

**The Royal Society of Edinburgh
Gannochy Trust Innovation Award Prize Lecture**

**New Antibiotics: From the Sea Bed to the Hospital Bed
Dr Andrew Mearns Spragg, CEO, Aquapharm Bio-Discovery Ltd**

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Dr Andrew Mearns Spragg, winner of the 2007 Gannochy Trust Innovation Award, set up Aquapharm Bio-Discovery, one of the UK's leading marine biotechnology companies. He described how why the world's oceans are an exciting source of new drugs, including Obicin – a promising new antibiotic from a marine microbe found on the company's Oban doorstep.

Man, according to Dr Andrew Mearns Spragg, isn't a very good chemist. Indeed, nature beats him hands down every time. So it is to nature that he and his colleagues are turning, to find new drugs and compounds with the potential to become world-beaters. Specifically, they are looking at the world's oceans, to find ways of exploiting the vast, untapped natural resources of the under-explored marine environment.

In the Gannochy Trust Innovation Award Lecture, winner Dr Mearns Spragg described setting up Aquapharm Bio-Diversity, explained why the oceans have such potential and spoke about the company's promising product pipe-line.

Dr Mearns Spragg, (35), set up Aquapharm in 2001. From modest beginnings, it now employs 17 people in its headquarters at the European Centre for Marine Biology near Oban in Argyll. The company's main focus is on developing novel anti-infectives, including antibiotics, but is also looking at developing natural products for personal and consumer health care applications – all based on marine life. It has a library of thousands of marine microbes, which it makes available to others, and has several extremely promising compounds of its own. Its lead compound, P216cm, a pseudopeptide, is in pre-clinical trials for use as an antibiotic and its first major licence deal was signed in December 2007 – what Dr Mearns Spragg called a great Christmas present for the business. In addition, the company last summer (2007) raised six million euros in its second major funding round.

The company started from a small base, against a background of the dot.com bubble, at a time when venture capitalists were shying away from investing. After a "lot of eating baked beans" and some hard-fought fundraising, however, Dr Mearns Spragg won start-up costs through SMART (a scheme run by the Scottish Government, intended to help small businesses to improve their competitiveness by developing new, highly innovative and commercially viable products or processes to the benefit of the national economy), the National Endowment for Science, Technology and the Arts (NESTA), Scottish Enterprise and some private money. That £200,000 meant he was in business.

A strong belief in the potential of marine biotechnology has underpinned the company's birth and growth. But why should this be? "The oceans are the cradle of life," said Dr Mearns Spragg, explaining that life began in the oceans around four billion years ago. About 3.5 billion years later, only a small proportion of the planet's total biodiversity managed to evolve mechanisms to cope with living out of water, leaving a far greater proportion of life to evolve and diversify within the oceans.

The life which remained in the ocean is of extraordinary diversity, capable of flourishing in incredibly varying environments, from life-containing enzymes which live in the high temperatures of volcanic vents to those which grow in the icy Arctic. These last, incidentally, are of interest to those who want to manufacture washing powders which work at very low temperatures.

Modern exploration techniques, including deep sea submersibles, mean that ocean life, even at tremendous depth, is more accessible than ever before. And it's well-worth exploring, said Dr Mearns Spragg, pointing out that the number of rare and new compounds from the oceans is growing exponentially, with more biodiversity even than the rain forests. Natural products, he said, tend to win out when looking for new drug leads, especially when compared to man's efforts. "Nature is the best chemist," he admitted, adding that 40 per cent of the top-selling pharmaceuticals today are derived from natural products. Over the past 25 years, marine plants,

invertebrates and micro-organisms have proved to be an excellent source of natural products, possibly because of the mechanisms they have developed to survive in hostile and competitive environments. More than 30,000 natural products have been reported from marine organisms in the last two decades and Aquapharm itself has identified (from its screening) alkaloids, peptides, macrolides and polyketides.

Aquapharm is not alone. Other companies across the world have been and are developing products from marine life. One example is Salinosporamide, an anti-cancer agent currently in human trials, which was discovered in California by the US company Nereus Pharmaceuticals Inc. and another is the product Yondelis, a product derived from sea squirts for soft tissue sarcoma, which received authorisation for use by Pharmamar in November 2007 from the European Medicines Agency (EMA).

Where there is biological diversity there is also chemical diversity, says Dr Mearns Spragg, adding that less than one per cent of all marine micro-organisms have been cultured to date.

Aquapharm's library of around 7,000 marine microbes is at the heart of the business, he says. As well as finding its own product leads, the company also makes its library – and innovative screening methods (patent applied for) – available to other organisations.

Promising discoveries from Aquapharm so far include a compound with anti-ageing properties, which has attracted serious interest from the beauty industry, and a small molecule, isolated from a new deep sea organism, which acts against the cause of dandruff. There have also been promising leads in finding anti-inflammatory drugs, which could help in the treatment of diseases including rheumatoid arthritis and diabetes.

However, Aquapharm's main focus is on antibiotics, partly because there is a worldwide need for effective new antibiotics as bacteria grow increasingly resistant to those which are already available. "There is a massive opportunity here," says Dr Mearns Spragg, outlining the major challenges of healthcare associated infections, particularly Methicillin-resistant *Staphylococcus aureus* (MRSA), including those developing resistance to the current battery of drugs. "There aren't enough compounds to keep up with drug-resistance," he says. "A huge number of current antibiotics will be less valuable than the plastic bottle they are kept in by 2010."

He described the costs – in human and commercial terms – of MRSA and other drug-resistant bacteria, which are a growing problem in communities, as well as hospitals.

Worldwide there are a number of new antibiotics both in development and in use, with billions of dollars in potential and actual sales. Aquapharm is well placed to tap into that market. In January 2008, its compound, P216cm, known as Obicin (after Oban), entered full pre-clinical trials. Research so far has shown it is active against a variety of MRSAs and Vancomycin-resistant enterococcus (VREs) and has potent activity against drug-resistant bacteria. The compound has also shown antifungal activity.

Another compound, which is showing real promise for Aquapharm, is P211E, which appears to act against gram negative bacteria and so is a potential treatment for bacteria including *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*. "It's really very exciting and we're ramping it up the priority list," he says.

Dr Mearns Spragg summed up the company as one with a strong team in place, with lead compounds moving into development, out-licensing agreements on technology and products and a valuable microbial library. On top of that, the funding is there to drive Aquapharm forward and more positive announcements are imminent. "We have good investors, with deep pockets and long arms," he smiled. "Look out for some interesting press releases coming out."

Questions

He was asked how samples from the deep ocean were cultured and if they didn't simply explode when brought to the surface. Dr Mearns Spragg responded that while some certainly did – and these were too expensive to bother with – there were new techniques to bring others up slowly and keep them viable.

Asked the biggest challenge in starting his business, he said it was getting 'angels' or investors to take him seriously. Receiving an RSE Enterprise fellowship was his 'first break', he said, because it gave him credibility.

One member of the audience asked whether the oceans and marine life were environmentally protected. Dr Mearns Spragg said that some countries, including Fiji, were more protective than others and insisted on companies signing up to 'conventions' to ensure that the impact on the marine environment was minimal.

Asked if man could invent fast enough to cope with the rate of bacteria adapting to current drugs, he said it was an ongoing battle. Better husbandry in prescribing antibiotics, cleaner hospitals and multi-drug therapies would all help.

Asked how he knew which microbes to look at, he said the targets were those which were high in DNA content because they had 'more chemistry', although other microbes also had potential.

Vote of thanks

The vote of thanks was given by Dr Russell Leather, the chairman of the Gannochy Trust, who praised Dr Mearns Spragg's 'remarkable achievements' and tenacity. On a more personal note, he described his own childhood delight at looking in rock pools and marvelling at the marine life, without realising what hidden treasure lay there. He also singled out the company name, Aquapharm, for praise. "It's a gem – clear, simple and wholly appropriate," he said.

Jennifer Trueland