EDISON

ReNeuron Group

Data update

Strong data in retinal therapy shows long effects

Pharma & biotech

ReNeuron has released further follow-up data from the ongoing human retinal progenitor cell (hRPC) trial, which shows a robust sustained averaged response. This data set completes the six-month data on eight patients and extends, for one individual, to 18 months, who showed a good net gain. The next dose level, two million cells in nine patients, remains delayed due to COVID-19. A filing to start a pivotal study is expected in the second half of CY21. Our indicative value remains at £107m.

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.

Impressive averaged response

What is impressive, in our view, is that the therapy, on average, appears to give a clear benefit quickly and then appears stable. In the current one million cell dose cohort, eight patients successfully underwent the procedure; two others had surgical complications, one of whom has fortunately recovered. In our analysis, we continue to look at the successfully implanted patients. With more data points, the net gain in mean visual acuity is now 8.9 letters at six months. One patient so far has 18-month data and displayed a strong response with an impressive 16 letter net gain.

hRPC cell-based therapy might treat any RP patient

Retinitis pigmentosa (RP) is an inherited, degenerative eye disease caused by one of over 100 different gene mutations. ReNeuron's hRPC therapy could potentially treat any RP patient, giving a big potential commercial advantage; competing gene therapies only treat specific mutations. ReNeuron has regulatory permission from the FDA to move to a two million cell dose level in its Phase /IIa trial. In the UK, a third trial site, in Oxford, has been approved. However, the COVID-19 situation has so far prevented this cohort from being recruited and treated. In H221, ReNeuron plans to seek approval for a pivotal hRPC study. A pivotal US trial may require a partner, perhaps with a valuable deal. We use a 25% probability of success for hRPC therapy in RP, with launch in 2024.

Valuation: Retained at £107m

Our indicative value remains £107m. We will reassess the hRPC valuation as data emerge but note the high deal values in the area with one totalling $250m plus royalties in June. Exosome deals to deliver RNA drugs, with another early stage collaboration announced, are promising but the projects are preclinical. Cash on 31 March 2020 is estimated to be about £8m, pending the year-end results due in July. We envisage a further funding need in FY21.

6 July 2020

Price	**141.5p**
Market cap	**£45m**
	$1.32/£
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	8.9	34.8	(41.0)
Rel (local)	12.7	16.8	(28.3)
52-week high/low	275.0p		75.5p

Business description

ReNeuron Group is a UK biotech company developing allogeneic cell therapies. Human retinal progenitor cells are also being studied for retinitis pigmentosa (in Phase I/IIa). There is a strong preclinical technology base in exosomes.

Next events

Further hRPC Phase I/IIa data	Ongoing
FY20 results	July 2020
hRPC pivotal study start	H221

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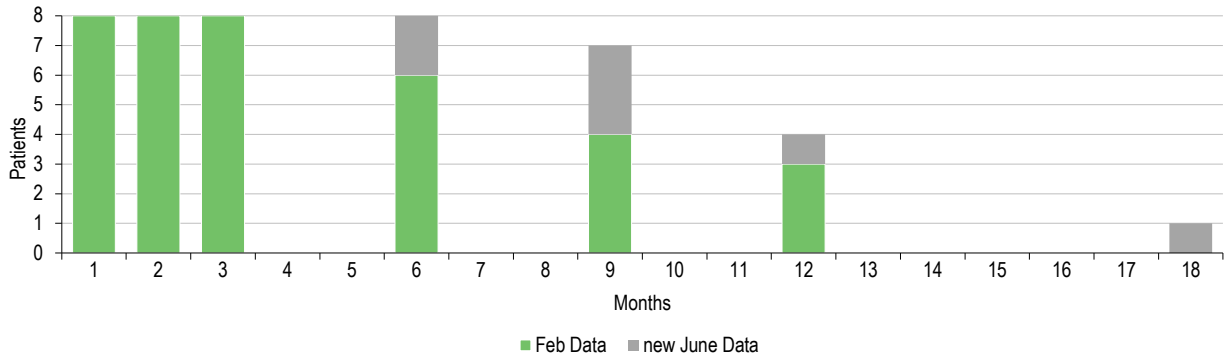
RPC data to 18 months

The June 2020 update on the US Phase I/IIa US trial (NCT02464436) adds extra data and takes the time course, in one case, to 18 months post-treatment.

In Exhibit 1, the additional data points are added to the January dataset. There are eight patients who had successful cell implantations.[1] The data for all of these are now complete at the six-month point and we have data on seven patients at nine-months post treatment. The 12-month data are now for four patients, up from three in January, and we have one report of 18-month data. By late 2020, the longer-term data will be more numerically robust.

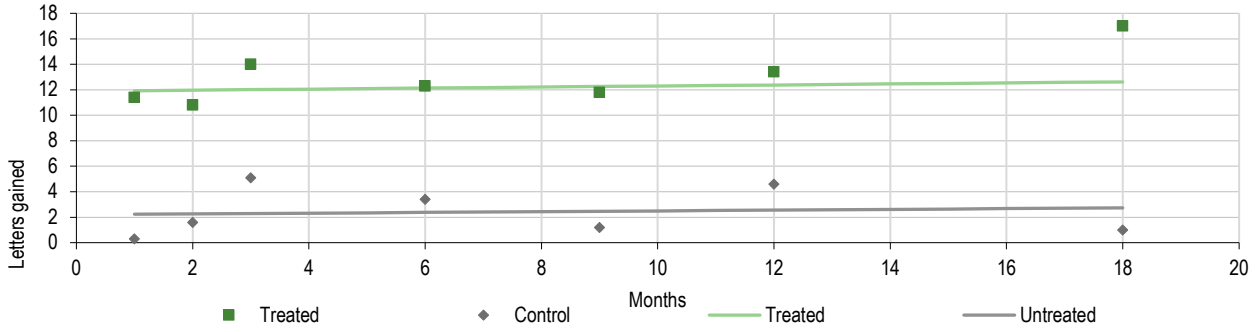
Exhibit 1: Patient data at various timepoints



Source: ReNeuron data graphed by Edison Investment Research

Exhibit 2 shows the time course, to which we have fitted simple lines of regression based on one- to nine-month data. We suspect there are a wide range of patient responses, but this detail is not disclosed. Hence, we rely more on the average six and nine-month data points rather than 12 or 18 months as these are small so far. The one 18-month patient has done very well (16 letter gain).

Exhibit 2: Mean letters gained in successfully treated patients over time



Source: ReNeuron, Edison Investment Research

The pattern looks stable and we would, on this simplistic analysis, expect to observe a net difference of about nine or 10 letters at a year. We look forward to the full presentation of the trial data.

[1] This excludes two subjects who experienced sight loss due to complications arising from the surgical procedure. One of these subjects has recovered back to at least baseline at one-year post treatment. We do not consider these issues are a cause for concern as we anticipate the technique will be improved with experience to reduce future risk. If surgical complications occur in a pivotal study, they would be present in the intent to treat analysis and so reduce the measured efficacy.

In our February note, we observed that the untreated eye seemed also to be doing unexpectedly well, but this apparent signal has decreased as more data has accumulated. For example, at nine months, the February data showed an untreated gain of six letters (n=4) but this is now a mean of 1.2 letters after another three patients' worth of data. Hence, on average, these further patients lost visual acuity vs baseline in the untreated eye but gained in the treated eye to give a similar net gain (the difference in mean change between treated and untreated eye remained approximately 10.5 letters at nine months, in both the June and February data sets).

What is impressive, in our view, is that the therapy appears to give a clear benefit so quickly and then appears stable on average. For gene therapies, there are general concerns over the long-term persistence of the treatment effects. Cell therapies are generally assumed to show very low persistence and survival after injection but perhaps these retinal cells have much more stable and persistent effects.

By the end of 2020, we expect there will be 12-month follow-up data on eight patients (compared to four currently), giving a better view of the long-term response. The trial has a two-year final endpoint.

US and UK expansion

An amended protocol submitted to the FDA, now approved, will enable the dose to be raised to two million cells. ReNeuron has approval to treat nine more patients at this dose in a Phase IIa extension of the study (in addition to the 10 Phase IIa patients already treated). In addition, a wider range of pre-treatment baseline visual acuity in patients will be eligible and the trial endpoints will be expanded to include microperimetry testing to measure and detect spatial changes in retinal sensitivity.

The trial currently runs at two US centres. The UK regulatory agency (MHRA) has now approved a UK site trial at the Oxford Eye Hospital where Professor Robert MacLaren, a recognised leader in the treatment of retinal diseases, will be the principal investigator.

These studies are temporarily delayed due to COVID-19 making it difficult to screen and treat patients. As restrictions lift, we expect the study to restart but there is no company guidance yet. As there will then be three centres, recruitment should be fast.

According to management, an application to start the planned pivotal study is now planned for H221. We have no indication of timeline or design. With the extended and delayed Phase I/II study and Phase II/III recruitment starting perhaps from late in 2021, or possibly in H122, we continue to prudently assume a 2024 launch after an expedited review.

jCell: A potential competitor?

US company jCyte is running an 84-patient Phase IIb RP cell therapy trial (NCT0307373), with completion (12-month endpoint) due in September 2020. The randomised, single-administration study tests two doses (of three million and six million) of hRPCs (termed jCell) against a sham comparator arm. jCell has FDA Regenerative Medicine Advanced Therapy designation.

A Phase I/II trial dose-ranging study with 28 patients in four dose cohorts was completed in July 2017. Patients in the higher-dose arms, one million and three million, had gains of 4.8 and nine letters, respectively, after a year. There were six in each cohort. Of the treated patients, 25 of 28 reported adverse events. Without publications, we cannot comment further.

Japanese eye specialist Santen licensed the rights to jCell technology in Europe, Asia and Japan in early June. The deal value was $50m in cash, $12m in a convertible note offering and up to an

additional $190m in milestones based on regulatory approval and initial sales. There will be a royalty on sales.

jCyte is a private academic spin-out company from the California Institute for Regenerative Medicine based at the University of California, Irvine.

Valuation: Retained at £107m

The hRPC programme is now ReNeuron's key project. As in previous notes, we have valued it on a partnered basis with a 30% royalty. This level assumes that ReNeuron funds the project.

However, there have been a number of deals in the genetic eye diseases area, for example Nightstar was acquired for $800m by Biogen in 2019. The Santen deal is noted above. Hence, partnering based on expanded Phase II data is possible and could be significantly value enhancing.

Alternatively, this type of specialist retinal therapy (subretinal implantation of hRPC) would only be expected to be carried out by a limited number of a specialists, potentially allowing direct sale by ReNeuron; this would require future investment in a small salesforce.

Our estimate of end-FY20 (31 March) cash is £8m. Cash use in the second half of CY20 might be lower than previously expected due to reduced trial activity and cessation of CTX patient recruitment. We retain our previous assumption that up to £30m might be raised in H2 CY20 to allow for expansion of hRPC studies and exosome developments.

The unchanged value basis is shown in Exhibit 3. This gives an overall value, including estimated March 2020 cash, of £107m, equal to 336p per share with about 32m shares in issue currently.

Exhibit 3: Valuation estimate

Product	Setting	Status	Launch	NPV (£m)	Peak sales ($m)	Probability of success	Royalty rate	rNPV (£m)	rNPV per share (p)
CTX	Stroke disability	Phase II	2027	59	1,388	15%	12.5%	6	20
hRPC	CRD	Phase I/II	2024	63	185	20%	30%	11	36
hRPC	RP	Phase I/II	2024	206	691	25%	30%	64	201
Fosun Partnership	N/A	N/A	N/A	31	N/A	N/A	N/A	17	53
Portfolio total				328				99	311
Cash (end March 2020 est)								8	25
Overall valuation								107	336

Source: Edison Investment Research. Note. Estimated amount for 31 March 2020.

Our financial estimates (Exhibit 4) are unchanged pending the publication of FY20 results in July.

Exhibit 4: 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

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