Reason to be hopeful

We’ve launched two major research initiatives.

We’re having an exciting year. The community is pitching in this year to help the Alpha-1 Foundation get some traction on some of our most important goals. In the spring of 2009, for the first time in Foundation history, we were given the challenge of matching a generous million-dollar grant.

And we made the goal. With tough economic times affecting families everywhere, it’s a remarkable achievement. Alphas have every reason to be proud of themselves.

When we reported our Million Dollar Match success at the Alpha-1 Association’s national education conference in June, we were delighted to have a second example of amazing generosity. Ruth and Gordon E. Cadwgan, Jr., announced the donation of a million dollars to the Alpha-1 Foundation from themselves and Gordon Cadwgan, Sr. (See Congratulations, page 9)

As often seems the case, the generosity could hardly have come at a better time.

This year, we awarded $1.3 million in new grants for Alpha-1 research. (See Tackling the Key Questions, page 16)

In addition to those peer-reviewed research grants, this year the Foundation is launching two major initiatives toward our goal of research for a cure. In the spring, we introduced The Alpha-1 Project, created “to accelerate the discovery, development and commercialization of cures, treatments and drug therapies for those with Alpha-1.”

And this fall we are launching our Liver Initiative.

The evidence mounts that Alpha-1 liver disease in adults is a growing problem. This may actually indicate a success: it may well be that Alphas are living longer than they did before current therapies for lung disease were available.

That is why the Foundation is redoubling our efforts on Alpha-1 liver disease this year. We are actively seeking out Requests for Proposals – asking researchers to request new funding for clinical research on Alpha-1 liver disease, especially in adults.

It’s an aggressive and ambitious series of goals, but we believe it is essential for the Alpha-1 community we serve.

This time of year, many of you have the opportunity to choose a charitable giving program at work for the coming year. If you’d like to take advantage of this to donate to Alpha-1 research, see our easy guide in this issue. (See Join our Workplace Giving Program, page 22)

For information about organizing a fundraising event to benefit Alpha-1 research, contact Angela McBride at 1.888.825.7421, Ext. 233, or amcbride@alpha-1foundation.org. To learn more about methods of giving, or to make an online donation, visit www.alpha-1foundation.org/belp/.

ALPHA-1

Practical advice, personal experiences, and pertinent news for people touched by Alpha-1

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Letters to the Editor. ALPHA-1 would like to hear from you. Please send letters to the editor at the Foundation or e-mail us at editor@alpha-1foundation.org. Letters may be edited for clarity and length.

The Alpha-1 Foundation is dedicated to providing the leadership and resources that will result in increased research, improved health, worldwide detection, and a cure for Alpha-1 Antitrypsin Deficiency.

* Diagnosed Alpha-1 Antitrypsin Deficient
+ Diagnosed Family Member

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What Alpha-1 means to me: Amber Albanese won the first of a monthly series of the Foundation’s Facebook Friend contests. See her pastel drawing at tiny.cc/albanese and facebook.com/alphafriend
Francis S. Collins is famous for many reasons:
- He is director of the US National Institutes of Health (NIH).
- As former director of the National Human Genome Research Institute, he led an international team which completed the sequence of the human genome.
- He led or worked with research teams that discovered key genes responsible for cystic fibrosis, Huntington’s disease, neurofibromatosis, and others.
- He's published three books, one predicting that genetics will revolutionize medical treatment.
- He's a religious scientist. His other two books express his conviction that science and religion are not contradictory.
- He’s well-known for wearing leather jackets while riding his Harley-Davidson, playing his guitar and performing his own songs, often spoofs of pop music hits.
- And in the world of Alpha-1 Antitrypsin Deficiency, Collins is famous for being an Alpha-1 carrier.

While a specific health condition like Alpha-1 may be relatively rare, genetic flaws are universal, Collins says: “Today, we have discovered that everyone is born with dozens of genetic glitches.” And he says we can very often change our behavior to alter the outcome of our genetic dispositions.

At a conference on “personalized medicine” last October, Collins told about having his own DNA analyzed by three commercial services. “I found out I was a carrier of the gene for Alpha-1 Antitrypsin Deficiency,” he said. “I didn’t know that before.”

Collins, who is 60, said he surprised himself by altering his own behavior because of the genetic testing. He began to exercise and lost 20 pounds after finding out he has a genetic predisposition to diabetes.

When President Obama named Collins to head the NIH in 2009, many critics, especially on the Internet, predicted Collins would bring a religious agenda to health research. Others pointed out the obvious: Collins has a long record of prominent scientific leadership with no trace of religious bias.

A LONGTIME FRIEND

John Walsh, president & CEO of the Alpha-1 Foundation, who is also president of the COPD Foundation, said of Collins: “We consider him a longtime friend of both the Alpha-1 and COPD communities. The leadership of Dr. Collins with the Human Genome Institute inspired our continued efforts to invest in research on Alpha-1, often called Genetic COPD.”

Walsh serves on the NIH Director’s Council of Public Representatives (COPR). “The confirmation of a new director will make the role of COPR vital and interesting to advance significantly the nation's capacity to protect and improve health,” he said.

Collins’ diagnosis as a carrier was not by any means his introduction to Alpha-1. Collins and Craig Venter, who led the commercial effort to complete sequencing the human genome, received the first “Alpha-1 Viking Explorers” award in 2002.

GENETICS AND PERSONALIZED MEDICINE

When he took over at NIH, Collins promised a push to turn cutting-edge science into better bedside care – especially care that can save health-care dollars. “We should be completely bold about pushing that agenda,” he told an interviewer.

Collins has a lot of faith in the ability of genetics to “personalize” medicine, meaning to focus medical treatment on someone’s individual needs. His 2010 book The Language of Life is subtitled DNA and the Revolution in Personalized Medicine.

“I would hope that in another five years it would be routine for people who come down with cancer to have the genome of their cancer completely analyzed and then to see what’s driving that cancer to
“OK, then, let’s look at the list of drugs that are available and what their targets are, and let’s do the match… It’s going to be very precise smart bombs that are going to work for your cancer and might not for the person down the hall.”

One triumph for Collins was hiring Harold Varmus as the new director of the National Cancer Institute. Varmus, a former NIH director, was president of Memorial Sloan-Kettering Cancer Center in New York for 10 years.

Varmus was awarded the Nobel Prize in 1989 for studies showing how certain normal genes can mutate and cause cancer, work that opened a new era in cancer research.

Varmus is expected to shake up the much-criticized federal cancer program. His hiring raised both excitement and fears. One criticism came from the non-profit Cancer Prevention Coalition:

“…the U.S. spends five times more than the U.K. on cancer chemotherapy per patient, although survival rates are similar. As an expert in cancer treatment, Varmus appears unaware that almost 700 carcinogens, to some of which the public is periodically or regularly exposed, have been identified by independent scientists. He also seems to be unaware that the more cancer is prevented the less there is to treat.”

**THE BIGGEST CHALLENGE**

The biggest immediate challenge for Collins is embryonic stem cell research. Federal funding for such research, which Collins calls “one of the most exciting areas of the broad array of engines of discovery that NIH supports,” was halted Aug. 23 by a federal judge’s ruling.

The NIH had to tell researchers in labs across the country that, in some cases, their work would have to shut down within days. Researchers who had already received funding could continue their work, but would not be able to apply for renewed funding. Fifty promising projects that were up for peer review were pulled. Twenty-two grants that were coming up for annual renewal this month were frozen.

“This goes beyond politics,” Collins told *The New Yorker*. “Patients and their families are counting on us to do everything in our power, ethically and responsibly, to learn how to transform these cells into entirely new therapies. It’s time to accelerate human-embryonic-stem-cell research, not throw on the brakes.”

The Obama administration has said it will appeal the judge’s ruling.

Another issue facing the new director is NIH funding, which has been flat for years. But Collins says funding will remain healthy despite the weak economy. He points to Obama’s decision to increase the NIH budget of $31 billion this year by $1 billion for fiscal year 2011.

Some researchers fear that the rush to translational research – translating research into drugs and therapies – will mean less basic research initiated by scientists themselves. But Collins told *Science* magazine: “The amount of additional funds that might go into focusing on translation are going to be maybe 1% or thereabouts of the overall NIH effort. That shouldn’t have a very big effect.”

In the same interview, Collins defended the push for new treatments: “The translational goals… get a lot of traction with the Congress, with the public. They should.” And elsewhere, he has pointed out: “We’re not the National Institutes of Basic Sciences. We’re the National Institutes of Health.”

Francis Collins sings and plays his own lyrics for the 1961 pop hit “Runaway” after his keynote address at the National Heart, Lung and Blood Institute’s annual meeting of public interest organizations in May, 2010.
Imagine this scene: It’s 1987 and a conference room is filled with the giants of Alpha-1 research. To name just a few of the doctors present: Ronald Crystal, then chief of the Pulmonary Branch, National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health; Claude Lenfant, then director of the NHLBI; Suzanne Hurd, another key member of the NHLBI Pulmonary Branch; as well as Bob Fallat, James Gadek, Aaron Janoff, and Gordon Snider.

The US Food and Drug Administration (FDA) had invited the group to discuss how to prove the effectiveness of intravenous augmentation therapy for the treatment of Alpha-1 Antitrypsin Deficiency. A definitive study needed to be designed — one that would evaluate whether patients with Alpha-1 did better when they were given the therapy, compared to patients who did not receive the therapy. This type of study is so well known it is usually referred to by its initials: an RCT (or Randomized, Controlled Trial).

Some questions needed to be answered:

What will be measured to see if the drug is working?

The answer was, the fall in FEV1 over time. FEV1 is the amount of air a person can force out of their lungs in one second, starting from the very top of a breath.

What is the usual fall in FEV1 in patients with Alpha-1 and how long does it take to see this fall?

The scientists didn’t know the exact answer. They estimated that Alpha-1 patients with lung disease lose about 100 to 150 milliliters over a one-year period.

How much of a decrease in the rate of decline would you consider to be important?

If a drug could decrease this decline by 30%, this would probably be a major slowing of disease over several years — especially since everyone’s FEV1 declines with age.

When you do a test measuring the FEV1 in someone with lung disease, how accurate is that measurement?

Everyone agreed the measurement of FEV1 is not perfect. (When people are told to, “Blow! Blow! Blow!” into a tube, and do the best they can, the results vary, even on the same day.) The experts gave their best estimate of the variability that would be seen in this test.

After this discussion, the biostatisticians calculated what the necessary study would look like. How many patients would need to be enrolled? How long would each need to be treated with drug — or left untreated? The answer was discouraging.

Researchers would have to enroll 250 patients who received augmentation therapy and 250 patients who did not (they would get a placebo, something like plain sterile water). They would need to follow each patient for three to five years. Neither the patients nor the researchers could know which group they were in during that entire time (This is called double-blinding a study).

Augmentation Therapy Today

Why the FDA approved augmentation therapy, the best evidence for it, and what’s needed now
The scientists were shocked. This would be a very large and long study, and therefore very expensive. And only about 500 patients with Alpha-1 lung disease who might qualify for such a study had been identified in the United States at that time.

In addition, nearly all those patients with Alpha-1 knew about this therapy and the studies that had been done at the NIH to show that it was safe and could raise alpha-1 antitrypsin levels in the lungs. At the time, there was no treatment available for Alpha-1 patients. They were clamoring for something—anything—to treat their genetic condition.

Most people left that meeting believing there was no way this study could be done, and that the FDA would not approve the new therapy. There weren’t enough patients and not enough money to pay for such a study, even if more patients could be identified.

THE FDA’S APPROVAL OF AUGMENTATION

Several months later, in December of 1987, the FDA announced that they had decided to approve the marketing of the first Alpha-1 augmentation therapy without an RCT.

The FDA relied on studies performed at the National Institutes of Health. NIH scientists had come up with the idea of getting normal alpha-1 protein from the blood plasma of healthy volunteers. They had designed and tested the methods for collecting and purifying the protein. They had tested this augmentation therapy in Alphas, trying a variety of doses, eventually settling on 60 mg/kg given intravenously every week.

The FDA said the NIH data was evidence of both safety and “biochemical efficacy” of augmentation therapy. The new drug was approved for those who had already been diagnosed with emphysema due to Alpha-1. The FDA reasoned that many people with Alpha-1 never get lung disease, and there was no way of predicting who would go on to get lung disease and who wouldn’t.

The new drug was named Prolastin. Its manufacturer was Cutter Labs, which had recently been acquired by Miles, the American division of Bayer, a European pharmaceutical company. The FDA required that Bayer and the NIH develop a registry of patients, with the goal of documenting the natural history of

Randomized, controlled trial may prove effectiveness at last

CSL Behring, the manufacturer of Zemairia, is currently completing enrollment of a randomized, controlled trial (RCT) that might give a conclusive answer on the effectiveness of augmentation therapy.

The study hopes to enroll 180 subjects for two years, the largest RCT ever done on augmentation.

The candidates needed for the trial are people with emphysema due to Alpha-1, between 18 and 65, with an FEV1 between 35 and 70 percent of normal. Demonstrating the difficulty in enrolling such a trial, 45 centers in the United States and Canada, 11 European countries and Australia were originally asked to help recruit volunteers four and a half years ago.

The primary measure for the study will be lung density as measured by CT scan five times during the study. Experts now agree that lung density measured by CT scans is the most accurate way of measuring lung function and the progress of emphysema.

Among the secondary outcomes to be studied will be exacerbations (worsening of symptoms), lung function tests, exercise capacity, quality of life and mortality. Investigators hope to finally close recruitment this month, with close to 180 subjects enrolled, and finish the two-year trial by September, 2012.

The study director is Othmar Zenker, MD.
Alpha-1 in at least 1,000 patients. Thus was born the NIH Alpha-1 Antitrypsin Deficiency Registry.

During the 1990s, a number of studies evaluated the effectiveness of augmentation therapy. Most, including the NIH Registry, enrolled whatever Alpha-1 patients they could find and compared the patients who happened to be taking Prolastin with patients who were not. None of these was the ideal RCT.

“Just the same, the results were encouraging,” said Robert A. Sandhaus, MD, PhD, the Alpha-1 Foundation’s clinical director and medical director of AlphaNet. “Study after study in the US and Europe suggested that Alphas receiving Prolastin had a slower rate of decline in lung function – and in some studies, longer survival – than those who were not receiving Prolastin. Based on the publication of these results, physicians were treating patients with augmentation with increased confidence in its effectiveness.”

In 2003, the FDA approved two additional augmentation therapy products, Aralast and Zemaira. Both were approved based on studies showing safety and biochemical efficacy that was comparable to Prolastin.

The FDA required that after the approval of each product, each company must perform an RCT to demonstrate clinical effectiveness. When Prolastin was replaced by Prolastin-C, a similar requirement was made. Two RCTs have been completed so far, neither large enough to prove the effectiveness of augmentation therapy.

A new RCT, sponsored by CSL Behring, has nearly completed enrollment (see Page 7, Randomized, controlled trial). This is the largest to date and may be the needed conclusive trial.

Another possibility, longer term, is the trial by Israeli biopharmaceutical company Kamada of inhaled alpha-1 protein, now enrolling patients in Europe. This trial is an RCT designed to investigate both the safety and effectiveness of alpha-1 protein taken by a nebulizer instead of intravenously. Glassia, Kamada’s intravenous augmentation product, was approved by the FDA in July and will be marketed by Baxter International.

THE COCHRANE REVIEW

The lack of a large, randomized, controlled trial has recently led to an attack on augmentation therapy. In July this year, the Cochrane Library published an article on augmentation therapy by Peter C. Gøtzsche and Helle Krogh Johansen.

The Gøtzsche article, preceded by a press release, reviewed two studies and concluded that augmentation therapy “cannot be recommended, in view of the lack of evidence of clinical benefit and the cost of treatment.”

The Alpha-1 Foundation made a blistering response in its own press release, citing major flaws in the Gøtzsche review.

Foundation President and CEO John Walsh said the review “does a disservice to rare disease patients everywhere. We hope that therapies for other rare conditions won’t become victims of the same poorly designed analysis.”

The Foundation quoted several responses to Gøtzsche from leading Alpha-1 researchers and clinicians. Robert Stockley, MD, Director of Research and Development at Queen Elizabeth Hospital, Birmingham, UK, commented:

“This conclusion was based on retrospective analysis of published data from only two small pilot placebo-controlled studies that were not powered to evaluate the effectiveness of augmentation therapy. This flies in the face of carefully crafted guidelines from the American Thoracic Society, the European Respiratory Society, the American College of Chest Physicians, and the American Association for Respiratory Care – all prestigious organizations that recommend augmentation therapy for the treatment of patients with lung disease due to Alpha-1.”

Danish researcher Asger Dirksen, MD, was the lead author of the only two studies reviewed by Gøtzsche. Dirksen, originally listed as a co-author of the Gøtzsche review, had his name removed before publication.

“After seeing the first draft I realized that our points of view were so far apart that collaboration with Peter Gøtzsche and his wife (Helle Krogh Johansen) would not be possible,” Dirksen said.

And Sandhaus added: “In selecting only these two small studies on which to base their sweeping recommendation, Gøtzsche and his co-author have ignored the wealth of other data in the medical literature regarding the effectiveness of augmentation therapy in Alpha-1.”

The Foundation’s Medical and Scientific Advisory Committee is preparing a formal response to Gøtzsche’s review for publication.
Thank you, everyone! We achieved our year-long effort to reach our Million Dollar Match.

In the spring of 2009, we were given the challenge of doubling a million dollars – matching every dollar donated – thanks to a generous grant from Talecris Biotherapeutics. We’ve been tracking progress on the Million Dollar Match in each issue of Alpha-1 magazine. And thanks to many generous donors and enthusiastic fundraisers, we made our goal in June.

Right after we announced this exciting news at the Alpha-1 Association’s annual education conference in Orlando, we heard more good news. Ruth and Gordon E. Cadwgan, Jr. announced the donation of a million dollars to the Alpha-1 Foundation from themselves and Gordon Cadwgan, Sr.

Gordon Cadwgan, Jr. explained the timing of the family’s donation for Alpha-1 research: “My dad, who’s 96, said, ‘I want to make a difference while I’m still here.’”

Gordon and Ruth Cadwgan live in West Palm Beach, FL, and are the co-leaders of the Alpha-1 support group in the area. Gordon is on the Foundation Board of Directors and both he and Ruth serve on the Foundation’s Development Committee.

The elder statesman of the family is Gordon E. Cadwgan, Sr., who retired at age 92 after 70 years as an investment banker. For many years, he has shared his financial success with charitable causes.

“The Alpha-1 Foundation is tremendously grateful for this gift,” said Foundation President & CEO John Walsh. “The Cadwgans’ amazing generosity comes at a time when the Foundation is re-doubling its research efforts to help find new therapies and ultimately a cure for Alpha-1.”

The full story behind the remarkable generosity of the Cadwgans and the long family history of charitable giving is on our website here: http://tiny.cc/Cadwgans

The Foundation invited Alphas to express their thanks to the Cadwgans, and we made a video and booklet with their responses – 52 of them. See them here: tiny.cc/cadwganvideo

Congratulations!

We matched a million.
Then a generous family gave us another million for our redoubled research

Ruth and Gordon Cadwgan with Gordon Sr., center

$1,000,000

To the top – thanks to you!
The Triple Threat

This is the first of a series on The Alpha Docs – the great doctors involved with Alpha-1 Antitrypsin Deficiency, both as researchers and clinicians.

G ordon Snider, MD, was a healer long before he was a scientist.

“Gordon is unique because of his career switch to researcher after 20 years as a successful clinician,” says Robert A. Sandhaus, MD, PhD, clinical director of the Alpha-1 Foundation.

Snider was among the ground-breaking researchers who showed how emphysema is created. The finding changed the direction of lung disease research for decades.

He founded the modern section of pulmonary medicine at Boston University School of Medicine and was chief of the medical service at the Boston VA Medical Center for 14 years.

He was also president of the American Thoracic Society and served on the Alpha-1 Foundation’s board for 10 years.

As if all that wasn’t enough, he became a great teacher, too.

The Foundation gave Snider a lifetime achievement award last October, at a Boston luncheon attended by more than a hundred colleagues and researchers he trained – many now leading researchers and clinicians themselves.

THE DISTINGUISHED EX STUDENTS

His former students have telling memories of Snider.

• Bartolome Celli, MD, of Brigham and Women’s Hospital in Boston and a lecturer in medicine at Harvard, calls Snider “one of those rare giants, a triple threat – a great researcher, a superb caregiver and teacher.”

• Steven Shapiro, MD, chair of the Department of Medicine at the University of Pittsburgh, says, “Probably Gordon’s biggest [research] accomplishment was showing that neutrophil elastase has the capacity to create emphysema in animal models. His group and others pioneered this concept and changed the focus of pulmonary research.”

Snider and colleagues showed that normal white blood cells called neutrophils can destroy lung tissue and create emphysema, one of the major causes of death in the United States and the world.

• David Center, MD – now Gordon L. & Ruth Snider Professor of Pulmonology at Boston University – says: “While there are many anecdotes about his legendary ability to interpret chest X-rays, what I took out of my experiences was not just his ability to interpret shadows on film, but his encyclopedic knowledge of medicine and his extraordinary memory. He made associations that were like the solutions to Sherlock Holmes stories.”

• Dario Maldonado, MD, whose research includes a widely quoted paper on COPD related to wood smoke in his native Colombia, recalls as a young resident reviewing X-rays with Snider over...
Snider chose the pulmonary field because of Snider, “a very stimulating teacher.”

THE BEGINNING OF PULMONOLOGY
Snider’s interest in pulmonology began with studying chest X-rays as a young resident in the 1940s. He credits an early mentor, Harry Wessler, MD, with, “melding the history of the X-ray and the physical generalization of the chest in a way I’d never seen before, and it sparked my imagination.”

The experience left such a strong impression that Snider decided to join the fledging ranks of the pulmonary field. “I took my pulmonary boards with just six other people. I was there at the beginning. After that, pulmonology developed very rapidly.”

Snider saw mostly tuberculosis patients in his early practice in New York and Chicago. But he felt the need to broaden his experience, first into emphysema and then into research.

Snider has written about a turning point in his career:

“From the mid 1960s on, I had been switching my research interest from tuberculosis to emphysema, but I was floundering as to what line of investigation to pursue.”

Eventually, with Boston University colleagues, he published a paper showing that the elastolytic properties of papain (an extract of papaya fruit) were responsible for the emphysema it caused in mice. This contributed to the now widely accepted idea that elastase/anti-elastase imbalance is a central cause of COPD.

“Of course, Alpha-1 was the major anti-elastase in the lungs,” Snider writes. “So began my love affair with Alpha-1 and a long career in experimental medicine focused on the pathogenesis of emphysema.”

THE TEACHING YEARS AT BU
At Boston University Medical Center, Snider developed and taught techniques for incorporating X-ray and pulmonary function tests. He also taught new doctors the importance of “listening to the patient, and then making the diagnosis.”

Sandhaus describes Snider’s teaching style: “Gordon had a knife-sharp intellect. He would tell you when you were heading in the wrong direction in a way that was direct without making you go to your room and cry.”

Snider’s mentorship couldn’t be taken for granted, Sandhaus adds. “Gordon did not tolerate fools well. If you worked hard, had good ideas and some intelligence, he was the best person to know. If you were lazy or foolish, he didn’t want to waste time dealing with you.”

How pivotal was Snider’s presence at Boston University? The BU Medical Center website still refers to the pulmonary division’s history in terms of pre-Snider, Snider, and post Snider eras.

Snider joined the Alpha-1 Foundation board in 1997. He feels that his major contribution to the Foundation was promoting basic research as well as focused Alpha-1 trials. “I suggested the idea of a research menu – we cannot just look for a cure in one place. Our best chance is to have a broad palette.”

Foundation President & CEO John Walsh agrees. “Dr. Snider’s leadership helped the Foundation establish a robust research agenda. He emphasized balancing basic and translational research to try to speed scientific discoveries into clinical practice. We were delighted to name our critical issues workshop series in Gordon’s honor.”

Snider is now retired in Massachusetts with his wife, Sarah (Sally) Everett, whom he met while both served on the Foundation board. Everett is currently working on a memoir about Alpha-1 and its impact on their lives.
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(Human)

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Kankakee, IL 60901 USA
US License No. 1767

Before prescribing, please consult full prescribing information, a brief summary of which follows:

INDICATIONS AND USAGE
Zemaira® is indicated for chronic augmentation and maintenance therapy in individuals with alpha1-proteinase inhibitor (A1-PI) deficiency and clinical evidence of emphysema. Clinical data demonstrating the long-term effects of chronic augmentation therapy of individuals with Zemaira® are not available.

Safety and effectiveness in pediatric patients have not been established.

CONTRAINDICATIONS
Zemaira® is contraindicated in individuals with a known hypersensitivity to any of its components. Zemaira® is also contraindicated in individuals with a history of anaphylaxis or severe systemic response to A1-PI products.

Individuals with selective IgA deficiencies who have known antibodies against IgA (anti-IgA antibodies) should not receive Zemaira®, since these patients may experience severe reactions, including anaphylaxis, to IgA that may be present in Zemaira®.

WARNINGS
Zemaira® is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. Because Zemaira® is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically the Creutzfeldt-Jakob disease (CJD) agent. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors at testing laboratories, and fractionation facilities are designed to reduce the risk of viral transmission. The primary viral reduction steps of the Zemaira® manufacturing process are purification (60°C for 10 hours) and two sequential ultrafiltration steps. Additional purification procedures used in the manufacture of Zemaira® also potentially provide viral reduction. Despite these measures, such products may still potentially contain human pathogenic agents, including those not yet known or identified. Thus, the risk of transmission of infectious agents cannot be totally eliminated. Any infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to CSL Behring at 800-504-5434. The physician should discuss the risks and benefits of this product with the patient.

During clinical studies, no cases of hepatitis A, B, C, or HIV viral infections were reported with the use of Zemaira®.

PRECAUTIONS
General - Infusion rates and the patient’s clinical state should be monitored closely during infusion. The patient should be observed for signs of infusion-related reactions.

As with any colloid solution, there may be an increase in plasma volume following intravenous administration of Zemaira®. Caution should therefore be used in patients at risk for circulatory overload.

Information For Patients - Patients should be informed of the early signs of hypersensitivity reactions including hives, generalized urticaria, tightness of the chest, dyspnea, wheezing, faintness, hypotension, and anaphylaxis. Patients should be advised to discontinue use of the product and contact their physician and/or seek immediate emergency care, depending on the severity of the reaction, if these symptoms occur. As with all plasma-derived products, some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate at this time. Parvovirus B19 may most seriously affect pregnant women and immune-compromised individuals. Symptoms of parvovirus B19 include fever, drowsiness, chills, and runny nose followed two weeks later by a rash and joint pain. Patients should be encouraged to consult their physician if such symptoms occur.

Pregnancy Category C - Animal reproduction studies have not been conducted with Zemaira®, Alpha1-Proteinase Inhibitor (Human). It is also not known whether Zemaira® can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Zemaira® should be given to a pregnant woman only if clearly needed.

Nursing Mothers - It is not known whether Zemaira® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zemaira® is administered to a nursing woman.

Pediatric Use - Safety and effectiveness in the pediatric population have not been established.

Geriatric Use - Clinical studies of Zemaira® did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. As for all patients, dosing for geriatric patients should be appropriate to their overall situation.

ADVERSE REACTIONS
Intravenous administration of Zemaira®, 60 mg/kg weekly, has been shown to be generally well tolerated. In clinical studies, the following treatment-related adverse reactions were reported: headache, injection site pain, dizziness, headache, paresthesia, and pruritus. Each of these related adverse events was observed in 1 of 89 subjects (1%). The adverse reactions were mild.

Should evidence of an acute hypersensitivity reaction be observed, the infusion should be stopped promptly and appropriate countermeasures and supportive therapy should be administered.

Table 3 summarizes the adverse event data obtained with single and multiple doses during clinical trials with Zemaira® and Prolastin®. No clinically significant differences were detected between the two treatment groups.

Table 3: Summary of Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Zemaira®</th>
<th>Prolastin®</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects treated</td>
<td>89</td>
<td>32</td>
</tr>
<tr>
<td>No. of subjects with adverse events regardless of causality (%)</td>
<td>69 (78%)</td>
<td>20 (63%)</td>
</tr>
<tr>
<td>No. of subjects with related adverse events (%)</td>
<td>5 (6%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>No. of subjects with related serious adverse events</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No. of infusions</td>
<td>1296</td>
<td>160</td>
</tr>
<tr>
<td>No. of adverse events regardless of causality (rates per infusion)</td>
<td>298 (0.29%)</td>
<td>83 (0.519)</td>
</tr>
<tr>
<td>No. of related adverse events (rates per infusion)</td>
<td>6 (0.006)</td>
<td>5 (0.031)</td>
</tr>
</tbody>
</table>

The frequencies of adverse events per infusion that were a0.4% in Zemaira®-treated subjects, regardless of causality, were: headache (33 events per 1296 infusions, 2.5%), upper respiratory infection (1.6%), sinusitis (1.5%), injection site hemorrhage (0.9%), sore throat (0.9%), bronchitis (0.8%), asthma (0.6%), fever (0.6%), pain (0.5%), rhinitis (0.5%), bronchospasm (0.5%), chest pain (0.5%), increased cough (0.4%), rash (0.4%), and infection (0.4%).

The following adverse events, regardless of causality, occurred at a rate of 0.2% or <0.4% per infusion: abdominal pain, diarrhea, dizziness, ecchymosis, myalgia, pruritus, vasodilation, accidental injury, back pain, dyspnea, dysphonia, hemorrhage, injection site reaction, lung disorder, migraine, nausea, and paresthesia.

Diffuse interstitial lung disease was noted on a routine chest x-ray of one subject at Week 24. Causality could not be determined.

In a retrospective analysis, during the 10-week blinded portion of the 24-week clinical study, 6 subjects (20%) of the 30 treated with Zemaira® had a total of 7 exacerbations of their chronic obstructive pulmonary disease (COPD). Nine subjects (64%) of the 14 treated with Prolastin® had a total of 11 exacerbations of their COPD. The observed difference between groups was 44% (95% confidence interval from 8% to 70%). Over the entire 24-week treatment period, of the 30 subjects in the Zemaira® treatment group, 7 subjects (23%) had a total of 11 exacerbations of their COPD.

HOW SUPPLIED
Zemaira® is supplied in a single-use vial containing the labeled amount of functionally active A1-PI, as stated on the label. Each product package (NDX 0053-7201-02) contains one single-use vial of Zemaira®, one 20 mL vial of Sterile Water for Injections, USP (diluent), and one vented transfer device.

STORAGE
When stored up to 25°C (77°F), Zemaira® is stable for the period indicated by the expiration date on its label. Avoid freezing which may damage container for the diluent.

Prolastin® is a registered trademark of Bayer Corporation.

Revised: January, 2007
Adapted from 19131-05

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
A month after John and Mary started going together in high school, she told her pastor, “This boy needs to be prayed for, because I think I’m going to marry him.”

Sure enough, they married a few years later (in 1947) in Cleveland, Ohio, their home town. Within a decade, they had seven children; clearly, parenthood suited them. A good thing, because their large family would become much larger.

**REHAB BY HARMONICA**

John Shook, now of Kissimmee, FL, turned 82 on May 20. He still goes to pulmonary rehabilitation classes twice a week. Perhaps that helps explain why he was the oldest Alpha attending the Alpha-1 Association national conference in Orlando, FL, in June.

Shook has been part of the twice-a-week pulmonary rehabilitation classes at Florida Hospital Celebration since 2002.

A staff respiratory therapist, Patricia Ross, decided to use the harmonica as a tool for pulmonary therapy after reading about the idea. Playing the harmonica strengthens the diaphragm muscles and helps with breath control.

The group called themselves the Harmonicats, after the pop music group from the 1940s. They breathed better, learned to play, and did local public performances. Shook is convinced harmonica playing is great therapy.

“I’ve seen folks wheeled in on a wheelchair. Then after they practiced, they would be able to walk on a treadmill for 15 minutes,” he says.

**IT’S ALL IN THE FAMILY**

The Shooks lived a fairly typical family life for nearly 20 years. John made his living as a firefighter, and Mary Lou was a stay-at-home mom raising their big brood. But like all families, they were not immune from tragedy.

In 1958, after years of an abusive marriage, Mary Lou’s sister committed suicide, leaving behind six children. The children lived next door to the Shooks, but their father forbade any contact. Even so, the children would sometimes sneak over to their aunt and uncle’s house.

“The kids would come over and ask for bread,” says Mary Lou. “They’d come over and say ‘We were going to have potatoes, but we’re down to the last one. Can we have some potatoes?’”

In 1965, seven years after the death of their mother, the father was jailed. The local authorities tried to find an appropriate home for the children, but the family was large, the county low on funds. They approached Shook to discuss the problem.

Mary Lou vividly remembers John’s response:

“He said, ‘Oh, bring them on, they’re family. We’ll take them.’ Let me tell you, my organized life became a little scattered!”

That added six children to the nine the Shooks already had — two still in diapers. (And they had two more children later. That made 17.)

How did they handle dinner time?

“We used a ping pong table,” says Mary Lou. “It was big enough for all of us to eat at once. It was important to sit down as a family. After dinner was family worship time. We read some scripture, or at least learned about everybody’s concerns, so we could pray for them.”
Perhaps the huge family was exactly the large support system John Shook needed to get through the obstacles life held for him.

He says smoke is not the only hazard to a firefighter’s lungs. “Fighting fires, I inhaled a lot of noxious chemicals and fumes, too. Great stuff for an Alpha!”

He paid the price. At 48, he was a fire brigade captain, but his lungs were severely damaged. He had to apply for a partial disability payment. It wasn’t enough to sustain his family, so he went to work part-time with the county engineers.

That same winter of 1976, he developed pneumonia that seemed to last forever. This began a long series of visits to lung specialists. One of them told Shook he had five years to live (and he hadn’t even been diagnosed with Alpha-1 yet).

**WORK, PRAYER, AND MIRACLES**

The disability check and the part-time job brought in just $300 a month. The girls got babysitting jobs; the boys delivered a paper route. And everybody knew the Shooks. Church and charitable agencies came by often with donations of clothing and other supplies. Somehow, the family got by.

One winter, the Shooks had to deliver disheartening news to their oldest four children. Two were freshmen in college, two were sophomores. The family was $1,000 short of the money they needed to pay the school tab. John and Mary Lou prayed for a month.

The day he was about to cancel his four children’s education for the coming semester, Shook received a phone call. A family from their church had a relative pass away and leave them $1,000. The family donated their windfall to the Shooks.

“We hung up the phone and cried a little bit,” says Mary Lou.

In the late 1970s, a nuclear plant was being built in Perry, Ohio. Shook became the plant fire chief, training the staff — but no firefighting. And he got three paid months off in winter, allowing the Shooks to travel to Florida for warmer weather.

During one of those Florida trips, a lung infection sent John to a hospital emergency room. The ER lung specialist tested him for Alpha-1 — and that’s how he finally got properly diagnosed. With the kids out of the nest, the Shooks moved to Kissimmee in 1994.

One great sadness came to the Shooks this year. Their daughter Karen died of Lou Gehrig’s disease in the spring.

At 82, John’s health has actually improved a bit. He’s been free of severe lung infections for two years now. He uses a nebulized medication that has reduced his need for other inhalers. He also continues Alpha-1 augmentation therapy.

The Shooks celebrated their 60th wedding anniversary in June of 2007. Like all their family gatherings, it was a big event, with children, grandchildren, and great-grandchildren. “I tried to count all our great-grandchildren this year. I got to 76, and gave up because birth announcements and notes about pregnancies kept coming in,” says Mary Lou.

Says their daughter Kay: “The love our family has for our parents is indescribable. I think my siblings would agree. We are so grateful to them for how much they have done for us.”
Can Alphas donate their body cells to be used in their own gene therapy? Do tobacco plants hold the secret to cheap, plentiful and super-safe augmentation therapy? Can an antibody stop the alpha-1 molecule from forming long chains, and therefore treat both lung and liver disease? These researchers want to find out all this, and more.

The Alpha-1 Foundation awarded these 11 scientists new Peer Reviewed research grants totaling almost $1.3 million this year:

**GENE THERAPY from ALPHAS:**

Andrew Wilson, MD, of Boston University School of Medicine, will study the use of gene therapy to increase the level of alpha-1 protein in the lung. Wilson plans to show that genes delivered directly into lung cells can protect alpha-1-deficient mice from both spontaneous and smoke-induced emphysema. He will also study how the alpha-1 protein limits inflammation in the lungs. The study will also test a new method using cells donated by living Alphas.

**BLOCKING PRODUCTION:**

N. Tony Eissa, MD, of Baylor College of Medicine, will study how the liver makes defective alpha-1 protein. Eissa wants to block production of defective alpha-1 without affecting other proteins.

**PLANT PROTEIN:**

Keith Davis, PhD, of the University of Louisville, will study the ability of plants to produce alpha-1 protein. (Ironically, tobacco is the plant being studied.) Alpha-1 protein, used in augmentation therapy for Alpha-1 patients with lung disease, is now purified from human blood plasma. If the protein could be produced from plants, this could increase the supply of alpha-1 protein, lower the cost of treatment, and increase safety.

**CUTTING THE CHAINS:**

David Lomas, MD, PhD, of the University of Cambridge, UK, will investigate the use of antibodies to prevent mutant alpha-1 protein from linking in long chains, or polymers. These proteins build up in liver cells, causing liver damage. In the lungs, they increase inflammation and lung damage. Lomas plans to show that mouse spleens can produce an antibody that would prevent alpha-1 molecules from polymerizing. If this can be done, the single alpha-1 protein would not get stuck in the liver, and might function normally in the lung – treating both liver and lung disease of Alpha-1.

**TREATING LIVER DISEASE:**

Nicola Brunetti-Pierri, MD, of the Telethon Institute of Genetics and Medicine, Naples, Italy, will investigate both drug and genetic therapies to treat Alpha-1-related liver disease. Some drugs can increase autophagy, the process by which cells actually digest themselves. This might slow or prevent the buildup of alpha-1 cells in the liver, which leads to liver disease in some Alphas.

Brunetti-Pierri also hopes to show that gene therapy can increase the number of lysosomes, compartments in liver cells responsible for clearing defective proteins.
AUGMENTATION and INFLAMMATION:

Noel G. McElvaney, MD, of the Royal College of Surgeons in Ireland, will study the effects of alpha-1 protein on neutrophils, white blood cells in the lung. Neutrophils produce molecules called reactive oxygen species (ROS), which can attack and damage both invading germs and human tissue. When there are too many ROS and too little alpha-1 protein, the lungs can be damaged.

McElvaney plans to show that alpha-1 protein controls ROS production in neutrophils, and that augmentation therapy is an efficient way to achieve this control.

IRON and LUNG DAMAGE:

Bernard Fischer, DVM, PhD, of Duke University Medical Center, believes that the enzyme neutrophil elastase causes an iron imbalance in lung cells, promoting free radical production that damages the lungs of Alphas. Fischer will test whether the drug deferasirox can bind up free iron in the cell, preventing the damage.

ALPHA-1 in CELL MEMBRANES:

Irina Petrache, MD, of Indiana University, says that recent research has shown that alpha-1 protein works not just outside cells, but actually enters the cells and reacts with cell membranes.

She will study alpha-1 protein by removing sugar molecules from the protein to see how this affects the ability of alpha-1 to enter the cells and interact with their membranes.

GENETIC DIFFERENCES in LIVER DISEASE:

Richard Sifers, PhD, of Baylor College of Medicine, will study how the alpha-1 protein is broken down in liver cells.

With biochemical studies and population analysis, Sifers hopes to show that a single nucleotide polymorphism (SNP) is a key modifier of the severity of liver disease in Alpha-1.

HOW SMOKING DAMAGES LUNGS:

Kamal Akhtar, PhD, of the Washington University School of Medicine, received a Postdoctoral Research grant. He will study elastic fibers in the lung and how they become damaged.

Alpha-1 antitrypsin protein normally protects elastic fibers from damage, but chemicals called oxidants in smoke can damage the alpha-1 protein so that it doesn’t function normally.

Akhtar will study how oxidants produced by cigarette smoke make elastic fibers more susceptible to damage and increase inflammation in the lungs.

PROTEIN RECEPTORS:

Angelia Lockett, PhD, at Indiana University, also received a Postdoctoral Research grant.

Lockett thinks that alpha-1 may protect lung cells by entering the cells through a receptor molecule. She hopes to find the receptor molecule. This might make it possible to develop treatments that increase receptors, so that more alpha-1 protein can enter lung cells and provide better protection against lung damage.
Alphas and many other people with chronic health conditions wait and hope for new and better treatments. It can be frustrating to excitedly follow the latest in research, only to be told that it will be years before drugs or treatments are available.

But there is new hope, especially for those with relatively rare health conditions.

Hidden among the 2,000 plus pages of the new national healthcare reform law is legislation aimed at reducing the long time between the discovery of ground-breaking research and actual new treatments for patients.

The Patient Protection and Affordable Care Act establishes a “Cures Acceleration Network (CAN)” in the director’s office at the National Institutes of Health (NIH). The network will “conduct and support revolutionary advances in basic research, translating scientific discoveries from bench to bedside.”

CAN will award research grants and contracts and support the development of “high need cures.” CAN will also work with the Food and Drug Administration (FDA) to expedite the development of these products.

Miriam O’Day, the Alpha-1 Foundation’s senior director, public policy, says this is exciting news for the Alpha-1 Foundation and all other research and patient advocacy organizations.

“It’s a really progressive idea” says O’Day. “Many progressive ideas don’t work the first time around. So, I’m sure there will be trial and error and refinement. But it is a great concept.”

The law defines a “high need cure” as a drug, biological product, or device that the NIH director determines is:

Goals of the Cures Acceleration Network:

- Promote innovation to support advanced research and development of “high need cures;”
- Accelerate development of these cures using medical products, behavior therapies or biomarkers; and
- Help to establish protocols that comply with FDA standards in all stages of development of a medical product.
• a priority to diagnose, mitigate, prevent or treat any disease or condition;
• and for which incentives of the commercial market are unlikely to result in adequate or timely development.

No specific diseases or conditions have been named as eligible to benefit from CAN’s support. O’Day says the Foundation should not wait to be included. “The Alpha-1 Foundation needs to establish Alpha-1 as one of the conditions recommended to benefit from CAN. This needs to be an ‘action item’ for us,” she says. “We need to ask for further definitions of ‘high need cures’ and what diseases should benefit. And then we need to advocate specifically for Alpha-1 research to receive CAN support.”

The Foundation was one of 75 patient advocacy and research organizations which signed a letter to both the House and Senate appropriations committees asking that the original $500 million allocated for CAN in fiscal year 2010 be fully funded. Ultimately, $50 million was earmarked for the CAN project. A diverse board with members representing the FDA and the research, venture capital and patient advocacy fields will oversee the execution of CAN.

**FDA, NIH JOIN FORCES TO SPEED DEVELOPMENT**

Another federal effort should also help to speed up development of new treatments.

The FDA and the NIH have agreed to establish a joint “NIH-FDA Leadership Council.” The Council will work to make regulatory considerations (product safety, quality and efficacy) a part of biomedical research planning. The Council will also work to ensure that the latest research science is a part of the current FDA drug and treatment review process.

Susan Shurin, MD, acting director of the NIH’s National Heart, Lung and Blood Institute (NHLBI), will serve on the Council. “This exchange between agencies should translate into better science and more transparency during the review process for drug development,” says O’Day. “And having the head of the NHLBI as part of the new Leadership Council can only be positive for Alpha-1 researchers and patients.”

The Foundation, along with the other members of the National Organization for Rare Disorders (NORD), have worked on another FDA-related initiative that will help not only Alphas, but everyone with a rare disorder. NORD and its members have lobbied hard for the FDA to become more “rare and neglected disease-oriented,” O’Day says.

“After working hard for the creation of an Associate Director of Rare Diseases position at the FDA earlier this year, NORD has recently learned that the work of this new position may now be greatly enhanced,” she reports. “As a result of our lobbying efforts, the Senate Appropriations Committee will soon consider a bill that provides $1 million to hire additional rare disease and orphan drug experts for this office.”

The bill also includes a $2 million increase for the FDA’s Orphan Product Development Grants. This program funds clinical research in rare diseases.

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**WANTED**

**THE FIRST HEROES OF ALPHA-1**

**WERE YOU IN THE FIRST ALPHA-1 REGISTRY?**

**FROM 1988 -1994, THE NIH REGISTRY FOLLOWED NEARLY 1,000 ALPHAS.**

**THEY CALLED THEMSELVES “THE BRANTLY BUNCH,” AFTER MARK BRANTLY, MD, THE DOCTOR WHO WORKED CLOSELY WITH THEM. THESE ALPHAS MADE AUGMENTATION THERAPY POSSIBLE. NO ONE KNOWS HOW MANY SURVIVE TODAY.**

**THE ALPHA-1 FOUNDATION IS EXPLORING THE POSSIBILITY OF AN “ALPHA-1 PIONEER REUNION” IN LATE 2011.**

**IF YOU WERE IN THE NIH REGISTRY, AND ARE INTERESTED IN A REUNION, CALL ANGELA McBRIE AT 1- 888 - 825 - 7421, EXT. 233, OR AMCBRIE@ALPHA-1FOUNDATION.ORG**

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www.alpha-1foundation.org
Videos for family AWARENESS

Alpha-1 Association’s Family Awareness DVDs are a new resource to create family awareness of Alpha-1 Antitrypsin Deficiency can be hard to understand. Explaining Alpha-1 to family members can be even harder.

Often, when Alphas tell their family about their diagnosis, they find that family members are reluctant to get tested. This is unfortunate, because testing can provide an accurate diagnosis and the opportunity to make lifestyle changes that help to maintain a healthier life.

The Alpha-1 Association wants to help make these conversations easier.

The Association has released its Family Awareness Videos as a new tool for Alphas to share with their families to discuss and understand Alpha-1 Antitrypsin Deficiency. The DVD contains information about what Alpha-1 is and how it affects the entire family. It is designed so family members can be informed before making a decision about getting tested for Alpha-1.

Robert A. Sandhaus, MD, PhD, clinical director of the Alpha-1 Foundation and medical director of AlphaNet, mentions in the video: “When you’ve identified a person with Alpha-1, you’ve actually identified a family at risk, since it is a genetic condition.”

This DVD, along with the Foundation’s “It’s All in the Family” brochure, can be used as an easy way to open a conversation about Alpha-1.

The DVD is divided into four parts:

• Family Matters
• Vital Organs – Liver and Lungs
• The Little Alphas – Our Children
• Genetics.

It features the stories of Alphas and their families, some of the obstacles they have had to face, and how they have overcome them. Participants in the video provide viewers with a better understanding of what it means to live with Alpha-1 and how families should be aware of the risks.

Testing for Alpha-1 is an important decision and family members should be well informed about testing options, the risks and benefits of testing, and which relatives are at greater risk. The Alpha-1 Association Genetic Counseling Program is an expert resource for patients and family members to help work through these complicated issues. Our certified genetic counselor, Dawn McGee, is available to talk about the diagnosis of Alpha-1, how it can impact the family, and ways to stay healthy longer. To speak to Dawn McGee, call the program’s confidential toll-free number, 1-800-785-3177.

The Alpha-1 Association is grateful to its board member Dell Witcher, who produced the DVD, and to the families and physicians who participated in the video and shared their stories.

The Family Awareness Videos can be ordered via email to aartiles@alpha1.org. The videos are also available online at www.alphal1.org.

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It’s easy: go to “Job Seekers” at www.vtsystems.org to apply today!!

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The COPD Foundation is a founding charity of Virtual Training Systems.

In order to qualify, you must be eligible to work in the US and be one or more of the following: disabled, veteran, caregiver, and/or a military spouse.
Some help getting to the Doctor

Foundation offers Alphas financial aid to visit CRC doctors familiar with Alpha-1

Finding a doctor who is knowledgeable about Alpha-1 can be a challenge sometimes. That’s why the Alpha-1 Foundation is offering a travel stipend of up to $500 to help Alphas and caregivers around the country to visit a Clinical Resource Center (CRC).

At these centers, Alphas can see a physician familiar with Alpha-1 and get answers about their condition. They can also find out more about how Alpha-1 affects their families. And they can learn about the testing choices available to family members.

More than 60 Clinical Resource Centers are located throughout the United States. A CRC specializes in patient care and education for those with Alpha-1. Some centers treat lung disease and others liver disease.

Centers often have other resources for Alphas such as transplant centers, support groups and pulmonary rehabilitation. Each center must meet certain criteria in order to be listed as a CRC through the Alpha-1 Foundation.

To qualify, Alphas must be newly diagnosed or have never visited a CRC. AlphaNet coordinators will help with the process. To find an AlphaNet coordinator, see the bottom of this article.

For information or to request a travel stipend, contact Pamela Arango at 888-825-7421 ext. 217 or parango@alphaone.org.

See the list of CRCs: tiny.cc/alphadocs
Find your state’s AlphaNet coordinator: tiny.cc/coordinator

Building Friends for a Cure and Team Alpha-1 Calendar of Events

<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
<th>Location</th>
<th>Contact Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>September 16</td>
<td>Alpha-1 Golf Tournament</td>
<td>Greenwich, CT</td>
<td>Ken Irvine <a href="mailto:airvine3@optonline.net">airvine3@optonline.net</a></td>
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<tr>
<td>September 25</td>
<td>“Get the Scoop on Alpha-1” Ice Cream Social</td>
<td>Fairmont, MN</td>
<td>Julie Liljenquist <a href="mailto:julie@NORWEKwithjulie.com">julie@NORWEKwithjulie.com</a></td>
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<tr>
<td>September 26</td>
<td>Team Alpha-1 Apple Cider Century Bike Ride</td>
<td>Three Oaks, MI</td>
<td>Berger Family <a href="mailto:mberger907@aol.com">mberger907@aol.com</a></td>
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<tr>
<td>October 1-3</td>
<td>Team Alpha-1 Escape to the Cape</td>
<td>Cape Cod, MA</td>
<td>Sue Binnall <a href="mailto:sbinnall@comcast.net">sbinnall@comcast.net</a></td>
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<tr>
<td>October 9</td>
<td>Brookside Croquet Championship In Honor of Todd Zinni</td>
<td>S. Nyack, NY</td>
<td>Brent Hirn <a href="mailto:croquet@optonline.net">croquet@optonline.net</a></td>
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<tr>
<td>November 20</td>
<td>2nd Annual Alpha-1 5k Walk Miami</td>
<td>Miami, FL</td>
<td>Angela McBride <a href="mailto:amcbride@alpha-1foundation.org">amcbride@alpha-1foundation.org</a></td>
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<tr>
<td>December</td>
<td>Building Friends for a Cure Training</td>
<td>Las Vegas, NV</td>
<td>Angela McBride <a href="mailto:amcbride@alpha-1foundation.org">amcbride@alpha-1foundation.org</a></td>
</tr>
<tr>
<td>2011</td>
<td></td>
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<tr>
<td>March 12</td>
<td>Celtic Connection</td>
<td>Needham, MA</td>
<td>Angela McBride <a href="mailto:amcbride@alpha-1foundation.org">amcbride@alpha-1foundation.org</a></td>
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<tr>
<td>April 2</td>
<td>Alpha-1 5K “Hero” Walk</td>
<td>Richmond, VA</td>
<td>Pam Vanscoy <a href="mailto:Pamvs2000@yahoo.com">Pamvs2000@yahoo.com</a></td>
</tr>
</tbody>
</table>

For fundraising event information, contact Angela McBride at 888.825.7421 ext 233 or amcbride@alpha-1foundation.org.
Patty Tew is a people person. She loves to invite people to her house to socialize. She can walk into a conference where she doesn’t know anyone, and leave with a bunch of new friends.

All of this got harder, and less enjoyable, when her health deteriorated a few years ago.

“I was getting sick more often and I was staying sick longer. I wasn’t getting well like I used to. An upper respiratory infection would go on for a solid two months,” said Tew, of Orlando, FL.

Actually, it was a respiratory infection that brought her to an emergency appointment with a physician assistant at her doctor’s office. A chest X-ray came out “normal”. The physician assistant was skeptical, and sent the X-ray out for another read. That’s when Tew found out she had chronic obstructive pulmonary disease (COPD). Her doctor tested her for Alpha-1, and sure enough, that’s what she had.

Shortly after her diagnosis, Tew was in touch with her AlphaNet coordinator. “For 13 months, he was the only Alpha I spoke to,” she said.

Those conversations began a series of events. Alpha-1 and its effects on people fascinated Tew. She became a support group leader in 2008, and took great satisfaction in helping other Alphas. And she decided if she were going to go back to work, she’d really like to be an AlphaNet coordinator herself.

So that’s what she did. In 2009, she put in a resume and eventually got the job as the AlphaNet coordinator for northern Florida and Georgia.

“It seemed a natural fit for me,” she said. “I very much enjoy Alphas. I like being around them. We’re all so different, and yet we all have much in common. We get together and there really is a sense of bond and family. It was easy for me to think of talking to them and serving them all day.”

### Join our Workplace Giving Program. Here’s how:

- **United Way:** Just write “Alpha-1 Foundation” on the “other” line of the payroll deduction form.
- **Combined Federal Campaign (CFC)** (postal workers, court employees, military, FBI, and IRS, for examples): Specify code 11717 to select the Alpha-1 Foundation.
- **A Matching gift Program** Many companies double, sometimes even triple, your charitable contribution.
- **Volunteering:** Many companies offer incentives to employees for volunteering. Some offer time off to volunteer, or make contributions to reward volunteer activities.
- **Invite friends** who participate in United Way, or who are federal employees, to increase our efforts in finding a cure.

Contact: Linda Rodriguez  
888.825.7421 ext. 237  
lrodriguez@alpha-1foundation.org
PROLASTIN®-C
Alpha1-Proteinase Inhibitor (Human)

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use PROLASTIN®-C (Alpha1-Proteinase Inhibitor [Human]) safely and effectively. See full prescribing information for PROLASTIN-C.

PROLASTIN®-C (Alpha1-Proteinase Inhibitor [Human]) Lyophilized Preparation

For Intravenous Use Only

Initial U.S. Approval: 1987

-------------INDICATIONS AND USAGE-------------

PROLASTIN-C is an alpha1-proteinase inhibitor that is indicated for chronic augmentation and maintenance therapy in adults with emphysema due to deficiency of alpha1-proteinase inhibitor (alpha1-antitrypsin deficiency). The effect of augmentation therapy with any alpha1-proteinase inhibitor (Alpha1-PI) on pulmonary exacerbations and on the progression of emphysema in alpha1-antitrypsin deficiency has not been demonstrated in randomized, controlled clinical trials. PROLASTIN-C is not indicated as therapy for lung disease in patients in whom severe Alpha1-PI deficiency has not been established.

-------------CONTRAINDICATIONS-------------

IgA deficient patients with antibodies against IgA.

-------------WARNINGS AND PRECAUTIONS-------------

- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions.
- This product is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease agent.

-------------ADVERSE REACTIONS-------------

The most common drug related adverse reactions during clinical trials in ≥ 1% of subjects were chills, malaise, headache, rash, hot flush, and pruritus.

To report SUSPECTED ADVERSE REACTIONS, contact Talecris Biotherapeutics, Inc. at 1-800-520-2807 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

-------------USE IN SPECIFIC POPULATIONS-------------

- Pregnancy: No human or animal data. Use only if clearly needed.
We’re all about better outcomes.

With PROLASTIN-C, you get more than just a leading alpha-1 treatment. You also get the leader in alpha-1 care—PROLASTIN DIRECT®.*

One simple call provides easy access to:

• Health management from AlphaNet
• Insurance reimbursement help
• Customized drug delivery and home infusion
• Prompt answers to questions about PROLASTIN-C therapy

Plus, PROLASTIN DIRECT® is fully staffed by alpha-1 specialists, all of whom are alphas themselves, so they understand, first hand, that there’s more to successful treatment than first-rate infusions.

To get started, call 1.800.305.7881

IMPORTANT SAFETY INFORMATION

PROLASTIN-C, Alpha₁-Proteinase Inhibitor (Human) is for adults who have emphysema caused by inherited alpha₁-antitrypsin deficiency. The effect of therapy with any alpha₁-proteinase inhibitor (alpha₁-PI) on pulmonary exacerbations and on the progression of emphysema in alpha₁-antitrypsin deficiency has not been demonstrated in randomized, controlled clinical trials.

PROLASTIN-C may contain trace amounts of IgA. Patients with known antibodies to IgA, which can be present in patients with selective or severe IgA deficiency, have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. IgA deficient patients with antibodies against IgA should not receive PROLASTIN-C due to the risk of hypersensitivity.

The most common side effects during clinical trials with PROLASTIN-C were chills, a general feeling of being unwell, headache, rash, hot flush, and itching.

PROLASTIN-C is made from human plasma. Products made from human plasma may carry a risk of transmitting infectious agents, eg, viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088

Please see brief summary of PROLASTIN-C full Prescribing Information on adjacent page.

*Formerly known as Talecris Direct®.