Science Will Win Podcast
Season 5
Episode 4 Transcript

[Theme music]

Sharsti Sandall:
…Anytime we put something in a patient, I want that to be useful. I want everything to matter.

[Theme music swells, then fades]

RON: Welcome back to Science! Will! Win!

I'm your co-host, Dr. Ron Gamble - I'm a theoretical astrophysicist, STEM educator, and science communicator.

And I'm joined here by my partner in crime – AND life –

RAVEN: Dr. Raven Baxter, a.k.a., "Raven the Science Maven!" I'm a molecular biologist and science educator.

RON: We've partnered with Pfizer to learn everything we can about some of the most exciting medical technologies today.

We've been taking turns leading episodes and DIVING deep into cutting-edge innovations in disease treatment and prevention.

For this episode—**our final episode**—I'm leading!

[Theme fades out]

RAVEN: Ron, how does it feel to close out Season 5 of Science Will Win?

RON: It feels both amazing and a little sad because, I mean, I've learned so much, and I've loved learning and sharing knowledge with you each episode.

RAVEN: Well, I'm so excited to hear what you have in store for us today!

[Musical transition]

RON: Well, we've spent this whole season talking about the drug discovery process…There are A LOT of steps—like years worth—that need to be followed. AND lots of trial and error involved.

RAVEN: And Ron, I think it's worth mentioning that the landscape of science is evolving. Not just the way we do science, but how we communicate. The old way was just publish, present, and move on. But during the pandemic, that stopped working. We had to take what we already knew and flip it for a new world.

RON: Yeah, the dynamic learning process, which is something that we kind of use in science communication and other areas of science, and learning other people's science even though we're an expert, has been a game changer for me. Science communication has definitely come a long way…how we talk about science discoveries, and even who gets to *join* in on the conversations has changed.

RAVEN: And this new era has definitely changed my process. I started reworking old approaches, turning research into stories and visuals people could actually connect with. It taught me that innovation isn't necessarily "reinventing the wheel". Sometimes it's about giving old ideas a new voice.

RON: I definitely feel you. This happens a lot in theoretical sciences, specifically my field of physics. Where we literally revive old ideas from the grave and test them with new methods.

RON: Today's episode is *all* about how scientists can rely on old questions, obstacles, ideas, and technologies to innovate something entirely new—in this new era. Because when something doesn't work in one context, it *might* go on to have a powerful purpose in others. I'm going to share with you what I've learned about antibody drug conjugates or ADCs.

RAVEN: Well, you know what's wild? Science never really lets a good idea go to waste. And antibody drug conjugates, or ADCs, are proof of that. Scientists started working on this idea decades ago, trying to make chemo treatments that are more focused on hitting cancer cells and not the rest of the body.

But back then, the tech…just wasn't there. The antibodies weren't specific enough, so they'd still hit too many healthy cells. The linkers, which connect the antibody to the drug, were too weak, so the chemo would leak out early and cause the same side effects we were trying to avoid. And then the payloads, those tiny chemo molecules, were hard to control.

But over time, we learned how to improve all of that. New generations of antibodies can spot cancer cells by their surface markers, kind of like recognizing a face in a crowd, for example. And chemists figured out how to build linkers that stay stable in the bloodstream but break open once they're inside the tumor. And the drugs themselves got way more powerful, so you can use less of them.

And now ADCs are actually being used to treat various types of cancers. And new ADCs are in development every year. So what used to be an 'almost idea" is now a reality. That's why I say science doesn't miss. Sometimes it just takes a couple of rounds to get the mix right.

RON: One hundred percent agree. And as you just previewed, ADCs are multifaceted because they require a bunch of different parts to be combined or "conjugated".

ADCs represent a careful mix of physics, chemistry AND biology. They harness the power of targeted antibody engineering AND potent chemotherapy.

But you know Raven, I can't help but throw in a little history. To better understand the potential of ADCs today, I thought we should look back to the past.

There are two crucial scientific breakthroughs that led to where cancer treatment AND the development of ADCs are today.

> *Phoenix Ho:*
> *The concept of chemotherapy started all the way back in the early 1900s, but then this concept of using antibodies to treat disease really had its roots, I think, in the 1970s when the process for developing monoclonal antibodies was uncovered. And so you have chemotherapy, you have antibodies, and then you have this idea that people are working on the chemistry of how to put the things together.*

RON: That's Phoenix Ho.

> *Phoenix Ho:*
> *I am currently a group lead in oncology early stage clinical development at Pfizer.*

RON: As a clinical drug developer, Phoenix's team works to advance the latest ADCs to their first human clinical trials. We asked Phoenix to help explain some of the history behind ADCs.

> *Phoenix Ho:*

There was a really famous German physician scientist named Paul Ehrlich, who in the early 1900s had this idea of a magic bullet. And really that idea is that, you know, you can use substances as medicine to give to people and have them differentially target the thing that you're trying to get rid of, whether it's an infection or whether it's a cancer cell while sparing normal tissue, something that's gonna treat the problem and have minimal side effects on the rest of the body. That idea is really the root of what we call chemotherapy, which is, generally speaking, just really potent medicine that we have to treat cancer.

RON: Today, chemotherapy remains a foundational treatment option in the standard of care for cancer.

Phoenix Ho:
The chemotherapy that is given to cancer patients is indiscriminate. It doesn't have a way of specifically seeking out the cancer cells or targeting the cancer cells other than that cancer cells are rapidly dividing.

RON: That's why other rapidly dividing cells, like the ones that make up our hair…

RAVEN: …They also get affected in the process.

RON: Right. So, the first concept of chemotherapy emerged. But as time went on, scientists began experimenting with another way to treat cancer—monoclonal antibodies. Which we talked about earlier this season.

Phoenix Ho:
Another really significant development in the history of cancer therapy, you know earlier in the 90s, was the development of this first monoclonal antibody to treat a solid tumor, was an antibody that was developed to target HER2 for the subset of breast cancer patients that have that marker. And so breast cancer then became an area where because there was a successful monoclonal antibody, there was then an effort to create an ADC out of that.

The idea here is can you put together a powerful cancer-destroying medicine like chemotherapy with the targeting ability of an antibody? And therefore, on the one hand, decrease the systemic or total body side effects of the drug, of the chemotherapy, while on the other hand, harnessing that targeting ability of the antibody, but then increasing potency by actually putting a payload on that antibody. So it's not just the immune system that's now fighting the cancer, but using the antibody to deliver so called a magic bullet to the cancer cells.

RAVEN: When we think about cancer treatment, chemotherapy is usually the first thing that comes to mind. And when we hear chemotherapy, I'm sure most of us immediately think about the side effects it can have, which can be really tough.

I think of ADCs as a ride-share for drugs. And they take the chemo payload and drop it off right where it needs to go. And instead of hitting every stop along the way, they're just going to their targeted destination.

So, I'm intrigued to hear about how a more targeted distribution of chemotherapy drugs could potentially reduce the toll of chemo on a patient's body.

RON: That's the goal and a perfect analogy. ADCs are engineered to bind to a protein that is highly expressed on cancer cells, but less present on normal cells. Scientists are designing ADCs to not only be highly targeted, but also to last longer in the body so that patients require less frequent doses.

> *Phoenix Ho:*
> *The first FDA approved ADC didn't occur until 2000. And it was a drug that was used to treat leukemia. In the 20 plus years that have followed, there's been an explosion of clinical and preclinical research and now over a dozen FDA approved ADCs across both solid tumor cancers as well as hematologic malignancies like leukemia and lymphoma.*

RAVEN: I feel like specificity has been a major theme across many of the therapeutic modalities we've talked about this season. It's a real signal of where we are in medicine and scientific discovery today. We're transitioning from sweeping solutions to a diverse range of distinct treatment options.

RON: Agreed.

So, Raven, we've covered two of the three main parts that make up an ADC. There's the antibody. Then, the payload or chemotherapy-like drug. And finally, one more. And here's a pop quiz for you Raven, can you help me out?

RAVEN: That would be…the linker!

RON: That's absolutely correct! We spoke to another scientist at Pfizer to explain more about ADC structure.

Sharsti Sandall:
My name is Sharsti Sandall and I am an executive director and head of ADC biology in the oncology research unit. So I lead a group of scientists that all work on our ADC therapeutics.

RON: When it comes to the parts of an ADC, Sharsti has a bit of a soft spot for the linker. Just like you Raven!

Sharsti Sandall:
This maybe the most underappreciated part of the ADC because its job is really just to keep the potent chemotherapy or the anti-cancer drug attached to the antibody. And it has to do this in a way that keeps it stable when it's circulating through the body and inactive. And then once the antibody binds to the cancer target and gets taken up by the cancer cell, it's a process we call internalization, which literally means that it is taken into the cancer cell. then it has to release the chemotherapy or the drug in the cancer cell so that it can go on and target its effector target so that it kills the cancer cell. So the linker has to be very controlled so that it's cleaved only when you want it to be cleaved.

RON: So, those are the ADC parts. But, assembling them is complicated because there are so many options to choose from.

Sharsti Sandall:
There's many variables for all of the parts. And so you can imagine that the number of permutations grows very quickly when you have three variables of the ADC. And just to make it more complicated, let me add one more piece. You can have varying amounts of drug to antibody ratios. We refer to this as DAR. So some of the antibody drug conjugates will only have like two copies of a payload and some will have up to eight. And there's even technologies that are being worked on to try to load up even more payloads. But every time you add something to the ADC, you change its physiochemical properties. And so you really have to tune this specifically for the payload as well as how potent it is and the target you're going after, so all of these things have to be kind of worked out empirically for each ADC.

RAVEN: Man, that sounds like serious brainwork. I've done experiments where you're juggling a bunch of variables at once, and honestly, it really does feel like trying to find a needle in a haystack. Every little change can throw the whole thing off.

And it's wild how with ADCs, one tweak to the linker or one extra payload can totally change how the drug behaves in the body. It's chemistry, biology, and math all fighting

for balance. And you can’t just guess your way through that. You have to test and tune A LOT of combinations until it hits that sweet spot.

And that kind of trial-and-error science takes patience. But when it works, it’s like hitting the jackpot.

RON: Trial and error happens a lot in my field as well. Sometimes we run an experiment, or even get the math wrong, and we have to test it again. And again. And again.

I was curious about how this works with ADCs. So, we spoke to Sharsti about how her team finds the best ADC combinations. Starting with how they identify target antigens.

> *Sharsti Sandall:*
> *So we have a really great collaboration with our clinical development group. What we call end-to-end workshops where we'll pull together the clinical group, commercial, and our researchers. And we'll have those moments of this is really what it looks like from the patient's perspective.*

RON: After identifying a target antigen, Sharsti's team has to identify the payload—or the anti-cancer drug—to pair with it.

> *Sharsti Sandall:*
> *There's no one formula. It works through many ways. And a couple of examples I'll share are, we still heavily rely on the scientific literature, both academic, mostly academic I would say, scientists that are publishing papers that spark ideas, as well as other drug development companies will sometimes publish papers and those will often spark ideas of, oh could try this drug as an ADC or oh look somebody described this new tumor antigen and it has this this function maybe we could block that so we often start with the literature.*
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> *The other place ideas come from, honestly, is the clinical experience. So I have a couple of examples in my own career where we've taken things all the way through from idea to the clinic and we've figured some things out that something didn't work as we planned. And so we came back to the lab and we said, well, it didn't work in this application, but what if we change this one thing and tried it in this different application and could it work? And so those are some of the most, I think, rewarding examples because they really turn what you might think of as a failure into successes. And you can also go a lot faster when you kind of are reiterating like that versus starting from scratch.*

RON: And one more cool thing that I learned about payloads Raven, scientists aren't just iterating on molecules they've created in the lab. As Phoenix explains, they're also iterating on molecules in nature.

> *Phoenix Ho:*
> *Going back decades, there's been an effort by scientists to look in the natural world for bioactive molecules and looking at rainforests, looking at the bottom of the ocean, because there's so much biological diversity in compounds that may not exist elsewhere in nature that can have medicinal properties.*
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> *There was a scientist that isolated a compound called dolestatin from a type of sea slug called a sea hare. And it turns out that this chemical that was isolated from this marine invertebrate is a really, really potent at stopping cells from dividing, which makes it really attractive as a potential chemotherapy drug, except that it is so potent that it's not feasible. It's too toxic to give to people just as chemotherapy. And so there were lot of iterations on that. Once this natural compound was discovered that scientists continued, chemists continued to tinker with it and created a synthetic version of it called auristatin. And that led to one of the first classes of payloads, this auristatin class of payload that is now utilized in multiple approved ADCs.*

RAVEN: Hold up, I love that. The fact that something from a sea slug helped inspire a whole class of cancer drugs is wild. It's a good reminder that nature really is the original chemist.

I've always thought it was so cool how the stuff we think of as "natural" medicine and "synthetic" medicine aren't really separate worlds. Like, so much of what we make in the lab starts out as nature's very own recipe. We just remix it, clean it up, and make it safe enough to help people.

RON: I never thought sea slugs would be something that could help out with cancer. But again, like nature provides, which is really awesome.

So, back to the process. When scientists are confident that they've got a promising molecule, they have to take it through preclinical studies.

> *Phoenix Ho:*
> *Phase one development is not for the faint of heart. And I think perhaps what I can say is that being in this environment, makes it as perhaps as optimal and as exciting as possible because what we have is an army of brilliant preclinical*

research scientists working before the program ever even gets to us in clinical development.

RON: The work done in the pre-clinical phase is crucial to making sure each ADC candidate has the best shot at success. Once that's complete, the potential ADC reaches Phoenix and his team.

Phoenix Ho:
By the time a program and an ADC gets to us in early clinical development our research colleagues have narrowed things down for us. They've gone through all of those preliminary steps of selecting the right antibody, optimizing the right linker, picking the right payload, and they've delivered to us what is a clinical candidate. What is exciting enough to take into the clinic and what we do, you know, our job in early drug development is to try to, as efficiently as possible, figure out how to dose this, show that it's safe to give to humans first and then increase the dose to a level where we begin to see some clinical activity, where we start to see it working.

And, you know, these cancer patients that are enrolling in these first human trials are, you know, typically very heavily pretreated. They've typically exhausted all the approved cancer treatment options for their disease. And so it's a high bar. But if this novel medicine is able to be dosed up to the point where we're starting to see responses, in these cancer patients, that's when we begin to get some hope that this could be the potential to become a medicine that's gonna help a lot of people.

RON: Potential is the key word here. Raven, do you know how many oncology drugs out of ten, make it past phase one development?

RAVEN: Not a lot. I wanna say maybe a couple out of ten…if that. Because phase one is no joke. You can have the best data in the world, and then once you bring humans into the picture, everything changes.

RON: You were close…it's just ONE out of ten. So the odds of an oncology drug making it out of phase one development are not that great. And Sharsti says that pushing through these inevitable setbacks is the hardest aspect of her job.

Sharsti Sandall:
I often describe scientists as stubborn optimists because we have to be really persistent.

You know, I often spend a lot of my time just keeping my team motivated and reminding them of how important our job is and that patients are counting on us.

We have to make hard decisions about which drugs to push forward. So it can feel a little bit heavy to know that your choices and decisions are going to potentially work for a patient or not work for a patient. There are many nights that I agonize and lose sleep. So that's hard.

RAVEN: You know, there's a lot of work that goes into this. And even though it is tedious work, it's also very rewarding. And the work that you're doing now is going to become the foundation of something that could potentially save someone's life. And every decision counts, time counts, funding counts.

So Ron, I think you did a great job walking through how ADCs work and what it takes to create them. It's been a little while since I've been involved in this work. Can you update me on how ADCs are impacting patients' lives right now? Especially, since we've made so many advancements and many ADCs are being used in cancer treatment today.

RON: So, yes, several ADCs have been approved worldwide to treat various types of cancers. When we asked Phoenix and Sharsti about this, they both named one disease that ADCs are making a huge impact in treating.

Phoenix Ho:
I think frontline metastatic bladder cancer is sort of a perfect example.

Sharsti Sandall:
The treatments for metastatic bladder cancer hadn't changed in many, many years until this, you know, ADC was approved there.

RON: According to the American Cancer Society, nearly 85,000 new cases of bladder cancer will be diagnosed in 2025. Bladder cancer is the 10th leading cause of cancer death in the United States. ADCs could have the potential to alter this reality.

Sharsti is referring to a 2023, FDA approved dosing regimen which combined an ADC with a checkpoint inhibiting immunotherapy. This is used to enhance the ADC's immune activation capabilities. It was a first of its kind dosing regimen to treat advanced or metastatic bladder cancer.

Phoenix Ho:

Up until very recently, the standard of care treatment for somebody who had metastatic bladder cancer was a really intensive chemotherapy regimen.

But it turns out that when you take one of these immunolcology drugs, put them together with an ADC, that is a chemotherapy free regimen. That ADC combination has changed the way that patients who have newly diagnosed metastatic bladder cancer are treated and made it possible for them to, you know, hopefully live longer and live better while receiving a regimen that avoids classic chemotherapy.

This is not far off science fiction anymore.

RAVEN: Chemotherapy is and will continue to be a very important part of cancer treatment. But to know that there are treatments advancing beyond that…that's major!

RON: I know! ADCs are changing the standard of care for bladder cancer. And I really wanted to learn more about the difference this could make for someone who has a personal connection to the disease.

RAVEN: I like where you're going with this. So what are we getting into?

RON: We've spoken a lot about patients throughout this season, but what about the caregivers out there?

They may not be experiencing treatment themselves, but when you take care of someone, you can develop your own close relationship to the disease or condition that they live with.

With that being said, Raven, I have someone I'd like you to meet.

Renee:
I am Renee Barron Gores and I am from the state of Michigan.

RAVEN: Okayyy, tell me more about Renee.

RON: Well, Renee is a writer who loves art and reading. She's a mother with three grown kids. And from 2018 to 2020, she was caregiver to her father, Bill Barron, who had bladder cancer.

Ron:

What was Bill Barron like? What kind of guy was he?

Renee:
Excellent sense of humor. Loved his family, hard worker…and very strong. The man was sometimes in a lot of pain and dealing with a lot of health issues and always would just like find the humor. I never really saw him really break down or have a very difficult time till like towards the very end of, of everything.

RON: Bill was 71 years old when he was diagnosed with bladder cancer. As someone who dealt with heart issues for a long time, Bill was used to frequent hospital visits. *But* on one particular visit, his doctors noticed something was wrong.

Renee:
It was around December of 2018 when he originally went to the doctor and then they discovered the tumors. So then he went and had a surgery to remove it and have it biopsied. And then that's when they discovered that it was cancerous.

He waited a while before really doing anything about it. So there's, as a caregiver, as his daughter, there was a little bit of anger in the beginning, honestly. Like, why did you wait? That type of thing. But then it just gets to the point where you have to support what decisions they're gonna make and you're gonna be there for them and support them along the way. He did kind of go down that road of regret and oh I should have stopped smoking or I should have done this but I just told him you got to move forward from that and no regrets and just we're gonna do what we need to do so.

Ron:
Absolutely. Can't hang on the what ifs, right? You just gotta keep going.

Renee:
Right, right.

So then in around January of 2019 is when we kind of started the process of the chemo and radiation, he first went to see if he would qualify for a trial…

RON: Chiming in here. At this point, the first ADC for bladder cancer hadn't been approved yet. While Renee and her family looked into an ADC clinical trial for Bill, it wasn’t a viable option.

Renee:

So then the next step was to do aggressive chemo and radiation, which was, they actually combined those two. So he would get chemo one day in the hospital and then when that was done go get radiation and then he supplementally have three days of chemo at home through a port and then he'd get a little break and then they would do radiation it was like kind of on and off between those two.

Ron:
Wow. So what was his, like, what was the mental health like?

Renee:
In the beginning, he would just try to be very upbeat. He always tries to find the humor in everything. He would joke, he'll joke with like the oncologist or the nurse, he never really complained. You could tell he was like in pain, but he would just try to make the best of it. He did have his moments where he'd get irritable or depressed, but he knew he had us there to help support him through it too.

RAVEN: And I know that Bill wasn't able to receive ADCs but I'm curious, how was his experience with the other treatments available to him?

RON: It was pretty intense—and honestly, it sounds like a bit of a roller coaster.

Renee:
Well, we didn't have a whole lot of options because he had kind of waited a while. So we would, met with his urologist and the oncologist and kind of came up with the best plan that he thought he could handle that would be best for him, which included the radiation and the chemo. And then that did work for a while. There was a short stint of time in the early summer of, I believe it was 2019, that they actually told him he was in remission and there were no more tumors.

RAVEN: It's complicated because that small period of remission could feel like a sigh of relief. But on the other hand, there's still that question of: could the cancer come back?

RON: That's a worry that I think a lot of people have. Recurrence is a very common factor of bladder cancer—that makes treating the disease even more challenging.

Renee:
And then he went from June until about three months later, then he went for his three month checkup and they said there was five tumors that had grown back.

So was very aggressive. And they grew back on his urethra and then in other spots on the bladder where it was more behind the bladder.

So then the best approach for that was to then, his urologist would surgically remove the tumors and get as much of them out as he could. And then they would do like an immunotherapy after the surgery, which is basically a bacteria that they inject and then it eats away at the cancer. But you have to like lay still for like two hours while they and let that do its job. Yeah, so.

Ron:
Which I'm sure is hard to do. That's... So it's... I can't lay still for two hours, let alone 20 minutes.

Renee:
Right. And to have to hold, you know, your bladder's already getting the punching bag, so to speak, from all of these surgeries and radiation. To me that was remarkable that he had his mind, almost a mind over matter with the body, like just making himself be that strong to hold that in and so that it can work and do its job.

RAVEN: That treatment regimen sounds incredibly intense. It must have taken so much strength and patience for Bill to go through that, especially having to lie still for hours while already in pain. That kind of endurance is something we don't always talk about enough. It takes a different kind of courage to keep showing up for treatment like that.

I'm curious how all of that started to affect his daily life as things went on. Did his symptoms start to change as the cancer progressed?

RON: They did. Renee noticed how his symptoms chipped away at the things he *loved* to do.

Renee:
He had to eventually stop working He liked to go out walking and that got harder for him….He loved cooking. He became quite the cook.

And as he progressed with the disease it was harder for him to cook and probably not safe so, because he would get real shaky and just you know being around the stove.

RAVEN: You know, when we talk about patient quality of life, these are the things that we're talking about. It's not just the pain. It's the ability to participate in your hobbies, do things that you love to do, contribute to society in the ways that you used to, have fun with your family, engage at the level that you want to. And all of these things are impacted when you are suffering from something as serious as cancer.

RON: Yeah, I completely understand the impact on quality of life. My condition, it definitely impacts the day to day. There's some things you can do, some things you can't do. And when your body is constantly changing, sometimes it feels easier to just give certain things up.

RAVEN: Yeah. You know, when you're going through a disease, a cancer, you're not alone, right? You're experiencing it along with your community—the people that care about you.

So what was all of this like for Renee? Because she also had to adjust to this new reality?

RON: Yeah, honestly it *was* something that affected the whole family.

> *Renee:*
> *Between my mom and I, because she still would have to go into work, we would figure out what the chemo radiation schedule was going to be. So then we would both try to be there to take him to it. So I could kind of be a support for her as well as be there for him.*
>
> *Ron:*
> *Full-time job, right?*
>
> *Renee:*
> *Right, right. It is and when you're in the moment and you're doing it, you don't really realize that you're actually doing another type of full time job. On top of the kids were still young then. Well, they were middle school, high school. So it was trying to navigate that as well.*

RON: On top of her new hours as a caregiver, there was a lot Renee had to learn about the science and treatment options for bladder cancer. *And* the healthcare landscape.

> *Renee:*

And that's another thing, just trying to navigate that for my parents and for my dad, trying to explain how that all works. You have to kind of always be on top of things. I didn't really show it but I had a few breakdowns quietly.

Ron:
You're human, that's okay.

Renee:
And back then too, I didn't really realize that there's resources for family members who are caretakers. And there's things you can do to get like respite, and I didn't realize any of that. I'm like, well, this is just what you do.

Ron:
Mm-hmm. Mm-hmm. You stepped up and I think that's admirable, yeah.

Renee:
I was just trying to navigate every day and keep it all together.

RAVEN: Well, as you know Ron, I worked as director of science communication at a medical center that specializes in complex chronic illnesses. And one of my first initiatives was to create a clinical manual that was a resource not only for patients, but also their caregivers. And I just wish that every caregiver had a manual for the illnesses that they are tending to.

RON: That would be monumental, for us on the patient side. And for caregivers. It would give us much needed advocacy in our health journeys.

So Raven, Bill's journey with bladder cancer lasted until 2020. That's, of course, a year we will never forget because of the onset of the COVID-19 pandemic. By that point, Bill's condition had continued to worsen, but the pandemic further complicated his situation.

Renee:
I want to say end of February 2020, he began, there was a lot of blood in his urine. So when he would urinate, there was like a lot of blood and some clots, which was very alarming. And he's like, no, it's just because of all my chemo and all my radiation.

And then my brother and I were like, no, this has been going on for a while. This is not just from that. This is kind of a huge warning sign that you need to go back.

So we got my brother and I kind of had a, I guess you say a come to Jesus with him about going back to the doctor. And then there he had, there was now it was progressing where there was tumors on his liver and more on his urethra.

And then COVID happened. I actually got COVID really bad myself in October of that year.

Ron:
Oh wow.

Renee:
So then I didn't wanna, I couldn't chance seeing him or being around him or anything. So then it wasn't until I could see him in November and I was like, he's not, he looked, he looked horrible.

RON: Bill Barron passed away from bladder cancer in December 2020.

In the time since, Renee has reflected on her experience helping her dad through treatment – and she has some advice for anyone taking care of a loved one with cancer.

Renee:
Listen to what they're saying and try to be supportive of what their choices might be. Even if you think that's not best for them, they're going through it and they're the ones that know how much more they can take or how much further they want to go with it.

RON: Renee also told me that she hopes the future of bladder cancer care addresses every aspect of the disease. Not just more treatment options. But, also mental health resources and advocacy for patients and caregivers.

And ADCs are an important part of building toward the future Renee is hoping for.

RAVEN: What else is on the horizon for ADCs?

RON: To put it simply—a lot. Phoenix says the future of ADCs is all about new payloads, new combinations, and new capabilities.

Phoenix Ho:
I hope that we are just at the tip of the iceberg and that this is the beginning of the chapter of ADC history. That original idea of putting a drug, putting a potent

chemical that could kill cancer cells on an antibody to make it targeted, to make a magic bullet, is just the start of iterating and creating whole new classes of payloads, whole new mechanisms of drugs that we can then put on antibodies and perhaps even using different vehicles, the things that have different properties than antibodies to target cells.

[Music shift]

RON: Well Raven, that's a wrap for this episode… and for this season of *Science Will Win!*

The breakthroughs we've talked about this season have covered so many corners of science and medicine. From discovery to design, from lab bench to bedside, it feels like we've been peeking through a window into the future, and that future looks really bright.

RAVEN: It does! There's so much passion, innovation, and teamwork behind all of this. It gives me chills sometimes, thinking about how far we've come and how much further we can go. It makes me proud and grateful to be a scientist in a time like this.

RON: I'm with you on that one.

RAVEN: And can I just say, I loved seeing you step into my world of molecules and biology this season. You handled it like a champ.

RON: Side quest conquered! I'll admit, it was a fun challenge, cuz you know those are not my skill sets. But…when do we get to do a version of this that's all about astrophysics?

RAVEN: I'd love to see it!

RON: I'll be crossing my fingers.

I hope everyone listening enjoyed this season of Science Will Win as much as we did. Thanks so much for coming along this ride with us.

RAVEN: That's all for now! And remember…

BOTH RON AND RAVEN: SCIENCE. WILL. WIN!!!!!

– CREDITS —

RAVEN: Science Will Win is produced by Acast Creative Studios and hosted by me, Dr. Raven Baxter,

RON: And me, Dr. Ron Gamble. Please take a minute to rate, review, and follow Science Will Win wherever you get your podcasts. It helps new listeners to find the show.

RAVEN: Special thanks to all of our guests and the Pfizer research & development teams. And thank you for listening!