# ReNeuron

## **CORPORATE PRESENTATION**

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#### **Re**Neur**o**n



### SUMMARY – RENEURON TODAY A LEADER IN STEM CELL BASED EXOSOMES TECHNOLOGIES

#### O Differentiated Exosomes technology platform in a growing market

- Delivery mechanism for variety of payloads
- Growing number of Partner Collaborations in a fast expanding area of scientific and commercial interest
- **Key advantage** of ReNeuron's stem cell derived Exosomes delivery technology is the ability to tissue match the exosome with the target tissue type
- 7 research collaborations ongoing with Big pharma, biotech and academic institutions

#### Induced Pluripotent Stem Cell (iPSC) Platform

- Offers the ability to further expand the tissue targeting of the Exosomes platform
- Under investigation in allogeneic CAR-T / CAR-NK cell therapies

#### **O** Two stem cell programmes out licensed / available for licensing

• CTX Programme for stroke disability and hRPC programme in retinitis pigmentosa out-licensed in China to Fosun Pharma. Available to out-license in other regions

#### Well-funded with cash at 30 Sept 21 of £17.4m

• Providing at runway until late Q2 2023



### MAXIMISING RETURN TO SHAREHOLDERS

#### **REVENUE STREAM 1:**

#### Partnered exosomes programmes

- o Building a Contract Development and Manufacturing Organisation (CDMO) model
- Working with multiple partners offers many shots on goal for success
- ReNeuron receives a contribution from commercial partners to enable the early stage research while co-owning IP of the resulting programme
- Progression of the programme to the clinic would require a licensing agreement
- Our aim is for ReNeuron to manufacture the therapeutic exosome while the partner leads the clinical development and commercialisation

#### Section 2 Constraints of the section of the sect

- Our Research team is lead by Stefano Pluchino (CSO) and Randolph Corteling (VP of Research), who have 30 years experience in the Exosomes field
- Our Manufacturing team have long experience in producing exosomes and cell therapies, having achieved two IND approvals and successfully completed several technology transfers

#### ReNeuron's Goals

- Maximise the number of partner programmes hence increasing the shots on goal in a low risk / low R&D spend manner
- Progress current partnerships towards a licensing event



## MAXIMISING RETURN TO SHAREHOLDERS

#### **REVENUE STREAM 2:**

#### O Proprietary exosome programmes

- Taking advantage of extensive internal research expertise to develop our own product candidates in pre-clinical development
- Successfully developed pre-clinical programmes could either be out-licenced or further developed in-house
- o Own product development offers larger upside potential

#### ReNeuron's Goals

- Produce further pre-clinical data highlighting the potential in these programmes
- To have a balanced portfolio of proprietary and partnered early-stage programmes

#### **REVENUE STREAM 3:**

#### Out-licensing and associated revenue for existing clinical portfolio

- Fosun Pharma: Deal terms secured of up to £80m in milestones as well as tiered royalties of 12-14%
- Ex-China CTX and hRPC: Seeking partners

#### ReNeuron's Goals

- To continue to progress the CTX and hRPC programmes with Fosun in China
- To complete ongoing discussions with Fosun on a Technology Transfer agreement
- Out-license the CTX and hRPC programme in other geographies
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Exosomes versatility has the potential to overcome various hurdles with many current delivery mechanisms

## EXOSOMES: THE NEW GENERATION DELIVERY TECHNOLOGY

#### Able to carry a wide range of payloads

- ✓ siRNA
- ✓ mRNA
- Soluble protein
- Membrane-assoc. protein
- Small molecules
- ✓ Genes (ExoAAV)

#### Tissue targeting / Tissue Specificity

- ✓ ReNeuron has potential to match exosome cell lines with target tissue (tissue matching)
- ✓ Use of external loading to further assist in targeting correct tissue

#### Multiplex payload

- ✓ Able to carry 2+ payloads
- ✓ Payloads can be carried internally and/or externally

#### Outline Utility and Safety profile

- ✓ No pre-existing immunity and ability to re-dose
- ✓ Good safety profile

## EXOSOMES: RENEURON GROWING IN A GROWING MARKET

- The Therapeutic Exosomes field is expanding quickly, growing significantly in recent years
- ReNeuron's number of partners has grown from two to seven in last 3 years
- Right Place, Right Time, Right Technology

Evox / TakedaCodiak / JazzEvox / LillyTotal \$0.8BTotal \$1BTotal \$1.2Brare diseasesCancerneurological targets

Increasing industry interest and hence commercial value of Exosome deals







## THE RENEURON ADVANTAGE: TISSUE FOR TISSUE MATCHING



#### **Exosomes Collaborations with Partners**

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

#### **Internal Programmes**

EXOSOMES

PARTNER AND

OWN

PROGRAMME

PIPELINE

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

## DELIVERY OF THERAPEUTIC PROTEINS WITH RENEURON'S EXOSOMES



\*In a preclinical setting

**ReNeuron** 

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

- Delivered by Intrathecal injection (lumbar puncture)
- Response observed only with Exosomes loaded with therapeutic protein
- (a) This area of the brain (the striatum) is affected in Parkinson's and Huntington's disease
- Exosomes have potential to transform effective drug delivery for key neurological diseases
- Patent filed Oct 2021

#### **NEXT STEPS**

- Perform functional studies to demonstrate clinical potential
- Planning to conduct *in vitro* functional studies in a variety of indications
- *In vivo* functional studies will follow for the most promising indications



### SUMMARY: THE OPPORTUNITY

#### © EXOSOMES – Right place, Right time, Right Technology

- o Accelerated investment to build IP and know-how in the Exosomes field
- Strengthen and progress our existing partnerships
- Establish new value creating industry partnerships
- Maximize the potential for ReNeuron in this fast growing area of Science

#### O Potential longer-term upside: iPSC platform, CTX Stroke disability and hRPC

- iPSC Platform earlier stage but with exciting potential in multiple areas
- o CTX in stoke disability progressing with Fosun in China
- Potential to out-license CTX and hRPC in other geographies

#### A leader in Stem Cell based Exosomes Technologies



## ReNeuron

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## Appendix



## STRATEGIC REVIEW SUMMARY

#### Retinitis Pigmentosa (RP) Review of Data

- Meeting of Scientific advisory board convened to discuss surgical related complications seen at the 2 million cell dose and also analysis of the 24 month data at the 1 million dose
- For the 2 million cell dose it was concluded that the rate of surgical complications would mean it would not be a viable commercial product
- For the 1 million dose, analysis of the 24 month data showed that four of the nine patients still showed a positive response versus baseline at 24 months

#### Occurrence Conclusions

- While the 1 million cell dose showed an average 9.9 letter improvement at 12 months, there was a large variation in the positive responses seen from +2 to +20 letters. To fully understand and identify which sub-populations were most likely to respond and also have a sustained response the company believes an additional phase 2 trial would be needed
- The Board concluded that the size of the investment required would not be in the best interests of shareholders
- It was therefore decided it would be better to complete the data package on the programme and look to out-license the programme to a third party
- With the growing market in Exosomes and increasing number of partner programmes, ReNeuron will focus its full efforts on maximising the opportunity in the Exosome market

## EXOSOMES: COMPARISON OF DELIVERY TECHNOLOGIES

	Lipid nanoparticles	Lentivirus	AAVs	Exosomes	
Gene delivery in <i>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)	

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\* 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

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

## Ability to produce Native, Passively-loaded and Engineered Exosomes



Providing an expanded range of Exosome products

CAR-T

**CAR-NK** 

UCL

**iPSC** Platform

UCL



## **IPSC COLLABORATIONS WITH UNIVERSITY COLLEGE LONDON**

#### © Collaboration with Dr. Claire Roddie, UCL

- ReNeuron to provide iPSCs from its CTX immortalised Neural progenitor cell line, which is available as clinical grade material
- UCL to assess for their ability to differentiate into functional T cells and natural Killer ('NK') cells
- If successful, the CTX-iPSC cell lines will be used to generate chimeric antigen ('CAR') T cells and/or CAR-NK cells

Dr. Clare Roddie said: "We are excited to work with ReNeuron to develop universal CAR approaches using their clinical grade CTX-iPSC lines. If preclinical testing is successful, we would hope to move towards clinical studies."

#### Solution Collaboration with Prof. James Philips and Dr. Rebecca Powell, UCL

- hiPSCs can be differentiated into Schwann cells via an intermediate Schwann cell precursor stage
- hiPSCs were reprogrammed from ReNeuron's clinical grade CTX neural progenitor line, which benefits from conditional immortalisation (CI)
  - Hence, once terminally differentiated, the cells will only divide in the presence of a synthetic molecule that is not present in the body, reducing the risk of tumour formation
  - The CI technology also appears to promote mature Schwann cell viability