

# ReNeuron

## 2022 PRELIMINARY RESULTS

*THE CUSTOMISABLE EXOSOMES DELIVERY PLATFORM  
OPTIMISED FOR SPECIFIC DRUG DELIVERY NEEDS*

4 July 2022

Iain Ross - Interim Executive Chairman

Catherine Isted - Chief Financial Officer

Dr. Randolph Corteling - Head of Research



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# A LEADER IN STEM CELL-BASED EXOSOME TECHNOLOGIES

## ◎ OUR SCIENCE

- Exosome delivery platform with a range of seven proprietary stem cell lines that can be customised and optimised for a particular payload and target

## ◎ OUR PEOPLE

- Highly skilled and passionate team of 35 professionals
- Deep knowledge across stem cell and stem cell-based exosomes research, CMC and regulatory with proven track record working with MHRA and FDA

## ◎ OUR KNOW-HOW

- CSO/Head of research >30 yrs experience in stem cell and stem cell-based exosomes with extensive knowledge of the biology of the field
- CMC team: experts in process/analytical development, manufacturing and technology transfer

## ◎ OUR PATENT ESTATE

- Third largest exosomes patent estate globally

## ◎ OUR PARTNERSHIPS AND PIPELINE

- Collaborations ongoing with Big pharma, biotech and academic institutions
- Exciting pre-clinical data delivery of a therapeutic protein to the brain



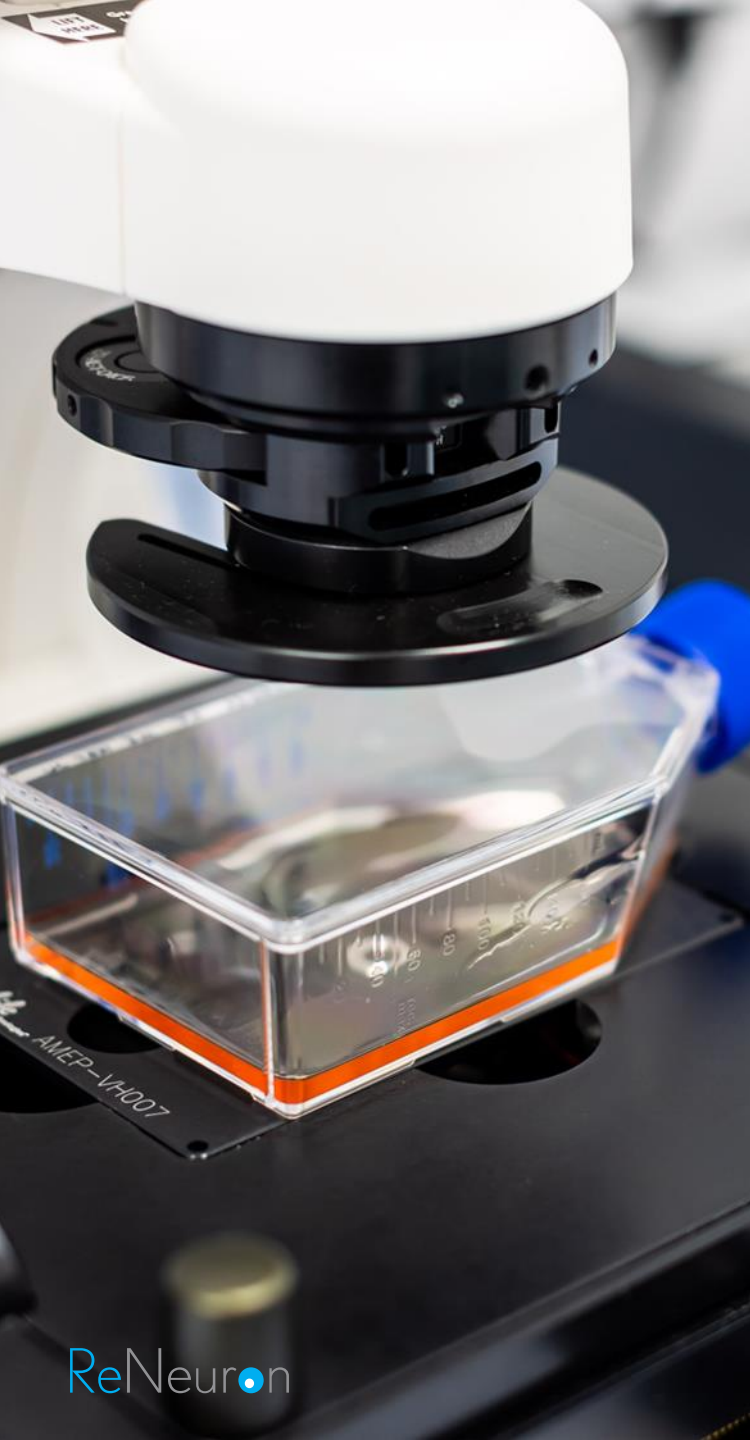
## ORGANISATIONAL HIGHLIGHTS

- In July 2021, Iain Ross was appointed as Non-Executive Chairman and following Olav Hellebø's resignation as CEO in February 2022, Mr Ross became Interim Executive Chairman until the appointment of a new CEO
- In October 2021, Catherine Isted, ACMA, joined the Board, replacing Michael Hunt as Chief Financial Officer
- Additionally, during the period, the Board was reconfigured with former Chairman, Dr Tim Corn and Non-Executive directors Mark Evans and Sir Chris Evans OBE stepping down. Two new independent Non-Executive directors, Barbara Staehelin and Martin Walton, have joined the Board
- Additionally, Dr Stefano Pluchino was appointed as Chief Scientific Officer and Dr Randolph Corteling as Head of Research, greatly increasing the Group's exosomes expertise





# Operational & financial highlights

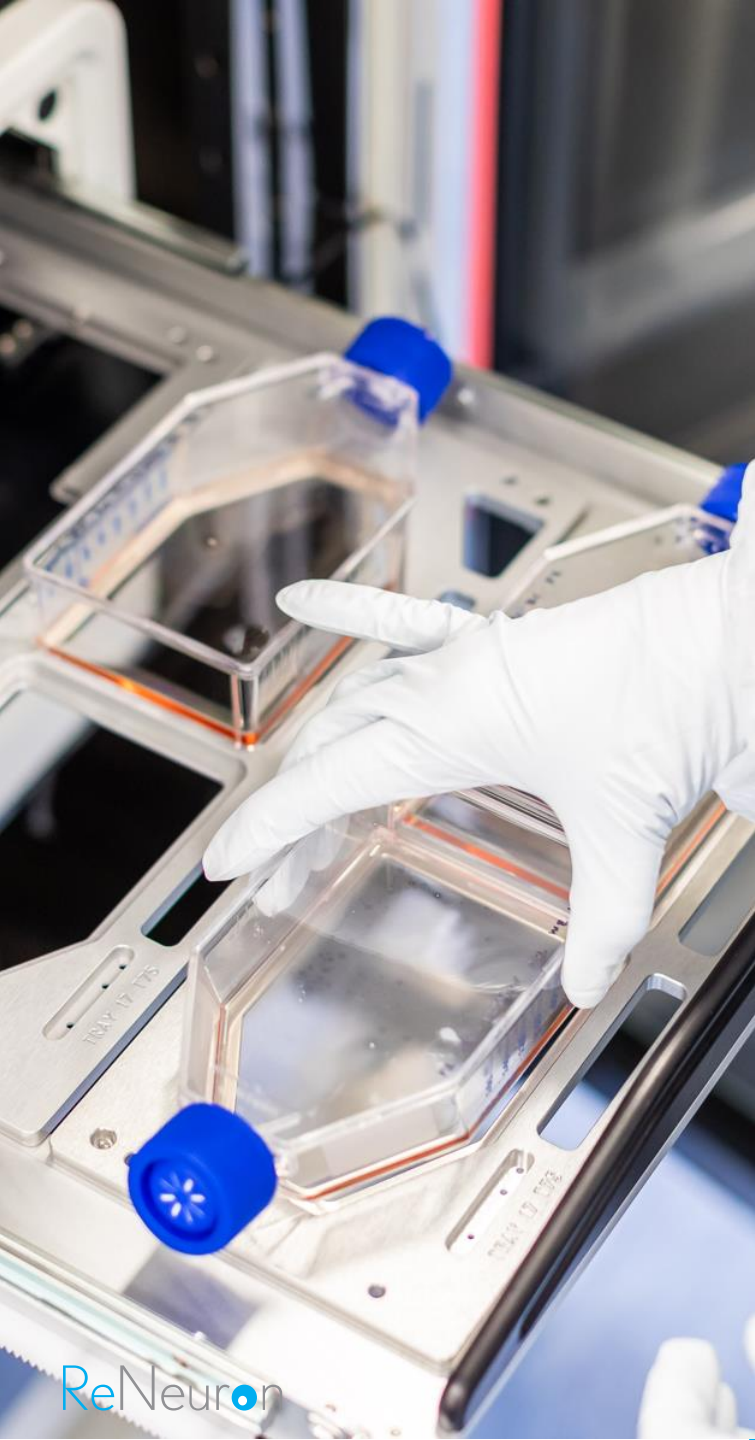


## FINANCIAL HIGHLIGHTS



- Revenue for the period of £403,000 relating to research and collaboration activities and royalty income (2021: £257,000)
- Loss for the period of £9.7 million (2021: loss of £11.3 million) reflecting lower costs
- Reduced costs incurred in the period of £11.6 million (2021: £13.2 million) primarily driven by lower R&D spend following the strategic decision to curtail clinical development activities
- Increased net cash used in operating activities of £7.4 million (2021: £6.1 million) with the prior year benefitting from the receipt of two R&D tax credits relating to financial years 2019 and 2020
- Cash, cash equivalents and bank deposits at 31 March 2022 of £14.5 million (31 March 2021: £22.2 million)
- Cash runway until at least mid-calendar year 2023





## OPERATIONAL HIGHLIGHTS

### ○ hRPC

- In January 2022, the Board took the decision to halt development of its RP programme as it became clear that a further phase II trial would be required
- The intention is to complete the data package and out-licence the programme to a third party

### ○ Fosun Pharma

- Fosun Pharma continues to progress development of CTX in stroke disability in China
- In January 2022 ReNeuron announced that it had signed an additional agreement, setting out the first step of the technology transfer of CTX into China
- In July 2022, a Supplemental Terms Agreement was signed. As a result, the Group expects to receive approximately £1 million over the next 24 months with up to a further £5 million over the medium to long term

### ○ Exosome and iPSC Platforms

- ReNeuron is now fully focused on its proprietary customisable exosomes platform
- Seven discovery-stage collaborations proceeding with global pharma, biotech and academic institutions, with the Group committed to adding new partnerships
- In October, pre-clinical data announced showing that ReNeuron's exosomes can effectively deliver therapeutic proteins to the brain to potentially treat neurological diseases
- Two iPSC collaborations signed with UCL for generation of CAR-T/CAR-NK cells and also production of Schwann cells for potential use in peripheral nerve damage repair





# Exosome and iPSC Technology Platforms



# WHY STEM CELL-BASED EXOSOMES?



## ⑥ A customisable, targeted delivery platform for complex drug modalities

- Proven ability to carry and deliver a variety of cargos including proteins and nucleic acids
- Can be genetically engineered to target specific tissues or cells
- Potential to deliver more than one bio-active cargo simultaneously
- Biological nanoparticles for intercellular communication - evades immune detection

## ⑥ Specific to ReNeuron's Platform

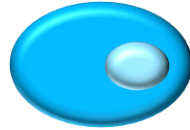
- Seven proprietary conditionally immortalised exosome producer stem cell lines
- Our catalogue of proprietary stem cells from neural and non-neural tissue differentiates us from many others in the field, we believe leading to a greater chance for success
- Years of experience and knowledge in the manufacture of consistent stem cell banks to GMP – 2 INDs
- Early preclinical animal data with our modified cortex stem cell derived exosomes delivering BDNF demonstrates greater efficacy compared to BDNF alone when targeting specific regions of the brain when administered intrathecally

# RENEURON'S USP: THE PORTFOLIO ADVANTAGE

THE CUSTOMISABLE STEM CELL EXOSOME DELIVERY PLATFORM, OPTIMISED FOR SPECIFIC DRUG DELIVERY NEEDS

## Standard Approach

Single cell line



Engineering

Exosome candidate



## Competitors – Single cell line approach

- Single cell line, single outcome
- 'One size fits all'

# ReNeuron

Exosome candidates

## Four Proprietary Neural Stem Cell lines

(Cortex (CTX), Striatum, Hippocampus, Ventral Mesencephalon)

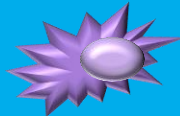


Engineering



## Three additional proprietary Stem Cell lines

(Retinal, liver, pancreatic)

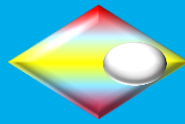


Engineering



CTX iPSC\*

Any Stem Cell



Engineering



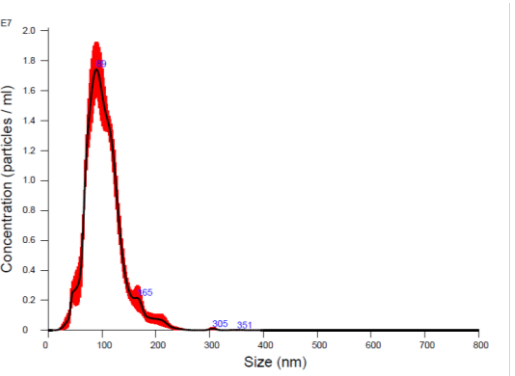
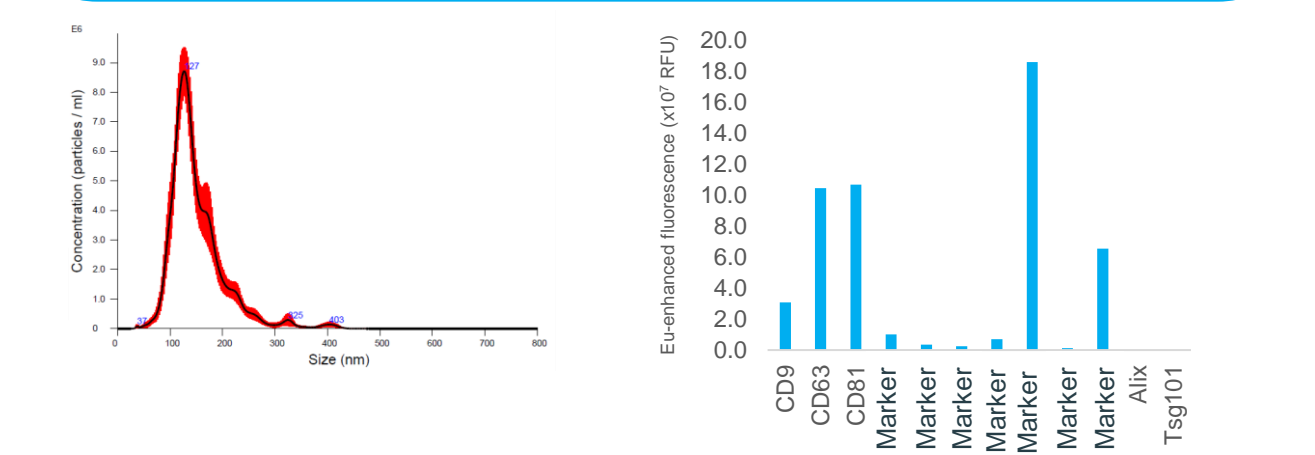
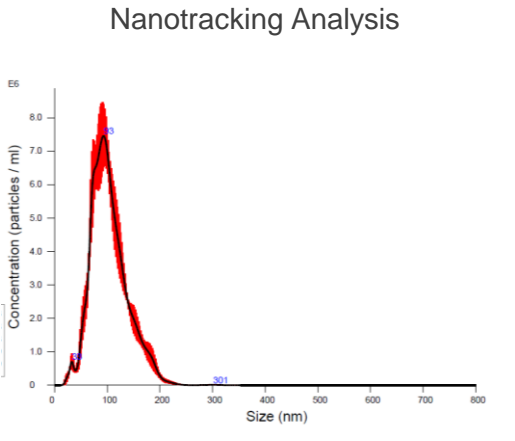
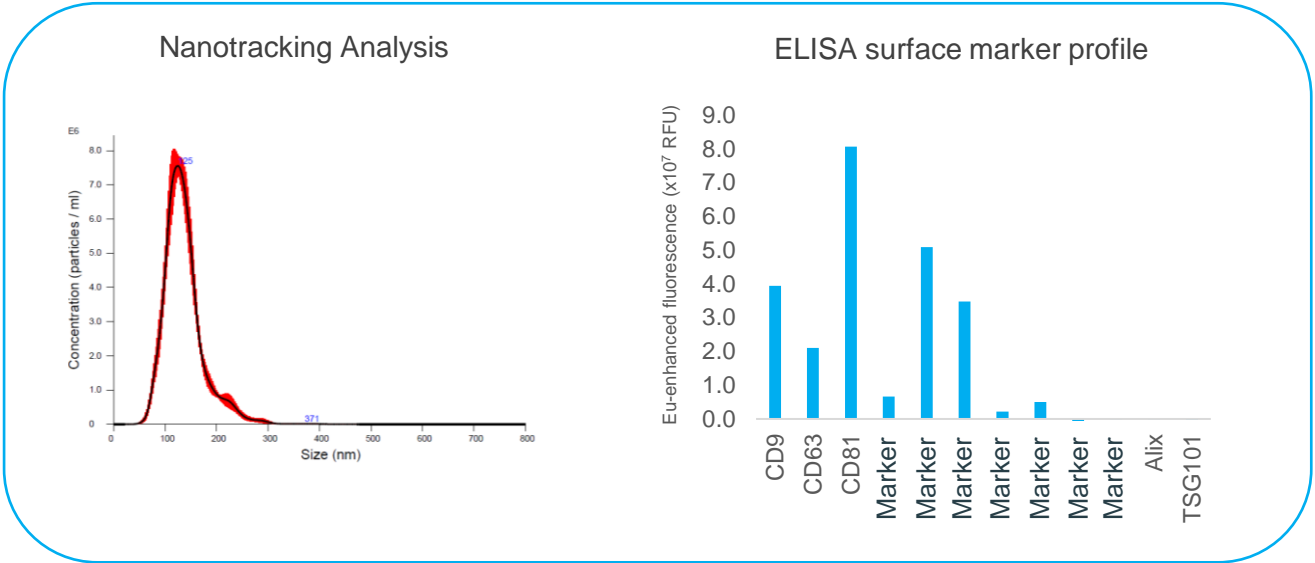
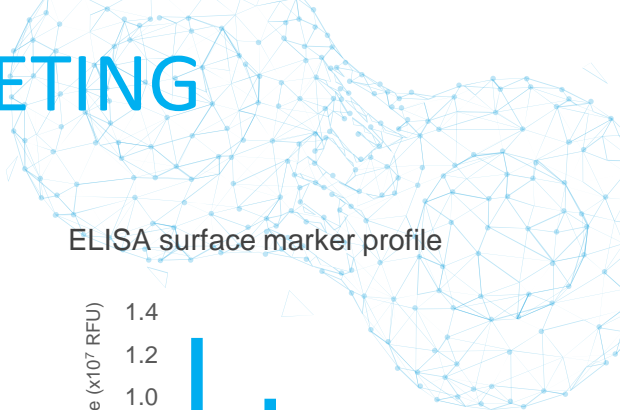
## ReNeuron – Portfolio of stem cell derived exosomes

- Exosomes have functional properties based on parent stem cell
- ReNeuron's seven conditionally immortalised stem cell lines allows exosomes to be customised and optimised for a specific payload and targets

## Producer stem cell line optimised for:

- Engineering efficiency
- Tissue targeting (on and off-target effects)
- Delivery (cytoplasm / nuclear)

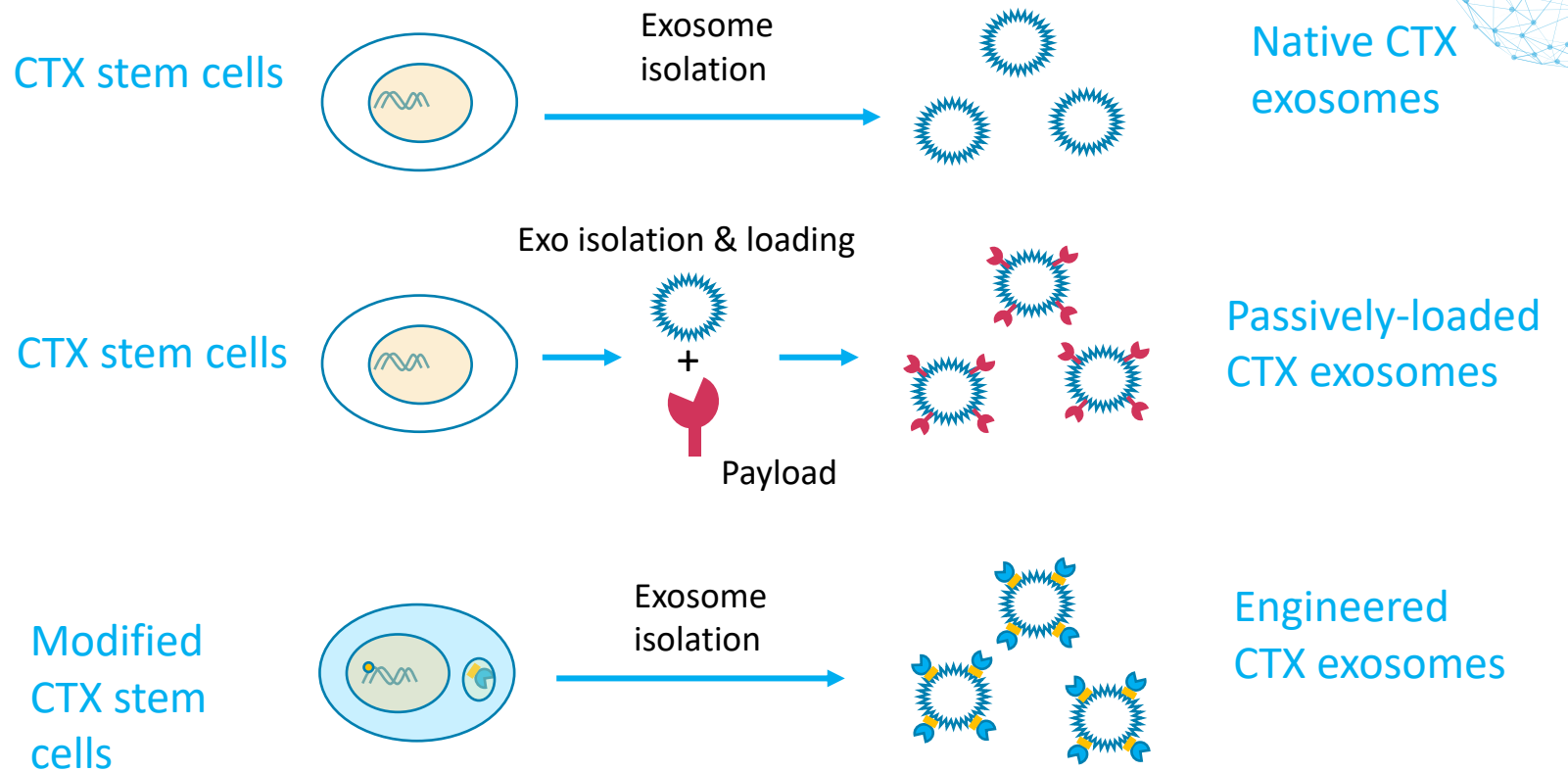
# DISTINCT CELL LINES ENABLING GREATER TISSUE TARGETING



Four of ReNeuron’s different producer cell lines, 4 different surface marker profiles

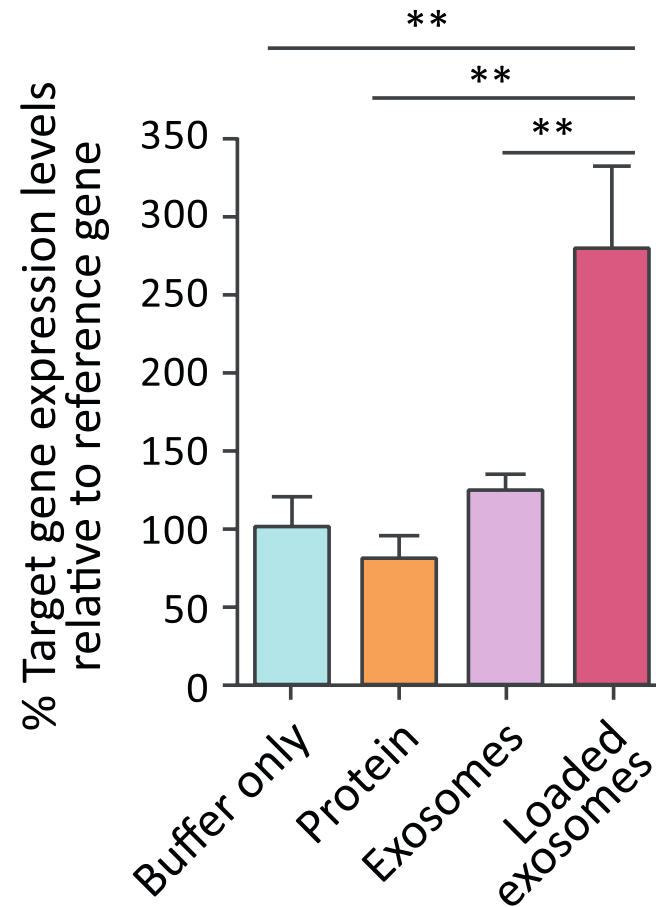


# ABILITY TO PRODUCE NATIVE, PASSIVELY-LOADED AND ENGINEERED EXOSOMES



Providing an expanded range of exosome products

# DELIVERY OF THERAPEUTIC PROTEINS WITH RENEURON'S EXOSOMES



**We believe this is the first time that a potentially therapeutic protein payload has been delivered to a specific site in the brain using exosomes\***

- Delivered by Intrathecal injection (lumbar puncture)
- Response observed only with exosomes loaded with therapeutic protein (BDNF)
- This area of the brain (the striatum) is affected in Parkinson's and Huntington's disease
- *In vivo* functional studies are ongoing

\*In a preclinical setting

# EXOSOMES PARTNER AND OWN PROGRAMME PIPELINE

## EXOSOMES COLLABORATIONS WITH PARTNERS

COLLABORATION	PAYLOAD	DISCOVERY	IN VITRO	IN VIVO POC	IN VIVO LATE STAGE
UNIVERSITY	Protein				
GLOBAL PHARMA	HDO*				
LARGE BIOTECH	siRNA				
SMALL BIOTECH	Peptide				
GLOBAL PHARMA	Plasmid				
MEDIUM BIOTECH	siRNA				
UNIVERSITY	Small molecule				

## INTERNAL PROGRAMMES

PROGRAMME	PAYLOAD	DISCOVERY	IN VITRO	IN VIVO POC	IN VIVO LATE STAGE
Exo-miR	miRNA				
EXO-GF	Growth Factor				
EXO-Cas	CRISPR gene-edit				

\*HDO: heteroduplex oligonucleotide





# INDUCED PLURIPOTENT STEM CELL (iPSC) PLATFORM

- ReNeuron's induced pluripotent stem cell (iPSC) platform technology can reprogramme proprietary neural stem cells into a pluripotent state able to differentiate into any other form of cell
- iPSCs retain the immortalisation characteristic of the stem cells from which they are derived, resulting in highly stable cell lines
- Technology has the potential to lead to “off the shelf” therapeutics
- Also has the potential to produce exosomes with tissue-specific targeting ability
- Collaborations with University College London investigating potential use of CTX-iPSC cell lines to generate CAR-T / CAR-NK cells and separately the ability to differentiate into Schwann cells for potential use in peripheral nerve damage repair



# Summary

## OUR GOALS FOR THE COMING YEAR

- **Build** a best in class end-to-end proprietary delivery technology and manufacturing platform and **continue to strengthen** our IP
- **Progress** our current partner programmes and **expand** with new named partners building a growing revenue stream
- **Undertake** further experiments and publish data proving the strength and versatility of our platform
- **Develop** our proprietary programmes focused on delivery of therapeutic proteins to the brain via ReNeuron's neural exosomes
- **Monetise** our legacy assets (CTX, hRPC)
- Further develop our **Induced Pluripotent Stem Cell** (iPSC) Platform

**Building a fully validated and sustainable proprietary 'drug delivery platform business' with strong scientific and commercial partners**



# ReNeuron

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# Appendix

# MEET THE RENEURON TEAM



**Iain Ross**  
Interim Executive Chairman

- Highly experienced board director with over 40 years' experience in the international life sciences and technology sectors
- Senior commercial roles at Sandoz, Fisons and Roche
- Former Chairman, CEO, Director roles at Celltech, Quadrant and Redx Pharma
- Current Non-Exec Chairman at Silence Therapeutics (NASDAQ:SLN)



**Catherine Isted ACMA**  
Chief Financial Officer

- c.25 years' experience in the healthcare and healthcare banking industry
- Formally part of the Financial Leadership team at Oxford Biomedica and instrumental in three capital raises totalling over £110m
- 19 years in healthcare in the city at Morgan Stanley, Nomura and Peel Hunt
- BSc in Chemistry and Chartered Accountant



**Dr Randolph Corteling**  
Head of Research

- 24 years' experience in medical research and drug discovery, spanning academia, biotechnology and the pharmaceutical industry
- Re-joined ReNeuron in Q1 2022 from Evox
- In 2007 joined ReNeuron where he established the first Exosomes programmes
- PhD in Medical and Surgical Sciences



**Suzanne Hancock**  
Head of Operations

- Suzanne joined ReNeuron in 2017 from GE Healthcare, where she spent c.12 years
- She has held a number of managerial roles leading global cross functional teams engaged in the development and delivery of new products in the Life Sciences and Cell Therapy Industry
- BSc in Applied Biological Sciences



**Prof. Stefano Pluchino**  
Chief Scientific Officer

- Appointed CSO in May 2021
- He is Reader in Regenerative Neuroimmunology and Honorary Consultant at the University of Cambridge
- Stefano is internationally recognised as a leader and pioneer in the field of regenerative neuroimmunology and Exosomes



**Shaun Stapleton**  
Head of Regulatory Affairs and Pharmacovigilance

- Joined ReNeuron in 2015 from Voisin Consulting Life Sciences where he was a Director and Vice President of Regulatory Science.
- Prior regulatory affairs positions at Eli Lilly and Boehringer Ingelheim, beginning his career in research with Imperial Cancer Research Fund
- BSc in Biochemistry



# CORPORATE AND MARKET INFORMATION



## Company Facts

- Listed on AIM (RENE)
- Cash position (31 Mar 22): £14.5m
- Cash runway guidance: Mid-calendar 2023
- At 30 June 2022
  - Share price: 27.75p
  - Market Capitalisation: £16 million (\$19 million)

## Major Shareholders holding over 3% of the Company's ordinary shares\*

Number of ordinary shares	% of issued share capital
Richard Griffiths and Controlled Undertakings	11.48%
Obotritia Capital KGaA	7.84%
Octopus Investments Nominees Ltd	5.89%
Rosetta Capital VI GP LP, on behalf of Rosetta Capital VI, LP	5.65%
Arthurian Life Sciences SPV GP Ltd, as GP of The Wales Life Sciences Investment Fund LP	5.27%

## LEGACY ASSETS – CTX AND HRPC

### ⑥ Fosun Pharma – ReNeuron’s partner in Greater China

- In 2019 ReNeuron signed an out-licensing agreement with Fosun Pharma for both CTX and hRPC in Greater China, totaling £80m in milestones as well as royalties of 12-14%
- In January 2022 ReNeuron announced that it had signed an additional agreement, setting out the first steps for the technology transfer of the CTX drug product into China
- In June 2022, ReNeuron signed a Supplemental Terms Agreement with Fosun Pharma. As a result, the Group expects to receive approximately £1 million over the next 24 months with up to a further £5 million over the medium to long term
- Fosun is building a 20,000 sqft GMP facility to manufacture CTX highlighting its commitment to the programme

### ⑥ hRPC

- In January 2022 following a decision to out-license the programme, work has been ongoing to complete the data package

### ⑥ ReNeuron’s Goals

- To continue to progress the CTX and hRPC programmes with Fosun in China
- To successfully complete the Technology Transfer of CTX to Fosun in China
- Out-license the CTX and hRPC programme in other geographies

# EXOSOMES: COMPARISON OF DELIVERY TECHNOLOGIES

	Lipid nanoparticles	Lentivirus	AAVs	Exosomes
Gene delivery <i>in vivo</i>	++	+++	+++	+++ (ExoAAV)
Safety profile	+	++	++	+++
Max payload size	+++	++	+	++
Pre-existing immunity	+++	+++	-	+++
Repeat-dose immunity	+	+	-	+++
Permanent effect	-	+++	+	+
Multiplex payload delivery (2+ payloads)	++	++	-	+++
Ease of manufacture	+++	+	++	++
Tissue targeting	+ (mainly liver)	+	+	+++*
Tissue specificity	-	-	-	+++*
Payload presentation	Internal	Internal	Internal	Internal & external
Payload repertoire	siRNA mRNA Soluble protein Small molecules Genes	Genes	Genes	siRNA mRNA Soluble protein Membrane-assoc. protein Small molecules Genes (ExoAAV)

\* ReNeuron predicts an comparative advantage in these areas by matching exosome source with target tissue

**Exosome Key Advantages:** Range of payloads, Tissue targeting, Multiplexed delivery, Redosing possible, Safety profile



# PRELIMINARY RESULTS

## Highlights for the year ended 31 March 2022



(£'m)	Year ended 31 March 2022	Year ended 31 March 2021
Revenue and other operating income	0.4	0.3
Research and development costs	(8.1)	(9.5)
General and administrative costs	(3.6)	(3.7)
<b>Operating loss</b>	<b>(11.2)</b>	<b>(12.9)</b>
Net finance income/(expense)	0.2	(0.5)
Taxation	1.4	2.1
<b>Loss for the year</b>	<b>(9.7)</b>	<b>(11.3)</b>

# SUMMARY BALANCE SHEET



(£'m)	31 March 2022	31 March 2021
Non-current assets	0.8	0.9
Current assets (excluding cash & bank deposits)	1.9	2.3
Cash and bank deposits	14.5	22.2
<b>Total assets</b>	<b>17.3</b>	<b>25.4</b>
Total liabilities	(7.4)	(6.4)
<b>Net assets</b>	<b>9.9</b>	<b>18.9</b>
Share capital	0.6	0.6
Share premium	113.9	113.9
Other reserves	42.5	42.5
Accumulated losses	(147.1)	(138.1)
<b>Total equity</b>	<b>9.9</b>	<b>18.9</b>

# SUMMARY CASH FLOW

(NON-STATUTORY FORMAT)

(£'m)	Year ended 31 March 2022	Year ended 31 March 2021
Cash flows from operating activities	(9.2)	(12.1)
R&D tax credit received	1.8	6.0*
<b>Net cash used in operating activities</b>	<b>(7.4)</b>	<b>(6.1)</b>
Capital expenditure	(0.3)	-
Proceeds from issue of shares (net of costs)	-	16.3
Lease payments	(0.2)	(0.2)
<b>Net (decrease)/increase in cash &amp; bank deposits</b>	<b>(7.9)</b>	<b>10.1</b>
Effect of foreign exchange rates	0.2	(0.5)
Cash at start of year	22.2	12.6
<b>Total cash and bank deposits at end of year</b>	<b>14.5</b>	<b>22.2</b>

\* Includes £2.9 million relating to the year ended 31 March 2019