ReNeuron

ReNeuron Group plc
Annual Report and Accounts 2020

Developing stem cell technologies to improve patients' lives

Leading the development of vital stem cell therapies ...

Our vision is to improve patients' lives through our proprietary stem cell technologies.

As a leader in cell-based therapeutics, we develop allogeneic stem cell technology platforms, stem cell derived exosomes and induced pluripotent stem cells.

INSIDE OUR REPORT

... improving patients' lives

hRPCs for retinal diseases

Exosome nanomedicine platform

iPSCs: expanding our therapeutic platform

CTX stem cell therapy for stroke

Our hRPC technology is in a Phase 1/2a trial in retinitis pigmentosa

- Retinitis pigmentosa (RP) is a degenerative eye disease.
- It is an inherited medical condition.
- Patients usually lose night vision in teenage years.
- Side vision is lost in middle age and central vision in later years.
- Currently, there is no treatment for most types of RP.

Our exosomes are a potential drug delivery vehicle

- There are many conditions that are difficult to treat because enough active drug is unable to reach its target.
- Our exosomes could provide that delivery system to enable drugs to more effectively treat these conditions.
- Our nanosomes are also potential therapeutics.

Our iPSCs can potentially expand our therapeutic platform

- New data show that our CTX stem cell line can be reprogrammed into induced pluripotent stem cells (iPSCs) and differentiated into other cell types.
- New cell lines can be rapidly created as cell therapy candidates or exosomes, targeting a broad range of diseases.

Our CTX cells have shown clinical potential in stroke disability

- There are 80 million stroke survivors worldwide.
- Out of this, 50 million patients are permanently disabled.
- Patients are dependent on social care for the rest of their lives.
- There are currently no treatments for stroke disability after the early phase.

Many patients suffer from medical conditions where their needs are unmet, impacting on the quality of their lives.

Our stem cell technologies have the potential to improve the lives of patients with unmet medical needs.

A year of progress towards improving patients' lives

Our progress to date

hRPC stem cell therapy candidate for retinal diseases

Positive interim efficacy data from patients treated in the Phase 2a segment of the ongoing Phase 1/2 study were announced in October 2019.

Subsequent long-term efficacy data from the study continue to show a meaningful clinical effect from the therapy at all time points post-treatment.

Clinical trial protocol amendment approved by the FDA and MHRA to expand the Phase 1/2a study.

Application approval received from the MHRA to open a site in Oxford, UK with Professor Robert MacLaren, a world-renowned leader in the treatment of retinal diseases, as Principal Investigator.

Read more about our progress with **hRPC stem cell therapy** on pages 16 to 17

Exosome nanomedicine platform

Expansion of intellectual property estate via the grant of a number of key patents covering our exosome technology platform. Patents were granted in China, Korea, Japan and Europe.

Grant-funded collaboration initiated with European Cancer Stem Cell Research Institute to develop novel systems to enable the delivery of therapeutic nucleic acids across the blood brain barrier using our exosomes.

In April and June 2020, we announced separate commercial collaboration agreements to explore the potential of our exosomes to deliver therapeutic agents to the brain.

Read more about our progress with **Exosomes** on pages 18 to 19

What's coming up

hRPC stem cell therapy candidate for retinal diseases

The Group expects to commence treating patients shortly in both the US and the UK under the revised approved study protocol, subject to a continued easing of COVID-19 related restrictions at the relevant clinical sites.

On this basis, the Company expects to present further data from the expanded Phase 1/2a clinical trial during the next twelve months and expects to have sufficient data from the study to enable it to seek approval in the second half of 2021 to commence a single pivotal clinical study with its hRPC cell therapy candidate in RP.

Exosome nanomedicine platform

Targeting our exosome technology programme towards value-generating business partnerships in which exosomes may be exploited as a potential third-party drug delivery vehicle.

The group is developing an exosome displaying proteins characteristic of the SARS-CoV-2 coronavirus with the objective of the exosome being used to deliver a vaccine against COVID-19.

Financial Highlights

Loss for the period of
£11.4m
(2019: £14.3m)

Cash used in operating activities
£14.3m
(2019: £11.9m)

Cash, cash equivalents and bank deposits
£12.6m
(2019: £26.4m)

Our progress to date

iPSCs: expanding our therapeutic platform

New data presented, supporting use of iPSCs to develop new immortalised cell lines as potential therapeutic agents for subsequent licensing to third parties.

Read more about our progress with **iPSCs** on pages 20 to 21

CTX stem cell therapy candidate for stroke disability

During the period we continued to progress the clinical development of our CTX cell therapy candidate for stroke disability.

Positive data from PISCES II Phase 2a clinical trial of CTX in stroke disability was published in a peer reviewed journal.

Patient recruitment in the US based PISCES III Phase 2b study was put on hold due to COVID-19 related restrictions, will remain suspended in the US for the foreseeable future; clinical trial sites will be kept open and patients already treated will be followed up over time in line with the clinical trial protocol.

Exclusive licensing partner in China, Shanghai Fosun Pharmaceutical Industrial Development Co., Ltd. ("Fosun Pharma"), continues to pursue development of CTX cell therapy in the licensed territory (Greater China including Hong Kong, Macao and Taiwan).

Clinical trial applications have recently been filed by Fosun Pharma to open clinical sites in the licensed territory.

Read more about our progress with **CTX stem cell therapy** on pages 22 to 23

Business development

Signing of an exclusive out-licence agreement with Fosun Pharma to commercialise hRPC and CTX programmes in the People's Republic of China ("Greater China").

Fosun Pharma is a leading healthcare group in China with extensive healthcare business interests worldwide.

We received £6.0m (before withholding tax) on signing and will receive up to £6.0m in near-term operational milestones and up to £8.0m in future regulatory milestone payments as well as post-launch profit threshold milestone payments and tiered royalties on sales.

What's coming up

iPSCs: expanding our therapeutic platform

The Group's iPSC platform enables the derivation of different stem cell populations that can be utilised for the production of exosomes with specific tissue targeting, or as new cell-based therapeutic candidates, thus providing further scope for a wide range of industry-based partnerships.

CTX stem cell therapy candidate for stroke disability

Clinical sites to be opened, by Fosun Pharma, in the licensed territory to build on the clinical data generated in the US.

The CTX cell therapy candidate will be made available for licensing in stroke disability outside China and will also be made available for licensing in other indications such as Huntington's disease.

For **scientific terms** see the glossary on pages 96 to 97

Business development

Discussions will continue with other commercial third parties regarding potential out-licence deals across all therapies.

We will continue to work closely with Fosun Pharma as it pursues the development, manufacture and commercialisation of our cell therapy programmes in Greater China, with the CTX programme for stroke disability being the initial focus of activities.

Group at a glance

Our stem cell-based therapies ...

hRPCs

Our hRPC stem cell therapy could change the lives of patients suffering from retinitis pigmentosa (RP) and also has potential utility in other eye diseases.

What are hRPCs?
Human retinal progenitor cells (hRPCs) are an allogeneic, cryopreserved cell-based therapy for treatment of retinal diseases.

What can they do?
hRPCs have demonstrated the ability to differentiate into functional photoreceptors and integrate into retinal layers in pre-clinical models; integration may also enable durable trophic support.

How it is used
Our therapy is initially targeting the inherited retinal degenerative disease, retinitis pigmentosa, by implantation of hRPCs into the retina.

Exosome platform

Our exosomes could change the lives of patients where current treatment options are limited.

What are exosomes?
These are nano-sized packages of information released by our neural stem cells.

What can they do?
Therapeutic agents can be loaded onto our exosomes and potentially be used to treat a host of medical conditions.

How it is used
Our exosomes can be delivered either locally or systemically depending upon the desired final destination.

iPSCs

Our iPSCs could expand our therapeutic portfolio, targeting a broad range of diseases.

What are iPSCs?
Induced pluripotent stem cells (iPSCs) are reprogrammed proprietary neural stem cells that are in an embryonic-like state.

What can they do?
iPSCs can be made to develop into any other type of stem cell.

What this means
iPSCs can be utilised as new cell-based therapeutic candidates or for the production of exosomes with specific tissue targeting.

CTX cells

Our CTX stem cell therapy could change the lives of patients suffering from stroke disability.

What are CTX stem cells?
Allogeneic, cryopreserved, immortalised neural stem cells for treatment of stroke disability.

What can they do?
CTX stem cells have the ability to differentiate into a repertoire of specific nerve and nerve support cells, as well as provide support for already present cells.

How it is used
Our cell therapy is directly injected into the brain near to the area damaged by the stroke.

... could improve the lives of patients

Key facts about retinitis pigmentosa

RP is an inherited, degenerative eye disease that results in the loss of peripheral vision followed by the loss of central vision[1].

The end result is blindness. One in 3,000 to 4,000 people are affected by RP[1].

Our therapy could potentially benefit patients suffering from this rare disease.

Read more about the marketplace for our **hRPC stem cell therapy** on page 09

Key facts about exosomes

Our studies have identified the potential of our exosome candidate as a drug delivery vehicle.

We are focusing on the use of our exosome technology as a novel drug delivery vehicle.

One of the key advantages of our exosomes is that they can cross the blood brain barrier.

Read more about the marketplace for our **Exosomes** on page 10

Key facts about iPSCs

There is a potential to expand our therapeutic portfolio by developing further therapeutic candidates for subsequent out-licensing.

There is a potential to produce exosomes with the ability to target specific tissues within the body.

Our iPSCs research platform provides further scope for a wide range of industry partnerships.

Read more about the marketplace for our **iPSCs** on page 10

Key facts about stroke disability

Around 800,000 strokes happen in the US each year[2].

Stroke mortality rate has decreased by 33% since 1996 suggesting that more people survive and are left suffering[3].

More people than ever might be able to benefit from our potentially life-changing therapy to reduce their disability, and dependence on others.

Read more about the marketplace for our **CTX stem cell therapy** on page 11

Key facts

40
patents worldwide covering cell-based therapies and exosome technology

4
key grant-funded collaborations with research institutes globally

For **scientific terms** see the glossary on pages 96 to 97

[1] RP Fighting Blindness

[2] Centers for Disease Control and Prevention

[3] National Institutes of Health

Chairman's statement

The year ended 31 March 2020 was a year of significant progress in both clinical and strategic development, providing growing confidence in the short and long term potential of the Company's programmes.

> We look forward to reporting further Phase 2a data from the ongoing study with our hRPC cell therapy candidate for retinitis pigmentosa over the next 12 months.

John Berriman
Non-executive Chairman

12 August 2020

Read more on our **hRPC stem cell therapy** on pages 16 to 17

Read more on our **exosomes and iPSCs** on pages 18 to 21

I am pleased to introduce the Group's results for the year ended 31 March 2020. It was a year of significant progress in both our clinical and strategic development, providing growing confidence in the short and long term potential of the Company's programmes.

We are increasingly encouraged by the positive interim data and duration of therapeutic response from the Phase 2a patients treated in the ongoing US Phase 1/2 clinical trial with our hRPC cell therapy candidate for retinitis pigmentosa. We are also pleased to have received regulatory approval from both the FDA and MHRA to expand the ongoing Phase 2a part of the study to treat patients with RP at a higher dose level, at clinical sites in both the US and the UK. We look forward to reporting further Phase 2a data from the study over the next 12 months.

We have successfully refocused our exosome technology programme towards value-generating business partnerships, in which our exosomes are being exploited as a potential novel vector for delivering third parties' biological drugs. This refocusing has culminated in the signing of two collaboration agreements post year-end with major pharmaceutical/biotechnology companies to explore the potential of our neural stem cell derived exosomes to deliver therapeutic agents to the brain. During the period, we also presented new data supporting the use of the Group iPSCs (induced pluripotent stem cells) to derive new immortalised cell lines as potential therapeutic agents for subsequent licensing to third parties.

We recently announced a strategic decision to focus the Group's resources on our retinal disease programme and our exosome and iPSC research platforms. Consequently, our stroke disability programme will continue through regional partnerships. In April 2019, we were delighted to sign an exclusive licence agreement with Shanghai Fosun Pharmaceutical Industrial Development Co., Ltd. ("Fosun Pharma") for the development, manufacture and commercialisation of both our CTX and hRPC cell therapy programmes in the People's Republic of China. Fosun Pharma is a leading healthcare group in China with extensive healthcare business interests worldwide. Clinical trial applications have recently been filed by Fosun Pharma to open clinical sites in the licensed territory to build on the Phase 2b clinical data already generated with the CTX cell therapy candidate for stroke disability in the US.

In addition to making our CTX cell therapy candidate available for licensing in stroke disability outside China, we further announced that the candidate is available for licensing in other indications. In support of this licensing strategy, we were pleased to have recently published positive data from the PISCES II Phase 2a clinical trial of CTX in stroke disability in the Journal of Neurology, Neurosurgery, and Psychiatry.

> ReNeuron has a clear focus to deliver value-generating data across its programmes over the next twelve months.

John Berriman
Non-executive Chairman

Additionally, we recently announced the publication of new positive non-clinical data relating to our CTX cell therapy candidate in Huntington's disease.

During the ongoing COVID-19 pandemic, the safety of employees, suppliers, clinical trial participants and all other people with whom the Group interacts has been of over-riding importance to us. The Group continues to comply with governmental advice and requirements across its operations in the UK and US, without significant impact on our priority internal research projects. In response to COVID-19, we also initiated a research programme focused on the potential utility of our proprietary exosomes as a delivery vehicle for SARS-CoV-2 coronavirus vaccines.

ReNeuron now has a clear focus on delivering value-generating data across its programmes over the next twelve months. Consistent with this new sharper focus and as a consequence of long-serving Non-executive Directors indicating their intention to retire from the Board (having served for nine years and thereby become non-independent under the QCA code of corporate governance), the non-executive membership of the Board will be progressively reconfigured, reducing the number of Non-executive Directors from six to four. This rationalised Board has the expertise necessary to support the Group's new emphasis on retinal diseases and commercial partnerships. I shall therefore not be seeking re-election at the coming AGM (along with my colleague Simon Cartmell) and Dr Claudia D'Augusta is also stepping down. The company is now stronger and more diversified than when I joined nine years ago and I am particularly pleased to be leaving it in the able hands of my successor chairman, Dr Tim Corn. Furthermore in recognition of the significant shareholding of Obotritia Capital KGaA and their ongoing support for the Company we have approved in principle their request to nominate a non-executive director for election to the Board.

Finally on behalf of the Board I would like to thank our employees for their commitment and determination, especially in the face of the COVID-19 pandemic. On behalf of all Directors and employees I would also like to thank our shareholders for their support as we continue to strive to make ReNeuron a great success.

On page 91 of this report is the Notice of the 2020 annual general meeting (AGM) to be held at 10.00 a.m. on 10 September 2020. A short explanation of the resolutions to be proposed at the AGM is set out on page 94. The Directors recommend that you vote in favour of the resolutions to be proposed at the AGM, as they intend to do in respect of their own beneficial holdings of ordinary shares.

John Berriman
Non-executive Chairman

12 August 2020

Our marketplace

Meeting market needs with our therapeutic candidates

$0.5bn – $1.6bn
Market potential for RP therapy[1]

Retinal diseases

Market need:

No approved treatment for vast majority of patients with retinitis pigmentosa (RP).

Market characteristics:

RP is an inherited, degenerative eye disease causing severe vision impairment and often blindness.

There is currently no general cure and limited treatment options for RP and sufferers remain reliant on both health and social care services.

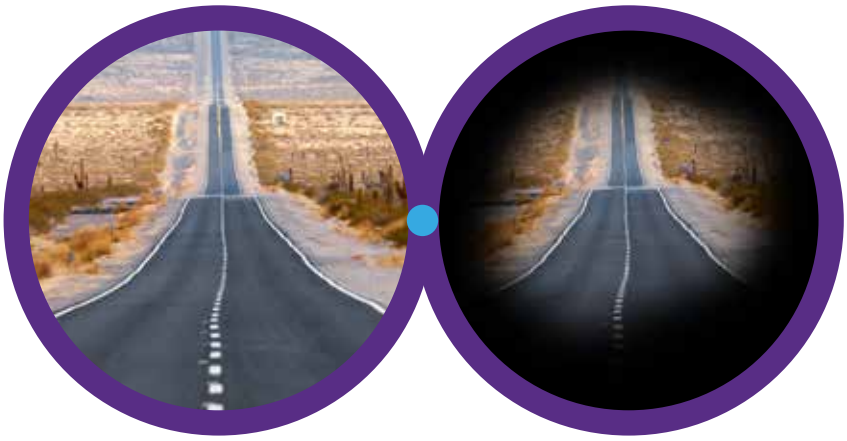
Current treatments target specific genes and therefore are only appropriate for a limited number of the RP population as there are over 100 gene defects causing RP.

As with all forms of blindness, the quality of the patient's life is significantly diminished.

Given that this condition is inherited it can affect every part of the patient's life; from their career to decisions around starting a family.

Other retinal diseases include Cone Rod Dystrophy (CRD), which frequently affects patients in childhood and has no cure.

CRD is an inherited orphan disease that affects roughly one in 40,000 people.



Normal vision

Retinitis pigmentosa

Our response

Our hRPC cell therapy candidate offers a number of potential advantages over alternative approaches to the treatment of RP.

Our cell therapy candidate is independent of the many specific genetic defects that collectively define RP as a disease, thereby allowing a much broader potential patient population to be eligible for the treatment.

Our research suggests that hRPC therapy may be able to slow or even reverse the progression of RP through its ability to differentiate into components of the retina and its ability to maintain existing photoreceptors.

Our therapy is cryopreserved, enabling on-demand shipment and use at local surgeries and hospitals.

Our hRPC therapy doesn't require immunosuppressants. The cells are injected directly to the site of retinal degeneration, allowing a greater chance of anatomic restoration of photoreceptor function.

(1) Analysts' estimates: Stifel March 2018, N+1 Singer April 2017, Edison May 2017.

Our marketplace

Drug delivery technologies

One of our primary objectives is the development of exosomes as a delivery vehicle targeting areas of significant unmet or poorly met medical need.

Exosomes have the potential to overcome the limitations of current delivery technologies.

Advantages of exosomes:

A key advantage of exosomes is their low immunogenicity, which means they do not provoke immune responses in the body. In comparison, delivery technologies such as Lipid Nanoparticles (LNP), are known for inducing a significant inflammatory response.

Other delivery technologies (e.g. Lipid Nanoparticles) are generally taken up by a certain type of pathway in the body which results in lysosomal destruction.

Exosomes however have the ability to be taken up by a number of different pathways, including cell fusion. If the exosome fuses to the cell membrane, its cargo will be directly released into the cell to have its desired functional effect.

There is a potential for exosomes to deliver medicine to specifically targeted areas. In comparison to other delivery technologies, such as GalNac conjugates, which can only delivery siRNA to the liver.

Crossing the blood brain barrier

Very few therapies successful cross the blood brain barrier (BBB), making central nervous system disorders difficult to treat.

Why does it make it difficult to treat?

If drugs do not cross the BBB easily, systemic administration (I.V.) is ruled out. Very high doses will need to be given to an efficacious dose to the brain.

If I.V. is ruled out, then local administration is an option, which is much more complex, expensive and less accessible. If higher doses are given I.V., the chance of off-target effects (side effects) increases significantly.

References: Vader et al. 2016 – Extracellular vesicles for drug delivery;

Ha et al. 2016 – Exosomes as therapeutic drug carriers and delivery across biological barriers.

Our response

Our exosomes can cross the blood brain barrier. We believe exosomes can do this due to the neural nature of their cell of origin.

This neural stem cell line produces exosomes with specific surface markers that allow the exosomes to cross the BBB and communicate with other cells within the brain.

For **scientific terms** see the glossary on pages 96 to 97

New cell-based therapeutic candidates

Human pluripotent stem cells offer huge potential for the entire field of regenerative medicine and cell therapy. Their capacity for unlimited expansion through self-renewal and ability to differentiate into any cell type within the body has the potential to produce an inexhaustible source of different cell types to treat a variety of indications.

A number of issues have so far impeded the clinical development of pluripotent stem cells.

More often than not, pluripotent stem cells require differentiating to adult stem cells or tissue progenitor prior to use as a drug product. However these cell types are extremely unstable and are difficult to manufacture at scale.

Our response

ReNeuron's iPS cells however, have a conditional immortalisation technology inserted which requires no further manipulation and increases the stability of the subsequent therapeutic cell lines for the rapid production of 'off-the-shelf' stem cell therapies.

Stroke disability

Market need:

Treatment options are limited, and they are only available within 4.5 hours of stroke onset.

Market characteristics:

Stroke is the single largest cause of adult disability in the developed world.

Stroke disability significantly affects a patient's quality of life, and the treatment and care of these patients is a burden on health and social care as well as family and caregivers.

There are currently no treatments for stroke disability after the early phase.

US

Stroke is the leading cause of morbidity and long-term disability in the US[2].

In the US, $34 billion is spent each year on stroke disability (this includes health care services, medications and lost productivity)[3].

UK

In the UK, the NHS spends £3.4 billion each year on stroke disability and the social care spend is £5.2 billion annually[4].

China

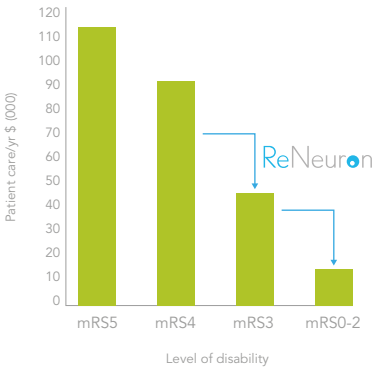
Stroke has the highest single-disease disability rate and is a financial and social burden in China. From 1993 to 2003, the average growth rate for the direct cost of stroke care was 18.04% per year.

In 2010, the average cost per capita of patients with a high risk of stroke was estimated to be US$517.8 per year. This heavy financial burden to the Chinese healthcare system will likely increase in the next 20 years because of the ageing population[5].

[1] Analysts' estimates: Stifel March 2018, N+1 Singer April 2017, Edison May 2017.
[2] Benjamin et al. (2017) Circulation 135, e146-e603.
[3] Centers for Disease Control and Prevention.
[4] Stroke Association.
[5] Chinese Stroke Association, World Stroke Organisation.

Swedish study

The graph on the right shows the results from a 2017 Swedish study which demonstrated that patient care cost can be reduced in proportion to a reduction in stroke disability. Our Phase 2b study targets patients with a mRS score of 3 or 4 and will be looking for an improvement of one or more points.



Our response

Our stroke therapy is the first cell-based therapy of its kind. Our CTX cell therapy aims to treat patients months or even years after their stroke.

The Phase 2a clinical trial (PISCES II) for our CTX cell therapy demonstrated that it can reduce a patient's global disability post stroke as assessed by mRS.

Our exclusive licensing partner in Greater China, Fosun Pharma, continues to pursue development of our CTX cell therapy.

$3.4bn
spent each year in the UK on stroke disability[1]

$34bn
spent each year in the US on stroke disability[1]

Our business model

Key resources

Intellectual
We use proprietary technology to produce our life-changing therapies.

Human
Our researchers and academic collaborators have industry-leading knowledge and this drives the therapy development process.

Physical
Our contract manufacturing organisations are instrumental in the production of our therapeutic candidates.

Financial
Funds are raised by commercial partnerships, the issues of shares and from grant funding bodies. These financial resources enable us to advance the development of our therapies.

Value chain

Develop best-in-class cell-based therapies for life-changing high-value products. ▶ Gain clinical validation for our therapeutic programmes, via robust clinical trials in well regulated territories. ▶ Realise value for our technologies and therapeutic programmes, via direct sales or substantial licence deals.

Our relationships

hRPCs
We are developing good relationships with inherited retinal disease specialists, who administer the hRPC therapy to study participants.

This will support the clinical development to advance this potential therapy to patients with inherited retinal disease.

Our licence agreement with Fosun Pharma for China also includes our hRPC therapy programme.

Exosomes
We are developing strong relationships with academic and clinical key opinion leaders in the area of neurology to oncology and beyond.

We also have relationships with commercial organisations who we will be collaborating with as we broaden our therapeutic pipeline.

We have established relationships with pharmaceutical companies to explore the use of our exosomes as a novel drug delivery vehicle.

We are working on a collaboration which focuses on loading gene silencing sequences into exosomes.

iPSCs
We continue to develop strong relationships with academic leaders in all areas of cell therapy to understand where the technology will have the biggest impact.

CTX cells
As part of the clinical trials for the CTX cell therapy for stroke disability, we develop strong relationships with the neurologists and rehabilitation doctors who care for the patients and the neurosurgeons who will administer the therapy.

Our exclusive licensing partner in China, Fosun Pharma, continues to pursue development of our CTX cell therapy for stroke disability.

Our relationships with academic institutions and other pharmaceutical companies enables us to explore the use of our CTX sell therapy to treat other indications such as Huntington's disease.

Our competitive advantages

We are positioned for success ...

1

With our proprietary technologies

- Our patent estate consists of over 40 patents worldwide covering our cell-based therapies, exosome and iPSCs technologies.
- A highly efficient, patented process is used to produce hRPCs on a large scale.
- Our CTX drug product is a proprietary allogeneic cell therapy produced by our well-established, scalable manufacturing process. (Allogeneic: recipients of cells are immunologically different from cell donor.)
- Our high-yielding human neural stem cell derived exosomes have proven ability to be loaded with siRNA, miRNA and proteins, and are able to cross the Blood Brain Barrier.
- Our iPSC platform technology engineers CTX neural stem cells into other forms of stem cell.

2

With our flexible cryopreservation process

- Our hRPCs and CTX cells can be cryopreserved, which provides flexibility in terms of scheduling patient treatment.
- This makes our product similar to conventional 'off-the-shelf' pharmaceuticals/biologics.
- Our cryopreservation process allows us to develop the therapies and transport them globally.

3

With our efficient development pipeline

- Our therapy development pipeline spans the pre-clinical and clinical development process.
- We have seen positive top-line efficacy data presented from Phase 2a patients in ongoing US Phase 1/2a clinical trial in retinitis pigmentosa. The ongoing Phase 2a study is to be expanded to allow for subsequent potential single pivotal clinical study and shorter route to market.
- There are significant clinical validation milestones due in the next 18 months in our ongoing clinical trial in retinitis pigmentosa.
- The exosomes we are harnessing for use are a by-product of our CTX cells and are derived from a GMP compliant process. They can be produced at an industrial scale without affecting the quality and consistency of the final product. They have potential as both a drug load/delivery vehicle and as a therapeutic.
- Our iPSC platform has potential for new targeted cell therapeutics and for exosomes based on non neural stem cells.

Our process for developing life-changing therapies

The clinical trial process

Pre-clinical trials	Clinical trials	Review and approval
Pre-clinical studies (in vitro and in vivo) are conducted to assess feasibility, efficacy and safety of any potential drug product prior to it being tested in humans.	**Phase 1** We carefully assess the safety of a biologically active substance in a small, select group of subjects. **Phase 2** We evaluate the efficacy and safety of our therapy in selected groups of patients. We further evaluate the efficacy and safety of our therapy in patients in a controlled, rigorous trial. **Phase 3** Once our therapy has shown preliminary efficacy and safety (in Phase 1 and Phase 2) we carry out larger-scale clinical trials.	Once a therapy has been deemed safe and effective, it is submitted for approval to regulatory bodies. These bodies review the available evidence and approve it if the benefits appear to outweigh the risks.

Development Pipeline

Programme	Indication	Pre-clinical	Phase 1	Phase 2	Next Milestones
hRPC	Retinitis Pigmentosa				Further data read-outs from expanded UK/US Phase 2a study in 2020 and 2021
CTX cells	Stroke Disability				Future clinical development with Fosun and other potential partnerships
Exosomes platform	Neurodegeneration, Oncology, Vaccines (e.g. COVID-19)				Proof of concept data from pharma/biotech research collaborations
iPSC platform	Oncology, Diabetes				Validation of technology and publication of pre-clinical proof-of-concept data in 2020

Progress in the last 12 months

hRPCs

Positive interim efficacy data from patients treated in the Phase 2a segment of the ongoing Phase 1/2 study were announced.

A total of 22 patients have now been treated in the Phase 1/2a study and a good safety profile has been established.

Subsequent long-term efficacy data from the study continue to show a meaningful clinical effect from the therapy at all time points post-treatment.

Read more on page 16

Exosome platform

Our focus has been on the potential of our exosomes as a drug delivery vehicle, providing greater scope for near-term third-party collaboration deals.

We have signed a grant-funded collaboration agreement with European Cancer Stem Cell Research Institute to enable delivery of therapeutic nucleic acids, such as small interfering RNA (siRNA), across the blood brain barrier using our exosomes.

A number of key patents were granted in regions such as China, Korea, Japan and Europe.

In April and June 2020, we announced separate commercial collaboration agreements to explore the potential of our exosomes to deliver therapeutic agents to the brain. The first of these agreements, with a major pharmaceutical company, focuses on the use of our exosomes for the delivery of novel gene silencing therapeutics. The second, with a major US biotechnology company, focuses on the use of the exosomes to deliver the US biotechnology company's neuroscience therapeutic candidates.

Read more on page 18

iPSCs

New data was presented, supporting use of iPSCs to develop new immortalised cell lines as potential therapeutic agents for subsequent licensing to third parties.

Further, it has been demonstrated that the mesenchymal stem cell lines generated can be grown at scale by virtue of our conditional immortalisation technology, enabling the efficient production of clinical-grade cell therapy candidates.

Read more on page 20

CTX cells

Patient dosing continued in the study PISCES III, a randomised, placebo-controlled clinical trial in 110 patients.

The protocol was amended which, amongst other changes, increases the number of patients to receive CTX therapy as opposed to placebo procedure.

Overall size of Phase 2b study increased from 110 to 130 patients across up to 40 sites.

Exclusive licensing partner in China, Fosun Pharma, continues to pursue development of CTX cell therapy in the licensed territory (Greater China including Hong Kong, Macao and Taiwan).

Clinical trial applications have recently been filed by Fosun Pharma to open clinical sites in the licensed territory.

Read more on page 22

Our progress towards improving patients' lives

hRPCs for retinal therapy

Pre-clinical data

- A rodent model of retinal degeneration was used to study the effects of our hRPC therapy.
- These hRPCs were injected subretinally (just beneath the photoreceptor layer of the retina).
- The results from this study demonstrated that these cells can treat retinal degeneration.

They are able to . . .

1 Preserve retinal structure and function.

2 Differentiate into components of the retina.

Initial Phase 1 element of combined Phase 1/2a trial

- This study was a single centre, open-label, dose escalation trial to assess the safety of hRPCs in patients with established retinitis pigmentosa.
- Three different doses of hRPCs were tested.
- Patients received a single, subretinal injection of one dose and were followed up for one year.
- It was determined that subretinal injections of hRPCs at the three doses tested were safe and well tolerated.
- We successfully developed a cryopreserved formulation of our hRPC stem cell therapy.
- This enables cells to be frozen for shipping/storage and be easily thawed at the point of clinical use.
- The success of this stage means that we were able to progress into the Phase 2a element of the combined Phase 1/2a study.

Figure 1 Long-term efficacy data from the phase 2a portion of the study.

Months post-treatment	**Mean change from baseline in visual acuity in treated eye***	Mean change from baseline in visual acuity in untreated eye*	Difference in mean change between treated eye and untreated eye*
1	**+7.9 letters (n=9)**	+0.2 letters (n=9)	+7.7 letters (n=9)
2	**+8.0 letters (n=9)**	+1.2 letters (n=9)	+6.8 letters (n=9)
3	**+10.8 letters (n=9)**	+4.4 letters (n=9)	+6.4 letters (n=9)
6	**+9.6 letters (n=9)**	+3.4 letters (n=9)	+6.2 letters (n=9)
9	**+7.1 letters (n=8)**	+1.2 letters (n=8)	+5.9 letters (n=8)
12	**+11.9 letters (n=5)**	+4.3 letters (n=5)	+7.6 letters (n=5)
18	**+17.0 letters (n=1)**	+1.0 letters (n=1)	+16.0 letters (n=1)

* Data as announced 29 June 2020, excluding one patient who experienced surgical complications and whose vision has not recovered to at least the baseline level of vision in the treated eye.

Initial Phase 2a element of combined Phase 1/2a study

- We progressed into the Phase 2a element of the combined Phase 1/2a study.
- We were able to expand our assessment of efficacy into RP patients that have a greater baseline level of visual acuity (clarity of vision).
- All three of the first cohort of subjects in the Phase 2a part of the study reported a rapid and significant improvement in vision, on average equivalent to reading an additional three lines of five letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart, the standardised eye chart used in clinical trials to measure visual acuity, as seen in Figure 2.
- Later cohorts comprised patients with a greater baseline level of visual acuity than those treated earlier in the study to assess preliminary efficacy in patient groups with differing levels of remaining vision.
- A total of 22 patients have now been treated in the Phase 1/2a study and a good safety profile has been established, with no patients experiencing product-related serious adverse events and two patients experiencing surgical procedure-related loss of vision (one of whom has now recovered their vision and is back to at least baseline at one year post treatment).
- In February 2020, interim efficacy data from the study continued to show a meaningful clinical effect from the therapy at all time points out to 12 months post-treatment.
- In June 2020, further long-term data from the study have been gathered from patients at six, nine, twelve and now, for the first patient treated, eighteen months follow-up. The Company is pleased to report that the latest data continue to demonstrate the efficacy of the therapy, with a clinically meaningful benefit being observed at all time-points. These results are particularly encouraging as RP is characterised by inexorable progression to blindness, with no therapy currently available for the vast majority of patients.
- The degree of efficacy varies between patients, with mean results in a group of subjects who had a successful surgical procedure, set out in Figure 1.
- An application approval has been received from the MHRA to expand the ongoing trial to a UK site.

Figure 2

What does this mean for future development?

Milestones in the next two years

Regulatory approval has recently been received from both the FDA and MHRA for the expanded Phase 2a study in RP patients. We expect to commence treating patients shortly in both the US and the UK under the revised approved study protocol, subject to a continued easing of COVID-19 related restrictions at the relevant clinical sites. On this basis, we expect to present further data from the expanded Phase 2a clinical trial during the next twelve months and expect to have sufficient data from the study to enable us to seek approval in the second half of 2021 to commence a single pivotal clinical study with our hRPC cell therapy candidate in RP.

At this point, other indications will be assessed alongside retinitis pigmentosa, such as cone rod dystrophy.

Our progress towards improving patients' lives

Exosomes as a novel drug delivery vehicle

Potential as a novel drug delivery vehicle

- Our studies have identified the potential of our exosome technology platform as both a novel therapeutic candidate and as a drug delivery vehicle. Our focus has been on the potential of our exosomes as a drug delivery vehicle.
- In April 2020, we signed a collaboration agreement with an experienced pharmaceutical company to explore the potential use of exosomes to deliver novel therapeutics. The collaboration will focus on the use of exosomes for the delivery of gene silencing sequences created by the pharmaceutical company.
- In June 2020, we signed a research evaluation agreement with a major US biotechnology company. This collaboration will focus on the use of our exosomes for the delivery of the US biotechnology company's neuroscience therapeutic candidates.
- We are developing an exosome displaying proteins characteristic of the SARS-CoV-2 coronavirus with the objective of the exosome being used to deliver a vaccine against COVID-19.

Scalability

- We have tested the production of exosomes through our grant-funded collaboration between University College London and the Cell and Gene Therapy Catapult.
- The data demonstrated the feasibility of scaling up the production of our exosomes utilising state-of-the-art bioreactor systems.
- This represents a significant advance towards an industrial scale production process without affecting the quality and consistency of the final product.
- As part of the collaboration agreement to use exosomes to deliver gene silencing sequences, ReNeuron will be paid by the pharmaceutical company for manufacturing and loading the exosomes in the initial phase of the collaboration.

What does this mean for future development?

- We will continue to develop our exosomes as a novel vector for delivering third- party biological drugs.
- We intend to pursue opportunities to capitalise on the significant scientific and life sciences industry interest in exosomes. We will do this by forming further value-generating business partnerships covering this exosome technology.

> We are progressing in the development of our exosomes platform, focusing on its use as a novel vector for delivering third party drugs.

Exosomes explained

What are exosomes?

The exosomes released by our CTX cells are nano-sized packages of signalling molecules.

Therapeutic agents can be attached to exosomes as cargo. Exosomes have the ability to deliver this cargo to specifically targeted cells in the body.

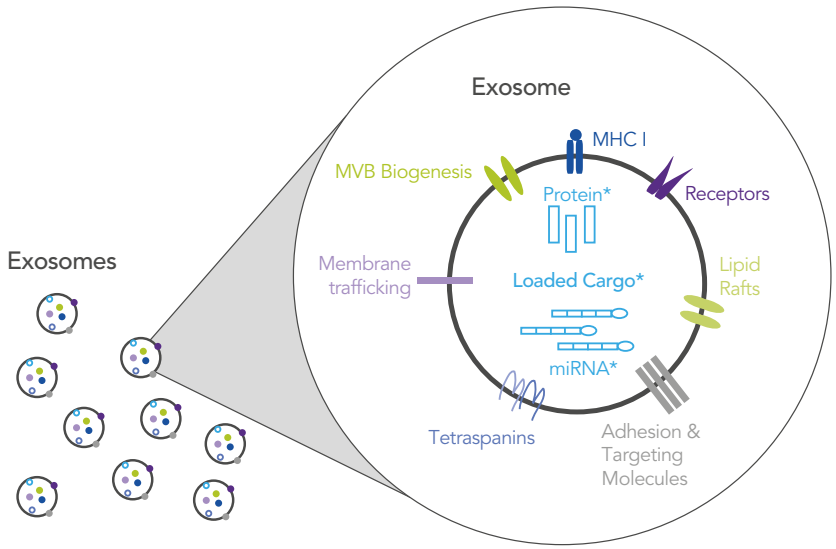
Advantages of exosomes as a delivery vehicle

- Natural carrier of nucleic acids and proteins, amenable for loading complex, hard-to-deliver therapeutic agents.
- Ease of bioengineering.
- Low immunogenicity.
- Intrinsically durable.

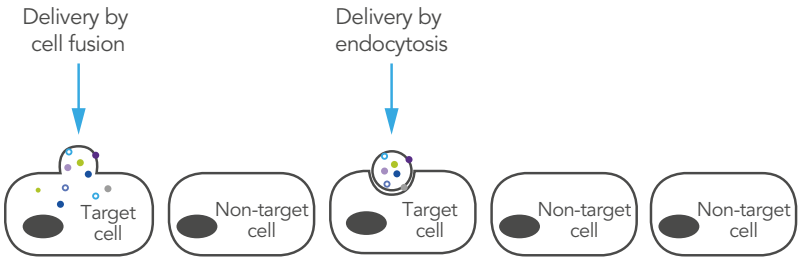
Advantages of ReNeuron's exosome technology

- Stable, consistent, high-yield.
- Proven ability to load miRNA and proteins.
- There is a potential for exosomes to work as a therapeutic in gene therapy.
- Able to cross the blood brain barrier.
- Could be engineered to target particular tissues.

Exosomes as a therapeutic delivery vehicle



There are two ways that cargo can be delivered, through:



Our progress towards improving patients' lives

iPSCs: expanding our therapeutic platform

A step towards developing further therapies in key areas of unmet need

Engineering CTX neural stem cells

- New data shows that our CTX neural stem cell line can be reprogrammed into induced pluripotent stem cells (iPSCs) and differentiated into other cell types.
- In essence, this means that the CTX neural stem cells can be reprogrammed back to being embryonic like cells that can be engineered into any other type of stem cell.

What is pluripotency?

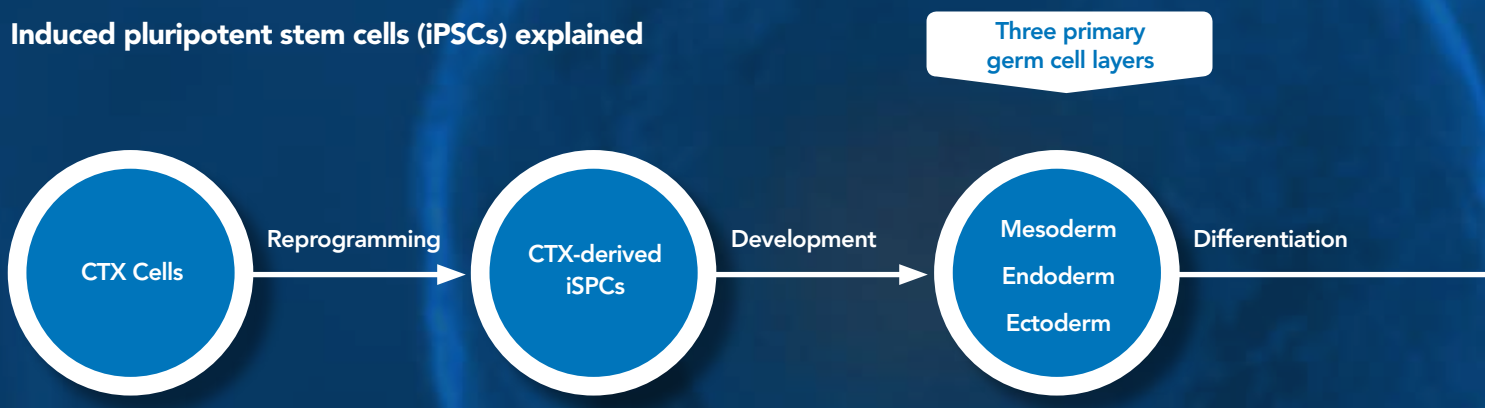
- Pluripotent stem cells are cells that have the capacity to self-renew by dividing and to develop into the three primary germ cell layers of the early embryo and therefore into all cells of the adult body.
- The new data demonstrate that CTX cells could be used to produce new conditionally immortalised allogeneic cell lines from any of the three primary germ cell layers which form during embryonic development. See below.

What does this mean for future development?

- Potential new cell lines can be efficiently created as cell therapy candidates targeting a broad range of diseases. A number of different cell lines are currently being developed.
- As a result, there is a potential to expand our therapeutic portfolio by developing further therapeutic candidates for subsequent out-licensing.
- There is a potential to produce exosomes with the ability to target specific tissues within the body.
- The maintenance of the immortalisation technology within these new cell lines may allow for the scaled production of 'off-the-shelf' allogeneic stem cells.

For **scientific terms** see the glossary on pages 96 to 97

Induced pluripotent stem cells (iPSCs) explained



> There is potential to expand our therapeutic portfolio by developing further therapeutic candidates for subsequent out-licensing.

Different cell lineages can be generated

New conditionally immortalised allogeneic (i.e. non-donor-specific) cell lines produced)

Potential for therapeutic agents used to treat diseases of unmet medical need

Scalability

Our immortalisation technology is retained which enables the efficient production of clinical-grade cell therapy candidates for subsequent licensing to third parties

Our progress towards improving patients' lives

CTX cells for stroke disability

Pre-clinical data

- A well-established rodent model of stroke was used to study the effects of our CTX cell therapy.
- The CTX cells were directly injected into the brain.
- Our results were particularly positive given that restricted blood supply to the brain, following a stroke, results in nerve cell death.
- The effects of our CTX cell therapy included the formation of new blood vessels, new nerve cells and new connections between nerve cells.

Clinical trials: Phase 1 study

- In this study, we included 11 stable, disabled stroke patients who were between six months and five years post-stroke.
- This study was a single centre, open-label, ascending dose trial to assess safety.
- The CTX cells were directly injected into the putamen (an area of the brain), and patients were followed up for over two years post-implantation.
- It was determined that these CTX cell injections at the doses tested were safe and well tolerated.

Clinical trials: Phase 2a study

- In this study, we included 23 disabled, stable stroke patients, who were between 2 and 13 months post-stroke.
- This study was a single arm, open-label trial using the highest dose tested in Phase 1. This trial was "single arm" because all the patients were administered the same dose.
- CTX cells (20 million cells) were directly injected into the putamen, and patients were followed up for 12 months post-implantation.
- No cell-related safety issues were identified.
- The Modified Rankin Scale (or mRS, a globally used measure of functional disability and dependence in stroke sufferers) was used as a secondary end-point for this study.
- As shown by the figure to the left, 7 out of 20 (35%) patients demonstrated a clinically meaningful improvement at 12 months post-implantation. An even higher response rate (6/12; 50%) was observed in pre-specified patients who had some residual upper limb movement at time of treatment.

Modified Rankin Scale (mRS)

0 No symptoms at all

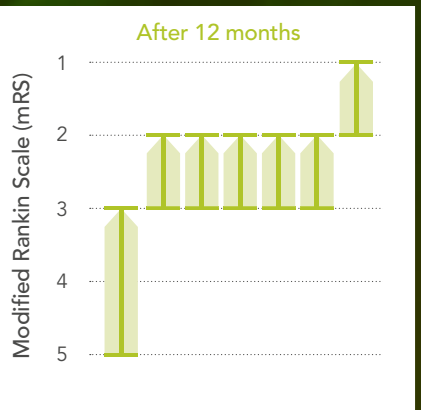
1 No significant disability despite symptoms

2 Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance

3 Moderate disability; requiring some help, but able to walk without assistance

4 Moderately severe disability; unable to walk and attend to own bodily needs without assistance

5 Severe disability; bedridden, incontinent and requiring constant nursing care and attention



Clinical trials: Phase 2b study

- Patient dosing commenced in the study PISCES III, a randomised, placebo-controlled clinical trial in 110 patients.
- We are seeking a one point or more improvement in the mRS scoring, at six months post surgery, in CTX-treated patients that have a mRS score of 3 or 4 at baseline.
- The study is being conducted in up to 40 sites, of which 12 surgical sites and 22 assessment sites have been activated.
- The protocol was amended which, amongst other changes, increases the number of patients to receive CTX therapy as opposed to placebo, with the size of the Phase 2b study increasing from 110 to 130 patients.
- Patient recruitment which was put on hold due to COVID-19 related restrictions, will remain suspended in the US for the foreseeable future; clinical trial sites will be kept open and patients already treated will be followed up over time in line with the clinical trial protocol.

What does this mean for future development?

Future milestones

- The CTX cell therapy candidate will continue through regional partnerships. Our exclusive licensing partner in China, Fosun Pharma, will develop the Company's CTX cell therapy candidate for stroke disability in the licensed territory (Greater China) where we have the potential to benefit from future operational and regulatory milestones under this out-license agreement.
- Clinical trial applications have recently been filed by Fosun Pharma to open clinical sites in the licensed territory to build on the clinical data already generated in the US.
- In May 2020, we announced the publication of new positive non-clinical data relating to our CTX cell therapy candidate in Huntington's disease (HD). The CTX cell therapy candidate will be available for licensing in HD and other indications.

Chief Executive Officer's review of performance

The decision we have recently taken to focus our in-house activities on our retinal disease and exosome-based programmes provides the Company with significant near-term opportunities to deliver value-enhancing data and commercial partnerships.

> During the period under review, and subsequent to it, we have continued to generate encouraging positive efficacy data from the ongoing US Phase 2a clinical trial of our hRPC cell therapy candidate in retinitis pigmentosa.

Olav Hellebø
Chief Executive Officer

12 August 2020

Review of clinical programmes

hRPC (human retinal progenitor cells) for retinal disease

During the period under review, and thereafter, we have made significant progress with our ongoing clinical programme targeting retinitis pigmentosa (RP). RP is a group of hereditary diseases of the eye that lead to progressive loss of sight due to cells in the retina becoming damaged and eventually dying.

The ongoing Phase 1/2a clinical trial is an open-label study to evaluate the safety, tolerability and preliminary efficacy of our hRPC stem cell therapy candidate in patients with advanced RP. The Phase 2a segment of the study, which uses a cryopreserved hRPC formulation, enrols subjects with some remaining retinal function and, thus far, has been conducted at two clinical sites in the US – Massachusetts Eye and Ear in Boston and Retinal Research Institute in Phoenix, Arizona.

In April 2019, initial data from the first cohort of three patients in the Phase 2a segment of the study were presented at the sixth annual Retinal Cell and Gene Therapy Innovation Summit in Vancouver, Canada. The data demonstrated a sustained improvement in visual acuity compared with baseline in these patients, as measured by the number of letters read on the ETDRS chart (the standardised eye chart used to measure visual acuity in clinical trials).

In October 2019, further positive efficacy data from the study were presented at the American Academy of Ophthalmology Annual Meeting (AAO) in San Francisco. At this point, 22 patients had been treated in the study, consisting of 12 patients in the Phase 1 segment of the study and 10 patients in the Phase 2a segment of the study. Eight out of the ten Phase 2a patients treated had reached at least the one month follow up time point. The visual acuity data presented at the AAO conference from the patients treated in the Phase 2a segment of the study continued to show the hRPC therapy's ability to deliver clinically meaningful signals of efficacy in a patient population where inexorable disease progression is the norm.

We announced further updates regarding the Phase 2a study in February 2020 and, more recently, in June 2020. This latest update summarised data gathered from patients at six, nine, twelve and, for the first patient treated, 18 months follow-up. The latest data continue to demonstrate the efficacy of the therapy, with a clinically meaningful benefit being observed at all time-points. The results announced in February 2020 excluded two subjects who experienced sight loss in the treated eye as a result of complications arising from the surgical procedure. In the June update, we reported that one of these two patients has now recovered their vision and is back to at least baseline at one year post treatment.

Also in June 2020, we announced that the Group had received regulatory approval from both the FDA and MHRA to expand the ongoing Phase 2a clinical

study to treat patients with RP at a higher dose level, at clinical sites in both the US and the UK. We intend to open the ongoing study to a highly experienced UK clinical site, the Oxford Eye Hospital, with Professor Robert MacLaren, a world-renowned leader in the treatment of retinal diseases, as Principal Investigator. These approvals will enable the treatment of up to a further nine patients in the Phase 2a extension segment of the study (beyond the ten Phase 2a patients already treated).

We expect to commence treating patients shortly in both the US and the UK under the revised approved study protocol, subject to a continued easing of COVID-19 related restrictions at the relevant clinical sites. On this basis, and as announced in June, we expect to present further data from the expanded Phase 2a clinical trial during the next twelve months and we expect to have sufficient data from the study to enable the Group to seek approval in the second half of 2021 to commence a single pivotal clinical study with our hRPC cell therapy candidate in RP.

Our hRPC cell therapy candidate offers a number of potential advantages over alternative approaches to the treatment of RP. Firstly, our cell therapy candidate is independent of the many specific genetic defects that collectively define RP as a disease, thereby allowing a much broader potential patient population to be eligible for the treatment. Secondly, the cells are cryopreserved, enabling on-demand shipment and use at local surgeries and hospitals. Finally, the cells are injected directly to the site of retinal degeneration, allowing a greater chance of anatomic restoration of photoreceptor function.

Our RP clinical programme has been granted Orphan Drug Designation in both Europe and the US, as well as Fast Track designation from the FDA in the US. Orphan Drug Designation provides the potential for a significant period of market exclusivity once the therapy is approved in those territories. Fast Track designation provides eligibility for an accelerated approval and priority review process by the FDA.

Exosome and iPS cell technologies

Our exosome technology is being exploited as a novel vector for delivering third party biological drugs. We have developed exosomes derived from our CTX human neural stem cell line that have a natural ability to cross the blood brain barrier and can thus be used to deliver therapeutics for diseases of the brain. These exosomes can be produced through a fully qualified, xeno-free, scalable process and the clinical-grade source cell-line ensures consistent exosome product. The exosomes can be loaded with a diverse range of potential therapeutics, such as siRNA/mRNA/miRNA, CRISPR/Cas9, antibodies, peptides and small molecules.

In July 2019, we announced the grant of a number of key patents in Europe, Japan, China and South Korea covering our exosomes and their methods of production. In August 2019, we announced a new grant-funded collaboration with the European Cancer Stem Cell Research Institute at Cardiff University to develop novel systems to enable the delivery of therapeutic nucleic acids across the blood brain barrier using our exosomes.

In April and June 2020, we announced separate commercial collaboration agreements to explore the potential of our exosomes to deliver therapeutic agents to the brain. The first of these agreements, with a major pharmaceutical company, focuses on the use of our exosomes for the delivery of novel gene silencing therapeutics. The second, with a major US biotechnology company, focuses on the use of the exosomes to deliver the US biotechnology company's neuroscience therapeutic candidates.

Further collaborations with pharmaceutical/biotechnology companies are anticipated to commence over the coming months. In response to COVID-19, we have also developed a proprietary exosome displaying the SARS-CoV-2 spike protein with the objective of out-licensing it for the potential delivery of COVID-19 vaccines.

In October 2019, we presented new data demonstrating the stability and scalability of new stem cell lines derived from our CTX human neural stem cells following re-programming to an embryonic stem cell-like state (induced pluripotent stem cells, or iPSCs). This means that we are able to take our CTX neural stem cells back to being stem cells that are able to differentiate into any other type of stem cell, including bone, nerve, muscle and skin. Further, we showed that the new stem cell lines generated could be grown at scale by virtue of the Group's conditional immortalisation technology, enabling the efficient production of clinical-grade, allogeneic ("off-the-shelf") cell therapy candidates.

As a result of the above findings, we are exploring the potential of our iPSC technology to be utilised to develop further new, immortalised allogeneic cell lines of varying types as potential therapeutic agents in diseases of unmet medical need for subsequent licensing to third parties. For example, the production of allogeneic haematopoietic stem cells from our iPSCs could potentially provide an alternative approach to those cancer immunotherapies currently in development that rely on the use of the patient's own T-cells. The iPSC-derived cell populations can also be utilised for the production of exosomes with specific tissue targeting, thus providing further scope for a wide range of industry partnerships.

CTX for stroke disability

During the period, we continued to progress the clinical development of our CTX cell therapy candidate for stroke disability, via our PISCES III clinical study, a randomised, placebo-controlled, Phase 2b clinical trial being undertaken in the US. Patients in the study are treated between six and 24 months after their stroke and are randomised to receive either CTX therapy or placebo treatment. The primary end-point of the PISCES III study is the proportion of patients showing a clinically important improvement (at least one point) on the modified Rankin Scale (mRS) at six months post-treatment compared with baseline. The mRS is a global

Chief Executive Officer's review of performance

measure of disability or dependence upon others in carrying out activities of daily living and is accepted by regulatory authorities as an appropriate end-point for marketing approval in stroke disability.

In February 2020, we announced that positive data from the PISCES II Phase 2a clinical trial of CTX in stroke disability had been published in the Journal of Neurology, Neurosurgery, and Psychiatry. PISCES II was a single arm, open-label study in patients living with significant disability resulting from ischaemic stroke. A total of 23 stable stroke patients with moderate to severe disability were treated with a single dose of 20 million CTX cells a median of seven months post-stroke. Clinically meaningful improvements in disability scales were measured out to 12 months post-implantation.

In June 2020, we announced that, following a review of programme priorities and resource requirements, we intended to focus the Group's resources on our retinal disease programme and our exosome and induced pluripotent stem cell (iPSC) research platforms. Consequently, we have suspended the PISCES III clinical trial in the US and our stroke disability programme will now continue through regional partnerships. Fosun Pharma, our exclusive licensing partner in China, will develop the CTX cell therapy candidate for stroke disability in the licensed territory (Greater China including Hong Kong, Macao and Taiwan) where the Company has the potential to benefit from future operational and regulatory milestones under this out-license agreement. Clinical trial applications have recently been filed by Fosun Pharma to open clinical sites in the licensed territory to build on the clinical data already generated in the US. Patient recruitment in the PISCES III study, which has been on hold due to COVID-19 related restrictions, will remain suspended in the US for the foreseeable future; clinical trial sites will be kept open and patients already treated will be followed up over time in line with the clinical trial protocol.

As part of the June 2020 programme update, we announced that our CTX cell therapy candidate would be made available for licensing in stroke disability outside China. We further announced that the CTX cell therapy candidate would be available for licensing in other indications where the candidate might have the potential to address the deficits in those indications. As an illustration of this potential, in May 2020 we announced the publication of new positive data relating to our CTX cell therapy candidate in the journal Stem Cells. The new data showed for the first time that our CTX human neural stem cell line can rescue deficits associated with an accepted animal model of Huntington's disease, a progressive genetic brain disorder.

Other activities

In April 2019, we announced the signing of an exclusive licence agreement with Fosun Pharma for the development, manufacture and commercialisation of both our CTX and hRPC cell therapy programmes in the People's Republic of China. Under the terms of the licence agreement, Fosun Pharma will fully fund the development of our CTX and hRPC cell therapy programmes in China, including clinical development and subsequent commercialisation activities. Fosun Pharma has also been granted rights to manufacture the licensed products in China. In return, ReNeuron received £6.0 million (before withholding tax) on entering into the agreement and will receive up to £6.0 million in near-term operational milestones and up to £8.0 million in future regulatory milestone payments. In addition, ReNeuron will receive post-launch profit threshold milestone payments derived from the licensed products, leading to total estimated milestone payments of £80.0 million provided all milestones and profit thresholds are successfully met, as well as tiered royalties at rates between 12% and 14% on sales of the licensed products in the Chinese market.

We continue to work closely with Fosun Pharma as it pursues the development, manufacture and commercialisation of our cell therapy programmes in the People's Republic of China, with the CTX programme for stroke disability being the initial focus of activities.

Summary and outlook

During the period under review, and subsequent to it, we have continued to generate encouraging positive efficacy data from the ongoing US Phase 2a clinical trial of our hRPC cell therapy candidate in retinitis pigmentosa. We are pleased to have recently received regulatory approvals in both the US and the UK to pursue this study in further patients at a higher dose level and we look forward to presenting further data from this extended study in due course.

Additionally, we have been very encouraged to see the potential of our exosome and iPS cell technologies emerge during the period, with further collaboration agreements expected in the near term to complement the agreements we have already signed with major pharmaceutical/biotechnology companies regarding our exosome programme.

The decision we have recently taken to focus our in-house activities on our retinal disease and exosome-based programmes provides the Group with significant near-term opportunities to deliver value-enhancing data and commercial partnerships. Our stroke disability programme will continue through regional partnerships and we are pleased to be working with Fosun Pharma as our partner for China, following the signing of the exclusive licence agreement for both our CTX and hRPC programmes in that territory during the period.

Olav Hellebø
Chief Executive Officer

Financial review

Michael Hunt ACA
Chief Financial Officer

12 August 2020

Revenues in the year amounted to £6.1 million (2019: £0.05 million), being an upfront licence fee of £6.0 million received from Fosun Pharma in respect of the license agreement signed with that company in April 2019, together with £0.1 million (2019: £0.05 million) of royalties from non-therapeutic licensing activities. Grant income of £0.1 million (2019: £0.8 million) has been recognised in other income. In 2019, other income also included £1.9 million relating to an exclusivity fee received during out-licensing negotiations.

Research and development costs in the year were £16.3 million (2019: £16.2 million) and accounted for 79% of operating expenses (2019: 77%). General and administrative expenses were £4.2 million (2019: £4.8 million), the decrease in costs being primarily due to reductions in staff costs and reductions in legal and professional fees over the prior year.

Finance income represents income received from the Group's cash and investments and gains from foreign exchange, with lease interest arising from the application of IFRS 16 shown in finance costs. Finance income was £0.6 million in the year (2019: £1.1 million), primarily reflecting reduced foreign exchange gains. The Group holds cash and investments in foreign currencies in order to hedge against operational spend in those currencies.

The total tax credit for the year was £3.0 million (2019: £2.9 million). This was offset by overseas taxation of £0.6 million (2019: £Nil).

As a result of the above, the total comprehensive loss for the year reduced to £11.4 million (2019: £14.3 million).

Net cash used in operating activities was £14.3 million (2019: £11.9 million), largely reflecting the operating costs incurred during the period, net of the Fosun Pharma licence fee of £5.4 million (net of withholding tax). The Group had cash, cash equivalents and bank deposits totalling £12.6 million at the year-end (2019: £26.4 million).

Directors' duties

The Directors of ReNeuron Group plc and its subsidiary companies are required to act in accordance with a set of general duties which are detailed in the Companies Act 2006.

As part of their induction, Directors are briefed on their duties and they are regularly updated by both the Company Secretary or external advisers. Directors may also seek advice on their duties at any time, either via the Company Secretary or externally. More details are set out in the Corporate Governance section on page 43.

Section 172 Statement

The Directors are required by the Companies Act 2006 to act in the way they consider, in good faith, would most likely promote the success of the Company for the benefit of its shareholders as a whole and in doing so, are required to have regard to the following:

- The likely consequences of any decision in the long term;
- The interests of the Company's employees;
- The need to foster the Company's business relations with suppliers, customers and others;
- The impact of the Company's operations on the community and the environment;
- The Company's reputation for high standards of business conduct; and
- The need to act fairly as between members of the Company.

In 2018, the Group adopted the Corporate Governance Code for Small and Mid-Size Quoted Companies from the Quoted Companies Alliance (the "QCA Code"). The QCA code is an appropriate code of conduct for the Group's size and stage of development. Details of how the Group applies the ten principles of the QCA Code are set out on pages 40 to 45.

The Chairman's and Chief Executive Officer's statements describe the Group's activities, strategy and future prospects including considerations for long-term decision making on pages 06 and 24.

The Board considers the Group's major stakeholders to be its shareholders, its employees and its suppliers.

Overview as to how the Board performed its duties

Shareholders

The Board is committed to openly engaging with the Company's shareholders and recognising the importance of an effective dialogue. It is important that shareholders understand the Group's strategy and objectives, so these must be explained clearly and feedback received and issues raised carefully considered. Details of shareholder engagement are set out in sections 2 and 10 of the Corporate Governance Report on pages 41 and 45.

Employees

The Group is a relatively small organisation and Executive Directors have regular day-to-day contact with employees at all levels, both formal and informal. The CEO regularly briefs employees on developments in the business and conducts question and answer sessions at these times. An Employee Engagement Group provides a more formal means of consultation with staff, and a Staff Engagement Survey is carried out annually.

Suppliers

The Board takes a close interest in relations with key suppliers whose performance is crucial to the Group's success. The Group endeavours to maintain good relationships with its suppliers and seeks to pay them promptly in accordance with the contracted terms. Where appropriate, the activities of suppliers are subject to audit.

Community and environment

The Board is mindful of the potential social and environmental impacts of the Group's activities. The Board is committed to minimising the environmental effect of the Group's activities wherever possible and seeks rigorous compliance with relevant legislation.

Business reputation

The Group operates in a highly regulated sector and the Board is committed to maintaining the highest standards of conduct. Staff behaviour is governed by appropriate policies, including anti-bribery policies, supported by a whistle-blowing process. There were no reported incidents in relation to this policies in the year ended 31 March 2020.

Sustainability

The Directors believe that operating the business responsibly is key to its long-term future and success.

People

The Group relies for its success on the intellectual qualities of its employees. Therefore it seeks to recruit and retain highly skilled and well-qualified employees.

Reward

The Group recognises the importance of a fair and competitive reward package which seeks to incentivise high performance and align the interests of the employees and the Group. Salaries are competitive, and the bonus scheme is based upon the attainment of both personal and corporate objectives. The Group also offers pension entitlement and health insurance or gym membership. Details of the Group's employee share schemes are set out in note 27 to the Financial Statements.

Diversity

The Board believes in a diverse and gender balanced workforce and the Group's Equal Opportunities Policy ensures the provision of equal opportunities in all areas of employment.

At 31 March 2020 the Group employed 29 men and 33 women.

Employee engagement

Employee engagement is described in the Section 172 report above.

Development

Employees have significant opportunities for learning and development, often identified from the annual appraisal process. Examples include PhD studies, process management and quality management skills such as six sigma black belt, as well as soft skill courses and various formal training courses identified as part of employees' annual personal development plans.

Health and safety

Keeping its employees safe is a priority for the Group. A Health and Safety ("H&S") Committee meets regularly, monitors performance and drives improvements through H&S Committee representatives. A number of employees work in a laboratory environment and are trained and required to comply with the relevant regulations and best practice. The H&S Committee reports to the Group's Senior Management Team and the Board.

The Group also offers Employee Wellbeing support.

During the COVID-19 crisis, the Group has made resources available to support the mental health needs of employees who may feel isolated by working from home.

Policies and procedures

The Group has a comprehensive Employee Handbook and supporting policies which set standards for ensuring that the Group's business activities are conducted in a responsible manner for the benefit of its shareholders, employees, research partners and suppliers. The Board believes that ensuring employees understand their responsibilities and act in an ethical way is vital to the Group's future success.

Patients

As explained earlier in this report, the Group's objective is to produce new stem cell therapies for the treatment of patients whose medical needs are currently unmet. The Group's two clinical stage candidates are in development for the treatment of patients suffering from retinitis pigmentosa and disability as a result of a stroke while research with exosomes has indicated their potential as a drug delivery system which can cross the blood brain barrier.

Exosomes may also have potential for use as a delivery vehicle for viral vaccines.

In April 2019 the Group licensed its hRPC and CTX products to Fosun, covering the Greater China market and will look to further patient access to its stem cell based therapies via future licensing arrangements in other territories.

Clinical trials

ReNeuron has established a standard set of Standard Operating Procedures ("SOPs") and policies which govern the conduct of the clinical trials which it sponsors. These SOPs and policies ensure compliance with internationally recognised and adopted standards together with national and international legislation in the relevant territories. They also ensure consistency across studies and programmes in the way that data is collected, analysed and stored. Compliance with the Group's SOPs and policies is monitored by its internal Quality Assurance department.

Our social impacts

The Group endeavours to maintain links with universities and local schools. University students and schoolchildren have visited the Pencoed site and been given an introduction to practical research based science. The Group has supported PhD research, and placements are provided from time to time.

Environmental impact

Due to the nature of the business, the Board considers that the Group has a low environmental impact. The Group seeks to minimise any environmental impact of its operations and complies with relevant regulations and legislation.

Risks and uncertainties

Risk	Potential impact	Mitigation action/control
Clinical and regulatory risk There are significant inherent risks in developing stem cell therapies for commercialisation due to the long and complex development process. Any therapy which we wish to offer commercially to the public must be put through extensive research, pre-clinical and clinical development, all of which takes several years and is extremely costly. The regulatory process is both complex and multi-jurisdictional.	**Clinical potential impact** The Group may fail to develop a drug candidate successfully because we cannot demonstrate in clinical trials that it is safe and efficacious. Delays in achieving regulatory approval may impose substantial costs on the business. If a product is approved, the regulators may impose additional requirements, for example, restrictions on the therapy's indicated uses or the levels of reimbursement receivable. Once approved, the product and its manufacture will continue to be reviewed by the regulators and may be withdrawn or restricted. **Regulatory potential impact** Reduction of an income stream through regulation could adversely affect the commercial viability of a drug product. Withdrawal of a drug product by a particular regulatory agency would prevent sale in that particular territory and may be followed by regulators in other territories.	The Group's internal development expertise and knowledge in its targeted clinical areas will enable it to develop therapeutic products in a manner which will substantially mitigate, but which cannot eliminate this risk in the future. The Group looks to employ suitably qualified and experienced staff. It also consults, where necessary, with regulatory advisers and regulatory approval bodies to ensure that regulatory requirements are met. Additionally, the Group seeks to foster a culture where quality is a key priority. Both it and its clinical and manufacturing partners comply with Good Clinical Practice and Good Manufacturing Practice and the Group employs rigorous processes in its research and development of therapeutic products. The Group uses experienced and reputable clinical research organisations in its clinical trials.
Intellectual property risk Intellectual property protection remains fundamental to the Group's strategy of developing novel drug candidates. The Group's ability to stop others making a drug, using it or selling the invention or proprietary rights by obtaining and maintaining protection is critical to our success. The Group manages a portfolio of patents and patent applications which underpin its research and development programmes.	There is a risk that intellectual property may become invalid or expire before, or soon after, commercialisation of a drug product and the Group may be blocked by other companies' patents and intellectual property.	The Group invests significantly in maintaining and protecting this intellectual property through the use of expert lawyers and patent agents to reduce the risks over the validity and enforceability of our patents. The protection of the Group's intellectual property is a significant consideration throughout the Group's contracting activity.

Risk	Potential impact	Mitigation action/control
Manufacturing and supply risk The Group's ability to successfully scale up production processes to viable clinical trial or commercial levels is vital to the commercial viability of any product.	**Manufacturing potential impact** Inability to sell a drug product on a commercially viable scale. Product manufacture is subject to continual regulatory control and products must be manufactured in accordance with Good Manufacturing Practice. Any changes to the approved process may require further regulatory approval. Availability of raw materials is extremely important to ensure that manufacturing campaigns are performed on schedule. **Supply potential impact** Substantial cost increases and delays in production which could adversely impact on the Group's financial results and cash liquidity.	The Group utilises reputable contract manufacturing organisations, experienced in meeting the requirements of Good Manufacturing Practice. The Group maintains contractual relationships with key manufacturers and suppliers to ensure availability of supply and sufficient notice of disruption. Additionally, the Group seeks to avoid reliance upon any single supplier or manufacturer.
Financial risk The financial risks faced by the Group include foreign currency risk, liquidity risk and risk associated with cash held on deposit with financial institutions.	These risks may adversely affect the Group's financial results and cash liquidity.	The Board reviews and agrees policies for managing each of these risks. The Group's main objectives in using financial instruments are the maximisation of returns from funds held on deposit, balanced with the need to safeguard the assets of the business. The Group does not enter into forward currency contracts. The Group holds currency in US dollars and euros to cover short and medium-term expenses in those currencies.
Fundraising risk The Group has incurred considerable losses since its inception and is dependent upon equity and public grant financing. It does not currently have any approved or revenue generating products.	The Group may not be able to raise additional funds that will be needed to support its product development programmes or commercialisation efforts. Any new funds raised may lead to dilution of existing investors.	The Group is continually seeking business development opportunities which enable it to support the future costs of development of its drug products and commercialise them successfully. Additionally, the Board places considerable emphasis on communication with shareholders and potential investors, to maximise the chances of successful future fundraising.
Cyber risk There is risk that third parties may seek to disrupt the Group's business, or perpetrate acts of fraud using digital media.	Loss of IT systems for a significant period may result in delays in the development and commercialisation of drug product. Fraud may result in financial loss.	The Group is focused on maintaining a robust and secure IT environment that protects its corporate data and systems. IT systems are continuously monitored and employees are trained to be aware of cyber security and the associated risks.

Risks and uncertainties

Risk	Potential impact	Mitigation action/control
Site and system disruption risk Unexpected events could disrupt the business by affecting its key facility, critical equipment, IT systems or a number of employees.	Loss of IT systems for a significant period or key employees may result in delays in the development and commercialisation of drug product.	The Group has developed a business continuity plan to ensure that it can respond effectively to identified risks. All critical equipment will have active service contracts in place. Business continuity insurance is in place.
Staff turnover risk The Group is dependent upon its ability to attract and retain highly qualified and skilled staff.	Loss of key staff could delay the development and commercialisation of drug product.	The Group offers attractive employment packages, including share incentive plans, and actively encourages employee engagement in the business. Employees also have significant opportunities for learning and development as well as promotion opportunities born out of the Group's staff appraisal and succession planning processes.
Risks associated with the departure of the United Kingdom from the EU ("Brexit")		
SME and Orphan Drug status Within the EU, the Group holds SME status, together with Orphan Drug Designation in respect of its hRPC product.	Loss of SME status and Orphan Drug Designation within the EU upon the United Kingdom's exit would expose the Group to increased costs of development and commercialisation of drug product within the EU.	The Group has incorporated ReNeuron Ireland Limited to enable it to maintain a presence within the EU and to manage and mitigate the risks and uncertainties surrounding the final outcome of exit negotiations between the United Kingdom and the EU.
Regulatory risks After Brexit, regulatory requirements for the development and approval of drug products and medical devices may diverge between the EU and the UK.	The EU is seen as a major future market for the Group's products. The regulatory divergence may complicate and slow the process of developing and commercialising drug product in the EU.	The Group has considerable experience of dealing with major overseas regulators including in the EU and the USA and will monitor changing requirements and adapt accordingly.
Currency risks The Group makes purchases of supplies and services overseas, notably in the EU and the USA.	Currency volatility or a post-Brexit depreciation of sterling may increase costs.	The Group will monitor the situation and will utilise the methods described under financial risk above to mitigate the risks.

Risk	Potential impact	Mitigation action/control
Risks associated with the COVID-19 pandemic and associated public health measures		
In common with many businesses world-wide the Group's activities have been disrupted by the economic effects of the public health measures enacted to contain the spread of the coronavirus.	Government measures implemented in the UK and the USA cause the ongoing clinical trials to be subject to delays in patient recruitment. The extent of the delay and the eventual cost implications are unknown. The Group's internal research projects may be delayed.	The Group will monitor the situation and when it is free to do so, will take appropriate action consistent with staff and patient safety. The Group implemented home-working wherever possible from 17 March 2020. Where staff have been required to attend the Group's premises, appropriate social distancing and hygiene practices have been implemented. Laboratory staff continue to work to safely maintain the Group's essential research work. Priority internal research projects are progressing to current timelines. Patient recruitment has been on hold in the Group's clinical trials due to the COVID-19 related restrictions. Wherever possible, follow-up consultations with existing patients are taking place remotely. Patient recruitment will re-commence subject to an easing of these COVID-19 related restrictions at the relevant clinical sites.
The Group's fundraising activities may be constrained by the continuing economic effects of the government measures to contain the spread of the coronavirus.	Loss of economic confidence in financial markets may either reduce the level of future funding available to the Group, or prevent it from raising funds within the necessary timescale.	The Board recognises the need for further fundraising in the near future and will continue its dialogue with shareholders and potential investors. The Board will fully consider all stakeholders' interests during this process.

In addition, and in common with other small biotechnology companies, the Group is subject to a number of other risks and uncertainties, which include:

- the early stage of development of the business;
- availability and terms of capital needed to sustain operations, and failure to secure partnerships that will fund late-stage trials and commercial exploitation;
- competition from other companies and market acceptance of its products; and
- its reliance on consultants, contractors and personnel at third-party research institutions.

Pages 08 to 33 of this Annual Report and Accounts comprise the Strategic Report for the Group which has been prepared in accordance with chapter 4A of part 15 of the Companies Act 2006.

Approved by the Board and signed on its behalf by:

Michael Hunt
Chief Financial Officer

12 August 2020