EDISON

ReNeuron Group

Global clinical pipeline strategy update

Clinical pipeline update

Pharma & biotech

ReNeuron continues to prepare for its Phase III chronic stroke study (due to start in H217) and has indicated that it is making progress with the US/EU regulatory authorities. It intends to submit an IND in the US in Q217 and shortly after in the EU. ReNeuron also announced that it now plans to expand its ongoing Phase I/II retinitis pigmentosa (hRP cells) study to 20 patients in Phase II and commence a Phase II study in a new indication: cone-rod dystrophy (CRD). As a result, it will not continue development of CTX in critical limb ischaemia (CLI). We maintain our rNPV at £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.

Phase III chronic stroke study set-up progressing

ReNeuron reported positive Phase II trial data (December 2016) for its CTX cells in chronic stroke patients. It has recently announced that it is on track to initiate the follow-on Phase III trial in H217. It is currently consulting with the regulatory bodies in Europe and the US, has an end-of-Phase II meeting with the FDA shortly and intends to submit an IND in Q217. The European clinical trial application will follow shortly after. Alongside this, discussions are ongoing with the Japanese regulatory agency, which could offer a conditional marketing approval. For more detail, see our March 2017 outlook note.

Ophthalmology clinical programme expanded

ReNeuron also recently announced the expansion of its ophthalmology programme, following successful development of a cryopreserved formulation of its hRP cells. It intends to expand the Phase II part of the trial in RP patients (20 patients vs six patients) to utilise the cryopreserved hRPCs and build a richer data set. We expect efficacy data readouts to now be in H218. Alongside this, it is also expanding development of hRPCs into CRD, with a Phase II trial application planned in H217. As a result of the expansion of its clinical programme, the CLI programme is on hold. A Phase I safety study in CLI has been completed with no significant adverse events, according to the company.

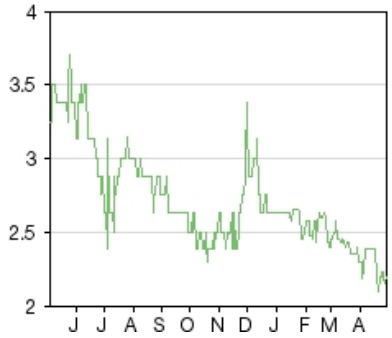
Valuation: Maintained at £291m, positive progress

We maintain our valuation at £291m. We have removed the CLI programme from the valuation, but this has been tempered by the inclusion of the CRD programme, an increase in the assumption of the price of hRP cell treatment and an updated £/$ conversion of 1.28 (vs 1.32). We believe ReNeuron is making positive developments by focusing on its clinical programme. There are a number of potential inflection points as it executes its strategy. We currently forecast a cash runway into FY19, which should enable significant advancement of its clinical programmes. At that point, it will either raise further funding and/or partner some of its programmes.

2 May 2017

Price	**2.20p**
Market cap	**£70m**
	£/$ 1.28
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	1.2	(14.6)	(32.3)
Rel (local)	(5.6)	(11.7)	(38.4)
52-week high/low		3.7p	2.1p

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

IND filing with FDA for Phase III stroke trial	H117
Initiation of Phase III stroke trial	H217
hRPC: safety data	H217
12-month follow-up from PISCES II stroke trial	H217

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Edison profile page

Updated clinical pipeline overview

ReNeuron has a broad clinical pipeline with multiple data readouts anticipated in the next couple of years. For a full company overview, please see our outlook note published on 23 March 2017.

Expanded ophthalmology programmes

ReNeuron has announced that it has successfully developed a cryopreserved formulation of its human retinal progenitor cell (hRPC) therapeutic candidate. This is a significant step forward as it enables shipping and storage, increasing the shelf life of the product and enabling potentially far-reaching commercialisation. This has enabled ReNeuron to apply to alter its current US Phase I/II clinical trial to switch from a fresh hRPC formulation for the final Phase I dose cohort (three patients). Alongside this it has allowed an expansion of its programme in ophthalmology. It intends to apply to extend the Phase II element of the ongoing Phase I/II clinical trial in RP to 20 patients (vs six patients) and expand it to a new indication: cone-rod dystrophy (CRD).

hRPC to be pursued in two indications

hRPC is currently being investigated in a Phase I/II study in retinitis pigmentosa (RP), in which the Phase I part is progressing as planned and the Phase II part is expected to be expanded to include 20 patients across additional US clinical study sites. The Phase I 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. Please see our July 2016 outlook note for a more detailed overview of RP and an outline of the trial design.

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 now expected later due to the additional patients in H218.

ReNeuron has announced its intention to expand the hRPC retinal disease programme into CRD. CRD is a group of rare eye disorders associated with the loss of cone cells in the retina that initially results in deterioration of central visual acuity (frequency 5-29%[1]) and colour vision (frequency 30-79%[1]). It is an inherited orphan disease (one in 40,000 people[2]) and generally starts in childhood, with no cure currently. The expansion to include a second indication is part of ReNeuron's strategy to evaluate the efficacy of its hRPC therapeutic candidate across a range of genetic diseases of the eye. It intends to file an application to commence a Phase II study H217.

Phase III chronic stroke study – H217

ReNeuron has indicated that the rate of patient improvement as measured in the Phase II study (motor scales, global impairment and activities of daily living 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 Phase III 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 endpoints 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 has met with the EU regulators and will be meeting with the US regulators shortly. It expects to file

[1] https://rarediseases.info.nih.gov/diseases/10790/cone-rod-dystrophy

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1808442/

an IND in the US in Q217 and shortly after in Europe. We believe there is potential readout from the trial in 2019. In addition to its progress in the US and Europe, ReNeuron is continuing to move forward in Japan, where it has also met with the regulatory agency (PDMA). The Japanese market offers an interesting opportunity as there are regulations that offer the potential for conditional marketing approval at an earlier stage of clinical development. We expect ReNeuron to find a partner to commercialise in Japan. For a more detailed overview of Phase II clinical stroke study data, see our March 2017 outlook note.

Exosome nanomedicine platform potentially in clinic H118

ReNeuron is currently engaged in preclinical work around its exosome platform. If the outcome of the preclinical work is positive, the company intends to start a Phase I clinical trial in H118. 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 to partner 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, please see our July 2016 outlook note.

Valuation: Maintained at £291m

We are maintaining our valuation at £291m. We have removed the CLI programme from our valuation, which has been offset by the inclusion of the CRD programme, an increase in the price of the hRPc treatment to $75,000 per treatment vs $50,000 previously and using an updated £/$ conversion of 1.28 (vs 1.32 before). We also now use our estimated FY17 cash of £44m (vs H117 reported cash of £60m). Exhibit 1 outlines our key assumptions around the CRD programme. Our assumptions for the other programmes remain the same. We noted in our previous report that pricing of $50k per eye treatment (RP and CRD programme) is conservative as a transformational disease-modifying treatment. We have reviewed this in our model, as stated above, but still believe it could be priced higher. We also note that we do not currently ascribe value to its exosome programme.

Exhibit 1: rNPV valuation and 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 completed	2020	765	1,633	25%	30%	175	5.54	1.76m strokes/yr (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 II ready	2020	94	147	20%	30%	14	0.45	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	2020	331	629	20%	30%	57	1.80	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).
Portfolio total				1,190				246	7.79	
Cash								44	1.40	FY17 estimated cash
Overall valuation								291	9.19	3,164m shares outstanding

Source: Edison Investment Research

We maintain our forecasts, as overall we expect the same spend as before the change in clinical programme mix. ReNeuron has a strong cash position (we forecast a cash runway to FY19), which should allow the company to significantly advance its 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 (H217);
- Phase I hRPC safety data in 2017;
- initiation of Phase II hRPC study in RP and CRD; and
- further preclinical data from the exosome nanomedicine platform (efficacy and toxicity).

Exhibit 2: 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: ReNeuron accounts, Edison Investment Research

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