Few discoveries in recent cancer research can match the importance of anti-PD-1/PD-L1 immunotherapies, perhaps the closest that medicine has come to a cure for cancer. When used against certain cancers, anti-PD-1/PD-L1 antibody drugs switch the immune system back on, which then attacks and drastically shrinks tumors. Currently immunotherapy drugs are FDA-approved against more than 10 cancers, and it’s likely that within a few years anti-PD-1/PD-L1 will be approved for 15 other types of cancers that have shown significant response in clinical trials.

The scientist behind these therapies is Lieping Chen, MD, PhD, United Technologies Corporation Professor in Cancer Research and Professor of Immunobiology, Medical Oncology, and Dermatology, and Co-Director of the Cancer Immunology Program at Yale Cancer Center. His discoveries have brought him many honors, most recently the 2017 Warren Alpert Foundation Prize “for transformative discoveries in the field of cancer immunology.”

With PD-1/PD-L1, the journey from discovery to FDA-approved was long. Dr. Chen conceived his theory about the tumor molecules that disable lymphocyte function in 1992. In 1999, he discovered the B7-H1 molecule (now also called PD-L1) and showed how the PD-L1 bound to PD-1 in a tumor’s microenvironment to shut down the immune response. When Dr. Chen blocked this pathway with monoclonal antibodies to stop the binding, the lymphocytes in the tumor woke up and attacked the cancer cells.

“Most people did not take this concept very well,” said Dr. Chen. “It was too new. The majority of immunologists were trying to boost the immune system, in hopes that would get rid of the cancer. The others didn’t believe that the molecules would work selectively in the tumor’s microenvironment.”

Despite that skepticism, the therapy eventually reached the clinic for the first time almost 15 years, until 2006. “We were using a primate study,” said Dr. Chen. “Many patients in the trial still had huge tumor burdens even after chemotherapy, radiotherapy, and targeted therapy, but with anti-PD-1/PD-L1 treatment, their tumors really regressed.”

Skeptics called the trial too small. Dr. Chen had to wait another six years before anti-PD-1/PD-L1 was tested in a large trial with more than 200 patients. Once again, all the patients had failed on every other treatment. Once again, the data about tumor regression was astonishing. In some patients the cancer disappeared and didn’t return. “People started to believe it was real,” explained Dr. Chen.

But this trial and others also showed that 40 to 60 percent of the patients didn’t respond to anti-PD-1/PD-L1 therapy. Those tumors are Dr. Chen’s new targets.

“From this therapy we learned that a tumor creates an immune inhibitory mechanism in its microenvironment,” he said. “So it doesn’t matter how much you boost the immune system in other parts of body, because these local tumor sites are so strong and can completely shut down immunity inside the tumor. My current research is driven by this idea—to go into the tumor microenvironment, tease out the molecular pathways, and study those to identify the fundamental mechanisms that allow cancer to shut down the immune response in tumors, especially that do not respond to anti-PD-1/PD-L1 therapy. Then, we will devise a therapeutic approach to fix those problems. It’s almost like starting from scratch again, and it’s really exciting.”

He and his 25-person lab are focusing on solid tumors with few effective treatments and poor survival rates—lungs, breast, colorectal, and pancreatic cancers. But this time he wants to shorten the lag time between discovery and clinical applications. He is doing that through strong alliances with pharmaceutical and biotech companies.

“We are changing the model a little bit,” explained Dr. Chen. “We want to cut down the time from discovery to clinical trial from 20 years down to two to five or maybe even three. It’s going to be faster and better.”

Among the pharmaceutical companies working with Dr. Chen are Pfizer and Boehringer Ingelheim. His newest alliance set a record for a biotech start-up: investors raised $67 million in 2016 for a new company called NextCure, based on Dr. Chen’s future breakthroughs.

Dr. Chen can’t talk yet specifically about the fruits of these partnerships except to say that a few drugs are getting closer to clinical trials. He is confident they will likely go to trial in mid-2018, just two-and-a-half years from the lab.

“This is the model we’re looking for,” said Dr. Chen. “Acceleration. It’s now obvious that there are pathways in some tumors that are immune suppressive, and I expect in the next few years many will be discovered so we can use immunotherapy against them.”