Company Note

Prelims

8 July 2021

ReNeuron Group plc (RENE.L)

hRPC study confirmed back on track

Recruitment has resumed in the US into the Phase 2a trial of the lead programme hRPC in retinitis pigmentosa (RP) after an investigation following the presumed bacterial infection that caused its temporary suspension last month. We expect resumption in the UK and Spain by August after regulatory confirmation. The quick resolution of this issue seems to have caused only a modest, one quarter, delay. The three-month data on the higher dose (2m cell) extension arm is due in Q4 2021 and will be important to attract a commercial partner. Good progress has been made in developing the exosome platform with enhanced targeting now shown. This is being evaluated by potential partners, but the hoped-for big biobucks deal has yet to be signed. The investment case rests on a significant future licensing deal for hRPC, the terms of which could mirror those achieved by competitor jCyte last year. Cash at the year-end was £22.2m, providing at least a 12-month runway.

- Recruitment has resumed into the higher-dose extension of the Phase 2a trial, after this was put on hold following a presumed bacterial infection following the first treatment in one centre last month. The independent Data and Safety Monitoring Board approved the resumption of enrolment after a case review. The restart has removed what could have been a major concern and delay. Three-month data from the 2m cell extension cohort should be available in Q4 2021 and could be the basis for seeking a licensing deal, possibly from mid-2022.

- In RP, ReNeuron is running about a year behind its near competitor jCyte, which appears to be gearing up for Phase 3. Both companies use hRPCs, but ReNeuron has a potentially more efficacious approach. jCyte appears to be looking at targeting predicted responders to its therapy, which may also render it suitable for only a proportion of RP patients. Around a dozen gene therapies are in development, but each of these can only target one of the 100 or so gene mutations that can cause RP.

- Cash and equivalents at 31 March totalled £22.2m, providing at least 12 months' funding. We estimate that with reduced cash use over 2022 and 2023, cash could be adequate till Q1 2023 excluding any hRPC or exosome deals. However, further cash or a deal will be required to run a pivotal hRPC study.

- We maintain our fair value at £204m (358p/share), based primarily on hRPC. We see the investment case resting of the terms of a future licensing deal for hRPC. Any deals involving exosomes, iPSC or CTX will provide upside to this figure.

Year End: March 31				
(£'000)	2020	2021	2022E	2023E
REVENUE	6,165	335	250	250
ADJ. EBITDA	-12,794	-11,770	-12,803	-12,870
ADJ. PBT	-12,655	-12,163	-13,188	-13,265
ADJ. EPS (p)	-39.8	-31.1	-23.2	-23.3
NET CASH)	12,625	22,203	11,164	211
EV/EBITDA (x)	N/A	N/A	N/A	N/A
PER (x)	N/A	N/A	N/A	N/A

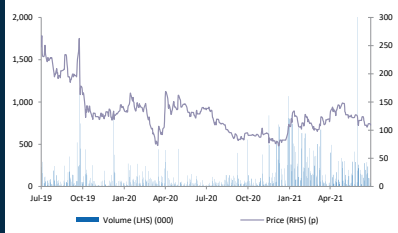
Allenby Capital acts as joint broker to ReNeuron.

Please refer to the last page of this communication for all required disclosures and risk warnings.

Corporate

Current price	109p
Sector	Pharma & Biotech
Code	RENE.L
Listing	AIM

Share Performance



	1m	3m	12m
RENE.L	-13.3%	-5.0%	-21.3%

Source: Thomson Reuters, Allenby Capital

Share Data		
Market Cap (£m)		62.0
Shares in issue (m)		56.9
52 weeks (p)	High	Low
	148.5p	72.5p
Financial year end		March

Source: Company Data, Allenby Capital

Key Shareholders	
Obotritia Capital	10.8%
R. Griffiths (inc. controlled)	8.0%
Octopus Investments	5.9%
Rosetta Capital	5.7%
Arthurian Life Sci	5.3%

Source: Company Data, Allenby Capital

Robin Davison

020 7065 2690

robin@equitydevelopment.co.uk

www.allenbycapital.com

Investment thesis

ReNeuron offers investors a play on the economics of a potential future licensing deal for its lead programme using human retinal progenitor cells (hRPC) for retinitis pigmentosa (RP). A deal on hRPC to fund a pivotal study and generate long-term returns could be struck anytime from mid-2022 but whether it is and, if so, on what terms, depends on the crucial data from the extension Phase 2a trial. Licensing negotiations for products of this type can sometimes develop into an acquisition, as it may be advantageous for the potential licensor as to gain complete control over the intellectual property (IP) and manufacturing/supply chain. Such an outcome, if it were to occur, may offer an attractive exit to ReNeuron's investors.

Major commercial advantage over alternative gene therapies

ReNeuron's hRPC therapy can potentially treat any RP patient, representing a major commercial advantage over the 12 or so gene therapies that are in development for the condition, each of which targets a specific rare gene mutation (around 100 of which are known). There is only one cell therapy-based competitor, jCyte, which is slightly further ahead in development but has still yet to enter Phase 3 trials.

jCyte uses a similar cell line but delivered in a different way (intravitreal vs sub-retinal), with ReNeuron's approach having potential advantages, in our view. In addition, we are uncertain whether the jCyte product can be frozen; if not, this makes logistics complex. These could be important clinical and commercial advantages for ReNeuron.

jCyte has already partnered its product with the Japan-based global ophthalmic company, Santen. As jCyte is privately held, its funding position is not known, but we presume that Santen is providing sufficient cash and resources to run the pivotal study. The Santen deal provided $50m upfront, a $12m convertible note and $190m in clinical and sales milestones, in exchange for global (ex US) rights, with double digit royalties on sales. This provides an obvious precedent deal value for ReNeuron.

Exosome platform technology and CTX cell therapy for stroke

ReNeuron also has an exosome platform technology – over which it hopes to secure non-exclusive license deals particularly for drug delivery – and its CTX cell therapy for stroke. The CTX product had been in a pivotal study but discontinued to focus resources on rhRPC and extend the cash runway. Development will now require a partner (it is licensed to Fosun in China and this gave a £6m milestone in FY20). ReNeuron also has earlier stem cell projects (in immunotherapy and diabetes) that could become the subject of deals from 2022. In particular, ReNeuron notes a potential pancreatic cell line that could be used to treat diabetes.

Cash runway to early 2023

ReNeuron's investment case is not particularly geared to financial metrics at this point, except to the extent that it allows the conduct of trials. Currently, ReNeuron has a cash runway to early 2023 in our view.

Sensitivities

ReNeuron is exposed to the risks typically associated with early-stage drug development, including major uncertainties over the outcome of clinical studies. Although it addresses opportunities in areas characterised by high unmet medical need, these areas are competitive and thus ReNeuron can be affected by the success and failure of competing approaches.

ReNeuron will have to secure licensing partner for hRPC and then will be entirely reliant on that company to complete clinical development, obtain registrations and commercialise resulting products. Licensing deals are standard practice in the biotech industry but there is no guarantee that one can be consummated and, if so, whether it will generate the expected economic returns after the initial upfront payments.

The economic value that can be realised in a licensing deal is difficult to predict, as it is determined by multiple external (competitive) factors as well as the intrinsic qualities of the programme.

Update: case review allows quick restart of hRPC study

ReNeuron is conducting an up to 33-patient open-label Phase 2 study of hRPC for RP (NCT02464436). To date, this has to date treated 10 patients at the original 1m cell dose and will enrol up to nine more in an extension study at a higher 2m cell. Visual acuity results from first cohort of patients have been reported and show good evidence of efficacy out to 12-months of follow up, but with a degree of variability of response.

The nine-person extension study uses the same cryopreserved hRPC formulation and test subjects with advanced RP with some remaining central vision but makes certain changes to explore if efficacy can be improved. In addition to the higher dose, it enrols a wider range of patients in terms of pre-treatment baseline visual acuity (VA). However, the principal change is that two blebs (small drops) of one million hRPC are delivered on either side of the functional retinal area. The cells are injected under the retina making this a fairly delicate procedure.

Prior to 2021, the study was being conducted at two clinical sites in the US, but the expansion allowed ReNeuron to add a centre in the UK and one in Spain (generally speaking, involving more centres improves the "quality" of the trial data, as it reduces the effect of subtle differences at individual locations).

According to ReNeuron, the presumed eye infection (bacterial endophthalmitis, which causes inflammation of the internal eye tissues) occurred in the first patient treated at one of the centres. The patient is now improving, though has not fully recovered, but infection was not definitive on culture (hence "presumed").

Recruitment resumed in the US

We understand recruitment has resumed in the US and will be permitted shortly in the UK. The Spanish restart may take until August. Four patients have been recruited so far, so ReNeuron will have to add the remaining five by September, as it expects to have three-month data from higher dose cohort in Q4 2021. This with the 12-month data from the low doses, will form the basis of the data used to gain a licensing deal.

ReNeuron has been seeking a licensee for the rHPC programme for some time, and we expect it would be providing updates to potentially interested parties that have signed a CDA (this is normal practice in biotech business development).

The study is testing the hypothesis that hRPC injected close to centre of the retina where most photoreceptors are situated, may support the remaining functional light-sensitive cells. The cells administered by subretinal injection in a bleb, which requires a precise operation and temporarily distorts the retinal structure. In the continuation of Phase 2, two blebs are being given near to functional retinal areas but not under them. This could support, by trophic factors, the nearby functional retina and potentially help to restore some function to the overlying degraded retina.

The effect of the treatment is measured in terms of visual acuity (VA), which provides an indication of patient's ability to resolve details and perform day-to-day tasks – but it is a variable parameter. VA is measured using the ETDRS2 chart, with results reported as the number of letters read correctly. The term often used is best corrected visual acuity (BCVA), which means that the patients wear glasses or contact lenses for the readings.

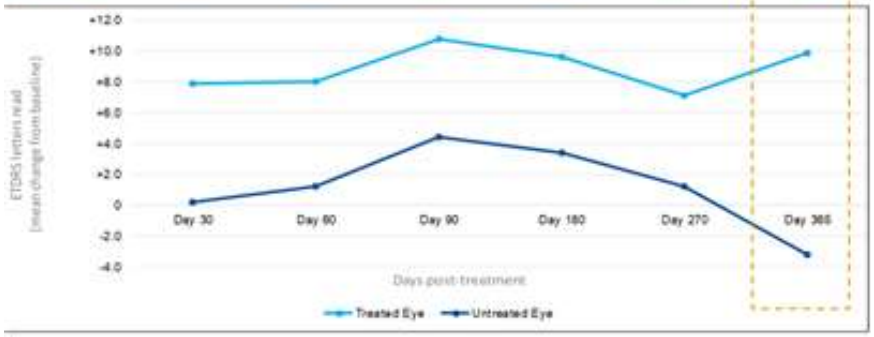
A one-line improvement in ETDRS (five letters) is not regarded as being clinically significant, whereas a ten letter-line gain would be. If a patient can read three extra lines (15 letters), their VA has doubled.

The therapy based on the 1m single bleb dose appears to give a clear benefit quickly and appears stable. However, one patient in the first stage also had a surgical complication on bleb implantation but subsequently recovered to baseline, reducing the reported averages. Another patient who experienced a surgical complication is not included as they have not recovered any sight in the treated eye.

Of interest is that at the nine- and 12-month points, there have been additional patients reported. The untreated eye now shows (after 12 months with seven patients), an average decline of -3.2 letters. In contract, the treated eyes on average gained 9.9 letter. This is an average net gain of 13.1 letters. This is impressive and appears consistent. However, we do note that patient numbers are small and the variability between patients appears to be high as seen in the second chart where gains ranged from two letters, insignificant but in the patient who experienced surgical complications, to 15 and 20 letters in two patients which is a doubling or more of visual acuity and clinically significant.

Exhibit 1: ETDRS results

	Day 30	Day 60	Day 90	Day 180	Day 270	Day 365
Treated Eye	+7.9	+8.0	+10.8	+9.6	+7.1	+9.9
Untreated Eye	+0.2	+1.2	+6.4	+3.4	+1.2	-3.2
Difference	+7.7	+6.8	+6.4	+6.2	+5.9	+13.1



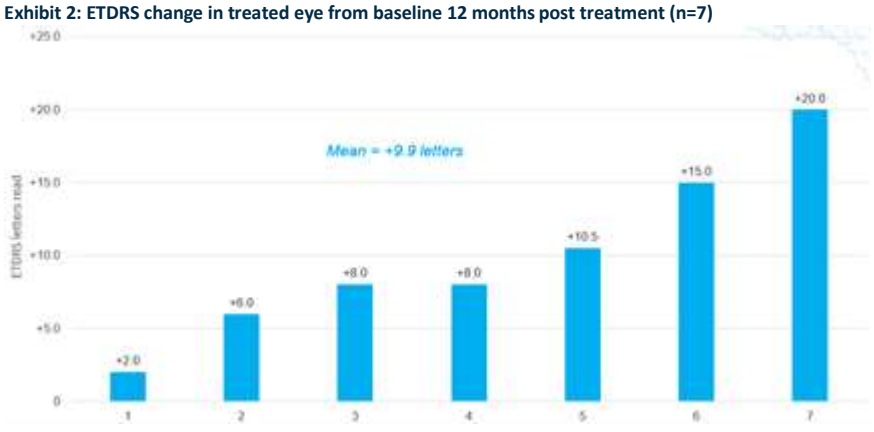
Additional Notes:

*excluding 1 patient (6003) with surgery-related vision loss

**One year follow up is now complete, but the availability of additional follow up data has been hindered by COVID-19

Source: Company

Exhibit 2: ETDRS change in treated eye from baseline 12 months post treatment (n=7)



Source: Company

Valuation

Fair value maintained at £204m (358p/share)

We maintain our fair value of ReNeuron at £204m (358p/share), based primarily on hRPC. The delay to the trial in mid-2021 will not be significant in terms of data acquisition and licensing. Any deals involving exosomes, iPSC or CTX would provide upside to this figure.

Financials

Revenues in FY2021 were £0.3m representing royalties from licensing activities and income from research collaborations (2020: £6.1m; £0.1m of royalties plus an upfront of £6.0m from Fosun). R&D costs were lower in 2021: £9.5m (2020: £16.3m), with general and administrative expenses reduced to £3.7m (2020: £4.2m). In both cases, there were lower than our model. We expect the full impact of the cost reductions made in H2CY20 to give lower admin expenses in FY22. We expect R&D expenses at about £10.5m over FY22 and FY23. With R&D tax credits of £2-2.5m a year, this gives an operational cash outflow of just under £11m a year. This implies that with £22.2m FY21 year-end cash, ReNeuron is funded for at least 12 months and potentially into Q1 CY23.

Disclaimer

Allenby Capital Limited ("Allenby") is incorporated in England no. 6706681; is authorised and regulated by the Financial Conduct Authority ("FCA") (FRN: 489795) and is a member of the London Stock Exchange. This communication is for information only it should not be regarded as an offer or solicitation to buy the securities or other instruments mentioned in it. It is a marketing communication and non-independent research and 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. The cost of Allenby research product on independent companies is paid for by research clients.

This communication is for the use of intended recipients only and only for distribution to investment professionals as that term is defined in article 19(5) of The Financial Services and Markets Act 2000 (Financial Promotion) Order 2005. Its contents are not directed at, may not be suitable for and should not be relied upon by anyone who is not an investment professional including retail clients. Any such persons should seek professional advice before investing. For the purposes of this communication Allenby is not acting for you, will not treat you as a client, will not be responsible for providing you with the protections afforded to clients, and is not advising you on the relevant transaction or stock. This communication or any part of it do not form the basis of and should not be relied upon in connection with any contract.

Allenby uses reasonable efforts to obtain information from sources which it believes to be reliable. The communication has been prepared without any substantive analysis undertaken into the companies concerned or their securities, and it has not been independently verified. No representation or warranty, express or implied is made, or responsibility of any kind accepted by Allenby its directors or employees as to the accuracy or completeness of any information in this communication. Opinions expressed are our current opinions as of the date appearing on this material only and are subject to change without notice. There is no regular update series for research issued by Allenby.

No recommendation is being made to you; the securities referred to may not be suitable for you and this communication should not be relied upon in substitution for the exercise of independent judgement. Neither past performance or forecasts are a reliable indication of future performance and investors may realise losses on any investment. Allenby shall not be liable for any direct or indirect damages including lost profits arising from the information contained in this communication.

Allenby and any company or persons connected with it, including its officers, directors and employees may have a position or holding in any investment mentioned in this document or a related investment and may from time to time dispose of any such security or instrument. Allenby may have been a manager in the underwriting or placement of securities in this communication within the last 12 months, have received compensation for investment services from such companies within the last 12 months, or expect to receive or may intend to seek compensation for investment services from such companies within the next 3 months. Accordingly, recipients should not rely on this communication as being impartial and information may be known to Allenby or persons connected with it which is not reflected in this communication. Allenby has a policy in relation to management of conflicts of interest which is available upon request.

This communication is supplied to you solely for your information and may not be reproduced or redistributed to any other person or published in whole or part for any purpose. It is not intended for distribution or use outside the European Economic Area except in circumstances mentioned below in relation to the United States. This communication is not directed to you if Allenby is prohibited or restricted by any legislation or registration in any jurisdiction from making it available to you and persons into whose possession this communication comes should inform themselves and observe any such restrictions.

Allenby may distribute research in reliance on Rule 15a-6(a)(2) of the Securities and Exchange Act 1934 to persons that are major US institutional investors, however, transactions in any securities must be effected through a US registered broker-dealer. Any failure to comply with this restriction may constitute a violation of the relevant country's laws for which Allenby does not accept liability.
By accepting this communication, you agree that you have read the above disclaimer and to be bound by the foregoing limitations and restrictions.

Research Recommendation Disclosure
Robin Davison is the author of this research recommendation and is employed by Equity Development as an Equity Analyst. Unless otherwise stated, the share prices used in this publication are taken at the close of business for the day prior to the date of publication. Information on research methodologies, definitions of research recommendations, and disclosure in relation to interests or conflicts of interests can be found at www.allenbycapital.com. Allenby Capital acts as joint broker to Reneuron plc.

Allenby Capital, 5 St Helen's Place London EC3A 6AB, +44 (0)20 3328 5656, www.allenbycapital.com