

Intent

BY KIM RIBBINK

CLEAR



Dr. Una Ryan
has made significant inroads
in the biotechnology world.

Not only has she helped to successfully navigate a company through major change, she has also played a key role in improving business conditions for other biotech companies. Now she is applying her forward-thinking approach to science and business to develop clean energy for both industrial purposes and save lives in poor nations.

Throughout her career, Una Ryan, Ph.D., has had a knack for understanding the bigger picture — be that as a scientist, a company leader, or even as a campaigner for the biotech industry at large.

From a scientific viewpoint, Dr. Ryan has thrown herself into a variety of research programs at all levels and has easily adapted to different therapeutic categories, continuously seeking out projects that have the potential to save lives.

As a businesswoman, she recognized the value of M&A in the biotech sector before the trend was popular, helping the fledgling company T Cell Sciences move from its focus on complement inhibitors to become a vaccines company, which was renamed Avant Immunotherapeutics and ultimately merged with Celldex.

Perhaps her biggest impact within the biotech industry has been the role she has played in battling for the long-term success of the industry and in particular the influence she was able to bring to bear on the Massachusetts legislature.

“I want to live and work in a state that has science- and business-friendly laws; I don’t believe change just happens, and I believe it’s important to support the industry beyond just my own company’s needs,” she says. “I like to be a part of educational efforts and be involved with groups that can influence the thinking of legislators. I want to work in a healthy industry and I enjoy doing things for the broader group — it’s a rising tide that lifts all boats.”

Dr. Ryan is a past chair of the Massachusetts Biotechnology Council, and she served on its board for 12 years, as well as the boards

of the Biotechnology Industry Organization, the New England Healthcare Institute, and the Board of Associates of the Whitehead Institute. She also is a member of the Strategy & Policy Council of the MIT Center for Biomedical Innovation and serves as a member of the Business Advisory Board of BIO Ventures for Global Health.

It’s her ability to see the bigger picture and broader desire to do good works that led Dr. Ryan to her next venture. As CEO of Waltham Technologies, which is focused on developing methods to clean water using blue-green algae, Dr. Ryan has the opportunity to lead a profitable company while making an impact on health in developing nations.

“With this technology, which is used to clean wastewater, in particular for the beverage industry, I can have my cake and eat it too,” she says.

REALIZING A DREAM

In many ways, Dr. Ryan’s journey has come full circle as she returns to one of her earliest scientific interests, water.

As a child, using a regular mercury thermometer, she worked out the anomalous expansion of water. She was fascinated by the unusual expansion properties of water and the differences between the molecular composition of the liquid in its solid, liquid, and gaseous states.

Waltham Technologies has its sights set on cleaning water, both at a commercial level for the beverage, food, and textile industries

and in the longer term to deal with contaminated water in both the developed and developing world.

“Water is the most precious commodity we have; it has had the biggest impact on civilization over the last 100 years,” she says. “Water is the difference between advantaged and disadvantaged people — having clean water and sanitation — yet, it remains a silent emergency. People talk about oil and carbon footprints; they don’t talk about our water footprint.”

The dream of making a difference and saving lives began when Dr. Ryan was a very young girl.

“My parents were overseas a great deal of time when I was growing up; I lived with my aunt in Oxford, England, who had a lot of friends who were missionaries,” she says. “I was surrounded by strong women.”

This was a generation of women, she explains, who had lost their husbands and brothers in World War I and who had overcome hardship to go on and do all types of jobs.

During her early years, Dr. Ryan was also influenced by the viewing of a movie about a little boy whose family had leprosy and who was taken away from his mother and father and all of his friends.

“I remember I was 5, and this movie broke my heart; it was then that I decided when I grew up I was going to cure these dreaded diseases,” she says. “That small voice of my childhood has remained with me over the years; I just want to save lives.”

Her scientific passion also never faded, and ultimately Dr. Ryan went on to study zoology, microbiology, and chemistry before earning her Ph.D. in cellular and molecular biology.

Research has played a major role in her life, and time and again Dr. Ryan has been recognized for her contributions to the scientific community.

In 1986, she received a MERIT (Method to Extend Research in Time) Award from the National Institutes of Health (NIH) to support her research. The award program extends funding for up to 10 years to a select number of investigators who have demonstrated superior competence and outstanding productivity during their previous research endeavors, and are leaders in their field with paradigm-shifting ideas. MERIT awards are intended to provide such investigators with long-term, stable support to foster their continued creativity and spare them from the



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burden of frequent application for research grants.

Researchers cannot apply for a MERIT Award; rather the NIH recognizes researchers who have demonstrated superior competence and outstanding productivity in research endeavors.

“I had been slaving away writing grants for years and didn’t realize that I had gotten very high scores,” she says.

Dr. Ryan was one of the first recipients of the award from the Heart, Blood And Lung Institute. Beyond the obvious joy in having a guaranteed 10 years of support, she says the award also drew attention to her research at the University of Miami, where she was working on pulmonary endothelial cells in the area of vascular biology.

EMBRACING CHANGE

Dr. Ryan’s expertise in the vascular field took her to Monsanto for a period as director of health sciences, with a joint academic position as research professor of surgery at Washington University School of Medicine in St. Louis.

When an opportunity arose to work in a different field, she jumped at it. Dr. Ryan took the position of chief scientific officer at T Cell Sciences, which was conducting research on complement inhibitors, an early part of the immune and inflammatory cascade.

“This opportunity was a break from what I’d done before, but I like change, so I wasn’t daunted by the fact that the company was operating in a completely different area,” she says. “The immune system is fascinating and there are many diseases caused by or of the immune system.”

The field and research programs so absorbed Dr. Ryan that she was frequently selected to tell the company’s science story to Wall Street.

“When I became CEO, this was an aspect of the job that I knew how to do and enjoyed doing,” she says. “I like explaining research and sharing my excitement about a project with people who aren’t scientists.”

Exposure to the way larger pharmaceutical companies operate through her time at Monsanto also proved invaluable in making the switch from head of science to head of the company.

As CEO of T Cell Sciences, Dr. Ryan began a series of merger and acquisition activities, a less-common move in biotech in the mid-1990s when she began implementing these growth strategies.

“At the time, biotech leaders tended to think about growing organically or by licensing more projects from academia,” she says. “While M&A is common practice in biotech today, at the time it wasn’t thought of as a way for companies like ours to grow.”

During her years at Monsanto, Dr. Ryan had been a member of the Monsanto Management Council, and putting companies together as part of a growth strategy was one of the many issues analyzed at council meetings.

“I also learned about post-patent strategies, how to deal with legal challenges, and many other aspects of business that one isn’t exposed to with start-ups,” she says. “I got a much more sophisticated and advanced company view than I would have received had I just grown up with a small company.”

Dr. Ryan’s first foray into the M&A world involved a merger of almost equals between T Cell and the Virus Research Institute (VRI).

“When we put the two companies together, I realized that neither name was appropriate for the new combined entity, so I decided to pick a new name and called the company Avant Immunotherapeutics,” she says.

During her 15 years at the helm of Avant Immunotherapeutics, Dr. Ryan oversaw several other moves. Avant acquired a small company in St. Louis called Megan Health that brought vaccine technologies to the table. Then Dr. Ryan and her team acquired the intellectual property assets of a small company in San Diego that gave them the ability to make their vaccines temperature stable.

“At the time I left Avant Immunotherapeutics, the merger with Celldex Therapeutics was completed,” she says.

Avant has since been integrated into

Celldex, which uses its immunotherapy platform to generate candidates for cancer and other difficult-to-treat diseases.

While Dr. Ryan's move to a biotech company focused on water treatment may appear to be a dramatic departure from her research background, there is a clear symmetry to the next leg in her career path.

During a conversation with Waltham Technologies Founder and Chief Scientific Officer Theresa O'Keefe, Ph.D., Dr. Ryan realized there was a strong overlap between what she had been doing at Avant

Immunotherapeutics and the technology Dr. O'Keefe was developing.

Waltham Technologies bioengineers algae so the organism's required production of Vitamin B12 is chained to the production of new genes. These introduced genes enable the organisms to rapidly digest contaminants in the water and produce valuable products. As algae cannot live without Vitamin B12, these new genes become a life requirement. Algae are photosynthetic; they can directly use sunlight for energy so the process will continue until all the waste is removed from the

water. The bioengineered algae recycle the waste into materials, such as industrial enzymes and oils for biodiesel.

"Theresa had applied to patent her technology using blue-green algae to clean water and make fuel, while at Avant we had been using bacteria as a manufacturing platform to make our vaccines — the bacteria were the organisms that grew in the bioreactors," Dr. Ryan says. "So I was very familiar with the concept of bacteria as a manufacturing platform."

A BROADER IMPACT

IN THE COURSE OF HER CAREER, UNA RYAN, PH.D., HAS BEEN A SIGNIFICANT AND HIGHLY REGARDED CONTRIBUTOR TO THE HEALTH OF THE BIOTECH INDUSTRY.

For many years, Dr. Ryan was on the boards of the Biotechnology Industry Organization (BIO) and the Massachusetts Biotechnology Council (MBC). Among her achievements were impacting biodefense legislation by ensuring vaccines were included in BioShield One and Two and helping to make Massachusetts a more friendly environment for biotech companies.

"I helped to push the state legislature to adopt an economic stimulus package long before it was fashionable, and that provided grants and low-interest loans to biotech firms," she says.

She also was instrumental in making sure Massachusetts adopted a streamlined permit process for plants and facilities, a critical need because once companies got to the manufacturing stage, they were leaving the state because of its complex permit rules.

"Our companies were being lured away by other states that were aggressively courting these up-and-coming companies just when they would have provided a lot of jobs and tax revenue back to the state," Dr. Ryan says. "With the help of some very good local legislators, we eased the permit process."

In a 2006 article published in *Nature Biotechnology*, Thomas Finneran, then president of MBC, described Dr. Ryan as a rock star, lauding her ability to describe the big picture of how biotech contributes to the state to legislators.

While Dr. Ryan's tenure on the boards of

MBC and BIO has expired, she says she very much enjoyed the time she spent with the two organizations. Because a quiet life is not her style, today she is involved with medical school and a nonprofit organization called the Institute for Pediatric Innovation (IPI). The IPI strives to move drugs that have been approved for adults through clinical trials to make them suitable for children.

She also has just been appointed to a Climate Change and Green Economy Council for the state of Massachusetts, which fits perfectly with her new role as CEO of Waltham Technologies, a company working in the clean energy space.

"I believe it's important to be involved with organizations that affect the industry," she says. "And our technology impacts all industries here — pharma, green technology, beer, everything."

In addition, Dr. Ryan commits her time to teaching and spending time with students. Throughout her career, she has maintained strong academic ties and today has an appointment at Boston University.

"I like to keep in contact with academia because I enjoy working with students," she says. "I also teach entrepreneurship and Sloan school management concepts at MIT."

In particular, Dr. Ryan likes to encourage women to enter the sciences. To that end she devotes time to address women in biotechnology. She was the keynote speaker at Women in Bio's annual dinner earlier this year.



Dr. Ryan says after she gives a talk she will always stop to speak with women on a personal level.

"I speak to women from an organizational point of view, but I also like to engage in an individual way," she says. "I give out my card so they can e-mail me. I don't know how to evaluate the impact of these encounters, but there are women around town who will stop to thank me for encouraging them and discuss how their business is doing. It's very rewarding."

Sometimes these encounters lead to new and exciting opportunities. For example, not that long ago Dr. Ryan got together with a friend who was looking to start a business based on a new bioengineered algae technology but didn't have business expertise. That friend was Theresa O'Keefe, Ph.D., founder and chief scientific officer of Waltham Technologies.

"Little did I know that I'd end up running the company," Dr. Ryan says.

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LEADERSHIP IN ACTION

Over the years, Dr. Ryan has proven her leadership credentials time and again. She takes what she refers to as a collegial approach to leading her team.

“My initial management style was very much familial — one big family pulling together — but as I began dealing with larger and larger organizations my style changed, and now I would say it is collegial,” she says. “I’m a decision maker; I don’t like to put decisions that need to be made up for a vote because I don’t think this process is satisfactory for anybody. I like to get people to come to a consensus, but when that’s not possible, I’ll hear the argument, make a decision, and move on. I have found that people like decisive leaders.”

While at Avant, she navigated the company through a series of key changes, managing

each move adeptly. What she says she is most proud of from her time at the company is managing through good times and bad.

“It’s very easy to be the CEO of a biotech company when the sector is soaring, but it’s hard when the market is down and there are clinical failures and disappointments,” she says. “Being able to keep the company going through the tough times as well as the good times is probably what I feel best about.”

When a significant problem arose at Avant — the company’s complement inhibitor performed poorly in trials — Dr. Ryan drew on her experience to overcome the challenge.

“I had to pick up the pieces and say to Wall Street, ‘now we’re a vaccine company’ and put the best face on it for investors so we could continue to raise money and keep employees working on the remaining programs,” she says.

Dr. Ryan recognizes that there are tough times ahead for the industry as it battles through the recession.

“The current financial environment will change the industry; there will be quite a lot of consolidation,” she says. “In times of crisis there is evolution — the weak don’t survive and those companies that do usually go on to great things, so perhaps there will be some good eventually. But it’s going to be very hard on the employees who lose jobs and the projects that will get lost along the way.”

She suggests the way forward will be a flight to quality, with companies picking their best programs and people.

“The ready money from Wall Street is gone, and companies need to find new ways of funding,” she says.

As an example, Dr. Ryan points to some of the creative ways in which disease foundations are supporting projects, and notes that the government also is coming up with new ways of funding research important to those in office.

“The margins we’re used to in the pharma industry may get narrower; we have to break with the old models and develop reasonable expectations,” she says.

It’s this very need for adaptation that in part prompted Dr. Ryan to shift her focus to a different type of technology.

“I want to have an impact, but I also want to avoid some of the areas that are still very uncertain,” Dr. Ryan says. “Investors hate uncertainty. Investors understand long timelines and expensive development processes if they know there’s a reward at the end. But uncertainty, in terms of timelines and expenses, is very unsettling for people. I think the regulatory process has been uncertain for companies and investors alike.”

Dr. Ryan is moving ahead cautiously at Waltham Technologies. Ultimately, her goal is to develop the technology at a commercial level for high-margin markets, in particular the beverage industry — breweries, wineries, and soda plants — while using the same technologies and nondilutive funding in the developing world to clean up wells, ponds, and rivers that have been polluted.

In the future, she expects she will revisit successful business plans of the past, forming partnerships to expand and grow.

“Right now, we’re so small that I don’t want to get distracted by clever business deals, but I do think growth by M&A is a very sensible way to build a company,” she says. ♦

WATERSHED MOMENTS

UNA S. RYAN, PH.D., OBE — RÉSUMÉ

2008 – PRESENT. President and CEO, Waltham Technologies Inc.

1996 – 2008. President and CEO, Avant Immunotherapeutics Inc. (formerly T Cell Sciences Inc.)

1993 – 1996. VP of Research and Chief Scientific Officer, TCell Sciences Inc.

1994 – PRESENT. Research Professor of Medicine, Whitaker Cardiovascular Institute, Boston University School of Medicine

1990 – 1993. Director of Health Sciences, Monsanto Co.

1990 – 1994. Research Professor of Surgery, Medicine and Cell Biology, Washington University School of Medicine

1980 – 1989. Professor of Medicine, Department of Medicine, University of Miami School of Medicine

1977 – 1980. Associate Professor of Medicine, Department of Medicine, University of Miami School of Medicine

1972 – 1977. Senior Scientist, Papanicolaou Cancer Research Institute

1972 – 1977. Assistant Professor of Medicine, Department of Medicine, University of Miami School of Medicine

1967 – 1972. Instructor in Medicine, Department of Medicine, University of Miami School of Medicine

1967 – 1971. Director, Laboratory for Ultrastructure Studies, Howard Hughes Medical Institute

EDUCATION

2009. D.Sc. (Honorary Doctor of Science), Bristol University

1968. Ph.D. (Cell Biology), Cambridge University

1963. B.Sc. (Zoology - Special Honors, First Class); B.Sc. (Chemistry - Subsidiary, First Class); B.Sc. (Microbiology - Subsidiary, First Class), Bristol University

AWARDS AND HONORS

2007. Albert Einstein Award for outstanding achievement in the life sciences

2002. Order of the British Empire (OBE)

1986 – 1993. MERIT Award, National Heart, Lung, and Blood

1972 – 1977. Established Investigator, American Heart Association

1967 – 1972. Howard Hughes Investigator

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CLINICAL RESEARCH

BY KIM RIBBINK

DEVELOPING Health



Saving lives and making a difference in poor nations has been a lifelong goal for Una Ryan, Ph.D., President and CEO of Waltham Technologies.

Dr. Una Ryan began to realize her dream of making a difference in the world when she was head of Avant Immunotherapeutics. Over time, the company, originally called T Cell Sciences, evolved into a vaccines company. One of the projects the company was involved with was taking the cell line for what became the GlaxoSmithKline vaccine Rotarix through Phase II clinical trials.

“It was a great achievement that GSK was able to get Rotarix to market and to have been involved with the product’s development,” she says. “This vaccine will save lives; there are 600,000 deaths from rotavirus across the world, so it’s very important.”

Avant also worked on single-dose oral cholera and typhoid fever vaccines.

“Even though these vaccines are not on the market yet, they are already saving lives,” Dr. Ryan says. “Children, who very well may be dying of these diseases, are getting these vaccines through clinical trials.”

It was during her time at Avant Immunotherapeutics that Dr. Ryan was first

able to realize her childhood ambition to address global health issues.

“It was very important to me that we get our vaccines to everyone, not just the people who could afford them,” she says. “We developed a plan whereby we would make and market vaccines for travelers, and at the same time develop the same vaccines for children in the developing world who were dying of these diseases.”

It was important, however, to ensure that the money they received from Wall Street investors went into profitable ventures, so to achieve the dual goal Dr. Ryan used nondilutive funds from the NIH and the Gates Foundation to develop the products for the developing world.

Her focus has long been on diarrheal diseases that afflict children.

“The focus has been on the big diseases — AIDS, malaria, and TB — that affect millions of adults in the developing world, but children under 5 are dying from diarrhea,” Dr. Ryan says. “Since the company was working in that area, I decided this would be my mission.”

Over time, frustration with development setbacks began to take its toll.

“It was taking so long to develop each vaccine, I thought we would have to pick off each diarrheal disease one by one through a 10-year process,” she says. “Then I remembered thinking if I could clean the water, I could take care of all of the diarrheal diseases with one technology.”

This was the big draw that brought Dr. Ryan to Waltham Technologies.

Her hope ultimately is to use a similar business plan to the one she devised at Avant; she wants to engage Wall Street and other investor funds to develop technologies for high-margin customers in the developed world and draw on nondilutive funding to clean up water in the developing world.

Dr. Ryan has been widely recognized for her contributions to biotechnology and seeking to advance health in developing nations.

In 2002, Her Majesty Queen Elizabeth II awarded Dr. Ryan the Order of the British Empire (OBE) for her services to the research, development, and promotion of biotechnology. In 2007, Dr. Ryan was honored as a recip-



ient of the Albert Einstein Award for outstanding achievement in the life sciences. In 2009, she received an Honorary Doctor of Science degree from Bristol University.

“Research can be difficult, business can be

hard, much of the time things don’t go well, and at times I was tired and frazzled, so it’s nice when somebody says well done,” Dr. Ryan says. “This is especially true when the acclaim comes in the form of the OBE. I love

“It was very important to me that we get our vaccines to everyone, not just the people who could afford them.”

my awards and I’m not ashamed to say how much pleasure they give me. I like to remember people who have been kind to me in my life and I try to touch other people, even if it’s just saying thank you; this helps, it makes you move forward again, and you don’t give up.”

When she received her honorary degree from Bristol, Dr. Ryan says one of the faculty told the story of her research life.

“It was like he was talking about someone else; it really is a pleasure to hear when the story is all put together,” she says. “I thought maybe it wasn’t all a waste of time.” ♦

A WATERSHED CAREER TRANSITION

IN 2008, UNA RYAN, PH.D., TOOK THE HELM OF WALTHAM TECHNOLOGIES INC. AS PRESIDENT AND CEO AFTER HAVING A CAREER-CHANGING CONVERSATION WITH HER FRIEND THERESA O’KEEFE, PH.D., FOUNDER AND CHIEF SCIENTIFIC OFFICER OF THE COMPANY.

Dr. Ryan was enthused by Waltham Technologies’ focus on developing and commercializing innovative methods to clean water, a goal that fit with her desire to end childhood diarrhea in developing nations.

WALTHAM TECHNOLOGIES’ MISSION

Access to clean water is the No. 1 cause of increased human life expectancy in the last 100 years. Contaminated water has disastrous effects on human and animal health in both the developed and developing world. Current methods for cleaning water are complicated, expensive, and consume large quantities of energy. Unfortunately, water decontamination is a required expense for most industries but creates no product. Waltham Technologies believes that a system that easily and profitably cleans water will rapidly provide great benefits to the beverage, food, and textile industries in the developed world. Future development will also provide far-reaching benefits for military needs and in emerging markets.

WALTHAM TECHNOLOGIES SYSTEM

Waltham Technologies’ system safely bioengineers algae so the organism’s required production of Vitamin B12 is chained to the production of new genes.

These introduced genes enable the organisms to rapidly digest contaminants in the water and produce valuable products. As algae cannot live without Vitamin B12, these new genes become a life requirement. Algae are photosynthetic; they can directly use sunlight for energy so the process will continue until all of the waste is removed from the water. The bioengineered algae recycle the waste into expensive materials, such as valuable industrial enzymes and oils for biodiesel.

THE MARKET

Many industries will benefit from this technology but the most rapidly accessed market is helping breweries, wineries, and beverage producers make a profit while cleaning their wastewater. These industries create between one and nine gallons of wastewater for every gallon of saleable product (almost 300 billion gallons of wastewater). This wastewater must be cleaned at great cost (worldwide, \$5 billion; in the United States, \$500 million). The Waltham Technologies system allows this waste to be recycled as industrial enzymes that are used extensively to simplify material preparation and cleanup, an estimated worldwide cost of \$2.3 billion. The enzyme market is projected to triple as emerging markets such as cellulosic

ethanol production develop. Providing a duplex wastewater cleaning to enzyme production system that is simple, safe to operate, and easy to insert in existing plants will provide these and other related industries with desperately needed solutions. Oils also produced by the algae provide an additional bioenergy product.

FUTURE POTENTIAL

Waltham Technologies expects to complete proof of concept in about one year. From this success, many other scientific goals will develop with their priorities determined by market conditions and board advice. As scientific success is created, other departments, including business development, marketing, engineering, and manufacturing will be assembled to build on the success of the company’s scientific creations. The first product is expected in about two years with full-scale marketable solutions available within four years. As the technology has widespread potential applications, the company plans to align with strategic partners for both early development and later global expansion. In addition, Waltham Technologies will issue licenses for specific applications as part of longer-term revenue generation.