IMMREVIEW

JULY 2021 | NEWSLETTER #35

When MedTech behaves like Biotech

TISSIUM's biomorphic, programmable polymer

IMMR Accelerating your innovative research

When MedTech behaves like Biotech

An interview with Christophe Bancel

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What gives your job meaning? For us, it is the privilege to have the opportunity to work with women and men from diverse backgrounds driving innovation to advance health care. Innovation in health care means solving unmet medical needs and coming up with new solutions for caregivers and patients. This is made possible by the synergistic work between researchers, physicians, engineers, and investors or funders. At the beginning of any medical revolution there is often a start-up company pursuing a vision, but wherever it stems from it always involves pioneers working tirelessly to bring their concept to reality. We are glad to introduce you to one of them.

Christophe Bancel is the Co-Founder and CEO of TISSIUM, a Paris-based, venture-backed start-up that is pioneering the development and commercialization of biomorphic, programmable polymers, novel biomaterials that once applied and activated are intended to be used for tissue repair and other indications initially in nerve repair, GI, cardiovascular and ENT. We had an opportunity to speak with Christophe about this innovative technology and its path from conception to reality.

Christophe Bancel
Co-Founder and
CEO of TISSIUM

Welcome Christophe, would you please begin by describing your core technology, what biomorphic, programmable polymers are and what unmet needs they are intended to address.

CB: If you look at surgeries, in many ways the techniques themselves have not really evolved for many years. The methods used to access organs and tissues have improved dramatically, moving from open surgery to minimally invasive surgery and now even to the use of robotics. However, once you are on the target tissue itself, these procedures have all been and are still traumatic. In other words, you damage the tissue while repairing it: You make holes, you use staples or sutures, you have to cut, you have to use tacks, anchoring systems, etc. All of those techniques are invasive and traumatic. All the great progress we've made with minimally invasive surgery and robotics, which brought tremendous value to patients, did not really change the way target tissues

are fixed. We believe that this limitation comes from the lack of materials, because if you want to change the technique fundamentally, you need new materials with new properties that can work in new ways.

And this is precisely what we have. It is a new material for tissue repair and reconstruction that was originally designed by a team at MIT. The material consists of a polymer that is constructed from components that are already present in the body, so it has a very attractive biocompatibility and biodegradation profile. We call the polymer biomorphic because it is a soft, elastomeric compound that will comply with whatever tissue to which it is applied to assist with healing. And once healing is complete, the polymer will bioresorb. The polymer itself is not comprised of a single monomer in a repeating sequence; rather, it's a combination of three monomers that are used together. We say the polymer is programmable because by combining the monomers in different proportions, or slightly modifying the structure of the monomers, the polymer's mechanical properties and speed of degradation can be altered. In this way, we can tailor-make polymers that will be better suited for one certain type of tissue or application versus another one. We don't believe that one polymer could work ideally on every single tissue in the body, because the way a bone behaves is very different from the way an artery would behave, or a lung, the bladder or a segment of intestine.

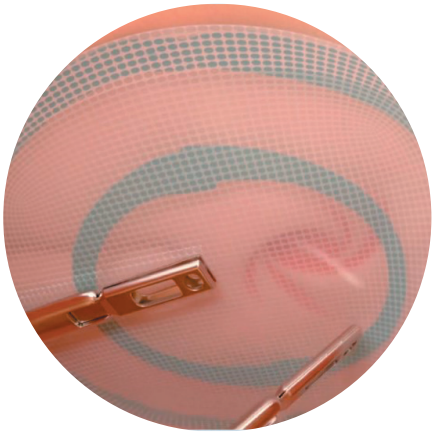
"OUR POLYMER CAN BE OPTIMIZED TO COMPLY WITH THE UNDERLYING TISSUE, AND THIS IS A KEY COMPONENT OF ITS SUCCESS."

Our polymer can be optimized to comply with the underlying tissue, and this is a key component of its success. For example, if you have a very strong and adhesive polymer that can seal soft tissues back together, but if it's also a very stiff compound that can't accommodate motion, that mechanical stiffness will be translated from the polymer to the underlying tissue and damage it and/or delay healing. However, if you have a compliant polymer for soft tissues, it can accommodate mechanical stress and better protect the underlying tissue, providing a better outcome.

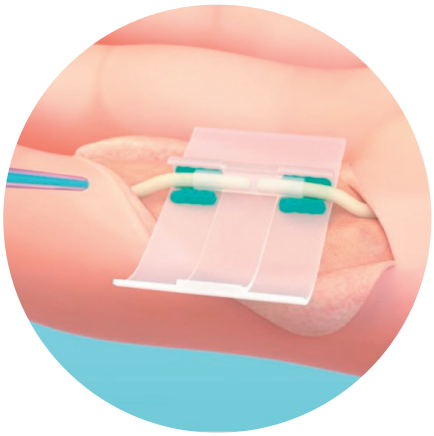
Seen through the eyes of the FDA or another regulatory body, how much can you modify the polymer's structure before it is viewed as a different medical device?

CB: The answer will change over time. Today, we are introducing a brand-new family of biomaterials. It's not simply PLGA [poly(lactic-co-glycolic acid], PLA (polylactic acid) or collagen – which are already well-characterized - that we are modifying. Right now this is a novel class of compounds at an early stage, so each preparation and indication will have to be fully evaluated. But looking 10 or 20 years down the road, as we gain more experience and predictability with these materials, things will change. So as you can see, we have a long-term view for the company. Look for example at WL Gore & Associates that pioneered Expanded Polytetrafluoroethylene (ePTFE, or Gore-Tex). They have built an amazing enterprise out of one single material, and they have been able to master it to really understand what it can and cannot do, and what the implications of this are when using it to design new products including medical devices. And over time, the perceived differences between different products that are constructed of ePTFE diminish. This is what we're trying to accomplish as well. That's our aspirational vision.

We're in the space of bioresorbable materials that are activated by light. Today we're using the polymer in two ways: One way is as an adhesive – to bring tissues together or to secure other medical devices to tissue. The other way we're using it is as a resin for 3D printing. Today, one of our product solutions is a combination of both components that use slightly different versions of the polymer: One is a prefilled syringe with an adhesive for nerve repair, and the other is a 3D printed chamber to secure and protect the repaired nerves.



Application of TISSIUM's polymer and its use in hernia repair.



3D printed surgical scaffold from TISSIUM's polymer in nerve repair.

From an FDA point of view these are currently two distinct chemical entities, so we have to provide all the details for each. But you can imagine down the road, when the FDA would have seen 7, 8, 9 or 10 products with the same chemistries, they would be ready to look at these the way they're looking at Nitinol, PLA, PLGA, as materials that are very standard even though different preparations of them can have differences. Our strategy is to develop our polymers both for our own products and also for devices that are designed for and/or with partners. At the beginning of course we had to just start with our own products. But as we are growing now and getting closer to having innovations ready for patients, We are beginning to have the right evidence to attract partners.

It gets even more complicated! We had to construct the platform from the bottom up. This material had never been produced, so we had to design manufacturing processes and scale them. We even had to establish our manufacturing capabilities because there were no subcontractors that had the required equipment, so we had equipment custom made for us. And now we have a facility that's under our full control, so we can start to expedite new program development. So we're not a typical Med Tech start-up developing a single product and working to get commercial traction to attract an acquirer. We are developing TISSIUM more like a biotech company, where we have programs that we will develop and commercialize on our own, and we will also have products that we will design with and for partners and license out. This is exactly like how Gore did it. With TAVI valves, the skirt is frequently made out of ePTFE. However, valve developers don't manufacture the ePTFE, they rely on companies like Gore for that material.

"WE'RE WORKING TO CREATE AN OPEN SYSTEM THAT INNOVATORS WHO HAVE A SPECIFIC NEED COULD ALSO UTILIZE, WHETHER IT'S FOR 3D PRINTING OF CUSTOM ELASTOMERIC DEVICES, OR CONNECTING TISSUES TOGETHER OR DEVICES TO TISSUES."

We're working to create an open system that innovators who have a specific need could also utilize, whether it's for 3D printing of custom elastomeric devices, or connecting tissues together or devices to tissues. Our strong IP position will allow us to do this without sacrificing our competitive advantage.

Following your biotech model, do you see becoming a publicly traded company in your future?

CB: I see financing as a means, not as a destination. My destination is to help patients, so that's not our focus. That being said, and I can't predict the future, I see that eventually, if we can demonstrate the benefit of using our platform, and if we can demonstrate our capacity to grow multiple verticals by ourselves and with partners, then accessing public capital could make sense.

Investors often expect laser focus from their CEOs, and to take even one new product into a new market is quite ambitious. You've been able to advance multiple programs in different disease areas. What have been some of the challenges and what have been some of your strategies?

We are very focused on the material – that's our DNA. Anytime we develop a new program, we use that as a use case to expand and highlight the versatility of the platform. First, we started with a cardiovascular sealant, which was a way to demonstrate the polymer's adhesive properties. After that, for the second program which was in the space of nerve repair, we had the idea for how to use our polymer for this, but we also needed a chamber to hold and protect the nerve, and we had to make this as well. We did this using 3D printing techniques, thus allowing us to highlight a new technical capability of the polymer. Then after that we designed a product in the hernia space, where we are improving the ability to secure an existing implant – a mesh - inside the abdominal cavity through a laparoscopic procedure. This allows us to demonstrate coating devices with our polymer, delivering them laparoscopically, and activating the polymer in a minimally invasive manner, thereby opening yet another new technical vertical. Each time we have done this we've also improved our internal capabilities.

Our cardiovascular first program took us six years to get to a validated proof of concept that was scalable, including having to build manufacturing capabilities. For the second program in nerve repair, we had to develop 3D printing of our polymer at an industrial, FDA-acceptable scale in a cleanroom environment. It took us four years total to develop that. And the hernia application took us one and a half years to develop.

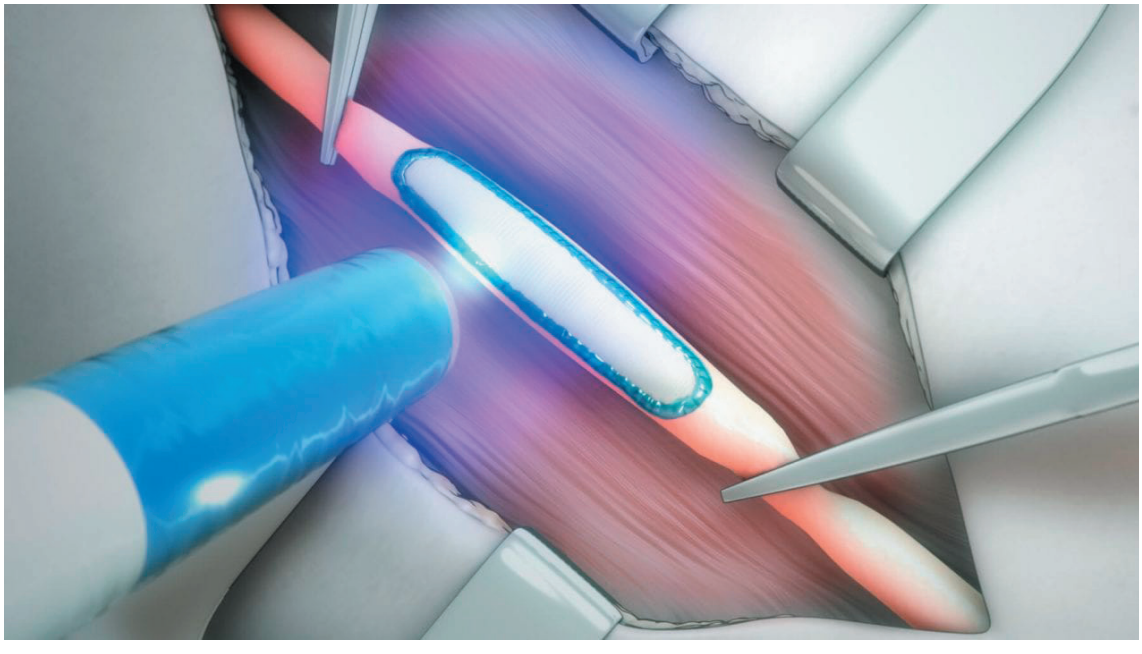
Anytime we go after a new vertical, we create a separate business. Each one is a company within a company. As soon as we decide to commit and advance the development of a new vertical, we create a fully owned affiliate that owns all the rights in that field. Today we have one affiliate for cardiovascular, one affiliate for hernia, and one affiliate for nerve repair, all of which are fully owned by Tissium. We engage quite early in our business design process with KOLs. Elise DeVries, our head of portfolio innovation strategy and an alumnus of the Stanford BioDesign program, drives the independent business case for each vertical.

The key challenge of our business model is that we cannot scale commercialization alone in all verticals. When we work in a specialty area where the target audience of surgeons is limited, there we want to go full speed alone, especially if on top of that we have the potential to have a portfolio of solutions in that vertical. With just one program in your platform it does not really make sense to build a sales force. However, if we can have two, three or four programs in a therapeutic area that requires limited sales support because you don't need to call thousands of surgeons, we want to own and run that business ourselves. For other therapeutic areas where we can make one product, or maybe two, and not a portfolio of solutions, and where we would need to reach thousands of surgeons, we want to partner and we want to slide into an existing portfolio, which again aligns with a biotech model.

"OUR APPROACH IS NOT TO JUST KEEP AND CONTROL OUR ASSETS. WE WANT TO PUT THEM IN THE HANDS OF THE RIGHT COMPANIES TO DEVELOP NEW PRODUCTS AND TO MAKE THEM ACCESSIBLE TO PATIENTS."

If we can partner one asset, we have time and resources to make a new one, and then to keep doing that. The difficulty for a company like ours is to reach a scale to be able to do this well before we can begin to find partners. Today our projects come from our own priorities. As we become established, hopefully people will call us with their own ideas on how we might work together. So our approach is not to just keep and control our assets. We want to put them in the hands of the right companies to develop new products and to make them accessible to patients. It's a twist on the single product focus that's typical in the Med Tech space.

Rendering of TISSIUM™ polymers helping to close a surgical wound. The viscous pre-polymer is activated on-demand, within seconds, using a visible blue light. The resulting bond is both adhesive and elastic, allowing the polymer to comply with the underlying tissue while remaining strongly adhered. ▼



Typically, venture capitalists invest with a limited time horizon within which to exit. Can you talk about the financing strategy that enables your vision?

CB: Fortunately, our investors are united in having a long-term vision. If I had on my Board people who were going in different directions, with short term vision, it would have been impossible to manage. In a company, the worst thing that can happen to you is to have misalignment at the Board level. It kills the greatest technology, the greatest people. If you have misalignment in the board, the company will fail. So I'm very fortunate today to have a very strongly aligned Board. They believed that it could be done, it could be big, but it would take time. It was never the idea that we could do something and sell the company in three years. We could not do that - we had to build a manufacturing facility! To develop that alone can take two to three years – if things go well.

"THE MORE WE PARTNER, THE BETTER WE'LL BECOME AT SUPPLYING, CREATING A VIRTUOUS CIRCLE THAT WE CAN LEVERAGE."

But tomorrow, if we are successful, we will be the sole provider of the polymer. Med Tech companies don't have the necessary facilities, people and know-how. Any partner that licenses in our technology is going to ask us to supply it. The more we partner, the better we'll become at supplying, creating a virtuous circle that we can leverage.

Have the approaching new European Medical Device Regulations impacted your development or strategy?

CB: We are not a company with multiple SKUs that would have to be recertified, and being a Class III medical device we are already working within highly rigorous regulatory requirements. The thing that is most worrisome is what remains unknown or not fully defined. With this in mind, we did make the decision to pivot our regulatory and market entry strategy to the US. And knowing that we would be able to leverage what we do in the US back to Europe. This will allow us to see how things unfold in Europe before we try to enter the market there. For us, as in any startup, especially when you don't have generate revenue, six months' delay can be catastrophic. Six months' delay for a big company is a hit. For us, it's death. So with all the uncertainties already in what we do, we decided to focus on where the environment is potentially a bit more predictable, stable and consistent.

And finally, having transitioned from Biopharma/Biotech into MedTech, what are your observations of the major differences between them?

CB: There are important parallels: In both fields, we're in a highly regulated industry. We're helping patients, so we have to do it right. It requires enormous investments, and for good reasons. The regulations are different, but we just learn these differences and adapt accordingly. One thing that's different is the timelines for scaling the business. Things go faster in the MedTech space. That is attractive to me and is more compatible with my character compared to my days in Pharma.

Christophe, this has been fascinating, thank you very much!

CB: And thank you as well.

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