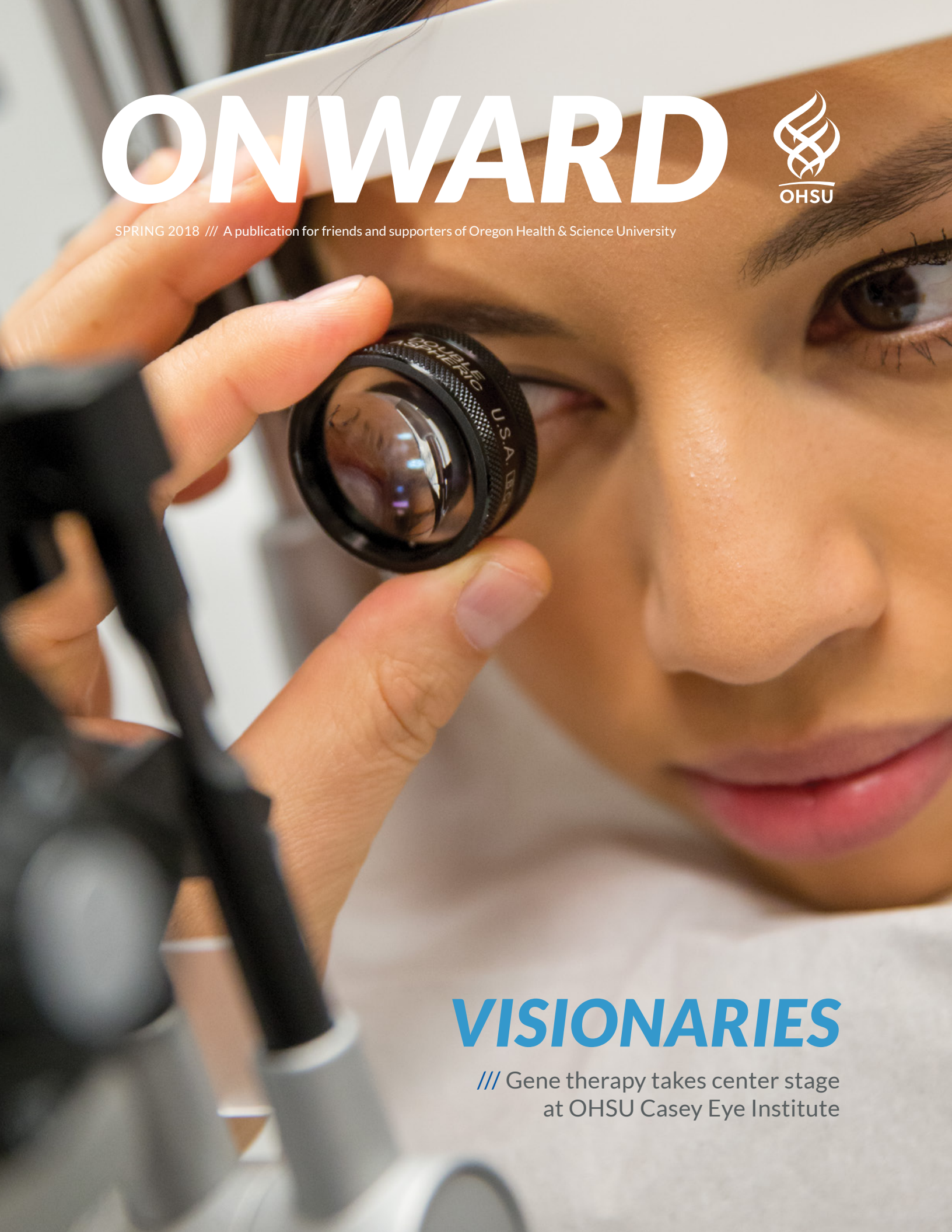
ONWARD

OHSU

SPRING 2018 /// A publication for friends and supporters of Oregon Health & Science University



VISIONARIES

/// Gene therapy takes center stage at OHSU Casey Eye Institute

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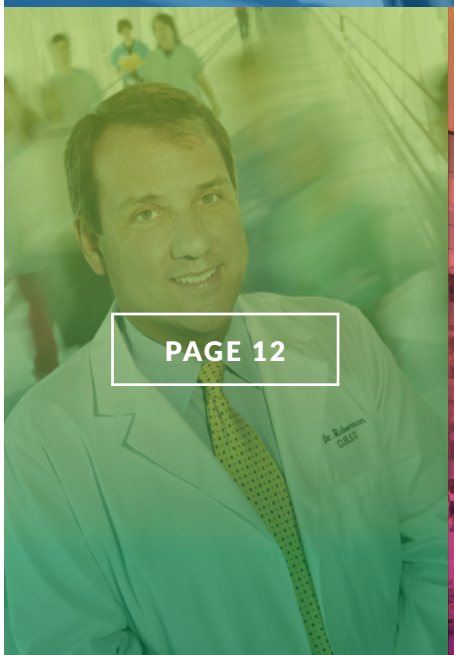

ONWARD
THE OHSU FOUNDATION MAGAZINE
SPRING 2018

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Elks Children's Eye Clinic renderings courtesy of NBBJ

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Welcome to **ONWARD**

It is with mixed emotions that I write this introduction to ONWARD magazine, as it will be my last. As many of you know by now, I plan to leave the President's Office at the end of the academic year.

My career at OHSU, which began nearly 40 years ago in 1979 as an ophthalmology resident, has been enormously fulfilling and gratifying. Through what has often felt like a series of happy accidents I became OHSU president, but in a lot of ways I feel exactly as I did as a young physician just starting my career. When I drive to work in the morning, I still feel the same excitement and gratitude and devotion to OHSU's mission today as I did when I first became a faculty member in 1985.

It's been a privilege to lead this extraordinary organization for the last 11-plus years, a period in which we've had a good deal of success. I want to be clear, though: I don't claim credit. All of our success is the result of the collective effort, collaborative spirit and commitment of the OHSU community. Success at OHSU is shared success.

OHSU's future is brighter than ever. Our mission is clear. Our people are the best and brightest and most committed I've ever had the privilege to know. And our community of supporters — all of you — provides the steady wind pushing us forward as we expand our national leadership in improving health care for all.

So while this is a farewell from my role as OHSU president, it is definitely not goodbye. After a brief sabbatical, I will remain connected to OHSU through a part-time faculty appointment in ophthalmology and my work in global health. Beyond that, I fully intend to continue supporting the success of this world-class institution in whatever capacity I can.

Thank you for the honor of serving OHSU and the state of Oregon.

Joseph E. Robertson, Jr., M.D., M.B.A.
President, OHSU

An eye-opening era in gene therapy

No one has looked at the colors on an iPhone with as much fascination as Annie Joiner has in the past couple of months.

That's because the 60-year-old Annie can see the "colors" on her phone — can see any colors actually — for the first time in her life.

She doesn't really recognize them as colors. After a lifetime of color-blindness, her brain has never tried to process such a thing before. Still, she sees them as somehow different.

And it's world-changing for Annie.

"It's very exciting for me," she says.

The changes occurred after Annie underwent eye surgery last December as part of a gene therapy clinical trial at the OHSU Casey Eye Institute. Annie has achromatopsia, which causes complete color blindness, light sensitivity and reduced sharpness of vision.

The most common form of achromatopsia is genetic. People are born with it. It comes from a mutation in a gene that normally helps our eyes react appropriately to light. In the clinical trial, an eye surgeon injects a normal copy of the specific gene — carried by a modified and harmless virus — under the retina of the eye. The hope is that the normal gene will then help trigger the proteins that will get her eyes working more normally.

So far, for Annie, it appears to be working.

There is much work to do before scientists will know whether the achromatopsia gene therapy treatment is successful. But human gene therapy in general — in which doctors replace a mutated gene with a normal one or "turn off" the actions of a disease-causing gene — has had a run of real success over the past few years. A number of gene therapy procedures, mostly in clinical >>>>

ACHROMATOPSIA

is a condition characterized by a partial or total absence of color vision. People with complete achromatopsia cannot perceive any colors; they see only black, white and shades of gray.

GENE THERAPY CLINICAL TRIALS UNDERWAY AT CASEY RELATING TO THIS CONDITION

/// Achromatopsia clinical trial participant Annie Joiner; below she is pictured the way she's seen the world throughout her life — in black and white — until a gene therapy clinical trial gave her a first glimpse of color.

trials, appear to effectively treat or cure a range of medical conditions, including those affecting the eye.

And Casey is helping to lead the way.

Casey is participating in more gene therapy clinical trials for eye conditions than any other center in the world. It boasts three physicians and surgeons who are international experts in inherited retinal disease; most centers have no more than one such expert.

Andreas K. Lauer, M.D, Chief of Casey's retina-vitreous division, Kenneth C. Swan Professor of Ophthalmology and vice-chair for education, is known for his success as an eye surgeon in clinical trials. In a few current national clinical trials, Casey is the only site selected to do the eye surgeries.

Casey is also becoming part of history: It is one of only seven sites in the country offering the first FDA-approved gene therapy for a genetic disease — a clinical trials success now available to patients.

The treatment is for the several thousand people born with a rare defect in the *RPE65* gene. The mutation causes severe visual problems from infancy and often leads to complete blindness.

Using the treatment, called Luxturna™, an eye surgeon injects a normal copy of the *RPE65* gene — again carried by a modified and harmless virus — into the retina of each eye of the patient. That normal *RPE65* gene is placed next to the patient's defective genes; it then helps the retina produce the normal proteins that the defective *RPE65* gene is not producing — which converts light to an electrical signal and restores the vision of the patient.

/// Dr. Andreas Lauer (center) consults with his team, including surgical nurses, a fellow and coordinators.

The treatment improved the vision of more than 90 percent of people participating in its clinical trials, with some moving from legally blind to not blind.

"This is a 'one giant leap for mankind' kind of moment," says Mark E. Pennesi, M.D., Ph.D., associate professor of ophthalmology and division chief of the ophthalmic genetics program at Casey. "This is one therapy for a rare disease, but it is the proof of principle — that gene therapy can work. This is really miraculous. And this is really just the beginning."

> "Gene therapy has the possibility of being able to change families' lives."
>
> **ANDREAS K. LAUER, M.D.** — Kenneth C. Swan Professor of Ophthalmology; Chief, Retina-Vitreous Division, Casey Eye Institute

Casey an international leader

Casey is among the handful of sites in the nation that will perform the procedure because of its team's national and international reputation in gene therapy and gene therapy eye surgery.

The team expertise and experience that Casey now boasts was hardly accidental, Casey physicians say. Casey's leadership in gene therapy is the result of the vision of David J. Wilson, M.D., the Margaret Thiele Petti and August Petti Chair of Ophthalmology and director of Casey, who anticipated how important gene therapy would become in treating eye diseases. And the foundation for Casey's gene therapy prominence was built through philanthropy: An important $1 million gift from Paul Casey eight years ago "was the spark that lit the fire," says Pennesi. >>>>

Gene therapy: A centerpiece of Casey expansion

The Casey Eye Institute building expansion will include an entire floor for the gene therapy program, providing more rooms for physicians to see patients, and more space for the advanced equipment needed for clinical care and research programs.

Added space will allow Casey providers to decrease the wait time for gene therapy clinical trials patients who often travel to Portland from throughout the country, says Mark E. Pennesi, M.D., Ph.D., associate professor of ophthalmology and division chief of the ophthalmic genetics program.

And Casey will build an unusual but important feature for centers that want to be part of major clinical trials: a life-sized maze. Top ophthalmology research centers have extensive human mazes that allows researchers to test how well a specific treatment may have helped visually impaired patients.

“You can change the illumination levels and test how well people navigate,” Pennesi says.

Only three U.S. centers currently have a maze large enough to satisfy requirements of the newest gene therapy research, Pennesi says.

David J. Wilson, M.D., Casey director, says the building expansion will allow Casey to remain a national leader in gene therapy.

“The resources you need for a gene therapy program are going to be something that not many centers can provide,” Wilson says. “We are already out in front. By building the infrastructure for this program, we’re enabling an entire industry in Portland."

That $1 million gift led to an additional $10 million in industry and philanthropic support for Casey physicians and scientists doing genetic therapy research.

"It does show how philanthropy can lead to a successful and thriving program," Wilson says. "It allowed us to build a program that then led to multiple millions in sponsored research. It put us in position.”

But leaders can’t rest, which is partly why Casey has embarked on an expansion plan that includes a new building featuring an entire floor devoted to gene therapy treatment and research (see more to the left).

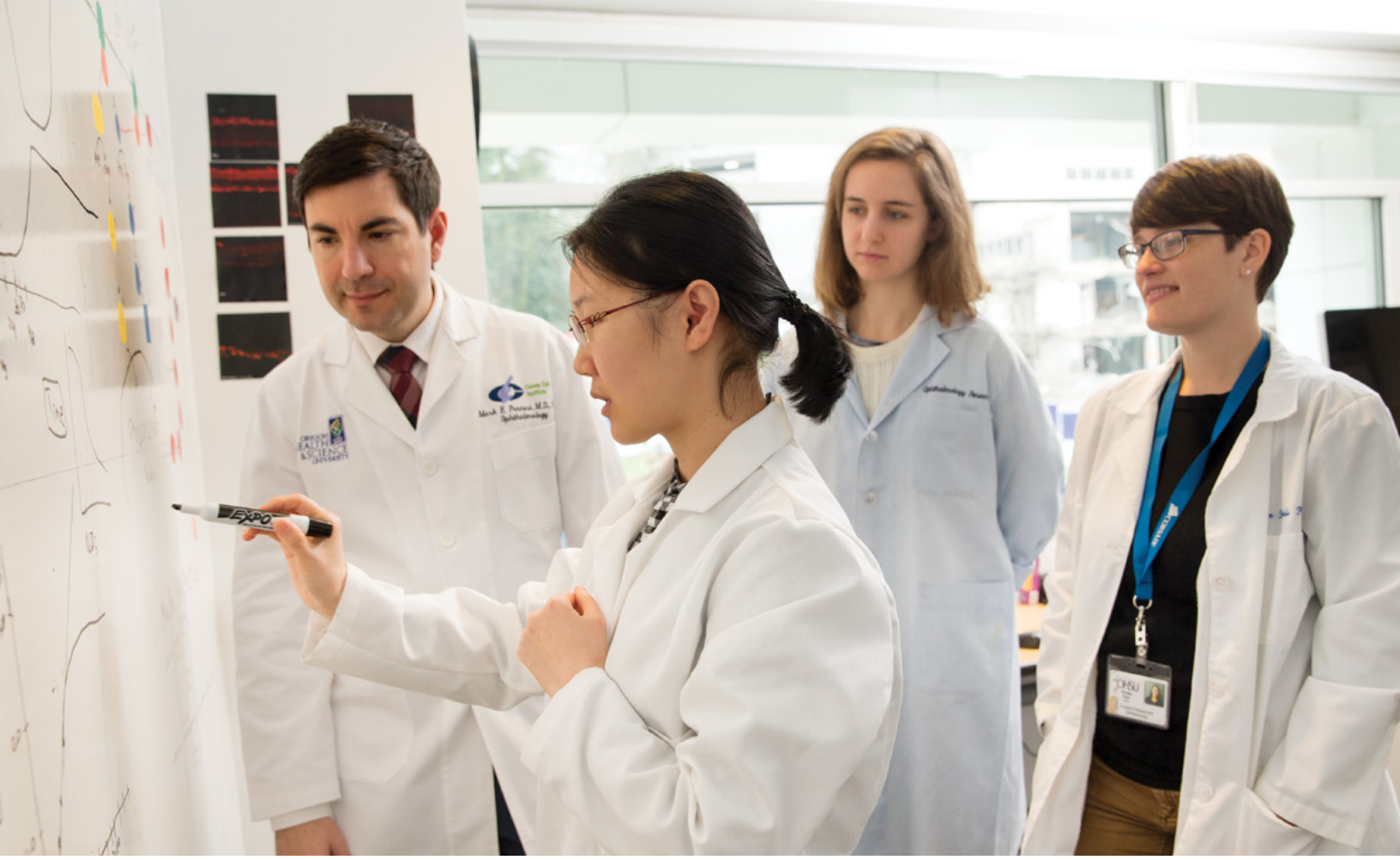
Hope for more hard-to-treat eye diseases

Wilson, Pennesi and Lauer each say they're excited about the gene therapy success of Luxturna, and their optimism is further fueled by how this success could lead to better treatments for a range of eye diseases, including much more common problems like age-related macular degeneration. Scientists hope that different gene or cell-based therapies might be able to do for other conditions what Luxturna does for *RPE65* disease. For example, they may be able to stop or reverse “wet” AMD, which affects more than 2 million mostly older people in the U.S.

One of those people is Zola Goodell.

Zola, a Portlander who turns 84 in April, is participating in a Casey clinical trial that is exploring whether gene therapy can treat AMD.

Zola has “dry” AMD in her right eye and the more rare “wet” AMD in her left. In dry AMD, yellowish or white deposits form under the macula at the center of the retina, causing the macula to deteriorate. In wet AMD, abnormal blood vessels underneath the retina form and



/// Dr. Mark Pennesi (left) working with his lab team on various approaches to protect the retina from degeneration.

> "This is one therapy for a rare disease, but it is the proof of principle – that gene therapy can work."
>
> **MARK E. PENNESI, M.D., PH.D.** – Associate Professor of Ophthalmology; Division Chief of the Ophthalmic Genetics Program at Casey Eye Institute

grow toward the macula, then often break and leak fluid, damaging the macula. Dry AMD progresses to wet AMD in 10 to 20 percent of people who have dry AMD. The wet AMD results in more rapid and severe vision loss.

Casey's clinical trial is testing a treatment for wet AMD, in which corrective genes are implanted in the retina with hopes of blocking the growth of the abnormal blood vessels. Zola had the surgery to implant the genes four years ago and goes to Casey for checkups every six months. During those check-ups — which will continue as part of the trial for the next 10 years — doctors draw fluid out of her eye to measure the levels of the protective proteins that should have been triggered by the genes administered to her in surgery.

Clinical trials often require some significant ongoing commitment by participants, and volunteers like Zola — and Annie — are vital for scientific research, and for almost all medical breakthroughs. Their participation might be even more important, and notable, in trials that involve eye surgery, says Lauer. >>>>

> "If I've been a part of something that makes life better for someone else, I'm delighted to do it."
>
> **ZOLA GOODELL** — patient in clinical trial at Casey Eye Institute

"There's a tremendous amount of emotional investment in coming to the decision to go ahead with such treatment," Lauer says, "There's risk potential with surgery — it's not like putting in an eye drop or ointment. There's a certain amount of trust that the patient places on the surgery team. This is a type of treatment where you need to get it right."

One thing is certain: With the promise that gene therapy is showing, the increasing knowledge gained through clinical trials is incredibly important, Lauer says.

"My hope is that gene therapy would allow people in the future to enjoy the beauty there is in this world," says Lauer. "Some of these people are not even born yet. Gene therapy has the possibility of being able to change families' lives."

For people like Annie and Zola, that's more than enough.

Annie was the first person in the United States with her type of achromatopsia to get the treatment she received. She knew there was some risk in the trial, but "there's always risk in anything," she says. The reward: it's already brought some improvement in her vision, and she believes there will be more improvement.

But Annie says she wanted to participate for reasons beyond her own vision. Achromatopsia runs in families — often skipping a generation — and her grandson has the condition. "His vision is worse off than mine," Annie says. "So anything that is learned from my experience might give him a chance to have improved vision."

Zola is driven by similar hopes.

Since she had her surgery, her retina has continued to create the protective proteins that the genes were supposed to trigger. She has noticed no further decline of vision in her left eye with the wet MD, and she no longer requires periodic eye injections.

Zola knows the treatment is unlikely to reverse her wet AMD. But that's not the point, she says.

She wanted to be part of the study because she believes helping scientists learn more about macular degeneration now may benefit someone with macular degeneration after she's gone. She has high praise for the Casey staff and the way they have shepherded her through an "easy and informative" study experience. "If I've been a part of something that makes life better for someone else, I'm delighted to do it," she says.

"If people don't volunteer to do these sort of things, medicine can't advance."

MACULAR DEGENERATION

is an eye disorder that causes progressive vision loss. The macula is responsible for sharp central vision, which is needed for detailed tasks such as reading, driving and recognizing faces.

GENE THERAPY CLINICAL TRIALS UNDERWAY AT CASEY RELATING TO THIS CONDITION

/// Wet AMD clinical trial participant Zola Goodell; the doctored image below shows the impact of age-related macular degeneration on the eye's ability to focus.

It was to be “Joe's Big Adventure,” as Joe Robertson still calls it, smiling.

And it was supposed to last only a few years.

As the small-town Indiana boy and newly minted M.D. pondered where he might complete his residency, he considered staying close to home. But he also had enough money for a single plane ticket. So he figured he'd try someplace where the hills were taller and the bodies of water bigger. He applied to be a resident in the ophthalmology program at Oregon Health & Science University.

"I intended to stay three years and go back to Indiana," Robertson says.

But OHSU somehow grabbed hold of him and never let go.

Over the next three decades, Robertson would move from resident to faculty member to eventually chair of the ophthalmology department and director of the Casey Eye Institute.

Today, as he prepares to retire after 11 years as president of OHSU, he finds himself reflecting on his early days at OHSU and his enduring connection to Casey.

“You felt an incredible sense of commitment from the people you worked with," Robertson says of his years at Casey. "There was a tremendous sense of belonging. That you were a part of something you felt a great sense of pride about. It was much more than a job. It was a way of being.”

From early in his career, Robertson specialized in vitreoretinal surgery, which is performed in the eye's interior, where the retina and the jelly-like substance called the vitreous are found.

He became interested in a condition called retinopathy of prematurity, found in premature babies and actually caused by the neonatal intensive care that saves their lives. The oxygen therapy given to the babies causes abnormal growth of blood vessels in their retinas. In the most severe cases, it can result in retinal detachment and permanent blindness. Thirty years ago, that was the outcome for most babies with severe ROP.

Robertson believed that, over the arc of his career, he could contribute to improving the treatment for this disease. As his surgical experience grew, more and more families from many Western states began coming to OHSU for care.

Today, Robertson’s hope for better outcomes for the tiniest patients has been realized. Most babies have their vision saved, in great part due to Casey’s pioneering work in research and new treatments for ROP, including the use of advanced digital imaging and technology to remotely diagnose the condition early enough to be successfully treated.

This is what can happen, observes Robertson, at a place as special as Casey, where very smart and driven people work together to advance medicine.

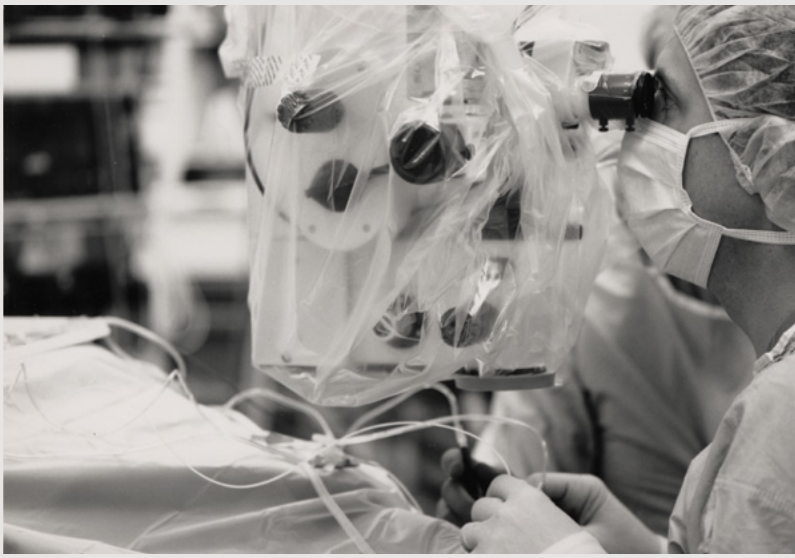
That collaboration and teamwork first came together as the Casey Eye Institute in 1991, when everyone in the department of ophthalmology began to work in a sleek new building near what was then the OHSU School of Dentistry building.

After Casey opened, teaching, research and patient care were no longer siloed. People from different disciplines saw each other every day, mingled at lunch, talked about ideas.

“It was transformational,” Robertson says. “Absolutely transformational.”

In the past decade, Robertson says he's watched with pride how Casey has gained greater national prominence under the guidance of Director David J. Wilson, M.D.

/// In 1987, Dr. Robertson was named director of the Vitreous Surgery Service in the Casey Eye Institute. He went on to become professor and chair of ophthalmology in the OHSU School of Medicine and director of the Casey Eye Institute in 1998.



"Under Dr. Wilson’s leadership, the Casey has undergone profound growth that would have been nearly unimaginable before he achieved it," Robertson says. "He has also guided Casey to become a player on the national and global scientific scene, with discoveries relevant not just to the eye but all of medicine.”

> “You felt an incredible sense of commitment from the people you worked with . . . It was much more than a job. It was a way of being.”
>
> **JOSEPH E. ROBERTSON, JR., M.D., M.B.A., President, OHSU**

Robertson's own memories of Casey are infused with a sense of camaraderie and dedication.

Performing surgeries long after midnight — because that’s when eye surgeons could get access to limited OHSU operating room time — as Jimi Hendrix blasted on a boom box. Getting to know medical residents and fellows whose talent, commitment and enthusiasm were always “a great antidote for cynicism,” Robertson says. And the challenges, victories and grit of hundreds of patients.

He recalls a 3-year-old boy, brought in by his distraught father, whose eye was impaled in a pumpkin carving accident. After several surgeries at Casey, the boy ended up with almost normal vision — and visited Robertson one last time a few years ago before he went off to college.

So often, Robertson says, patients exhibit “incredible perseverance and character. What you see in patients serves as an inspiration in your own life.”

He will carry that inspiration forward in retirement, along with the many friendships he has made, as he begins the next phase of “Joe’s Big Adventure.” ■

THE POWER OF PLACE

The OHSU Casey Eye Institute will break ground this summer on the Elks Children's Eye Clinic, a new 60,000-square-foot building next to its existing facility. The project is being funded through philanthropy, and will provide more space for three of Casey's most crucial programs:

Elks Children's Eye Clinic

The Oregon State Elks Association has invested nearly 70 years and more than $40 million in its partnership with OHSU's opthalmology department. That collaboration continues with this new clinic space, which will become the hub of Casey vision screening and treatment programs serving thousands of children in our region each year.

Macular Degeneration Center

Age-related macular degeneration is the leading cause of legal blindness in the U.S., and it's on the rise as our population ages — a 100 percent increase in AMD patients is predicted by 2050. Casey scientists are leaders in developing innovative therapies to attack this complex disease. The new Macular Degeneration Center will include expanded space for research and clinical trials.

Gene Therapy Center

Casey is a world leader in the growing field of ocular gene therapy, hosting more clinical trials than any other eye center in the world. Patient volume is expected to triple within five years. The Gene Therapy Center will occupy a full floor of the new building, allowing dramatic expansion of clinical trials capacity.
(see page 8 for more).

/// **Top left and right:** Architects' renderings of the new Elks Children's Eye Clinic to be built adjacent to the current Casey Eye Institute.

WHAT THE NEW BUILDING WILL DO

- Double the capacity to serve patients and conduct groundbreaking research
- Increase space and equipment for clinical trials — including a life-sized human maze that allows researchers to test how well a specific treatment helps visually impaired patients
- Significantly expand childhood vision screening and unique pediatric care programs

The construction of the current Casey Eye Institute facility in 1991 was the catalyst for profound growth in every facet of the institute's mission: serving patients, discovering new treatments and training specialists. The new building will create the same kind of momentum.

"We wanted to create an environment that is receptive to those with visual impairment. We are striving to create a health delivery environment that is not only about having resources to allow for leading-edge advances in eye care and its delivery, but also to be mindful about the people we are serving."

ANDREAS K. LAUER, M.D.
Kenneth C. Swan Professor of Ophthalmology; Chief, Retina-Vitreous Division, Casey Eye Institute

Please consider making a gift in support of the Casey Eye Institute Capital Campaign, and help create a future where no one has to go blind. To make a gift, please visit:

OnwardOHSU.org/supportcasey

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