

A GOAL FOR LIFE

For Friends and Supporters of the Ara Parseghian Medical Research Foundation



May 2013

Dear Friends:

When we started the Ara Parseghian Medical Research Foundation, nearly nineteen years ago, very little was known about Niemann Pick Type C Disease (NP-C), other than it was always fatal. Now, due to the generosity of countless donors and volunteers, and the relentless effort of a multitude of investigators and NP-C families, NP-C research has made huge strides. With a better understanding of the disease process, researchers are now concentrating their energy on developing treatments for children worldwide who suffer from the ravages of NP-C.

In football terms, we started deep in our own territory and have picked up significant yardage. The goal line is within reach as several potential therapies are either in trials or moving in that direction. In January 2013, a trial began at the National Institutes of Health with a promising drug, Cyclodextrin, being administered to children. The APMRF played a crucial role in getting Cyclodextrin to trials, including recognizing it as a potential drug candidate, doing extensive analysis in understand the drug's potential benefit and by supporting pre-clinical animal trials to determine dosages and safety concerns. The Foundation has also supported a natural history study at the National Institutes of Health which has led to the development of markers that determine disease progression and will be used in the clinical trial to determine the effectiveness of the drug. In addition, another group of promising drugs is also progressing to trials.

The team is suited up, the play has been called but we must keep the ball on the field. With the research in the "Red Zone" we must keep moving forward, advancing the research.

This is where your help is greatly needed. It is essential that we continue to fund therapeutic research so we can defeat NP-C disease. It is not enough to say we "understand what is happening in the disease process." We will only win this battle when an effective therapy is available to all NP-C children. You have helped us march down the field; now help us score a victory!

Please consider a significant multi-year pledge. An envelope is enclosed for your convenience. At a time when the federal government is falling way behind in its ability to fund medical research, it is imperative the private sector steps forward to promote critical research. NP-C research is of vital importance, as it can provide valuable insight into other diseases such as cholesterol disorders including heart disease, stroke and Alzheimer's.

With deep gratitude,

Cindy K. Parseghian

President

CYCLODEXTRIN Clinical Trial Begins

Because of the hard work and dedication of APMRF funded researchers, a clinical trial to evaluate a drug candidate called cyclodextrin as a possible treatment for Niemann-Pick disease type C1 (NPC), started in January 2013. Scientists from the NIH's National Center for Advancing Translational Sciences (NCATS) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) will conduct the clinical trial at the NIH Clinical Center.

The NPC Phase I clinical trial will test multiple doses of cyclodextrin in nine patients. Forbes Porter, M.D., Ph.D., senior investigator and NICHD clinical director, and Nuria Carrillo, M.D., will conduct the trial. Dr. Porter also is conducting a natural history study of NPC to collect health information from patients to understand how the disease develops. The natural history study, which has been funded by APMRF, is critical to understanding the clinical significance of a treatment for NPC patients.

The goal of the Phase I clinical trial is to determine a safe dose of cyclodextrin that will support an expanded Phase II trial to begin to evaluate the effectiveness of the drug. The team already is in the initial stages of collaborating with the Network for Excellence in Neuroscience Clinical Trials (NeuroNEXT), which is administered by the NIH's National Institute of Neurological Disorders and Stroke, to plan a Phase II multicenter trial.

In 2009, the NIH Therapeutics for Rare and Neglected Diseases (TRND) program, now led by NCATS, selected NPC cyclodextrin as one of its initial pilot projects to repurpose cyclodextrin from its conventional use as an ingredient in other drugs to a therapeutic for this rare disorder.

"Initiation of this clinical trial is the culmination of two decades of basic and clinical research to understand and develop therapies for NPC," said Porter. "The efforts of the collaborators who make up the TRND NPC team have greatly accelerated translating cyclodextrin from the laboratory to the clinic." The TRND NP-C team includes many APMRF funded researchers who discovered the potential of cyclodextrin as a therapy candidate, along with testing the drug in several animal models to determine safety and efficacy.

The APMRF and TRND supported animal toxicology studies to evaluate the safety of cyclodextrin and all necessary regulatory efforts and also supported the development of an NPC biomarker. The biomarker test detects in the blood a modified cholesterol molecule specific to neuronal cells in the brain that would increase as a result of treatment with cyclodextrin.

"A crucial part of the NCATS mission is to collaborate within and beyond the NIH on projects to improve and accelerate the translational research process and deliver tangible improvements in human health," said NCATS Director Christopher P. Austin, M.D. "The cyclodextrin project is an important step in the development of both a potential treatment for a devastating disease that ravages the bodies and minds of its victims and a more efficient way to do translational projects."

Reaching this trial stage required collaboration among government, industry, patient advocacy groups and academic researchers. Dr. Porter summed it up, "Support by parent support organizations is critical to developing therapeutics for rare diseases. NPC has benefited from the efforts of a number of groups. However, the strong and longstanding support of APMRF for both basic and translational work truly laid the foundation and was absolutely critical for the Cyclodextrin trial that we initiated earlier this year. APMRF's support of basic science research led to the discovery of Cyclodextrin as a potential therapy of NPC and APMRF support for the NIH Natural History study allowed us to obtain the clinical experience and identify the biomarkers that are the focus of the current trial." (add this quote)

The APMRF has funded researchers at the University of Texas, Southwestern, Washington University School of Medicine, St Louis; Albert Einstein School of Medicine, New York City, the University of Pennsylvania, Philadelphia, the

(cont'd. on page 3)

Science Update (cont'd. from page 2)

University of Arizona, Tucson and the University of California, San Francisco We want to also thank and acknowledge the support of other NP-C family organizations that have helped promote the research efforts including the International Niemann Pick Disease Alliance, the National Niemann Pick Disease Foundation, and Support Of Accelerated Research for Niemann –Pick Type C. Johnson and Johnson Pharmaceutical Research & Development has provided cyclodextrin for the trials.

HDAC Meeting

APMRF sponsored a one day meeting on April 10, 2013 at Cornell University's Weill College of Medicine where a group of 15 researchers shared recent developments in HDAC inhibitors; a class of compounds that interfere with the function of histone deacetylase. HDAC inhibitor treatment appears to dramatically reduce cholesterol accumulation in NP-C mutant fibroblasts and therefore is being studied as treatment for NP-C disease. Further research is being conducted on HDACs to determine their effectiveness and potential safety risks. There are still many steps to be taken before an HDAC will move into clinical trials but by bringing these research experts together, it is hoped that collaborations will be expanded and pursued to help determine the full potential of a HDAC treatment, in the shortest possible time frame. We wish to thank Dr. Frederick Maxfield for his help in coordinating this effort.

Heartfelt Thanks...

Thank you Verna Burrows!

For the past 8 years, Verna has organized "A Touchdown for Ty" to raise money and awareness for NP-C, the disease that plagues her 16 year old grandson, Ty Quandt. Verna's great spirit, energy and determination has been a source of inspiration to all who know her. Our thanks go out to all of the supporters and volunteers who have made this event a true success. Verna and her husband, Roy, have done a fabulous job over the years in raising contributions to help all NP-C children. We extend a deep gratitude to all those involved in this Las Vegas event.

Happy Birthday Coach!

On April 20th, at the University of Notre Dame, a celebration took place honoring Coach Ara Parseghian's 90th birthday. Ara's football players, assistant coaches, friends and family members gathered to toast his accomplishments, both on and off the football field. A highlight of the evening was the presentation of a most meaningful birthday present, a contribution of



Photos courtesy of Mike and Susan Bennett, Lighthouse Imaging

\$300,000, collected from dinner attendees and many others, to APMRF to support continuing research efforts.

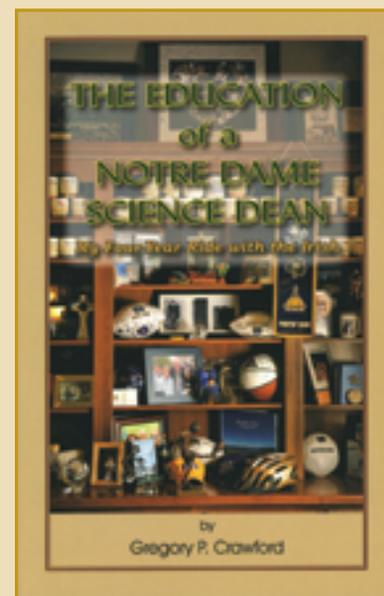
Ara closed the evening with an invitation for 10 years down the road when he celebrates his next big birthday: "I want you here when I turn 100."

(cont'd. on page 4)

Heartfelt Thanks... (cont'd. from page 3)

“The Education of a Science Dean”

University of Notre Dame College of Science, Dean Greg Crawford is one of NP-C's loyal champions. In addition to fighting NP-C disease through his dedication, involvement and support for the NP-C research being conducted at Notre Dame's Center for Rare and Neglected Diseases, Greg has spent the last 3 summers biking across the country to spread the word about this rare disease, meeting families and greeting ND alumni along the way. Most recently, Greg has written and published the book “The Education of a Science Dean: My Four-Year Ride with the Irish”, which expresses how grateful Greg is to be a part of the ND family. “Working with Coach Parseghian in the fight against NP-C, he says, fulfills his childhood dream of playing for a ND Coach as his Great Uncle Pomp played for Knute Rockne”... The dream of following Pomp's footsteps onto the Notre Dame football field may have faded with my childhood, but the chance to participate in the mission of his beloved university was irresistible.” Greg's commitment and passion to this cause “knows no bounds”. Dean Crawford has donated all proceeds from the sale of his book to the Parseghian Foundation. The book is available at the Hammes ND Bookstore and through Corby Books.



Coach Matt Painter

Inspiration is Contagious

Purdue University men's basketball coach, Matt Painter represented The Smith Family BReaK Thru Fund, a fund held at the Parseghian Foundation, in the Infiniti Coaches' Charity Challenge 2013. Coach Painter had an ambitious goal to win – he was competing against 47 rival coaches from the nation's top NCAA Division I men's basketball programs in a fan-vote challenge. Coming in second place for the Midwest region Coach Painter was awarded \$5000 for the charity of his choice – The Smith Family BReaK Thru Fund. Thank you to Coach Painter, to INFINITI and to all who voted!

Students who care...

Service to the community is an essential part of the experience at St. Gertrude's High School, an independent Catholic college preparatory school for young women, in Richmond, VA. Again, this year, students

held a pizza party and bake sale to raise money for APMRF in honor of Ashton Friedl. We thank the Junior Class and this caring community for continuing to help the fight against NP-C disease.



Ashton Friedl

Mark Your Calendar

June 12, 2013

The seventh annual **"Irish Legends Golf Classic"** will be held at the Lost Dunes Golf Club in Bridgman, Michigan. Legends Ara Parseghian, Lou Holtz and current fighting Irish football coach Brian Kelly support this wonderful golf outing that supports their foundations. For information contact Angela Monger at (800) 628-9922, Ext. 503 or acmonger@sap-corp.com

June 13-15, 2013

The annual **"Michael, Marcia & Christa Parseghian Scientific Conference"** for Niemann Pick Type C research will be held on the campus of the University of Notre Dame. Researchers will gather for three days to discuss the advances in NP-C research. This yearly meeting helps to form collaborations and determine the direction of NP-C research.



June 21-24, 2013

The second annual **"Parseghian Classic"**, a 3-day golf tournament, will be held at the magnificent Pebble Beach Golf Resort. Golfers will play a round of golf at The Links at Spanish Bay and another at the Pebble Beach Golf Links. The all-inclusive event includes a welcome reception and dinner, a putting tournament and, a final reception and dinner with a performance by special guest, singer/songwriter, Amy Grant. Full golf and non-golf packages are available. Visit parseghianclassic.nd.edu for additional information.



June 25 - August 2nd, 2013

Notre Dame Dean of Science, Greg Crawford will be taking his bike on the **"Road To Discovery"** again! His journey will take him from California to Maryland, meeting with NP-C families and Notre Dame Clubs along the way. This will be the fourth cross-country journey for Greg who continues to bring hope to NP-C families, while raising awareness of the disease, and collecting contributions for NP-C research.



Dean Greg Crawford on the Road to Discovery

August 3, 2013

The sixth annual **BReaK Thru Fund Golf Outing** will be held at the Lafayette Elks Country Club in Lafayette, Indiana. Hosted by the Smith family this event is held in honor of their 3 children, Braden, Reilly and Keaton who have NP-C. The BReaKThru fund supports NP-C research at Purdue University. For information contact Trent Smith at: info@breakthrufund.org



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Ara Parseghian Cup Match

*"Win, lose, every player and coach knows that this was for the greater good."
-Dave Sitton*

On March 10, 2013, the spirited and rugged game of RUGBY brought together the University of Notre Dame and the University of Arizona rugby teams for the inaugural *Ara Parseghian Cup Match*. U of A Coach Dave Sitton, a longtime friend of the Parseghian family and foundation, launched and coordinated this wonderful event which is the first of many to benefit APMRF's research efforts.

U of A prevailed over ND but all players and attendees agreed that the real winner was the fight for NP-C disease. "We knew we were doing the right thing as a university and a rugby program to start this for the foundation, but I don't think we understood the true importance of it until we sat at the breakfast on Saturday morning," remarked Notre Dame head coach Sean O'Leary. "...The team understands that we're playing for a greater cause and it has really touched them. I just can't wait for the Fall when we host Arizona up at Notre Dame."

Next year's match will take place on the Notre Dame campus in October 2013, the match in 2015 will be returning to Tucson.

We would like to thank Tucson Medical Center for their generous sponsorship, U of A Coach Dave Sitton and ND Coach Sean O'Leary and the all of the team members who shared their Spring Break working together for an important cause.

