

# The Mesothelioma Applied Research Foundation

*Our mission is to eradicate mesothelioma as a life-ending disease.*



## BREATH OF HOPE

Spring 2005

INSIDE THIS ISSUE

### Message from the Executive Director



Last month the U.S. Justice Department indicted W.R. Grace & Co. for the "human and environmental tragedy" Grace caused in the tiny mountain town of Libby, Montana. The vermiculite Grace mined from Libby and spread all over the town was contaminated with a particularly lethal form of asbestos.

The indictment is an important step toward justice for the people of Libby. But "justice" must mean very much more than punishing Grace. Dangerous exposures from the contaminated vermiculite and scores of other companies' asbestos containing products have been widespread - while the government has often looked the other way - throughout our working and living environments. For those who are sick or likely to become sick - in Libby and the entire country - true justice requires finding a solution. We must develop ways to treat asbestos disease and reduce the suffering.

This is why MARF focuses so aggressively on funding practical research aimed at curing meso. In fact, MARF is funding research at Libby's Center for Asbestos Related Diseases to help develop the exciting new SMRP meso detection and monitoring test. This research will directly benefit the people of Libby, and meso patients and those at risk throughout the world.

The Libby project is one of eleven excellent projects going forward thanks to grants from MARF in 2004. Read more about them in Focus on Research. We awarded over \$1,000,000 in research grants last year. This is about equal to the amount of applied meso research the National Cancer Institute funds annually!

Your generosity is what enables MARF to fund this critically needed meso research. Your response to our

year-end annual appeal, which raised \$276,000, specifically made three of the grants possible. See the included Annual Report for details on MARF's 2004 expenses and fundraising. We are committed to financial transparency and accountability to you, our donors and supporters.

Craig Kozicki's profile is an inspiring example of why we believe a solution to the meso tragedy is within reach. It also demonstrates the importance of clinical trials. Craig's courageous decision to participate in an experimental protocol made a huge difference in his life; it has also advanced the science and is helping patients who come after him. Another person who is advancing the science is Dr. Steven Albelda, a leader in gene therapy research. Dr. Albelda has joined MARF's Science Advisory Board, and in his profile you can read more about him and his exciting work.

At MARF's First International Mesothelioma Symposium last year, many of you heard Dr. Albelda and other leading meso experts describe the important progress being made. Save the date! We are thrilled to announce the second annual Symposium, and hope to see you there. We will email hotel and registration info soon.

On all these fronts, we are making progress together toward solving the meso tragedy. But true justice requires the federal government not just to prosecute a company, but to take responsibility for its own role and join in the effort to end the suffering. MARF's Federal Mesothelioma Research Funding Petition calls on the government to do this. We are close to our initial goal of 10,000 signatures, and will forward the Petition to the Senate Appropriations Committee. But this is just a first step; obtaining a federal commitment to meso research will require a major, sustained grassroots effort. We will have more details about how you can help in this effort over the coming months.

I thank each of you for joining with MARF to be part of the solution.

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## BELIEVE IN A CURE

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## Craig Kozicki, Meso Survivor

"EVEN THOUGH MY ORIGINAL SURGEON KNEW VERY LITTLE ABOUT TREATING MESO HE ADVISED ME TO SEEK OUT CLINICAL TRIALS AND NEW TREATMENTS."

For all who ask, "Is there hope of surviving meso, what steps can someone take to get there, and what can life be like afterward?" Craig Kozicki's story is inspiring. In 1998, at just 42 years old, Craig Kozicki was diagnosed with peritoneal meso. Today, Craig is about to turn 49, and in July he will celebrate his 7 year anniversary as a survivor. With his wife Shelly and daughter Emily he lives an active and full life, each day with a little more gusto. Craig faced meso, was able to overcome it, and has resumed a nearly normal life again.

With a degree in Chemical Engineering from Wayne State, Craig once again works full time (as a manufacturing manager for Solutia), plays sports, and takes vacations like any other man in the prime of his life. He also devotes his time to educating and supporting other meso patients and families as they travel the difficult road he knows intimately.

Craig's initial treatment ran 10 months and involved two surgeries, chemotherapy, and radiation under the care of Drs. Robert Taub and John Chabot of Columbia Presbyterian in NYC. Craig was one of the first to undergo this multi-modality treatment. It is now extending the lives of other meso patients, but at the time it was still new and highly experimental.

Craig admits that both physically and psychologically, his life differs from what it was before mesothelioma. "I've just graduated from a six-month to an annual review cycle with my doctors. That's kind of scary since I can't help but wonder when I feel a pain or a twinge whether I



Emily, Craig and Shelly Kozicki

might not be having a recurrence." Craig experienced one recurrence already. In November of 2001 he detected a growth, which a CT scan confirmed as a tumor in the rectus muscle of the stomach. In 2002, his

surgeon, Dr. Chabot, removed the tumor and surrounding tissue, replaced it with a mylex patch, and ordered a cycle of radiation. "With this cancer it's hard not to wonder with every little ache and pain if something isn't brewing," states Craig, "but in general I have a positive outlook and approach each day with the intention to live it to the fullest." The longer Craig has survived, the more long-term his outlook has become.

One of the most uplifting things that Craig does is to take calls from meso patients and families. "You can just hear

the relief in their voices when they first talk to somebody that has gone through this experience and survived. There are so few positives in the media, the medical community, and on the internet that talking to a survivor makes a real difference." Craig knows that meso's rarity and track record of mortality make it difficult for any doctor to provide positive feedback to new patients. "You can't really blame the doctors," says Craig. "They are working from their own experience and I'd rather they were honest with me than mislead me about my diagnosis or prognosis. On the other hand, without input from survivors and resources like MARF, patients would never know they had options."

Craig himself balanced the fatalistic prognosis - based on statistics - that his doctors initially gave him, against his own scientific understanding of data analysis. He determined that if he did everything he possibly could to provide for his own best treatment, he might move his data point to the "long-term survivor" end of the statistical scale. "Even though my original surgeon knew very little about treating meso he advised me to seek out clinical trials and new treatments, which led me directly to Dr. Chabot and Dr. Taub. I felt so comfortable after discussing my situation with them that I never felt it necessary to look further."

Throughout the arduous process of frequent travel from Missouri to NYC, treatment, complications, and side-effects, Craig was determined to stay active and not fall into moping and feeling sorry for himself. He managed to work 3 to 4 hours a day, mostly from home. He walked and did household tasks, being careful not to overextend himself. Craig felt very fortunate when he compared his own experience to what his research had led him to expect.

During treatment, Craig placed his trust firmly in the hands of Drs. Taub and Chabot, but he remains a big believer in staying in control of one's own treatment and making very informed choices about what protocols are suggested. "The patient needs to be the strongest advocate for his or her own case. After all, treatment is a team effort and the patient has the most to lose. Don't be afraid to challenge the doctors, ask questions and stay on top of the treatment being recommended." Wise words from someone truly qualified to give them.

The full story of Craig's treatment and recovery is on MARF's website in the Patient Education section, under Patient Profiles. Visit [www.marf.org](http://www.marf.org).

## Dr. Steven Albelda Joins MARF's Science Advisory Board



To strengthen our expertise in meso research, MARF has added to our Science Advisory Board one of the leaders in meso gene therapy research, Steven M. Albelda, M.D.

Dr. Albelda is the William Maul Measey Professor of Medicine in the Department of Medicine, Associate Director of the Pulmonary Division, Director of Lung Research, and Co-Director of the Thoracic Oncology Laboratories of the University of Pennsylvania Medical Center. He has been a member of the Penn community since 1975 when he enrolled in the Medical School after graduating summa cum laude from Williams College. He graduated with his M.D. in 1979 at the top of his class, continued his post-graduate training at Penn, and began his clinical practice there, with Board Certifications in Internal Medicine, Pulmonary Medicine, and Critical Care Medicine.

As a pulmonary physician, Dr. Albelda frequently interacted with patients who had lung cancer or meso. Frustrated by the inadequacy of these patients' treatment options, he established a translational thoracic oncology research laboratory in conjunction with Penn's Dr. Larry Kaiser, aimed at moving research from "bench to bedside."

A main focus of the lab has been researching gene therapy for meso. Gene therapy is the incorporation of new DNA into an organism's cells, usually by a "carrier" such as a virus modified so that it cannot cause disease. Dr. Albelda believes meso is a good candidate for gene therapy because the tumor cells tend to be confined to one easily accessible cavity, and there is evidence that

the tumor is vulnerable to the body's own white blood cell immune response that is strongly triggered by the gene therapy.

His initial research in gene therapy focused on the use of a "suicide gene" and led to Penn's first gene therapy clinical trial. Toxicities were minimal, and two patients showed a six-year survival. However, this apparently resulted not from the "suicide" effect of the gene, but from a strong immune response triggered by the therapy.

Dr. Albelda's lab has therefore refocused on immuno-gene therapy, inserting into the cancer cell a cytokine with strong anti-tumor activity - Interferon-beta. In mice, just one dose led to a 70-100% survival, so Dr. Albelda's team has begun a phase I dose escalation clinical trial. 10 patients have been treated. Eight have been evaluated and half of these have shown clinical responses (either stable disease at 3 or 6 months or tumor regressions). A new trial using two doses, plus intratumoral injection, is planned to begin later this year.

Dr. Albelda's expertise in basic research has been widely recognized. He holds research grants from the National Institutes of Health (NIH), and in 1985 received a prestigious Physician-Scientist Award from the NIH's Lung Division. He has published over 170 peer-reviewed papers, and is on the Editorial Boards of, among others, Gene Therapy and Cancer Gene Therapy.

MARF is very grateful for Dr. Albelda's commitment to meso patients and expertise in meso research, and we are honored that he has joined us in our mission to eradicate the disease.

### HAVE YOU SIGNED?

Help urge Congress to join the fight against meso by funding the **National Mesothelioma Research and Treatment Program.**

If you have not yet signed the petition, use the link from MARF's homepage: [www.marf.org](http://www.marf.org), or visit [www.thepetitionsite.com](http://www.thepetitionsite.com) and search "mesothelioma".

ARE YOU MISSING IMPORTANT NEWS AND UPDATES?

IF YOU DID NOT RECEIVE OUR FEBRUARY EMAIL REGARDING THE PETITION, YOU MAY NOT BE ON OUR EMAIL LIST.

TO RECEIVE IMPORTANT UPDATES, INCLUDING DETAILS OF THE SYMPOSIUM, MAKE SURE YOU ARE ON OUR EMAIL LIST. SEND US AN EMAIL.

DO YOU HAVE A QUESTION OR COMMENT? SEND US AN EMAIL.

WE WANT TO HEAR FROM YOU!

[NEWS@MARF.ORG](mailto:NEWS@MARF.ORG)

# MARF Annual Report - 2004

## Programs

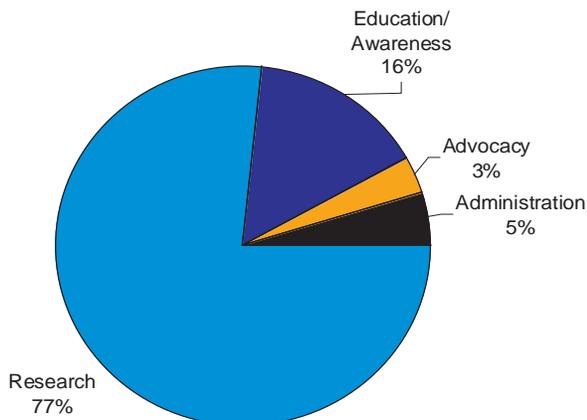
MARF pursues its mission through three programs:

Research - MARF directly funds the most promising, innovative research aimed at developing effective treatments and ultimately a cure for meso. MARF's International Symposium on Mesothelioma also advances the research, by promoting scientific understanding, idea-sharing and collaboration among the experts.

Education, Support and Awareness - Through its website, educational materials, Symposium, staff, and volunteer network, MARF offers support to meso patients and families, and helps educate them and their local doctors that there are centers specializing in meso, there are treatments which are beneficial, and there is hope. MARF also works to raise the general public's awareness of the disease and the urgent need for a cure.

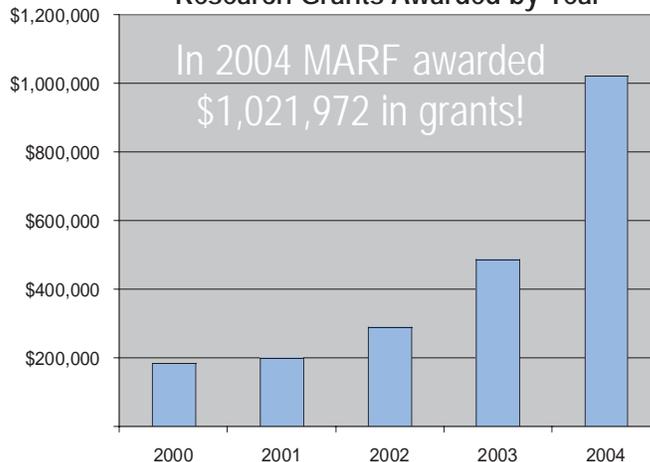
Advocacy - MARF is active in Washington, D.C., advocating that the federal government address its responsibility and begin funding meso research at least proportionate to other cancers.

<b>RESEARCH</b>		<b>\$1,059,652</b>
Grant Funding	\$914,637	
Symposium*	\$135,015	
IMIG Meeting**	\$10,000	
<b>EDUCATION, SUPPORT, AND AWARENESS</b>		<b>\$209,558</b>
Activities and Materials	\$134,402	
Symposium*	\$75,156	
<b>ADVOCACY</b>		<b>\$45,457</b>
<b>ADMINISTRATION</b>		<b>\$66,251</b>
Fundraising	\$36,489	
Management	\$29,762	
<b>Total</b>		<b>\$1,380,918</b>



**Expenses by Percent of Total**

## Research Grants Awarded by Year



## 2004 Program Highlights:

Receives and reviews 32 high quality research proposals from around the world for its competitive grants cycle.

Awards nine competitive grants (approx. \$100,000 each, paid half in 2004 and half in 2005), plus an additional \$135,000 to two special MARF projects, for a total of \$1,021,972 in research grants awarded.

Conceives the annual International Symposium on Mesothelioma series, and organizes the First Symposium in Las Vegas.

Obtains ranking minority Senator Harry Reid's attendance at Symposium and commitment to meso research funding.

Institutes quarterly newsletter to help educate and unify the meso community.

Volunteer network grows to over 100 members.

\* Two-thirds of Symposium expenses are allocated to advancing meso research, and one-third to educating patients/family and community physicians.

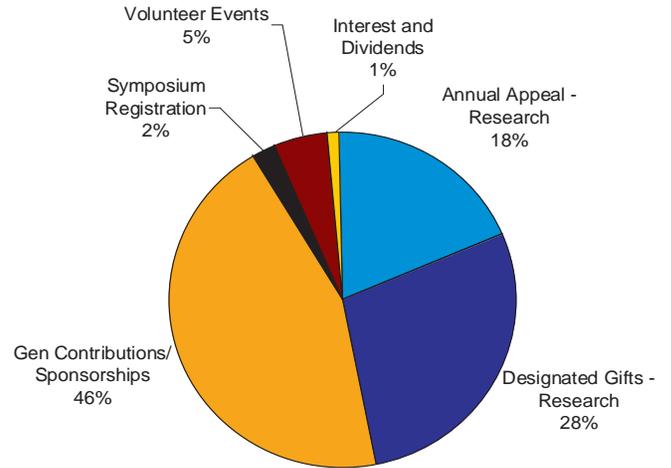
\*\* MARF support for International Mesothelioma Interest Group Scientific Meeting

## Fundraising

MARF raises funds to support its work through: Direct mail solicitations including the annual appeal, special gifts from patients and families, direct appeals to attorneys and companies involved in asbestos litigation, special events (both MARF-organized and volunteer-organized), planned giving and estate planning, and memorial and honorary contributions. MARF is a tax-exempt organization under section 501(c)(3) of the Internal Revenue Code, and gifts to MARF are deductible as charitable donations.

### Income Sources

Annual Appeal - Research	\$276,844
Designated Gifts - Research	\$425,546
Gen. Contributions/Sponsorships	\$666,178
Symposium Registration	\$35,407
Volunteer Events	\$75,151
Interest and Dividends	\$17,890
Total	\$1,479,126



Income Sources by Percent of Total

### 2004 Fundraising Highlights:

The SimmonsCooper law firm pledges to MARF a percentage of its attorneys' fees on each mesothelioma case, expected to total approximately \$1 million per year beginning in 2005.

Donors respond to MARF's Annual Appeal with over \$275,000 in gifts, enabling MARF to fund three additional research grants.

The Worthington law firm gives \$200,000 to MARF.

The children of Alvin Rehbeck contribute \$100,000 to MARF to endow a research grant in their father's memory.

Major U.S. corporations begin giving to MARF for meso research.

Volunteers raise over \$75,000.

## MARF gives a special thanks to our major donors of 2004:

### \$100,000 - \$200,000

Roger G. Worthington, P.C.  
SimmonsCooper, L.L.C.  
The Children of Alvin Rehbeck  
*in memory of Alvin Rehbeck*

### \$50,000 - \$100,000

Waters & Kraus, L.L.P.  
Brayton Purcell, L.L.P.  
Janet Simkins  
*in memory of Ron Simkins*

### \$25,000 - \$50,000

Barbara Hoffacker  
*in memory of Hans Hoffacker*  
Bergman Senn Pageler & Frockt  
Scott Monk  
*in memory of William Lee Monk*  
Pfizer, Inc.  
General Electric Company  
Wise & Julian, P.C.  
Stanley, Mandell & Iola, L.L.P.  
Viacom Foundation  
Dow Chemical Company  
MAFCO Worldwide Corp

### \$10,000 - \$25,000

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*in memory of Judith Koranda*  
Peggy Sterling  
*in memory of John Sterling*  
The David Law Firm, P.C.  
Clara Anderson  
*in memory of Rodney Anderson*  
Verda Mae Lewis  
*in memory of Paul M. Lewis*  
Vicki Cronin  
*in memory of Paul Coen*  
June Breit  
Travis Bales  
Janet Love  
*in memory of Thomas H. Love*  
Kirsten Silva  
*in memory of Edward Silva*  
Mark Jones  
*in memory of Melinda Jones*  
The Lanier Law Firm, P.C.  
Sieben Polk LaVerdiere & Dusich, L.L.P.  
Marcia Abbott  
*in memory of Michael D. Abbott*

## Focus on Research

One of the most exciting recent developments in meso research is the promising new biomarker, SMRP (Serum Mesothelin Related Protein). With a simple blood or urine test, this marker can distinguish meso from other malignancies, and from inflammatory conditions such as asbestosis. Even more promising is that the concentration of SMRP rises with increasing burden of meso and falls with successful treatment. All of these factors point to SMRP as a powerful tool for early detection and diagnosis of meso, as well as for monitoring response to treatment and recurrence.

In order to develop this tool and make it standard in the detection, diagnosis and treatment of mesothelioma, important studies still must be performed. "Normal" ranges of SMRP must be defined in non-asbestos exposed individuals, and in asbestos-exposed but non-cancer bearing individuals. These "normal" values can then be compared to the concentration of SMRP in meso patients. Through its recent 2004 round of competitive grants, MARF is funding Dr. Brad Black and his colleagues at the Center for Asbestos Related Diseases (CARD) in Libby, Montana to perform these critical studies.

Tragically, Libby is the site of the W.R. Grace mine that spread asbestos-contaminated vermiculite throughout the town, and shipped it all over the country. Hundreds of Libby residents have died of asbestos diseases. W.R. Grace & Co. and seven of its employees were recently indicted for knowingly creating this danger and conspiring to hide it. The CARD provides clinical services to Libby residents who need diagnosis and coordination of care for any asbestos related disease. It has collected multiple serum samples from individuals exposed to asbestos and is a unique, ideal setting for the important work of defining SMRP levels in asbestos exposed populations. This research will help the people of Libby, following the awful tragedy that occurred there. By participating in this research, they in turn will be helping meso patients around the world.

A second grant from MARF's 2004 round of awards goes to Dr. Richard Kornbluth at the Veterans Medical Research Foundation in San Diego. He and his colleagues will seek to develop a novel method of immunotherapy, using the patient's own immune system to eradicate the mesothelioma tumor. The immune system contains "killer" T-cells which normally recognize and destroy the cells of a growing tumor. In meso patients however, these immune cells are not properly activated, resulting in increased and un-regulated growth of the tumor.

Using an immunomodulator protein known as CD40 Ligand (CD40L) to stimulate the immune cells has been reported to eradicate mesotheliomas in mice, but a form of CD40L that can be effectively delivered to human meso tumors has not been found. Dr. Kornbluth will use a new technology to formulate CD40L in a special structure, so that it can be more powerfully delivered to the tumor and better activate the immune cells. Dr. Kornbluth will test this new formulation in mice in order to determine whether a clinical trial in meso patients is appropriate.

MARF's reviewers were excited by the innovative nature of Dr. Kornbluth's research, and its potential to trigger a clinical trial for the benefit of meso patients. Dr. Kornbluth's work also underscores the important role the VA can take in overcoming the disease. Meso is a service-related disease, and dedicated, outstanding researchers – including those working with the VA like Dr. Kornbluth – are making progress. The VA should join with MARF in a serious commitment to fund this research.

Alimta (Pemetrexed) is now well known as the first agent with significant activity – in combination with cisplatin – in the treatment of advanced meso, and the only FDA approved treatment for meso. Alimta decreases cell growth by blocking the actions of folic acid. Specifically, Alimta inhibits the activities of two enzymes: Thymidylate Synthase (TS) and Glycinamide Ribonucleotide Transformylase (GARFT), which cells use to copy their DNA so they can divide and grow (DNA synthesis). While all this is known, little is known about the mechanisms of acquired resistance to Alimta and why meso tumors stop responding to Alimta treatment.

Dr. David Goldman at Albert Einstein College of Medicine is one of the leading researchers in how tumors acquire resistance to specific drugs such as Alimta. Studies in tumors other than meso indicate that drug resistance can occur when either (1) the drug is actively transported out of the tumor cells, or (2) compensatory pathways are activated so DNA synthesis can continue even in the presence of the drug. One such compensatory pathway utilizes an enzyme called MTAP (methylthioadenoside phosphorylase). When present, MTAP serves as a "back-up" mechanism which cells use to continue DNA synthesis and therefore to continue division and growth.

With his 2004 MARF grant, Dr. Goldman and his colleagues will investigate specifically in meso small molecule inhibitors that have recently been developed for MTAP. He will seek to confirm that Alimta treatment in combination with these MTAP inhibitors will overcome

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TREATMENT AND  
RECURRENCE."

## Research, continued.

meso tumors' resistance to Alimta and improve meso patients' response to treatment. These important combination studies will yield results that can be rapidly translated into the clinic for improved patient therapy.

Dr. Goldman's entire project will be funded by a \$100,000 gift to MARF from the children of Alvin Rehbeck. Alvin was diagnosed in September, 2002 with bi-phasic nonresectable meso. Alvin's son Tim called MARF E.D. Chris Hahn who told him about obtaining Alimta on a compassionate use basis. Alvin went on Alimta and responded well at first. In gratitude to MARF, and to continue in the fight against meso and help other families, Alvin's children made the gift to MARF, to fund a grant in their father's memory. We are very pleased to be able to use this generous gift to advance Alimta therapy for the sake of other patients. Under the terms of his grant, Dr. Goldman will credit the "Alvin Rehbeck Memorial Grant" in all publications and presentations describing his work.

MARF also awarded grants to the following cutting-edge projects in 2004:

Paul Bass, M.D., Ph.D. - Netherlands Cancer Institute: Malignant Mesothelioma and Thalidomide; A Translational Research Project

Cecilia Camacho-Hübner, M.D. - St. Bartholomew's Hospital, William Harvey Research Institute, University of

London: Development of Novel Therapeutic Strategies for Malignant Pleural Mesothelioma: Targeting the IGF System

Robert Cameron, M.D. - University of California, Los Angeles: Comparison of Adjuvant Treatments for Mesothelioma, Including Hyperthermia, COX-2 Inhibition, Cpil-4 Toxin Therapy, and Standard Chemotherapy

Bin Liu, Ph.D. - University of California, San Francisco: Defining and Targeting Mesothelioma-Specific Internalizing Cell Surface Receptors for Novel Therapeutics

Gregory Otterson, M.D. - The Ohio State University Research Foundation: Epigenetic Changes in Mesothelioma

Harvey Pass, M.D. - Karmanos Cancer Institute: Soluble Mesothelin/MPF-Related Protein (SMR) Levels in Mesothelioma

Ravi Salgia, M.D., Ph.D. - University of Chicago: Studies of C-Met in Mesothelioma

Bernadette Scott, Ph.D. - Monash University, Clayton Victoria, Australia: Pre-clinical Studies of a Novel Therapeutic Strategy for Malignant Mesothelioma

## VNN

(Volunteer Network News)

We will soon be sending a new volunteer handbook to all MARF Volunteer Network members. The handbook is full of excellent information about providing support to patients and family members in need as well as detailed information on how to produce a fundraising event and raise awareness in your community. If you are not a part of the Volunteer Network and would like to get involved, visit [www.marf.org](http://www.marf.org) and fill out a volunteer application. Volunteers are needed to help provide support to patients and family as well as raise awareness of meso, raise money for research, and advocate for meso research funding.

The Children of Ron Trainer will be hosting a bowling fundraiser on September 10, 2005 in Sinking Springs, PA. They will be offering food, fun, a raffle, and of course... bowling. If you would like to help or participate contact Tina at [calltina2travel@comcast.net](mailto:calltina2travel@comcast.net).

Rob Grayson, MARF's Director of Development and Volunteers, and volunteer Keogh Visconti will be running the Anchorage, Alaska Marathon on June 18, 2005 to raise money for MARF. Rob, who lost his father to multiple myeloma in 1997, has set a personal goal of \$10,000 and Keogh, who lived in Manhattan during the events of 9/11, has set a goal of \$3,000. We wish them luck on the race and look forward to hearing details of their adventure.

In just a few weeks MARF will be offering Awareness Bracelets through the Volunteer Network. The bracelets are dark blue - the MARF color, have embossed on them "Believe In A Cure", and will be \$3.00 each. If you would like to help distribute them or use them at your event, contact the MARF office so we can send you a batch.

"ALIMTA INHIBITS THE ACTIVITIES OF TWO ENZYMES ... WHICH CELLS USE TO COPY THEIR DNA SO THEY CAN DIVIDE AND GROW. [BUT] LITTLE IS KNOWN ABOUT THE MECHANISMS OF ALIMTA AND WHY TUMORS STOP RESPONDING TO ALIMTA TREATMENT."

# The Mesothelioma Applied Research Foundation

Our mission is to eradicate mesothelioma as a life-ending disease.

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Congressman Bruce F. Vento

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**MARF's Second Annual  
INTERNATIONAL SYMPOSIUM ON  
MALIGNANT MESOTHELIOMA**

**LAS VEGAS, NEVADA**

**OCTOBER 6 - 8, 2005**

