



# THE SPLIT VOTE: UROGEN AND THE FDA

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## The Split Vote: UroGen and the FDA

**Stephanie Sirota:** There are nine jurors in a room. Your job? Convince this advisory committee of your drug's safety, that the benefit outweighs the risks. But here's the challenge. Only two of those jurors actually understand how your drug works and the system in the body that it targets. They're specialists. The other seven are not. Under these circumstances, how do you convince a regulatory body that your drug is not only safe, but it's an essential therapy that changes the treatment paradigm and will transform patients' lives?

I'm your host, [Stephanie Sirota](#), Partner and Chief Business Officer at RTW Investments. And today I'm excited to welcome the CEO of [UroGen Pharma](#), [Liz Barrett](#). Before that, she served as CEO of Novartis Oncology and also held several senior leadership roles at Pfizer. Liz, thank you so much for joining us.

**Liz Barrett:** Thank you so much for having me. And— I have PTSD from your introduction. (LAUGHTER)

### Liz Barrett's Pharma Journey

**Stephanie Sirota:** Well, good. We're going to get into that.

So, tell us a little bit about your pharma journey. What is it like to climb the corporate ladder at a large company, and what do you attribute your success to, both at Pfizer and Novartis?

**Liz Barrett:** I would have never guessed I would be where I am today. I started my career at Kraft Foods and then went to Johnson & Johnson. Their biggest business was the pharmaceutical business.

I always joke that I used to think it was really important what kind of toothbrush you use, because I was the brand director on Reach toothbrushes.

I actually started reaching out to people on the pharmaceutical side. I started at a small company called Ortho Biotech. My claim to fame is I launched the first DTC ever in oncology.

It's hard to work in cancer and not feel very personal about it, because either you experience it, someone close in your family, or you know someone who has had cancer. When I started in cancer 30 years ago, five-year survival was actually very low.

I felt like I was given an opportunity.

**“My career decisions have always been around, ‘Where can I make the biggest impact, and am I being challenged? Am I learning? Am I giving?’”**

**Stephanie Sirota:** Was it hard for you to make the transition from Big Pharma to biotech?

**Liz Barrett:** Actually, it wasn't. I've been able to be successful in large companies but also had this in my mind that I would one day do the biotech thing.

I was having too much fun. You know, things were going well. I was continuing to grow.

When I got the call, I said, "Well, you know, I'm not really ready at this time."

And Arie, who's our chairman, he just said, "Just come in and talk to us." And it was really after speaking to our chief medical officer, Mark Schoenberg, who's still a practicing urologist, I was like, "I've been in cancer for 30 years, and I really didn't know much about urothelial cancers."

Nothing had really been done in this space and the idea that we had a drug and a technology that worked, I saw the data, and it was very compelling.

So being able to build a company at the same time, feel like you're really making an impact on patients and their lives and on human health, that was always very compelling for me. And that's why I finally made the jump.

**Stephanie Sirota:** That's great. What about the risks, though? I mean, even, you know, early data doesn't always translate into getting across the finish line.

**Liz Barrett:** At the time, I guess I wasn't as worried. I had done well in pharmaceuticals, and obviously I'm always a believer that, "Look, if it doesn't work out, I can go back to Big Pharma, if I really wanted to."

So, the risk wasn't really driving it so much as it was, "Will it be something that I can get excited about?"

## **UroGen: the product and the pipeline**

**Stephanie Sirota:** Let's get into the meat of UroGen.

**Liz Barrett:** Sure.

**Stephanie Sirota:** For context, let's assume that most of the listeners are not urologists. So, in layman's terms, can you tell me about UroGen's pipeline?

ZUSDURI™ and JELMYTO® are your two drugs. Tell us a little bit about the patients that you're aiming to help.

**Liz Barrett:** Being a businessperson in a science world, you have to take the time to understand the science.

We have a very unique, innovative technology that this chemist developed around urothelial cancers. Think about the upper tract of the urothelial as well as bladder cancer.

Any time you deliver medicine to an area in the urothelium, it just gets voided out very quickly with urine.

But what you do is you put an active medicine—in the case of both of our products that are on the market now, it's mitomycin C, a well-known chemotherapeutic agent. If you use it either systemically or in aqueous solution in the body, there are side effects associated with it.

Our gel—it allows it to release the medicine over a several-hour time period. So, when you think about it, one it's delivered locally. You don't have the systemic side effects that you have with systemic chemotherapy.

It's able to get to where typically these patients are treated with surgical procedures. And so, the doctor goes in and literally cuts out the tumors in both the upper tract and in the bladder. But the problem is, you can only cut out what you can see.

In the upper tract, a lot of time, you can't even reach the tumor because it's behind the kidney. So, these patients get their kidney removed. You're in a situation where the average age is in the 70s and 80s and these patients are losing their kidney. Everybody knows that age alone is a factor for reduced kidney function.

So even though, yes, you can live with one kidney, you don't prefer to live with one kidney.



You are talking about from your kidney down to your bladder, and cancers grow throughout that area. And then the bladder, they're very similar if you think about the actual cancer itself.

They're both low-grade cancers. They're both urothelial cancers and genetically very similar.

Physicians are excited about it, but patients are as well, because the side effects are mostly mild to moderate.

**Stephanie Sirota:** Are these cancers identified early on, or when do they get diagnosed?

**Liz Barrett:** Most patients will present with blood in the urine. Some will be high grade. Some will be low grade.

In non-muscle invasive bladder cancer, most patients actually do have low grade. Bladder cancer isn't one disease. If you have high grade, there's a risk of progression, so you want to treat it more aggressively. And then obviously as you get into muscle invasive bladder cancer, that's a different sort of situation.

**Stephanie Sirota:** And how long is the treatment?

**Liz Barrett:** Once a week for six weeks, and then you're done.

**Stephanie Sirota:** What is the recovery like? Do patients—

**Liz Barrett:** Recovery, there's not a lot of downtime. As a matter of fact—they can leave the—

**Stephanie Sirota:** Walk out of the office.

**Liz Barrett:** Walk out, go to the grocery store, go back to work.

**Stephanie Sirota:** Tell me a little bit more about the RTGel<sup>®</sup>, the technology of your delivery mechanism, that it's novel. And I understand that it's a liquid when chilled, but then it solidifies with body temperature.

Tell us a little bit about why that is so important as an innovation in this area.

**Liz Barrett:** It's a polymer-based technology. It's called RTGel because it's reverse thermal, which means that it's liquid when it's cold.

If it's mixed with the active and you put it in an ice bath before, it turns to a liquid. And then as it hits the warm temperature of the body, it turns to a gel.

For ZUSDURI as an example, one of the details that we say, "Have a patient sit there for 15 minutes just to make sure." But it doesn't even take that long.

If you actually held it in your hand— then you would see that it very quickly turns to a gel and then again disintegrates over a several-hour time period with normal urine flow and is excreted from the body very naturally, not having any concerns about blockage or anything.

It's a very elegant solution.

**Stephanie Sirota:** What other treatments are available to patients. Are you first line or—?

**Liz Barrett:** For JELMYTO, we're for low-grade upper tract urothelial carcinoma (LG-UTUC), period. For the bladder, for ZUSDURI, it's for low-grade recurrent intermediate-risk, nonmuscle-invasive bladder cancer.

So, we are a treatment for both low-grade tumors. And we actually are the only drugs approved in both of those areas.

Now it's been interesting since we've been there, now that the high-grade drugs are starting to do studies to come into our space at low-grade intermediate-risk— nonmuscle-invasive bladder cancer (LG IR NMIBC).

So, the market will get more crowded. Being in oncology for 30 years, people would ask me about competitors.

More medicines for patients with cancer, the better, because unfortunately these aren't cures. Patients recur. So, having more medicines on the market for patients is good for patients, and that makes it good for us.

**Stephanie Sirota:** And it's good competitively.

**Liz Barrett:** And to educate physicians. You know, we're changing behavior now. The current standard of care is surgical intervention. Without these medicines, they would just continue to do repetitive surgery. The more companies you have out there talking about alternatives, that's a good thing.

## The FDA vote on UroGen

**Stephanie Sirota:** Let me take you back. On May 21st of this year, you attended an FDA panel assessing ZUSDURI's risk-benefit profile. And that must have been a really nerve-wracking moment for you. You sat there waiting for the votes to be cast. What was going through your mind?

**Liz Barrett:** I don't like to get ahead of my skis. When we had a break at the ODAC, things seemed to be going well.

I said, "Guys, don't get ahead of yourselves. I've been to way too many ODACs in my time to know that anything can happen."

I just remember sitting there being like, "Don't make any facial expressions. (LAUGHTER) You don't want anybody reading your face."

**"I just remember closing my eyes at that point, just dropping my head. Dr. Pazdur said, 'We think this is a split vote. You know, we'll be talking to the sponsor.' But at the time, you're just like, 'I can't believe this.'"**

**Stephanie Sirota:** For our listeners, the ODAC is the Oncology Advisory Committee, and they are permanent oncology voters on their panel. Now it's up to them to invite specialists to join, which should have been urologists. But you only had two urologists that had been invited to join this panel of nine people.

Was that worrisome, that it wasn't packed with specialists who knew the disease well?

**Liz Barrett:** Definitely. There's a benefit to being in the oncology division and then also a risk. For urothelial cancers that get treated by urologists, you would argue that maybe it should be in the urology division of the FDA.

But because obviously it's cancer, it's in the oncology division.

The positive about oncology division is they understand cancer. And they are used to seeing drugs for the first time coming in the space.

But the bad news is they do not understand urothelial cancers. I cannot tell you how many times we tried to educate that low-grade cancers don't progress to muscle invasion. Every time we met with them, they kept bringing that up as the concern.

We were happy with the two panelists that they did invite. But, yes, we had hoped they would have invited a couple of others. And unfortunately, one of the permanent members is a kidney cancer doc, a specialist, but he wasn't there that day. So, we did go in with the deck stacked against us.

**Stephanie Sirota:** The vote was split four yeses to five nos—

**Liz Barrett:** Right.

**Stephanie Sirota:** You were shy a single vote. So, your stock dropped— (LAUGH)

**Liz Barrett:** Yes. (LAUGH)



**Stephanie Sirota:** —by more than 50%, down to, like, \$4 a share. And normally it's quite difficult, actually, for FDA to approve a drug after a negative outcome like this. What was your reaction? Were you angry? Were you frustrated?

**Liz Barrett:** We actually already had planned time to debrief after the ODAC. We all go back to the room, and everybody's, I think, just shell shocked, just in shock.

And I said, "Okay, I can't— I can't talk right now. I can't sort of debrief right now. I need to go. And then we'll get back in touch." And I left alone.

I got to the train station, and I called Arie, who's our chairman. I always crack up about him, because the reason I ended up at UroGen is he wouldn't take no for an answer.

And that's exactly what he said to me. "Don't take no for an answer (LAUGH)." I said, "Okay, what are we doing? Let's figure this out." I'm a problem solver.

I contacted Jim, who's our head of regulatory, and said, "Okay, I want you to reach out to them and say, 'Dr. Pazdur said let's talk.' So, figure out when we could talk."

I made a couple calls myself. It's kind of one of those things. We are going to do everything that we can to have a positive outcome here.

Dr. Pazdur agreed that he would come to our meeting in person. But the meeting wasn't for ten days. And so, you can imagine, the hardest time was those ten days between the time we reached out to the FDA, and we actually had our meeting.

And when we had the meeting, they really understood how they confounded the issue by bringing up and asking, "Well, should we have randomized control studies?" Well, you shouldn't ask that question, (LAUGH) ahead of asking for approval of it on a single-arm study.

We had been perfectly fine with doing a randomized control trial. The problem is we couldn't get the FDA to agree. They wanted us to demonstrate superiority. They didn't want to do a placebo control study.

We didn't want to do adjuvant. And the reason we didn't want to do adjuvant is, part of the biggest benefit is you don't have to do surgery. So, if you can get the type of results without doing surgery, why would you put patients through that?

There was information that wasn't really clear to the panelists. What was interesting is they said they were only going to listen.

So, they sent us these questions. And I said to the team, "We will go in person."

Mark sort of challenged them in the sense of, "We were definitely willing to do the study. But you guys didn't agree."

In my closing, I really talked about the fact that we had an agreement with the FDA. We're a small company. We never would have done a study that we didn't have agreement with the FDA if it could be the basis for an approval.

And then I talked about my history in oncology and the compelling data, and how important it was for patients. They also want to bring medicines that can help patients as well.

We left there on a really good note. They said, "Okay, well, let us debrief, and we'll get back to you."

We got basically a draft label the same day after our meeting. But then we can't talk about it, right? Everybody's asking us questions, and we went quiet. I left the FDA meeting and flew down to Florida for our national launch meeting.

I had to address our sales team, the entire commercial organization without knowing whether we were going to get approval or not.

**Stephanie Sirota:** What about investors? Because did you have investors calling you up and asking you what happened? You had to juggle between preparing for your FDA conversations but then also the investor conversations—

**Liz Barrett:** We had to go dark, so we couldn't talk to investors.

At that point after the meeting, we were highly confident we were getting approval. But we couldn't tell anybody that, right? That gave us a little bit of air cover. I did say that we all still continued to feel like there was a path forward after the ODAC.

It's so funny, because after that event, somebody said, "Well, Liz looked really worried, you know, on the Zoom call." And it's amazing how investors try to read into everything you say and every facial expression that you make. (LAUGH)

**Stephanie Sirota:** (LAUGH) Everyone wants to try to glean something.

**Liz Barrett:** Right. And ultimately, the FDA recognized the unmet need. So, we were able to get ZUSDURI approved.

## **UroGen and RTW's relationship**

**Stephanie Sirota:** You have a poker face. They were wrong. (LAUGHTER) We've been invested in UroGen for some time on the equity side, and also, on the royalty side. Can you share a little bit about the relationship that you've developed with RTW?

**Liz Barrett:** We initially did the royalty deal with RTW. And RTW was not an investor in UroGen.

I didn't really deal a lot with RTW. Our CFO did. And when she left, I called Tony. I said, "Just wanted you to know we're still open for business. Everything's great."

That's when I started my personal relationship with RTW. Over the years, it's been the best of relationships.

RTW has invested a lot of money in our company. They really want to support and guide— but without a heavy hand. And for a CEO of a small publicly traded biotech company where the stock has been up and it's been down, there's nothing better than that.

And so, I am very grateful to RTW, extremely grateful for the relationship that I've built with Tony, and Gotham, and Rod over the years. And that's unique. I have a lot of confidence and a lot of belief in what we're doing and where we're going as a company. And could not ask for a better partnership than what we have with RTW.

**Stephanie Sirota:** Oh, thanks. We really appreciate that. One of the things that we strive to do is really have a depth of understanding, try to match that as much as we can, to really understand what it is that you're working on, what challenges companies that we invest in are facing. Now for our investor audience who's listening to this, we all think about risk-reward every day. How should they think about the uncertainty you face?

**Liz Barrett:** It is a show-me story. All I can say is, "Be patient."

We still have a lot to prove. The people in the commercial organization will tell you that it's the hardest job they've ever had, down to the sales rep.

Because it's not a pill or an infusion. It's a procedure. So, you sort of have this drug device. There's a lot of logistical and operational burden on the practice. And that's hard, because any physician— the key is to make sure it fits seamlessly into their practice.

They're not about changing for you. We really have to do everything we can to make it as easy as possible on them.

But you can only make it so easy, because the drug has to get mixed. It has to get chilled. It's a more complex sell.

And that's why we're trying to tell our investors, "Okay, you know, we are highly confident that this will be a successful launch and a successful medicine."

**Stephanie Sirota:** And you're trying to do this yourself commercializing. You're not, you know, partnering with pharma. And maybe tell us a little bit about why you feel like you're best equipped to do that.

**Liz Barrett:** The good news is in this space you don't need a large commercial infrastructure.

And what's nice about it is we do have revenue with JELMYTO in a commercial organization. And yes, JELMYTO didn't end up being as big of a drug as we thought it would be.

I think we set expectations. We expected it to be bigger. But I think we have been successful with JELMYTO.

We definitely underestimated physicians around the operational, logistical burden of it. And so, things are so much easier with ZUSDURI.

To share the value with a larger company doesn't make a whole lot of sense, because, again, we have a leverageable infrastructure that we have in place, so able to be able to do it.

## Liz Barrett's leadership style

**Stephanie Sirota:** Can we talk a little bit about your personal brand of leadership? What are some of the key tenets that you live by as CEO?

**Liz Barrett:** I'm a direct communicator.

**"I'm a big believer in integrity, and honesty, and transparency, sometimes maybe too honest (LAUGH)."**

What people that have worked for me talk about is that I was probably the hardest person they ever worked for because I really challenged them.

But they learned the most. And for me as a leader, there's probably nothing better that someone can say about you.

You challenge your people, but you support them. So, I've always been one of those willing to go to bat for us.

And I can think of times where it's uncomfortable to do so. Over time, I learned, you know, to be a better leader by just coaching people.

But I've worked with people where I'll give them feedback, and they've been in their career 20 years, and they'll say, "That's the first time I've heard that," when it really wasn't. It's just no one sort of stepped up to talk to them.

The role that I'm in today, that's a very fine line that you have to walk, because we're a publicly traded company, and you have to be very careful about what you say when.

I had a boss at Pfizer that said to me, "You know, you lead by your values." I would say that's probably what has driven me and the type of leader that I am.

**Stephanie Sirota:** I'm curious. Are you the same person at work as you are at home?

**Liz Barrett:** No, I'm a pushover at home, although my kids would never say that. At work I'm never really satisfied.

I'm always challenging people just to do a little bit better. I've challenged my kids to do that. Just be the best version of yourself. Do something you love.

I didn't know that 30 years ago, but the ability to be able to make a living in doing what I love has been fantastic.

**Stephanie Sirota:** I've also discovered later on in my Wall Street career of 25 years that when you love what you do, and the people that you're doing it with, then it doesn't feel like work. But maybe tell us a little bit about why you do what you do. What is your "why?"

**Liz Barrett:** What we get to do is develop and discover medicines that have a huge impact on patients, and on their families, and really on the world. There's nothing better than that.

I mean, I have meaning in my work, right? My kids. That's the meaning of my life. They're my world. When they get to see what their mother does, they're very proud. Since they were young, they also understood that I loved what I did.

That makes a huge difference when you think about them, and their lives, and how they're going to grow. And so, if you're fortunate enough, as we both are, I think that there's no more meaning than that. My mother died when I was five years old.

**Stephanie Sirota:** Oh, I'm sorry.

**Liz Barrett:** She died of liver disease. She wouldn't die today. And I can't tell you how many people when you think about cancer, my brother is in remission from cancer, and how many people have impacted your life that have had cancer or died from cancer.

**“But the fact that we get to be part of that solution and really helping people live better, longer lives, what more could you ask for?”**

**Stephanie Sirota:** Right? No, that's unbelievable. We say the same thing at RTW. We get to participate in one little piece of this overall major innovation story.

**Liz Barrett:** Yes.

**Stephanie Sirota:** We are really mission-driven investors. And it makes us feel like we're doing a little piece of good in that big puzzle that is going on.

**Liz Barrett:** I guess the only thing I'll say is probably more than a little piece. Because guess what? We couldn't do what we do if you didn't do what you do. I did not appreciate that working for a large company. But boy, do I appreciate that working for a small biotech company.

**Stephanie Sirota:** Liz, thank you so much. It was wonderful to see you today, and I wish you continued success.

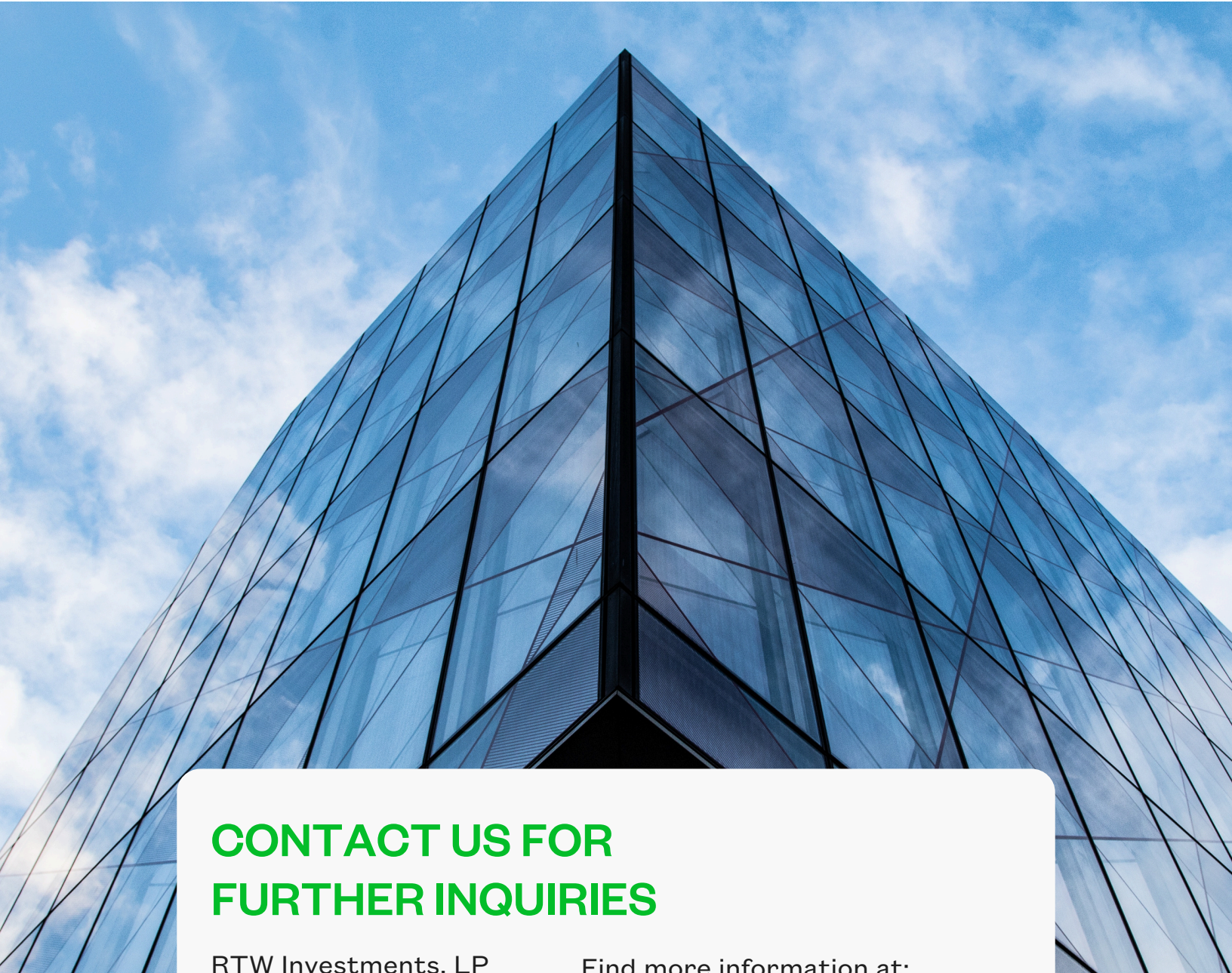
**Liz Barrett:** Well, thank you for having me.

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