Karen Jagoda: Welcome to the Empower Patient Podcast.com Show. I'm Karen Jagoda, and my guest today is Dr. Nerissa Kreher. She is the Chief Medical Officer at Tiburio, it's T-I-B-U-R-I-O dot com, and they're dedicated to advancing novel treatments for rare neuroendocrine tumors and rare endocrine diseases.

Karen Jagoda: So, I want to welcome you to the show today, Nerissa, and really appreciate you taking a few minutes to talk about a topic that we haven't talked enough about, which is the endocrine system. So welcome.

Nerissa Kreher: Thank you, Karen. I'm happy to be joining you today.

Karen Jagoda: It's amazing to me how few people really know what the endocrine system is or what endocrine diseases are. That's just from my own random sampling of folks I've been talking to this last week. So, could you start us off with just a little bit about what the endocrine system is and what endocrine diseases really are, and what they impact?

Nerissa Kreher: Certainly. So the endocrine system consists of a number of glands that produce substances called hormones and these hormones help to regulate a number of different bodily systems. So some of the endocrine glands that listeners might be familiar with include the thyroid gland and that gland is important for metabolism. Other glands include the pituitary gland, which we'll be talking more about today, and that gland is called the Master Gland because it produces a number of hormones that regulate various bodily systems. So, the endocrine system is a very important system and is one of the key regulators of all of our bodily function.

Karen Jagoda: That's a pretty simple statement about a pretty dramatic role that it plays. So, tell us a little bit about the kinds of diseases that you are studying and the kinds of diseases ... The kinds of causes that these diseases we might be able to identify.

Nerissa Kreher: Certainly. So at Tiburio, we are focused on rare endocrine disorders, and many endocrine disorders are indeed rare. We believe that there is a continued unmet need for improved therapies for many of these rare endocrine diseases and our mission is to develop transformative therapies to fill this need.

Nerissa Kreher: You know, in the endocrine world, people are familiar with drugs such as insulin, which helps diabetes, an endocrine disorder. Thyroid medication, which helps thyroid deficiency. But there are other disorders where it, like you said, may be unusual for people to know about and one of those is pituitary tumors. Pituitary tumors happen and occur at the base of the brain, and often times, they can cause various hormone deficiencies or they may just cause issues related to their large size and compression of other structures.
Karen Jagoda: And so, who is most likely to develop those kinds of tumors?

Nerissa Kreher: Yeah. So pituitary tumors, or adenomas, which we are focused upon, occur mainly in adults, although rarely in children and they’re most commonly diagnosed between the ages of about 40 to 50 years of age. So, in that fourth and fifth decade. There typically is not a differentiation between males and females, so they can occur in both genders. And really, other than that, they can occur in anyone. There’s not a specific genetic predisposition that we’re yet aware of.

Karen Jagoda: Okay. So what might be the trigger for them to develop? Is it environmental? Is it lifestyle? How do you sort of predict who might develop these?

Nerissa Kreher: That’s a great question. And unfortunately, we don’t know the answer to that. There are not any specific environmental, as I mentioned, or genetic features that help us to predict that, and thus, that leads to many times patients with pituitary adenomas and especially non-functioning pituitary adenomas to have symptoms that can be somewhat nondescript, like headaches, and these tumors can grow quite large because the patient doesn’t have a well-recognized predisposition that would help a physician to diagnose these pituitary tumors.

Karen Jagoda: And so, I’m assuming there’s no blood test available right now that would identify that that was growing in the body.

Nerissa Kreher: That’s right. No easy blood test. Once a physician is suspicious of a pituitary adenoma, they can do a set of hormonal tests that may help point them in certain directions, but there’s no one specific task that says, "Yes or no, you have a pituitary adenoma."

Karen Jagoda: And so, doctors who identify patients who do have them, what are the current therapies for these people?

Nerissa Kreher: Right. So, I’ll specifically answer regarding non-functioning pituitary adenomas. And let me just differentiate that because that’s what we are focused on first at Tiburio.

Nerissa Kreher: So, pituitary adenomas as a whole can represent two different buckets. The first bucket is functioning pituitary adenomas. And by functioning I mean those pituitary adenomas make excess hormones, and secrete that hormone, and can lead to disorders of growth hormone access, that would be called acromegaly. So, that type of pituitary adenoma specifically makes too much growth hormone, as an example.
Nerissa Kreher: Now, non-functioning pituitary adenomas, they don't make excess hormone. However, they do grow, and the area where they are, at the base of the brain, is close to very critical structures that are important for vision, there are arteries nearby that help blood flow to the brain, and so, these non-functioning pituitary adenomas, although they don't make excess hormones, they cause significant problem by compressing on these critical structures at the base of the brain.

Nerissa Kreher: So, the current therapy for non-functioning pituitary adenomas is an invasive surgery, typically by a route called transsphenoidal, so the surgeon goes in through the nose to get at the tumor. That invasive surgery may be followed by radiation therapy.

Nerissa Kreher: And then, because, as I mentioned, these tumors are near very critical structures, regardless of surgery, the tumors can grow back, and often times the surgeon is not able to take out all of the tumor. And so, regardless of that invasive therapy and adding radiation therapy for some patients, the patients still require lifelong monitoring by radiologic methods, like MRI. And patients typically live with this ongoing concern that they could have a pituitary tumor that may regrow at the base of their brain.

Karen Jagoda: Okay. There is no medical way of sort of addressing it without going in and cutting it out. And I hear this so often about cancer patients, that there's always this worry that it's going to grow back. So, that's what you're dealing with as a challenge here. And so, tell us a little bit about your lead clinical drug candidate TBR-760 because that's where the exciting news is here, isn't it?

Nerissa Kreher: That's exactly right. And you summed it up nicely. There is no drug therapy for patients with non-functioning pituitary adenoma, currently, and so TBR-760 is a chimeric-peptide. It's called a dopastatin molecule, and that's because it binds to two different types of receptors. One is the dopamine receptor and one is the somatostatin receptor.

Nerissa Kreher: And both of these receptor types are present on non-functioning pituitary adenomas. So, by dually-binding both of these receptors with TBR-760, we've shown in early development that we can inhibit the growth of non-functioning pituitary adenoma more effectively than if you use a drug that binds one of those types of receptors alone, or even if you use two drugs that bind both receptors. So, by dually-binding both with one molecule, we believe we are developing a therapy that will be able to treat non-functioning pituitary adenoma.

Karen Jagoda: And what stage of clinical development is this drug right now?
Nerissa Kreher: Right. So we are moving the drug into a late-stage clinical trial. And it's previously been studied in a Phase I trial, which is in healthy, normal volunteers. In that study, we were able to develop the upper limit of dosing that is well-tolerated by patients.

Nerissa Kreher: And it was then studied in a Phase II clinical trial, in a different rare endocrine disorder, the one that I mentioned previously, acromegaly. And again, in that patient population the drug was well-tolerated. So now, Tiburio is focused on starting a clinical trial for patients with nonfunctioning pituitary adenoma by the early part of 2020. And that trial, we are planning on conducting in multiple countries throughout Europe as well as the United States.

Karen Jagoda: That's extraordinary. And are you sort of the first ones out of the gate looking at this particular ... The NFPAs? Is that really a breakthrough in this field or have some others kind of led the way before you?

Nerissa Kreher: No, we are the first, which is very exciting for us. And I'll say very exciting for the clinical community, as well. As I've been out speaking with physicians who take care of patients with NFPA, there is much clinical excitement about the fact that we are starting a clinical trial for patients with NFPA. And this would be the first drug that has, you know, the potential for being approved for the treatment of non-functioning pituitary adenoma.

Karen Jagoda: So, what other therapies are in Tiburio's pipeline that you can mention today? Because I know sometimes you can't talk about stuff that y'all are working on, but can you give us a flavor of how else you're able to apply this knowledge?

Nerissa Kreher: Certainly. So, we have one other compound that's called TBR-065. It's another chimeric-peptide and we are currently exploring target indications for that peptide in various rare endocrine disorders. We haven't landed on that yet, but we hope to do that soon, and look to further develop 065, as well.

Karen Jagoda: So before we run out of time today, I just have to ask you how you found yourself at Tiburio as the Chief Medical Officer? You've got quite a lot of knowledge here. Can you just give our audience a little bit about how you found yourself here?

Nerissa Kreher: Sure. I'd be happy to. So I am a pediatric endocrinologist, and that means I'm a doctor that takes care of these endocrine disorders. And I specifically focused in my training on pediatrics.

Nerissa Kreher: However, I moved out to the Boston area about 15 years ago, and have worked in the Boston Biotech environment for the last 15 years. And most of that time I have spent developing drugs for rare diseases, and often time rare endocrine
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diseases. So Tiburio was especially interesting to me because it allowed me to
go work on clinical development of drugs, but also clinical development of rare
endocrine disorders.

Karen Jagoda: And you still have a lot of enthusiasm for this field, it sounds like. So are you
thinking that this is the beginning of the next phase of really understanding of
the endocrine system? Are we starting sort of the next level of really being able
to attack these kinds of diseases?

Nerissa Kreher: So, I think so. There's a lot of excitement. As we continue to learn about the
genetics of various diseases, as we start, you know, or continue, to understand
and receptor profiles, tumors like NFPA, I think there is a lot of development
that continues and remains to be done for the endocrine system and for
multiple other systems. So, I always remain excited about working on therapies
to help patients, especially in the endocrine world.

Karen Jagoda: Thanks to my guest today, Dr. Nerissa Kreher, Chief Medical Officer Tiburio,
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Jagoda, and you've been listening to the Empowered Patient Podcast.com
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