ReNeuron

Corporate Presentation

Michael Hunt, Chief Financial Officer

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ReNeuron Snapshot

Multi-asset, allogeneic cell therapy company with lead programs in clinical development in the US

- CTX stem cell therapy candidate for stroke disability:
  - Positive long term data from Phase IIa clinical trial
  - IND approval for Phase IIb, placebo-controlled clinical trial. To commence in 30 US centers in H1 2018
- hRPC stem cell therapy candidate for retinal diseases:
  - Retinitis Pigmentosa program - Phase IIa study underway at Mass Eye and Ear Infirmary, Boston
  - Phase IIb studies planned to commence in 2018 in Retinitis Pigmentosa and Cone Rod Dystrophy
- Exosome nanomedicine platform:
  - Positive pre-clinical data with ExoPr0 exosome therapy candidate demonstrates potential of ExoPr0 to target multiple diseases
- Solid foundations:
  - Cash position - $61m
  - Strong management team and solid institutional investor support
  - Clinical operations managed from newly established office in Lexington, MA

Unique platform technologies

Originally derived from single neural stem cell

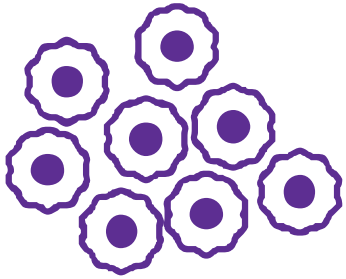
CTX cell line

CTX

Clinical pipeline in vascular and neurological indications

CTX-derived exosomes

Potential to broaden therapeutic pipeline beyond cell-based programs



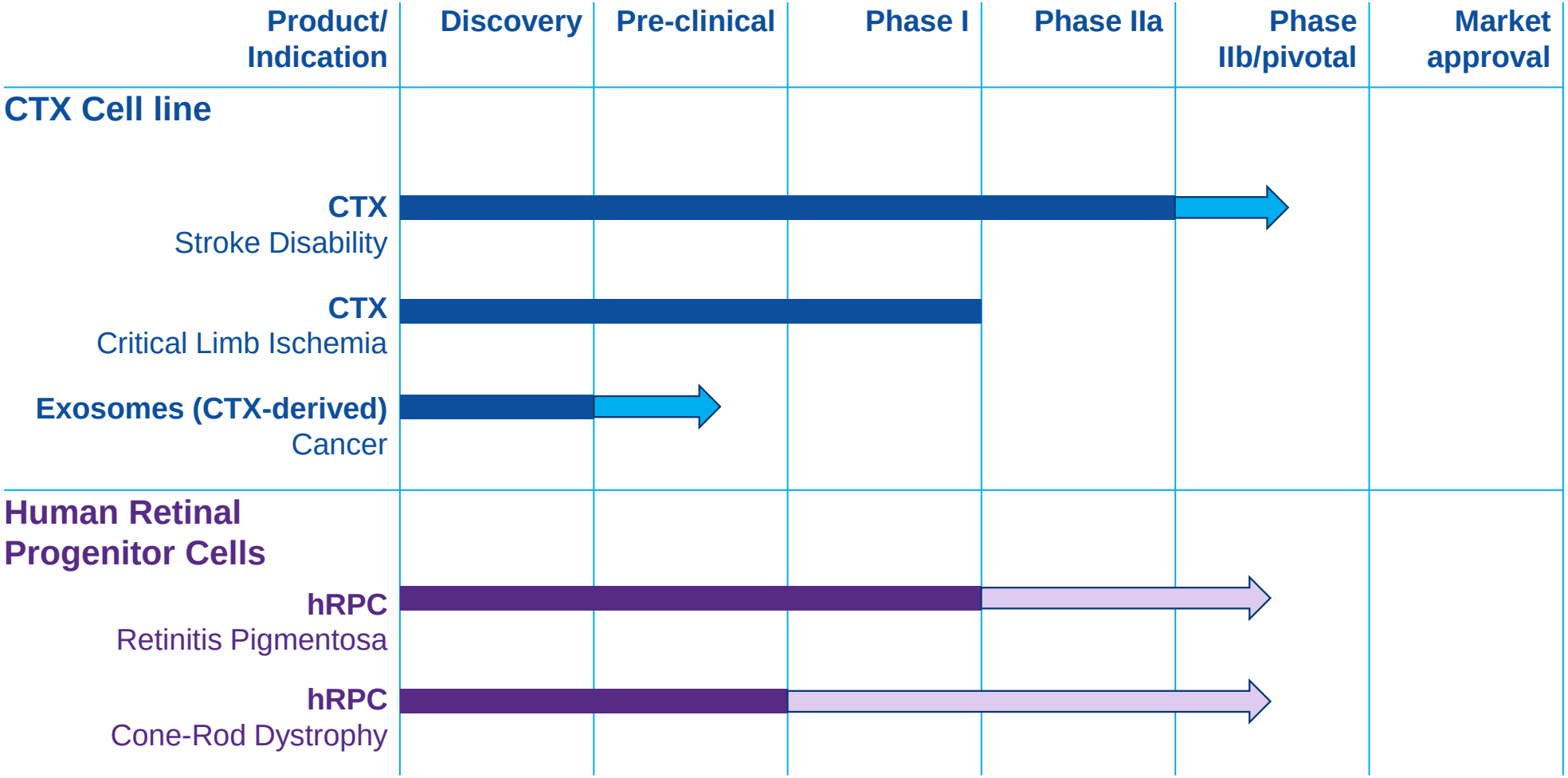
Retinal stem cell population

Human Retinal Progenitor Cells (hRPC)

hRPC

Targeting retinal degenerative diseases

Pipeline



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Starting in 2018

Well backed and well funded

- **UK-quoted (AIM)**
- **Backed by major generalist and specialist life science institutional investors:**

35.5%	9.5%	9.3%	5.7%
Woodford Investment Management	Wales Life Science Fund	Invesco	Aviva

£45.3 million (US$61 million)

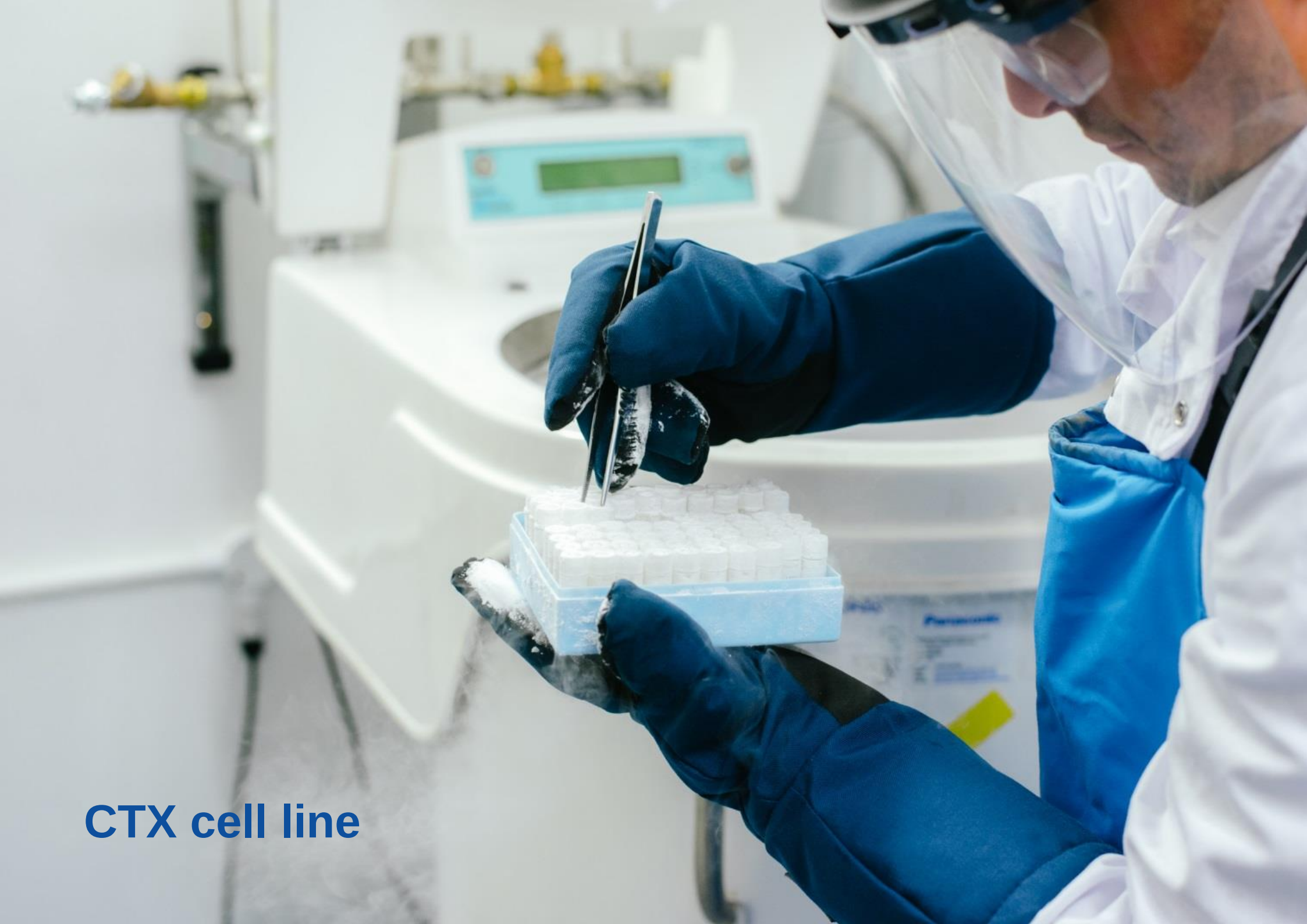
Cash on balance sheet (as at 30 September 2017) – runway into H1 2019

Market potential according to analyst estimates*

Indication	Assumptions	Peak Annual Sales
CTX for stroke	1.76 million strokes/year (total US/EU/Japan) 85% survival, 85 % ischaemic Peak penetration 5% US/EU/Japan Treatment cost $40,000 EU to $60,000 US/Japan	$1.1bn - $3.9bn
hRPC for RP	Prevalence 1:4000, ~244,000 cases (total US/EU/Japan) Peak penetration 7.5% US/ EU Per-eye treatment cost $50,000 EU to $100,000 US/Japan	$0.5bn - $1.8bn

- Applicability of hRPC in other hard-to-treat ophthalmic diseases could provide upside potential
- Longer-term upside from exosome platform

*Stifel July 2016, N+1 Singer April 2017, Edison May 2017

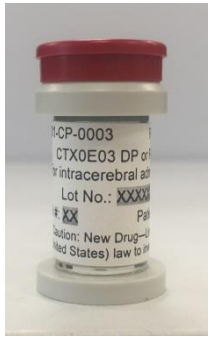


CTX cell line

CTX cell product

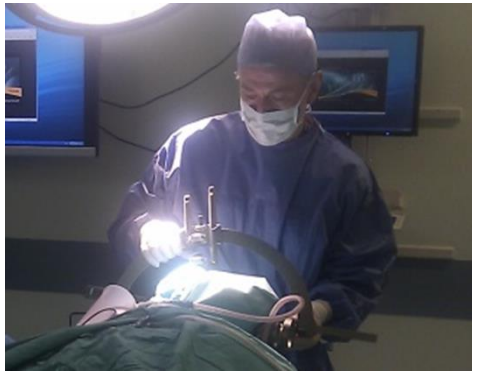
CTX - an allogeneic, cryopreserved human neural stem cell product

- Manufactured under cGMP with a 6 month shelf life
- Product to be readily ordered, shipped and stored at the hospital
- CTX platform allows for commercial scale manufacturing at attractive COG
- Excellent safety profile - no immunogenicity issues post-administration



CTX delivered in cryo-shipper

Straightforward, controlled thawing at hospital site



Administer to patient ‘on demand’

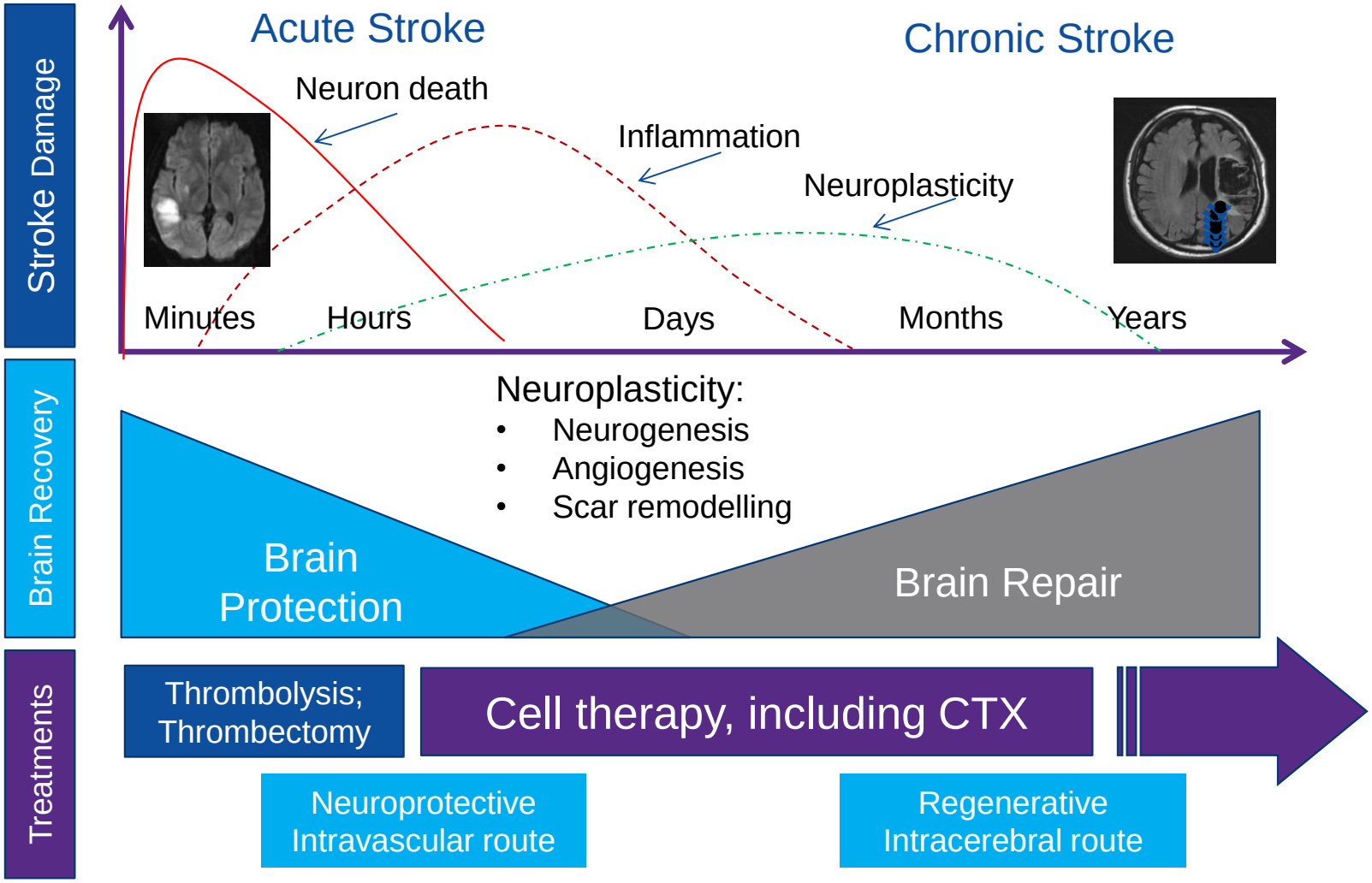
Similar to a conventional ‘off-the-shelf’ pharmaceutical / biologic drug

CTX for stroke disability: unmet medical need

Lifetime risk of stroke:
1 in 5 women
1 in 6 men

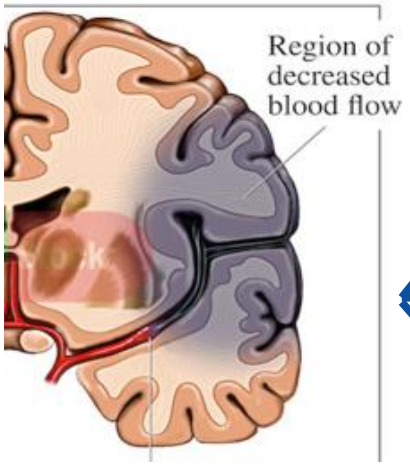
- Stroke is the single largest cause of adult disability
- Annual health/social costs: >$70 billion in the US
- Only one pharmaceutical treatment option available within 4 hours of stroke onset
- No treatment options available for stroke patients months to years later
- CTX administration promotes repair in the damaged brain

Two distinct cell therapy strategies for stroke



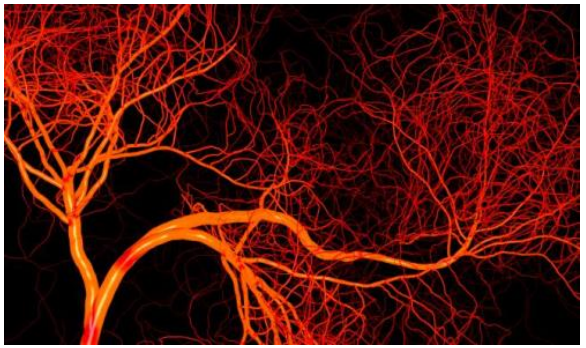
ReNeuron is a pioneer in treating chronic stroke patients

CTX promotes anatomical plasticity in the brain

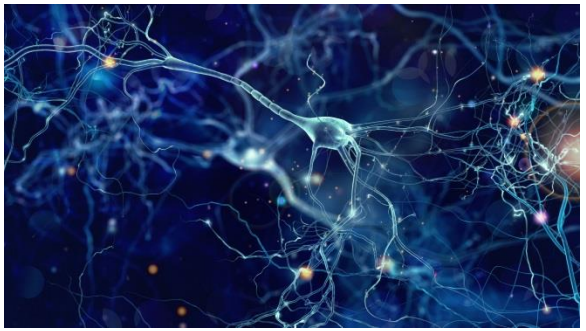


Implanted CTX cells modulate the immune system to promote repair by

Formation of new blood vessels (angiogenesis)



Formation of new neurons (neurogenesis)



Formation of new connections between neurons (synaptogenesis)

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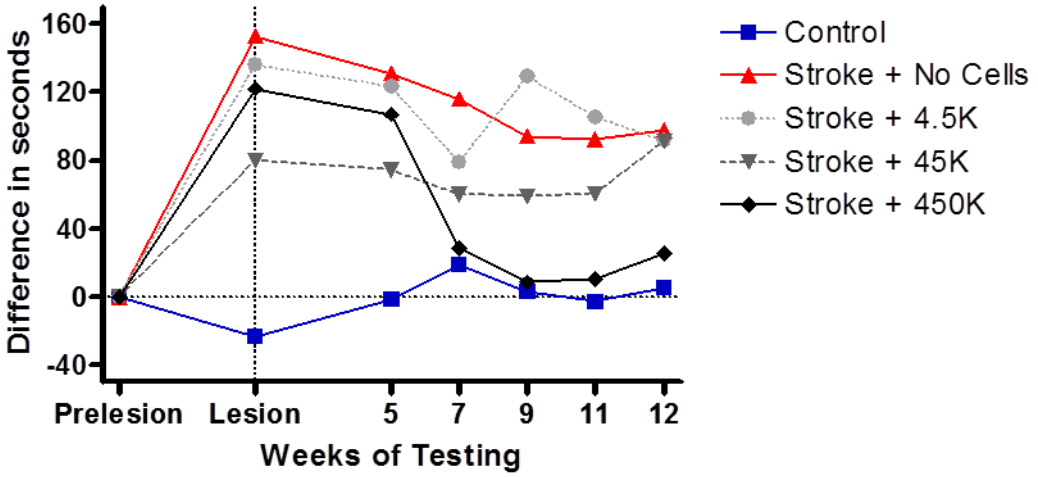
Strong pre-clinical proof of concept

- MCAO* in the rat used to model stroke damage in similar regions of the brain to those seen in stroke patients
- Panel of behavioural tests to characterise dysfunction and recovery
- Injection of CTX into same region of brain as in the patients
- Reductions in “permanent” disabilities
- Restoration of function weeks after CTX administration
- Dose response demonstrated – unique in field of cell therapy
- Motor-related efficacy demonstrated with CTX in other models of neurological disease

Reduction in permanent dysfunction



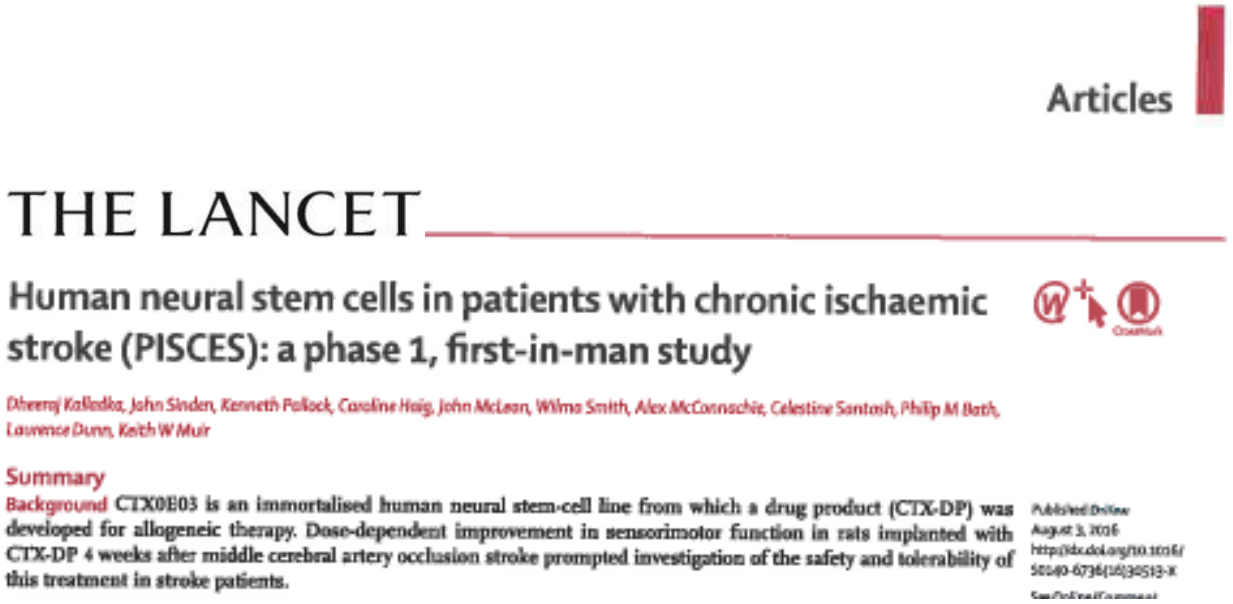
CTX administration led to recovery of tape removal from the affected forelimb in a dose dependent manner

Stroemer et al. Neurorehab Neural Repair 2009

Well validated pre-clinical models predict efficacy in chronic stroke

* Middle cerebral artery occlusion

CTX for stroke disability: Phase I data published



Articles

THE LANCET

Human neural stem cells in patients with chronic ischaemic stroke (PISCES): a phase 1, first-in-man study

Dheeraj Kalladka, John Sinden, Kenneth Pollock, Caroline Haig, John McLean, Wilma Smith, Alex McConnachie, Celestine Santosh, Philip M Bath, Lawrence Dunn, Keith W Muir

Summary

Background CTX0E03 is an immortalised human neural stem-cell line from which a drug product (CTX-DP) was developed for allogeneic therapy. Dose-dependent improvement in sensorimotor function in rats implanted with CTX-DP 4 weeks after middle cerebral artery occlusion stroke prompted investigation of the safety and tolerability of this treatment in stroke patients.

Published Online August 3, 2016 http://dx.doi.org/10.1016/S0140-6736(16)30513-X

- Phase I dose escalation safety study published with 24 months follow up
  - 11 disabled, stable stroke patients, 6 months to 5 years post stroke
  - Single, straightforward neurosurgical procedure, Doses at 2, 5, 10, 20 million cells
- No cell-related or immunological adverse events
- Significant improvement in NIH Stroke Scale, 3 patients improved in Modified Rankin Score

PISCES II – Completed Phase II study

- Aim of the PISCES II study:
  - To demonstrate effect of CTX cells on improving outcome of patients during rehabilitation phase following an ischemic stroke
  - To provide further safety data in a larger group of patients
- Inclusion Criteria
  - Male and female patients; aged 40-89; 2-12 months after a stroke
  - Upper limb dysfunction (Inability to pick up a 1” cube and place on a shelf)
- Study Procedures
  - CTX 20 million cells injected into brain (putamen) on affected side, Follow up for 12 months
- Outcome measures
  - **Modified Rankin Score**, Barthel Index, ARAT, Fugl-Meyer
- Treated 23 patients in 8 centres across the UK
- Median Age: 62 yrs (41-79), Median time from stroke to treatment: 7 months (2-13)

PISCES II efficacy – summary of all key endpoints

Test	Responder definition	3 months n/N (%)	12 months n/N (%)
ARAT Test 2	≥2 points	1/23 (4%)	3/20 (15%)
Total ARAT	≥6 points	3/23 (13%)	5/20 (25%)
Modified Rankin	≥ 1 point	7/23 (30%)	7/20 (35%)
Barthel Index*	≥9 points	8/17 (47%)	8/16 (50%)

- Six and 12 month results were similar so six months will be proposed as primary measure in future studies

Reduction in disability after CTX administration – maintained to 12 months

* Six patients had a baseline score >90 and could therefore not meet the criteria of a responder (maximum score = 100). Therefore n=17 at 3 months.

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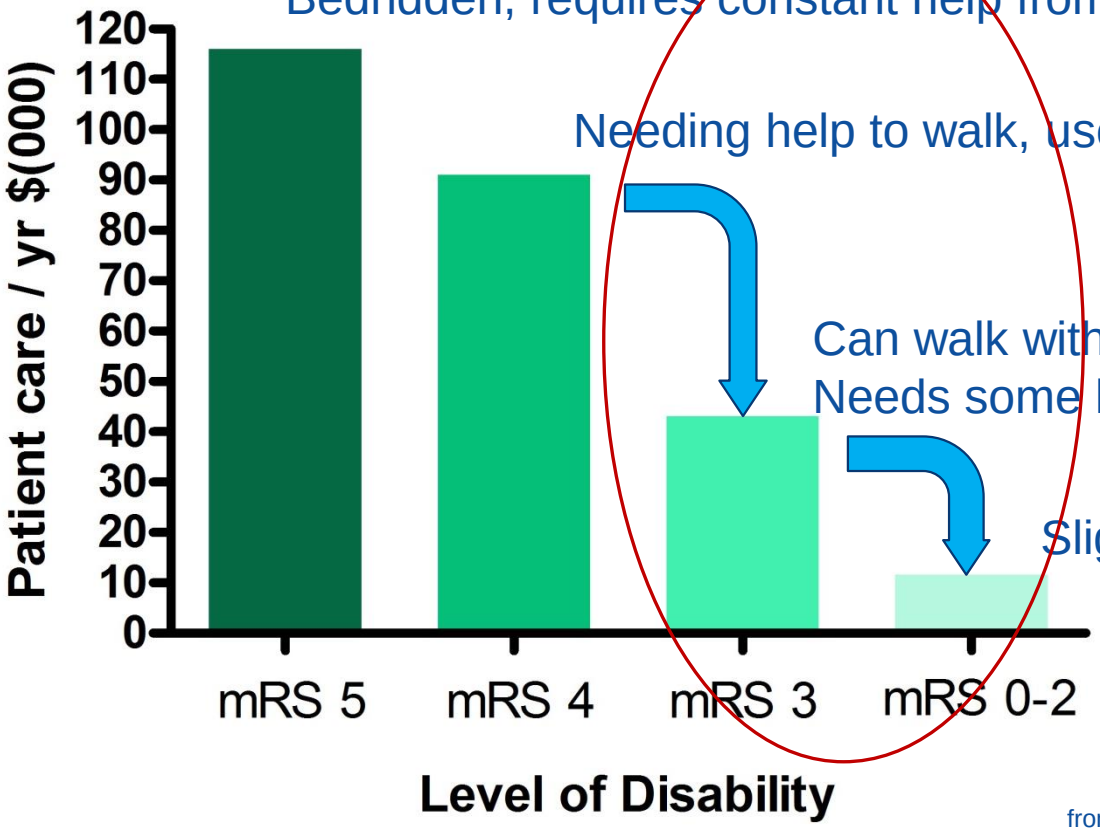
PISCES III

- IND approved – study to commence in US in HI 2018
- Randomised, placebo-controlled Phase IIb study
- n=110 patients, 1 to 1 randomisation, CTX 20 million cell dose as used in PISCES II
- Entry criteria:
  - Ischemic stroke 6-12 months previously
  - modified Rankin Score (mRS) of 3 or 4
  - Some residual Upper Limb movement
- Primary endpoint:
  - Response as measured by mRS six months post treatment
- Key Secondary endpoints
  - Response measured by Barthel Index
  - Improvement in Lower Limb and Trunk function: Timed Up and Go test
  - Improvement in Upper Limb function: Chedoke Arm and Hand Activity Inventory (CAHAI)
  - Durability of Response measured out to 12 months

Costs of disability – mRS scale



Bedridden, requires constant help from others

Needing help to walk, use toilet, bathe

Can walk with appliance,
Needs some help at home

Slight to no disability

from Lekander et al 2017, 42,114 patients from 2007-2012
Costs from Sweden, translated into $

Reductions in disability result in substantial reductions in patient care costs

Human Retinal Progenitor Cells

Retinal platform

- The intrinsic regenerative capacity of cells in retina is limited[1,2].
- Any preservation of retinal structure/function balance can greatly impact vision loss associated with retinal disease
- Our program is based on sub-retinal injection of hRPCs
  - Pre-clinical testing program demonstrates:
    - Rescue of photoreceptors to preserve vision
    - Maturation of injected hRPCs into retinal neurons/glia
  - Frozen formulation in clinical trial
    - Ship and thaw on demand
- Collaborations:
  - Schepens Eye Research Institute (Harvard Medical School)
  - Massachusetts Eye and Ear Infirmary (MEEI)
  - University College London – Institute of Ophthalmology, UK
- Initially targeting inherited retinal degenerative diseases
  - Characterized by progressive loss of photoreceptors

Broad application across a range of retinal diseases

[1]Ader et al (2014) Regenerative Biology of the Eye, A Pebay (Ed), doi: 10.1007/978-1-4939-0787-8_8; [2]So and Yip (1998) Vis Res 38, 1525-1535.

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hRPCs may slow visual loss associated with inherited retinal disease (IRD)

Retinitis Pigmentosa: primary loss of rod photoreceptors.

45 causative genes/loci (non-syndromic)[1]

Cone Rod Dystrophy: primary loss of cone photoreceptors.

10 cloned genes/3 loci (non-syndromic)[2]

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

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[1]Hamel (2006) Orphanet J Rare Disease 1, 40;
[2]Hamel (2007) Orphanet J Rare Disease 2, 7.

Retinitis pigmentosa (RP)

- RP is an inherited, degenerative eye disease[1,2]
  - Onset varies from early childhood to 20s to even later
  - Early stage main symptom is night blindness
  - Progressive loss of peripheral vision (ie tunnel)
  - Incidence of RP is 1:4000 in US and worldwide
  - Estimated treatment population of 275,000 in the US and EU
- Orphan Drug Designation in EU and US & Fast Track Designation in US
- Phase I/II study ongoing in the US
  - Phase I dosing complete August, 2017
  - Phase I safety data readout in H2 2017
  - Phase IIa commences H2 2017
  - Phase IIa readout H2 2018

NORMAL VIEW

VIEW WITH
RETINITIS PIGMENTOSA

www.eyehealthweb.com/retinitis-pigmentosa

[1]Hamel (2006) Orphanet J Rare Disease 1, 40;
[2]https://nei.nih.gov/health/pigmentosa/pigmentosa_facts

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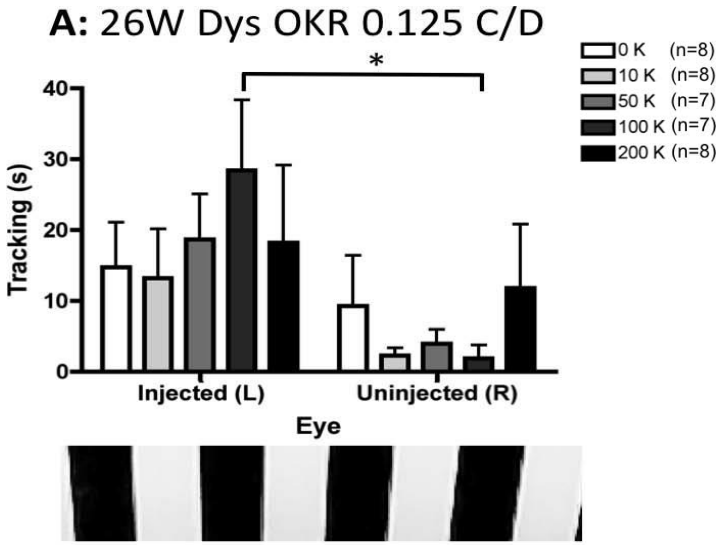
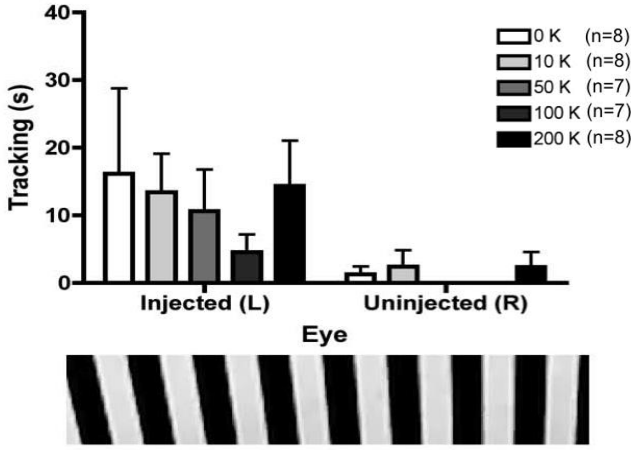
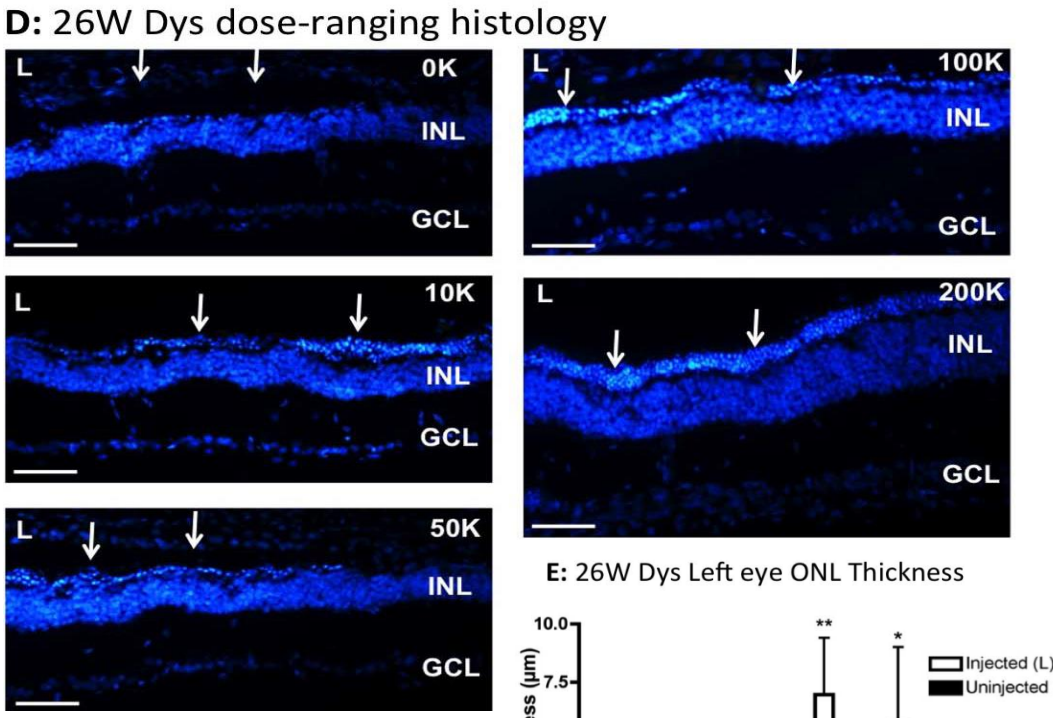
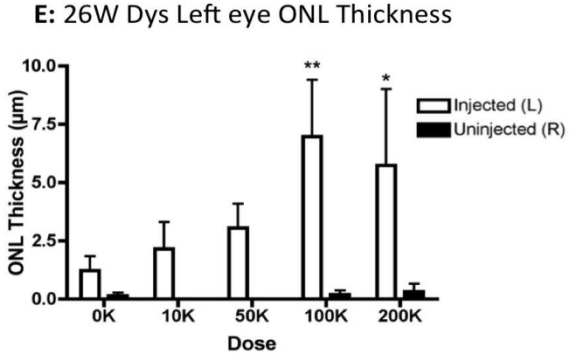
hRPCs reduce retinal degeneration and visual deterioration in RCS dystrophic rats

26 weeks post-implantation









Both structural and functional efficacy of hRPCs observed 6 months post-implantation

Semo et al (2016) Trans Vis Sci Tech 5(4), 6

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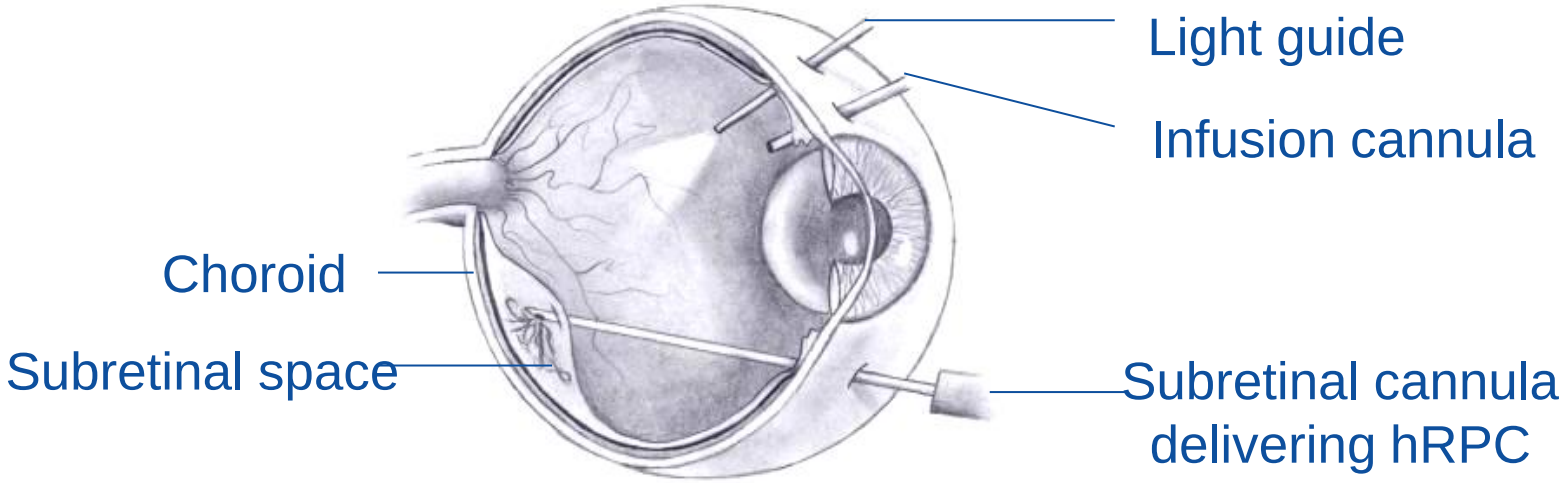
Clinical development in RP – Ongoing Phase I/IIa

- FIH, dose escalation study in subjects with established RP in the US (NCT02464436)
- Phase I - 3 dose groups of 3 subjects each
- Phase IIa - 6 additional subjects at highest, safe dose
- Primary endpoint is safety, with visual acuity, visual field, retinal sensitivity and retinal structure as secondary efficacy measures
- Measurements in both treated and untreated eyes for comparison
- Phase I/IIa clinical site – Massachusetts Eye & Ear Infirmary, Boston (PI: Dr Eric Pierce)
- Scheduled to readout in H2 2018



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Proposed hRPC studies: RP (Phase IIb) and CRD (Phase II)

Objective:
Efficacy, Safety and Tolerability of subretinally transplanted hRPCs

Primary endpoint:
Change in best-corrected visual acuity, from baseline to 6 months post-implantation

Subject Population:
Subjects (>18 yo) w best Corrected ETDRS visual acuity in both eyes within LogMAR +1.3 to +0.5 inclusive (20/400 to 20/63)*

Approximate # US sites:
5

- Both studies planned to commence in 2018

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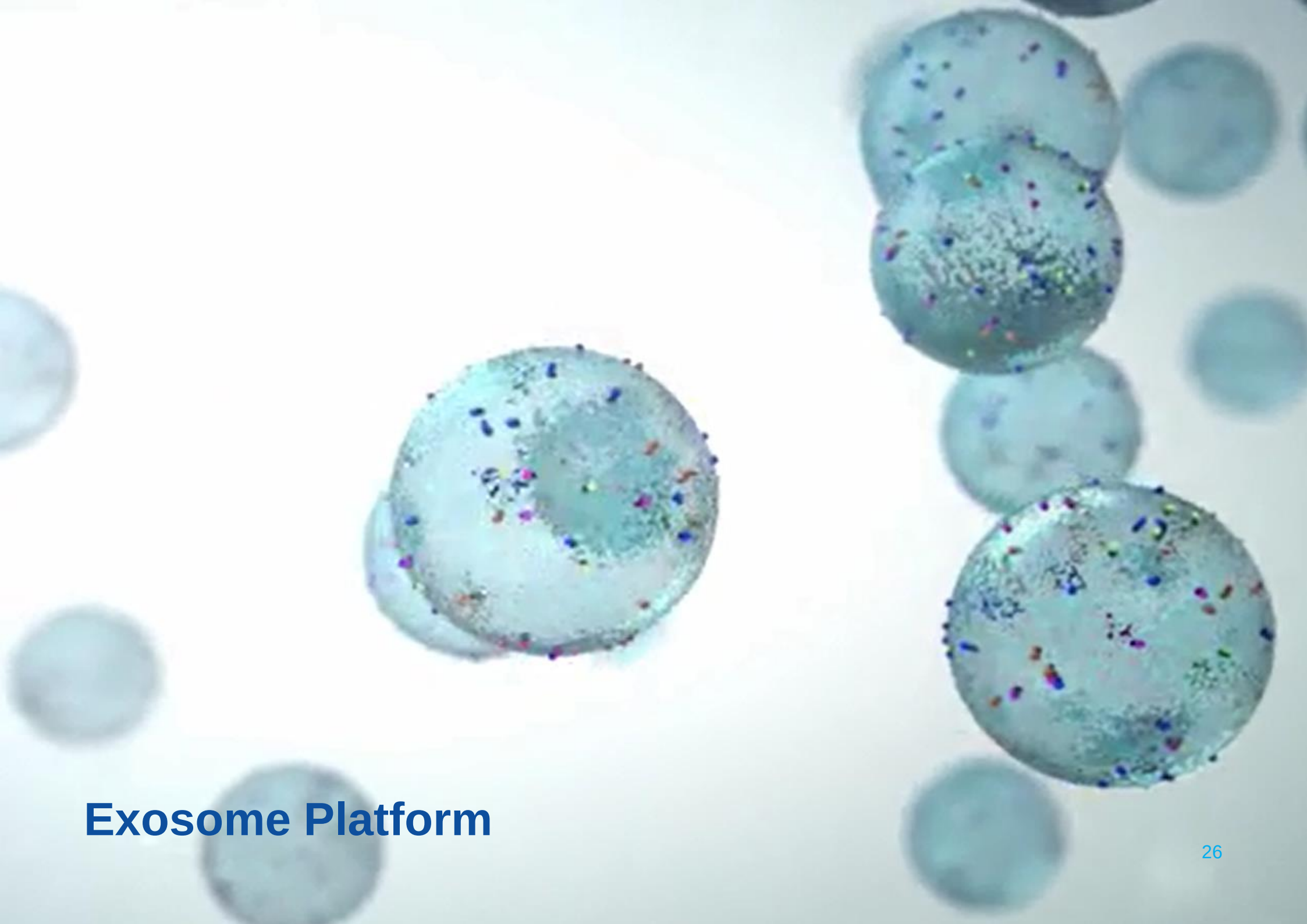
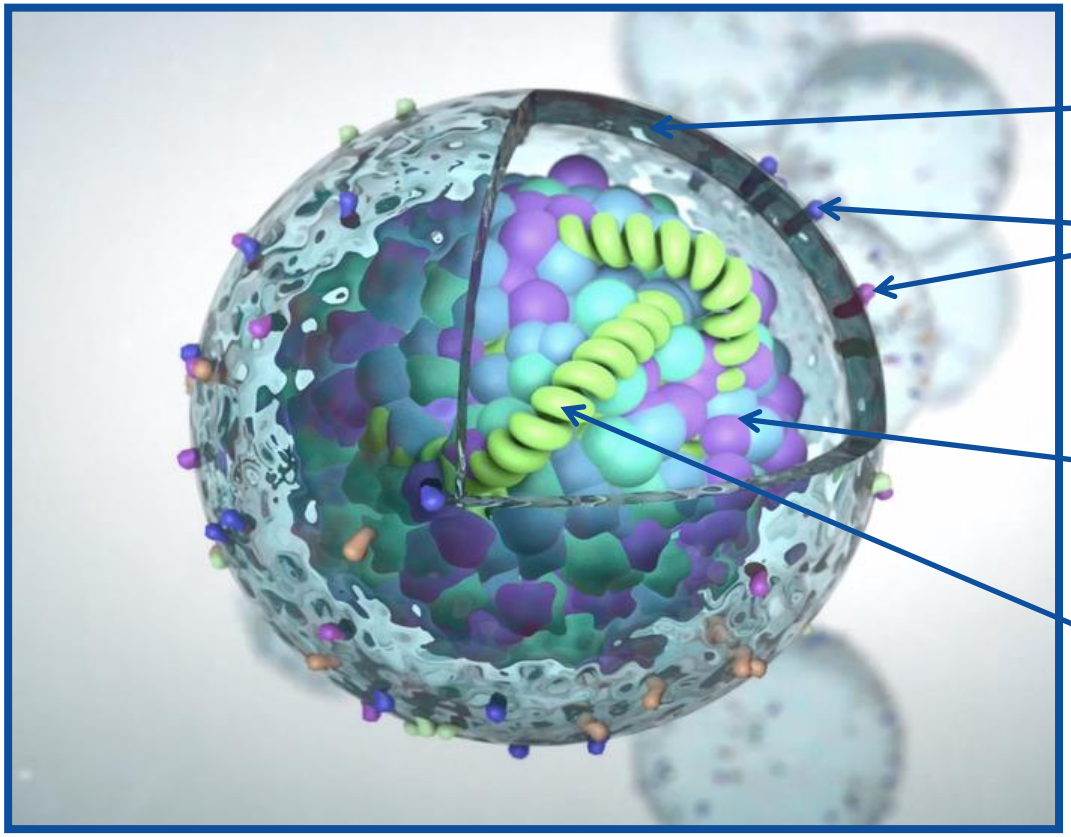


Exosome Platform

Exosome therapeutics

- Nano-scale vesicles (30-100nm) released by most cell types as a means of intercellular communication
- Considered to be a naturally-occurring liposomal delivery system
- Contain and transport bio-active lipids, proteins and nucleic acids



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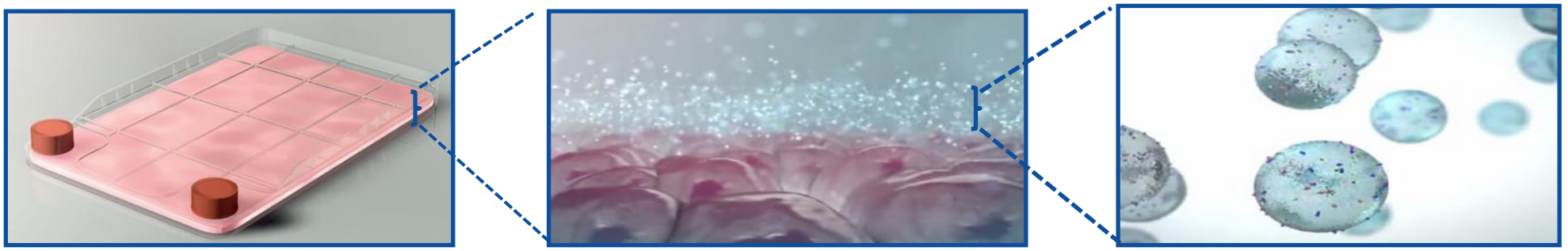
Three distinct applications for CTX-derived exosomes

- Base platform can be rapidly modified using different approaches to produce alternative products for specific applications:

Endogenous CTX Exosomes | **Bespoke CTX Exosomes** | **CTX Exosomes Delivery System**



Culture Conditions

- Modification of e.g. growth / environmental conditions tailored to specific effects and/or targets

Modification of Producer Cells

- Directed expression through genetic modification for specific trafficking of desirable exosome cargoes

Extracted exosomes

- Post-production loading of exogenous cargoes, e.g. siRNAs, proteins, small-molecule inhibitors

ReNeuron

A global leader in stem cell-derived exosome manufacture

- Exosome platform established at ReNeuron in 2011
- Significant IP portfolio established
- Qualified, scalable GMP process
- Proprietary clinical-grade producer cell line (CTX), giving high yields
- Stable and consistent product
- Established analytics
- Broad anti-cancer properties identified pre-clinically in lead candidate (ExoPr0)
  - Initial clinical trial planned for 2019 in a solid tumor indication

Future clinical milestones by program

CTX for stroke disability

- H1 2018 – Phase IIb commencement
- H2 2019 – Phase IIb data

hRPC for retinitis pigmentosa

- H1 2018 – Phase IIb commencement
- H2 2018 – Phase I/II longer-term data
- H1 2020 – Phase IIb data

hRPC for cone-rod dystrophy

- H2 2018 – Phase II commencement
- H2 2020 – Phase II data

Exosomes for cancer (solid tumors)

- H1 2019 – Phase I commencement
- 2020 – Phase I data

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