

GENENTECH MARKETED PRODUCTS



■ Genentech manufactures and markets six pharmaceutical products in the United States for several serious medical conditions and promotes a seventh for various cancer indications. The first component of Genentech's strategy for growth is to maximize sales of its marketed products by protecting and increasing market share or market size and by leveraging new indications for the products. In 1996, Genentech received regulatory clearances for new indications for three of its products. In early 1997, through an agreement with Roche, Genentech added Roferon-A for various cancer indications to its product portfolio.

PRODUCTS AND APPROVED INDICATIONS:

Protropin (somatrem for injection) growth hormone

- Growth hormone inadequacy (GHI) in children

Nutropin [somatropin (rDNA origin) for injection] growth hormone

- GHI in children
- Growth failure from chronic renal insufficiency up to the time of renal transplantation
- Short stature from Turner syndrome*

Nutropin AQ [somatropin (rDNA origin) injection] liquid formulation growth hormone

- GHI in children
- Growth failure from chronic renal insufficiency up to the time of renal transplantation

Pulmozyme (dornase alfa) Inhalation Solution

- Cystic fibrosis patients with moderate and advanced* disease

Activase (Alteplase, recombinant), a tissue-plasminogen activator

- Acute myocardial infarction
- Acute massive pulmonary embolism
- Acute ischemic stroke*

Actimmune (Interferon gamma-1b)

- Chronic granulomatous disease

Roferon-A* (Interferon alfa-2a, recombinant)

- Several types of cancer

* New indication or new to portfolio



GROWTH HORMONE



Genentech employees pause to celebrate. Years of hard work led to an announcement in December 1996 that the FDA cleared for marketing Nutropin for the long-term treatment of short stature associated with Turner syndrome. This chromosomal disorder can cause numerous problems, most notably short stature. During 1996 the team also filed for U.S. regulatory clearance to market growth hormone for growth hormone inadequacy in adults.

Leading the field through service and support

Genentech is the only company to market in the United States three different growth hormone products, one of them for three indications, and the only company to offer a convenient liquid version.

Competition against Genentech's growth hormone products increased during 1996, with four competitive products now on the U.S. market and one additional product kept off the market as a result of ongoing patent litigation. Despite this, Genentech maintains a two-thirds market share. Though some market share loss is possible, Genentech will work to maintain a majority market share by continuing to partner with the pediatric endocrinology community in helping these physicians understand and enhance their patients' growth and development. Genentech's Medical Affairs group provides valuable information to these physicians through postmarketing studies unique to the field.



Genentech also will continue to defend its patent position against one product on the market for which litigation continues, and against another product which is not marketed due to an injunction against it.

In a continuing effort to enhance ease of use, Genentech is working in collaboration with Alkermes, Inc. to develop a sustained-release growth hormone product that would reduce the need for daily injections and potentially offer a significant competitive advantage.

Eighteen-year-old Maisha Lauer (photo above) is a high school senior who had a predicted height well below five feet because of Turner syndrome. However, she was able to receive treatment with Nutropin as part of a clinical trial. Today she is 4 feet 11 and $\frac{7}{8}$ inches tall (she calls it 5 feet) and happy to have received the therapy. Based on clinical trials of growth hormone in Turner syndrome patients such as Maisha, in 1996 Nutropin received regulatory clearance for the treatment of short stature related to Turner syndrome.



Opportunities exist primarily
in disease and young patients



PULMOZYME



Genentech's Pulmozyme Core Team plans an Early Intervention Trial to determine the long-term two-year effectiveness of Pulmozyme in young cystic fibrosis patients with preserved lung function. The team used data accumulated through both clinical studies and Genentech's Epidemiological Study of Cystic Fibrosis to plan this trial. It is scheduled to begin in 1997.

Working to help the full spectrum of cystic fibrosis patients

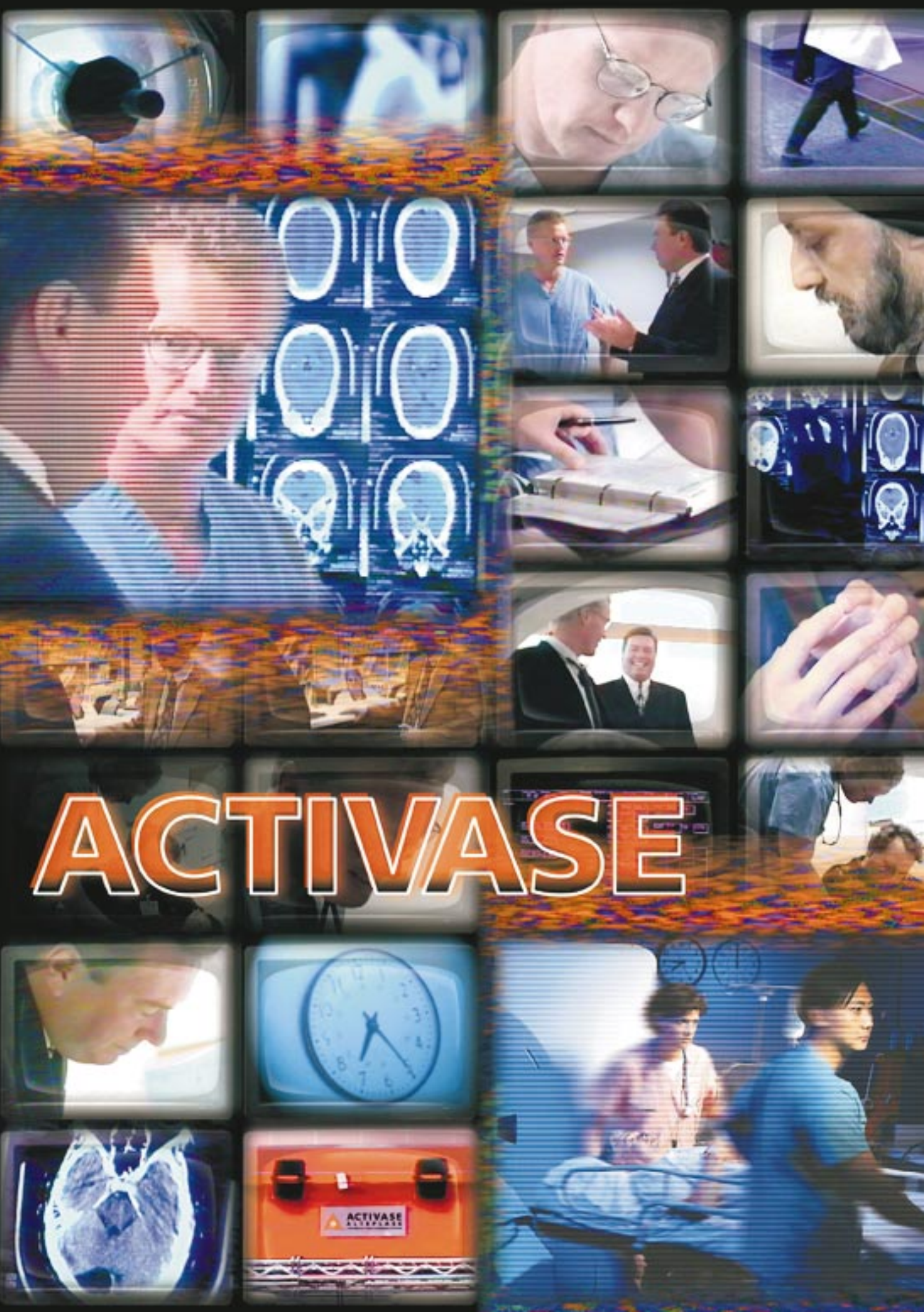
Cystic fibrosis is a genetically inherited, progressive disease that can begin with no or mild symptoms when the patient is very young. Over time, patients' health can deteriorate so that normal breathing becomes increasingly difficult and hospitalizations become more and more frequent. Ultimately, cystic fibrosis can progress to death, usually by age 30.

In 1994, Genentech received regulatory approval to market Pulmozyme for the management of cystic fibrosis patients from age five with mild to moderate disease. While this patient population benefited greatly from the medicine, Pulmozyme was not approved for management of very sick patients whose disease had progressed to a point where breathing is routinely compromised and infections are frequent. Genentech continued to study the medicine in these patients and in 1996 received clearance to market Pulmozyme for patients with advanced disease. This indication is especially beneficial to help keep patients healthy as they await lung transplants.

The question remained whether early intervention with Pulmozyme can benefit young patients with preserved lung function. Genentech is currently planning a clinical trial, to begin in 1997, to determine if it can. Through such continued study, Genentech's goal is to help all cystic fibrosis patients lead fuller, healthier lives.



Twenty-eight-year-old Stacy Hawes (photo above) is on "beeper status" for a lung transplant as a result of the cystic fibrosis with which she was diagnosed at age two. As the disease has progressed, Stacy has experienced increasingly frequent hospitalizations, lately about every six months. While she waits, Pulmozyme treatment helps keep her healthy enough to work full-time in the cable television industry and to qualify for a lung transplant. In 1996, Pulmozyme received regulatory clearance for the treatment of patients, like Stacy, with advanced cystic fibrosis.



ACTIVASE

ACTIVASE
SLEEPERS

The Message Is Urgency

Genentech representative Tim Yarnik has been working with Drs. Douglas Kabbes and Narinder Arora at Saint Anthony's Hospital in Effingham, Illinois, to help the hospital develop an urgent protocol for treating acute ischemic stroke with Activase, in an effort to improve outcomes of the hospital's ischemic stroke patients. The protocol involves predetermined steps: quick assessment; immediate paging of specialists needed to make a formal diagnosis if stroke is suspected; and fast administration of Activase within three hours of symptom onset if acute ischemic stroke is confirmed and the patient or patient's family agrees to the treatment. With the new protocol, these steps happen within one hour. Though still being fine-tuned at the time of her stroke, the hospital's stroke treatment protocol was essential to the successful treatment of Rosetta Bolander (opposite).

New indication for Activase gives hope to acute stroke patients

Activase received regulatory clearance for the treatment of acute ischemic stroke within three hours of symptom onset in June 1996. As a result, stroke—currently the country's leading cause of adult disability—joined heart attacks and trauma as medical conditions for which emergency treatment may reduce the risk of permanent disability. The approval was based upon data from a nationwide clinical trial, which showed that eligible patients treated with Activase within three hours were at least 33 percent more likely to recover with minimal or no disability than those treated with placebo.

Following the approval, Genentech worked closely with the National Institute of Neurological Disorders and Stroke, which, with more than 50 professional medical organizations from several health care fields, developed a blueprint for a national plan for rapid stroke treatment. The goal of this watershed effort is to help the medical community to quickly mobilize hospital teams and patients for optimal treatment of acute ischemic stroke.

Genentech is also involved with the American Academy of Neurology's national consumer and professional education campaign, the Stroke Awareness Response Treatment (START) Initiative. Besides further educating the medical community, this program focuses on public education with this key message: **Know the symptoms of stroke, and seek treatment fast.**



The Symptoms of Stroke

- Weakness/ numbness in the face, arm or leg, especially on one side of the body
- Sudden dimness, blurred or decreased vision, particularly in one eye
- Difficulty speaking or understanding speech
- Unexplained dizziness, loss of coordination, or sudden falls
- Sudden or severe headaches with no known cause

When 67-year-old Rosetta Bolander (photo above) experienced the symptoms of a stroke in September, 1996, she and her family knew to seek treatment quickly because of reports on Activase they had seen on television. Rosetta improved within half an hour of being treated with Activase and recovered with no signs of damage, much to the delight of her six children, 17 grandchildren and two great grandchildren.

Leader for heart attack treatment

Activase currently leads the thrombolytic market in the United States. In 1996, Activase's market share climbed to approximately 80 percent from approximately 75 percent at the end of 1995.

Activase as a heart attack treatment faces challenges to its share of the thrombolytic market and to the size of that market. Genentech is vigorously facing these challenges.

In 1996, Boehringer Mannheim announced that the FDA licensed its heart attack drug, Reteplase (brand name Retavase®). Genentech believes Reteplase infringes Genentech patents and has filed a patent infringement action against Boehringer Mannheim.



Genentech also is currently developing in Phase II clinical trials a second-generation t-PA, called TNK, which is potentially more effective and faster to administer than t-PA.

Despite Activase's strong market share, the overall size of the thrombolytic therapy market during 1996 has declined by about 6.5 percent compared to 1995 as a result of some heart attack patients receiving angioplasty rather than thrombolytic therapy and others receiving therapy through ongoing large-scale clinical trials. This decreased market size has led to a 1996 decline in sales from 1995. However, a study reported in the *New England Journal of Medicine* in October 1996

demonstrated no significant mortality difference between primary angioplasty and thrombolytic therapy, but that rates of procedures and costs were lower for patients who received thrombolytic therapy. In addition, angioplasty is an invasive procedure requiring specialized equipment and facilities and is currently available at a limited number of hospitals in the United States.

The Symptoms of Heart Attack

- Uncomfortable pressure, fullness, squeezing or pain in the center of the chest lasting for two minutes or more
- Pain spreading to the shoulders, neck, jaw, arms or back
- Dizziness, fainting, sweating, nausea and/or shortness of breath

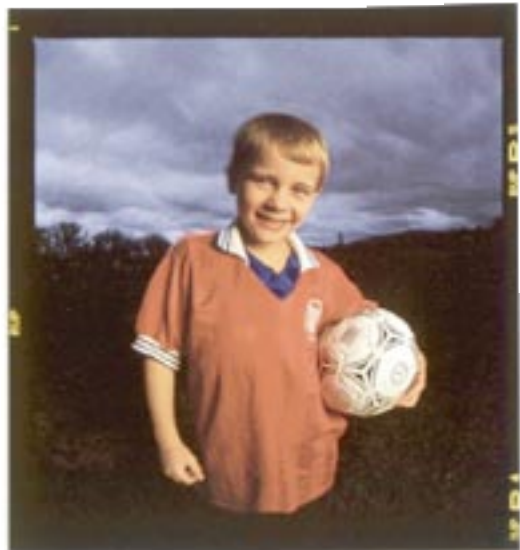
When what he thought was early morning indigestion persisted and worsened, 48-year-old Dalvinder Matharu (photo above) called his local hospital, who advised him to call 911. He was transported to the hospital, and was diagnosed as having an acute myocardial infarct—a heart attack. After physicians quickly treated him with Activase, he felt relief within minutes. Since his heart attack, Dalvinder has adopted a heart-healthy lifestyle, with a healthy diet and consistent exercise schedule.

A c t i m m u n e

Keeping healthy, despite CGD

Patients with chronic granulomatous disease (CGD) have a defect in their immune system that leaves them vulnerable to repeated, severe infections, which often require hospitalization and can cause death. Actimmune reduces approximately threefold the frequency of serious infections requiring hospitalizations. Of the approximately 400 patients in the United States with this very rare, inherited disease, most are children. Actimmune helps these patients stay healthy so they can lead a more normal life.

It was not until after his brother died of chronic granulomatous disease in 1994 that 8-year-old Ronald McFarland (photo at right) was diagnosed with the same inherited disease. Ronald's mom, Kim, says that before the diagnosis, Ronald was sick and hospitalized often with mold pneumonia and bladder problems. Since he started treatment with Actimmune two years ago, Ronald has not been hospitalized and rarely misses school.



R o f e r o n - A

Roferon-A paves the way into the oncology market

Through a 1997 agreement with Roche, Genentech now promotes Roche's Roferon-A in the United States for its approved oncology indications, including hairy-cell leukemia, AIDS-related Kaposi's sarcoma and Ph-positive chronic myelogenous leukemia. As Genentech builds an oncology business, the experience it gains through promoting Roferon-A will provide significant benefit.

Programs for Marketed Products

Some of Genentech's efforts relate to all six of its marketed products. Two marketing programs are described below:

Patient assistance programs

Genentech believes all patients who need its marketed medicines should receive them, regardless of economic or insurance status. Since its first product reached the market in 1985, the company has had programs in place to help ensure this happens. Today, Genentech offers reimbursement information programs, featuring a reimbursement hotline, to provide information on and assistance with various payment resources available to patients.

Genentech also has programs to ensure that even qualified patients who are not eligible for reimbursement can get the treatment they need. Over the past twelve years, Genentech has provided more than \$200 million worth of pharmaceuticals free of charge through various programs for un- or underinsured patients in the United States.

Managed care

Genentech's managed care group is committed to partnering with customers to ensure it meets the needs of both patients and health care providers. The company has had a managed care staff in the field for more than a year, working to help medical providers recognize the benefits of Genentech products for their patients. As Genentech's development pipeline produces new products, the managed care group will play an essential role by preparing managed care organizations for novel therapeutics. By being well educated ahead of time, these organizations will be more readily able to integrate the products into their systems as the new medicines reach the market. In support of these efforts, Genentech's health economics group provides valuable information about the economic and quality-of-life benefits of Genentech products. This information is becoming increasingly necessary to provide the best patient care with the most efficient use of resources within a cost-conscious environment.

Genentech's Medical Affairs group also works with the company's marketed products, continuing clinical investigation efforts once a product has reached the market.

Genentech Observational Clinical Studies		
Study Name	Participating Groups	Patients Included in Study
National Cooperative Growth Study (NCGS)	>650 pediatric endocrinologists	>27,000 patients treated with growth hormone
CRI Arm of North American Pediatric Renal Transplant Cooperative Study*	Pediatric nephrologists	Children treated with growth hormone for growth failure related to chronic renal insufficiency
National Registry of Myocardial Infarction (NRFMI)	>1,500 participating medical centers	>750,000 heart attack patients
Epidemiological Study of Cystic Fibrosis (ESCF)	Almost 200 centers	>19,000 cystic fibrosis patients

*Genentech sponsors the CRI arm of NAPRTCS, but, unlike the other studies listed here, it is not a Genentech study.

Observational clinical studies

To provide physicians, hospitals and managed care organizations valuable information to help them optimize patient care, Genentech's Medical Affairs group continues clinical investigation of its marketed products after they

reach the market. The table above indicates the variety of observational clinical studies Genentech conducts in cooperation with clinical investigators or sponsors.