Building a "virtuous circle" of investment in healthcare: Q&A with Lumira Ventures

FEATURING

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Read commentary from Torys for the latest legal and industry trends in our article "AI healthcare companies: navigating the cutting edge of technology with Canada's regulators". And for more industry insights, read our in-depth Q&As featuring Abubaker Khalifa, MD, Co-founder and COO, Moonrise Medical and Saumik Biswas, CEO, President and Founder at Tenomix.

As a long-time player in the sector, what does building a sustainable and robust healthcare innovation ecosystem mean to you?

Peter: It means three things to me. First, it means exactly what you said. It's sustainable. It means it's a continuous and meaningful flow of ideas, capital, and people that allow best in class, and first in class, innovation to be developed, identified, and supported.

I think a robust ecosystem is about value capture, which means that if we build companies in this country, we want to capture the value from those companies. So, that means we cannot have our best and most innovative companies be funded primarily by third parties that are not domiciled in Canada and have most of the value of that process accrue to third parties.

And then finally, to really have a robust ecosystem, you must be impactful. And obviously the beauty of life sciences is that it is impactful every day. The impact story for patients is obviously very easy. On the industry side we create high value jobs that leverage all those students who are in our academic centers doing undergraduate degrees, masters and PhDs. It is incumbent on us to figure out ways to make sure that those people stay in this country, that we can provide them with robust jobs and the kind of career they can be proud of over the next three or four decades. In addition, the universities and academic centers who are creating this IP need to have ownership stakes in that IP and in those companies. So, as these companies are built, scaled, and successfully monetized that value attributes to the scientific and clinical innovators and then comes back into the economy for those universities and institutions and allows them to recycle it.

What does Canada have, and what does it still need to do, in order to achieve this objective?

Peter: There is little doubt we have the science, clinical and academic expertise. We have some of the leading academic centers across the country. We have some of the leading hospitals in different therapeutic areas, whether it's SickKids or Princess Margaret, or any of a dozen other clinical environments.

> If we do this right, we create the next generation of jobs for the students being trained within our academic environments. We create a virtuous ecosystem between our academic centers and companies, with capital flowing back into academic centers. We create transformative products for patients that address unmet needs.

We have an emerging class of impressive entrepreneurs, and entrepreneurs who have built companies multiple times, but that's still a small group. We have a core group of domestic investors which is positive, but it's lacking in scale and breadth—and none of them have scaled to the size of our global peers. We have gaps in terms of the staging in capital: both in the early- and later-stages. If we look at places like the E.U., the U.S. or China, the simple reality is we are just not competing on scale with the firms coming out of those markets. Many of those firms are being powered by significant government capital and I think that's a big challenge. You need a robust ecosystem to make this work, and we don't really have that today.

We also don't have a funding ecosystem for venture capital that is akin to any of our peers. In the U.S. our peers raise most of their money from either endowments or pension plans, and there is deep engagement in the space. We don't have that same engagement here in Canada.

What is the role of government and others in the ecosystem in achieving these objectives?

Peter: I think there are two roles for government. There's the direct role, and the indirect role. The direct role involves procuring early innovation and providing muti-level funding. For example, there is a general belief that the U.S. government is very hands off and doesn't play a big role in the venture ecosystem, but that's fundamentally not true. The U.S. ecosystem exists because the U.S. government put in place procurement, and multiple layers of federal and state funding to support venture.

The second part is indirect engagement, which features smart policy. One of the smartest venture policies we've seen in this country emerged in the 2009-2012 time frame when the Ontario, Québec, and Federal governments all launched initiatives that provided incentives for third party capital to join them in funds-of-funds structures. That capital was then deployed to GP led funds and capital was, in turn, invested in the next generation of innovative Canadian companies.

Programs such as these, where we see a continuum of entities and funding, have really been at the core of funding within the Canadian ecosystem for venture. The beauty is that those early government supported fund-of-funds investments are actually generating real returns for those governments. They aren't grants. They aren't giveaways. They aren't concessions. Through these programs the government has received all the ancillary benefits of building high value jobs, creating more robust economies, getting engaged in the innovation ecosystem and at the same time, generating a real and meaningful return on their capital for Canadians.

That's how you build a virtuous ecosystem. So, there is clearly a huge role for governments to play. It's both direct, and indirect, but most importantly it's about smart, sustained and engaged policy.

Why is it important to achieve this objective?

Peter: If we do this right, we create the next generation of jobs for the students being trained within our academic environments. We create high value jobs, and we create a virtuous ecosystem between innovation and academic centers. Through building companies and having capital flow back into academic centers, we create transformative products for patients that address unmet needs. And for groups like us, we create returns for our investors, our pension plans, high net worth individuals, and corporations. And so again, it's all about a virtuous circle. It's about patience, impact and a cycle that benefits everyone. And if we do that, I think we transform the Canadian economy.

What therapeutic areas within biotech are you most excited about? Where do you see unmet needs?

Suman: One that we are definitely very excited about is oncology. About 40% of all invested dollars today go toward companies that are developing drugs against various oncology indications, which makes this the single largest therapeutic area to receive VC investments.

We have seen huge strides in developing novel therapies over the last two decades across various cancer types, which has been fueled by an influx of capital, leaps of innovation and a better understanding of the underlying cause of these cancers. However, many of these drug approvals have been focused or clustered within just a few subtypes of cancer including lung, breast, genitourinary, leukemias and lymphomas; whereas other cancer types, such as brain, head and neck, pancreatic, ovarian, GI, colorectal and many others have seen a low to modest number of drug approvals at best over the last two decades. While we have seen some great innovation come through, there is still a lot of unmet need that must be addressed for various cancer patients today.

How has the field of oncology evolved over the last few years?

Suman: There has been a paradigm shift in the way many oncology patients are managed today. Historically, patients were treated with highly nonselective agents called chemotherapeutic drugs that kill cancer cells, but also destroy normal, healthy, dividing cells. These result in extremely poor quality of life for patients, as well as high levels of toxicity, which are unbearable.

Recent years have seen the advent of targeted therapies, which are a stark difference from the way cancer was managed for many decades. In fact, there was a recent review article published by authors at the FDA and the NCI that evaluated trends in oncology drug approvals from January 2000 to October 2022. This report showed that there were 206 distinct oncology products approved across over 500 or so different cancer indications—and over 90% of those approvals were targeted therapies.

Leaps of innovation including sequencing the human genome, the use of multi-omics techniques such as transcriptomics, proteomics, or using in-silico/AI-enabled drug discovery approaches have collectively contributed towards the development of these targeted therapies.

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> [Life sciences companies] need to think about how to commercialize and distribute all while being eight to 10 years away from any customer feedback. It's a very different industry with no positive feedback loop from customers in the short term.

Some classes of targeted therapies that were approved in the last two decades that are worth pointing out include kinase inhibitors, antibodies, immunotherapies, cell and gene therapies and antibody drug conjugates. We expect to see continued innovation across these classes and several next-generation modalities.

What are some other breakthrough discoveries and approvals that you have been most excited about?

Suman: The last decade saw the approval of practice-changing medicines and several “firsts” within various drug classes. Some cancer types saw drug approvals after decades of no new therapies approved. While it is difficult to recount every single one of them, there have been a few that I have been excited about:

- 2011 marked the approval of the first immune checkpoint inhibitor, Ipilumumab (CTLA-4 inhibitor) for advanced melanoma, as well as abiraterone acetate (CYP17A1 inhibitor), a targeted therapy reducing androgen production for metastatic castrate resistant prostate cancer, which was transformative in the prostate cancer treatment.
- 2014 was a significant year for immunotherapy, since the first PD-1 targeting immune checkpoint inhibitor, pembrolizumab (Keytruda) was approved for certain patients with melanoma, with subsequent approval across multiple indications.

- 2015 saw the approval of the first cyclin-dependent kinase inhibitor, palbociclib (CDK4/6) for postmenopausal women with ER-positive, HER2-negative metastatic breast cancer. This was followed by subsequent approval of two other CDK4/6 inhibitors, which has been game-changing in the way breast cancer patients are managed.

- 2016 saw the approval of the first BCL-2 inhibitor, venetoclax, for chronic lymphocytic leukemia and the approval of the first PD-L1 targeting checkpoint inhibitor, atezolizumab for locally advanced or metastatic bladder cancer, making this the first approval in bladder cancer after 30 years.

- 2017 was the year that marked the approval of the first CAR-T therapy targeting CD-19, tisagenlecleucel (Kymriah) for children and adults up to the age of 25y with unresponsive/ relapsed B-cell acute lymphoblastic leukemia.

- 2021 was a historic year that saw the approval of the first inhibitor against a target that was previously considered undruggable for decades. KRAS is a well-established driver of many tumors and has been an elusive target due to difficulties identifying a druggable pocket. The approval of sotorasbib (KRASG12C) for non-small cell lung cancer patients with the mutation was a significant milestone in drug discovery.

- In 2023, one of our portfolio companies, HistoSonics, the developer of the novel Edison system, which uses non-invasive focused ultrasound technology to mechanically destroy and liquefy tumors, received FDA approval for patients with primary and metastatic liver cancer, making it the first and only histotripsy platform available in the U.S. This addresses a huge unmet need within patient populations that were previously ineligible for surgery and lacked treatment options.

Peter: With this non-invasive treatment, patients don't get cut, poked, or prodded. They don't have any chemotherapy. They don't lose hair, and they don't have ancillary like side effects. They literally have this procedure noninvasively and then go home the next morning. This is going to be game changing for patients with liver cancer.

2023 was also the year another one of our portfolio companies, enGene, went public through a SPAC with Forbion European Acquisition Corp. It is currently conducting a pivotal study for its non-viral gene therapy for BCG-unresponsive non-muscle invasive bladder cancer. This drug is being developed as a monotherapy and does not require combination with a device or BCG or PD-L1 / PD-1 therapies and has the potential to be highly beneficial to patients.

What do you look for in entrepreneurs that are creating a product for some aspect of human health?

Jacki: When speaking to investors, you want them to feel your passion for the journey you are on. You want to demonstrate that you are far more knowledgeable in all aspects of the program than they would be able to ascertain by doing a little bit of background research in the area.

An entrepreneur requires extraordinary drive and tenacity—it's hard to take an idea or a new product that you've discovered in the lab and move it forward. It's tough out there when you're wanting to move your idea to the next level to secure funding, to find partners and to have people come and work with you on your project. You're going hear a lot of no's. You're going to get a lot of questions, and you're going to have to work through those no's and those questions and understand why you are hearing them and what you can learn from them. Finally, having a good network of mentors and advisors is extraordinarily important. These should not just be names on a slide, but people that, if we speak to them, they will confirm your deep engagement and passion for what you are doing.

Particularly in life sciences, what's important for entrepreneurs to have a view on?

Jacki: Unlike other sectors, the life sciences industry is highly regulated. You will need to understand all regulatory considerations along with ways to take your product from concept to something that can be used in humans. On top of this, each jurisdiction may have different ideas of what constitutes a "safe" product, characteristics your product needs to be first administered into humans and even the type of evidence you need to provide.

You may have the most innovative product to treat a particular disease, be able to show the regulatory authorities that it is safe to enter the clinic and that it has a profile to make a difference from the early animal studies, but it takes much more than this to have a successful product. Having insight into market dynamics early can have a huge

impact in the design of your product. How will the product be dosed if a therapeutic? How will the clinical workflow need to be changed to adopt your product? What attributes will be needed for health systems to be convinced that your product provides meaningful improvements to patient outcomes to justify premium pricing?

You need to know, as best you can, where your product will enter the market, your REAL market size, steps needed for reimbursement, who will administer or prescribe your product and the dynamics they live and work in, the clinical program you will need to embark on to eventually gain regulatory approval, and who your competitors are. Working backwards through all of this will help guide you forward.

Peter: With IT, for example, you can launch a product and, in a year, get customer feedback. Life science entrepreneurs have to wait years for customer feedback. They need to do a lot of R&D to get to the product—without getting any of that feedback from the customer, because they don't have product approval. They need to figure out how to get the regulator, and how to get reimbursement in place. They need to think about how they're going to commercialize and distribute, and they have to do all of that while being eight to 10 years away from any customer feedback. It's a very different industry with no positive feedback loop from customers in the short term.

What advice can you give to first time entrepreneurs who are planning to present their vision to investors?

Jacki: The number one thing is, know your audience. Are you speaking with a venture capital group, an angel group, a government agency, family office, or friends and family? Make sure you do your research to understand what they're looking for and the way to present to each audience.

If you're speaking with a sector specific venture capital group, you are going to need to be prepared and do your homework and go into much more detail and focus less on general background. For a group that may not be as sector specific, you may need to spend more time on background and be less technical.

I can't tell you how many times entrepreneurs show a market size slide which includes everything under the kitchen sink in it, when the real market size for their product is a tiny slice of the overall market. For example, you may have a product that addresses one particular patient type that has cancer—don't show your market being all patient types that have cancer as your TAM. Your market size is going to be your vertical in the area your product or service is within.

Be clear where you want to move your program to with the funding you are asking for—including the milestones the funding will achieve. You will need to understand what the incremental steps are and present cogently how you will achieve those millstones.

What is your 10-year forecast for the industry?

Suman: I think there will be continued innovation and better medicines that bridge existing treatment gaps. The last couple of years have been challenging for many companies that were not able to raise capital, had to make cuts to their programs or staff. I believe this serves as a reminder for everyone in the biotech ecosystem to remain thoughtful and diligent, because ultimately, these decisions can have a material impact on patients' lives.

Jacki: AI and machine learning are providing new tools to harness copious amounts of data that we can capture, store, and analyze, which was unimaginable even just a decade ago. These tools have begun to, and will continue to, speed the process of uncovering new scientific innovations and turn these innovations into safe and effective products tailored to the needs of patients.

Oncology treatment and screening has benefited tremendously from these tools. We now know from the innovations of the human genome project spawned more than 20 years ago that no two cancers are identical, and we are now learning how to treat an individual's disease rather than treating all patients alike. Until this last year, there were no therapeutics available to stop the progression of Alzheimer's disease and we now have the first therapeutic for AD on the market. With many new innovations following behind.

Using large data sets, machine leaning and AI we will be able to target therapies for patients in the very early stages of developing dementia through the analysis of blood samples, perhaps changes in speech patterns, eye movements or retinal scans. None of this would be possible without these new tools.

The future continues to hold tremendous promise to continue to decrease morbidity and provide better health for

humanity.

Peter van der Velden is a seasoned entrepreneur and investor with over 28 years of experience across various industries, including life sciences, information technology, and consumer sectors. Throughout his career, Peter has excelled as an entrepreneur, partner, and mentor, collaborating with successful management teams across various ventures and roles. He is recognized for his results-driven approach and expertise in venture and buyout investing, transaction structuring, strategic planning, business development, and operational management. As the Managing Director of Lumira Ventures, Peter oversees overall business operations and actively engages in growth equity investments, particularly in companies transitioning from development to sales and marketing. His investment focus encompasses non-traditional and consumer-oriented medicines, spin-outs, restructurings, and public companies. Additionally, he plays an advisory role with both federal and provincial governments, contributing to healthcare innovation and innovation financing policies.

With over 20 years of life science, IT and business development executive-level experience, Jacki Jenuth is a key member of the senior investment team sourcing, conducting diligence on, structuring deals terms for and working closely at the board level with portfolio companies. Jacki has a strong reputation for providing the focus, clarity and cohesion required to drive projects from efficient inception to effective completion. Jacki focuses on early to mid-stage private companies involved in all aspects drug discovery and development utilizing a variety of platforms from complex biologics to small molecules in a variety of indications including oncology, neurology, rare disorders and inflammatory diseases. In addition to her investment activities, Jacki also directs all aspects of Lumira Ventures' information technology initiatives having developed a world class venture capital analytics platform. Prior to joining Lumira Ventures, Jacki worked at Base4 and Open Text Inc. where she developed, sold and provided support for enterprise content management solutions targeted to the biotechnology and pharmaceutical industry in North America and Europe.

Suman Rao comes from a strong life science background, with special expertise in oncology and developing multi-targeted strategies to treat advanced cancers. Suman joined Lumira in 2021 as an Associate and focuses on conducting scientific and technical diligence of investment opportunities. She remains extremely passionate about understanding drivers of complex diseases and through her work at Lumira Ventures, hopes to bring novel therapies to patients by promoting cutting-edge technologies and medicines. Prior to joining Lumira Ventures, Suman worked in healthcare consulting at L.E.K. Consulting in Boston as a Life Sciences Specialist. During her time at L.E.K., she provided strategic advice on growth opportunities, pipeline expansion, potential M&A partnerships and financial modeling. Her clients included start-ups, biotech and pharma companies developing cell & gene therapies, protein degraders, small molecules and RNA-based therapies within oncology, neurology, rare diseases and ophthalmology.

To discuss these issues, please contact the author(s).