Bertrand Ducrey â?? CEO, Debiopharm

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In a wide-ranging interview CEO Bertrand Ducrey introduces Debiopharmâ??s unique business focus on drug improvement, drug delivery, and drug targeting; recent progress in oncology, including an FDA breakthrough designation and out-licensing deal for its head and neck cancer product; as well as a host of other topics, including the companyâ??s investment fund, AI integration, and antimicrobial resistance (AMR).

Can you begin by introducing yourself to our international audience?

Currently, I am heading the life science activities at Debiopharm. I have been fortunate to have been able to build my career at Debiopharm, starting as a formulation scientist, moving on to developing and industrializing our triptorelin formulations, and finally now as CEO. Over the years I have seen the company grow from 40-50 people when I first arrived to now nearly 450. In my time with the company, we have been able to multiply our manufacturing capability tenfold and build our three innovation pillars: drug improvement, drug delivery, and drug targeting. These three remain to this day.

As CEO, I manage all the development activity, from filling the pipeline to developing drugs and out-licensing products. Two years ago, I also became senior vice president for the life sciences, covering manufacturing, development â?? Debiopharm International -, and investment, via the Debiopharm Innovation Fund. Itâ??s thrilling to see how the company continues to evolve and expand in expertise over time.

What is the scope of Debiopharmâ??s life sciences footprint today and what has changed since we last spoke back in 2017?

We currently have the strongest pipeline in Debiopharm history. Since we last spoke, Debiopharm has moved forward in cancer research with a new drug for head and neck that got a breakthrough designation from the US FDA. This has seen very promising results in terms of survival over three-year data in Phase II trials. These impressive results led to our recent out-licensing deal with Merck KGaA, Darmstadt, Germany, who will take on the development and commercialization of the product. We are currently co-conducting the Phase III trial TrilynX for head and neck cancer patients and aiming for market approval in 2024.

Since 2017 we have decided to put a strategic emphasis on *radiopharmaceuticals*. Within this we take a â??theranostic (therapeutic + diagnostic) approach which gives us the ability to both identify, treat and monitor the patient. The idea is to deliver radiotherapy safely. For that, we licensed two programs, one of which is in Phase I (debio 1124) and the other in late preclinical stage (debio 0228).

In targeted therapies, we have in-licensed an antibody drug conjugate from Immunogen (debio 1562) to develop in haemotological cancer. It is currently in Phase II trials.

Oncology seems to be an increasing area of focus for Debiopharm. Would that be a fair assessment?

It is the major pillar of our strategy. We are still working on antibiotics and anti-infectives, but we have shelved projects in autoimmune disease, for example. We have now decided on this as a strategy and the results are extremely positive so far.

Another aspect of your strategy is the â??no research, development onlyâ?? (NRDO) model. Could you explain how this works and its importance?

This is another important point. It is in our DNA to look for and assess opportunities. We assess around 500 potential product opportunities per year with the aim of in-licensing only one or two.

The NRDO model means that we are not in the market ourselves, except for a very small presence in Switzerland with our triptorelin pamoate product. Having only one product in one country helps us to understand the market realities and needs of our clients â?? pharma companies â?? and where we can add something new.

Our â??no researchâ?? maxim means that we do not engage in basic research. However, via our three pillars â?? drug delivery, drug improvement and drug targeting â?? we are able to apply research.

In drug delivery, for example, we have been very successful with the long-lasting formulation of triptorelin.

In drug improvement, when you develop a drug, you understand its liability, how well it works, and what can be improved. We have the ability to apply what we learn in order to create a different drug or to expand it into a new indication. It has been done successfully with xevinapant and the 4028

program weâ??ve just out-licensed to Merck.

For drug targeting, we invest in in-licensing, but we have developed our own proprietary technology to build ADCs called Multilink. This can be applied in-house and other companies can in-license it to allow a higher load of drug on the antibody and to load different drugs on the same antibody. Weâ??ve just announced a collaboration with Multiling and a Korean company called Genome & Company.

What profile of drug candidates does Debiopharm look for, in what stages of development, and what are some of the evaluation metrics you use?

Even if we are in constant growth, we try to have some equilibrium in the pipeline between advanced programs and early assets. While we do in-license programs or products which are currently in Phase II, our main focus is on preclinical oncology or antibiotic assets. This is because our current workload in clinical development, where we have six programs, is very high and takes up a lot of resources. We are currently looking mainly preclinical assets where we can bridge with our drug development capabilities. Debiopharm aims to see how much value it can bring to a program before it decides to in-license.

Given the highly competitive in-licencing field today, how do you ensure that Debiopharm chooses the right drug candidates?

In-licensing activity is very competitive. For new technology and promising new assets, Big Pharma is able to put a lot of money down at a very early stage. However, in specific areas we are able to see the potential of a drug earlier than our competitors. A good example is our radioconjugates, a field in which there are currently very few players. The same is true of our recent success xevinapant; with our internal scientific team weâ??ve anticipated before others the potential of this product in H&N cancer in combination with radio and chemotherapy. It was not obvious nor mainstream, but we were able to translate a promising idea into promising results. That is where we think a little bit differently.

When we develop a product, we are fully dedicated and do not have competitor products focused on the same target. The benefit of partnering with Debiopharm is our focused expertise and our dedication to each compound in our pipeline. If a start-up or small biotech comes to us to present an asset, we are dedicated to it and do not allow any competitor product into our development program, which can be a risk in larger pharmaceutical companies with several programs running on the same target.

We have a good track record, having developed two blockbusters, and one recently out-licensed therapy with FDA Breakthrough Designation. This success shows that we are able to move an asset from the preclinical stage to registration, bringing value for the licensing partner.

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Ipsen CEO David Loew told us that although some areas of oncology are overcrowded, there are niche tumours with one to five percent prevalence, equating to peak drug sales of between USD 300-800 million, that Big Pharma is not interested in. To what extent is this Debiopharmâ??s strategy?

I think we can be a little more ambitious. Some mid-sized pharma companies can find a place with products in that USD 300-800 million market size that are not first choice for Big Pharma. However, for us, our in-licensing partners could be this type of mid-sized pharma but could be Big Pharma too. For us, it is important to be clever and integrative enough to show the highest value to each asset of the pipeline and find the right partner dedicated for further development.

One of Debiopharmâ??s drugs has been given FDA breakthrough designation, what types of agreements will you go after next?

As mentioned, xevinapant, an oncology asset being developed for the treatment of head and neck cancer, received this recognition from the FDA and was recently licensed to Merck KGaA, Darmstadt, Germany. In Phase II, the compound showed very impressive results when given in combination with chemoradiotherapy in helping patients to have control over their disease and living longer. We were thrilled to reach an agreement with a partner that has such solid expertise in head and neck cancer and worldwide commercialisation capacity.

For the other clinical assets in our pipeline, we are always looking for the right partner to conduct additional studies with and bring products to the market. As of now, our focus in on two of our other oncology compounds, naratuximab emtansine (Debio 1562), an antibody-drug conjugate for patients with a subtype of non-Hodgkinâ??s lymphoma in Phase II, and our Phase I WEE1 kinase inhibitor Debio 0123 in Phase I. We always are open to aligning with potential partners and we are actively seeking them.

Taking drugs forward to commercialization can be quite complicated and risky. Thatâ??s why we go as far as our expertise brings value, then we out-license programs when we recognize that a partner company could bring even more. At some point, you need significant power to execute a lot of parallel development activity.

You have been in position for nine years; how many targets have gone into Phase III in this time? What is the success rate?

Debiopharm has been able to conduct several Phase III trials on already registered products for different indications and formulations.

The most difficult part is to conduct these Phase III trials on products which are new or best-in-class. Many doors need to be opened to access the right development path and align with the authorities. We have seen with the breakthrough designation of xevinapant that the FDA is very committed to supporting us in the development. They see the value and want us to be successful in bringing the safest and most efficient products to patients.

Developing ten innovative drugs in Phase III at the same time is not something that Debiopharm can manage. It is very important that we show strong signs of efficacy for our partners. This could be after Phase Ib or Phase II in the classical way or via accelerated approvals, which is a topic we are actively looking at and exploring every opportunity to attain.

How big of an impact has technology like AI made to Debiopharmâ??s journey so far and what do you foresee as its influence on the companyâ??s future trajectory?

We have already been using this technology for many years, but we see a potentially greater impact in the future from using AI-based technology to conduct clinical studies in a clever manner. First of all, it can be difficult to process large amounts of data. For this reason, we invested in BC Platforms, a world leader in genomic data management solutions, which specializes in data mining and data analytics. This investment helps us accelerate the speed of access to information and to gain knowledge from other clinical studies.

Another investment we made in France, Nova Discovery, focuses on conducting *in silico* pre-clinical and clinical studies. Creating this *in silico* model is very ambitious. Our vision is to reduce the number of patients in trials and avoid having patients in the comparator arm who cannot benefit from innovation directly; when we make a double-blind study, the control arm does not benefit from the innovative therapy. For ethical reasons, itâ??s important that we can find other ways in order to allow the patient to have access to an innovative life-saving treatment as soon as possible. Finally, being able to have much more access to science through *in silico* trials will accelerate development and create faster access for patients to better drugs.

Debiopharm is also active in antimicrobial resistance (AMR); is that an ethical commitment or do you see commercial potential in this field?

We see a need. In the past year we have learned that pandemics are a high risk for the global population. There is a risk within a pandemic of bugs becoming resistant to all possible antibiotics. If we were a publicly listed company it would be difficult to explain to investors the need to develop antibiotics, as it is not necessarily a financially appealing field. However, there is a need to find solutions and we consider it our duty as responsible citizens to bring forward new treatments. The current pandemic shows that when a problem arises, all actors need to work together to find solutions.

We need to anticipate that and take financial risk. However, if we take this financial risk, we need to de-risk potential bacterial pandemics, which could affect the entire population in the future. We are currently working on three pathogens considered by the WHO to be â??criticalâ??, where people are dying of antibiotic resistance and where something needs to be found. 20 years from now, if we do nothing, we will have much more, the risk of people dying from antibacterial resistance will be higher than cancer. It is important for us to be a pioneer in building an antibiotic pipeline and we hope that other companies will join us; preparing new weapons to fight with antibiotics is not a huge effort. Developing one drug is USD one billion; with ten to 20 drugs over the next ten to 15 years, we can manage that.

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Are pharma executives receptive to that message about the importance of AMR?

Some companies are sensitive to it. For certain bugs that are major concerns in developed countries, some pharma companies can see a potential benefit and value. However, we are working against gonorrhoea, which is more present in developing countries, where a solution is needed urgently. It is also present in some Western countries and resistance is a major risk in the US, but they are generally able to find a solution via a cocktail of antibiotics. Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), a global non-profit partnership dedicated to accelerating antibacterial research to tackle the global rising threat of drug-resistant bacteria, supports two of our programs and we are looking for more institutional support, but we also need more effort at the government level.

When we fight a pandemic, itâ??s not country-specific, but more a global effort. In the last four years, we are seeing a lot of nationalism, politically speaking. A clear ambition to work in a collective manner worldwide is lacking and I hope, as the US re-joins the WHO, we will see a strong international commitment to work on this. Currently, the US, which is the major player in the pharma industry, is supporting several programs. CARB-X is US-based and there are other investors there. The same is true of the Biomedical Advanced Research and Development Authority (BARDA). It is a good opportunity for Europe to build something as well.

The US was thinking of what they call the Pasteur Act, if a company reaches the market, they get one payment covering all the development costs plus some benefit. We need this new way of thinking about developing antibiotics as insurance. The best antibiotic to bring to market is one that is not overused to avoid risk of resistance. Payment cannot be made like in pharma on volume; rather it has to be considered as a service. The only medical intervention that has had a more positive impact on life expectancy than antibiotics is vaccines; therefore, we need a concerted effort to create new ones.

Debiopharm also has an investment fund focusing on digitalization and data. What is its philosophy in terms of where it invests and what it expects in terms of returns?

It is a strategic investment fund with the idea of helping us develop drugs in a better manner. The initial idea was to develop into diagnostics and biomarkers ten to 15 years ago. After that, we moved to digitalization, which we need for patient monitoring and follow-up in real life and during clinical studies.

We invested in Kaiku Health, a company based in Helsinki, and a US company called Carevive, which does patient monitoring. The idea is to add tools for diagnostics and biomarkers identification. We are currently working with two companies for digital diagnostics. One, Nucleai, is an Israeli company using AI for tumour pathology. For us that is a tool to better understand tumour type and best treatment for patients.

Given the way that Debiopharm operates is extremely global, what is the benefit of still being based in Switzerland?

We have something like 40 nationalities in our company and are quite open to people and technology. We have a stable situation in Switzerland with our facilities here and our location between Martigny and Lausanne is a very attractive value proposition for people moving here. For us it is simple to have everything in the same place and, pre-COVID, we were able to travel everywhere quite easily.

However, Switzerland is something of a Sleeping Beauty; everything works well here, and we are very well positioned in various competitiveness and innovation rankings, but we perhaps need to wake up and look more towards our competitors like the US, UK, China, and Israel. Israel really nurtures start-ups and innovation and could be a good model for Switzerland where we need to better link our ecosystem together.

We need to develop this permeability between basic research at our very good universities and the network of pharma and biotech start-ups in the country. Innosuisse is already working on this but it is not enough. A strong message has to come from the top to align everybody. If we remain working in silos, we have no chance, especially compared to big countries like the US and China. We need to have some strategic areas to align on.

Switzerland is still over-concerned about universities being influenced by the private sector and whether we should add some firewall between these actors. In Japan, the strategy now is about translational science, and taking basic research for the benefit of patients.

Switzerland is always said to be a pharma country, but we actually have very few innovations coming from here; most come from North America. Homegrown innovation is something that could be developed more here.

Additionally, we are very strong in manufacturing and precision, with a culture of watchmaking. There is a good fit for pharma manufacturing, so I hope we create more interaction linking innovation to universities, teaching hospitals, and pharma companies.

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What initiatives is Debiopharm putting in place to contribute to this much-needed ecosystem?

We will soon launch a new initiative soon called Idea-L â?? â??Ideaâ?? plus â??Lâ?? for the Geneva Lake area. With this initiative, we want to link up with universities and the world-leading teaching hospitals in Lausanne and Geneva to work together, share ideas, and provide support for the innovative ideas developed here.

We can build this strong network locally and expand that pilot to the rest of Switzerland and even more globally. Co-innovation needs close collaboration and cutting out silos, something we hope to achieve through this project.

Having access to this pipeline of innovation means that we learn a lot. It is an opportunity for us to know more about what is coming and help more academic people to push their ideas further via grants and support.

What would you like your colleagues around the world to think of when they hear Debiopharm?

Debiopharm is a networking company. We link innovation from start-ups and universities to the market across pharma. We know that we cannot do anything alone and that we need collaboration with other actors in the industry. Therefore, we are creating and developing this network.

The beauty of our model is that, although we are now approaching mid-sized status, we are not a huge organization and we can adapt quickly to change. We are a middle size company with a start-up spirit. If we want to apply new digital tools and a new digital mindset, it is easy to promote new ways of working within our company.

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