Representative Lauren Matsumoto: If you haven’t listened to our brand new podcast on the 30th anniversary of the Americans with Disabilities Act, I really encourage you to check it out! As a legislator and a moderator of a podcast in this series previously, I’ve found WIG resources created in collaboration with the SEED initiative of the Office of Disability Employment Policy to be really valuable – a lot of great ideas for future legislation.

In addition, we’d also like to help legislators reach their constituents by recording a radio Public Service Announcement in time for National Immunization Awareness Month. The COVID-19 pandemic has us all asking questions, and a public service announcement can definitely help to answer them. So, please contact Women In Government for more information about all of this.

Please don't go anywhere - we have another great presentation for you today: “It Takes Two – Type 2 Inflammation.” Before I introduce the next session, I just wanted to quickly remind everyone that WIG is still planning on hosting an in-person conference in Orlando, Florida in November. I am really looking forward to this conference! Stay tuned for registration and agenda updates.

So now, please join me in welcoming the speakers for our segment on “It Takes Two – Type 2 Inflammation.” I am happy to have Carole Huntsman, Head, Sanofi Genzyme North America and U.S. Country Lead on the call with us. She's been with the company for eight years and has over 25 years of pharmaceutical and biotech experience. Additionally, Carole was commissioned as an officer in the US Army. Thank you so much for being here today. Carole, the virtual podium is yours!

Carole Huntsman: Thank you so much Representative Matsumoto. I'm pleased to be with all of you here today to share some information about Sanofi and the work that we're doing to help patients who suffer from Type Two Inflammation.

My name is Carole Huntsman, as Representative Matsumoto said, and I've recently been named the new Head of Sanofi Genzyme in North America. In this role, I'm responsible for rare disease, oncology, and immunology. I'm pleased that I can be part of this session today to raise awareness about a very important health condition, Type Two Inflammation.
Sanofi has been an active participant and partner with Women In Government for well over a decade. We appreciate all of the work that WIG and its members have done on educating state legislators and public policy members about important health issues and support their efforts to shape public policy to better patient lives.

I’m happy to be able to introduce our speaker today. Dr. Mandeep Kaur is Vice President, Head, North America Medical for Dupixent at Sanofi Genzyme. She's a physician - in fact, a dermatologist by training - and Mandeep has over 15 years of research and development experience in both drug and device development. She will share with you the characteristics of the disease and its impact on patients and their families.

Now, it’s my pleasure to turn it over to Dr. Kaur.

**Dr. Mandeep Kaur:** Thanks, Carole. Thank you so much for such a kind introduction. And again, thank you to WIG and the amazing, powerful people on the call who make it happen. It’s an absolute honor to be here.

As we look at the slide, I just want us to start thinking about someone we know, or maybe ourselves who might be impacted by this disease state. I think this is the conversation we want to have today. Carole mentioned that we are committed to the science part of this conversation, and at Sanofi, it's a very patient-centric organization, so you will probably hear a lot about how we consider patients as a center of these conversations and how their impact is our impact when you talk about the disease.

As you look at these disease states on the slide, we talk about lungs, we talk about skin, and we talk about the upper airway. One thing that I just want to mention is as we look at these disease states – Asthma; Atopic Dermatitis, which is a chronic inflammatory form of eczema; or Chronic Rhinosinusitis with Nasal Polyps, which I understand can be a little mouthful sometimes - but I would say these are well understood chronic inflammatory diseases.

I also want us to focus not only on the diseases, but on the words chronic and inflammatory. As you can imagine with the word chronic, it means that these are the diseases that are impacting patient’s lives for a very long time. When we talk about chronic, in some cases, this is a lifelong disease. When we talk about asthma - a chronic inflammatory disease of the lower airway which is characterized by coughing, wheezing, difficulty breathing - in some cases the asthma attacks are so severe that these patients have to go to the emergency room or have a hospitalization to further get it treated.
When we talk about atopic dermatitis, which is a chronic inflammatory form of eczema, it's a rash – something that you can consider and think about and say hey, it's just a rash. But it's a rash on the skin that can cause such intense, persistent itching and skin dryness that it leads to, in some cases, crusting, redness, and oozing. And in some cases, because of the intense itching, before a patient knows it, the patient already have a bacterial infection going on. So this chronic inflammatory disease plays such a critical role in a patient's life who's suffering from that.

Chronic rhinosinusitis with nasal polyps is also a chronic inflammatory disease and it's an upper airway disease. As we know, the upper airway and the lower airway is separated by the epiglottis in the throat. The way the chronic rhinosinusitis with nasal polyps works is it's basically something stuck in your nose. You can see with these patients there's constantly pressure building up in their sinuses, and you could say but that's basically sinusitis.

Well, there's a sinusitis component, but this has been happening for many years in those patient populations, and it's basically like having a grape stuck in your nose. You would have difficulty breathing, you'll have nasal congestion, you're going to have discharge and what we've heard from these patients is that there's also a reduced sense of smell and a reduced sense of taste, which is such an important part of everyday life.

These patients are suffering a lot with these disease states. Often diseases like atopic dermatitis and asthma have been viewed as atopic, meaning that there's an underlying tendency or predisposition to allergic reactions. So while all these responses are often triggered by the environment, the excessive chronic inflammation that underlies them has the same features.

Let me share an example. Airborne allergens like pollen – we're all are familiar with that, and pollen season is coming up very soon. Pollen can trigger an allergic response in those with pollen allergies and induce an asthma attack. The same pollen can come in contact with the skin and induce an itchy rash in someone with atopic dermatitis. Although these symptoms are different, the body's reacting to the pollen with a specific type of inflammation that spans across atopic dermatitis and asthma.

In the U.S., as you can see on the slide, millions of people have these diseases. These diseases not only appear different from the outside, but they can also vary in prevalence and age of onset. I think that's very critical to understand when we're thinking about these disease states. I'm sure you have heard – if you know someone or someone in your family or your friend is affected by it – things like oh, this happened when they were young, but then they outgrew it, or I never had this problem when I was young and now that I’m in an adult age group I'm getting it, so I don't know what's going on.
The prevalence and the age of onset is different for these diseases as well. Many are common, and they can be lifelong diseases like asthma and atopic dermatitis, but then some can appear in the adult age group like chronic rhinosinusitis with nasal polyps. But the interesting fact I also want to share is that even atopic dermatitis and asthma can be adult onset only, so there's a lot of variations. This is going to be one of the challenges I'm going to be talking about later in the presentation.

Any of these diseases may coexist with each other in the same person, and I think that's very critical to understand. Some patients might have one disease only, some might have a coexisting condition, and I think that's where it's very important because that's how the whole type two inflammation plays a critical role.

So, a little bit about when I mentioned the term coexist – let me give you some facts to support it. Up to 50% of adults with atopic dermatitis also self-reported asthma. Around 13% of adults with moderate to severe atopic dermatitis also self-reported chronic rhinosinusitis with nasal polyps. Up to 48% of adults with chronic rhinosinusitis with nasal polyps also have asthma. You can see how the coexistence of the diseases plays a critical role, and that's why when we are talking about a certain pathway or a certain treatment or a certain awareness, I think that it’s very important to understand the overlap in some of these diseases as well.

When you think about the patient perspective, it has always been my focus, not just being a physician by training but also seeing those patients and hearing their stories by being very fortunate to work for organizations that also support patient care to that extent. When you talk about the burden of the disease on patients and their families, I want to emphasize the word burden. I know it's a very strong word, and there's always that component of you don't know how the impact is and who gets impacted.

Is it the patient who is suffering from it or someone else? Or is it the community that it takes a toll on? I think it's all of the above, the reason being that the patient is going through a journey – a very impactful journey that's impacting the quality of life but also impacting the families and the caregivers that play a very critical role. Their lives are also impacted by someone suffering from this disease state as well.

I can share my own story really quickly. My kids have atopic dermatitis and asthma. I had atopic dermatitis and never got diagnosed. I think I self-diagnosed it when I became an adult, but I didn't have a treatment when I was growing up. Also, my father has asthma and nasal polyps. Understanding the burden of disease and how it takes a toll on a family plays a very critical role to understand these diseases and how these different inflammatory components play a role in that.
When we think about these diseases more there are some challenges, like how do we control these different signs and symptoms that I referred to you before? There's a challenge because in some cases, there are chronic symptoms that we have discussed – for example the rash, the itchiness, the oozing and the crusting – the signs and symptoms of atopic dermatitis. These signs and symptoms wax and wane, because there is the onset of disease, there's the prevalence of the disease, so there's that component.

The option that is available in some cases is long term corticosteroids use. As you can imagine, first there is a safety component because these drugs are not approved, but at the same time, these are the only option. They might give you a quick benefit, but it's got a long term side effect on top of that.

When you start thinking about something like asthma or chronic rhinosinusitis with nasal polyps patients, their option is if you have a severe asthmatic attack, you're going to get hospitalized. There's increased risk of that burden to live with. Then with chronic rhinosinusitis with nasal polyps patients, the only option available at this point is nasal surgery, which doesn't have a long-term effect – it has an effect to kind of further support it.

This is where the challenge of control for these patients is very, very important and very important to understand that as well. When we talk about people with one or more moderate to severe diseases characterized by underlying Type 2 Inflammation, they may have unpredictable, persistent or uncontrollable symptoms that can lower their health-related quality of life.

Impact on quality of life, the last line on this slide, is something I do want to mention. When a disease has taken control over your life, it's going to impact productivity at school, it's going to impact productivity in daily activities. The part that I also want to emphasize is sleep disruptions. I have to say that as women, there is a lack of sleep in our conversations and we are always catching up on sleep, but think about a patient with atopic dermatitis.

I'm going to show you a visual where you are constantly, constantly itching – the word is persistent itch. When you look at the data that's available about persistent itch, 90% of the patients say that at least one night a week they cannot sleep because of itch. 50% of the patients say that they cannot sleep for five nights a week because of persistent itch. 61% of the patients say that the itch is severe and unbearable. 86% of the patients say that there's a daily presence of itch in their lives and more than 60% of the patients are itching at least 12 hours a day.

Think about it. I know I've been talking about impact and the burden of the disease on these patient populations, but think about when your life revolves around the disease, what you see with regard to
decrease in daily activities or mood disturbances and anxiety. It's all interlinked. Not to mention these diseases are costing billions of dollars to the society and patients for direct health care costs and indirect health care costs, such as absenteeism, missed work, and missed school days. In the U.S. alone the costs are estimated to be more than $80 billion for asthma and more than $5 billion for atopic dermatitis. So the impact is significant on that level as well.

So, I have shared the patient’s voice in these conversations, which is something that I feel very, very strongly about, but I also want to share some of these quotes directly from the patients who are impacted by this. As you can see, the word is personal burden of these diseases on patients. What are those personal burdens?

On the left side of this of the slide, we’ll start with Tammy, who has asthma and allergies. When her asthma is really bad, she stays home, and she says inside. She can only watch everything from a distance. So, you can think about how she's feeling and what she can't experience because she's not feeling well.

Jason – and I have met all of them and I can tell you I know their detailed stories – when he was 12, he missed the first two weeks of sixth grade. My son is going to sixth grade, so I can understand that. School plays such a critical role in their lives, and when Jason came back to school, he somehow became the center of attention, which he didn't want, and that was a trigger for him to itch. Remember the data I’ve shared with you about the persistent itch of these patient populations.

Or Amelia, she had a great opportunity to present in front of the CEO of a company – that morning she had a flare up because that was the trigger. The stress is a trigger, and she had to pass on that opportunity because of polyps, and she spiraled out of control for a couple days because it definitely impacted her quality of life from that perspective, and it was really upsetting for her.

This is the life that they are leading on a regular basis. The burden that they carry, the impact that it have on these patients - and there are a lot of patients - plays a critical role in that piece as well.

How is Type 2 Inflammation connected? I think I've shared that throughout the chronic inflammatory component tied to the coexisting component as well. They are connected because Type 2 Inflammation is a normal part of the body. It’s important for the body to fight off certain kinds of infections, but the excessive form of Type 2 Inflammation leads to the disease. The recent science has shown that excessive Type 2 Inflammation – a specific kind of overactive responsive immune system – can underlie seemingly unrelated diseases such as atopic dermatitis, asthma, and chronic rhinosinusitis with nasal polyps. That
underlying Type 2 Inflammation may help explain some of the unifying features of these diseases and why these diseases may coexist, which we have talked about earlier as well.

Though these diseases and their symptoms are different, there are commonalities stemming from the underlying Type 2 Inflammation. As you can see here the commonalities unite people with these diseases, which are the drivers of the diseases.

So, the first one is the genetic component. I think genetic component plays a critical role. Genetics of Type 2 Inflammation may explain why some people experience more than one of these diseases throughout the course of their life and why these diseases can have a huge impact on not just the one who’s suffering but also on the caregivers and families as well.

Then, environmental triggers absolutely play a part. Environmental triggers that can exacerbate Type 2 Inflammation can include irritants, allergens, pollutants, and UV radiation – especially when the barriers like skin or airway are compromised. When you start scratching or you not able to breathe properly, constantly reinforcing that piece again and again is leading to the skin barrier or the airway barrier to be compromised. Of course, with that compromised barrier, that leads to the other aspects, including in some cases where the barrier can be so compromised that it might also lead to multiple infections.

So, over time, Type 2 Inflammation can lead to the loss of function in the tissues - like skin for atopic dermatitis or airway tissue in asthma. This can make them more susceptible, as I mentioned, to infections leading to more inflammation, and that's where the excessive Type 2 Inflammation is the reason, and the coexisting of the diseases kind of come together.

But despite these similarities in drivers of diseases with underlying Type 2 Inflammation, the way these diseases manifest can look very different depending upon the interaction with genetic and environmental factors. So, it depends upon where you are, what you are doing, what your genomic structure is, and it plays a very critical role in how this is coming together as well.

As mentioned before, Type 2 Inflammation is a normal part of the process and is important in fighting off certain diseases and infections. There are several types of inflammation, as you can see – B cell, Eosinophil, TH2, ILC2 – several types of Inflammation Type 2 cells are one of the specific targetable pathways and it's defined by certain signaling proteins, immune mediators and immune cells, like TH2 cells. The TH2 cell is a pathway it is named after.
I will say a lot of work is done in this field where the scientists are mapping out the specific components of Type 2 Inflammatory Pathway and their interactions, and it's all to better understand how this pathway can contribute to a disease. So, a lot of work is going on in understanding how we can move forward with that as well.

Of course, there is an emerging science about Type 2 Inflammation. I focused on three diseases today, but looking at Type 2 Inflammation and the kind of overactive response we're getting to the immune system, there are other diseases. There are ongoing studies happening in understanding the contribution of the role of Type 2 Inflammation to, for example, eosinophilic esophagitis (EoE) and Aspirin-exacerbated respiratory disease, which is also called AERD. Then there are also food and environmental allergies because, as you can imagine, when we are talking about allergies to begin with, those are considered a trigger factor in that as well. There are different components of diet on that level that play a part as well.

As we wrap up this conversation, I hope that you know this is important and this was helpful, not just for everybody on the call, but also hoping that the people suffering with this disease understand that they are not alone in this. I think that's very critical because sometimes it's just bringing people together that plays such a critical role in understanding the disease.

Also, the knowledge of the Type 2 Inflammation can help them understand why their disease may be unpredictable and explain why there might be coexisting diseases for them as well. We also believe that understanding how excessive Type 2 Inflammation plays a role in the disease can help people to ask the right questions, advocate for personalized care, and address a specific Type 2 Inflammation that underlies the disease.

So with that, thank you again for the opportunity, and I’m looking forward to an engaging conversation.

Representative Lauren Matsumoto: Thank you so much for that presentation. I see our first question is from Representative Wendy Thomas. What is the impact of diet on Type 2 Inflammation?

Dr. Mandeep Kaur: I think there's a lot of different ways of looking at diet in this conversation. One of those things is to determine is diet a trigger? I know there's a lot of data on that, but how much of Type 2 Inflammation plays a part in it still needs to be evaluated. As I shared with you, the Type 2 science is emerging on that level. Looking at food allergies is one way of looking at it, as well and there are ongoing studies for that. So, there's definitely a correlation.
I think there’s more to come on that from a conversation standpoint with some factual data supporting it as well.

**Representative Lauren Matsumoto:** The last question is my question. This is such an important issue. I think the question I’m always wondering is what can we do as state policymakers to help?

**Dr. Mandeep Kaur:** I will answer first on that and then I’ll ask my colleagues Kathryn, Karla, and Carole who are on the call as well if they want to add to it. First, thank you! I think this is definitely the beginning of many conversations on this topic, I hope. I think awareness, education, and support for these patients suffering from these diseases is the most critical piece of what we can do to support them.

Carole, if you’re still on the call, Karla, or Kathryn, would you like to add anything?

**Carole Huntsman:** I think just to continue to support the patient communities is very important. I think clearly there are a lot of patients in need, particularly with asthma as one of the most common diseases that patients suffer with. So, I think continuing to be aware of the needs that patients have in the community would really be our number one ask. Thank you.

**Kathryn Lavriha:** Mandeep, this is Kathryn Lavriha from Sanofi State Government Affairs, and we appreciate the support of Women In Government on these issues because I think the forum today shows that many of you probably were surprised to even learn about this disease.

What we have found in our previous experience at the State Capitol is that once you go back and start talking to the other legislators and to your colleagues, they say we didn’t even know this was a problem. How can we address these issues? You form a caucus, and you begin to talk with the Secretary of Health. Is there funding in the budget for these kinds of diseases?

I think it’s the next step from raising awareness to really talking about – you know, we have state employees who are off work. Why? They may have some form of atopic dermatitis, but we just think that they’re not showing up for work.

So, I think if you go back and talk to your colleagues, form a caucus so they can share stories, and talk with the Secretary of Health to see what else we can do within the state budget to raise awareness and address these kinds of chronic conditions would be very helpful. Thank you.
Representative Lauren Matsumoto: Thank you to everyone for all of that wonderful information! Just to let everybody on the webinar know, if you'd like to hear more about this topic, WIG is producing a podcast which will be coming up later this year, so stay tuned for that.

I'd like to just say thank you again to all of our speakers and thank you to all of our sponsors and member companies for supporting the session today.

Please don't forget to join us again next week, Wednesday, July 1st at 3pm eastern time for our third WIG Summer Summit segment. You'll be hearing from our special guest Shelby Kerns, Executive Director of the National Association of State Budget Officers, and we'll also be having exciting programming around the 30th anniversary of Americans with Disabilities Act.

Please encourage your legislator colleagues and legislative staff to register for the remaining events in the series at https://www.womeningovernment.org/ again, that's https://www.womeningovernment.org/.

Thank you so much again for joining us, and stay safe!