For Vision Research, Wayne Streilein’s Legacy is Hope
As many of you now know, J. Wayne Streilein, M.D., the then Charles L. Schepens Professor of Ophthalmology at Harvard Medical School, and President and CEO of The Schepens, passed away very suddenly in March of this year. The past few months have been a difficult time for many of us. The personal loss of a friend, the loss to the scientific community of a real giant in the field of immunology and a truly creative “big science” thinker, and the loss to the Institute of an impassioned and visionary leader, have all led to a time of mourning, introspection, and challenges. This issue of Sightings is dedicated to Wayne, and presents a glimpse of his tremendous scientific contributions and legacy of leadership at the Institute. I want to express my sincere condolences to all whom have been touched by this event, and to acknowledge the impact of the sadness and shock we have experienced as an organization. It has also given me a sense of hope and optimism to see how individuals rose to the challenge of shepherding the Institute through this interval, even while confronting great personal loss. It speaks very highly of Wayne as a leader that individuals were in place at The Schepens who were equal to this challenge. Darlene Dartt, Dave Conlon, Nina Collins and other members of the staff have shown tremendous strength and wisdom at a time when the way was not at all clear. They have been a great help to me, and were instrumental in setting the stage for the arrival of Dr. Michael S. Gilmore, our new Director of Research, who joined the Institute in September.

Dr. Gilmore will also serve as the Acting Chief Executive Officer of The Schepens Eye Research Institute, in addition to the roles for which he was recruited, that of the DeWalt and Marie Ankeny Director of Research and the Charles L. Schepens Professor of Ophthalmology at Harvard Medical School. Dr. Gilmore was very generous with his time in the months after Wayne’s passing, shuttling back and forth between Oklahoma City and Boston in order to get up to speed and get started with the work of leading the Institute. Over the past six months, I have gotten to know him quite well, and I could not be more delighted to have him on board. Mike is both an outstanding scientist and an excellent administrator. In “Ask a Scientist” (page 8), Mike discusses his primary field of research interest—bacterial infections of the eye—a field in which he is an internationally recognized leader. In addition to cutting-edge research, he brings his experience as the Vice President for Research at the Oklahoma Health Sciences Center, where he oversaw the entire extramural grant program (in excess of $100 million per year), to the Institute. Joining the Institute under such challenging circumstances, Mike Gilmore has proven himself to be a natural leader who is compassionate, resourceful, and wise. I believe that we have many important opportunities before us, and Dr. Gilmore has the vision and creativity to capitalize on them.

This issue of Sightings also serves as the Annual Report for The Schepens Eye Research Institute. The statement from our Chairman of the Finance Committee (page 15) also presents an image of Wayne’s legacy, in the form of his many successful initiatives that have come to fruition over the past fiscal year. Since August of 1999, the Institute has undergone major renovations, dramatically changing the landscape of its research facility. The ambitious project of rejuvenating the Staniford Street laboratory building was completed in August of 2004. The 20 Staniford Street laboratories are now part of an “open concept” design that is meant to create a spacious and airy feel through the use of glass and natural lighting. Open-grid ceilings and colorful walls in royal blue, gold, and brick red complete the updated look of the 42-year-old building. On
The success of this proposal attests not only to the strength of The Schepens faculty and the Harvard Department of Ophthalmology, but also to Dr. Streilein’s ability to think creatively and inclusively about large scientific questions. A center dedicated to moving vision science forward through the collaboration of luminaries from many scientific disciplines seems a fitting addition to the premier vision research institution in the world.

In the week before the Democratic National Convention, Congress met to approve the Defense Department budget in advance of the summer recess. With the recent transfer of power in Iraq proving a significant challenge, and the war on terrorism continuing on many fronts, they met to choose those initiatives that would meet the critical defense needs of the country. The Defense Appropriations Committee chose to set aside $2 million to fund the FY05 research proposal from the Center for Excellence in Military Low Vision Research at The Schepens. As one of the few critical organs unprotected by body armor, the eye is particularly vulnerable, and many eye injuries have been sustained by soldiers in the Iraq and Afghanistan Theaters. Cognizant of the value of SERI research and technologies for deriving new battlefield and surgical treatments, Dr. Streilein created what has come to be known as “the government initiative” in 1999. The purpose of this initiative was to engage the SERI research enterprise in militarily relevant research projects—projects which eventually formed the basis for the Center for Excellence in Military Low Vision Research.

The success of the Center has been many years in the making. Wayne believed strongly in the value of presenting the world’s foremost vision scientists with the military’s ocular challenges to develop technologies that would address both the critical needs of the military, and that would also benefit the aging civilian population. Members of Congress from both sides of the aisle have come to understand the importance of the Center’s research to meeting the ocular challenges faced by active-duty soldiers and veterans, and appreciate the close working relationship that the Center has developed with its partners within the Department of Defense.

Wayne, with incredible foresight, has given us so much to build upon. With successful national-level initiatives, a state-of-the-art research facility, and a world-class Director of Research, The Schepens is poised to lead the vision research community in curing blindness by developing new technologies to prevent visual loss and restore sight. As I look at the road ahead, I see many opportunities stretched out before us, and I think of Wayne with gratitude for preparing us so well for this journey.

Sincerely,

Kennett F. Burnes
From the Acting CEO

Visualize SERI

Each of us has a key role to play in developing a future where we, our parents and eventually our children can have additional years of productive, independent and fulfilling life. Right now, as a nation, we spend approximately $68 billion to treat eye disease and visual loss, but we invest less than one percent of that in research. How much will new social agencies cost to help with the loss of independence of our aging population? How much could be saved by each additional day of independence for our elderly? Investing in research is not just the right thing to do, it is good national management.

There is no question that great technological advances are out there, it is only a question of when they will come. The ability to make these advances is limited only by the number of scientists engaged in their pursuit; the number of scientists is only limited by the resources available to provide laboratories, reagents and equipment.

I would urge each of us to ask ourselves, and to ask our friends, “What is the value of independence?”—our parents’ independence, our children’s independence, our own independence?

SERI scientists have a role to play.

With the untimely loss of Dr. Wayne Streilein’s leadership in research on corneal transplantation and inflammation, and his leadership at the helm of the institution; and with the planned relocation of two internationally renown senior scientists, Drs. Ann Elsner and Steve Burns, to pursue great opportunities, fewer SERI scientists will be available to confront the daunting challenges associated with our aging population. As SERI works to recover from these losses, each SERI scientist will be asked to shoulder ever more of the load to maintain our standing as the nation’s top vision research institution.

I will have an important role to play. Friends of SERI, SERI scientists and its Board of Trustees have a right to expect that the institution—founded on the technologic breakthroughs, innovation and vision of Dr. Charles Schepens and nurtured to its current preeminence through Dr. Streilein’s leadership, brilliance and dedication—will function with laser-like focus on developing the vision-saving technologies of tomorrow. I look forward to the challenge and to delivering on that expectation.

What will the SERI of the future look like? There are no limits to what we can do. There are only limits to our imagination, to our dedication, and to our effort. As we begin a new era at SERI, at the dawn of a new century, at a time when literally millions of our loved ones could benefit from the technologies we develop, I hope you will join me in being bold as we visualize SERI, and in working shoulder to shoulder as we bring that vision to fruition.

Sincerely,

Michael S. Gilmore, Ph.D.
Since his death on March 15, 2004, scientists, journalists, friends, and family have paid tribute to J. Wayne Streilein, M.D. They have described with great eloquence his work, his life, his contributions to science, his passionate search for truth, his creative energy and mind, his extraordinary talents as mentor, teacher and friend, his humor and his elegance as a human being.

According to those who knew, loved and worked with him, Wayne Streilein was all these things. For those who suffer from blinding eye diseases and those who strive to cure them, he was more. For them, he was and will always be a symbol of hope—a hope that will continue to inspire and drive his students, fellows and colleagues as they carry on his work at The Schepens Eye Research Institute and around the world, a hope for a cure that will help sustain those suffering from macular degeneration, glaucoma, and other debilitating eye diseases.

His legacy of hope is in our memory of his enormous natural optimism about the ultimate success of vision research and in a body of knowledge (previously unknown) about the special way the eye functions in the face of injury, disease or infection. He, more than any scientist in the past century, according to colleagues and experts in ocular immunology, has expanded understanding of what is known as the eye’s “immune privilege,” and his, as much as anyone’s, work has and will continue to reveal ways to harness and manipulate the eye’s own special properties for future cures.

Although during his career Streilein’s genius dramatically touched the fields of dermatology, transplantation, neonatal tolerance, genetics and clinical medicine, his romance with the intricacies of the human eye began early in his career and it was an affair that lasted until the day he died.

Born and raised in Johnstown, Pennsylvania, Streilein earned a chemistry degree at Gettysburg College and his M.D. at the University of Pennsylvania. He went on to hold positions at the University of Pennsylvania and the University of Texas (UT) Southwestern Medical School in Dallas. After leaving Texas he was appointed Chair of the Department of Microbiology and Immunology at the University of Miami School of Medicine. In 1993, he was recruited as Director of Research for The Schepens Eye Research Institute, and soon after was named President of The Schepens and Vice Chair of the Department of Ophthalmology at Harvard Medical School.

Streilein was first exposed to the concept of immune privilege while at the University of Pennsylvania by his mentor, Dr. Rupert Billingham, a colleague of Dr. Peter Medawar, a Nobel Prize winner for his formal proposal of the concept. Intrigued by their work and ideas, Streilein began his own journey of groundbreaking discovery.

Immune privilege is a condition or ability of a few critical organs in the body, which prevents or suppresses the body’s normal inflammatory immune response to foreign proteins such as bacteria. Tissues whose function could be damaged by such responses are believed to have immune privilege and include the testes, the reproductive tract, the brain, and the eye.

According to his peers, Streilein early on became the world leader in researching immune privilege in the eye. He believed that evolution had given the eye “immune privilege” because the tissues of the eye were fragile, unable to regenerate, and easily and permanently damaged by the “traditional” inflammatory response of the immune system. Permanent damage to those tissues meant permanent damage to vision.

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Thoughts about Wayne Streilein: As expressed over the past few months...

“His family hold dear to their hearts his love and wisdom, his talent and interest in music and continue to be inspired by his multifaceted quest for learning that he shared so generously with his wife and colleague, Joan, and their children, children’s spouses and their grandchildren.”
—The family of Dr. J. Wayne Streilein

“Wayne Streilein was a towering figure in ophthalmology and immunology. In the field of ocular immunology, he was without doubt the leading scientist of his generation.”
—Professor Santa Jeremy Ono of UCL, in an article in UCL News.

“Wayne Streilein was a skillful and ingenious investigator and team leader, who had a profound influence on his collaborators and students. He was also an inspiring teacher.”
—Dr. Leslie Baruch Brent, London, in an article in The Guardian

“Wayne Streilein is one of the premier scientists of his generation and of this century. I see him as a citizen scientist of the world. He was a great man in ocular immunology, but beyond that, vision research did not own him exclusively because he was also internationally recognized for his work in immunology as a basic discipline.”
—Dr. Paul A. Sieving, Director of the National Eye Institute

“For the past three decades, Wayne Streilein was the unquestioned major intellectual force in ocular immunology. He trained more people in this field, both in the U.S.A. and internationally, than anyone else in the world.”
—Dr. Henry Kaplan, Director of the Kentucky Lions Eye Center at the University of Louisville, in an article in The Lancet

“He helped develop the laws of transplantation. Wayne was an extraordinary researcher who contributed much to our knowledge of ocular immunology, especially the role of immune privilege in promoting survival of corneal allografts and in preventing rampant intraocular inflammation.”
—Dr. Sally Atherton, Chair of the Department of Cellular Biology and Anatomy at the Medical College of Georgia, in an article in The Lancet.
And finally...

“It is impossible to summarize the life of contributions of a truly remarkable individual such as J. Wayne Streilein. Perhaps the most fitting way is to refer to the words he used to describe his relationship with his mentor, Rupert Billingham, and his philosophy of science. Shortly after Billingham’s death, Wayne sent his current and former fellows the following note.”
—Dr. Jerry Y. Niederkorn, University of Texas Southwestern Medical School at Dallas, in an article in Transplantation

“Throughout our lives we experience losses through the deaths of individuals whom we know well and love. In my advancing maturity, I have come to realize that these are not merely irreplaceable losses. They can also be bittersweet opportunities to ponder the connectivities among individual lives and the growth and evolution of shared ideas. I am cognizant of the flow of ideas that have passed to and through me and I am fortunate to have found trainees willing to receive these ideas and able to fashion them into discoveries that bring truth closer and closer.”
—J. Wayne Streilein

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One of his first and most significant contributions was his development of the research model of anterior chamber-associated immune deviation (ACAID). In this early work, he was the first to show that a “deviant” immune response occurred in the anterior chamber of the eye, which prevented the rejection of, or gave immune privilege to, foreign or transplanted tissue and helped them to survive.

In his thinking and his studies of this phenomenon, Streilein went far beyond even the theories of his mentors about immune privilege in the eye. Billingham and Medawar believed that immune privilege in the eye was the result of barriers posed by lack of access to the immune system because the eye had few lymphatic or blood vessels for transporting messages to the immune system. Streilein found that there were numerous players and regulatory processes that helped the eye maintain its privileged status.

ACAID was just a part of hundreds of observations and papers over the course of three decades in which Streilein and his research team painstakingly documented the myriad of tiny yet essential interactions within various parts of the “healthy” eye that protect it, and at the same time prevent it from rejecting foreign matter.

And his observations never stopped. In the past several years, he published a number of studies that continued to clarify the role of immunology in the eye. In one recent study, he showed that inflammatory processes in the eye might be the first step in the formation of glaucoma. In another, in the Journal of Experimental Medicine, he demonstrated that the pigment epithelium of the eye’s iris produced a molecule that stopped the action T lymphocytes immune cells, which, in the eye, can be potentially damaging.

SIGNIFICANCE FOR BLINDING EYE DISEASES

Streilein’s discoveries about the mechanisms that create the “normal” immune privileged state of the eye help to explain why most corneal transplants survive. It also, according to experts, explains why, when those mechanisms are not working correctly because they have been damaged by injury or disease, or a person’s own genetic predispositions, transplants of corneal and other tissues, such as retinal tissue, cannot survive.

(continued on page 14)
Ask a Schepens Scientist: A Profile

Eye Infection Expert to Head The Schepens Eye Research Institute

Michael S. Gilmore, Ph.D., was installed in September as Acting Chief Executive Officer and the Dewalt and Marie Ankeny Director of Research at The Schepens Eye Research Institute. In addition, he will serve as Charles L. Schepens Professor of Ophthalmology at Harvard Medical School, a professorship named for the founder of The Schepens Eye Research Institute.

Gilmore served as Vice President for Research at Oklahoma University Health Science Center for the past three years, where he also held the titles of M.G. McCool Professor of Ophthalmology and George Lynn Cross Research Professor in the College of Medicine. During his tenure as Vice President for Research, Gilmore had primary responsibility for a $100 million+ annual research portfolio, which grew 40 percent during his tenure. This research management experience set Gilmore apart from other outstanding scientists vying for the position.

Scientifically, Gilmore is an internationally recognized expert on antibiotic resistant infections, particularly resistant staphylococcus and enterococcus “Superbugs.” He organized the First International American Society for Microbiology Conference on Enterococcus in Canada in 2000, and produced the definitive textbook on this leading cause of resistant, hospital-acquired infection. His research has been published in leading journals, including Science, Nature and Proceedings of the National Academy of Science.

His research is aimed at developing new strategies for treating these infections, including infections of the eye. “We identify the critical events in infection that result in permanent injury, such as visual loss or death, and develop new ways to intercede. Ultimately our goal is to create new, more effective antibiotics to destroy these bacteria, or at least limit the destructiveness of the infection,” says Gilmore. Gilmore serves on numerous review panels for NIH, NSF and FDA, as well as on several corporate scientific advisory boards.

Michael S. Gilmore, Ph.D.

Dr. Gilmore was selected from among the leading senior researchers in vision science in the world. A candidate was sought who was an internationally recognized leader in the field, and who also possessed the vision, creativity and energy to lead the world’s premier vision research institute. The mission of The Schepens Eye Research Institute is to cure blindness by developing new technologies to prevent visual loss and restore sight.

According to Kennett F. Burnes, Chairman of the Institute’s Board of Trustees and President and Chief Executive Officer at Cabot Corporation, “Mike embodies all the qualities of leadership, scientific talent and humanity for which The Schepens Eye Research Institute stands, and continues to need, as it moves forward in the years to come.”
A native of Providence, Rhode Island, Dr. David Snyder spent part of his youth in North Falmouth, Massachusetts. He completed his bachelor’s degree in marine biology in 1971 and his M.D. in 1975, both at Brown University. Following an internship at University of Southern California/Doheny Eye Institute and a residency at Illinois Eye and Ear Infirmary, Snyder became a fellow in retinal and macular diseases at Schepens Retina Associates.

A private-practice ophthalmologist for 26 years in Delray Beach, Florida, Snyder specializes in diabetic, macular and retinal vascular diseases. He is also a Corporator of The Schepens Eye Research Institute and on the Board of Directors of Brown University School of Medicine.

Q: I have heard about some new drugs for age-related macular degeneration. Can you give me an update on standard treatments and on the new drugs, particularly anti-VEGF drugs?

A: One of the most exciting areas of basic research today involves the study of angiogenesis, blood vessel growth, and its flip side—anti-angiogenesis, which arrests blood vessel growth. These two phenomena have been under study in the laboratory of Dr. Patricia D’Amore, a senior scientist at The Schepens Eye Research Institute, for a number of years. The anti-VEGF drugs you have been hearing about for age-related macular degeneration are based on work she and others in her field have done.

To understand how these drugs fit into the AMD treatment picture, here is a little background.

WHAT IS AMD?

Age-related macular degeneration is actually a group of diseases, all of which cause the deterioration of the macula, the tiny light sensitive center of the retina responsible for sharp vision needed for reading and color perception. There are two major forms of AMD—dry and wet.

DRY AMD

Dry AMD causes age spots called drusen that slowly develop on the macula, first causing distorted vision and, ultimately, over a period of years, severe central vision loss.

Although there are few treatments for dry macular degeneration, results of the National Eye Institute’s Age Related Eye Disease Study suggest that certain nutrients slow progression. Many clinicians, therefore, now suggest that patients take one Centrum with lutein daily and four OcuVite® Preservision tablets daily along with lots of dark green leafy vegetables as a source of lutein and xanthanthine. They also encourage patients to stop smoking, which has been shown to be a risk factor for AMD.

In addition, there is now interest in certain drugs not designed specifically for AMD, but which seem to have a protective effect through an anti-inflammatory process, against macular degeneration. Among those drugs are Lipitor® and Celebrex®. Lipitor is a drug, known as a statin, that has been used to lower cholesterol. Celebrex is a member of a class called selective COX2 inhibitors, which are used to treat rheumatoid arthritis.

WET AMD AND ANGIOGENESIS

Wet AMD is the result of bleeding or fluid leakage from fragile blood vessels that, scientists believe, proliferate in the retina in the eye’s misguided attempt to protect a damaged retina. The leakage blurs vision and scars the macula. Experts like Dr. D’Amore have discovered that this “angiogenesis” in wet macular degeneration is controlled by a chemical called vascular endothelial growth factor (VEGF), which is known to stimulate vessel growth in damaged or ischemic (of oxygen deprived) tissue.

Many approved treatments for wet AMD are focused on blocking the action, or eliminating the results, of VEGF-165, the most active form of the chemical in humans.

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Ms. Hudson-Wilson is widely published, and her record of service within the real estate industry and the community is extensive. A Counselor of Real Estate and member of the Real Estate Roundtable, she is an Urban Land Institute Trustee, and a founding member and past President of the Real Estate Research Institute. A former Chairman of the Pension Real Estate Association (PREA) and current member of Lambda Alpha International, she is also a Corporator of The Schepens Eye Research Institute. In addition, she has served on AIMR’s Candidate Curriculum Committee, and was a CFA examination grader. Prior to founding PPR, Ms. Hudson-Wilson was Director of Portfolio Strategies and a member of the Board of Directors of Aldrich, Eastman & Waltch, and held senior research positions at John Hancock Properties, Inc. and UNUM Life Insurance Company. She holds a B.A. cum laude in economics from the University of Vermont and an M.A. in economics from Boston University, where she also pursued further post-graduate studies. She is a Chartered Financial Analyst.

Dr. Thaddeus (Ted) P. Dryja, M.D.

Dr. Dryja is the David Glendenning Cogan Professor of Ophthalmology at Harvard Medical School and the Director of the David G. Cogan Eye Pathology Laboratory and the Ocular Molecular Genetics Institute at Massachusetts Eye and Ear Infirmary. He received his M.D. from Yale University School of Medicine and went on to do his residency and fellowship in Ophthalmology at Massachusetts Eye and Ear Infirmary as well as a fellowship in genetics at Children’s Hospital in Boston. He is board certified in Ophthalmology and in Clinical Molecular Genetics. Dr. Dryja is a member of the National Academy of Sciences and is the recipient of numerous awards and honors, including the prestigious Cogan Award from the Association for Research in Vision and Ophthalmology. Dr. Dryja’s clinical interests include ophthalmic pathology and hereditary diseases of the retina. Dr. Dryja and his wife, Maureen, live in Milton, Massachusetts.
Debbie and Maryanne Steen are identical twins who share a special talent of powerful voice and perfect pitch. The twins, a mere 20 years old, have been steadily entertaining audiences both large and small since grade school. This year, Debbie and Maryanne agreed to give a special performance at the Institute’s Fifth Annual Eye Ball fundraiser, *A Night for Sight*, on November 5, 2004.

Identical twins frequently share an unspoken bond uniting them in a manner most siblings don’t experience. In addition to their musical talent, they share the struggle of navigating this world without vision. Debbie and Maryanne, born prematurely, are blind as a result of retinopathy of prematurity (ROP), a condition that occurs in over 16 percent of all premature births.

Infants born months premature have immature eyes. The blood vessels that nourish the retina (the image-capturing area of the eye) are often missing. In some cases, blood vessel growth proceeds normally after birth, connecting the retina to the optic nerve. In others, blood vessels are triggered to grow at a very rapid pace. Bleeding from these fragile new vessels interferes with vision and also causes scarring. The resulting scar tissue pulls on the retina, tearing it and/or causing it to detach from the back of the eye. A number of vision-enhancing techniques have been developed and refined (many of them at The Schepens) to prevent and treat ROP including indirect laser surgery, the scleral buckle, and the open-sky vitrectomy.

Preserving or restoring even a little vision does a lot for these infants, enabling them to read, write and generally live more independent and productive lives. Unfortunately, those with the most severe form of ROP, as is the case with the Steen twins, cannot be helped by existing treatments. According to their grandmother Nancy Steen, they are well-rounded, well-adjusted siblings, finding solace in their ability to bring joy to others through their musical talents.

The girls were first introduced to the Institute in 1997 by their grandfather, Joseph Steen, during his tenure as State Commander of the American Legion. As Commander, Mr. Steen selected The Schepens Eye Research Institute (SERI) as the recipient of the funds raised by members of the American Legion of Massachusetts.

Mr. Steen’s efforts yielded more than $40,000 for SERI research, and he achieved this goal while also educating his fellow comrades about eye disease, vision impairment, and learning to strive with limited or no vision. He chose to present the donation with the help of his then 13-year-old granddaughters who showcased their talent by performing for Legion members.

One of the officers, James Army, was so moved by the girls’ talent, he vowed that he would designate half of the donations raised by the American Legion to the Institute when he became Commander. SERI reaped the benefits of that pledge this summer when Commander Army presented the Institute with a generous donation to further our research in an effort to prevent future generations from experiencing the same impairment.

Debbie and Maryanne chose a gift of music to honor their grandfather’s noble efforts on their behalf, thus inspiring others to give generously; a melodic notion.

"Debbie and Maryanne have shown us so much and given us the enjoyment of voices like angels and lack nothing through their darkness."

— Proud grandmother Nancy Steen
The lives of Theodora (Pinkie) Lang and Marie Ankeny had been intertwined for a century until Pinkie’s death last March at the age of 100. The identical twin sisters, born in 1903 in St. Paul, Minnesota, were extremely close. Even after they married and started their own families, they would travel around the world on a nearly annual basis. London was among their favorite places to visit, and celebrating their birthdays in the British capital with family and close friends became a tradition that continued well into their nineties. In fact, Institute founder Dr. Charles L. Schepens attended some of these functions.

Perhaps their most significant common trait was their strong sense of philanthropy. Pinkie’s primary interest was in pediatrics and she gave generously of her time and resources to the St. Paul Children’s Hospital, even serving as President of its Board of Directors at a time when such positions were not typically held by women. One of Marie’s strongest philanthropic interests is eye research, and in particular The Schepens Eye Research Institute, which Marie Ankeny and her family have been supporting since 1958. In fact, the Ankenys endowed the Institute’s DeWalt and Marie Ankeny Director of Research position to which Dr. Michael Gilmore was appointed in September, and which had been held by the late Dr. J. Wayne Streilein from 1993 to 2000. More recently, the Ankenys family pledged $1 million toward the Institute’s laboratory renovations.

Pinkie Lang did not have serious eye disease. However, the retinal afflictions that plagued Marie’s family fostered Pinkie’s connection to The Schepens Eye Research Institute. In the late 1950s, Marie’s husband, DeWalt H. Ankeny, Sr., suffered retinal detachments that threatened to rob him of his sight. Although nowadays detached retinas are repaired with relative ease, at that time such a condition would often lead to blindness. Mr. Ankeny had been seen by several physicians who had been unable to treat him effectively. It was only when Dr. Charles L. Schepens operated on Mr. Ankeny that his vision was restored. Using a surgical technique that he had developed at the Retina Foundation (the predecessor to The Schepens Eye Research Institute), Dr. Schepens was able to successfully reattach Mr. Ankeny’s retinas. Decades later, when one of Marie’s retinas became detached, Dr. Schepens and his associates used the same procedure to save her sight. These experiences resulted in Marie’s great fondness for Dr. Schepens and forged her commitment to support eye research and help those whose eye diseases cannot be cured at the present time.

As a final expression of her love for Marie, Pinkie made a significant contribution to support The Schepens Eye Research Institute’s efforts to rid future generations of blindness. Several years ago, Pinkie funded a charitable remainder trust. This trust provided Pinkie with income for the rest of her life. Upon her death, the trust terminated and funds were distributed to The Schepens. Pinkie’s kind act serves to honor her sister. Furthermore, it gives hope to those suffering from incurable blinding diseases that we may one day find a cure for them, much like we were able to find a cure for DeWalt and Marie Ankeny’s retinal detachments.

To learn more about how you can provide for The Schepens Eye Research Institute in your will or trust, please contact George Constant at (617) 912-2572 or (877) 724-3736 (toll free). constant@vision.eri.harvard.edu

The William Wolff Society recognizes and honors those who include the Institute in their estate plans.
The Institute is very grateful for the continuing support of our clinical partners in presenting the annual Eye & Vision Research Symposia Series. We are particularly grateful for the generosity of Mr. John Palmer of The Magnifying Center and to Ms. Victoria McCullough for their commitment in supporting the Symposia Series.

The 2005 Series schedule is:

Monday, February 7
Boca Raton Marriott
9 a.m.–Noon

Tuesday, February 8
Vero Beach Museum of Art
9 a.m.–Noon

Thursday, February 10
The Sarasota Hyatt
1:30 p.m.–4 p.m.

Friday, February 11
Ft. Myers Harborside Center
9 a.m.–Noon

Saturday, February 12
The Philharmonic Center for the Arts, Naples
9 a.m.–Noon

Plans are well underway for the 2005 Florida Eye & Vision Research Symposia Series. Thousands of Florida’s year-round residents and “snowbirds” will once again hear the very latest on advancements in eye disease research and the latest clinical treatments next spring. The Schepens Eye Research Institute joins forces with several Florida-based Schepens clinical faculty members at the annual Eye & Vision Research Symposia Series.

Those attending the 2005 Symposia Series will learn the latest updates on macular degeneration, optic nerve disease, glaucoma, diabetic retinopathy and dry eye syndrome. This year, Ankeny Director of Research and Acting CEO Michael S. Gilmore, Ph.D., will be introduced to the Florida audiences. The Institute’s Patient Liaison, Rich Godfrey, will also join Dr. Gilmore. They plan to share the program with David Snyder, M.D. (clinical faculty member and Corporator of The Schepens) of Delray Eye Associates, along with Florida Eye Institute (Vero Beach) clinicians, Sarasota Retina Institute clinicians and clinical faculty from Retina Consultants of Southwest Florida.

A VERY SPECIAL PALM BEACH RECEPTION

On Wednesday, February 9, Mr. and Mrs. Leo Vecellio will host a special invitation-only reception in Palm Beach to benefit The Schepens. Katie Vecellio is a member of the Board of Trustees, and Leo serves as a Corporator for the Institute. They have been constant supporters of the Institute for the past two decades, and are truly regarded as among our most philanthropic friends. In fact, the newly remodeled laboratory of Darlene A. Dartt, Ph.D., will soon be named in their honor as an acknowledgment of their generosity.
At the present time, photodynamic therapy using Visudyne with cold diode laser therapy is the best approved treatment for abnormal new vessels in the macula. Additionally, injection of a type of cortisone called Kenalog right into the eye, in conjunction with photodynamic therapy, has become the standard of care in this country. Kenalog seems to have anti-angiogenesis properties as well as anti-inflammatory effects. With a series of these two methods of treatment, clinicians like myself can eradicate abnormal macular blood vessels in approximately 80 percent of patients.

Today, the new anti-angiogenesis (anti-VEGF) drugs getting public attention take these treatments a step further. They are designed to prevent abnormal blood vessels from growing in the first place. All of these drugs are still being tested by the FDA.

Here are the leading candidates:

- **MACUGEN™** by EyeTech and Pfizer. This drug is a man-made chemical formed by building blocks of protein, called an aptamer, which binds with VEGF and blocks its action. It is injected into the eye every six weeks.

- **LUCENTIS™** by Genentech and Novartis. This is an antibody fragment known as ranibizumab (rhu-Fab), which also binds to VEGF to block its action. This drug is injected into the eye every four weeks.

- **RETAANE®** by Alcon. This is the steroid anecortave which is injected behind, but not into, the eye and has strong anti-angiogenesis properties and anti-matrix metalloproteinase properties. Matrix metalloproteinases (MMP) are enzymes needed for blood vessels to grow into the retina. Blocking the action of MMPs helps to eliminate abnormal blood vessels from the retina.

- **SQUALAMINE** by Genaera. This strong anti-angiogenic compound is injected into the body rather than into the eye.

- **VEGF Trap.** This new synthetic molecule with strong anti-angiogenic effects is a very potent inhibitor of VEGF.

We look forward to the release of some of these drugs as early as 2005. My general sense is that one or two will emerge as the predominant treatment, probably in conjunction with other drugs and lasers in the next few years, thus arming ophthalmologists with much more effective treatments for these serious diseases of the retina.
FY04 marked a significant year in strengthening the financial stability of the Institute. We ended FY04 with a $7.1 million surplus, which resulted from increased federal revenue, continued disciplined spending, and some one-time events. The investment in our building renovation program is nearing completion and shortly we will have a state-of-the-art research facility for our scientists to continue their important work toward finding cures for eye diseases and blindness. The Institute’s unrestricted and restricted endowment are growing stronger, building a solid financial infrastructure to continue to support current research and be in a position to take advantage of future growth opportunities.

A synopsis of the Institute’s financial picture for the fiscal year ending June 30, 2004 shows total assets of $74.7 million, which increased $10.1 million from the previous year. The increase is primarily due to an increase in pledges receivable of $0.9 million, an increase of $2.6 million in our long-term investments, and an increase in our land, buildings and equipment of approximately $8.6 million, reflecting the construction during FY04 which will be completed in early FY05. These additions are offset by the reduction of our construction advance of $0.3 million, a reduction in our long-term debt of $0.2 million, an increase in our deferred support of $1.1 million, reflecting advance payments of certain research programs, and an increase in our accounts payable of approximately $0.4 million, reflecting the construction activity.

The increase in liabilities of $1.0 million is primarily due to an increase in deferred support of $1.1 million, and an increase in our accounts payable obligations of $0.4 million offset by a reduction of long-term debt of $0.2 million, and a reduction of our construction advance of $0.3 million.

Total equity (net assets) of $46.0 million increased by $8.9 million. The increase results primarily from the increase in our investment in the physical plant of $8.6 million, an increase in our long-term investments of $2.6 million, an increase in our temporarily restricted net assets of $2.0 million and the receipt of $2.5 million from our key man life insurance policy. These increases were offset by the reduction of cash in our building fund of $4.8 million.

Total unrestricted revenue of $33.5 million increased $6.4 million over the last fiscal year primarily due to increased operating revenues of $1.4 million (mainly federal grants and contracts), the receipt of $3.4 million in building fund contributions, proceeds from the key man insurance policy of $2.5 million and an increase of $0.7 million in bequests, offset by deferred revenue released from donor restrictions of $1.5 million less than FY03.

Total operating expenses were $26.2 million, an increase of $0.6 million primarily due to increased funded research programs.

In summary, FY04 follows prior years in becoming a building block for the future of the Institute, supporting our research, programmatic and building initiatives.

Robert L. Gable
Chair, Finance Committee

“The Institute’s unrestricted and restricted endowment are growing stronger, building a solid financial infrastructure to continue to support current research and be in a position to take advantage of future growth opportunities.”
## Financials

### Statements of Financial Position

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cash in interest-bearing accounts</td>
<td>$3,663,902</td>
<td>$5,967,672</td>
</tr>
<tr>
<td>Funds held in trust by others</td>
<td>726,741</td>
<td>696,118</td>
</tr>
<tr>
<td>Trustee-held bond funds</td>
<td>3,608,221</td>
<td>3,405,947</td>
</tr>
<tr>
<td>Pledges receivable, net</td>
<td>1,897,694</td>
<td>989,956</td>
</tr>
<tr>
<td>Grants and contracts receivable</td>
<td>475,894</td>
<td>680,966</td>
</tr>
<tr>
<td>Prepaid expenses and other assets</td>
<td>315,575</td>
<td>137,996</td>
</tr>
<tr>
<td>Land, buildings and equipment, net of accumulated depreciation</td>
<td>33,094,867</td>
<td>24,494,299</td>
</tr>
<tr>
<td>Long-term investments at fair market value</td>
<td>30,866,196</td>
<td>28,272,507</td>
</tr>
<tr>
<td><strong>Total assets</strong></td>
<td>$74,649,090</td>
<td>$64,645,461</td>
</tr>
<tr>
<td><strong>Liabilities and Net Assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accounts payable and other accrued expenses</td>
<td>1,761,654</td>
<td>1,348,661</td>
</tr>
<tr>
<td>Construction advance</td>
<td>9,628,778</td>
<td>9,907,282</td>
</tr>
<tr>
<td>Accrued payroll</td>
<td>587,968</td>
<td>631,002</td>
</tr>
<tr>
<td>Deferred support</td>
<td>2,961,311</td>
<td>1,788,212</td>
</tr>
<tr>
<td>Annuity obligations</td>
<td>100,000</td>
<td>100,000</td>
</tr>
<tr>
<td>Long-term debt</td>
<td>13,575,000</td>
<td>13,795,000</td>
</tr>
<tr>
<td><strong>Total liabilities</strong></td>
<td>$28,614,711</td>
<td>$27,570,157</td>
</tr>
<tr>
<td><strong>Commitments and contingencies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Net assets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unrestricted</td>
<td>11,712,453</td>
<td>6,609,677</td>
</tr>
<tr>
<td>Board designated</td>
<td>6,409,342</td>
<td>4,383,542</td>
</tr>
<tr>
<td>Temporarily restricted</td>
<td>14,470,841</td>
<td>12,530,953</td>
</tr>
<tr>
<td>Permanently restricted</td>
<td>13,441,743</td>
<td>13,551,132</td>
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<tr>
<td><strong>Total net assets</strong></td>
<td>$46,034,379</td>
<td>$37,075,304</td>
</tr>
<tr>
<td><strong>Total liabilities and net assets</strong></td>
<td>$74,649,090</td>
<td>$64,645,461</td>
</tr>
</tbody>
</table>
## Statements of Activities

### Years ended June 30, 2004 and 2003

<table>
<thead>
<tr>
<th></th>
<th>2004</th>
<th>2003</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Changes in unrestricted resources:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Operating revenues:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Federal grants and contracts</td>
<td>$18,661,453</td>
<td>$17,478,860</td>
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<tr>
<td>Contributions</td>
<td>2,042,787</td>
<td>1,023,919</td>
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<tr>
<td>Contributions—Building Fund</td>
<td>2,223,558</td>
<td>—</td>
</tr>
<tr>
<td>Bequests</td>
<td>1,924,899</td>
<td>1,162,298</td>
</tr>
<tr>
<td>Non-federal grants and contracts</td>
<td>2,928,735</td>
<td>2,829,946</td>
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<tr>
<td>Income on long-term investments</td>
<td>409,436</td>
<td>211,428</td>
</tr>
<tr>
<td>License and royalty fees</td>
<td>494,291</td>
<td>629,023</td>
</tr>
<tr>
<td>Proceeds from key man life insurance policy</td>
<td>2,518,159</td>
<td>—</td>
</tr>
<tr>
<td>Other</td>
<td>177,790</td>
<td>74,709</td>
</tr>
<tr>
<td><strong>Total operating revenues</strong></td>
<td>$31,381,108</td>
<td>$23,410,183</td>
</tr>
</tbody>
</table>

|                                |               |               |
| **Net assets released from restrictions:** |               |               |
| Contributions—satisfaction of program restrictions | 1,334,448 | 2,504,123 |
| Income on long-term investments—satisfaction of program restrictions | 827,293 | 1,187,097 |
| **Total resources released from restrictions** | 2,161,741 | 3,691,220 |
| **Total unrestricted revenues** | $33,542,849 | $27,101,403 |

|                                | 2004          | 2003          |
| **Operating expenses:**         |               |               |
| Research                       | 19,486,915    | 18,917,855    |
| Management and general         | 6,105,588     | 5,812,123     |
| Fundraising and public relations | 648,670      | 903,830       |
| **Total operating expenses**   | $26,241,173   | $25,633,808   |

|                                | 2004          | 2003          |
| **Unrestricted income from operations before net unrealized losses on investments:** |               |               |
| Net unrealized losses on investments | (173,100)   | (14,151)      |
| **Increase in unrestricted net assets** | $7,128,576 | $1,453,444 |

|                                | 2004          | 2003          |
| **Changes in temporarily restricted net assets:** |               |               |
| Contributions                   | 912,211       | 634,420       |
| Realized gains on sale of investments | 1,616,712   | 2,175,518     |
| Net unrealized gains (losses) on sale of investments | 570,985 (1,560,242) |
| Income on long-term investments | 1,001,721     | 699,123       |
| Net assets released from temporary restrictions | (2,161,741) | (3,691,220) |
| **Increase (decrease) in temporarily restricted net assets** | $1,939,888 | (1,742,401) |

|                                | 2004          | 2003          |
| **Changes in permanently restricted net assets:** |               |               |
| Gifts and bequests              | 50,000        | 92,138        |
| Transfers per donor             | (159,389)     | —             |
| **(Decrease) increase in permanently restricted net assets** | (109,389) | 92,138 |
| **Increase (decrease) in net assets** | 8,959,075 | (196,819) |

|                                | 2004          | 2003          |
| **Net assets at the beginning of the year** | $37,075,304 | $37,272,123 |
| **Net assets at the end of the year** | $46,034,379 | $37,075,304 |
**EMERITUS SENIOR SCIENTISTS**
Adler, Alice J., Ph.D.
Cintron, Charles, Ph.D.
Doane, Marshall G., Ph.D.
Refojo, Miguel F., Sc.D.
Schepens, Charles L., M.D.

**SENIOR SCIENTISTS**
Azar, Dimitri, M.D.
Burns, Stephen, Ph.D.
D’Amore, Patricia, Ph.D.
Dana, Reza, M.D., M.P.H.
Dartt, Darlene A., Ph.D.
Delori, François, Ph.D.
Elsner, Ann, Ph.D.
Gilmore, Michael S., Ph.D.
Gipson, Ilene K., Ph.D.
Joyce, Nancy, Ph.D.
Kazlauskas, Andrius, Ph.D.
Lorenzi, Mara, M.D.
Peli, Eliezer, O.D.
Stein-Streilein, Joan, Ph.D.
Sullivan, David A., Ph.D.
Webb, Robert H., Ph.D.
Zieske, James, Ph.D.

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Ksander, Bruce, Ph.D.
Taylor, Andrew, Ph.D.

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Fine, Elisabeth, M., Ph.D.
Lashkari, Kameran, M.D.
Young, Michael, Ph.D.

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Chen, Lu, M.D., Ph.D.
Darland, Diane, Ph.D.
Gerhardinger, Chiara, M.D., Ph.D.
Gregory, Meredith, Ph.D.
Masli, Sharmila, Ph.D.
Mo, Jun Song, M.D., Ph.D.
Ng, Tat Fong, Ph.D.
Rawe, Ian, Ph.D.
Rios-Garcia, Jose, Ph.D.
Romeo, Giulio R., M.D.
Woods, Russell, Ph.D.
Zhang-Hoover, Jie, M.D., Ph.D.

**ADJUNCT SENIOR SCIENTIST**
Snodderly, D. Max, Ph.D.

**ADJUNCT ASSOCIATE SCIENTIST**
Klassen, Henry, M.D., Ph.D.

**ADJUNCT ASSISTANT SCIENTIST**
Ruberti, Jeffrey, Ph.D.

**EMERITUS CLINICAL SENIOR SCIENTISTS**
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Toletino, Felipe I., M.D.

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Dohlman, Claes H., M.D.
Hirose, Tatsu, M.D.
McMeel, J. Wallace, M.D.
Miller, Joan, M.D.
Trempe, Clement L., M.D.
Weiter, John, M.D.

**INVESTIGATORS**
Greiner, Jack V., D.O., Ph.D.
Rubin, Peter, M.D.

**CLINICAL ASSOCIATE SCIENTISTS**
Colby, Kathryn, M.D., Ph.D.
Grosskreutz, Cynthia, M.D., Ph.D.
Pasquale, Louis, M.D.
Schaumberg, Debra, Sc.D.

**ADJUNCT CLINICAL SENIOR SCIENTISTS**
Bonini, Stefano, M.D.
Kenyon, Kenneth R., M.D.
Kinoshita, Shigeru, M.D., Ph.D.

**ADJUNCT CLINICAL ASSOCIATE SCIENTISTS**
Arai, Mikki, M.D.
Fletcher, Donald, M.D.
Wing, Glenn L., M.D.

**ADJUNCT CLINICAL ASSISTANT SCIENTISTS**
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Ghuman, Thomas, M.D.
Hughes, Mark S., M.D.
Raskauskas, Paul, M.D.
Sang, Delia, M.D.
Usomoto, Nari, M.D.
Walker, Joseph, M.D.

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Susan Hudson-Wilson

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David L. Conlon
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Physical Plant and Risk Management
Frances Ng
Director of Human Resources
Schepens Receives NIH “Roadmap” Grant

Institute to join forces with experts from other biomedical and technological fields in battle against blindness

Harvard’s Schepens Eye Research Institute has been awarded a grant from the National Institutes of Health to form teams of basic and clinical researchers from many disciplines to find cures for blinding eye diseases such as macular degeneration, diabetic retinopathy and glaucoma. The Institute competed with hundreds of organizations for the award. It is the only eye research institute to receive this type of award. The grant is part of a larger initiative known as the “NIH Roadmap,” which seeks to find new ways to solve problems that have not yielded to traditional research. NIH announced the recipients of these special awards on September 30 in Bethesda, Maryland.

“This is an exciting opportunity to bring enormous energy and new brain power to solve some of the most complex puzzles in eye research,” said Darlene Dartt, Ph.D., Director of Scientific Affairs at The Schepens, who is heading up the project. The Institute plans to combine forces with other components of the Harvard Medical School Department of Ophthalmology, including Massachusetts Eye and Ear Infirmary, and other Harvard teaching hospitals by enlisting top investigators exploring diseases as diverse as Alzheimer’s, rheumatoid arthritis and heart disease to be part of a “think tank” to cure blindness.

According to Michael Gilmore, Ph.D., Ankeny Director of Research and Acting Chief Executive Officer of The Schepens Eye Research Institute, “This award demonstrates that NIH recognizes eye disease as one of the most important problems facing the rapidly aging population. The selection of The Schepens Eye Research Institute as the location for that program reflects the national leadership of Schepens and the Harvard Department of Ophthalmology in the search for new cures for blindness.”

For more information about the NIH Roadmap, please visit the Web site at: http://www.nihroadmap.nih.gov. For additional information about the Schepens’ Roadmap grant, go to http://www.theschepens.org/nih_roadmap.htm.