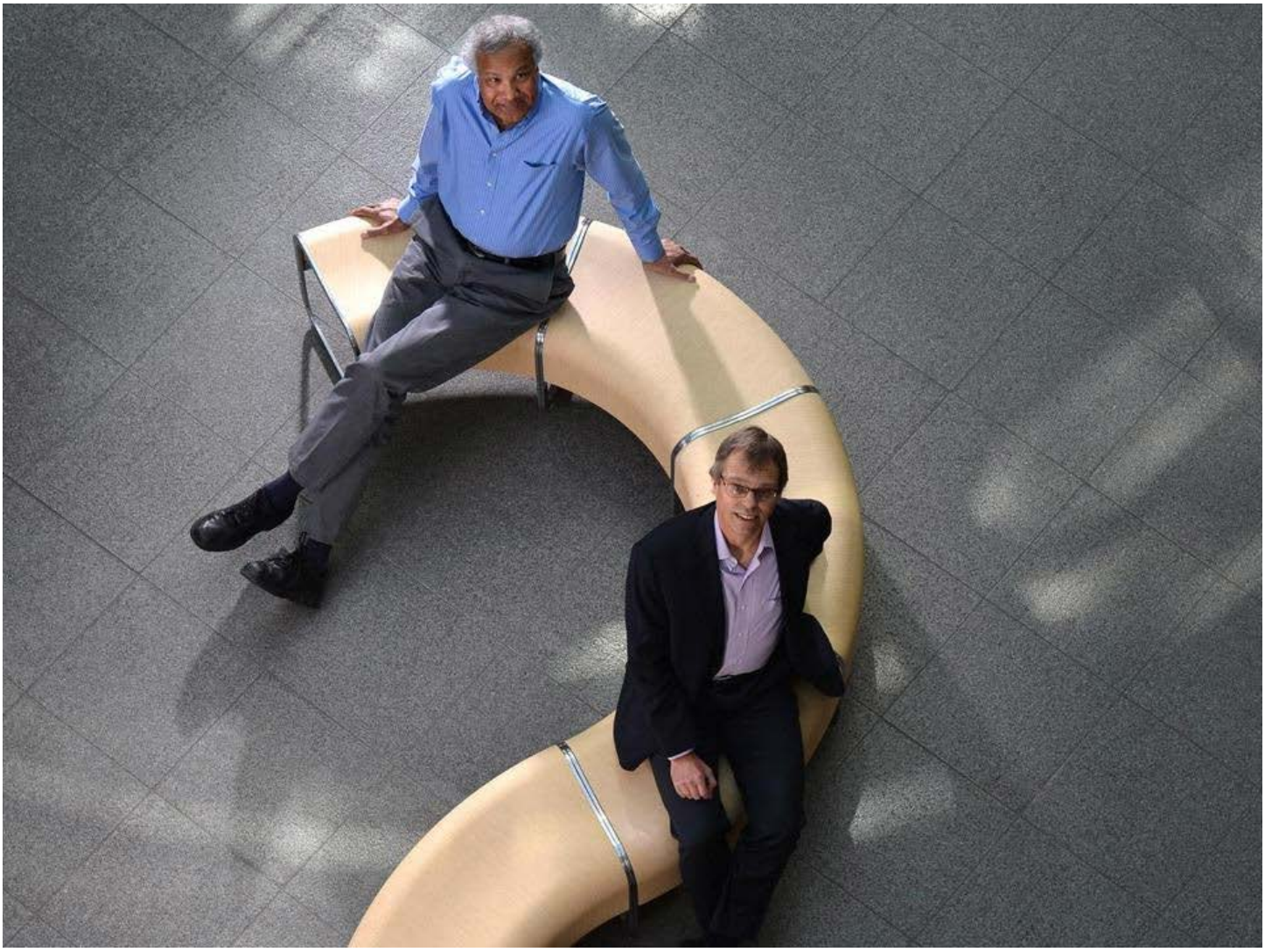
The Boston Globe

GAME CHANGERS

ImmunoGen’s breast cancer therapy took time

By **Robert Weisman | Globe Staff**



ESSDRAS M SUAREZ/GLOBE STAFF

Ravi Chari (top) and John Lambert helped to develop Kadcyla at ImmunoGen.

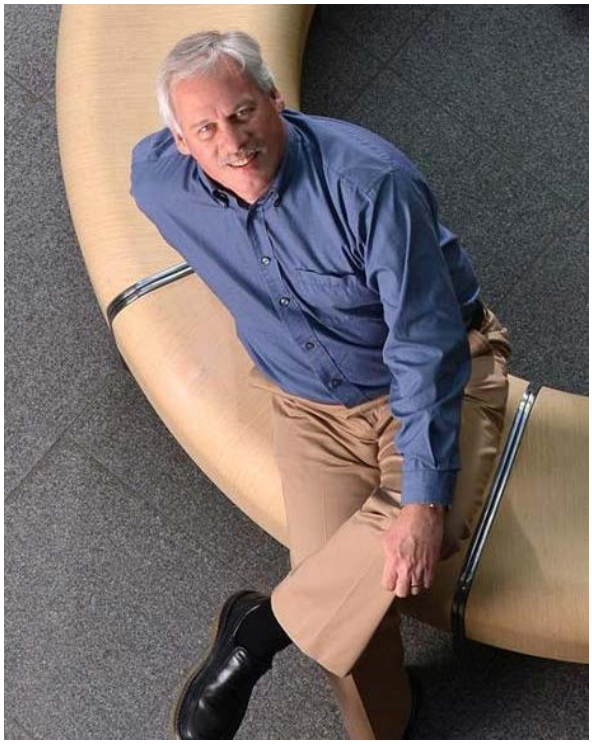
Patients and doctors applauded last year when the powerful new breast cancer therapy Kadcyla made its market debut, following a long and winding journey to approval for what many view as a miracle medicine.

The Genentech division of Swiss drug giant Roche AG got the nod from US and European regulators to sell Kadcyla. But the innovative “payload platform” that enables the drug to bind to tumors — releasing targeted, cancer-killing toxins that don’t harm surrounding healthy cells — was painstakingly developed over three decades by ImmunoGen of Waltham.

“It was 30 years of beavering away,” said chief scientific officer John Lambert, who was ImmunoGen’s second employee.

In the early 1980s, the dawn of the biotechnology age, scientists and investors saw the potential to exploit a type of protein known as monoclonal antibodies to deliver toxic chemicals directly to tumors. ImmunoGen was spun out of the Dana-Farber Cancer Institute's predecessor hospital in Boston to investigate the concept.

After several dead ends, its researchers created a "linkable derivative" of maytansine, a compound extracted from the bark of an African tree. "It gave us a chemical handle," Lambert recalled. "Now we had something we could put on cancer cells and kill them."



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Bob Lutz, vice president of translational research and development at ImmunoGen.

But scientists still had to find a way to link that derivative to an antibody and a method of getting the combined payload into the targeted tumor cells. That work would give birth to a new class of drugs, complete with their own delivery system. They were called antibody-drug conjugates.

It took many more years to overcome the technical challenges. Once they were met, Lambert wrote to scientists at Genentech, which had won approval for its breast cancer drug Herceptin in 1998. By using ImmunoGen's linker and delivery system, he said, "we could turn a drug into a superdrug."

After what Lambert describes as "a four-year dance," Genentech licensed the ImmunoGen technology. Early last year, Kadcyla became the first antibody-drug conjugate to win full approval from the Food and Drug Administration.

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In the process, it positioned the technology platform to become a growing force in cancer drug research. ImmunoGen itself has nine other experimental drugs — three wholly owned and six in partnerships — using the same approach.

"Kadcyla's approval was a validating event," said ImmunoGen chief executive Daniel M. Junius. "Patients are seeing clear efficacy with better tolerability."

Lorraine Heidke-McCartin, a Hanson woman diagnosed with HER2-positive breast cancer in 2006, was treated with more than a dozen drugs — many causing severe side effects — before she began taking the drug candidate that was to become Kadcyla, under an expanded access program in late 2010. Her tumors and swollen lymph nodes quickly began to shrink, and since the end of 2011, her doctors have seen no sign of the disease.

"It's been a blessing," said Heidke-McCartin, who works at a Holbrook church and baby-sits her seven grandchildren. "Previously I was fighting a losing battle. By putting the poison right where it needs to be and not throughout the body, this drug has made so much difference for patients. You don't lose your hair, you don't have all the side effects. I can live my life."

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