EP.89 - Murat Kalayoglu FINAL

Narrator: You're listening to *BioTalk* with Rich Bendis, the only podcast focused on the BioHealth Capital Region. Each episode, we'll talk to leaders in the industry to break down the biggest topics happening today in BioHealth.

Rich Bendis: Hi, this is Rich Bendis, your host of *BioTalk*. And as you know, we interview successful, emerging leaders, entrepreneurs within the BioHealth Capital Region. And we've got a repeat performance today. It's really nice to go back and see those who have progressed nicely with their companies and their careers, and talk about that success, and some of the great things happening in the BioHealth Capital Region. So today, we have Murat Kalayoglu, who is the Co-Founder, President, and CEO of Cartesian Therapeutics, located in the heart of the BioHealth Capital Region in Montgomery County. Murat, welcome back to *BioTalk.*

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Murat Kalayoglu: Thank you, Rich. It's great to be back.

Rich Bendis: Thank you. All the listeners are excited to hear about the progress you've made and everything that has happened in the last couple years since we last talked. But for those who didn't know you before, why don't you give a brief introduction to your background and how it led to your current career with Cartesian?

Murat Kalayoglu: I was trained as a physician-scientist. I got my MD/PhD degree at University of Wisconsin, Madison. My research was in immunology and in particular, role of infectious agents in atherosclerotic heart and vessel disease. And then went off to do an internship out in the Bay Area, where I ended up meeting my wife, who's also a physician, doing her internship out there. And then we moved out to Boston, where I did a residency in ophthalmology at Harvard, where I met my long-time partner, Mike Singer, who was also doing residency there. He and I decided that the practice of academic medicine was not for us.

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We left and started down the road of starting companies. Between the end of residency and our first company, I went and got an MBA at MIT Sloan. Mike finished up his residency; he was a couple years behind me.

And then we went off and started our first company. It was called HealthHonors Corporation. That was a way to use principles of behavioral economics to drive healthy behaviors such as medication adherence and weight loss and exercise and these kinds of things. We in essence used some Skinnerian conditioning, basically intermittent reinforcement, motivate people through some of the concepts around gambling to take on some healthy behaviors. We ended up growing that and selling it to a company called Healthways, now Tivity Health. Started that in 2006 and sold it in 2009. Shortly after, ended up starting our second venture together called Topokine Therapeutics.

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That was a more traditional biotech type of venture where we took a concept that we had observed in the clinic in treating patients with glaucoma, the disease of high pressure of the eye. Recognized that one of the drugs that we were using to treat these patients, called Xalatan, ended up reducing the fat around the eye, and we determined that this drug, when reformulated into a gel, could actually penetrate right through the skin and have a direct effect on fat reduction. And so we figured, well, why don't we take this drug and make it into a gel and use it to treat patients directly with the fatty eyelids and fatty chins. It's basically a medical aesthetics and dermatology ophthalmology company we ended up creating from concept. And we took it to advanced clinical trials and registration studies before selling that to Allergan, now AbbVie. And so that was in 2016. And a week later, we ended up banding together again, and this time with a third co-founder of ours, who's currently our chief medical officer, Metin, and started Cartesian.

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And so we've been doing Cartesian ever since Spring of 2016.

Rich Bendis: So your first two were up in Boston. Is that correct? So what brought you down to this region?

Murat Kalayoglu: Back in 2008, my father-in-law passed away. And so my mother-in-law lives here in Takoma Park. My wife grew up here, in Takoma Park. My parents are in Turkey. My brother is down in Alabama. My wife Liz's family is in Seattle. So family is all separated. We were up in Boston. We figured, well, why don't we move down, and have our kids a little closer

to grandma, and have Liz be a little closer to her mom. And so we ended up just packing bags and moving here. It has been great, because I didn't move here necessarily for the actual ecosystem; I moved for family. But I was very pleasantly surprised that we actually have this incredible ecosystem that allows me to be able to do just the kind of things that I was doing up in Boston.

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Rich Bendis: We are fortunate that you landed here and you've decided to stay, because you could operate these companies anyplace else in the country. And it's nice to see them growing. We'll talk a little bit about your ability to attract talent to the company too, later. But more importantly, you're on the third startup and venture with the same individual. Mike, as you mentioned. Mike Singer. Normally, marriages don't last beyond one time, and you're on your third marriage with Mike. Tell me, what's the secret to success there?

Murat Kalayoglu: I apply a lot of the principles I've learned from my marriage to Mike to my marriage with Liz.

Rich Bendis: [laughs]

Murat Kalayoglu: And vice versa. I'm honestly not kidding you. [laughs] It really is amazing how it really takes a degree of respect and commitment to your business partner as your spouse, to ensure that the marriage is successful, in either scenario. And so Mike and I, I think really, we complete each other, Rich, in that he's really smart, and me, not so much.

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It allows us to be able to—I might be a bit more risk-taking, and he tends to sort of pull me back a little bit and talk some sense into me. And together we've had some degree of success. And most importantly just have to sort of enjoy being able to work with each other. And he's just such an amazing and kind and brilliant person that I've just been so fortunate to get to know over the years. He's a friend way before he was a business partner.

Rich Bendis: It sounds like you have two soulmates. The third time we do a *BioTalk*, we're going to have both of your partners. You're going to have your wife

and Mike on with you, and then we'll talk about this real dynamic and how it works. That would be interesting. So getting back to the business, though, with Cartesian, why don't you introduce our listeners to Cartesian, and how it was created and what it does today?

Murat Kalayoglu: The genesis that Cartesian really dates back to is my brother getting diagnosed with cancer, Hodgkin Lymphoma, back in 2014, 2015.

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This is right around the time when Topokine was generating some just great clinical data. I started to think, well, I could continue a career in medical aesthetics, but I could also go and do something about folks like my brother who were getting diagnosed with cancer every day. And I ended up wanting to shift gears and talked to Mike about it. He also had a family member that was diagnosed with multiple myeloma. And I've had members of my family with myeloma. So we figured, let's go and hunt the most interesting technology out there and bring it in and start a company around it. So we went and licensed some technology from the NIH from the Kopenderfer Lab and sort of the Rosenberg group over there and came up with just a terrific technology around a CAR-T that was able to target a unique antigen called B-cell maturation antigen, with the chimeric antigen receptor T-cell approach.

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And we can talk about what that technology entails, but it's in essence a CAR-T for BCMA. So we ended up approaching them, and it took a while to negotiate an exclusive, but we were successful. And in 2016, we formally launched the company around that technology to engineer cells through non-viral methods. We can get into the benefits associated with that—to make them potent yet safer to be able to treat patients earlier in the disease paradigm. The one thing about multiple myeloma is that it's really hard to treat this disease after the third or fourth or fifth relapse. And the disease always relapses, no matter how often you end up treating it, and the remissions become shorter and shorter. So it's really important to throw the kitchen sink when the patient is first diagnosed, along with all the great therapies that they have access to, to really push the patient into as deep and durable of a response as early on as possible.

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It’s always easier to treat a disease, whatever disease it is, if you're treating it early. But it’s especially true with multiple myeloma. So we ended up designing from the bottom up a program that allowed us to be able to go after a front line myeloma setting. We had to go through all the safety studies first of course, in the most advanced patients. That’s from a regulatory perspective. You sort of have to do that. So it took us a while to get there. But we finally ended up launching, just recently, a study where we're using a CAR-T for the first time in RNA cell therapy, an RNA CAR-T to treat a front line cancer, and that cancer happens to be multiple myeloma. That study is up and running. Now along the way, we developed a lot of know-how and technology that allowed us to be able to use the same engineering concepts of RNA and cell therapy such that we ended up expanding beyond cancer and beyond myeloma into autoimmune diseases, into respiratory diseases.

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We intend to go into cardiovascular diseases over the next 12 months. So as often happens, as you well know, in these types of ventures—new discoveries are made on an ongoing basis. So as these opportunities came up, we ended up branching out such that today, we're an RNA cell therapy pioneer, with six assets in development, three in clinical development, and three in pre-clinical development. All of those three are expected to matriculate into clinical development over the next 12 months. And really a dedicated team of scientists. We have more advanced degrees than employees here at Cartesian, where you sort of bring everyone together under the same roof, and you create this fully integrated team, where we do discovery in-house. Regulatory work is here. We have our own GMP cell manufacturing facility we've built from the ground up a couple years ago. We have our own quality management systems, quality control labs.

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We release product here internally. We do clinical operations. So everybody is under the same roof, and that allows us to be able to make relatively rapid progress to the point of where we're filing one to two INDs a year. Our approach is to bring game-changing therapies using the

safety and potency of RNA cell therapy into not just oncology but beyond oncology as well.

Rich Bendis: Your introduction to Cartesian has stimulated so many questions that I have. But before I get into that—I want to talk a little bit later about your vertical integration, which is very rare for emerging bio companies, which you've been able to do, which is very intriguing, and a lot of listeners would be interested in that. The other thing is it sounds like you have a platform technology right now that might create the opportunity to create some more spinouts and we might have some baby Cartesians coming down the road with some of these new INDs that you're doing. But I'll talk about that later. But one of the more important things, as we go back to the beginning, we have NIH in our backyard.

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We have 6,000 scientists at 27 different research institutes in Bethesda in Montgomery County. And you don't hear as much about companies licensing technology from NIH, because they always talk about how difficult it is. You successfully did this back in 2016, and that's when they had a centralized tech transfer office, versus now being decentralized. So I would imagine you probably worked with Mark Rohrbaugh and his team back in 2016 when you did that. So talk a little bit about the process of licensing technology from the NIH, and the challenges as well as the benefits of doing so.

Murat Kalayoglu: It's always difficult to be a relatively small company, or even before a company—a couple of folks—approaching a massive organization, especially if it's a government organization. Things happen at different time scales. Often making a decision once every couple of months is considered fast in a large organization. [laughs]

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And of course a couple months can mean a lot for a smaller organization. So it's frustrating. But if you go into these types of discussions with a set of expectations that it's going to take a while, and just plan accordingly, then I think things tend to work out more often than not. Ultimately everybody is on the same page. NIH is looking to license these technologies because they have the same interest about patients as you do. There's just more bureaucracy just by definition. And our experience

was certainly frustrating, but at the same time, we persisted. And we ended up getting exclusive rights to what is now recognized to be the originator patent that is the foundational patent that covers all the CAR-T BCMA therapies out there for myeloma and beyond. Then we actually ended up going back to them and getting additional license for other diseases, and based on that foundational relationship, I think that went a lot more smoothly.

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So I certainly respect the boundaries and the difficulties that folks at NIH are limited by. The individuals certainly want to do more. But I think over the last several years, you've seen an attempt to decentralize and make some of these processes go even faster, and I certainly commend that.

Rich Bendis: Congratulations. I think that's something that people don't understand—the unbelievable asset base that NIH has, and how approachable they can be. Even though it may be frustrating and bureaucratic, the scientific content and assets that they have within their portfolio is amazing. One of my goals and I hope for this region is we'd love to see more Cartesians evolve out of NIH that can create their companies in our region, stay here, and then continue to do multiple licenses like you've done. So congratulations on that success. In addition to the licensing there, you've also been very successful in raising non-dilutive financing through SBIR grants at NIH.

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Do you want to talk a little bit about your strategy there, Murat?

Murat Kalayoglu: Yeah. We've raised a total of about $7 million in grant funding. The vast majority of that has come from the NIH, from three different institutes—the NHLBI, the NCI, and the NIAIDS—with phase two SBIRs, each of which support in part one of the three clinical studies that are currently enrolling. And then in addition we just recently found out that we had received the Maryland Stem Cell Award as well for Descartes-30 in ARDS study that we're doing. And that portion will be used to fund a part of the study at the University of Maryland up in Baltimore for that clinical trial. And so the total amount of $7 million is, over just the last couple years—that's a significant amount for us and a meaningful amount that allows us to be able to do things that we otherwise wouldn't be able to do.

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And we're certainly grateful that the NIH has recognized the foundational science that supports a lot of the development around RNA cell therapy as a new therapeutic category.

Rich Bendis: I think what the SBIR grants do is enable you to look at new therapeutic areas where you can take your RNA platform and develop it, which is what NIH is looking for. So it's a win-win for both NIH as well as for Cartesian. So congratulations on that funding as well as the Maryland Stem Cell Grant funding. Let's go back a little bit. You talked about your philosophy about having everything under one roof. It's rare that you see the level of integration you have of all the different disciplines at a company of your stage, because a lot of that is contracted out or done through strategic partnerships. Why have you gone in this direction, and what do you attribute your success to?

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Murat Kalayoglu: We never intended to. Topokine, our previous company, we started that company, Rich, in 2009, with the two of us, and we sold it to Allergan in 2016 with the two of us. And along the way, we had taken a company from concept to late-stage clinical trials having outsourced everything. We didn't even have an office. I worked out of home and so did Mike, and we were all virtual. So when we started Cartesian, it was with that philosophy and mindset that we thought that we could replicate that model that had worked so well, in the world of cell therapy. And it didn't take that long [laughs] for us to recognize that it just wasn't going to work with cell therapy, and that we had to shift our mentality and philosophy 180 degrees.

Rich Bendis: Took more than two men and a truck?

Murat Kalayoglu: [laughs] Right, right. Bottom line, I'll give you an example. We thought, okay, we're just going to go ahead and outsource—there's a local CRO that we figured we would outsource some of the early pre-clinical work to.

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We looked at the timelines. We looked at their relative unfamiliarity with some of these cell therapy-based engineering technologies. Some of the difficulties that we encountered around how some of those studies would translate from a regulatory perspective to clinical and labeling studies. And we recognized that they didn't know any more than we did. Or if they did, that they certainly didn't know what it was that we were trying to do, and the way we were trying to do it. Cell therapy up until then had been very focused in sort of a conventional way of engineering cells with DNA. To date, it's still very focused in that area. But conventional cell engineering, which is engineering cells with DNA at the genomic level, making irreversible changes, it has come to be conventional in the sense that most everybody is doing that kind of work.

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And there are certain standards that are now being placed that allow the CDMOs to manufacture with standard batch records and everything, certain units of machines that are dedicated for a given type of production to support that type of therapy. These kinds of things are emerging, but from the very beginning we recognized that if we weren't going to do the conventional way, if we were going to use RNA instead of DNA to engineer cells to make them safer, to confer upon them druglike properties, and all the sort of benefits associated with RNA instead of DNA, we recognized we had to come up with an entire new manufacturing strategy. And that translated to the fact that we needed to bring everything in-house. And so that's why we moved up here to Quince Orchard Road here, and just a stone's throw away from AstraZeneca and Novavax here, and piggybacked on a total building renovation to build our GMP cell manufacturing facility right next to our D laboratories.

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We've been doing this for the last couple years now, and I can tell you that if we hadn't done that, there's no way that we would have been able to get a product and much less three products into the clinic as quickly. It takes a lot of thinking and learning iteratively from each and every run. Our entire manufacturing team is comprised of MDs, PhDs, or MD/PhDs. We've populated our group in order to extract as much information as possible from each and every production run. And that's really important

in early clinical development, especially in an area where you're really the pioneer, so that you can make it better over time. And that wouldn't have been possible if we had taken the same philosophy as our previous company and just outsourced everything.

Rich Bendis: It's a really interesting strategy and it's working, so congrats on that. But it does take good development partners. You have to have a really good real estate partner to work with, as you're growing, because it's just two men starting it, or two guys starting it, and then all of a sudden—how many employees do you have now?

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Murat Kalayoglu: We have 20. But you're absolutely right. You can't build a company in isolation. You [laughs] definitely need an ecosystem. So our colleagues here at Scheer and ARE, from a real estate perspective. All of our vendors that support us for all our reagent supplies, equipment. Some of this equipment is very sophisticated, as you well know, in cell and gene therapy. All the folks that have provided us guidance along the way from our advisors to consultants, et cetera. All that really needs to be—I think personally—sort of physically co-located, within a relatively condensed environment that allows us to be able to move at lightning speed. And that's what Montgomery County has been able to provide us.

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Rich Bendis: You're creating a little mini Cambridge right here in Montgomery County because you've been able to attract all the resources you need, right in your own backyard. And the other thing you always talk about is the ability to recruit highly qualified team members, and you talk about the qualifications you have in your team now. Talk a little bit about how your team has evolved, and where have you basically attracted all of these people to come into Cartesian?

Murat Kalayoglu: We're probably I would say about 50/50 in terms of within Maryland and ex Maryland. The folks that are within Maryland come from all over, from Frederick or down in Silver Spring, to Baltimore area. And then I think the folks that have relocated here we've recruited either internationally or from California. We have a number of university professors that have come from Tennessee and other places. So for folks to sort of pack up their bags and come to Cartesian, obviously you have to believe in the

technology, et cetera, but they're also looking for an ecosystem beyond Cartesian.

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And from a personal perspective, from a family perspective, obviously the region has got everything—big city like Baltimore and DC just a stone's throw away, as well as all what Montgomery County has to offer. But on top of that, from a professional and career perspective, the sort of window here, the 270 window, Montgomery County in particular, is just great. You've seen in particular over the last year the explosion of opportunities in manufacturing, in cell therapy, in gene therapy. So it's not that difficult for us to recruit some incredible talent.

Rich Bendis: And then you talk about the CAR-T. If you look at the explosion, we're becoming a neat little hub and cluster in CAR-T and cell therapy with some of the companies that have set up manufacturing operations, have decided to come from Boston, down to Montgomery County. And that's great for your employees as well because you don't want to be in a region where there's a one-trick pony and if it doesn't work you don't have the ability to go to other companies.

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Now you have a number of other companies surrounding you, where you actually have the ability to get talent, or they know they're more secure within the region.

Murat Kalayoglu: That's exactly right. Rich, you've been so instrumental in this. And you've always recognized that there is a critical mass beyond which things start to accelerate and snowball. And I think we're at that critical mass, where people start to think about generations of companies. You have not just a handful of companies. Your job security after an acquisition or a merger, something, it's still very bright, without having to relocate to a different state just because a company disappears. And from a management perspective, investors love folks that have had a couple of exits. So if an entrepreneur after a successful exit is able to stay and start their next company in the same region, and if you sort of amplify that, over dozens and potentially hundreds of such exits, you start to reach critical mass where everything starts to become more, as you put it, more Cambridge-like.

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So things just get easier, I think, from this point forward.

Rich Bendis: You talk about investors, and we've talked about the non-dilutive funding, but you've had a great deal of success with your equity funding as well. That also comes to being able to identify a really strong partner, not just an investor. So talk a little bit about your equity strategy and your growth there in the couple rounds you've done.

Murat Kalayoglu: We've been just fortunate to be in a portfolio of an institutional investment firm called Schooner Capital. They're a private investment firm, started in 1971. They're based out of Boston. They're generalists and they invest across stage and sector in both public and private companies, and have a very interesting and growing portfolio of life science investments that they've been successful in over the last decade or so. So Mike and I started our first company at their offices—HealthHonors in 2006—at their offices.

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And they took a chance with us back then, and we've had that partnership with them ever since. And given that they're an evergreen fund and they've been supportive, they've seen a couple exits from our companies, that partnership continues to grow. Now, as companies grow, the access to capital certainly needs to grow as well beyond a single sort of institutional partner. And so we are in the process of sort of contemplating how best to sort of grow that, whether it's to access capital from the public markets or through additional institutional investors, et cetera. And I think a lot of that thinking is evolving together with the kind of progress that this region is seeing in terms of attracting investment dollars.

Rich Bendis: We're hopeful we'll see you at the next IPO. We've had I think 12 or 14 in the first four months of this year, in this region, IPOs, which it's a record year. And if you look at the venture capital financing plus the IPOs, this place is really hot.

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The moons are aligning right over this region right now. And we don't have to really take a back seat to San Francisco or Boston. We just need more of the same.

Murat Kalayoglu: That is exactly it. Those are incredible numbers. I didn't know that. That's just unbelievable.

Rich Bendis: It is amazing. We're talking to Murat Kalayoglu, who is the Co-Founder and President and CEO of Cartesian Therapeutics. And one last thing that we'll talk a little bit about is that in addition to running this company, you're an angel investor as well. You've done in addition to the three companies, two of which you've exited successfully, plus Cartesian which is growing well, you like looking at other entrepreneurial opportunities which you could seed a little bit. Talk a little bit about that.

Murat Kalayoglu: Mike and I have been doing a little angel investing since the Topokine days. We have a portfolio of—well, he's got a few more I think in his portfolio—but I've got about a dozen or so such investments, mostly in life sciences, that I've made over the last several years.

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And we continue to be interested in these types of opportunities in the sense that from an investment perspective of course, because it's an area that we think we know a few things about, sort of both on the medical device side and the drug side as well as the diagnostic side. But in addition, I think it's fun. And it's especially fun to see entrepreneurs building their enterprises in the same sort of ecosystem that I'm trying to do the same in. And so there's a lot of opportunity to compare notes and interact with folks that are looking for a little capital to get something going. And if they've got something that's highly promising and they're highly motivated, highly committed, why not take a little bit of a risk and sort of help them along to see their dreams come true. So these types of investments I think all just really depend on the entrepreneur sort of growing their business to a point where they're able to attract a degree of institutional capital.

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We do sometimes coinvest with institutional investors. But more often than not, these are, as you said, seed investments. So the ability to

attract that kind of institutional capital again is in part a function of the region. It's more difficult to make an investment in non-Maryland states.

Rich Bendis: [laughs]

Murat Kalayoglu: The fact that we've made a couple investments in our sort of local community here in life sciences and growing companies. Just throw out a couple names—Remedy Plan Therapeutics. Just a really terrific up-and-coming company run by Greg Crimmins. GiveHero is another terrific company. These are just terrific companies that have great management, great prospects, and I'm just really happy and proud to be a part of them.

Rich Bendis: Generally people are so focused on their business they don't have time to give back to the community, but you've had some success.

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You and Mike both have had success. So it's refreshing to see that you're willing to reinvest some of those dollars that you've been able to earn through your exits that you've had, back into other entrepreneurs that can hopefully follow the same pathway that you and Mike have. So I congratulate you on that, Murat. So keep it up, and I'm sure that people are going to find a way to your doorstep as a result of this *BioTalk* and say, "Hey are you open for business for me?" As we close this podcast, you have an open mic now. Anything you'd like to convey to the listeners that we haven't discussed that you'd like to share?

Murat Kalayoglu: I think we've covered a lot, haven't we? I'd just like to reinforce how instrumental you have been to this region, to this community, Rich. Through the podcast, through all your efforts at BHI, all the conversations that you have, all the time, effort, and energy that you spend in putting a spotlight in the kind of progress that this region is making. I really want to thank you for this conversation and all of the others that I've had with you and all the work that you've been doing.

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Rich Bendis: I appreciate that very much. Wasn't expected, Murat, but it takes a village, and we're just two people as a part of this large village we have in the BioHealth Capital Region. So I want to thank Murat Kalayoglu, who is the Co-Founder, President, and CEO of Cartesian Therapeutics, one of the

fastest-growing companies in Montgomery County and the BioHealth Capital Region. And as I promised—and hopefully I'll get rid of this cold so I won't be as froggy next time—we're going to bring back his partner Mike, and his wife, and do a three-way and talk about how all these things work in the future. So stay tuned, listeners. We'll be back with Murat in the future.

Murat Kalayoglu: Thank you.

Narrator: Thanks for listening to *BioTalk* with Rich Bendis.

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