Stefan Hendriks – Global Head Cell & Gene, Novartis Oncology

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Stefan Hendriks, Global Head of Novartis Oncology's Cell & Gene division outlines the company's progression to becoming the global leader in cell and gene therapies, the strategy he has put in place for the business, and the key issues of manufacturing and access.

Stefan, you became global head of cell & gene for Novartis Oncology in July 2019. Could you briefly highlight your career trajectory up to that point?

I have had the privilege to work across many different roles, areas and countries. I began with AstraZeneca in the commercial space, initially in very operational roles but subsequently with expanding responsibilities. In 2002, I joined the management team of Bristol-Myers-Squibb (BMS) in the Netherlands, leading the specialty care unit, overseeing therapeutic areas such as virology, neuroscience, immunology and oncology, and launching a number of new products. This was the beginning of my experience leading cross-disciplinary teams and launching products.

In 2007, my international journey started. I first moved to Vienna to become general manager of BMS Austria and also part of the management team for Central Europe. This exposed me to different healthcare systems in different countries. In 2009, my family moved to Paris where I became European brand leader for virology, and subsequently led the HIV franchise for Europe. Leading this business gave me the opportunity to grow closer to patient communities. I also had to

participate in ethical discussions about pricing and access at a global level, and became involved in label expansion and other aspects of lifecycle management.

In 2012, I then moved to BMS headquarters in New Jersey, the US, as a global launch lead for Hepatitis C, during an exciting period where the industry was moving away from interferon-based treatments, with very limited efficacy, to all oral treatments that only needed to be administered for a couple of weeks, and cured Hepatitis C 95 per cent of the time. My initial major focus was Asia due to the genotype of Hepatitis C that our product targeted. That was another opportunity to familiarize myself with global markets and global product launches.

After that, I became global franchise lead for cardiovascular diseases and subsequently took over as commercial lead for oncology in the US domestic market, which was a great opportunity to manage and work with a large oncology sales team that comprised nearly a thousand people at that time. What was really defining was the chance to see the hugely positive impact immuno-oncology treatments had on patients, including some already at the stage of hospice care. That totally changed the way I engaged with my work.

After that, I moved to Novartis where I lead the Biosimilars business unit for Sandoz. While I had experience running cross-disciplinary teams as franchise lead, as a business unit leader I became responsible for the whole process, from development to manufacturing to commercialization to business development. After a year, my current boss, Novartis Oncology CEO Dr. Susanne Schaffert, asked me to assume my current position as the global head of cell and gene.

Novartis Oncology is the global leader in cell and gene therapies. What do you see as the major milestones of Novartis Oncology’s journey within this space?

Cell and gene therapies are truly transformative. With CAR-T therapies, we are entrusted to work with a patient’s own living T-cells. That is a huge responsibility as we have to know where the cells came from and monitor them carefully every step of the way. Within the pharma industry, companies always try to be patient-oriented but with cell and gene therapies, that has to be a part of our DNA because we are working with the patient’s own living cells! That sense of purposefulness and responsibility is truly amazing and inspiring, and it does not end with the extraction and manufacturing process, it also carries forward to the distribution, to the services we provide, and to our partnerships with hospitals, all of which are essential if patients are to benefit from these transformative therapies.

There have been many defining moments for us. We have seen so many firsts: our therapy was the first CAR-T to reach the market, it was the first CAR-T to be approved for two indications, and it was the first CAR-T to reach global markets, with initial approvals after the US and Europe in Canada, Australia, Japan and a couple of other Asian markets – and more coming. Today, this therapy is reimbursed in 27 markets globally and we have onboarded, qualified and trained over 285 hospitals in the world. I am very proud of that.

Being the first mover in these markets, our teams had to partner with local healthcare systems and payers to explain the value of CAR-T and to find innovative ways to create access for patients. Healthcare systems are not built for one-time, potentially curative, treatments so there was a period of acclimatization. Value is also defined differently in each market so it was essential to listen and understand our partners in order to create a common understanding of the value that CAR-T therapies can deliver, and then to develop and offer innovative models to support access.

Another significant achievement is that we have now built the largest and most comprehensive manufacturing platform for cell and gene therapies in the world. We currently have five – soon to be six – active manufacturing sites across four continents.

What strategy have you outlined for the business moving forward?

From all my previous roles, I have learnt that it is essential to define clear and strategic focus areas for any business, to ensure that cross-functional teams are working seamlessly together. Once the teams know their North Star, they can be empowered to work towards it.

We have identified three strategic pillars for the business. The first is the commercialization of CAR-T therapies, which means ensuring that we bring them to as many patients as we can, across different areas. We are currently running six CAR-T clinical trials and we are looking to add a couple more indications.

The second is ensuring that our manufacturing is competitive in terms of process robustness and capacity, which is why, as I mentioned, we have established a number of sites, this year in France, Switzerland and Japan, and we expect the sixth to be open in Australia in the coming months.

The third is creating an exciting pipeline. Even as we focus on commercialization of approved CAR-Ts, we also need to dedicate resources to build our portfolio. We are working on a next-generation manufacturing platform that has the potential for higher efficiencies, shorter turnaround times and hopefully better outcomes. It will also allow us to preserve a different subtype of T-cells that we

believe will have a positive impact on durability of efficacy. Using this platform, we are developing a portfolio of novel CAR-Ts, addressing multiple antigen targets across different malignancies.

We are also constantly scanning the business landscape and speaking with other players to identify interesting areas for partnership, for instance, in solid tumors or in allogeneic CAR-T therapies. We are definitely willing to invest if we see the right opportunities.

We are also looking to partner on the data front. We have generated a lot of manufacturing and clinical data, as well as real world evidence (RWE), so we have started to partner with IT players such as Microsoft on AI, as well as Carnegie Mellon University (CMU) to develop advanced analytical models. All these efforts are intended to further improve the cell and gene development and manufacturing processes so that we can provide better outcomes for patients.

As you have emphasized, despite the tremendous achievements made within the cell and gene space, it is still a very new area. When we spoke to the FDA and EMA regulators on cell and gene therapy, both emphasized the importance of manufacturing and the importance of close collaboration with industry on this topic. What is your perspective on this?

I agree with them. As I alluded to, since we were the first to launch a CAR-T therapy, we were also the first to build a great collaborative partnership with regulators across the world. We had the opportunity to learn together, and there is still a lot to learn regarding what it takes to deliver safe and high-quality products to patients. We have made significant progress on this over the past few years, and I am particularly proud that we have been able to open and qualify multiple manufacturing sites even through the global pandemic. We are also generating and analyzing manufacturing data to identify opportunities to make the manufacturing process even more robust, again in collaboration with the regulators.

One of the learnings we have gained is that we should have a nice mix of in-house manufacturing capabilities and external partnerships. We need the former because we need to build that manufacturing expertise ourselves, but we also need to enrich and complement those in-house capabilities, which is why we have formed collaborations with, for instance, Fraunhofer-Institut for Cell Therapy and Immunology in Germany, the Foundation for Biomedical Research and Innovation (FBRI) in Japan, Cell Therapies in Australia, and Cellular BioMedicine Group (CBMG) in China. When it comes to these partnerships, geography is not as important as the expertise and experience of our partners. We are looking for companies and institutions with the same value and quality

standards that Novartis holds.

It is also important for us to develop an extensive manufacturing network globally – that is part of our mission to deliver these transformative therapies to more patients around the world. We went as broadly and as quickly as we could to build our global capacity in a balanced manner.

Cell and gene therapies are so personalized and they involve patients, healthcare practitioners and hospitals in much closer capacities than many other types of therapies. How have patients and hospitals responded to cell and gene therapies?

Certainly, when patients are educated about these therapies, they are excited about their potential benefits. We are continuing to work on generating longer-term data on CAR-T therapies. In the American Society of Hematology (ASH) conference this year, we will present the 40-month data of our original pivotal trial. We also have real world evidence now, in addition to the randomized clinical trial data.

There is still a lot of work to be done in terms of educating patient and medical communities about the value of these potentially curative therapies. For instance, we are currently conducting a trial for second-line lymphoma but we are seeing many patients being referred for a CAR-T therapy only after three, four or even five rounds of chemotherapy. It would be great if we could reach these patients earlier and give them higher chances of a cure.

In terms of the hospitals and healthcare practitioners, they are also excited! CAR-T therapy offers hope for patients who have gone through multiple rounds of chemo and other therapies without success, most of whom would have been sick for years, many of whom are children. It is horrible for the treating physician to have to deliver the news that there are no more treatments left to be tried. CAR-T therapies offer another therapeutic option that is potentially transformative for the patient, so physicians are highly motivated to partner with us.

What is important is that we work with doctors and hospitals to ensure that they are trained and experienced in these new therapies. Typically, the centers need to see at least a certain number of patients in order to become experts. We are in an interesting position because the hospitals are our customers but they are also the suppliers of the starting material, the patient’s T-cells, so they need to be well-trained and certified, which takes effort. If hospitals were not motivated to administer these therapies, they would not go through all that effort.

If hospitals and physicians need to be trained in different processes for different types of CAR-T therapies, would that be a bottleneck moving forward when it comes to the adoption of these therapies?

There are many players right now in the field but I do not think all of them can build the capabilities needed to develop, commercialize and manufacture new CAR-T therapies. Even after that, you need to have organizational capabilities to scale distribution, training and education. Therefore, I expect to see some consolidation within the cell and gene therapy industry, so that ultimately hospitals will not have to deal with too many players.

Novartis Oncology has been working to expand access to CAR-T therapies globally. One of the initial concerns in the US and Europe when CAR-T therapies reached the market, was their price Are you seeing similar concerns in other regions?

Not particularly. It comes down to the quality of dialogue we build over value. The total value of CAR-T therapies as a one-off treatment that is potentially curative, that could eliminate the need for any future therapies and health services, that would allow patients to return to normal lives, is transformative. We have been able to leverage our experience of commercializing and launching CAR-T therapies in the US and Europe. We bring those learnings to other markets when it comes to engaging with payers and regulators. It is about building that dialogue about what value means to them, understanding their challenges, and then finding innovative solutions and models.

As long as we focus on patients and finding solutions to help them, we can go a long way. If you think about how fast we have entered the 27 markets where patients can now access approved CAR-T therapies, that is about as fast as – or even faster than – normal oncology products. But different countries have different needs, and of course, not all countries have the necessary level of technical advancement to implement cell and gene therapies either.

In general, we have seen a lot of excitement around our CAR-T therapies. Regulatory authorities globally have been very collaborative and responsive. There is a lot of enthusiasm.

Besides cell and gene therapy, Novartis Oncology also has three other technology platforms. How complementary are they to cell and gene therapy?

At Novartis Oncology, we do not believe that cancer is one single disease. It is a very complex range of conditions offering different challenges. Our ultimate aim is to move towards a cure for cancer, so we need to be able to leverage different platforms and strategies. This is why Novartis Oncology has acquired four different technology platforms: targeted therapy, immuno-oncology, radio therapy, and cell and gene therapy.

We certainly want to increase the adoption of cell and gene therapy. Limitations in terms of systems and infrastructure still exist but we strongly believe that cell and gene therapy will play an important role in the way human diseases will be treated in the future. Cell and gene therapy is currently characterized by fast-moving cyclical innovation, but this allows us to assess what is truly innovative, to incorporate that into the next generation of therapies, and to constantly raise the bar.

Cell and gene therapy is a very hot space within the industry and many other companies of different shapes and sizes are also building their capabilities here. How is Novartis Oncology acquiring, training and developing the skills and capabilities needed in your teams?

There are many smart and educated people in the industry but what is really crucial in cell and gene therapy is the passion to help patients and to be extremely curious and adaptable. We are working in an extremely complex environment so people need to be willing to learn, to experiment, to iterate, and to improve.

It is also critical to be a team player. Bringing these complex solutions to highly dynamic marketplaces is a team sport, as everything is so integrated. We always have to take the 360-degree view.

A final message as we close 2020?

The most important thing I want to say is that I am extremely proud of what our teams have achieved. In this extraordinary year with the global pandemic, they have not missed a beat. They kept all manufacturing sites operational so that not a single batch of drugs was missed. Even when all passenger flights were stopped, our teams found alternative transportation at very short notice. On top of all that, we have opened new sites and expanded our pipeline initiatives. These are truly amazing accomplishments, so I want to convey my gratitude to the teams.

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