1986 letter the committee sent to *Nature* which introduced the new name. The media and most researchers followed the World Health Organization’s suggestion to use both names until the imbroglio was solved. It took an agreement signed by President Ronald Reagan and French Prime Minister Jacques Chirac in 1987 to formalize the naming of HIV and to share patent rights to the technology for detecting infection of the virus.14

Meanwhile, at the NIH, the pressure mounted to find “something to fight AIDS.” Sam Broder of the NCI had received permission to set up an AIDS drug initiative but did not get a significant budget nor any additional staff. His small team was quickly overwhelmed. Who could help fight this retrovirus? Gallo remembered Erik De Clercq’s article that he had published in one of his *Cancer letters* of 1979, and recommended testing the effects of suramin on this virus. It produced a remarkable result. Suramin did not kill infected cells but blocked viral replication.

Broder called Erik De Clercq in October 1984 to congratulate him. In its latest issue, *Science* had accepted an article about suramin as an option to conduct human trials. Broder’s Japanese post-doctoral fellow, Hiroaki Mitsuya, co-authored the article with Gallo. They extensively referenced De Clercq’s findings. It pleased De Clercq tremendously, but notwithstanding the prestigious article, AIDS remained far from his mind in 1984. He had just returned from the British branch of Searle in High Wycombe, where he had to cope with the news that the company no longer was interested in BVdU. It was not clear what prompted Searle’s decision to cut its ties with both Walker and De Clercq. Was this sudden disaffection due to the new CEO, Donald Rumsfeld, former secretary of defense under the Ford administration? Rumsfeld wanted to streamline the company by shedding a number of global subsidiaries in order to focus on its core business.

The disastrous reports about a Japanese trial with BVaraU, a drug with close resemblance to BVdU, would later compromise the British-Belgian compound even further. The Japanese did not realize that their drug was incompatible with an anti-aging supplement, fluoro-uracil, that is very popular among adults there. Administering their drug to people with herpes had caused more than eleven deaths. Because of the close similarity in name, the two drugs, BVdU and BVaraU, created confusion; they were forever conflated with one another in the Anglo-Saxon world.
In October 1984, the media were more interested in Belgian scientists from the Institute for Tropical Medicine in Antwerp. Many of the patients with AIDS in French and Belgian hospitals came from central Africa. Once the hypothesis of an Africa link was triggered, Peter Piot’s expertise was in demand because of his previous experience with viruses originating in Africa. He had been a member of an investigative team in the 1970s that found the reservoir of the Ebola virus. It allowed the Institute in Antwerp to isolate the virus from the infected serum of a missionary nun. The virus was then more thoroughly analyzed at the Centers of Disease Control and Prevention, which named the virus after the Ebola river.¹⁵

A CDC mission that went to Zaïre along with Peter Piot’s group came back with devastating stories.¹⁶ AIDS in Africa was not a so-called gay disease because the virus equally infected men and women. It was most prevalent, not among the poor, but among the educated elite who often had more sex partners than the average person.¹⁷

These reports were instrumental to universalize the disease in the western world and lay the groundwork for an international AIDS conference in Brussels in 1985. A few months after the Institute in Antwerp had introduced the famous ELISA tests in Belgium, the conference encouraged several African governments to organize blood screenings and create national committees that would consolidate information about the epidemic.¹⁸

Many Africans, however, felt they were being blamed for the epidemic. The suggestion that the AIDS virus originated from African monkeys was a particularly insulting form of racism. Many claimed that the virus had evolved in the West and was introduced in Africa by visitors, United Nations soldiers or foreign businessmen. Others asserted that the virus had been released into the native population through the distribution of tainted polio vaccines. A few leaders suspected a form of biological warfare, spread by European governments in order to cripple the independence of their former colonies. Public denial became a formidable obstacle in dealing with the epidemic in Africa.¹⁹

The representatives from 50 African nations, present at the Brussels conference, issued a statement saying there was no conclusive evidence that AIDS originated in Africa.
Chapter X
From passivity to action

*The world of science may be the only existing participatory democracy. Science is an immensely supportive activity. Its support is both intellectual—the sharing of knowledge—and emotional—the sharing of purpose.*

— Salvador Luria

**A pivotal year**

On a breezy day in March 1985, while making his rounds of the academic research institutions, Julius Vida, a licensing director from Bristol-Myers, appeared in De Clercq’s office and asked if there is any product he would like to develop together with the American drug maker. He was a most agreeable man who knew how to impress De Clercq with his soft spot for chemistry. Vida had studied with the renowned scientist, Robert Woodward, at Harvard who was considered the most artful of master chemists in his era. Long before he received the Nobel Prize in Chemistry he had become a cult figure among scientists, even his idiosyncrasies, like his fixation with the color blue, were legendary.

With his old-world charm, Julius Vida belonged to the more sophisticated kind of Americans. He introduced De Clercq to top class restaurants in Brussels where cuisine and fine wines fused together like sublime chemistry, places where a young university professor would not often set foot. But on one of their outings, De Clercq accidentally said too much. He spoke of a new class of antiviral compounds and had to hold his tongue so as not to give away any more details until the compounds were properly patented and enshrined in a publication. “Come back next year,” he told Vida, who immediately responded with an invitation to visit Bristol-Myers in the United States.
The discovery of a new class of antiviral compounds, the acyclic nucleoside phosphonates, was one of De Clercq’s most thrilling experiences. Holý’s compounds, HPmPa and PMEA, had come to life in the assay systems that his first Japanese postdoctoral fellow, Takashi Sakuma, had introduced in Leuven.¹

De Clercq had been working with Holý unabatedly for almost a decade. They seldom saw each other, except for a few international conferences like the FEBS meeting in 1978 and the intimate workshop in Kyoto, Japan with seven other chemists and the Nobel Prize winner Khorana, in 1982. Most of their collaborative work was done over the phone or by correspondence. This time, however, he had to share his joy with Tony Holý in person. He accepted to act as chairman of a symposium on virology in Bechyne Castle not far from Prague. It was a good excuse to visit his friend at the IOCB and celebrate their invention in one of Holý’s favorite restaurants: the century-old Red Wheel, near the convent of St. Agnes, the patron saint of Bohemia. It was also another opportunity to bring compounds to Leuven; his coat stuffed with plenty of new vials.

It was precisely in these happy times that De Clercq was struck the most dreadful blow he had ever experienced, with the sudden and unexpected news that his boss, Piet De Somer, had died. The abrupt loss of a legend left him and everybody else in Leuven in a profound state of shock. De Somer looked so vigorous not long before when he was hosting the Polish pope, John-Paul II, in Leuven. Never before had a pope visited this University, the oldest of all Catholic universities in the world.²

A few weeks before De Somer died, the United States beckoned De Clercq with travels to Bristol-Myers, a lecture at the US Army Medical research facility in Fort Detrick, Maryland and an urgent invitation from Sam Broder at the National Cancer Institute. At the NCI, a group of about fifty scientists with only a few Europeans, discussed whether there was an agent which could be effective against replication of the AIDS virus.

Sam Broder did not say much about the human trials the NCI had been conducting with suramin. The very first drug to act against a retrovirus showed promise in the lab. When tested on patients, the decrease in viral load was impressive indeed but the side effects from the weekly injections were just too toxic. Broder shared his consternation over the pharmaceutical companies in the US. Not a single one was interested in looking for
a drug against AIDS! He had called all of them, from the largest to the smallest start-up, but all claimed there was no market.

The only firm with a different attitude was the North Carolina-based company, Burroughs Wellcome. Even though Wellcome did not want to work with retrovirus samples, the company had given the NCI some promising compounds to analyse. One of them, AZT, could become a drug against HIV. The representative from Wellcome, present in the room did not want to divulge too much information: “I can only say it is a nucleoside analog, but it is not acyclovir.” This came as a shock to De Clercq. He had never imagined a nucleoside analog could be active against a retrovirus. So far, he had only used nucleosides with DNA viruses of the herpes family.

The Burroughs Wellcome compound, AZT, was revealed in greater detail a few months later, in the October edition of the Proceedings of the National Academy of Sciences (PNAS). De Clercq raced excitedly over to one of his younger colleagues in the department of medicinal chemistry, Piet Herdewijn, waving a copy of the article. He kept trying to convince the younger chemists in the Rega Institute to work on nucleosides. AZT had been synthesized in 1964 as an anti-cancer agent by Jerome Horwitz of the Detroit Cancer Center, but was not potent enough to become a cancer drug. It was nevertheless acquired by Burroughs Wellcome and kept on the shelf. Thanks to his previous association with the company, Sam Broder remembered the compound when he was at the NCI. Horwitz had synthesized other dideoxynucleosides: d4T (stavudine), ddI and ddC. Could they also become drugs against HIV?

When De Clercq asked Herdewijn whether he could produce a similar compound as AZT, he received an answer within a month. By November 1985, Herdewijn had synthesized d4T, but did not know yet whether it was active against HIV. To assay this compound there was only one option: sending it to the National Cancer Institute lab in Washington.

A fortuitous coincidence: De Clercq’s assistant, Jan Balzarini, was about to take up residency for his year-long sabbatical at the NCI to study the workings of HIV assays. He could test Herdewijn’s d4T, it complemented perfectly Mitsuya and Broder’s program as they had obtained the other dideoxynucleosides ddI and ddC, synthesized by Horwitz in the sixties.

The Christmas season was just around the corner. An eventful year
Cold War Triangle

filled with both sorrow and promise was coming to an end. After De Somer’s death in June, Erik De Clercq was named the Head of the Rega Foundation, a legal entity that managed the funds following the break-up of Rega and Rit. At the Rega Institute itself, the succession as the head of the institute was proving an impossible task. All five of De Somer’s assistants, except one, felt a calling to become his successor. As there was no consensus, De Clercq, who had absolutely no interest, was designated not only as the Head of the Institute but also as Director of the Microbiology Department in the medical faculty. The youngest member of De Somer’s inner circle who had never been in charge of a team larger than five people was suddenly entrusted with the unique legacy of his boss.

De Clercq was still mourning the passing of Piet De Somer, and tried to overcome his grief by writing an article for Nature about the phosphonates that Holý had prepared and the antiviral activity that had been discovered in Leuven. If everything worked well, it could be published before the end of the following year. At the end of his article, he added a suggestion: “One day these compounds should be investigated for their capacity to fight AIDS!”

By the end of 1985, after four years of indifference, the general public in the US and the rest of the world was slowly becoming aware of AIDS. The disease was given a face after Hollywood heartthrob, Rock Hudson, sought treatment at the American hospital in Paris. He had joined hundreds of other Americans who had flocked to the hospital hoping to receive Montagnier’s experimental drug HPA-23. The announcement he had AIDS was a bombshell.

Weeks before Hudson died, President Reagan was asked during a press conference whether he would support a massive government research program against AIDS like the one that Nixon launched against cancer? He surprised everybody when he pronounced the word “AIDS” for the first time and assured it would be a top priority for the US government: the 1986 budget would earmark half a billion dollars for research on AIDS! However, once media attention receded, his proposal was reduced by twenty-two percent in Congress and Senator Jesse Helms started adding his notorious amendments to every appropriations bill, limiting research and prevention of AIDS in the US.
A triangular collaboration is set in motion

The first cold weather of 1986 brought Julius Vida back to the Rega Institute. He was eager to learn more about the new class of antiviral compounds. However, De Clercq kept tight-lipped as his article in *Nature* had not yet been published. He did not feel like sharing any information and only mentioned that he had been working with a chemist in Prague. He was certain that Vida, however, would be too discouraged to go anywhere behind the Iron curtain, as was the case with most of his interlocutors. Julius Vida, however, was of Hungarian origin, and before emigrating to the US, had studied in Budapest and often traveled to Prague. Instead he bubbled over with excitement, and immediately made travel plans to visit Prague.

Vida loved the contrarian nature of Czechs. Even Prague’s river, the Moldau, expressed contrarianism. The river cleaves the city in two, not unlike the Danube between Buda and Pest. All rivers in Central Europe flow to the Black Sea, whilst the Moldau heads in the opposite direction and joins the North Sea. Vida was saddened to see how Communism and Soviet rapacity had brought this country to its knees. He was not deterred by the air of neglect that lingered over the city. The baroque churches and Italianate palaces with marble staircases, the ornamental ceilings peeling with broken plaster were just waiting to spring back to life.

The meeting with Tony Holý was filled with expectations. The suave pharma representative, polished from Harvard, and passionate about nucleosides and nucleotides, found a laboratory thriving under adversity, a hidden treasure grove. The news that a representative of an American company came to see Holý at the IOCB generated a lot of nervous energy around him. *Inventia*, the office for defending intellectual property rights, was immediately put on high alert. In the meeting, Julius Vida got straight to the point and asked if Bristol-Myers could examine Holý’s compounds.

Vida realized early on that Holý and De Clercq were like two sides of the same coin. He sensed that De Clercq treasured his first big discovery, BVdU. In order to coax his willingness to cooperate, Vida arranged for a meeting with one of the big bosses in New York. The Vice President of research, Giulio Vita, reigned supreme over the posh Manhattan headquarters at 345, Park Avenue. The elegant building and all the hushed
formalities surrounding the VP duly impressed the Flemish scientist.

De Clercq prepared a presentation on BVDU, a compound similar to what Gertrude Elion had discovered, but promised more activity in a wider range of herpes viruses. Giulio Vita had a short attention span, however. The instant he learned that Searle had already produced the drug and returned the license, the meeting was over. “I am not interested in violated virgins,” he grumbled. The talk with Giulio Vita would have been the definite nail in the coffin of BVDU if scientists in East Berlin had not salvaged the drug. After the Berlin Wall came down, it became a popular drug all over Europe.7

In 1986, however, it seemed as if De Clercq went from one failure to the next. In Washington, his assistant, Jan Balzarini, had tested d4T against the AIDS virus in Sam Broder’s lab. He had not found any noteworthy activity however. TheATH8 cells used in Sam Broder’s lab were possibly not reactive enough. Yet, it was in the same cell line that activity of nucleosides of the same family like ddI and ddC was detected. The mystery was never solved.

The only silver lining in those days was the visit in Leuven of a junior Bristol-Myers executive: The Associate Director of Anti-Infective Chemistry, John Martin. Though unassuming, the thirty-five year old scientist had already acquired quite some feathers in his cap. De Clercq’s lecture at Bristol-Myers in Syracuse had piqued his curiosity. His colleague, Julius Vida, only added grist to the mill with his gushing comments about Leuven and Prague. Martin could not contain his excitement knowing that De Clercq and Holý were working on phosphonates. He wanted to know everything about it.

Before moving to Bristol-Myers, John Martin had synthesized the new antiviral, gancyclovir. While he was at Syntex, he had also synthesized phosphonates when nobody was interested in this field. The boss of research, John Moffatt, who had explored phosphonates in the late sixties was pleased, but the company never wanted to investigate these further. When he left the Californian company in 1984, Martin was not able to take the results of his experiments with him since the intellectual property belonged to Syntex. It had been a gnawing frustration.

John Martin’s arrival in Belgium, just at the start of a sacrosanct holiday, delayed his encounter with De Clercq. He used the May 1 weekend
to travel to Bruges and soak up the age old traditions permeating that part of the world. He had read many articles written by the newly minted Director of the Rega Institute and knew him from the times he had visited the West Coast. Their first encounter took place at the Syntex conference hosted by Thomas Merigan in 1981, where De Clercq gave a lecture on “Selective Antiviral Drugs.” John Martin vividly remembers their second meeting at a Symposium on Antiviral Agents organized in Seattle by the American Chemical Society in March 1983. It was a great honor for both Martin and De Clercq to be chosen as two of the main speakers for the prestigious event.

When Martin finally sat down with De Clercq, he was pleasantly reminded of how well the virologist could communicate in the universal language of chemistry and introduce him to Belgian beers at the same time. It reassured John Martin that he was on the right track in his renewed pursuit of the phosphonates.

Martin subsequently flew to Prague to visit Tony Holý at the IOCB. They had met each other before at several international conferences but never had the chance to deepen their acquaintance. He found Holý sitting at a small desk with a pile of photocopies and reprints 1.5 meters high, which if it were to fall over would surely have knocked him out and ruined the experiment as well. Most of the space in his laboratory was taken up by his technician, a tall imposing woman several years his senior. He was astonished to see how Holý and his assistant were working with homemade reagents without any protection, no laminar flow hoods, nothing. His lab was as plain as a kitchen.

Holý overcame his innate suspicion and distrust and showed his American visitor the center of Prague. They walked around the old town with its narrow streets and cobblestone alleys. It was a great feeling to cross the fourteenth century Charles Bridge and walk up the hill to the castle. Martin sensed the city’s hidden beauty behind the walls polluted with the soot of brown coal. John Martin’s acquaintance with Prague and his immediate trust in Tony Holý, cemented the Cold War triangle, the triangular collaboration set in motion by Julius Vida.

Upon his return in Connecticut, John Martin was approached by a very charming female CIA officer. “Could he debrief her about his contacts with Holý?” she asked, fluttering her eyelashes. He had to disappoint
Cold War Triangle

her. He declined and strongly advised her not to enlist Holý as an asset in Czechoslovakia. Politics and science don’t mix!

Launching an AIDS laboratory in Leuven: the story of d4T

De Clercq was wondering what could have gone wrong. He was tinkering with all the steps necessary to assay Piet Herdewijn’s d4T and kicked himself for not being able to carry out the test himself. Just then, one of the visiting fellows, an assistant professor in ophtalmology from the University of Pennsylvania named Herbert Blough, ambled into his office. He was on a two-month mission in Europe, combining work at the Rega Institute with research at the Pasteur Institute in Paris and wanted to test some compounds to see whether they could be active against AIDS. Almost as an afterthought, he mentioned the vials with HIV viruses he carried, courtesy of Luc Montagnier.

De Clercq felt quite helpless since his only assistant was in Washington. There was just a postdoctoral fellow from Japan working with him who was busy testing Holý’s compounds and a student in pharmacology, Rudi Pauwels. He was about to leave the Rega Institute as his two-year contract was coming to an end; an internship in a nearby pharma company took up all of his time. De Clercq nevertheless called on Rudi, kindling his curiosity:

Could he interrupt his work to help a professor from Philadelphia? He has found some compounds that could work against AIDS and wants to test them against the virus samples he brought with him!

Rudi jumped on the occasion, eager to help. He came back to the Institute immediately. He showed Blough where to change into a protective suit to enter a lab that, at best, had minimal safety levels. All technicians fled when they heard the professor possessed vials with the AIDS-virus. One technician, named the “mother of the laboratory,” remained in the area and told Rudi Pauwels what to do in order to prepare the cells. Just as Blough was going to open the vial, he suddenly remembered he had to make an urgent phone call and began acting very nervous. The fear of the virus was too strong. He pretended he had to urgently leave for Paris.
“Could Rudi Pauwels continue the testing?” he meekly asked. “Step in a protective suit, open the vial, and do the test.” Rudi did just that and, a few days later, found a very mild action against HIV. An article was prepared for publication, Herbert Blough was never seen again, but AIDS had made its entry as the new research topic for the Rega Institute!8

Rudi had tasted the thrilling experience of working with the AIDS virus. His hunter’s instincts got the upper hand. It felt like playing Russian roulette. He was barely twenty-five years old, but he considered the fight against HIV a military mission. He was now sure he wanted to work on one thing: installing an AIDS lab at the Rega Institute.

As the AIDS laboratory was being set up, everybody objected to bringing the virus into his or her side of the building. Negotiating with his colleagues for more space was not De Clercq’s forte. Rudi Pauwels had noticed that the university hospital was about to move to another location. The emergency department had already liberated some space and the basement of the clinic linked to the Rega institute by an underground corridor. Even though there were no windows, it seemed like a perfect place to start working with the virus.

Rudi cajoled Jan Desmyter, head of clinical virology lab at the university clinic to step in. It was a happy confluence of minds. Desmyter had been thinking of bringing the virus to Leuven for research ever since he met Luc Montagnier. Thanks to his Parisian contacts, the institute had ready access to virus samples, but the tricky part was to multiply them.

Rudi Pauwels worked day and night to set up an AIDS assay system. He collected all kinds of cell-lines to see where HIV multiplied best. For HIV to infect cells, it must dock with a receptor that sits on the surface of those cells. Pauwels managed to acquire Japanese leucocyte cells that had been weakened through pre-infection with the leukemia virus and had plenty of CD4 cells. The MT2 and MT4 cells from Naoki Yamamoto’s lab in Tokyo were a delight. They were unusually sensitive to HIV. Ironically, Yamamoto’s lab was at that time also developing the d4T compound.

Rudi did not only have a nose for finding the right cells but he also invented a completely new system to assay HIV. It was much simpler to use than the traditional assays that involved measuring the cytopathogenicity and required a double check under a special microscope, a cumbersome device. With Rudi’s system one could detect HIV activity
with the naked eye, on the basis of colors: brown for infection, light yellow for protection. He had managed to automate the assay by introducing robots which he had fabricated in his garage at home. His assay system became the talk of the science community. The article that was published later in the *Journal of Virological Methods* received a gold star in the citation index. For over twenty years, it was considered the best system around and used in just about every lab in the world!

At first, no technician wanted to work with Rudi Pauwels for fear of being infected by the virus, but help was on the way. A new Japanese post-doctoral fellow, Masanori Baba, arrived in Leuven. He was the student of one of De Clercq’s best Japanese friends who came to his NATO conference at Les Arcs. There and then he asked to join De Clercq’s lab. Applying for financial aid took a while, but he obtained the very prestigious *Fellowship from the Japan Society for the Promotion of Science* (JSPS). Baba had remarkable skills and brought with him two more assay systems to the Rega Institute: a test for adenoviruses and a new test for varicella-zoster viruses.

As one of his first assignments, in August 1986, he assayed Piet Herdewijn’s d4T compound. Baba found immediately that the compound was very active against HIV. It was a complete turnaround from the testing that was done eight months earlier at the NCI lab! This time, the patent lawyer in the Netherlands was contacted immediately. As to a publication, De Clercq looked for a journal that would publish swiftly and not wait an entire year for all peer reviews to arrive. He found a journal in Madrid that promised to publish within three months.9

De Clercq asked Bristol-Myers whether they would be interested in the drug. Julius Vida confirmed that they were. Actually, they had already acquired another compound of that same family, ddI and planned to offer this drug for “compassionate use” to the gay community. They also knew there was something in the works in Bill Prusoff’s lab in Yale. Bristol-Myers would go with whoever would get the patent first. The race between the two universities was on.

The patent lawyer in the Netherlands took an unusually long time. There was no reaction, even though the article had been sent to the publisher. A few months later, in late 1986, De Clercq’s friend at Yale, Bill Prusoff, filed his patent. Filing meant he was first in line to be awarded