American film and television star Rock Hudson was diagnosed with HIV on June 5, 1984. He died from AIDS-related complications just 15 months later.

British musician, singer and songwriter Freddie Mercury was diagnosed with AIDS in 1987 and died on November 24, 1991, age 45.

In the mid-Eighties and early Nineties, the deaths of Rock Hudson and Freddie Mercury garnered worldwide attention. HIV/AIDS was proving to be a relentless, indiscriminate, fast-spreading global pandemic.

As the virus leapt through entire communities, it also caught the fascination of Dr. Paul Janssen, the founder of Belgium-based Janssen Pharmaceutica. He gathered together a small group of scientists at the University of Leuven’s Rega Institute to study HIV and AIDS. Within that group was young protégé Rudi Pauwels, a virologist who theorized that by blending science and technology, he could possibly develop a solution that might change the fate of the virus and the lives of hundreds of thousands of people.

“Tibotec, focused on discovering new treatments for HIV. And it was headquartered in our garage, believe it or not!” explains Pauwels. “But while we were discovering the first molecules, it became clear that something was fundamentally missing.”

In the early ‘90s, it was observed in patients taking the first generation of HIV drugs that the virus went away but grew rapidly again leading to another rampant outbreak.

“In 1994, I decided together with my wife to create a company, Tibotec, focused on discovering new treatments for HIV. And it was headquartered in our garage, believe it or not!” explains Pauwels. “But while we were discovering the first molecules, it became clear that something was fundamentally missing.”

The healthcare landscape of the early Nineties was still based on the premise - if you feel pain, we’ll relieve your pain. If you’re coughing, we’ll stop your cough. When it came to HIV, physicians relied on basic trial and error. If Drug A or B didn’t work, then maybe they combined a few of them. And if then they didn’t work, they changed to other molecules.

“But my friend was no longer responding to the drugs,” says Dr. Stoffels. “So we performed a diagnostic test, analyzing not only the drugs he’d been taking, but also some experimental new drugs. And what we found was that while he was resistant to the two medicines he had been prescribed, the virus would likely respond to some of the experimental drugs we had included. All based on the virus samples that we got from him directly. This is personalized medicine.”

Pauwels became convinced that the next-generation anti-HIV drugs could not be developed without having a profound understanding of how HIV replicated in a patient; how it changed, how it evolved, how it tried to evade molecules, and so on. Therefore the next logical step was to somehow access and study an HIV patient sample to measure the extent to which the virus was resistant or not resistant to a drug. But what HIV patient?

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Pauwels and Dr. Stoffels rushed to get the doctor on the drugs that, according to the diagnostic test, would yield a better response.

“And that was one of the most beautiful moments we’d ever experienced in our lives. Our patient began taking the new
drugs, and instead of dying, he lived," says Pauwels. "That’s what this is all about. There’s nothing magic about it." This new treatment methodology was revolutionary. It flouted traditional approaches that employed large clinical studies with thousands of patients. It reasoned that, if you have an illness, you don’t care that a drug has been tested on patient groups who’ve shown that with a very high or a low P value the probability of response is X. You just want to know, ‘Am I going to respond?’ That’s the only thing that really counts.

When word of Pauwels and Dr. Stoffels’ test in Africa began to spread, physicians were astounded. Key opinion leaders in the international medical community such as Dr. Marcus Conant in the US, and Professor Brian Gazzard in the UK also had HIV patients who weren’t responding to treatments. This new technology offered hope.

And so, in 1995, Virco was born. Professor Gazzard, with some money from the Freddie Mercury fund, helped to buy the company’s first equipment. Meanwhile, relying on savings, loans from their families and a few grants, Rudi Pauwels and Dr. Paul Stoffels created Virco with the sole mission to develop diagnostic solutions that could help physicians tailor and optimize therapies for individual patients suffering from HIV.

**Using data to drive therapies**

A major question in 1997 was could resistance testing make sense in clinical practice? Could physicians prospectively use the information revealed in clinical labs to positively influence care and treatment? With the VIRA3001 study, conducted in collaboration with GlaxoSmithKline, Virco set out to find the answer.

“This landmark study compared the virologic outcome in 272 patients who were failing their current antiretroviral regimens,” says Dr. Stoffels. The patients were divided randomly into two groups: In the phenotype group, physicians were given Virco’s Antivirogram® (AVG) test result to help select a new treatment regimen. In the Standard of Care group, doctors selected a new regimen without using resistance information.

The study showed that the prospective use of AVG test led to a better virologic outcome. Physicians prescribed more ‘active’ drugs in the AVG group, and the overall use of more active drugs was associated with a significantly better virologic response.

“Following that study, in the early years we were really able to guide therapy. And later, we were able to go a step further and use the information to develop the next generation of drugs able to combat multiple drug-resistant strains of the virus. Drugs like such PREZISTA and INTELENCE all came out of this exercise,” explains Stoffels.

“Paul and Rudy were generating great science that laid the groundwork for the rapid uptake of HIV resistance testing,” adds Werner Verbiest, former Head Virco (2001-2011). “From 1998 to 2005, what Virco did from a technology perspective formed the foundation for the fastest uptake of a diagnostic ever known. Resistance testing went from concept to market to acceptance relatively quickly.” Over time the healthcare industry witnessed a significant reduction of patients with a detectable viral load. Because the right drugs were being picked, there was less need for resistance testing. “So the great story here is that the goal was not to sell more tests, but instead to ultimately get to a day when you wouldn’t even have to do the test!” says Verbiest.

**Getting every stakeholder on board**

More than 15 years later, Virco has unlocked the complexity of HIV resistance in patients. But to do so, the technical challenges the company has had to overcome have been enormous. “We had to, for example, make massive investments in a very specialized lab infrastructure, because the kinds of tests we were running could not be done
everywhere. So we decided to design and build our own laboratory infrastructure,” says Pauwels.

“Very early on in the process, we also decided to inform the US Food and Drug Administration (FDA) of our findings, which proved to be a very canny decision,” adds Dr. Stoffels. At the time, the FDA was keen to know what the resistance profile was of HIV drugs, and pharma companies weren’t able to provide this information. “But we could. So the FDA encouraged companies to use our tests in order to get their approvals.”

Thanks to that, Virco was able to complete its lab and attract the interest of other companies who provided additional resources upon which the company could build a solid foundation.

Virco, (acquired by Johnson & Johnson in 2002 and today fully integrated into Janssen Diagnostics, a Johnson & Johnson company), has since created a database of more than 650,000 HIV sequences, the largest outcomes-driven in the world.

Another challenge came in convincing its pharmaceutical peers that the diagnostic tool could be of value, even if at first glance it seemed otherwise.

“As word spread about what we were doing, a number of skeptics in the pharmaceutical industry asked ‘Why would you do that?’ Until then, the mantra had been that pharma companies spent a lot of money developing drugs and in order to recoup that money, they needed to be able to market their drugs to as many patients as possible,” explains Dr. Stoffels.

Virco, on the other hand, introduced technology that could help physicians say to patients, “You’ll be better off taking drugs A and D and not B and C”. From a drug marketing perspective, this shift in approach was seismic. Why would pharmaceutical companies want to segment markets and risk making less profit by doing so?

“Well, our answer has been consistently, you can only do the right thing,” says Pauwels. “If you have a test that can predict with a high degree of certainty whether or not a patient is going to respond to a treatment, can you ethically justify giving the patient treatments even if they are likely not to work?”

“You only want the drug to be given to people who can benefit from it. That’s how you create more value for the patient, more value for society and as a result, more value for your company,” adds Dr. Stoffels.

“Fortunately, everybody understands this now. We accept that water always runs down, and in terms of ethics, we should advance medicine in such a way that we develop the technologies that help us to, at the individual patient level, identify the root cause of their problem,” says Pauwels. “If we understand the root cause, then we can maybe do something about it. And our argument is that ultimately for the patient, for the physician, for the payers, and for society, this is the most economical way to do it.” Which leads us to the next challenge for Virco’s pioneering diagnostic, reimbursement.

In the US, before a payment agency like the Center for Medicare Services (CMS) can make a decision about payment for diagnostics, a CPT (Current Procedural Terminology) code has to be generated by the American Medical Association (AMA). That code signifies that the diagnostic is deemed to be mainstream and relevant.

In the 2002/2003 timeframe, though resistance testing technology was becoming accepted, an algorithmic approach wasn’t considered mainstream, and as such, the AMA had not assigned it a mainstream code. Instead it was assigned a CPT3 code, which basically branded it as an ‘in development’ technology. As far as payment is concerned, a CPT3 code is challenging for adoption. “With that code, basically the AMA was saying ‘we recognize it, but it’s not established,’ which makes it really hard to generate access to the patient!” explains Verbiest.
So Virco’s US company embarked on an ambitious campaign to get a CPT Category 1 code. “We worked on patient advocacy and ensured that the legislative community in Washington understood how important this was. We also collaborated with the American Clinical Lab Association. The main idea was to educate people and let them know that this technology had ‘arrived’.”

The campaign needed to demonstrate to the American Medical Association’s CPT Editorial panel that the diagnostic was 1) in widespread use; 2) scientifically validated and supported by peer review journals and 3) clinically relevant. Fortunately the advocacy and science voices were heard, and the AMA granted the Category 1 code in 2005.

“This was one of the first examples where, in essence, a sophisticated algorithm was treated no differently in a CPT approach than a routine laboratory test. We were able to prove that a good understanding of diagnostic information could yield results that could replace what used to be done in a lab, and at far less cost,” says Stoffels.

Once the code was granted, the Center for Medicare Services then had to decide how to integrate this new CPT Code into the following year’s fee schedule. The traditional approach for determining a payment for a lab test is ‘cost plus’: x amount to do the test, plus a markup. “Though it only costs pennies to send data over the Internet, we had to prove that the huge investment in developing the algorithm and keeping it fresh were also worth considering. We really had to educate the FDA that though it costs pennies to do the transaction, it costs millions to keep the technology up to date,” says Stoffels. “Fortunately the payment they eventually assigned did take into consideration the investment that had been made. In fact, I’d argue that this was an early example of moving away from valuating the diagnostic and instead determining worth on the outcome.”

**A fair price for life-saving information**

In the early 90s, if you were diagnosed with HIV, it was essentially a death sentence. If you were lucky you had maybe two to three years to live. And so giving drugs was the right thing to do because having an AIDS patient deteriorate was not only enormously unpleasant and painful, it was also extremely costly for the individual and society.

Today, thanks to Virco’s diagnostic testing, HIV is a chronic, manageable disease like diabetes, for those who have access to the medicines. It’s rare to even see HIV patients in an intensive care unit.

“I think the value the healthcare system places on information is still significantly low,” laments Dr. Stoffels. “If you look at what we do from a reimbursement and payer perspective, we get a very limited amount of money for the test. But if you look at the difference it makes with patients, it’s quite significant. For a drug, a pharma company may get multiple thousands of dollars a year. For diagnostic, it would get multiple hundreds of dollars. That’s a tenfold difference, even though the diagnostic might be as important to the patient as the drug itself.”

What Virco demonstrates is that if its tools are applied in such way that drugs achieve positive response rates of 80 to 90 percent in patients, then maybe a higher price for it is justified.

“We should be rewarding outcomes,” emphasizes Werner Verbiest, Global Head Janssen Diagnostics. “Whether it’s a medical device, diagnostic or a therapeutic, in the end, it’s about keeping people healthy. Governments, policymakers, HMOs, all of them should look long term, beyond the next quarter of sales or the next election cycle. They should be thinking, we have X amount of patients infected with HIV - how can we keep them alive? And how can we bring them back into society so that they can return to work and also have a social life like anyone else?”
“We collectively are entering a very delicate phase in healthcare. We have essentially added 25 years to the life of humans globally, and that’s costing us four trillion dollars a year, or roughly 10 percent of the world’s GDP. So with an aging population, there’s increasing pressure to deliver advances in medicine more affordably,” says Pauwels. “On the pharmaceutical side, therefore, we have to become smarter. And that’s where Virco shines as an example, because not only have we helped patients manage their disease using drugs already available, but we’ve also played a role in the development of a number of very effective new drugs.”

Case in point, every single drug Tibotec (acquired by Johnson & Johnson in 2002) has selected in Phase One trials has reached the market. To highlight the significance, it’s important to know that in the pharmaceutical industry, a Phase One drug has on average a 10 to 15 percent chance to get to market. Every drug Tibotec has selected, however, has gotten there.

“And that has to do with two things,” stresses Pauwels. “First, we picked the right molecules. Secondly, I truly believe that tools like Virco played an important role in helping us to develop better drugs.

“Edurant TMC-278, for example, is a further evolution from Etravirine TMC-125. And that evolution was partially a result of understanding what the viruses were doing in patients, taking the results back to the development lab, and creating a synergy between clinical and basic research.”

**Holistic healthcare**

Virco also challenges the healthcare community to break down its siloes.

“This is a medical device; this is a diagnostic; this is a drug. That’s also how the industry is organized, and I don’t believe anymore in that model,” explains Verbiest. “For example, I don’t see myself as part of pharma organization. We are a healthcare company. It’s like the iPhone. What is it? Is it a phone? A computer? A toy? A camera? It’s all of the above.

“We also need to go to a model where things are much more integrated and disease-focused. And this shift must happen not only within the industry but also among regulators and the reimbursement environment so that we jointly create a new model where creativity and innovation are rewarded in addition to outcomes.”

Adds Dr. Stoffels: “I think in the end, being rewarded for outcomes at the patient level, whether it’s a pill the makes the difference or a pill plus diagnostic information is where we are headed. Recognizing the value of that combination is essential and that is where policymakers and reimbursement agencies have a role to play. The policymakers will have to put legislation in place to support it, and the payers will have to pay for it, because frankly, if it’s not reimbursed, it won’t be developed. It’s as simple as that.”

VircoType and other diagnostics promise a whole new holistic approach to healthcare.

“Beyond HIV, we see that already in oncology and hepatitis C. Virco is an early example of where the traditional ‘chemical’ part of medicine is transforming to be a more integrated solution that is part drug and part diagnostic. Combined we can understand where the patient is in the disease, when they should be treated, and with what. And if the treatment doesn’t work, we can explore what else the patient should be treated with,” explains Pauwels. “I’m not saying that every drug will have a diagnostic. But the whole concept surrounding how we handle a particular condition could lead to early markers of a disease long before a patient is even aware that they’re getting sick.”

Wouldn’t it be wonderful if we could identify cancer a lot earlier so that – assuming there is a treatment available – physicians could intervene with a much higher likelihood of a cure?

And here’s another question: The knowledge that physicians, pharmaceutical R&D teams and scientists gain about diseases grows daily, but how can we bring that closer to the patient/physician experience? Can we bring technology used in Virco’s extraordinary labs into every hospital? Can we bring it to other parts of the world, where maybe they don’t have the super laboratory infrastructure Virco has?

“I believe the answer is yes,” answers Pauwels. “It’s exactly what needs to be done next.”

**HOW VIRCOTYPE WORKS**

VircoType is an electronic service through which the Virco team is able to interrogate a sequence generated locally from a patient sample. The lab first takes the patient sample and performs the sequence. Next that sequence is sent back to Virco. Virco then reports on the result, which basically tells the physician or the virologist in the lab, for which drugs the patient is still eligible, and for which they are not.