

Paul Major (Bellevue) – Innovations To Fix a Broken System

Tom Yeowart: Paul, welcome to the podcast. Thank you very much for coming on.

Paul Major: Thank you for having me.

Tom Yeowart: So, let's start at the very beginning. I think you did biochemistry at university and then moved into the City and started as a sell side analyst. I'd love to hear more about your early career and what prompted you to choose the City rather than the healthcare industry itself?

Paul Major: So, when I was a very young child, like most young children, most boys, I wanted to be like a truck driver or something like that. And then I rapidly moved on to wanting to work in medicine, to be a doctor. And then when I was a very impressionable age, 10 or 11 or something, my brother was poorly and ended up in paediatric intensive care and I went to visit him, and it was a horrific experience. And I thought, I don't want to do this. But I had this love of science. So gradually I discovered biochemistry, the background to life, for want of a better word, and decided that was what I wanted to study, and I wanted to be a scientist and make great discoveries, but I wasn't exactly sure how it all works. So, I did a couple of placements and for my sins, again, thinking about medicine and trying to make the world a better place, my first placement was in paediatric pathology. So, if you don't really like medicine, dead babies are definitely not the way to go. So, anyone who's thinking about a career in this area, paediatric pathology, I would strongly urge you not to go into. And then my second placement was in genetic engineering and breeding of plants and things like that, which was fascinating because it was so economically important and so exciting and then so incredibly slow. And I think broadly, I didn't really enjoy lab work very much. It was very laborious.

So, I thought if I'm going to sell out, I might as well do it properly. I became an investment banker at SG Warburg in corporate finance, working gazillion hours a week. I ended up in the healthcare investment banking team. I did a bit of a stint in global M&A, so I did lots of different transactions, ended up in healthcare. And then I discovered the research side and I thought, well, this is really interesting, so I ended up as a sell side analyst. That was okay, but bulge bracket banks, it's a bit procedural and boring. So, then I went to a start-up called Redburn, which became quite a large firm, and unfortunately for me, didn't move strategically in the direction that I was supportive of. So, then I started to look at other things. Thought I'd do some kind of non-exec work and

then ended up in a very circuitous way, having a conversation with Bellevue about starting a fund. And the rest, as they say, is history.

Tom Yeowart: How would you describe Bellevue itself to the uninitiated?

Paul Major: Bellevue's been going since the early nineties. It started off as a kind of integrated bank brokerage asset management firm. But gradually has morphed toward being solely an asset management firm. Is pretty much a healthcare shop in terms of heritage and also assets under management. So, we run a high teens number of different healthcare products with specific focuses on geographies or sub-sectors of healthcare. Different approaches. We have private equity, VC stuff, all the way through to public markets. Even though some of your listeners might not have heard of Bellevue, everyone who runs a healthcare company has heard of Bellevue.

So, what it means is that they're always keen to see us on their shareholder register. So, it's a great calling card to get you access to companies and all sorts of different people, which is critical to making all of this work because it's not just about the companies you want to invest in, it's also about the companies adjacent to the companies you want to invest in so you can understand the competitive landscape and innovation.

George Viney: Can we go back to your time as a pharma analyst and from my perspective, analysing a pharma company is very different from analysing pretty much every other company. Every other company, you don't take a product line and do a DCF out to 2040 or something. So, what did you learn that generally applies to company analysis and investing from being a pharma analyst full-time.

Paul Major: Two things, I guess. Pharma companies are rubbish at R&D, really bad. So that would be my first learning. My second is that if you're going to work in healthcare, you mustn't fall in love with the science. The very way you approach your example though is fascinating. So, you talked about analysing a product. Well, actually the product in and of itself is not important. What's important is understanding an end market, understanding the value to society of that end market, understanding the competitive landscape, the unmet medical needs, and then ascertaining whether or not there are products that show the potential profile that meets those needs at an appropriate economic value.

Medicine is full of areas where you could develop new drugs, better drugs, but people choose not to simply because the drugs we've got are good enough.

Classic example is all these ulcer medications. We had a huge amount of innovation in the eighties and early nineties in that regard. AstraZeneca could develop another Nexium if they wanted to, but since it cures something like 98% of people in six, eight weeks, it's pointless. You have to focus on the right things, and I think that's applicable in every area of healthcare. The value of intellectual property, how you market a product, convincing doctors to change a surgical technique, for example, is a much higher hurdle to cross than, why don't you try a couple of patients on this different pill for the same ailment that you are used to prescribing for. So, I'm not sure that it's necessarily that different.

The other thing that's been fascinating about the pharmaceutical industry is its gone through this really, really interesting period. The drug market essentially became deregulated from a sales and marketing point of view in the mid-nineties. We had a huge wave of innovation in the early to mid-nineties around the whole genetic information side so that we could understand why do some patients not respond to certain drugs. And so, if you were the CEO of one of the big drug companies in the early nineties, you got out of bed in the morning, you opened the curtains, your company grew 18% before you even had a coffee so you didn't have to be a very good manager. So, they never really understood how to do R&D properly and to make it reproducible.

The problem with pharma is that actually R&D doesn't scale. Because if you go into a lab and you meet somebody who's a really interesting, clever, dynamic person, these tend to be actually quite challenging individuals. Why does somebody upend medical dogma? Because actually they're quite intellectually arrogant. They think everybody else is wrong and they're right. Those people are very, very hard to manage. So as soon as you get big organizations that are very process driven, they crush the spirit out of people, and they don't deliver. What you want these people to do is you want to give them a lab, give them loads of money, and then every three or four years check in and say, have you've got anything interesting for us? That's the key to success.

So, many of your listeners will know that the Swiss pharmaceutical Roche, acquired in the early 2000's, Genentech. What's interesting about Genentech is it undeniably ushered in the biotechnology revolution, actually creating synthetic molecules and using them therapeutically, revolutionized the treatment of cancer with Avastin, Herceptin. All of that took place in a bunch of labs in south San Francisco in the late eighties through to the mid-nineties. And they were recruiting from a pool of people who'd all done undergrad at Stanford. Now, exactly at that same period, Roche, opened a facility in south San Francisco to do R&D, to take advantage of all this clever stuff that was going on

around Silicon Valley. And in the 10 years that Genentech changed the world, they invented absolutely nothing. Now these are the same people. They're friends with the people that work at Genentech. Their kids go to the same school. They probably socialize together. Why is it that one of them changed the world and the other one did absolutely nothing? That's the fascinating thing about this whole industry is to understand what really is innovation? How do you deliver it?

Another interesting example is a company that we are very keen on called Vertex. So, Vertex revolutionised cystic fibrosis over the last 10 years. When we started the trust, we obviously looked at Vertex because they'd been amazingly successful and they were making enormous amounts of money, so much cash, they kind of didn't know what to do with it. They decided to diversify massively away from cystic fibrosis into all sorts of different diseases. And what was really, really interesting is they were all kind of moon shots. So initially you'd look at that and you think, well, we're going to apply a typical probability of success, which is you're going to fail 90% of all this stuff, and they haven't.

They've actually done really, really, really well, in some big areas. The first gene editing drug that gets on the market, people closest to launching a cure for type one diabetes, a fairly sizable market, non-opioid post-operative pain. So totally different areas of medicine. And what's really interesting is, again, they're almost behaving like a venture capitalist. They're saying, right, we found some really interesting people doing some really clever science that could genuinely make a difference. We are going to fund that and see what happens. And that's the kind of difference between them and a Glaxo. So, it's not about the science, it's not about the individual drugs. It's about understanding how you deliver innovations that society will pay for and can be transformational for your business.

Tom Yeowart: I'm intrigued on the point you're just talking about where you look at Vertex, it's been very successful in one area. It's now being very successful in other areas. But to your point, it is deploying a venture type method to that success. And venture capital is all about you get one or two things right, which pay for the sort of multiple things you get completely wrong. When you look at a Vertex and you invest behind it, what are the other factors you look for to get comfort that their model is one which is going to be more successful than not?

Paul Major: That's a great question. Firstly, we don't ever assume anyone can be serially successful because the empirical evidence is they can't. So, this is

where you come maybe much more to a project-by-project basis. But the fundamental thing for us, and this is what differentiates us from a lot of other healthcare funds. So, we are not a pharma fund, we are a broad healthcare fund. We are a conviction fund. So, we can have a maximum of 35 positions. 29 has been our average. We're about 27 at the moment. We think 30 issues is kind of the sweet spot. We will not buy anything until we've seen compelling clinical data that supports what the company's doing.

This whole journey with Vertex, they started talking about this stuff five years ago. We didn't invest in it until a couple of years ago because we wanted to see tangible progress. We are long-term investors. We are typically hoping to be invested for a kind of three-to-seven-year timeframe. That period of time will cover the launch of all of these interesting projects that Vertex is doing. What we don't assume is in late 2030s, early 2040s, they're going to do it again. It's possible that they might, they'll certainly have generated a boat load of cash if they're genuinely successful with what they've got now. So, they can either continue to acquire or they can fund further things. But you have to look at each one on a case-by-case basis. But I do think there is a sort of cultural element to all of this.

So, we wrote in one of our fact sheets about oncology. We are not really interested in investing in oncology. It's not because we don't care about cancer. It's not because we don't think cancer is important. But there's just too many people chasing too few targets. You cannot get an edge on who's ultimately going to be successful. If you're the 13th pi3 kinase inhibitor in phase one trials. I mean, I don't know, are you better than the other 12? Are you worse? So, the logical thing to say is half of these are going to work because we know that the target is a valid target, therefore actually your share of the market, it might be a big market, is pretty small. So, then it becomes much less exciting from a risk reward point of view, given the massive costs.

And similarly, you look at kind of medical devices. You can sit there, and you can say, well, we've got the Smith & Nephew's or the Zimmer's or the Stryker's. And they're predominantly involved in large joint orthopaedics? Well, basically it's titanium rods, screws and some glue, and the current devices last about 25 years. The average person that gets one's in their mid-fifties, does the world need better large joint ortho? Not really. Are you going to be able to generate massive returns from being successful in the area? What people don't really understand, I think, is that if you did develop a new system for hips or knees, you have to deploy a load of instrumentation into the market to enable surgeons to fit your new gadget. And that from a working capital point of view, can be a billion-dollar investment. So again, return on capital employed, not really very

exciting. So, I think you've got to look at the complexity of healthcare and distill it down to simple questions of what are the key problems that society faces? What do the solutions to those problems look like? Who's most likely to deliver? And that's, that's what we do

George Viney: Before we get onto those problems and needs. Healthcare investing puts a lot of people off because there's a lot of jargon, but there's a lot of different disciplines that are required. Medicine, which you mentioned, but also an understanding of statistics, trial design, trying to understand the science at a basic level before you can start mapping as to what the competitive set looks like. But what you're describing here is sort of general principles that a non-specialist could apply. It's judgment. Are there other elements such as game selection or market selection that are applicable here? Or the focus on a culture of innovation, that is broadly applicable not just to the healthcare industry in the way that you practice your investing, but more broadly?

Paul Major: One of the things that frustrated me when I was on the sell side, and we tried very hard not to do, was people love to use jargon and make things complex. You don't need to. It's very, very simple. You are selling widgets at the end of the day. They might have a complex basis to their understanding, but when you walk into a showroom to buy yourself a new BMW, you don't have to understand the complexities of the engine management system and the software behind it. And how a heated seat works. It's kind of the same thing.

I'll give you a classical example. So, we own a company called Outset Medical. Nobody's heard of Outset Medical. Why do we own Outset medical? Well, if you look at kidney dialysis, kidney failure is increasing as a disease for all sorts of lifestyle related reasons. Principally linked to type two diabetes in an aging population. There are 2.6 million people in the US receiving some form of dialysis treatment, kidney failure. They're on that journey and there aren't enough kidneys going around for them to all get a replacement kidney, so they're all going to end up on dialysis. A few years ago, Donald Trump signed a piece of legislation that said by 2020 something, 80% of those patients have to have been offered the opportunity to receive dialysis at home.

You cannot receive dialysis at home with traditional dialysis equipment. You would need to

Paul Major: a room the size of your garage into a medical facility just for all the ancillaries to make it work. But there are companies, two of them, that

provide home dialysis units that are basically the size of a commercial under the counter fridge, and they're plug and play, touchscreens and all this kind of thing. Connected to the cloud for remote monitoring and blah, blah, blah. So, two companies. One of them is private. So, 2.6 million people. 1% of them today receive home dialysis. They receive something called peritoneal dialysis, which basically is where they inflate your abdomen full of fluid and then suck it out while you are asleep. Except of course you can't sleep because you are being inflated and deflated like some kind of pregnant whale, by a noisy machine throughout the night. So, if that doesn't kill you, the person sharing the bed with you will probably kill you. It's just not practical, right? So, there's only a few tens of thousands of people receiving that. So, when we look at a market like that, it comes back to the area under the curve. The TAM. It's huge. It's going to happen. We can only invest in one of those two companies. And as long as there's no structural impediment with regard to the technology, it's unsafe, it's hard to use, whatever it might be, in the end, if you're a long-term investor, which we are, you are going to be rewarded for owning something like that.

So, you can make these things really complicated. But the reality is actually it's very, very simple. It's what ails society, can it be fixed? Can it be fixed in a way that's practical and deliverable? Can it be fixed in a way that's economically viable? Can it be fixed in a way that the medical profession will accept, that patients will accept?

Tom Yeowart: Can we take a step back and explore some of those issues in a bit more detail? You invest in a very specific way. The premise of your approach is that the healthcare system is fundamentally broken. There are significant challenges which are only getting worse. Could you talk about those challenges and then also your approach to investing behind productivity and that sort of thing.

Paul Major: If you read a newspaper in the UK, they will tell you the healthcare system's broken. Okay, we know that. And then they will tell you it's a political problem due to underfunding or not prioritizing the right things. And yet, when we look at the United States, totally different healthcare system, Spain, Italy, France, Germany, they are all struggling with the same issues. You can't get enough staff. You've got increasing mortality, lowering of life years lived well. So, life expectancy has stopped improving. But of the years you get, you will spend an increasing proportion of those, and this is really critical, in poor health at the end, which is very, very expensive.

And this all sort of circularizes together. So, if you look at the distribution of healthcare expenditure for a human being. When your mother is pregnant with

you, the healthcare expenditure belongs to you. So, if you were to draw a chart for somebody's life, you'd see it's very high at the beginning, those first 9-10 months of your existence, and then it drops away to almost nothing. And then, if you're a woman where you get into fertile years, sort of late twenties through to late thirties, where you might start having children, again expense goes up, plateaus off, then you get into the fifties, and it starts to climb and climb and climb. And the most expensive period of your existence will be the last three or four weeks of life that you have, which for most people tragically, ends in a hospital bed.

So just from an economic standpoint, because the population is aging, and people don't drop off the end of the cost curve fast enough. I know this is all very crass. There's a cost multiplier effect. So, for example, if population grows at one and a half percent let's say, in the UK, the healthcare demand will grow at about 5% because those new 1.5%, they don't actually cost any money. But the people that don't die at the other side, they cost a huge amount. So, when you have this political discussion and the Conservatives have been in power for 20 years and they say, we've always increased the budget in real terms, above inflation. That's true. It's just not enough. And then you have the other thing, which is if only we gave all these systems enough money, they'd work. Well, that's not true either. So, we are short of about a hundred thousand staff in the NHS right now. So quick question for the two of you. Are there more or less qualified frontline staff in the NHS today measured as full-time equivalents versus the end of 2019 before the pandemic? And how much more or less are there?

George Viney: I think there are more. Well, I know there are more because I've done my homework and I read your literature, but the punchline is, I don't remember what the number is.

Paul Major: It's a teens percentage. But again, if you think about a newspaper, you wouldn't believe that, would you? You'd think that all the doctors and nurses have retired because of terrible working conditions post covid. So, we have a hundred thousand vacancies in the NHS. The simple reality is not enough people want to work in this industry to bridge that gap and we are recruiting as many people as we can find. We're going all around the world. The Philippines has got no nurses because they're all working in the NHS because we are actively going to the Philippines as a country to poach their nurses. But what about the people in the Philippines? Is that really how we should solve our healthcare crisis? So, then you come back to a really fundamental point, which is, if the system that we have doesn't scale, and it's not just the UK that has a

deficit of staff, it's everywhere, we need to find solutions that enable people to be massively more productive.

People spend enormous amounts of time not doing what they were trained to do. So, paperwork about a third of their time, they complain they don't have enough time, they're literally running from one patient to another to meet their basic medical needs, and not invest the time into giving them proper quality care. If you think about this like a production line, you come into the healthcare system, you get intervened with and then you come out the other side. It's bottlenecks everywhere. And so, the key to all of this is not the next generation of whizzy drugs. It's not hiring more people. It's not paying people more money. Whether you think that they deserve more money or not, that's irrelevant. It's not going to fix your problem. It's just going to increase your bill. So, the solution is productivity tools that enhance people's ability to spend time looking after patients.

And some of this stuff, people are not going to like, the whole electronic triage. Your first conversation with your GP is a telephone based one, for example. That is a necessary step in improving productivity because you come back to the data and the NHS' own data shows you that 25% of all interactions between a patient and a GP are concluded to be not medically necessary after they've taken place.

The other thing that's fascinating, there's a company that's been working with a number of NHS trusts looking at what people actually do in an appointment and it's a bit like those conversations everybody's had where the gas board dig up the road outside your house and then three weeks later, the electricity board dig up and then BT dig up. Why couldn't you all just work together, dig one big hole, fix everything, and then it wouldn't be such a problem. The same thing, believe it or not, is true when it comes to patients. So, you'll come in and then they'll send you an email the next day saying, we noticed when you came in and we looked at your records that we haven't had a blood pressure reading from you for five years. Would you mind coming in? We'll take your blood pressure. If you'd have just used a little bit more insight, you could have taken the blood pressure while they were in the room, and you were discussing their runny nose or whatever it is that they'd contacted you for in the first place. So again, there are tools that show you that you can get 70, 80% productivity enhancements with these sorts of things.

The other thing we need to do, and this is very difficult in this kind of PC world that we live in these days where people don't like to talk about, you know, people being fat or having poor lifestyle choices. The reality is Pareto's law

applies in healthcare as it does in everything else in life. 80% of the problems come from 20% of the population, and you can predict who they are long before they have problems. If you are sedentary, if you have self-reported poor diet, you smoke, you drink too much and you're overweight, you are going to be back with type two diabetes and various other musculoskeletal problems, because your joints are going to struggle under the weight of all the excess fat and everything else.

Those people should be intervened with, with constructive help. What are the barriers to you eating healthy? What are the barriers to you exercising? How can we help you psychologically, financially, whatever it might be, and do genuinely preventative medicine. Now, this is something that is finally beginning to happen in the US. It's taken 10 or 15 years, but the data is in, and the data shows you that if you are a GP and you've got 2000 people on your roster, a bit of computational analysis, run some funky algorithms, you can identify who those people are. So come in, we're going to do a wellness check, we're going to help understand what are your problems?

So, a lot of what we invest in, when you look at it, software companies and things, you might think, why on earth are these guys investing in a software company? Because the answers to some of these problems are so simple that it's just understanding how to help people navigate the system, make better decisions, all those sorts of things. It's, it's really interesting.

George Viney: The origins though of the crisis that we find ourselves in is in a way more disturbing than the headlines would suggest. It suggests it's an economic problem or a political one. But what you are saying is there's a cultural problem at two levels. One, with the management of the system, and that's proving hard to change. But then also cultural problem with wider society in the way that we live our lives. And that's hard to change too. So, there's no single fix here. What you are describing is there's a problem at many levels that have these causes, and you have to attack them on an individual basis.

Paul Major: So, there's a few things to unpick there. So, you're absolutely right that the origin of mass healthcare is a post-World War settlement. World War II, what can we do for all these troops that have gone out and given their lives for our freedom, we can give them healthcare. But that was a very reactionary system. You have a malady, you seek treatment, we patch you up. So, if you actually go back and you start searching the medical literature for the idea of preventative healthcare, you won't really find any studies prior to the early nineties, that talk about the benefits of intervening early to prevent people from becoming unwell with things that are chronic conditions.

Why do we have these problems now? People joke about the number of heart attacks they've had now because actually they tend to be mild in nature and quite manageable. And we have all these coronary interventions, stents and other things, bypass surgeries that we can do that mean that we've dramatically reduced those really awful cardiovascular events where someone has a horrific stroke or a heart attack and then they literally keel over and die in that moment. So, lots of the problems we have now are simply because people don't die of the things they used to die of. So now you have this chance for your body to start to wear out.

So, most people in their late forties, early fifties will have significant signs of arthritis in their major joints. Your body's not really designed to live beyond the age of the female menopause, because from an evolutionary point of view, you're redundant at that point. So, stuff wears out. We're only now beginning to uncover the kind of degradation and degeneration of the body to understand how to kind of intervene and then what the right interventions are. So, we are in the early innings of understanding how to manage elderly people. And in the meantime, the healthcare system was never designed to cope with them. They didn't exist. So, we're now trying to fix a problem that didn't previously exist.

So, there's a lack of planning. There's the glacial kind of pace of all of this. It's like most things, how do things break, slowly at first and then very quickly, and that sort of feels like healthcare. Why did we launch this fund five years ago? What's changed? When we think about it as kind of a series of simple problems that need to be fixed, the solutions to those are now presenting themselves, and a huge amount of it has got to do with cloud, the internet, mobile phones, because it provides a level of connectivity that enables us to analyse, in real time, how people actually behave and what the impacts of those behaviours and interventions are.

Analysing healthcare data is really, really tricky. We have different lifestyle factors, and we all lie to our doctors. So, when they ask you how much you drink, whether or not you smoke, what you eat, you lie to them. So, they've got no good baseline data about what people are actually like. So, if, if you were doing a study, you have to do massive data sets and complex analysis to get to the truth of why does this person need a new hip and this person doesn't, when we've matched them for all these other things. And we've only really recently got to the point where the computational systems and the power is there to be able to do this analysis. And then we can start to identify what the problems are.

There aren't many, but there are some benefits of the pandemic. One of them is people were forced to experiment with critical care. There was no textbook for

Covid, and Britain should be very proud. We led the world in some of the interventions that dramatically reduced mortality from Covid. And it's worth thinking that it went down by a factor of five if you were hospitalized in the space of about 12, 18 months. That's pretty incredible.

One of the things that Covid has done is it's made people realize that lots of things they used to do aren't necessarily perfect and it's worth experimenting and trying new approaches to things that are established in order to maybe have better outcomes. And what we can start doing now is we can do comparisons. So, this group of 10,000 people got this intervention, this group of 10,000 people got that intervention, match them, controls, look at them. What are the outcomes? 1, 3, 5 years? What were the costs? Oh, okay, we should all be doing it like this, not like that. And is that sort of stuff that gives us the confidence that we can start to make meaningful impacts on these things.

The challenges are again cultural because people don't like change. Doctors are no different. They're very inherently conservative people. You've taken an oath, do no harm. If someone comes in and says that technique that's out of date, you don't want to do it like that, you want to do it like this, you're going to take some convincing. It's going to take some time; it's going to take some robust data to make you kind of change. And then similarly, the public as well. It is paradoxical, is it not, here in the UK that everybody says the NHS is amazing and brilliant and it needs to be protected whilst also complaining that it's absolutely rubbish and doesn't provide any care that they actually think is worth anything. So how do you square that?

George Viney: Paul, you said earlier on that the problems we're experiencing in the UK are replicated in other countries, but there's one country which is an obvious outlier, and that's the US in terms of the spend per capita or GDP, but then the clinical outcomes seem to be far inferior to what you see in other countries. Why is that?

Paul Major: That's a common, I would say, misperception. So, on the spend per capita, you're absolutely right, percentage to GDP massively higher. Roughly one and a half to two times. Healthcare outcomes on average don't look better and, in many areas, look much worse. But that is to do with inequality of access. If you actually look at higher end care. Theirs is better than ours. As a relatively affluent person, who would be well insured, well provided for by your employer if you lived in the US, you are far better off there than you are here. That's just true. But in aggregate, they have a system where the safety net doesn't work in anything like the same way as ours does, and that pulls down there. So, I think we have to differentiate the quality of care versus the

more social elements of this. And I'm not in any way saying that the US is right in what it does. For example, you look at infant mortality statistics there and they're absolutely scandalous.

So why is the US the way it is? Two or three things are problematic. The first thing is that if you go to med school in America, you pay yourself and it's very, very expensive. So, it's about a quarter of a million pounds to get trained in the UK, I would imagine it's more in the US. You are going to own that debt yourself. And they've had this historical model, which is fee for service. So, in other words, the more things I do to you, then the more I get paid. So, there's no disincentive for me to be conservative in any kind of treatment approach that I would give. The second is litigation. So, the fear of litigation drives behaviour because people are absolutely terrified of being sued because it's so disproportionate, the cost. And that's one of the interesting things you've seen over the last 20 years. 20 years ago, if you qualified as a doctor in America, you would want to set up in private practice. Now everybody works for a big hospital group because they can't afford the liability insurance anymore.

I'll give you a classic example of overtreatment in the US. So, when my eldest son, who's like 18 now, when he was about two or three, he banged his head on some playground equipment when he was playing in a park. And one of my colleagues who worked in our New York office, exactly the same thing happened to his son on the same weekend and they're the same age. So, my son, took him to minor injuries because he never really had a fall before, I didn't really know what to do. And they looked and they said he's absolutely fine. Give him some Calpol, if he starts being a bit weird, bring him back. That was it, right?

So, my colleague goes to the hospital in New York and first thing they say this kid needs a head CT because he's banged his head and he's got a nosebleed or whatever. So, he's all right, we're going to anesthetize him. We're going to give him a general anaesthetic so he can lie still in a CT scanner. So that's what they did. And then they were in the hospital for like 12 hours and then they ended up having to stay overnight because they wanted to monitor him. So, the bill for this thing would've been like \$10,000 or something like that. And they've unquestionably endangered the life of this child by giving him a general anaesthetic when he didn't need one. And funnily enough, the conclusion of all of this was he was absolutely fine. That's driven by fear. That's driven by the one in a million chance that poor kids got a hematoma.

Now, what's really interesting, is this transition toward value-based care. So, this idea of actually reward doctors for maintaining the health of their patients

over a long period of time. And this started about 10 years ago. So originally these deals were upside generated, the carrot of a bit more money if the wellness of your patients had improved above their demographic baseline. There are all these actuarial tables of people's health, and so if you're doing better after five years, we'll give you a bonus for want of a better word. Now they're moving to the other system, which is put all your patients on this. We'll give you an even bigger bonus if they do really well, but if they do badly, then you pay as well. So that ensures there's a minimum service level.

And again, this is moving away from the fee for service. So hopefully that means less overtreatment, which lowers cost. I don't know what you can do about the litigation side of things. The last person to try tort reform in the US was George W. Bush. He didn't get anywhere with it because funnily enough, most of the people in Congress are lawyers. Turkeys don't vote for Christmas. Medical malpractice is a huge industry. So, I don't think you are really going to address the cost issue until you address the litigation side of the equation.

Tom Yeowart: You've talked about why given all the issues with the healthcare system and aging demographics and all those things that we need productivity solutions as a core part of the solution. And you are investing essentially in more disruptive companies. Companies that are younger, trying to solve the problems that they see in front of them. But what does that mean for the incumbents themselves who have grown big based on the existing problems within the system but also have the scale to potentially affect change.

Paul Major: I don't think it's necessarily that negative for them, for the simple reason that we are volume limited on what we can do because of the bottlenecks that we've discussed. So actually, in a world where you can do more, you'll just do more. And so, I don't think that there's necessarily a negative situation, but it's more a question of, if you are an investor, you know, particularly in the current environment where we have inflation, probably persistent, we have a slowing economy, we have enormous pressures on the consumer. If you're planning for your retirement or long-term wealth preservation, what do you really want? You want visible quality growth, right? You want stuff that you can be absolutely certain it's going to happen. There are low levels of risk to it, and it's predictable.

And healthcare very much ticks that box because it's demographically driven. As long as there are people, there will be healthcare, because illness is unavoidable and there are more people, they are generally richer in global terms than they've ever been. And that will continue to be the direction of travel.

Therefore, they will spend more on healthcare because they can and therefore it will continue to grow.

But we know the system doesn't work as is, and we know it has to undergo profound change. We know what that change has to achieve and where the most likely points of intervention are. And they're the strands that we follow when constructing our portfolio. Now we want to have a broad approach across that because the timing of these things is, by definition, uncertain. Things can always go wrong. You want to have diversity across that piste of opportunity. But at the same time, the reason we tend toward the innovative and smaller companies is because they provide high levels of operational gearing into these changes. At the end of the day, if Pfizer were to find another amazing drug that could transform things and sell \$2-3bn a year, right now nobody's going to notice because Pfizer's making \$20-30bn, or it was, selling covid vaccines, for example.

And that's why we tend toward more focused companies. And they tend to be smaller and younger because this is a very fast-moving industry and lots of these things are disruptive innovations. Funnily enough, as I said earlier, turkeys don't vote for Christmas. So, a lot of time people, don't want to reinvent the wheel. So, for example, one of our big holdings is a company called Axonics who makes these nerve stimulation things to prevent incontinence. Very, very clever. What they've done is they've basically taken a device that was invented by Medtronic, they're all ex-Medtronic people, that wasn't really very good, and they've made it smaller and cooler and better. And they've launched this thing and now Axonics is growing 30% a year and they're taking all this market share and they're revolutionizing the treatment of incontinence. Medtronic could have done that. But they didn't because they've got a thousand different businesses. Why are we bothering with this small little hundred-million-dollar product line, when the question they should have been asking themselves is why is this a hundred-million-dollar product line? Why isn't it a \$500 million product line? And could we make it better? Yes, we can. Well, let's do that. They didn't because their focus was elsewhere. So that's why we like focused companies.

Tom Yeowart: How do you gain confidence in the durability of the competitive advantages of these companies because often when you are growing at a fast pace, you are transforming part of the industry, it can attract even more venture capital money. So, what are the forms of competitive advantage for these companies and how do you gain confidence in the long term?

Paul Major: That's a really interesting question, that's probably the thing that occupies the most of Brett and my time. It's difficult to articulate how fast

moving some of this stuff is. So, for example, when we talk about life science tools, which is equipment used in labs, people make the analogy it's the picks and shovels of the gold rush. Well, I wouldn't necessarily choose a pick or a shovel because they haven't changed for thousands of years. I'd say it's more like a steam shovel from 1920. Now we have these hugely capable excavators. Back then we had these one-dimensional machines, but they could do the work of hundreds of people.

And we own this company called Pacific Biosciences, and they do genetic sequencing, but they do this very high-fidelity sequencing that enables you to really understand the structural elements of the genome, which is quite important for lots of diseases. But the point I want to make is when we started owning this company, they had a machine, and they were replacing with a better machine called the Sequel II. And then in the time that we've owned it, they replaced the Sequel II with the Sequel IIe, and they've just launched a machine called the Revio, which is, I think, 16 times more powerful than the Sequel IIe.

This is only first innovation of the Revio, and they're already working on a version that's 64 times faster than the Sequel IIe. So, they're already on the next iteration, the next iteration. There aren't many things where somebody comes out and says, here's something that's 64 times better than what you had before, which in itself is 15 times better than what we had 10 years ago. So, the pace of change is incredibly fast. You have to keep following what's going on. You have to meet the private companies, the disruptive innovators, the key opinion leading physicians in all the different areas of medicine to understand what does the treatment of X look like 5, 10, 15 years from now? What's possible? What's out there? Who might deliver it? And you just have to not get caught in the sunk cost fallacy that just because you are the market leader today, you are going to be the market leader in five- or 10-years' time. Because there are no guarantees in an industry that makes itself obsolescent every five to 10 years, which is pretty much true across all of healthcare.

George Viney: And the thing that gives you confidence that they can sustain innovation over time is coming back to this point about the quality of the people, the ability to attract and retain the brightest minds and keep them happy and productive.

Paul Major: And also understanding what innovation looks like. Innovation doesn't have to be a completely new thing. It's really born of an understanding; how does my product get used in the real world.

George Viney: So, it's not just good ideas, but it's also understanding of the customer and solving their problems in a systematic way.

Paul Major: Yeah. It's interesting as well with physician education because so much of this has got to do with how do you prep the market before you launch a product? Particularly around surgical stuff. Physicians are incredibly conservative. It's a big responsibility when someone's laying on a table and you've cut them open that you are going to do your very best in that situation. So, when you're turning around and saying, don't do it like that, do it like this. Put my new widget or gadget in. What information do they need to be confident doing that?

You often look at innovations and then you just go, that's just not going to work because it doesn't seem practical. There are certain things that give people the ick, they don't like putting patches or drugs or creams in certain places in their body, or pessaries or whatever it might be. And so, solutions that are based around things like that, they're not going to work. We know, it doesn't matter how good it is, if you compare a pill with an injection, you are going to lose about seven times more people. So, when someone says, oh, we've got this great idea. We're going to replace X with Y, when it's an injection, you sit there and think, oh, unless they're really, really, really ill, that's not going to happen.

George Viney: Paul, you've articulated why you are biased towards the more disruptive businesses. Some of them are not making a lot of money today but have the promise to be making lots of money in the future. How do you go about valuing them in a way that's accurate, responsible, but also doesn't do the simple thing of just giving it a 25% haircut because it might not work?

Paul Major: There's lots of interesting things to unpick there. So, the first thing is we probability adjust everything that we do. So based on where you are in the journey toward commercialization, we have all sorts of data about probabilities of technical and regulatory success. There you go. My first bit of jargon, that we can apply, but based on large data sets of what's happened historically. Related to that we apply higher discount rates. So, we are very discounted cashflow kind of driven people. We apply discount rates that are commensurate with the level of maturity of the company. We assume additional financings in our models. Obviously discuss that with the companies. You can generally have a reasonable idea on what your cost to go to market is, and you just need to factor that in appropriately.

We try very hard not to attribute meaningful value beyond visible and patent protected innovations. Now you can't penalize people twice. So, the other side

of that is equally, if you don't believe that they're going to do anything beyond what they're doing, you shouldn't be assuming they're going to spend a huge amount of R&D in the meantime pursuing something that has no value, because that would be kind of nonsensical. And then we look at all sorts of different scenarios around commercialization and market share penetration. You know, we're checking all those things. What does our out-year number imply in terms of penetration of the market? Is that realistic? So, you are back solving to check that you've not gone a bit crazy. And we're generally quite cautious.

Now we do all of that work in isolation. So, when we've decided, we are going to model something up, Brett and I, one of us will choose to do the primary analysis and kind of lock ourselves in a room and do that, and the other person will take the other side of the argument and try and pull apart the assumptions to make sure that they're robust. Once the first stage of that is done, we will then look at it in a market context because it's worth bearing in mind as well that how you make money is by having a high level of conviction that the market is wrong one way or the other. So, your view in isolation is not actually very important. If everybody's already manifestly ahead of you and that's built into the valuation, you're not going to make any money. You're just taking an enormous amount of risk.

So, once we've done that primary analysis, we also look at what's the market expecting, what's the cadence of the uptake? Is that realistic? Map out what's the journey of the share price over that sort of three- or five-year period? Because the other point about this is once you own it, you are an active manager of a position at that point. So, you have to understand the journey, is the market head of itself, behind itself. What do you do? Generally, we buy things when they go down. The market is unfortunately, very short term. You get short term overreaction to something, that's an opportunity to increase. Equally, if we are sitting there and something goes up a lot and we don't think it deserves to, we'll take some off the table.

Clearly that's been a very challenging approach over the last sort of 15 months because we've had this very macro focused market where people are overly fixated on discount rates, and overly fixated on funding risk. So, we've always used discount rates that are reflective of the industry's risk. So, we've never been lower than seven for anything, and we're often up sort of nine, 10 for some things. And that's always been the case. So, the fact that interest rates happen to be low a few years ago and high now, we are not going to be seduced into that.

The other thing relates to this reluctance around funding. And I think good companies are always able to raise money. And we've had a number of

successful fundraisers within our portfolio even during 2023, because if you're doing it at the right time for the right reasons, and it's post a gating event that gives people confidence that you'll continue to hit the markers for the development of your business and the prosecution of your strategy, why shouldn't they give you more money?

The problem that we have at the moment, I think, is that on the back of the pandemic, lots and lots of not very high-quality companies came to market very quickly, probably earlier than they should have done. There was also this bolus of these SPAC transactions, which generally speaking have been quite low grade as well. What's happening now is that natural selection is asserting itself. So, the companies that haven't progressed, don't deserve, frankly, any more funding from investors, are struggling to get that funding and they're circling the death spiral now.

And when you look at some of the all-comers indices, Russell 2000 and NASDAQ Biotech where just by virtue of IPO-ing or SPAC-ing, you end up in the index. Those things are dragging down the performance of those indices and people are saying, well, look, I just need to be in these mega cap companies that don't need funding because they're doing much better.

And it creates this kind of self-reinforcing situation such that it is paradoxical to us, at this point in time where people are talking about the S&P and the multiples being very, very full relative to historical norms. And if you look at mid-cap healthcare it actually stands aside from a lot of that and doesn't look expensive relative to history. It actually looks, in some cases, quite reasonable value.

Tom Yeowart: That's a good place to turn to our closing question, which is if you were to go back to the start of your career, Paul, what piece of advice would you give yourself?

Paul Major: Aside from never working in paediatric pathology, what advice would I give myself? I think working in corporate finance was incredibly educational, so I certainly would encourage people to spend a bit of time doing that if they're interested in working in finance, it really is the crucible of learning. It's like doing a compressed MBA in the evenings and the weekends. I think the sell side is not what it was. So, if I was counselling a younger version of me, I would be, don't do sell side analysis. You're not able to do what you want to do anymore. And it's a limited value as a consequence of that.

Tom Yeowart: Thank you very much for coming on.

Paul Major: Thank you.