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FEBRUARY 2022

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"It was never my intention to be CEO," says Bernard Coulie. In fact, when the Belgian-trained M.D., Ph.D. arrived in the U.S. in the late 1990s, he had only thought about being a doctor. "Coming from Europe to be a gastroenterologist at the Mayo Clinic in Rochester, MN, was a big deal," he relates. Though much of his time at the Mayo was split between clinical practice and lab/bench-type research, he'd also done some sponsored R&D for the likes of Regeneron and Novartis. And before he knew it, J&J came knocking with an opportunity to enter industry — back in Europe. "I talked well, was able to organize, got promoted into management, and before long was overseeing European R&D related to internal medicine."

However, the Big Pharma was going through a leadership change, and Coulie grew fatigued of frequent restructurings. So in 2006, he left to cofound ActoGeniX N.V., a small biotech in Belgium. Initially, he worked as the head of research and then chief medical officer, which made sense, as ActoGeniX was a microbiome company. In 2010, however, Coulie suddenly found himself taking on the role of CEO. "Because the other guy left for something else," he clarifies. But the investors trusted him, and he oversaw the company through an eventual acquisition by the former Intrexon (now Precigen) in 2015. "Sometimes you have to make decisions and direct a company toward an exit you might not have wished for when you started," he concedes. While that part of his first startup experience may have left a bad taste in his mouth, what didn't was having the opportunity to work on front-running technology — not what's trendy at the time, but what's going to be hot in the future. Now if he could ever do that again. ...

INTRIGUED BY THE SCIENCE

Following what he would call a lackluster exit, Coulie worked briefly as a chief medical officer for hire. Then someone introduced him to Mark Levin, a partner at Third Rock Ventures (TRV). "By then it was the summer of 2015, and we met at their offices in Boston," Coulie states. "He liked me. I liked their model of advancing disruptive areas of science and medicine [i.e., what's going to be hot in the future]. So they started looking for an opportunity for me to join one of their portfolio companies."

At the time, TRV was in the process of setting up Pliant Therapeutics to develop new treatments for fibrotic diseases based on technology out of University of California San Francisco (UCSF).

"I could see that the science was still way ahead of us; data still needed to be generated, and that's always filled with risk, uncertainty, and hurdles," recalls Coulie. But from his perspective, at least the capital formation looked to be well in hand, enabling him to focus on what he knows best. "The science is something I can judge myself, and as a physician scientist, I know exactly what the challenges are when working in high hurdle indications."

Working in an area of high medical need was important to Coulie when he was considering his next move. And as Coulie evaluated Pliant Therapeutics, it appeared to have a unique proposition. "It was not an oncology company, not a cell therapy company, and not another CAR-T, all of which were very hot at the time, but one focused on fibrotic diseases." He joined Pliant Therapeutics in the fall of 2015, initially as a consultant CEO. "I had to get my visa taken care of, which happened in January 2016, and we launched the company shortly after."

STARTING A SECOND STARTUP REQUIRED A TISSUE TEAM

In February 2016, Pliant Therapeutics announced a $45 million Series A and its planned focus of using the therapeutic capabilities of integrin biology and TGF-β signaling to develop treatments for fibrotic diseases in the lungs, liver, kidney, skin, heart, and gastrointestinal tract. "While we may have started with a unique proposition, when talking with other people in pharma and investors, what we were doing was certainly not considered the next big thing," Coulie comments. "'Show us some data,' seemed to be the rallying cry. It took about two years for that to change." In part, this was because they were developing something new, which means they had to figure out the narrative to best communicate what it was they were doing. "As we gained a better understanding of biology and greater clarity around endpoints, people started to see the possibilities of venturing into fibrotic diseases, and we started to become positioned as a leader."

The team had hypothesized that there was a mechanism that selectively activates the master regulator of fibrosis, but in fibrotic tissue alone, which was supported by mouse and monkey data. They started working diligently trying to prove this was the right approach before jumping into large Phase 2 studies.

The problem, though, was around animal models and fibrosis. "These models have been around forever but are limited in their ability to mimic the chronic condition of fibrosis. That's because there is no such thing as a spontaneous fibrotic disease in animals; you must do something to the animal to create lung or liver fibrosis.

Their solution was to use human tissue, which had been used to interrogate biology in academic settings for a long time, but Coulie and his team weren't aware of any companies using it in this manner. In fact, there wasn't even a commercial supplier of any sort at that time, which has since changed. But because of Pliant's unique relationship and sponsored research agreements with UCSF and Stanford University, it was able to get access to human tissue from patients undergoing transplants. "We'd get an explanted lung, which was highly fibrotic, or an explanted liver, which was very sick, and we'd take a piece of it and run that in our tissue lab, enabling us to test drugs on fresh actively fibrotic tissue, which is what you are trying to treat in real patients. This allows you to measure things you cannot measure in a real patient, unless you start taking biopsies of their liver or lung, which is something you don't want to do."

With that solution came a new challenge. Getting that tissue, which must be fresh, means having folks available 24/7 to pick it up. "You can't really predict when a transplant will take place, as these tend to be driven by when an organ becomes available," Coulie explains. He credits Johanna Schaub, Ph.D., as the scientist who drove the

development of the "tissue team." "There were no protocols. There was nothing in the literature, so the team had to figure it out." Basically, the academic institutions they are working with (Stanford & UCSF), call Pliant when they have an appropriate organ available. The company doesn't use a transport service; their scientists pick up the tissue and take it to their lab, since Pliant, Stanford, and UCSF are within a few miles of each other.

Getting access to the tissue and getting the tissue to the lab were just the beginning. It took Pliant a year to figure out how to best use the liver tissue before it died in the lab. "The lung was a little bit shorter," Coulie contends. "We've expanded into kidney tissue and recently started using heart tissue." As with every organ, protocols needed to be set up, as every organ is different. "There's always a validation period, and that takes time, too," he adds. And while startups are known for having a high sense of urgency, Coulie emphasizes patience. "It's critical you take your time on such foundational components, no matter what, because those data will be priceless."

Coulie credits strong relationships with academic institutions as critical to Pliant's success. "Yes, we have agreements, and there's a small fee to make sure we all stay friends," he states. For example, the company gets tissue from Stanford as part of a sponsored research agreement, while tissue from UCSF involves a fee. But Coulie says, when it comes to academics, it isn't about the money. "We publish tons of abstracts, and the researchers providing us with tissue are part of those abstracts." According to Coulie, scientific collaboration, in the truest sense of the word, is how you build strong relationships with academicians.

DATA DRIVES SEMINAL PARTNERSHIP

The efforts began by the tissue team proved a real game changer for any conversation with investors and pharma because the data produced at Pliant proved almost too good. "Initially, we didn't even believe the data ourselves," Coulie contends. But it isn't just the data; it is how they are presented (i.e., the narrative). "We have a very thorough publication strategy that is not just sending out press releases; it's a steady stream of abstracts, poster presentations, and oral presentations at important annual liver and lung meetings." Next, the company began expanding into other indications, creating a steady flow of "peer-reviewed news." "That's what this is all about, the scientific data. Because it's not just investors looking at it; our peers also need to review and accept it. But remember, many investors in life sciences are Ph.D.s or M.D.s, and the only thing they are interested in is the same thing I'm interested in — the data and science."

DO YOU HAVE A MENTOR ON YOUR BOARD?

As Pliant Therapeutics prepared to go public in the summer of 2020, Bernard Coulie knew he needed some additional independent directors to serve on the board. So he and his team put together a profile for the type of person they were seeking. "Someone with public company CEO and board experience was desired, but I also added the word 'mentor,'" he says.

After narrowing a list of dozens, David Pyott, the former Allergan CEO, came out as the lead candidate. The two had a planned one-hour call for their first engagement, which ended up lasting two hours. "Then we had another very long call, and I was blown away; I knew I could learn so much from him."

Since 1998, Pyott has served on more than half a dozen boards and tended to do so for a long time. For example, he spent 17 years on Allergan's board and more than 20 on Avery Dennison's. Today, he serves on four, with the most recent addition being Pliant Therapeutics in January 2021. Given Pyott's career accomplishments, it isn't hard to imagine that he gets plenty of offers from which to pick. So why choose Pliant? What made it stand out? "When I looked at the position specification, it struck me very quickly that this is a group of people who are strong in science, with several having company formation skills," Pyott states.

Pyott believes that any good board discussion should have a variety of viewpoints. "If a board is operating properly during meetings, remarks build on remarks, and you can actually come up with some really cool new ideas on how to do stuff differently." To that end, he interviewed with six of the company's board members, including the CEO. "You have to assess people personally to best determine whether you're going to be a fit for a board, and if the board is a fit for you," he continues.

When it comes to assessing the company, especially one that's public, Pyott says it pays to go beyond the reading material provided. "I like to review perhaps a year's worth of analyst reports, being sure to pay attention to those that are less enthusiastic." He also suggests looking at the IPO filing, as you want to make sure there aren't any surprises buried in the S1. "I think it a reasonable expectation that you know a lot about the company before you ever attend your first board meeting. That way you are in a better position to offer sound advice," he counsels. Another thing he did was to see who the principal investors were. Knowing at least one, he called to get their take on Pliant, using the subterfuge that he was looking at a personal investment in the company. "Be thorough so you don't miss on some huge point," he reminds.

So did having the word "mentor" included in the role description make a difference when Pyott was assessing Coulie and Pliant? "Somebody indicating they want to be mentored sends the message that they want to learn. They want to change. They want advice. They want tradeoffs. They want to improve." And while Pyott notes he enjoys mentoring, to be worthwhile it must go both ways. "Any opportunity along these lines should provide for two-way learning, so be sure to be assessing this aspect while doing your diligence," he counsels.

In 2019, a Pliant scientist was presenting at a major annual liver conference. Turns out someone from Novartis was sitting in the audience and perked up when the human tissue data were discussed. According to Coulie, Novartis was very familiar with the animal model data but had never seen anything like Pliant's human tissue data. Later that year, the two inked a $416 million collaboration, which included Novartis investing in Pliant. That deal catalyzed interest in other investors heading into J.P. Morgan 2020. "Suddenly a lot of investors wanted to be part of the story, and we did a $100 million crossover round that February."

Looking back, Coulie says Pliant and Novartis actually began collaborating before the deal was signed. "We were doing experiments for them already, for which they agreed to pay us retroactively, because they were in such a hurry and clearly convinced as to the quality of work we were doing." Coulie takes this as a positive sign because although most deals are done out of economic necessity, he asserts that the ultimate collaborations are driven by scientists and clinicians who connect with each other and feel there is a common purpose/goal between their organizations.

The Novartis deal certainly made the path to a Pliant IPO much clearer, and by going public, the company then had access to a new group of investors. "The public markets enable you to access really long-term investors, and you need those as you enter into later stage and more expensive trials that can take six to 12 months."

In March 2020, Pliant was starting to test the IPO waters in Boston at the Cowen conference. "Next thing we know, there's been a coronavirus infection at the Biogen global R&D meeting taking place in a hotel next door," Coulie says. And as soon as everyone got home, the whole world changed as the lockdowns spread. There were no Zoom calls. There was no video. "We were on voice calls with our bankers trying to figure out what was the right thing to do." Fortunately, the company's CFO had come from Citigroup, bringing a wealth of banking experience. "We really didn't have anything to lose by pursuing, so we just behaved as if doing a virtual roadshow and IPO was normal." He notes there was an unexpected benefit that all the press around COVID-19 brought to Plaint during this time. "Early on, there was talk around whether COVID patients were going to have lung fibrosis long term, which certainly helped our story." In the end, Pliant went public (NASDAQ: PLRX) on June 3, 2020, raising roughly $144 million.

While fundraising in any manner is a challenge for biopharma CEOs, Coulie warns that, "From day one, you should be thinking and strategizing around a company's pipeline, or you may end up in a place you cannot turn back from." For example, the company's lead indication for its PLN-74809 asset is idiopathic pulmonary fibrosis (IPF). While IPF has a high medical need (i.e., incidence of 10/100,000/yr.), it is also fairly high risk, as the clinical development path is long and complex, the biology poorly understood, and the field littered with failures. "Our approach is based on a methodical derisking from preclinical stage [i.e., fresh patient tissue], into clinical stage [i.e., biomarker work and target engagement using PET imaging], which takes time. But by better understanding the drug's behavior, we are derisking the outcome of large and expensive pivotal trials." Exploring where else a product may bring value (i.e., a secondary indication) can help further offset risk. "This is how we came up with our secondary indication in primary sclerosing cholangitis [PSC]." Both indications will have Phase 2A readouts this year, and if positive, propel the company to its next stage of pivotal and registration trials. Those take time and will require new capital to expand the team and support systems. At the same time, Coulie notes the need to start preparing for the commercial stage and building the rest of the pipeline. "Although Pliant has to be a fibrosis company — and true to that mission and vision — it cannot be a one-trick pony if we truly hope to help patients," he concludes.

BE STRATEGIC WHEN DISCLOSING DATA

It's been said that data are the new oil; their value comes only after they've been refined. For Pliant Therapeutics, this has certainly proven true, but Bernard Coulie says you want to be very deliberate in how you disclose such data. "Usually, it begins with a given data set being discussed amongst the research staff." This might lead to a conversation around what it would take to put together an abstract before a deadline for a certain international meeting. Then, it goes to IP to make sure everything being disclosed is covered by patents. "We don't want to create prior art that prevents us from doing any patent publication." Assuming that goes well, then it goes to what is called a disclosure committee to make sure the messaging is right. "Because we are now a public company, that adds a level of complexity." According to Coulie, it might take a year's worth of work to generate one abstract. The next step could be combining multiple abstracts into a manuscript to be submitted to a meeting or journal. For example, in October 2021, the company published its first big manuscript in *Respiratory Research*. However, you won't find Coulie as one of the coauthors. In fact, when it comes to publishing, he has some very specific advice to fellow scientist CEOs. "Don't put yourself on those to try to boost your resume because you really need to have participated in a scientific way, in the thought process and execution, to be listed as a coauthor."