One of four major initiatives announced last fall as a result of the unprecedented influx of donations resulting from the 2014 ALS Ice Bucket Challenge is Neuro Collaborative, which employs a three-pronged approach drawing on the unparalleled expertise of three labs. One of these labs, located at Cedars-Sinai Medical Center in Los Angeles under the direction of Clive Svendsen, Ph.D., is developing a Stem Cell and Motor Neuron Core Facility with the purpose of creating clinical-grade induced pluripotent stem cell (iPSC) lines.

iPSCs have emerged as a key research tool and potential source of therapeutic cells in ALS. As the cell lines become available, they will be openly shared with the ALS research community. “The idea is,” said Dr. Svendsen, “to essentially create ALS in a petri dish.”

Cedar-Sinai is at the forefront of this kind of research, and the lab is working with the C9orf72 gene, which is the most common genetic cause of ALS, responsible for up to 40 percent of inherited cases and about six percent of sporadic cases. The same mutation is also

Continued on page 6
The Most Rewarding Year of My Career

Message from The ALS Association President and CEO Barbara J. Newhouse

Having just recently completed one year of service with The Association, I can safely say that this has been the busiest, most exciting and most rewarding year of my career. The ALS Ice Bucket Challenge has forever changed the landscape in the fight against ALS and set the bar for all healthcare and disease-related nonprofit campaigns.

In just a few weeks, ALS went from relative obscurity to a household name. At least for the present, fewer and fewer people who are diagnosed with this dreadful disease have to explain what ALS is to family, friends and even strangers. As an artifact of this incredible increase in awareness, more and more people are getting involved with this cause. They are making donations—which is the life source of our ability to fund research and provide support and resources to people and families living with ALS everyday—as well as becoming involved with ALS advocacy efforts. At our recent National ALS Advocacy Day and Public Policy Conference, a record 1,100-plus advocates, including 131 people living with the disease, came to learn about the latest research and the public policy priorities and carried their message to Capitol Hill.

This awareness has not just spread with the general public but also within the research community. The number of submitted research proposals has increased from 198 to 500 in the past year. And, The Association has been able to triple the amount of spending on research. We were also able to double the amount of funding from the national organization to our 44 ALS Association Certified Centers of Excellence, which are providing the multidisciplinary care recognized by the American Academy of Neurology as state-of-the-art care for people with ALS.

The ALS Ice Bucket Challenge provided a backdrop to convene a “Collaboration for a Cure” meeting of every major ALS organization in the country to discuss how the entire ALS community can use this important opportunity to extend the impact of the challenge into the future. Out of this meeting came a commitment to work together to continue the momentum toward finding effective treatments for ALS as quickly as possible.

We simply cannot stop now. It takes between $1 and $2 billion (with a “B”) dollars to bring just one drug through the FDA-approval pipeline, a process we are also working to streamline, by the way. That’s ten ice bucket challenges! We are asking everyone to join the “Challenge ALS” team to create a world without ALS. In the words of ALS Ice Bucket Challenge co-founder Pat Quinn: “Every August until a cure.”

Corporate Partner Moves the ALS Cause Forward

Quantum Rehab®, a Pride Mobility Products® Corporation company that designs and manufactures complex rehabilitation solutions for individuals with comprehensive mobility needs, has supported The ALS Association for a number of years. However, two years ago, Quantum became an ALS Association Premiere-Level National Partner.

As a national partner, Quantum supports important ALS Association events, including the Walk to Defeat ALS®, which raises funds to sustain care for people with ALS and their families, while also supporting ALS research.

“It is truly our honor to support The ALS Association and the amazing work it accomplishes through its local chapters across the country,” said Quantum product marketing director Megan Kutch, M.S., OTR. “Our missions toward serving those living with ALS align, and we whole-heartedly support the quality-of-life programs and the research performed by The ALS Association.”

Quantum contributes funds to cover free seat lift elevators for those living with ALS. Many Quantum employees took the ALS Ice Bucket Challenge, and in the last two years they have contributed nearly $750,000 to the fight against ALS.

Quantum employees take the ALS Ice Bucket Challenge.
Patrick O’Brien was just 30 years old when he was diagnosed with ALS. An award-winning filmmaker and DJ, O’Brien made moving films about the disabled, never imagining that he himself would be among that population. Ten years after his diagnosis, O’Brien is still writing and producing thought-provoking films—thanks to his indomitable spirit, the revolutionary technology at the Leonard Florence Center for Living (LFCL) in Chelsea, Mass., and the support of the ALS community.

O’Brien’s latest film, “TransFatty Lives,” recently premiered at the prestigious Tribeca Film Festival in New York City. Lauded by both critics and attendees, the film won the “Top Audience Award,” which is the highest possible honor. Additionally, the film was featured at the International Documentary Festival in Montreal.

Diagnosed with ALS in 2005, O’Brien lived in a nursing home in Maryland for four years before moving to the LFCL in 2010. The Center, part of the Chelsea Jewish Foundation, was the first urban Green House® skilled nursing center in the country and features a permanent residence dedicated to caring for individuals living with ALS. The home is equipped with the latest computer-operated technology to allow individuals with ALS as much independence as possible. Although O’Brien needs round-the-clock ventilation, he lives an active and busy life. In addition to producing films, he travels, attends concerts, sporting events, movies and premiers.

The ALS Association has been a terrific support system for O’Brien. In particular, Lynn Aaronson, ALS Association Massachusetts Chapter Executive Director, and Jan Obermann, Care Services Manager, have visited him at the LFCL. “I am grateful for their support and the tireless efforts of the local ALS community,” said O’Brien.

“The first time I met Patrick at the Leonard Florence Center, he was reclining in his wheelchair,” said Aaronson. “As I passed by him I said hello. He typed into his assistive speech device and replied, ‘hey good looking, what’s cooking!’ Patrick has a keen sense of humor and is a creative and talented movie producer.”

The film “TransFatty Lives”—so named because O’Brien is known by the name of TransFatty for his love of donuts and other junk food snacks—depicts O’Brien’s personal reflections since being diagnosed, which include falling in love and having a child. The humorous and poignant documentary examines what it is like to live when you know you are going to die.

“Patrick displays such incredible courage and powers of inspiration,” said Chelsea Jewish Foundation CEO Barry Berman. “Every day, he gives us an incredible gift through his humor, his talent, his spirit and, above all, his friendship. It is an honor to have him in our lives.”

Two days before the festival, O’Brien received a congratulatory letter from New Jersey Governor Chris Christie. In the letter, the Governor cited O’Brien’s incredible passion, talent, bravery and optimistic outlook. As he put it, “The screening of your film will serve as an inspiration to people worldwide who are fighting their own battles, while raising awareness for ALS.”

To watch a trailer of “TransFatty Lives” visit http://transfattylives.com/trailer.
Antisense and Nonsense

Continued from page 1

sides are said to be complementary, meaning “matching opposites.”

The major purpose of DNA is to store the instructions for making proteins, which are the workhorses of every cell. In order to make a protein, the nucleotide sequence from one side of the DNA is used as a template to assemble a complementary (matching-opposite) strand of RNA. RNA is chemically similar to DNA, again with four types of nucleotides, but instead of T it uses U. If the DNA template strand is TAAGTC, the RNA formed will be AUUCAG. Because its job is to carry the DNA message, it is called a messenger RNA (mRNA).

This mRNA is called a “sense” strand, and it is used to make protein. Any strand that is complementary to it is called an “antisense” strand. With that under our belts, we can explain ASO therapy.

The goal of ASO therapy is to destroy mRNA that would otherwise cause harm to motor neurons, either through making a mutant protein such as SOD1, or through being present in excess, as results from the C9orf72 mutation.

ASO therapy takes advantage of a cell’s defense mechanism against viruses. Normally, a cell’s DNA doesn’t pair directly with its own RNA. Some viruses also contain RNA, and when they inject their RNA into a cell, it can pair with the cell’s DNA. The formation of this “DNA-RNA hybrid” is a signal that the cell is infected. The cell marshals an enzyme to destroy the RNA.

In ASO therapy, a short DNA-like molecule is introduced into a cell. The molecule is created to be complementary to the target mRNA, from either SOD1 or C9orf72. The mRNA carries the “sense” sequence and the DNA-like ASO carries the “antisense” sequence. They pair up, triggering the viral defense mechanism to destroy the cell’s own mRNA, releasing the ASO to pair up with another mRNA, and so on. In this way, the level of mRNA is reduced, reducing the harm to the cell. Experiments in models have shown that ASO therapy has the potential to reduce the death of motor neurons. Clinical trials are being developed to test this in people with ALS.

Nonsense-mediated Decay

Recently, researchers have identified NMD as potentially important to understanding the normal function of two ALS-related proteins, called FUS and TDP-43. NMD is a cellular quality-control process that destroys mRNA when it contains a certain kind of mistake, called a “nonsense codon” or “premature stop codon.” NMD helps regulate the levels of FUS and TDP-43. Excess accumulation of these proteins contributes to some cases of ALS. In the recent study, researchers showed that increasing a protein that contributes to NMD helped protect motor neurons in models of the disease. More work will be needed to determine how to exploit this pathway for development of new therapies.

Both ASO therapy and NMD involve the cell’s own abilities to maintain itself. As researchers learn more about these and related processes, they hope it may be possible to harness these and other cellular defense systems in the fight to keep motor neurons healthy and slow the progress of ALS.

Company Puts People with ALS First

Located near Nashville, Tenn., Permobil, Inc., assembles and ships thousands of power wheelchairs every year from its state-of-the-art facility. They put a priority on serving people with ALS. When someone with ALS places an order, it is immediately moved to the front of the production line.

A proud supporter of the Walk to Defeat ALS® for more than six years, Permobil has contributed close to $1.3 million through monetary and product contributions to The ALS Association.

“Permobil was founded in the late 1960s on the principle of helping people through innovation, so until a cure is found, we will continue to stand with The ALS Association and people living with ALS,” said marketing director Barry Steelman. “They are a big part of why we do what we do.”

Permobil is also The ALS Association’s longest standing national partner. They participate in several Walks to Defeat ALS across the country and donate 40 seat lifts annually to The ALS Association Chapter network.

‘Permobil was founded...on the principle of helping people through innovation...we will continue to stand with The ALS Association and people living with ALS.’

—Barry Steelman
Marketing Director
Permobil
It’s hard to image that less than a year ago ALS was a disease that few had ever heard of outside the mention of Lou Gehrig. Yet, with the ALS Ice Bucket Challenge came an outpouring of awareness and astonishing generosity to the tune of $115 million. Your generosity has brought hope and the ability to provide expanded services and support to people living with ALS today.

It all started with a golfer in Florida by the name of Chris Kennedy. When Kennedy took the challenge in mid-July last year, the then little known stunt was not tied to a specific charity. Instead, participants selected the charity of their choosing, and Kennedy thought taking the challenge might bring some cheer to a relative with ALS, Anthony Senerchia. Kennedy nominated Senerchia’s wife to take the challenge next.

News travels quickly across social networks. Soon word of the challenge had traveled from the Senerchias’ small New York town to Pat Quinn in Yonkers, N.Y., who himself was diagnosed with ALS in March of 2013. Within two weeks’ time, word reached Quinn’s charismatic friend Pete Frates in Boston, Mass., who was diagnosed with ALS a year earlier. Due to his extensive network of friends both on- and off-line, Frates along with help from Quinn gave the ALS Ice Bucket Challenge the push it needed to become a household name.

Together, these four lives touched by ALS have significantly helped to accelerate the pace of scientific research by having made the ALS Ice Bucket Challenge the hottest way to cool off during the hot summer months. See how generous ALS Ice Bucket Challenge donations are making a world of difference in the lives of people with ALS right now:

http://www.alsa.org/fight-als/ibc-progress.html
a cause of frontotemporal dementia. In ALS, continued Dr. Svendsen, “Genes load the gun and the environment pulls the trigger.”

Working with the iPSCs in the dish, researchers can test potential therapies and look for a positive outcome. Once a candidate therapy is identified, the researchers’ goal is to harvest cells from a person with ALS, treat those cells and place the cells back into the patient.

“It is commonly known that ALS has many forms and develops in a variety of ways,” said Dr. Svendsen. “Using this approach, we hope to provide a therapy especially suited for a particular patient, thus increasing the likelihood of producing a positive result.”

In addition to the research lab, Cedars-Sinai has an ALS Association Certified Treatment Center, under the direction of Robert Baloh, M.D., Ph.D., which administers the kind of multidisciplinary care recognized by the American Academy of Neurology to demonstrate longer and high-quality of life for those with ALS.

“There are many advantages of having an ALS research lab under the same roof as a treatment center,” said Dr. Baloh. “Researchers and clinicians are able to exchange ideas more easily and collaborate on new approaches and treatments.”

Dhruv Sareen, Ph.D., who directs the iPSC core facility at Cedars-Sinai is also an important member of the team and thinks this technology has the power to understand more about the disease process. “Studying a patient’s own motor neurons, using cutting-edge methods across large numbers of ALS patients will now allow us to discover processes that may be failing in these cells,” said Dr. Sareen.

“The Cedars-Sinai Medical Center and Drs. Svendsen, Baloh and Sareen are important members of our Neuro Collaborative team,” said ALS Association Chief Scientist Lucie Bruijn, Ph.D., M.B.A. “We appreciate their efforts to help The Association to put ALS Ice Bucket Challenge funds to good use as we look to discover effective treatments for ALS.”
Decades of Love—and a Gift of Hope

By Katie Sweeney

Don Mills has many reasons for supporting The ALS Association.

His wife of 42 years, Edna Mills, died of ALS in 2000. Decades earlier, Edna’s father and uncle also died of the disease.

Today, Don has yet another reason to support The Association: the future health of his three adult children.

“I’m particularly interested in research that’s focused on the familial aspect of ALS, because it seems like there’s a definite link in our family,” said Mills, 79, who recently established a charitable gift annuity for The ALS Association to support ALS research. “My kids might be at risk.”

Don and Edna’s life together began in 1957, when they met in the then-quiet seaside town of Ventura, Calif. Edna was a legal secretary, and Don had graduated with an architectural engineering degree from California State Polytechnic University, San Luis Obispo. They met in the church choir and were quickly smitten.

They married a year later and settled in Ventura. Don began what would be a 43-year career in civil engineering, designing water supply facilities throughout Southern California. Meanwhile, they started a family, and Edna stayed home to raise their children: Colleen, David and Carol.

“She was energetic, enthusiastic, caring and loving,” Mills continued. “She had lots of friends, so she was our social secretary, too!” he added, laughing.

Edna also was a committed volunteer. Among other activities, she spent three decades volunteering for the Ventura County Fair, served on the Ventura Parks and Recreation Commission for 12 years, helped update the city’s charter, was active in raising funds to renovate the city’s pier and was named “Citizen of the Year” by the Chamber of Commerce.

The first sign of illness appeared in May 1999, when she began having trouble lifting the front of her foot, a condition called “drop foot.” A month later, Edna was diagnosed with ALS.

Edna’s disease progressed rapidly, but she remained committed to her volunteer work, continuing to serve on the Parks and Recreation Commission and attending the dedication ceremony for the Ventura Pier’s new terminus, which was named “Mills’ End” in the couple’s honor.

Just five days after that ceremony, on April 5, 2000, Edna passed away peacefully at home after a 10-month battle with ALS. She was 63.

“I feel fortunate I was able to care for her,” said Mills. “We made every day count.”

Today, Mills stays busy as a volunteer, using his engineering skills to assist with rehabilitation projects at his church and Channel Islands National Park. He also has three grandsons in college.

He and Edna began supporting The ALS Association in the early 1990s, and Don has continued that support. Recently, when a CD matured and his bank offered a minuscule interest rate, he used the funds for a charitable gift annuity, providing him with an attractive payment rate and substantial annual income that is guaranteed for his life.

“The ALS Association is at the forefront of ALS research, and it’s so important to support this effort,” he explained. “Little by little, the knowledge is growing. That’s what gives me hope for the future.”

Get a Tax Deduction and Retirement Security with an ALS Association Charitable Gift Annuity!

Current Payments and Payment Rates

Here are a few payment rates and payment amounts based on a donation to the ALS Association of $20,000 and one beneficiary. Contact us for your exact payment amount, based on your age and number of beneficiaries.

<table>
<thead>
<tr>
<th>If your age is</th>
<th>70</th>
<th>75</th>
<th>80</th>
<th>85</th>
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<td>Your payment will be</td>
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<td>5.8%</td>
<td>6.8%</td>
<td>7.8%</td>
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<td>Your annual payment will be</td>
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<td>$1,160</td>
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These payments are based on a donation of $20,000, one beneficiary and rates effective July 1, 2014. Rates subject to change. Not available in all states.

We recommend you seek the advice of an estate and/or tax professional in connection with any gift.

For more information or a no obligation proposal, call (916) 723-4262 or email mwelling@alsa-national.org
The 2015 Walk to Defeat ALS events are off to a great start! With 35 Walks already done, and 140 still to come, this year is sure to be the biggest and best Walk season yet!

The Walk to Defeat ALS provides an opportunity to bring hope to people with ALS, to raise money for a cure and to join together to fight for something that has touched each of us.

Share your story. Inspire others. Empower your community.

Never before have we been in a better position to fuel our fight against this disease. The time is NOW. Find a Walk near you:

www.walktodefeatals.org

Pat Quinn, person with ALS and co-founder of the ALS Ice Bucket Challenge:

“I remember Walk day, pulling into the Walk site and thinking, ‘This is it. There is no turning back now.’ We had over 100 people show up, won biggest team of the day, and raised over $25,000! It was a huge success for our team, as well as a personal feeling of hope. If this many people will come out to support me, we can make a change. The Walk to Defeat ALS is a truly inspirational event and one I will look forward to every year. Being diagnosed with ALS was not something I could control, but deciding to fight is something I can.”