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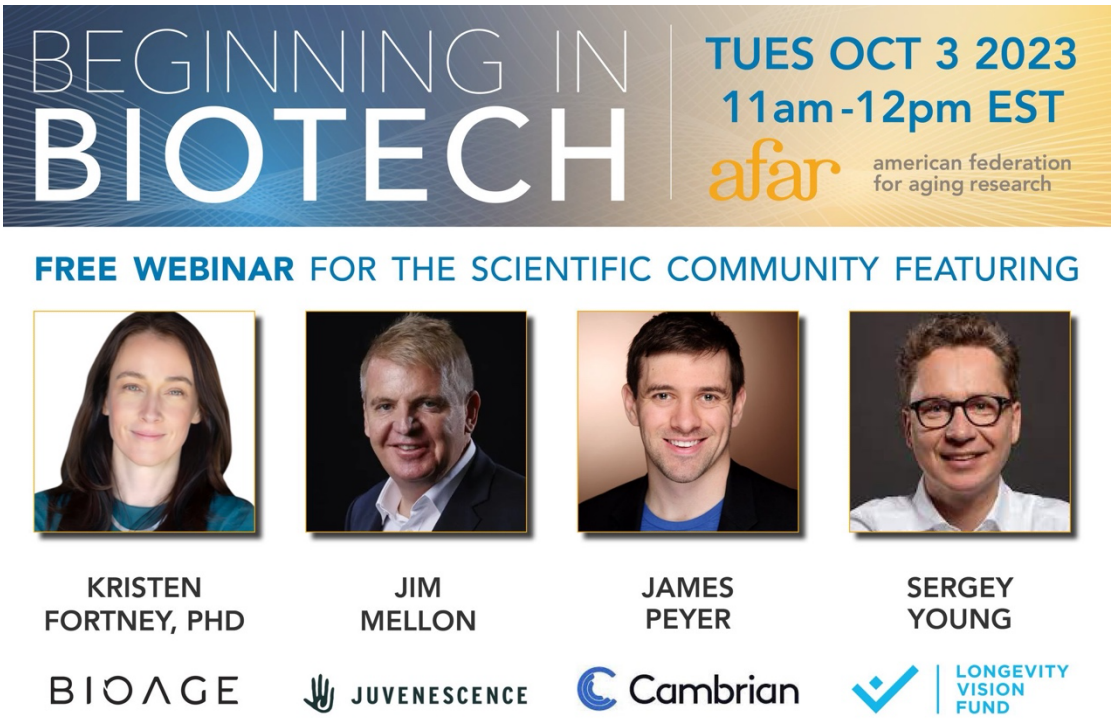

BEGINNING IN BIOTECH: INSIGHTS FROM INSIDERS

TRANSCRIPT

SERGEY YOUNG (SY):

Welcome to "Breakthroughs in Biotech: Insights from Insiders," organized by American Federation for Aging Research. Your moderator today is Sergey Young. I'm a founder of Longevity Vision Fund, and I'm very proud to be a board member of AFAR.

For 40 years, the American Federation of Aging Research has been advancing the science of healthy aging. AFAR has provided roughly around $200 million to more than 4,000 investigators all around the world. AFAR also works with public and private funders to support high quality grant programs and advanced aging research.

Now, meet our speakers today.

First is Kristen Fortney, Ph.D. She's the CEO and co-founder of BioAge. In fact, Kristen is also an AFAR grantee. So that's why we really proud to have her on board today!

Next is Jim Mellon, prominent longevity investor again, AFAR board member, co-founder, and deputy chairman of Juvenescence.

Another good friend is our guest, CEO and co-founder of Cambrian Biopharma, James Peyer.

So, welcome to our webinar. Let's go!

SERGEY YOUNG (SY):
Each of you entered the field of healthy aging from unique places and unique perspectives. Why and how did you decide to focus your interests and your talents aging biotech. And if you don't mind, I would like to start with Kristen, please.

KRISTEN FORTNEY (KF):
Thanks, Sergey. Great, to be here, everybody. So yeah, from a personal perspective, I went into the field of aging science very deliberately for my Ph.D., coming from more of a quantitative background in in math and physics and computational biology. And I was very deliberately motivated by the idea that that everyone here is likely familiar with that. There are these interventions that can dramatically extend life and health spanning animals. And if that could be translated to humans, the potential would be enormous. Right? So, for my Ph.D., I focused on applying Omics technologies to identify biomarkers and drug targets relevant to aging. And then for my postdoc, which was supported by AFAR and for which I'm very grateful, I actually got to study mechanisms of longevity in humans who are already aging very well—like there are a lot of people living examples that we can do better. People live, you know, past the age of a hundred with functional muscle, with functional brain.

And that was very related to the work at BioAge. So, making the transition into longevity biotech again, I was personally really excited about the idea of developing medicines that positively impact human lives, human healthspan. And while a lot of really important work happens in academia, that's sort of the first of many steps that you need to take to get a medicine out there.

SY:
Perfect. Thank you, Jim, please.

JIM MELLON (JM):
Thanks! Okay. Well, I'm the only person on this call who doesn't have the scientific credentials that the rest of you do. I studied philosophy, politics, and economics at university, which is not really relevant to what we're discussing today, but luckily, about 20 years ago, when I stopped being a fund manager, I teamed up with a couple of friends, and we got to back biotech companies in the days when biotech was hot. And we've had a couple of good successes. One was called Medivation was acquired by Pfizer, and the other one called Bio Haven, which was acquired by Pfizer as well. My other partner, Greg Bailey, who, many of you will know., is actually obsessed with staying alive in a healthy condition for a long period of time, and he does the stuff that we should all be doing, and I'm sure some of you do it. But most of us probably not including restricting his calorie intake and doing lots of exercise, and you know, being stress free, etc., etc. And he wanted to pursue the aging field from the point of view of supplementation, prevention, clinics and all that sort of stuff. And over time we agree. But actually, we would go down the road of drug development.

And so, Juvenescence is a company—and Greg and myself put about $100 million dollars of our own money into the company—and I believe that this whole industry has vast opportunity, and it's right now, at this time that we're at an inflection point where money, success. and excitements are combining to create great opportunities, but particularly for people like myself. Because, you know, having just lost my father at the age of 94 he lived a long life, but you know, if the therapies are available in 10 years, time were available to him before he died. I think. It would have been a very different situation for our family, and I want, everyone that I know and love to benefit from all the great stuff that all these companies are undertaking.

SY:
Thank you. Thanks for sharing, Jim. James?

JAMES PEYER (JP):
There's a couple of different narratives that anyone can tell about how they ended up where they are right, and so probably the most prominent that comes to mind for me is how if Kristen approached the space from the computational and kind of tech side of things and made their way, made her way into biology, I came from it from more of a philosophical path in some ways. Because when I really started getting excited about aging was when I was a teenager, and I had sort of the existential crisis of, well, what

is? What does life mean? What is our purpose here, you know, those big philosophical questions. And as this was all happening, my grandfather was dying of cancer in his 80s. And as I watched him very unwillingly go from living a full life to succumbing to his cancer, I thought to myself, "All right. Well, this is the endpoint for all of us?"

So, what greater thing could we struggle for than trying to maximize health and to get as much well lived life as we can while we are here for ourselves and those around us. So instead of going into math, or into physics, or something like that, I'm going to spend my life working on this aspect of biology, and then went towards my Ph.D., based on that sort of philosophical grounding.

SY:
Beautiful, very interesting story, James—very much related to how I end up with investing in longevity. Second question is for everyone as well. What is the hardest thing that you have found about running the new company in a longevity and aging space? I want to start with Kristen again, please.

KF:
Yeah, sure. I mean, there are a lot of things that are incredibly challenging about starting a new company in biotech, period. This is a very challenging industry where the failure rates at every stage are incredibly high. But to focus in, perhaps, especially on aging, like, "What are the unique challenges to our field?"

Part of it is, for example, at BioAge we have a platform to find targets relevant to aging. So, great: You have an aging drug and aging mechanism. Now, what? What's your clinical trial? What's your first indication? How can you show that it's doing what you think it's doing in humans without waiting 20 years? Without spending tens of millions of dollars? So a lot of work that we do—that I'm sure lots of the other companies here focus on as well as—is looking at, "What's that first disease indication?" And even, "What's that first mechanistic proof of concept I can do in a really efficient clinical trial? How can I de-risk that in animals?" And this is challenging, too, because often you have to do this in naturally aged animals which are not a common model, right?

So that's one example of what's challenging sort of just carving a path forward where you have to select a particular disease first but still retain the promise, what all of us want is these ultimately to be drugs that are taken by healthy people past a certain age, true aging drugs. So, sort of carving that path forward to not losing sight of the bigger picture as you execute on these near-term milestones.

SY:
Thank you. Jim?

JM:
Well, I don't run Juvenescence. We have a guy called Richard Marshall, who comes from Astra who runs it, and he's absolutely outstanding. But what I would say is that when we started Juvenescence, which was 6 and a bit years ago, the main impediment to us was that we had too much money rather than too little money, to be quite honest, and that there were too many wackos who were promising the elixir of life! I'm not going to mention any names, but we know who these people are, who promised that that people could live to a thousand years, and the first person amongst us was 200, you know, was going to live to 200, etcetera, etcetera.

All of that did the industry no favors at all. So what Kristen's saying is that you know you have to focus on near term commercial opportunities that may have a link to aging measured by biomarkers, by clocks and so forth. But we absolutely have to be in the clinic with our products and laser focus on having near term applications, which is what we are.

I think there are still plenty of charlatans out there in the industry. But it is now gaining institutional respectability, which is the most important thing for it to succeed, and I've got no doubt I don't know how it's going to be done. It may be done by Cambrian and by BioAGe and possibly by Juvenescence and other companies that you've invested in Sergey. But in the next 10 years, we're going to have some remarkable successes which will offset the unfortunate failures that have characterized the industry up to up to now, which is another factor that unfortunately has added lead weights to our boots in terms of making progress.

SY:
Thank you, James, please.

JP:
So, I would echo Kristen's characterization that specifically applied to the aging field. I think this question of how to select the right indication for your drug or for your innovation is the hardest problem to get right. And given that the theme of today is getting into biotech, I'm going to give a slightly different answer, which is not just if you're starting a new company. But in general, if you're making the jump from academia to biotech, I think one of the things that took longest for me to hammer into

my head is how all of the science—in terms of doing research, understanding mechanisms, and ultimately finding a drug that, in my case, could extend lifespan or treat a disease or something—is part of a process of getting a drug out there and to patients and on the market, and especially the middle bits of preclinical, between discovering that tool compound and getting a drug into clinical trials. It's important to understand that that's where most people in biotech work, right? They are trying to figure out how to take that discovery and get it from target to hit, to lead to candidate to in development. And each of those phases have so much work backed into them that—especially coming from the genetics and biology background)—I had no appreciation for before coming into the field. And so, I think that's the flag that I wave to people who are entering the space now: to actively search out those pockets of ignorance there and understand how hard transitions are.

SY:
Very interesting, thank you. The next question is for Jim because it's more from an investment perspective. So, Jim, for a new investor entering this space, what advice would you give them about where to start? If people want to invest in aging, research, aging, longevity: where to start?

JM:
Probably to invest in your fund! I do think that spreading your risk across multiple opportunities is a good idea. I wouldn't put all my eggs in one basket. And it, it's it would be a good idea to invest in a fund. There are number of funds now, of which I think yours was probably the first, that invests in opportunities across the longevity space. So, I would recommend investing in a fund. I think it's too hard for investors coming you to the space to just invest directly in an individual company unless they're institutional investors, and they have a large pot of money, and they can invest in multiple companies. But I wouldn't invest in just one company.

SY:
Yeah, I completely agree. I think it's just too early to make one bad investment, and I would always look at the portfolio of interest and investments as well. I agree. Well, the other perspective is for people who just want to start a new project or create startup and enter the space. So, a question to Kristen and James: what advice would you give them which can actually make or break their success?

JP:
So, the most important thing I guess to talk about right now is to understand the market that we're in right now. Early-stage biotech is actually in a really tough place,

and companies that got started. Or in the bull years right from 2014 up through 2021, they had very different rules than biotech companies that are starting today, especially early preclinical efforts and early preclinical efforts today are so hard to get funded unless you've already got sort of a bird in the hand. And so, [you need] really creative business strategies and access to funding and so on.

The advice that I give is: you almost need that before saying, "I'm going go out on this little, on this, on this big adventure." Which is not a very optimistic message to send, but the funding environment for early preclinical stage stuff is just so bad right now. I don't want to occupy too much more airtime. But that access to funding and that network is the number one thing that is determining success or failure for companies today. More so even than the quality of the scientific idea.

SY:
Perfect. Very interesting. Kristen, please.

KF:
To echo James. It is hard right now. It's a hard time to start something new. Which is a shame, right? Because a lot of these new ideas that are going to be especially impactful. New targets, right? I would say that biotech right now, like investors, are looking more for targets that have already proven themselves in the clinic. So, things that are really new biology, new insights that can be more transformative are going be funded as much. That will get better, because medicines work, medicine save lives. So, I think everyone expects the sector to recover.

But in the meanwhile, if you're someone early career, and you have an idea—a target—that you're really excited about, what can you do? I think you can get to meaningful milestones with grant funding. And from turning this into a real product perspective, I would say that one of the most important things you could do it's just to get help. I would completely agree with what James said. one of the things that you learn when you got into a company is that: You find a great target? Great. You know your most model works wonderful? Great. You even have a, you know, a lead drug? Wonderful. But there's so much else to do, and you can do. You can de-risk a lot of that early, and you can learn a lot more about what that landscape looks like by speaking with the right people, and they'll want to talk to you. It's usually a very open community of people who've been successful in drug development. They love to hear about new, exciting ideas. You can get a lot of really informative feedback. That informs what you do, by having those conversations, by bringing on the right advisors and mentors.

SY:
Perfect. Very interesting. You just answered my next question: what are the key stakeholders and relationships that you need to develop earlier on? And what you would add: prospective investors? Funding partners? Anyone else?

KF:
That's a great question. The right partners and investors will differ, based on the stage of your company, too. That it'll be a different class of people who are excited about your scientific idea versus are excited about the later stage data and the prospects there. And in some ways, this network will go organically over time. I mean, all of us start with zero in our network. We find those initial believers and they sort of build over time. But in terms of what's the most valuable: yes, of course, access to capital right. Someone who is excited by your idea and will pay for it.

And this can be a seed investor. This can also be a Grant agency. There are a lot of new opportunities there as well, especially for that first couple of 1 million to get you to really important preclinical milestones. But you need to find expertise. Especially, I would say, on the clinical front. With chief medical officers, I initially thought, "Oh, you know we don't need that for a few years, you know, clinic is so far away." But that really, where you're aiming for in the clinic—that sort of constrains your preclinical development in a lot of useful ways.

There's a lot of things you want to do very early, and you can get a lot of perspective by talking to somebody about. You know what indications are practical on a clinical setting, and how you can build for that over time. So clinical: I would say it's probably the most important for us.

But course there's all the different aspects that we've that we've touched on during this conversation, whether it's regulatory or commercial, or even just chemistry. And you know, a lot of the models used in academia are not considered to be translational or in biotech, because they don't, aren't very predictive of drug success. You want to learn about that early as well.

SY:
Thank you, Kristen. I just remembered that was just reading a book from Dan Sullivan, and the whole notion of the book is every time you face a new problem, think “who,” not “how,” right? And if we can retain the spirit of your answer, and especially helping young scientists, entrepreneurs to network. I think the world is just abundant of so much expertise.

And the worst thing to do is just try to solve the problem [yourself] and be your own boss. you never want to reinvent the wheel. You don't need to. If it's a problem that someone else has solved, reach out and get their help Because it's hard enough focusing on the new things.

The next question is for Jim. Jim, we just discussed today that it's just great to work on your portfolio level, you know, just investing in different hypothesis and different ideas as well. But what are the common bottlenecks for growth in in your portfolio of interest and in your portfolio of investments, in aging, research, aging field and longevity? Is access to resources? Regulations? Access to capital? Scientific talent?

JM:
I think there's a danger for people who are coming into this industry of spending too much time in conferences. And going to what a basic echo chambers for the same people, talking to each other in a self- congratulatory mode. So, I do think the organizations, like a longevity pharma biotech association, are very worthwhile in terms of networking opportunities for new entrants to the field.

I mean, I can't emphasize just how difficult this all is. The problem is that although the best science is probably in the United States, generally speaking, in the United States, it's an extremely expensive place to do business, especially in California, as we all know, and you can run through money incredibly quickly in the U.S. If there was a way in which you know, cheaper locations could be used for research and trials, and so forth, and yet be acceptable to the FDA. that would be a big positive for our industry, because the United States, for some reason, manages to burn through 3 times more money than, for instance, comparable companies in
in Europe on a per outcome basis.

I think that also teaming up as we've done, because we don't have the strong research background that Kristen and James have with research institutes, where we can back their scientist entrepreneurs in companies is a good strategy for people like us who are, you know, not aging specialists. As an example, we've got joint ventures with the Buck Institute, and so forth. And that way we are linking up with research institutes that need money and need guidance from a business point of view and provide us with a starting point for technology.

But it's a difficult thing. I wouldn't advise people to go to every single conference around, because I just think you're wasting your time and your money, probably, and

you'll just meet the same people and talk to the same people all the time. But you should join the critical organizations, and you should try and link up with the key research institutions, and of course read as much as you can as well, which is what all of us do. Just read as much stuff as you can, and gradually you'll find out what the good stuff is what the bad stuff is, and that will be a big step forward to success.

SY:
Thanks, Jim. Speaking of bottlenecks, we have an interesting question from the audience: “Would the TAME (Targeting Aging with Metformin) study help you raise funds for your companies, or have a different approach for another clinical trial that would be lucrative?” Let's start with James.

JP:
So, I think the answer to this question is tied in with a topic we touched on at the beginning, which is about, how do you pick the right indication to bring drugs that target aging into the clinic? And so, TAME and other trials that that kind of try to do the same thing. These are prevention trials, right? Something where you give a relatively healthy group of people an intervention, and then you see how long you can keep them healthy. Can you keep them compared to a placebo more healthy, less likely to get a new, a new condition? And this is sort of the best and highest use of what a drug developed in the aging space is supposed to do.

But from the perspective of building a company and ending up in biotech today, it's actually a second order problem, right? The first order problem is, how can we get a drug to show safety and efficacy and get on the market today? And then the second order problem is all right. Now, how do we expand the applicable uses of this drug toward closer to prevention if the drug is suitable to do that?

And so TAME, or another primary prevention trial, would be an enormous boom for the industry, because the way that that we could then talk about it is today.

I'll give you an example when we raise money for Cambrian, which has now been a fair amount of money like 175 million dollars, what we say is, "We're going to take each of these drugs meet 15 different drugs. All have applications to prevention and longevity in some way." And what we told our investors is set the value of that to 0. Assume that it has no value. And now let's just talk about the value of each of these for the specific diseases that they're going in for.

And that's fine, especially as the industry is getting started. But as soon as you have a proof of concept for one of these indication expansion and prevention type of trials, then we can start pointing in that and say, you know the value of that. It is going to be non-zero and here is the path kind of like the tracks in the snow that we can follow to get there. That right now is still a bit of a you know, a winter wonderland that needs to be explored.

SY:
Perfect. Thank you. I actually like the idea of integrating audience question in our conversation. So, if you don't mind, I'll ask another one. And Kristen, if you can address this one: What would you do differently if you had to restart your company again?

KF:
What would I do differently? Gosh, I mean a lot of things, right? Mostly it feels like you could do what mattered faster right? There's a lot of directions that you, you know, you would know, or would be less fruitful. So, bringing in the right expertise faster focusing on areas that I now know or like translational, have a clear path faster.

I think an important question is, "Imagine a world where the TAME Trial worked. What would that mean for the industry?" And I think all of us talk about how the aging field as it exists today is so much more widely accepted than 10 years ago. 10 years ago, there was maybe there was Calico. Now there's a whole bunch of us that are near R &D, or in the clinic, and even large Pharma is starting to look towards aging, but they're not really spending on it yet. Right?

So, I think we're all excited by the prospect of an aging mechanism that's sort of clinically validated, and how that could unlock further interest in the field. So that's another aspect: that one of our drugs could be [brought to market because of] TAME. That's going to be a really an important transition point, I think, for the industry. We're still very much at the beginning, right? In some ways we've gone so far—like there's 20 odd drugs in the clinic that I think are targeting aging mechanisms, right? But look at the pipeline of any large pharma like Novartis, or something that's got over 100 different mechanisms, and, like, aging biotech still has a long way to go!

SY:
I agree. Very interesting. Well, let's talk about the other bottleneck, which is biomarkers for aging. And that's the question for James, why is it a big challenge, and is there anything that you do within your portfolio which address that?

JP:
So, I think this is a perfect one to come after the discussion we just had about tame right? Because if we talked about prevention trials being sort of a second order question. In this space, I would say, the biomarkers are the third order question depending on how who you talk to and how they want to approach the space.

The way that I look at it is, that at the start you have to get a drug approved and on the market for something. And the biomarkers that come out of those sorts of studies are not like aging clocks, right? There are usually specific biomarkers tied to the molecular mechanisms or the specific disease that's being addressed in those first studies. So, when we talk about aging biomarkers, I leave that out.

Then you have studies like what theme would be right? Prevention-focused outcome studies where you hope to learn at long last whether these different putative biomarkers, like aging clocks and others really work, whether they're really correlated with outcomes?

And then you finally get to sort of what I think of as the final form. You know you have your 3 Pokémon stages, and this is the third Pokémon stage of the aging space! Where now, all of a sudden, if you have a validated biomarker or set of biomarkers, then that that can prevent disease risk. Now you can run trials that measure the biomarker and not the outcome which reduces the cost and time of running trials by an order of magnitude and that will really let the field fly.

And so, I think that this is one of the big joint goals for the field. There are a number of different approaches. I think we're going. We're seeing a lot of thoughtful exploratory work begin to happen here at Cambrian; we have spent almost all of our data science energies on creating a foundation, where we can measure all of the differentiative aging clocks in each of our clinical trials and then integrate them into the same database. And there's going to be a bunch of efforts and hopefully, coordination between efforts from different groups to kind of play with these. But I think we'll really start seeing the spending and the urgency of this ramp up. Once the milestone Kristen talked about—having one of the aging mechanisms validated in the clinic—
is kind of conquered, then we're going to see an explosion looking at this.

SY:
Thank you. Well, the next question is about AI. (How can we avoid discussing that?) I guess it's for Kristen and for James: how important can AI be for starting longevity

startup today? And is it Must-Do, or it can be integrated at the latest stage of development?

KF:
I mean, yeah, it depends on what it's for, right? But I think that, unbiased, data-first approaches, still have a lot to teach us, you know about aging biology and about novel pathways that matter. And that's how we're approaching discovery at BioAge. Aging Biology—it's still an early day of science. We're still making big discoveries, you know, every few years. So, looking in a more unbiased way instead of under the under the lamp post, I think, will yield important new targets.

So that's sort of taking AI that's taking software and algorithms to the right data sets to find targets. I actually think in in the nearer term where AI is going to be, you know, more important for biotech generally is I think we have seen advances in terms of finding a molecule, right? If you have a target that you know you want to hit, and you could build something that hits it and has the properties that you want : that's a really hard, complicated problem that we are seeing AI accelerate whether it's predicting what will stick to your protein, or whether it's something like iterative DNA encoded libraries where you're measuring billions of molecules, and they're binding affinity and learning what sticks really well from the data.

So, I think that those hit to lead in in biotech in general is a really hard problem. So, I think that we always use a component of that when we can, but there are aspects, of course, of biotech that are not going to be revolutionized anytime soon. And that's things like clinical trials themselves; we're terrible at predicting what's going to happen in the clinic—even after we do all this mouse work, even after we do all this mouse safety work. And in in large part, that's because we can't simulate how a human is going to respond to a drug, and we can't train a model to simulate that because we lack the data, what are the data sets? They're going to train your AI to behave like a human right? So, I think that's further off.

But I think there that components of AI are going to become critical and aspects of drug discovery development across the board. For aging and other fields that are newer. I think that's important in target discovery.

SY:
Perfect, thank you. James?

JP:

I don't have too much to add, except a mantra that I've unapologetically stolen from the chief AI officer at Accentia. What she said is that there are some AI companies in biotech that are bouncing around out there that are really AI companies. But for most efforts in biotech, the important thing is to be a computer-literate company, not exactly an AI company. And so, when we think about our strategy at Cambrian, we're not a bunch of AI people, but we use all of these tools across the whole ecosystem and try to integrate them and think critically about, how do we become a modern computer literate biotech company or pharma company. I think for especially people coming from the scientific world or the biology and chemistry world, asking that question and keeping that fresh in your mind, as the landscape is changing rapidly, will move you in the right direction.

SY:
Yes, thank you. 80% of the companies at the Longevity Vision Fund use AI as an enabler. But I think we're living in the world where AI will become, you know, accessible rather than something that you would need developed from the day one inside your startup. Otherwise, it's just too demanding specifically for this this whole theme of AI.

So, let's talk a little bit about fundraising, about access to capital. And before I turn to Jim, I wanted it to ask the question to James and Kristen. Where should young entrepreneurs start to find seed funding for an idea? Kristen, please.

KP:
Gosh, there's still a very a few places in the world where it helps to have a physical advantage. For me, founding BioAge in California, I think, was really critical, because there's just a lot of there's a large community of people who do see investing who will do investing and ideas that are higher risk, higher reward, which is still most things in aging, you know. I think that that's been democratized a bit, right? There are more video pitches So you can still access this community, even if you're not physically located there.

But I would say, go and go and visit, even if you're just going to some aging conferences that are in the Bay area. There's a ton of them all the usual seed investors go there, too. If there's other groups, you can, you know, present some pitch and get your story out where you'll sort of get access. I feel like there's a large community of folks that do specially the earliest side of longevity investing, and they are well represented at the usual conferences as well as, I would say, especially in California.

JP:

I would add on that seed is definitely the easiest right now. Series As, Bs, and Cs are where we're seeing the compression in the space. And so, in addition to what Kristen mentioned, the obvious shout out that I would give that was cool news in the space is that a longtime friend of all of ours, Laura Deming, along with Alex Colville, just closed their new Age1 Fund, which grew out of the Longevity Vision Fund, and it's doing explicitly early stage investing in the space. And there's, I think, a series of folks around that Cambrian is also still doing some. I actually signed the docs for a new spin out that we're doing with an AFAR-affiliated academic actually just a couple of weeks ago.

SY:
Thank you. Jim, the question to you: So, what does the field need to achieve for the next 5 years or so to attract new sources of capital, new entrepreneurs, new sciences?

JM:
I'm sure we can all agree on this: it's basically visible success, isn't it? I mentioned earlier on that the failure of some high-profile companies like Unity and RestoreBio didn't do any favors for the sector, and especially since there was a lot of attention paid to the founders of those companies, and particularly in Unity, there was a very high profile [disappointing result] and so we just need some success. And I feel that, Kristen's going to have success. James is going to have success. I think that we're going to have a big announcement next year, which will be a successful announcement. So just we need lots of these companies to have something that people can hang their hat on. Say, actually, aging is a field I want to invest in.

Something you talked about is seed funding. In the UK, we have incredibly good tax breaks for early-stage investors and venture capital and biotech. The taxpayer can get basically all their tax back if they invest in a venture capital company or a venture capital fund. So, if you're looking for a seed investor, there are plenty of them in the UK. All you have to do is to set up a branch in the UK, and you can get that money. And honestly, it's worthwhile, because, as far as I'm aware, it's not available anywhere else in the world, and you get basically half your money back. If you make the investment, and if it fails and you've only lost half your money.

JP:
The thing I would add on to that, Jim, is that if there are budding biotech entrepreneurs in the audience here. I would make a shout out for contacting Risa Star, who is the executive director of the LBA (Longevity Business Association), which is starting to be a bit of a hub for getting that network that we were talking about and finding investors that are interested in that space? I think the LBA is on the verge of

even creating a portal through which you can access. Kind of and see who is out there in the ecosystem that wants to be doing this stuff actively.

SY:
Yeah, I would also mention that a number of early-stage companies that we're looking at right now use non diluted funding. You know how AFAR grants is just, you know, one of the examples of that. So, we shouldn't—every time we think about the capital, it should not be capital from commercial investors. But it's gonna be pro bono, granting type of capital as well. So, I think it's very important as well.

Kristen, you mentioned already the challenges of transitioning from academic setting to a private research environment. And I can see there's a question around this: traditional research institutions can better partner with private companies? James, do you have any advice how we can actually address this? Turning scientists to entrepreneurs: the biggest challenge of our life and our work.

JP:
I have probably less of a San-Francisco-entrepreneur-forward view on this in that I actually think that we have no shortage of entrepreneurial talent in the longevity space. I think that makes me a minority within our within our group. I think that the thing that many folks who want to be entrepreneurs in the longevity space should do is go work for a much bigger organization to learn the traditional ropes of drug development, and then let the connections between their enthusiasm about the space kind of sync up with experience that that comes from a completely a more traditional field. And then let those things fuse together into slightly more mature organizations. That that's in general the pattern of success that that you see in biotech. Not that there are not exceptions. There are scores.

But my advice to people is generally, you know, it's not always the best idea to say, "Okay, I just finished my postdoc, let's go start a company," and figure things out along the way. (Even though you know that's very close to what I did. That's kind of what Kristen did.) It's not the wrong model. but I think that where there's almost the greatest good to be done for the field is to bring in people who have an interest in this space, but then also have expertise developed and other stuff to come in. (That's a bit of a crotchety old man view. I respect that.)

SY:
Very interesting. We have more interesting question from the audience, I just want to link it with the questions that we discuss before. So, the question has something with it

drugs, because the default mode is longevity aging is "Let's work on drugs." But this is the question to all of you: if you were to launch a new company today, which scientific or technological areas would you focus on today? Let's start with Jim.

JM:
I think we would avoid all the mistakes we've made so far. That would be a that would be a good starting point. And I don't want to go into those mistakes, but they've been there been plenty of them. I think I would focus on nearer term commercial opportunities rather on moonshot stuff. And if I, you know, could relive the moment. But everything is a learning process. And you know, as with James and with Kristen, we're going to have plenty of clinical assets by the end of next year and we hope to be able to drive at least 2 or 3 of them into commercial applications. And that's what you need in biotech, and could we get 5 or 6 companies comparable to our companies to do the same. We have a very viable industry, and what I hope is that the traditional for big pharma companies don't come along and buy all the companies up, and then, you know, go back to the normal ways, because this is an industry that deserves to be nurtured and not acquired at an early stage. We really need all of us to try and keep going for as long as possible before selling out to the big boys.

SY:
Thank you. Kristen?

KF:
Sure. I think those things that will have the largest impact are going to be drugs, you know, or gene or cell therapies, or maybe even organ transplants, right? there's sort of categories of things. I think there are questions around diet, and that's a different kind of business model. I mean, there are some companies that are doing that like Prolong. But then how do you sort of have scientific rigor? And then how do you profit at the end? And it's a very different type of activity, and I think that's interesting science, too, but I think a lot of that can probably be done in a non-commercial setting.

SY:
And there's a question from the audience as well (and do remember that our audience is not only US-based, but from all around the world): “What are the different geographies that you would reach out if you need something other sources of capital or scientific talents, during a trial outside the US? And what is the geographical aspect of your work, or you can actually be more international in what you do?”

JP:

I can maybe jump in on that. I'll jump in on that one first cause I was smiling a little bit when Jim was saying, “If only you could have access to the UK.” That is almost the business case thesis for Cambrian: I started my first company, which was the Apollo Ventures Fund, in Germany, actually, and a bunch of the early-stage research that I helped turn into companies before starting Cambrian was great European science that we then housed in American corporate entities. Israel has actually been doing this with a Tel Aviv research site, and a Boston-based operational team for a long time. And so, I think that biotech almost more so than any other of the deep technology industries can function in a highly globalized environment., right? Biotech people were on Zoom [around the world] before the pandemic 8 hours a day.

So, I think that that structure of a US or UK- kind of center of gravity. But then with tendrils, wherever the academic breakthroughs are happening across the world, is a great model. The clinical trials that we're on running are about are about to start are actually all ex-US even though all of our companies are US. And it's only in later stage, larger phase, 2 B phase, 3 trials that you want to make sure that you're opening US sites to comply with. FDA. So yeah, I think there's this highly globalized environment.

The only really sad thing that I would just throw in here that that is happening is the decoupling with China. And so, you know, I think there was a time 5 years ago where a lot of us were quite enthusiastic about the increased in IP. Things were on the upswing, and it seemed like there was going to be a greater enmeshment between the scientific ecosystems between us and China. But now that's going in the opposite direction. And so, I think we're missing out on a lot of great brain power there from our Chinese colleagues. But other than that, I think the rest of the world is just becoming more and more enmeshed scientifically. And it's becoming easier to run things all across the rest of the world.

KF:
Absolutely. Yeah, absolutely. A lot of biotech development opportunities and activities are international. And I hadn't, you know, realized that early on either. But just to give you a very concrete example: for one of our drugs going into phase one next year, we did a DNA encoded library screen in China. We did all the hit to lead discovery with China. They've been a wonderful partner. Like a lot of that. We don't have our own chemistry internal.

You don't need to have your own chemistry internally. You can run that through. You know what is a very cost, effective, very high quality. There is a drug that when it goes into the clinic next year, the phase one will be likely in New Zealand or Australia, where

you could run a phase one trial for roughly, half the cost of what it is in the us, but it's perfectly acceptable to FDA, and where you also have a faster startup as well, which is also highly relevant to a biotech, because time is money. Keeping your operation alive for every month is very costly. Right? So those are some aspects of how we are.

JM:
Can I just say something here? So okay. And that is that you know, I think some entrepreneurs are still living in the era of 2 or 3 years ago, and fancy the evaluations as being very high. And there's a famous Silicon Valley saying, I don't know who said it: "The time to eat the canopies is when they're being handed around." I think you really have to accept, as James emphasized earlier on that, this is a really tough time to raise money in biotech, and if you are offered money, I give it a very good thought through, and accept it, probably rather than you know. Try and hold out for higher evaluation, and in terms of where the pots of money off of starting companies I mentioned the UK. Obviously, there's a lot of money in the US. But I think those are the 2 key areas—you and I know the Middle East very well, Sergey—but that's for a later stage stuff. And honestly, it takes years and years and years of effort to make those relationships work. And for a startup company, it's just not going to happen.

SY:
True. We have only 3 min to run, and I have a final question to 3 of you. And the question is: I guess from my experience, it's easier to sell the longevity and aging research field to, you know, older person. Like I'm 51, you know, so I can roughly understand what are the benefits for me today or in the future. So what is the deal for younger generation of scientists and entrepreneurs? Even if younger people aren't worried about themselves, they certainly are worried about their parents and their older relatives. I mean, they'll be worried about their children one day. So I think that's very compelling.

JP:
The way that I conceptualize this, and we've been asked this question in many different ways... I'm pretty sure Kristen and Jim and I did a podcast together whose explicit, full hour was just Jim asking me and Kristen, “What's with all the young people in aging?” And my answer to this is that I think aging is just where some of the most exciting things in biology generally are happening, over the last 10 and the next 10 years. So just like you saw a huge rush into oncology after the discovery of oncogenes, a huge rush into genomics after we sequenced the genome. Right? I think that the breakthroughs in aging research are just bringing cause.

There's so much opportunity. There are so many unanswered questions scientifically that it is just bringing people in because that's where our science has progressed. And I think that's actually the best thing about where this space is right now is it's just it's not a, "Oh, what about aging research?" It's actually, "Oh, my God! Aging research is going to take over the way that we look at biology and medicine!"

SY:
Perfect, thank you.

JM:
My final point is that this is not just a nice idea for people like Bill Gates to live longer and Jeff Bezos to parade around on his expensive boats or put rockets to Mars. This is an imperative for society. We are living in a demographic crisis like none other before. By 2070, half of the G7 will be over 65 years old. Unless we can keep those people healthier for longer working longer. We're going to have a whole load of 90- to 100-year-olds who will be incapable of being looked after by themselves, and there won't be enough young people to look after them. We need to do something to extend healthy lifespan, otherwise societies will just literally break down. This is as important a crisis as the climate crisis is just not as visible. Japan currently has 125 million people; by 2100, it will have less than 50 million people. Singapore will be one third of its current population. By the year 2100 Korea will be half of its current population. So, there is an absolute imperative for what you guys are doing, what we're all doing to change to the trajectory of aging. It's really important, not just. It's a nice idea. It's something we have to do.

SY:
Thank you, Jim. And thanks to everyone who joined us today—either a speaker or attendee —we would like to have your support and your involvement in AFAR. So go to www.afar.org and you know we would like to collaborate and receive your support to the extent that you can, and you want.

I think it was amazing conversation. I want to do more and more of this, and thanks to everyone for their time today, and I'm very excited about our field and where it's all going. Thanks to everyone for the time today!