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## IMPATIENCE AND UNDERSTANDING **DR. BRIAN DRUKER**

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If you lived in New York City in 1900, you faced the industrial revolution of the 19th century, plus severe overcrowding owing to massive immigration. NYC had no running water and no sewage system. Infectious diseases were rampant. In the US, the life expectancy in 1900 was 47 years. If you had a child, he or she had a one in ten chance of dying before age 4. Pneumonia, tuberculosis, and diarrheal diseases were the top three causes of death, accounting for 30% of all deaths.

Despite this bleak picture, scientists and politicians of the day were optimistic. They predicted that these infections would be eradicated. What led to this optimism was the establishment of the germ theory of disease, which held that infectious agents, not mythical forces, caused diseases. Just before the turn of the 20th century, Louis Pasteur had introduced a vaccine for rabies and Robert Koch had identified the bacteria that caused tuberculosis. There was real cause for optimism and a new mantra: “If you understand a disease, there is hope for a cure.”

The scientific breakthroughs of the 1900s translated into enormous gains against infections. In the early 1900s, public health measures such as chlorination of water, pasteurization of milk, improved sanitation and refrigeration made our food and water supplies safe.

Antibiotics, not even conceived of in 1900, were introduced in the late 1930s. Penicillin was first used in 1942, when a 33-year-old woman was hospitalized with life-threatening pneumonia. She was delirious, and her temperature reached 107 degrees. Treatment with sulfa drugs, blood transfusions, and surgery had no effect. As a last resort, her doctors injected her with a tiny amount of an obscure, experimental drug called penicillin. Overnight, her temperature dropped to normal, and the next day she was no longer delirious. She survived to marry, raise a family, and one day she met Sir Alexander Fleming, who discovered penicillin. These were magic bullets for treating infections, the likes of which had never been seen before. Disease after disease fell to these agents.

The other major advance in the 1900s was the introduction of vaccines. Many of us can remember the polio epidemic of the 1950s. Hospital ward after hospital ward was filled with iron lungs. In 1952 alone, there were 60,000 cases of polio reported in the US. In

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1955, the Salk polio vaccine was introduced; by 1965, only 72 cases of polio were reported annually. Diseases like smallpox have been eradicated with vaccination. Mumps, measles, and rubella, the diseases that we all grew up with, are now memories.

In the year 2008, we face new challenges. Cancer is the second-leading cause of death in this country. It accounts for 25% of all deaths. Hopeless encounters between doctors and cancer patients are common.

But scientists of today are as optimistic as our counterparts were 100 years ago. That's because in the last decades of the twentieth century, we have established the gene theory of cancer. The genes in our cells that lead to cancer have been identified. And like a century ago, when the hope was that this understanding would lead to effective treatments, we have new hope for fighting cancer.

But we have more than hope: we have proof. Gleevec tells us that by understanding cancer, we can develop effective treatments. Over the past three decades, cancer researchers have identified the precise abnormality that causes the white blood cells to grow uncontrollably in a particular form of leukemia called chronic myeloid leukemia. In collaboration with Novartis Pharmaceuticals, my laboratory has developed Gleevec, a drug that completely shuts down this specific abnormality. In clinical trials, virtually all of our patients have had their blood counts return to normal, and in up to three quarters of our patients we can no longer detect leukemia cells in their bone marrow. Remarkably, the once-a-day pill treatment has been well tolerated, with minimal side effects. In short, it is a simple, effective treatment that disables the cancer without disabling the patient. Today, more than 100,000 lives have been saved by Gleevec. In May of 2001, Gleevec was approved by the FDA in record time. Now, the five-year survival rate is 95% for this previously fatal leukemia. People diagnosed with this leukemia were once told they had five years to live, or less; now we are projecting 30.

Let me put that five years in perspective. LaDonna, a retired dietician from southwest Washington, came to my clinic seven years ago. She could barely walk because her spleen, normally the size of a fist, had swelled to the size of a football, compressing her stomach so that she couldn't hold down any food. She was losing two to three pounds a day. She had only weeks left to live when she came to see me; she had purchased a burial plot and picked out the music for her funeral. Within a week on Gleevec, she was able to walk again. Her spleen shrunk and after a month her blood counts had returned to normal.

I have a picture of LaDonna from five years ago where she is playing with her three grandchildren, including a sixteen-year-old, a thirteen-year-old and a three-year-old she wasn't supposed to meet. He's named Will, because he was her will to live. She recently gave me a new picture. It was from her eldest grandchild's wedding; she's 21. Her thirteen-year-old is now 18 and has graduated from high school, and her three-year-old is now 8 and just completed third grade.

Targeted therapy, once considered science fiction, is now part of the mainstream.

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There are over 100 targeted cancer therapies in clinical trials and over 200 in development. Every drug company's cancer pipeline has moved from chemotherapy drugs to targeted agents. Hundreds of biotech companies have been formed to develop targeted therapies, and the buzzword in the industry is personalized medicine.

Gleevec has shown cancer doctors that we too can develop medicines that are like magic bullets, medicines that work quickly and effectively on patients for whom there previously was no hope. But just as penicillin does not treat all infections, Gleevec won't work against all cancers. We need to develop treatments like Gleevec for many more cancers. Just as antibiotics are not the only treatment for infections, so we need to take a broad-based approach to treating cancer. We certainly need more drugs like Gleevec. But we also need a better understanding of the power of the immune system so that we can harness it to attack cancer, and we need a better understanding of what places us at risk of developing cancer so we can develop strategies to prevent it. All of this requires a greater understanding of the genes involved in cancer.

We live in challenging times. We have many distractions. Funding levels for research are decreasing. But there are incredible opportunities in cancer research. I fully believe that we have the technology in hand to solve the cancer problem. It is no longer a matter of if, but when. But we need increased research funding to accelerate the pace of our discoveries. Gleevec tells us we are on the right track, but we can't be complacent. We can't be patient. We must seize this momentum to reach the finish line of curing cancer.

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**Dr. Brian Druker** is an Investigator of the [Howard Hughes Medical Institute](#) Director of the [OHSU Cancer Institute](#) and JELD-WEN Chair of Leukemia Research at OHSU. Upon graduating from the University of California, San Diego School of Medicine in 1981, Dr. Druker completed his internship and residency in internal medicine at Barnes Hospital, Washington School of Medicine in St. Louis, Missouri. He then trained in oncology at Harvard's Dana-Farber Cancer Institute. Dr. Druker then returned to the lab to begin his research career studying the regulation of the growth of cancer cells and the practical application to cancer therapies. His work was instrumental in the development of Gleevec (imatinib), a drug that targets the molecular defect in chronic myeloid leukemia (CML). After completing a series of preclinical studies, Dr. Druker spearheaded the highly successful clinical trials of imatinib for CML. Imatinib is currently FDA approved for CML and gastrointestinal stromal tumors (GIST). His role in the development of imatinib and its application in the clinic have resulted in numerous awards for Dr. Druker, including the John J. Kenney Award from The Leukemia and Lymphoma Society, the AACR-Richard and Hinda Rosenthal Award, the Warren Alpert Prize from Harvard Medical School, the American Society of Hematology's Dameshek Prize, the Lance Armstrong Foundation's Pioneer of Survivorship Carpe Diem Award, the American Cancer Society's Medal of Honor, the Kettering Prize from General Motors Cancer Research Foundation, the David A. Karnofsky Award from the American Society of Clinical Oncology, the Robert-Koch Award, and the Keio Medical Science Prize from the Keio University Medical Science

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Fund. He was elected to the Institute of Medicine of the National Academies in 2003, the American Association of Physicians in 2006, and the National Academy of Sciences in 2007.