Vaccines business overview

Dr Moncef Slaoui

Good afternoon everyone. I am Moncef Slaoui, Chairman of GSK Vaccines. I have been with GSK for 27 years, most recently as the Global Head for R&D over the past eight and a half years.

My presentation today is going to be in three parts. In the first part I will quickly give a broad introduction to the Vaccine business in general for those of you who may not be very familiar with it. Then in the second part I will give you some specifics about the GSK Vaccine business and an analysis of its performance over the past 10 years and how, using that, we extracted learnings that have allowed us to define our strategy going forward.

Then in the last part I will tell you about our ambition for this business over the next five years, where we expect to grow our top-line in the mid to high single digits and achieve a margin clearly north of 30%.

Starting with a broad overview.

The Value of Vaccination

Vaccination is by far the most impactful intervention for public health after clean drinking water. Therefore its value-add is undisputed. Many different segments of the populations are vaccinated. The one we are all familiar with is infants and toddlers, but there are also very important segments like adolescents, adults, within adults there are a number of at-risk populations like healthcare workers or travellers and others, and then the elderly population.

When you look into it all these segments, some of which are covering many birth cohorts, are growing significantly. Just as an example it is projected that we will have more than a billion people aged over the age of 60 by 2020.

There are also a number of very important diseases for which there is a need for vaccines. You can see them on the slide there. Some of these vaccines may help define new segments for immunisation in the population and I will be hinting at that later on my presentation.

Vaccines is an attractive business

If I look at the performance of the global business in general it has experienced quite a significant growth over the past 10 years at a CAGR of 16 or 17%; clearly double that of

the pharmaceutical industry. It is now at about £17 billion in sales and, as Andrew said, there are only four major players in this business and the reason for that is barriers to entry.

You can see on the slide also that GSK post-transaction is clearly in the lead with 27% market share. The barriers to entry in this business relate, for example, to the levels of capital investment required prior to having Phase III data; very high risk investments. If I take pneumococcal vaccine that we have developed, *Synflorix*, we invested almost £400 million before we had the first Phase III data available to us.

Complexity of manufacturing is another very significant barrier. If I take again *Synflorix*, it takes 24-28 months to release a batch. It takes 550 quality control checks before you are able to release a batch. Trust me, you have 550 opportunities to fail your batch; very complex.

Finally, combination vaccines are very important. If you take infant vaccine, combinations are a critical means to enhance coverage through immunisation and in the pertussis area. If you don't have five or six vaccines combined in one shot, you can't enter the game. Significant financial portfolio and technical barriers to entry, which explains why there are very few players and very few players are able to enter this game.

In contrast to the pharmaceutical business, intellectual property plays partly the same role and a different role. It is the same role because of course, for freedom to operate you need to have your patent coverage, but in contrast to the pharmaceutical industry there is no patent cliff, there is no cliff upon patent expiry. The vaccine business is a very long term, very sustainable business where life-cycle management plays a very important role. As a consequence for that, for instance, if I take our R&D budget in GSK Vaccines, about 50% is allocated to active life-cycle management and the other 50% to new product discovery and development.

Finally, maybe not familiar to all of you, but it is a good, profitable business with profit margins comparable to those of the pharmaceutical industry. A very attractive, very long term fundamental growing and good profit margin business with undisputed value-add to society.

GSK Vaccines: a snapshot

If I move now to the second part of my presentation and give you a view about some nuggets on GSK Vaccines. GSK Vaccines was founded in 1947; it was a biotech company and it was acquired in 1968 by Smith, Kline & French. I joined the company as a bench scientist in 1988. I was employee number 602 globally. Today we are 16,000, inclusive of the Novartis transaction. We have about 2,000 scientists in the organisation, spread over

seven sites across the continents, the Americas, Europe and Asia; very productive R&D between the two companies – 14 new vaccines approved over the past 10 years, by far the best-in-class and a very broad footprint for manufacturing; we have 14 manufacturing sites, again in the Americas, Europe and Asia, producing last year 850 million doses of vaccine, in certain years more than a billion doses of vaccine. We are commercially present in 177 countries, thanks to the fact that we are part of GSK and to the fact that vaccines are commercially distributed through our pharmaceutical organisation, as Abbas, our President for Pharmaceuticals will describe to you and, as Andrew told you, it is a capital intensive business. We have invested a little bit over £4 billion over the past 10 years in maintaining and enhancing our supply network.

Strong track record of growth

If I now look at our performance over the past 10 years you can see that the business grew its top-line at a CAGR a little bit north of 8%, more than doubling the top-line excluding the Novartis participation. This growth took place despite the fact that we have a significant gap in our product portfolio in the US; I'll describe that to you in a minute. The US has been by far the biggest contributor to the growth of this market over the past 10 years. The growth also took place despite self-imposed constraints in the supply of certain of our vaccines because we have made the decision to be very proactive in investing and enhancing our network, our supply network, our manufacturing processes to make sure we meet and exceed the ever growing regulatory requirements and make sure we don't end up having significant vaccine shortages, as have happened with others because of regulatory actions; significant growth. I will tell you more about our US product portfolio.

Broadest vaccines portfolio offering worldwide (pre-transaction)

This is our worldwide portfolio comparing the GSK portfolio to that of our competitors and you can see the portfolio organised by segments – paediatric, adolescents, etcetera and you can see we have a very broad, the broadest portfolio in the industry.

Broadest vaccines portfolio offering worldwide (pre-transaction)

If I look at our portfolio in the US, you can see that we have two significant gaps – we have a gap in the paediatric segment, where we are lacking the measles mumps rubella vaccine – there is a "P" next to that because it is a product in Phase III trials – I'll tell you about it in a minute. We have a gap in the paediatric portfolio because we don't have a pneumococcal vaccine approved in the US: we have it outside of the US. We also have a gap because we don't have a meningitis vaccine in the US, where we have it outside of the US. In the adolescent population again, clearly, we have a gap because we are lacking the meningitis portfolio in the US.

Clear opportunities for growth going forward because when we have the products approved in the US, we have a really good commercial performance with *Pediarix* in the pertussis arena, we are first in market share. With hepatitis we are by far first in market share and with *Boostrix*, for instance, we are second in market share. *Cervarix* is an exception; we have an uncompetitive product label and therefore we have a very small market share. Clear opportunity for growth by focussing on product approvals in the US, both existing products and new products.

Vaccines business

We extended our analysis of the performance of the business over the past 10 years to see how do we score vis-à-vis what we believe to be the key success factors for a vaccine business in general. We believe there are six key success factors for a vaccine business; you can see them on the left-hand side of the slide: supply sustainability, supply predictability, supply reliability are critical to all the stakeholders, critical for the success of the vaccine business.

Achieving recommendations for mass vaccination are critical for penetration of new vaccines. Having the breadth of portfolio in each one of the segments of the population is critical because there is significant synergy between the products within the portfolio. Having the breadth of the geographic footprint to be able to generate the kind of volumes that allow us to then play appropriately the price volume equation is critical in this business. Of course, like all innovation based businesses, having a productive R&D organisation and, in this case specifically, an organisation able to run clinical trials that sometimes include 100,000 subjects across the world, is very important. We score ourselves as, humbly, best-in-class in five out of the six business critical factors. We are very good on the sixth one, ex-US – we have room for improvement and an opportunity for growth in the US with our product portfolio.

Our strategic focus

This has helped us define our strategy going forward. Our strategy going forward, as we established last year, relies on five key pillars. One, reliability of supply – invest to have reliable, predictable supply. Two – succeed in the US with our existing products and new products, achieve approval and achieve competitive labels. Three – bolster our innovation pipeline with particular focus on success in the US and worldwide. Four – enhance our pool of talent, again particularly the kind of talent that will allow us to succeed effectively in the US on product approvals and finally, laser sharp focus on execution of the strategy. Those are the five key pillars of our strategy and the Vaccine Executive Team is absolutely focussed on them.

Our strategic focus

Importantly, if you look at the Novartis transaction, it squarely catalyses an acceleration of the key pillars of the strategy.

We have been very pleased since March 2 to have the first view at the manufacturing network of Novartis and I can tell you because of the challenges they have had early in the 2000s with the regulatory agency, significant investment has been made and everything we have seen we are very pleased with.

Clearly the addition of the Novartis portfolio enhances and allows us at least partially to close the gaps we have in the US; I will show you that in a second. Then through the presentation you see how it also accelerates the two other key pillars of our strategy.

Strong portfolio synergy post-transaction

I am going to now show you the impact on the product portfolio. In red you can see the new products from Novartis. Immediately *Menveo*, which is the only meningitis ACWY combination vaccine approved in the US for the two months and above population, it immediately provides us with a vaccine that nobody else has in their portfolio for the paediatric segment and clearly filling the gap in the adolescent segment with both *Menveo* and *Bexsero*, the meningitis B vaccine indicated for adolescence in the US.

Key focus areas for 2015-2016

We will now move to the third part of my presentation, to share with you our plans and ambitions going forward between 2015 and 2020. I elected to slice it into three periods: 2015 and ’16, short term, ’17 and ’18, mid-term and ’19, ’20 and beyond, long term.

Starting with 2015 and ’16 we have three critical areas of focus; three critical things to achieve. First we need to succeed with the Novartis integration. It started on March 2 and I can tell you we are pleased with the progress, we feel confident we will be able to deliver on the £400 million synergies extraction that we committed to and, as Andrew said, this will be achieved by 2017; in fact 50% of that will be achieved by the end of 2016.

We have already integrated the first two layers in senior leadership of the organisation and, importantly, 40% of the second layer of the new GSK Vaccine organisation comes from Novartis. This gives you an idea on how quickly and how remarkably we have been able to access a very experienced talent pool of vaccinologists from all dimensions. We have already almost achieved the integration at the commercial operations level in the countries and advanced our integration at the manufacturing and supply level, but only at the above site level, like engineering or quality, not at site level because we have decided not to

create any disturbance to the reliability of supply into the sites. We are going to take our time to understand how best to do it and of course we will do it.

Then we have taken the opportunity of the transaction to transform GSK Vaccines R&D. We have created now three major centres in this R&D organisation. A centre based in Belgium, which will be mostly focussed on viral vaccine drug discovery and development, and that is an area of historical strength of GSK Vaccines. A centre in Siena, Italy, that will be mostly focussed on discovering and developing bacterial vaccines and that is an area of historical strength of the Novartis vaccine company.

Vaccines global R&D centre in US

Finally, a new centre based in Rockville in the US, Maryland, that will be our new third global centre for vaccines discovery and development. It will integrate all R&D activity that existed in the US and enhance them from bench work in discovery all the way to active life-cycle management.

The centre will be focussed – there is a picture of it here – on vaccines that are aimed at succeeding in the US. They may be only US specific or they could be for worldwide basis, but they will be driven and developed by teams in the US. We believe that this location will allow us to attract the best and the brightest of scientists from the huge talent pool available in the US. We believe that this location in Rockville, a few miles away from key stakeholders, from the FDA to the NIH, to other stakeholders, will help us better define and understand the criteria for effective, efficient development of vaccines that will be approved and have the appropriate labels.

This centre used to be the HGS facilities in Rockville, Maryland. We have recycled it for our vaccine organisation. This will be a cornerstone to our US strategy to succeed. We have already started to execute on it.

Proactive upgrading of supply network

The second key focus in 2015 2016 is to continue to invest to upgrade our manufacturing network and manufacturing processes to make sure we continue to comply and exceed regulatory requirements. It comes at a price; the price is a certain level of constraint in the supply of certain vaccines – pertussis containing vaccine and hepatitis A containing vaccine; this constraint will lapse beyond 2016. You can see on the picture there our new pertussis vaccine facility built in Belgium that will start to deliver commercial products in 2018 or 2019.

Key growth drivers

Finally, the third critical area of focus, of course, in the short, mid and long term is to drive the opportunity with the Novartis portfolio in particular, but also the whole portfolio of GSK vaccines, provides us through the commercial operations we have. We see low single digit growth in 2015 at the top-line, driven primarily by the Novartis meningitis portfolio and traveller portfolio and within that primarily *Menveo* in the US and Europe, *Bexsero* primarily outside of the US because of the highly restricted indication currently we have, and *Synflorix* and *Rotarix* vaccines outside of the US or our flu quadrivalent vaccine in the US.

In 2016 we see an acceleration of the growth of the top-line to the mid-single digit, driven primarily this time by, of course, the momentum behind the products I cited, but also the expected enhancement of the adolescent indication for *Bexsero* in the US at the ACIP that will be meeting in October. A good start to the period.

Key growth drivers

If I now look at the next period, 2017-2018, we see an acceleration of the growth at the top-line to the mid to high-single digits, that will be driven by the momentum behind the meningitis portfolio and the traveller portfolio, the momentum behind *Rotarix* and *Synflorix* and the flu quadrivalent, but importantly also driven by the new product launches that will characterise this period.

We will be launching three new products: one I am not going to expand on, but it is a world first and a demonstration of our technical capabilities, which is the malaria vaccine. The second one is the measles mumps rubella vaccine combination in the US; I told you about it before. It is a product that is in Phase III trials. We are going to file it in 2017 and launch it in 2018 in the US. It is a very important product because it will not only participate into our top-line, but also clearly the leverage it provides across the rest of our paediatric segment.

***Shingrix* HZ(su): Significant opportunity to prevent herpes zoster**

The most important of our product launches is *Shingrix*. Andrew already told you a little bit about it. This is a vaccine against shingles, or zoster. This is a disease that goes by the same virus that provokes chickenpox in children and we have this disease when our cell mediated immune system is waning down or affected. It can be depressed through medication, like in cancer patients with chemotherapy or through infections, like in aids patient, but more commonly, just through ageing. In fact from the time you are from 50 years of age and beyond your risk for shingles starts to increase. Every 10 years that risk doubles. By the age of 90 30-40% of people will have experienced shingles. Across four decades of birth cohorts, the risk of shingles increases. It is an enormous medical need to

an enormous population. I told you this population in the above 60s will be above a billion by 2020.

Our vaccine is based on a platform science that we have invested in for 25 years now, which is the adjuvant technologies. In fact, what made this vaccine successful, which is the adjuvant AS1, is the same adjuvant that we use in our malaria vaccine in a different dosage. That adjuvant is used in six week old newborn babies. It is the same adjuvant we use in here in a different dosage; twice more concentrated here.

Thanks to this technology, as you can see in the paper we have published in the *New England Journal* last week, we have achieved remarkable efficacy, above 97% across the age brackets – everybody above 50, but also in the above 60 and the above 70 and in the above 80. It is remarkable because the currently exiting vaccine, which is a one dose live attenuated vaccine, achieves about 55-60% efficacy in the younger elderly, but efficacy went down to the 30% in the 70 years old and beyond and it is counter-indicated in those who need it the most, the immunocompromised individuals, so a clear almost doubling of the effectiveness of the vaccine with our shingles vaccine.

It comes at no price in terms of safety. We have no imbalance in serious adverse events with this vaccine, as you can see in the publication and we have an acceptable tolerability at the injection site and at the time of immunisation.

This vaccine is going to be filed in 2016 in the US, Europe and Japan. We have two still ongoing Phase III trials, one in 70-plus year old individuals to bolster our claims in that population that needs it the most and one in immunocompromised where we can have an indication because our vaccine is a recombinant, not a live attenuated vaccine.

In terms of the size of the commercial opportunity all I'll tell you is the current vaccine with its very limited efficacy, which then results in very limited penetration, only 7 or 8% of the population who needs it got it. It sold $868 million last year in the US. We have significant expectations for this vaccine.

If I look now still beyond this period, but starting in '17/'18 to our pipeline development, what products will be entering late state development? I am excited to share with you three products that will be in late stage development during this period and we will be launching early in 2020 or slightly later.

The first one is a combination of *Menveo* and *Bexsero*, that provide a vaccine that covers meningitis ACWY, so you have to really know your alphabet, and it is really a vaccine that we will be the only company able to have that vaccine in the foreseeable future. We are the only ones that have the two components required. It is a vaccine that is important

because it carries the possibility to provide the meningitis B universal mass immunisation indication. Today *Menveo* has universal mass immunisation recommendation in the US. *Bexsero*, the meningitis B doesn't have it yet; we don't expect it to have it in October, we will expect a broader indication than today, but not a full universal mass immunisation. This is a very significant opportunity to increase our market share and improve the penetration of the meningitis immunisation.

The other vaccines that I would like to tell you about will be entering or in late stage development in '17, '18 and beyond are the group B strep vaccine and the RSV vaccines. These are two diseases that are extremely deadly and with very high morbidity in very young infants. In fact, the highest risk is from the day of birth through about eight to 12 weeks of age. The only way to immunise effectively neonates in that age bracket is to immunise their mothers during the third trimester of pregnancy. We know for these diseases that having antibodies gives you protection and we know if we immunise, if a mother has higher titres of antibodies she will transfer those antibodies to her baby, either through the placenta and later through breast feeding.

We have completed Phase I trial with our RSV vaccine; we are very pleased with the outcome and we are preparing to enter Phase II studies in pregnant women as we speak. We are in advanced Phase II development with the group B strep vaccine which came to us through the Novartis transaction.

We believe that these vaccines, once available in the 2020s, when combined in our portfolio with the *Boostrix* vaccine and the quadrivalent flu vaccine, two vaccines for which there is already a recommendation for vaccination in third trimester pregnant women, we will create a critical mass of vaccines targeted to this potential new segment in the population for immunisation, a segment by definition equal in size to that of the birth cohort, paediatric segment and with extremely high awareness for good health. A significant opportunity for growth beyond what I have described to you with our products.

Key growth drivers

If I sum up, looking at our growth opportunities in the top-line we see that from 2015 onwards to 2020 we expect overall a mid to high-single digit growth at the top line, roughly we think about a third of that will come from our new product launches, principally *Shingrix*, roughly a third of that will come from the meningitis portfolio and to an extent the traveller portfolio acquired from Novartis and roughly a third of that will come from the GSK legacy products, particularly *Synflorix*, *Rotarix*, *Flu QIV*, etc.

Now because this is over a period of four and a half/five years, there clearly are sensitivities I would like to share with you – two sensitivities. One is around *Pediarix* sales in

the US, which may be impacted by the approval of the hexavalent pertussis vaccine from Sanofi that may be approved in the fall, or later. Depending on when it is approved and critically depending on the label this vaccine will have, particularly in terms of fever in infants, it will have an impact on *Pediarix*, we have taken that into account, so it can go upwards or downwards.

Secondly, clearly, the uptake, the speed of uptake, access and penetration of *Shingrix* is also something that can have an upward or a downward impact on the overall perspective, but we feel confident we are able to achieve the kind of digits I have just told you about.

Margin improvements

If I now look at our bottom-line you can see that we are starting from a point with the integration of the loss making business from Novartis that has been challenged vis-à-vis where we stood before, and I know Simon will be telling you much more specifics around that. From 2015 and onwards we see an accelerating improvement in our operating margin, driven by the three principal cost lines: significant improvements on the cost of goods lines related to the increasing volumes in our new product launches, significant improvement on the R&D line relative to the sales line because of highly disciplined investment decisions in R&D and a significant improvement on the SG&A line because of the leverage as compared to the pace of growth in the top-line. We expect to achieve margins clearly north of 30% by the end of the period in 2020.

We also expect to continue to invest capital investments to enhance and upgrade our manufacturing network; such an essential element of the sustainability and performance of the business.

Positioned to be a global leader for a very long time

I hope you share my excitement and ambition for this business. We have an absolutely crystal clear strategy for the business. We are absolutely focussed on flawlessly executing on that strategy. We have already started – you can see from what I have presented to you. We believe that *Shingrix* is going to be a transformative part of our business. We believe that the meningitis portfolio we have acquired from Novartis in our hands is going to be transformative and we believe that our base products will continue to growth this business.

We feel confident that we will be able to deliver the mid to high single digit top-line growth at an above 30% margin. We think it is great for GSK Vaccines to be part of GSK; we would never have the kind of reach we have commercially outside of a pharmaceutical

organisation and we know that GSK is very happy to have GSK Vaccines participate in the kind of operating margins and growth that we participate in.

Thank you. I would like now to introduce Abbas Hussain, President of Pharmaceuticals.