

TISSIUM CEO's Vision Is To Make The Tissue Recon Label Stick



CHRISTOPHE BANCEL, CEO TISSIUM

Christophe Bancel, CEO of French medtech innovator TISSIUM, has made a career in various parts of the health care products industry, identifying business opportunities, founding, directing and leading ventures, and planning for contingencies. The ex-Serono and UCB executive is now testing his adaptability and leadership qualities by bringing a versatile class III synthetic polymer device into key markets.

BY ASHLEY YEO

Spotting the commercial opportunity for meaningful medtech innovation that improves workflow and fits into the value-based health care arena is a particular skill. Driving forward regulatory and reimbursement strategies at the same time requires different types of expertise, but for the CEOs of promising, smaller medtech companies, these roles are often combined.

TISSIUM's Christophe Bancel is one who fits the profile and has his own way of addressing processes. Key for him is that a company's core technology are compatible with a platform-based approach, but this is not always the case.

A sense of realism plus contingency planning are further elements of the leader's skill set.

TISSIUM CEO Christophe Bancel was talking to fellow founder of the company, Jeffery Karp, when the subject turned to a Massachusetts Institute of Technology (MIT) project being developed by Maria Pereira. The technology was a biocompatible liquid polymer, and Bancel was attracted by the claim that it could suture the heart of newborns. Pereira's technology was claimed to support faster healing and obviate the need for traditional suturing.

Seeking to take the idea further, Bancel envisioned a technology ecosystem built around the synthetic polymer, and up to four formulations, initially, to address different clinical needs. Bancel, now 45, already had a track record of innovation development in commercial circles, and had set up the iBionext funding vehicle for start-ups. Evidently, he had the bandwidth for another challenge – one he acknowledged, in an interview with *In Vivo*, is his most exciting to date.

"To start with, we took an indication that was relatively simple – an add-on to vascular sutures – with the idea of spinning the technology out in different directions." With Pereira joining the venture at inception, being central to the company and having since been elevated to chief innovation officer, TISSIUM set about launching a clinical trial in humans. The trial was in 2016; and in 2017, the product was CE marked as an add-on in vascular reconstruction.

Vascular reconstruction was the springboard for the planned wider R&D program extending into new formulations for additional indications that now include peripheral nerve repair, a second-generation specific cardiac application, and, soon, the gastrointestinal (GI) field. The platform element is crucial: Bancel envisaged the company more as a tissue reconstruction specialist than simply a provider of a technology.

Bancel's idea was to do different formulations to match clinical needs using designs

that had a lot of commonality. “We see investment as a fixed cost, and the first step to conquer. We were fortunate to be successful in the first stage of the company’s life, and now we’re at the second stage – phase 2 – expanding into the portfolio of solutions, and leveraging the activities of the past.” Phase 1 of TISSIUM’s business plan was validating the technology and getting ready; phase 3 is spinning out new business opportunities, including 3D printing and drug delivery applications.

TISSIUM’s business model does not involve selling polymers as a basic component, rather it designs kit solutions. The selling point to clients is that one of its kits will have the right biomechanical properties to allow them to implement solutions that are tailor-made for surgeons.

TISSIUM’s first innovative tissue reconstruction product is called SETALIUM Vascular Sealant. Looking to the bigger picture, Bancel decided early on to grow the company by building its own manufacturing capabilities. Its 1,150-m² facility is at a brand-new site in Roncq, near Lille, north-eastern France, and is being set up to produce all versions of TISSIUM’s polymer, sterile and ready to use in a pre-filled syringe and packaged in a box with the right accessories for the surgeon.

Contingency Planning

TISSIUM designed the platform in a way that, once successful, it could be scaled up. But contingency plans were also being laid. “You always have in mind that the plan could fail. But with the critical data, we felt relatively strongly that if we were able to translate the technology, it would work.” In the early days, the company was producing 5g batches; now it is producing human-grade polymer, class III bioresorbable medical device implants by the kilo.

Bancel admitted that it took TISSIUM “a certain time” to develop the first formulation, but now it has three variations of the polymer, which can be used in different set-ups. It also retains the ability to use the polymer in its liquid form, as a sealant or adhesive. In parallel, it uses the polymer as a resin.

“We pick a specific application and proceed based on user case,” explained Bancel. As such, TISSIUM develops everything that supports the user case, knowing that, if successful, it can pivot to other

applications, using the same building-block technology. The second application, peripheral nerve repair, is a bid to design nerve conduits that protect the nerve and allow growth inside.

3D Applications

The company can now additionally print 3D medical device implants with extremely high resolution, all bioresorbable in the body. This application is used in the production phase, but it is not yet ready for personalized applications. “The one application where 3D is truly personalized is at the bench, and our technology may lead to that, but not in the short-term,” stated Bancel. The approach TISSIUM has selected for its new material is to use 3D printing as a means of manufacturing complex architecture. “Down the road, when we have fully industrialized our capabilities, we will be able to do customization and design specific implants for patients with the same system,” he added.

Bancel is clear. “First things first; we must demonstrate that we can make complex medical devices using our own resin with high-quality manufacturing processes using 3D printing. Once the system is validated for a few products, it will be easier to switch to personalized medicine.”

User Case Focus

Success in developing medtech innovations requires the core technology to be compatible with a platform-based approach. “That is not always the case. There can be great technologies that are specific and cannot be expanded into a portfolio,” Bancel observed. “What we have tried to do is set a long-term vision, typically from a small start, and focus on the user case, pick a specific hands-on project that we can develop and learn from along the way, expand that, and then grow fast. That’s the plan.”

“We see ourselves as an innovation engine,” said Bancel. TISSIUM’s strength is its capacity to identify which clinical needs its polymers can provide a solution for. “Now that we have designed an internal process of how to move from R&D to clinical human validation, we can leverage our work across indications. That expedites our work. We learn from experience about how to streamline in-

FUNDING TO DATE

TISSIUM raised €8m (\$9.04m) in 2013. In 2016, it raised a further €22.5m in a series A led by Sofinnova Partners and Bpifrance. For its series B, the company is planning to raise around \$40m.

novation, and can then go quickly to validation in human clinical trials.”

Learning From Mistakes

Part of the management process involves learning from past mistakes. “We had this vision, based around the planned phases, about how we should design the organization for five or 10 years down the road,” explained Bancel. The plan set out how, if TISSIUM is to be successful, the company would make decisions at different time-points to prepare itself for expansion. “That’s why we wanted to set up our own manufacturing capabilities. We are a relatively small medtech company and yet, now, we are equipped to serve a breadth of supply needs with a diversity of polymers.”

TISSIUM set up its own plant precisely because it did not want to be dependent on certain subcontractors for its very innovative processes. “When you do real core innovation, you don’t find people to do what you need them to do – because it’s new.” He continued, “We had to design new processes for our products – it was complex – but if we were to design effectively, we could use the template for any new product in the future. It was a key asset.”

Bancel said TISSIUM had a very strong IP position, including in composition of matter, application and accessories. “And now we also have control of the supply.”

The idea is that the more differentiated products that TISSIUM produces, the more it will be able to optimize its costs, controlling both the upstream and the downstream. “And in the middle, we have design processes so that we can accelerate innovation and have exclusivity. “We are a design factory of innovation around our polymers.”

A Time To Partner?

But TISSIUM won’t do it all by itself. It wants partners in targeted areas,

acknowledged Bancel. “We want to be really good at what we do, and to partner in areas where we are not, so we can learn from others.”

TISSIUM’s polymers will be available for third parties who want to work with the company, but Bancel feels that these products need to be more than research-grade technology. “If clients want a final commercial solution, we don’t want to provide them with a ‘half-baked’ solution, be they a large medtech or a small start-up.”

Partners also need to know that they have protected technology. “The beauty is now we can provide the core platform where the technology is effectively complete, and the partner can go straight to commercialization.” TISSIUM wants to partner with companies with products already in place, that have customer bases and know how to approach surgeons in each of the target countries.

Making The Lille Plant Digital

Bancel is determined that TISSIUM remains ahead of the pack and at the forefront of the processes by which businesses evolve. In 2018, it conducted two crucial digitalization projects that ostensibly do not affect current business, but which will make a lot of difference to commercial prospects over time: one focused on the quality system (QS); and the other on financing and supply processes. The plant now shares an enterprise resource planning (ERP) system that had already been implemented company-wide, making it a fully electronic, pay-per-lot facility. This allows the running of projects in parallel without any constraints on quality. The unit also has 300 m² of clean rooms (four) and a 140-m² analytical laboratory.

The Lille facility is validated, and is running “on hold.” Bancel said, “We are waiting to update our dossiers with the new output. The plant has been designed so that we can increase capacity at each of our reactors producing the liquid product, so we can monitor and increase capacity as necessary.” The plant employs 12 of TISSIUM’s 45 staff, all based in Paris or at the Lille plant.

TISSIUM is working in two geographies, the US and Europe, and is advancing three new products, one is in development, and two in research. All are used in surgical procedures in the

TIMINGS FOR REGULATORY WORK

TISSIUM’s first product, for use in vascular reconstruction, is CE marked, and the company will start investigational device exemption (IDE) work this year with the FDA. In 2020, TISSIUM will begin discussions with the Chinese authorities. In parallel, it will start clinical trials for its nerve program at the end of next year (2020), and will keep more or less the same program and timings for the other cardiovascular applications. GI is being lined up as a project for 2020–21. The first fundraising proceeds were used partly to secure CE approval of the initial product, while the second injection of funding was used to demonstrate that TISSIUM could “spin” the platform, that is, scale the technology, including manufacturing. “Most companies underestimate the cost and complexity of manufacturing and scale, which enables interaction with third parties. For us, it meant digitizing all our processes, so there were no bottlenecks,” said Bancel.

OR – hospital-based products – some for open surgery and some for minimally invasive surgery.

Competitive Landscape

Analyzing where TISSIUM faces rival technologies or procedures means looking at each specific product individually. “From a platform point of view, we are a unique breed, as our polymer family does not have specific competition,” noted Bancel. The tissue reconstruction field is not really defined per se, he said, and in TISSIUM’s case, it means bringing tissues together to heal in a variety of procedures – GI, open and minimally invasive in certain cases.

There is no competition to TISSIUM in the procedure of bringing the nerves back together. The standard nerve repair process is a complex technique involving suturing. “Our quick and simple technique allows them to be glued together.”

Commercial penetration is always a

challenge, and clinicians and surgeons need to be convinced of the benefits of the technology. That requires significant effort. “If we are successful, I am sure people will try to imitate us,” Bancel said. Accessing in a real-world OR scenario takes a long time, and this is a constraint of the system. “This is something we take into account when we bring our technologies to market.”

The current plan is to do soft launches in four selected countries at the end of this year (2019), in the EU and beyond. The reimbursement codes are already available.

TISSIUM Above All

Where does TISSIUM sit in the roster of companies and ventures that Bancel’s name and efforts are behind? (See box, page 29.) “This is the company that could have the biggest ramification in terms of spread; it’s a brand-new material we are working on, and at the raw state. What makes us different is the materials and we have full control of the IP.”

The question for the CEO now is how to transfer that raw value into a business that can be monetized and grow into a large sustainable organization. “The challenge is how you scale and manage speed of development. So far we have done a good – not excellent – job.” Bancel expressed pride in his team, and said the next two years would be a very exciting time for the company. “That’s when we’ll unleash the power of the platform.”

What If...

The key for Bancel was broaching the “what if” questions, such as: what if we could remove or replace sutures in surgeries? “We believed we could do a much better job, which is why we created the company.”

The what-ifs answer the demand pull. “It’s not a one-direction process, but that process *should* start from the demand,” he stressed. The technology is seen as an enabler. “Our role is as an entrepreneur, making sure we answer the right questions. We always take a lot of time to ensure we can answer the what-if questions now, that is, at the outset.”

The other golden rules are to identify both the value of the market and where there is a need, and then make sure that the company can improve the care of the patients. Equally essential, the technology

iBIONEXT – A START-UP STUDIO

Bancel's varied record of health care projects includes being the co-founder of iBionext, a venture that supports health care technology companies from creation to growth, and aims to transform innovation into products for patients. iBionext styles itself as a management company and start-up studio specializing in the creation and development of disruptive health care start-ups. It began in October 2012 with three companies, TISSIUM being one of them, and currently has nine companies, employing 300 people, with some of them showing fast growth. "It was set up by people who were willing to design a place where companies could develop innovative technologies for patients and answer the 'what if' questions," said Bancel.

must improve the efficiency of the health care system by helping the surgeon.

Commercial Plans

As far as the company's commercial plans go, in terms of growth, "We want to have an approach where we can partner with local payers and know the market. We want a selection of specific distributors," said Bancel. The first launch will be defined as a user case. He reiterated that TISSIUM's products have a very strong competitive advantage – as a fully synthetic product and devoid of animal or human proteins, the technology fits well in those geographies that have been looking for products that need to observe local and cultural criteria.

The vascular sealant application is "just the start," and besides cardiac and nerve, GI and ophthalmology applications are among the R&D options for TISSIUM's proprietary technology. The next stages include not just more of its own products, but also designing for third parties, including the larger medtechs. The immediate goal is to use the new chemistry and build the industrial capability to produce the polymer at scale.

One of the advantages is that, for tissue reconstruction, the developer can play with the ratios – with different proportions leading to distinct properties. The polymers are bioresorbable and fully hydrophobic, don't react with blood, and don't dilute, unlike fibrin- and bovine-based sealants. They polymerize on being mixed and on a light stimulus. The texture is user-friendly in surgical procedures. The product moves from its unpolymerized liquid, viscous state into a polymerized, solid yet flexible state.

The Bancel Approach

Driving the whole concept into life, Bancel breathes pragmatism and a flexible approach. "I have very high aspirations for what we're trying to embark on with my team. I am extremely optimistic – but also paranoid! Life will not always treat us easily. We plan for the best and we manage for the worst."

Elsewhere, he said the staff needed to be themselves, a tenet he applies to himself too. "Don't try to be somebody else." He added, "I tend to be hands-off – I trust my team to know what's good for the company. I hire smart people. And I put the right people in the right jobs and that helps us make the right decisions."

But with value-based health care coming onto the agenda – steadily, if not super swiftly – TISSIUM's technology solutions could be seen as fitting well into the concepts that promote affordable, patient-centered solutions. "I hope so – that's what we try to do. What is key is that a product should be assessed on its value – not on its cost. It's about the value that it brings to the system, whichever way that is defined."

The challenge with the value-based approach is that you need to define metrics to be able to define value. "Managing things by cost is extremely easy – it's what we've all been doing until now. But managing things by value needs a definition of value – which can also be subjective. This is maybe why there has been a struggle to get on with VBHC," Bancel opined.

Crucially, he says there is a need to convince people of value, and a need to communicate with data. "At TISSIUM we define products with a very specific value. The one-size-fits-all approach is not the one we want to pursue."

MULTI-TASKING

Christophe Bancel, MSc (Master in Biochemistry and Molecular Biology, University of Tokyo), MEng (Ecole Centrale Paris), MBA (INSEAD, Paris), currently has two jobs, besides the CEO role at TISSIUM; he is both the co-founder and a venture partner of iBionext, set up in October 2012 to support health care technology companies from creation to growth. Before 2012, he was director of BrainEver, a biotechnology company focused on neurodegenerative disease treatments based on a homeoproteins platform; and prior to that he founded Prophesee, a French developer of innovative sensor technology for applications in all fields of artificial vision. He held various roles at UCB, ending a six-year stint there as general manager of the CNS franchise business in France. This was preceded by a 30-month posting managing endocrinology portfolio sales at Serono in France. He started his career in a business development role at the biotech Transgene, after which he co-founded and directed at Faust Pharmaceuticals (now Domain Therapeutics).

The Technology

The original technology for TISSIUM's synthetic polymers came out of research and intellectual property from the laboratories of Professor Robert Langer (MIT), and Professor Jeffrey M. Karp (Brigham and Women's Hospital), who co-founded TISSIUM, formerly Gecko Biomedical, in 2013.

The management team chose to rebrand the company to more accurately reflect its mission. While it was perceived as being focused solely on the development of adhesion technology, recent milestones illustrate the company's dedication to shaping the new era of tissue reconstruction, leading to a brand refresh under the name TISSIUM. TISSIUM competitors include companies like J&J's Ethicon, BD (Bard) and Baxter, among others. ▶

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Comments:

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