As we begin 2015, it is my pleasure to share my reflections about our accomplishments of the past year and my optimism about the new year.

It is my privilege to acknowledge your role in making this possible. We accomplished a great deal in 2014. The Scripps Research Institute (TSRI) continues to be recognized around the world for its research. As highlighted in these pages, high-impact findings ranged from inventing a breakthrough tool to disrupt a gene involved in a majority of cancers to developing new chemical transformations with profound implications for drug development. With public support and philanthropy, we have come from TSRI discoveries that address serious medical needs—from the Ebola crisis to Parkinson’s disease and so many others.

As highlighted, a vibrant independent research institute. The search for a permanent president and CEO is ongoing.

Thank you for helping TSRI reach $16.9 million in philanthropy revenue in FY 2014! Your gifts help support TSRI’s life-saving research.

The Scripps Research Institute (TSRI) serves humanity by creating new knowledge in the biosciences, applying it to high-return research, advancing emerging fields and speeding the application of research to patients in need.

While grants and contracts provide funding for a significant portion of the institution’s research activities, gifts from individuals and private foundations provide a critical source of funding for high-risk, high-reward research, achieving meaningful and significant results in the new year.

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Jim Paulson
Chairman of the Board and CEO

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A team led by researchers from the Scripps Research Institute (TSRI) continue to make strides in the quest to understand the fundamental processes of life and advance human health. Here is a small sampling of highlights from 2014.

**TSRI DANISH DRUG FOR MULTIPLE SCLEROSIS AND ULCERATIVE COLITIS ADVANCES**

In 2014 the team—a collaboration between TSRI and Novo Nordisk A/S—announced positive new data were released in two separate clinical trials of a drug candidate first discovered and synthesized at TSRI. The molecule, ZMapp, is a mix of monoclonal antibodies that target Ebola virus and Middle Eastern Respiratory Syndrome coronavirus (MERS-CoV). The researchers hope that the drug could fight the virus before it has a chance to replicate within the body. The researchers also hope to investigate the implications for animal models. The molecule, taken orally, improved the function of MYC, a regulator involved in a majority of cancers when produced in the brain. Nerve cells appear to make more of the Alzheimer’s protein. Now TSRI biologists have identified a signaling pathway that stimulates weight loss and may also protect against diabetes. “This pathway works with the gut-brain connection to promote the formation of brown fat cells during weight gain and prevents diabetes,” said TSRI Associate Professor Floyd E. Romesberg, who led this research. “This chemical mechanism of life on Earth in all its diversity is encoded by only two pairs of bases,” said TSRI Associate Professor Floyd E. Romesberg, who led this research. “This chemical mechanism of life on Earth in all its diversity is encoded by only two pairs of bases,” said TSRI Associate Professor Floyd E. Romesberg, who led this research.

**MIMIC OF ‘GOOD’ CHOLESTEROL COULD FIGHT HEART DISEASE AND STROKE**

A team led by researchers from Scripps Florida and the Mayo Clinic has identified a mimic of “good” cholesterol that shows promise as a new drug to prevent and treat cardiovascular disease, according to new research. This is the first time a compound has been identified that can mimic the function of high-density lipoprotein (HDL), also known as “good” cholesterol. The new approach holds promise for helping patients with heart disease and stroke, said team leader TSRI Professor M. Reza Ghadiri (above). The new approach builds upon a previously identified, unique multidisciplinary environment in chemistry and biology at TSRI allowed this progression to clinical trials.

**REVEALED: WEAK SPOTS IN EBOLA’S DEFENSES**

The structural images of Ebola virus are like enemy reconnaissance, helping researchers develop vaccines and drugs that could help stop the deadly disease. In a new study, a team led by Jin-Quan Yu (above), who is Frank and Katherine Harvey Institute for Research and Medicine, and Skaggs Scholar and Founding Dean of the Skaggs School of Pharmacy and Pharmaceutical Sciences, reported on a new approach for Alzheimer’s prevention and therapy.”

**NEW STRATEGY TAKES AIM AT ALS, FRONTOTEMPORAL DEMENTIA**

The study found that drugs that can boost the production specifically in the median eminence region of dopamine neurons, a part of the brain that helps control movement, could improve certain aspects of the Alzheimer’s disease. “The new study shows that drugs that can boost the production specifically in the median eminence region of dopamine neurons, a part of the brain that helps control movement, could improve certain aspects of the Alzheimer’s disease,” said TSRI Professor Joel N. Blumoff. “But now we realize that it could indicate a new approach for Alzheimer’s prevention and therapy.”

**NEW Approach TO TREAT PROSTATE CANCER**

In addition to exploring potential new drugs for breast cancer, researchers are battling prostate cancer, a disease that affects 1 out of 7 men in the U.S. The team hopes that their new approaches will lead to new treatments for prostate cancer. “Prostate cancer is still a large problem today,” said TSRI Professor M. Reza Ghadiri (above). The new approaches hold promise for helping patients with heart disease and stroke.

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**BRAIN BROWSER NON VULNERABILITY FOR VACCINE DEVELOPMENT**

In good news for the effort to develop a vaccine against AIDS, a team has uncovered a non-vulnerable site on the HIV virus. “When sites show that for the first time that targeting this vaccin -

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Recently published studies report that an increased ability to burn fat at characteristic times also may be a factor in weight loss and may also protect against diabetes. “This pathway works with the gut-brain connection to promote the formation of brown fat cells during weight gain and prevents diabetes.”

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The new study suggests that drugs that can boost the produc -

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**Biomedical Advances from 2014**

**THE ENSKY TAKES AIM AT MULTIPLE SCLEROSIS AND **
**PERIPHERAL NERVES**

A team led by researchers from Johns Hopkins University School of Medicine has developed a new treatment for multiple sclerosis (MS) and peripheral nerve damage called MSK-2. The therapy is designed to promote repair and regeneration of damaged nerve tissue. The team used a combination of stem cells and an innovative delivery system to deliver the therapy directly to the site of injury. The results showed significant improvement in nerve function and reduced inflammation in animal models. The researchers are planning to conduct clinical trials in the near future to test the therapy's effectiveness in patients.

**NEW TECHNIQUE TO PRODUCE CARBON DIOXIDE FROM **
**DRUG METABOLITES AND WATER**

Scientists at the Scripps Research Institute (TSRI) have developed a new technique to produce carbon dioxide (CO₂) from drug metabolites and water. This process could be a valuable source of CO₂, which is currently derived from burning fossil fuels, and could help reduce greenhouse gas emissions. The technique involves using a catalytic reaction to convert the drug metabolites and water into CO₂, which can then be used in various applications such as food processing, beverage production, and industrial processes.

**BEYOND NON VIOLABILITY FOR VACCINE DEVELOPMENT**

In an effort to develop a vaccine against AIDS, a team has discovered a new technique that uses heat and cold to induce the formation of non-viral particles. These particles can be used as a delivery system for the vaccine and have shown promise in early-stage studies. The researchers are now working on improving the stability and effectiveness of the particles to make them suitable for use in human trials.

**DISCOVERY MAY LEAD TO IMPROVED BREAST CANCER TREATMENTS**

A team of researchers has identified a new target for breast cancer treatment. They found that a specific protein, called myc, is overactive in breast cancer cells and can lead to the development of drug resistance. The researchers developed a new drug, called TIC10, that targets this protein and shows promise in early-stage studies. Further research is needed to determine the safety and efficacy of the drug in clinical trials.

**NEW TECHNIQUES TO PROTECT ANTIBODY PROJETS FROM **
**HARMFUL AGGREGATES**

Researchers at the Scripps Research Institute and other institutions have developed new techniques to protect antibodies from harmful aggregates, which are a common cause of drug failure. The techniques involve using small-molecule drugs to stabilize the antibodies, which can extend their shelf life and improve their effectiveness. These techniques could have significant implications for the development of new treatments for a variety of diseases, including cancer, HIV, and Alzheimer's disease.

**UNDRUGGABLE TARGET TO BLOCK TUMOR GROWTH**

A team of researchers has identified a new target for cancer treatment that could potentially block tumor growth. They found that a protein, called MYC, is overactive in many cancers and can lead to the development of drug resistance. The researchers developed a new drug, called RPC1063, that targets this protein and shows promise in early-stage studies. Further research is needed to determine the safety and efficacy of the drug in clinical trials.
REVEALED: WEAK SPOTS IN EBOLA'S DEFENSES

A team led by researchers from California Institute of Technology (Caltech) and the University of California at Berkeley has identified a potential entry point for Ebola virus, a highly lethal pathogen, in human cells.

“This finding offers new possibilities for the therapeutic activity of small molecules that target the virus,” said team leader TSRI Associate Professor of Chemistry Andrew Ward (above), whose work was featured in the journal Science in February. "We have a significant lead on finding new small-molecule drugs that could treat Ebola," he said.

The enzyme that is first targeted by the virus’ spike protein is the receptor that allows the virus to enter cells. The research team, led by Andrew S. Wilson, Ph.D., Chair of the Skaggs Institute for Chemical Biology at TSRI, demonstrated that the small-molecule drugs, called "unigniters," can block the virus from entering human cells.
From the President

As we begin 2015, it is my pleasure to share my reflections on our accomplishments of the past year and my optimism for the future of The Scripps Research Institute (TSRI).

This year, TSRI continued to be recognized around the world for its research. As highlighted in these pages, high-profile findings ranged from inventing a breakthrough method to disrupt a gene involved in a majority of cancers to developing new chemical transformations with profound implications for drug development. Wide public exposure also came from TSRI discoveries that addressed unmet medical needs—from the Ebola crisis to autoimmune diseases including multiple sclerosis and ulcerative colitis.

The high quality of TSRI's faculty was acknowledged this year with numerous awards, honors, federal grants and rankings that bring recognition to TSRI. To name only a few of these, Dale Boger and Benjamin Cravatt were elected to the National Academy of Sciences and Gerald Joyce was elected to the National Academies Institute of Medicine, Chi-Huey Wong won the Wolf Prize in Chemistry, Erica Ollmann Saphire was elected to both the American Association for the Advancement of Science and American Academy of Microbiology. In addition, based on citations per paper Thomson-Reuters listed 11 TSRI faculty members as among the "World’s Most Influential Scientists."

Also this year, U.S. News & World Report reaffirmed that TSRI’s Kelllogg School of Science and Technology is among the nation’s best in the biological and chemical sciences. The program is now ranked second in the specialty of biochemistry, sixth in the specialty of organic chemistry, seventh overall in chemistry and ninth overall in the biological sciences. We applaud the faculty, students, alumni and donors who have built the Kelllogg School's well-deserved reputation for excellence.

Notable among this year’s philanthropic supporters are the late Jean and Keith Kellogg, committed friends of higher education who provided more than $5 million in support to TSRI over time through outright and planned gifts. Jean passed away earlier this year and has further enriched the Kelllogg family legacy at TSRI by providing a bequest that will be used to support first-year graduate students and Alzheimer’s disease research. Another significant unrestricted bequest to TSRI was made by the estate of Allan and Beverly Gale of San Diego.

This year we also renewed our collaboration with the International AIDS Vaccine Initiative (IAVI) to extend our joint work at the Neutralizing Antibody Center for the next five years, supported by $6.5 million in funding in 2014, which includes approximately $4.4 million from the Bill & Melinda Gates Foundation. The Gates Foundation also provided TSRI with up to $3 million in direct support for operations and equipment, including the powerful new Titan cryo-electron microscope. A federal grant of $13 million was also awarded to support HIV research at the institute.

The National Institutes of Health also awarded a significant grant to establish a center for excellence at TSRI to fight Ebola. This effort was fueled by a crowdfunding campaign that raised more than $200,000 from more than 800 contributors to purchase two badly needed machines to speed work to find new therapies for the disease. As part of the campaign, an anonymous foundation provided a $25,000 matching gift, and the Shaffer Family Foundation gave a gift of $100,000 to match its support for postdoctoral and graduate students in the laboratory of Dr. Jerold Chun.

In Florida, to name just a few of our supporters, the Klarman Foundation made gifts totaling $200,000 for two postdoctoral training fellowships under the direction of Patrick Griffin, whose laboratory is laying the groundwork for new treatments for immune disorders, diabetes and osteoporosis. The Men’s Golf Association at the Ballenisles Country Club provided more than $160,000 to fund a prostate cancer research fellowship and the Frenychian’s Creek Women for Cancer Research Group surpassed $1 million in cumulative giving in support of women’s cancer research. Peter and Janice Brock made a $100,000 pledge to fund blood cancer research. Also, Abby Jablin made a $100,000 gift to fund cardiovascular research in memory of her father, Dr. Paul A. Hurwitz, who practiced pulmonary medicine.

As we conclude celebrations of Scripps Florida’s 10th anniversary, it is notable that our Florida campus has attracted a total of more than $412 million in grants from federal sources—including a $5.7 million grant from the U.S. Department of Defense in 2014 to create an artificial immune system—as well as generous gifts from foundations and donors. As a testament to the quality of research, the Florida campus has generated more than 100 domestic and foreign patent applications and 40 technology licenses. We take pride in these accomplishments and look forward to our next 10 years as part of the Florida community.

On a personal note, I am proud to be a member of this institute and want to thank all of you for your support in this time of transition. Currently, the Board of Trustees and faculty are called in the goal to chart a future for TSRI as a vibrant independent research institute. The search for a permanent president and CEO is ongoing.

It is my privilege to acknowledge your role in making this year’s scientific achievements possible and to ask for your continued commitment to work together to advance critical biomedical discoveries in the new year.

Warm regards,

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FINANCIAL HIGHLIGHTS

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TSRI REVENUES, FISCAL YEAR 2014

% INTERNAL AND OTHER GRANTS
% INVESTMENT INCOME
% PHILANTHROPY
% OTHER

TSRI EXPENSES, FISCAL YEAR 2014

% BIOLOGICAL RESEARCH
% GRADUATE SCHOOL
% MANAGEMENT/GENERAL
% FUNDRAISING/OTHER

PHILANTHROPY REVENUE SOURCES, FISCAL YEAR 2014

% FOUNDATIONS
% INDIVIDUALS
% PLANNED GIFT/STATE
% CORPORATIONS