



# CORPORATE PRESENTATION

January 2021

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# RENEURON TEAM AND KEY CLINICAL ADVISERS



**Olav Hellebø**

Chief Executive Officer

Olav has held leadership roles internationally at big pharma companies, including Novartis and Schering Plough, and biotechs including Clavis Pharma ASA. Product launches include the TNF-blocker Cimzia whilst at specialty biopharma business UCB



**Michael Hunt ACA**

Chief Financial Officer

Michael qualified at Ernst & Young after which he joined Bunzl plc before focusing on healthcare at Biocompatibles International plc and then ReNeuron. He sits on the board of the US-based Alliance for Regenerative Medicine and other industry bodies



**Dr. Rick Beckman**

Chief Medical Officer

After a career as an ophthalmologist in academics, then private practice, Rick moved into leadership roles at large companies including Allergan, Alcon and BD. He then moved on to serve as CMO at ophthalmology-focused biotechs including Neurotech, Ophthotech, and Clearside.



**Dr. Tim Corn**

Chairman



ReNeuron



**Dr. Mike Owen**

Non-executive Director



GlaxoSmithKline



**Sir Chris Evans**

Non-executive Director



**Mark Evans**

Non-executive Director



## Clinical Advisors

### Dr Jason Comander

Associate Director of the Inherited Retinal Disorders Service at Massachusetts Eye and Ear Infirmary and Assistant Professor of Ophthalmology at Harvard Medical School



### Prof. Robert MacLaren

Professor of Ophthalmology, University of Oxford, directs research into new treatments for blindness. Co-founded Nighstar Therapeutics, which was acquired by Biogen.



### Dr Timothy Stout

Chair of the Ophthalmology Department and Director of the Cullen Eye Institute at Baylor College of Medicine.



### Dr Jordi Monés

Macula and Vitreoretinal Specialist and Researcher. Director of the Institut de la Màcula and the Director, Principal Investigator and one of the founder governors of the Barcelona Macula Foundation: Research for Vision.



### Dr Karl Csaky

T. Boone Pickens Director, Molecular Ophthalmology Laboratory and Clinical Center of Innovation for Macular Degeneration.



# RENEURON: HIGHLIGHTS



**Leading clinical stage cell therapy company with presence in the UK and US**

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**Proprietary allogeneic retinal and neural stem cell therapy platforms**

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**Lead programme an Orphan Drug treatment with Fast Track Designation targeting retinitis pigmentosa (RP) – positive early Phase 2a clinical data with study ongoing**

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**Planning to commence pivotal RP clinical trial in H2 2022, with top-line data targeted for 2024, ahead of market approval application**

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**Proprietary exosome programme – collaborations ongoing with pharma & biotech, with further collaborations anticipated**

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**Well-funded following recent £17.5m capital raise. Strong newsflow expected in the next 12 months, including extended RP Phase 2a clinical data read-outs and exosome pre-clinical proof-of-concept data**

# PROPRIETARY PLATFORM TECHNOLOGIES



## hRPC

Human Retinal Progenitor Stem Cells with sub-retinal delivery enabling engraftment

Cryopreserved formulation allows global ship-and-store

Positive early Phase 2a data in ongoing retinitis pigmentosa study

Partnered with Fosun Pharma for China



## Exosome Platform

High-yielding 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. 3 pharma collaborations ongoing



## iPSC Platform

CTX-based induced pluripotent stem cell platform

Neural stem cells engineered into other forms of stem cells while preserving the immortalisation

Potential to create allogeneic CAR-T cell therapies and pancreatic islet cells



## CTX Cells

Immortalised neural progenitor stem cell line

Positive clinical data in stroke disability. Potential in Huntington's disease, TBI and other indications

Out-licensing strategy  
Partnered with Fosun Pharma for China

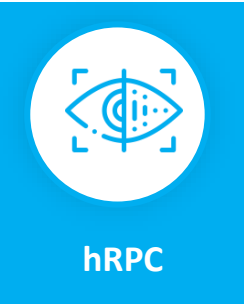
Example  
Peers

# INTERNAL RESEARCH AND DEVELOPMENT PIPELINE



Programme	Indication	Pre-clinical	Phase 1	Phase 2	Next Milestones
Human Retinal Progenitor Cells	Retinitis Pigmentosa				<ul style="list-style-type: none"><li>• Further data read-outs from expanded Phase 2a study over next twelve months</li><li>• Pivotal trial to commence in H2 2022, subject to Phase 2a data</li></ul>
Exosome platform	Neurodegeneration, Oncology, Vaccines (e.g. COVID-19)				<ul style="list-style-type: none"><li>• Proof of concept data from current research collaborations expected in H1 2021</li><li>• Additional collaborations expected over the next 12 months</li></ul>
iPSC platform	Oncology, Diabetes				<ul style="list-style-type: none"><li>• Validation of technology and publication of pre-clinical proof-of-concept data</li></ul>
CTX cell line	Stroke Disability				<ul style="list-style-type: none"><li>• Currently partnered in China with <b>FOSUN</b> 复星</li><li>• Open for partnerships outside China</li></ul>

# MATERIAL VALUE INFLECTION POINTS TARGETED OVER NEXT 12 MONTHS AND BEYOND<sup>(1)</sup>



✓ RP Phase 2a extended study - first subject treated in US

RP Phase 2a initial study – 12 month data on all subjects

RP Phase 2a extended study - first 'non-US' subject treated

RP Phase 2a extended study - last subject treated



RP Phase 2a extended study - 3 month data



AMERICAN ACADEMY OF OPHTHALMOLOGY\*

RP Phase 2a extended study - 6 month data

FDA meeting re pivotal study design

Potential out-licensing deals on full Phase 2a data

RP pivotal study commences

RP pivotal study top-line data

Q3 2020

Q4 2020

Q1 2021

Q2 2021

Q3 2021

Q4 2021

H1 2022

H2 2022

2023

2024



Further pharma collaborations

POC data for delivery of siRNA by CTX-derived exosomes

POC data for delivery of functional proteins by CTX-derived exosomes



INTERNATIONAL SOCIETY for EXTRACELLULAR VESICLES

Potential out-licensing deals on POC data



**Lead  
Programme**  
hRPC in retinitis  
pigmentosa

# RETINITIS PIGMENTOSA: AN UNMET NEED



RP is an inherited, degenerative eye disease<sup>1,2,3</sup>

- Incidence of 1:4,000 in U.S. and worldwide



>100 genes identified containing mutations leading to RP<sup>4</sup>



Treatment available only for patients with a single gene defect (RPE65)



Patients with all other types of RP (c98% of patients<sup>5</sup>) have declining vision eventually leading to severe visual disability in most

**Therapeutic benefit of hRPC approach not dependent on genetic cause**

<sup>1</sup> Hamel (2006) Orphanet J Rare Disease 1, 40;

<sup>2</sup> [https://nei.nih.gov/health/pigmentosa/pigmentosa\\_facts](https://nei.nih.gov/health/pigmentosa/pigmentosa_facts);

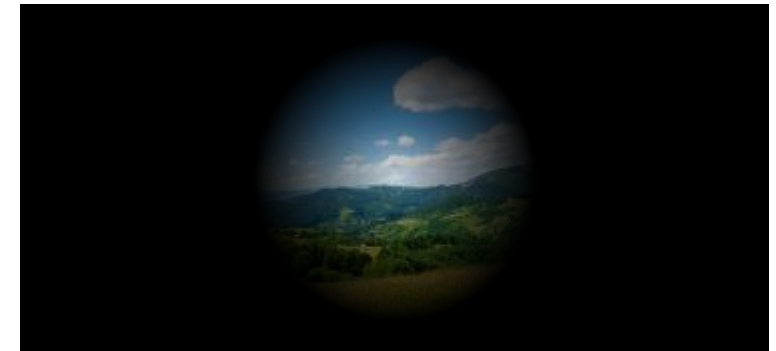
<sup>3</sup> NORD

<sup>4</sup> <https://www.genome.gov/13514348/learning-about-retinitis-pigmentosa/>

<sup>5</sup> [www.nice.org.uk/guidance/hst11/chapter/2-The-condition](http://www.nice.org.uk/guidance/hst11/chapter/2-The-condition)



**Normal View**



**View with Retinitis Pigmentosa**

# 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 potential across a range of eye diseases, initially targeting inherited retinal degenerative diseases

Orphan Drug Designation in EU and US in RP and FDA Fast Track Designation



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

Collaborations with Schepens Eye Research Institute (Harvard) and University College London

Proprietary technology enabled development of GMP manufacturing process

Cryopreserved formulation provides nine-month shelf life and enables local treatment worldwide



**High commercial potential**

RP is a large orphan market.  
Attractive pricing precedent set by Luxturna

Mechanism of action independent of genetic cause

Commercially viable formulation

# CLINICAL DEVELOPMENT

Phases 1 and 2a

## Phase 1

Single ascending dose in subjects with established RP

- Subjects with very poor visual potential
- Four cohorts, three subjects each (n=12)
- Formulation changed from fresh to cryopreserved cells

**Established safety in cryopreserved formulation**

## Phase 2a

10 subjects with established RP

- Patients with better visual potential
- 1m cell dose

Primary endpoint

- Safety

Secondary measures

- Visual acuity, visual field, retinal sensitivity and retinal structure

**Established efficacy signal, continued safety**

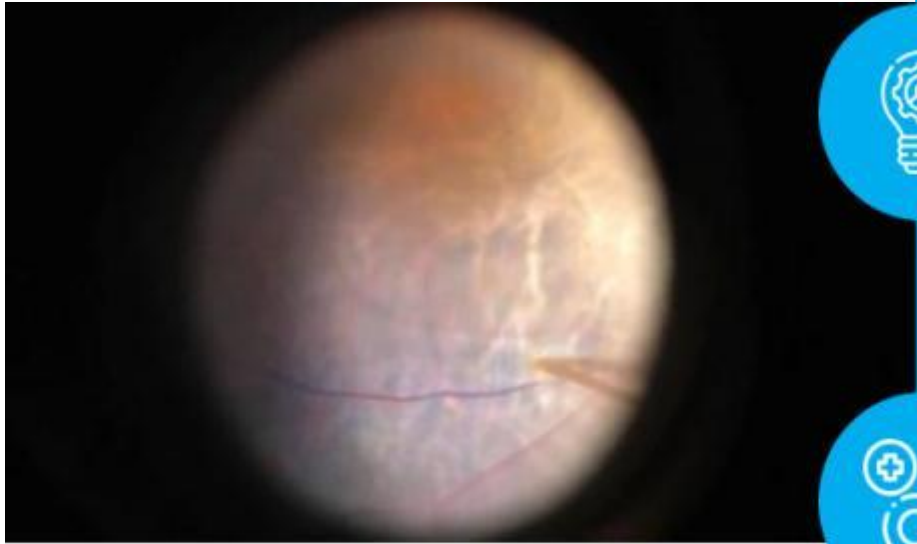
## Existing Clinical Sites

Massachusetts Eye & Ear Infirmary, Boston

Retinal Research Institute, Phoenix

# SURGICAL TECHNIQUE

## Sub-retinal Injection



**Well established technique used commercially with Luxturna®**



**Allows correct anatomic placement of cells for integration into the retina**

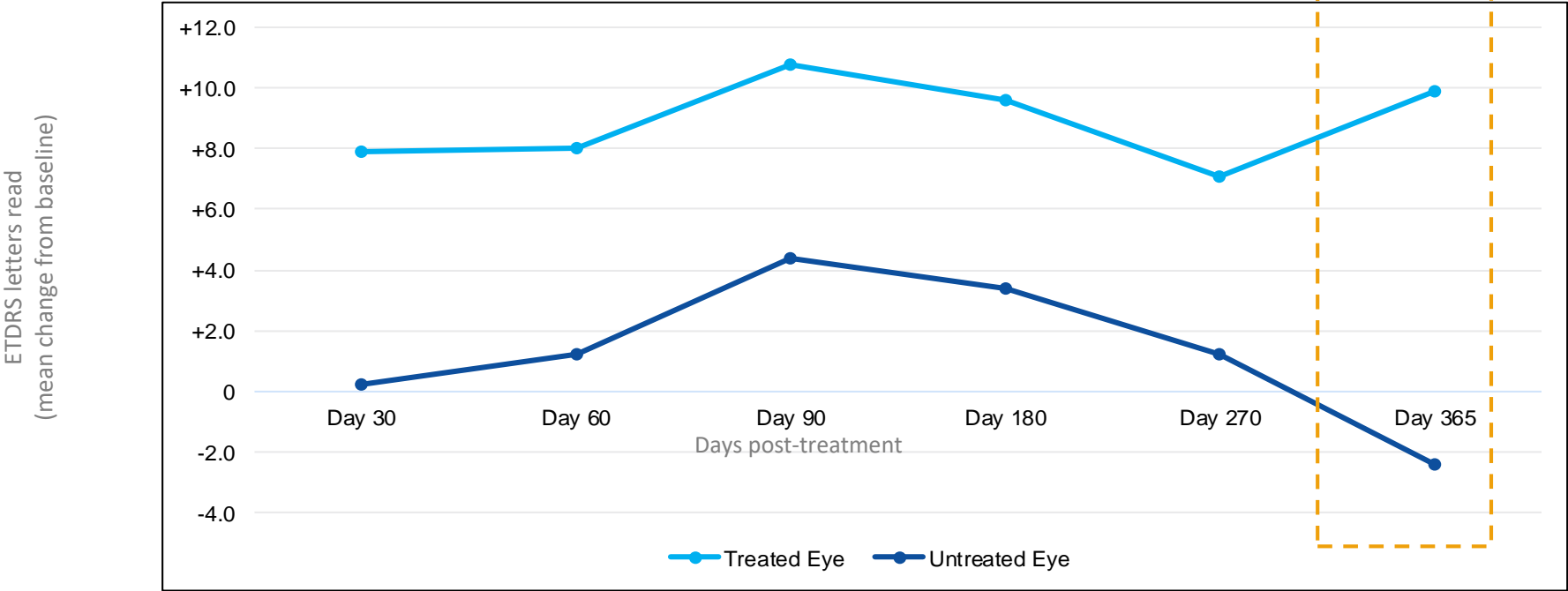
- Can serve as a depot for prolonged production of trophic factors
- Can allow for differentiation into photoreceptors with proper connections to other cells needed for vision

# PHASE 2a EFFICACY RESULTS

Mean changes in ETDRS letters read (treated eye vs untreated eye)



	Day 30 (n=9)	Day 60 (n=9)	Day 90 (n=9)	Day 180 (n=9)	Day 270 (n=8)	Day 365 (n=7)
Treated Eye	+7.9	+8.0	+10.8	+9.6	+7.1	+9.9
Untreated Eye	+0.2	+1.2	+4.4	+3.4	+1.2	-2.4
Difference	+7.7	+6.8	+6.4	+6.2	+5.9	+12.3



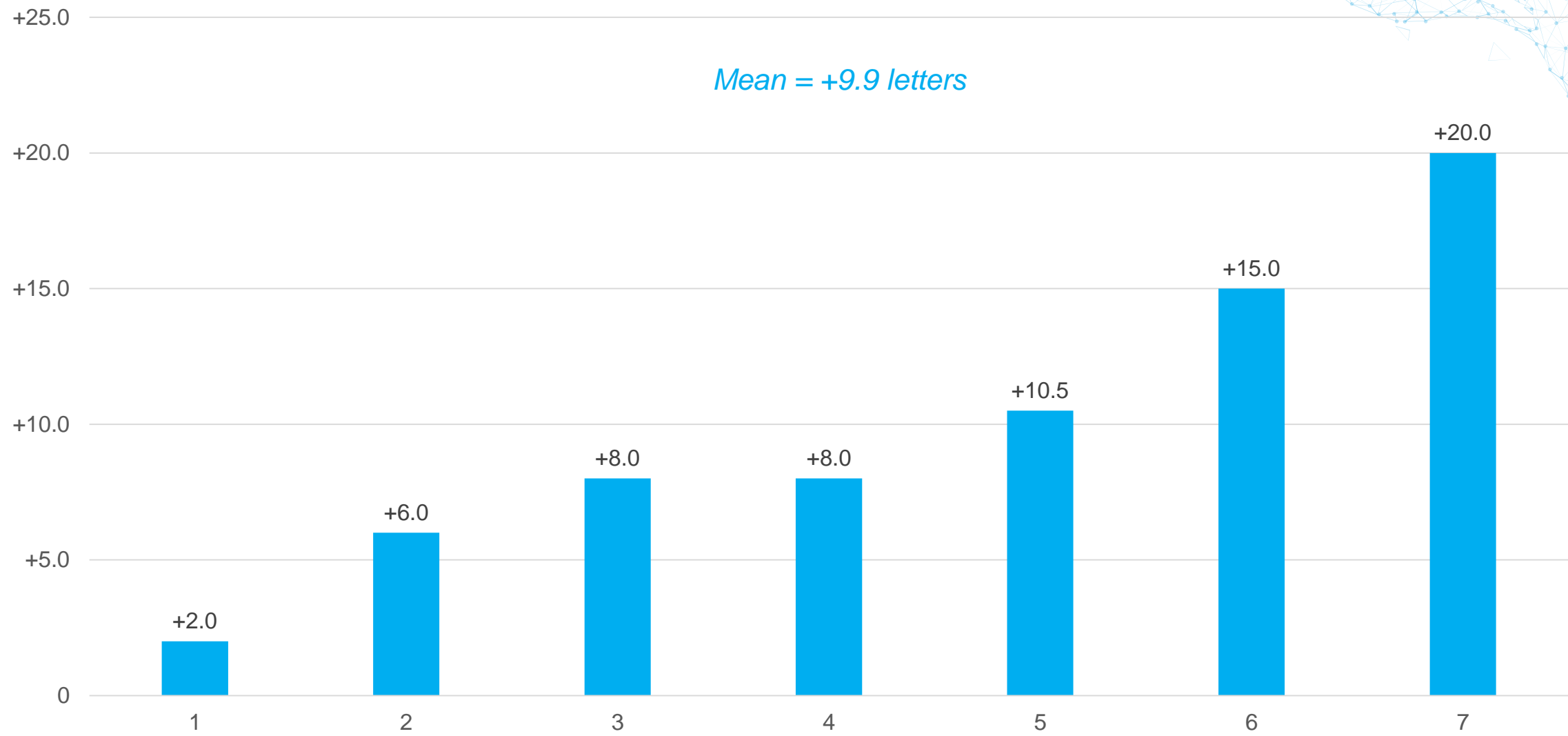
**Additional Notes:**

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

\*\*Two patients have so far been assessed at 18 months. One patient has gained 17 letters from baseline in the study eye and one letter in the non-study eye. The second patient has gained six letters from baseline in the study eye and 22 letters in the non-study eye.

# INDIVIDUAL PATIENT IMPROVEMENTS AT 12 MONTHS

ETDRS change from baseline 12 months post treatment (n=7)



# CLINICAL DEVELOPMENT: PHASE 2A EXTENSION

Modifications to better hone efficacy signal



## Phase 2a Extension

### 9 additional subjects with established RP

- Dose escalation: from 1m to 2m cells
- Require ability to perform micro-perimetry – should allow retinal sensitivity to be an indicator of efficacy
- Additional baseline VA's to ensure patient reliability
- Modified surgical technique to target bleb placement: injection sites chosen to avoid areas of viable retina

### Primary endpoint

- Safety

### Secondary measures

- Visual acuity, micro-perimetry, visual field, retinal sensitivity and retinal structure

### Additional Sites Added

Oxford Eye Hospital, Oxford, UK  
(Prof Robert MacLaren)

Two further sites planned,  
one in Europe and one in the US

# RETINITIS PIGMENTOSA: THERAPY LANDSCAPE



Company	Technology	Stage	Comment
<b>ReNeuron</b> (AIM, market cap: £61m*)	Cell therapy	Phase 1/2a	Cryopreserved formulation
<b>jCyte Inc</b> (US, private)	Cell therapy	Phase 2b	Not cryopreserved; used to date in California and Massachusetts
<b>Spark Therapeutics</b> (acquired by Roche in 2019 for \$4.3bn)	Gene therapy	Approved and marketed, Luxturna for RPE65	Addresses only about 2%** of RP patients
<b>Nightstar Therapeutics</b> (acquired by Biogen in 2019 for \$800 million)	Gene therapy	Phase 2/3	UK company co-founded by Prof Robert MacLaren
<b>MeiraGTx</b> (Nasdaq, market cap \$695m*)	Gene therapy	Phase 1/2	-
<b>AGTC</b> (Nasdaq, market cap \$114m*)	Gene therapy	Phase 1/2	-

\* Market capitalisations as at 7 January 2021

\*\* [www.nice.org.uk/guidance/hst11/chapter/2-The-condition](http://www.nice.org.uk/guidance/hst11/chapter/2-The-condition)

# RETINAL PLATFORM NEXT STEPS

Material newsflow and value inflection points over the next 15 months and beyond



## Collect long term data in normal dose subjects

- Most patient visits restarted post-Covid restrictions
- All 22 patients will be followed to at least 24 months post treatment

## Recruit high dose expansion study

- First patient treated September 2020
- Enhancements in patient selection, dose, surgical technique and efficacy assessments



## Further efficacy data to be presented at retinal conferences over the coming twelve months

- AAO/ASRS/ARVO are the key conferences in ophthalmology
- 3 months data on all 9 Phase 2a extension patients to be presented at ASRS in July



## A single further clinical trial is planned before filing for marketing authorisation

- Randomised, not placebo controlled
- Three patient groups (high dose, low dose and observational cohort)



Assess other indications alongside RP (e.g. Cone Rod Dystrophy)

Partnering strategy to be based on full Phase 2a data

The background features a stylized illustration of several cells. Each cell has a translucent green outer membrane and a bright purple, textured nucleus. Inside the cells, there are smaller, colorful vesicles in shades of red, blue, and green. In the upper right corner, there is a blue wireframe network diagram consisting of interconnected nodes and lines, resembling a molecular or neural structure.

# Exosome platform

# EXOSOMES: BIOLOGICAL NANOPARTICLES



Nano-scale vesicles released by most cell types as a means of intercellular communication



Naturally occurring liposomal delivery system

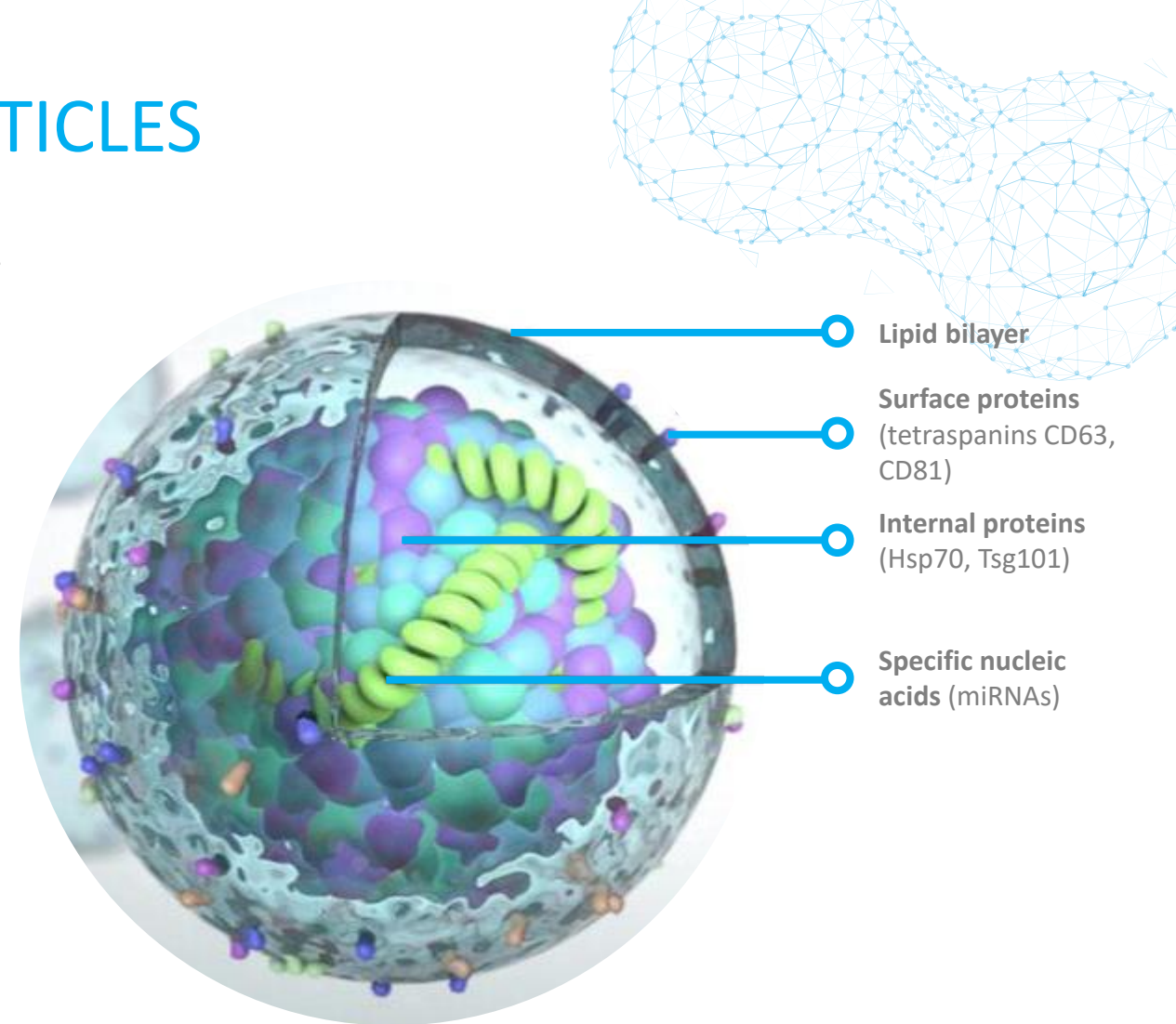


Contain and transport bio-active lipids, proteins and nucleic acids



Potential as a drug delivery vehicle and as a therapeutic

- Current focus is on drug delivery
- Collaborations in place and further ones under negotiation



**Increasing industry interest in and commercial value of exosome deals**

# ADVANTAGES OF RENEURON'S EXOSOME TECHNOLOGY



Favourable distribution  
across the blood  
brain barrier



Proven ability  
to load miRNA  
and proteins



Stable, consistent,  
high-yield,  
clinical-grade product



Fully qualified xeno-free,  
optimised, scalable  
GMP process



Established  
analytics



Modifiable to carry siRNA/mRNA,  
CRISPR/Cas9 proteins,  
small-molecule inhibitors



Engineered to target  
particular tissues

# PROOF OF CONCEPT DATA EXPECTED IN H1 2021



**hNSC-Exosome Platform** (for delivery across the blood brain barrier)



## **Significant research collaborations ongoing**

- Three current undisclosed industry leading partners
- Focused on delivery of siRNA and mRNA
- Goal to deliver in-vivo proof of concept data
- Trials financed by partners

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**Further research collaborations under review, focused on delivery of other novel therapeutics including antibodies**

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**ReNeuron owns equal co-development rights to new therapeutic modalities**



# Summary

# VALUE REALISATION

## Recent deals in cell therapy for retinitis pigmentosa and exosomes research

### Santen deal based on Phase 2 data in RP\*



- jCyte Inc signed an ex-US licensing deal for its jCell product in May 2020 with Santen Pharmaceutical
- jCell is a Phase 2b retinal progenitor cell suspension for RP

### Deal terms

- \$50m upfront
- \$12m convertible note
- \$190m of milestones
- Double-digit royalties

### Exosome deals based on pre-clinical POC data\*



Total: \$72.5m  
neuro-muscular  
targets  
  
Codiak listed on  
Nasdaq in October  
2020, raising \$83m



Upfront: \$20m  
Total: \$1,230m  
neurological  
targets



Total: \$882m  
rare diseases



Upfront: \$56m  
Total \$1,076m  
cancer

# SUMMARY



**Major value creation opportunities in the coming 12 months for hRPC**



**New data from expanded Phase 2a study of hRPC in retinitis pigmentosa to be presented at major conferences next year**



**Competitor data support ReNeuron's approach in RP**



**Potential of cell therapy in ophthalmology underlined by recent JCyte/Santen Pharmaceutical licensing deal**  
\$252m in upfronts and milestones for ex-US rights plus double digit royalties



**Exosome programme being advanced through partners while retaining rights**



**High level of industry interest in exosomes reflected in recent licensing deals**  
Deals totaling more than \$2bn in upfronts and milestones based on proof of concept data

# ReNeuron

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