Fluorouracil – It is an FDA approved cancer therapy (also known as Adrucil®, Carac™, Efudex®, Fluoroplex®) that blocks nucleotide synthesis via thymidylate synthase and in turn this inhibits both DNA and RNA synthesis. Through this mechanism, it should have negative effects in cell division. The first efficacy study is completed, and the data looked positive, especially for male survival. The data were as follows: in male mice we saw a 9% delay in disease onset, 5.5% extended survival and a 19.5% effect in neuroscore. We are in the process of two concurrent repeats of the same dosing regimen. Neither repeated study looks like it will demonstrate the same positive effect that we saw the first time.
I’m sure many of you have heard by now that Dr. Rick Olney, the Director and Founder of the ALS Center at UCSF, has himself been diagnosed with ALS. Dr. Olney is a trusted ally in our fight and the news of his diagnosis has profoundly affected the staff at ALS TDF. Dr. Olney first came to our attention in late 2000 as the physician caring for Vanna Forrester, the mother of Sean Scott, our Vice President of Drug Development. Sean described firsthand a level of care at the ALS Center which would be the envy of any medical center for any disease. Dr. Olney is a giant in the ALS field who is a willing and compassionate friend to those in need. Time and time again, patients have told us stories about Dr. Olney going the extra mile on their behalf.

In our collaborative efforts with Dr. Olney designing trials, he has always made it clear that ALS will be ultimately cured. Many of you will remember Olney’s efforts to unravel the intrathecal IGG mystery in the summer of 2001, when he performed the procedure under very controlled conditions to determine its merit. He made similar efforts with many drugs and treatments, always working to separate fact from fiction on behalf of his patients and the community at large.

Dr. Olney’s resignation as Director of the ALS Center at UCSF is a loss not only to ALS patients in San Francisco but also to ALS patients and researchers across the globe. In the words of my friend Sean, “Rick has been a longtime friend and a devoted warrior against ALS; the irony and heartbreak of this diagnosis is disturbing beyond words.”

We redouble our efforts in the face of this new challenge, determined to help those Dr. Olney dedicated his life to and now Dr. Olney himself. This team is more resolute then ever to finish what we started together.

“Rick has been a longtime friend and a devoted warrior against ALS; the irony and heartbreak of this diagnosis is disturbing beyond words.”

SEAN SCOTT, ALS TDF VICE PRESIDENT, DRUG DEVELOPMENT

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Thalidomide – It is an FDA approved treatment (Thalomid®) for Hansen’s Disease, commonly known as leprosy. Among its many effects, thalidomide is a potent inhibitor of proinflammatory cytokines TNFalpha and IL-1beta. In addition, it has anti-angiogenic effects which might account for its efficacy in multiple myeloma as well as its serious teratogenic effects. Last autumn we presented at the Society for Neurosciences 34th annual meeting the results of our first full efficacy study of thalidomide at 200 mg/kg, orally, once daily. The data showed 12% delay in disease onset in males and 6% in females; 4% effect in survival for males and 3.5% in females and a 13% neuroscore for males and 8.5% in females. We are in the process of two concurrent repeats of the same dosing regimen.

In addition, through these studies we will be evaluating the effects of thalidomide on gene expression in the spinal cord to evaluate the primary reason(s) for thalidomide’s effects in ALS.

Pilot Studies
Genzyme Transgenics Corporation (GTC) is our new mouse provider! Last autumn we switched from having our transgenic mice bred in Maine to a local facility in Massachusetts owned by Genzyme. GTC is now providing us with all our mice, and we are currently in the process of revalidating these mice in terms of age of disease onset, disease progression and survival, and gender differences. Scientifically, one big bonus of having GTC breed, genotype and deliver our mice includes their quantitative genotyping of all the sires (breeding males) of our colony to ensure that all the mice we test in efficacy studies have the same high copy number and consistent expression of the SOD1 transgene.

Nicotine – Nicotine is an OTC drug that is readily available and can be dosed in many forms (patch, gum). Over the last several years, an increasing number of studies have shown that nicotine is neuroprotective in models of Alzheimer’s disease and Parkinson’s disease, and retrospective clinical studies apparently support these findings, with lower incidence of either disease in nicotine users vs. non-users. The neuroprotective effects of nicotine and other regulators of alpha7 nicotinic acetylcholine receptor has been documented for many years, and it may be a compound effect that includes inhibition of microglial activation, enhancement of both NGF and BDNF expression and possibly antioxidant effects. We recently completed a 25 day pilot study dosing nicotine orally in drinking water at 40 mg/kg or via ICV cannulation dosing 10 µg/mouse/day and found that neither route provided therapeutically relevant concentrations of nicotine to the spinal cord consistently. In the future we may consider taking a fresh look at dosing nicotine utilizing our newly developed spinal cord catheter, but presently we are focused on secondary effects in studies where nicotine is dosed peripherally.

FOR MORE INFORMATION:
Visit www.als.net and click on “In Our Lab” to view our drug pipeline and more.
In January, ALS TDF began the expansion of its laboratory space in order to perform crucial gene therapy and stem cell experiments. While we continue our dedication to the pursuit of drug or small molecule therapies, we are adding gene therapy and stem cell tests to our comprehensive testing program because we believe they will play an important role in developing a treatment or restorative regimen for ALS patients.

Because these experiments will require handling live materials such as human stem cells and replication deficient viruses, the new lab facility was built to meet strict Biosafety Level 2 (BL2) guidelines. Special vents, HEPA filters, and autoclaves will allow staff to take the extra precaution of treating mice and housing as potentially infectious. Many of the features of the new facility were physically built by the staff who will conduct the new research, using donated weekends and late nights to knock down walls, lay floors and place new equipment.

The lab expansion should be completed and the new experiments begun within the next month. The first
programs will quickly determine the scope of our BL2 future and immediately impact the course of our entire discovery effort.

ALS TDF runs the world’s largest animal drug testing program for ALS. Our existing lab houses 800 mice at any given time, with as many as 8-12 full efficacy studies running concurrently. We are thrilled that the new facility and expanded testing program will help us find a cure even faster.

LABORATORY DEFINITIONS

**BL1 Laboratory** – Utilized in experiments with non-living, well characterized substances. Agents tested in this lab category are generally stable and pose no significant hazard to laboratory staff.

**BL2 Laboratory** – Meets government specifications requiring training to handle living and potentially pathogenic agents. Both lab and staff adhere to rigorous confinement and sterilization policies.
INNOVATIONS CONTINUED FROM PAGE 1...

“ALS TDF’s ability to pump drugs directly to the spinal cord of a mouse is an impressive and unprecedented development that should speed drug discovery for ALS.”

Fred Vinick, Senior Vice President, Drug Discovery, Genzyme Corporation

we can now pump drugs around the clock into the lumbar spinal cord. These osmotic pumps are good for 28 days and can be changed when empty. This technique has previously been impossible due to the incredibly small scale of the operation and device.

“ALS TDF’s ability to pump drugs directly to the spinal cord of a mouse is an impressive and unprecedented development that should speed drug discovery for ALS,” commented Fred Vinick, Senior Vice President, Drug Discovery, Genzyme Corporation.

The first drug studies have commenced using the new intrathecal catheter. Because the device doses directly and continuously to the mouse spinal cord we can achieve drug levels that are much greater than pumping into the brain. Preliminary results suggest that levels of drug reaching the spinal cord are fifty times higher than those achieved using brain delivery.

Initially, pump implant surgeries required a two hour procedure. Within a few months, ALS TDF streamlined the process to accommodate over 40 animals in half a day, sufficient to begin full efficacy studies. Studies are ongoing to monitor surgery impact on lifespan and neurological function.

“I believe that getting drugs to the spinal cord is going to be a requirement for successfully treating the SOD mouse. The development of the mouse spinal catheter and pump system now makes this treatment possible,” noted Sean Scott, Vice President of Drug Development, ALS TDF.

ALS TDF is optimistic about the projects planned for the near future pending resources. Along with drug testing, the goal is to deliver promising gene silencing technologies such as siRNA and antisense without the need to use a gene therapy for delivery. Gene therapy, while exciting, presents numerous safety and delivery challenges that could be circumvented with this approach. Preliminary research looks very positive for these molecular therapy programs as they are the best prospects for fast, minimally invasive therapies.

By keeping pace with the new discoveries realized every day in medical science, ALS TDF intends to lead the way with advanced technology and to share innovative insights with any organization or group focused on curing ALS and other neurological diseases.

These advancements in ALS research would not have happened without the incredible grassroots fundraising of the family and friends of Mary Lou Krauseneck, an ALS patient. In our next newsletter, we will share some exciting news about their upcoming involvement with our Drug Delivery Program and their amazing fundraising efforts. ✦
Symptoms of ALS impact mobility and can compromise an individual’s comfort and energy level. However, there are several options for improving movement and quality of life while reducing body stress that can make a big difference in day to day living. These tips can help make physical changes a little less stressful for both patients and caregivers.

**SEAT LIFTS**

Lift seating is an option for people with lower extremity weakness. Lifts are designed for chairs, baths, and commodes, and there are many distributors nationwide. If you are beginning a search for a lift online, one suggested website is www.all-lift-chairs.com. Also, it is important to keep your bed at a comfortable height. Bed risers can be purchased at hardware stores or Bed, Bath and Beyond for less than $20.

**WHEELCHAIRS**

Opting to get a wheelchair will allow you to maintain a higher energy level. Wheelchairs vary in cost and functionality; getting the right fit for your height, weight and ability are important when making your selection. Most insurance companies will pay for only one wheelchair, so it is advised to work with a seating specialist to ensure a proper selection. Your neurologist or physical therapy group can easily direct you to the best local dealers, but it may be helpful to do some independent research as well. Some suggestions include:

- Invacare www.invacare.com 1.800.333.6900
- Permobil www.permobileusa.com 1.800.736.0925

You may also choose to buy a used wheelchair from a local resident or from the Internet. Having a local maintenance and repair service for your wheelchair can come in handy if problems arise. Additionally, the ALS Association and the Muscular Dystrophy Association can sometimes provide wheelchairs through their loan closet programs. Contact your local chapter for details.

**VEHICLES**

If you are in need of a new handicapped friendly vehicle, you might want to take a look at Vantage Mobility International www.vantageminivans.com. Their dealer locator can assist you with buying new and used vehicles.

Finally, having a Handicapped Parking tag will make traveling and access much easier. Applications are available from your local Department of Transportation or Motor Vehicles. Remember to take the registry form to your next appointment for physician signature.

Mary Beth Parks, R.N.,
Patient Services Specialist
email: mbparks@als.net
phone: 617.441.7250

FOR MORE INFORMATION:
Family Inspires Research Grant from the Commonwealth by Elizabeth Hayes

Like other families currently battling ALS, the Brooks/Shambo family is putting up a fervent fight and will not back down. On September 21, 2004 the ALS Therapy Development Foundation honored ALS patient Joseph Shambo and his brother-in-law Paul Brooks along with several legislators from the Commonwealth of Massachusetts to thank them for their efforts resulting in a research grant of $150,000 to ALS TDF for research. Public officials included former Speaker of the Massachusetts House, Thomas Finneran, current Massachusetts House Majority Leader, John Rogers, former Representative Kevin Fitzgerald, current Representatives Timothy Toomey and Alice Wolfe, as well as the Mayor of the City of Cambridge, Michael Sullivan. Joe’s wife Maureen, father-in-law Paul Brooks, Sr. and home health aide Dawn Pelletier were also in attendance. The group was received by ALS TDF staff, then toured the laboratory and animal facility.

After the tour and reception, Representative Rogers stated, “The ALS Therapy Development Foundation fosters hope for so many families in
this state and in the nation for people who are afflicted with ALS. With $150,000 in the state budget, we are investing in research towards a cure, an investment that will continue to inspire hope for families waiting for a cure."

Inspiring hope for other families faced with the daily challenges of ALS was exactly Paul Brooks’ motivation for introducing his life long friend John Rogers to ALS TDF. Paul, a successful contractor and resident of North Attleboro, Massachusetts met ALS TDF founder James Heywood at one of the organization’s Night At Fenway events that he attended with brother-in-law Shambo. As he tells it he was, “very impressed with Jamie; it’s important to organize services, but it’s another thing to actively work to find a cure.”

Three years later, Brooks worked to pull together his resources to urge support from the Commonwealth. “Joe and I worked together to determine how I could best dedicate my time and energy to this cause.” By activating his network and promoting the research, Paul enabled ALS TDF’s first official support from the legislature, which he hopes will serve both to renew and increase support from Massachusetts and inspire other families to engage their own connections for maximum benefit. Paul says, “It is time for our legislators to step up to the plate, not just in Massachusetts, but across the country. ALS is truly a family disease and I see what my sister Maureen goes through on a daily basis. It affects not only the 30,000 people living with ALS today, but every single member of their families.”

Joe applauds his brother-in-law’s efforts as well. “I am extremely proud of Paul for his dedication to the cause. Without his persistence and perseverance this Bill would not have happened. Paul used his resources to reach out for all ALS patients and Massachusetts officials responded.” He emphasizes, “You don’t have to be a celebrity or Major League Baseball player to make a difference - although it doesn’t hurt!”

The ALS Therapy Development Foundation is now working together in partnership with the Massachusetts Department of Public Health on a multi-faceted research project made possible by the FY 2005 award. We look forward to providing highlights from the completed project in our next newsletter and will make the entire report available to the public online. We are grateful to Paul, Joe and all of the legislators who worked to sponsor this award and thank them for their efforts on behalf of our work to develop treatments for ALS. ✦
George and Daphne Hatsopoulos’s support of ALS TDF is very important to us, most significantly because they have contributed generously although no one in their family is affected by ALS.

Dr. George Hatsopoulos is one of the most innovative and entrepreneurial engineers in the country. He is an accomplished businessman, engineer and inventor and has won prestigious awards in the technical and business fields, including the Heinz Award in Technology (1993), in recognition of his significant scientific and industrial accomplishments. In addition, he is a member of the National Academy of Arts and Sciences as well as the National Academy of Engineering and was inducted into the Academy of Distinguished Entrepreneurs at Babson College in 2000.

Dr. Hatsopoulos is best known for founding Thermo Electron Corporation which makes everything from artificial hearts to analytical instruments. It has spawned more than a dozen other companies that produce measurement instruments and biomedical research products. More recently, he started Pharos (meaning lighthouse in Greek) which primarily develops advanced medical devices.

The Hatsopoulos first learned about the ALS Therapy Development Foundation through Dr. John Heywood, who taught with George at the Massachusetts Institute of Technology. Their involvement at ALS TDF started through George’s relationship with Professor Heywood. The two later met with John’s son, and d’Arbeloff Founding Director of ALS TDF, James Allen Heywood. They learned more about ALS TDF and were further inspired to increase their involvement by Jamie’s methodology and enthusiasm to find a treatment and cure.

“Given the Hatsopoulos’s amazing history of effective investment in technology and development, their support and endorsement of our laboratory reflects very well on the accomplishments of our R&D team and our future,” says James Heywood.

George began college at the National Technical University of Athens and received his Bachelor’s,
Master's, Engineer's and Doctorate degrees, all in mechanical engineering from MIT. His wife, Daphne came from Greece as well to attend Wellesley College. In 2000, the Hatsopoulos Laboratory for Micro-Fluid Dynamics was created at MIT by a generous contribution from the couple. Their dedication to science and engineering is clear in all they have done in the field both professionally and philanthropically.

The Hatsopouloses have two accomplished children following in their footsteps. Their son, Nicholas, is a Professor of Neuroscience at the University of Chicago and their daughter Marina is an entrepreneur who founded and runs the company Z Corp. She is also the mother of four children.

We greatly appreciate the generosity the Hatsopouloses have shown over the years. We wish to thank them for their involvement and the encouragement they bring to our laboratory and team. Their involvement instills a certain confidence in our team as we carry the knowledge that we are supported by the best in the business.

Dear Friends,

When Jeff and I discovered ALS TDF we found a source of hope. We were impressed with their approach, and the personal motivation behind it.

A lot has changed since then, and we continue to search for a cure. With your help, Driving 4 Life has raised nearly two million dollars. Thank you all for contributing to the success of the campaign, and making a huge difference.

Now that I’m an official member of the ALS TDF team, I’m excited to be dedicating all of my energy to Driving 4 Life as Founding Director, and feel blessed to be working with such an incredible group of people.

We have a great line-up of events for the 2005 golf season and I encourage all of you to find an event near you by going to our recently revamped website: www.driving4life.org.

Thank you again for all you have done, and I look forward to working with you all.

Sincerely,
Kim Julian

FOR MORE INFORMATION:

Support Driving 4 Life by visiting www.driving4life.org
When Faye Magneson was diagnosed with ALS last October, no one could have anticipated just how strongly the South Bend, Indiana community would pull together to support her in this new chapter of life. But that is exactly what they did, and have continued to do every day since.

Shortly after Faye’s diagnosis, a committee including Faye’s two sisters, mother, and many friends formed Friends for Faye and chose to benefit research at ALS TDF. According to Faye, ALS TDF is “a foundation that is truly dedicated to research and a cure. The people here not only have a scientific mission to stop ALS but a personal mission as well.” Now, just four months later, more than $70,000 has been raised for ALS research and hundreds of people in South Bend can put a real face to a disease many had only heard about.

Friends for Faye began their campaign by sending out a letter that Faye wrote to over one thousand friends and family members. Letters were mailed to just about anyone the committee thought might want to help Faye and her efforts to support a cure for ALS. The response was both outstanding and humbling, because Faye, a retired physician, has dedicated her life to improving the lives and health of her patients, all of whom were looking for a way to show their gratitude.

Shortly after the letter writing campaign, Faye’s sister, Beth, created lapel pins with the Friends for Faye slogan, “We’ll Never Give Up” as a way for the community to show their love and support for Faye. The pins were so successful that car magnets with the same slogan were recently developed to help increase awareness of ALS and the need for more research.

But still, people wanted to do more. Recently a committee headed by Faye’s close friend, Jody Freid, has been working tirelessly to host a golf tournament on June 20 in Faye’s honor. The event will be held at the South Bend Country Club with a reception and auction to follow.

The staff of ALS TDF is incredibly grateful to have the support of Friends for Faye. Like all of those involved with their fundraising efforts, we here at ALS TDF will never give up.

FOR MORE INFORMATION:

Please visit Friends for Faye: www.als.net/ffc/fmagneson
TRI-STATE TREK
Twenty cyclists left Newton, Massachusetts on July 18, 2003 and rode into history. Traveling by bike through some of the most beautiful back roads in Massachusetts, Connecticut and New York, the group arrived in White Plains, New York three days later completing the first annual Tri-State Trek.

Now, the Tri-State Trek has joined forces with ALS TDF to raise awareness and funding for ALS research. Registrations have already started and riders are joining us from across the country. All proceeds from the 270 mile ride, which runs from July 15th to the 17th, will benefit the research center at ALS TDF.

Please consider joining us as a rider, a volunteer or a sponsor. We welcome teams of cyclists or volunteers who wish to support the ride in honor or in memory of a loved one by riding all or a portion of the 270 mile event, or staffing one of the rest stops along the way. Sponsorship opportunities are available and a great way for you or your company to show your support of this important cause.

A Cure is Coming! participants will reenact Paul Revere’s historic midnight ride in reverse to help raise awareness of ALS in the greater Boston community. Participants will begin at the Lexington Battle Green at 9 am with an historic sendoff!

The journey will begin in Lexington through Arlington and into Medford where a lunch will be held at Medford City Hall Plaza. After lunch, the ride will continue through Medford into Somerville and Charlestown until finally reaching the historic Old North Church in Boston’s North End Neighborhood where a reception and candlelight vigil will be held.

FOR MORE INFORMATION:
To register please contact Jamie Manganello at jmanganello@als.net or call at 617.441.7256

A CURE IS COMING!
ALS TDF in conjunction with Ride for Life present A Cure is Coming!, a 12 mile ALS awareness and fund-raising ride/walk taking place in Massachusetts on Saturday, April 16, 2005
Thank you!

Driving 4 Life

D4L Wristbands!
Look for them at your local pro shop!
Or call Rob 617.441.7200

DRIVING 4 LIFE INVITATIONAL
On September 27th, 2004 in Bedminster, New Jersey, Driving 4 Life hosted its first national golf event for ALS research. The First Annual Driving 4 Life Invitational Presented by Celgene attracted more than 92 players from across the nation who enjoyed an early opportunity to play the new and prestigious Trump National course. The event exceeded its fundraising goals and raised more than $110,000 for ALS TDF.

Following a brief golf clinic and brunch at the Trump National clubhouse terrace, golfers played a net best ball tournament at the beautiful par 72 golf course. At the reception, Dr. Robert Hariri, President of Celgene Cellular Therapeutics, spoke eloquently about ALS TDF and his commitment to ALS research.

Joining Dr. Hariri at the podium that evening were Honorary Chairperson Kim Julian, best selling author John Feinstein, ESPN analyst John Buccigross, and Bill Leahey, former PGA TOUR caddie and close friend of Bruce Edwards.

Thank you to our sponsors and committees for making the first Driving 4 Life Invitational a resounding success.

Honorary Chairperson
Kim Julian

Honorary Committee Chairman
Dr. Robert J. Hariri

Honorary Committee
Ernie Accorsi
Senator Jon S. Corzine
Gwyn Edwards Dieterle
John Feinstein
Joe Lacava
Senator Frank Lautenberg
Rebecca Lobo
Steve Rushin
Christine Todd Whitman
Carl Vigeland

Event Committee Chairpersons
Chris and Jackie Martin

Event Committee
Susan Airey
Harry DiSimone
Malcolm Goodridge
Jill Kaufmann
Keith Melanson
Beverly Rivkees
Regina Rear

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Save the date!

DRIVING 4 LIFE INVITATIONAL 2005
September 12th, 2005
Trump National Golf Club
Bedminster, NJ
HMS HOST GOLF CLASSIC, TAMPA, FLORIDA
For the second year in a row this event raised more than $25,000 for Driving 4 Life in October 2004. Special thanks to Jeff Yablun and Doug McGuiness for making this event a special one.

THE SECOND ANNUAL OLSON ALS FOUNDATION GOLF TOURNAMENT, FORT WAYNE, ILLINOIS
This annual event again was a resounding success for ALS research of the SOD mouse. “As long as we all hang in there and band together...we will soon wipe out ALS,” says E.J. Olson, organizer of the event.

CRONAN FAMILY TOURNAMENT, PEABODY, MASSACHUSETTS
Held September 27 2004 in memory of family patriarch, “Cubby” Cronan, the day of golf was a memorable one for all involved. The event was the first fundraiser held by the Cronan family to benefit Driving 4 Life.
ALS 101

ALS 101 is a seminar designed for patients and their loved ones to better understand the basic biology and science of ALS, learn about what goes wrong in the body with ALS, and find out what researchers are focusing on to find effective treatments and a cure.

During ALS 101, you will have the opportunity to meet James Heywood and the ALS TDF staff. You can ask specific questions about research and treatments, and you will develop skills to sift through information on emerging treatments to help you have productive conversations with your doctor. To date, hundreds of patients from the U.S. and around the globe have attended ALS 101.

For a list of ALS 101 dates and locations, please visit:
www.als.net/als101 or call 617.441.7200

“ALS 101 makes me feel at ease knowing that I’m getting the most up-to-date information in a concise presentation.”

-Brent Paulhus