Acceptance speech

18 June 2026

Michel Sadelain, awardee in the Biology and Biomedicine category (18th edition)

I first want to thank the BBVA Foundation, the international prize committee and the Spanish National Research Council for this extraordinary honor. The Premios Fronteras del Conocimiento are prestigious awards that resonate from Bilbao and Vizcaya around the world. I am honored to share this award with Carl June and congratulate him for his achievements.

The journey that brings me here began forty years ago, when I started to imagine how we could teach T cells to perform any task of our choosing, such as identifying and destroying cancer cells. T cells are essential constituents of our immune system, which successfully fight many viral infections but struggle against cancer. To teach T cells first required establishing technology for introducing genes in natural, patient T cells and designing composite receptors, which I named chimeric antigen receptors in 2003, that would guide the T cells to execute their assigned mission. The CAR molecules we designed perform multiple duties to ensure that the T cells recognize their target, multiply, migrate to track down hidden cancer cells, and maintain their capacity to eliminate cancer cells over time – for weeks, and sometimes longer. We hoped we might someday bring our CAR T cells to the clinic, and so needed to identify a suitable target molecule found in many cancers. We selected CD19, which, when we chose it in the mid-1990's, was not the superstar it has since become. It fulfilled all of our expectations: by 2003, we published that we could effectively treat a range of leukemias and lymphomas in mice using genetically engineered human T cells. The only way to advance this therapeutic concept, which most in academia or industry rejected at the time, was to do it yourself. I am so, so grateful to Dr Isabelle Riviere for having suspended her own research pursuits to come set up with me the infrastructure and processes that enabled us to obtain FDA approval to conduct a clinical trial in patients with relapsed refractory leukemias. We infused the first patient in New York in June of 2007. Our clinical results and those reported by Carl rapidly demonstrated the extraordinary potency of this medicine and convinced the scientific, medical, regulatory and industrial

worlds of their promise. The first CAR therapies, both targeting CD19, were approved by the US FDA in 2017 and EMA in 2018. There are by now hundreds of laboratories across the world exploring the potential of CAR T cells to treat an ever-expanding array of pathologies.

These new medicines are not inert molecules like most medicines, but programmed cells charged with performing a defined task. In 2012, I nicknamed them "living drugs", to stress their ability to multiply and persist, sometimes for years, following a single administration. CD19 CAR T cells are not only – for some patients – curative; they are administered only once, a very unique hallmark. They can have side effects, but we are learning fast to control their occasional toxicities; the next step will be not to treat but prevent these side effects, which will allow these life-saving therapies to be used more broadly. The range of their potential usefulness is rapidly growing: after certain leukemias and lymphomas, multiple myeloma was the next cancer to be successfully treated by CAR T cells. While so-called "solid tumors" remain a challenge, CAR T cells are showing great promise in rheumatology, neurology and overcoming transplantation barriers. There is hope that they could also be harnessed for intractable infections, neurodegenerative disorders and pathologies associated with senescence and fibrosis. The advent of CD19 CAR T cells paves the way for many more discoveries and applications yet to come. A path has been opened for reprogramming functions in human cells that can be safely used to treat severe disorders that we are otherwise unable to control.

The next generation of scientists, physicians and engineers who will make these discoveries will not face, as we did, the sarcasm and sometimes the contempt that some held for cell therapies and genetic engineering. I am grateful to all those who worked with me or supported me over the years, in particular the brave ones who risked their careers when this work was labelled as science fiction. I already mentioned the critical contribution of Isabelle Riviere. I also want to mention Renier Brentjens, who joined my lab against the advice of many colleagues, Tom Kelly and Harold Varmus, who allowed me to work at Memorial Sloan Kettering Cancer Center when this was all very uncertain, and Katrina Armstrong and Roy Vagelos, who, at Columbia where I work today, support the vision of promoting cell therapies for a broad range of pathologies. To my past and present lab members I express my heartfelt gratitude: it takes curious, smart, creative, rigorous, skillful, passionate, committed and generous individuals to advance big ideas, especially when they don't fit prevailing dogmas.