December 13, 2023 / Long live your dog

[HALF SECOND OF SILENCE]

[BILLBOARD]

SCORING <Wag The Dog>

NOEL KING (host): The “dog” arm of a San Francisco based biotech firm called Cellular Longevity says it has developed a new medication that will help large-breed dogs live longer.

“Loyal”: that’s the name of the dog arm / partnered with the pharma company Crinetics to develop the medication; it should be on the market very soon.

If your first reaction is “that’s fantastic!” followed by … sorry? Dog arm? Crinetics? You’re in good company.

Scientists may be googley-eyed over this new med, but animal ethicists are on edge.

*<CLIP> REBECCA WALKER (UNC professor): Well, I'm, I'm not saying I necessarily think it's wrong. I mean, you asked me if I would do it.  
NOEL: Yes, you're right. You're an ethicist and it's good for you to draw that distinction.  
REBECCA: Yeah.*

NOEL: Coming up on Today, Explained: long live your dog.

SCORING OUT

[THEME]

*<CLIP> THEME, BUT WITH BARKS*

NOEL: It’s Today, Explained. I’m Noel King. Emily Mullin is a staff writer at WIRED Magazine. She covers biotechnology. And she’s also a dog person.

EMILY MULLIN (WIRED staff writer): I do not have a dog. But my parents do. He is a he's a very sweet English cream golden retriever who's sort of lazy and does his own thing, but he's – We love him.

NOEL: I have a lot of adjectives to describe my pug and sweet is not one of them…

EMILY: <laughs>

NOEL: …but I love him so much.

EMILY: <laughs>

NOEL: Emily recently wrote about a company called Loyal, which made some big news.

EMILY: This San Francisco biotech company has just cleared a key FDA hurdle on the path to getting a drug approved to extend the lifespan of dogs. So they haven't gotten approval yet. There are still a couple more steps in that process, but this is sort of the first major step. Based on initial data the company has submitted to the FDA, the agency has basically said this drug has a reasonable expectation of success. And that's kind of a big deal for the FDA to do because it has never approved a drug for life extension, for longevity, for animals or humans. So this is kind of a sign that the FDA is ready to take this idea seriously.

NOEL: How far back? I mean, listen, I think a lot about medicines for humans and the advances that have been made since – god, time immemorial, right? – How long have scientists been studying life lengthening drugs for dogs?

EMILY: Well, scientists have been interested in this general idea of life extension for a long time.

SCORING <Innovator>

EMILY: In the 1980s and 90s, they identified the first genes that modulate life span. And they did this in worms first. And since then, there have been studies in different lab animals, rodents, fruit flies, more worms. And scientists have shown that certain genes seem to be key regulators of lifespan in these animals.

*<CLIP> LOYAL FOUNDER AND CEO CELINE HALIOUA: The genes that control dog size, and specifically make big dogs live a shorter life – is all connected to one of the most well-understood and OG longevity pathways there is. Because the first time they showed with a single gene mutation that they could make worms live a longer life: they made that worm genetically like a chihuahua.*

EMILY: So, Loyal with this drug is specifically trying to lengthen the lifespan of large and giant-breed dogs. And there's this well-known inverse relationship between dog size and how long they live. So you probably know that Great Danes, Irish Wolfhounds, Bernese Mountain Dogs: these dogs only live six, seven, eight years. And yet the smallest of the dogs that humans have bred, Chihuahuas, for example, can live up to 20 years. And so there's this inverse relationship here. And scientists have pinpointed one potential driver, a hormone called IGF-1 that seems to be present in high levels in these large dogs and in low levels in small dogs.

SCORING OUT

EMILY: And, of course, humans have been breeding dogs for hundreds of years for certain characteristics, and that has resulted in this big disparity in dog sizes. I mean, purebreds are very inbred. And in fact, several studies have shown that mixed breed dogs, on average live longer than purebred dogs.

*<CLIP> HALIOUA: Basically when people were breeding for size – our thesis is that they accidentally gave dogs an accelerated aging disease. Basically, the things that control the dog growing really quickly in puberty don’t fully turn off…   
FORMER “DAILY SHOW” HOST JON STEWART: Woowwww.   
HALIOUA: … then the dog ages at a faster rate and dies sooner.*

NOEL: So big dogs have higher levels of a hormone called IGF-1 and they die more quickly than smaller dogs. What does IGF-1 do? And is it fair to say it's killing large dogs more quickly?

EMILY: Well, one explanation for why large dogs have shorter lives than small dogs is that maybe they're aging at a faster rate. And IGF-1 has been linked to growth and bone size, and it plays a role in metabolism. So what Loyal is trying to do is reduce the levels of this hormone throughout the body of these large dogs. And they say that in initial studies of a little over 100 dogs, that they have been able to bring this level down to what is seen in medium sized dogs. So we're not talking about getting rid of this hormone completely or bringing it down to levels in small dogs. But Loyal says that at least in the initial studies it's done, that it can actually do this in large dogs and bring this hormone to levels seen in medium-sized dogs.

NOEL: Would it affect their bone growth and their metabolism?

EMILY: So with this drug, Loyal aims to treat dogs that are at least seven years old.

NOEL: Ohhh.

EMILY: The company hasn't really said how this drug is going to affect dog's health at that age, we don't really know exactly the mechanisms behind how it's working, and the company has kept some of that information close. So we don't exactly know yet. And right now, the company is planning a bigger trial of around a thousand dogs. That's going to start either next year or in 2025 to do this bigger efficacy study. And what's going to happen is they'll have a placebo group and an experimental group. And of course, some dogs won't receive the drug will receive a placebo. Some dogs will. They're enrolling people's pets in this trial. So if you have a large or giant breed dog out there who, you know, you might be able to get your dog enrolled in this trial.

NOEL: God, I wish I could get my pug enrolled in this trial.

EMILY: <laughs>

NOEL: I want – I want him to live forever. How do dogs, how do dogs receive this treatment? I mean, is this something where you have to take them to a hospital to get it done? Or is this as simple as, you know, it's a pill you grind up over their food?

EMILY: So for now, this drug is an injection designed to be given in a veterinarian's office every 3 to 6 months.

NOEL: Hmm.

EMILY: So to get conditional approval of this drug from the FDA, the company has already shown that there's a reasonable expectation of effectiveness, but it still has to conduct this larger study. It also has to show the FDA that this drug is safe for dogs and it has to show that the drug can be manufactured safely and reliably. Once it does that, the company can then ask the FDA to conditionally approve this drug. And a conditional approval is essentially a temporary approval, which is going to allow Loyal to market the drug for up to five years. And at that point, at that five years, the conditional approval is going to expire. So Loyal is going to have to show in this large trial of around a thousand dogs that it does work or else it has to take the drug off the market. But if it does have this great data showing it does in fact extend the life of these large dogs, then the drug will be fully approved by the FDA.

NOEL: Are there any side effects of this medication?

EMILY: Well, we don't really know yet because Loyal has said it has tested this drug so far in about 130 research dogs. But at least in the initial tests of this drug, they didn't see any major cause for concern. A couple of dogs had runny stools for a couple of days after treatment…

NOEL: Aww.

EMILY: … but nothing serious. But again, that's what this bigger trial is for.

NOEL: You know, I have a question sort of on behalf of the skeptics about the investment in this versus the investment in things that are useful for human beings. Right. So I imagine there are people out there who would say there are bigger scientific questions. We still haven't figured out cancer guys. Why are we, why are we putting time and money into this when loyal and companies that work on this are asked those questions? What do they say? Is it just about well, you know, pets are people, too.

EMILY: Well, I think Loyal’s goal – and I think a big goal of the life extension field – is to bring a drug to humans is the ultimate goal. Right. To figure out how we can extend not just people's lifespan, but the number of healthy years that they have. Humans have IGF-1 as well, and too much of IGF-1 in people also leads to health problems. So I think there's definitely potential here for maybe an application to humans if it does work in these dogs.

SCORING <Singing Dog>

NOEL: Emily Mullin, staff writer at WIRED where she wrote "A Life-Extension Drug for Big Dogs Is Getting Closer to Reality,” you can find it on WIRED dot com. Coming up: so it sounds like good news for pet owners, BUT: is it ethical? We’re gonna call an ethicist. An animal ethicist. It’s a real thing.

[BREAK]

[BUMPER]

*<CLIP> “ALL DOGS GO TO HEAVEN” (1989), CHARLIE: Where am I?  
 HEAVEN DOG: This is the Great Hall of Judgment.   
 CHARLIE: Judgment?!*

*HEAVEN DOG: Oh, not to worry, Charlie. You’ll go to heaven. All dogs go to heaven. Unlike people, dogs are naturally good and loyal and kind.   
CHARLIE: Huh. That’s true.*

NOEL: Today, Explained. We’re back with Rebecca Walker. She’s a professor of social medicine and philosophy at the University of North Carolina Chapel Hill, and she focuses on animal research and ethics. Including: our relationship with what she calls “companion animals.”

REBECCA WALKER (UNC professor): <laughs> I think the word companion animal can be confusing for people. So I just mean by that: pets. I think people are really too focused on their own interests, in their relationship with the animal and not thinking enough about what life is like from their point of view.

NOEL: For instance, Professor Rebecca?

REBECCA: Well, I mean, I – <laughs> I don't know if I should say this, but I think giving your pet drugs to extend their life by a little bit just so you can spend a little bit more time with them, would be a prime example of that kind of problematic attitude, because I, I think it's probably not in the best interest of the animal.

NOEL: Rebecca has a cat, a few chickens, and a golden retriever named Pepper. So I asked her: would she give this Loyal drug to Pepper?

REBECCA: No, certainly not this drug at this time. But generally, I think probably not. Medications all have risks and side effects. She's a perfectly healthy dog. She's not in a position to communicate with me how she's feeling about any drugs that I might be giving her other than, you know, her behavior or her sort of, you know, medical signs that aren't necessarily going to track, you know, how she's actually feeling. So, you know, why would I give her a drug that could harm her and at best expand her life for a few months? I think that might be in my interest, but I doubt it's in her interest.

NOEL: Let's dig into that a little bit more. So among the distinctions that I want you to kind of just spin out a little bit are: If a dog is sick, we give them medication. What's the difference between a dog is sick? And so we give him or her medication and a dog eventually is going to die. And now there's this, this drug that can make them live longer?

REBECCA: So the things I would be concerned about is: amongst them, I think when we're when we're behaving for the sake of other people and we're we're doing actions that are primarily with respect to thinking about their interests, it's important that we don't confuse what we want with what they really have an interest in. And so for I could, I think for, you know, a human being who maybe they have a big project that they're working on or something that they've been sort of trying to get finished their whole life. And, you know, they just need a couple more months of life to, to get it done. Maybe for them this would make sense because it would give meaning to their life as a whole. But dog lives aren't like that, right?

*<CLIP> DOG BARK SFX*

REBECCA: They're sort of really driven by their day to day welfare and not by those kind of big projects. So I think you need to think about the dog life from her point of view and what's good for her.

*<CLIP> TWO DOG BARKS SFX*

REBECCA: And is it is it worth the risk of having some unpleasant experiences or unpleasant reactions just to sort of add a little bit more life from her point of view? I think for us, because they live a lot less than we live, we think of their short lives as, as, you know, tragically short. But from her point of view, things are quite different. So I think, if she was experiencing an illness or, you know, suffering from a disease or disability, that would be a really different situation because then it would be in her interest to give her a medication. Even in that case, it often happens that people may treat animals or extend their lives beyond what is actually in their interest because they just can't let them go.

NOEL: So. All right, so we have this company make this announcement. And so we understand that people who own or guard or live with large dogs will soon be able to make this decision for themselves. From an ethical standpoint, what should people consider before they think about giving a medication like this to their pets?

REBECCA: So I think there are a few different things.

SCORING <Keep Your Friends Close>

REBECCA: One, I think this issue about whether an animal is a healthy animal or a sick animal is really important. And so you really need to do a risk-benefit sort of analysis on their behalf, which, again, I think is really difficult for us to do because our interests are all kind of caught up in wanting them to live longer and, you know, thinking about sort of the benefit they provide to us by being part of our lives. So I think it's really important to for people to as much as they can to remove themselves from that equation and try to think about things from the point of view of the animal. But also in that regard, I think one thing for people to be aware of upfront is that when this drug hits the market, if it does so under this FDA conditional approval, it won't actually have been proven effective to extend an animal's healthy lifespan. And the sort of rhetoric around it sounds really positive. And people are, you know, obviously hopeful that it will be effective.

*<CLIP> FOX FIVE: Scientists could be on the brink of a big breakthrough when it comes to helping four-legged friends live longer…*

*<CLIP> NBC NEWS: … giving you possibly an extra year of cuddles, fetch, and slobbery kisses.*

REBECCA: But it does mean that veterinarians can be prescribing it and owners can be thinking they're doing something that's going to help their pet live longer, but it's not actually necessarily the case. So whether it actually works will depend on getting the full results of the clinical trials that are still going to be ongoing at the point that it's approved.

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NOEL: We heard in the first half of the show that this type of drug could someday be available to humans. Now, you've drawn this distinction, which is my dog, as much as I love him, is never going to retire and start learning another language and travel and develop hobbies. Gugli is always just going to have walks and treats, and that's about it. But human life can be really fulfilling past a certain point. Do you think, like, life-extending drugs for humans are something that is ethically interesting, tricky, dubious?

REBECCA: I'm not worried about it just because it's life expanding, I mean, so typically in bioethics, we make a distinction between medical interventions that treat or prevent disease or disability and those that enhance us in some way. And I think that the way that the people who are promoting this drug have been talking about it, they've been talking about it as a kind of a prevention and particularly preventing death.

*<CLIP> HALIOUA: One of the cool things about how at least we’re trying to approach it is: we’re looking at preventative medicine. And specifically, one way to think about it is: statins. A large percentage of the adult US population is on statins to reduce their risk of future cardiac events. That’s what I think an aging drug should be.*

REBECCA: But it's pretty clear that it falls into the enhancement category in terms of that distinction. So we're trying to add more life to a normal life span. And I'm I'm not that worried about that because our what's normal in terms of our lifespan has changed dramatically over the centuries and in result to environmental shifts and, you know, even just plain old sanitation. So I guess what I'm more concerned about is lifespan is already really closely associated with wealth. And these drugs might be expensive and might give better off people even more access to longer life. So there's a certain fairness issue and access issue that I think would be really important to consider. I also think that, you know, we're sort of always looking for a kind of fountain of youth or a way to expand and extend our lives instead of recognizing the reality that we are all going to die and the importance of doing the best we can with what we have. And so I just sort of feel like this is kind of one more way of adding to that problematic perspective.

NOEL: It sounds like your point of view is that we should think maybe a bit less about extending the lives of our pets and think more about improving the quality of the lives of our pets. How should we do that, other than the obvious?

REBECCA: Yeah, well, I think one important thing we can think about is how animals are bred for human interests. And I was saying before, I'm more concerned with how we're already relating to animals. So just for example, take my golden retriever, right? There's some evidence that their lifespans have been going down as they've been bred more intensively to have particular kinds of looks. You know, we should, we should think first about how we're creating animal breeds and lines in ways that already diminish their lifespan before we think about taking the livestream that we've already shortened and lengthening it by adding a drug into the mix. <laughs> So I think that that's kind of more what I'd be interested in us looking at.

SCORING <Rock n Dogs>

NOEL: Today’s show was produced by Amanda Lewellyn. She has a little brother (dog) named Opie. It was edited by Matthew Collette, Orzo’s dad. It was fact-checked by Laura Bullard, mom of Murf and Muzzy. And it was engineered by David Herman who is a cat person: Robocop and Smalls. This is Today, Explained and it’s the second time this year we’ve put our pets’ names in the credits.

One more thing before we go, we're working on an episode about millennials dreading motherhood. Are you a millennial? I know that a lot of you are. If you were born between 1981-ish and 1996-ish and you're feeling some type of way about becoming a parent, please give us a call and tell us about why that is. Our number is 202.643.0314. Keep your message brief, please, and we might use it in the show, heads up. 202.643.0314. Thanks for doing this.

SCORING OUT

**[10 SECONDS OF SILENCE]**