Our progress for developing life-changing therapies

Development Pipeline

Programme	Indication	Pre-clinical	Phase 1	Phase 2	Next Milestones
hRPC	Retinitis Pigmentosa				Further data read-outs from expanded Phase 2a study expected Q4 2021 Pivotal trial to commence in H2 2022, subject to Phase 2a data
Exosomes platform	Neurodegeneration, Oncology, Vaccines (e.g. COVID-19)				Additional proof of concept data from current research collaborations expected in 2021
iPSC platform	Oncology, Diabetes				Validation of technology and publication of pre-clinical proof-of-concept data
CTX cell line	Stroke Disability				Currently partnered in China with FOSUN 复星 Open for partnerships outside China

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 outweigh the risks.

hRPC for retinal diseases

26 patients have been treated in the Phase 1/2a study including 4 in the expanded Phase 2a.

New clinical sites opened with sites in the US, EU and UK.

Subjects followed out to 12 months show a clear efficacy signal with a favourable risk/benefit profile.

Read more

See pages 18 to 19

Exosome nanomedicine platform

Our focus has been on the potential of our exosomes as a drug delivery vehicle.

7 ongoing research collaboration projects ongoing with both commercial and academic partners.

Our medium-term goal is to deliver in-vivo proof of concept data.

Read more

See pages 20 to 21

iPSCs platform

Our iPSCs can develop into new conditionally immortalised cell lines as potential therapeutic agents for subsequent licensing to third parties.

New conditionally immortalised cell lines generated from our iPSC platform as potential therapeutic agents for cancer immunotherapy and type 1 diabetes.

Research collaborations under negotiation and ongoing to validate the technology and publish pre-clinical proof of concept data.

Read more

See pages 22 to 23

Our progress towards changing 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 1a 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.

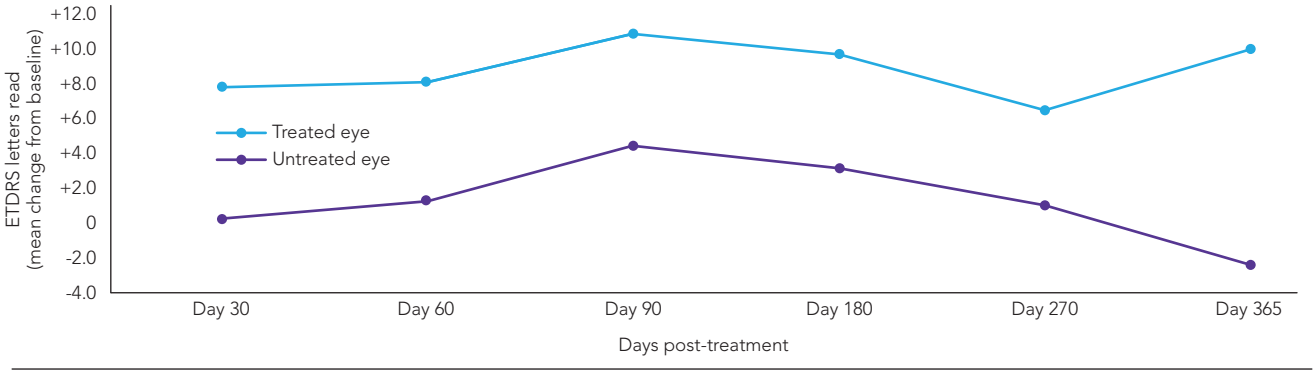
Initial Phase 2a element of combined Phase 1/2a study

- 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).
- Later cohorts comprised of 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 were treated in the Phase 1/2a study and a good safety profile was established, with no patients experiencing product-related serious adverse events.
- As seen on Figure 2, the mean change is visual acuity from baseline for nine of the subjects showed a clinically significant improvement beginning early, equivalent to reading approximately 2 lines, on the standardised eye chart used in clinical trials to measure visual acuity, as seen in Figure 1.
- The data continues to demonstrate the efficacy out to 12 months 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.

Figure 1

Figure 2: Phase 2a Efficacy Results, Mean changes in ETDRS letters read (treated eye vs untreated eye)

	Day 30 (n=9)	Day 60 (n=9)	Day 90 (n=9)	Day 180 (n=9)	Day 270 (n=8)	Day 365 (n=7)
Treated eye	+7.9	+8.0	+10.8	+9.6	+7.1	+9.9
Untreated eye	+0.2	+1.2	+4.4	+3.4	+1.2	-3.2
Difference	**+7.7**	**+6.8**	**+6.4**	**+6.2**	**+5.9**	**+13.1**



*excluding 1 patient with surgery-related vision loss **Some patients have not completed due to COVID-19

Extended Phase 2a study

Extended Phase 2a study

- Our extended study includes enhancements in patient selection, dose, surgical technique and efficacy assessments. We aim to treat a total of nine subjects with established RP, with a dose escalation from 1m to 2m cells.
- In January 2021, we opened a new US site, the Casey Eye Institute, Oregon Health & Science University and two further clinical sites have since been opened, one in Spain, the Institut de la Màcula, Barcelona and one in the UK, the Oxford Eye Hospital, Oxford.
- Four out of the nine additional subjects have been treated to date but a presumed case of bacterial endophthalmitis led to precautionary temporary study enrolment suspension. However, following a completed investigation, and with Data & Safety Monitoring Board approval, the study has reopened to enrolment in the US with amendments being filed to reopen in the UK and Spain.

What does this mean for future development?

Next milestones in the next two years

- Three-month data from extension segment of Phase 2a study expected to be available in Q4 2021.
- Our partnering strategy to be based on full Phase 2a data.
- The Company anticipates that, subject to the sufficiency of this expanded Phase 2a data, it will be able to seek regulatory approval to commence a pivotal clinical study in the second half of 2022 with its hRPC cell therapy candidate in RP.
- At this point, other indications will be assessed alongside retinitis pigmentosa, such as Cone Rod Dystrophy.

Exosomes as a novel drug delivery vehicle

What are exosomes?

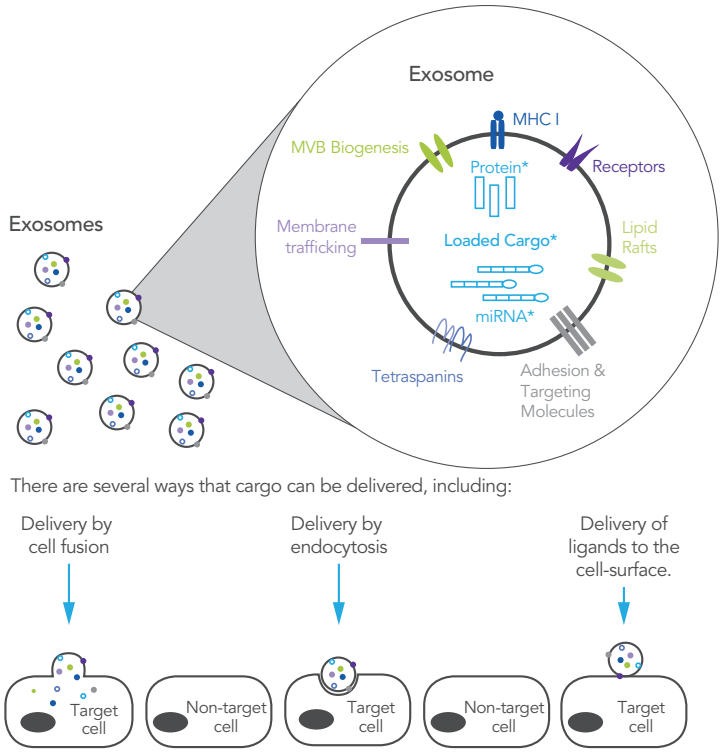
What are exosomes?

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

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

Our studies have identified the potential of our exosome technology platform as both a novel therapeutic candidate and as a drug delivery vehicle.

Exosomes as a therapeutic delivery vehicle



Pre-clinical research

- We have shown highly efficient loading of nucleic acid payloads in our exosomes.
- Our exosome candidates have also demonstrated functional payload delivery, both in vitro and in vivo, to the brain and peripheral tissues via repeat-dose intravenous administration.
- Evidence of target knockdown was observed in key peripheral tissues including heart, kidney and skeletal muscle organs, suggesting these exosomes have the potential to deliver payloads to therapeutically-meaningful levels to a variety of tissues.
- We have successfully decorated the surface of our exosomes with a specific tissue-targeting peptide. This proprietary peptide was modified to enhance binding to the exosome surface, resulting in a 10-fold increase in surface binding compared with unmodified peptide.
- The next phase of this collaboration aims to confirm that the peptide promotes exosome targeting to additional tissues in vivo. This peptide platform has the potential to generate further targeting peptides to that which would rapidly expand the therapeutic reach of our exosome candidates.

Multiple industry-based collaborations in progress

Industrial collaborations

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.

In November 2020, we signed a collaboration agreement with a major pharmaceutical company, focusing on the potential of our exosomes to deliver DNA cargoes for expression of therapeutic genes in the brain.

Academic collaborations

As of March 2021, there are two ongoing collaborations with leading academic institutions in the UK and mainland Europe, focusing on the delivery of CNS-targeting growth factors and siRNA to the brain.

We have demonstrated engagement of target receptors in the CNS by exosome-loaded growth factors during a recent pilot study.

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 develop further exosome candidates derived from a panel of additional producer cell lines owned by the Company. These exosome candidates have the potential to broaden the repertoire of tissues and indications that the Company is able to target.
- Our medium-term goal is to deliver in-vivo proof of concept data.
- 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.

Our progress towards changing patients' lives

iPSCs: developing our therapeutic platform

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

Engineering CTX neural stem cells

We have shown that despite the presence of the conditional immortalisation technology, the CTX neural stem cell line can be reprogrammed into Induced Pluripotent Stem Cells (iPSCs).

This will allow us to create new cell types necessary for the treatment of many indications for which cellular therapies were previously unavailable.

What is pluripotency?

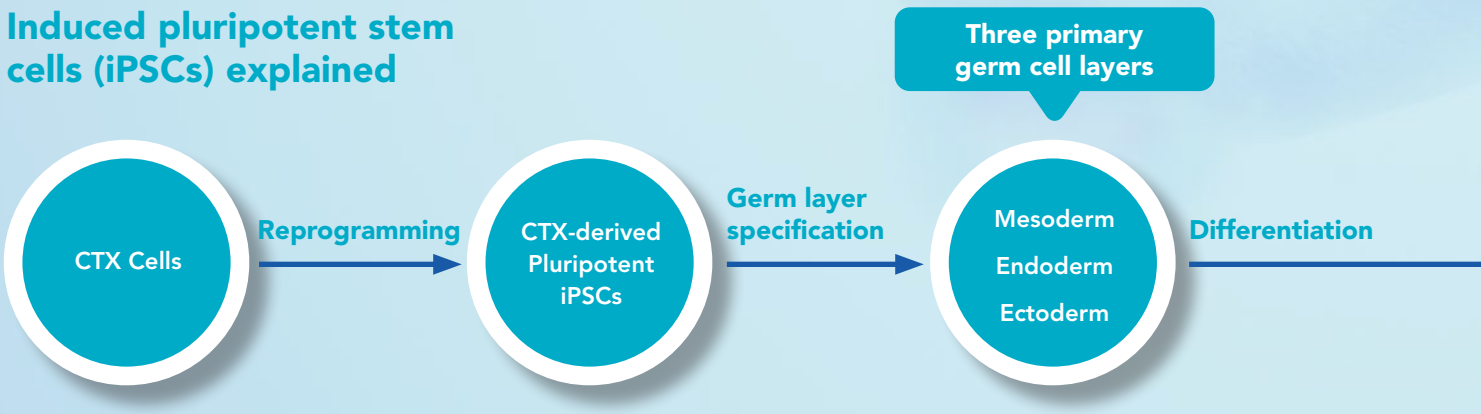
Pluripotent stem cells such as iPSCs can both self-renew (divide indefinitely whilst maintaining their phenotype) and also differentiate to generate cells of the three primary embryonic germ layers (and thence, all cell types found in the human body).

CTX-iPSCs could therefore be used to produce conditionally immortalised allogeneic cell types of any type required for cell therapy.

Pre-clinical research

- As proof-of-principle, we have generated clinically-relevant cells of several types from CTX-iPSCs, including hematopoietic progenitors and effectors, mesenchymal stem cells, pancreatic ß-cells and neural lineages.
- We are working on a process to produce pancreatic progenitor cells from our iPSCs and from these, ß-islet cells. We will then aim to scale up this process prior to phenotype analysis and confirmation of the glucose responsiveness of the derived, mature ß-islets.

Induced pluripotent stem cells (iPSCs) explained



Pre-clinical research

- We are in discussions with a further commercial third party to apply CTX-iPSC-derived ß-islet cells as an allogeneic cell therapy candidate for type 1 diabetes.
- We have differentiated our iPSCs into hematopoietic stem cells, lymphoid progenitors and, of great interest for cancer immunotherapy, NK and killer T-cells.
- We have been collaborating with a commercial third party to explore the possibility of large-scale in vitro expansion of iPSC-derived hematopoietic stem cells and discussions are ongoing with other interested parties in the immunotherapy field.

What does this mean for future development?

- New cell types can be efficiently created as cell therapy candidates targeting a broad range of conditions. Discussions are ongoing with interested parties, including in the cancer immunotherapy space.
- As a result, there is an opportunity to expand our therapeutic portfolio by developing candidates for subsequent out-licensing, and providing cells for partners to develop their own cell ATMPs from CTX-iPSCs.
- There is great potential to produce exosomes from both iPSCs themselves and CTX-iPSC-derived differentiated cells, with the ability to target specific tissues within the body.
- We think that the presnce of the immortalisation technology within these new cell types will allow for the large scale production of 'off the shelf' allogeneic stem cells.
- Our medium-term goals are to further validate our technology, publish pre-clinical proof of concept data and to generate clinical grade iPSCs incoporating the conditional immortalisation technology for therapy and commercial development.

Different cell lineages can be generated

Multipotent adult stem cells and tissue progenitors of many cell lineages

New cell therapeutics for the treatment of potentially any unmet medical need caused by acute or chronic cell loss

Scalability

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