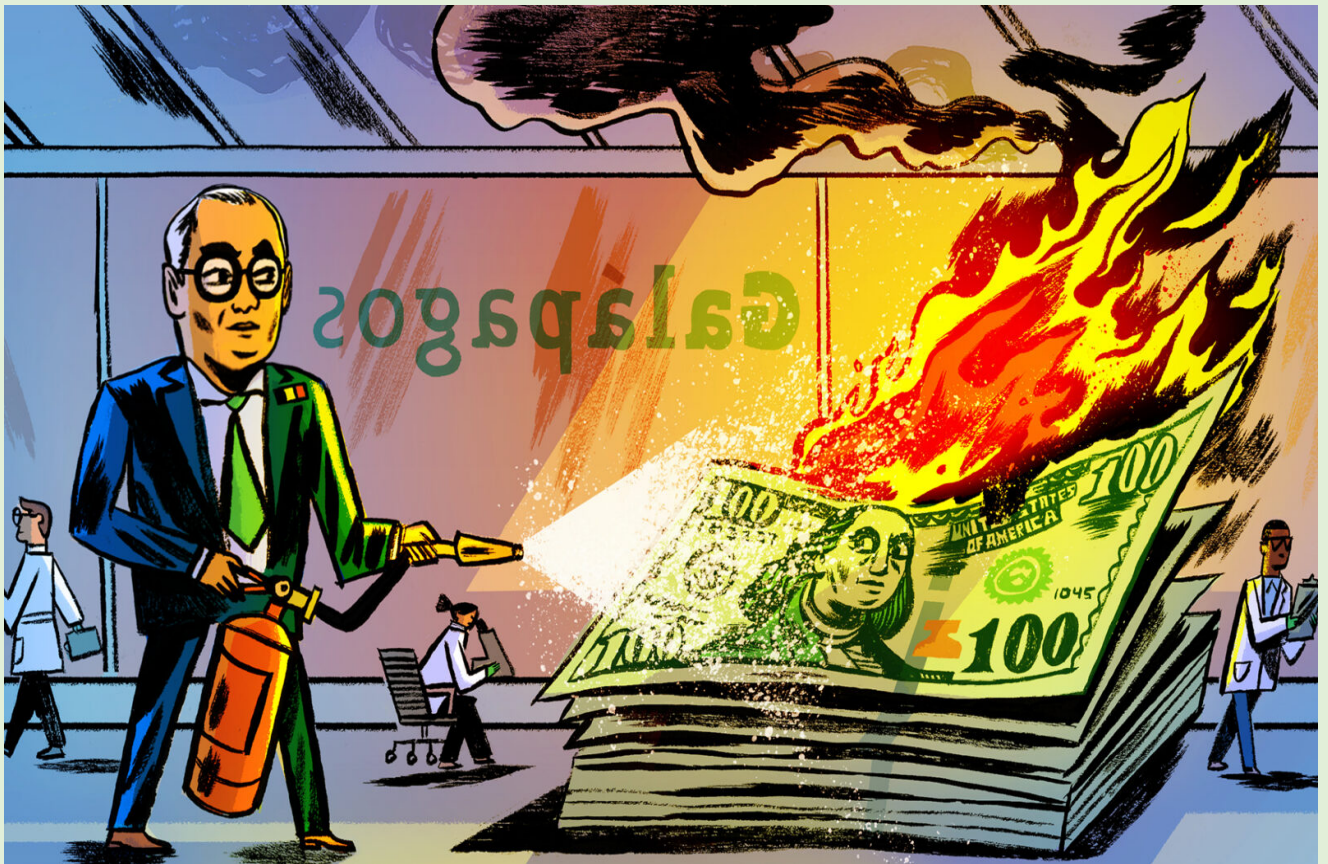


## BIOTECH

In Belgium, a native son returns to resurrect the drugmaker Galapagos — and ‘to get the trust back’



By Damian Garde  
May 18, 2023



MIKE REDDY FOR STAT

**There is, according to Wall Street, no worse investment in biotech than Galapagos NV.**

The Belgian company trades at an enterprise value approaching negative \$2 billion. That means its liquid assets, mostly cash, are worth more than the company itself. It means, according to the market, that every dollar Galapagos puts toward inventing new drugs would be better spent doing pretty much anything else.

“Basically the company is being valued as though they are lighting that cash on fire,” said Emily Field, an equities analyst at Barclays in London.

It's not, to be clear. Instead, a series of 11th-hour failures, a broader biotech crash, and the macro effects of escalating interest rates have conspired to turn Galapagos' financial fortunes upside down over the past three years. Now the company's enterprise value, the lowest in the entire drug industry, has made it a source of befuddlement, fascination, and, to some investors, hope for a massive return.

The latter is due entirely to Paul Stoffels, a 61-year-old biotech eminence in his native Belgium. An infectious disease physician by training, Stoffels is plainspoken and professorial, immediately recognizable among his pharmaceutical peers for the full and defiantly black eyebrows beneath his lucent white hair. Stoffels spent nearly two decades at Johnson & Johnson building a reputation as a superlatively skilled drug hunter, identifying promising medicines and striking canny deals to acquire them. In 2022, with Galapagos at its nadir, Stoffels ended his brief retirement to become its chairman and CEO, a native son who made good in the U.S. returning to Belgium to save the nation's banner biotech company.

It's a narrative pivot for Galapagos, which spent more than 20 years in the high-risk, high-reward game of inventing medicines from scratch on the belief that its scientists were simply better than their counterparts around the drug industry. The rewards never quite materialized, but Galapagos got rich in the process, amassing more than \$4 billion in cash from the deep-pocketed partners who bet on its research. The company's future, in the eyes of investors, will be whatever Stoffels chooses to spend that money on.

**“There is no magic formula to create value in one bang,” Stoffels said in an interview. “You have to get the trust back. You have to have a product portfolio. You have to show progress, and you have to show results. And while I’m very impatient to grow that value, you have to do it on solid grounds.”**

Stoffels was among Galapagos' co-founders in the 1990s, back when the entire Belgian biotech industry was confined to a single office park in a Flemish city called Mechelen. Decades of mergers, spinouts, and startups would ultimately condense the nation's biotech footprint and scatter his former colleagues around the world. One of Stoffels' first moves as Galapagos CEO was getting some of that old band back together, reuniting with colleagues from his yesteryear startup that successfully developed medicines for HIV.

“What is important is to get credibility in our business,” said Pierre Raboisson, Galapagos' head of drug discovery who previously worked with Stoffels at the Belgian biotech Tibotec. “What I like to say is either we are able to discover drugs or we are not. There's nothing in between.”

Paul Stoffels in 2020

Paul Stoffels came out of a short-lived retirement to become CEO and chairman of Galapagos.

Galapagos' stock price suggests the path to credibility will be long. But some investors see a colossal turnaround in the making. To Oleg Nodelman, founder and portfolio manager of the San Francisco-based biotech investment fund EcoR1, Galapagos' comically depressed valuation presents what could be an era-defining opportunity.

“I haven't seen something this left for dead and abandoned honestly in my career,” said Nodelman, whose fund has amassed a roughly 5% stake in Galapagos, according to the company's most recent disclosures. “If I said to someone, ‘Here's this new opportunity: The company has \$4.5 billion in cash. The CEO is Paul, who has brought over 25 new drugs to

market and is one of the premier drug hunters alive today, and you get to invest at a negative \$2 billion valuation,' people would just laugh."

U.S. biotech giant Gilead Sciences is making the same wager. Most of Galapagos' enviable bankroll came from Gilead in a handsome partnership deal that hasn't exactly aged well, giving the company a stake in its Belgian counterpart's reboot.

"We have somebody I would definitely put a bet behind, Paul Stoffels, now running that," Gilead CEO Daniel O'Day said at the STAT Breakthrough Summit earlier this month. "Paul happens to have a bit of a track record of innovation," he said, grinning at his own understatement.

Every conversation about Galapagos comes back to Stoffels. He has a blank slate, a lot of money, and a claim to the industry's most expansive Rolodex. One year into his tenure as CEO, he has heard innumerable variations of the question, "What are you going to buy?" And he has, characteristically, a professorial answer.

"Excel sheets don't drive our business," Stoffels said. "I learned, in my long career in pharma, it's not the biggest number that makes the biggest return; it's the smartest selection of products that makes the biggest return."

Before Stoffels was Galapagos' CEO, he was its neighbor. In 1995, the hotspot for Belgian biotech was Mechelen, halfway between Brussels and Antwerp, where a single street was home to Tibotec, a firm developing drugs for HIV, and Virco, a startup at work on viral diagnostics. Stoffels had left a leadership role at nearby Janssen Pharmaceutica, already a J&J subsidiary, to work with both startups at once, serving as chairman of Tibotec and CEO of Virco.

The allure was robots. Tibotec and Virco were founded on the then-cutting-edge technology of using machines to rapidly screen would-be drugs against a particular biological target. At Tibotec, the robots were testing scores of compounds against HIV in search of working medicines. At Virco, they were testing different strains of the virus against existing medicines to craft tests for drug-resistant HIV.

By the end of the decade, the fruits of the Human Genome Project had illuminated thousands of potential targets for new medicines, promising a revolution in drug discovery and convincing Stoffels and his colleagues to widen the aperture of their robotic pursuits. Galapagos Genomics began in 1999, co-founded by Tibotec and a Dutch vaccines company called Crucell, to take what was working in HIV research and apply it to other diseases. Each firm put in \$5 million, and Galapagos set up on the same block as its Belgian forebears.

"The three companies were literally next to each other here in Mechelen: Tibotec, Virco, and Galapagos," Stoffels said, gesturing as if pointing to each firm's place on the same street. "And we used three times the automation of robotic screening for three different purposes."

It was all going according to plan until the dot-com crash. Tibotec had identified antivirals that could outfox HIV's many mutations and was ready to test them in larger clinical studies, but raising money in a depressed market proved difficult. In 2001, the company merged with Virco to pool its resources. The following year, after struggling to get its research funded, Tibotec-Virco accepted a \$320 million buyout offer from J&J, securing the company's future and returning Stoffels to Janssen, where he began his pharmaceutical career a decade before.

"I learned, in my long career in pharma, it's not the biggest number that makes the biggest return; it's the smartest selection of products that makes the biggest return."

## **PAUL STOFFELS, GALAPAGOS CHAIRMAN AND CEO**

The merger set in motion Stoffels' ascent within J&J, first as head of the company's virology business, which turned Tibotec's discoveries into a series of approved medicines for HIV and hepatitis C. Then, in 2009, as the world's largest drugmakers stared down patent cliffs, J&J put Stoffels in charge of its entire research operation, tasking him with building a pipeline that would see the company through to the next decade and giving him the job that would cement his reputation in the industry.

Under Stoffels, J&J established "Project Playbook," a pharmaceutical prospectus that took a baseball scout's view of the entire drug industry. The company identified a few focus areas, including blood cancer and autoimmune diseases, and then tasked its scientists with simply learning everything there was to know about every drug in development. The resulting intelligence got mapped onto bull's-eye-shaped charts for each disease, with each molecule placed according to how close it was to approval. In the center were the all-but-sure things that J&J would have to pay a premium to license, but out on the fringes were early-stage drugs that might be more obtainable. That's where Stoffels paid particular attention.

On the highlight reel of Stoffels' deals is ibrutinib, a cancer drug developed by a firm called Pharmacyclics. In 2011, impressed by ibrutinib's early data in lymphoma, J&J paid \$150 million in cash for a 50% stake in the drug's commercial future. It would prove to be a rainmaker. The drug succeeded in a series of subsequent trials, leading AbbVie to pay \$21 billion for Pharmacyclics and the other 50% of ibrutinib just four years later. Sold under the brand name Imbruvica, the drug has since become the standard of care for certain blood cancers and brings in about \$8 billion a year.

In 2012, Stoffels' group homed in on daratumumab, an antibody treatment for multiple myeloma then in Phase 1 development. J&J paid its inventor, the Danish firm Genmab, a total of \$135 million upfront for worldwide rights to daratumumab. Ten years later, it's approved as Darzalex and accounts for \$8 billion in sales.

In all, J&J won approval for 25 novel therapies during Stoffels' time as head of research, including, he noted with pride in his interview with STAT, seven drugs on the World Health Organization's list of essential medicines. Many came from the company's internal labs, but most traced their roots elsewhere, scouted through Project Playbook, licensed from outside J&J, and cultivated through partnership.

"Really I used my experience with Tibotec of sourcing external science and working with small companies to get more ideas," Stoffels said. "The world is your lab. Learn from other people, collaborate, and with that find new opportunities and develop new opportunities. You don't have to own everything."

Meanwhile, in Belgium, Galapagos was making its name doing the exact opposite. Maintaining the spirit of its foundation, the company spent decades operating as a cottage pharmaceutical enterprise, conducting its own basic research to find drug targets and then spinning up molecules to attack them.

By 2019, Galapagos was a \$10 billion company with a home-brewed pipeline of medicines for arthritis, eczema, cystic fibrosis, and a chronic lung disease called idiopathic pulmonary fibrosis. The crown jewel was filgotinib, which Galapagos CEO Onno van de Stolpe took to calling "pipeline in a product" thanks to its potential benefits for rheumatoid arthritis, Crohn's disease, and a host of related inflammatory conditions.

The company's zenith came that summer, when Gilead, which had already licensed filgotinib, paid Galapagos \$5 billion in cash to enter into a decade-long relationship and get the rights to six drugs in clinical trials and 20 more in the early stages of research. O'Day, Gilead's CEO, likened the partnership to the one between Roche, his former employer, and Genentech, which led to the Swiss company's four top-selling medicines. The deal was a public affirmation of Galapagos' business model, and the money guaranteed the company could prolong its independence regardless of market forces, something Tibotec and Virco could never manage.

Then, piece by piece, it all fell apart. The first shock came a year after the Gilead deal, when the Food and Drug Administration rejected filgotinib's application for approval in rheumatoid arthritis, citing a safety issue. In time it became clear that the FDA would never be comfortable with filgotinib at its highest tested dose, and the drug wouldn't be competitive at a lower one, leading Gilead to abandon the effort to win approval in the world's most lucrative market for medicines. Galapagos' share price fell by a third.

It would get worse. In 2021, ziritaxestat, Galapagos' treatment for idiopathic pulmonary fibrosis, failed in a Phase 3 trial, instantly nullifying years of study and hundreds of millions of dollars invested in its development. The setback, SVB Securities analyst Geoffrey Porges wrote in a note to clients, was "a reminder for investors that while Galapagos has been a very successful drug-discovery organization, their performance as drug developers has been less impressive." Earlier-stage treatments for osteoarthritis and eczema failed, too, and so did the company's AbbVie-partnered cystic fibrosis medicines.

**Galapagos had lost 70% of its value since filgotinib's rejection, trading below its cash reserves for the first time.**

**"They went from having a drug that was about to be approved in the U.S. to having no late-stage pipeline at all," said Field, the Barclays analyst.**

In August, Galapagos said van de Stolpe would retire once the company found a replacement, ending his two-decade tenure. Two months later, Stoffels, having led J&J's development of a vaccine for Covid-19, announced his retirement, effective Dec. 31, 2021. The plan was to rejoin Galapagos' board of directors, on which Stoffels had served before J&J bought Tibotec. "But then the board came back," Stoffels said. "The CEO is leaving. Do you want to do the turnaround at Galapagos and become the CEO?"

He said yes. On April 1, 2022, Stoffels went home to Belgium and began his tenure. Galapagos had lost the faith of investors, but it still had Gilead's money. And now it had the architect of Project Playbook to piece together its future.

Galapagos immediately embarked on a rebrand. A cheerful marketing video called it "the dawn of a new era," unveiling a Gatorade-adjacent monogram, some hashtags, and the implicit promise that the company's future would be brighter than its dismal recent past.

"Bringing in Paul and his emphasis on business development clearly signifies that the old Galapagos is over," said Phil Nadeau, an equities analyst at TD Cowen in New York. "But in biotech generally, business development has a non-perfect hit rate."

In June 2022, the Stoffels administration did its first deals, paying about \$150 million total for the privately held firms CellPoint and AboundBio. The acquisitions, announced on the same day, marked Galapagos' entry into CAR-T cancer treatment, which involves genetically modifying a patients' own immune cells to attack tumors, and an embrace of therapeutic antibodies, each a stark contrast to the company's decades-long focus on small-molecule research.

**The stock price hardly budged. Small-dollar deals for companies no one had heard of were not quite the transformational moves the market wanted from Stoffels. And because Galapagos' newly acquired assets were so early in development, even investors with longer time horizons struggled to see an entry point, Nadeau said.**

Stoffels sees it differently. Buying AboundBio reunited him with John Mellors, a colleague from the early days of Tibotec and Virco. And bringing in a CAR-T therapy gave Galapagos a foundation for its ambitions in oncology. Just as their old company studied HIV's adaptive mutations to find powerful antivirals, their new one will learn from cancer's evasive maneuvers to develop counter-punching immunotherapies, Mellors said.

"We both witnessed the extraordinary success of treating HIV and want to do that again to the best of our ability," he said. "It was truly transformative, and the opportunity to do that in cancer is just a dream."

CAR-T is a crowded field, and Galapagos' first cell therapy attacks the same tumor target as approved and entrenched medicines from Novartis, Bristol Myers Squibb, and its friends at Gilead. But Galapagos' offering is different. Traditional CAR-T relies on a roughly month-long process of extracting immune cells, genetically engineering them, and then infusing them back into the patient. By acquiring CellPoint, Galapagos got its hands on a bedside technology that promises to do the same thing in about seven days using a pod-shaped machine that looks like a backyard grill from the world of "Spaceballs." Galapagos is years behind its rivals, but if early trials of its point-of-care CAR-T are successful, the company believes it has a platform to match and eventually exceed the technology's pioneers.

To Stoffels, neither acquisition is by itself a transformation of Galapagos but rather a tile in an in-progress mosaic, alongside a reboot of the company's drug-discovery operation, early-stage drugs from the prior administration, and deals yet to be signed.

**"Putting all your money on one or two big acquisitions is very risky in our position," Stoffels said. Just as with Project Playbook, the strategy is not to "bet the ranch" on the center of the bull's-eye, he said, but to make strategic wagers out on the margins, where the next Imbruvica or Darzalex might be available.**

**Setting Galapagos right — and convincing the market the company isn't shoveling cash into a furnace — will be an iterative process.**

**"It's not hope, not prayers," Stoffels said. "It should be value, driven by data and products."**