

Genzyme Corporation (formerly GelTex Pharmaceuticals, Inc.)

Anti-Infectives Would Eradicate Viruses

*As the genetic code began to unravel in the early 1990s, scientists began to explore new options for treating diseases. One possibility involved creating molecules akin to "super-antibodies" that would detect and bind to particular pathogens, flushing them from the body before infection could spread. This new treatment method could significantly reduce healthcare expenditures, could recover worker productivity lost to sick days, and could usher in a new generation of medical treatments designed to eradicate viruses rather than just treat their symptoms. To this end, GelTex Pharmaceuticals, Inc., sought to create custom molecules, called "anti-infectives," that would seek out viruses, bond to them, and render them harmless. The viruses targeted by GelTex were *C. parvum* and human rotavirus, which cause diseases that attack the gastrointestinal tract of individuals with lowered resistance such as children, the elderly, and HIV/AIDS patients.*

GelTex's research could potentially create a pathbreaking technology for curing viruses that would generate substantial economic spillover for employers and the U.S. economy. In 1994, the Advanced Technology Program (ATP) awarded GelTex \$2 million to pursue a three-year effort to develop these anti-infectives. At the end of the ATP-funded project, however, healthcare industry issues had forced GelTex to abandon its research plan. In 2000, Genzyme Corporation acquired GelTex and the two companies continued their drug development efforts. Knowledge that GelTex had gained during the ATP project allowed Genzyme to expedite some drug development functions.

COMPOSITE PERFORMANCE SCORE

(based on a four star rating)

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Research and data for Status Report 94-01-0147 were collected during October - December 2001.

Current Methods Only Treat Symptoms of the Virus

As anyone who has had the flu knows, antibiotics do not work on viruses. Typically, medical professionals can only treat a patient's fever, sore throat, and cough while the virus runs its natural course through the body. Similarly, treatment for the viruses *C. parvum* and human rotavirus, which cause viral gastroenteritis, involved only treating the symptoms of the ailment. Improvements in virus treatments could not be made unless methods of actually killing the viruses themselves were found, which was the focus of GelTek's proposed research.

Killing Viruses Marks a Major Shift for Medical Treatment

GelTex developed a program to research molecular recognition polymers that would act as anti-infectives, binding to the viruses, neutralizing them, and passing them harmlessly through the gastrointestinal tract. Viruses attack by attaching to human cells at specific points, injecting viral ribonucleic acid (RNA) into the human cell where the RNA replicates, forming new viruses, and then moving on to infect other human cells. The proposed anti-infectives would be engineered with an outer "skin" of receptors that would bind to a virus,

occupying the very receptors that bind to and infect human cells. These polymers would be used to neutralize the reproduced viruses, preventing their continued onslaught on the human body. Unable to bond with and infect new cells, the neutralized viruses would either be passed out of the body through waste products or would die inside the body without infecting new cells, thus allowing the patient to recover much faster.

Anti-Infective Technology Could Save Billions of Dollars

In the early 1990s, the healthcare industry projected that the successful treatment of *C. parvum* could save the nation \$135 million annually. Moreover, since rotavirus affects 3.5 million American children annually, better treatment could generate savings of up to \$1 billion in treatment costs and economic losses from parents' lost work time while caring for their children. If this research program proved successful, the next step would be to neutralize other viruses that could result in much greater savings for the U.S. economy. Therefore, ATP awarded GelTex \$2 million to conduct research with the goal of eliminating viruses through the development of its anti-infectives.

Healthcare Industry Concerns Cause Early Termination of Research

During the ATP project, a number of changes in the healthcare industry required that GelTex redirect its research. In the second quarter of 1996, GelTex discovered that a pharmaceutical company was making rapid progress toward introducing a vaccine that would limit the market for an oral rotavirus treatment. At the same time, GelTex was making rapid progress toward developing the *C. parvum* anti-infective. As a result, the company directed its resources away from rotavirus and toward its *C. parvum* program.

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By May 1997, GelTex had identified three lead compounds with which to conduct final *C. parvum*

testing, but again the market shifted in an unfavorable manner for GelTex. The "drug cocktail" of protease inhibitors for HIV/AIDS patients became available in mid-1997. This combination therapy drastically reduced the incidence of *C. parvum* infections among HIV/AIDS patients. With fewer patients catching the virus in the first place, the potential market for a *C. parvum* anti-infective shrank to the \$25 million to \$75 million range. Based on costs to get a drug through the lengthy Food and Drug Administration trials process, this market was too small for investors to pursue. Therefore, with three months remaining on the ATP project, GelTex ceased work on its anti-infective for *C. parvum*.

ATP Award Leads to External Funding

ATP funding lent credibility to GelTex's efforts and aided in attracting additional capital. One year after the initiation of its ATP project, GelTex went public. The company continued to fund infectious disease research after the ATP award ended, more than doubling the staffing level for the program to 14 full-time equivalents. In 2000, GelTex was acquired by Genzyme, and the combined firms used the knowledge that GelTex had gained during the ATP project to continue their drug development efforts.

Conclusion

ATP awarded cost-shared funds to GelTex in order to implement a research plan to develop an "anti-infective" that would eliminate viruses from the human body rather than just treating the symptoms. The healthcare industry and the U.S. economy as a whole stood to benefit from a successful research effort through more effective healthcare and fewer work days lost to illness or time spent caring for sick children. From human rotavirus alone, the economic benefits from successful treatment could reach \$1 billion.

Despite this promising beginning, various changes in the healthcare marketplace led GelTex to abandon its research. Other treatment options for the two viruses tested during the research project entered the marketplace, diminishing the possibility for successful commercialization. After GelTex was acquired by Genzyme in 2000, the knowledge gained from the ATP-funded research assisted the companies' continued drug development efforts.

PROJECT HIGHLIGHTS

Genzyme Corporation (formerly GelTex Pharmaceuticals, Inc.)

Project Title: Anti-Infectives Would Eradicate Viruses
(Molecular Recognition Polymers as Anti-Infectives)

Project: To develop anti-infectives that bind to, and render harmless, *C. parvum* and human rotavirus that attack the human gastrointestinal tract.

Duration: 2/1/1995-1/31/1998

ATP Number: 94-01-0147

Funding (in thousands):

ATP Final Cost	\$2,000	25%
Participant Final Cost	<u>5,860</u>	75%
Total	\$7,860	

Accomplishments: Although changes in the healthcare marketplace ultimately forced GelTex to halt its anti-infective program for rotavirus and *C. parvum*, the ATP project enabled in vivo research on a non-influenza virus for the first time. As a result of the ATP-funded research, GelTex committed significant funds to infectious diseases, more than doubling staffing levels. Further, after returning to rotavirus research in late 1998, GelTex received the following patents:

- "Ionic polymers as anti-infective agents"
(No. 6,034,129: filed June 24, 1996, granted March 7, 2000)
- "Polyvalent polymers for the treatment of rotavirus infection"
(No. 5,891,862: filed September 20, 1996, granted April 6, 1999)
- "Acid-functionalized saccharides as polyvalent anti-infectives"
(No. 5,821,312: filed June 25, 1997, granted October 13, 1998)
- "Ionic polymers as toxin-binding agents"
(No. 6,007, 803: filed September 19, 1997, granted December 28, 1999)
- "Antiviral polymers comprising acid functional groups and hydrophobic Groups"
(No. 6,060,235: filed September 19, 1997, granted May 9, 2000)

- "Polyvalent polymers for the Treatment of Rotavirus Infection"
(No. 6,187,762: filed April 5, 1999, granted February 13, 2001)

- "Anionic polymers as toxin binders and antibacterial agents"
(No. 6,270,755: filed April 3, 2000, granted August 7, 2001)

- "Anionic polymers as toxin binders and antibacterial agents"
(No. 6,290,946: filed May 11, 2000, granted September 18, 2001)

- "Ionic Polymers as Toxin-Binding Agents"
(No. 6,290,947: filed June 19, 2000, granted September 18, 2001)

Commercialization Status: Due to changes in the healthcare industry for *C. parvum* and human rotavirus, GelTex was unable to take its research beyond the laboratory. The knowledge gained from this project has assisted Genzyme (after it acquired GelTex in 2000) in further drug development activities.

Outlook: In late 1998, GelTex renewed its focus on rotavirus research. Some products may well result from the ATP-funded research.

Composite Performance Score: * *

Number of Employees: Seven employees at project start, 14 at project conclusion, 5,000 at Genzyme (which acquired GelTex) as of December 2001.

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