BY KIM RIBBINK

WITH A PIONEERING SPIRIT THAT HAS LED HIM TO TACKLE EMERGING FIELDS OF SCIENCE, RUSSELL M. MEDFORD, M.D., PH.D., IS STRIVING TO ENSURE THAT ATHEROGENICS, THE COMPANY HE COFOUNDED IN 1993, IS CREATING BREAKTHROUGH MEDICATIONS FOR CHRONIC INFLAMMATION.

Dr. Russell Medford

ENTREPRENEURIAL SPIRIT IS ABOUT TAKING RISKS AND FORGING NEW PATHS, which is what defines Russell M. Medford, M.D., Ph.D. From the start, Dr. Medford has been drawn to pioneering research — investigating questions that don't necessarily have immediate answers and addressing problems that require leaps into unchartered territories. As a student of cellular and molecular biology in the 1970s, he was part of an emerging field.

"We were writing the book, so to speak, as we were going along," he says. "None of the research had been codified; unlike today, there were no books available with laboratory protocols nor were there companies that could simplify tasks such as isolating RNA or DNA. It was hit or miss. Blazing a trail turned out to be a component of science that I enjoyed, and this has followed me through my professional career."

One of the joys of academia and working as a professor of medicine was the opportunity to learn something that no one else knew and communicating that information to others in the scientific world.

"The 'ah-ha' experience of discovering something new and being able to enlighten colleagues around the world is a wonderful feeling, and it's those moments that I cherish because they are few and far between," he says. "It's probably not dissimilar to climbing a mountain peak that no one has climbed before."

Dr. Medford, president and CEO of AtheroGenics Inc., cofounded the company in 1993 with the goal of translating raw scientific research into therapeutics for the treatment of chronic inflammation. With the company's lead product, AGI-1067, in Phase III trials, Dr. Medford is close to seeing his vision become a reality.

"The process of translating science into an actual medicine in order to make a difference in people's lives is extraordinarily challenging but it is extraordinarily rewarding because we're doing something that few people can do or have an opportunity to do," he says. "It is a blessing to be in a position through science to have an impact on so many people's lives."

A SENSE OF WONDER

The rigorous and reductionist approach that scientists in the field of eukaryotic molecular biology — the study of complex organisms — were taking to understand and explain complex systems held enormous appeal for Dr. Medford and encouraged him to focus on the field.

PHOTOGRAPHY: Becky Stein

shing Science Forward

"This was a discipline that offered insights into how cells and organs functioned and those in the field were able to ask specific and powerful scientific questions that gave very precise answers on the nature of how genes were regulated and how these genes expressed proteins to control functions," Dr. Medford says.

He began his research as a graduate student at Albert Einstein College of Medicine in New York and was encouraged by his mentors to apply for the American Cancer Society Special Post-Doctoral Fellowship, a competitive internship that sought to bridge the gap between basic research and clinical medicine.

"I wrote a research proposal and surprisingly enough, even though I was in competition with assistant professors for this fellowship, I was awarded a multiyear grant that enabled me to complete my graduate studies," he says. "The grant also allowed me to go to medical school on a full scholarship plus a fellowship stipend to get me through my Ph.D. and M.D.," he says.

Early on, Dr. Medford knew the direction he wanted to take — academic research.

"I was attracted to answering fundamental questions in science and nature," he says. "I love clinical medicine, but being a good scientist and being a good clinician are two very demanding mistresses and one can't be married to both at the same time with equal commitment."

He chose to grapple with the questions regarding disease and the human condition, but remains deeply respectful of the practitioners of medicine.

"Clinical medicine requires an understanding of disease as the abnormal expression of genes or dysfunction of organs as well as emotions, interactions, and social structures," he says. "Being a physician is not just science, it's also philosophy and social work."

For Dr. Medford, the discipline of science is a thrill because of the passion and excitement of doing something new, of making a difference, of learning new things.

FORGING A NEW PATH IN TREATING CHRONIC INFLAMMATORY DISEASE

AtheroGenics Inc. began operations in 1993 with the mission of discovering, developing, and commercializing novel drugs for the treatment of chronic inflammatory diseases, such as atherosclerosis, rheumatoid arthritis, and asthma.

To that end, the company has developed a proprietary drug-discovery technology platform called vascular protectant, or v-protectant, for treating diseases of chronic inflammation.

The company's v-protectants are therapeutic small molecules that block oxidant signals. Oxidant signals lead to the production of selected inflammatory proteins, including VCAM-1. These inflammatory proteins attract white blood cells, or leukocytes, to the site of chronic inflammation. Leukocytes destroy infective agents and promote healing but can also amplify chronic inflammation.

The company's lead compound, AGI-1067 for the treatment of atherosclerosis, is completing a 6,000-patient Phase III clinical trial in 250 clinical sites in four countries. The company believes that AGI-1067 may treat all areas of the coronary artery susceptible to atherosclerosis in a way that cannot be achieved with any existing therapy.

"The drug inhibits the signal that controls the expression of a small number of genes in the coronary artery that carry white blood cells, which are the mediators of the chronic inflammatory response; therefore those white blood cells or leukocytes don't congregate in the areas of the blood vessel that lead to the atherosclerotic plaque, which ultimately is the cause of heart attack and stroke," says Russell M. Medford, M.D., Ph.D., scientific cofounder, president, and CEO of AtheroGenics. "This is very different from anti-inflammatory approaches that try to block the binding of receptors that are expressed on the outer surface of cells. We're reaching into the cell and inhibiting its ability to express some of those genes in the first place."

Dr. Medford says that if the ARISE study (Aggressive Reduction of Inflammation Stops Events) is successful, the company hopes to file an NDA in 2007.

"The NDA would be nearly the end of a journey that began with the founding of the company in 1993 based on developing the first drug in a new class of anti-inflammatory agents that, if successful, could bring in a new approach for the treatment of heart disease," he says.

In addition to AGI-1067, the company is investigating AGI-1096, a novel antioxidant and selective anti-inflammatory agent that is being developed to address the accelerated inflammation of grafted blood vessels, known as transplant arteritis, which is common in chronic organ transplant rejection.

"Science is a great motivator that I draw inspiration from," he says.

Encouraging the ideas of young scientists is one of the great joys for Dr. Medford and one of the great challenges since this requires an ability to translate scientific knowledge into real-world examples for researchers and physicians starting out in their careers.

As a company leader, he seeks to generate enthusiasm in those he works with, not just among the scientists, but all of the professionals who make up AtheroGenics.

The leap from academia to cofounding a company was demanding on a number of fronts.

"Scientists in academia and in industry are two cultures separated by a common language," Dr. Medford says. "In academia, it's about asking basic, fundamental questions. In a pharmaceutical or biotech environment, it's about taking an academic approach and integrating a host of additional skills and people — chemists, pharmacologists, physiologists, clinical development experts, toxicologists, and regulatory experts — into a team and translating that science into testable hypotheses that lead to a goal, which is a clinical product or a therapeutic."

A second challenge for an academician switching to industry is coming to grips with the demands of raising capital. In an academic setting this requires applying for grants to pay salaries. In industry, funds are used for a great many other things in addition to wages.

"In the biotech and pharmaceutical industries, investment capital allows us to take the next steps to move ideas to reality; we have to respect the risk and be cognizant of the return on investment expected," Dr. Medford says. "The concept of building value in the development of a drug and the evolution of science during that time are important concepts that I learned when I made the transition to private industry."

Perhaps most challenging, however, is the fact that such a significant career change — particularly one involving risk-taking — requires a willingness to move out of a comfort zone.

"Academics spend years mastering the language and the semantics of arcana," Dr. Medford says. "To found a biotech company, I had to move outside of my comfort zone; I had to recognize that my expertise and background are only one part of the puzzle and that success depended on convincing and engaging experts in other fields to join me. Ultimately, that's what makes an individual entrepreneurial — having the courage to embrace uncertainty."

CARVING A NICHE

In the early 1990s, Dr. Medford and R. Wayne Alexander, M.D., Ph.D., at the time professors at Emory University, discovered a novel mechanism within arterial blood vessel walls that could control the excessive accumulation of white blood cells without affecting the body's ability to fight infection.

The two scientists surmised that atherosclerosis — the disease that leads to heart attacks and strokes — was an inflammation of the coronary arteries and that the abnormal inflammation that characterizes the disease was regulated by an abnormality in the signaling of genes inside the coronary arteries based on oxidation-reduction reactions, which involve a change in the oxidation state of the atoms or ions involved.

"At the time, this was a new concept; all risk factors that lead to heart attack and stroke — ele-

SCIENCE FRICTION

IN AN EXCLUSIVE INTERVIEW WITH PHARMAVOICE, RUSSELL M. MEDFORD, M.D., PH.D., SCIENTIFIC COFOUNDER, PRESIDENT, AND CEO OF ATHEROGENICS INC., TALKS ABOUT HIS CONCERNS ABOUT THE FUTURE OF ACADEMIC MEDICINE.

The world of academic medicine faces challenges on many fronts, according to Russell M. Medford, M.D., Ph.D., scientific cofounder, president, and CEO of AtheroGenics Inc.

"Academic researchers are under constant pressure to support their research with funding from a variety of sources, such as the federal government and private institutions," Dr. Medford says. "The vagaries of public policy that impact scientific research in the United States have a direct impact on scientists who are just beginning their careers. It is often a challenge for researchers to establish a track record with the federal government to win research support."

The situation, Dr. Medford believes, has reached almost a crisis point in terms of continuing support for young scientists. And the impact this could have on scientific research and ultimately on the pharmaceutical industry is a major cause for concern.

"The health of our industry — the biotechnology and pharmaceutical industry — is intimately tied to the health of the academic infrastructure in this country," he says. "This is where we get the new ideas. Science is inherently not predictable; we don't know what the next insights are going to be in human disease.

"If we don't have a vibrant, basic science infrastructure at the university level, the new ideas, the new science, the new insights, the new AtheroGenics will not happen," Dr. Medford continues.

With that in mind, Dr. Medford maintains a position as an adjunct clinical professor of medicine at Emory University so he can continue to play an active supporting role in academia.

"The research infrastructure and support of research in the biological sciences are something that the industry must take a strong look at because if we lose that infrastructure, if we lose the inherent health of our scientific base in the United States, our ability to develop new drugs out of that science will be crippled," he says.

This also means the industry must not try to direct academic research. While focus on outcomes is crucial, Dr. Medford maintains that it is critical for the industry to respect the individual passions and interests of investigators in academic institutions.

"Academia must be protected against the goal of product, which is so crucial in the industry," he says. "If we distort the mission of academic science by making it goal-directed for products, we lose the essence of novelty and pure science that is absolutely necessary."

IN SCIENCE, THE MOST IMPORTANT ELEMENT IS ASKING THE RIGHT QUESTION

vated cholesterol, hypertension, diabetes, cigarette smoking — have a final common pathway," he says. "They induced an abnormal chronic form of inflammation in the coronary arteries."

Putting that hypothesis to the test — hoping that it might lead to a new class of therapies to treat heart disease — required courage, but it was a chance Dr. Medford and Dr. Alexander, scientific cofounder of AtheroGenics and a company director, were eager to take.

Today, the company is focused on the discovery, development, and commercialization of novel drugs for the treatment of chronic inflammatory diseases, such as atherosclerosis, rheumatoid arthritis, and asthma.

How AtheroGenics forges its path depends on bringing together the various areas of expertise to pose the question or hypothesis and follow it through to fruition. The path for all scientific endeavors begins with posing the right question.

"In science, the most important element is asking the right question; the answer itself is of secondary importance because we never know what the answer is going to be when we set up a hypothesis," he says.

In its early days, when AtheroGenics had just a small group of employees, Dr. Medford spent much time alongside his staff in one-on-one interactions that helped him get to know his people well — their fears, frustrations, excitements, and passions.

The challenge as the company grows, he says, is to maintain that connection with all members of the staff.

"I have an open-door policy; I spend as much time as I can with the employees in the research labs, clinical labs, data management," he says. "I spend time in the break room so I can answer questions and interact with the staff.

"To me, the biggest challenge is retaining the core passion that a small company must have to be successful and translating that sense of purpose as the company grows and the distance between the founders of the company and the employee base grows wider," he says.

STEERING THE SHIP

AtheroGenics has come a long way in less than 15 years. To start, the company went public in 2000, then in late 2005 AtheroGenics formed a worldwide commercialization deal with AstraZeneca for AGI-1067, a deal Dr. Medford describes as one of the biggest of that year.

The agreement provides AtheroGenics with milestones and royalty payments on sales of AGI-1067, with AstraZeneca being responsible for the worldwide commercialization of the drug. AGI-1067 is in Phase III trials for the treatment of atherosclerosis. In addition, AtheroGenics will field a 125-person specialty salesforce, funded by AstraZeneca, to copromote the drug in the United States, targeting office-based cardiology practitioners.

"We are going to use the success of AGI-1067 as a way to transform from a research and development company to a fully fledged commercial pharmaceutical company," Dr. Medford says.

Deals such as this have certainly been a boon for Dr. Medford and his senior management team, but in particular the CEO regards his most important role as being able to attract and retain talented and committed people.

"I have always understood that while outstanding science is absolutely necessary, it is not sufficient for the development of a successful company or a successful therapeutic product," he says. "Therefore, I've focused on bringing in very talented executives and experts to help me build this company."

Another important job for the CEO is to communicate an understandable vision of what the company is trying to accomplish.

"Firstly, it's important to make public presentations so the investor community understands our progress and our challenges going forward," Dr. Medford says. "Second, we're communicating a vision and hope for many people. When I make a presentation I find that because our lead product, AGI-1067, is targeted toward heart disease, a condition that many people in the room have, are likely to develop, or know someone who has or has died of, the personal impact of what we're trying to do is apparent."

As important as the successes are, Dr. Medford says it's equally important to appreciate the failures, which should not be considered negatively, as long as they happen fast.

"When an unproductive line of work is eliminated, it allows the company to pursue a new line of inquiry," he says. "This is cause for celebration because it allows for future successes."

Equally important to the company's vision is ensuring that there is a work-life balance.

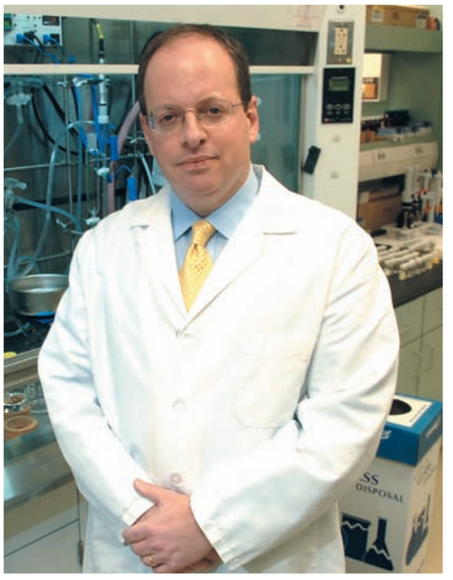
"When you're committed to a dream, you're spending most of your time working," he says. "But for me, my family is the No. 1 priority, and I would venture to say that's probably the case for most of our employees. The challenge has been to compartmentalize work from the most important thing in our lives — our families."

To ensure that balance, Dr. Medford says he enjoys biking, tennis, and sailing with his wife, who is the deputy national VP of research for the American Cancer Society in Atlanta, and spending time with his two teenage daughters. In addition, the busy executive derives a great deal of joy in making short film documentaries for personal use.

In addition, Dr. Medford maintains an adjunct professorship at Emory University, a role he regards as critical. (For more information, see the box on page 60.)

He is also active in the broader healthcare community, sitting on the board of directors of the Biotechnology Industry Organization (BIO), as well as committing time as chairman of the Georgia Biomedical Partnership, the state affiliate of BIO.

"I find parallels between helping political leaders develop policy and building a company; it's about bringing a group of people from very different backgrounds — scientists, non-scientists, politicians, policy experts — into the same room, getting them to share a vision, and helping them to achieve that vision," he says. ✦



SCIENCE IS A GREAT MOTIVATOR

JOURNEY OF DISCOVERY

RUSSELL M. MEDFORD, M.D., PH.D. — RESUME

DEC. 1995 – PRESENT. Scientific Cofounder, President, and CEO, AtheroGenics Inc., Alpharetta, Ga.

1994 – 1995. Scientific Cofounder and Executive VP, AtheroGenics Inc., Alpharetta, Ga.

2001 – PRESENT. Adjunct Clinical Professor of Medicine, Emory University School of Medicine, Atlanta

1994 – 2001. Associate Professor of Medicine (Tenured), Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta

1994 – 1997. Member, Program of Genetics and Molecular Biology, Division of Biological Sciences, Emory University, Atlanta

1994 – 1997. Director, Molecular Cardiology Research Center, Department of Medicine, Emory University, Atlanta

1989 – 1994. Assistant Professor of Medicine, Division of Cardiology, Department of Medicine, Emory University School of Medicine, Atlanta

1987 – 1989. Instructor, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston

COMMITTEE MEMBERSHIPS

2006. Board of Directors, Biotechnology Industry Organization, Washington, D.C.

2004 – PRESENT. Chair, Georgia Biomedical Partnership, Atlanta

2004 – PRESENT. Member, BIO Emerging Companies Section Governing Board, Atlanta

2004. Chair, GA Life Sciences Summit '04 Program, Atlanta

2004. Member, BioScience Executive Committee of the Metro Chamber of Commerce, Atlanta

2003 – PRESENT. Board of Directors, SEBIO

2003. Board of Directors, Governing Body, BIO's Emerging Companies Section, Atlanta

2003. Chair, GA LifeSciences Summit – National Program Committee, Atlanta

2003. Vice Chairman, Georgia Biomedical Partnership, Atlanta

2002. Member, Techlinks Life Sciences Advisory Committee, Atlanta

2001. Chairman, Special Review Committee, Gene Therapy Program Projects, National Heart, Lung, Blood Institute (May)

2000. Acting Chairman, National Institutes of Health, National Heart, Lung, and Blood Institute Program Review Committee (June)

1997. Member, NIH, NHLBI's Program Project Review Committee (June)

1993 – 1996. Member, Program Committee, Council on Basic Science, American Heart Association

1991 – 2001. Member, Special Review Committee, NIH, National Heart, Lung, and Blood Institute

1991 – 2001. Member, Site Visit Scientific Review Committee for Specialized Centers of Research, NIH, National Heart, Lung, and Blood Institute

1991 – 2001. Member, Site Visit Scientific Review Committee for Program Projects, NIH, National Heart, Lung, and Blood Institute

EDUCATION

1983. M.D., Albert Einstein College of Medicine, N.Y.

1982. Ph.D., cell and molecular biology, Albert Einstein College of Medicine, N.Y.

1978. M.S., cell and molecular biology, Albert Einstein College of Medicine, N.Y.

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PharmaVOICE welcomes comments about this article. E-mail us at feedback@pharmavoice.com.