

PULMONARY FIBROSIS FOUNDATION

# Breathe

## BULLETIN

VOLUME 12 | ISSUE 02

FALL 2012



# in this issue

BREATHE BULLETIN VOLUME 12 | ISSUE 02 FALL 2012



©ISTOCKPHOTO.COM/NICOLAS\_

## SPECIAL INTEREST

### RESEARCH, CLINICAL TRIALS, AND THE DRUG DEVELOPMENT PIPELINE

- 04 Q+A with A. Bruce Montgomery, MD: Developing and Bringing a Drug to Market
- 08 Clinical Trials
  - 08 The Basics
  - 13 Finding a Clinical Trial

## REGULAR FEATURES

### PROFILES

- 14 My Experience in a Clinical Trial
  - 14 As Told by Marj Korn
  - 16 As Written by Neal Busk
- 18 Research and Clinical Trials at Stanford University: A Discussion with Glenn D. Rosen, MD

### RESEARCH

- 22 How Does the PFF Impact the Pulmonary Fibrosis Research Community?
  - 22 Pulmonary Fibrosis Foundation Research Fund
  - 24 PFF Research Program — Awards, Partnerships, and Sponsorships
- 26 Recent News in Pulmonary Fibrosis Research

### PFF NEWS

- 30 PFF Summit 2013
- 31 Ways to Give

*Breathe Bulletin* is published biannually by the Pulmonary Fibrosis Foundation. Opinions expressed by the authors are their own and do not necessarily reflect the policies of the Pulmonary Fibrosis Foundation.

#### Disclaimer

The material contained in this newsletter is for educational purposes only and should not be considered as medical advice. Consult your health care provider for treatment options.

The mission of the Pulmonary Fibrosis Foundation (PFF) is to help find a cure for idiopathic pulmonary fibrosis (IPF), advocate for the pulmonary fibrosis community, promote disease awareness, and provide a compassionate environment for patients and their families.

© 2012 Pulmonary Fibrosis Foundation, All Rights Reserved

**Pulmonary Fibrosis Foundation**  
230 East Ohio Street, Suite 304  
Chicago, Illinois 60611-3201  
888.733.6741  
[www.pulmonaryfibrosis.org](http://www.pulmonaryfibrosis.org)

COVER IMAGE: ISTOCKPHOTO.COM/HAYDENBIRD



# LETTER FROM OUR PRESIDENT AND CEO

## DEAR FRIENDS,

Welcome to our latest edition of the *Breathe Bulletin*. This issue will focus on current research initiatives and includes an in-depth discussion on the critical importance of clinical trials from multiple perspectives. I hope that you will find this issue as interesting as I do.

The Pulmonary Fibrosis Foundation serves many roles in fulfilling our mission. One important aspect is to bring valuable new information to patients, their families, and caregivers. With that in mind, a focus of this issue of the *Breathe Bulletin* is clinical trials—their impact on patients and their importance in developing new and better medical interventions. There is fundamental and detailed information about clinical trials from the National Institutes of Health with a link for current trials.

Additionally there are interviews with Dr. Glenn Rosen (who does both translational research and clinical trials at Stanford University) and with Dr. Bruce Montgomery (who has developed a number of successful therapies for patients with cystic fibrosis). I found their interviews to be very informative and full of hope. We are extremely fortunate to have them on our Medical Advisory Board.

Finally, and significantly, there are two patient stories, told in their own words, about their experiences in clinical trials. These are the heroes in the pulmonary fibrosis community. Without their participation successful therapies will not be found. However, that is not to say that the decision to participate is correct for everyone; participation is a deeply personal decision that should be made with the guidance of one's physician.

All of us at the Foundation hope you remember to visit our website often at [www.pulmonaryfibrosis.org](http://www.pulmonaryfibrosis.org). It's a great resource for anyone who wants to learn more about pulmonary fibrosis and has more detailed information on all of the topics in the *Breathe Bulletin*.

As always, we greatly appreciate your participation and support.

Sincerely,

A handwritten signature in black ink that reads "Daniel M. Rose". The signature is fluid and cursive, with a large, stylized "R" at the end.

**DANIEL M. ROSE, MD**

President and Chief Executive Officer

# Q+A

## Q+A WITH A. BRUCE MONTGOMERY, MD

### Developing and Bringing a Drug to Market

#### **How did you become interested in research, and specifically drug development?**

I was trained in internal medicine, and 29 years ago I was doing a pulmonary critical care fellowship at UC San Francisco, and one of the hospitals there is San Francisco General. So I showed up to do my fellowship in pulmonary critical care, and it was basically day zero, ground zero of the AIDS epidemic. And what got me interested in research was realizing that I didn't have the drugs to treat these patients.

I was very interested in figuring out a way of treating, and then preventing, this pneumonia that AIDS patients would get. I worked with an old friend of mine from Seattle, Robert Debs, and we invented an aerosolized medication that prevented the pneumonia that AIDS patients got, and we pretty much eliminated that as a problem in HIV. Survival when we first started was six weeks, and we moved that out to about 18 months; and that gave the researchers enough time to try and test the antiviral agents that have totally changed the disease.

Therefore, I got interested in research after realizing that we didn't have the answers for all the patients, and I said, "let's develop some better answers." I've always been focused in the area of developing new therapies for unmet needs in pulmonary disease; I got interested because my patients weren't doing well.

#### **What was the genesis for Pulmozyme® and the inhaled antibiotics TOBI® and Cayston® that are used to treat cystic fibrosis?**

I was working in an area of what is now called translational medicine, which is taking ideas from the lab and doing proof of concept studies in humans. Once we were able to demonstrate the validity of a concept, we would pass it off to a larger team that would take the idea through the approval process.

Pulmozyme was based on an idea of a drug that Merck had actually developed. Pulmozyme is a DNase enzyme, which means it cleaves DNA. In 1947, Merck had developed a form of bovine DNase. This was before cystic fibrosis (CF) patients lived long enough to get lung disease, and Pulmozyme worked in some lung diseases. Unfortunately, being from the cow, it caused a lot of allergic reactions, and so it was pulled from the market in about 1970.

One of the people at Genentech, a guy named Steve Shak, came across this old history and said, "gee, we now have the ability to make a human DNase," and he went ahead and did that. Then I did the initial studies, and we went ahead and tried it in CF patients. We were able to improve their lung function by about 5% and decrease the number of exacerbations.

So the whole genesis was actually taking an old idea that worked but was unsafe because of allergic reactions, and then saying, hey, we can solve that problem.

Similarly, the inhaled antibiotics TOBI and Cayston were developed to basically deal with the chronic infections cystic fibrosis patients get. With TOBI there had been some academic work with inhaled tobramycin, some of the studies seemed to work and some didn't. The key thing that we figured out was that the tobramycin would actually bind to sputum; therefore, we needed to give ten times the dose we thought we had to give, and if we gave a big enough dose, it worked.

We developed an effective formulation and got a more efficient nebulizer. The combination of those two things allowed us to consistently deliver the high dosage that led to the efficacy, and that has really changed the natural history of cystic fibrosis. TOBI alone has probably added over a decade to a typical CF patient's life.

**"What we need to do is really good science and good trials, and we'll eventually find something."**



Cayston, on the other hand, which is another inhaled antibiotic, came about because patients can't take the same antibiotic forever because of bacterial resistance—you need more than one bullet in your gun. And what's the second bullet? Cayston. Aztreonam is the key chemical, and it's been around as an antibiotic. Actually, some doctors had been off-label experimenting with it, getting very mixed results.

After examining what they were doing, I made the realization that the commercial intravenous doses of aztreonam actually contained an incipient ingredient, which neutralized the acid base level. I realized that this ingredient would unfortunately lead to inflammation and damage to the lung tissue. So the genesis of the idea was that I'd switch out the ingredient that neutralized the pH and create something that was safe for the lungs.

We then took it into clinical trials, and the long story short is, it works spectacularly, and it eventually got approved. So basically, it was taking ideas that were sort of half-baked, figuring out what the problems were, carrying them through, and finally getting something that is safe and effective for humans.

**Without a real clinical trial, it would have been impossible to make this a reality.**

But you also needed a real drug. The real drug, that was the easy part, and then the five-year part is the good clinical trials. Even though I'm considered to be the person who developed these drugs, one has to put it in context that in order to take a drug through development, it's about a minimum of a couple hundred man-years or woman-years worth of work. I'm not that old, so clearly I've had a large team. Some people may claim differently, but it takes a large team of talented people that are experts in toxicology and pharmacology in order to determine if the drug is safe and effective.

You've got to really make sure that your drug is safe, that results are reproducible, that the drug can be stored, and finally that it can be given safely. Also we have to know that we have tested it in enough patients to make sure there's not a rare side effect, which could be dangerous. So all this takes time and money. But when you get it approved, you can do spectacular things for patients.

**From start to finish, was that ten years, twenty years?**

Interestingly enough, the development timeline for Pulmozyme was about five years, TOBI four years, Cayston nine years. If you've got some previous data on something and you're adapting it, you can save some time.



A. Bruce Montgomery, MD

**“You’ve got to really make sure that your drug is safe, that results are reproducible, that the drug can be stored, and finally that it can be given safely.”**

**How do you expedite drug development?**

The rules are pretty flexible from the U.S. Food and Drug Administration (FDA). So for instance, if you have a disease that doesn't really kill people, it can be a problem. I'll give you an example, acne—you better make sure that when you get that drug approved, it's been tested in literally thousands of patients and there are really no major side effects.

If you have a disease that is fatal and you show that you're actually improving outcomes in some way, the FDA is far more lenient. Let's say there's a rare side effect that kills one in 1,000 people, but it saves 15–20% of the people, they're going to think that is acceptable. The good news for idiopathic pulmonary fibrosis (IPF) is that everyone appreciates this is a bad disease, and so the agency is more likely to allow you to take risk. With IPF, you're in the 300 patient range, so if you had 300 patients showing the drug is safe and you had efficacy, you could get the drug approved.

The problem, though, with drug development is we've been forever fooled. We do a small study in idiopathic pulmonary fibrosis, the results look really good, and then we do a large study and they don't pan out, and that's really disappointing to patients.

What we've seen with so many drug trials going on, and the smaller the trial, the more chance for—you know—problems. If you do a very, very large trial, the chances of a fluke result are smaller. We're sort of running out of things that people say work in a small trial. We've tested all those things, and they don't work. And so now we know, and now we can focus on trying some of these newer agents. There's really nothing that needs to be fixed at the FDA. What we need to do is really good science and good trials, and we'll eventually find something.

Unfortunately you need a winner to know what biomarker actually is predictive, because how do you know if a biomarker is predictive unless you have what is called the positive control or the one that shows it actually works? So the first drug that works is going to really help get the other drugs through because it will give us an idea if there were things early in the trial that gave us the clue that this drug was working.

*continued on next page >*

**What are your thoughts regarding therapies currently in development? For instance, LOXL2 developed by Arresto and subsequently purchased by Gilead. Do you have any thoughts on the potential efficacy of other drugs in development — BIBF 1120, STX-100, and CTO 888?**

Full disclosure, I was the Senior Vice President in charge of respiratory therapeutics at Gilead when we bought Arresto, so of course I thought it was a good idea. We spent a lot of money buying it. So I'm biased on that. LOXL2 basically interferes with what is called the TGF-beta fibrosis pathway—I don't know if it's going to work or not, but it's a logical bet, and it's going into clinical trials. I think it's a very interesting compound and well worthy of testing.

BIBF 1120, which is the Boehringer Ingelheim compound, is a tyrosine kinase inhibitor. Clearly there was a wonderful paper in the *New England Journal of Medicine* that showed some efficacy. I think the question with this compound is: is there a dose that is safe enough and tolerable enough for patients? Can you thread the needle between safety and efficacy? Sometimes a drug could work, but the side effect profile is such that it's not tolerable. Is there a dose that people can tolerate and has efficacy? I think these trials, which are currently ongoing, have been extremely well-designed to answer that question.

STX-100 [Stromedix/Biogen], which you also mentioned, targets the alpha V beta 6 integrin. There's enough biology there to think this might work. Unfortunately, we don't have any good animal models for IPF. Since the animal models don't replicate the mechanism that is going on in humans, you really can't do an effective animal efficacy model and say, okay, this thing works. You really have to go to the humans, and this is an interesting bet.

Finally, the last one you've asked about is Centocor's CTO 888. It basically goes after a monocyte chemo-attractive protein and tries to block that, which may be important in the cascade of lung fibrosis.

It's a little like stopping traffic into Manhattan. If you want to stop traffic going into Manhattan, and you block the Holland Tunnel, you're pretty effective, because there's less traffic getting into town. However, if you go further down the pathway and you block Fifth Avenue, there's always Seventh, First, and the other avenues.

So the question is, do these compounds block a certain pathway? Are they early enough in the cascade, and there are no other mechanisms that go parallel to it, so that even though you block it, the process still continues? And that's a question that can only be answered in clinical studies. A wreck on Fifth Avenue doesn't necessarily block all traffic going uptown, but if you block the Holland Tunnel, you're pretty effective.

I think one of the key questions about all these trials is, do they block pathways early enough and are there other pathways around this, because the body is completely full of redundant pathways to do something. And that's probably evolutionary, you don't want to have something so critical that one genetic defect will completely kill you. Usually there are multiple ways of doing things.

So I think all these things are good bets, and may actually lead to effective therapies. In HIV medicines we found blocking viral replication with one drug would work for a little while, two would work a little better, but when you gave three, then you blocked everything, and you had phenomenal results. What we might find is that, yeah, these drugs all work a little bit in clinical trials by themselves, but when we put the combination together, then we have that kind of magic potion that we're all looking for. In the end I think it's probably going to be combination therapy. It's going to be "two plus two is equal to ten" type of stuff. We've got to keep trying and doing really good clinical trials.

**“Every patient who enrolls in a trial and takes a risk is a true hero to me, because they’re putting their life on the line to see if they can advance science.”**

## Will we be able to get beyond randomized trials with the use of biomarkers?

I don't think we'll ever get beyond performing randomized trials, but we could probably make trials a lot smaller if we knew what biomarkers were really predictive of efficacy. If you're going the right direction at six weeks rather than six months, then you could do a lot of very short-term trials with a whole bunch of agents and screen a lot in 20 or 30 patient trials rather than having to do these 200–300 patient trials. The biomarkers aren't going to get us beyond randomized trials. What they're going to do is get us beyond very large randomized trials and into focused, short-term trials that give us answers quicker.

## How can the patient community become more engaged with drug development?

The more research that we have and the more agents we test, the more likely we are to come to an answer. So the patients can help by asking their centers, "Are you set up for research, can you do trials?" That should be something that they ask their docs. That's sort of an expectation at these centers for excellence, that excellence implies they should be doing good research.

The second thing is—we need more heroes. Every patient who enrolls in a trial and takes a risk is a true hero to me, because they're putting their life on the line to see if they can advance science. The attitude from the patient is that there's no greater contribution than to say, "Okay, I'm going to put my life on the line. I'm going to sign up for this thing and find out if something works." In IPF it's important!

And we have a genetic component. There are some patients that have family members that may eventually get this disease, and if you're the person who volunteers and you find out that something works, then maybe your family will benefit down the road. Signing up and volunteering for studies is the greatest thing they can do, and I strongly encourage it.

These docs know what they're doing, and I want to explain what's going on and give people hope. Because that's what everybody wants—hope. We can't give up. If we put our mind to it, we'll figure this out. It's just a matter of us not giving up, continuing to try, cutting our losses, and just to keep making bets. We've got a lot of great bets on the table, and hopefully one or two or three will come through. If one comes through, that's just a beginning.

# "Let's develop some better answers."



©ISTOCKPHOTO.COM/NICOLAS

### About A. Bruce Montgomery, MD

A. Bruce Montgomery, MD, is the Chief Executive Officer at Cardeas Pharma, a privately held pharmaceutical company dedicated to the development and commercialization of inhaled antibiotics to treat serious, hospital-acquired respiratory infections.

Dr. Montgomery has more than 25 years of drug development, operations, and financing experience, including positions at Genentech, PathoGenesis, Corus Pharma, and Gilead Sciences. He led development of the only three currently marketed antimicrobials for inhalation, (aerosolized pentamidine, Tobramycin Inhalation Solution [TOBI®], and Aztreonam Inhalation Solution [Cayston®]) and initiated multiple other programs that have resulted in drug approvals, including Pulmozyme®, Xolair®, and Raptiva®. Dr. Montgomery has raised over 200 million dollars in venture and public financings.

Prior to founding Cardeas, Dr. Montgomery served four years as Senior Vice President of Gilead Sciences, and six years as Chief Executive Officer of Corus Pharma, a specialized biotechnology company focusing on infectious disease and respiratory drugs that he founded, and which was acquired by Gilead in 2006.

Dr. Montgomery also served as Executive Vice President of Research and Development at PathoGenesis Corporation until its acquisition by Chiron in 2000.

In 1998, the FDA Commissioner recognized Dr. Montgomery with a special citation for leadership in the development and approval of TOBI. For this work, Dr. Montgomery also received the 2009 Inventor of the Year award from the University of Washington. In 2010, Dr. Montgomery received a scientific achievement award from the Cystic Fibrosis Foundation for his work on Pulmozyme, TOBI, and Cayston, which collectively have extended the average life span of cystic fibrosis patients by over a decade. In 2011, he received a career achievement award from the International Society for Aerosols in Medicine.

Dr. Montgomery received his B.S. in Chemistry (Magna cum Laude, Outstanding Chemistry Major [Merck Award]), and M.D. (Alpha Omega Alpha Honor Medical Society) from the University of Washington, Seattle. Dr. Montgomery is a board certified internist and pulmonologist. He has served as a board member for ZymoGenetics, and is currently on the board of Alder Pharmaceuticals. In 2012, Dr. Montgomery was honored as one of the top 150 living graduates of the University of Washington College of Arts and Sciences in conjunction with the 150th anniversary of the university.

Dr. Montgomery is a member of the Pulmonary Fibrosis Foundation Medical Advisory Board.

## What are clinical trials and why do people participate?

Clinical trials are part of clinical research and at the heart of many medical advances. Clinical trials look at new ways to prevent, detect, or treat disease. Treatments might be new drugs or new combinations of drugs, new surgical procedures or devices, or new ways to use existing treatments. The goal of clinical trials is to determine if a new test or treatment works and is safe. Clinical trials can also look at other aspects of care, such as improving the quality of life for people with chronic illnesses.

People participate in clinical trials for a variety of reasons. Healthy volunteers say they participate to help others and to contribute to moving science forward. Participants with an illness or disease also participate to help others, but also to possibly receive the newest treatment and to have the additional care and attention from the clinical trial staff. Clinical trials offer hope for many people and an opportunity to help researchers find better treatments for others in the future.

# CLINICAL TRIALS THE BASICS

## What is clinical research?

Clinical research involves people like you. Individuals volunteer to participate in carefully conducted investigations that are designed to discover better ways to treat, prevent, diagnose, and understand human disease. Clinical research also includes “longitudinal” studies that examine the natural history of an ailment and provide important information about disease progression.

### THE IDEA

Motivation for a clinical trial often originates in the laboratory. After a researcher tests a new therapy or procedure in the laboratory and performs appropriate animal studies, only then are the most promising experimental treatments moved into clinical trials. During a trial, more information is gained about an experimental treatment, its risks, and its effectiveness.

## THE PROTOCOL

Clinical research is conducted following a carefully designed protocol. The protocol is structured to safeguard the participants’ health and answer specific research questions. A protocol describes the following:

- Who is eligible to participate in the trial
- Details about tests and procedures that will be performed
- Medications and dosages that participants will receive
- The length of the study and what information will be documented

A clinical study is led by the principal investigator (PI) who is often a physician. Members of the research team regularly monitor the participants’ health to determine the study’s safety and effectiveness.



## What is clinical research? (cont.)

### PROTOCOL REVIEW

At all sites where clinical trials are performed, the study must be approved and monitored by an Institutional Review Board (IRB). The IRB ensures that the risks of the clinical trial are minimized and are worth any potential risks. An IRB is an independent committee that consists of physicians, statisticians, and members of the community. The committee makes sure that the clinical trials are ethical and that the rights of participants are protected. Federal regulation requires all institutions in the United States that conduct or support biomedical research involving people to have an IRB approve and periodically review the research.

### SPONSORS

Clinical trials can be sponsored or funded by various organizations and can include: individuals, foundations, medical institutions, pharmaceutical companies, and federal agencies such as the National Institutes of Health and the Department of Veterans Affairs.

### INFORMED CONSENT

Informed consent provides prospective participants with all the key facts about a clinical trial before deciding to participate. To help someone decide whether or not to participate, members of the research team thoroughly explain all the details of the study. Translation or interpretive assistance can be provided for participants with limited English proficiency. The research team provides an informed consent document that contains details about the study, including its purpose, duration, required procedures, and who to contact for further information. The informed consent document also explains risks and potential benefits. The individual then decides whether to participate. Throughout the study participants are updated on any important or new information as it becomes available. Informed consent is not a contract. Volunteers are free to withdraw from the study or to refuse particular treatments or tests at any time; however, this can make them ineligible to continue the study.

### TYPES OF CLINICAL TRIALS

There are different types of clinical trials.

- **Natural history studies** provide valuable information about disease progression.
- **Prevention trials** look for better ways to prevent a disease from occurring or returning. Interventions may include medications, vaccines, or lifestyle changes.
- **Screening trials** test the best way to detect specific diseases or medical conditions.
- **Diagnostic trials** determine better tests or procedures for diagnosing a particular disease.
- **Treatment trials** test new treatments, new combinations of drugs, or new approaches to surgery or radiation therapy.
- **Quality of life trials** (or supportive care trials) explore and measure ways to improve the comfort and quality of life of people with a chronic illness.

### PHASES OF CLINICAL TRIALS

Clinical trials are conducted in “phases.” Each phase has a different purpose and helps researchers answer different questions.

- **Phase 1 trials:** This initial study investigates an experimental drug or treatment in a small group of people (20–80) to evaluate its safety and identify side effects.
- **Phase 2 trials:** The experimental drug or treatment is administered to a larger group of people (100–300) to determine its effectiveness and to further evaluate its safety.
- **Phase 3 trials:** The experimental drug or treatment is usually administered in a randomized and “blinded” fashion to a larger group (1,000–3,000). This phase will determine the efficacy of a particular therapeutic intervention, monitor side effects, compare it with standard or equivalent treatments, and collect information that will allow the experimental drug or treatment to be used safely.
- **Phase 4 trials:** After a drug is approved by the FDA and made available to the public, the investigators track its safety and gather more information about a drug or treatment’s risks, benefits, and optimal use.

*continued on next page >*

## What is clinical research? (cont.)

### SOME CONCEPTS TO UNDERSTAND

Typically, clinical trials compare a new product or therapy with another that already exists to determine if the new one is as successful as, or better than, the existing one. In some studies, participants may be assigned to receive a **placebo** (an inactive product that resembles the test product, but without its treatment value).

Comparing a new product with a placebo can be the fastest and most reliable way to demonstrate the new product's therapeutic effectiveness. However, placebos are not used if a patient would be put at risk—particularly in the study of treatments for serious illnesses—by not having effective therapy. Most of these studies compare new products with an approved therapy. Potential participants are told if placebos will be used in the study before they enter a trial.

**Randomization** is the process by which two or more alternative treatments are assigned to volunteers by chance rather than by choice. This is done to avoid any bias with investigators assigning volunteers to one group or another. The results of each treatment are compared at specific points during a trial, which may last for years. When one treatment is found superior, the trial is stopped so that the fewest volunteers receive the less effective treatment.

In **single-** or **double-blind studies**, also called single- or double-masked studies, the participants do not know which medicine is being used, so they can describe what happens without bias. “Blind” (or “masked”) studies are designed to prevent members of the research team or study participants from influencing the results. This allows scientifically accurate conclusions. In single-blind (single-masked) studies, only the patient is not told what is being administered. In a double-blind study, only the pharmacist knows; members of the research team are not told which patients are getting which medication, so that their observations will not be biased. If medically necessary, however, it is always possible to find out what the patient is taking.

## Who participates in clinical trials?

Many different types of people participate in clinical trials. Some are healthy, while others may have illnesses. A **healthy volunteer** is a person with no known significant health problems who participates in clinical research to test a new drug, device, or intervention. Research procedures with healthy volunteers are designed to develop new knowledge, not to provide direct benefit to study participants. Healthy volunteers have always played an important role in research.

Healthy volunteers are needed for several reasons. When developing a new technique, such as a blood test or imaging device, healthy volunteers (formerly called “normal volunteers”) help define the limits of “normal.” These volunteers serve as controls for patient groups and are often matched to patients on characteristics such as age, gender, or family relationship. They receive the same test, procedure, or drug the patient group receives. Investigators learn about the disease process by comparing the patient group to the healthy volunteers.

Factors like how much of your time is needed, discomfort you may feel, or risk involved depend on the trial. While some require minimal amounts of time and effort, other studies may require a major commitment in time and effort on behalf of the volunteer, and may involve some discomfort. The research procedure may also carry some risk. The consent process for healthy volunteers includes a detailed discussion of the study's procedures and tests.

A **patient volunteer** has a known health problem and participates in research to better understand, diagnose, treat, or cure that disease or condition. Research procedures with a patient volunteer help develop new knowledge. These procedures may or may not benefit the study participants.

Patient volunteers may be involved in studies similar to those in which healthy volunteers participate. These studies involve drugs, devices, or interventions designed to prevent, treat, or cure disease. Although these studies may provide direct benefit to patient volunteers, the main aim is to prove, by scientific means, the effects and limitations of the experimental treatment. Consequently, some patients serve as controls by not taking the test drug, or by receiving test doses of the drug large enough only to show that it is present, but not at a level that can treat the condition. A study's benefits may be indirect for the volunteers but may help others.

All clinical trials have guidelines about who can participate, called **inclusion/exclusion criteria**. Factors that allow someone to participate in a clinical trial are “inclusion criteria.” Those that exclude or do not allow participation are “exclusion criteria.” These criteria are based on factors such as age, gender, the type and stage of a disease, previous treatment history, and other medical conditions. Before joining a clinical trial, a participant must qualify for the study. Some research studies seek participants with illnesses or conditions to be studied in the clinical trial, while others need healthy volunteers.

Some studies need both types. Inclusion and exclusion criteria are not used to reject people personally; rather, the criteria are used to identify appropriate participants and keep them safe, and to help ensure that researchers can find new information they need.

## What do I need to know if I am thinking about participating?

### RISKS AND BENEFITS

Clinical trials involve risks, just as routine medical care and the activities of daily living. When weighing the risks of research, you can consider two important factors:

- the degree of harm that could result from participating in the study; and
- the chance of any harm occurring.

Most clinical studies pose the risk of minor discomfort, which lasts only a short time. However, some study participants experience complications that require medical attention. In rare cases, participants have been seriously injured or have died of complications resulting from their participation in trials of experimental therapies. The specific risks associated with a research protocol are described in detail in the informed consent document, which participants are asked to sign before participating in research. Also, a member of the research team explains the major risks of participating in a study and will answer any questions you have about the study. Before deciding to participate, carefully consider possible risks and benefits.

### POTENTIAL BENEFITS

Well-designed and well-executed clinical trials provide the best approach for participants to:

- Play an active role in their health care.
- Gain access to new research treatments before they are widely available.
- Receive regular and careful medical attention from a research team that includes doctors and other health professionals.
- Help others by contributing to medical research.

### POTENTIAL RISKS

Risks to participating in clinical trials include the following:

- There may be unpleasant, serious, or even life-threatening side effects to experimental treatment.
- The study may require more time and attention than standard treatment would, including visits to the study site, more blood tests, more treatments, hospital stays, or complex dosage requirements.

## What questions should I ask if offered a clinical trial?

If you are offered a clinical trial, feel free to ask any questions or bring up any issues concerning the trial at any time. The following suggestions may give you some ideas as you think about your own questions.

### THE STUDY

- What is the purpose of the study?
- Why do researchers think the approach may be effective?
- Who will fund the study?
- Who has reviewed and approved the study?
- How are study results and the safety of participants being checked?
- How long will the study last?
- What will my responsibilities be if I participate?

### POSSIBLE RISKS AND BENEFITS

- What are my possible short-term benefits?
- What are my possible long-term benefits?
- What are my short-term risks, such as side effects?
- What are my possible long-term risks?
- What other options do people with my disease have?
- How do the possible risks and benefits of this trial compare with those options?

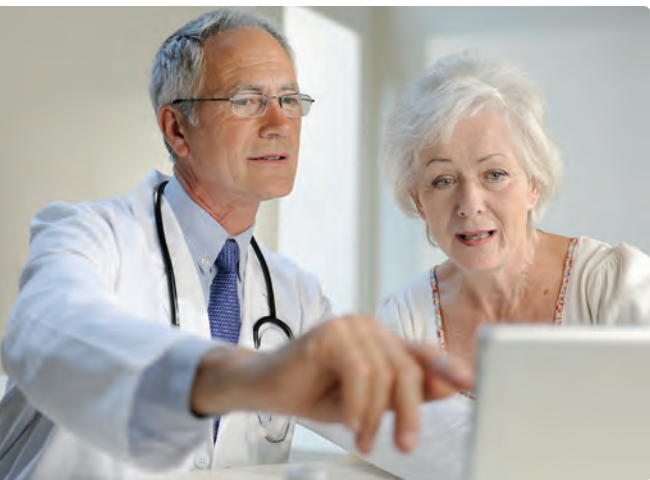
### PARTICIPATION AND CARE

- What kinds of therapies, procedures, and/or tests will I have during the trial?
- Will they hurt and, if so, for how long?
- How do the tests in the study compare with those I would have outside of the trial?
- Will I be able to take my regular medications while in the clinical trial?
- Where will I have my medical care?
- Who will be in charge of my care?

### PERSONAL ISSUES

- How could being in this study affect my daily life?
- Can I talk to other people in the study?

*continued on next page >*



©ISTOCKPHOTO.COM/PEEPO

## What questions should I ask if offered a clinical trial? (cont.)

### COST ISSUES

- Will I have to pay for any part of the trial such as tests or the study drug?
- If so, what will the charges likely be?
- What is my health insurance likely to cover?
- Who can help answer any questions from my insurance company or health plan?
- Will there be any travel or child care costs that I need to consider while I am in the trial?

### TIPS FOR ASKING YOUR DOCTOR ABOUT TRIALS

- Consider taking a family member or friend along for support and for help in asking questions or recording answers.
- Plan ahead what to ask—but don't hesitate to ask any new questions you think of while you're there.
- Write down your questions in advance, to make sure you remember to ask them all.
- Write down the answers, so that you can review them whenever you want.
- Ask about bringing a tape recorder to make a taped record of what's said (even if you write down answers).

Questions courtesy of Cancer.gov.

## How am I protected?

### ETHICAL GUIDELINES

The goal of clinical research is to develop knowledge that improves human health or increases understanding of human biology. People who participate in clinical research make it possible for this to occur. The path to finding out if a new drug is safe or effective is to test it on patient volunteers. By placing some people at risk of harm for the good of others, clinical research has the potential to exploit patient volunteers. The purpose of ethical guidelines is both to protect patient volunteers and to preserve the integrity of the science. Ethical guidelines in place today were primarily a response to past research abuses.

### INFORMED CONSENT

Informed consent is the process of learning the key facts about a clinical trial before deciding whether to participate. The process of providing information to participants continues throughout the study. To help someone decide whether to participate, members of the research team explain details of the study. The research team provides an informed consent document, which includes such details about the study as its purpose, duration, required procedures, and who to contact for various purposes. The informed consent document also explains risks and potential benefits.

If the participant decides to enroll in the trial, the informed consent document will be signed. Informed consent is not a contract. Volunteers are free to withdraw from the study at any time.

### IRB REVIEW

Each clinical trial in the United States must be approved and monitored by an Institutional Review Board (IRB) to ensure that the risks are minimal and are worth any potential benefits. An IRB is an independent committee that consists of physicians, statisticians, and members of the community who ensure that clinical trials are ethical and that the rights of participants are protected. Federal regulation requires all institutions in the United States that conduct or support biomedical research involving people to have an IRB approve and periodically review the research.

## further reading

**For more information about clinical trials, please visit:**

- **NIH CLINICAL RESEARCH TRIALS AND YOU** [www.nih.gov/health/clinicaltrials](http://www.nih.gov/health/clinicaltrials)

**For more information about research protections, please visit:**

- **OFFICE FOR HUMAN RESEARCH PROTECTIONS** [www.hhs.gov/ohrp/](http://www.hhs.gov/ohrp/)
- **CHILDREN'S ASSENT TO CLINICAL TRIAL PARTICIPATION** [www.nichd.nih.gov/health/clinicalresearch/aboutclinicalresearch.cfm#3](http://www.nichd.nih.gov/health/clinicalresearch/aboutclinicalresearch.cfm#3)

**For more information on participants' privacy and confidentiality, please visit:**

- **NATIONAL INSTITUTES OF HEALTH, HIPAA PRIVACY RULE** [privacyruleandresearch.nih.gov](http://privacyruleandresearch.nih.gov)

**For more information on safety and monitoring, please visit:**

- **THE FDA'S DRUG REVIEW PROCESS: ENSURING DRUGS ARE SAFE AND EFFECTIVE** [www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm](http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143534.htm)
- **NATIONAL CANCER INSTITUTE, MONITORING THE SAFETY OF CLINICAL TRIAL** [www.cancer.gov/clinicaltrials/learningabout/patientsafety/monitoring-safety-of-trials](http://www.cancer.gov/clinicaltrials/learningabout/patientsafety/monitoring-safety-of-trials)



## What happens after a clinical trial is completed?

After a clinical trial is completed, the researchers carefully examine information collected during the study before making decisions about the meaning of the findings and about further testing. After a phase 1 or 2 trial, the researchers decide whether to move on to the next phase or to stop testing the agent or intervention because it was unsafe or ineffective. When a phase 3 trial is completed, the researchers examine the data and decide whether the results have medical importance.

Results from clinical trials are often published in peer-reviewed scientific journals. **Peer review** is a process by which experts review the report before it is published to ensure that the analysis and conclusions are sound. If the results are particularly important, they may be featured in news media and discussed at scientific meetings and by patient advocacy groups before they are published. Once a new approach has been proven safe and effective in a clinical trial, it may become the standard of medical practice.

Ask the research team members if the study results have been or will be published. Published study results are also available by searching for the study's official name or Protocol ID number in the National Library of Medicine's PubMed® database at [www.ncbi.nlm.nih.gov/pubmed](http://www.ncbi.nlm.nih.gov/pubmed).

## How does the outcome of clinical research make a difference?

Only through clinical research can we gain insights and answers about the safety and effectiveness of drugs and therapies. Groundbreaking scientific advances in the present and the past were possible only because of participation of volunteers, both healthy and those diagnosed with an illness, in clinical research. Clinical research requires complex and rigorous testing in collaboration with communities that are affected by the disease. As clinical research opens new doors to finding ways to diagnose, prevent, treat, or cure disease and disability, clinical trial participation of volunteers is essential to help us find the answers.

**Adapted from:** National Institutes of Health. "Clinical Trials: The Basics."  
Last reviewed on January 11, 2011. Accessed August 14, 2012; available at <http://www.nih.gov/health/clinicaltrials/basics.htm>.

# FINDING A CLINICAL TRIAL

## VISIT CLINICALTRIALS.GOV

ClinicalTrials.gov is a searchable registry and database of federally and privately supported clinical trials conducted both internationally and in the United States. ClinicalTrials.gov provides comprehensive information about a trial's purpose, who may participate, locations, and contact information. This information should be used in conjunction with advice from health care professionals.

Visit [www.nih.gov/health/clinicaltrials/CTgovSearchTips.htm](http://www.nih.gov/health/clinicaltrials/CTgovSearchTips.htm) for tips on finding trials on ClinicalTrials.gov.

## SEARCH THE NIH CLINICAL CENTER

The National Institutes of Health (NIH) maintains an online database of ongoing clinical research taking place at its Clinical Center, which is located on the NIH campus in Bethesda, Maryland. Studies are conducted by most of the NIH institutes and centers. The Clinical Center conducts a wide range of clinical research that includes rare diseases, chronic health conditions, and studies involving healthy volunteers. Information can be obtained by searching the diagnosis, signs, symptoms, or other significant key words.

Search at [clinicalstudies.info.nih.gov](http://clinicalstudies.info.nih.gov).

## JOIN A REGISTRY OF VOLUNTEERS

ResearchMatch is an NIH-funded initiative to connect 1) people who are trying to find research studies, and 2) researchers seeking people to participate in their studies. It is a free, secure registry that enables interested individuals to volunteer and become involved in clinical research studies that will contribute to improving our understanding of many important health issues.

Register at [www.researchmatch.org](http://www.researchmatch.org).

**Adapted from:** National Institutes of Health. "Clinical Trials: Finding a Clinical Trial."  
Last reviewed on June 7, 2012. Accessed August 14, 2012; available at <http://www.nih.gov/health/clinicaltrials/findingatrial.htm>.

# profiles

## MY EXPERIENCE IN A CLINICAL TRIAL

### As Told by Marj Korn

Even as a kid I knew something would happen to my lungs. My parents were chain smokers, but I never smoked, never had a cigarette. And I was fairly athletic growing up. I got into my forties just fine. But probably around my mid-40s I started noticing something, close to when I moved to Colorado to be near my daughter. I just blamed it on the altitude when it was hard to do hikes with my friends; I was really out of breath and would be lagging far behind them. I love to dance and I was out of breath dancing, which had never happened. It was around 2000 when all these things started happening. But I was a bit overweight, not in the greatest shape, so it was easy to blame it on that.

My name is Marj Korn and I live in Arvada, Colorado, just outside of Denver. My children, a son and a daughter, are grown up and I have five grandchildren. There were several signs along the way that pointed to my pulmonary problems, but like so many others, I always blamed it on something else.

Most of my career was in HR—human resources and recruiting for several large corporations. I was always in the limelight and part of a stressful environment as a senior manager for a corporation in Connecticut. It was 2010, while on a business trip in a New York City hotel, that I awoke with a really strange feeling; I was very lightheaded and thought I couldn't breathe. It passed within a few minutes so of course I continued my day.

Coincidentally, I had an appointment for a regular physical in early 2010. Near the end of the appointment my physician asked if there was anything else I wanted to share. Thankfully I decided to tell her about the episode on that business trip, even though it had long passed. She thought it could have been a mini-stroke and ordered cardiac tests. Then we discussed my dry cough. The cough started suddenly in 2010 and just wouldn't stop—yet another sign, but I blamed it on allergies. My heart was fine, but on the treadmill I became out of breath very quickly. My results all pointed in one direction. The stress test revealed lung problems and when the chest X-ray results came back we saw the irregularities in my lungs.

This began the next phase of understanding my disease and doing something about it. By then I was living in Colorado and decided to go to National Jewish; I had read so much about their work. I saw Dr. Huie and had a ton of tests—blood tests, radiology, and breathing tests. When he heard the crackling sounds in my lungs he was pretty sure that I might have idiopathic pulmonary fibrosis (IPF). I was still hoping it would turn out to be something else, but my biopsy in March of 2011 confirmed his suspicion of IPF and I began the process of acceptance. And yes, I must mention my children... my daughter has been extremely supportive, and so has my son.

Dr. Huie mentioned clinical trials and the PANTHER-IPF trial that was being conducted. He explained the pros and cons and that while in a trial I'd get excellent care because of the monitoring of my health required by the study. And of course I could be helping myself and possibly helping others by finding a cure for this disease. I already knew about how some clinical trials worked—my father was in a trial for an Alzheimer's drug. I might get the medicine they are researching, or I might get the placebo. I weighed the pros and cons. There could be negative results but I was told the trial would be stopped if that was happening. And with that in mind, I just said, "let's go with it." Either way, if it could help others and myself, it would be the thing to do.

“I weighed the pros and cons.”



Marj Korn and her daughter Kim.

**“And I could be helping myself, but I also want to help the research, give back, help others, and do everything I can.”**

The trial made me discipline myself, remembering to take all the pills I was given, writing it down. And I had a follow-up every three months with a questionnaire about my physical and mental health. At the same time they were monitoring my cognition—flashcards and tests like that. And I found out my memory was good! But because of the trial I was always taking pills and keeping track of them. I was very conscious of having a disease and it takes its toll psychologically. But it also improved my care and the attention I received. There were regular physicals and blood draws, so if something was going wrong an alarm should go off.

I was in the trial about eight months and then I received a phone call. Without much explanation I was told to stop taking all the drugs except for one. I went in to see Dr. Huie and he told me that they were finding a higher rate of death and disease progression for people in the trial—not something I was prepared to hear. But I was on the placebo. It made me feel somewhat better, but also hesitant about participating in other trials.

This is a very hard thing to go through—psychologically and emotionally. And I could be helping myself, but I also want to help the research, give back, help others, and do everything I can. It's important to get more people to participate in trials and it's the right thing to do. It's an important message, too, to know that although the doctors think that participating in clinical trials is in the best interest of research, they put the patient's best interest above that. It was proven to me that if the doctors notice a decline, they will stop the trial immediately and will not jeopardize your health.

As I look back I was, and still am, proud to have been in a trial. I told everyone about it. I was empowered, proud that I was doing this not only for myself but also for others that were ill and those that might get IPF in the future. I wasn't helpless. I'm helping to find a cure. And depending on the trial, I would do it again.

I recently repeated the same tests I had a year and a half ago when I was first diagnosed and haven't declined much at all, and that's great. But breathing is getting a little tougher and I wear my oxygen more than I used to. I'm thinking about moving closer to sea level, “the flatlands” as I call them, where I can walk more without oxygen and enjoy a milder climate. But my family is here, making it a difficult decision.

Right now it's all about my quality of life and what will make me happiest. This disease makes me look at things differently—the decisions I'll have to make. But I'm also an optimist and I will probably do another trial. I want to participate more, contribute more, and increase awareness of what this disease is.

**“I was empowered . . .  
I wasn't helpless. I'm  
helping to find a cure.  
And depending on  
the trial, I would  
do it again.”**

# profiles

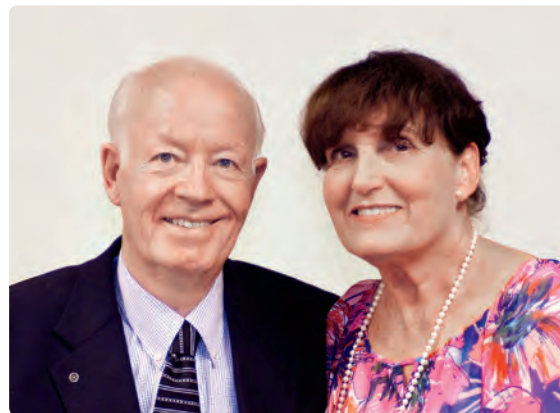
## MY EXPERIENCE IN A CLINICAL TRIAL

### As Written by Neal Busk

My name is Neal Busk, age 74, and I live in Richfield, Utah, a small city surrounded by tall mountains and red rock scenery. My family consists of my wife, Judy Shell Busk, five children, thirteen grandchildren, and two great-grandchildren. How fortunate I have been that I have lived long enough to see my family grow and to know and love them. There are many who, because of idiopathic pulmonary fibrosis (IPF), did not or will not have that wonderful experience. I retired from 15 years as a chemistry, physics, and math teacher in California, Japan, Germany, and Richfield. After that, I purchased a small electronics retail business and I retired from that business after 20 years.

Twenty-two years ago, shortly after my mother died of IPF in 1989, it seemed to me that while I was singing there was a problem with shortness of breath. So I had a breathing test and it showed about 70% lung capacity. There were no other symptoms at that time and I was told that perhaps it was just small lung capacity. Perhaps my symptoms at that time had nothing to do with IPF. Then nine years ago, while on a trip to the Midwest, I got an ear infection and also started to cough a lot. My family doctor, Mark W. Greenwood, MD, was acquainted with my mother, Golda Pectol Busk, and my older sister, Carol (who had died of IPF four years earlier in 1999). Shortly into the exam, he diagnosed me with having IPF.

Fairly soon after my sister died, I got a letter from Dr. Mary Beth Scholand at the University of Utah Hospital. She had discovered that two members of the family had died of IPF. She told us about a medical study that was being done and asked if my family would like to participate. Of course we did. We had already participated in a study at the University of Washington that my sister had enrolled us in before she died.



Neal Busk with his wife Judy Shell Busk at their fiftieth wedding anniversary.

Knowing that my mother had died of IPF and Carol, my sister, was dying of it, it was urgent for my whole family to participate, including a sibling of my mother, and easy for us to do.

So when I was diagnosed with IPF, I was well aware of IPF research and Dr. Scholand. I immediately called Dr. Scholand and asked her who was the IPF expert in Utah. Without hesitation, she said, "I am." After a thorough interview and exam with her, and a biopsy by Dr. Bull, she confirmed the diagnosis of IPF. Because of an alert and knowledgeable family doctor and excellent help at the University of Utah, the final confirmation took less than two months. Having watched my mother and sister struggle and suffer with IPF and die two years after their diagnoses, and knowing the mortality statistics of IPF, I was obviously struck with fear as well as concern for the rest of the family, especially my children, two younger sisters, and my brother John.

Nine months later, my brother John was also diagnosed with IPF. Now the family members with IPF had climbed to four. He is two years older than me and I had hoped that he would help take care of me. Now we are in this together.



## **“Be as proactive as you can. You will feel better about your situation in life and you just might help yourself and/or someone else.”**

Dr. Scholand told John and me of a clinical trial at National Jewish Health in Denver with the experimental drug bosentan. I had heard of clinical trials but did not know the details. Options were discussed at the time as well as risks, etc. John and I felt we had no option but to join. We had everything to gain and nothing to lose. If it did not help us, perhaps our sisters and children would someday be helped, as well as many others. We really did not hesitate. Perhaps our only concern was one of privacy of information and after considerable consultation with the doctors, our concerns were lessened, if not totally alleviated. It boiled down to a balance of trusting the medical profession and our intense desire to join the study and help others in some way, if not ourselves. Because of the inherited component and the possible consequences of this for our families, we had a significant criterion: would it possibly help our families? The answer was yes and our families supported this decision and all joined in giving blood samples and having baseline tests for an additional genetic study separate from the bosentan trial.

The trial did change my daily life. It made me feel proactive knowing that I was not sitting back just counting the time before IPF would kill me. It made me feel that I was contributing in some small way to find a cure for IPF, the disease that had taken my mother and sister and was now invading my brother as well as me. It made me feel that perhaps I was helping my two sisters, my children, and grandchildren should they come down with IPF. I had a very concrete reason to live and to enjoy what life I have left. The quarterly eight hour drive and, later, the semiannual drive to Denver were sometimes difficult, especially in the winter. It was mostly enjoyable though and allowed more time to visit with John and to visit with our wives when they would go with us. I miss those visits with Dolly Kervitsky and Dr. Kevin Brown at National Jewish and the others who gave such wonderful care. There were the blood draws, the breathing tests, the six-minute walk tests, and the CT scans. Then came the follow-up visits with Dolly and Dr. Brown and his thorough examinations. I couldn't have had better care. The small amount of time it took and the inconvenience of matching schedules were of little importance.

Today I am really struggling with my health. Post-polio syndrome is hitting me hard and it is very difficult to walk. The effort to walk seems to exacerbate the breathing problems. I am on oxygen and CPAP at night and spend much of the day with a portable machine. I still do a little yard work. Frustration often sets in when I am unable to do what I used to do and I'm sure my mood is sometimes not very positive. But life goes on with many good times with family and friends. I can't complain. I have had the opportunity and blessing to live much longer than I thought possible considering the rapid deaths of my sister, Carol, and my mother after their diagnoses with IPF. My sister had just turned 63 two weeks before she died; Mother was 76.

Having IPF has also given me the opportunity to lobby two years in Washington, DC, during IPF week on the Hill. That was a good experience and I learned a lot about how funds for medical research are acquired and what must be done. My assignment was to tell my family's story, a story that is all too common for others with IPF, a disease that is so little known and understood. Also, my brother and I, with some of our children, have participated in a genetic study at Johns Hopkins Hospital with Dr. Mary Armanios. She has also been an excellent person with whom to work.

We have an IPF support group at the University of Utah that has educational programs which are very helpful to many. It is also enjoyable to see people we have met at previous meetings and to hear their experiences. My message to the group has always been and always will be: join a study if at all possible. There is nothing to lose and much information to be gained. Be as proactive as you can. You will feel better about your situation in life and you just might help yourself and/or someone else. Join a clinical trial. What do you have to lose?

## **“It made me feel that I was contributing in some small way to find a cure for IPF, . . .”**

# RESEARCH AND CLINICAL TRIALS profiles AT STANFORD UNIVERSITY



Glenn D. Rosen, MD, at the Foundation's  
*Breathe Benefit* 2012 where he was  
recognized for his Albert Rose Established  
Investigator Award.

## A Discussion with Glenn D. Rosen, MD

### **Was there anything in particular that made you want to do idiopathic pulmonary fibrosis (IPF) research?**

It was a combination of seeing patients in my general clinic with the disease, and really being frustrated over our inability to do much to help those patients. At the same time I felt challenged, fascinated, and frustrated by this process that is unique to the lung and is characterized by this continuous cycle of injury and abnormal repair.

### **What do you think are the biggest challenges in getting new IPF therapies into the pipeline?**

There are several challenges—hopefully some of these are being mitigated. One is reacting to the sense of urgency, as we tend to do, not only in medicine but in general, especially when we're all frustrated by the lack of progress. Another is moving things too quickly into the clinical sphere. Sometimes the initial enthusiasm really clouds objectivity regarding the potential of treatments.

Another challenge has been in the development of an animal model for IPF. Bleomycin induced fibrosis or transforming growth factor beta overexpression doesn't really replicate the disease, and so we're kind of stuck with an animal model that doesn't mimic the human disease.

The last challenge is the IPF patients themselves. Not only is the disease heterogeneous, but it's really very difficult to predict who's going to get worse, how rapidly the disease is going to progress, and when the best time is to intervene. Sometimes the diagnosis is made late in the course, when it's obviously more difficult to treat the patient.

So, I think to summarize, the challenges have been a lack of intensive, scientifically rigorous research, the lack of accurate surrogate animal models, and patients that are very heterogeneous and have disease progression that is hard to predict.

**“The best thing I can recommend,  
if you are potentially eligible for clinical  
trials, is to enter a clinical trial.”**

**What type of conversation do you have with patients when you discuss clinical trials with them?**

The conversation I have with patients, and the way I lay it out is that we don't have an effective therapy now. The best thing I can recommend, if you are potentially eligible, is to enter a clinical trial. We can't predict whether the therapy will be effective or not. If it really is effective, it might help you in your lifetime, or if you have a familial form of the disease, it might help your family members.

There's also the reality that anything we do may have the potential to delay or slow the progression of this disease, improve your quality of life, and hopefully increase the length of one's life—this is what we're trying to achieve. I always try to instill some sense of hope and realism when I talk about these trials.

We get a lot of referrals and the patients have been told by their physicians that there's nothing that can be done, that you need to get your affairs in order, and just go and try to maximize what little time you have left. That's not the way we approach things and it's not true. It's not an accurate depiction of what really happens. Everybody's different. Everyone has a unique genotype and makeup, individuals react differently to drugs, and disease progression can vary greatly. Also, lung transplantation is often an option. The majority of lung transplants today are being done for lung fibrosis. So we really look at the individual, and we approach the conversations about trials with patients in that way too.

We offer the opportunity to consider enrollment in all open trials. Some patients will be eligible and not others. Clinical trials really provide the opportunity to not only potentially help now, but also gain valuable knowledge about the disease. One way to understand the disease better is to identify a treatment that actually works for the disease.

**Do studies' inclusion/exclusion criteria ever present a big challenge in recruiting your patients?**

They do. One way to lessen this is for a center to get involved in several trials that have different inclusion and exclusion criteria. Whether one agrees or has issues with their criteria, these are the criteria that have been established, and we make it clear that some trials will be more challenging to enroll in than others.

**“I would say that the value of participating in research and clinical trials is that these trials, especially ones coming along now, are based on very careful and very deliberate and exhaustive pre-clinical scientific studies that are really targeted for IPF.”**

**What trials are you active in right now?**

We are currently enrolling patients in the [InterMune] Phase 3 pirfenidone trial. We are also participating in the [Boehringer Ingelheim] BIBF 1120 and the Gilead AB0024 trials. Both are now closed to enrollment. Additionally, we are in the process of starting the [Stromedix] trial with the anti-alpha V beta 6 [integrin] that blocks activation of TGF-beta.

There are about three or four more trials that we're going to be starting up in the next six months.

**What type of responses do you see in patients who participate in clinical trials? Is there fear, trepidation, hope?**

Again, it's interesting. I think one of the advantages of being in a center like Stanford is patient contact—patient contact is more frequent because they are participating in trials and we are acutely aware of what's going on with the patient. This is reassuring to the patient and it's reassuring to us.

We address comorbidities. We're very careful about getting patients involved in activities like pulmonary rehabilitation. We also offer the potential of lung transplantation to those patients who may be eligible. We have this conversation early in the process.

In terms of psychological well-being, pulmonary fibrosis is psychologically and physically very debilitating and very challenging for patients and family members. Discussions about end of life care are also very difficult conversations, it is helpful to be in a situation where we see patients more frequently, and it makes having these conversations a little easier. Even if we're not their primary pulmonologist, we have this connection.

*continued on next page >*

**What new compounds are being investigated for PF and do you think that multi-drug therapy will prove to be effective?**

Yes, a lot of new compounds are being investigated.

There is investigation into an antibody against a lysyl oxidase family member, LOXL2 [Gilead]. Interestingly, this antibody appears to be preferentially or predominantly expressed during abnormal wound healing, not during normal wound healing, which obviously would tend to make it have less side effects in patients.

LOXL2 is an antibody that thus far in early Phase 1 and 2a clinical trials has been well tolerated. Very minimal or almost no side effects have been reported when given as an infusion. The pre-clinical data looks really outstanding with the antibody not only inhibiting fibrosis in the lung but that it may also limit fibrosis in other organs. LOXL2 has also been shown to be quite effective in reversing fibrosis in the bleomycin model. We are hopeful that a Phase 2 study will be initiated soon.

Other compounds being investigated are:

STX-100 [Stromedix/Biogen], which is another humanized monoclonal antibody with anti-fibrotic activity. This antibody seems to block expression of TGF-beta, which is a key player in fibrosis.

FG-3019 [FibroGen] has some encouraging Phase 2 trial data from their anti-connective tissue growth factor (CTGF) antibody.

AM152 [Bristol-Myers Squibb] is a lysophosphatidic acid 1 (LPA1) antagonist. It is an oral compound that has completed Phase 1 clinical studies and will hopefully soon move on to Phase 2a trials.

Whatever drives lung injury, just trying to block scar—which is downstream from the injury—may not be enough because the body will continue to generate that injury. We're looking at some studies that were supported by the Pulmonary Fibrosis Foundation to look at telomerase in potentially regulating the injury.

Whatever it is, we're going to need compounds that work in synergy, and not in opposition. Maybe one could block more scarring and one could help the lung heal better. I think that's going to be critically important.

What ultimately I think we will need to do is develop an effective combination of therapies for this disease to not only prevent the formation of scar tissue, but also somehow facilitate healing.

**“What ultimately I think we will need to do is develop an effective combination of therapies for this disease to not only prevent the formation of scar tissue, but also somehow facilitate healing.”**

**If you had a general message about the value of patients participating in research and clinical trials, what would it be?**

I would say that the value of participating in research and clinical trials is that these trials, especially ones coming along now, are based on very careful and very deliberate and exhaustive pre-clinical scientific studies that are really targeted for IPF.

For the first time, I think, in our fight against this disease there are a lot of drugs in development and in trials that may be effective because they target the specific disease process, pathways, and genes which are abnormal in the disease. So participating now, I feel, offers more hope than it ever has.

It's really critically important for patients to participate because every person is different, and how they respond to one drug or another drug is unknown. IPF is a broad diagnosis, and a general diagnosis, but everybody's a little different about how they respond to drugs and how they will progress.

The more we understand about how the disease progresses—and the only way to really do that is to be part of a clinical trial—and how patients respond to therapy, the more we'll be able to help that individual and others in the future.



©ISTOCKPHOTO.COM/CHERKO



**How do you respond to patients who are apprehensive about participating in a randomized clinical trial where they might get a placebo as opposed to the medication that's being tested in the trial?**

I think that's a very valid question. Nobody wants "the placebo."

But the way I address patients who have concerns about receiving the placebo versus the study drug, is that we tell the patients we are treating you as an individual and we are here for you, and we want to do what's best for you. So if you're getting side effects from a drug, or you're progressing, or you're not feeling well, whether it has anything to do with a trial drug or not, and you're progressing in the trial, we will think of alternatives—whether it's pulling you out of the clinical trial, considering you for transplantation, or considering another clinical trial.

It's not always the case that we can do all that, but our first priority is the patient. It would be nice if everybody got a drug that was effective, but we also tell patients that we don't know if that drug is effective, and the only way we can really ascertain whether it's effective is to compare it against patients who don't get that drug.

We also tell the patient that they have choices, and we work with them. We work as a group. It's very easy to feel alone with this disease, like it is with any chronic disease, and we really try to develop a team approach and work closely with the patients and caregivers.

**Do you see a difference in the populations of patients who are interested in participating in open label trials, as opposed to a blinded clinical trial?**

We do have a subset of patients who, if the opportunity is there, will choose the trial in which they know they're getting the drug and there's no placebo. Those types of trials are not always available. The fact that they're getting the drug can be counterbalanced by the fact that they don't know if it's safe or effective.

**So it's more of a self-selection process that you're seeing? It isn't any particular age group that is self-selecting these different trials?**

Sometimes it's disease activity. If the patients are declining more rapidly, and if the data from a pre-clinical study looks really encouraging, then they don't really want to take the chance of getting a placebo. It doesn't tend to be an age dependent thing as much as how severe or active the disease is.

**Do you have any other suggestions? What else do you think patients can do to become involved in drug development, and how do you feel about national advocacy being beneficial to the research community?**

This is a devastating disease. It's really important that we learn from the patients, we remain open-minded about opportunities, and we don't give patients the wrong messages. We don't want to tell them that there's no hope. We really want to give them some perspective as to what are the options, and what are the alternatives?

We really need to learn from all of our patients. We have the opportunity, as a group, as the PF community, to pull together, and to target specific research to better understand this very complex disease. We're starting to do more genomics research because we need to understand the unique differences in patients' genomes. Beyond understanding their genome, the next level is to understand how genes regulate the expression of other genes that really cause the disease.

So just as it's emphasized or recommended that we use a multidisciplinary approach to make the diagnosis of IPF, we really need multiple disciplines to mine different ways of thinking and attacking this disease. That's why I think national advocacy is important. It brings together patients, family members, scientists, and legislators to work as a team, and working in parallel will offer hope for our patients and ultimately lead to effective therapies.

**“It's very easy to feel alone with this disease, like it is with any chronic disease, and we really try to develop a team approach and work closely with the patients and caregivers.”**

**About Glenn D. Rosen, MD**

Dr. Rosen has been on the faculty of the Stanford University School of Medicine since 1993. He is presently an Associate Professor of Medicine in the Division of Pulmonary and Critical Care Medicine. Dr. Rosen's laboratory research focuses on translational studies in pulmonary fibrosis; specifically, his laboratory studies mechanisms involved in the pathogenesis of pulmonary fibrosis and then applies the application of these discoveries to the development of novel treatments for fibrotic lung disease. Recent work in his laboratory has revealed novel functions of telomerase in pulmonary fibrosis and additional studies are focused on the genetics of pulmonary fibrosis. Dr. Rosen has published broadly, is active in clinical trials in idiopathic pulmonary fibrosis, and works with biotechnology companies in the development of novel anti-fibrotic therapeutics.

He is the Clinical Director of the Stanford Interstitial Lung Disease Program in the Center for Advanced Lung Disease. Dr. Rosen's active clinical and research program in interstitial lung disease gives him insight into how to apply basic research discoveries to help patients with advanced lung disease.

Dr. Rosen is a member of the Pulmonary Fibrosis Foundation Medical Advisory Board and is the recipient of the PFF's 2012 Albert Rose Established Investigator Award for his research "Analysis of Novel Functions of Human Telomerase RNA in IPF."

# HOW DOES THE PFF IMPACT THE PULMONARY FIBROSIS RESEARCH COMMUNITY?

## Pulmonary Fibrosis Foundation Research Fund



©ISTOCKPHOTO.COM/CHEPKO

One of the primary goals of the Pulmonary Fibrosis Foundation (PFF) is to fund research that will ultimately lead to successful therapies for pulmonary fibrosis (PF). As part of this commitment, the Foundation supports new research through grants funded solely by the PFF and through partnership grants with other organizations.

The PFF Research Fund was established with the primary goal of funding innovative grants that offer a high likelihood of advancing research that could translate into successful therapies.

### Primary Objectives

#### Fund innovative and promising research

- **I.M. Rosenzweig Young Investigator Awards:** These awards of up to \$50,000, given over a two-year period, encourage young investigators\* to maintain and enhance their interest in PF research during the early stages of their academic career. (*\*individuals within five years of completion of their formal training*)
- **Albert Rose Established Investigator Awards:** These awards of up to \$50,000, given over a two-year period, allow established investigators\* to explore innovative areas of research that may not yet be eligible for federal grants. (*\*individuals who have demonstrated a clear record of successful independent research as defined by publication record and current or previous funding from a major organization*)
- **Special Needs Awards:** These awards, granted periodically as needs arise, provide funds for investigators and institutions to “fill the gaps” of financial need where unique circumstances exist and additional funding will help advance an exceptional research effort.
- **Partnership grants with the American Thoracic Society and the American College of Chest Physicians:** These unique partnerships allow the PFF, in collaboration with leading lung health organizations, to jointly award grants focusing on PF.

#### Provide donor grant guidance and administer donor-advised funds

The Foundation provides oversight for a donor wishing to make a restricted gift to a specific institution (or institutions) or support a specific research project. The Foundation receives a small percentage of the total grant to administer the grant and to provide oversight.

#### Foster funding opportunities for PF research

The Foundation continually seeks ways to increase research funding through partnerships with industry, governmental agencies, and other foundations.



## Current Areas of Interest

The primary goal of awarding grants through the PFF Research Fund is to support projects that offer a high likelihood of improving the understanding of pulmonary fibrosis in the following areas:

- **Basic Science** – Studies that are conducted to increase the fundamental understanding of the disease process on a molecular and cellular level. This type of research can provide the scientific basis for later stage research.
- **Translational Research** – These studies “translate” basic science into meaningful treatments and clinical applications, oftentimes bringing knowledge learned in animal model studies into human study.
- **Clinical Medicine/Research** – Studies that are performed to determine the safety and efficacy of medications, treatment regimens, and diagnostic procedures in humans.
- **Social Science/Quality of Life** – Studies that look at the general well-being of individuals undergoing specific treatment modalities, including medications as well as supportive therapies (nutrition, exercise, respiratory therapy, and psycho-social support).

## The Role of Peer Review

The PFF Research Fund operates its grant making initiatives with the understanding that approval for funding must rest in the hands of a credible, peer-review committee of experts. Members of the Research Advisory Committee review all accepted applications. Funding decisions are made on the basis of scientific merit, originality, and responsiveness to the purpose of the specific grant award. A complete list of the Research Advisory Committee members is available at [www.pulmonaryfibrosis.org/medicalboard](http://www.pulmonaryfibrosis.org/medicalboard).

## 2013 GRANT CYCLE

The call for letters of intent to submit a full application for a 2013 grant was announced on October 23, 2012 with a submission deadline of November 26, 2012. Review by the Research Advisory Committee takes place November through December with notifications of acceptance to submit a full application being communicated to investigators in January of 2013. Full grant proposals from investigators are due mid-February. Review takes place February through May and award recipients will be notified in June. Grant recipients are acknowledged at the PFF's annual dinner, *Breathe Benefit*, in October. Learn more at [www.pulmonaryfibrosis.org/research](http://www.pulmonaryfibrosis.org/research).

# research

## PFF Research Program — Awards, Partnerships, and Sponsorships

### 2012 PFF RESEARCH FUND AWARDS

#### General Research Grants

- Dr. Erica Herzog of Yale University – “Prospective Evaluation of IPF Biomarkers” (Year 2)
- Dr. Aldo T. Iacono of University of Maryland – “Open Label Use of Inhaled Cyclosporine in Lung Transplant Recipients” (Year 3)
- Dr. Daniel J. Kass and Dr. Naftali Kaminski of University of Pittsburgh – “Targeting the Relaxin Pathway in Pulmonary Fibrosis” (Year 2)
- Dr. David J. Lederer of Columbia University – “Subclinical Interstitial Lung Disease in MESA: The MESA Lung Fibrosis Study”
- Dr. Imre Noth of University of Chicago – “miRNA Expression in Patients with Rapidly Progressive IPF Versus Stable IPF” (Year 2)
- Dr. Patricia J. Sime of University of Rochester – “Translational Studies of New Therapeutic Targets & Biomarkers in PF” (Year 2)
- Dr. Andrew Tager of Massachusetts General Hospital – “Profibrotic Mechanisms of the LPA Pathway”

#### I.M. Rosenzweig Young Investigator Awards

- Dr. Haitao (Mark) Ji of University of Utah – “Design and Synthesis of Selective Beta-catenin/T-Cell Factor Inhibitors for the Treatment of Idiopathic Pulmonary Fibrosis” (Year 1)  
*Funded by a grant from InterMune, Inc.*
- Dr. Rebecca Keith of University of Colorado, Denver – “Therapeutic Targeting of PTPN-13 in Idiopathic Pulmonary Fibrosis” (Year 1)

#### Albert Rose Established Investigator Awards

- Dr. James S. Hagood of University of California, San Diego – “Extracellular Vesicles Alter Cell Phenotype in Pulmonary Fibrosis” (Year 1)
- Dr. Glenn Rosen of Stanford University – “Analysis of Novel Functions of Human Telomerase RNA in IPF” (Year 1)

#### ATS/PFF International Partnership Grants

- Dr. Anthony Shum of University of California, San Francisco – “Defining the Molecular Basis of Interstitial Lung Disease in Rheumatoid Arthritis” (Year 1)
- Dr. Anne Holland of La Trobe University, Australia – “Where Does Pulmonary Rehabilitation Fit in the Management of Pulmonary Fibrosis?” (Year 2)

#### ATS/PFF/CPF Young Investigator Partnership Grants

- Dr. Jia Guo of University of Rochester – “Fibrocyte Differentiation is Regulated by Yin Yang 1 in Pulmonary Fibrosis” (Year 2)
- Dr. Yan Sanders of University of Alabama at Birmingham – “Epigenetic Regulation of Caveolin-1 by TGF-beta Mediated Signal Pathway in Lung Fibroblasts” (Year 2)

### 2012 PARTNERSHIPS

- 17th International Colloquium on Lung and Airway Fibrosis (ICLAF)

### 2012 SPONSORSHIPS

- American Thoracic Society – Fibrosis Across Organ Systems Symposium
  - National Jewish Health – Familial Pulmonary Fibrosis Genetic Counseling Program
  - Pittsburgh International Lung Conference
  - University of Maryland – Hales Lung Conference
  - University of California, San Francisco – “Update in Interstitial Lung Disease: Diagnosis and Management” CME Course
  - University of Minnesota – Annual PF Educational Symposium
  - Yale University – Sixth Annual Yale Fibrosis Symposium
- As of November 2012.



## 2013 PFF RESEARCH FUND AWARDS

### General Research Grants

- Dr. Aldo T. Iacono of University of Maryland – “Open Label Use of Inhaled Cyclosporine in Lung Transplant Recipients” (Year 4)
- Dr. Daniel J. Kass and Dr. Naftali Kaminski of University of Pittsburgh – “Targeting the Relaxin Pathway in Pulmonary Fibrosis” (Year 3)
- Dr. Imre Noth of University of Chicago – “miRNA Expression in Patients with Rapidly Progressive IPF Versus Stable IPF” (Year 3)

### I.M. Rosenzweig Young Investigator Awards

- Dr. Haitao (Mark) Ji of University of Utah – “Design and Synthesis of Selective Beta-catenin/T-Cell Factor Inhibitors for the Treatment of Idiopathic Pulmonary Fibrosis” (Year 2)  
*Funded by a grant from InterMune, Inc.*
- Dr. Rebecca Keith of University of Colorado, Denver – “Therapeutic Targeting of PTPN-13 in Idiopathic Pulmonary Fibrosis” (Year 2)
- I.M. Rosenzweig Young Investigator Award (Year 1)\*
- I.M. Rosenzweig Young Investigator Award (Year 1)\*

\*To be announced June 2013.

### Albert Rose Established Investigator Awards

- Dr. James S. Hagood of University of California, San Diego – “Extracellular Vesicles Alter Cell Phenotype in Pulmonary Fibrosis” (Year 2)
- Dr. Glenn Rosen of Stanford University – “Analysis of Novel Functions of Human Telomerase RNA in IPF” (Year 2)
- Albert Rose Established Investigator Award (Year 1)\*  
*Funded by a grant from Boehringer Ingelheim*
- Albert Rose Established Investigator Award (Year 1)\*

\*To be announced June 2013.

### ATS/PFF International Partnership Grant

- Dr. Anthony Shum of University of California, San Francisco – “Defining the Molecular Basis of Interstitial Lung Disease in Rheumatoid Arthritis” (Year 2)

### CHEST Foundation Partnership Grant

- Clinical Research Award in Pulmonary Fibrosis\*

\*To be announced October 2013.

## 2013 SPONSORSHIPS

- Interstitial Lung Disease Program at University of California, San Francisco, Stanford, and UC Davis – 3rd Annual ILD Patient Seminar
- Vermont Stem Cell Conference

As of November 2012.

## LEANNE STORCH SUPPORT GROUP FUND

Named for the Foundation's former Executive Director, Leanne Storch, who was diagnosed with pulmonary fibrosis in 2003, the Leanne Storch Support Group Fund honors Leanne's continued passion for supporting those affected by the disease. Groups may apply for awards of up to \$500 per award year, to be used towards meeting programming, educational materials, or location requirements. Six awards were granted in 2012 and up to eight awards will be granted in 2013. Applications for the 2013 awards will be accepted beginning May 2013.

### 2012 Leanne Storch Support Group Award Recipients

- Dr. Kathleen Lindell of University of Pittsburgh Medical Center, Dorothy P. & Richard P. Simmons Center for Interstitial Lung Disease Support Group
- Myrna Taylor and Grace Jacobson, RN, of Eastern Idaho Regional Medical Center, Eastern Idaho Pulmonary Fibrosis Support Group
- Dr. Hyan Kim and Melinda Bors, RN, BSN, MA, of University of Minnesota, Minnesota Pulmonary Fibrosis Patient Support Group
- Dr. Maryluz Fuentes of Baptist Medical Center South, IPF Support Group of Montgomery
- Donna Serlin, RRT, of Edwards Hospital, Edwards Hospital Pulmonary Fibrosis Support Group
- Dr. Anoop Nambiar of University of Texas Health Science Center at San Antonio, San Antonio Pulmonary Fibrosis Support Group

# RECENT NEWS IN research PULMONARY FIBROSIS RESEARCH

## Boehringer Ingelheim Completes Enrollment of Pivotal Phase III Studies for Nintedanib (BIBF 1120) in IPF

Boehringer Ingelheim Pharmaceuticals, Inc. announced that clinical trial enrollment has been completed for two Phase 3 studies evaluating the safety and efficacy of nintedanib (BIBF 1120), an investigational compound, in patients with idiopathic pulmonary fibrosis (IPF).

In June 2011, the U.S. Food and Drug Administration (FDA) granted nintedanib orphan drug status, which identifies compounds for rare diseases.

“With no FDA-approved treatments, today’s standard of IPF care is limited to oxygen therapy and lung transplant for some patients,” said Dr. Kevin R. Flaherty, a study investigator and associate professor in the Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, University of Michigan Health System. “IPF patients desperately need safe and effective treatments to not only reduce the decline in lung function and eventually decrease mortality, but also to stabilize health-related quality of life and delay or reduce sudden worsening of symptoms, or acute exacerbations. These are hallmarks of IPF and are often times unpredictable and can cause death.”

The two global Phase 3 studies are identical in design, constructed as double-blind, randomized, placebo-controlled trials with a 52-week duration, matching twice-daily 150 mg dosing, and the same inclusion criteria and endpoints. The primary endpoint is the annual rate of decline in forced vital capacity (FVC), or the volume of air that is expelled into a spirometer following maximum inhalation. Reductions in FVC are reflected in impaired ventilation capacity of the lungs. Measuring FVC is a part of the examination conducted in patients with lung disease and is scientifically accepted as an assessment of treatment efficacy in IPF patients. Secondary endpoints include health-related quality of life, exacerbations, respiratory mortality, overall survival, and on-treatment survival. The trials have enrolled a total of 970 patients in 20 countries.

## About Nintedanib

Nintedanib is an investigational small molecule tyrosine kinase inhibitor (TKI) in development by Boehringer Ingelheim for IPF. It targets three growth factors: the vascular endothelial growth factor receptor (VEGFR), fibroblast growth factor receptor (FGFR) and platelet-derived growth factor receptor (PDGFR). These receptors have been shown to be potentially involved in development of pulmonary fibrosis. By blocking these signaling pathways that are involved in fibrotic processes, it is hypothesized that there may be potential to reduce disease progression, and thereby slow the decline in lung function.

**Source:** Boehringer Ingelheim Press Release, September 26, 2012  
*Content edited for space.*

## Thalidomide Shown to Improve Cough in IPF

In a recent small study thalidomide demonstrated significant efficacy in treating patients with debilitating cough related to idiopathic pulmonary fibrosis (IPF). In the 1960s thalidomide, which is manufactured by Celgene, was commonly used for morning-sickness. It was shown to be linked to birth defects and was therefore discontinued. Currently it has been employed to treat certain types of cancers.

In a 20-person trial recently published in the *Annals of Internal Medicine*, coughing was reduced by about 63% in patients with IPF who were given thalidomide. While patients on the medication experienced some side effects including constipation, dizziness, and malaise, each opted to keep taking thalidomide after the trial ended.

Researchers hypothesize that the drug’s effects on the immune system may make it a potential treatment for IPF, although a previous trial did not demonstrate any benefit. The recent study did suggest that thalidomide helps relieve the dry, debilitating cough that afflicts as many as 80% of IPF patients. “We noticed the people on thalidomide, (that) their cough went away,” said Maureen Horton, a study co-author and Associate Professor of Medicine and Environmental Health Sciences at the Johns Hopkins School of Medicine. “They came to us and said, ‘Hey, you cured my cough.’” In today’s report, adverse events were found in 74% of patients on thalidomide, compared with 22% on placebo.

Celgene markets thalidomide under strict regulations to prevent pregnancies while patients are on therapy. Celgene also sells a next-generation therapy, Revlimid®, for multiple myeloma and myelodysplastic syndromes.

The results warrant a larger study to evaluate thalidomide or Revlimid's effects on cough in IPF, and potentially to assess whether they may work to treat the disease itself, Horton said. The results "will encourage patients and frustrate them because thalidomide is not FDA-approved for this indication and they're not going to be able to get this," Horton said. "My goal is to gain enough interest to do further studies," she said.

**Source:** Meg Tirrell, *Bloomberg News*. "Celgene's Thalidomide Shown to Improve Cough in Ailment." September 17, 2012. Accessed September 17, 2012; available at <http://www.bloomberg.com/news/2012-09-17/celgene-s-thalidomide-shown-to-improve-cough-in-ailment.html>.

**Original journal article:** Horton MR, Santopietro V, Mathew L, et al. "Thalidomide for the treatment of cough in idiopathic pulmonary fibrosis: a randomized trial." *Ann Intern Med* 2012 Sep 18;157(6):398-406.  
*Content edited for space.*

### **FibroGen Presents Updated Results of Phase 2 Trial of FG-3019 at 2012 European Respiratory Society Meeting**

FibroGen, Inc. presented the most recent results from its Phase 2 trial of FG-3019; the title of the presentation was "Phase 2 Trial of FG-3019, Anti-CTGF Monoclonal Antibody in Idiopathic Pulmonary Fibrosis: Preliminary Safety and Efficacy Results."

The results showed that at six months more than 60% of study participants had stability or substantial improvement in their lung fibrosis as measured with high-resolution computed tomography (HRCT). In a disease for which fibrosis is expected only to progress in severity, this is a notable finding. The initial improvement in HRCT appeared to persist in nearly all of the subjects for whom 12-month HRCT analyses were performed. Furthermore, improved or stable lung function demonstrated a strong, statistically significant correlation with decreased or stable lung fibrosis. Preliminary results also confirmed a trend associating improvements in lung fibrosis with increasing blood levels of FG-3019.

Given the promising results observed so far, FibroGen expects to initiate a randomized placebo-controlled trial. If improvements of fibrosis and pulmonary function are confirmed in larger and more rigorous studies, these observations would suggest that FG-3019 may have the capacity in some IPF patients to extend life by delaying or by reversing the normal progression of fibrosis.

#### **About FG-3019**

FG-3019 was developed to inhibit the activity of CTGF, a common factor in chronic fibrotic and proliferative disorders in which persistent and excessive scarring can lead to organ dysfunction and failure. In addition to the Phase 2 study of FG-3019 in patients with IPF discussed above, FibroGen is currently conducting clinical studies of FG-3019 in two additional diseases, pancreatic cancer and liver fibrosis. FG-3019 has been well tolerated, with no apparent significant adverse reactions in studies involving over 300 patients.

**Source:** FibroGen, Inc. Press Release, September 5, 2012  
*Content edited for space.*

### **InterMune Reports New Analyses from the RECAP Study of Esbriet® (pirfenidone) at the European Respiratory Society Meeting**

InterMune, Inc. announced that new analyses of data from the RECAP extension study of Esbriet® (pirfenidone) were presented at the 2012 Annual Congress of the European Respiratory Society (ERS) in Vienna, Austria by Dr. Ulrich Costabel of the Ruhrlandklinik, Essen, Germany.

The RECAP study is an ongoing open-label extension study evaluating the long-term administration of Esbriet in patients who completed InterMune's Phase 3 CAPACITY program. The CAPACITY program (studies 004 and 006) was designed to evaluate the safety and efficacy of Esbriet in IPF patients with mild-to-moderate impairment in lung function.

Dr. Costabel presented new analyses of forced vital capacity (FVC) and survival in patients who received placebo in CAPACITY and were newly treated with Esbriet in RECAP. These analyses show that patients with mild-to-moderate IPF newly-treated with Esbriet in RECAP for 60 weeks had similar FVC and survival outcomes when compared to those treated with Esbriet for the same duration in CAPACITY.

Dr. Costabel commented, "The population in this RECAP analysis represents the fourth large, well-defined cohort of IPF patients to be treated with pirfenidone and followed prospectively for more than one year. FVC and survival outcomes in the RECAP patients treated with pirfenidone were highly consistent with those in pirfenidone-treated patients in three previous randomized, controlled Phase 3 studies. While these data should be interpreted with due regard to the limitations inherent to the open-label study design of RECAP, the results provide further support for the role of Esbriet in the treatment of patients with this devastating disease."

The results of this study, coupled with additional information presented at ERS during a poster discussion session on the long-term safety data in IPF patients treated with Esbriet for up to 7.7 years, provide further evidence to support the clinical efficacy and safety of Esbriet in patients with IPF.

*continued on next page >*

# research

## About RECAP

RECAP is an open-label extension study for patients who participated in the Phase 3 program for Esbriet, known as CAPACITY.

## About Esbriet® (pirfenidone)

Esbriet is an orally active drug that inhibits the synthesis of TGF-beta, a chemical mediator that controls many cell functions including proliferation and differentiation, and plays a key role in fibrosis. It also inhibits the synthesis of TNF-alpha, a cytokine that is known to have an active role in inflammation.

The European Commission granted marketing authorization for Esbriet in adults for the treatment of mild-to-moderate IPF. The approval authorizes marketing of Esbriet in all 27 European Union member states. Esbriet has since been approved for marketing in Canada, Norway, and Iceland.

InterMune is conducting a Phase 3 study, ASCEND, to support the regulatory registration of Esbriet for the treatment of IPF in the United States and expects to complete patient enrollment of the study around the end of 2012.

**Source:** InterMune, Inc. Press Release, September 3, 2012  
*Content edited for space.*

## Evidence for Adult Lung Growth in Humans

Researchers have uncovered the first evidence that the adult human lung is capable of growing back, at least in part, after being surgically removed. In an observational study, researchers used MRIs with hyperpolarized helium-3 gas to show that existing alveoli (the tiny, air-exchange units of the lung) actually increased in number after a 33-year-old woman had her entire right lung removed due to cancer.

The study showed a 64% increase in the number of alveoli in the woman's lung 15 years after surgery. "The research clearly shows that some form of lung growth can occur in the adult human," said study author James Butler, an Associate Professor of Medicine in the Department of Medicine at Harvard Medical School in Boston.

The new alveoli were all shaped similarly. "It's striking, the degree of homogeneity of the new alveoli, as if the lung was responding to something," Butler added. The cause of the new growth could be stretching of the tissue, perhaps by exercise, he suggested.

Over a period of 15 years, data measuring lung size and capacity were collected, using common respiratory tests (called FEV and FVC) measuring how much air can be taken in and blown out with deep breaths. In the early months after surgery, the lung responded as researchers would expect. The total lung volume increased and the lung density fell below normal. But, the lung tissue volume gradually started to increase and the density returned to a level normally seen when a deep breath is taken, suggesting the growth of new tissue.

The ability of the lung to regenerate, potentially triggered by exercise, makes sense, said Dr. Norman Edelman, a professor of medicine at Stony Brook University and Chief Medical Officer of the American Lung Association. "When the lung develops in utero [when the fetus is developing], the pulling force of the diaphragm is an important stimulation for the lung to grow," he said. "But, of course, the practical application of the research is a long way off." Butler said the next step is to do a study involving more people over time.

**Source:** *HealthDay*. "Study Gives First Evidence That Adult Human Lungs Can Regrow"  
Accessed July 19, 2012; available at <http://consumer.healthday.com/Article.asp?AID=666800>.  
**Original journal article:** James P. Butler, Ph.D., Stephen H. Loring, M.D., Samuel Patz, et al.  
"Evidence for Adult Lung Growth in Humans" *N Engl J Med* 2012; 367:244-247 July 19, 2012  
DOI: 10.1056/NEJMoa1203983  
*Content edited for space.*

## MicroDose Therapeutx and Moerae Matrix Announce Collaboration to Develop Novel Inhaled Treatment for IPF

MicroDose Therapeutx, Inc. and Moerae Matrix, Inc. announced in June that they have signed a collaboration agreement to develop a dry powder inhalation product of Moerae's novel MK2 inhibitor, MMI-0100, for the treatment of idiopathic pulmonary fibrosis (IPF). The collaboration will involve the development and supply of a pulmonary drug delivery system for Moerae and/or its partners utilizing MicroDose's proprietary inhaler technology in support of chronic administration.

"We are pleased to be partnering with a recognized industry leader in pulmonary drug delivery to advance development of MMI-0100 for IPF," said Cynthia Lander, PhD, Chairman and Chief Executive Officer of Moerae Matrix. "MicroDose's piezo-driven dry powder inhaler platform is the optimal technology for delivering our first-in-class peptide therapeutic for treatment of IPF."

MMI-0100 is a selective inhibitor of MAPKAP kinase 2 (MK2), a key terminal kinase in the transforming growth factor beta (TGF- $\beta$ )/p38 signaling pathway. By targeting a terminal kinase, MMI-0100 has the potential for greater specificity of action and lower off-target toxicity than other anti-fibrotic agents that address targets higher in this important pathway.

"IPF represents an enormous unmet medical need and delivering a drug directly to the lung that inhibits a down-stream kinase in the TGF- $\beta$ /p38 pathway is extremely appealing. It is very likely that multiple drugs that interfere with different components of fibrosis will be needed to combat IPF and MK2 inhibition is a novel and exciting target for drug development in this devastating disease," said Paul W. Noble, MD, Professor of Medicine, and Chief, Division of Pulmonary, Allergy and Critical Care Medicine, Duke University Medical Center.

Development of MMI-0100 for treatment of IPF is being funded in part with federal support from the National Heart, Lung, and Blood Institute (NHLBI), part of the National Institutes of Health (NIH) in the Department of Health and Human Services (DHHS), under the Science Moving Towards Research Translation and Therapy (SMARTT) program (NHLBI Contract No. HHSN268201100017C).

**Source:** MicroDose Therapeutx, Inc. Press Release, June 20, 2012  
*Content edited for space.*

## Study Finds Commonly Used Three-Drug Therapy for IPF Harmful

A combination of three drugs used worldwide as the standard of care for idiopathic pulmonary fibrosis (IPF) puts patients in danger of death or hospitalization, and should not be used together to treat the disease, according to the surprising results of a rigorous independent study.

The study, which was published in the *New England Journal of Medicine*, was conducted by the IPF Clinical Research Network, and funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

"The findings show the importance of testing even those treatments that doctors give routinely for any type of condition—to see if they truly help, and don't harm, patients," says University of Michigan Health System lung specialist Fernando Martinez, MD. Martinez and his colleagues report that patients in the mild-to-moderate stages of the progressive lung-scarring disease had a far higher chance of dying or being hospitalized if they were taking a three-drug combination of prednisone, azathioprine, and N-acetylcysteine (NAC), compared with those patients taking a placebo.

Additionally, the three-drug combination yielded no improvement in lung function, or even slowing of loss of lung function, compared with placebo. Results from a group taking the single drug, N-acetylcysteine, are still being gathered and analyzed. This evidence is from a randomized, placebo-controlled, double-blind trial that included patients with a definitive diagnosis of IPF who were treated at 25 centers taking part in the IPF Clinical Research Network or IPFNet. The study was stopped early when an interim analysis showed signs of harm from the three-drug therapy. The findings should cause physicians worldwide to discontinue using this combination to treat IPF patients similar to those in the trial, say the authors. The dramatic finding of harm from a standard treatment should cause physicians to apply rigorous testing methods to other types of treatment, and highlights the importance of independent federal funding for such studies, said Martinez.

The study is called PANTHER-IPF (Prednisone, Azathioprine, and N-acetylcysteine: A Study that Evaluates Response in Idiopathic Pulmonary Fibrosis). Except for a donation of NAC and a matched placebo by the company that makes the drug, there was no industry support for the work. The PANTHER-IPF trial was designed to test a standard therapy in a rigorous way.

**Source:** University of Michigan Health System Press Release, May 20, 2012  
*Content edited for space.*



**SAVE THE DATE!**

**DECEMBER 5–7, 2013**



**HYATT REGENCY LA JOLLA AT AVENTINE  
LA JOLLA, CALIFORNIA**



The Summit will feature an innovative two-day continuing medical education program for physicians, researchers, registered nurses, and allied health professionals. Additionally, there will be separate sessions for patients, family members, and caregivers to address the growing educational needs of the pulmonary fibrosis community.

**Visit [www.pffsummit.org](http://www.pffsummit.org) for more information.**

To pre-register, or for additional information, please email [summit@pulmonaryfibrosis.org](mailto:summit@pulmonaryfibrosis.org) or call 888.733.6741.

For sponsorship opportunities, please contact Cara Schillinger at [cschillinger@pulmonaryfibrosis.org](mailto:cschillinger@pulmonaryfibrosis.org) or 312.265.2184.

**PRESENTED BY** **Pulmonary Fibrosis**  
**FOUNDATION**

## WAYS TO GIVE

Many of the valued donors to the Pulmonary Fibrosis Foundation (PFF) support us by giving a gift in memory of a person who died of pulmonary fibrosis (PF) or in honor of someone living with PF. You may be one of these supporters. These gifts are vital to our success in serving the PF community by helping to find a cure, increasing awareness and advocacy, and supporting those affected by this disease. Donors like you have provided much of the support needed by the PFF during our first decade.

**Did you know there are many other ways to help support our mission and make a difference?** You've read about patients, learned about how we support research, and been inspired by how our volunteers raise awareness and funds. There are many ways to support the Foundation. You don't have to know someone with the disease to support our important initiatives.

- **You can simply go to our website** — go to [www.pulmonaryfibrosis.org](http://www.pulmonaryfibrosis.org) — and click on the “DONATE” button. Follow the prompts to give securely and quickly online using your credit card
- Or, if you prefer, **you can mail a check** to:  
Pulmonary Fibrosis Foundation, 230 East Ohio Street,  
Suite 304, Chicago, Illinois 60611-3201
- Another option? We would love to talk with you.  
**Call us to give a donation** over the phone — 888.733.6741

**It's also possible to double or triple your gift with a matching gift from your employer.** Visit [www.pulmonaryfibrosis.org](http://www.pulmonaryfibrosis.org) to learn more about employer matching gifts. And you may work for a company that supports their employees' causes through their own philanthropy or marketing sponsorships. Inquire if your employer offers financial support for nonprofit organizations and let us know.

**Please consider including the Pulmonary Fibrosis Foundation in your estate plan.** Contact your financial advisor to get started.

**And if you have not already done so, please give us your email address.** In addition to emailing you updates about the Foundation and other PF-related news, it's easy to contribute by clicking on the “DONATE” button in the email.

The Pulmonary Fibrosis Foundation, and everyone struggling with this terrible disease, is deeply appreciative of your support for our mission.

# Pulmonary Fibrosis FOUNDATION

## BOARD MEMBERS

**Daniel M. Rose, MD\***  
PRESIDENT AND CEO

**Patti Tuomey, EdD\***  
CHIEF OPERATING OFFICER

**Joseph Borus, Esq.\***  
SECRETARY

**Thomas E. Hales\***  
TREASURER

**Ritu S. Baral\***

**Daniel Beren, Esq**

**Kevin K. Brown, MD**

**Jennifer A. Galvin, MD**

**Michael C. Henderson\***

**Julia Willis O'Connor**

**John Ryan**

**Carl Salzano**

**Stephen A. Wald, PhD**

**Matthew C. Williams**

\*EXECUTIVE COMMITTEE

## STAFF

**Daniel M. Rose, MD**  
PRESIDENT AND CEO

**Patti Tuomey, EdD**  
CHIEF OPERATING OFFICER

**Dolly Kervitsky, RCP, CCRC**  
VICE PRESIDENT, PATIENT RELATIONS

**Cara Schillinger**  
ASSOCIATE VICE PRESIDENT,  
COMMUNICATIONS AND MARKETING

**Scott Staszak**  
CHIEF FINANCIAL OFFICER  
AND ASSOCIATE VICE PRESIDENT,  
INFORMATION TECHNOLOGY

**Jennifer Bulandr**  
DIRECTOR, COMMUNITY AFFAIRS

**Daeshawna Cook**  
COORDINATOR, COMMUNITY EVENTS

**Zoë Dirks**  
SENIOR PROJECT MANAGER

**Wendy Escobar**  
COORDINATOR, FINANCIAL OPERATIONS

**Courtney Firak**  
COORDINATOR, SUPPORT SERVICES

**Amanda B. Miller**  
COORDINATOR, DEVELOPMENT

**Elizabeth Price**  
MANAGER, DATABASE ADMINISTRATION

## MEDICAL ADVISORY BOARD

**Kevin K. Brown, MD\***  
CHAIRMAN

**David W. Kamp, MD\***  
MEDICAL DIRECTOR

**Jesse Roman, MD\***  
CHAIRMAN, RESEARCH  
ADVISORY COMMITTEE

**Marvin I. Schwarz, MD**  
PAST CHAIRMAN

**Timothy S. Blackwell, MD\***

**Jeffrey T. Chapman, MD**

**Harold R. Collard, MD\***

**Rany Condos, MD**

**Gregory P. Cosgrove, MD\***

**Aryeh Fischer, MD**

**Christine Kim Garcia, MD, PhD**

**Andreas Günther, MD\***

**Susan S. Jacobs, RN, MS**

**Naftali Kaminski, MD\***

**Joseph Lasky, MD\***

**Andrew H. Limper, MD\***

**Kathleen Lindell, PhD, RN\***

**James E. Loyd, MD\***

**David Lynch, MD\***

**Fernando J. Martinez, MD, MS\***

**A. Bruce Montgomery, MD**

**Imre Noth, MD**

**Ralph J. Panos, MD**

**Ganesh Raghu, MD**

**Luca Richeldi, MD, PhD\***

**Glenn D. Rosen, MD\***

**Patricia J. Sime, MD\***

**David A. Schwartz, MD\***

**Moisés Selman, MD**

**Charlie Strange III, MD\***

**Robert Strieter, MD**

**Jeffery J. Swigris, DO, MS\***

**Janet Talbert, MS, CGC**

\*RESEARCH ADVISORY COMMITTEE

# Pulmonary Fibrosis

## FOUNDATION

230 EAST OHIO STREET SUITE 304 CHICAGO, ILLINOIS 60611-3201

# we've moved!

PFF'S NEW  
HEADQUARTERS

230 EAST OHIO STREET | SUITE 304 | CHICAGO, ILLINOIS 60611-3201



©ISTOCKPHOTO.COM/LAFLOR

### Questions about familial pulmonary fibrosis?

Talk to a qualified genetic counselor at National Jewish Health

FAMILIAL PULMONARY FIBROSIS GENETIC COUNSELING PROGRAM

**800.423.8891** EXT 1097

SPONSORED BY A GRANT FROM THE PULMONARY FIBROSIS FOUNDATION

# 800.423.8891



©ISTOCKPHOTO.COM/DMBAKER

### Find out about clinical trials. [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Up-to-date information on clinical trials including:

PURPOSE • PARTICIPATION REQUIREMENTS • LOCATIONS • CONTACT INFORMATION



PHOTO BY CHRIS OWYOUNG

# BROADWAY save the date BELTS!

## FEBRUARY 25, 2013 BIRDLAND JAZZ CLUB

Enjoying the print version of our *Breathe Bulletin*? Sign up for the electronic version to:

Help the PFF save printing costs • Reduce impact on the environment • Easily forward to family and friends

Email [info@pulmonaryfibrosis.org](mailto:info@pulmonaryfibrosis.org) or call **888.733.6741** to change your *Breathe Bulletin* preferences or to be added to our mailing list.

## JOIN OUR EMAIL LIST

[www.pulmonaryfibrosis.org](http://www.pulmonaryfibrosis.org)