

FIGHTING CANCER: USHERING IN A NEW ERA OF MOLECULAR MEDICINE

By unraveling the molecular causes of disease, biomedical research is paving the way for promising new therapeutics and ushering in the next era of medicine. This approach is known as molecular medicine and, in its most individualized form, precision medicine. Gleevec®, a drug used to treat chronic myelogenous leukemia (CML, a rare type of blood cancer), was among the first successful molecular medicines. This was achieved, in part, thanks to powerful scientific techniques and government efforts encouraging drug development for rare diseases. The NIH's National Cancer Institute (NCI), along with many other public and private organizations, played a vital role in developing Gleevec®.

ABOUT CHRONIC MYELOGENOUS LEUKEMIA (CML)

CML is a type of cancer caused by an abnormal chromosome, called the Philadelphia chromosome, which leads to uncontrolled growth of white blood cells that build up in the bone marrow and blood. The Philadelphia chromosome is created when two different chromosomes break and switch ends. When DNA sequences from both chromosomes are combined, it creates the cancer-causing gene *BCR-ABL*. Gleevec® is a targeted precision medicine therapy that blocks the protein kinase produced by the *BCR-ABL* gene, preventing the overproduction of white blood cells. In 2010, there were nearly 70,000 people in the U.S. with CML,⁵ and about 6,000 people are newly diagnosed with CML each year.^{6,7}

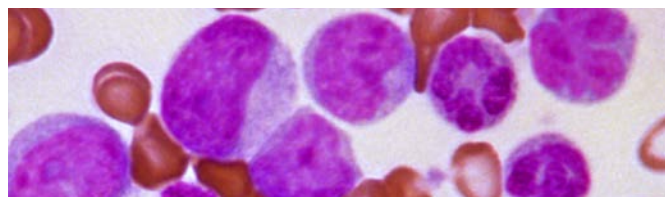
MOLECULAR MEDICINE: BEFORE AND AFTER GLEEVEC®



THEN

- In the 1950s, new techniques to study cells and the chromosomes within them were just starting to be developed; researchers began linking chromosomal abnormalities to specific human diseases.
- Until the 1990s, medications to treat cancer were limited to non-specific chemotherapy that killed many healthy cells in addition to cancerous cells.³
- The standard chemotherapy treatment for CML was not very effective and could cause serious side effects.
- Industry had little incentive to invest in therapeutic development for rare diseases.

The five-year survival rate for CML patients was less than 30%.¹



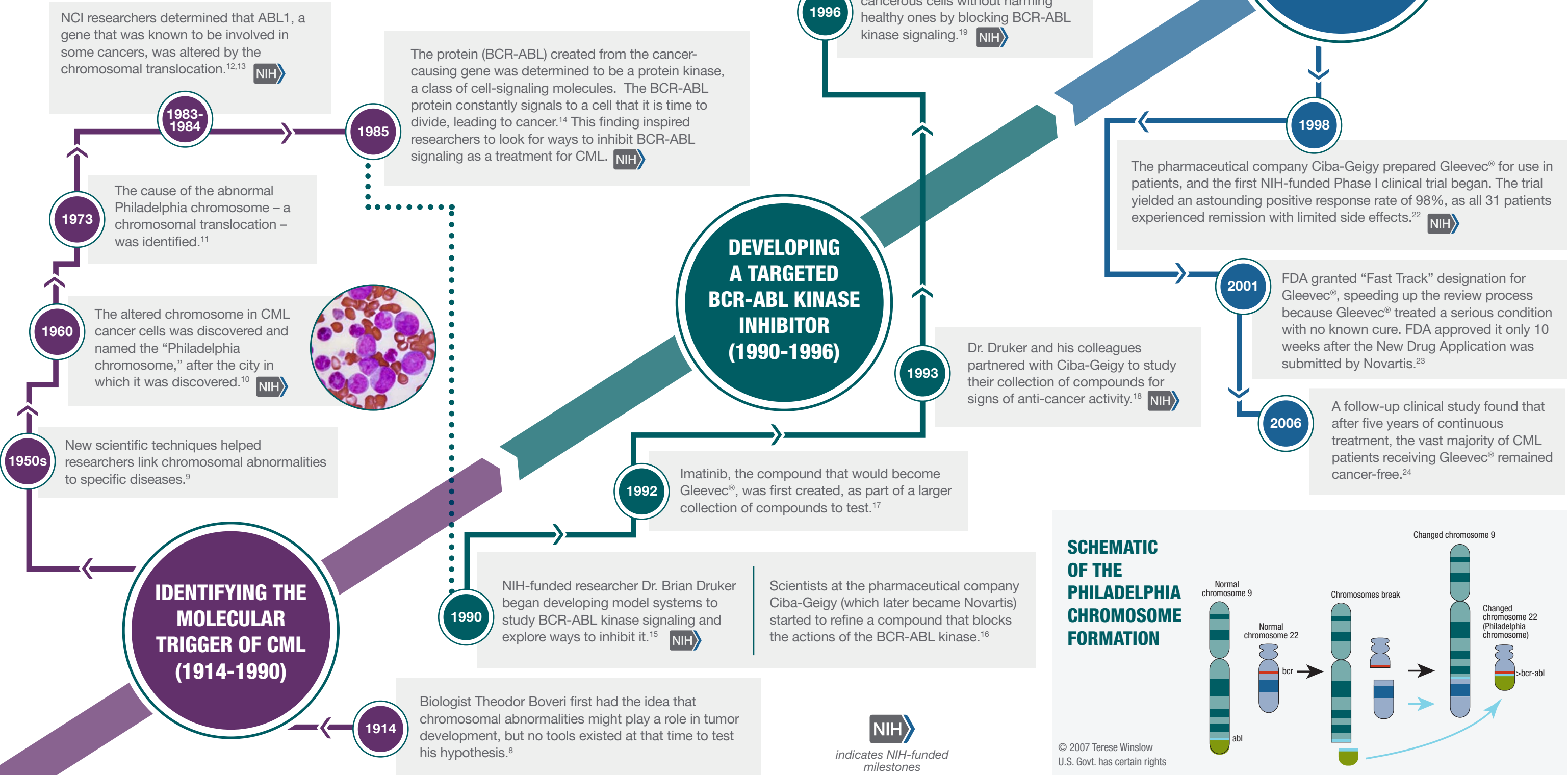
NOW

- Gleevec® was FDA approved in 2001. Among the first precise cancer treatments, Gleevec® preferentially targets the growth of cancer cells.
- Gleevec® is standard therapy for CML patients.
- Patients with a new diagnosis of CML are now expected to live 30 years post-diagnosis, essentially a normal lifespan.⁴
- Building on Gleevec's® success, dozens of other drugs targeting the same class of molecules are now available to treat cancer and other diseases.

CML patients treated with Gleevec® have an 89% five-year survival rate.²

RESEARCH-TO-PRACTICE MILESTONES FOR GLEEVEC®

For more information on the supporting evidence and research sponsors for the following milestones, see the Web appendix table.



IMPACTS OF GLEEVEC®

Gleevec® is a “first-in-class” drug that many consider to be a forerunner of molecular medicines. Its success was proof that knowledge about the underlying biological mechanism of a disease could help scientists design powerful, targeted strategies to kill cancer cells without harming healthy cells.

KNOWLEDGE

- Gleevec® was the first cancer drug approved by the FDA that directly targeted a signaling molecule inside the cell.²⁵
- The dramatic effectiveness of Gleevec® stimulated an ongoing surge of new research into the treatment potential of kinase inhibitors. For imatinib alone, more than 12,000 scientific articles have been published in the last 15 years.²⁶
- The success of Gleevec® spurred the development of other kinase inhibitors for CML and for other types of cancer. These newer kinase inhibitors, many based on the structure of Gleevec®, are improving survival rates for patients with CML and other diseases.²⁷



HEALTH

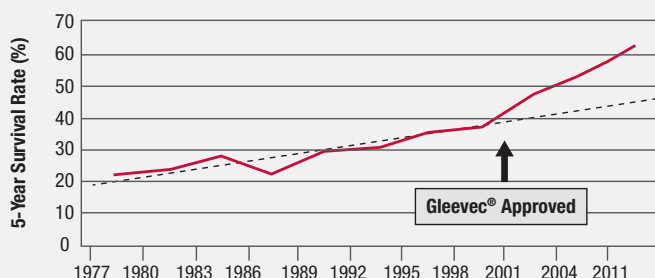
- Patients with a new diagnosis of CML are now expected to live 30 years post-diagnosis, essentially a normal lifespan.²⁹
- Worldwide, more than 600 clinical trials have been undertaken on Gleevec® for new disease indications and drug formulations.³⁰
- Gleevec® is now approved to treat multiple cancers, including gastrointestinal stromal tumors (GIST), in adults and children.³¹

Five-year survival rates for CML patients treated with Gleevec® currently top 89%.²⁸

SOCIETY

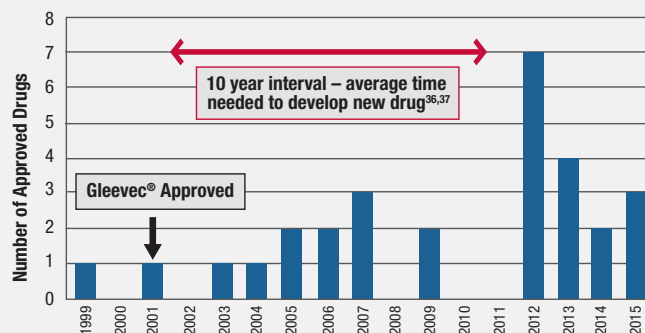
- Far beyond its impact on CML, Gleevec® helped to pave the way for a new industry of medications that are tailored to the specific genetic changes that cause a disease.
- More than 15 major pharmaceutical companies have pursued kinases as viable targets for new product development.³⁴
- By the end of 2014, more than 39 drugs targeting different kinds of kinases were approved by the FDA (see Figure).³⁵

CML Survival Rates Increased Dramatically after the Introduction of Gleevec®



Above: Five-year survival rates for patients with CML (including some patients not treated with Gleevec®) have doubled since Gleevec® was introduced, from about 30% in the early 1990s to over 60% today. The dotted line indicates the expected survival rate without Gleevec®. Source: NCI's Surveillance, Epidemiology, and End Results (SEER) database.³²

Gleevec® Stimulated New Drug Development: Number of FDA-approved Kinase Inhibitors by Year



Above: The approval of Gleevec® in 2001 initiated a flood of activity in drug discovery and development related to protein kinases. In 2012, roughly 10 years after Gleevec® came to market, a record number of kinase inhibitors were approved.^{36,37}



By the late 2000s, more than 100,000 CML patients worldwide had been treated with Gleevec®.³³