Bringing CYTOPOINT to life—from an idea to an injectable
A discussion with some of the scientists behind the development of CYTOPOINT

CYTOPOINT is an innovative monoclonal antibody (mAb) therapy that represents an important advancement in the treatment of canine atopic dermatitis. It is an in-office injectable that specifically targets interleukin (IL)-31 to help provide long-lasting and safe itch relief for 4 to 8 weeks.

On August 10-11, 2016, we interviewed some of the scientists who helped develop CYTOPOINT to get an inside look at how this groundbreaking treatment was conceived, created and tested.

**ANDREA GONZALES** [Research scientist, allergy and immunology]: The development of CYTOPOINT really started with APOQUEL® (oclacitinib tablet). We began by paying attention to how that was working and focusing on what we still didn’t understand about canine atopic dermatitis.

**STEVE DUNHAM** [Antibody engineer]: We knew APOQUEL was inhibiting the activity of several cytokines.

**GONZALES**: So we started by looking at cytokines that we thought might be involved in itch. We knew APOQUEL could inhibit multiple Janus kinase–dependent cytokines, but could we get away with just inhibiting one?

**DUNHAM**: We chose to focus on IL-31, based on some data that came out in the mid-2000s, demonstrating a strong pruritic response in mice overexpressing IL-31. It was a bit of a flyer to think that it was the most important cytokine in natural disease. The only way to prove that IL-31 was an important pruritogen was to generate an antibody that eliminated IL-31 from the equation. If it worked [reduced pruritus], we knew it would be an excellent, more targeted therapeutic option.

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The fewer cytokines you can inhibit, the less likely you are to interfere with the immune system in a time of need.

GINA MICHELS [Lead clinician, CYTOPOINT™ program]: And after all this, we needed the approach to translate into the field.

DUNHAM: We knew from the model that our antibody was very effective at eliminating IL-31–mediated activity.

MICHELS: The data from the field agreed [with the laboratory data]. It showed we were actually inhibiting IL-31 very early—within 1–3 days. Initially, we had thought if it did work at all, it might take a couple of doses. And we also saw a significant improvement in the skin lesions.

We were basically rewriting the textbook in terms of the management of atopic dermatitis in dogs, showing that inhibition of a single cytokine can have a dramatic impact, not only on the itch, but also on helping remove skin lesions.

The field safety study itself was a pretty unusual study design for a field study, since we couldn’t exclude any medications. Dogs in the study were allowed to receive other medications. This allowed us to truly compare adverse event (AE) frequencies between the placebo and treatment group. And we saw no difference in AEs between the groups.

MATTHEW KRAUTMANN [Researcher, safety studies]: It was the first time that we used a T-cell–dependent antibody response test in a target animal safety study. And that’s just one example of how the entire approach to safety was adapted based on principles from human biopharma experience.

GINA MICHELS: Meanwhile, as a team, we communicating our science and our mechanism of action very early on. When we started, veterinarians were still very focused on IgE and mast cells as primary drivers for this disease, and we had to work to change that mindset, to help them understand that cytokines are likely driving the disease, particularly cytokines from T cells. We worked across the organization from researchers to the communications folks to really get a nice disclosure plan in place so that we could talk about our research.

KRAUTMANN: It was an incredibly interdisciplinary process. We had protein chemists, cell biologists, immunologists, vaccinologists, toxicologists, pathologists, and clinicians all working together. There needed to be quite a bit of dialogue in order for us all to come to a common understanding and to communicate inside and outside the organization, and in that sense it’s the most fun I think I’ve ever had in this job.

DUNHAM: I distinctly remember when the first read from the clinical data came back, and it’s a feeling I’ll never forget. We were the first people in the world to understand the significance of the role of IL-31 in natural disease, in any species. I’ve been working in science for 20 years and it was almost a feeling of euphoria.

It makes you proud of what you’re doing. You know it’s making a difference in dogs with atopic dermatitis and for their owners as well.

KRAUTMANN: I actually have a dog on CYTOPOINT. She had a really bad case of atopic dermatitis and other drugs hadn’t helped, and I was about ready to put her down, but we’ve put her on this antibody and now she looks normal.

DUNHAM: It makes you proud of what you’re doing. You know it’s making a difference in dogs with atopic dermatitis and for their owners as well.

CYTOPOINT is now available as a single in-office injection that can help reduce clinical signs of canine atopic dermatitis for 4 to 8 weeks. Feedback from the Conditional License program continues to be very positive, reflecting improvements in the long-term quality of life of dogs and their owners. In some cases, veterinarians and owners report that the impact has been truly life-changing.
Compliance and the human-animal bond
A discussion with Patrick Flynn, DVM, Senior Professional Services Veterinarian, Human-Animal Bond Team Lead, Zoetis Inc.

Ask a veterinarian how well his or her clients comply with medication schedules, and you’re likely to hear that most are reasonably close to the mark. Ask the pet owners the same question, and you may get a very different answer. One study found that veterinarians, on average, estimated that 15% of clients had trouble pilling their dogs as directed; the actual number reported by clients was 66%. Only 6% said they had never missed a dose.

“[Atopic dermatitis] can impact the dog’s bond with the owners. They’ll say, ‘I don’t even want to sleep with him anymore’ or ‘I don’t want to take him for a walk because I’m afraid I’m gonna be judged.’ Veterinarians don’t always have the full picture of the suffering that’s going on in the home.”

According to Patrick Flynn, DVM, “the problem with medications many times is on the other end of the leash. It’s not the pet.” Dr Flynn, who was in veterinary practice for 12 years, is now pursuing a Master’s degree in the nascent field of anthrozoology, the study of human-animal relations. “You’re challenging veterinarians when you say that their clients aren’t doing what they say—because the clients are human.” Evidence suggests that compliance is a serious issue in human medicine as well, even when lives are at stake. “There’s an amazing study of postal workers who were given an antibiotic [during the 2001 anthrax scare that killed 5 people] to protect them from anthrax, and only 60% of them finished the medication.” And this was for something that was life-threatening.

It is difficult enough for humans to comply with their own medication; the difficulties increase when a pet is the patient. Part of the reason, says Dr Flynn, is that chronic illness and medication administration can disrupt the cherished bond between owners and their pets.

“Dogs are hyper-social, as we are. They enjoy their social unit, and they appreciate being valued. When the dog is afflicted with skin disease, which is outward, gross and smelly, and not something you want to touch, the dog is rejected by its social group. ‘You’ve got that nasty hot spot. You smell like yeast.’ All of a sudden the members of the pack are making disgusted noises and the dog is being rejected for a reason he doesn’t even understand. So it can impact the bond with the owners—they’ll say, ‘I don’t even want to sleep with him anymore,’ or ‘I don’t want to take him for a walk because I’m afraid I’m gonna be judged’”—and it also goes the other way around. The dog’s bond with the human is damaged too. Veterinarians don’t always have the full picture of the suffering that’s going on in the home.”

Veterinarians, on average, estimated that 15% of clients had trouble pilling their dogs as directed; the actual number reported by clients was 66%.1

The need to give medication to the dog, Dr Flynn explains, has the potential to further erode the human-animal bond. “Some dogs don’t tolerate the medication; some dogs go from being very friendly family pets to being aggressive, which puts the client at risk; there are the throw-up dogs, and the dogs whose owners just give up. And there are the amazing ‘artists’ whose owners will swear up and down that

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they gave the dog all the medication, and one day they move the couch and find a pile of pills. There are certainly dogs that will gladly eat anything that’s covered in peanut butter, but even then it’s challenging to dose it at the right time. There’s a big difference between ‘every 12 hours’ and ‘twice a day.’”

Research has shown the mutual benefit of the human-animal bond, and the value in protecting it. “What the individual pet gives to the family at home is the equivalent of a medication. Pets give as much as they get. In the Odendaal study in 2003, he looked at owners with their dogs. They were separated, in different rooms, and they took baseline readings of multiple hormones in both dogs and owners. Then they allowed the owners to spend about 20 minutes playing with their dogs, and they measured hormones again. And they found that oxytocin doubled in people. We now know that oxytocin decreases blood pressure and decreases heart rate—it does a lot of really calming things in a mammalian brain. It’s the same neurochemical bond that’s happening in a new mother to help her bond with the baby. And the dogs’ oxytocin levels doubled as well. It’s a true two-way street that a healthy relationship can give.”

“The biggest block to compliance is from people who are just living their lives. They’ve got children, they go to the gym, and they forget. Life is one of the biggest barriers to getting it done.”

For dogs that resist pill ing, alternative treatments may offer a solution that reduces stress on the animal-owner bond. “The dog is thinking, ‘What’s wrong with you? I thought we had a relationship, and now every 12 hours you’re wrestling me to the ground and shoving something in my mouth that I don’t want!’ And that’s something that a treatment like CYTOPOINT™ can really help with, because it can help restore that bond on both sides.”

Compliance may always be a challenge, Dr Flynn concedes. “The biggest block to compliance is from people who are just living their lives. They’ve got children, they go to the gym, and they forget, or they give it as often as they can. Life is one of the biggest barriers to getting it done.” Working with the schedules of owners and the preferences of dogs by exploring alternative forms of medication has the potential to make life better for both dogs and their families.

Patrick Flynn, DVM, pictured with a young warthog at a meeting of the Florida Veterinary Medical Association PAC.

Zoetis is a proud sponsor of the Human Animal Bond Research Initiative (HABRI), which strives to gather, fund and share scientific research demonstrating the positive health impacts of companion animals on people. Learn more at https://habri.org/.

Interview with Dr Patrick Flynn conducted August 10, 2016.

A novel approach to treating canine atopic dermatitis—views from Conditional License participants

Canine atopic dermatitis has historically been a challenging disease to treat. The emergence of a monoclonal antibody for canine treatment is a significant advancement in more targeted therapies. With the launch of CYTOPOINT™, veterinarians now have another tool in their arsenal to help manage this chronic condition.

On June 15, 2016, we spoke to some Conditional License participants to learn about their clinical experiences with CYTOPOINT.

How do you recommend and explain CYTOPOINT to your clients?

LAURA STOKKING, PhD, DVM, DACVD, Dermatologist, Veterinary Specialty Hospital, San Diego, CA: [We tell them that] CYTOPOINT is an excellent addition to our armamentarium against canine atopic dermatitis. Rather than needing to find the treatment that is the least likely to suppress the immune system, or the least likely to cause side effects, or one that is going to be the least likely for the owner to forget, we have a treatment that is safe and effective, and can be administered once monthly.

“We finally have the opportunity to use the same cutting-edge medicine that is used in people.”—Dr Lindsay McKay

LINDSAY McKay, DVM, DACVD, Dermatologist, Aurora Animal Hospital, Aurora, IL: Clients really need to understand that we finally have the opportunity to use the same cutting-edge medicine that is used in people. Now we can explain to them that, with CYTOPOINT, we have done the work to figure out the molecule that is causing all of this itching, and we can take it out of play, and do it very safely and very effectively.

TOM LEWIS, DVM, DACVD, Dermatology for Animals, Gilbert, AZ: I tell clients that there are different interleukins (ILs), and some have positive roles in the body and some have negative roles. Blocking IL-31 doesn’t seem to have any negative impact. This concept appeals to clients. Additionally, CYTOPOINT is a once-monthly injection given in the office, so the owners don’t have to do anything at home.

“In my practice, some of our patients have struggled their whole lives. Now we have this new product that’s so effectively blocking IL-31, and patients’ lives have changed.”—Dr Tom Lewis

When it comes to selecting patients, which dogs are the most appropriate candidates?

LEWIS: With CYTOPOINT, there is no age contraindication, so I have frequently used this product in patients under 1 year of age.

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ROD ROSYCHUK, DVM, DACVIM, Staff Dermatologist, Colorado State University, Fort Collins, CO: The majority of our patients on CYTOPOINT™ are on chronic therapy, but we do use it intermittently for short or seasonal issues. I think we are going to be using even more of it in the future [in seasonally affected dogs].

BRUCE HANSEN, DVM, DACVD, Dermatologist, Springfield, VA: CYTOPOINT is just as good in chronic cases [of atopic dermatitis] as it is in acute cases.

DR ROYCHUK: It’s been a great treatment for us to use in individuals who are on other medications where we’re trying to avoid drug interactions. We have a number of clients who also like the convenience of not having to remember to give pills on a regular basis, and we can use it for long-term therapy.

“I’m the miracle worker who has provided this wonderful therapy ... so [clients] heap that praise upon me.”—Dr Rod Rosychuk

DR STOKING: CYTOPOINT definitely has a role as a first-line treatment for atopic dermatitis.

How do you work up patients, and how do you begin CYTOPOINT?

DR HANSEN: The first thing to do to establish the diagnosis and the type of drug that we use is to make sure we get all of the infection cleared. Thereafter, we need to make sure there are no parasites, and we need to complete a food trial, if it’s non-seasonal. Once parasitic disease and food allergies are ruled out, I generally will recommend either CYTOPOINT or APOQUEL while I perform allergy tests and potentially start allergen-specific immunotherapy.

How have your clients reacted to CYTOPOINT?

DR McKay: They are seeing only positives. I get emails with pictures of dogs that are actually sleeping, and they’re not red anymore, and they are comfortable and calm. The owners just honestly got to a point where they never really thought that would happen.

DR LEWIS: In my practice, some of our patients have struggled their whole lives. Now we have this new product that’s so effectively blocking IL-31, and patients’ lives have changed and their itch has gone, or at least dramatically subsided.

DR ROSYCHUK: The obvious overall efficacy has made my clients very pleased with us, and this reflects very well on me. I’m the miracle worker who has provided this wonderful therapy for them, so they heap that praise upon me.
Don’t miss these important veterinary meetings

NORTH AMERICAN VETERINARY COMMUNITY CONFERENCE (NAVC) 2017

February 4-8, 2017
at the Orange County Convention Center, Orlando, FL

The NAVC conference, with over 16,000 veterinary professionals and guests from around the world, offers a huge variety of advanced learning opportunities, extraordinary innovations and meaningful connections to keep veterinary professionals moving in exciting new directions.

This year’s conference will feature:

+ Over 1,200 CE Credit Opportunities, including panels, hands-on labs, master classes, behind-the-scenes tours and sessions designed to fit your schedule

+ Two NAVC Exhibit Halls, filled with more than 650 exhibitors demonstrating new products, services and equipment to take your practice or career to the next level

+ IGNITE!, featuring TED-like talks interspersed with hands-on learning in breakout sessions intended to spark fresh ideas and new perspectives about the future of the veterinary profession

+ The latest diagnostic approaches

DON’T FORGET TO VISIT ZOETIS AT BOOTH 2419!

And don’t miss these Zoetis-sponsored presentations:

Innovation & Technology: New Therapies for Common Skin Diseases

Sunday, February 5, 2017, 1:45 PM–4:50 PM

Drs Andrea Gonzales, Natalie Marks, Lindsay McKay, Mark Papich and John Angus

NAVC Live Theater: Introducing CYTOPOINT: Next Generation Therapy for Canine Atopic Dermatitis

Sunday, February 5, 2017, 12 PM
Monday, February 6, 2017, 3:30 PM
Tuesday, February 7, 2017, 12 PM

Dr John Angus

To learn more about the NAVC conference or to register, visit navc.com.
UPCOMING EVENTS

WESTERN VETERINARY CONFERENCE (WVC) 2017

March 5-9, 2017
at the Mandalay Bay Convention Center, Las Vegas, NV

The annual meeting of the WVC offers the most practical and cost-effective professional development available, presented at a world-class, yet affordable destination. You will have the chance to learn from leaders in your field and gain knowledge that you can put to use immediately in your practice. With over 1,000 hours of CE to choose from, the conference is your opportunity to earn all required CE in one place.

The WVC also offers an unparalleled opportunity to network with peers. Nearly 15,000 veterinary professionals attend WVC, of whom over 6,000 are veterinarians.

DON’T FORGET TO VISIT ZOETIS AT BOOTHs 4319 AND 4524!

And don’t miss these Zoetis-sponsored presentations:

Not Just Skin Deep: The Game-Changing Science of Allergic Itch
Monday, March 6, 2017, 2:00 PM-2:50 PM
Room: Mandalay Bay F, Level 2
Drs Douglas DeBoer and Andrea J Gonzales
Immunotherapeutics like monoclonal antibodies (mAb) offer exciting new options for treating allergic itch. Learn how these biologic therapies can aid in the long-term management of canine atopic dermatitis. This session will also review mAb pharmacology and key efficacy and safety studies.

Switch Off the Itch: Practical Application of New Therapies
Monday, March 6, 2017, 3:00 PM-3:50 PM
Room: Mandalay Bay F, Level 2
Drs Douglas DeBoer and Natalie Marks
Learn how to provide rapid relief for your allergic patients. Keep them itch free during a diagnostic workup, without the negative effects of traditional therapies.

Atopic Dermatitis: Building a Lifelong Treatment Plan With Sustainable Therapy
Monday, March 6, 2017, 10:00 AM-10:50 AM
Room: Mandalay Bay F, Level 2
Drs Douglas DeBoer and Lindsay McKay
Canine atopic dermatitis is a lifelong disease—don’t let your patients and their owners suffer. Discover how monoclonal antibodies (mAb) can help control the disease even in very young and seasonal patients and provide solutions to help manage lifestyle, compliance and comorbidity concerns.

Challenging Our Beliefs About Anti-Infectives: A Human Medicine Perspective
Monday, March 6, 2017, 5:00 PM-5:50 PM
Room: Mandalay Bay F, Level 2
Drs George Zhanel and John Angus
Ready to rethink some of our most basic beliefs about anti-infectives (AIFs)? Learn how much resistance, treatment duration and compliance can actually affect clinical outcomes, and get expert advice on judicious use of AIFs, including how to maximize therapeutic efficacy and minimize selection of resistant microorganisms.

To learn more about the WVC conference or to register, visit WVC.org.

IMPORTANT SAFETY INFORMATION

Do not use APOQUEL in dogs less than 12 months of age or those with serious infections. APOQUEL may increase the chances of developing serious infections, and may cause existing parasitic skin infestations or pre-existing cancers to get worse. APOQUEL has not been tested in dogs receiving some medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporines. Do not use in breeding, pregnant, or lactating dogs. Most common side effects are vomiting and diarrhea. APOQUEL has been used safely with many common medications including parasiticides, antibiotics and vaccines.

For more information, please see the full Prescribing Information.

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THE INSIDE STORY:
LAUNCHING CYTOPOINT

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