# 1 Cancer Drug Development

## *Challenges in a Competitive Market*

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## ABSTRACT

In the 1940s, a leak from a leftover canister of mustard gas prompted scientists to take a closer look at the myelosuppressive implications of nitrogen mustard for treating acute leukemia (then deemed a fatal disease). A new era of hope and possibility started with a mere accident, an inadvertent gas leak from a canister of nitrogen mustard. The era of genotoxic drug development had begun. Subsequent decades would herald remarkable advances in oncology medicine—in molecular understanding, scientific method, diagnostic tools, and therapeutic options.

Improved techniques and better diagnostic tools were enabling doctors to detect more cancers earlier. Improvements in the diagnosis and treatment of infectious and cardiovascular diseases were increasing the number of patients living long enough to contract cancer. An aging population contributed to a greater incidence of cancer and, consequently, higher therapeutic demand. Both the number of patients on cancer medicines and the duration of their treatment were growing. The "war on cancer," as declared by President Nixon, and the increased public perception of the "Big C" was further fueling the demand for anticancer agents. Genomically based, targeted therapies had begun to offer real hope: better efficacy and tolerability were providing the potential to live longer.

Between 1991 and 1995 the number of drugs in oncology development grew rapidly. One company, Bristol-Myers Squibb, demonstrated the opportunity to gain commercial success in a market once thought of as strictly niche.

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Apparent breakthroughs and frustrations, and emergent challenges and unmet needs, motivated and confounded a pharmaceutical industry that recognized the extraordinary opportunity inherent in the development of anticancer agents and the difficulties associated with turning such theoretical opportunities into a thriving, viable business.

With the common belief that cancer was a growing issue that had to be solved, biopharmaceutical companies seemed particularly well positioned to capture a significant proportion of a market in which traditional cytotoxic and hormonal therapies were expected to yield to targeted and novel therapeutics in the coming years.

In the early 2000s, many companies found that the promise of genomics was feasible, but not all approaches, and, in fact, few approaches, would actually work—there was a dose of reality. Bortezomib/Velcade is a case study of a company, Millennium, taking a completely new approach to treating cancer and bringing a novel drug, with a new mechanism of action to approval and market launch.

**Key Words**

Cancer; reality of cancer drug development; circumventing the pitfalls in cancer development; bortezomib; velcade; oncology; commercial; cancer team composition; cancer development collaborative approach; FDA; drug approval.

## 1. INTRODUCTION

In the 1940s, a leak from a leftover canister of mustard gas prompted scientists to take a closer look at the myelosuppressive implications of nitrogen mustard for treating acute leukemia (then deemed a fatal disease) *(1)*. A new era of hope and possibility started with a mere accident, an inadvertent gas leak from a canister of nitrogen mustard. The era of genotoxic drug development had begun. Subsequent decades would herald remarkable advances in oncology medicine—in molecular understanding, scientific method, diagnostic tools, and therapeutic options *(1)*.

Improved techniques and better diagnostic tools (better mammography, helical computed tomographic scans, and magnetic resonance imaging; serum-based screening tests such as prostate-specific antigen, CA-125, and α-fetoprotein; and molecular pathology testing) were enabling doctors to detect more cancers earlier. Improvements in the diagnosis and treatment of infectious and cardiovascular diseases were increasing the number of patients living long enough to contract cancer. An aging population contributed to a greater incidence of cancer and, consequently, higher therapeutic demand. Both the number of patients on cancer medicines and the duration of their treatment were growing. The "war on cancer," as declared by President Nixon, and the increased public perception of the "Big C" were further fueling the demand for anticancer agents *(2)*. Genomically based, targeted therapies had begun to offer real hope: better efficacy and tolerability were providing the potential to live longer.

By 1991, 126 oncology compounds were in development in laboratories around the world. By 1995, that number had grown to 302, with 138 companies managing oncology clinical pipelines (Millennium, data on file). Still, difficult questions challenged the nascent genotoxic drug development industry. Paclitaxel (Taxol®), which went on to become the top-selling oncology drug in history, generated $1.5 billion in sales in 1999. Bristol-Myers Squibb (BMS) had proved that launching a blockbuster oncology product was possible, despite the small and increasingly fragmented cancer-patient population *(3)*. (BMS also