Our marketplace

Retinal diseases

Market potential for RP therapy[1]

$0.5bn – $1.6bn

Incidence in U.S. and worldwide[2,3,4]:

1:4,000

Number of genes identified containing mutations leading to RP

>100

Market need:

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

At the moment, treatment is only available or patients with a single gene defect (RPE65).

Patients with all other types of RP (c.98% of patients[5]) have declining vision eventually leading to severe visual disability in most.

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.

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

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.

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, such as 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

Notes

1. Analysts' estimates: Stifel March 2018, N+1 Singer April 2017, Edison May 2017.
2. Hamel (2006) Orphanet J Rare Disease 1, 40;
3. https://nei.nih.gov/health/pigmentosa/pigmentosa_facts;
4. NORD
5. www.nice.org.uk/guidance/hst11/chapter/2-The-condition

Our response:

A differentiated, allogeneic cell-based therapeutic approach to retinal disease

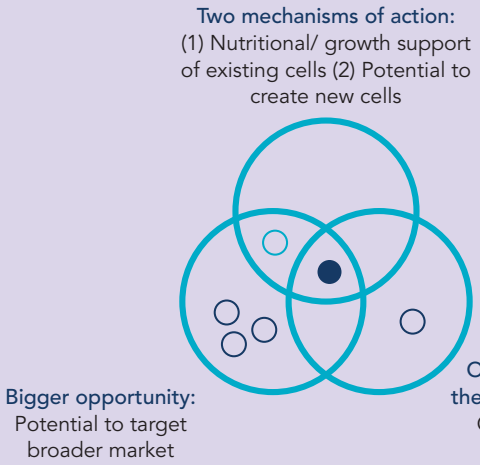
Our research suggests that our hRPC therapy may be able to slow or even reverse the progression of RP through its ability to differentiate into components of the retina and its ability to maintain existing photoreceptors.

Our stem cells are placed into the actual anatomic location where the retinal cells are degenerating. This creates the potential for the cells to integrate into the tissue where they can provide durable nutritional and growth support as well as potentially evolve to become new retinal cells and make the neural connections to enable sight.

The cells are injected directly to the site of retinal degeneration, allowing a greater chance of anatomic restoration of photoreceptor function.

Insight into the therapy landscape targeting retinal diseases

Our hRPC cell therapy candidate offers a number of potential advantages over alternative approaches to the treatment of RP within the therapy landscape. Our candidate meets the following criteria:



Proprietary manufacturing process allows for stable, high-quality and high-quantity GMP production

- Collaborations with Schepens Eye Research Institute (Harvard) and University College London
- Proprietary technology enabled development of GMP manufacturing process
- Cryopreserved formulation allows on-demand shipment and use at local surgeries and hospitals. It provides nine-month shelf life and enables local treatment worldwide.

High commercial potential, targeting a higher addressable market

- Orphan Drug Designation in EU and US in RP and FDA Fast Track Designation
- Broad potential across a range of eye diseases, initially targeting inherited retinal degenerative diseases
- Attractive pricing precedent set in the marketplace
- Commercially viable formulation
- Agnostic to genetic type, so potentially targets entire RP market

Our marketplace

Drug delivery technologies

Exosomes deals totalling more than

c.$2bn

in upfronts and milestones based on proof of concept data[1]

Market need:

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

Market opportunity:

There is increasing industry interest in and commercial value of collaboration deals, focused on delivery of novel therapeutics.

Market characteristics:

We focus on exosomes because the technology has the potential to overcome the limitations of current delivery technologies.

Drug delivery technology with the potential to target a range of areas

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

Immunosuppresive need

A key advantage of exosomes is their low immunogenicity, which means they are less likely to provoke immune responses in the body. In comparison, delivery technologies such as Lipid Nanoparticles (LNP), are known for inducing a significant inflammatory response.

Favourable transport within cells

Exosomes are naturally transported within cells much more efficiently than synthetic vehicles such as Lipid Nanoparticles which are prone to rapid destruction by lysosomes.

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.

Crossing the blood brain barrier (BBB)

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

Why does it make it difficult to treat?

Intravenous (IV) or systemic administration is usually favourable due to it's simplicity and broad drug distribution. If a drug cannot cross the BBB efficiently, the dose might have to be increased, which increases the risk of off-target side effects. Alternatively, drugs can be administered locally to the central nervous system, but this is technically complex, expensive and carries additional risks.

Notes

1. Company Information

References:

Vader et al 2016 – Extracellular vesicles for drug delivery; Ha et al 2016 – Exosomes as therapeutic drug carriers and delivery across

Our response:

A differentiated drug delivery approach to target areas of significant unmet medical need

Exosomes can cross the blood brain barrier

We believe exosomes can do this due to the neural nature of their cell of origin.

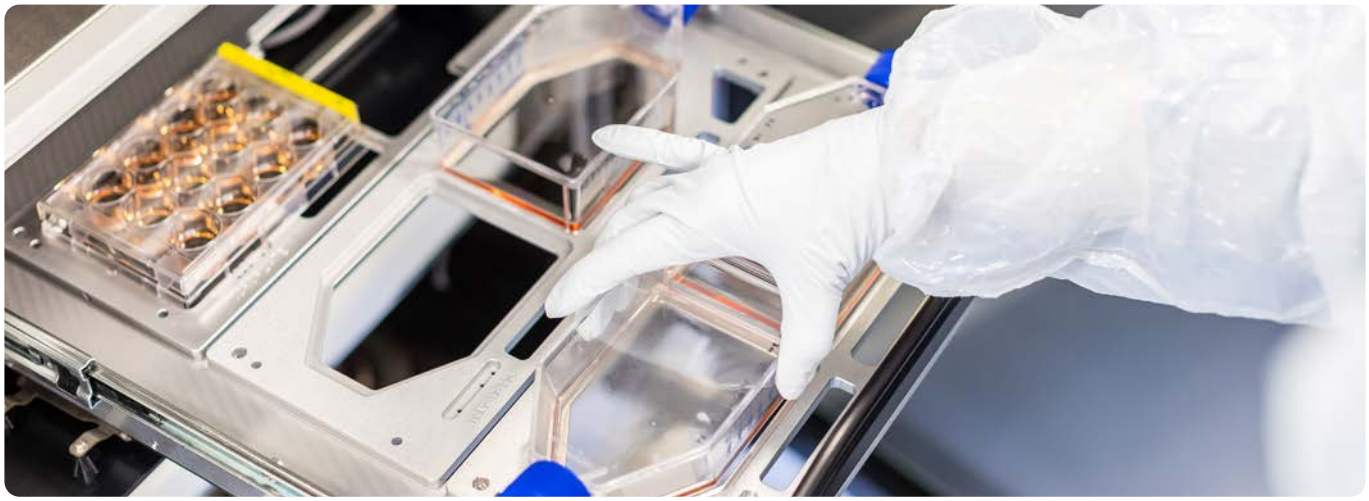
This neural stem cell line produces exosomes with specific surface markers that we believe allow the exosomes to cross the BBB and communicate with other cells within the brain.

Strong, proprietary technology gathering industry interest

Our current focus is on drug delivery, with funded collaborations in place with further ones under negotiation.

Advantages of ReNeuron's exosome technology:

- Favourable distribution across the blood brain barrier
- Modifiable to carry siRNA/mRNA/CRISPR-Cas9 proteins, small-molecule inhibitors
- Proven ability to load miRNA and proteins
- Engineered to target particular tissues
- Potential for our exosomes to work in gene therapy
- Fully qualified xeno-free, optimised, scalable GMP process
- Established analytics
- Stable, consistent, high-yield, clinical-grade product



Our marketplace

New cell-based therapeutic candidates

Market opportunity:

Human pluripotent stem cells offer huge potential for the entire field of regenerative medicine and cell therapy.

Market characteristics:

Human pluripotent stem cells' 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:

Potential to expand our therapeutic portfolio by developing further therapeutic candidates

ReNeuron's iPSCs however, have a conditional immortalisation technology inserted which we believe 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.

This also makes feasible large scale banking and purification of partially-or fully differentiated cells for therapy.

Advantages of ReNeuron's iPSC technology:

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

Potentially, any indication where cell loss is a problem is a candidate target for iPSC-based therapeutics, including heart damage, Parkinson's disease, or Huntingtons's disease

Generated cell lines can be grown at scale, enabling the efficient production of clinical grade cell therapy candidates