



# Partnership

## PROGRESS IN PARTNERSHIP

The success of Genzyme Transgenics is directly linked to the partnerships it has developed with major pharmaceutical and biotechnology companies. In 1999, the Company initiated and extended collaborations with a number of companies that recognized both the potential of transgenic technology to meet their protein production requirements and the leadership role Genzyme Transgenics has taken in this growing field. Timely execution of existing partnership programs in 1999 resulted in the Company's ability to achieve milestone payments totaling nearly \$7M.

Genzyme Transgenics' primary focus is on using transgenic technology to produce monoclonal antibodies in partnership with companies actively conducting clinical development of this promising new class of therapeutics. In 1999, between new partnerships and existing collaborations, Genzyme Transgenics developed founder goats transgenic for several different monoclonal antibodies/Ig

fusion protein projects. The Company is developing a transgenic version of Remicade® in a collaboration with Centocor. Also, Genzyme Transgenics is developing transgenic versions of eight additional monoclonal antibodies/Ig fusion molecules, the cell culture versions of which are currently in clinical trials, including D2E7 and MAK195 for BASF/Knoll, CTLA4Ig and an Ig fusion molecule for Bristol-Myers Squibb, Antegren® for Elan Pharmaceuticals, BR96 for Seattle Genetics, PRO542 for Progenics and a therapeutic recombinant protein for Alexion. The indications for these products include arthritis, HIV/AIDS, cancer and autoimmune diseases. These corporations are currently conducting human clinical trials with cell-culture produced versions of their proteins and are having Genzyme Transgenics produce them transgenically. The strategy is to transition to transgenic-derived product in order to meet market demand. The status of the cell culture and transgenic versions of these products is shown in the chart below.

Partner	Product Name	Indication	Development Stage Cell Culture/Plasma Product	Development Stage Transgenic Product
<b>MONOCLONAL ANTIBODIES / IMMUNOGLOBULIN FUSION PROTEINS</b>				
Centocor	Remicade®	Crohn's Disease; Rheumatoid Arthritis	Marketed	Transgenic goats identified.
BASF/Knoll	D2E7	Rheumatoid Arthritis	Phase III clinicals	
Elan Pharmaceuticals	Antegren®	Neurological Disorders	Phase II clinicals	
Bristol-Myers Squibb	CTLA4Ig	Rheumatoid Arthritis	Undisclosed	Transgenic goats under development.
Bristol-Myers Squibb	Undisclosed	Organ Transplant Rejection; Autoimmune Disorders	Undisclosed	
Alexion Pharmaceuticals	Undisclosed	Undisclosed	Undisclosed	
Progenics Pharmaceuticals	PRO542	HIV/AIDS	Phase II clinicals	
<b>PLASMA PROTEINS</b>				
Genzyme Corporation	Antithrombin III	Anti-clotting	Marketed	Transgenic product in Phase III trials.
Fresenius AG	Human Serum Albumin	Blood Expander	Marketed	Transgenic cows producing HSA identified.

## *Focusing Our Partnerships on Monoclonal Antibodies*

Monoclonal antibodies represent one of the biotechnology industry's greatest successes. As a result, the last several years have witnessed the clinical success, regulatory approval and commercial launch of several breakthrough monoclonal antibody therapies by a number of companies including ReoPro<sup>®</sup> for use in various acute cardiac conditions, Rituxan<sup>®</sup> for B-cell non-Hodgkin's lymphoma, Synagis<sup>®</sup> for treatment of viral respiratory disease in premature babies, Herceptin<sup>®</sup> for breast cancer, Remicade<sup>®</sup> for use in Crohn's disease and rheumatoid arthritis and Zenapax<sup>®</sup> for acute transplant rejection. These clinical successes, the availability of technologies for making fully human molecules and drug discovery technologies that identify potential antibody targets, will continue to drive the development of new antibody-based therapeutics for which Genzyme Transgenics and its technology can be uniquely enabling.

Therapeutic antibodies are typically administered in larger doses than other protein therapeutics and in repeated doses to treat chronic illnesses. Their continued success is driving the need for commercially feasible production methods yielding significantly higher quantities than currently available using traditional protein production methods. While the annual worldwide requirement of a typical recombinant protein may approach 10 kilograms, Genzyme Transgenics believes that many antibodies will require supplies in excess of 100 kilograms annually. Current cell culture methods (the only traditional method available for producing monoclonal antibodies) generally cannot produce the requisite high volumes needed for antibody therapeutics, are not economically feasible and require significant capital investment. Genzyme Transgenics believes that the high expression levels which can be achieved using transgenic technology will enable the pharmaceutical industry to meet these market demands.

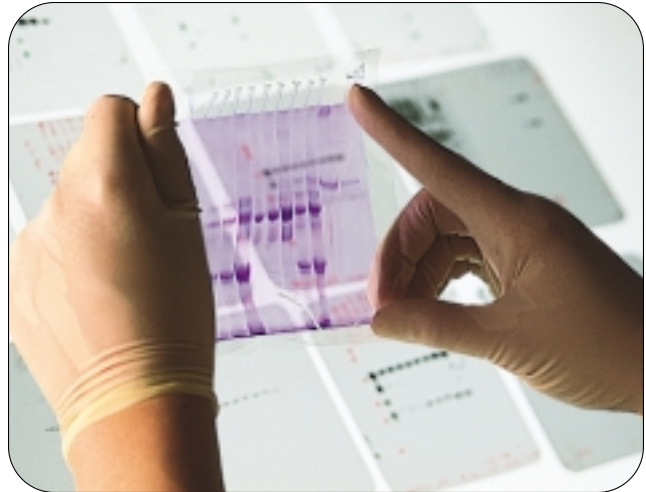
*“At Bristol-Myers Squibb, we are developing novel ways of treating autoimmune disorders such as rheumatoid arthritis. Our partnership with Genzyme Transgenics is directed to helping us produce these proprietary biologic compounds in a cost efficient manner that will allow us to continue our research and to benefit patients in the future.”*

— Ronald Pepin, Ph.D.  
*Executive Director, External Science and Technology  
Bristol-Myers Squibb Company*

*“After purposeful evaluation of various production methods, Alexion decided that Genzyme Transgenics’ technology held great promise for the high volume manufacture of our product at attractive costs.”*

— David Keiser  
*Executive Vice President,  
Chief Operating Officer  
Alexion Pharmaceuticals*

Genzyme Transgenics entered into two strategic alliances in 1999 in order to facilitate the purification of transgenic proteins from milk. Genzyme Transgenics signed a letter of intent with Lonza Ltd. of Basel, Switzerland, a worldwide leader in custom manufacturing, under which Lonza will work in partnership with Genzyme Transgenics on a project by project basis, to provide downstream purification capabilities for transgenically produced monoclonal antibodies and other therapeutic proteins. In addition, an alliance was formed with DSM Biologics to provide development and downstream purification capability for the initial phases of the Human Serum Albumin project. These alliances enable Genzyme Transgenics to provide a complete package of services to its partners for production of therapeutic proteins.





*“The milk of transgenic cows is a safe, pure and economical source of human albumin. Recent breakthroughs by Genzyme Transgenics in this technology and its rapid development promise to revolutionize the albumin market and could provide many other medical and healthcare products as well.”*

— Wolfram Eichner, Ph.D.  
*Head of Biotechnology  
Fresenius AG*

During 1999, the Company achieved several milestones under a collaboration with Fresenius AG for the production of Human Serum Albumin (“HSA”). These milestones included the demonstration of expression of HSA in the milk of transgenic cattle at a concentration that is consistent with making it a commercially viable product. The therapeutic use of HSA is indicated in situations of blood loss and decreased blood albumin levels which can occur in a number of serious medical conditions, including shock and burns. HSA is currently sourced from human plasma, with current worldwide sales of approximately \$1.0 billion.

The progress, partnerships and strategic alliances that Genzyme Transgenics has developed over the past year have become the strong foundation for the Company's success and continued growth. Genzyme Transgenics is continually evaluating new technologies and complimentary alliances in order to advance the Company's leadership position in the transgenic production of therapeutic proteins.