Interview: Ronald Scott â?? CEO, Basilea, Switzerland

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Ronald Scott, CEO of Basilea, a biotech company that was spun out of Roche in 2000, talks about launching its first two products, Zevtera and Cresemba; the milestone agreement with the Biomedical Advanced Research and Development Authority (BARDA) to develop Zevtera for the US market; and

about the companyâ??s partnering strategy for the development of its oncology portfolio.

Could you start by giving our readers an overview of Basilea, a company that was spun-off from Roche 16 years ago?

Basilea was established as a spin-off from Roche in the year 2000. We started with the full research assets of a pharmaceutical company in the area of antibiotics and antifungals. Initially Roche owned 100 percent of our shares before selling the majority of them to private investors. In 2004 Basilea went public on the SIX Swiss Exchange. We started the company with pre-clinical assets from Roche. Today we have two branded compounds that are on the market: Zevtera (generic name ceftobiprole) a broad-spectrum intravenous antibiotic which is effective against Methicillin-resistant Staphylococcus aureus (MRSA), as well as Cresemba (generic name isavuconazole), an intravenous and oral azole antifungal, both of which were discovered at Roche. Since then we have augmented our discovery platform with compounds for oncology. From our foundation we have enjoyed certain opportunities, as well as facing a number of challenges. Initially the FDA did not agree with the way our then partner was conducting certain trials with Zevtera. We have since launched other indications of the product in several European countries and just this year we reached an agreement with the Biomedical Advanced Research and Development Authority (BARDA) to develop the product also for the US market.

At the center of BasileaÂ´s portfolio strategy is resistance, considered one of the biggest issues facing healthcare institutions globally. How do you explain that so few companies are looking at tackling resistance, and why is a company like Basilea at the forefront of fighting this issue?

There is a very significant medical need related to overcoming the development of resistance. It is a continual challenge, both in the area of anti-infectives, as well as in oncology. Just as antibiotics, or other anti-infectives, lose their ability to fight a pathogen, the same challenges occur in oncology: people who are successfully treated for cancer but subsequently suffer a relapse. Part of the issue is tumors that no longer respond to, or become resistant to, cancer therapies. We are focused on this issue, where there is also a considerable medical need.

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It is true that many of the big pharma companies have moved out of R&D in the area of antibiotics. This is a multifaceted issue, which includes the manner in which pricing of new antibiotics is determined. Many anti-infectives, and antibiotics, are becoming genericized. When you develop a new product, the regulatory authorities require you to use the standard of care as a clinical comparator that may now be a generic drug. In Europe the pricing agencies consider the price of the comparator drug used in clinical trials, which, as mentioned, may now be a generic drug. Basilea is very active in looking to clinically distinguish the programs that we are working on, to be able to achieve not only good results for patients, but also an economic benefit for the company and our investors. We have a subsidiary in China that provides important chemistry work for us, in particular the group helped us in the synthesis and scale up of our antibiotic and also our other drugs . Whenever we develop a new compound, we always consider the profile of the drug that we are looking for that will allow an economic return that justifies the significant investments that are required. Luckily government agencies have, to some extent, stepped in where large pharma has moved out. Basilea works, for example, in partnership with the US government, which is paying for the majority of the late-stage development costs to bring our antibiotic to US patients. There are certain restrictions when it comes to gaining access to capital, and paying for phase three clinical trials requires considerable funding. It is extremely expensive to run phase three clinical trials, and the same is true for anti-infectives. The assistance from government agencies is now key to be able to bring new antibiotic compounds to market.

What was it about Zevtera (ceftobiprole) that the US government was prepared to invest a considerable amount of money in this project?

It comes back to medical need. Ceftobiprole is bactericidal, it kills certain bacteria including resistant Staph bacteria altogether. Unlike many other drugs, it does not merely slow the growth, allowing your immune system to then overcome the bacteria but it kills the bacteria. In certain areas it works very quickly. A challenge for the healthcare domain is in areas such as blood-stream infections, which require long treatment periods relative to skin infections. Blood-stream infections require more than a treatment of 7 to 10 days. For some areas, such as heart valve or bone infections, it can take over a month. Physicians claim that the current antibiotics may become less effective during the treatment period. If you have an infection in your heart valve and the medication is not working as effectively regarding the treatment, this is a significant medical risk. It is because of unmet medical need and because ceftobiprole may be effective against certain pathogens that may pose a bioterrorism threat, that the US government is interested in our drug. Ceftobiprole is already on the market in Europe under the brand name Zevtera. We know that we can manufacture the drug. We also have a significant amount of data related to the product from clinical trials and patients in the market. It is both the profile of the drug, and the clear medical need, that makes Zevtera attractive.

How significant was the agreement reached with BARDA to bring Zevtera (ceftobiprole) to the US market?

The US is an important market for both antifungals and even more so for antibiotics. The US represents around 20 to 30 percent of worldwide sales of antifungal medications for severe

infections. For branded hospital antibiotics it represents around 60 percent. For the more recently launched antibiotics, that number is probably closer to 70 to 80 percent. The manner in which the US treats infections is somewhat different to other countries. The US also has high resistance rates, relatively speaking, which only increases the medical need. We were very pleased to have been able to enter into a collaboration with BARDA.. Without BARDAâ??s support, we would not be able to fund the trials to potentially bring the drug to US patients.

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After the successful launch of Zevtera in several key European markets, Basilea has made public a strategy of increasing market access for both Cresemba and Zevtera. Can you give us an update on how this strategy is unfolding?

We have just started to launch our anti-fungal product, Cresemba, in Europe. It was launched last year by our license partner, Astellas, in the USA. The reception of the drug has been excellent. There is a high medical need, driven primarily by cancer patients: with weak immune systems they are most susceptible to fungal infections. There are spores all around us from fungi, and people are exposed to them in their daily lives. If you have a weak immune system, they can start to grow. Such infections can be deadly. For aspergillosis, one of the more common types of mold infections, you have a mortality rate of 30 to 50 percent with treatment. If you do not treat mucormycosis, an emerging mold, quickly with an effective drug, the mortality rate goes from 40 to 80 percent. The opportunity for such infections is increasing. With an ageing population in Europe, the US and Asia, the likelihood of patients with weak immune systems and cancers increases, driving a considerable medical need. With limited treatment opportunities, and the excellent profile of Cresemba, the drug has been well received.

In additional territories we are entering into distribution agreements. In August 2016 we reached a distribution and supply agreement for Cresemba for the Middle East and North Africa (MENA) region with Hikma Pharmaceuticals, building on a previous agreement we signed with them concerning Zevtera. We are entering into similar discussions regarding a number of Asian countries, as well as Central and Southern America and the Nordic countries. For Basilea to have economies of scale there are certain major countries that we can operate in. We have a collaboration with Quintiles, who are providing a contract sales force, helping to establish our products quickly in a number of European key countries. In other countries, where the financials do not support us going it alone, setting up our own affiliates, we are looking at distribution agreements, where we plan to make some additional announcements this year.

We are pursuing the same strategy when it comes to Zevtera. Indeed, there is considerable commercial overlap between our antifungal and antibiotic businesses. In the markets where we are located there is around 70 percent overlap between the target hospitals. It therefore makes sense for us to conclude distribution agreements that include both drugs.

Can you tell us about the development of your oncology portfolio?

When we set up the company we received the patents and pre-clinical work of Roche in the area of antibiotics and antifungals. We also received a copy of the Roche compound library. Initially we did not have the resources to focus on oncology. Eventually we started working on the compound library, while we also added to it. This was the source, through medicinal chemistry, of our lead compound in oncology. The anti-cancer drug candidate BAL101553 is developed as a tumor checkpoint controller (TCC) and is being investigated in oral and intravenous (IV) formulations. The investigational drug is being developed for the treatment of diverse cancers, including tumor types unresponsive or resistant to standard therapeutics. Our oral and the continuous IV infusion

formulations are currently being investigated in two separate phase 1/2a clinical studies in adult patients with advanced solid tumors. We plan to partner this drug prior to entering clinical phase three, although we can work on certain indications ourselves in earlier phases of clinical development. This year we plan to enter in glioblastoma studies, an area of high medical need for brain cancer. Glioblastoma is the most common and aggressive primary brain tumor, and is often associated with poor prognosis for patients.

Our other anti-cancer drug candidate, BAL3833, is a phase 1 oral anti-cancer drug candidate (panRAF-SRC kinase inhibitor) targeting cell proliferation signaling pathways that are associated with tumor growth and the development of resistance to current therapies. Basilea is developing BAL3833 under a license agreement with a consortium of organizations including The Institute of Cancer Research, London, Cancer Research Technology, the Wellcome Trust and The University of Manchester.. The strategy is to work with additional partners to help pay for the phase three clinical trials in our oncology portfolio. We are also actively looking at biomarkers. We do a lot of work in this area to be able to determine which tumor types we should enter into clinical trials. We are very proactive in this regard, focused on small molecules.

How would you characterize the Swiss biotech scene?

Switzerland has a number of excellent universities. The number of patents that are generated per capita is one of the highest in the world. The country is also home to some of the worldÂ´s largest pharmaceutical companies. There are a lot of resources, from both universities and industry, in the life sciences area, which make Switzerland a natural place to have a biotech start-up company. While the tradition of start-ups is more extensive in the US, the infrastructure required for a start-up is present in Switzerland. The country also has one of the most open markets in Europe. It is a great place to conduct business.

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While Basilea has generated a comfortable cash position, today it is still generating losses. When do you expect to see the company start delivering profits?

Our ambition is to be profitable within the next two to three years. Investors who are active in the biotech area understand both the opportunities and challenges that the industry faces.

Over the last few years we have delivered on all of our milestones: in terms of product approvals, the launch of our drugs, and partnering with the likes of BARDA. Today we look forward to delivering on our commercial objectives, generating revenue from the successful launch of our drugs, while at the same time continuing to move our development portfolio forward. The foundation of our business is the science. We started off as 46 scientists from Roche and me. Going forward, science will remain the basis of our company; using our research and development capabilities to bring new medicines to patients.

What is it that motivates you most in your job?

The ability to form a company and be able to bring new medicines to patients, where there is a significant medical need, is extremely motivating. The excellent people we have working at Basilea are another factor. While we do not possess a large infrastructure, our people choose to work with us because the environment working at a smaller mid-size company is different: you can individually really make a difference. The level of responsibility here is great, we count on each of our employees. Healthcare is an extremely complex area. I saw this first hand at Roche, where I spent a decade. Coming from the financial world, I saw how complex the development, approval, and

commercial processes can be. The area is highly regulated; you need experts to be able to optimize the opportunities that you have. Being flexible is an extremely important part of being successful. Our people are key in this regard.

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