ReNeuron

# Shareholder Presentation
# AGM Trading Update
# September 2019

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# AGM update – Operational Highlights

**hRPC**

- Dosing of final patient cohort underway in ongoing US Phase 1/2a clinical trial in retinitis pigmentosa
- Top line data from all treated Phase 2a patients to be presented at the American Academy of Ophthalmology Annual Meeting in October 2019

**CTX Cells**

- Patient dosing ongoing in placebo-controlled US Phase 2b clinical trial in stroke disability
- Further initiatives being pursued or evaluated to boost patient recruitment into the study
- Top line data from Phase 2b study now expected in H1 2021

**CTX-Derived Exosomes**

- Programme primarily focused on use of exosome technology as a drug delivery vehicle
- Grant-funded collaboration with Cardiff University to deliver therapeutic nucleic acids across blood brain barrier using ReNeuron's exosomes
- Key patents over ReNeuron's neural stem cell-derived exosomes granted in Europe, Japan, China and South Korea

**Business Development**

- Work commenced under out-licence agreement with Fosun Pharma to commercialise hRPC and CTX programmes in China – initial focus of the collaboration is the CTX programme
- Discussions ongoing with other commercial third parties regarding potential out-licence deals

# 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

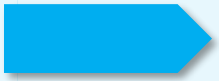
**CTX Cells**

- 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**

- Nano-sized vesicles from CTX cells
- Potential as drug load/delivery vehicle and as a therapeutic

# Pipeline with Near & Medium Term Catalysts

| Programme | Indication | Pre-clinical / Phase 1 / Phase 2 | Next Milestone |
|---|---|---|---|
| **hRPC** | **Retinitis Pigmentosa** |  | Top line Phase 1/2a data read out expected Q4 2019 |
| **CTX cells** | **Stroke Disability** |  | PISCES III, pivotal, multi-centre U.S. Phase 2b study, data read out expected H1 2021 |
| **Exosomes** | **Drug Delivery** |  | Collaboration / Partnering deals targeted |

# Human Retinal Progenitor Cells (hRPC)

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# Human Retinal Progenitor Cell Therapy

## hRPC: unique, 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 and high quantity GMP production

- Collaborations with Schepens Eye Research Institute and University College London
- Proprietary technology enabled development of GMP manufacturing process to support clinical application
- Cryopreserved formulation provides for commercially viable shelf life and allows for worldwide shipment on demand

# Retinitis Pigmentosa: An Unmet Need

- RP is an inherited, degenerative eye disease[1,2,3]
  - Primary loss of rod photoreceptors; secondary loss of cones
  - Onset varies from early childhood to 20s/30s
  - Early stage main symptom is night blindness
  - Progressive loss of peripheral vision, then central vision
  - 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 U.S.
- FDA Fast Track Designation

NORMAL VIEW

VIEW WITH
RETINITIS PIGMENTOSA

**Therapeutic benefit of hRPC approach not dependent on genetic causes of IRD**

**No approved treatment for the vast majority of patients with RP**

[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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# 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
  - Cohorts 1-2:  250K, 500K fresh cells
  - Cohort 3-4:  1 MM cryopreserved cells
- Reformulation into commercial, cryopreserved formula with 6+ month shelf life

## Phase 2a

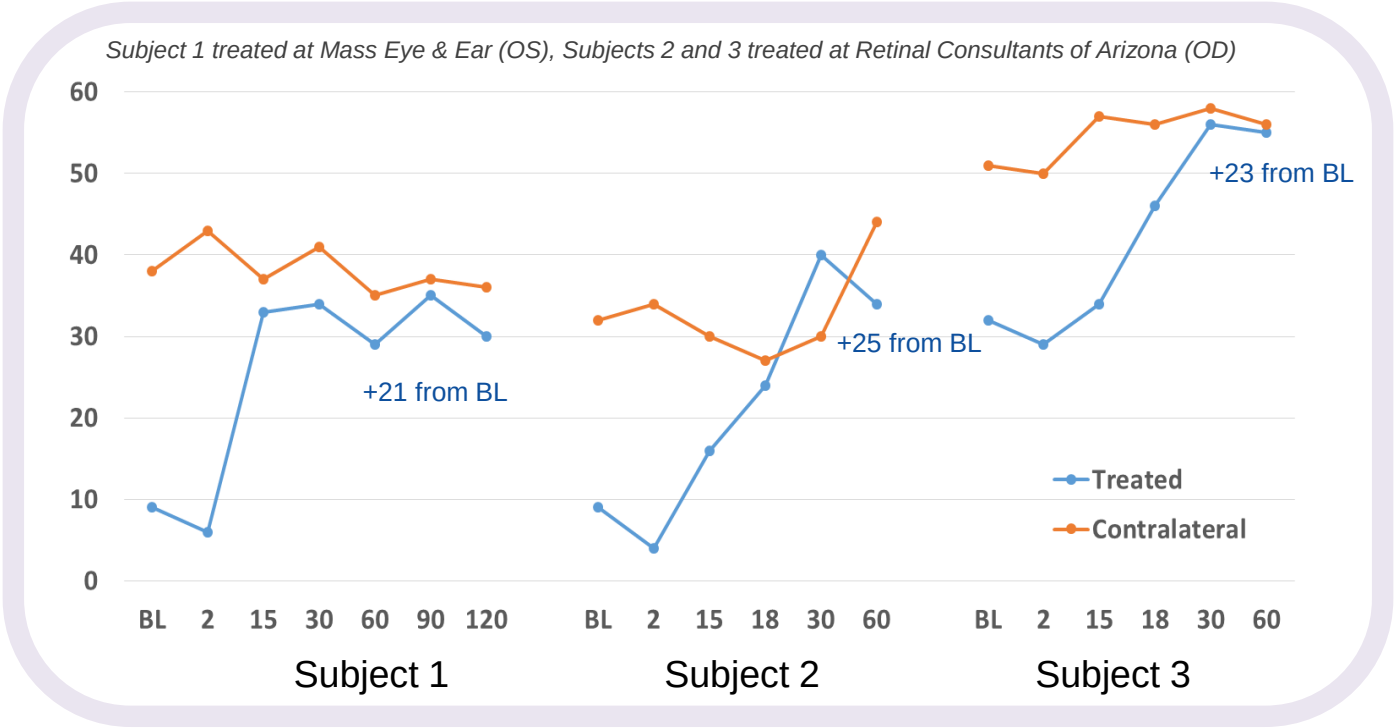
- 6-12 additional subjects with established RP
  - Subjects with better visual potential
  - Cohort 5: three subjects, 1 MM commercial, cryopreserved cells
- Primary endpoint: safety
- Secondary safety/efficacy measures: visual acuity, visual field, retinal sensitivity and retinal structure

## U.S. Clinical Sites

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

# Cohort 5 Efficacy Results*

## Changes in Letters Read (ETDRS chart)




* Sixth annual Retinal Cell and Gene Therapy Innovation Summit, Vancouver, Canada – April 2019

# Cohort 5 Efficacy Results

- Strongly positive visual acuity data
- 4-line gain on ETDRS chart
- FDA guidance considers a 3-line improvement as clinically significant (responder)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# hRPC Platform Next Steps

- Build further safety data in RP using commercial formulation
- Treating patients with more intact retinas in order to further assess efficacy potential –
  - further Phase 1/2a readout at AAO meeting in Oct 2019
- Conduct controlled multi-centre Phase 2b trial in RP
- Assess other indications

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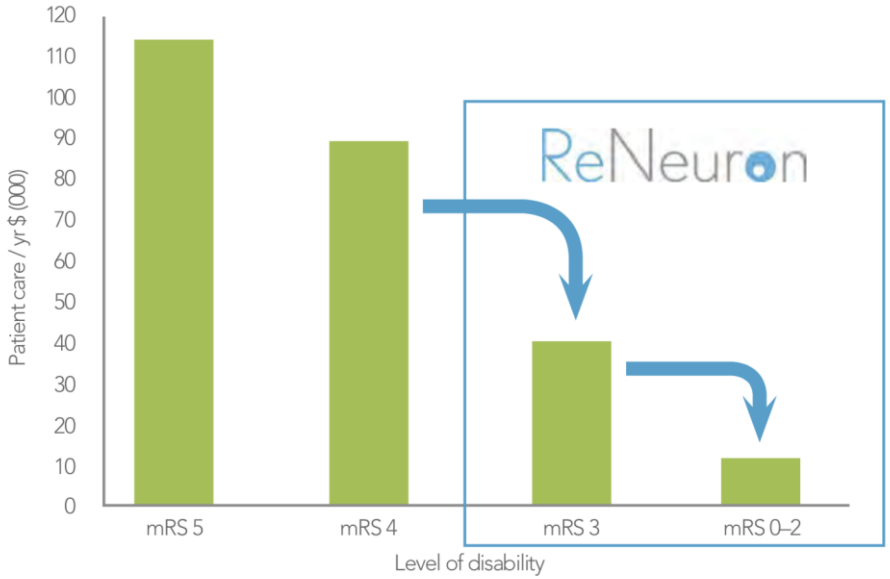
[1]Benjamin et al (2017) Circulation 135, e146-e603;
[2]Otwell et al (2010) Am J Health Pharm 67, 1070-1074;
[3]Hatem et al (2016) Front Hum Neurosci 10, 442

# 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

110 subjects - 1:1 randomization to placebo (sham) surgery

- Age 35-75 inclusive
- Ischemic stroke that includes supratentorial region (CT/MRI confirmed)
- 6-12 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

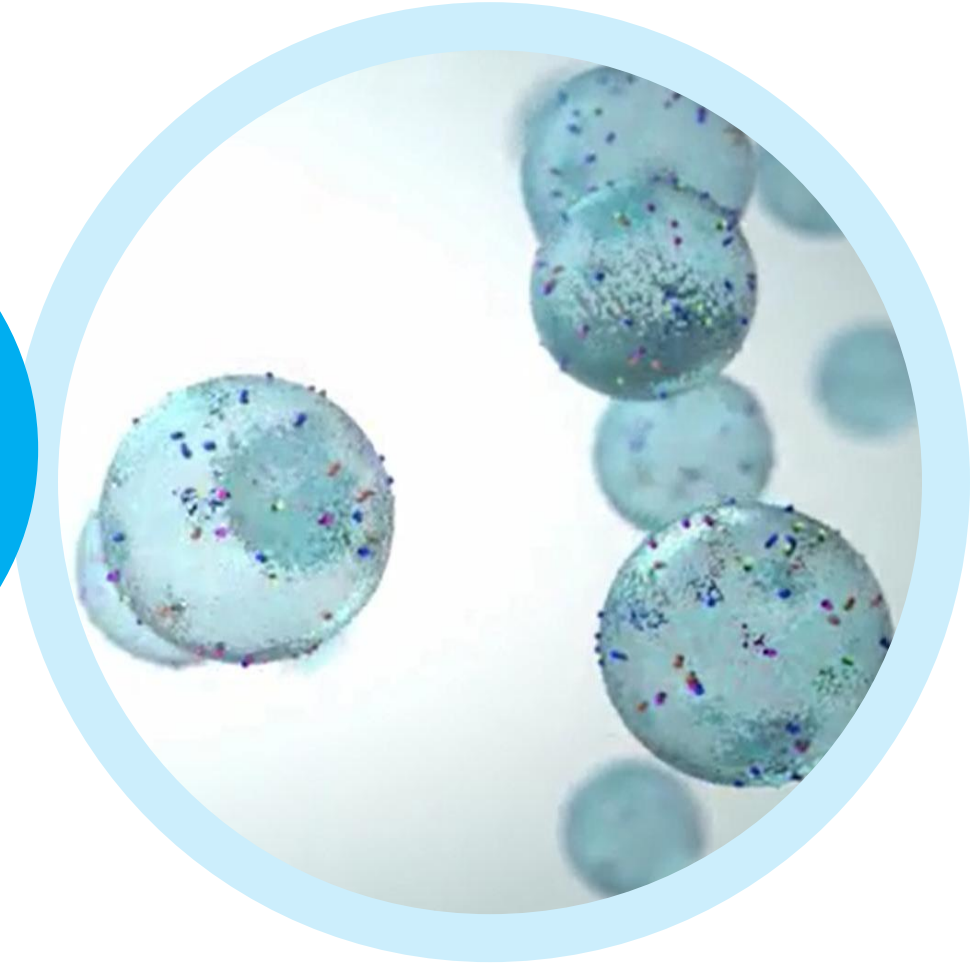
Secondary Endpoints* (1, 3, 6, 9, 12 mos post-tx)

- 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**

- 15 surgical sites and 22 patient assessment sites identified and approved
- Initial sites activated and patient dosing in progress
- CTX Drug Product batches in stock or scheduled for manufacture
- Top-line read-out expected in H1 2021

# CTX-Derived Exosomes



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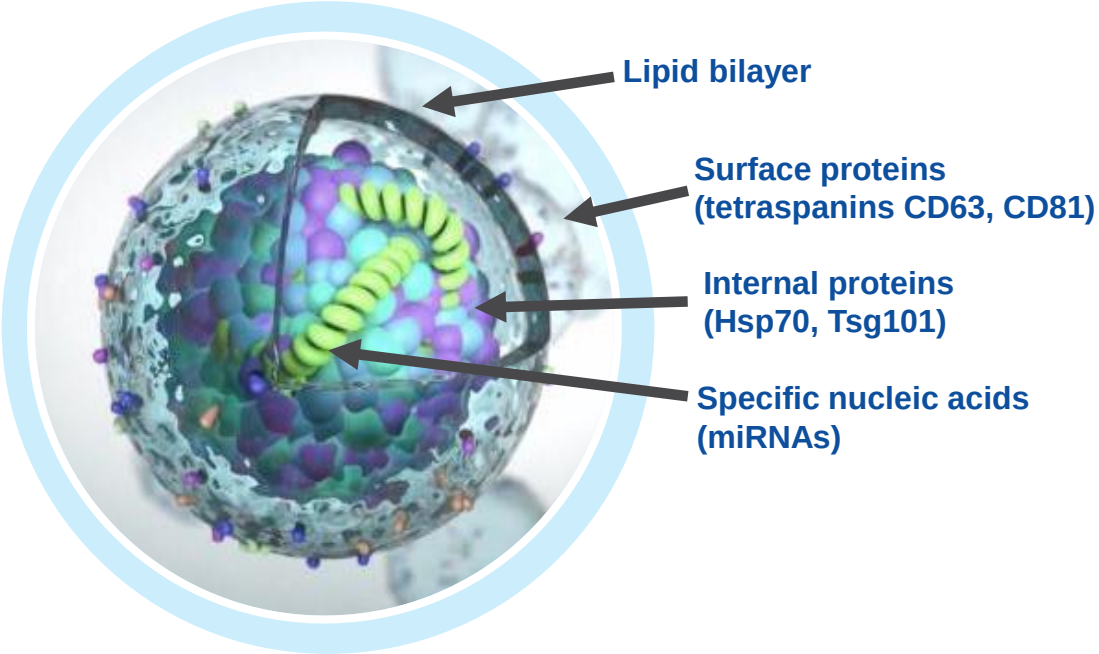
# CTX-Derived Exosomes: Biological Nanoparticles

- 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




**ExoPr0**

- First CTX-derived exosome candidate
- 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 ExoPr0 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

# Summary

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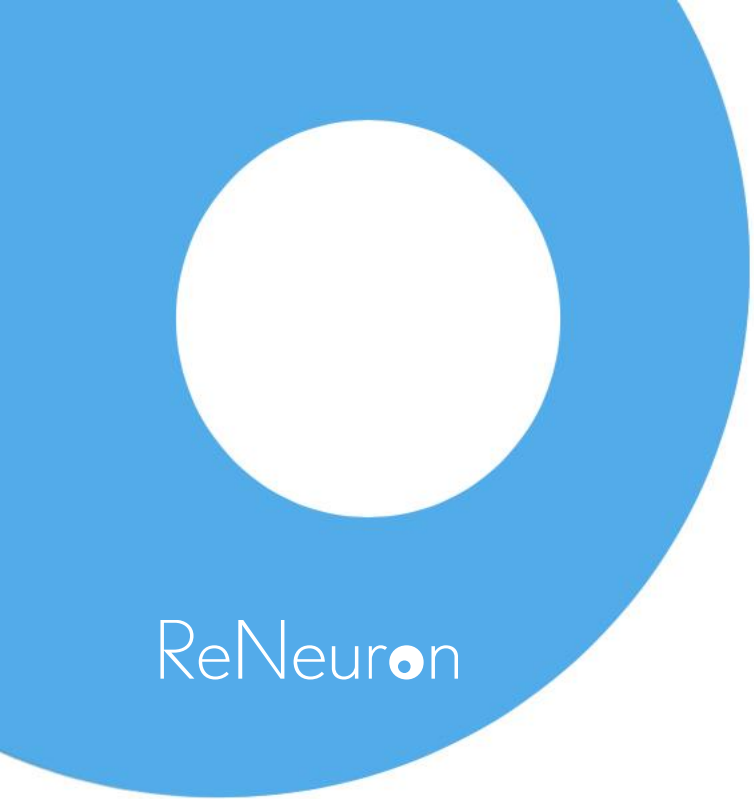
# Summary

- 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 over the next 24 months
- Near/medium term opportunities for value-generating partnering/collaboration deals




Pencoed Business Park | Pencoed | Bridgend | CF35 5HY | UK
T +44 (0) 203 819 8400 | E info@reneuron.com
www.reneuron.com
Ticker: RENE.L