Emmanuel Hanon – Senior VP, Vaccines R&D, GSK

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In an exclusive interview, GSK's Senior VP for Vaccines R&D Dr Emmanuel Hanon discusses how the sharing of GSK's adjuvant technology with a wealth of scientific institutions and companies globally can contribute to the rapid development of a safe and effective COVID-19 vaccine. Dr Hanon outlines the challenges inherent in manufacturing potential vaccines at scale and bringing them to market, as well as where the vaccine industry stands today in terms of innovation and public perception.

What resources is GSK investing into tackling the COVID-19 pandemic and what is your role in the global race to find a vaccine?

The strategy that GSK has pursued from the very beginning of the crisis has been to focus on collaboration. It is a strategy based on bringing together the strengths of the various players within the vaccine industry and other expert organisations. One of GSK's key expertise areas is the adjuvant technology. Here in Belgium we have been working for over 20 years on discovering a series of substances – adjuvants – that we use in our vaccines to impact their potency. That impact can lead to an enhanced immune response and longer protection after the vaccine has been given.

In a pandemic setting, another important impact of the adjuvant technology is its antigen sparing potential. Indeed, the antigen quantity – the identity card of the virus that is put into the vaccine – can be strongly reduced whilst still getting a sufficient immune response. With that approach we

can significantly increase the quantity of vaccine doses produced, contributing to protecting more people.

This is why – starting at an early stage of the COVID-19 pandemic – we have made our adjuvant available to several scientific institutions globally. We have several agreements in place, including one with Sanofi, another important vaccine manufacturer, and others in Asia, Europe, and North-America. We hope that this combined effort will lead to a number of successful COVID-vaccines that will use our adjuvant becoming available for people around the world at significant scale.

How big a challenge is the development of a COVID-19 vaccine for the industry?

It is important to note that finding a vaccine is only one part of the task at hand, one that is complex and important, but it's not the only part of the process. We are in an unprecedented situation where, at record speed, we need to discover a vaccine that works, demonstrate that it is safe and effective, and be able to produce it at a large scale. There are more than seven billion people on the planet and the virus will continue to circulate unless people are immunised against it with an effective vaccine. The only way to achieve this is either through a very efficient vaccine or allowing everyone to get infected and thus build what we call "herd immunity" in the population, which could have devastating consequences given the death rates of COVID-19.

The major research, development and industrial challenge facing the vaccines industry in parallel to the actual development of vaccine candidates, is to be able to produce billions of doses of safe and effective COVID-19 vaccines.

How useful are previous experiences with other coronaviruses such as SARS and MERS in the race to find this vaccine?

This is one of the reasons why the vaccine development against this specific coronavirus is proceeding more quickly than standard timelines. On average, it takes between 10 and 20 years to discover, develop, get approval, and commercialise a new vaccine. However, some companies have projected timelines of 12 to 18 months for a COVID-19 vaccine to become available, or even earlier. This might be – in part – possible thanks to the research that has been done over the past decade on SARS and MERS coronaviruses. The research has helped scientists to understand which antigen needs to be put in the COVID-19 vaccine, which is a process that can take up to 10 years for other pathogens.

The second reason that time will be saved is the ongoing intense collaboration across the industry, academics, governments, and regulators to find ways to accelerate the review of the file and the approval to start clinical trials whilst applying the high standards of patient safety.

Thirdly, there are a lot of people getting infected and getting the disease. Usually, the situation is not so intense and fewer people are infected when developing a vaccine against a disease that is not in a pandemic state. Therefore, the duration of trials can take several years. However, some COVID-19 vaccine candidate trials are projected to last just a few months. With a lot of cases, these trials will be in a better position to demonstrate the vaccine's efficacy.

How difficult will it be to bring a vaccine to market that is efficient but also safe?

There needs to be data on this generated from independent sources. It is not a company alone that decides to make a vaccine available. Independent regulatory authorities assess the totality of data generated and the risk-benefit balance, assess and document the side effects observed in the clinical trial versus the efficacy of the vaccine in preventing severe disease and hospitalisation. The regulatory authorities will finally approve (or not) a vaccine for use.

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The second aspect is information. It is the role of vaccine experts and authorities to communicate about vaccines and what they represent. Not one vaccine is 100 percent efficacious or has no potential side effects at all. People need to understand that it is a risk-benefit balance. The responsibility of the manufacturer is to thoroughly document the information he collects in his clinical trials. Transparency is critical for GSK and also applies to other companies in the pharma industry. The distribution of the vaccine at a super large scale is going to require a lot of communication and information to the public to understand the benefits and risks of a vaccine in a factual and science-based way.

The real challenge will lie in the production of this vaccine. What will need to be implemented to ensure that production of the quality and scale necessary can be launched?

In this unprecedented situation manufacturers are not competing against each other but are instead all competing against the virus. It will be great news for humanity if several companies are able to deliver successful vaccines. There are billions of people that will need to be immunised.

Both existing and new innovative platform technologies are being used to develop and produce future COVID vaccines.

Existing platforms benefit from significant infrastructure (e.g. manufacturing capacity) established which can help in producing doses at scale. Several vaccines have proven to be effective and safe with the existing platforms. The collaboration between GSK and Sanofi falls into the existing platform category.

Several players using new technologies are working hard to develop potential effective COVID vaccines, often in partnership with governments, universities, and other organisations. This is very encouraging and increases the chances to find several effective COVID vaccines that will become available for people around the world.

For the past few years, the voice of the anti-vaccination movement has been gaining a lot of traction globally. Could COVID offer a one-time opportunity for the pharma industry to send a message about vaccines? What does pharma have to do to get the message right?

The role of companies is to research, develop and manufacture qualitative vaccines. We need to generate as much data as possible, make this data available for full assessment, and the summary of that assessment has to be made available to the general public.

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I believe there is better awareness of the importance of vaccination and the huge impact infectious diseases can have on people, societies at large and the global economy. We all experienced it during the global pandemic where there is no vaccine available. However, trust in vaccines and vaccination will always remain an important point of attention. Even before COVID, we saw a worrisome resurgence of vaccine preventable disease such as measles, due to complacency or decreasing confidence levels.

At GSK, we are committed now to develop and manufacture, in partnership, vaccines that have an acceptable safety profile and will help prevent COVID, frankly at unprecedented scale and speed. That is our contribution. Authorities have a very important role to make sure people understand the importance of vaccination, the potential risks and also their approach to manage the COVID situation, including when vaccines will be available. This might differ from countries across the world.

Over the last three months, I have been trying to predict what will happen, but it has been a difficult task. Whether this will be an opportunity or challenge to address vaccine hesitancy, we do not have a choice. We need vaccines to tackle this global health crisis, and we need to do the maximum we can, including ensuring that everyone is informed properly in an understandable way, where journalists also have a role to play.

What has been the impact of the crisis on how you organise your work at GSK vaccines? Will there be any long-term changes because of it?

The vaccine division has been defined as a critical business, so we have continued to work effectively throughout this pandemic. We are producing millions of vaccines every day that are saving children around the world. 70 percent of our vaccines go to developing countries.

We continue to work while respecting the safety of our people, this is crucial as our mission is to protect people around the world from vaccine-preventable diseases – also and especially in times of a global health crisis. We have implemented measures to manage the distancing required and our way of working in the future will undoubtedly be different. I believe that the post-COVID world will be a different one from our world before this pandemic, we might never go back to where we were before. Society is undergoing a huge change in terms of behaviour and how we work.

In 2014, a major product swap between Novartis and GSK saw a lot of analysts predicting a gloomy future for GSK, with many doubts about GSK's portfolio strategy. However, since then, GSK's vaccines portfolio has outpaced the company's more traditional pharma portfolio in terms of growth. How are you aiming to continue that success story in terms of technology as well as therapeutic fields of focus?

Firstly, we work very closely across GSK R&D and collaborate with our colleagues in the pharma organisation as we have complimentary expertise that is hugely beneficial for both parts of our

organisation. The big differentiator for us versus others has been and it will continue to be innovation: investing in the future, finding new platform technologies that can be applied to more diseases and will allow us to enter into new fields. The two new fields that we are prioritising are therapeutic vaccines and antimicrobial resistance (AMR).

Most vaccines used today prevent the appearance of a disease in the population; vaccinating people before they are exposed to a pathogen. For example, flu vaccines are administered to patients before flu season. Therapeutic vaccines on the other hand have the ability to treat an ongoing disease or to prevent the cyclic evolution of that disease. GSK has several vaccine candidates in our platform that have this property. Our vaccine preventing shingles is one example and has 90 percent efficacy, across different ages. It is administered to people many years after they have been infected by the virus and is still able to recalibrate the body’s immune system against the virus so that it never comes back, or at least does so with very low frequency.

We have another set of vaccines in our pipeline which target RSV – a virus that causes respiratory disease. It can become a very severe disease and we are working on protecting children and older adults with three different vaccine candidates in development.

The other field of huge interest for GSK is AMR – antimicrobial resistance. We realise how dramatic it is to be faced with a pathogen for which there is no treatment. Multi-resistant bacteria such as tuberculosis or gonorrhoea are progressively accumulating resistance to traditional antibiotics. There is a huge complementary intervention that can be made using vaccines. Vaccines can be used to prevent certain infectious diseases and thereby prevent the use of antibiotics, as well of the misuse of antibiotics, for example for flu. This way, the development of antibiotic resistance is slowing down.

It is already well documented that resistance does not develop, or at least develops much slower, against vaccines. That is another really interesting avenue to investigate.

What are some of the most important recent innovations in vaccinology?

Over the last 20 years, we have seen the introduction of new platform technologies. This means working on a certain vaccine approach and, once you have collected the learnings of that approach, you can apply this to different pathogens and create a family of vaccines. This is what we have done in Belgium with the development of our adjuvant technology, where we use a given adjuvant in several different vaccines.

The benefit of a platform technology is that you make the investment once, but it benefits a variety of vaccines.

The other up-and-coming technology in vaccines is messenger RNA vaccines. The fundamental change with this technology is that the process of creating these vaccines is extremely fast. In messenger RNA, the antigen – the identity card of the virus or bacteria, a genetic code – is able to be programmed, somewhat akin to 3D printer. The body produces its own vaccine as the body's own cells will produce the antigen that can react against a pathogen, leading to the immune protection.

Another reason why messenger RNA manufacturing is so quick is that the manufacturing process of a molecule for a given vaccine does not change depending on which molecule you produce. In other words, your manufacturing site becomes a multi-antigen manufacturing site, instead of having a manufacturing site for one antigen only (as it is the case for more traditional vaccines). Companies working on messenger RNA are first to enter into clinical testing for a COVID-19 vaccine candidate. However – to date – no messenger RNA based vaccine has been licensed for any disease.

That allows for major economies of scale in the investment needed for vaccine development. We have the messenger RNA technology in house, but our strategy to develop a COVID-19 vaccine is to use a well-established platform. By doing this, we have potentially higher chances of success but will also be able to produce many doses of a successful vaccine. It does not, however, mean that we are not investing in messenger RNA technology, which we believe represents the future of vaccines.

How far away are we from the widespread emergence of personalised vaccines and to what extent does this represent a revolution in terms of business models for the vaccines industry?

The notion of personalisation is a hot topic in the pharma industry today. Smartphones with health checks drive behaviour, and consumers can easily buy microbiome tests that provide information about the myriad of bacteria and viruses in your gut. Every day a publication links a specific bacterium in your gut with a specific chronic disease.

There is a possibility that in the future, the population will be fragmented into mini populations with specific criteria defined either by mobile application or by specific diagnostics to be done at home.

These might trigger specific behaviours and, among this behaviour, the use of a vaccine may make sense.

GSK is not, today, pursuing personalised vaccines to this extent. Other companies use messenger RNA technology to move quickly between the genetic part of a pathogen and a vaccine candidate. They may be able to use the technology to make vaccines tailored against for example cancer in a patient. This is a powerful example that I would call personalised vaccination. There are still a lot of challenges in this field, but it is not impossible.

You have advocated for better planning and forecasting from the health industry on purchasing, which could be an incentive for pharma companies to reinvest in vaccines. How?

> We cannot easily predict epidemiology, but it is important to plan demand and understand countries' needs when making a vaccine for a given disease.

Most vaccines available today are recommended by public health authorities. If they get approval by the regulatory bodies, but are not recommended or funded by the public health authorities, they might not be used and this eventually could mean 10 to 15 years of R&D wasted – to say it bluntly. We see big differences across the world but also within Europe across national immunisation programs on how new vaccines are introduced, or existing vaccines extended to other age groups such as elderly people.

We have frequent interactions with leading experts in Belgium and universities to understand what society's medical need is going to be for a specific intervention. But this is not trivial – even with the sophisticated insights and models we have today. Nobody would have predicted that we should have made a coronavirus vaccine one year ago, but that is completely evident today.

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What is the importance of Belgium within the GSK group? What functions are carried out in the country and why does it still make sense today to locate them in Belgium?

Belgium is quite a unique place in terms of science and technology. There are many universities in Belgium, and many have a lot of experience in vaccine development. Several vaccine companies from the US come to Belgium to conduct clinical trials. GSK Belgium today has 17 scientific collaborations on vaccine clinical trials with Belgian research institutions.

The headquarters of GSK's global vaccines division is in Belgium and more than 9000 of our employees work across our three sites in Rixensart, Wavre, and Gembloux. Within our global network, we produce around 2 million vaccine doses every day that go to over 150 countries. In 2019, we invested one billion euros in R&D and, over the last 10 years, we have invested three billion euros in Belgian infrastructure. Our site at Wavre is the largest single concentrated vaccine manufacturing site in the world. GSK is a heavyweight in terms of vaccine R&D and Belgium is at the heart of that.

The recent creation of an anti-infectious unit for human challenge studies by Professor Arnaud Marchant (ULB – University of Brussels) and Professor Pierre Van Damme (UA – University of Antwerp) is another sign of the level of expertise the Belgian university environment has to offer. The political environment is also supporting this as they are investing in this public-private partnership. This is enabling the discovery of new vaccines together with the strong industry knowledge and capabilities we have in Belgium.

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