EDISON

ReNeuron Group

Stroke study

Clinical pipeline progressing as planned

Pharma & biotech

ReNeuron reported in December 2016 positive Phase II trial data for its CTX cells in chronic stroke patients, despite not meeting the three-month time frame of a two-point improvement in its primary outcome measure, the Action Research Arm Test (ARAT). As a result, the company has confirmed that it will progress to a pivotal controlled clinical study in 2017. Beyond CTX, we expect safety and efficacy data from its retinitis pigmentosa (RP) trial in 2017 and Phase I data from its critical limb ischaemia (CLI) trial. Our rNPV has increased to £291m.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
03/15	0.0	(10.3)	(0.50)	0.0	N/A	N/A
03/16	0.0	(12.8)	(0.44)	0.0	N/A	N/A
03/17e	0.0	(19.5)	(0.58)	0.0	N/A	N/A
03/18e	0.0	(31.3)	(0.93)	0.0	N/A	N/A

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

Stroke Phase II data review

PISCES II was a single arm, open-label study in patients with stable paresis (partial paralysis) of an arm 4-12 weeks following an ischaemic stroke. The primary end point of a minimum two-point improvement in the ARAT was not met within the pre-specified three-month time period, although three patients met the criteria at three, six and 12 months after treatment respectively. Also, clinically relevant end points were seen in other efficacy measures, with 15/21 patients achieving a clinically relevant and sustained response on at least one measure. Importantly, CTX was shown to be well tolerated, with side effects only relating to the surgical procedure.

Next steps for CTX in stroke

ReNeuron now intends to apply to US and EU regulators for permission to start a randomised, placebo-controlled, pivotal clinical trial in 2017, with potential read-out in 2019. We expect this to take place predominantly in the US and potentially some European sites, with a focus on measures of disability and daily living, such as the Barthel Index (BI) and Modified Rankin Scale (mRS), as these are particularly favoured by regulators. ReNeuron is also conducting an observational study, from which we expect insight into the natural time course of disease progression, which we also expect to be considered in the next trial design.

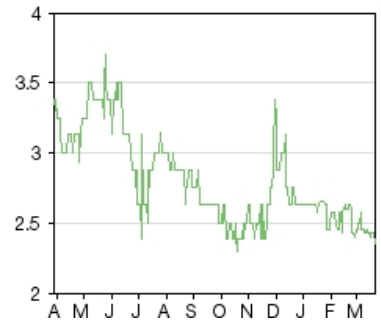
Valuation: Increased to £291m

Our rNPV-based valuation has increased to £291m (vs £278m), as we have rolled the model forward to 2017. ReNeuron is well-funded (£60m cash at end September 2016), which should enable it to execute on an expanding clinical trial programme. This could result in a number of key inflection points, including initiation of a pivotal Phase III study for CTX in stroke (H117), initiation of a Phase II clinical trial for CTX in CLI in 2017, Phase I/II human retinal progenitor cells (hRPC) data in 2017 and further preclinical data from the exosome nanomedicine platform (efficacy and toxicity).

23 March 2017

Price	**2.35p**
Market cap	**£74m**
Net cash (£m) at 30 September 2016	60.0
Shares in issue	3,164.6m
Free float	60.5%
Code	RENE
Primary exchange	AIM
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(10.5)	(10.5)	(30.4)
Rel (local)	(11.7)	(14.9)	(41.1)
52-week high/low		3.7p	2.3p

Business description

ReNeuron is a UK biotech company developing allogeneic cell therapies. CTX neural stem cells are in development for ischaemic stroke disability (Phase III planned) and critical limb ischaemia (Phase I), and human retinal progenitor cells (hRPCs) are being studied for retinitis pigmentosa (Phase I/II).

Next events

CTX: start stroke Phase III study	H117
CTX: CLI Phase I data/Phase II study start	H117
12-month follow-up from PISCES II stroke trial	H217
hRPC: safety and efficacy data	2017

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Edison profile page

Investment summary

Company description: Gaining traction as trials progress

ReNeuron is a UK clinical-stage company developing a portfolio of stem cell-based therapies. Three programmes are in clinical development; the lead programme, CTX, is about to start a pivotal Phase III study for ischaemic stroke disability and is currently in a Phase I dose-escalation study for CLI. The company was established in 1998, listed on AIM in 2005 and has 55 employees. In 2013, ReNeuron raised £25.3m (gross) through a placement of 1,014m shares at 2.5p to new investors including Invesco, Abingworth and the Wales Life Sciences Investment Fund, and secured a £7.8m grant package from the Welsh government to build a new manufacturing and research facility in South Wales. Following this, in 2015, it raised £68.4m (£65m net) through a placement of 1,367.4m shares at 5p per share. Woodford Investment Management (WIM) is now the biggest shareholder, with c 36%, having acquired a large part of Invesco's previous holding, following Neil Woodford's move from Invesco to WIM. Olav Hellebø was appointed CEO in September 2014.

Valuation: Increased to £291m

We have rolled our model forward to 2017 and therefore increased our valuation to £291m (vs £278m) or 9.2p per share. We note that this does not include a contribution for the earlier stage exosome nanomedicine platform as it is currently preclinical. We expect to revisit this when its first target is taken into the clinic in 2018. ReNeuron is well-funded (into FY19 on current forecasts), which should enable it to execute on an expanding clinical trial programme, resulting in a number of potential key inflection points over the next 24 months, including: initiation of a pivotal Phase III study for CTX in stroke (H117); initiation of a Phase II clinical trial for CTX in CLI in 2017; Phase I/II hRPC data in 2017; and further preclinical data from the exosome nanomedicine platform (efficacy and toxicity).

Financials: Well-funded to progress

On our forecasts, ReNeuron is funded into FY19, which should enable significant advancement of the two pivotal clinical studies (stroke Phase III and RP Phase II/III), advancement of the CLI Phase II study and Phase I exosome study in glioblastoma multiforme. With £60m in cash at the end of September 2016, ReNeuron has the resources to progress to potential valuation inflection points and continue to develop its broad portfolio. We expect ReNeuron to continue accelerating its investment in operating activities, particularly within R&D, in line with the progression of its clinical pipeline.

Sensitivities: Reducing as it progresses

ReNeuron is subject to the risks typically associated with drug development, including the possibility of unfavourable outcomes in clinical trials and regulatory reviews, success of competitors and commercial decisions by partners or potential partners. Specifically, it will be the outcome of the CTX Phase III stroke trial that will determine the product's eventual commercial potential. The industry's track record of R&D in stroke is poor, so this is a particularly high-risk indication. Recruitment of patients into stroke and CLI trials has also historically been a rate-limiting factor for a number of clinical studies and ReNeuron may face similar constraints in the future. Hence, there can be little assurance that our current estimates for completion of the trial programmes and subsequent next steps, particularly the stroke study, will be met. ReNeuron is well-financed and has reasonable visibility on the regulatory and clinical pathways, following discussions with the regulators, compared to a few years ago. Nonetheless, it is still exposed to the sensitivities normally associated with novel drug development.

Stroke study review – PISCES II

ReNeuron recently presented positive Phase II trial data for its CTX cells in chronic stroke patients. The Phase II trial evaluated standardised CTX neural stem cells, injected into the putamen of the brain on the affected side, in a 21-patient Phase II trial for reducing disability following an ischaemic stroke. It specifically looked at improving patient outcomes (or not) during the rehabilitation phase. The PISCES-II study has been described as a futility study, designed to provide a clear and definitive signal of efficacy with CTX cells. Alongside this, it also builds on the body of safety data from the Phase I trial. For an overview of the PISCES I study, our update report following the publication of results in The Lancet can be found here. The Phase II trial design is outlined below.

Exhibit 1: PISCES-II clinical study design

Trial design	Overview
Aim	To determine whether treatment with 20m CTX cells can improve recovery in the use of a paretic arm in acute stroke patients, in order to justify a larger controlled pivotal study.
Summary design	UK, multiple centre (10 sites), open-label, single arm (no comparator), study
Design details	21 pts; 40-89 years; stroke occurred within previous 2-12 months; patient had to have a paretic (loss of movement) arm at both four and eight weeks after a stroke (<5% chance of recovering use of arm). ARAT score of 0 or 1 at baseline, NIHSS*) upper limb motor score of 4, 3, or 2.
Primary end points	≥2-point improvement in ARAT score, six months post-treatment. Specifically, test number 2 of ARAT (grasp a 2.5cm^3 block and move it from A to B positions in <60 seconds) with paretic arm; seeking five responders out of 41 patients.
Secondary end points	Multiple 12-month assessments, including changes in: ARAT scores for upper limb function; modified NIHSS; Rankin Focused Assessment version of the mRS; BI; and safety/tolerability.
Start date	June 2014
Completion dates	Three-month follow-up data presented Q416, end 2017: full-study data analysis.

Source: Edison Investment Research, www.clinicaltrials.gov * National Institute of Health Stroke Score

Within the study, 21 patients were treated with a median time from stroke to treatment of seven months (2-13). These patients have been treated across 10 UK sites with eight UK sites having treated at least one patient. Baseline demographics include:

- male: 52%; female: 48%
- white: 95%
- median age: 62 years (41-79)
- site of ischaemic infarct:
  - cortex: 53%
  - subcortex: 14%
  - cortex and subcortex: 33%

The primary outcome measure was a minimum 2-point improvement in the ARAT #2. The choice of the ARAT response as an outcome is to provide a robust (and non-subjective) indication of what the benefit would be in the 'real world', rather than simply reporting the statistical significance of a defined clinical parameter. The issue is that ischaemic stroke exhibits a great deal of heterogeneity, with the site and size of the infarct, as well as the natural rate of recovery affecting the responses seen. The ARAT scale is well documented as being sensitive, reproducible and an accurate measure of recovery in upper-extremity motor function. It was chosen as a positive outcome would help demonstrate the degree of independence gained – for instance, the ability to feed oneself – and so help drive the reimbursement debate positively.

Meanwhile, assessments according to the standard stroke scales (mRS, BI) were also included as secondary end points, and positive outcomes on these measures are also important when considering further development options and commercial potential. Any pivotal study would likely include these stroke scales, and they may well become the primary end points used, given regulatory confidence and familiarity with them. Please note NIHSS scale was not reported on as an outcome measure as patients who are able to enter a stroke clinical trial all have very 'good'

NIHSS scores (necessary for informed consent for example). The scale is not sensitive enough to be used in rehabilitation and therefore used in this study as a baseline score and inclusion criteria but not focused on as an outcome. An overview of the stroke assessment measures are shown in Exhibit 2.

Exhibit 2: Summary of stroke end-point measures

Name	Purpose of the Test	Elements	Clinically Meaningful Change
mRS (Modified Rankin Scale)	Global rating scale of functional independence	0-5 categories of mild to severe disability Low Number = Better	Scores 0-2 considered good outcome or Improvement of 1 category
B-I (Barthel Index)	Measure of independence and mobility in Activities of Daily Living	10 items of ADL 0-100 points; higher score indicates more independence High Number = Better	9 or more points increase
ARAT (Action Research Arm Test) ("Total ARAT")	Upper limb function test	19 tests of Grasp, Grip, Pinch and Gross Movement , 0-57 points High Number = Better	6 or more points increase
F-M (Fugl-Meyer)	Performance based assessment of sensorimotor function following stroke	0-226 points total 0-100 motor points High Number = Better	10 or more points in motor subscale

Source: Company information

Results overview

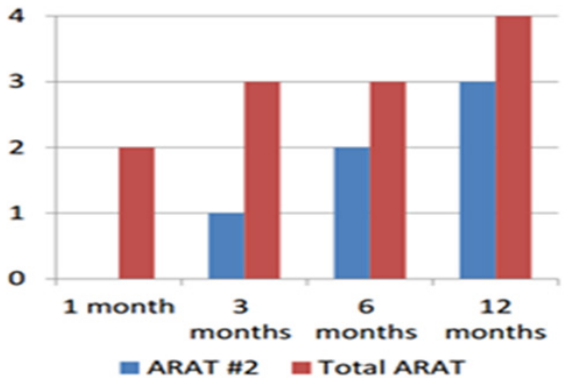
Primary end point – ARAT #2

The ARAT #2 was the primary end point for the study. The test involves lifting a wooden block from a desk up on to a 30cm shelf and is graded on the following scale:

- 0 = no part of task completed
- 1 = some effort but does not perform task
- 2 = performs task within 5-60 seconds
- 3 = performs task within 5 seconds

All patients entering the study started with a test score of 0 or 1, ie they could either complete no part of this test – for example, they couldn't lift their hand up on to the desk (score 0) – or showed some effort but could not grasp (score 1). Three patients showed a two-point improvement in the ARAT (defined as clinically significant see exhibit 2): one at three months, one at six months and one at 12 months (see Exhibit 3). It should be noted that the primary end point was for two patients to reach the two-point improvement within three months, which wasn't achieved; however, according to the company, the improvements seen have been sustained to date. In the total ARAT score (used to assess finer motor function, ie smaller objects), there were four responders with a six-point or more increase (defined as clinically significant see exhibit 2). Exhibit 3 also details the total ARAT scores.

Exhibit 3: PISCES II efficacy – ARAT



Source: Company information

BI (measure of independence)

The BI measures a patient's performance on activities of daily living; for example, eating, moving from bed to chair, dressing, etc. 8/21 patients had a greater than nine-point change from baseline (clinically significant as defined in exhibit 2). Interestingly, 6/21 patients were deemed to demonstrate a BI score of 90+ at baseline and therefore unable to reach 'responder' status. This means that 8/15 responded (53%).

Exhibit 4: BI

21	FEEDING	0 = unable 5 = needs help cutting, spreading butter, etc., or requires modified diet 10 = independent
22	BATHING	0 = dependent 5 = independent (or in shower)
23	GROOMING	0 = needs to help with personal care 5 = independent face/hair/teeth/shaving (implements provided)
24	DRESSING	0 = dependent 5 = needs help but can do about half unaided 10 = independent (including buttons, zips, laces, etc.)
25	BOWELS	0 = incontinent (or needs to be given enemas) 5 = occasional accident 10 = continent
26	BLADDER	0 = incontinent, or catheterized and unable to manage alone 5 = occasional accident 10 = continent
27	TOILET USE	0 = dependent 5 = needs some help, but can do something alone 10 = independent (on and off, dressing, wiping)
28	TRANSFERS (BED TO CHAIR AND BACK)	0 = unable, no sitting balance 5 = major help (one or two people, physical), can sit 10 = minor help (verbal or physical) 15 = independent
29	MOBILITY (ON LEVEL SURFACES)	0 = immobile or < 50 yards 5 = wheelchair independent, including corners, > 50 yards 10 = walks with help of one person (verbal or physical) > 50 yards 15 = independent (but may use any aid; for example, stick) > 50 yards
30	STAIRS	0 = unable 5 = needs help (verbal, physical, carrying aid) 10 = independent

Source: Edison Investment Research

Exhibit 5: PISCES II efficacy – BI

Source: Company information

Fugl-Meyer (motor assessment measure of upper and lower limb)

Fugl-Meyer data were introduced part-way through the study (to capture leg motor activity and to assess its suitability as a future study endpoint) and so data are only currently available on eight patients. Among those eight patients, three responded on the combined upper and lower limb motor function tests, all at three months post-treatment. For details of the test, click here.

mRS (global assessment of disability and dependency)

The mRS is often used in acute stroke studies. Within this study, to date, seven out of 21 patients demonstrated a clinically significant mRS improvement (for definition see exhibit 2). Seven patients improved by at least one category, with one patient improving by two categories.

Exhibit 6: mRS

0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead

Source: Edison Investment Research

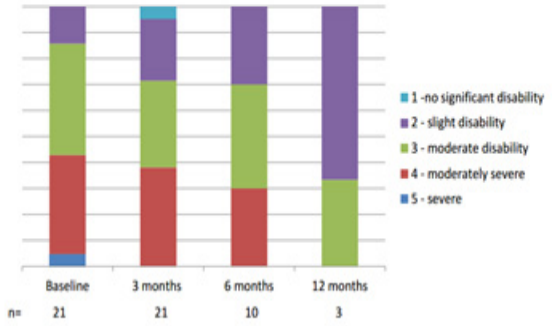
Exhibit 7 outlines the results of starting mRS, last measured mRS and when the improvement was first measured. Exhibit 8 shows the shift in mRS scores from the baseline, with the majority of patients only measured through the three-month period at this time. It is clear that the proportion of patients in categories 1 and 2 are growing, which is encouraging.

Exhibit 7: PISCES II – mRS

Starting mRS	Last Measured mRS	Improvement first measured - months
5	3	1
4	3	1
3	2	1
3	2	1
3	2	3
2	1	3
3	2	6

Source: Company information

Exhibit 8: PISCES II efficacy – shift in mRS scores



Source: Company information

Safety overview

This study has built on the safety data obtained from PISCES Phase I. From Phase II the company reported:

- 18/21 patients (86%) experienced an adverse event (headache, chest infection, pyrexia and falls).
- Procedure was generally well tolerated (patients discharged after one-day recovery), with the majority of adverse events attributable to surgical procedure.
- One adverse event attributed to study drug (HLA antibody in blood, with temporal reactivity and no intracerebral symptoms).
- Seven patients experience severe adverse events. These were attributed to the stroke itself or surgical complications, e.g. vomiting, headache and infection.
- One death resulting from sepsis of unknown origin but not deemed attributable to the treatment, seven months post-treatment. Patient was 73 years old with a history of repeated infections.

Next steps – pivotal, controlled, randomised study

ReNeuron has indicated that the rate of patient improvement as measured in the Phase II study (motor scales, global impairment and ADL independence) exceeded what it expected would be due to natural recovery alone. As a result, ReNeuron is planning to progress clinical development of its

CTX cell therapy candidate in patients with disability due to ischaemic stroke, in a pivotal, controlled, randomised study. We expect this to take place predominantly in the US with possibly a few sites in Europe, and while it is too early to state what the primary end points may be, we do expect it to utilise the scales already outlined here in Phase II, albeit potentially with a different emphasis. In particular, we expect a focus on measures of disability and daily living such as BI and mRS, as these are particularly favoured by regulators. ReNeuron now plans to meet with the US and EU regulators to discuss the details of its pivotal trial, which it aims to commence in mid-2017, with a potential read-out in 2019. In addition to this, ReNeuron is continuing to advance its CTX cell therapy candidate in Japan, where we expect it to find a partner.

Ongoing observational study – OSIS

ReNeuron is also conducting an observational study called OSIS, which ran alongside the PISCES-II trial. The intention was to facilitate recruitment into the Phase II study (by pre-screening patients), while also potentially providing a comparable patient population dataset, although it is not a controlled placebo group. Data have not been presented from this yet; however, we expect them to provide important insight into the natural time course of disease progression in stroke patients, and this in turn should feed into the pivotal trial design.

Opportunity for CTX in stroke

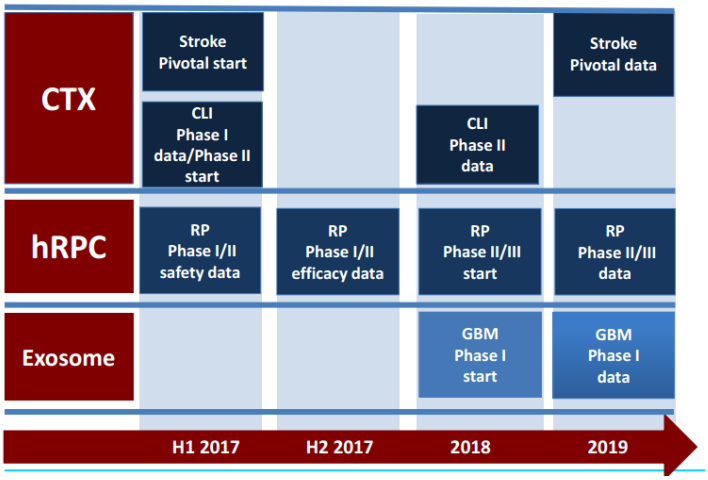
Stroke is the fifth-leading cause of death in the US and is a major cause of adult disability. About 800,000 people in the US (and 150,000 in the UK) have a stroke each year, of which around 85% are ischaemic (caused by a blood clot) and the rest are haemorrhagic (caused by a ruptured blood vessel). This could be expected to rise as a consequence of ageing demographics in the US, Europe and Japan, although the actual incidence rate may be declining as a result of better education and preventative measures for those at risk. Approximately half of the survivors experience disability that has an adverse impact on their life. The economic costs of stroke are high in terms of the direct costs of providing medical care to patients, but the indirect costs (lost productivity, long-term care and quality of life) are the larger burden on society. The direct costs of stroke are estimated at $33bn a year in the US, with a similar amount for European markets. The use of pharmacological agents in the treatment of ischaemic stroke is currently limited to the use of thrombolytic agents in the acute phase.

Tissue plasminogen activators (t-PAs), like alteplase (Genentech), have regulatory approvals but must be administered within three to four hours of a stroke, which ultimately restricts the use of t-PAs to just 5-8% of patients. Alteplase gained FDA approval in 1996 and subsequent attempts by multiple large pharma and biotech companies to develop new treatments for stroke, both for acute and chronic stages, have been unsuccessful. As such, stroke is widely regarded as a high-risk area of development.

Broad clinical pipeline – update

ReNeuron has a broad clinical pipeline with multiple data readouts anticipated in the next couple of years. In addition to the stroke programme, it also has a Phase I trial in CLI and a Phase I/II trial in RP. For a full company overview, click here. An overview of ReNeuron's upcoming potential newsflow is outlined below.

Exhibit 9: ReNeuron newsflow overview



Source: Company information

Phase I/II trial – hRPC for RP progressing

hRPC is currently being investigated in a 15-pt Phase I/II study, which is progressing to plan. The trial has three dose cohorts with three patients in each and currently two of the three safety dose cohorts have completed. The study is being conducted at the Massachusetts Eye and Ear Infirmary (Boston) and is the first clinical trial activity in the US for ReNeuron. A more detailed overview of RP and an outline of the trial design can be found here.

hRPC has received both fast-track designation (accelerated approval and priority review) and orphan drug status for RP in the US, and orphan drug status in Europe, thus ensuring seven and 10 years of market exclusivity, respectively, following any approval. Initial safety readouts are expected in H117, with efficacy data (six additional patients at the highest safe dose) in H217. If positive, it could lead to a pivotal Phase II/III trial starting in 2018, possibly treating 120 patients and with readout potentially in late 2019.

CTX: CLI Phase I data expected H117

A second clinical programme that uses ReNeuron's standardised CTX neural stem cells focuses on CLI. The CTX cell therapy candidate for CLI is in a six-patient Phase I ascending dose safety trial in the UK. Data from this study are now expected in H117. For a more detailed overview of this study, please click here.

Exosome nanomedicine platform potentially in clinic H118

ReNeuron announced in 2016 that it had been awarded a £2.1m grant from Innovate UK for this programme. It is using the funds to develop its manufacturing capabilities alongside further preclinical work. If the outcome of the preclinical work is positive, the company intends to start a Phase I clinical trial in H118 (previously H217). We expect this could be granted orphan indication status if successful, which has the benefit of market exclusivity post-launch. There is also the potential for ReNeuron partnering with this programme, as exosomes could be a target vehicle for drug delivery. To view published data click here and for a more detailed overview of the programme click here.

Underpinning the clinical progress – manufacturing

Following the efficacy and clinical progress of ReNeuron's product pipeline, a key determining factor in a cell-based therapy's commercial uptake is manufacturing capability. Here, ReNeuron is

well-placed, having invested significant effort in developing robust and scalable processes for the large-scale manufacture of CTX cells. It has established methods to scale up the manufacture of the cell lines, including rapid cell culture techniques, cryopreservation methodologies, potency assays and the development of protocols for automated manufacturing processes. As part of this, ReNeuron is establishing a manufacturing and development facility at Pencoed Technology Park in South Wales (having received a grant from the Welsh government). The 25,700 sq ft facility has been fitted out to house R&D laboratories, clean rooms for automated cell culture and office accommodation. The GMP facility will have sufficient capacity to support early commercialisation.

Sensitivities

ReNeuron is subject to the risks typically associated with drug development, including the unpredictable outcomes of clinical trials, the risks of development or regulatory delays (for instance, the FDA requiring additional clinical data), unexpected changes in clinical practice (eg as a result of competitor breakthrough products being developed), an altered reimbursement environment (such as in countries with social healthcare systems) and success of competitors (for details, please click here to view previous notes) and commercial decisions by partners or potential partners. ReNeuron is well-financed and has reasonable visibility on the regulatory and clinical pathways, following discussions with the regulators, compared to a few years ago. Specifically, it will be the outcome of the CTX Phase III stroke trial that will establish the product's eventual commercial potential. ReNeuron has a high reliance on the continued, timely and visible progress of its key clinical programmes – which, if positive, would lead to the need for further finance and/or the need to establish worthwhile partnerships with a larger player, to further develop and commercialise any eventual product.

Valuation

We have rolled our model forward to 2017 and therefore increased our rNPV-based valuation to £291m, or 9.2p per share. We do not currently include a contribution for the earlier stage exosome nanomedicine platform as it is preclinical. We expect to revisit this when its first target is taken into the clinic in H118. Our key model assumptions are summarised in Exhibit 10.

Exhibit 10: ReNeuron valuation model and key assumptions

Product	Setting	Status	Launch	NPV (£m)	Peak sales ($m)	Probability of success	Royalty rate	rNPV (£m)	rNPV per share (p)	Key assumptions
CTX	Stroke disability	Phase II data	2020	741	1,633	25%	30%	169	5.35	1.76m strokes/year (US 800k + EU 800k + Japan 155k); 85% ischaemic; 85% survival; 50% disability; 10% peak penetration; treatment cost $50,000 (US/Japan) or $40,000 (EU).
CTX	CLI	Phase I	2022	161	670	20%	20%	27	0.87	CLI prevalence 0.25%-0.30% in 40+ years; 35% ineligible for revascularisation surgery; 85% survival; peak penetration 10% (US) or 5% (EU/Japan); treatment cost $20,000 (US/Japan) or $15,000 (EU).
hRPC	RP	Phase I/II-ready	2020	220	443	20%	30%	35	1.09	RP prevalence 1 in 4,000; 10% advance to severe vision loss per year; peak penetration 20% (US/Japan) or 15% (EU); per-eye treatment cost $50,000 (US/Japan) or $40,000 (EU).
Portfolio total				1,121				231	7.31	
Cash (H1 2017)								60	1.90	H117 reported cash
Overall valuation								291	9.21	3,164m shares outstanding

Source: Edison Investment Research

ReNeuron is well-funded (into FY19 on current forecasts), which should enable it to execute on an expanding clinical trial programme, resulting in a number of potential key inflection points over the next 24 months, including:

- initiation of a pivotal Phase III study for CTX in stroke (H117);
- initiation of Phase II clinical trial for CTX in CLI in 2017;
- Phase I/II hRPC data in 2017; and
- further preclinical data from the exosome nanomedicine platform (efficacy and toxicity).

Price and probability scenarios

The field of cell therapy has a considerably higher cost of goods than small molecules or biological molecules. ReNeuron appears well-placed in this context as its stem cell treatments can be easily scaled to commercial quantities (at reasonable costs), they are administered 'off-the-shelf' and do not have onerous supply chain requirements and currently there is no need for immunosuppressive co-treatments. Alongside this, ReNeuron's development focus is on therapeutic areas where the cost burden is high and current treatments are inadequate, hence providing a strong cost benefit rationale for reimbursement.

We note that our peak sales estimates and treatment costs for the hRPC programme and stroke programmes could be conservative as transformational disease-modifying treatments could be priced significantly higher. Given the relatively early stage of development of ReNeuron's stem cell technology, and the higher than-average risk involved in the lead indications, particularly stroke, we have been cautious in terms of the probability of success (raised to 25% following the Phase II data). We do, however, assume a relatively high treatment price ($50,000) for stroke at this stage. This is driven by the assumption that a one-off treatment with CTX cells has the potential to provide a significant improvement in the quality of life of disabled patients, which is one of the key criteria behind reimbursement decisions (eg QALY).

In Exhibit 11, we show the indicative valuations that may result from further positive clinical data, which would justify a higher probability of success, but potentially also in the treatment price that could be secured, which would be dependent on the extent of the impact on daily living for these patients.

Exhibit 11: Sensitivity analysis – CTX in stroke

Stroke sensitivity			
Probability of success	**Cost of treatment with CTX cells**		
	$25,000	**$50,000**	**$75,000**
10%	0.6p	1.8p	3.1p
25%	2.4p	5.6p	8.8p
35%	3.7p	8.1p	12.5p
50%	5.6p	11.9p	18.2p

Source: Edison Investment Research

Financials

Following the £68.4m (net raise of £65.2m) capital raise in July 2015, ReNeuron has been accelerating its investment in operating activities, particularly in R&D, given the proposed clinical programmes for CTX, hRPC and the exosome nanomedicine platform. We have reviewed our current forecasts and adjusted them slightly as the company is in preparation for its Phase III study as a result we expect capex and R&D costs to ramp up in FY18. We continue to expect an increase in R&D spend due to the Phase III study in stroke, Phase II study in CLI, RP Phase I/II study and subsequent start of Phase II/III, and the exosome nanomedicine platform reaching the clinic. We now forecast R&D in FY17 of £16.4m (vs £19.5m) and £27.9m (vs £24.0m) in FY18. As a result of

this we have also reduced our forecasted tax credit to £1.2m (vs £2.8m) in 2017 and £1.6m (vs £3.4m) in 2018. We have also reduced slightly our SG&A costs to £4.1m (vs $4.6m) in 2017 and £4.3m (vs £5.1m) in 2018. Finally, we expect capex to increase in FY18 alongside the increase in expenses resulting from the Phase III Stroke trial. We now forecast £1.8m (vs £0.4m) in FY18.

ReNeuron is well-funded (H117 cash of £60m) and therefore well-positioned to deliver on a range of clinical and operational milestones that could be transformative. We forecast a cash runway into FY19, which should enable significant advancement of the two pivotal clinical studies (stroke Phase III study and RP Phase II/III study) and Phase I exosome study in GBM. At that point, ReNeuron will either raise further funding and/or partner some of its programmes

Exhibit 12: Financial Summary

£'000s	2013	2014	2015	2016	2017e	2018e
Year end 31 March	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS						
Revenue	17	22	30	29	29	29
Cost of Sales	0	0	0	0	0	0
Gross Profit	17	22	30	29	29	29
R&D expenses	(4,786)	(5,829)	(7,250)	(10,272)	(16,435)	(27,940)
SG&A expenses	(2,319)	(2,824)	(3,693)	(4,015)	(4,095)	(4,300)
EBITDA	(6,966)	(7,857)	(10,269)	(13,632)	(19,895)	(31,549)
Operating Profit (before GW and except)	(7,088)	(7,969)	(10,394)	(13,724)	(19,968)	(31,677)
Intangible Amortisation	0	0	0	0	0	0
Exceptionals	0	0	0	0	0	0
Operating Profit	(7,088)	(7,969)	(10,394)	(13,724)	(19,968)	(31,677)
Other	0	0	0	0	0	0
Net Interest	29	149	91	878	493	371
Profit Before Tax (norm)	(7,059)	(7,820)	(10,303)	(12,846)	(19,475)	(31,306)
Profit Before Tax (FRS 3)	(7,059)	(7,820)	(10,303)	(12,846)	(19,475)	(31,306)
Tax	714	754	1,397	1,492	1,168	1,878
Profit After Tax (norm)	(6,345)	(7,066)	(8,906)	(11,354)	(18,306)	(29,428)
Profit After Tax (FRS 3)	(6,345)	(7,066)	(8,906)	(11,354)	(18,306)	(29,428)
Average Number of Shares Outstanding (m)	748.7	1,425.0	1,788.8	2,609.3	3,164.6	3,164.6
EPS - normalised (p)	(0.85)	(0.50)	(0.50)	(0.44)	(0.58)	(0.93)
EPS - FRS 3 (p)	(0.85)	(0.50)	(0.50)	(0.44)	(0.58)	(0.93)
Dividend per share (p)	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET						
Fixed Assets	1,620	1,772	2,033	6,963	7,242	8,872
Intangible Assets	1,272	1,272	1,591	1,591	1,591	1,591
Tangible Assets	213	225	161	361	640	2,270
Other	135	275	281	5,011	5,011	5,011
Current Assets	4,602	22,347	14,054	64,894	47,003	16,654
Stocks	0	0	0	0	0	0
Debtors	341	676	400	1,421	1,421	1,421
Cash	3,547	20,917	12,382	60,709	44,413	13,354
Other	714	754	1,272	2,764	1,168	1,878
Current Liabilities	(1,164)	(2,036)	(2,345)	(4,199)	(4,199)	(4,199)
Creditors	(539)	(1,234)	(1,150)	(3,700)	(3,700)	(3,700)
Short term borrowings	0	0	0	0	0	0
Short term leases	(1)	(1)	(1)	(1)	(1)	(1)
Other	(624)	(801)	(1,194)	(498)	(498)	(498)
Long Term Liabilities	(150)	(366)	(606)	0	0	0
Long term borrowings	0	0	0	0	0	0
Long term leases	0	(2)	(1)	0	0	0
Other long term liabilities	(150)	(364)	(605)	0	0	0
Net Assets	4,908	21,717	13,136	67,658	50,046	21,327
CASH FLOW						
Operating Cash Flow	(6,637)	(6,718)	(9,124)	(11,920)	(19,201)	(30,840)
Net Interest	(1)	0	0	0	0	0
Tax	616	714	879	0	2,764	1,168
Capex	(37)	(121)	(380)	(293)	(352)	(1,758)
Acquisitions/disposals	0	0	0	0	0	0
Financing	5,601	23,435	0	65,195	0	0
Dividends	0	0	0	0	0	0
Other	30	61	91	345	493	371
Net Cash Flow	(428)	17,371	(8,534)	53,327	(16,295)	(31,059)
Opening net debt/(cash)	(3,974)	(3,546)	(20,914)	(12,380)	(65,708)	(49,413)
HP finance leases initiated	0	(3)	0	1	0	0
Other	0	0	0	(0)	0	0
Closing net debt/(cash)	(3,546)	(20,914)	(12,380)	(65,708)	(49,413)	(18,353)

Source: Edison Investment Research and ReNeuron

Contact details	Revenue by geography
ReNeuron Group Pencoed Business Park, Pencoed, Bridgend CF35 5HY +44 (0) 203 819 8400 www.reneuron.com	N/A

Management team

Chairman: John Berriman	CEO: Olav Hellebø
John Berriman was appointed to the board in July 2011 and became chairman in March 2015. He is the chairman of Autifony Therapeutics and past chairman of Heptares Therapeutics (sold to Sosei in February 2015) and Algeta (sold to Bayer in 2014 and previously listed on the Oslo stock exchange). He is also a non-executive director of Cytos (listed on the SIX Swiss exchange). Previously he was a director of Micromet (until its sale to Amgen in 2012) and Abingworth Management, an international healthcare venture capital firm. Previously, he spent 14 years with Celltech Group and was a member of its board when it listed on the London Stock Exchange in 1994.	Appointed CEO in September 2014. Previously CEO of Clavis Pharma, a Norwegian oncology company, from February 2010 to June 2013. Before that he was senior VP, UCB Pharma (2004 to 2010), COO of Novartis UK (from 2003 to 2004) and for 10 years prior to that held a series of senior roles at Schering Plough, the last as head of the company's oncology biotech division in the US. He graduated summa cum laude in international business studies from Hofstra University, New York, and has an MBA from IESE, Barcelona.
CFO: Michael Hunt	**CSO: Dr John Sinden**
Joined ReNeuron in 2001 as CFO, was appointed COO in 2003 and CEO in 2005. Skilfully guided the company through the difficult period to 2014 and has since returned to the CFO role. Previously spent six years at Biocompatibles International (sold to BTG) where he held a number of senior financial and general management roles. His early industrial career was spent at Bunzl. He studied economics at UCL..	Scientific co-founder and a director of ReNeuron since October 1998. Previously Reader in Neurobiology of Behaviour at the Institute of Psychiatry at Kings College London. He graduated in psychology from the University of Sydney, with a PhD in neuroscience from the University of Paris at the College de France. He held post-doctoral appointments at Oxford University and the Institute of Psychiatry before joining the permanent staff of the Institute in 1987.

Principal shareholders	(%)
Woodford Investment Management	35.5
Wales Life Sciences Investment Fund LP	9.5
Invesco Ltd	9.3
Aviva & its subsidiaries	5.7

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