

# Transgenics: THE PROCESS

## HOW TRANSGENICS WORKS

### therapeutic proteins:

Proteins used to maintain health or treat disease in humans.



The core business of Genzyme Transgenics is the production of valuable human **therapeutic proteins\*** in the milk of transgenic animals. Transgenic animals carry genetic information allowing them to make these human therapeutic proteins. Once they are produced, the therapeutic proteins can be efficiently purified for use. This process offers an effective, reliable source of valuable biopharmaceuticals that would otherwise be available only from blood, tissue extracts or cellular bioreactors.

Genzyme Transgenics has primarily focused on the use of goats for the production of antibodies and many other proteins. A variety of factors, including a high milk yield, protein content, short gestation period and time to maturation make goats particularly well suited for biopharmaceutical development and scale-up for commercial product.

### Milk Protein Promoter DNA:

*Directs transgene expression to the mammary gland during lactation.*

### Protein Coding DNA

*The cloned gene for a therapeutic protein.*

### Transgene Expression Vector

*A combination of the milk protein promoter and the protein coding DNA.*

### Isolation of Fertilized Eggs

*The transgene is microinjected into fertilized eggs.*

### Embryo Transfer into Recipient Females

*Recipient females serve as surrogate mothers who carry microinjected embryos to term.*

**fig: 4.1**

Schematic overview of the production of transgenic animals.



Jack Green (*Vice President and Chief Financial Officer*) "1998 was a year of transition for Genzyme Transgenics, yet, at the same time, the Company remained committed to the development of all its scientific programs.

This commitment facilitated our efforts to expand the value of the Company and solidify the potential impact of transgenics in the development of new therapeutics."

### Testing for Presence of the Transgene

Animals carrying the transgene for the targeted therapeutic are identified.

### Mating of Transgenic Founders

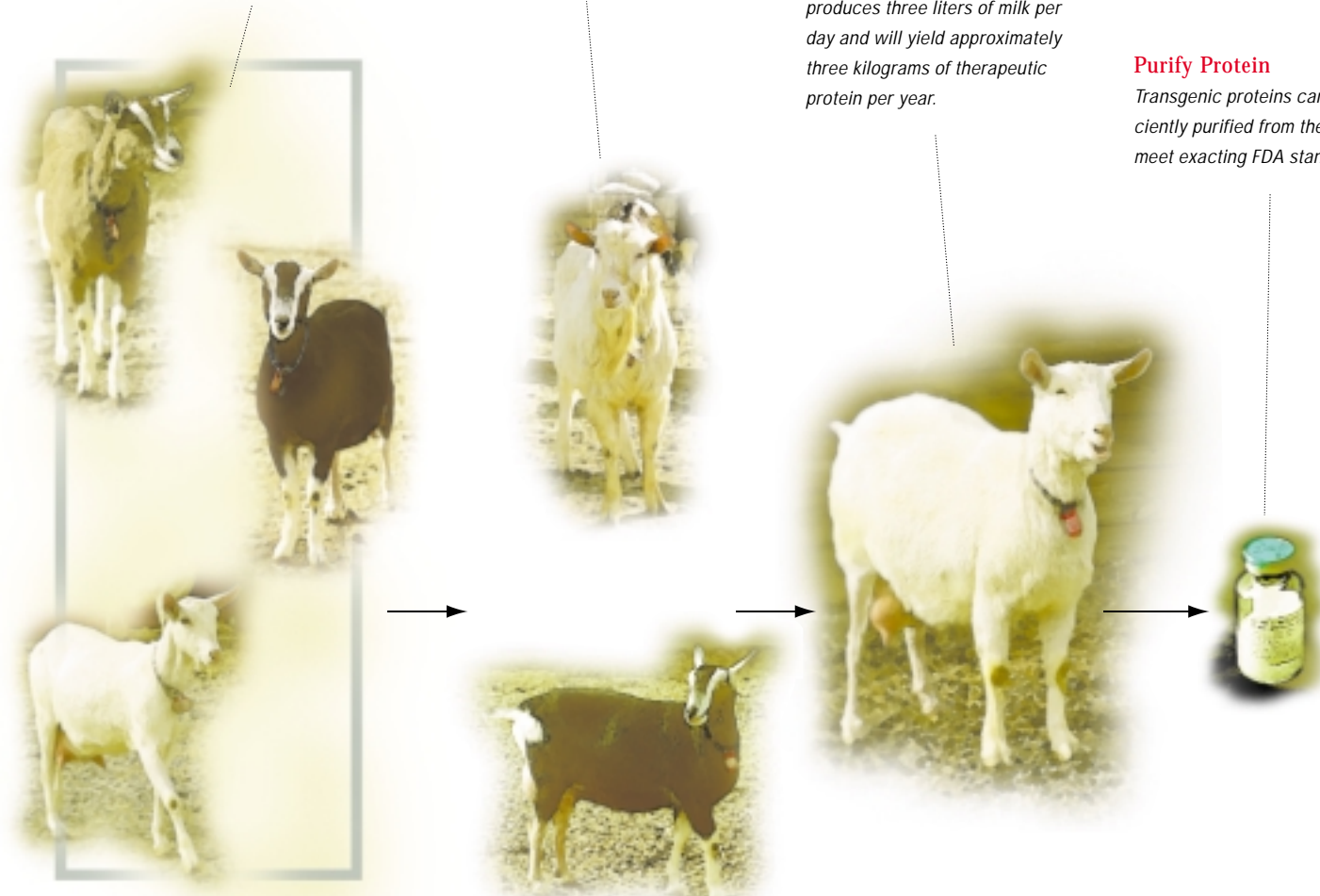
First generation carriers of the transgene are called "founder" animals. Female offspring of these animals serve as the production herd.

### Milk Transgenic Female

The therapeutic proteins are expressed in the milk of transgenic females. A single goat typically produces three liters of milk per day and will yield approximately three kilograms of therapeutic protein per year.

### Purify Protein

Transgenic proteins can be efficiently purified from the milk to meet exacting FDA standards.



### WHY TRANSGENICS?

Transgenic production of recombinant proteins offers a broad spectrum of benefits over traditional cell culture methods. On a scientific level, these benefits include the potential for development of hard-to-express proteins, the creation of **unique molecules\*** and their expression at commercially attractive levels. On the manufacturing side, transgenics offers flexible scale-up through herd expansion, reduced capital requirements and risk and the prospect of large-scale, cost effective production.

### unique molecules:

Modified versions of existing pharmaceuticals which can enhance specific features or benefits, such as pharmacokinetics or biological activity.

Sandra Nusinoff Lehrman, M.D. (*President and CEO*) "Our primary mission is, through transgenic technologies, to enable unique therapeutics for the ultimate benefit of people with serious illnesses and diseases.

To ensure the fulfillment of this mission, we support internal research and development and cultivate strategic alliances and partnerships with key biotechnology and pharmaceutical firms that will help us increase shareholder

value. By extension, this enables us to increase our value to the people we seek to serve."