Diabetes Management

Novo Nordisk's Senior Vice President provides insight into diabetes care

Alan Moses* speaks to Daphne Boulicault, Commissioning Editor: Dr Alan Moses was educated at Duke University and Washington University School of Medicine and received medical training at Barnes Hospital, the NIH and Tufts-New England Medical Center. He is board certified in Internal Medicine and Endocrinology and Metabolism. He worked for 24 years at Harvard Medical School in basic and clinical research, patient care, teaching and medical research administration where he achieved the position of Professor of Medicine while serving as Chief Medical Officer of the Joslin Diabetes Center. His research interests have been in endocrine cell growth in response to peptide growth factors, the pathophysiology of severe insulin resistance and novel treatments for diabetes mellitus. Since joining Novo Nordisk in 2004, Dr Moses has held positions of increasing responsibility in Clinical Development and Medical Affairs and now serves as Senior Vice President and Global Chief Medical Officer. In this role he has responsibilities across the full spectrum of Novo Nordisk's diabetes focus from drug discovery, through drug development and the implications of diabetes for the company and for patients, healthcare professionals and for healthcare systems.

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Q Could you give us an overview of your career to date?

I trained in medicine and undertook research at the NIH, not specifically in diabetes but mainly aligned with diabetes. I completed my specialty training in Endocrinology and went into Private Practice for a few years, as the Head of Endocrinology at a community teaching hospital aligned with one of the major Universities in the Boston area. From this position I was invited to enter a more 'typical' academic career in setting up a laboratory at one of the Harvard teaching hospitals, where I was active for almost 20 years, in various roles including basic and clinical research. I ran the Clinical Research Center at the teaching hospital and in fact set up a training program for Clinical Investigators, between Harvard and the Massachusetts Institute of Technology; this program was a prototypical training program of the time and is still in existence today. From here I became Chief Officer responsible for Clinical Operations at the Joslin Diabetes Center where I remained for 5 years. Novo Nordisk then came knocking at my door and offered me my current position.

Q Following your years in the clinic & in academia what inspired you to join Novo Nordisk?

While considering Novo Nordisk's offer I realized that I would perhaps have the potential to affect a greater number of lives from within the pharmaceutical industry than in an academic role. So I 'crossed over to the dark side', as some would say, and it has been anything but dark – it has been really fascinating and a unique opportunity for me in

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particular. As someone who used to teach drug development (as part of the training program I mentioned previously) I was able to pontificate on the appropriate response to a disease state or drug development and here was an opportunity to have a 'hands-on' role in the process. There is not a day that goes by when I do not learn something new; it is an incredibly stimulating role and I hope in some small way I have contributed – and will continue to contribute – to the development of better medications and better outcomes for patients with diabetes.

My more personal motivation for joining Novo Nordisk was my son's diagnosis of Type 1 diabetes during my time at the Harvard teaching hospital. This was a major milestone for my son and for my family as a whole, but also for me in terms of recognizing that I really needed to commit myself to making a difference to the lives of diabetes patients. What I have found at Novo Nordisk is that this commitment is evident in many individuals within the organization, whether on the sales, medical or research side of things. A close connection to diabetes drives a lot of them in their work – it is of course unfortunate when anyone is touched by diabetes, but it is a strong unifying force within the company.

I believe this spirit is linked to the founding of Novo Nordisk in 1922. Marie and August Krogh heard reports of a newly discovered hormone, insulin, during a trip to the USA. As a sufferer of Type 2 diabetes, Marie was particularly interested in these accounts; in gaining permission to manufacture and sell insulin in Scandanavia, Nordisk Insulinlaboratorium was born. There is continuity throughout our history that makes Novo Nordisk a different kind of company.

Q What particular lessons have you learnt from your years at Novo Nordisk?

The personal experiences I have had, both as a clinician and as the father of someone with Type 1 diabetes, have certainly allowed me to focus attention on issues such as drug development and the application of drugs to the individual care of the patient. I also try and highlight how we need to think beyond HbA1c as a marker. It is a very important marker in terms of clinical efficacy, but it is less important to the individual patient than how they can live their day-to-day lives. As a company, we try to incorporate this into the drugs we develop, how we test these drugs and how our labeling will allow physicians to use them, although this often requires a lot of clinical experience after a drug is approved.

Payers often say 'show me that this drug works in this patient group or under these circumstances' which is information that may not be available, but restricting the availability of these drugs impedes our ability to collect these data. I would maintain that the cost of drug therapy in diabetes is a small proportion of the total cost, and an increase in this cost would be entirely appropriate if it could reduce the overall cost of the disease in terms of complications. We think too often of the price of a drug rather than the value of a drug and I believe that health authorities in particular need to change their mindset on this.

Q How have your years in the clinic shaped your opinion of the current state of diabetes care? In your opinion, what should be the priorities going forward?

One of the things I have learnt from the clinic, and I think I was a pretty good doctor among my other responsibilities, was that diabetes treatment needs to be individualized. When I first started out in endocrinology choices were extremely limited within diabetes, at least in terms of what doctors could offer patients. On the other hand, what I began to appreciate as a clinician was that every patient is different; they do not necessarily require different medication, but each patient has to live with their condition in different ways. Patients must accommodate their life in some unique way in order to survive, both medically and emotionally, in the environments in which they work, live and play. I found this very striking.

Even to the end of my days caring for patients, I would sit down with them and the first thing I would ask is 'How are you doing?' and the next thing I knew I would be handing them a box of Kleenex because they would break down describing the challenges their diabetes presented them on a daily basis. So even with good medicines, knowing how to apply those medicines effectively and knowing how to match those medicines to the medical and social needs of the patients is something I believe is critical. And it is an aspect which is still not appreciated enough today.

This is one of the reasons that Novo Nordisk tries to find out as much about patients and families as possible. The DAWN™ study program (Diabetes Attitudes, Wishes and Needs;

NovoNordisk, Denmark) is an effort to find out what it is like for patients to live with diabetes. Furthermore, our CEO, Lars Rebien Sørensen, instituted a Youth Council for young people with diabetes to advise himself and the company on the gaps in terms of how they live with diabetes. The deficits in care are many and they can be overlooked by the health authorities and even physicians. This is particularly the case with generalist physicians, who deal with many patients with both Type 1 and 2 diabetes and do not have the time to delve into the issues faced by individual patients. This sort of input is extremely important to us, because it helps shape the kind of research we conduct in order to deliver better therapies or better approaches to therapies using the medication we already provide.

Q How do you see the adoption of individualized diabetes care affecting healthcare providers?

This is a really important consideration and one that I think many countries are struggling with in different ways. If you take the developing world, the main challenge is making the diagnosis and doing something as opposed to nothing.

With a system like the National Health Service, on the other hand, the diagnosis has generally been made and it is a matter of educating both caregiver and patient sufficiently to ensure the best possible outcome. Personally, I think this is going to devolve away from the physician and move toward other healthcare providers and electronic assists. There are a number of online and cell phone-based technologies that are being aggressively worked on now, which may provide optimal outcomes when used in conjunction with the appropriate medication by enabling a continuous education process for the patient. This process will nonetheless be directed by the healthcare provider.

Additionally, as data are collected and become more widely available I believe physicians will be able to become more directly involved in population management. They will be more able to identify the outliers, those patients who are not doing well and focus the resources on these individuals. This will help enormously in the overall cost of care, by reducing hospitalizations and complications, as well as improving population management in understanding how to apply the best medicines to the majority of patients.

Q What work needs to be done to make this a reality & where are we now? How does Novo Nordisk plan on achieving these targets?

At Novo Nordisk, we aim to use our available products, in late-stage development or in the market, to understand the appropriate population in which to apply these medications and at what stage of the disease (in particular with Type 2 diabetes) and combine medications into a single injectable, like Ryzodeg® (insulin degludec/insulin aspart; Novo Nordisk, Denmark) and Xultophy® (insulin degludec/liraglutide; Novo Nordisk, Denmark). These combination treatments provide opportunities to use a single medication with greater efficacy and a better safety profile to achieve the desired goals in a patient, based on their individual profile.

Patient adherence is another aspect of diabetes care we concern ourselves with; it is one thing to develop the right medication and apply it to the right patient at the right stage, but it is another to assess how likely these patients are to apply them in their everyday lives. One of the main challenges faced by the pharmaceutical industry in this regard is the disparity between what is required from a regulatory perspective (the kinds of trials that are needed to get a drug approved) and how much or little these trials actually inform the use of the drug in a real-world setting. Indeed the whole question is: how can you conduct a so-called real-world study? In essence, as soon as it is a study it is no longer 'real world'. However, the ability to acquire data from a real-world setting is still limited by our technology and data-access systems. Something I anticipate seeing over the next decade, or longer, is improved data enabling better decision-making. At Novo Nordisk we are thinking about how to conduct studies, including trials, in order to better inform us as to the directions we should take.

Q Do you believe a cure for Type 1 diabetes is a possibility?

Is it a possibility? Of course. But we need to be careful in how we define a 'cure'. The 1990's was the 'decade of the cure'; well it is 2014 and we are not there yet. A cure means that a treatment is applied and never has to be applied again – we have a long way to go here. Even in regards to β-cell replacement, growing cells in a laboratory and encapsulating them in such a way that they are not destroyed by the body's immune system, the likelihood that occurs once and never again

is a long way off. Nonetheless, this would be an unbelievably effective treatment.

My personal belief is that in Type 1 diabetes, while a cure should be the goal, the 'artificial pancreas' will go a long way as a treatment option. It is a technology solution that is not a cure, but if done right will make an enormous difference in the lives of Type 1 diabetes patients. For Novo Nordisk, creating faster-acting insulins to work within this closed-loop system is a project in development. In addition, if a GLP-1-based therapy like Victoza® (Novo Nordisk, Denmark) can dampen the excursions of glucose in combination with this type of technology we would have a very effective method of improving patient outcomes. This would reduce the chance of hyperglycemia and allow Type 1 diabetes patients to lead daily lives largely unaffected by this disease.

Nevertheless, Novo Nordisk is very involved in stem cell biology and in efforts to coax stem cells into becoming β cells and in large enough quantities that they can be applied pharmacologically.

Q What are you excited for in 2015 & beyond? How will these developments impact clinicians?

The 2015–2016 are big years for Novo Nordisk; we have lots of products coming to fruition in terms of clinical trials and making their way into the market, some of which I have already touched on. Ryzodeg (insulin degludec/insulin aspart) is being launched in some markets already. We are very excited about Xultophy (insulin degludec/liraglutide) and its potential to make a difference to patients who are unable to achieve control on basal insulin alone. This insulin and GLP-1 combination is also becoming available now. We are hoping that liraglutide 3 mg will be available in the obesity space, at least in some parts of the world.

We are completing clinical trials on our faster-acting insulin, Victoza for Type 1 diabetes and a once weekly GLP-1 analog called semaglutide that seems to be the most efficacious of the GLP-1 analogs that have been tested to date. Semaglutide is particularly exciting as it too can be used in combination with other drugs.

The 'wild card' in all of this is our large Phase II study on oral GLP-1. We are not certain what the results will be. My own bias is that this particular product will take a little longer to perfect because we are really forging new ground here. Nonetheless, I think this is incredibly exciting in terms of its potential.

We are also continuing to work on our insulin products, once-weekly insulin for example. We know that this will work but the question is: how easy will it be to use? Are there certain patients for whom it is particularly appropriate? Do we think about basal insulin in a new way with this new insulin? There are all sorts of situations in which we need to think about this. Again, this is in the early phases of clinical development, but it is in clinical development.

Q Novo Nordisk supports WHO's Action Plan for the Prevention & Control of Non-Communicable Diseases 2013–2020, what actions have been put in place to achieve its targets?

I think the Cities Changing Diabetes program is a very tangible example of the work we are doing in support of this. Almost 70% of the global population will live in cities by 2050 and we know that urban lifestyles are driving a sharp rise in non-communicable diseases such as diabetes. This program is our commitment to tackle the urban diabetes epidemic, as almost two-thirds of people with diabetes are living in cities. It is also something that I believe has the potential to make a real impact as we fulfill our three goals: to gather data and begin to identify and understand the factors that promote the development and progression of diabetes in the world's cities; to share this insight and valuable best practice with cities across the globe and to form action plans in collaboration with policy-makers, health authorities, the private sector and the voluntary sector to catalyze concerted action on the ground.

In fact, Novo Nordisk has very recently been ranked second in the world on the 2014 Access to Medicine Index, which speaks further to the points I have raised. Two of our initiatives were highlighted: the Base of the Pyramid project and the Changing Diabetes in Children program. The Base of the Pyramid project aims to improve diagnosis, treatment and diabetes education for the working poor in developing countries by applying an integrated approach in conjunction with faith-based organizations. With this project we are trying to tackle the public health issues associated with the diabetes epidemic. The Changing Diabetes in Children program provides treatment, patient education and medicine free of cost to children living with

Type 1 diabetes in low-income countries. Here we are attempting to ensure that all children with Type 1 diabetes have access to basic medicines. It is important to remember that in 2014 it would not be unusual for a child with Type 1 diabetes, in an area such as Sub-Saharan Africa, to die without a diagnosis being made; within 6 months of a diagnosis being made because they could not gain access to life-saving medicines or because of a decision made by the parents due to the resources that would be necessary to keep them alive.

Q Novo Nordisk has established the World Diabetes Foundation in 2002, in response to the deficits in diabetes awareness & healthcare in developing countries. What have you accomplished so far & what do you hope to achieve in the next 10 years?

The World Diabetes Foundation (WDF) is another prime example of how we support the WHO's Action Plan for the Prevention and Control of Non-Communicable Diseases in developing countries. Since its establishment, over US$111 million have been applied to the process of helping more than 100 countries around the developing world to set up sustainable efforts to combat diabetes within their populations. From creating diabetes clinics in Tanzania, when we began the program there were zero and now more than 400 diabetes clinics have been established by WDF in Tanzania and the number of patients being treated has increased even more dramatically, to developing limb prostheses or providing eye-screening programs in India. These are the kinds of efforts and projects which have resulted from the WDF and that make a substantial difference both in terms of diagnosis and, most importantly, in preventing or treating the complications which arise from diabetes.

We are full steam ahead with these projects and secured another 10 years of funding around a year ago. One of the challenges for WDF is this: if you have money and applications for projects, how can you be assured that the money will be used effectively, in other words, that it will have impact on the target populations for these specific projects. In regards to the Base of the Pyramid project, we learned to engage with faith-based organizations around the globe that seem to have a commitment which extends beyond that of local governments. This strategy has so-far been successful. The newly-appointed Managing Director of WDF, Dr Anders Dejgaard, is extremely engaged in the process and in tackling this.

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