Johan Van Hoof â?? Global Therapeutic Area Head of Vaccines, Janssen

> We need to be sure we are not complacent. We have to keep an eye on emerging infections and continue to invest in vaccines and other preventative health measures

10.12.2020

Tags:

Global, Vaccines, Janssen, Coronavirus, Ebola, HIV

Dr Johan Van Hoof, global therapeutic area head of vaccines for Janssen, shares his extensive career experience in vaccines; the learnings from Janssenâ??s Ebola vaccine; and his key message to the global community on vaccines.

Johan, could you start by briefly outlining your extensive career experience in vaccines?

I am a medical doctor by training, I joined the pharma industry in 1985 and I have been working in the vaccine industry since 1987. I spent the first few years at Pasteur MÃ©rieux, now Sanofi Pasteur, and then, after a short stint at Chiron Vaccines, I joined GSK where I spent ten years, including time as head of vaccine development. I joined the Johnson & Johnson Family of Companies (J&J) in 2005 as s Vice President, Data Management and Early Clinical Development. I later held roles as R&D Chief Operating Officer and Head of the Global Development Organization. In 2011, J&J acquired the vaccine company Crucell, which I headed up, and for a number of years now, I have been the Global Therapeutics Head for Vaccines.

Throughout my career, I was able to develop in-depth and hands-on experience across clinical development, QA/QC, regulatory affairs and CMC, which has been exciting and useful because vaccines is a field with a lot of interaction between the technical and clinical sides.

The global vaccines market is largely dominated by four Big Pharma players. Against that backdrop, what role do you see Janssen playing?

Our strategy is to focus on well-defined areas where we can bring new, unique and transformational vaccines to address high unmet medical needs, and in doing so, become an important vaccine player globally.

The areas we are focusing on at the moment are respiratory infections like respiratory syncytial virus (RSV) and a universal flu vaccine; a preventative vaccine for HIV, where many have failed in the past; and vaccines for bacterial diseases, because we think vaccines can be a part of the solution for the problem that is antimicrobial resistance (AMR) today. For example, we are developing a vaccine for *Escherichia coli (E. coli)*, which is a major cause of disease, sepsis and death, especially in the elderly.

How has Janssen invested in vaccine development technology platforms? Given the complexity of vaccine R&D, is it an area where it is better to have as many tools in the toolbox as possible?

We certainly want to have multiple tools in our toolbox but it is not about acquiring or developing a technology just to have it. At the center of our thinking is the disease that we want to tackle â?? we look at what we might need to design a vaccine, and then we either develop that tool internally or acquire it externally. For instance, adjuvants are something you acquire or produce based on whether it is needed within your development strategy.

For our bacterial vaccines, for instance, for *E. coli*, we are using bioconjugation, where a bacterial surface polysaccharide from a pathogen is attached to an immunogenic protein.

For other diseases like HIV, RSV and the Zika virus, we are working with non-replicating vectors, specifically the adenoviral vector type 26 (Ad26). We have been developing this for over ten years and we have accumulated a lot of experience. Across these various projects, we have seen consistent results in both antibody production â?? humoral immunity â?? and T-cell responses â?? cellular immunity. This is also the platform used for our investigational COVID-19 vaccine candidate, and while we are still at a very early stage, our Phase 1 data has also shown indications of robust humoral and cellular immune responses. Our Ad26 platform was also used in the development of our Ebola vaccine regimen, which was approved by the European Commission earlier this year. The vaccine regimen contains two doses, our Ad26 vaccine and an MVA vaccine we in-licensed from Bavarian Nordic. Through all these different projects, we have vaccinated over 114,000 people, all within a controlled clinical trial setting, so we have been able to observe and evaluate the safety profile of this platform. There is a level of confidence there and we can be reassured that the backbone of the Ebola vaccine, for instance, has been used many, many times in other people.

Janssenâ??s Ebola vaccine was approved by the European Medicines Agency (EMA) in July 2020. What are some of the learnings from this successful project?

There have been many learnings from Ebola but an important one is the value of partnerships. We formed partnerships across many different aspects of basic science and clinical research, and on the funding side, we worked with US institutions like the Biomedical Advanced Research and

Development Authority (BARDA) as well as European entities like the European Commission through the Innovative Medicines Initiative (IMI). Half of the funding came from Janssen and the other half came from public sources.

What was really important in these collaborations was to ensure that we agreed on well-described and clear goals and responsibilities with our partners. It is critical to agree on, and then adhere to, the strategy. Perseverance is also key because it takes time to reach the finish line. The EMA approval is good news, and we are continuing to work on US regulatory approval.

Applying that lesson to the current COVID-19 global pandemic, it has been incredible to see all the partnerships being formed between stakeholders in the development of a vaccine to help address the global pandemic. There has also been intense dialogue with agencies, who have been very responsive with quick turnarounds on industry questions. Other aspects like the standardization of pre-clinical model tests in conjunction with academic and research institutions, and the World Health Organization, have also been essential. The discovery of this novel coronavirus is not even a year old so it is truly remarkable to see how much work has already been done â?? and that would not have been possible without all these close partnerships.

Janssen Ebolaâ??s vaccine is a two-dose regimen. How might this potentially affect its distribution and supply chain logistics, especially in the West African countries where Ebola is endemic?

It is always logistically easier to have a single dose than two doses but we have to note that many of the vaccines currently used in emerging markets â?? with success â?? require more than one dose. Global distribution and supply chain logistics function as a well-oiled machine, with UNICEF and regional and local vaccine distribution channels and centers, and most entities are quite accustomed to a multi-dose vaccination approach. Therefore, it is a matter of leveraging those experiences and practices, not reinventing the wheel. It is not for companies to say how governments should run their vaccination programs but for me, the fact that it has worked multiple times in the past is very encouraging, and should, in my view, make it feasible for the Ebola vaccine and other multi-dose vaccines going forward.

In general, there are many considerations when it comes to vaccine supply chain and logistics. For instance, having to store a vaccine at negative 20 degrees Celsius is more compatible with existing vaccination distribution channels than having to store it at negative 70 degrees Celsius â?? which is the case for the other Ebola vaccine that has been developed â?? but even then, that challenge can be overcome. I think with the right will and planning, everything can be overcome.

Coming to COVID-19, vaccine R&D efforts have proceeded at an incredible speed, and more public and media attention has been paid to the vaccine industry than perhaps ever before. How has this impacted Janssenâ??s work?

The pandemic is unprecedented, so the enormous attention is understandable. Certainly, one of the challenges of the media hype and attention is people wondering how the industry can be advancing so quickly on vaccine development. What are the risks involved? It is important to keep in mind that, even as the pace of vaccine R&D has been incredibly fast, we have placed the safety of clinical trial volunteers and meeting quality standards in general as our priority. The timelines are a lot faster than typical but that is because many R&D aspects are being conducted in parallel where normally we would follow a sequential path to minimize overinvesting. With the urgency of the pandemic, we

understand these risks are worth taking. There has also been a lot more money and resources invested in all these efforts, including the funding of at-risk manufacturing and production, so that the industry at large is ready to begin manufacturing as soon as a vaccine is approved. Therefore, we have to remember and emphasize that no compromises are being made to safety and quality standards.

As an industry, we should always be transparent but the lesson here has been that we need to be even more proactively transparent than before. This is why, for instance, COVID-19 vaccine manufacturers have published our clinical study protocols publicly. Many pharma companies also pledged recently not to respond to external pressures to file for regulatory approval, waiting until there is sufficient evidence for the safety and efficacy of the product. We need to maintain transparency so that people feel they can understand about our R&D processes and do not perceive ongoing COVID-19 vaccine development efforts as a black box.

This is a challenge facing the entire industry, not just Janssen. We have a role to play but we are not the only ones. I think it is extremely critical to be transparent about the efficacy, the safety, and any potential side effects of any product we develop, so that the public can be informed and so that policymakers can make their decisions with the same level of transparency. Progressively, in this way, I believe we can build and reinforce trust in vaccines.

Another priority area for Janssen is the development of a HIV vaccine, which has been seen by many as the Holy Grail of the industry. What progress has been made here?

Having worked in this field for a long time, we have developed various generations of a HIV vaccine, applying the principles of translational medicine. The idea is to work with preclinical and animal models, particularly non-human primates (NHP), until we see promising levels of protection, at which moment we enter Phase 1 human trials to compare NHP and human responses. In that way, going back and forth, we have improved our HIV vaccine formulations, and a few years ago, we reached a point where one particular formulation had as much as over 90 percent protection compared to placebo vaccinated animal models. Even after six challenges, 66 percent of the NHP were still protected, which was when we started doing in-depth analyses of immune markers to see which were correlated with protection. Based on that, we could see what type of immune response was needed for animals to fall within that category of being protected after six challenges. These were animals with a certain level of antibodies and a certain level of cell-mediated immunity â?? and with those thresholds, we saw over 94 percent of animals protected after six challenges. Through our initial Phase 1 and 2 data, we saw that it was possible to also achieve those thresholds in humans, which was very encouraging. We started subject enrollment for a Phase 2b trial in high-risk women in South Africa in 2017, who have now been vaccinated and are being followed up on, and we hope to have a readout of that trial by mid-2021.

HIV vaccine development comes with a lot of risk, and we are still in the middle of the process but we are cautiously optimistic about our vaccine candidate.

With many public observers having seen the breakneck speed at which COVID-19 vaccine R&D has proceeded, are you concerned that unrealistic expectations are being set for vaccine R&D in general, for instance, with some wondering why a HIV vaccine has still not been developed after 30 years when it seems that we might have a COVID vaccine soon?

In many ways the development of a COVID-19 vaccine is easier than developing a HIV vaccine. I think the main reason there is still no HIV vaccine after 30 years is the scientific challenge. With COVID-19, we know that the majority of people clear the virus without any issue, many are asymptomatic, and only a relatively small percentage suffer serious symptoms. As a result, we know that neutralizing antibodies is the solution to clearing COVID-19, and so we were able to develop vaccines demonstrating protection in animal models almost as soon as the virus was discovered. This was fundamental.

On the contrary, almost no one clears HIV themselves. Even now, we do not know with certainty what kind of immune response is needed to overcome HIV, which makes it extremely difficult to develop a vaccine for it. There has been a lot of disappointment with HIV vaccines because the HIV virus is extremely smart, mutable and adaptable. In the 1990s, after the identification of the cell receptors that act as a gateway for HIV, many vaccine candidates were developed based on the viral envelope proteins with which they interact. However, they did not work, and the next generation of vaccines that was developed was designed to generate cell-mediated immunity. The current generation of HIV vaccines is based on the combined effect of immune responses (both cellular and humoral) which target a particular part of the viral envelope. The hypothesis is that these antibodies, with Fc related functionalities other than classical neutralization, will result in protection. Hopefully they work but if not, we will have to move on to the next generation. But it is important to remember in R&D that we learn from failure, tremendously, as we have learned additional insights each time, which has helped HIV vaccine research advance.

The other thing is that the timeline for COVID-19 vaccine development is extremely aggressive due to the nature of the global pandemic and the widespread and unrelenting impact across communities worldwide. Unlimited resources have been thrown at this on both the regulators and manufacturers sides. It is not a normal situation; looking at the workload, teams are working 24/7, which is just not sustainable in the long run. Companies could not afford to run more than one project of this magnitude and speed at one time.

Having been in the industry for over 30 years, what is a key message you would like to send to the global community?

Vaccines have been the most cost-effective health intervention in the world after clean water. Thanks to the success of vaccines, the negative effects of infectious diseases have been significantly mitigated. We need to be sure we are not complacent. We have to keep an eye on emerging infections and continue to invest in vaccines and other preventative health measures. This has been a wake-up call for everyone and we need to reflect on how we can become better prepared for future pandemics.

See more interviews