

# A GOAL FOR LIFE

For Friends and Supporters of the Ara Parseghian Medical Research Foundation



In 1994, when the Ara Parseghian Medical Research Foundation was launched, very little was known about Niemann Pick Type C disease. As we begin our 22nd year, we are in awe of the body of work that has been achieved through the conscientious and passionate work of so many researchers, and made possible by the generosity of thousands of individuals, corporations, foundations and NP-C families. This journey continues and we have a deep gratitude for what is being accomplished and we have great hope that these efforts will provide a bright future for those affected by NP-C disease.

## SCIENCE UPDATE

Vtesse, a biotechnology company located in Gaithersburg, MD, is developing a form of cyclodextrin (VTS-270) for the treatment of Niemann Pick -Type C disease. The National Institutes of Health first conducted a Phase I clinical trial with VTS-270 over the last two years testing its safety in children with NP-C. This trial was based on the result of research supported by the APMRF that showed that NP –C mice and cats lived longer when administered cyclodextrin.

Vtesse has raised \$25 million from investors to support the NIH-led VTS-270 trial and will work with researchers to launch a second, larger trial this fall. The second trial will enroll 51 patients in the U.S. and Europe. Vtesse has worked diligently to get a protocol agreed upon by both the United States Food and Drug Administration and the European Medicines Agency. Twenty testing sites will be opened in the USA and Europe.

Preliminary results from NIH Phase I trial, suggest that the rate of disease progression had slowed down (based on a standardized measure) in children treated with VTS-270 in the Phase I trial as compared to the rate in an age- and disease severity-matched cohort obtained from a separate natural history study of NP-C patients. The analyses also show that children treated with VTS-270 demonstrated improvement in several disease areas.

In the Phase I trial, among the 12 children treated with direct administration of VTS-270 into the cerebrospinal fluid via an intrathecal administration for more than six months and up to 12 months, the overall NPC score showed a slowing down in the rate of decline. In these patients, when the scores for impact on hearing were removed, the NPC score showed disease stabilization and halting of progression. Areas of cognition and speech have shown improvement of the disease state for participants in the study; while ambulation, fine motor skills, cognition, swallowing, and memory demonstrate slowing down of decline. Measurements of eye movement and hearing appeared to have worsened among participants in the Phase I trial.



Clinicians have administered more than 250 intrathecal administrations of the drug to study participants thus far with minimal administration-related side effects. Vtesse plans to submit more complete Phase I clinical trial results for presentation at a scientific meeting later this year. More details about the study can be found at [www.clinicaltrials.gov/ct2/show/NCT01747135](http://www.clinicaltrials.gov/ct2/show/NCT01747135).

“This initial analysis of the data look encouraging and this therapy may make a meaningful difference for children with NPC,” said Ben Machielse, Drs., President and Chief Executive Officer of Vtesse, Inc. The pivotal trial design will be randomized and controlled, and our planned implementation of the trial underscores the essence of our commitment to the NPC patients and their caregivers.

In addition, Vtesse has started a patient queue for each of the sites in the US. It is important to know how many patients are interested in being screened for inclusion in the trial. Each clinical trial site needs to be prepared for the number of patients they potentially may need to enroll. If you would like more information about the trial or if you would like to be placed in a patient queue, please contact Carrie Burke, head of advocacy at Vtesse. She can be reached at [Carrie@vtessepharma.com](mailto:Carrie@vtessepharma.com) or 240-801-9268 or go to: [www.thenpcstudy.com](http://www.thenpcstudy.com)

## SCIENTIFIC CONFERENCE UPDATE

Over 70 attendees gathered from around the globe at the annual Michael, Marcia & Christa Parseghian Scientific Conference for Niemann-Pick Type C (NPC) Research on June 11-13 at the University of Notre Dame. Hosted by the College of Science and the Ara Parseghian Medical Research Foundation (APMRF), the conference featured presentations from NPC researchers who shared their most recent findings, including work to better understand the rare disease and to find new opportunities for the development of NPC therapies.

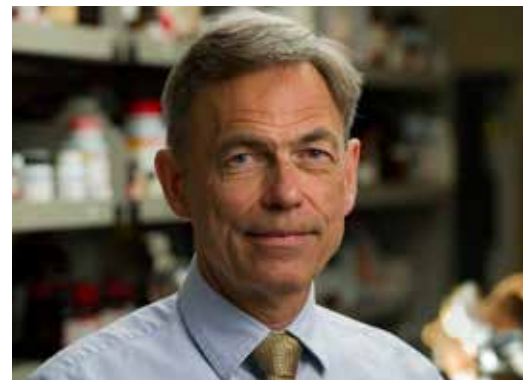
The conference kicked off on Thursday afternoon with a presentation from Stanford University's Suzanne Pfeffer, professor of biochemistry, who is studying the role of membrane proteins in cholesterol trafficking. An additional highlight of the session was the exciting work of Guosheng Liang, associate professor of molecular genetics at the University of Texas Southwestern Medical Center. Liang is using new gene editing technology in order to create a new NPC mouse model and is looking in to potentially applying the same method for gene therapy in those afflicted with NPC. The day concluded with a reception and dinner at the campus' banquet facilities in the Morris Inn with presentations from Cindy Parseghian, president of APMRF and P.J. Brooks, Ph.D., health science administrator for the Office of Rare Disease Research at the National Institutes of Health (NIH).

On Friday, Paul Helquist and Olaf Wiest, professors of chemistry and biochemistry at the University of Notre Dame, presented their most recent efforts to design and synthesize cholesterol analogues that are now available to structural biologists to probe the transfer of cholesterol between proteins, a critical process related to NPC. Several other researchers including Ed Holson, director of the medicinal chemistry group at the Broad Institute; Fred Maxfield, professor and chairman of biochemistry at Weill Cornell Medical College; and Dan Ory, M.D., professor of medicine, cell biology and physiology at Washington University Medical School; presented their most recent findings on the use of histone deacetylase (HDAC) inhibitors to combat NPC. Suhail Alam, Ph.D., a researcher in Notre Dame's Boler-Parseghian Center for Rare and Neglected Diseases, presented a study of the effect of a combination therapy on a mouse model of the disease. The morning concluded with updates on two current clinical trials through presentations from Denny Porter, M.D., Ph.D., of the NIH and Ben Machielse, president and CEO of Vtesse, the company that is ushering cyclodextrin through the next clinical trial. Dr. Porter is leading the clinical trials of SAHA, an HDAC inhibitor, and was the lead investigator on the Phase 1 cyclodextrin trial.

On Friday afternoon, Kevin Vaughan, associate professor of biological sciences at Notre Dame, presented results of live imaging of NPC cells, which demonstrated the potential importance of the motor protein StARD9 in cholesterol transport. Ethan Perlstein, the founder and CEO of the San Francisco-based startup company Perlstein Lab, presented their efforts to build a platform for high-throughput, whole-animal drug screens for NPC. Wrapping up the session, Rich Taylor, associate vice president for research and professor of chemistry and biochemistry at Notre Dame, updated the conference on his group's discovery of a new class of compounds, RNA splicing modulators, which have the ability to correct cholesterol trafficking in NPC cells. After a vibrant afternoon with poster session presentations, the day wrapped up with a visit and dinner at South Bend's Studebaker National Museum.



Suzanne Pfeffer, Ph.D.



Paul Helquist, Ph.D.

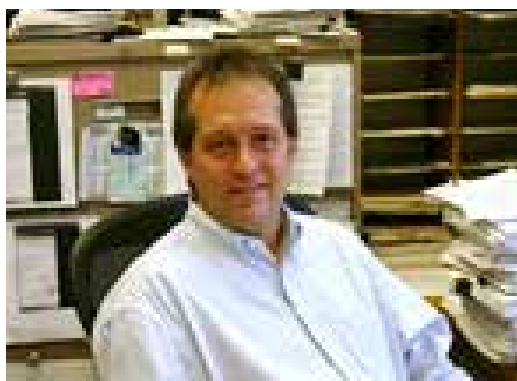


Fred Maxfield, Ph.D.



Denny Porter, M.D., Ph.D.

## SCIENTIFIC CONFERENCE UPDATE *continued*



David Thompson, Ph.D.

This year's conference concluded on Saturday morning with several additional presentations, including details on the mechanism of action of cyclodextrin-mediated reversal in NPC disease. David Thompson (Purdue University) described his lab's efforts to analyze cyclodextrin-based polyrotaxanes for improved pharmacokinetics and biodistribution. The final speaker of the conference was Joyce Repa (UT-Southwestern) who described her recent studies of the biological effects of cyclodextrin and HDAC treatment on NPC1-/- mice.

The next Michael, Marcia & Christa Parseghian Scientific Conference for Niemann-Pick Type C (NPC) Research will be held in June 4-7, 2016 in Tucson, AZ at the beautiful Westin La Paloma Hotel.

### CURRENTLY FUNDED RESEARCH - JULY 1, 2015

**Paul Helquist**, Ph.D., Professor & Associate Chair for Research, The University of Notre Dame, Olaf Weist, Ph.D., Professor & Director of computer-Aided Molecular Design The University of Notre Dame – TITLE: "Design and Synthesis of Small Molecule Agents for Studies and Treatment of NP-C Disease"

**Frederick R. Maxfield**, Ph.D., Professor and Chairman, Biochemistry, Weill Medical College of Cornell University – TITLE: "In vitro tests of the efficacy of therapies for NP-C disease"

**Daniel S. Ory**, M.D., Alan A. and Edith L. Wolff Distinguished Professor of Medicine at Washington University, School of Medicine – TITLE: "Histone Deacetylase Inhibitors for Treatment for NPC1 Disease"

**Suzanne Pfeffer**, Ph.D, Professor and Chairman of Biochemistry, Stanford University, School of Medicine – TITLE: "NPC1-mediated export of cholesterol from lysosomes"

**Forbes D. Porter**, M.D., Ph.D., Senior Investigator, Eunice Kennedy Shriver National Institute of Child Health and Human Development – TITLE: "Inhibition of Necroptosis in NPC1 disease: A Novel Therapeutic Approach"

**Stephen L. Sturley**, Ph.D., Associate Professor, Columbia University Medical Center – TITLE: "Modifying NP-C disease and defeating the blood-brain barrier"

**Charles P. Venditti**, M.D., Ph.D., Senior Investigator, National Human Genome Research Institute, National Institutes of Health – TITLE: "Adeno-associated viral (AAV) gene therapy to treat Niemann-Pick disease, type C"

**Charles H. Vite**, DVM, Ph.D., Associate Professor, Neurology, University of Pennsylvania, School of Veterinary Medicine – TITLE: "Postsymptomatic cyclodextrin therapy in the NPC1 cat"

## FORD MUSTANG RAFFLE



### TICKETS ARE STILL AVAILABLE. BUY NOW!

It is not too late to purchase raffle tickets for this incredible 50th Anniversary Limited Edition 2015 Ford Mustang. In creating an ode to its own icon, Ford will only offer 1964 copies of the car this fall and they will come in Wimbledon White, the same color applied to the first Mustang off the line in 1964. This is sure to become a collector's edition.

Tickets are available online for \$25 each or 5 for \$100 at [www.parseghian.org](http://www.parseghian.org) or you can contact us directly at (520) 577-5106. The drawing is on November 19, 2015. Entries must be received by November 6, 2015.

In appreciation for our supporters, the Parseghian Foundation will also enter ticket purchasers in our tandem give-away at no additional charge. Winners of this will receive Coach Ara Parseghian autographed items to include:

**Grand Prize:** 4 Box Seat Tickets to a Notre Dame Football Game in fall 2016.

**First Prize through Fifth Prize:** Notre Dame football autographed by Coach Ara Parseghian

**Sixth through Tenth Prize:** An autographed print of Coach Ara Parseghian.

We are extremely grateful to Jim Click and the Jim Click Automotive Team for their continued support of APMRF and for this opportunity to raise significant dollars for NP-C disease through the Millions for Tucson Raffle.

#### MARK YOUR CALENDAR

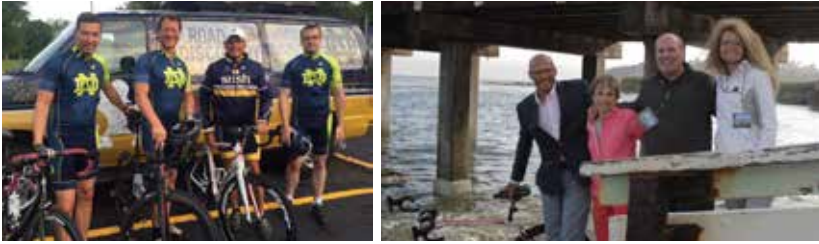
##### June 4-7, 2016

The annual "Michael, Marcia & Christa Parseghian Scientific Conference" for Niemann Pick Type C research will be held on June 4-7, 2016 at the Westin La Paloma, Tucson, AZ. Researchers will gather for three days to discuss the advances in NP-C research. This yearly meeting helps to form collaborations and determine the future direction of NP-C research. For additional information contact Jenna Rangel at [Jenna.Rangel@nd.edu](mailto:Jenna.Rangel@nd.edu)

##### June 24-27, 2016

The fifth annual Parseghian Classic, a 3 day golf tournament, will be held at the wonderful Pebble Beach Golf Resort. Golfers will play a round of golf at Spyglass Hill golf course and another at Pebble Beach Golf Links. The all-inclusive event includes a welcome reception, Putting Contest and dinner with a special guest performance. Full golf and non-golf packages are available. Contact Kim Kirkpatrick at [Kimberly.Kirkpatrick.18@nd.edu](mailto:Kimberly.Kirkpatrick.18@nd.edu) for more information. Please also read Heartfelt Thanks, on page 5, for details on the 2015 event.

## HEARTFELT THANKS



Greg Crawford, Notre Dame Associate Provost, completed his fifth cross country bike ride this past summer bringing the grand total to 15,000 miles. Along the way, he visited with alumni clubs and families affected by NPC. Greg's treks have represented his and Notre Dame's commitment to supporting research into this devastating disease with the goal of developing a treatment or a cure. It also celebrates Notre Dame's partnership with APMRF.

Greg's journey began on Long Island, NY with a reception hosted by John & Heidi Passarelli at Friar's Head. The last leg of the journey was celebrated at the Parseghian Classic in Pebble Beach, CA. Greg started the Pebble Beach weekend with a symbolic bike tire dip into the Pacific Ocean, mirroring the dip in the Atlantic Ocean a month earlier.

The goal to raise \$1 million this past summer was surpassed – close to \$1.2 million was raised that will benefit NPC and other rare disease research at Notre Dame's Boler-Parseghian Center for Rare and Neglected Diseases.

We wish to thank the many Notre Dame Clubs, NP-C families, friends and sponsors who along the way held events, raised funds and supported this amazing effort with enthusiasm and encouragement. We are forever grateful to Greg's commitment to making a difference in the lives of NP-C patients.

"It has been an honor to ride for the children and families affected by NPC, and I am so happy they have embraced the ride and our scientific efforts at Notre Dame. We are on this journey together, and we will keep supporting each other until we have crossed that finish line. Thank you so much for the inspiration you have been to me on this journey across the country." --Greg Crawford

Thank you to the sponsors who generously supported the Road to Discovery and the Parseghian Classic.



## PARSEGHIAN CLASSIC



The 4th annual Parseghian Classic took place on June 26-29, 2015 and was an incredible event. With the perfect combination of ocean view golf, luxurious accommodations, delicious cuisine and excellent service – all of which was made possible with the heartfelt commitment and generosity of all who attended. Singer, songwriter Amy Grant once again brought her musical talent and her devotion to helping raise NP-C research funds and performed at the closing dinner. This year's event, with the largest turnout yet, was filled to capacity with a waiting list. We ask.... "How can this get any better?" Well, we are going to try....and you can help by joining us next year! Mark your calendars.... June 24-27, 2016.



## Ara Parseghian Medical Research Foundation

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## IN MEMORY OF KEATON SMITH



### **September 24, 2000 – May 22, 2015**

Our hearts reach out to the Smith family. Keaton, age 14, lost his courageous battle with NP-C disease on May 22.

An 8th grade student at Battle Ground Middle School in West Lafayette, IN, Keaton was involved in and enjoyed many activities in spite of the challenges he faced. He played on the Tippy Stars Baseball Team and was a huge fan of Purdue men's and women's basketball teams. His fun loving spirit and wonderful smile will be remembered by the many whose lives he touched.

Trent & Julie Smith, Keaton's parents, created the BReaK Thru Fund, held at APMRF, in honor of their 3 children with NP-C disease. Their steadfast commitment has contributed significantly to raising awareness and funds for NP-C research.

Keaton is preceded in death by his sister, Riley, who passed away at age 15 in 2014 and his brother, Braden, who passed away at age 10 in 2006.

Please keep Trent, Julie and daughter, Chandlar, in your thoughts and prayers.