



BY KIM RIBBINK

THE Discovery Bug

GRAHAM ALLAWAY, PH.D.

WHETHER DR. ALLAWAY IS EXPLORING THE OPEN SEAS IN HIS SINGLE-HANDED LASER OR INVESTIGATING UNCHARTED AREAS IN VIROLOGY, HE ATTENDS TO BOTH WITH EQUAL PASSION, COMMITMENT, AND FOCUS.

// **In small companies, people are pulling in the same direction; it's truly a team effort.**

For private companies in particular, there are far fewer rules and regulations to contend with so decisions can be made by consensus.

And that's motivating. //

Twice in his career Graham Allaway, Ph.D., has been at the center of significant discoveries in the field of HIV: first identifying the co-receptor to HIV, CCR5, and then uncovering a novel way to inhibit the disease, called maturation inhibition. Both discoveries are a testament not only to Dr. Allaway's deep scientific skills and expertise in the area of virology, but also to his commitment to teamwork and building groups of enthusiastic, engaged employees.

"My approach is to try to foster a team environment and to encourage people by focusing on the positive rather than dwelling on the negative," says the president and chief operating officer of Panacos Pharmaceuticals. "In my experience, having a collegial environment where people can have input into the programs and direction of the company is the best way to move projects forward."

With a focus on creating a cohesive approach and bringing everyone's ideas on board, Dr. Allaway has helped build a company that not only has a pipeline of promising anti-infective drug candidates but also has a happy, engaged workforce.

"We've had very little turnover in staff since we formed the company — much lower than often exists at small companies," he says.

Panacos focuses on the development of oral drugs with novel mechanisms of action to treat major viruses resistant to existing drugs. The company has its corporate headquarters in Watertown, Mass., and its R&D facility in Gaithersburg, Md.

For Dr. Allaway, one of the great joys of the scientific world is its internationalism, and he says even when Panacos was a young startup in 2001 with just a dozen people on board, it had a truly global feel about it, with someone from every continent aside from Australasia and Antarctica.

That global feel is right for the English-born and raised scientist. He spent a couple of years in Canada as a postdoctoral fellow. He has spent time in the United States, where he cur-

rently lives. And in between, he briefly returned to the United Kingdom.

"Science is a very international business, which means, at least from a work perspective, there wasn't much of a culture shock in moving between countries," he says. "One of the great things about this business is the opportunity to meet and interact closely with people from different cultures around the world."

THROUGH THE MICROSCOPE

A fascination for all things related to biology — from whole organisms to cell biology, molecular biology, and ecology — led the young Graham Allaway to a degree in zoology at Oxford University.

During summer vacations, the Oxford student worked for a government research institute, where exposure to invertebrate virology piqued his interest in studying and understanding viruses.

"I worked on an ecology project for the Natural Environment Research Council's Institute of Invertebrate Virology, mostly in Wales," Dr. Allaway says. "We were looking at the spread of a virus that infects the spruce sawfly, how the virus spreads through the forest plantations, and what could be done to control the pest."

The experience led him to a master's degree in tropical and temperate entomology at Imperial College London. His work involved the ecology of viruses, particularly how they spread between insect larvae. Thereafter, he undertook his Ph.D., whereby he began looking at different viruses and characterizing the viruses by their molecular and physical structure.

"It was an exciting time to be doing this type of research as a number of new techniques were just becoming available," Dr. Allaway says. "Restriction enzymes, for example, were just being used in the late 1970s to cut up



pieces of DNA for cloning and other purposes. We used those techniques to analyze the DNA genome of insect viruses that we had isolated as well as to classify and compare those viruses."

Around that time, Dr. Allaway became interested in how viruses get into cells and specifically wanted to know what were the receptors for viruses on cells, an area that was largely unknown. This interest led Dr. Allaway to two big career changes — a shift into mammalian viruses and a transatlantic move to undertake a postdoctoral project at Memorial University in Newfoundland, Canada.

"The huge medical need for antiviral therapies means that, from a commercial perspective, there are many more opportunities in human pathogenic viruses, and scientifically these are equally or more fascinating than the insect pathogenic viruses," he says.

Though Dr. Allaway was fascinated by both academic and government research, such as that conducted by the National Institutes of Health where he spent six years, he began to weigh the pros and cons of staying in that world.

"Academia and government research had many attractions; I could move wherever I liked from a scientific perspective, assuming funding was available," he says. "While I was at the NIH, I began to realize that there wasn't much opportunity to take a research discovery forward to its practical application."

It was that desire to be involved with a project from start to finish that inspired Dr. Allaway to join the biotech industry.

“Working for small biotech companies has enabled me to remain involved in fundamental scientific research but also to translate that into the development of important medicines, at the same time having the business development challenges that go with that,” he says.

LANDMARK DISCOVERIES

Dr. Allaway has truly made his mark on the scientific world.

“At Progenics and Panacos I was involved in the most important scientific discoveries that I’ve made in my career — one at each company — both in the areas of HIV,” he says.

The first, at Progenics, was the discovery of the HIV coreceptor, CCR5, which resulted from a collaborative project between Progenics and the Aaron Diamond AIDS Research Center (ADARC) in New York.

Scientists had known for many years that a specific molecule, or receptor, on the surface of immune cells allowed HIV to enter cells. But

research indicated that this receptor, called CD4, alone was not sufficient and that some other molecule or molecules were involved in HIV infection of immune cells.

In the mid-1990s, a scientific race ensued to identify the coreceptor, and it was Dr. Allaway with his colleagues at Progenics and ADARC who discovered the role of the chemokine receptor CCR5 in HIV infection.

“Right away, we realized the potential of CCR5 as a target for drug interventions to block HIV infection, and work continues at Progenics in that area, as well as at a number of large pharmaceutical companies,” he says.

At Panacos, a similar situation evolved, wherein Dr. Allaway and his team — through a collaboration with the University of North Carolina at Chapel Hill — identified a potent drug that seemed to work differently from most approved HIV drugs. This discovery has the potential to lead to a desperately needed new drug since resistance to the two major classes of currently approved treatments — reverse transcriptase inhibitors and protease inhibitors — has been building, resulting in increasing rates of treatment failure.

“Basically we started up the company around that discovery, as well as some other projects, and during the period between 2000 and 2002 we discovered that the drug had a completely novel and unexpected way of inhibiting HIV infection, which we now call maturation inhibition,” Dr. Allaway says.

Virus maturation is a process that occurs at the last stage in virus replication when the virus is released from infected cells. The company’s lead compound, bevirimat (formerly known as PA-457), is the first of a new class of HIV drugs called maturation inhibitors that work at the end of the life cycle of the virus.

As HIV buds out of an infected cell to spread the infection around the body, bevirimat blocks that process, preventing the virus from maturing properly so it becomes noninfectious and can’t spread.

“Last year, we completed an important Phase IIa study in HIV-infected patients showing that bevirimat is a potent inhibitor of HIV in patients and that it’s very well tolerated, so we’re moving it forward into late-stage development,” Dr. Allaway says. “We recently initiated a Phase IIb study where we are studying bevirimat’s antiviral activity and safety when dosed to patients in combination with currently available HIV drugs. This is how bevirimat will be used when it reaches the market.”

The science aside, Dr. Allaway says working in the biotech industry, particularly for a small company, is liberating.

In government institutes — be they in the United Kingdom or the United States — there is a structure and formality with regard to how

INTO THE FUTURE

Panacos Pharmaceuticals is engaged in the discovery and development of novel therapeutics and technologies to combat major viral diseases, including human immunodeficiency virus (HIV). With several products in the pipeline, including one in Phase II development, Panacos’ midterm goal is to successfully develop one or more products and get them onto the market.

Leading the pipeline charge is bevirimat, which is the first in a new class of HIV drugs called maturation inhibitors. Bevirimat blocks HIV maturation by inhibiting the final step in the processing of the HIV Gag protein. The resulting virus particles are structurally defective and are incapable of spreading infection around the body.

“For the scientists at Panacos, there’s a medical, almost humanitarian, goal that gives them the day-to-day motivation to come in and work hard, that is to continue moving bevirimat forward and get it to market,” says Graham Allaway, Ph.D., president and chief operating officer at Panacos.

In addition to bevirimat, the company is working on a number of other programs.

“For example, we’re bringing forward second-generation maturation inhibitors, and we plan to start clinical testing for one of those later this year,” Dr. Allaway says. “We also have a program to identify small-molecule, orally available drugs that target one of the first steps in HIV infection, that is the fusion of the virus to the cell at the beginning of the virus life cycle. There we have identified a number of very exciting and novel fusion inhibitors that we’re now optimizing with the goal of getting one of those into clinical testing next year.”

Consideration also will be given to in-licensing additional products as well as other business options to help Panacos become a successful pharmaceutical company.

Looking further into the future, Dr. Allaway says Panacos is keeping its options open with regard to partnering to bring drugs to market.

“There are advantages and disadvantages to partnering; we’ve had a lot of interest from large pharma companies that would like to partner with us to develop bevirimat because of its potential value,” he says. “From our perspective, if we partner we could take advantage of some of the resources that large pharma companies have — the salesforce, the financial resources, the development experience, and so on — but it would also mean giving up some control and value.”

One thing in the company’s favor with regard to going it alone is that the area of HIV does not require a huge salesforce and it is possible to be successful with about 100 sales people in a market such as North America.

“We’ll continue to evaluate our options and do whatever we think will bring the most value to the company and also help us to expedite development and get the product to the market as soon as possible,” Dr. Allaway says.

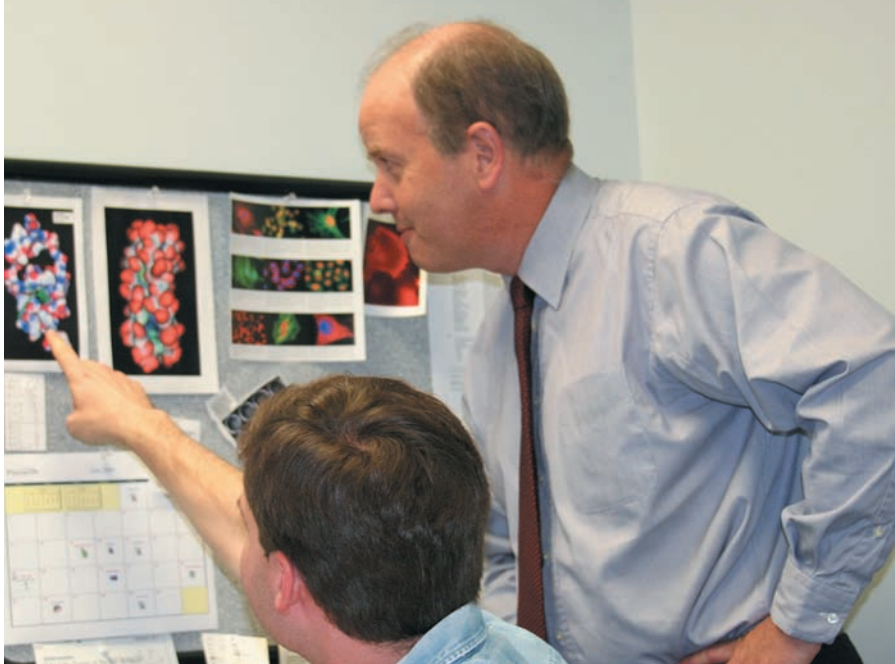
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direction is passed through the various layers of bureaucracy to those working in the lab.

“In small companies, however, people are motivated to pull in the same direction; it’s truly a team effort with everyone making an important contribution,” he says. “And for private companies in particular, there are far fewer rules and regulations and fewer layers of bureaucracy to contend with so decisions can

be made rapidly. And that’s both efficient and rewarding.”

MATCHING SCIENCE AND BUSINESS

Dr. Allaway joined Progenics in 1990, and since then he has had the opportunity to get

involved in all aspects of the business — from clinical development to business development to meeting with investors.

With a desire to expand his business experience, Dr. Allaway took the CEO position at Manchester Biotech, a British incubator company that Manchester University started with the goal of building new biotech companies from technologies coming out of the university.

One of the companies Dr. Allaway helped to start up was Renovo, which just went public this year.

“As with any new venture there were some very exciting opportunities at Manchester Biotech,” he says. “But there wasn’t as much funding available as we had hoped, and for various reasons I decided to look for other opportunities.”

The fit Dr. Allaway was looking for emerged in 1998 — at Boston Biomedica.

“The company was doing work in the diagnostic area but had got involved in a small side project in a collaboration with Professor Kuo-Hsiung Lee, Ph.D., at the University of North Carolina to discover novel HIV drugs,” Dr. Allaway explains. “Some interesting compounds came out of that partnership, and the company realized that there was a great deal of potential, which was beyond its resources, know-how, and business plan.”

The idea was to spin the findings into a new company, Panacos, which became an independent, private company in November 2000 through a round of venture financing.

Dr. Allaway was the founding CEO of Panacos, leading it through early-stage financing and helping it to secure investments from venture capitalist firms A.M. Pappas & Associates and Ampersand Ventures.

Two years ago, Panacos brought on board a CEO — Samuel (Skip) Ackermans who had experience in late-stage drug development — and Dr. Allaway took the role of chief operating officer. In that role, Dr. Allaway played a key role in the March 2005 merger with V.I. Technologies Inc., a biotechnology company

ALL THE WAY TO THE TOP

GRAHAM ALLAWAY, PH.D. — RESUME

2003 – PRESENT. President and Chief Operating Officer, Panacos Pharmaceuticals Inc., Gaithersburg, Md.

1999 – 2003. Founding CEO, President, Board Member, Panacos Pharmaceuticals, Gaithersburg, Md.

1998 – 1999. Senior VP, Drug Development, Boston Biomedica Inc., Boston

1997 – 1998. CEO, Board Member, Manchester Biotech Ltd., Manchester, United Kingdom

1990 – 1997. Head, Therapeutic Development Group, Associate Scientific Director, Progenics Pharmaceuticals Inc., Tarrytown, N.Y.

1984 – 1990. Visiting Fellow and Visiting Associate (NIDR), National Institutes of Health, Bethesda, Md.

1982 – 1984. Postdoctoral Fellow, Medical Faculty, Memorial University, St. John’s, Newfoundland, Canada

EDUCATION

1982. Ph.D. Virology; Imperial College, London University, United Kingdom

1978. M.S. Entomology; Imperial College, London University

1976. M.A. Zoology; Pembroke College, Oxford University

BOARDS AND COMMITTEES

2005 – PRESENT. Board Member, Enterprise Investment Fund, Maryland Department of Economic Development, Baltimore

2003 – PRESENT. Reviewer, Small Business Innovative Research (SBIR) Grants, National Institutes of Health, Bethesda, Md.

1996 – 1998. Adjunct Associate Professor of Microbiology and Immunology, New York Medical College, Valhalla, N.Y.

developing products designed to improve the safety of the world's blood supply. That deal turned out to be particularly fortuitous for Panacos, though less so for V.I. Technologies, Dr. Allaway says.

Panacos had reached a point where it needed to raise more money to start clinical development for bevirimat, but it was a difficult private market to raise capital. Not wanting to give the company away, management needed to find another solution. That solution arrived with V.I. Technologies, which had developed a promising technique to inactivate pathogens in red cell units used in blood transfusions. But just before the deal was set to close, data indicated a serious problem with V.I.'s product. So the deal was recut, allowing Panacos to become public through a reverse merger that gave Panacos more than 80% of the combined company. Since then, with the positive outcome from its Phase IIa trials, Panacos has managed to raise another \$85 million on the public markets.

Eager to keep abreast of what's happening

in the world of biotech, as well as to give back to the business community that helped Panacos survive and thrive, Dr. Allaway takes on several roles outside the workplace.

From time to time he works for the Small Business Innovation Research Grant (SBIR) review committee, which focuses on HIV and related grant applications. SBIR grants helped Panacos in its early years with financing. Dr. Allaway also is on the board of the Maryland Department of Economic Development's Enterprise Investment Fund, a venture financing program that Dr. Allaway describes as one of the most successful in the country.

"The state of Maryland was one of the early investors in Panacos, and I'm very pleased to be able to help them," he says. "It's also a fascinating opportunity to get into a broader range of biotech areas and help, to the extent I can, companies in their early start-up phases."

Through his various company experiences, as well as his involvement on different boards and committees, Dr. Allaway has learned a

great deal about the complexities of running a small business. Though the programs and possibilities at Panacos truly excite Dr. Allaway, the potential for burnout in such an intense environment is evident. So he finds ways to clear his mind, through skiing and, in particular, sailing, which he finds truly therapeutic.

"I have a couple of small sailing boats — a single-handed Laser and a two-person dinghy, that I usually sail with my daughter," he says. "Racing sail boats is one of the most complex sports in the sense that there are so many variables with regard to how the boat is set up, changing wind directions, strategy and tactics, and so on. When I race, it's a complete release; it's impossible to think about anything else." ♦

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



The National Institute of Allergy and Infectious Diseases (NIAID) stated in a report in May 2006, that since 1987, investigators supported by the NIAID have enrolled more than 23,000 volunteers in 96 HIV vaccine clinical trials to test at least 58 different vaccine candidates.

Yet an effective vaccine still remains elusive.

"No one really expected that it would be this difficult," Dr. Allaway says. "Back in the 1980s, people anticipated that a vaccine would be available within maybe 10 years or so. Whereas now, 20 years later, I do not expect that there will be an effective treatment for HIV available in the next 10 years. There's really nothing on the horizon."

PONDERING WORLD CONCERNS

IN AN EXCLUSIVE INTERVIEW WITH PHARMAVOICE, GRAHAM ALLAWAY, PH.D., PRESIDENT AND CHIEF OPERATING OFFICER OF PANACOS PHARMACEUTICALS, TALKS ABOUT THE HUGE INTERNATIONAL PROBLEM OF HIV INFECTION.

FOR ANY SCIENTIST WORKING IN THE AREA OF INFECTIOUS DISEASES, IT'S IMPOSSIBLE TO OVERLOOK THE HUGE GLOBAL TOLL OF HIV INFECTION.

According to the 2003 Joint United Nations Program on HIV/AIDS, 38 million adults and children worldwide are infected with HIV. In 2003 alone, almost 5 million people became newly infected with the virus, and more than 3 million people died of AIDS. In North America and Europe, about 1.6 million people are living with HIV/AIDS, and 80,000 were infected with HIV in the past year.

"These days most people are aware of the daunting scale of the problem, given all the articles about it," says Graham Allaway, Ph.D., president and chief operating officer at Panacos Pharmaceuticals.

Given the huge impact of the disease and how difficult it is to treat, one of the big problems is getting treatments to people in the developing world.

"It's difficult enough treating the disease in a country with very advanced medicine, like the United States; but in developing nations, where people are dying in huge numbers, the question is how can the world begin to tackle the problem of containing

HIV infection and helping the sick?" Dr. Allaway asks. "HIV is a complicated disease to treat, but we have made progress over the last 10 to 15 years in terms of making life better for HIV-infected patients. But that's just the couple of million people in Western countries, and even there it's not perfect.

"While some progress has been made, I don't envy the people in the World Health Organization and the other groups who are trying to get more drugs to people in Africa — it's just an incredibly difficult logistical exercise," Dr. Allaway says.

For many years, the hope has been to discover a vaccine against HIV, since that would be a much easier and cheaper way to tackle the disease. Vaccines undoubtedly are the Holy Grail, Dr. Allaway says, given what has been achieved in other diseases. Polio, for example, has been almost eradicated through vaccination, and smallpox has been eradicated.

THE PROBLEM IS THAT DEVELOPMENT OF A PREVENTIVE VACCINE IN THE HIV AREA HAS TURNED OUT TO BE AN IMMENSELY DIFFICULT UNDERTAKING.

Dr. Allaway says large amounts of time, effort, and money have been invested by governments, academic groups, and companies, with no significant progress.