ADVANCE MEDICINE

AstraZeneca Japan President Stefan Woxström shares his healthcare vision

By C Bryan Jones

Biopharmaceutical company AstraZeneca says science is at the heart of everything they do. With an unprecedented six new treatments expected to come to market in 2018, the company has life-changing breakthroughs in store for patients in Japan. Guiding efforts here is Stefan Woxström, who relocated in January from Sweden, where he headed up the company's operations in the Nordic and Baltic countries. *The ACCJ Journal* sat down with Woxström to find out more about AstraZeneca's approach to healthcare and why 2018 is a milestone year.

How are you adapting to Japan?
It's a fantastic country. Culturally, it's very different, so it's exciting to explore something new. From a business perspective, Japan has some of the best scientists in the world, and a lot of innovation in science.

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What stands out between healthcare in Sweden and Japan?

I think what Sweden is very good at is using digital tools for healthcare and opening up healthcare registers so that patients can read their own medical records. This is very beneficial, because you can gather real-world evidence much more quickly. Soon, every patient who steps into a clinic in Sweden will, through their data, be contributing to medical trials.

I think Japan can benefit from that experience. We have started to explore opportunities to work with the government and other stakeholders in Japan in this area. I understand that Japan is launching a new medical information database network, so we're very willing to share what we've learned from our experience in Sweden.

What is precision medicine and why is it important?

We should start from the standpoint of the patient. Imagine a patient suffering from cancer. They want the most effective treatment as soon as possible and to avoid delays caused by treatments that are not effective for them. For patients with severe diseases, time is critical. By performing a diagnostic test on that patient, you can identify which treatment will give them the highest probability of an effective response. This is what we're striving for with precision medicine, to offer follow-up testing of patients to ensure they get the right treatment at the earliest opportunity.

As well as being very good for patients, it's also good for governments, because they don't have to pay for medicines that don't work. And, for us, it's very good because we want to make sure that the right drug reaches the right patient as soon as possible. That's our goal. I really think all stakeholders benefit from precision medicine.

Today, it is becoming much more common to test every patient. For lung cancer, the first thing you do is test the DNA of the tumor. Understanding the DNA opens up new treatment options. With so many options available, it makes sense to screen patients to determine the most appropriate one.

This is called next generation sequencing. Japan is now testing patients very efficiently using this method. For most of our new medicines, we have already defined the biomarkers physicians should look for to see how well patients are likely to respond.

What does 2018 hold for AstraZeneca?

We aim to make this a milestone year for patients in Japan. We're introducing three new lifesaving medicines. On top of that, we have three first-to-market indications, which will offer better treatment options than those currently available. Four of these new treatments are in oncology, where the magnitude of the disease burden is quite serious. That represents an unprecedented number of new treatments within a single year for AstraZeneca.

At the same time, there's a lot of pressure on the company to make sure all these launches go well, because we want to treat patients as quickly as possible. Our task is to address unmet needs.

Are there any changes you have made to prepare?

We are very prepared, both at the global and local levels. When you work with a pipeline, things don't always come quickly, so we have plenty of time to prepare. One major change we made was to reorganize the company into three therapeutic areas: respiratory diseases; cardiovascular and metabolic diseases; and oncology. Last year, we also conducted a local review of our capabilities to ensure that we're fully prepared to deliver new medicines to patients.

Tell me about the lifesaving medicines.

Let's start with lung cancer. AstraZeneca already has a long heritage of lung cancer treatment. We pioneered the world's first molecular targeted treatment called TKI [tyrosine kinase inhibitors] for first-line treatment of non-small-cell lung cancer in 2002. And, in 2016, we also launched a first-of-its-kind second-line treatment for those patients who have developed resistance to first-line treatment. If patients have a certain type of DNA called EGFR T790M, you usually see a strong response to this treatment. Our latest data has shown that, when you start with this medicine as a first-line treatment, the length of patient progression-free survival nearly doubles compared with the current standard of care. It brings lots of benefits to patients and we shouldn't keep it only in second-line treatment. I think that was a major breakthrough.

We're also actively developing treatments for earlier stage lung cancer, called stage III, where there's been virtually no progress in the past 20 years. Today, those patients are

receiving chemoradiotherapy, which works temporarily, but eventually nearly every patient will relapse and the disease will start to progress again.

Until now, there is no effective treatment option after chemoradiotherapy and all we could do after chemoradiotherapy is "watch-and-wait." However, our new medicine is a biologic, also known as immuno-oncology therapy. It works with the cancer immune system, so the immune system can eliminate cancer cells. If patients are treated with immuno-oncology as a follow-up treatment to chemoradiotherapy, the cancer's progression can be arrested for a much longer time. It's a breakthrough for patients in this important area of treatment.

We're also looking into a drug for patients with specific types of ovarian and breast cancer. For example, we're looking at breast cancer patients with a rare hereditary BRCA mutation. Until now, there's been no treatment developed specifically for "hereditary" breast cancer in Japan. But, we have had a breakthrough in identifying patients with the BRCA mutation that enables them to have longer progression-free survival than with current treatments. Again, we're talking about precision medicine here. These are several examples of how we are testing patients and being more precise in treatment.

Another new treatment we're offering is for severe asthma patients. Asthma is a very serious disease. We often forget how severe it is, because we have very effective treatments. Many asthma patients can live a normal life, but a few still cannot. These patients struggle with everyday activities such as playing with their children or cooking. They can't be outside during temperature fluctuations or weather changes because they feel terrible. These patients are frequently in healthcare facilities seeking help for acute asthma, and they're afraid of being exposed to a lot of environments. They are living a very tough life and there haven't been a lot of good treatment options available to them.

This is a breakthrough for us because we can offer a biologic treatment that mitigates the inflammation mechanisms that cause severe asthma. We've seen that patients have experienced reduced symptoms and positive results.

We also have a new indication for our PPI [proton pump inhibitor]. The interesting thing about PPI is how much it's used. In many parts of the world, we have had patent expiries, but we continue to develop this drug. We now have a new indication for children that just got approved earlier this year.

We are also offering a new way of taking the drug—a sachet—so you can just pour the drug in a glass and drink it. It's much easier to swallow for many patients, not only for children, but also for the elderly and anyone who has problems taking a capsule. I think we are showing our commitment to patients by continuing to develop a drug in the late phase of its lifecycle.

There are many reasons to use PPI in pediatrics, but the most important thing is testing and documenting products for children—not just adults. We have a lot of documentation on adults, but children might have a different metabolism—and you need to know that.

What is involved in being first to market?

We're coming first to market with a drug for patients with stage III NSCLC lung cancer, and also treatments for breast and ovarian cancer.

There are a lot of benefits for us as a company, because we can drive the market. But it's also a huge responsibility, since we want to make sure patients can access those medicines as quickly as possible. As the first-mover, there's a lot of pressure on us, but we have a huge commitment to patients to get them on effective treatments quickly.

That's where we see the biggest challenge. To make that happen, all healthcare professionals must be informed and alerted to these new treatments, and we must make sure the testing process is working smoothly.

In precision medicine, testing becomes critical. How do you make sure every doctor knows how to test? Tests are usually biopsies, so healthcare professionals need to be trained on

how large a sample they need to take. But it could also be blood tests, which are simpler. You need to make sure that you have labs that can do these tests across Japan, so you don't have long lead times. Setting that system up for every new drug is a challenge. It's a worthy challenge, but it is a challenge.

Why is real-world evidence important?

We often talk about Big Data. What we're talking about is data that is being created every second—it's a lot of data. We know there are articles being published, but there are also patients going into healthcare, getting diagnoses, taking tests, getting treatment, perhaps being hospitalized. All that information is captured in the system. When you start to have a lot of data in the system, you ask, "Are we using that data to draw conclusions around safety, efficacy, and are there other types of treatments that we could look into?"

Real-world evidence is a way of capturing data. If you take that data and apply a methodology, you can start publishing this as evidence. It needs to be very robust, with a clear methodology, and at AstraZeneca we've proven that we're quite good at this. When I worked in Sweden, we published one of the largest real-world evidence studies ever conducted in the diabetes field in top-tier journals such as The Lancet and Circulation. This data is peer reviewed, but it also told a different story from so-called randomized clinical trials. These approaches are actually very complimentary. The most important thing here is that you are driving science very fast, because the data is already out there.

We want to make sure we provide the right drug to the right patient as quickly as possible.

How has real-world evidence advanced in recent years?

We see many more publications citing real-world evidence. We also see how the methodology has been developed. It's being recognized, trusted, and used. I think that's a very good development. If we can accelerate progress in science, we can get more effective and safer treatments to patients. That's a huge opportunity for a country like Japan, where there is a lot of data available. How can we capture that data and create science to develop better healthcare for Japanese patients?

Our breakthrough in diabetes was the CVD-REAL. CVD means cardiovascular disease and REAL means we are doing it in real life. For the first study, we focused on six countries: Denmark, Norway, Sweden, Germany, the UK, and the United States. We looked at diabetes patients on a new type of treatment versus those on standard care. We brought about 300,000 patients into this trial. When we compared these two groups, we could see a clear difference in hospitalization and mortality. This was interesting, because the same has been shown in other so-called randomized control trials, so we could actually confirm this finding.

Then we did a specific Nordic trial called CVD-REAL Nordic, focused only on Nordic countries [Denmark, Norway, and Sweden]. We looked at 90,000 patients and more outcome measures, but confirmed the same result. These types of trials appearing in Circulation and The Lancet repeatedly has built trust. We see now that healthcare systems, specifically in the Nordics countries, are paying close attention to the results of the RWE and the CVD-REAL trials. I think this type of data represents a breakthrough in how we examine treatment options for patients. I am confident that we will be seeing more real-world evidence used in the future.

We're also seeing this become a factor in decisions on reimbursement, particularly in Sweden, which has also started pilots using real-world evidence as the basis for evaluation. My dream for Japan is using real-world evidence to get medicines more quickly to patients. That's our aim. I hope that I can contribute to making this happen in Japan during the time I'm here.

Do you see the role of artificial intelligence (AI) growing?

Absolutely. I think AI could be used everywhere in the world. In the pharmaceutical industry, AI is an area we'll start exploring alongside real-world evidence. The United States is already very advanced, but Japan also has an opportunity to lead in this space because they have both the speed to deal with advanced treatments and a thriving technology sector.

How can we combine those factors and start exploring AI? I'll give you one example. Many people around the

world suffer from a respiratory disease called COPD, or chronic obstructive pulmonary disease. In Japan, diagnosis of COPD could be improved. What if we could use AI to find patients who are former or current smokers, above a certain age, and who frequently visit healthcare providers for airway infections? And what if we could also diagnosis those patients correctly and start treating them? That's how we can effectively use AI—input an algorithm with the desired parameters, confirm the diagnosis, and treat patients with the most effective options.

Why is collaboration between companies, government, academics, and healthcare providers important?

AstraZeneca is actively participating in about 600 collaborations globally and we are constantly adding more. Generally, we think that you can achieve much more through a partnership approach. Academia, healthcare providers, government, and also pharmaceutical companies all want to bring lifesaving medicines to patients. We're all aiming for the same thing.

Consequently, we make significant investment into research and development in Japan. By sharing more of that work and getting more input from healthcare and academia, we can ensure that we're doing the type of research Japan needs the most. Drawing from our network across the globe, AstraZeneca has a lot of experience in the pharmaceutical industry that we're willing to share with academia and healthcare providers. Academia is also a huge source of scientific discovery. I'm talking specifically now about real-world evidence.

What is the MID-NET database?

The Japanese government aims to launch a database called MID-NET in April, which will record data from about 4 million patients. This is a very good opportunity to start exploring broader applications of real-world evidence—especially for academic research. I believe the number of recorded patients will have to be increased eventually, but it's a very good start. The government's commitment to launching a system like this is a good signal. If we can collaborate to further develop the potential of MID-NET, it will be very beneficial for Japan and Japanese patients.

What does the future hold for AstraZeneca and patients?

At the moment, we're focused on making the six launches we're planning for this year a success. Looking ahead, we have very high expectations for our pipeline and future launches. Our mission is to be one of the top companies in Japan by 2021.

In parallel to these business goals, we want to create momentum by exploring every opportunity available to us through technology. We aim to optimize our use of real-world evidence to create science in Japan and explore the possibilities that AI will help us unlock. That's how we will generate sustainable growth at AstraZeneca over the coming years while continuing to deliver the best possible treatment options to patients in Japan. ■