Bascom Palmer Eye Institute
UNIVERSITY OF MIAMI HEALTH SYSTEM

November 14, 2024

Laura Beckwith
Executive Director
Helen Keller Foundation
Suite 101, 2208 University Blvd.
Birmingham, AL 35233

Re: Nomination of Professor Robert MacLaren for the 2026 Helen Keller Prize for Vision Research

Dear Ms. Beckwith,

I am pleased to support Professor Robert MacLaren's nomination for the 2026 Helen Keller Prize for Vision Research.

Professor MacLaren is a highly regarded physician scientist whose innovative research program at Oxford University has led to clinical evaluation of several gene therapies for inherited retinal diseases for which there are no current treatments.

Professor MacLaren's research initially focused on choroideremia, a rare inherited retinal disease mainly affecting men. The first symptom is impairment of night vision, often occurring in early childhood, followed by progressive narrowing of the field of vision that eventually culminates in blindness, most commonly in late adulthood. Subsequent to the publication of promising initial results (MacLaren et al., *Lancet* 2014) of a first-in-human gene therapy trial (NCT01461213) led by Professor MacLaren, followed by the publication of additional data providing evidence of the long-term benefit of the gene therapy (Edwards et al., *NEJM* 2016; Xue et al., *Nature Med* 2018), an international Phase III trial (NCT03496012) sponsored by Biogen has evaluated the safety and efficacy of this gene therapy in 170 choroideremia patients in the USA, Canada and Europe – the largest retinal gene therapy trial conducted in the world at the time. Although this trial did not meet the primary endpoint of a 3-line gain in vision, a 2-line gain endpoint was met and the results of this trial will support further progress towards regulatory approval for this disease (MacLaren et al., *Nature Med* 2023).

Another important inherited retinal disease targeted by the MacLaren laboratory is X-linked retinitis pigmentosa, the most common variant of a group of genetic retinal diseases known as retinitis pigmentosa (RP), which collectively are the lead cause of untreatable blindness in young people in the developed world. Most RP patients are legally blind by the age of 40. Development of a gene therapy for X-linked RP was particularly challenging as the affected *RPGR* gene has an unusual genetic code with several hundred repetitive guanine and adenine nucleotide sequence repeats that makes the gene very unstable and prone to mutations, which is why X-linked RP is one of the more common inherited retinal diseases. However, the MacLaren laboratory successfully used a codon optimization approach to re-program the genetic code of the *RPGR* transgene to make it more stable, without affecting its function (Fischer et al., *Mol Ther* 2017). A subsequent clinical trial (NCT03116113) sponsored by Biogen, evaluating first-in-human testing of this gene therapy for X-linked RP, showed reversal of visual field loss (Cehajic-Kapetanovic et al., *Nature Med* 2020) and sustained improvements in visual function (Von Krusenstiern et al., *JAMA Ophthalmol* 2023). More recently, I had the pleasure to report the results of the phase II/III trial which, although under-recruited due to COVID-19, nevertheless showed a statistically significant improvement in mean microperimetry and low luminance visual acuity (LLVA) in treated eyes compared with controls (Lam et al., *Ophthalmology* 2024). Most significantly, Prof MacLaren raised commercial funding and designed two prospective natural history studies, one for

choroideremia and one for X-linked RP with over 200 patients in each study (MacLaren et al., *Am J Ophthalmol* 2024; MacLaren et al., *Ophthalmol Sci* 2024) These seminal studies of such magnitude documenting a single gene disorder are unlikely ever to be repeated.

In testament to his academic leadership, it is also notable that Professor MacLaren has recently co-founded Beacon Therapeutics as a spinout from the University of Oxford with $115M of equity at launch and an additional $170M at series B. This new company has incorporated the assets from the Biogen X-linked RP programme as well as buying out AGTC, a former spinout from the University of Florida. This company is now advancing gene therapy for X-linked RP using the full-length codon-optimized *RPGR* transgene in a phase III trial across multiple US and EU sites.

Age-related macular degeneration (AMD), the leading cause of vision loss in people over the age of 50, has been a major focus of international gene therapy research. Dry AMD is the most common form of the disease, impacting 85-90% of people with AMD. As dry AMD advances, the disease progresses to the atrophic form, called geographic atrophy, an irreversible degeneration of the photoreceptors resulting in a gradual and permanent loss of central vision. Overactivation of the complement system has been strongly correlated with the development and progression of dry AMD. As the Complement Factor I (CFI) protein regulates the activity of the complement system, it is believed that increasing CFI production could dampen overactivity of the complement system; thereby reducing inflammation and preserving eyesight. An initial clinical trial (NCT03846193) sponsored by Gyroscope Therapeutics, evaluating first-in-human testing of a gene therapy for dry AMD co-developed in the MacLaren laboratory at Oxford University (Dreismann et al., *Gene Ther* 2021) provided evidence that the gene therapy is well tolerated and results in sustained increases in vitreous CFI levels in the majority of patients, as well as decreases in the downstream complement proteins associated with over-activation of the complement system. This program is currently on hold but was successfully licensed to Novartis.

In addition to his development and clinical evaluation of novel retinal gene therapies, Professor MacLaren has also progressed the field of retinal gene therapy by his development of an improved surgical technique for subretinal administration of gene therapies, involving preliminary macular detachment with balanced salt solution (BSS), followed by injection of gene therapy into the preformed subretinal bleb (Xue et al., *Eye* 2017). Careful propagation of the BSS bleb during the initial detachment step also permits safe detachment of the fovea – an important innovation for treating cone photoreceptors with gene therapy. Professor MacLaren has trained several retinal surgeons in the USA, for instance at the Bascom Palmer Eye Institute in Miami, which is ranked as the number one center of excellence in ophthalmology in the USA, in this two-step approach for subretinal administration of gene therapy using an automated injector, which is now regarded as the preferred surgical technique in this field.

In summary, Professor MacLaren's significant research contributions to the development of retinal gene therapy are indisputable, and I have no hesitation in recommending him for the 2026 Helen Keller Prize for Vision Research.

Sincerely,

Byron L. Lam

Byron L. Lam, MD
Professor, Mark J. Daily Chair
Bascom Palmer Eye Institute
University of Miami Miller School of Medicine

THE UNIVERSITY OF SYDNEY

SAVE SIGHT INSTITUTE

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Laura Beckwith
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2208 University Blvd.
Birmingham
AL 35233
USA

January 19, 2025

Dear Ms Beckwith,

RE: Nomination of Professor Robert MacLaren for the 2024 Helen Keller Prize for Vision Research

It gives me great pleasure to recommend Professor Robert MacLaren for the 2025 Helen Keller Prize for Vision Research. Professor MacLaren has made significant contributions to treating previously incurable vision disorders through sustained translational research focusing on cell therapy, gene therapy, retinal prostheses and the surgical delivery of these treatments.

In 2016, Professor MacLaren performed the world's first operation inside the eye using a surgical robot. The robot was employed to dissect the internal limiting membrane from the retina in a patient undergoing surgery for a macular hole. In the first phase of this pilot trial (NCT03052881), led by Professor MacLaren, the robotic surgical device was compared to standard manual surgery in a prospective randomized controlled clinical trial, demonstrating the advantage of robotic surgery for precise and minimally traumatic removal of retinal scar tissue (TL Edwards et al., *Nat Biomed Eng* 2, 649 (2018)). In the second phase, the robotic device was used to place a fine needle into the subretinal space to safely administer a subretinal therapeutic substance – an innovation showing its potential future utility for the delivery of gene or cell therapies to the retina (J Cehajic-Kapetanovic et al., *Am J Ophthalmol* 237, 104 (2022)). Professor MacLaren's pioneering use of robotic eye surgery was included by the British Broadcasting Corporation (BBC) as one of its medical breakthroughs of 2016. The Telegraph newspaper also mentioned it as one of the top eight robotic healthcare breakthroughs in its STEM Awards 2018.

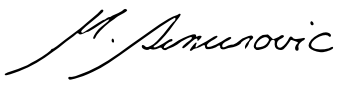
Professor MacLaren is also to be commended for his significant research contributions in the use of surgically implanted electronic prostheses to replace the lost photoreceptors in the eyes of patients suffering from degenerative retinal diseases. In the early 1990s, several research groups began the development of electronic retinas. Two alternative strategies emerged – an epiretinal (anterior to the retina) implant exemplified by the Argus II device manufactured by Second Sight Medical Products Inc. and a subretinal (posterior to the retina) implant exemplified by the Alpha IMS and second-generation Alpha AMS devices developed by Retina Implant AG. Image capture in the Argus II device relied on external cameras, which relayed visual information to the epiretinally located electrode array. The Alpha IMS and Alpha AMS devices, on the other hand, employed integrated photodiode arrays which were directly stimulated by ambient light transmitted to the retina and hence functioned in a very similar manner to the layer of light-sensitive photoreceptors present in healthy retinas. Although the Alpha IMS and Alpha AMS devices were more complex than the Argus II device and consequently took longer to develop in clinical practice, they had the advantage that there was no external camera device visible around the face, which many blind patients appreciated because they did not wish to draw attention to themselves in public. In addition, the photodiode arrays followed normal eye movements, which simulated the synkinetic experience of natural vision. Essentially, the subretinal implant acted both as the image sensor and electrical stimulator in one self-contained unit, similar to the normal photoreceptor array. It was far more

complicated than the Argus II but could produce a much more normal visual experience. Working with Retina Implant AG, Professor MacLaren helped develop the surgical technique for implanting a subretinal electronic retina in a complex 10-hour operation. His successful pilot trial of the second-generation Alpha AMS device (NCT02720640) indicated that electronic retinas could restore a certain degree of functional vision to patients with end-stage retinal disease and no useful sight (TL Edwards et al., *Ophthalmology* 125 (3), 432 (2018).), with one patient reporting the highest gain in visual acuity achieved to date with an artificial retina (J Cehajic Kapetanovic et al., *Acta Ophthalmol* 98 (7), 736 (2020). These positive outcomes, showing that after many years of blindness, patients were once again able to detect light and recognize objects, including being able to read the time on a clock, were highlighted on the front cover of the *National Geographic* magazine and in several popular television science documentaries.

A key issue in delivering new therapies – such as gene and stem cell therapy – to the retina is the efficacy of the surgical approach in delivering correct doses to patients. Although early work acknowledged the importance of standardizing approaches, it failed to address the inherent difficulty in reliably identifying the correct plane between the neural retina and the supporting retinal pigment epithelium when performing sub-retinal injections. Professor MacLaren recognized that difficulties in correctly identifying the surgical plane could lead to significant variations in dose delivery. This led to the development of the so-called 2-step approach, in which the correct plane for drug delivery is identified first with an inert "balanced salt solution" prior to the second step of delivering the therapeutic solution itself. This approach has subsequently been adopted by most vitreoretinal surgeons. Furthermore, my group has recently confirmed in a randomized controlled trial (ACTRN12619001121156) that the 2-step approach pioneered by Professor MacLaren leads to significantly less variance than the preceding 1-step approach (MP Simunovic et al., *Retina* 43 (1), 158 (2023). [2] MP Simunovic et al., *BMJ Open* 11 (12), e049976 (2021; final data under review for publication and to be presented at ARVO 2025) which it has effectively replaced.

I had the opportunity to participate in Professor MacLaren's ground-breaking work in retinal robotic surgery and electronic retinas while working as a clinical research fellow in his clinical team at Oxford University 10 years ago. His outstanding academic achievements are well-known in the gene and cell therapy field. However, it is unusual for academics to be involved in leading translational medical research whilst also being active surgeons/surgical innovators. In summary, his surgical achievements are unusual for an academic and warrant recognition. I am delighted to nominate Professor MacLaren for the 2025 Helen Keller Prize for Vision Research in view of these significant achievements.

Yours sincerely,



Matthew Simunovic **MB BChir PhD FRANZCO**
Professor of Ophthalmology and Visual Science
Save Sight Institute, University of Sydney

Senior Consultant Ophthalmic Surgeon
Sydney Eye Hospital & Sydney Children's Hospitals

BIOSKETCH (NIH format: standard PHS 398 form)

NAME: MacLaren, Robert Edward

eRA COMMONS USER NAME: MACLARENR

POSITION TITLE: Professor of Ophthalmology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Edinburgh, UK	MB ChB	07/1990	Medicine
NHS Scotland Deanery – Foundation School (Royal Infirmary of Edinburgh, Western General Hospital), UK		07/1991	Medicine (General Surgery)
NHS London Deanery – South Thames Foundation School (Guy's Hospital, St Thomas' Hospital), UK		07/1992	Medicine (Accident and Emergency)
University of Oxford, UK	DPhil	05/1996	Neuroscience
NHS Oxford Deanery – Oxford Regional Rotation (Radcliffe Infirmary, Royal Berkshire Hospital), UK	FRCS	02/1999	General surgery
NHS London Deanery – North Thames Rotation (Moorfields Eye Hospital, Western Eye Hospital, Hillingdon Hospital), UK		02/2003	Ophthalmology
Moorfields Eye Hospital, UK Residency and Fellowship training	FRCOphth	07/2005	Vitreoretinal surgery
University of Oxford, UK	PGDip	09/2006	Learning and teaching in higher education
UCL Institute of Ophthalmology, UK Post-doctoral scientist		09/2008	Retinal gene therapy

A. Personal Statement

Please refer to my biography at: www.ndcn.ox.ac.uk/team/robert-maclaren.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – 2024	Scientific Founder and Director, Beacon Therapeutics, USA
2014 – 2018	Scientific Founder and Director, Nightstar Therapeutics, USA (acquired by Biogen Inc., USA)
2009 – Present	Honorary Consultant Ophthalmologist, Oxford Eye Hospital, UK
2009 – Present	Professor of Ophthalmology, University of Oxford, UK
2006 – Present	Honorary Consultant Vitreoretinal Surgeon, Moorfields Eye Hospital, UK

2006 – 2014	Honorary Consultant Ophthalmologist, Great Ormond Street Hospital for Children, UK
2006 – 2011	Principal Investigator, UCL Institute of Ophthalmology and University of Oxford, UK (Clinician Scientist Fellowship, Academy of Medical Sciences and The Health Foundation, UK)
2006 – 2008	Senior Clinical Research Fellow, UCL Institute of Ophthalmology, UK
2005 – 2006	Locum Consultant Vitreoretinal Surgeon, East Surrey Hospital, UK
2004 – 2006	Clinical Research Fellow, Moorfields Eye Hospital, UK
2004 – 2006	Postdoctoral Research Fellow, UCL Institute of Ophthalmology, UK
2003 – 2004	Fellow in Vitreoretinal Surgery, Moorfields Eye Hospital, UK
1999 – 2003	Specialist Registrar in Ophthalmology, NHS London Deanery (Moorfields Eye Hospital, Western Eye Hospital, Hillingdon Hospital), UK
1996 – 1999	Senior House Officer in Ophthalmology, NHS Oxford Deanery – Oxford Regional Rotation (Radcliffe Infirmary, Royal Berkshire Hospital), UK
1995 – 1996	Captain, Royal Army Medical Corps, Section Commander, 16 Armoured Field Ambulance (active duty as a military doctor in the Former Yugoslavia conflict)
1992 – Present	Bodley Fellow and College Lecturer in Human Anatomy, Merton College, Oxford, UK
1992 – 1995	DPhil Student, University of Oxford, UK (Clinical Research Training Fellowship, Medical Research Council, UK)
1991 – 1992	Senior House Officer in Accident and Emergency, NHS London Deanery – South Thames Foundation School (Guy's Hospital, St Thomas' Hospital), UK
1990 – 1991	House Officer in General Medicine and General Surgery, NHS Scotland Deanery – Foundation School (Royal Infirmary of Edinburgh, Western General Hospital), UK

Honors

07/2024	The Doyne Lecture and Medal, 107th Oxford Ophthalmological Congress, Oxford, UK
04/2024	The Ophthalmologist Power List 2024: Top 100 most influential people in ophthalmology worldwide, UK
09/2023	Lecturer of the Year award, University of Lugano School of Medicine, Lugano, Switzerland
02/2023	Award Lecture, University of Miami and Elsevier Winter Symposium in Molecular Neuroscience, Miami, USA
09/2022	Keynote Lecture and Award, 120th German Ophthalmological Society Meeting, Berlin, Germany
08/2020	Vice Chancellor's Innovation Award (Overall Winner and Winner of Inspiring Leader Category), University of Oxford, UK
08/2020	King Khaled Eye Specialist Hospital Memorial Lecture and Award, Riyadh, Saudi Arabia
03/2020	The Lang Lecture and Medal, Royal Society of Medicine, UK
09/2019	Clinical Service of the Year Award, Macular Society, UK
05/2019	The Keeler Lecture and Medal, Royal College of Ophthalmologists
04/2019	Gold Clinical Excellence Award for NHS service delivery, Department of Health and Social Care, UK
12/2018	Sir Adrian Cadbury Lecture and Medal, Midland Ophthalmological Society, UK
09/2018	Achievement Award, American Academy of Ophthalmology, USA
05/2018	Fellowship, Academy of Medical Sciences, UK
04/2018	The Ophthalmologist Power List 2018: Top 100 most influential people in ophthalmology worldwide, UK
11/2017	Richardson Cross Lecture and Medal, Southwest Ophthalmological Society, UK
10/2017	Fellowship (by election), American College of Surgeons, USA
10/2016	Keynote Lecture and Award, 19th European Vision and Eye Research Congress, Nice, France
04/2016	The Ophthalmologist Power List 2016: Top 100 most influential people in ophthalmology worldwide, UK
03/2016	Senior Investigator Award (renewed in 2020), National Institute for Health and Care

	Research, UK
01/2016	Principal Fellow Award, National Institute for Health and Care Research Oxford Biomedical Research Centre, Oxford, UK
10/2015	Keynote Lecture and Award, 113th German Ophthalmological Society Meeting, Berlin
06/2015	Scientist of the Year Award, Retina UK, UK
10/2014	Hope for Vision Arsht Lidsky Lecture and Prize, University of Miami, Miami, USA
09/2014	EURETINA Lecture, 14th EURETINA (European Society of Retina Specialists) Congress, London, UK
09/2014	EURETINA Innovation Award (Runner-up), 14th EURETINA (European Society of Retina Specialists) Congress, London, UK
07/2014	Jessie Mole Lecture and Medal, British Retinitis Pigmentosa Society, UK
05/2013	Pfizer Ophthalmics Carl Camras Translational Research Award, ARVO (Association for Research in Vision and Ophthalmology) 2013 Annual Meeting, Seattle, USA
10/2010	Percival Hay Medal and Lecture, North of England Ophthalmological Society, UK
05/2006	Clinician Scientist Fellowship, Academy of Medical Sciences and The Health Foundation
01/2006	King James IV Professorship of Surgery (first eye surgeon), Royal College of Surgeons of Edinburgh, UK
07/2005	Founder's Cup and Medal, Oxford Ophthalmological Congress, Oxford, UK
07/2005	Students and Trainees Prize (Ophthalmology Section), Royal Society of Medicine, UK
01/2005	Gold Medal (Trainee of the Year Award), Moorfields Eye Hospital, London, UK

C. Contributions to Science

1. **First-in-human clinical trial of a gene therapy for choroideremia**: Choroideremia is a rare inherited retinal disease affecting approximately one in 50,000 people. The first symptom of the condition is usually an impairment of night vision which often occurs in early childhood. This is followed by progressive narrowing of the field of vision, as well as a decrease in the ability to see details, culminating in blindness, most commonly in late adulthood. In 2011, I led a first-in-human Phase 1/2 clinical trial of a gene therapy for choroideremia (NCT01461213). The initial publication (*Lancet* 2014) of the promising initial outcomes observed in the first 6 patients was followed by the publication of additional data (*New England Journal of Medicine* 2016; *Nature Medicine* 2018) providing evidence of the long-term benefit of the gene therapy for choroideremia. The full results of the phase III clinical trial have recently been published (*Nature Medicine* 2023).
    a. **MacLaren RE**, Groppe M, Barnard AR, Cottriall CL, Tolmachova T, Seymour L, Clark KR, During MJ, Cremers FP, Black GC, Lotery AJ, Downes SM, Webster AR, Seabra MC. Retinal gene therapy in patients with choroideremia: initial findings from a phase 1/2 clinical trial. Lancet. 2014;383:1129-37. DOI: 10.1016/S0140-6736(13)62117-0.
    b. Edwards TL, Jolly JK, Groppe M, Barnard AR, Cottriall CL, Tolmachova T, Black GC, Webster AR, Lotery AJ, Holder GE, Xue K, Downes SM, Simunovic MP, Seabra MC, **MacLaren RE**. Visual Acuity after Retinal Gene Therapy for Choroideremia. N Engl J Med. 2016;374:1996-8. DOI: 10.1056/NEJMc1509501.
    c. Xue K, Jolly JK, Barnard AR, Rudenko A, Salvetti AP, Patrício MI, Edwards TL, Groppe M, Orlans HO, Tolmachova T, Black GC, Webster AR, Lotery AJ, Holder GE, Downes SM, Seabra MC, **MacLaren RE**. Beneficial effects on vision in patients undergoing retinal gene therapy for choroideremia. Nat Med. 2018;24(10):1507-1512. DOI: 10.1038/s41591-018-0185-5.
    d. **MacLaren RE**, Fischer MD, Gow JA, Lam BL, Sankila EK, Girach A, Panda S, Yoon D, Zhao G, Pennesi ME. Subretinal timrepigene emparvovec in adult men with choroideremia: a randomized phase 3 trial. Nat Med. 2023;29(10):2464-2472. doi: 10.1038/s41591-023-02520-3.

2. **First-in-human clinical trial of a gene therapy for X-linked retinitis pigmentosa**: X-linked

retinitis pigmentosa is an incurable genetic disease that causes blindness in men. This is the most common variant of a group of genetic retinal diseases known as retinitis pigmentosa (RP), which collectively are the lead cause of untreatable blindness in young people in the developed world. Sight loss in X-linked RP begins with night blindness (i.e. loss of night vision) in adolescence, followed by a gradual loss of peripheral vision which results in progressively worsening tunnel vision, and ultimately complete blindness. In 2017, I treated the first patient participating in a first-in-human Phase 1/2 clinical trial of a gene therapy for X-linked RP (NCT03116113). The development of this gene therapy was particularly challenging as the affected gene has an unusual genetic code that makes it very unstable and prone to mutations, which is why X-linked RP is one of the more common hereditary retinal diseases. However, my team successfully used a codon optimization approach to re-program the genetic code of the gene concerned to make it more stable, without affecting its function (*Molecular Therapy* 2017). The initial results of the clinical trial are positive (*Nature Medicine* 2020).

a. Fischer MD, McClements ME, Martinez-Fernandez de la Camara C, Bellingrath JS, Dauletbekov D, Ramsden SC, Hickey DG, Barnard AR, **MacLaren RE**. Codon-Optimized RPGR Improves Stability and Efficacy of AAV8 Gene Therapy in Two Mouse Models of X-Linked Retinitis Pigmentosa. Mol Ther. 2017;25(8):1854-1865. DOI: 10.1016/j.ymthe.2017.05.005.
b. Cehajic-Kapetanovic J, Xue K, Martinez-Fernandez de la Camara C, Nanda A, Davies A, Wood LJ, Salvetti AP, Fischer MD, Aylward JW, Barnard AR, Jolly JK, Luo E, Lujan BJ, Ong T, Girach A, Black GCM, Gregori NZ, Davis JL, Rosa PR, Lotery AJ, Lam BL, Stanga PE, **MacLaren RE**. Initial results from a first-in-human gene therapy trial on X-linked retinitis pigmentosa caused by mutations in *RPGR*. Nat Med. 2020;26(3):354-359. DOI: 10.1038/s41591-020-0763-1.

3. **First-in-human clinical trial of a robotic surgical device**: In 2016, the first person in the world underwent robotic surgery inside the eye in an operation that I performed at the John Radcliffe Hospital in Oxford. The operation used a remotely controlled robot to dissect a membrane 100th of a millimeter thick (that was distorting the patient's vision) off the retina of his right eye – an extremely delicate operation that is a very demanding procedure for a surgeon to do safely by hand. The robotic surgical device was developed with Preceyes BV, a Dutch medical robotics firm established by the University of Eindhoven. In the first phase of this pilot trial, known as the Robotic Retinal Dissection Device (R2D2) study (NCT03052881), the robotic surgical device was used to peel membranes off the delicate retina without damaging it (*Nature Biomedical Engineering* 2018). In the second phase, the device was used to place a fine needle under the retina for therapeutic injections, demonstrating its potential utility for retinal gene therapy (*American Journal of Ophthalmology* 2022).
   a. Edwards TL, Xue K, Meenink HCM, Beelen MJ, Naus GJL, Simunovic MP, Latasiewicz M, Farmery AD, de Smet MD, **MacLaren RE**. First-in-human study of the safety and viability of intraocular robotic surgery. Nat Biomed Eng. 2018;2:649–656. DOI: 10.1038/s41551-018-0248-4.
   b. Cehajic-Kapetanovic J, Xue K, Edwards TL, Meenink TC, Beelen MJ, Naus GJ, de Smet MD, **MacLaren RE**. First-In-Human Robot-Assisted Subretinal Drug Delivery Under Local Anaesthesia. Am J Ophthalmol. 2022;237:104-113. DOI: 10.1016/j.ajo.2021.11.011.

4. **Restoration of functional vision in blind patients using electronic retinas**: In 2015, the first of six patients in the UK underwent surgical implantation of a second-generation Alpha AMS electronic retina, manufactured by Retina Implant AG, in a clinical trial (NCT02720640) that I led at the John Radcliffe Hospital in Oxford. The second-generation subretinal electronic photodiode array has several improvements over the first-generation Alpha IMS device, including a greater number of pixels, a better power profile, and other enhancements to extend its operational longevity such as improved durability and corrosion resistance. The successful outcomes of the study (*Ophthalmology* 2018), provided striking evidence that electronic subretinal implants could

restore a certain degree of functional vision to patients with end-stage retinal disease and no useful sight, thus improving these patients' general quality of life and returning to them an increased level of independence. After many years of blindness, patients were once again able to detect light and recognize objects, including being able to read the time on a clock. The gains in visual acuity are the highest achieved to date with artificial retinas (*Acta Ophthalmologica* 2020).

a. Edwards TL, Cottriall CL, Xue K, Simunovic MP, Ramsden JD, Zrenner E, **MacLaren RE**. Assessment of the Electronic Retinal Implant Alpha AMS in Restoring Vision to Blind Patients with End-Stage Retinitis Pigmentosa. Ophthalmology. 2018;125(3):432-443. DOI: 10.1016/j.ophtha.2017.09.019.
b. Cehajic Kapetanovic J, Troelenberg N, Edwards TL, Xue K, Ramsden JD, Stett A, Zrenner E, **MacLaren RE**. Highest reported visual acuity after electronic retinal implantation. Acta Ophthalmol. 2020. DOI: 10.1111/aos.14443.

D. Publications

Please refer to my PubMed profile at:
https://pubmed.ncbi.nlm.nih.gov/?term=MacLaren+RE&sort=date&size=200.