Deborah Dunsire â?? CEO, Lundbeck

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Speaking exclusively to PharmaBoardroom, Lundbeckâ??s global CEO Deborah Dunsire describes the progress in the strategy she put in place to â??revitalise and refreshâ?• the Danish firmâ??s pipeline upon taking the role three years ago. Following two recent acquisitions, Lundbeck now has a much broader focus across neuroscience including areas for which biomarkers can be established and are therefore relatively de-risked. Dunsire also touches on a growing awareness of mental health issues post-COVID, potential in the CNS field more broadly, and the advantages of running a global company from Denmark.

From a leadership and culture perspective, what are the key specificities and challenges of running a foundation-owned company like Lundbeck?

Having a foundation as the majority shareholder and owner gives us a long-term perspective. Lundbeck has existed for over 106 years, so having ownership that wants to ensure the company continues to be successful, grow, and increase in value for decades to come is very valuable. Some public companies with only public shareholders have a much shorter-term perspective, meaning that making investments that take a longer time to mature is not so easy.

We also have the benefit of having 30 percent of our equity traded publicly. Having institutional shareholders, pension funds, and normal investment funds as shareholders brings a level of market discipline to the mix. I feel that it is a great blend and a model unique to Denmark, where multiple big Danish companies are either totally or partially owned by foundations. This gives great stability to

companies that have grown up in Denmark and has enabled those companies to continue to grow and be headquartered in the country.

As a contrast, Sweden had some very impressive pharma companies like Astra, which ultimately merged with British firm Zeneca to become AstraZeneca and is now headquartered in the UK. While this merger has been very successful, there is now no longer such a significant Swedish company. Because of the foundation ownership, Danish companies have been able to withstand the short-term downswings that come with loss of exclusivities, and which sometimes lead to mergers or acquisitions, and instead progress within Denmark.

Given this ability to plan for the long-term, what strategy did you put in place when you arrived at Lundbeck three years ago, how much has been achieved so far, and what is still a work in progress?

The strategy we put in place was to revitalise and refresh Lundbeckâ??s pipeline, which is our path to the future, in the short-, medium-, and long-term. Lundbeck had had some pipeline failures, so our focus was on addressing that by both expanding the pipeline and rebuilding it. We have made tremendous progress towards this goal.

Firstly, we looked at Lundbeckâ??s core competencies and unique skills in the field of neuroscience, having been dedicated to that area for the last 70 years. We articulated the purpose of the company as a tireless dedication to restoring brain health so that every person can be their best. That is the North Star that guides us. Once this was established, we formulated a strategy around what needed to be done within our business to transform brain health and achieve our goals.

We decided that we had to capitalize on Lundbeckâ??s experience in neuroscience by looking at many different areas in the field, not only a narrow segment. Historically, our research had focused quite narrowly on Alzheimerâ??s, Parkinsonâ??s, mood disorders, and schizophrenia, but our capabilities go way beyond that. Therefore, we opened up the lens to bring in more disease areas within neuroscience because that better leverages our skills. That allowed us to bring in pipeline products through acquisitions that, while not necessarily in those four traditional areas of focus, were still in our neuroscience sweet spot.

The first acquisition, Alder BioPharmaceuticals, brought a new focus on neuropeptides, which are involved in areas like migraine, cluster headaches, and other specialty pain syndromes. We brought a new product to market for chronic and frequent episodic migraine, which was a totally new area for the firm. However, although this is a new area, it is still in the neuroscience space and our commercial organisation is still dealing with the neurologists and headache specialists to whom they are well accustomed. Our migraine drug also represents the companyâ??s first ever global launch; previously we have always done so through partnerships. That is enabling us to continue to build our organisation and leverage those skills around the world.

We also brought in some pipeline products. Lundbeck has another neuropeptide-focused product that will enter Phase II trials later in 2021, indicated for specialty pain and potentially migraine. Both products are antibody or biologic products, a new capability for Lundbeck, which has a heritage in small molecules. Biologics have been used very successfully in many different categories of medicine, from rheumatoid arthritis to multiple sclerosis, and these drugs in migraine and specialty pain have a very specifically targeted effect using a biologic agent. Through the acquisition, we brought in colleagues with capabilities in biologics development who sit in our Seattle site, formerly Alderâ??s facility, for the first time. Therefore, we have both products and capabilities coming into Lundbeck.

Another important acquisition was Abide Therapeutics, a company based in La Jolla, California. That brought in a pipeline of drugs which harness the therapeutic potential of the endocannabinoid system; a system which occurs naturally in the brain and is sometimes mimicked with cannabinoids or cannabis. We believe that there is tremendous value in being able to use naturally occurring compounds to address various diseases such as epilepsy and spasticity in multiple sclerosis.

In addition to the Abide pipeline, we have retained their sites in La Jolla, San Diego because it brought a different research focus. All in all, we are rebuilding our pipeline, bringing in new biologies, new approaches, and new technologies, while also leveraging what we have built up over the years in new directions. Lundbeck has begun to redirect its research focus into areas where we have a good understanding of the biology and, importantly, biomarkers that can help us understand and de-risk the programs during development. Lundbeck had never really had activities in areas with a lot of biomarkers, so this is another new capability being introduced within our internal drug discovery and development.

We have also made progress on digitalisation, utilising machine learning and AI in both our R&D and our commercial organisation. As the world changes, every company needs to adapt, which is what we are doing.

While Lundbeck has made tremendous progress on its pipeline rebuilding strategy, we have also given strong support to our strategic brands; the drugs that are available to patients today and which generate the revenues and profits that allow us to invest in R&D.

Finally, we have also been looking at our organisation and figuring out how to change the way we work for the better, become more agile in terms of decision-making speed and quality of decisions, ensure that diverse perspectives are heard, and leverage virtual tools to make our global business even more seamless.

Lundbeckâ??s financial reporting shows a marked increase in R&D expenditure and a move into areas for which biomarkers can be established. What impact do you see this having on the companyâ??s pipeline?

Having biomarkers will accelerate the decision making around whether a drug can go all the way or not; both in terms of moving it forward more quickly or deciding to stop it earlier, thereby freeing up resources to work on more promising areas. Additionally, biomarkers can be used to make clinical trials smaller as they allow researchers to see a bigger effect size. More precisely designed clinical trials using biomarkers become smaller, quicker, and less expensive and decisions to either stop or accelerate a program can be made more swiftly. Working in this way comes with several different benefits in terms of de-risking and speeding up the pipeline.

What do you see as the main opportunities and challenges of moving into the biologics field? Are the high investment costs needed balanced by biologicsâ?? potential effectiveness in the long-term?

Because the biologics are protein molecules/antibodies with a specific target, they tend to have more predictable biomarkers whereby their effects can be seen more clearly and have fewer off-target toxicities. Small molecules can affect receptors other than the target which must be considered in their development. However, biologics tend to affect only one receptor because that is what they are designed to do, creating a potentially clearer path from a safety perspective.

Biologics *are* more expensive at the early stages of development because their scale up requires cellular systems and is not as easy as the chemical process with which our small molecules are made. Even at scale they carry a higher cost of goods, but there are returns to be made based on having quicker drug development and more certainty on the target.

Drawing on the recent experience of launching Lundbeckâ??s migraine franchise, what have been the key takeaways for the organisation and for your teams?

Entering a new field teaches us that there is always more to learn. Something I have learned in this process â?? even though I am a physician and have treated migraine patients â?? is the full debilitating impact of chronic migraine. As we have interacted with more patients, the medical need has become even more compelling and clear. In the Top Five markets globally, there are around 134 million people who suffer from migraines, the majority of which from acute migraines, which occur episodically a few times per year. These people do not need our product.

However, our clinical trials were done in groups that have between four and 14 migraine days every month, with the second trial group containing people that have between 14 and 28. Often these come with nausea or the inability to be in a dark place, making it an incredibly disabling illness for those who suffer such frequent migraines.

As we have begun to better understand the disease and its impact on patients, we have become even more motivated by how our drug can make a difference. Many patients around the world have given up on therapy altogether given the side effects of some older therapies and have adjusted their lifestyles, including stopping work, in order not to have to take any medication. We think that the migraine market will continue to expand because these people who have been diagnosed with migraine and have given up on treatment will come back.

Additionally, this is the first time that Lundbeck has launched a product administered via intravenous infusion. The fact that the drug is delivered directly into the bloodstream means that it begins to work immediately and has a very fast effect. However, it does mean that patients must attend an infusion centre or physicianâ??s office for the treatment. This has necessitated some work on our side to make the patient journey as seamless as possible.

We have been very pleased with how patients experience the product. While we naturally looked at the data when we acquired Alder, this data is now being borne out by the people we deal with, which is extremely rewarding. Lundbeck sees this as a growth product all the way through to the mid-2030s when its patents expire.

The recent FDA approval of an Alzheimerâ??s drug, the first in over 17 years, has generated a lot of discussion about efficiency; what is your take on the debates swirling around new CNS products coming onto the market?

There is always a need for improved therapy. In migraine, for example, the industry has been bringing new tools forward that made a difference for patients, but they just were not quite good enough. However, as understanding of the biology advances and new technologies like biologics become available, a step change becomes possible. We can say for instance, in depression, that the current therapies are not good enough, but that they offer tremendous benefits to patients struggling with mental illness. Within depression, Lundbeck developed a product that enables people to function better at work because it does not depress the speed of processing. Other products can

also handle depression but dull the ability to think and process, leading to people struggling at work. Additionally, some previous products treated the depressed mood but were linked to treatment-emergent sexual dysfunction, whereas our product was not.

We are making some advances, but we want to make even more. In the discussions around Alzheimerâ??s disease, a small advance is not good enough, but it does not mean we should not accept small advances in the meantime. There needs to be an acceptance of the small wins while we continue to search for the big step changes.

Some analysts have argued that regulators need to continue giving approvals to CNS drugs in order to incentivise drug developers to keep investing in the field. Do you agree?

I do. In the case of the new Alzheimerâ??s drug, it depends on the biomarker and whether it is likely to predict clinical benefit. I spent a lot of my career in oncology, where the benefit of those biomarkers is very apparent; if a patient has a specific mutation in their lung cancer, it predicts that they will respond to an agent that addresses the protein produced by that mutation. What the field is debating in Alzheimerâ??s disease right now is whether a reduction in beta amyloid really going to predict for a clinical benefit? The FDA is saying that they think it is likely to predict; that is where the debate is. Certainly, the use of biomarkers as a pathway to approval does attract investment because you can move ahead of waiting for very long-term outcomes.

Mental diseases are highly heterogenous and no two people experience conditions like depression in exactly the same way. Given this fact, what can the impact of AI-driven analyses of real-world evidence be in learning more about mental illness and improving the drug development and discovery process?

We are striving to find more ways of accessing data. To find trends using machine learning, there is a need for greater access to large and anonymised data sets. The world is getting there but the data in many countries is in disparate places. In the US, for example, when someone want to change their insurance provider, suddenly there is nowhere to keep their longitudinal data and it becomes challenging to carry out large-scale analysis. However, in Denmark, where peopleâ??s health data are kept within just a few systems, there is unique potential.

This is something we talk about with the Danish Medicines Agency and Ministry of Health. We would love to be able to access that data and understand whether it can help us to find more responsive patient subsets so that we can do smaller clinical trials, get higher responses in patients, and treat fewer people who will not benefit from a particular treatment. This is still an emerging field and one that needs to be managed thoughtfully, with strong ethical boundaries. It is appropriate to move carefully, although I do wish we could move a little more quickly in that direction.

What are the Danish governmentâ??s key concerns around sharing data â?? even anonymised data â?? with pharma companies like Lundbeck?

It is about working out the parameters that need to be in place and bridging the outside world with the big data systems that are not anonymous because they contain actual patient data. I have not found resistance to the concept, more a thoughtfulness and carefulness. It is a complex issue that is partly technical and partly emotional. How the Danish population feel, whether they understand how

their data is being used, and how the gap is bridged with peopleâ??s ownership of their own data are key concerns and a lot of discussion is still ongoing.

The fallout from the COVID-19 pandemic has seen an increased awareness of mental health issues among general populations and governments, with high-level dialogues now taking place and dedicated budgets being set aside for the field. What are your hopes around the de-stigmatisation of mental health as well as greater awareness, diagnosis, and funding?

One of my biggest hopes is that we can destigmatise mental health. People facing mental health challenges should feel comfortable raising them with their physicians, understand that they are not alone, and be able to access the help and care they need. *Society should better understand that mental illness is illness*. This can be more permanently impactful in some cases, but in general â?? as in depression and schizophrenia â?? it is episodically impactful.

There needs to be a better understanding of how we deal with mental health issues in the workplace; we can make accommodations for people with mental health issues in the same way that we do for people with physical ailments. Talking about mental health and the impact that circumstances and environment has on mental health elevates our ability to reduce stigma.

Additionally, in policy settings Lundbeck advocates strongly for parity of care. In certain countries, partly because of stigma and partly because of the way that health budgets are allocated, mental health receives less budget per capita than diabetes or heart disease. For example, in the US, insurance pay-outs for mental diseases tend to be much less than for physical diseases and some areas â?? such as drug counselling â?? have traditionally not been covered by insurance at all. Because there is no measurement for mental disease in the same way as for physical diseases and many patients may look outwardly fine, there has tended to be an unwillingness to pay. We need to continue changing this narrative to ensure parity of care.

How is this growing global awareness of mental health issues impacting the way in which Lundbeck is conducting its business?

We are looking closely at how best to bring the patientâ??s lived experience into everything we do, from the discovery and design of drugs right through to the structure of our clinical trials. Partly thanks to COVID, we are now looking at virtualising clinical trials, effectively allowing patients to participate in elements of a trial remotely, which makes trial participation less impactful on them.

Another important area is building in metrics which are important to the patient. For example, migraine studies have traditionally tended to focus on the headache itself, whereas in fact often the most bothersome symptom for a patient is nausea or the inability to be in light.

We are also using digital biomarkers to measure patients when they are away from the clinic. In Parkinsonâ??s disease, we partner with a company that makes a shoe insole that helps understand the patientâ??s gait and whether it is improved by a medicine. Measuring that digitally while the patient is going about their daily life is much richer than doing it through a 15-minute consultation once a month on a clinical trial. We are trying to get that real time data to enrich our ability to measure things and are working with patients, not only once a product has been approved, but all the way through the clinical development process.

Lundbeck recently issued its financial results for the first half of 2021; what are you pleased about, where is there room for improvement, and what will be your areas of focus moving forward?

These results were strong, particularly for our patent protected â??strategic brandsâ?? which are today Lundbeckâ??s main growth drivers. Across all our regions these brands returned to double digit growth in Q2 as the impact of the COVID-19 pandemic lessened.

One of our main challenges this year was the loss of exclusivity for our hypotension in Parkinsonâ??s disease product, which has been enormously successful. Following the loss of exclusivity in February, we saw nine generics approved, an unexpectedly steep level of discounting, and very aggressive behaviour from the generics firms in terms of attracting patients. That led to a decline in that brand of about 75 percent, having initially planned at the beginning of the year for a 50 percent decline, and meant that the first half of 2021 was overall lower than the first half of 2020. While we expected a dip, we had not expected such a significant drop in revenues.

To remedy this, our attention will be focused on our newly launched product in migraine as well as our other big strategic brands in depression and schizophrenia and keep that growth going. We are also moving our pipeline forward with new compounds coming into Phase I and plans to forward some into Phase II.

Will inorganic growth play a significant role in your future or do you already have the capabilities you need following the Alder and Abide deals?

Our acquisition strategy is somewhat opportunistic. Lundbeck has been built over many years through a mix of internally discovered compounds and external partnerships, licensed products, and acquired products. We are going to keep that focus going forward, continuing to advance our own pipeline but always with an eye for promising external opportunities. Some of those external opportunities will not be acquisitions; for instance, two of our strategic brands today came from a partnership with the Japanese company Otsuka. We are looking at partnerships, licenses, and acquisitions and, while acquisitions tend to be the most newsworthy of the three, they do not represent the only strategy with which to build a business. It needs to be a good strategic fit that allows us to give value to Lundbeck shareholders. With some of the biotech valuations being very high right now, we are not going to do acquisitions if it does not create value for shareholders.

Despite its modest market size, Denmark punches well above its weight on several metrics within the life sciences. From your perspective, what does the country have to offer internationally?

In Denmark there is excellent collaboration and dialogue between the public and private sectors. While there is not necessarily always agreement, there is a real opportunity for dialogue here. This can be seen in the countryâ??s Life Sciences Strategy which came out of several years of dialogue; with industry coming up with proposals of what was needed, government and other partners commenting and pushing back, the Strategy being refined, and an eventual agreement that it is an important societal priority. There is government investment behind the Life Sciences Strategy, but it comes out of an open back and forth dialogue with industry. This is a very constructive path forward and one which could serve as an example to other countries.

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