AN AUDIENCE WITH…

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GlaxoSmithKline

Last year, GlaxoSmithKline (GSK) surprised the industry with its decision to trade its oncology business for Novartis' vaccine business. But the US$20-billion asset swap made GSK the largest vaccine company in the world, says Moncef Slaoui, Chairman of Vaccines at GSK. He talks with **Asher Mullard** about the rationale for the swap, the future of vaccines at GSK, and the implications for the company's remaining discovery and early-stage development oncology programmes.

Why did you trade your oncology business for Novartis' vaccine business?

The rationale was really deeply rooted in the strategy of the company, in that we have realized that the key to success in the medium- and long-term is that you either need to be the first into something or the biggest in something. Otherwise, your chances of success at the commercial level become very low. Unless you are very strong, your opportunities to optimally capture the value you have invested for are very low. And that's why although we were being successful in the oncology field, we were being less successful with these products than if they were in the hands of others that were bigger than us in oncology.

The second part of this deal was the acknowledgement that the current pricing pressures in pharma are challenging, particularly in the oncology area. In oncology, the challenge is that the average response for a drug may be 6–12 months' extension in disease-free survival, for which industry charges very significant prices — in the hundreds of thousands of dollars. And it gets higher when you start talking about combination treatments. With vaccines, by contrast, the health economics are compelling. Nobody questions vaccine pricing or the impact of vaccines on public health. There is also an accepted tiered-pricing approach with vaccines, whereby different countries with different gross domestic products are charged different prices, to make sure that humanity benefits from the public health impact.

We ended up with what we think is really a very attractive transaction, strengthening both companies. We are very happy to see our oncology portfolio in the hands of Novartis, where I think more patients will actually get access to it. And with this deal, we are now clearly the largest vaccine company in the world, and we are very pleased with the portfolio that we have.

Our focus is now on making sure that we play the volume-pricing equation — that is, higher volumes and lower prices — in a responsible way. But this has no implications whatsoever on our investment in and commitment to innovative medicines. We are not walking away from innovation, or from developing transformative medicines.

But whereas the oncology market is booming, the vaccine market has been flat for the past few years. What does this mean for your strategy?

We are in a business that has 10–15-year cycles, so I don't think 1 or 2 years should be the benchmark. And if I look over the past 10 years, the compound annual growth rate was 17% for the vaccine business and 8% for the pharma business. So the vaccine business is a growth business.

A second important point is that the margins in the vaccine business are comparable to those of the pharma business. The cost structure is different, in that with vaccines the cost of goods are higher but the cost of selling is dramatically lower. For pharmaceuticals, the costs of goods are somewhat lower, but the costs of selling are much larger.

A third point is what I call the 'area under the curve'. Vaccines are a perpetuity business. The hepatitis B vaccine that we launched in 1988 is still reaching its peak sales, and the notion of generics is hard to see in vaccines, especially with the development of combination vaccines and the enormous capital cost associated with producing vaccines. By contrast, in oncology there are challenges around the patent cliff on the one hand and the sustainability of the current prices on the other. And oncology pricing is an enormous challenge to the health system, and we are convinced that at some time — and we don't know when that time will be — the pricing model will be significantly challenged.

How does the cost of vaccine development compare with the cost of new drug development?

It depends on what you put into the cost of development. If we include not only the costs of discovery and clinical development, but also the costs of process development and manufacturing investments, the overall cost of development is comparable. But now the risk profile is different, because in vaccines a lot of the cost of development goes into developing what we call immunization platforms. Our herpes zoster virus vaccine, for example, is built on a new adjuvant platform. And we use that same adjuvant in our malaria vaccine. And it looks like that adjuvant is also a great immunization platform for vaccines for the elderly. So although we have invested 25 years of work into adjuvant platforms, once you have the right adjuvant for a particular population the risk and feasibility of developing lots of other vaccines changes dramatically. It is much harder to put a number on the actual cost of developing a vaccine, because the first vaccine that you use to validate a particular immunization platform is going to carry most of the cost of developing an immunization platform, and then subsequent vaccines benefit.

What other immunization platforms are you working on?

One other platform uses non-replicating live vectors, which others are working on as well. That's why we acquired Okairos 2 years ago, and this platform improves the feasibility of quite a lot of vaccines that

depend on cell-mediated immunity. And if we can achieve cell-mediated immunity with non-replicating vectors, these vaccines will be intrinsically safer than those that use replicating vectors, because there won't be any risk of infecting the vaccine recipients. The first of these vaccines, which wasn't really in the original plan, is our Ebola vaccine, which is now in clinical trials.

We acquired another platform earlier this year from GlycoVaxyn that allows us to make glycoconjugate vaccines against bacterial infections. Two of our glycovaccine programmes are in the clinic. One programme is a partnered programme with Crucell and Johnson & Johnson on urinary tract *Escherichia coli* infections. The other is a *Shigella* spp. vaccine for *Shigella*-mediated diarrhoea.

Another platform is a nucleic-acid-based vaccine platform for what are called self-amplifying mRNA vaccines, which we acquired from the Novartis transaction. We are preparing to advance an mRNA vaccine into the clinic.

The theme here is that we invest in a particular platform, validate it in particular projects and then use it on a series of projects.

Beyond these platforms, new segments of the population are also opening up as vaccine recipients. Take pregnant women, for example. The highest burden of disease morbidity and mortality in paediatric medicine is between 0 and 3 months of age, before most vaccines can be given to babies and before the immune system is fully formed. But during the third trimester of pregnancy, when the embryo is fully formed, mothers are able to transfer antibodies to their babies. So we and others are working on immunizing mothers in their third trimester in such a way that the mother can transfer antibodies to their babies both through the placenta and also after birth through lactation to provide protection for a period of 3–6 months.

Another approach that is really interesting is the use of vaccines in chronic diseases that can be exacerbated by infections. In chronic obstructive pulmonary disease (COPD), for example, if you get infections from certain bacteria, you lose further lung capacity and function, worsening your COPD. So one approach we are taking now is to immunize people who have COPD against the bacteria that provoke exacerbations. The potential here is to actually have the most effective intervention against COPD progression that there is, because these bacteria are responsible for about 50% of the exacerbation cases in COPD.

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A similar situation occurs for diabetes patients, who are at risk for hepatitis B through their renal dysfunction and requirements for dialysis. There is a number of other diseases like this that could be improved by what I call chronic disease prophylactic vaccines.

Q ***What vaccine development lessons did you learn from the Ebola outbreak?***

A positive is that, remarkably, the industry was able to respond. We did in 6–7 months what usually is done in 6–10 years. And others did that too. That's good. But, at the same time, the disruption it provoked was enormous and unsustainable. We cannot have that as a model. The key learning for me is the critical need for better preparedness.

We have made quite an elaborate recommendation to the US government, to various other governments, to the Biomedical Advanced Research and Development Authority and to the World Health Organization to create a specific approach whereby GSK would make our platforms and expertise available through an institution, to be led by ourselves, to make vaccines against a long series of known pathogens and biothreats. This proposal is being discussed at a Group of 7 (G7) conference that is being held as we speak, and there is a strong interest to go in this direction. We'd make vaccines — not in the hundreds of millions of doses, but in the few millions of doses — that would allow us to move quickly and mass-produce more vaccines when needed.

We have to be realistic here. For most of these pathogens, you cannot do a clinical trial outside of an outbreak. But we could take these vaccines and stockpile them just short of having demonstrated efficacy in humans, but of course having demonstrated efficacy in animal models and having demonstrated safety. And then as soon as there is an outbreak, we can gather further evidence for efficacy.

The biggest problem, frankly, is that there are no incentives for the industry to invest otherwise. We don't know if there is going to be an outbreak. And, we don't know if there is money to be made when there is an outbreak. It is more our corporate responsibility to do this. Yet we cannot do this alone for ten different diseases. We can't sustain that. But we can make these platform technologies that we have developed for over 20 years or more available at no cost, with no licensing costs. We think we can run an institute that discovers, in parallel, two vaccines and take them from zero to Phase II trials within a period of about 3 years for a budget of $50–60 million. And this would allow us to really tackle, on an ongoing basis, about 70 identified pathogens that could potentially cause outbreaks or be used as biothreats.

Q ***Coming back to the GSK–Novartis asset swap: despite your rationale for divesting of the oncology business, you are also still running some oncology discovery and early-stage clinical development programmes. How does this work?***

Our mission is to discover either new medicines or people who will discover new medicines. Interestingly, we've found that we may not always be the best commercialization party. And therefore, once we have a medicine that has reached Phase II proof-of-concept trials, we have to ask ourselves a question: are we the best group to commercialize this medicine, or is somewhere else better suited for it? Both answers can be equally good and can provide appropriate return for our shareholders and appropriate improvements in public health. In oncology, we have a very good portfolio and great ideas, particularly in epigenetics and immuno-oncology. Honestly, if these drugs work out to be great, we will most likely partner them. If they are amazing, we may build a new approach to commercialize these medicines. We'll see.

Q ***How has this deal impacted morale on the oncology teams?***

It would be disingenuous to say that it wasn't a shock to our organization, particularly for our development organization. But I think our discovery teams have understood that it is the decisions that count and not the words, and our decisions show them that we are still investing very significantly in our discovery oncology programmes and in early clinical proof-of-concept programmes. We look forward to having some transformational oncology programmes coming out of GSK to show that this is what we meant to do, that this is what we did, and that we could deliver on our word.