.)	(4,341)	(5,004)	(3,373)	(3,995)	(3,763)	(3,138)
Intangible Amortisation	0	0	0	0	0	0
Exceptionals	0	0	0	0	0	0
Operating Profit	(4,341)	(5,004)	(3,373)	(3,995)	(3,763)	(3,138)
Other	0	0	0	0	0	0
Net Interest	(169)	(191)	(224)	(231)	(243)	(296)
Profit Before Tax (norm)	(4,510)	(5,195)	(3,596)	(4,226)	(4,007)	(3,435)
Profit Before Tax (FRS 3)	(4,510)	(5,195)	(3,596)	(4,226)	(4,007)	(3,435)
Tax	553	942	447	667	597	627
Profit After Tax (norm)	(3,957)	(4,254)	(3,149)	(3,558)	(3,409)	(2,808)
Profit After Tax (FRS 3)	(3,957)	(4,254)	(3,149)	(3,558)	(3,409)	(2,808)
Average Number of Shares Outstanding (m)	192.2	192.5	194.0	211.0	214.1	214.1
EPS - normalised (p)	(2.1)	(2.2)	(1.6)	(1.7)	(1.6)	(1.3)
EPS - FRS 3 (p)	(2.1)	(2.2)	(1.6)	(1.7)	(1.6)	(1.3)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0	0.0
Gross Margin (%)	75%	67%	72%	68%	73%	72%
EBITDA Margin (%)	N/A	N/A	N/A	-209%	-153%	-82%
Operating Margin (before GW and except.) (%)	N/A	N/A	N/A	-230%	-164%	N/A
BALANCE SHEET						
Fixed Assets	5,642	4,713	5,273	4,919	4,738	4,613
Intangible Assets	4,218	4,218	4,218	4,218	4,218	4,218
Tangible Assets	661	495	1,055	701	519	395
Other	764	0	0	0	0	0
Current Assets	5,267	2,237	1,782	3,478	1,746	2,719
Stocks	301	331	403	388	388	388
Debtors	903	1,047	779	1,158	753	1,174
Cash	4,064	858	600	1,931	604	529
Other	0	0	0	0	0	627
Current Liabilities	(7,431)	(7,414)	(9,000)	(9,352)	(9,755)	(10,221)
Creditors	(692)	(479)	(808)	(931)	(1,086)	(1,254)
Short term borrowings	(6,526)	(6,726)	(7,951)	(8,191)	(8,439)	(8,737)
Short term leases	0	0	0	0	0	0
Other	(213)	(209)	(241)	(230)	(230)	(230)
Long Term Liabilities	(180)	(303)	(255)	(262)	(1,762)	(4,762)
Long term borrowings	0	0	0	0	(1,500)	(4,500)
Long term leases	0	0	0	0	0	0
Other long term liabilities	(180)	(303)	(255)	(262)	(262)	(262)
Net Assets	3,299	(767)	(2,200)	(1,217)	(5,034)	(7,651)
CASH FLOW						
Operating Cash Flow	(5,143)	(4,210)	(3,201)	(3,375)	(2,756)	(2,993)
Net Interest	24	9	2	9	4	2
Tax	(23)	856	434	(23)	0	0
Capex	(206)	(15)	(9)	(25)	(76)	(83)
Acquisitions/disposals	0	0	0	0	0	0
Financing	0	24	1,556	4,794	0	0
Dividends	0	0	0	0	0	0
Other	8	0	0	0	0	0
Net Cash Flow	(5,340)	(3,335)	(1,218)	1,380	(2,827)	(3,075)
Opening net debt/(cash)	(3,210)	2,462	5,868	7,351	6,260	9,335
HP finance leases initiated	0	0	0	0	0	0
Other	(332)	(71)	(265)	(288)	(248)	(298)
Closing net debt/(cash)	2,462	5,868	7,351	6,260	9,335	12,708

Source: Edison Investment Research, company accounts. Note: FY15 and FY16 include increases in long-term debt, which is indicative of the company's funding requirement; this could be achieved through licensing agreements with upfront/milestone payments, or the issuance of debt or equity.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
245 Park Avenue, 39th Floor
10167, New York
US

Sydney +61 (0)2 9258 1161
Level 25, Aurora Place
88 Phillip St, Sydney
NSW 2000, Australia

Wellington +64 (0)48 948 555
Level 15, 171 Featherston St
Wellington 6011
New Zealand