

PRIVATE PHILANTHROPY DELIVERS NEW INVESTIGATIONAL AGENT FOR EWING SARCOMA TARGETED CLINICAL TRIAL FOR EWING SARCOMA NOW OPEN

Private foundations and families of children impacted by Ewing Sarcoma know that more innovative treatments are desperately needed, and they realized it was up to them to make it happen. Led by the Rutledge Foundation, they approached Mary Crowley Cancer Research who shared the same objective, but required funding to accelerate the project. They partnered to implement a plan for private donors to assume funding responsibility for the pre-clinical laboratory studies that ultimately delivered a NEW targeted investigational therapy for Phase I clinical testing at Mary Crowley.

The first patient has received the investigational therapy for Ewing's Type 1 and is currently undergoing a response evaluation. The Principal Investigator for the clinical trial is Dr. Maurizio Ghisoli located at Medical City Dallas. The investigational agent, pbi-shRNA EWS/FLI1 Lipoplex, is the only agent currently under investigation in the U.S. that targets the EWS/FLI1 translocation, or *driver gene*, specific to Ewing Sarcoma. Developed by Dallas biotech company Strike Bio, Inc., this agent utilizes a platform RNA interference technology that, if proven, could be applied to multiple other cancers with elusive targets. Mary Crowley and donors are already in the process of expanding this technology for more sarcoma subtypes.

Patients with rapidly recurrent Ewing Sarcoma have less than a 10% chance of surviving more than five years. Despite this serious need, new cancer therapies for children generally lag years behind those for adults due to the smaller pediatric cancer population and fewer funding sources. Private philanthropy has proven crucial to development of novel approaches in pediatric cancers. Mary Crowley has dedicated research efforts to impact Ewing

Sarcoma, now offering access to three clinical trials for patients with the rare disease. In 2009, Mary Crowley began exploring adult RNAi anti-cancer technology and its potential application for children fighting Ewing's. The resulting immunotherapy is now in Phase II testing at multiple sites across the U.S. including Mary Crowley.

"Since 2012, we have enrolled more than 24 children with advanced Ewing Sarcoma on innovative molecular and immunotherapy trials. I am excited to offer these patients access to cutting edge clinical trials," said Maurizio, Ghisoli, M.D.

Special gratitude to those making this new Ewing Sarcoma therapy a reality and especially to the Rutledge Foundation:

Aileen and Jack Pratt Foundation, Alan B. Slifka Foundation, Carson Sarcoma Foundation, Crowley Carter Foundation, Dani's Foundation, Don and Linda Carter, Family and Friends of Sam Day, Helen L. Kay Charitable Trust, Hillcrest Foundation, Horace C. Cabe Foundation, Hyundai Hope on Wheels, Marilyn Augur Family Foundation, Speedway Children's Charities-Silver Dollar at the Ranch, The CHEMOWARRIOR Foundation, The Crystal Charity Ball, Triumph over Kid Cancer, W.P. and Bulah Luse Foundation, and Young Texans Against Cancer

For more information about this clinical trial, contact:

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UPDATES

Our Science



TUMOR MICROENVIRONMENT

BY DR. JAMES STRAUSS, MARY CROWLEY PRINCIPAL INVESTIGATOR

The Tumor Microenvironment (TME) has become the focus of a number of investigational studies at Mary Crowley in recent months. Oncologists have known for some time that a tumor mass is composed of many kinds of normal cells in addition to the cancer cells themselves. The non-malignant cells can have different functions such as constituting the blood vessels that supply the tumor. Cells from the immune system such as lymphocytes are also part of the TME.

Several drugs have been developed that are helpful in cancer treatment because of their effects on the non-malignant cells in the tumor. Drugs such as bevacizumab and ziv-aflibercept that suppress the formation of new blood vessels are the best example. The new area of interest is the lymphocytes and related non-malignant immune system cells in the tumor. The development of the "checkpoint" inhibitors - anti-CTLA4 antibody, anti-PD1 antibody and anti-PD-L1 antibody (Yervoy®, Opdivo®, and Keytruda®) has shown that tumor cells are able to block the immune system from attacking the cancer, and that in some cases this block can be removed.

However, there are other factors located in the TME that can also inhibit the desired attack by immune cells. Some of these immunosuppressive factors are the depletion of tryptophan by the enzyme IDO and excess levels of adenosine. Two clinical trials in progress at Mary Crowley are designed to reverse these effects.

Other immunosuppressive cells within the TME are called regulatory T cells or Treg cells. Two current clinical studies at Mary Crowley are designed with agents to decrease the number of Treg cells in combination with a checkpoint inhibitor. With these 4 clinical trials, and others in development, Mary Crowley is offering a new approach to stimulate the immune response.

WELCOME NEW BOARD MEMBER, TRICIA GEORGE

We are honored to have Tricia George serve on our Board as a Crystal Charity Ball Community Liaison for 2016 and 2017. Her experience will bring fresh perspectives for discussion and greatly enhance the Board's oversight. The Mary Crowley appointment will add to her list of community responsibilities. She presently serves on the Executive Committee of Callier Center for Communication Disorders; on the Board of Mercy Street; on the Texas Committee of the National Museum of Women in the Arts in Washington, D.C.; and she is a member of Crystal Charity Ball and the Junior League of Dallas.



MARY CROWLEY TO LAUNCH NEW WEBSITE

We are pleased to announce our new website launch in early January 2017. You will notice improved navigation and these additions:



NEW:

- **Patients and Families:**
Educational section including Cancer Basics, Tumor Type Definitions, What to Expect as a Patient at Mary Crowley, Downloadable Forms, Questions about Clinical Trials and more
- **Groundbreaking Research:**
Scientific articles that represent the foundation of our research, Peer Reviewed Articles, Abstracts and Poster Presentations
- **Community Partners**
- **News Highlights**

IMPROVED:

- **Access to Clinical Trials by Disease Type and Molecular Target**
- **Library of Patient Stories**
- **Donation Platform**
- **Mobile Optimization**

VISIT www.marycrowley.org TODAY!

MARY CROWLEY FALL FORUM: Game Changing News About Cancer Research

On Tuesday, September 27th, Mary Crowley Cancer Research hosted a panel of expert physician investigators, moderated by award-winning journalist Rena Pederson, discussing Game-Changing News About Cancer Research. Honorary Chairs Cindy Brinker Simmons and Marilyn Augur welcomed over 120 guests to Dallas Country Club.



Pictured Left to right: Dr. John Nemunaitis, Dr. Neil Senzer, and Dr. F. Charles Brunicardi

Dr. John Nemunaitis, Mary Crowley Executive Medical Director; Dr. Neil Senzer, Mary Crowley Scientific Director; and Dr. F. Charles Brunicardi, Mary Crowley Board Member and Professor and Vice Chairman at UCLA School of Medicine, spoke from their individual areas of expertise about the future of cancer diagnostic technology and how the molecular profiling of patients optimizes their alignment to personalized targeted therapeutics.

SPECIAL BULLETIN:

See Mary Crowley peer-reviewed publication in *American Society of Gene and Cell Therapy*, August 2016:
GMCSF/bi-shRNA Furin Autologous Tumor Immunotherapy Poster

PHILANTHROPY

Bringing Hope

2016 ALLISON'S HOPE GALA



Pictured: Linda Cassens Founder of Allison's HOPE, Carley Rutledge, Gian Cervo, and Pat Brown VP of Strategic Development

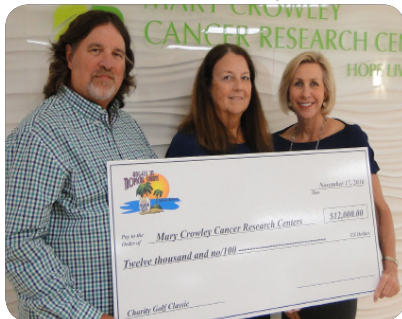
On November 12, 2016, Allison's HOPE hosted their 12th annual benefit at the LeClaire Room in Edwardsville, Illinois. This year's Black Tie and Blue Jean affair was about INSPIRING HOPE. The event accomplished their goal with the featured speaker, Carley Rutledge, who told her triumphant story

starting with her diagnosis of Ewing Sarcoma at age fifteen. Not wanting to undergo more chemotherapy, she and her family contacted Mary Crowley Cancer Research for immunotherapy research options. Carley described her experimental therapy at Mary Crowley as a success, which allowed her to attend college and now graduate school. "I am not the only patient that this has happened to at Mary Crowley, as many others have been impacted and returned to living normal lives" said Carley.

The event also featured classic Rock and Roll from the Robert Perry Band and the Original Mojos. To date, Allison's HOPE has raised more than one million dollars for Mary Crowley and has been pivotal in providing patient access across the globe to ground-breaking clinical trials, research and HOPE.

ANGELS IN TROPICAL SHIRTS GIVE \$12,000

Anita and Kelly Brown are proud Parrotheads who love spending time with friends at the lake.



Pictured: Kelly and Anita Brown and Ellen Dearman, VP of Development

Since 2009, they have organized fundraising events for non-profits in Dallas and Cedar Creek Lake area, through their non-profit, Angels in Tropical Shirts. Anita and Kelly first heard about Mary Crowley when

a friend was enrolled onto a Mary Crowley clinical trial. Anita had recently lost her mother and brother to lung cancer. They supported Mary Crowley for the first time in 2013.

In 2016, they established the first annual Angels in Tropical Shirts Golf Tournament and selected Mary Crowley as the beneficiary of a **\$12,000** grant. Anita said, "Too many of our friends and family have been affected by cancer. The innovative clinical trials that Mary Crowley offers were not available for my mother and brother, so we are happy to help Mary Crowley serve more cancer patients."

YTAC SUPPORTS TRIPLE NEGATIVE BREAST CANCER CLINICAL TRIAL

Young Texans Against Cancer (YTAC) awarded a grant of **\$25,000** to support Mary Crowley's innovative immunotherapy clinical trial for Triple Negative Breast Cancer (TNBC). Found in about 15% of breast cancer patients, TNBC is one of the most aggressive types of breast cancer. This grant will help Mary Crowley open another immunotherapy trial for TNBC patients.

RUTLEDGE FOUNDATION TO FUND SECOND TARGETED EWING'S THERAPY

Since 2010, the Rutledge Foundation has led other Ewing Sarcoma families and foundations to support Mary Crowley Cancer Research in the development of new therapies for children and young adults. Their advocacy and fund-



ing substantially contributed to the recent opening of the first targeted clinical trial for Type 1 Ewing Sarcoma at Mary Crowley. Their next collaborative research initiative will facilitate the development of a second targeted therapy for Type 2 Ewing Sarcoma. Both developments will fill a gap within this underserved population, because 85% of all Ewing's patients are either Type 1 or 2.

This additional development represents a significant goal for those families whose children were diagnosed with Type 2 and had insufficient treatment options. The Sam Day and Lilli Curry Fund through the Rutledge Foundation and the Alan B. Slifka Foundation, in honor of Max Ritvo, combined their funding to expedite initiation of this project.

Representatives of the Rutledge Foundation met with Mary Crowley Principal Investigator Maurizio Ghisoli, M.D., and Ellen Dearman, VP of Development (pictured above), to present a check in the amount of \$245,000 which will fund the preclinical laboratory work for the Type 2 Ewing Sarcoma therapy. Contingent upon the research results, the trial is estimated to open early 2018.

WHEEL TO SURVIVE

Be The Difference Foundation presents Wheel to Survive - an indoor cycling fundraiser that promotes awareness of ovarian cancer, supports programs for women battling the disease, and provides research funds for a cure. Join the Mary Crowley Wheelers for HOPE on Sunday, February 26th, 9AM - 3PM at the Jewish Community Center of Dallas. Visit marycrowley.org for more information.



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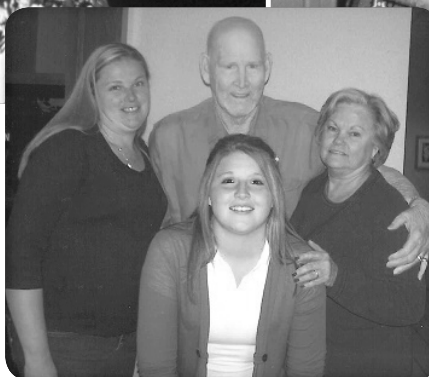
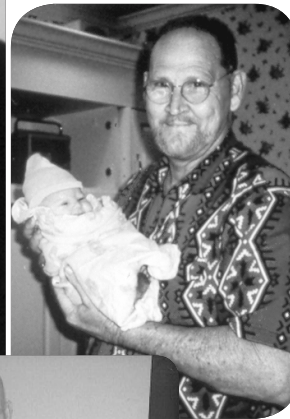
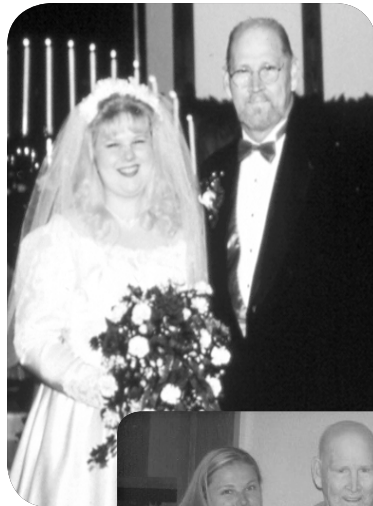
Twenty Year Story of **HOPE**

As one of our first patients, Grover L. Cummings is a legend at Mary Crowley. We celebrate Grover's undeniable courage and determination to survive cancer. Initially, he just wanted to live long enough to see his daughter, January, get married, even though physicians had only given him six months to live.

In 1994 at the age of 55, Grover discovered a lesion on his back. It appeared benign but the physician removed it out of caution. The biopsy revealed that the lesion was melanoma. From 1994 to 1996, Grover underwent four more major surgeries. The melanoma first metastasized to his lung. Not long after the lung surgery, the melanoma appeared in his intestines. The third time his cancer appeared, physicians said operating was futile, but Grover found one surgeon who would operate.

Grover, the 6'4" gentle giant, continued to fight. A physician told Grover he might be a candidate for a new clinical trial.

Grover found his way to an office filled with unopened boxes and Dr. John Nemunaitis, who had just moved to Dallas. He asked the young oncologist to keep him alive so he could attend his daughter's wedding;



Dr. Nemunaitis accepted the challenge. But scans revealed the cancer had progressed to his brain and had to be removed before the clinical trial could commence. Dr. Nemunaitis called several neurosurgeons before finding one who would remove a brain tumor from a terminal cancer patient. This was Grover's fourth surgery, which was then followed by full brain radiation.

Dr. Nemunaitis subsequently enrolled Grover onto the clinical trial that he hoped would keep him alive through the wedding. Grover and Dr. Nemunaitis were elated with the results. **GROVER WALKED HIS DAUGHTER DOWN THE AISLE!**

Not only that, Grover continued to improve year after year with no evidence of cancer. The rest is a 20-year history. Grover lived to enjoy the birth of January's daughter, who turned 18 in 2015, and he continued to spend time with his beloved family.

Grover also did not want to die of cancer, and he received that wish as well. He died in December of 2015 of pneumonia and NOT

CANCER, at the age of 75.

*What better way to commemorate the 20th anniversary of Mary Crowley than to reflect on Grover's 20 year survival and the **HOPE** he gave to all of us.*