ReNeuron

Interim Results Presentation

For the six months ended 30 September 2019

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A Leader in Cell-Based Therapeutics

Leading clinical stage cell therapy company
Sites in the UK and Boston, US

Proprietary allogeneic stem cell technology platforms

Two clinical stage therapeutic candidates targeting unmet medical needs

Significant clinical validation milestones over the next 24 months

Proprietary Platform Technology

hRPC

- Human retinal progenitor stem cell line
- Cryopreserved formulation allows global ship-and-store
- Positive early Phase 2a data in retinitis pigmentosa
- Partnered with Fosun Pharma for China

CTX Cells

- Immortalised neural progenitor stem cell line
- 12 month shelf life (cryopreserved)
- Positive Phase 2a results in stroke disability
- Partnered with Fosun Pharma for China

CTX-Derived Exosomes & iPS cells

- High-yielding human neural stem cell-derived exosomes
- Proven ability to load exosomes with siRNA, miRNA and proteins
- Favourable distribution of exosomes across the Blood Brain Barrier
- Potential as drug load/delivery vehicle and as a therapeutic
- CTX-derived induced pluripotent stem cells (iPSCs) offer further licensing potential

Clinical Programme Pipeline

Programme	Indication	Pre-clinical	Phase 1	Phase 2	Next Milestone
hRPC	Retinitis Pigmentosa				Further data read-outs from expanded Phase 2a study in 2020
CTX cells	Stroke Disability				PISCES III, pivotal, multi-centre U.S. Phase 2b study, data read-out expected mid-2021

Interim Results – Operational Highlights

hRPC

- Positive top-line efficacy data presented from Phase 2a patients in ongoing US Phase 1/2a clinical trial in retinitis pigmentosa
- Ongoing Phase 2a study to be expanded to allow for subsequent potential single pre-approval clinical study and shorter route to market
- Further top-line efficacy data from expanded Phase 2a study expected to be presented during 2020

CTX Cells

- Clinical trial protocol amendments and other initiatives in place to accelerate patient recruitment in ongoing US Phase 2b clinical trial
- Significant increase planned in overall number of patients to receive CTX therapy as opposed to placebo procedure in Phase 2b study
- Overall size of Phase 2b study increased from 110 to 130 patients, with top line data expected in mid-2021

CTX-Derived Exosomes & iPS cells

- Grant-funded collaboration initiated with European Cancer Stem Cell Research Institute to enable delivery of therapeutic nucleic acids using CTX-derived exosomes
- New data presented, supporting use of CTX-derived iPSCs to develop new immortalised cell lines as potential therapeutic agents for subsequent licensing to third parties

Business Development

- Exclusive out-licence agreement with Fosun Pharma to commercialise hRPC and CTX programmes in China
  - ReNeuron to receive upfront, near term and estimated success-based milestone payments of £80.0 million plus double-digit royalties on sales
- Discussions ongoing with other commercial third parties regarding potential out-licence deals across all of ReNeuron's programmes

Interim Results – Financial Highlights

(£'m)	**Six months ended 30 September 2019 (Unaudited)**	Six months ended 30 September 2018 (Unaudited)	Year ended 31 March 2019 (Audited)
Revenue and other operating income	**6.1**	2.4	2.7
Research and development costs	**(9.2)**	(7.5)	(16.2)
General and administrative costs	**(2.6)**	(2.6)	(4.8)
Operating loss	**(5.7)**	(7.7)	(18.3)
Net finance income	**0.6**	0.9	1.1
Taxation	**1.2**	1.5	2.9
Loss for the period	**(3.9)**	(5.3)	(14.3)
Net decrease in cash and deposits	**(5.1)**	(6.7)	(11.0)
Cash and deposits at start of period	**26.4**	37.4	37.4
Cash and deposits at period end	**21.3**	30.7	26.4

Human Retinal Progenitor Cells (hRPC)

ReNeuron

Human Retinal Progenitor Cells (hRPC)

hRPC: allogeneic cell-based therapeutic approach to retinal disease

- hRPCs differentiate into functional photoreceptors and integrate into retinal layers in pre-clinical models; integration may also enable durable trophic support
- Broad therapeutic potential across a range of retinal diseases
- Initially targeting inherited retinal degenerative diseases

Proprietary manufacturing process and controls allow for stable, high quality and high quantity GMP production

- Collaborations with Schepens Eye Research Institute and University College London
- Proprietary technology enabled development of GMP manufacturing process
- Cryopreserved formulation provides 9 month shelf life and enables local treatment worldwide

Retinitis Pigmentosa: An Unmet Need

- RP is an inherited, degenerative eye disease[1,2,3]
  - Incidence of 1:4,000 in U.S. and worldwide
- >100 genes identified containing mutations leading to RP[4]
- Orphan Drug Designation in EU and US
- FDA Fast Track Designation

NORMAL VIEW

VIEW WITH
RETINITIS PIGMENTOSA

Therapeutic benefit of hRPC approach not dependent on genetic cause

[1] Hamel (2006) Orphanet J Rare Disease 1, 40;
[2] https://nei.nih.gov/health/pigmentosa/pigmentosa_facts;
[3] NORD
[4] https://www.genome.gov/13514348/learning-about-retinitis-pigmentosa/

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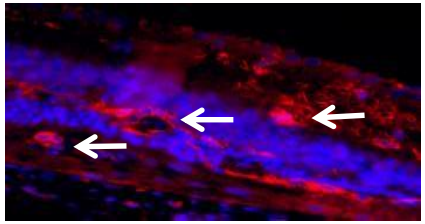
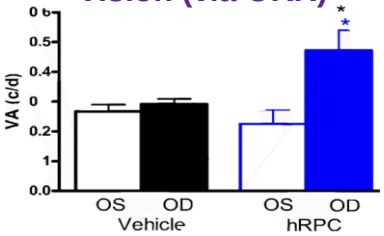
Pre-clinical Studies Support RPC Potential in Degenerative Retinal Disease

hRPC in RCS Dystrophic Rats
12 Weeks Post-Injection

hRPC Survival



Vision (via OKR)

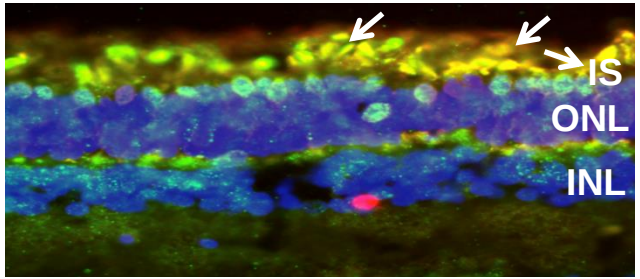


hRPC (red)/photoreceptors (blue); white arrows indicate hRPC cells within retinal layers

OKR = optokinetic response; OS = oculus sinister (left eye); OD = oculus dextrus (right eye)

- Evidence that hRPC:
  - Integrated into host retina
  - Provided trophic support of host cells
  - Preserved vision based on OKR

pRPC in Pigs
4 Weeks Post-Injection



Transplanted donor cells (green); transplanted donor cells becoming photoreceptor cells (yellow) in the host retina (blue)
IS = inner segments; ONL = outer nuclear layer; INL = inner nuclear layer

- Evidence that pRPC:
  - Differentiated into retinal cells
  - Integrated into host retina
  - Required no immunosuppression

Pre-Clinical Data Support a Durable Response

Species	Time after Treatment	Incidence of Survival
Dystrophic RCS & Normal Rats	**28 weeks**	77%; 23/30 dystrophic RCS rats 70%; 7/10 normal control rats
NIH-III Nude Mice	**39 weeks**	33%; 15/45
Mini Pigs (allogeneic study mimicking the clinical scenario)	**12 weeks**	81%; 21/26 At 12 weeks a number of surviving pRPCs appeared to have migrated into the photoreceptor layer up to a depth of 2-3 layers, indicating cell integration.

RPC cells survive for long periods in all species and survival is unaffected by the presence of disease

Clinical Development – Phase 1/2a

Phase 1

- FIH, single ascending dose in subjects with established RP
  - Subjects with very poor visual potential
  - Four cohorts, three subjects each
  - Dose escalated to 1m cells
  - Formulation changed from fresh to cryopreserved cells
- Established safety in 1m cell dose in cryopreserved formulation

Phase 2a

- 6-12 additional subjects with established RP
  - Patients with better visual potential
  - 10 subjects treated
- Primary endpoint: safety
- Secondary measures: visual acuity, visual field, retinal sensitivity and retinal structure

U.S. Clinical Sites

- Massachusetts Eye & Ear Infirmary, Boston, Jason Comander, MD, PhD
- Retinal Research Institute, Phoenix, Pravin Dugel, MD

Phase 1/2a Recent Summary Results*

- Patient recruitment status:
  - 12 Phase 1 patients treated (>12 months follow up)
  - Phase 2a (ongoing)
    - 10 patients treated, follow up period:
      1 month: n=8; 3 months: n=6; 6 months: n=4; 9 months: n=1
- Good safety profile (n= 22):
  - No immune-related adverse events
  - No drug product related serious adverse events
  - 2 patients with surgical procedure related vision loss (one AE, one SAE):
    - Consistent with nature of sub-retinal injection procedure; one moderate and likely permanent, the other severe, but improving
- Clinically meaningful efficacy signals consistently seen:
  - Rapid and profound in some patients, more gradual in others

* American Academy of Ophthalmology Annual Meeting (AAO) in San Francisco – October 2019

Phase 2a Recent Efficacy Results*

Months post-treatment	Mean improvement in visual acuity in treated eye	Mean improvement in visual acuity in treated eye (excluding two patients with procedure-related vision loss)	Mean change in visual acuity in untreated eye
1	+8.3 letters (n=8)	+14.5 letters (n=6)	+ 1.6 letters (n=8)
2	+5.4 letters (n=8)	+13.0 letters (n=6)	+ 2.8 letters (n=8)
3	+6.1 letters (n=8)	+17.8 letters (n=6)	+ 6.8 letters (n=8)
6	+18.5 letters (n=4)	+28.7 letters (n=3)	+ 7.8 letters (n=4)
9	+12.0 letters (n=1)	+12.0 letters (n=1)	- 1.0 letter (n=1)

"We're excited by the progress of ReNeuron's hRPC therapy. From the Foundation's perspective, any gain in vision, or even stabilisation, is a major step forward for patients with RP as currently it is a condition where progressive loss of vision leads to blindness."

Benjamin R. Yerxa PhD, Chief Executive Officer –– Foundation Fighting Blindness (14 Oct 2019)

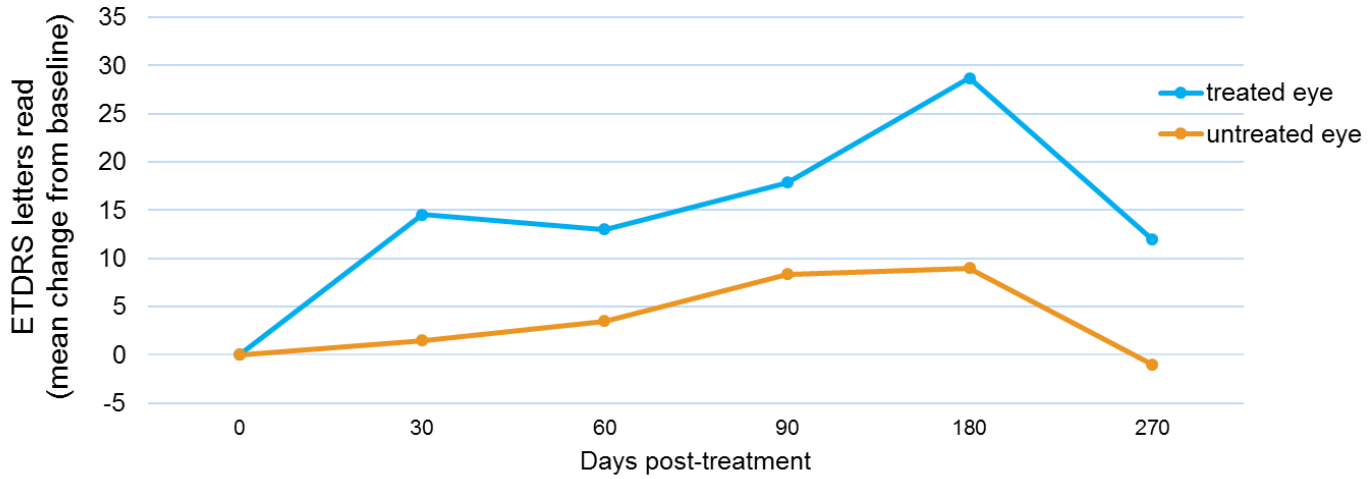
* American Academy of Ophthalmology Annual Meeting (AAO) in San Francisco – October 2019

Phase 2a Recent Efficacy Results*

ETDRS letters read: Phase IIa portion

Mean changes in treated eye vs untreated eye

Mean change:* *(per timepoint)*					
	+14.5 (n=6)	*+13.0 (n=6)*	*+17.8 (n=6)*	*+28.7 (n=3)*	*+12.0 (n=1)* *treated eye*
	+1.5 (n=6)	*+3.5 (n=6)*	*+8.3 (n=6)*	*+9.0 (n=3)*	*-1.0 (n=1)* *untreated eye*
	+13.0 (n=6)	*+9.5 (n=6)*	*+9.5 (n=6)*	*+19.7 (n=3)*	*+13.0 (n=1)* *difference*



**excluding 2 patients with surgery-related vision loss*

hRPC Platform Next Steps

- Expand ongoing Phase 2a study to generate further and longer-term follow up efficacy data in a larger group of RP patients:
  - Potential modifications in patient selection and surgical strategy to enhance safety and amplify current efficacy signal
  - Subsequent potential single pre-approval clinical study, allowing shorter time to market
- Further top-line efficacy data from expanded Phase 2a study expected to be presented during 2020
- Assess other indications alongside RP (e.g. Cone Rod Dystrophy)

CTX Cells

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CTX Cell Therapy

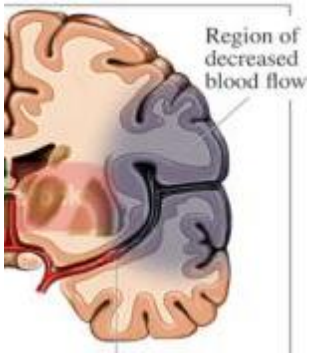
CTX: allogeneic, cryopreserved, human neural stem cell product

- Promotes anatomical plasticity in the brain
- Excellent safety profile – no immunogenicity issues post-administration
- Manufactured under cGMP with a 12 month shelf life

Commercially Attractive

- Product can be easily ordered, shipped and stored at the hospital
- Delivered in cryo-shipper, controlled thawing at hospital site
- Administer to patient ‘on demand’
- Commercial scale manufacturing at attractive COGs

CTX Promotes Anatomical Plasticity in the Brain



Cells stereotaxically implanted in the putamen - modulate immune response to promote repair

Potential Mechanism(s) of Action[1,2]

- Stimulate neurogenesis
- Cell trans-differentiation
- Stimulate/ restore synaptic activity
- Modulate inflammation
- Release of paracrine factors
- Stimulate angiogenesis

- Symptomatic relief of disability
- Tissue restoration and/or repair

[1]Pollock et al (2006) Exp Neurol 199, 143-155;

[2]Sinden et al.(2017) Stem Cells Dev 26, 1078-1085

CTX for Stroke Disability: Unmet Medical Need

- Stroke is the leading cause of morbidity and long-term disability in the U.S.[1]
  - 1 in 6 people will have a stroke in their lifetime
- Financial burden
  - $34 billion annually in stroke-related costs in the U.S[1]
  - Direct medical stroke-related costs projected to triple from 2012 to 2030[1]
- Limited treatment options
  - Only one drug available, for use within 4.5 hours of stroke onset[2]
  - Rehabilitation provides most benefit in first month, very little beyond six months[3]

CTX administration promotes repair in the damaged brain

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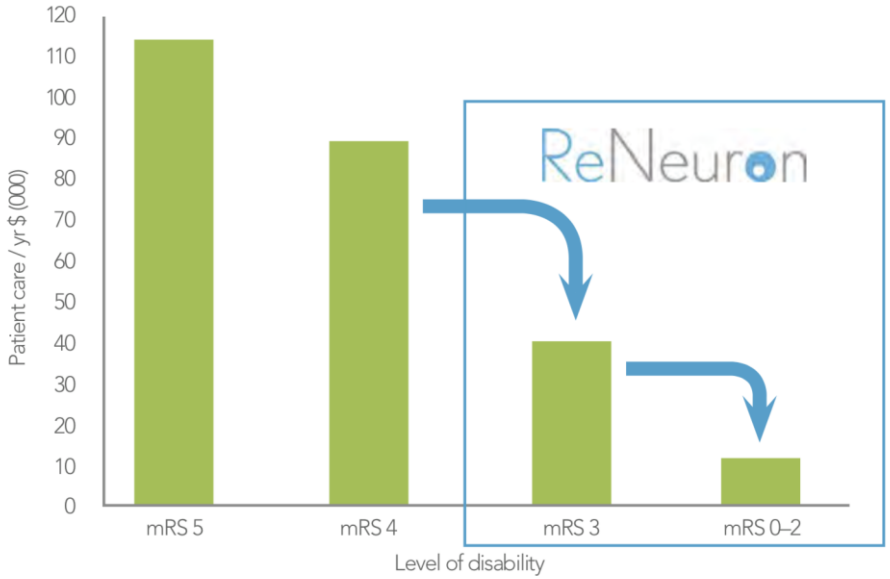
[1]Benjamin et al (2017) Circulation 135, e146-e603;
[2]Otwell et al (2010) Am J Health Pharm 67, 1070-1074;
[3]Hatem et al (2016) Front Hum Neurosci 10, 442

Severity of Functional Disability Measured by Modified Rankin Scale (mRS)



Source: Company data; adapted from Lekander et al 2017, 42,114 patients from 2007-2012, costs from Sweden translated into $

mRS 5: Bedridden, requires constant help from others

mRS 4: Needing help to walk, use toilet, bathe

mRS 3: Can walk with appliance, needs some help at home

mRS 0-2: Slight to no disability

Reductions in disability result in substantial reductions in patient care costs

CTX in Stroke Disability: PISCES II Study Results

Phase 2a, single arm, open label study

- 23 disabled, stable stroke patients, 2 to 12 mos post-stroke
- 20 MM CTX cell dose
- Clinically meaningful improvements in disability scales measured out to 12 months post-implantation
- No cell-related safety issues identified

Very promising results for chronic stroke disability, supportive of a larger, randomised, placebo-controlled Phase 2b study

Time	Total subjects		Patients with NIHSS upper limb score < 4 at baseline	
Month	N	Responders* (%)	N	Responders* (%)
Baseline	23	-	14	-
3	23	7 (30.4%)	14	6 (42.9%)
6	22	6 (27.3%)	13	5 (38.5%)
12	20	7 (35.0%)	12	6 (50.0%)

*number of subjects with ≥ 1 point improvement in mRS (% of N observed at day of visit)

Greatest mRS improvements in subjects with residual movement of the affected arm (NIHSS UL <4)

PISCES III Study Design and Status

PISCES III

Phase 2b, Randomised, Placebo-Controlled Study

130 subjects - 2:1 randomisation to therapy v. placebo (sham) surgery

- Age 35-75 inclusive
- Ischemic stroke that includes supratentorial region (CT/MRI confirmed)
- 6-24 mos post-stroke
- mRS 3 and 4
- Some residual arm movement

Primary Endpoint*

- >1 pt improvement from baseline in mRS at 6 mos post-treatment

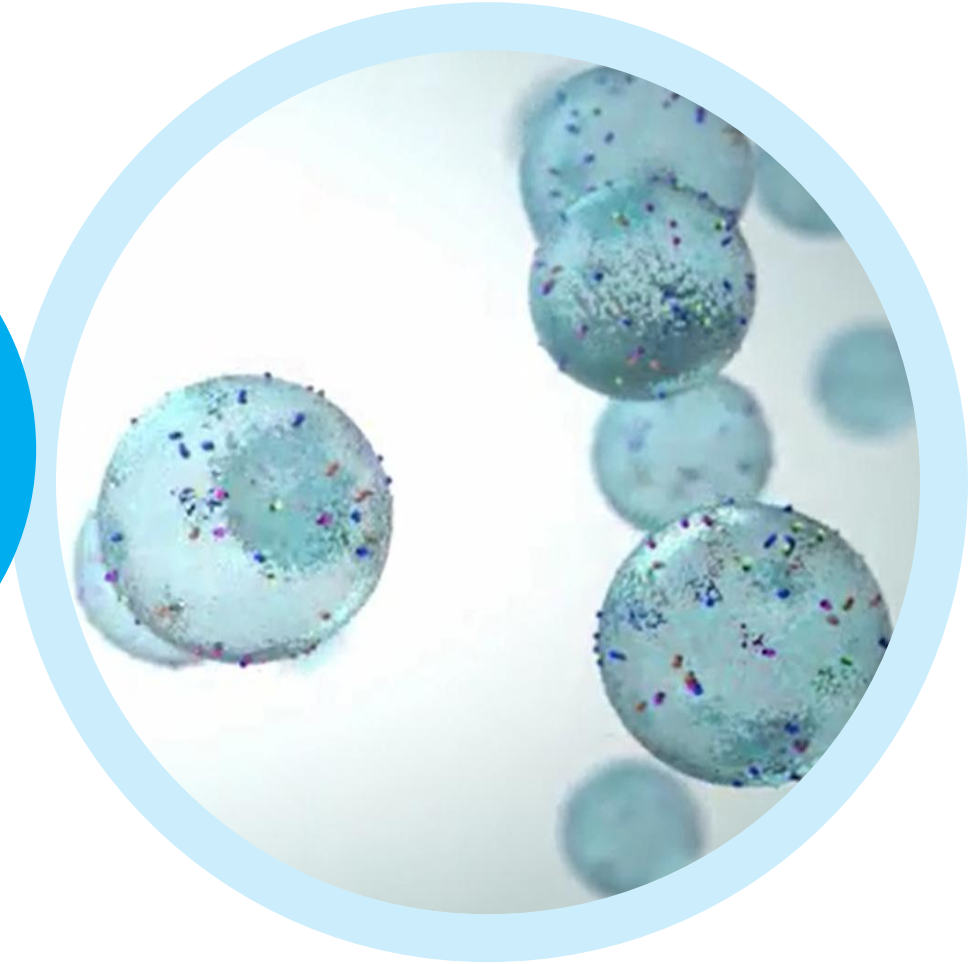
Secondary Endpoints* (1, 3, 6, 9, 12 mos post-tx)

- Barthel Index (ADL independence)
- Timed Up and Go test (lower limb and trunk function)
- Chedoke Arm/Hand Activity Inventory (upper limb function)
- NIHSS (impairment scale – neurological outcome and recovery)
- Fugl-Meyer Assessment (performance-based impairment index)
- EQ-5D-5L (QoL)

Current Status

- 12 surgical sites and 21 patient assessment sites now activated across US
- Clinical trial protocol amendments and other initiatives in place to enhance patient recruitment and enlarge data set for CTX-treated patients in study
- Top-line read-out expected in mid-2021

CTX-Derived Exosomes and iPS cells



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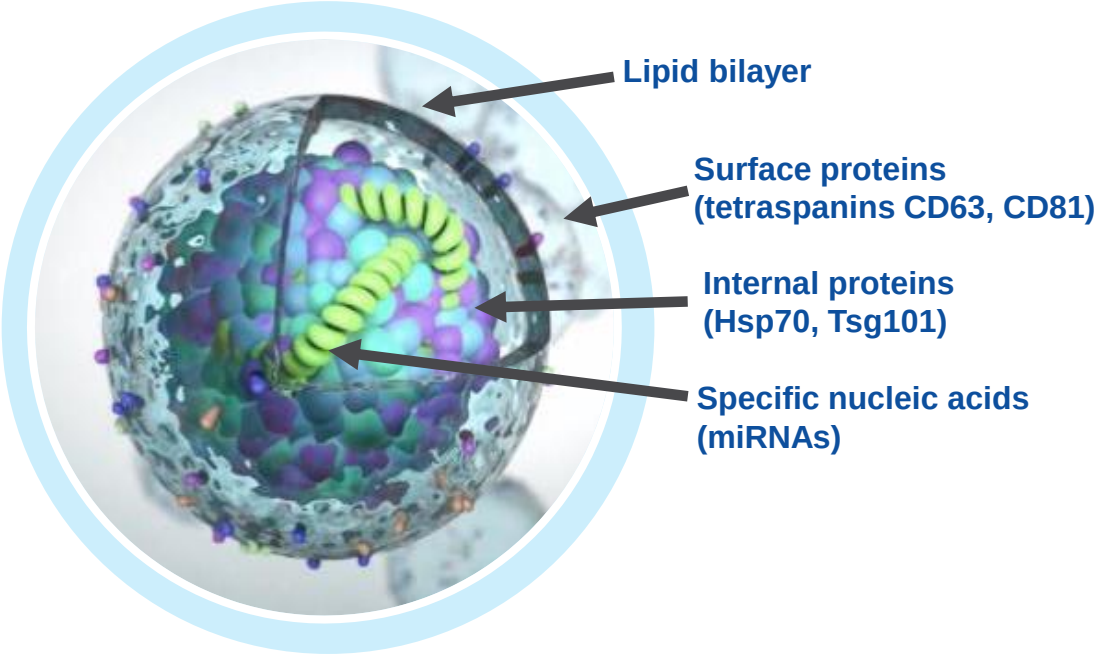
CTX-Derived Exosomes: Biological Nanoparticles

- Nano-scale vesicles released by most cell types as a means of intercellular communication
- Naturally occurring liposomal delivery system
- Contain and transport bio-active lipids, proteins and nucleic acids



- First CTX-derived exosome candidate derived
- Potential as a drug delivery vehicle and as a therapeutic

ReNeuron's CTX-Derived Exosome Technology

Advantages of exosomes as a delivery vehicle

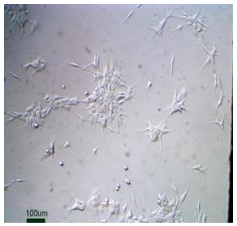
- Natural carrier of nucleic acids and proteins, amenable for loading complex, hard-to-deliver therapeutic agents
- Ease of bioengineering
- Low immunogenicity
- Intrinsically durable, membrane texture order of magnitude harder than synthetic liposomes

Advantages of ReNeuron's exosome technology

- Stable, consistent, high-yield, clinical-grade product
- Fully qualified xeno-free, optimised, scalable GMP process
- Established analytics
- Proven ability to load miRNA and proteins
- Modifiable to carry siRNA/mRNA, CRISPR/Cas9 proteins, small-molecule inhibitors
- Favourable distribution across the blood brain barrier
- Engineered to target particular tissues

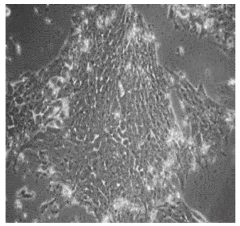
CTX-derived induced pluripotent stem cells (iPSCs)

Pluripotency



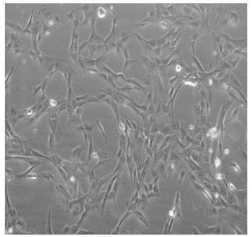
CTX0E03 Cells

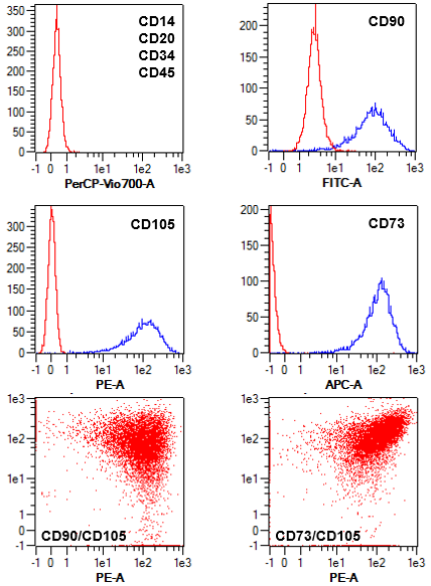
OCT4, KLF4,
SOX2, C-MYC



Human Pluripotent Stem Cells

Conditionally immortalised derivatives (MSCs) from CTX-iPSCs





- CTX cells can be rapidly and efficiently reprogrammed into a pluripotent state
- CTX-derived iPSCs retained immortalisation technology: key for consistency and scale up
- Potential:
  - New therapeutic candidates for subsequent out-licensing
  - Production of exosomes with tissue-specific targeting

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Summary

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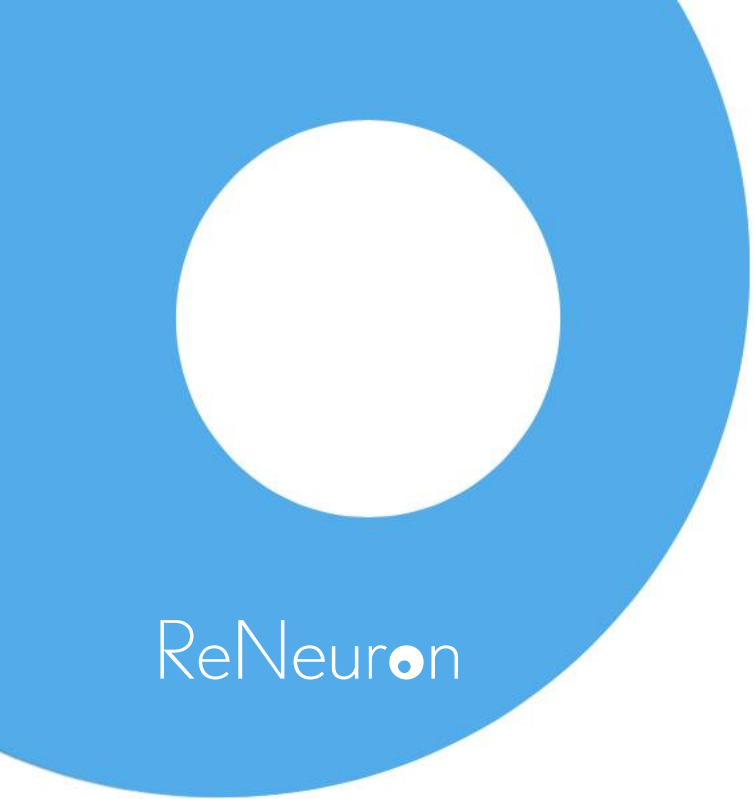
Summary

- A global leader in cell-based therapeutics – sites in UK and Boston, US
- Allogeneic stem cell technology platforms – patented, scalable & cost effective
- Targeting diseases with large unmet medical needs
- Significant clinical milestones in retinal and stroke programmes in 2020 and 2021
- Near/medium term opportunities for value-generating partnering/collaboration deals



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