EDISON

ReNeuron Group

Interim results

A transformational year

Pharma & biotech

2019 has been a transformational year for ReNeuron, marked by impressive initial data from the human retinal progenitor cells (hRPC) programme in retinitis pigmentosa (RP) and the initiation of a China partnership with Fosun Pharma (milestone payments of up to £80m and double-digit royalties). In the RP programme, positive data were presented at the AAO annual meeting in San Francisco on eight patients, which further reinforces the data presented earlier in the year. However, long-term durability of effect remains a key question. Further data are expected in H120. In ReNeuron's CTX PISCES III trial in stroke disability patients, the company recently updated its trial design to improve the speed of patient recruitment. Data are expected in mid-2021. We value ReNeuron at £197m.

Year end	Revenue (£m)	PBT* (£m)	EPS* (p)	DPS (p)	P/E (x)	Yield (%)
03/18	0.9	(21.0)	(55.66)	0.0	N/A	N/A
03/19	2.7	(17.2)	(45.34)	0.0	N/A	N/A
03/20e	6.1	(22.8)	(60.33)	0.0	N/A	N/A
03/21e	3.1	(30.8)	(83.69)	0.0	N/A	N/A

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

hRPC efficacy remains impressive in RP

The data set for hRPC in RP continues to mature. Due to differences in patient enrolment dates, follow-up times varied; however, all eight patients had reached at least three months of follow-up at the time of the recent data update (data presented at the American Academy of Ophthalmology (AAO) Annual Meeting in San Francisco). The eight patients at three months presented a mean ETDRS letters read change of 6.1 (vs 6.8 in untreated eye), however, the data were negatively confounded by two patients who had surgery related adverse events leading to vision loss. Removing these two patients, the remaining six patients demonstrated a mean ETDRS improvement of 17.8 (vs 8.3 in untreated eye) at three months.

Financials: Interim results

ReNeuron has reported results for the six-month period ending 30 September. Revenue increased substantially year-on-year to £6.1m (vs £0.03m in the six-month period ending 30 September 2018) as a result of the Fosun Pharma upfront. R&D costs rose 22% to £9.2m (vs £7.5m) as a result of the progression of the clinical hRPC and CTX programmes, while admin costs remained flat at £2.6m. Tax income fell to £1.2m (vs £1.5m). ReNeuron recorded an improved net loss for the period of £3.9m (vs a £5.4m loss in six-month period ending 30 September 2018). Cash and equivalents of £21.3m should enable a cash reach into 2021.

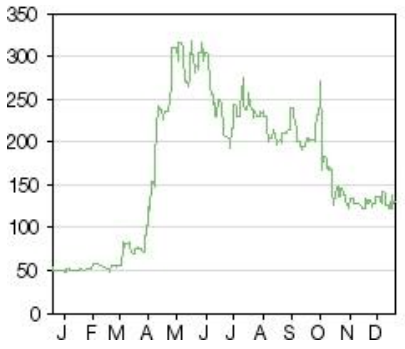
Valuation: £197m vs £198m previously

We value ReNeuron at £197m or 624p per share, versus £198m or 625p per share previously. We have rolled forwards our model, and updated for FX and cash. Additionally, we have increased the probability of success of hRPC in RP to 25% (vs 20% previously) and pushed back CTX launch to 2024 (vs 2023 previously).

19 December 2019

Price	**130p**
Market cap	**£41m**
	$1.32:£1
Cash (£m) at 30 September 2019	21.3
Shares in issue	31.6m
Free float	99.7%
Code	RENE
Primary exchange	LSE
Secondary exchange	N/A

Share price performance



%	1m	3m	12m
Abs	(3.0)	(35.0)	140.7
Rel (local)	(6.5)	(37.5)	110.7
52-week high/low		325.00p	47.50p

Business description

ReNeuron Group is a UK biotech company developing allogeneic cell therapies. The first pivotal Phase IIb trial for CTX neural stem cells for chronic stroke disability is underway. Human retinal progenitor cells are also being studied for RP (in Phase I/IIa).

Next events

Further hRPC Phase I/IIa data	Ongoing
Chronic stroke US Phase IIb study readout	Mid-2021
FY20 results	July 2020

Analyst

Dr Daniel Wilkinson +44 (0)20 3077 5734

healthcare@edisongroup.com

Edison profile page

Investment summary

Company description: Stem cell therapeutics

ReNeuron is a UK clinical-stage company developing a portfolio of stem cell-based therapies and technologies. Its two lead clinical assets are the human retinal progenitor cell (hRPC) line for the treatment of retinitis pigmentosa (RP) and the CTX cell line for the treatment of stroke disability. In a Phase I/IIa trial, the company is testing an hRPC product in patients with RP. Positive data have been presented to date, with additional Phase IIa data expected in H120. ReNeuron is currently enrolling patients (a total of 130 patients is expected) in a Phase IIb study investigating whether CTX will improve a patient's functionality following a stroke (6–24 months after). Initial data are expected in mid-2021. Additionally, the company has early-stage exosome and induced pluripotent stem cells technologies. ReNeuron was established in 1998, listed on AIM in 2005 and has approximately 60 employees.

Valuation: £197m or 624p/share

We value ReNeuron at £197m or 624p/share, vs £198m or 625p/share previously. We have rolled forward our model, in addition to updating for FX rates and net cash. Our valuation is based on a risk-adjusted net present valuation (rNPV) of CTX in stroke patients (274p/share), hRPC in RP patients (175p/share) and hRPC in cone rod dystrophy (CRD) patients (35p/share), Fosun partnership (72/share), in addition to a cash position as of 30 September of £21.3m (67p/share). We have updated our probability of success in the RP programme to 25% (from 20%) as early data continue to impress. With data now expected for the CTX programme in mid-2021 (from Q420 at time of our last published note) we now expect the launch of CTX in 2024 (versus 2023 previously). We have also updated R&D costs for the programme with the expansion of the number of patients expected to be enrolled.

Financials: Funded into 2021

ReNeuron has reported results for the six-month period ending 30 September. Revenue increased substantially year-on-year to £6.0m (vs £27,000 in the six-month period ending 30 September 2018) as a result of the Fosun Pharma upfront. R&D costs rose 22% to £9.2m (vs £7.5m) as a result of the progression of the clinical hRPC and CTX programmes, while admin costs remained flat at £2.6m. Tax credits fell to £1.2m (vs £1.5m). The Fosun Pharma upfront more than offset rises in R&D and decreases in tax income as ReNeuron recorded a net loss of £3.9m for the period. Cash and equivalents of £21.3m should enable a cash reach into 2021.

Sensitivities: Early days in the cell therapy sector

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 and the evolving data from the Phase I/IIa hRPC in RP that will determine the company's eventual success. The cell therapy industry remains in its infancy and ReNeuron's ability to navigate significant hurdles that arise from an evolving regulatory, manufacturing, logistical and pricing/reimbursement landscape will be critical to is success. In its CTX programme, ReNeuron is operating in a therapeutic area (stroke) with a poor track record for success with well know difficulties in recruiting patients, so this is a particularly high-risk indication. However, we note that many failures in the field have been in acute stroke studies where placebo effects can be high, while ReNeuron is focusing on the chronic downstream disability caused by a

stroke. In the RP programme, long-term durability of responses and safety will be critical to its success.

A transformational year for the hRPC programme

Initial data announced earlier in the year for the hRPC programme in RP, followed by further announcements covering the maturing data set, have revealed a product with substantial promise in a difficult to treat disease. Retinitis pigmentosa (RP) is an inherited, degenerative eye disease that can be caused by any of over 100 different gene mutations. Historically there has been no disease modifying treatments available for the disease and approved treatments have focused on managing symptoms of the disease. However, cell and gene therapies are offering new opportunities to either correct or replace these defective genes. Most notable is the approval in 2017 of Luxturna for RPE65 mutated retinal dystrophies, including patients with RPE65 mutated retinitis pigmentosa. However, while new treatments like Luxturna are offering new hope to a small group of patients, the disease remains a major unmet need with many therapies in development focused on addressing single mutations and not the whole pool of mutations. ReNeuron's hRPC therapy is a cell-based therapy and is not mutation specific, which means it could potentially address the whole RP patient population.

hRPC: Opportunities for single therapy in multi-mutation RP

Cell and gene therapies offer a unique prospect of dramatically improving a patient's outcomes through one-off administration of a product. Gene therapies are typically focused on replacing or editing one or a few genes, and while often extremely effective, these are by their nature limited to narrow patient populations. Cell therapies are not limited to a single gene defect and instead look to replace a flawed cell population with a correct one.

Cell therapies typically take two forms, autologous or allogenic. Autologous therapies utilise a patient's own cells, while allogenic therapies utilise a central donor. As a patient's own cells, autologous therapies benefit from being compatible and will not promote an immune reaction. However, each product must be custom made for each patient, which involves technical manufacturing and logistics. Allogenic products on the other hand are often from a single or a few donors. While the products have the potential to produce an immune response in a patient (graft versus host, hosts versus graft), the relative simplicity of manufacturing (one product for all) and the ability to be readily used (off the shelf) present substantial benefits. Additionally, the probability of an immune response can be reduced via either correct engineering of the cells or utilising them in an immune limited organ like the eye.

ReNeuron's human retinal progenitor cells (hPRC) are allogenic (isolated from fetal retina) and can differentiate into various components of the retina. This allows for a range of defects to be corrected from one product. To date ReNeuron has no reported cases of immune reactions with its hPRC products in the eye. While initial clinical testing was done with fresh cells, the company has developed a cryopreserved formulation (with a nine-month shelf life). This has been tested safely in patients; however, formulation work is ongoing as the small bleb that is formed at the site of operation has been seen to take longer to resolve then with fresh cells.

Phase I/IIa trial design

The Phase I trial enrolled 12 patients with severe eyesight problems (all patients were legally blind with an ETDRS letter score ranging from 0–1 with only one patient able to read one letter). The dose was escalated in the trial from 200,000 to 1,000,000 cells, with the patients at the highest dose receiving the cryopreserved formulation. Safety was the primary endpoint and the trial reported a good profile.

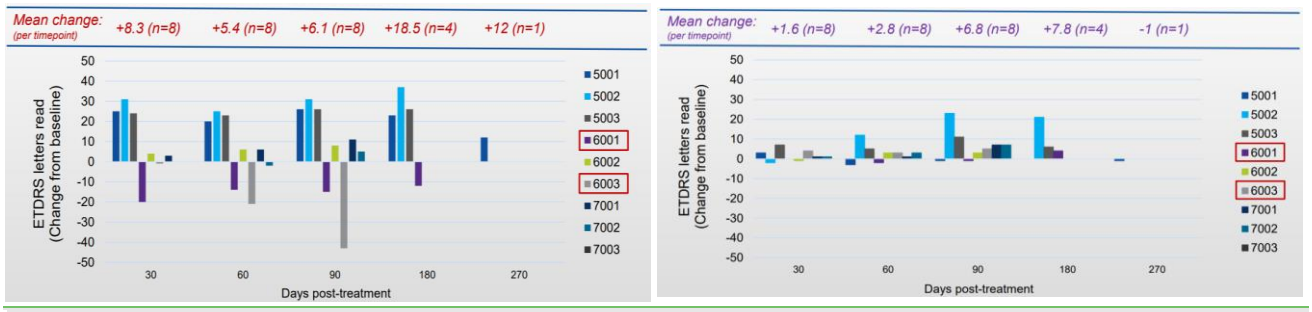
In the Phase IIa part of the trial, 10 patients were enrolled with better eyesight at baseline than in Phase I part (ETRDS range of 9 to 56 at baseline). Patients were all treated with 1,000,000 cryopreserved cells. The primary endpoint is change in ETDRS letters read from baseline to 24 months post-treatment. Interim visits at one, two, three, six, nine, 12 and 18 months are being undertaken. A clinical meaningful improvement in sight is an improvement of 10–15 ETDRS letters (two to three lines on the ETDRS chart). ReNeuron is currently in discussions with regulatory authorities to expand the number of patients in the Phase IIa trial by up to an additional 12 patients. In the company's view this would enable only one subsequent pre-approval study and could enable a quicker route to market.

AAO data maintain early but impressive trend

Efficacy data presented by ReNeuron at AAO (in San Francisco in October 2019) on its hRPC therapy continue the impressive trend seen in data earlier in the year. Exhibit 1 highlights the per-patient changes from baseline in ETDRS letters read. Comparing the mean and individual trends of ETDRS improvement over nine months it is evident that ReNeuron's hRPC therapy is having a positive effect on a patient's sight. However, with small patient numbers, particularly at the longer follow-up times, more data are needed to clarify the treatment effect. As more patients hit longer-term follow-up, the persistence, safety and value of the therapy will become clearer.

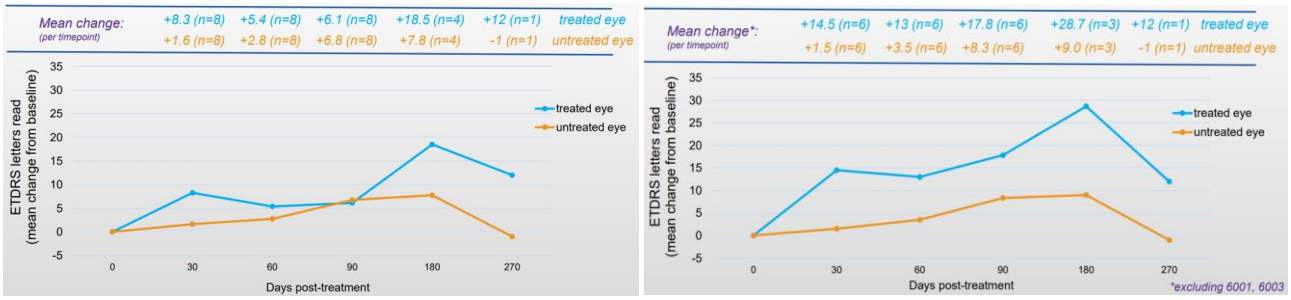
The mean improvements of the whole patient population (currently eight patients' data available) were confounded by two patients who had procedure (surgery) related adverse events leading to vision loss. All eight patients had reached three months of follow-up at the time of the most recent data presentation. At this time period, no mean improvement in the treated eye over the untreated was observed (Exhibit 2: 6.1 vs 6.8 respectively), although four out of the eight patients had an ETDRS improvement over 10, with three out of four achieving above 20 ETDRS improvement. When the two patients who had surgery-related adverse events were removed from the data (Exhibit 2), the remaining six patients demonstrated a mean ETDRS improvement of 17.8 (vs 8.3 in untreated eye) at three months. In four patients who had achieved six months of follow-up, a mean improvement in Early Treatment Diabetic Retinopathy Study (ETDRS) letters of 18.5 was observed compared with 7.8 in the untreated eye. One patient had achieved nine months of follow-up and demonstrated an ETDRS improvement of 12 versus -1 in the untreated eye.

Exhibit 1: ETDRS letters read (Phase IIa) in treated eye (left graph) and untreated (right graph)



Source: ReNeuron AAO presentation

Exhibit 2: Mean ETDRS changes (Phase IIa) of treated eye vs and untreated (left graph). Subjects with vision loss excluded (right graph)



Source: ReNeuron AAO presentation

Regulatory bodies, notably the US FDA, have been keen to rapidly accelerate these new life-changing cell and gene treatments to approval. For example, the only approved retinal gene therapy Luxturna was approved (on data from 41 patients) on a measured change from baseline over one year in a in a multi-luminance mobility test (as assessed by the ability of a subject to navigate a course accurately and at a reasonable pace at different levels of environmental illumination). ReNeuron could gain approval with a similar package; however, more mature data and further discussions with regulators are needed in order to crystallise the path to approval.

Safety in line with expectations

Safety to date has been in line with what is to be expected for the type of surgical treatment. Patients in the Phase I/II study had to undertake vitrectomy surgery and subretinal injection of the hRPC product. Vitrectomy surgery is a common procedure that often involves three small incisions in the white of the eye to allow access to the vitreous gel (jelly like material). The vitreous gel is often partly or fully removed to allow access to the retina, at which point a subretinal injection is carried out.

To date, one patient has had a retinal pigment epithelium (RPE) tear and another has persistent subretinal fluid. This is consistent with what has been observed with other advanced therapies. For example, in the two clinical trials required for Luxturna's approval, 10% (n=4/41) of patients who underwent a similar surgical procedure had a retinal tear, which compares to 12.5% (n=1/8) of ReNeuron's patients treated to date. Side effects when performing these surgical procedures are dependent on the health of a patient's eye; improved selection of patients who have healthier eyes may enable ReNeuron to decrease the incidence of adverse effects. However, we expect ReNeuron to continue to observe similar side effects as its trial progresses. We believe hRPC's current Phase I/II safety profile would be acceptable to regulatory agencies, however long-term evolution of the data will ultimately inform this.

Competitive landscape: Biogen/Nightstar advancing

Few competitors exist in RP. However, through its acquisition of Nightstar, Biogen is quickly advancing a product through clinical trials that aims to address a sub-population of RP patients. Biogen is developing NSR-RPGR (AAV8-RPGR), a gene therapy for X-linked retinitis pigmentosa (XLRP). XLRP is typically associated with men and is thought to account for 10–15% of the total RP population (source: NCBI). It is often characterised by a mutation in the GTPase regulator (RPGR) gene, which leads to loss of photoreceptor cells and a gradual deterioration of vision, potentially leading to complete blindness.

NSR-RPGR is an AAV (adeno-associated virus) vector carrying the RPGR gene. It is being tested in a Phase I/II trial and is currently undergoing a Phase II/III dose expansion (XIRUS). Data to date have been positive with the latest Phase I data presented at AAO in San Francisco in October

2019. 18 patients were included in the data set, with safety as the primary endpoint. There were 65 reports of adverse events, 52 of which were mild and 40 of which were resolved. 18 events were related to the surgery and 13 believed to be related to the treatment. One severe adverse event occurred, which was resolved. Improvements in microperimetry (a visual field test) occurred in 50% of treated eyes compared to 8.3% of untreated eyes at one month. At three months, 33% of treated eyes experienced an improvement in microperimetry, while no untreated eyes experienced improvement. At six months, 36.6% of treated eyes saw improvement and again no untreated eyes experienced improvements.

CTX cell line for treatment of stroke disabled patients

ReNeuron's most advanced product is a conditionally immortalised neural stem cell-derived CTX cell line for the treatment of stroke disability. CTX has been tested in a Phase IIa clinical trial (PISCES II) and ReNeuron is now recruiting patients in a Phase IIb clinical trial (PISCES III). The trial is expected to enrol 130 patients (2:1 ratio of treatment arm to placebo arm) with initial data expected in mid-2021. The primary endpoint is the number of patients who achieve an improvement in Modified Rankin Scale (mRS) by ≥1 point (Exhibit 3) at six months from baseline. mRS is a scale designed to measure the levels of disability in patients who have suffered a neurological disability like a stroke. The scale is ranked from 0 to 6, with 0 identifying patients who are healthy with no symptoms and 6 patients who are deceased. The six-point mRS endpoint was used as a secondary endpoint in the Phase II study (PISCES II), which found that the response rate was maintained 12 months post-transplantation. 35% of patients demonstrated a clinically meaningful improvement at 12 months post-implantation.

PISCES III: Adjusted trial design to improve enrolment

The PISCES III trial is designed to monitor improvements in the function of stoke patients who remain disabled six to 24 months following their treatment. The trial is split into a treatment arm and a control arm; both patient populations undergo surgery to the skull, with patients in the treatment arm receiving an injection of CTX to the site of the stroke. Patients in the placebo arm do not receive any therapy. Only patients with an mRS of 3 (moderate disability – requires some help but can walk unassisted) or 4 (moderate severe disability – requires assistance to walk) could be enrolled into the trial. The study will enrol patients at 40 centres.

Trial enrolment has been slower than expected to date; one factor that may have led to this is patients' reluctance to undergo invasive surgery when they have only a 50% chance of receiving treatment. To speed up enrolment, ReNeuron has increased the chance for patients who enter the trial to receive treatment. Two-thirds of patients in the trial (86 out of 130 patients) will now receive treatment compared with half previously. The company has expanded the number of patients enrolled to 130 from 110 previously in order to maintain the correct statistical powering of the trial with this change in trial design. Additionally, the company has expanded the window of patients who are eligible for treatment and it now includes those who are six to 24 months post-stroke from six to 12 months previously. We note the Phase IIa trial was in patients who were two to 12 months post-stroke and it is unknown if this expanded patient population will receive similar, better or worse outcomes than the previously selected population.

PISCES II: Positive data in secondary endpoints

The Phase II trial evaluated CTX injected into the putamen of the brain on the affected side. It was a 21-patient Phase II trial with the primary aim of determining whether CTX could reduce disability and improve patient outcomes during the rehabilitation phase. The trial failed to meet its primary

endpoint of a two-point improvement in ARAT #2 (grasp a 2.5cm^3 block and move it from A to B positions in <60 seconds) in two patients.

In the key secondary endpoint of improvement in mRS (Exhibit 3), 35% of patients responded at 12 months post-treatment by at least a one-point improvement in mRS. In patients with some residual upper limb movement, a greater than one-point improvement was seen in 50% of patients at 12 months. This patient population is the target population of the Phase IIb study (PISCES III).

Exhibit 3: Modified Rankin Scale (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

The procedure was generally well tolerated (86%, 18/21 experienced an adverse event of some kind), with seven patients experiencing a severe adverse event. These were attributed to the stroke itself or surgical complications, eg vomiting, headache and infection. One death resulted from sepsis of unknown origin but was not deemed attributable to the treatment.

Significant global market in stroke

Stroke is the fifth most common cause of death in the US and 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.

New pricing dynamics emerging

It is widely recognised by payors and prescribers that cell and gene therapies could provide huge clinical benefit and in some conditions be curative, but the high potential cost of such therapies remains of concern. Allogenic approaches like those being developed by ReNeuron will be needed to bring down costs. Additionally, substantial long-term data will be a critical part of the reimbursement equation, as evidenced by the recent struggles of cell therapies with initially immature data packages like Kymriah and Yescarta, or gene therapies like Luxturna or Zolgensma to gain appropriate reimbursement.

In August 2017, the FDA approved Novartis's CAR-T Kymriah for use in paediatric patients with acute lymphoblastic leukemia (ALL), priced at $475,000 for the one-off treatment. This initiated a debate on how much these innovative therapies are worth and subsequent approvals of other costly cell and gene therapies such as Luxturna ($425,000 for one eye), Yescarta ($373,000) and Zolgensma ($2.1m) have fuelled these discussions.

All of these therapies face ongoing discussions with payors over what is the appropriate pricing model for the treatment. Some companies are offering payment over time if selected efficacy milestones are hit. However, while this is operationally and logistically possible with a small number of approved therapies and relatively small patient populations, this will prove substantially more difficult with an increasing number of approved therapies. A recent example is Novartis securing a contract in Germany for an outcomes-based payment structure with GWQ ServicePlus, which represents approximately 13 million medical insurance policyholders. The contract is arranged so that Novartis will repay part of the drug cost to GWQ if certain undisclosed survival outcomes are not reached. We note this is a temporary pilot programme until the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband), which represents 90% of the population of Germany, concludes its negotiations with Novartis. In the UK, after extensive discussions, the National Institute for Health and Care Excellence (NICE) approved Kymriah in paediatric ALL in September 2018 and more recently (February 2019) in DLBCL. Originally NICE did not deem Kymriah cost effective in DLBCL; however, further negotiations have led to a lower price. Of direct relevance to ReNeuron and its hRPC programme is the recommendation by NICE for the use of Luxturna (for the treatment of inherited retinal dystrophy arising from mutation in RPE65 gene) in the NHS at an unknown net price but assumed substantial discount. If ReNeuron can maintain a low cost base for its allogenic products, it will offer them a substantial competitive advantage over any autologous therapies.

As the sector grows and systems are put in place, we believe many of the reimbursement challenges faced by cell and gene manufacturers will be addressed; however, it remains one of the key sensitivities for the sector as whole.

Next-generation platforms: Exosomes and iPS cells

ReNeuron continues to develop its next-generation technologies, notably its exosome and induced pluripotent stem cells (iPS) platforms. Within the body, exosomes are mediators of cell-to-cell communication and can carry various cellular components including proteins and RNAs. The function of exosomes is twofold, firstly to transport cellular components and secondly to protect them from breakdown until needed. ReNeuron has developed a stem cell CTX derived exosome platform. In August 2019, the company announced a grant-funded collaboration with the European Cancer Stem Cell Research Institute at Cardiff University to develop CTX stem cell-derived exosomes for the delivery of therapeutic nucleic acids across the blood brain barrier.

ReNeuron has developed a process for reprogramming the CTX neural stem cells into CTX-derived, induced pluripotent stem cells (iPSCs). This essentially enables the stem cells to then differentiate into any type of stem cell (including bone, muscle and skin) and not just nerve. In October 2019 the company presented data that demonstrated the stability and scalability of these cells. The company is currently exploring multiple CTX=iPSC derived cell lines with the aim of out-licensing the technology.

Fosun Pharma: Near-term revenue stream

In April 2019, ReNeuron announced it had signed an out-licence agreement with Shanghai Fosun Pharma ('Fosun') a Shanghai and Hong Kong listed (market cap c £6.7bn) pharmaceutical company. The deal included a £6m upfront payment with a further £6m expected in near-term operational milestones and an additional £8m in future regulatory milestones. We expect the £6m of near-term operational milestones to be split evenly between £3m of revenue in 2021 (financial year ending 31 March 2021) and 2022 (financial year ending 31 March 2022) and include them in our

revenue forecasts. ReNeuron is also eligible to receive an additional £60m in sales-related milestones and a tiered royalty rate of between 12% and 14%.

The deal is focused on the development, manufacture and commercialisation in China of ReNeuron's CTX and hRPC cell therapies. Fosun is responsible for the funding of development and commercialisation activities. Initially ReNeuron will supply CTX and hRPC cells until the appropriate tech transfer has been undertaken, after which Fosun will undertake its own manufacturing.

Sensitivities: Early days in the cell therapy sector

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 and the evolving data from the Phase I/IIa hRPC in RP that will determine the company's eventual success. The cell therapy industry remains in its infancy and ReNeuron's ability to navigate significant hurdles that arise from an evolving regulatory, manufacturing, logistical and pricing/reimbursement landscape will be critical to is success. In its CTX programme, ReNeuron is operating in a therapeutic area (stroke) with a poor track record for success with well know difficulties in recruiting patients, so this is a particularly high-risk indication. However, we note that many failures in the field have been in acute stroke studies where placebo effects can be high, while ReNeuron is focusing on the chronic downstream disability caused by a stroke. In the RP programme, long-term durability of responses and safety will be critical to its success.

Valuation: £197m or 624p/share

We value ReNeuron at £197m or 624p/share vs £198m or 625p/share previously. We have rolled forward our model, in addition to updating for FX rates and net cash. Our valuation is based on risk adjusted net present valuation (rNPV) of CTX in stroke patients (274p/share), hRPC in RP patients (175p/share) and hRPC in cone rod dystrophy (CRD) patients (35p/share), Fosun partnership (72p/share) in addition to a cash position of £21.3m (67p/share) at 30 September. We expect the £6m of near-term operational milestones to be split evenly between £3m of revenue in FY21 and FY22 and include them in our revenue forecasts. The £8m in regulatory milestones we expect to be split across the approvals of both CTX and hRPC in China with remaining £60m sales milestones split across the lifetimes of both products. We have assumed an average royalty rate of 13%.

We have updated our probability of success in the RP programme to 25% (from 20%) as early data continue to impress. With data now expected for the CTX programme in mid-2021 (from Q420 at the time of our last published note), we now expect the launch of CTX in 2024 (versus 2023 previously). We have also updated R&D costs for the programme with the expansion of the number of patients expected to be enrolled.

Exhibit 4: Valuation summary

Product	Setting	Status	Launch	NPV (£m)	Peak sales ($m)	Probability of success	Royalty rate	rNPV (£m)	rNPV/ share (p)	Key assumptions
CTX	Stroke disability	Phase II	2024	392	1,388	25%	30%	87	274	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).
hRPC	CRD	Phase I/II	2024	63	185	20%	30%	11	35	CRD prevalence 1 in 40,000; 30% advance to severe vision loss per year and abnormal colour vision; peak penetration 20% (US/Japan) or 15% (EU); per-eye treatment cost $75,000 (US/Japan) or $50,000 (EU).
hRPC	RP	Phase I/II	2023	275	691	25%	30%	55	175	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 $75,000 (US/Japan) or $50,000 (EU).
Fosun partnership	N/A	N/A	N/A	N/A	N/A	25%	13%	23	72	
Portfolio total				818				176	557	
Cash at 30 September 2019								21.3	67	
Overall valuation								**197**	**624**	31.8m shares outstanding

Source: Edison Investment Research

Financials: Fosun upfront increases cash reach

ReNeuron has reported results for the six-month period ending 30 September.

Revenue increased substantially year-on-year to £6.0m (vs £0.03m in the six-month period ending 30 September 2018) as a result of the Fosun Pharma upfront. Other operating income consisted wholly of government grants of £0.06m, down from £2.40m (£0.51m government grants plus £1.89m exclusivity fee received during licensing negotiations) in the associated period in 2018. We do not forecast any substantial further revenue for the second half of the financial year and forecast full year (FY20 – 31 March 2020 year-end) revenue of £6.1m.

R&D costs rose 22% to £9.23m (vs £7.54m) mainly as a result of the progression of the PISCES III clinical trial, with hRPC also contributing. Admin costs remained flat at £2.58m. We retain our full year R&D forecasts at £24.7m. However, we now increase our FY21 R&D spend to £28.6m (vs our previous forecast of £27.9m) to reflect the expected increase in patient numbers and extended timeline in the PISCES III study.

ReNeuron continues to hold some cash and investments in US dollars to hedge against operational spend and a strengthening of the US dollar. Financial income dropped to £0.59m (vs £0.89m) as a result of a decreased foreign exchange gain for the period of £0.42m (vs £0.75m).

Although tax credits for the period increased over 2018 to £1.85m (vs £1.46m), total tax income fell as ReNeuron paid international tax of £0.60m on the Fosun upfront resulting in total tax income of £1.25m (vs £1.46m).

The Fosun Pharma upfront more than offset rises in R&D and decreases in tax income as ReNeuron recorded a net loss of £3.9m for the period. We forecast a net loss for the full financial year (ending 31 March 2020) of £19.2m.

Cash consumed by operations reduced to £5.15m in the period vs £7.54m in 2018. Cash and equivalents of £21.3m should enable a cash reach into FY21. To bridge this funding gap, we have increased our illustrative debt in 2021 to £30m (from £16m previously). This was driven by a more expanded R&D cost than originally anticipated.

Exhibit 5: Financial summary

£'000s	2018	2019	2020e	2021e
Year end 31 March	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS				
Revenue	897	2,720	6,094	3,094
Cost of Sales	0	0	0	0
Gross Profit	897	2,720	6,094	3,094
R&D expenses	(16,657)	(16,240)	(24,685)	(28,634)
SG&A expenses	(4,616)	(4,779)	(5,078)	(5,586)
EBITDA	(20,222)	(17,915)	(23,448)	(30,965)
Operating Profit (before amort. and except.)	(20,376)	(18,299)	(23,575)	(31,032)
Intangible Amortisation	0	0	0	0
Exceptionals	0	0	0	0
Operating Profit	(20,376)	(18,299)	(23,575)	(31,032)
Other	0	0	0	0
Net Interest	(591)	1,064	792	240
Profit Before Tax (norm)	(20,967)	(17,235)	(22,783)	(30,792)
Profit Before Tax (FRS 3)	(20,967)	(17,235)	(22,783)	(30,792)
Tax	3,352	2,887	3,579	4,152
Profit After Tax (norm)	(17,615)	(14,348)	(19,204)	(26,640)
Profit After Tax (FRS 3)	(17,615)	(14,348)	(19,204)	(26,640)
Average Number of Shares Outstanding (m)	31.6	31.6	31.8	31.8
EPS - normalised (p)	(55.66)	(45.34)	(60.33)	(83.69)
EPS - FRS 3 (p)	(55.66)	(45.34)	(60.33)	(83.69)
Dividend per share (p)	0.0	0.0	0.0	0.0
BALANCE SHEET				
Fixed Assets	912	1,522	1,682	1,959
Intangible Assets	186	186	186	186
Tangible Assets	726	632	792	1,069
Other	0	704	704	704
Current Assets	41,706	29,988	11,684	15,849
Stocks	0	0	0	0
Debtors	1,285	834	834	834
Cash and deposits	37,411	26,386	8,082	12,247
Other	3,010	2,768	2,768	2,768
Current Liabilities	(5,949)	(7,402)	(7,402)	(7,402)
Creditors	(5,949)	(7,261)	(7,261)	(7,261)
Short term borrowings	0	0	0	0
Short term leases	0	(141)	(141)	(141)
Other	0	0	0	0
Long Term Liabilities	0	(864)	(864)	(30,864)
Long term borrowings	0	0	0	(30,000)
Long term leases	0	0	0	0
Other long term liabilities	0	0	0	0
Net Assets	36,669	24,108	5,965	(19,593)
CASH FLOW				
Operating Cash Flow	(14,887)	(11,947)	(18,808)	(25,733)
Net Interest	383	342	792	242
Tax	0	0	0	0
Capex	(235)	(239)	(287)	(344)
Acquisitions/disposals	0	0	0	0
Financing	0	0	0	0
Dividends	0	0	0	0
Other	0	0	0	0
Net Cash Flow	(14,739)	(11,844)	(18,304)	(25,835)
Opening net debt/(cash)	(53,061)	(37,411)	(26,380)	(8,076)
HP finance leases initiated	0	0	0	0
Other	(911)	813	0	0
Closing net debt/(cash)	(37,411)	(26,380)	(8,076)	17,759

Source: ReNeuron accounts, Edison Investment Research

Contact details	Revenue by geography
ReNeuron Group Pencoed Business Park, Pencoed, Bridgend Wales CF35 5HY +44 (0)20 3819 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 Confo Therapeutics, Autifony Therapeutics and Depixus. John was a 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 a non-executive director (NED) of Autolus, and was a NED 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, Olav was previously CEO of Clavis Pharma, a Norwegian oncology company, from February 2010 to June 2013. Before that he was senior VP of UCB Pharma (2004–10), COO of Novartis UK (2003–04) 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 the IESE Business School-Barcelona.
CFO: Michael Hunt	
Michael joined ReNeuron in 2001 as CFO, was appointed COO in 2003 and CEO in 2005. He skilfully guided the company through the difficult period to 2014 and has since returned to the CFO role. Michael 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.	

Principal shareholders	(%)
Schroder Investment Management	16.58
Link Fund Solutions	16.42
Arthurian Life Sciences	9.5

Companies named in this report

Novartis, Gilead, Spark Therapeutics, Roche, Biogen, NightStar

General disclaimer and copyright

This report has been commissioned by ReNeuron Group and prepared and issued by Edison, in consideration of a fee payable by ReNeuron Group. Edison Investment Research standard fees are £49,500 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the research department of Edison at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Crown Wealth Group Pty Ltd who holds an Australian Financial Services Licence (Number: 494274). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

This document is prepared and provided by Edison for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document.

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

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
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia