



Part 2: Investing to Scale in Health: How Health Drives the Economy

Esther Krofah 00:05

Okay. We're here for part two, focused on "Investing to Scale in Health: How Health Drives the Economy." I'm very excited about this panel that we have here in front of us. We have innovators; we have the health systems represented. We have cross-border and regions that are represented as well, as we talk about how health is really the driver for global sustainability in the economy. The two of them are tied together. We can't leave one out without the other. And I think countries are increasingly recognizing that. So as we talk about these subjects, before we get into that, like, how do we actually gain the benefit of our investment in health? I'll love to talk about what are we seeing from an innovation perspective? What is exciting to you? As you look across your therapeutic areas of focus, as you look across your health system, what are the innovations that are hitting you from a health perspective? Cynthia, why don't we start with you?

Cynthia Chen 00:59

So, hi, everyone. It's a great pleasure to being here today. I'm Cynthia Chen, the founder and chairlady of Pulnovo Medical. So the first indication Pulnovo is treating is called pulmonary hypertension. As some of you may know, pulmonary hypertension is a deadly disease that takes away people's ability to exercise, to work, to walk, or providing care for the families. According to WHO, there are five groups of pulmonary hypertension, and the heavy economic burden lands on the first two groups. So, Group 1, which stands for pulmonary arterial hypertension, which abbreviation for PAH patients are younger, generally diagnosed in their 30s. Many of them were women at their best working and childbearing years. The second largest indication is Group 2, which is pulmonary hypertension combined with left heart disease patients. Those patients are older, often age over 65, require extensive caregiving and repeated rehospitalization. So one group of these patients loses the best functional and working years of their life, and the other group pulls working age or family out of labor force and restrain health budgets. So in one of the largest US registrational study, at least, over, three out of four patients have marked or severe limitation on physical activity while when they diagnosed. So, we are providing a breakthrough technology called PADN, which stands for pulmonary artery denervation technology. We use invasive ablation technology and a catheter to ablate the abnormal sympathetic nerve activation for those patients to ultimately reduce the overload of the heart and reduce the pulmonary artery pressure. And this is what we're doing for the innovation. And for the standard of care right now, without optimal medication, the average lifespan of those patients are only 2.8 years. Even with optimal medication, which cost patients over \$250,000 all the way

to \$500,000 per year, the five-year survival rate is only 50 percent. But with PADN treated patients, the longest patients that we follow up has survived over 12 years, and regain functionality, go back to their work, to go back to their family. And this is what we're trying to do and bring the technology worldwide right now.

Esther Krofah 03:36

And that is the hope that every patient wants access to, which is when you're diagnosed with a devastating condition that you're working on. Is there a technology? Is there a therapeutic? Is there an intervention that can extend not just life, but quality of life as well? So, Jude, I'd love for you to just share as well from your perspective as you look across your therapeutic areas of focus. Where is this innovation? What is the innovation that patients are excited about seeing?

Judith Love 04:02

I think in one of the areas we look at. So, I'm Jude Love, the Regional President for Novartis, and I cover Asia Pacific, Middle East, and Africa. But we cover cardiovascular disease, oncology, neuroscience, and immunology. And I think if I just focus in on one area, for oncology for a moment, what strikes me is I was a registered nurse when I first got into the industry over 30 years ago. And the advances in medicine are quite stark, I'd have to say. So, in the last ten years, we've taken patients that have had a certain types of cancer, blood cancers, where their prognosis has been very poor. So, they've failed a lot of treatments. They've got refractory disease, and they didn't have a lot of hope. Roll forward. And now today, one-off treatment where the doctor would extract the immune cells from that individual patient. Then those cells would be transported and actually re-engineered in a laboratory to then come back and be put back into a patient. And the result here is that those cells then hunt down and attack the cancer cells. It is remarkable. One-off treatment, and patients that would have faced a very bad outcome are still alive a decade later. So these are the sort of advances that are not incremental. They're transformative.

Esther Krofah 05:40

And Eric, I'll come to you and then I'll come back to you, Wai Hoe. Can you tell us a little bit about the innovation that you're seeing, certainly from China's perspective? Huge biotech industry, it is continuing to grow rapidly, a lot of investment in immunology, rare disease, cell and gene therapy. What are you excited about? What are you seeing?

Eric Tse 06:00

I think there's from the larger perspective with the shortest perspective. I'll first introduce myself. I'm Eric from SBP Group. We're listed in Hong Kong. Our ticker is 1177. So, basically, we're focused in oncology, respiratory, surgery, analgesics, hepatitis, immunology, and CVRM. I'll say it's like from the macro perspective, China has been experiencing very high-speed growth in early discovery as well as in clinical trials. So, a lot of new drugs innovations coming out. Right now, globally, there's around, China already occupies over 40 percent of the global innovation as well as clinical trials right now. So, basically, the biggest hub for innovation. So, right now, we're experiencing faster trials and even more candidates are arising from the early discovery session. So, one is driven by innovation, so, early discovery, also speeding up by some speed of the AI, which some companies are listing to A-shares and H-shares as well. And the other is the speed of clinical trial. So, why we see that there's a huge growth is because China right now, one, has a massive population, 1.4 billion population. But it also has current one of the world's best, or in all the regions, of social facilities, in terms of hospital, in terms of clinical data, and speed of enrollment in patients in clinical trials. So, there's a huge group. And right now, only China has this ecosystem or have this all the facilities to carry out or speed up all of the trials, as well as with a global standard of

data. Other places that have the population, rather, does not have the standard of care that can be taken or the data cannot be, let's say, as prepared as that of China. So, with the innovation speed in engineering and then the other of carrying out clinical trials, right now, China is one of the only places in the world that has that capability. So this is also the reasoning why MNCs and other pharmaceutical companies, health-care companies, all try to take part in China's innovation right now. Also taking the speed, especially most of the firms are interested in early discovery as well as development opportunities in China right now.

So, in the past two years, we've also stepped into globalization from a domestic market more into a global market. Last year, we partnered with MSD, our PD-1/VEGF, with a total package of \$4 billion; upfront was \$888 million. This year, we had two already so far. Earlier, we partnered our JAK/ROCK with Sanofi, with a total package of \$1.5 billion; upfront is \$135 million. And then, recently in July, we just partnered with AZ, our PDE3/4, which is a total package of \$1.9 billion, and upfront of \$200 million. We're seeing more deals to come. So, by every year, we're expecting, let's say around, at least one to two continuous out-licensing. We're seeing more and more new co-opportunities development as well. And then, right now, I think AI is the other term that everyone is seeing. So, we're also a very, let's say, group that has history, but also a very young, has a young leadership and young team right now. So, we are one of the earliest players in the traditional field that took an approach in terms of AI as well. So, I'll say it's like, in terms of AI-generation of drugs and pharmaceutical, there's a generation of 1.0, 2.0, 3.0. 1.0 is basically the era of AIDD. So, we put it in a global perspective, I would say that there's thousands of firms that claim to have this capability. But I'll say tier one, they only have months of differences. Right now, we've already shrunken all the time passage from years, three to five years, up to maybe half a year within a year. So, there's only months of difference. But 2.0 is really on the mechanism of different modality or delivery system or undruggable drugs targeting our undruggable drugs. These are the, I think, more penetrating and innovations that we should look—focus more on. And the third is on large language model systems, on larger models that focus on novelty distribution. So, we also have distributions on and investments in all of these fields as well. I'll just stop there, so you have more time.

Esther Krofah 10:54

Well those are incredible areas of focus. And certainly we're seeing the out-licensing, the early Phase 1 trials, IND, investigator-initiated trials in China that are really speeding up. So as I heard from Cynthia, from Jude, and from you, we're speeding the pipeline to innovation. And, in fact, we're accelerating it through all of the infrastructure investments that you just talked about in China. So, Wai Hoe, as you hear all of this and you're the health system on the back end that needs to implement these innovations, how are you thinking about this landscape? So, you have a budget that you need to manage. You have a wave of new therapeutics or medical devices that are coming. How are you preparing your health systems to adopt these technologies?

Ng Wai Hoe 11:40

Yeah. So, I think I'll approach this more from a population health approach because I think the topic of our, this whole topic is really about how healthy populations can actually promote economic growth for our nation. And healthy people do lead to a healthy nation. So, I guess at the health system perspective, when we look at the entire continuum of care from primary health care all the way to hospital care, tertiary and quaternary, it would largely be if we put investments more upstream, in a more preventive and early diagnostic realm. I think that's where we will actually give the greatest benefit to the population. So, I think firstly, if we can invest more in keeping people healthy, preventing the onset of disease, diagnosing them early, treating them and curing them early, so you have a less long tail of the burden of disease, we'll try to put our investments in that. Now, the second point is that actually a lot of health care may not be, need not be that costly. Because if you consider for every—for all the

investments that we make in health care and health-care budgets, there is this term known as social determinants of health, where actually about 70 percent of health outcomes does not actually come from putting in a lot of expenses, does not come from hospital care, doesn't come from specialty care, doesn't come from expensive technologies and surgeries. It's actually common sense measures: healthy lifestyle, eating healthy, sleeping well, not smoking, and so forth. And if we invest in programs in the communities, and invest in those and keep people healthy, I think that's where we will actually have a lot of cost savings. I think the third thing that we really need to look at is behavioral nudges, because 70 percent of health outcomes come from social determinants. If many of you are like me, I know that I shouldn't eat fried chicken. But I do eat fried chicken. And I love to eat fried chicken. I eat it very regularly. And I think we need to look at how—

Esther Krofah 13:56

Just not every day.

Ng Wai Hoe 13:57

—yeah. Just every other day. I mean, I don't have cheat days, I have cheat weeks and cheat months. So, the thing is, I think we do need to look into investments into programs and things to actually improve the behavioral, not just to help people, to promote, make it easy for them to be healthy. I think the fourth bucket investments is, I would say, looking at things from the population base, from a large group of people: invest in data, invest in data platforms, understanding the demographics of the people that you look after, their pre-existing diseases, the demographics, their profile, so that we can tailor treatments accordingly and put the investments into the vulnerable groups, the groups that require intensive health care and really utilize a lot of health care. Certainly from the SingHealth experience, we have a small proportion of people, about one-third of our patients, consume three-quarters of our health care, the entire health care that we actually provide. So, we target these certain groups, if we understand the data, understand the demographics. And I think that's where investments into data, data platforms, data analysis is important. And I think lastly, the thing is, at the end of the day, big data needs to be transferable to n equals to one. And that's where precision health is. And that's where I think we need to put some investments into contextualizing the large data that is actually applied across the entire population, and yet personalize it to n equals to one to every single individual so that we can provide that precision health and that personalized care to that particular patient. So, I think these will be the five buckets that I would look at. Yeah.

Esther Krofah 15:52

So, Jude, I would love for you to respond to that, because what Wai Hoe has described is a population health platform. Invest in data, predictive analytics, targeting where we see the most cost relative to where we can achieve the most outcomes. And, to me, there's a tension between let's innovate and create more new medicines, and let's invest in prevention and wellness and sleeping and eating and all the things that are primary factors for prevention. It's not necessarily about the new medicines itself. How do you, representing this region, balance the need between prevention and innovation and who should be investing where?

Judith Love 16:35

It's a great question, and I think the million-dollar question. They're not mutually exclusive. So, I think it's really important that actually we do focus on prevention. We focus on infrastructure. We ensure that patients can actually reach the medicines that are being, where the innovation is actually occurring. And I think that's the whole point. From a benefits perspective, we're innovating every day. But the key here is those innovations aren't necessarily reaching the end user. So, the innovation is not the question for me. The piece is why is that not

happening? And Novartis actually worked with an external provider to do some market research recently. And we looked at a whole lot of different market archetypes. So, four different countries, from self-funding, right through to government-funded countries, and those that had a mixed model in between. Now, the thing here, I think, is that most consumers know that medical advances have been taken, that they know that they can get medicines that will make a fundamental difference to them. But, actually, eight out of ten patients that were or insured consumers that we spoke to felt that there was a barrier for them actually getting access to that medicine because financial burdens. What does that mean? It means that at the end of the day, the conversation in the physician's room doesn't go to what is the best treatment. It goes, "What can we afford?" Now, when we think about that affordability piece, who should wear that? Not just the government on their shoulders. Right? I think each individual should be prepared. They should actually understand what, that they may actually face a risk of a health event happening sometime in their life and plan for it. We've got a whole stakeholder group that really needs to work alongside the public system. The private, so finances, et cetera, need to actually be focusing also on providing and closing that gap. And I think three things are really important here. One is an awareness as individuals that in our lifetime there is a chance that we will be unwell. It's a horrible thing to say out loud, but we need to plan for that. We need to understand what that looks like. I think we also need to be able to start early enough. So, the prevention piece, I totally understand. Actually, prevention, early screening, ensuring that you catch diseases early, this is fundamental to actually keeping people in the workforce. So, it's important that we actually look at these, and we can't do it alone.

Esther Krofah 19:31

Yeah. I hear from you that everyone needs to work together. We need all parts of—

Judith Love 19:35

Completely.

Esther Krofah 19:35

—the ecosystem to work together.

Judith Love 19:37

Yes.

Esther Krofah 19:37

And is it because you fundamentally believe that if we do invest in either new medicines or prevention, we do help, actually, with this economic question that I raised at the top? Which is, you have healthier individuals; they can go back and participate in the workforce. We're able to see the full benefit—

Judith Love 19:53

Exactly.

Esther Krofah 19:53

—of their full quality of life if we're able to intervene early.

Judith Love 19:56

Exactly. And if I think about employers, for example, you can imagine a time where you have early screening; you catch the disease early. And what that means is that the medicines or the treatment they get can actually make them healthier to get back to the workforce. And health is everyone's responsibility. I think it's a shared accountability.

Esther Krofah 20:19

In this region, do you see employers playing a much greater role in paying for new, innovative medicines?

Judith Love 20:25

I think employers play a role. Financial advisers play a role. You know, we talk about retirement and ensuring we're ready for that. But how many times do you actually have a health-related discussion to say, "Have you planned for the risk of a health event?" That doesn't necessarily happen. And then if we look at insurers, they're not keeping up with the changes that are actually happening in innovation. So, the coverage is not there. It's right across the board. And innovation only creates value if it gets to the end user.

Esther Krofah 20:59

Yeah.

Judith Love 20:59

If it doesn't. Then, it doesn't.

Esther Krofah 21:03

And Cynthia, this is something that you're thinking about as well as you're developing your medical device, which is a relationship between the providers, the health system, and their willingness to adopt new technology. What do you think is needed to invest in new innovation?

Cynthia Chen 21:16

Well, as we discussed earlier this morning with Judith, I think we are encountering the same situation challenges everywhere globally for to bridge the gap between the fundamental of breakthrough technology all the way to, not only getting FDA approvals, but what happen after approvals. So, from our perspective, I think, physicians ultimately adopt what can translate and change the patient's outcome. Health system and investors ultimately adopt what they trust to scale. But, fundamentally, it's only the clinical evidence that can speaks to both. So, when we started Pulnovo 13 years ago, from 2013, we didn't rush to capital market, but we spent 13 years building up robust clinical data all over the world. Last month, we just announced the global first registrational study in treating Group 2 patients with concept to 65 to 80 percent of patient population that we are doing right now in Europe, and we become the Asia-first and China-first medical device technology being published on *New England Journal of Medicine*. In the same time, we secured seven FDA approvals alongside, including three FDA Breakthrough Device designations within the past six years. So, breakthrough technologies like PADN ultimately create value that health system can measure. Taking our *New England* trial study result as an example. So, adding PADN to the standardized heart failure medication eventually reduce the risk of clinical worsening events by over a half over a two-year span,

and also reduce all kinds of recurring clinical events by a third in the long-term follow-up. And we are also seeing a holistic improvements in all hemodynamic data and health status. So, that's what we need for those patients. And when patients are getting better, and health budget goes further, physician, hospital, health-care system, and investors all have a willingness to say yes. And this is a return in investing in health.

Esther Krofah 23:38

Eric, countries increasingly are thinking about affordability. So, are you concerned about so many innovations rushing all the way through regulatory, and then you hit a huge bottleneck in adoption? How do you think about the global scale of technology with this conversation? Because you can certainly say, "Do we need more innovative medicines or do we need more investment in prevention?" Do you think about the tension between the two?

Eric Tse 24:03

Well, I would say right now, globally, it's still a market of care, of treatment, rather than of prevention right now. So prevention, I think, it will move towards it. Talk of prevention came already, starting from two years ago. Right? So, for us, in terms of prevention, we do have some of our pipeline within as well, mostly revolve around siRNAs. So, for example, we have our own Lp(a) P669 dual targets, APOC3. All these targets, I think it's more to CVRM areas. But, we're very [inaudible] in making annual dosage. So, right now, most of the dosage are all like three months to half a year dosage. But ours is, right now, we can see 12 to 14 months of data. So I think these is a perspective in terms of prevention. But I think whoever can address the market of prevention is more a global market first. So that's, I think it's still quite, quite far away from China. China, on the other hand, is trying to have all population, basically, can be taking the care. So that, which means there's a price cut, a haircut on the pricing. So, I think it is really the country that has to decide on whether you want to give incentives on more innovation to come. Right? Or, to have a lower price on the innovation. So, one of our collaborated projects with GSK, bepirovirsen, the first cure towards hepatitis B, basically. Right now, it's already listed in Japan. Soon, it will be listed, this month it will be in the US and then China. So, I will anticipate there will be a price difference, for sure. But one of the other reasons is China occupies almost half of the world's patients in hepatitis B. Right? But it is one of the first, very first ones for 35 percent curation for hepatitis B. So, I think this to these patients is bringing them a hope, a faith of hope right there. And the other is like innovations right now that we're seeing that's very different, for example, HER2 bispecific. We have the global first, or global best at it as well. This year, [inaudible] will have our BLA very soon on our product that we have both efficacy and as well as safety nets, 30-fold of that of ADC, of Daiichi Sankyo. So, I think all of this is like when we are doing innovation, we are aiming for whether you're doing first-in-class. So, the best, sort of first to the market. Or, you're doing very specified, different to the rest of your competitors. And then some of our, the new delivery system or mechanism. For example, tumor microenvironment. This one, we're also one of the global first. So, basically, the molecule or the target only reacts in tumor environment. So, in tumors but not normal cells. So, in the end, for targets like CTLA-4, 4-1BB, Nectin-4, very effective but very potent targets. A lot of sides, grade three or worse effects. We can have the 30 times in terms of one gram—one milligram—originally, they might be very, very, very potent already, but we can make it 30 grams, but even having it very safe delivery system. So, all of these, I think, will change towards something new to the market.

Esther Krofah 27:51

Yeah. And, Wai Hoe, health systems are constrained. The reality is that, as Minister Ong said also in the opening panel that you have a budget, it's capitated, you're only given a certain amount. You have to manage the overall health of that population. And you're constantly making decisions in real time. We see a technology that has a potential benefit, but yet there is a cost that's associated with that. How do you work through the dynamics of

what you want to test and pilot within a health system, and what you think is better fit for a general population health strategy?

Ng Wai Hoe 28:26

I think it's always good to start from a real clinical problem, a real clinical need. And innovations need to address a wicked problem and an area where there's a huge clinical demand, real clinical need, that will move the needle in terms of patient care, outcomes, and also delivering value of care, and containing health-care costs. So, I think let's start off with a problem-driven approach where real clinical needs are. And I think a lot of pilots don't really, frequently don't scale. And I think as we develop these innovations, it's important to ensure that these innovations are adaptable; they are easily adopted into the workflows of a health system. Because I think health systems are largely conservative by nature. Physicians are creatures of habit. They don't really actually like change. They like change when it happens to someone else, but they don't like change when they have to change and adopt. So, I think it's important that the innovation doesn't disrupt the way they work too much, doesn't disrupt the system too much, because that will enhance adoption into the system, and that will enhance scalability. Because I think, at the end of the day, the innovation needs to be scaled up within the health system. And I always like to say that health care is "glocal." On the one hand, our problems are global, but a lot of health care is very much local, and we do need to then understand the local regulatory barriers, the governance, the financial system, the compensation systems. Because, if insurance is not going to compensate and pay for the drug or the device, it's not going to be scalable. So, I think we then need to, once we reach the scale of getting it to be adopted and kind of accepted by the clinical community, don't forget about the regulatory environment and the financial and compensation and remuneration part of the equation. And that differs from jurisdiction to jurisdiction.

Esther Krofah 30:38

Right. I think that's exactly right, with where do we end up with who is going to pay for that and which budget does it come out of? And it certainly can no longer just be one budget. We have to think about it holistically. We are out of time, but I do want us to go down the line with just some closing thoughts. We started this panel by talking about how health drives economic prosperity. Where would you like to see greater investment from the health stakeholders in order for us to see a better economic return?

Cynthia Chen 31:10

For Pulnovo, earlier this year, Medtronic has led our \$100 million Series D round, along with Sequoia and my existing shareholder, OrbiMed, LAV, and EQT. And every penny of this funding is going into our largest US registrational study in treating Group 2 patients. So, just a matter of timing. So for Pulnovo, we've been always invested in clinical trials because we wanted to get this technology faster and better to the market. And in the meantime, because of the first product is commercially available in more than 12 countries right now, we are also investing heavily in global commercialization across the Middle East and Europe. Both emerging markets and local investors that are expected to invest in more portfolios like us to expand the cardiovascular care for the local population. This is also why EQT invest in us two years ago. So adding one more new markets for us means more skilled physicians and providing more solid clinical data that can eventually help us with the adoption of the technology worldwide.

Esther Krofah 32:21

Yeah, excellent. Jude?

Judith Love 32:23

I think there's three areas. Prevention. If we catch disease early, then we can get better treatments and you have more choices and people can return to work. And I think that is really important from society's perspective. I also believe that getting innovative treatments actually to patients that need it is absolutely critical. And the third one is, I would invest in building the ecosystem, the health-care capacity. And that, as I said before, is not just the government. It's actually financial services. It's policy makers. It's industry. It's the health-care system. Everyone coming together.

Esther Krofah 33:08

Yeah. Wai Hoe, where should we invest?

Ng Wai Hoe 33:10

Yeah. So I think I'll end where I started, that really healthy people, healthy workplace, healthy economy, healthy nation. So, I would say that for whatever budgets that we have, if we invest in keeping people healthy in our preventive space, then we will have a lot more budgets left over because people will still fall sick. But if we invest more in preventing, in preventive health, keeping populations healthy, then for those who fall sick, we have a lot more resources to focus on them, to get them well, and to get them healthy again.

Esther Krofah 33:44

And Eric, where would you like to see greater investment as you see us speeding innovation, development, ecosystem?

Eric Tse 33:51

Well, I would say if you pick a ground in health care to invest, SBP is a good target. Well, I think in general, I think number one, invest in companies or corporations, especially in the Asia side of the world, I think. Leaderships that has a continuous tenures for, let's say five to 10 years, or even above. So I think continuously in the management is very important. Number two, I'd say in larger stakeholder shareholders have an over 25, 30 percent above of the shares, they will keep the stock price or everything, the equity to be more valuable, I think is one other bit. Number three, right now I think there might be very huge disruptions towards the entire industry. So, AI is definitely one of the key questions of how it will impact the entire industry. So, either look into right now, but it's way too early to see who's coming and who's not. So, either invest in companies that has an eyesight or foresight before what will happen or are doing a lot of investment prior to beforehand. Or, to stay put, and to see who will be coming later. So, that will be some of my personal, what I do for myself.

Esther Krofah 35:21

Yeah. Well, I think there's an opportunity for all of us to re-examine which part of the ecosystem we're working in, and that all of us need to work together. It's really the collective action that we're going to need in order for us to see a healthier population. Let's get the right medicines to the right patient at the right time, but also let's invest in that overall ecosystem. So, please join me in thanking our panelists for a great conversation.

Announcer 35:42

Thank you for attending our lunch program. Be sure to utilize the mobile app to stay up to date on the latest programming changes.

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