Jake 02:18
Thank you, Eric, for joining me on the show today, I really appreciate you taking the time. You are the founder and CEO of Elysium health, really innovative health company that I've been tracking for a while and think is super exciting, all these things that you're working on. But you've got a long story before that of a lot of successful stints along the way investing and now entrepreneurship. It would be great if you could sort of start off the show for those who aren't familiar with you or with the ECM by just walking us through that story really, as early as you're willing to start to where you are today and what you're doing today.

Eric Marcotulli 02:56
Thank you, Jason, and thank you for having me. And I'm happy to do that. I think I could go back, I would say probably to my college graduation, because I don't know how much it'll resonate with people. But it's it's a winding road filled with a lot I think of serendipity for me, in terms of how I ended up here. And I don't think that's particularly unique in terms of entrepreneurial experience. But in any event, I think what's what's partly interesting for me is I I was an athlete in college, I was a wrestler, and sort of from the very beginning, he the the path to at that time. So we're in the mid aughts, if you will, I graduated undergrad in 2007. And sort of as you enter college, in this particular setting, there was really only one track and that was investment banking. And so I like many others. Also, as an econ major said, Well, I guess I'm going to be an investment banker, and kind of just steeled myself for that in the early years of college and through internships and other things over the summers. throughout college, I realized that that was absolutely not the life for me. And you know, funny as these things go, I said to myself, well, that must mean that I have to be a management consultant, if I'm not going to be an investment banker, right, that's the only alternative, at least at this point. That's what I believe. And I remember my senior fall I interviewed at all of the major consulting shops, a handful of the smaller boutique ones and, and even some of the larger corporate ones that I really had no intention of ever working for, and it didn't really matter whether I did or not, because I didn't get any offers from that. And so I entered into the second semester of my senior year with no job prospects and you know,

all of my my peers sort of already you know, accepted positions and knowing where they're moving and here I am in February with with no opportunities and I I get a ping from our Career Center. airbases from a venture capital fund, which at that point, I had never heard of either the fund or venture capital itself. And it was Bain Capital ventures. And the the note said that they were looking for analysts, and this is their first class of it. And basically what it turned out is, you know, they want it to be more proactive, I think now, it's very, very common, but this is, you know, going back almost 15 years, you know, a lot of these especially you're looking at private equity funds, in this particular case, becoming earlier stage in their focus, what you see is much more relationship driven, or even process driven banker, lead, etc. And so, you know, now it's kind of weird even think that there wasn't a lot of proactivity and networking, but in this particular case, there wasn't. And so very interesting and appealing opportunity for me to try and identify young, fast growing technology companies and getting the opportunity to reach out to them and effectively convinced them to take our money while simultaneously learning about what they were doing. And I would never have stumbled into that had I actually taken, you know, one of these prior positions. And so I ended up at Bain and just had a wonderful experience there. And one of the things that I learned was, I felt like I was sitting on the wrong side of the table, I was constantly talking to entrepreneurs who sounded like they were just so incredibly dedicated to what they were doing. And, and more than that, just inspired every day to to wake up and put their feet on the floor and go do something. And while I love my job, I just I didn't have that level of enthusiasm and passion. And so I said, you know, I'd like to make a change. And I didn't really know how to do that. And so I thought maybe business school was, was the way I went to business school and fully intended on pursuing this idea of entrepreneurship, but did what I always now caution people not to do against even then my better judgment, which was, I tried to start a bunch of companies just for the sake of being an entrepreneur just for the sake of starting them. And those all failed or petered out. I mean, there was a point where I had one idea that I liked that I couldn't even recall if I were to try, but I remember vividly that it required about a $20,000 investment. And I wasn't willing to do that out of my own pocket, I wasn't willing to approach friends and family and I knew if,

if that was the case, that this was not something that I was going to dedicate myself to for 10 years. And, you know, with that in mind, I got a I got an inbound from Sequoia Capital and had some conversations with them about leading mobile investing for their their growth fund. And you have to remember, this is now 2011 or so. So the iPhone is only four years old. And while I'd come into business school thinking, Hey, you know, you're going to be an entrepreneur, all of a sudden, I had this opportunity to travel the West Coast, immerse myself in Silicon Valley and, and do something that I hadn't, up until that point in my life been able to do, or have the opportunity to do and so I thought and also, you know, Bane is an incredibly amazing fun top tier fund. And I think having the opportunity also to then work at Sequoia for me was was very, very interesting. And so I thought maybe it was just the space, I was focused on maybe infrastructure software investing at Bain Capital was different to me somehow, and that no mobile in California would be different. And so I took the position, with with great enthusiasm. And then as these things are apt to happen. About two months before I graduated, I did a case study in one of my classes on entrepreneurship, and it was on a company called Sirtris pharmaceuticals. So Jake, I don't know if you've ever heard of Sirtris

Jake 08:41
only from listening to your podcast in preparation for this.

Eric Marcotulli 08:45
Right? So it's interesting, because there's a small number of people who know it very, very well. And, and most people don't, but it is also a very sort of divisive company and outcome in terms of the the broader longevity and aging, both field and then I would say, market when you go to the sort of commercial side of things. And so anyway, I'd never heard of them. They were a Boston based company and pretty high profile, which we learned to the case. But here I was having never heard of them either. And so a couple things just about the case. The whole premise of this case is you are the protagonist as you are in business school in every particular case, and you have to make a decision as you do and again, every case and for Sirtris The, the the problem, the tension here, is there a pharmaceutical company and they have a molecule that they think is stopping slowing or reversing

a fundamental process of aging. And because aging is not a disease, and because the the molecule that they discovered was natural and its origins, there was an opportunity, from a business model standpoint to go direct to consumer Right to create a consumer facing healthcare company. However, because there weren't very many models, or at least good and reliable models for studying aging itself, the early research that was done in, for instance, mouse models was done on disease models, right? So you're looking at things like cancer and cardiovascular disease, and the data is very promising. And that fits right that maps, the idea is that aging is this fear connected series of degradations. And that solving for aging. And these processes of aging are going to have a multitude of potential impacts, as opposed to just going after, for instance, a singular form of cancer. And so because of that, the other opportunity would be to enter into a more traditional drug development path, where you're looking to modify the molecule one, so it's potentially more effective, but really, so you can get a patent on the molecule, because that's where the economic return resides. And that's your, that's your other path. And they're very different business models. And then there's a third, which is, you know, do they want to license their intellectual property away to a much larger pharma company, and you spend the better part of 90 minutes sort of debating this right. And just to give you a sense for the case, and where, where I was in all of this, just to back up the molecule What they discovered. It was a lab at MIT, run by Leonard garante. And his postdoc, David Sinclair, who was now at Harvard, they discovered a class of genes called sirtuin genes. And these genes are now affectionately referred to as longevity genes. Because what they found was, well, they found a series of things. The first was that these genes were found in in all living organisms, so conserved across species. So that's always interesting, right, discovering a new gene. But what they found from an activity standpoint was really interesting, they found that they acted as the guardians, if you will, of the genome. So they actually both from an information standpoint, protect DNA, they are responsible for DNA repair, but also DNA protection in terms of preventing DNA damage, but also they confer structural benefits to so if you think about your DNA is this warehouse or a library, they're not just the sort of librarians who are who are the filing system, making sure the books are on the shelves, and in good condition in the right places, they're actually

the in many cases, helping the building itself with the security guards that are locking the doors and whatnot. And so that's a pretty critical role and something that was new. And then the most important thing that they found was that in all of these living things, that that actually age, right, because there are certain organisms for some jellyfish that don't age or have the ability to, to sort of go back to an embryonic state, that the activity level of these genes degrades over time. And so that was, that was a huge deal. They took that a step further. And they showed that if you're able to activate these sirtuin genes, these genes later in life, when the activity begins to degrade, that it confers all sorts of benefits, right? So you see these mice living to the human equivalent of 120 years old, and they're healthy to, you know, 119 and 11 months, you put a funnel down their throat and feed them nothing but but fat, and they don't gain weight. If they have cancer, the cancer goes away, then they took that a step further in the genetically modified mice to actually never lose that sirtuin activity. And that showed exactly the same benefit. And so on the back of this discovery, it was a it was a huge deal at the time. The postdoc, David gets the offer to run sort of the aging research effort at Harvard, which he accepts, and being younger and entrepreneurial he screens for molecules that will activate these tunes, right? The idea that, hey, can we find a natural small molecule activator of these, because we can genetically modify humans, or at least at the time, we could write with CRISPR, and everything else that's now entered into the conversation. But by and large, you still probably want to find some sort of oral intervention, right? If it's if it's safe and effective. And so they do they find this molecule called resveratrol, Jake, you may have heard of that a lot of people have. And this is a derivative of red wine. And it's shown efficacy and activating these longevity genes. These are twins in mouse models. And for a while there was this great excitement, you can actually go go back and look, there's this massive spike globally and red wine sales, I think it's Oh 70809, something of that sort. And there's, you know, all kinds of periodicals and publications with you know, the red wine molecule, the you know, the the fountain of youth molecule. And people thought this was the answer to the French paradox, which is something I wasn't familiar with. But you know, that there exists this paradox, which is the French eat nothing but high saturated fat diets, right think croissants and cheese, and they smoked like chimneys, yet

they have among the lowest incidence of cardiovascular disease in the European Union. And obviously, that's the number one killer right in developing worlds. So you're faced with this this tension, right? This natural molecule and a potential path to market that's faster. But it's characterized by charlatanism and savvy marketing, right the consumer space than it is r&d and rigor and scientific pursuit. And on the other side, you're facing a very, very low likelihood of success, right? It's, you know, a minuscule, less than, you know, tenths of a percent chance, right, that you go from a mouse discovery to 10 years later and approved therapeutic. And you debate the merits of these right again, for, as I said, 90 minutes or so. And I was firmly in the first camp, Jake, I said, I can't understand how anybody can read the same case that I read and not immediately want to take this product for themselves and give that to their their family and their friends as well. And I was only one of two people who felt that it mainly because people were really attached this idea that the the consumer health world again, was was not a good place to be. I think the only other markets that might have been considered worse at the time were something like used car sales, and, you know, people who call you repeatedly for gym memberships. Right? And so it was interesting, because at the end of the case, right, the the sort of aha moment or gotcha moment in this particular instance, was they never had to make a decision. They were acquired by GlaxoSmithKline. For I think it was $720 million, or something they're in cash. And, you know, we know what GlaxoSmithKline does, they make drugs. And so that really added for me something special, right? I took a step back leaving that class and I was absolutely floored. I said, I didn't know that aging was a scientific pursuit, let alone a legitimate one, too, I didn't know how much progress we had made. Right? It was previously To me, this is a morphus unstoppable force. And yet now we're, we're able to not only identify the processes that drive it, but potentially intervene, and now even measure it and quantify it, which is, which is incredible. And the fact that the scientists were, you know, at MIT and Harvard, the fact that, you know, Glaxo was buying this for the price that they did an all cash after just what was a handful of mouse states. And it ended up failing, it ended up ultimately being internalized attacks. So and again, I don't have any insider information here in terms of it. But what I've heard is that they've made it into the clinic many years later with skin condition, related assets. And I think while

those are very important, large potential market opportunities, I don't necessarily think that it was what the original promise held. But I was really fascinated by this. I moved to California a couple months later, I, I was working at Sequoia i was i was investing there. And I started cold calling the scientists that were involved in the search worst case, and just immersing myself in this world and traveling to Stanford and Berkeley and UCSF where they have a very open sort of environment and community where people can come and sit and listen to researchers in the field of Beijing give talks on the State of the Union, and was everything from students to Nobel Prize winners. And it was very obvious to me at that point, Jake, that we were at this critical juncture in a slew of areas that I think added up to an opportunity that to me was, was something I had to pursue. And the first was, you know, not just what I said about aging, and all the things that I learned about it personally, but that, you know, we were making a lot of progress we were on the cusp of, in my opinion, and I certainly think this is borne out even faster, in many ways than I probably anticipated. But we're on the verge of a series of discoveries that were just fundamentally going to reshape our thinking not just about aging, but about human health and, and human longevity. And then to, you know, revisiting this idea of choosing one of these business models, right, I thought, you know, for whatever reason, 15 years ago, or so people didn't want to pursue these idea of platform companies, or you couldn't possibly build a direct to consumer company that also did studies and diseases, and then also did other things as well. And to me, I thought that was a huge opportunity. Because when you're addressing a fundamental process of aging, you're not limited, again, to one specific area of health or one specific, you know, health state, right? So you can make a drug or you can make a medical food or a dietary supplement or a diagnostic, and those things could go after, right, neurodegenerative diseases, human health and performance, right on the non disease side or a million other things. And so, long winded way of getting here, but I think, you know, all of that added up to I was really sucked into this and going back to the founder of search David Sinclair, you know, his mentor, the the lab where these discoveries were made plenty who rented MIT, one of the scientists, I called, just wholeheartedly agree with me in these ideas. And so we, we came together around this idea and Lenny became my co founder, our chief scientist.

Jake 19:54
Wow, that's an awesome story and certainly a lot of serendipity woven throughout. You know, I don't think there's very many people who remember so vividly a case study from business school, but you saw, obviously a seed of something in there and, you know, spent your your time at Sequoia, which I tried to feel too bad for you about that. But, you know, after a couple of years there, you decided to finally jump out and, and do the thing that it sounds like you went to business school in first place really to do, which was to find a way to be an entrepreneur, you had mentioned, like, you know, you felt like you were on the wrong side of the table, really, really liked the way that these entrepreneurs, just how passionate they seemed about what they were doing. But you were sort of forcing it at first, you're like, Alright, I want to be an entrepreneur. So you want to be an entrepreneur for the sake of being an entrepreneur? And these couple of companies flamed out or, you know, never got started in the first place. How did you know, you know, you're on a great track, like at that point, right? A couple years into Sequoia, post Business School at Harvard, you know, Princeton, Bain, like you're on this track. And I know from spending some time in banking myself, like, you're surrounded by a bunch of other people who are sort of like, operating on sort of like a track mindset. And you're either like ahead or behind, like, your brand is good or better, or it's worse. What gave you the conviction? Finally, to know, okay, with illicium, and your first product basis, this isn't me starting a company, for the sake of starting a company, this is me, really, you know, there's a high opportunity cost on quitting the position that you were in at the time, if things don't work out, what gave you the conviction that this was finally the right idea to go and become a founder?

Eric Marcotulli 21:49
Yeah, you know, I think it's a couple of things. Jake, it's it. And I, I always go back to, you know, there's some famous court case, and I can't remember what it is, I should probably learn it because this has come up so much. But I remember at the heart of this case, it might have been like the 60s, but it was going back a while and it was it was centered around pornography. And part of the ruling had to deal with, you know, how do you define it? And I remember the justice, I

think it was a Supreme Court case and the justices responses, you know, I know it when I see it. And so, you know, that is something I always tell people without maybe the the intro part there all the time. But, you know, for me, it was it was, after all of that, after all of the knowing maybe I wanted to do this, but not having conviction around an idea. There's a moment where it clicks, and you sort of just know it. And, you know, that's happened over and over again. And I think a lot of entrepreneurs would say that, that, you know, there are times when you'll go through decision making processes are really tough times, you just don't know. And then something, something happens and it clicks and you just have the confidence. And then I think it becomes more about pattern recognition and knowing that, but to actually put concrete examples against that, I think, you know, there were really two things. The first was, I can again, vividly remember driving to work on Monday mornings, and there was a there was a guilt element to it. And for me, it was driving to work, and saying, I don't enjoy this the way that I feel like I should. I'm a big proponent Jacob of doing something that you actually enjoy. Right? I think, I think it's definitely a characteristic more so of our generation and younger generations as well. And breaking from what I think previously was a different ethos and mindset. But, you know, for me, and I think it's difficult out of college, certainly, right, you have to pay your dues, and, you know, all of those sorts of things. And I do believe in that as well. But there, there does come a time when you get to make your own decisions. And I think that that's changed as well, right. I think we've empowered younger people, which is fantastic. But for me, it was, you know, late 20s driving in my car with this, this, as you said, I was a very fortunate person in terms of the path that I was on. And, and I did love what I was doing. But at the same time, I just also wasn't incredibly happy and not as not as fulfilled, I would say I was missing that element of it. And I again, I remember driving to work on Monday mornings and just not feeling that way. And then the second thing is, every waking moment that I had free. I was going in immersing myself, as I said in this, this brand new space that, you know, to me, I would have never thought that being in an FDA regulated environment was something you know, given how I grew up, given the things that I had optimized for in terms of academics and everything else, early career work, the ability through an approval process, you know, tackling diseases, you know,

that's a really, really high bar, and steep learning curve, right. And so it's it's very, very daunting in terms of taking it on and so, you know, for me, it was much more about not thinking about that and just enjoying the subject matter and you know, I started I did and maybe others do too, but you start to see opportunity everywhere, and so the are almost two ends of a seesaw, I feel like because they're they're sort of battling each other. And you get to a point where I said, it then turned into guilt where I felt, jeez, there's a million people who would line up maybe more out the door to have the opportunity that I do. And yet I feel like I'm being called to do something else. And so, for me, that's where it culminated was, it just got to the point where, you know, you start flirting with the idea, I think, and then you pursue it. And I did a lot of stress testing. You know, part of that was, if you look, we've, we've assembled an advisory board, it's it's fairly unique in terms of what we've done. But we have about three dozen, probably more, if you count our sort of collaborators as well, we have about three dozen meeting scientists on our advisory board. And the reason for that isn't because we love unwieldy meetings. I call it The Brady Bunch meetings when you know, we're on zoom down, you see all the faces. But the reason for that is aging is a multidisciplinary problem. It's you know, it's multifactorial, and so, you know, for us to really solve it, we don't just need one type of person, we need a lot. So people who explicitly study aging people study neuroscience, or cancers, or immunology, people who are data scientists or Bioinformatics, biostatisticians, etc. And as part of that, I said, one of the easiest litmus tests here of whether this idea holds water is maybe I can reach out to some Nobel Prize winners, right, I'd been seeing them speak at these events. And there had been a Nobel Prize awarded in the field of aging, for the discovery of telomeres and their role in the aging process. And so there were definitely people out there who could offer perspective. And I found this was, I think, the moment where I really realized something was there. And when you ask about connection, this was this was certainly the moment if not one of the key moments, it was I expected to be told to go play in traffic by these individuals. And one, I found them to be very welcoming. And to not only were they willing to take my call, but they were interested. And they were enthusiastic. And many of them said they would be a part of it when I asked them. And so, you know, I went from just asking is this a, an idea that's worth pursuing to

suddenly surrounded by now, I think, at this point eight or so Nobel Prize winners as part of the advisory group that that helps us think through product development and clinical trials. And I think at that point, when you have that level of a kind of enthusiasm for an idea that's taking shape, and that's new, especially one that you're passionate about idea at that point, it's a no brainer, I think, you know, not pursuing it is the worst idea.

Jake 27:37
Yeah, now, it sounds like there was a number of factors that just compiled and compiled and compiled and built up over the course of your time at Sequoia where, you know, at a certain point, you got to take the leap, so that you can have the Monday car ride to do something that you feel like, you know, understanding that things that Sequoia were, were, you know, good by a lot of people's perspectives, it's all relative. And if you're not doing the thing that you feel you need to be doing, then, you know, totally understandable to sort of let that build up and want to go do that thing. Your first product was basis. And I assume this was sort of the the idea around which the company originally was built. Can you talk about how basis works and what it is I know, it's about an ad plus, and, and serve twins. But for the, for the novice listener who's not super familiar with the science, what's the sort of fundamental explanation about what these things are, and why they matter and how it all works?

Eric Marcotulli 28:36
It was it's good, I gave a brief overview, I use brief and air quotes, you can't see me right now. But of searchers, because a lot of it was work that was carried over. And, you know, while David was working on Sirtris and you know, pioneering the use of potential small molecule activators of these longevity genes, right? These are two ns, Lenny, and many of his and David's peers were sort of really nose to the grindstone on the lab side of the equation really studying this further. And what they actually found was that the sirtuins were degrading in their activity over time, because they were dependent upon a fuel a fuel called na D. So you just mentioned that. And then a D is this critical coenzyme. In short, for the audience, without any, you'd be dead in 20 or 30 seconds. It's a, a fundamental coenzyme that's involved in processes as important as ATP production, right? We

remember high school biology and energy creation, mitochondria, powerhouses of the cell, etc. 101. So na D is, is this sort of currency, if you will, of the cell. It's used for almost everything. And so tunes are no exception. And so part of the idea here is, well, if you can restore levels of an ad, right, as they're declining due to age, they create this ad rich environment, then you're going to see a lot of these things that depend on it. Right, continue to perform as they should. And then Lenny's view was, you know, they've already demonstrated in animal models, multiple animal models, right? That activation of sirtuin genes when they're not degraded, right has all of these additional benefits. And so, really, it was it was Lenny's hypothesis, right from the outset of our conversations that if you could do both of those things in a single approach, if you could replete, restore boosts levels of an ad, and then activates for two ends, you're going to have an incredible product on your hand. So that was the hypothesis behind basis. And you know, the very first clinical trial that we did was to show that we could take people who were older life, so 60 7080 years old, and we administered the product basis to them for two months. And what we what we observed was, and again, this was placebo controlled, we looked at a 40% increase after 30 days that was sustained after the next 30 days after two months. And so we don't have a tremendously detailed scientific understanding of how much energy declines in humans due to aging the senses, it's by about 50%. So you know, being able to replete to 40%, in that period of time, means you're, you're right there, in terms of where you want to be. And we've subsequently shown that we activate certain ones as well. And, and not only that, but that there's a synergistic effect as, as Lenny had initially hypothesized between the two. So a number of different studies we've done and looked at the individual ingredients, and then the combination and you see a, a, either a result that exceeds right the first two individually, or you observe a result where there is no result for the individual components, but there is for the combination. And so we've taken basis, now into a series of other clinical environments. So in terms of sort of the health side of the equation, the non disease or non prescription side of the equation, we have just completed a non alcoholic fatty liver disease study. So this is a really interesting space Jake one because it says disease in the name, but it's not a disease, it's actually a precondition to a liver disease called Nash. And what's really

interesting is Nash has one of these, you know, sort of on the rise, dietary induced, it's basically the fibrosis of the liver. And it's has zero treatments. If you look across basically every major pharma portfolio, in the startup landscape, there are a ton of efforts looking to solve Nash, but just like in kidney disease, once the tissue is byproduct, very difficult to reverse it. And so you know, you'd rather treat it in the in the precondition, and it's estimated that about, I think, 180 to 100 million Americans have it now today, and that a billion people worldwide have, and it's on the rise, right? It's even in the rise of children. And so we're sort of in the readout phase of that now be publishing a study on it. But you know, we've got some incredible results there in terms of reducing toxic liver enzymes, reduction of bad actor, fatty acids that are linked not only to liver diseases in the future, but also cardiovascular diseases. And so, you know, in that case, you're looking at reversing a precondition state and potentially preventing some of these really big, and in many cases, you know, not very well solved or addressed health states right now. And, you know, we've also looked at on the health side of the equation, the relationship between basis and aging itself. So we have another product called index, which sits in the bioinformatics side of the world, and really the diagnostic side of the product portfolio. And so what index does is it's looking at sort of what's called methylation patterns, which is epigenetic signatures of gene expression. And it can actually tell you with a with a spit test, or even a pinprick of blood, how fast you're aging, or how old you are biologically versus chronologically, and the way that that's defined just for the sake of understanding is all cause mortality all cause risk for disease, morbidity and mortality. And so you don't have this quantification, right? Do these analysis very, very large data sets, we can actually begin to quantify aging at the individual level, too. And so one of the things we've done is we've just looked at the relationship between na D levels, as you had asked earlier, and rate of aging. And what we've found, and this is statistically significant. Again, it's it's sort of internal data at the moment, but we've found a relationship between levels of an ad and your rate of aging. So the lower your levels of an ad are, the faster you age, and then vice versa is true. So there's that. And then we've actually shown this is the beginning of what's really exciting of where we are in the space. We've actually shown that customers right in serving customers of

hours, those who use it for one year or longer, you see a reduction in their biological age that persists for one and two years after when we're looking at the longest standing customers of the product. And what's interesting also about that is these are people who are already chaste starting healthier than the average. So these and that's not surprising, right? If people are coming in, they're interested in this field, they're educated, they're opting in to, you know, product focus on cellular aging, right, you think they're probably doing other things that are good for their health as well. And so these people are starting off healthier than 75 80% of people at a minimum, and you're still seeing a reduction in the rate of aging. And again, statistically significant. And so, you know, we're entering into the space on the basis side of it, where you're, we're starting to learn the clinical benefits of it, but we're also being able to actually tie it directly to aging, which is really exciting, in my opinion.

Jake 35:42
So let's clarify that last point a little bit, because I think it's super interesting, you're basically saying that you've got this product index, which tells you your biological age, not to be confused with your chronological age, which is, you know, the biological age is a much better representation of like I said, like, all cause mortality, and, you know, the number doesn't really matter, it's what your, you know, body, what kind of shape your body is really in. And so imagine that, you know, people are taking the test, and then they're taking basis for a year two, taking the test again, and they've actually gone backwards, they've gotten younger, in terms of their biological age. What I mean, you mentioned that these people are, you know, they tend to be on the healthier side, which for the reasons, he says, Not surprising, but I'm curious what's like your, you know, taught like, most obvious sort of case study like customer a, in terms of like, Okay, this person's pretty healthy, 60 year old, as opposed to, for example, like, do you have 30 year olds taking this thing? And then they're 25? Or is it more like 65? And then they're 60? Or is it like 65? To 64? Is it a meaningful reversal? I'm curious, just like to get into the nitty gritty of what you're seeing in terms of the reversal, because that's something that I think a lot of people, you know, as recently as five years ago, just probably wouldn't have thought was possible.

Eric Marcotulli 37:02
Yeah, well, I'll say a couple of things. It's a great question. They the the first answer, which, unfortunately, will, undoubtedly be disappointing for a certain group, and if not a lot of people is that the vast majority of people, and again, I don't have the exact percentages, but when I say vast majority, I mean, it's well, more than 50%. And probably, you know, in the two thirds if not higher camp, but again, I don't have the exact figures are within call it two to three years of their chronological age. So you know, again, what you're going to find is that a 35 year old, most of the time is going to be somewhere in the call it 30 to 33 to 3738 range, you're not going to deviate that much. And the other thing is, as you get older, actually, the test becomes in many ways narrower. And the reason for that is in the most literal sense, survivorship bias, right? Because as those people who have the worst sort of side of the aging coin continue, you're sort of left with people who are much more in line with what you would expect from an actuarial standpoint. Right? So, you know, someone who's 75, chronologically is likely going to be very, very close to 75, biologically as well, right, just based on that methodology. Now, there are outliers. But you know, I think that's point 1.1. Is the you know, the the great majority of people are within that. The other thing there that will be disappointing is we have yet to see, and again, this, this makes a lot of sense. We have yet to see somebody who's going to be 20 years, for instance, because you asked for the extremes, right? We haven't yet seen. And there are some tests that will tell you this, but if you think about it, it's just the methodology would make no sense. And certainly in our platform, you've never seen this, but you're not going to get someone who's 20 years older or younger than that. And that makes sense, right? We've never had a human outlier. And as we understand all of humanity who's lived to 150, right, we have a whole bunch of people who have made it to 100, we have a very, very small number of people who've made it to 110. And then an even smaller number of people who've made it a little bit above that, right. And so you would expect if somebody was this incredible outlier on this test, you would also see it, you know, that would be the people who are in the range that I was just talking about, but we've never also, as you know, had somebody who's aged to 200 or something of that sort, there's always

been an upper limit. So that's that's kind of piece one. And then piece two is really now entering into the realm now that that measurement tool is available. We're only now entering into the realm of we're understanding what will impact it and how right I think ultimately that opens the door for things like personalization at the individual level. I think really, this is the key to personalization. It's one of the things we're obviously working on. But you know, if you were to say well, can I can I take there has been a study I think was very small key people looking at the combination of hormones like growth hormone and testosterone, maybe dapa and showed a small reversal over the course of a year and older men I believe it was but you We're only now on the cusp of really understanding the second part of your question, which is what are those things? how, you know, how are we actually going to be able to reverse it?

Jake 40:08
Great. Yeah. So and that's, you know, a little bit disappointing come coming from the company that I'm hopeful make people live a little bit healthier and a little bit longer. But at the same time, it does make sense that, you know, people tend to be relatively in line with their, their chronological age, and hopefully will continue to find things with your guys help that, you know, will enable people to, you know, have those reversals and stay young, a little bit longer and just work at the margin until it's a more meaningful impact. I want to touch on your third product, which we haven't mentioned thus far. I don't know if it was third in chronological order to use the aging term but but basis, we talked about index we talked about, you got a third product, which is focused on the brain would love just sort of the high level overview on that. And then I understand if you're able to share that there's another product coming very soon. And maybe we can release this podcast after it's out so that you can share a bit about that and what that's all about?

Eric Marcotulli 41:10
Absolutely. So matter is a little bit easier, I think, to understand for a couple reasons. One, it's about brain aging, as opposed to aging in general. So a little bit more tangible in that regard. But also, there was a lot of human work that was done when Alicia entered the picture. And we learned of this work years ago, and had been working

with the University of Oxford, where all of this research was conducted over that period of time. And we ended up launching the product about a year ago, a little over it was June of 2020 mid pandemic, which was interesting for a lot of reasons that we can talk about, but the short on on matter is the following. So the researchers at Oxford had hypothesized that a particular amino acid, a bad acting amino acid, called homocysteine exhibited high levels in patients with neurodegenerative diseases and cardiovascular diseases. And as they studied this, they had the hypothesis that reducing it would have beneficial effects in those diseases potentially. But as they start, you know, as they got deeper into the work as these again, things are apt to happen, they found that homocysteine was actually increasing in healthy people, too. So suddenly, it was this age related change, similar to an ad decline that we talked about earlier. And so what they found is that homocysteine was going up in, in even Healthy People, everybody. And they said, Well, maybe the opportunity is even bigger than we thought maybe the idea here is that homocysteine is somehow driving brain aging. And I didn't know this, Jake. At the time, it was it's a pretty terrifying stat to learn, but your brain will atrophy. I mean, if you think about atrophy, in general, it's it's something we're familiar with, right? If you look at the musculature of an 80 year old versus a 60 year old, right, it's, it's pretty starkly different 60 to 40 year old, also different, but that that 20 year difference between the latter group and the former group is is, you know, geometric, right. And so, this is very similar, the brain loses about, I think, in all 20% or so, of its mass as we age, which I mean, if you think about that, it's it's terrific. And what they were looking at could reduction of homocysteine arrest or slow again, the, the atrophying of the brain and, and by the way, that atrophy comes with cognitive decline, as well. And the slopes are almost identical. If you look at the slope of atrophy, on average, and then the the rate of cognitive decline again, even in healthy people, on average, they're identical. And so what they did was they looked at the metabolic regulatory pathways for this amino acid, they formulated a multi small natural molecule approach, and ratioed it based on the contributing weights of the inputs to that regulatory pathway. And they administer it over the course of two years in people who were older individuals, again, in their 60s 70s. Beyond, and who had self reported memory concerns, mild memory concerns, I think, because they

wanted to really know test this on people who were otherwise healthy, but also I think, have an indication whether it work in these more severe states as well. And they looked with fMRI imaging, very expensive at that time and gold standard at this group over the two year period. And what they found again, this was placebo controlled. What they found was was nothing short, in my opinion of incredible which was in the product group.

Eric Marcotulli 44:44
The treatment group after two years, the rate of atrophy in the brain, specifically in the areas associated with memory and learning. So these are the areas you really want to pay attention to. They slowed the rate of atrophy by 86% in comparison In a placebo and so you look at these images and they're on our web page, if people actually want to go and look at them, they're they're Stark to look at. I mean, if you think about you basically at 86%, almost fully arrested it right? If you think about a cruel, right over time, interest rates, for instance, if you're at 86%, you're doing a whole heck of a lot to make sure that that slowed. So, obviously, there was there was some cognitive benefit that was conveyed, although this study was not powered for that. So that's the next foray for us is to actually look at the benefits potentially, that would be associated with the slowing of the atrophy from a cognitive at a memory standpoint. But there's an index component to this as well. So just like we looked at nav levels, and their relationship with the rate of aging, we also analyzed samples, tissue samples from this study in the participants from it. And we found that there is the opposite relationship that na D has in the case of homocysteine, as your levels of homocysteine go up, your rate of aging goes up, right. And that makes sense. We know it's a bad actor, we know it's doing bad things, right? It's, it's literally causing atrophy of the brain tissue. And so you would expect that higher levels of it would have negative effects. And that's true. So in the case of an ad, as it's going down, you're seeing a bad effect. So you want to boost it in the case of homocysteine that's going up, you're seeing biological age and rate of aging go up. And so we've actually furthered that. And we're now working today to develop a test that would measure using index your rate of brain atrophy specifically, we're hoping to do it in those areas associated with learning and memory, because that would give us a whole slew of

potential opportunities to one look at in diseases, right, we actually diagnose some of these neurodegenerative conditions, right? We don't have good biomarkers today, we don't have any diagnostic tools, but in healthy people as well, understanding cognitive function, understanding the the things that the product would have efficacy towards. So that's the second product, that's matter.

Jake 46:54
And was that a hint at the next product that you have upcoming or that's something separate?

Eric Marcotulli 46:59
No. So the upcoming product is it's a new intervention. It's its name is format. And format is in the space of immuno senescence. So there's a there's a part of the aging field that has come into its own of the last kind of decade called cellular senescence. And again, for the audience, the idea is that, at some point your cells at any given moment, you probably have millions of cells that are doing it reached the end of their functional lifespan. And we have systems of course in the body, from the immune side of things that go and they recycle the components that can be recycled, and then they eliminate the products that cannot be reused. And as we age, those processes fail. And what happens is, you end up with an accumulation of these end of life cells that should be repurposed or eliminated, and they're not. I always liken it to driving in Boca ratone. Jake, I don't know if you've been but you know, you have these really large old like Lincoln's on the road, and people driving very slowly, probably shouldn't have their license, right. And, you know, one is it gunks up the highway, right, it actually jams it up. But more than that these cells are actually dangerous. They're called zombie cells, because they can infect other otherwise healthy cells. And that causes inflammation and cellular failure, and all of these other really bad things, sort of the way that one of these cars can cause damage to another vehicle on the road if it's not operated correctly. And so the idea behind set analytics or treating the senescence cells is sort of like cleaning a pipe in your house, right? There's this buildup, and you want to flush them out. And that's exactly sort of what we've decided we've decided to actually step system. It's it's pretty novel in terms of how these products work, we have one product, which is a daily product that's

really looking at has a number of complexes in it, but there's two that I would highlight here. The first is what's called a toffee G, you can think of that as the recycling portion of the of the immune system, right? going out and taking those cellular components that can be reused and allowing them enabling them to be reused supporting that process in the aging context, right. So not allowing it to decline or continuing its maintenance. The other piece, there is oxidative stress, right? inflammation, we know, is a huge, huge issue when it comes to all kinds of states of health, right? And I'm not talking about disease related inflammation, right? That would be more acute. This is just over time that comes with aging. And again, it's the immune systems job to fight this. But as the immune system declines, it's unable to do that. So that's, that's a part that's taken daily. And then the Senna lytic piece of it, which I was just referring to, is an add on that you do in high dose fashion only for two days out of each month. So it's not something you want to do every day. You don't want to portray no for instance, down the pipes every day with a little bit right. You want to wait until there's that build up and then you want to flush it out and so many people are are taking some of these types of products today and they're doing so incorrectly, they're taking them on a daily basis in a low dose format. When the data at least the data that we're seeing and that we're generating internally shows that you should be doing it. And so for us, the idea is really it's it's a new way of approaching immune health. It's it's also a new way of approaching I think, overall health, wellness and aging itself. And we will be incorporating index over time into that looking again, at the impact of these different things on biological aging and rate of aging.

Jake 50:30
Yeah, that sounds super exciting. Last question here. I know we're, we're coming up on time. Put yourself back in your old shoes, you're a venture capitalist, again, you're looking at the field of aging. What's most exciting to you? What do you see, for the next you know, 510 plus years? Obviously, you're going to be all in on illicium. But including an outside of that. What do you foresee for the space as a whole, which I think a lot of people, including myself are just so excited to see unfold over the next, you know, decade and decades to come?

Eric Marcotulli 51:05
I think for at least in the context of illicium. There's two things right. The first is I think will begin to show. And this isn't unique to us. I think we'll see it from others as well, both in the health side of the equation, the consumer side and the disease and drug side is you know, so really meaningful progress and improvement when we're talking about things like impacting aging itself. Right. And I think that's, that's just we've been waiting for the, since the dawn of time, right? Since we could think and write for, you know, things that actually can demonstrably measurably impact aging itself. And that will obviously come with a lot of other health benefits. And so that's from the intervention side of it. One of the areas I'm most excited about, I think you could probably hear it is the diagnostic side, right index. And I think, you know, technologies like epi genetics, and things that are looking at spaces like that, taking the genetics field into the new generation of technologies, I think it's just gonna open up doors to insights that we've just never even thought possible before. And so, you know, things that literally were science fiction, we're now beginning to live and for me, that's really, really exciting. I think beyond that, you know, obviously can't downplay the potential enormity of CRISPR. Right, I think, you know, even this past week, there's a new paper published out of phones NGS lab at the brode, around, you know, send sem D, and it's a really interesting way that they might have solved one of the key challenges of getting, you know, CRISPR, edited, changes to be adopted system wide in the body, which has been a huge challenge to date. And even for things like MMR mRNA vaccines. And so, you know, that is one thing. And then I'd say, the biggest promise a lot of this has, if you put all that together is personalization. You know, we've heard about this, this for a long time, it's a buzzword. No one has solved it, right. I mean, if someone had solved it overnight, this would be a trillion dollar company, right. And we would have heard incredible things from people. And so I think, you know, all of these things being put together over the next five and 10 years, if not faster, I think, you know, we're gonna be at the end of one level really personalizing things and seeing meaningful improvement.

Jake 53:15

Awesome. Well, thank you so much for taking the time and for doing what you're doing. I'm super excited to see what the future holds for illicium. I want to give you the opportunity to point people to, you know, wherever they can go and, and follow progress and everything like that. And maybe it's just a website, and I will give a plug you made a generous offer, people can go and if they go and buy the annual or semi annual subscription to basis or matter using the code Jake, they'll get 10% off. So that's an illicium health.com. And that expires October 1 2021. Anywhere else you want to direct people to go learn more about why you're doing it and follow updates as they come. No, I think that's it. Awesome. Well, hello, thanks again, and I'm looking forward to seeing what's next. Jake, thank you very much.