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NIGHTSTAR THERAPEUTICS: CATCHING THE EYE

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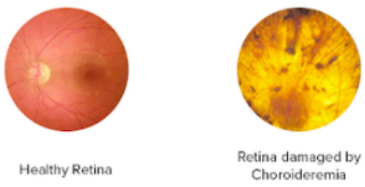
Nightstar Therapeutics is a London-based clinical-stage gene therapy company developing treatments for inherited retinal diseases that lead to progressive blindness. Nightstar was born as a spinout from Oxford University, co-founded by Professor of Ophthalmology, Robert MacLaren. The company's pipeline of therapies focusses on rare eye diseases that have no currently approved treatments, presenting a clear unmet medical need for patients. As a result, investors have been keen to tap into this potentially lucrative gap in the healthcare market. Indeed, since Nightstar's initial public offering (IPO) on the USA's biotech-friendly NASDAQ stock exchange market in September 2017, it has grown to boast a market capitalisation of $500 million.

Nightstar celebrates its IPO at the Nasdaq Market Site in Times Square, New York, September 2017, Credit: Globe Newswire

The company has two clinical programs currently in development, as part of a much larger pipeline of proposed retinal treatments. Their lead program is 'NSR-REP1', a Phase 3 genetic treatment for patients with Choroideremia (CHM). CHM is an X-linked degenerative retinal disease which presents itself as night blindness in children, followed by loss of peripheral vision in middle-age and eventual loss of central vision. Nightstar's treatment aims to stop disease progression and halt deteriorating vision. The epidemiology of CHM shows that it is almost exclusive to males affecting 13,000 potential patients in the US and major European markets.



Choroideremia is characterised by a progressive deterioration of rod receptor cells in the eye's retina, Credit: Choroideremia Research Foundation

Choroideremia's underlying pathophysiology is characterised by mutations in the CHM gene on the X chromosome. The wild-type allele typically produces Rab escort protein (REP-1) in retinal rod photoreceptor cells, a protein that plays an important role in intracellular protein trafficking and waste removal. Reduced expression of REP-1 leads to a progressive deterioration of retinal rod cells, which are responsible for vision in low light intensities. Rod cells contain a receptor protein called rhodopsin, which undergoes conformational changes when it absorbs light, leading to the generation of electrical signals which are sent to the brain via the optic nerve. Since these rod cells are concentrated around the edges of the retina, early signs of the disease are a loss of peripheral vision in childhood before further narrowing or "tunnel vision" presents itself later in life. In patients over the ages of 50, deterioration can extend into a tiny pit in the macula, called the fovea, which contains cones cells that are responsible for colour vision and function best in relatively high light intensities. As a result of damage to the fovea, central visual acuity ceases and total vision loss sets in.

It is clear that Nightstar are attempting to solve unmet medical needs. The ongoing NSR-REP1 Phase 3 trial, known as the 'STAR trial' is the most clinically advanced candidate for CHM worldwide. Alongside the STAR trial, the company have been conducting an observational study since 2015 - the 'NIGHT study' - in which CHM patients have been enrolling at multiple sites in the US, Canada and Europe. The idea of the NIGHT study is to understand the history and progression of disease in untreated patients, which will provide a well-characterized worldwide CHM patient population. When used in tandem, NIGHT and STAR can be used to evaluate the significance of visual improvement in treated patients

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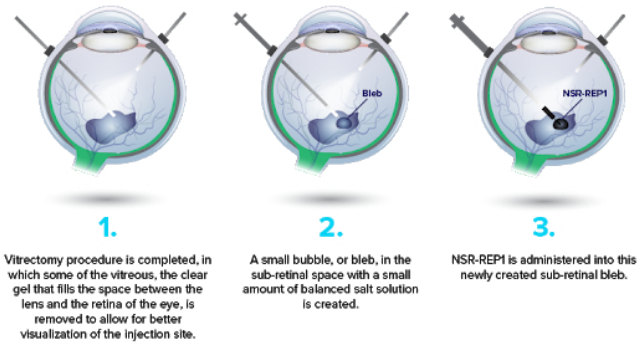
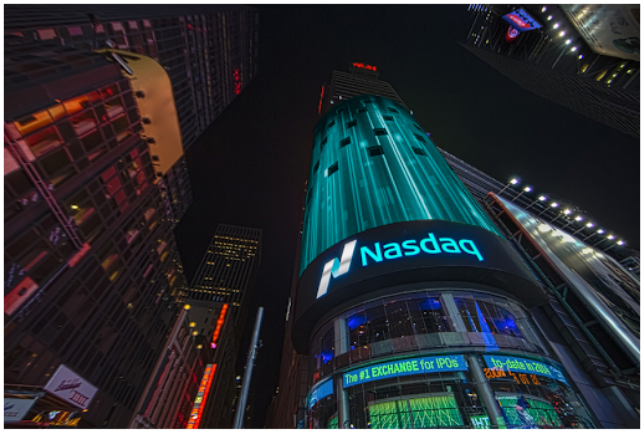


Nightstar's NSR-REP1 gene therapy requires a 3-step surgical procedure in CHM patients, Credit: Nightstar

The CHM gene therapy treatment is comprised of an AAV2 viral vector containing recombinant human complementary DNA, or cDNA, that will produce functional REP-1 within the eye. A surgeon injects the product into the eye's sub-retinal space, between the outer layers of the retina. The functional CHM gene is designed to enhance expression of REP-1 protein, thus reducing the accumulation of waste products in retinal cells and preventing a decline in vision.

The results of Nightstar's Phase 1/2 trial were published in Nature Medicine last year. Visual acuity significantly improved in each of the 14 treated patients, with 6 patients gaining more than one line of vision. Having been initially tested in Oxford Eye Hospital, Nightstar believe the procedure could be available for widespread use within 5 years.



Nightstar's popularity on the world-stage of investment will increase as its clinical programs progress, Credit: Fierce Biotech

Nightstar's second clinical gene therapy treatment is for X-linked Retinitis Pigmentosa. Similar to Choroideremia, the disease progresses in males from an initial loss of peripheral vision, followed by a progressive narrowing of vision that can reach the fovea and cause total blindness. Mutations in the RPGR gene lead to a lack of protein transport and deterioration of photoreceptors in the retina. The 'NSR-RPGR' gene therapy for the disease is currently at a Phase 1/2 clinical trial stage, yet it may not be long before it reaches Phase 3 and becomes a leading treatment, alongside its CHM brother.

Nightstar's success in developing treatments for retinal diseases has been profound and its potential to deliver life-changing therapies to patients around the world cannot be underestimated. Whilst investors understand that the biotech market can be volatile with fears of clinical trials not living up to expectation, it seems that for now at least, Nightstar is making all the right moves.

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