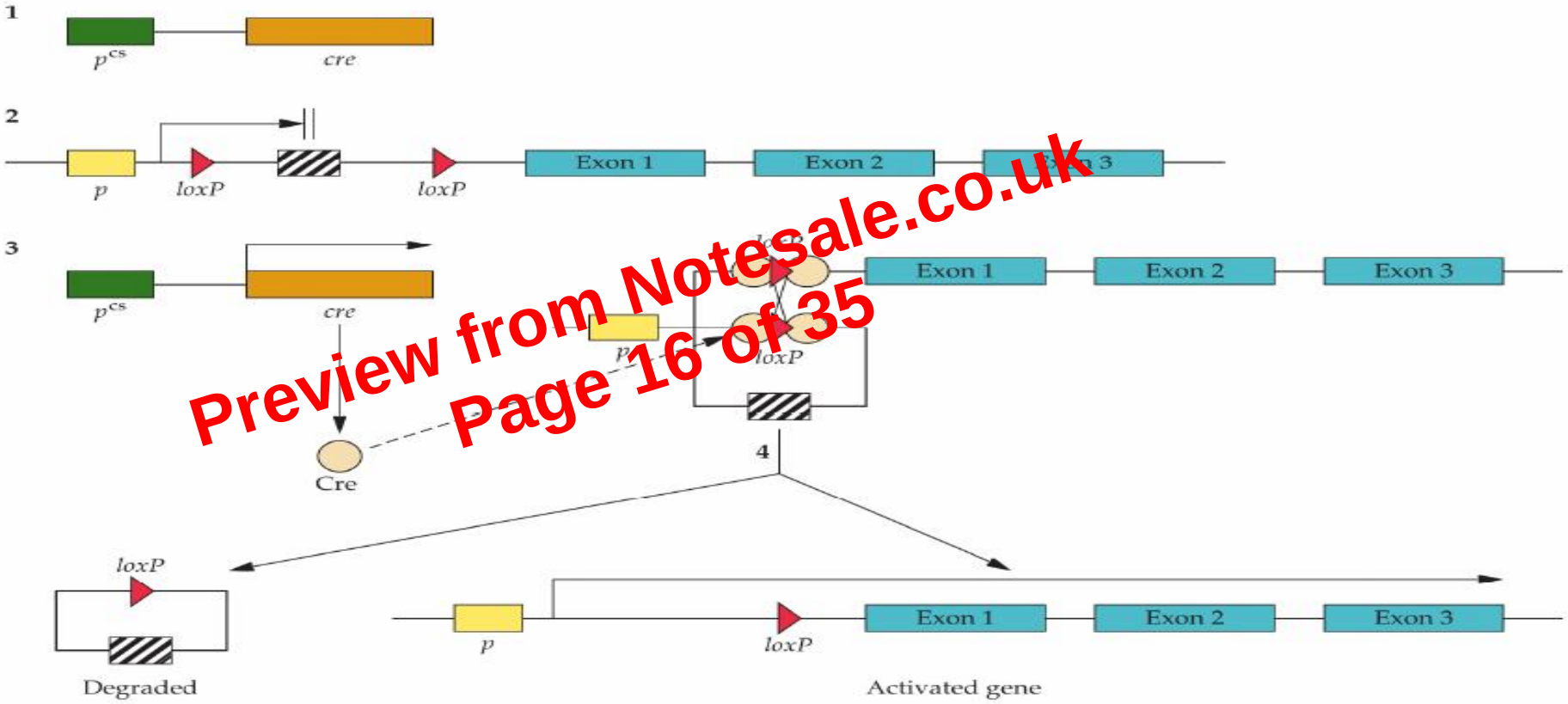

FIGURE 21.12 Cre–*loxP* recombination system for activating a transgene in a specified cell type. (1) The *cre* gene is placed under the control of a cell-specific promoter (p^{cs}) and established as a transgene in a line of mice. (2) A piece of DNA with *loxP* sites that flank a transcription termination sequence (hatched box) is cloned between a promoter *(p)* and the first exon (Exon 1) of a gene. (3) The construct with the *loxP* sites is introduced into a chromosomal site of embryonic stem cells by homologous recombination, and a transgenic mouse line is established with these cells. The two transgenic lines are crossed. In cells where both constructs are present, the Cre recombinase (beige circle) is synthesized, and two Cre molecules bind to each *loxP* site (dashed arrow). (4) The *loxP* sites undergo recombination (×), leading to the excision and circularization of a *loxP* site and a transcription termination sequence that is eventually degraded and the formation of a transcriptionally active transgene that is retained in the chromosome. The right-angled arrows denote transcription, and the parallel vertical bars indicate termination of transcription.

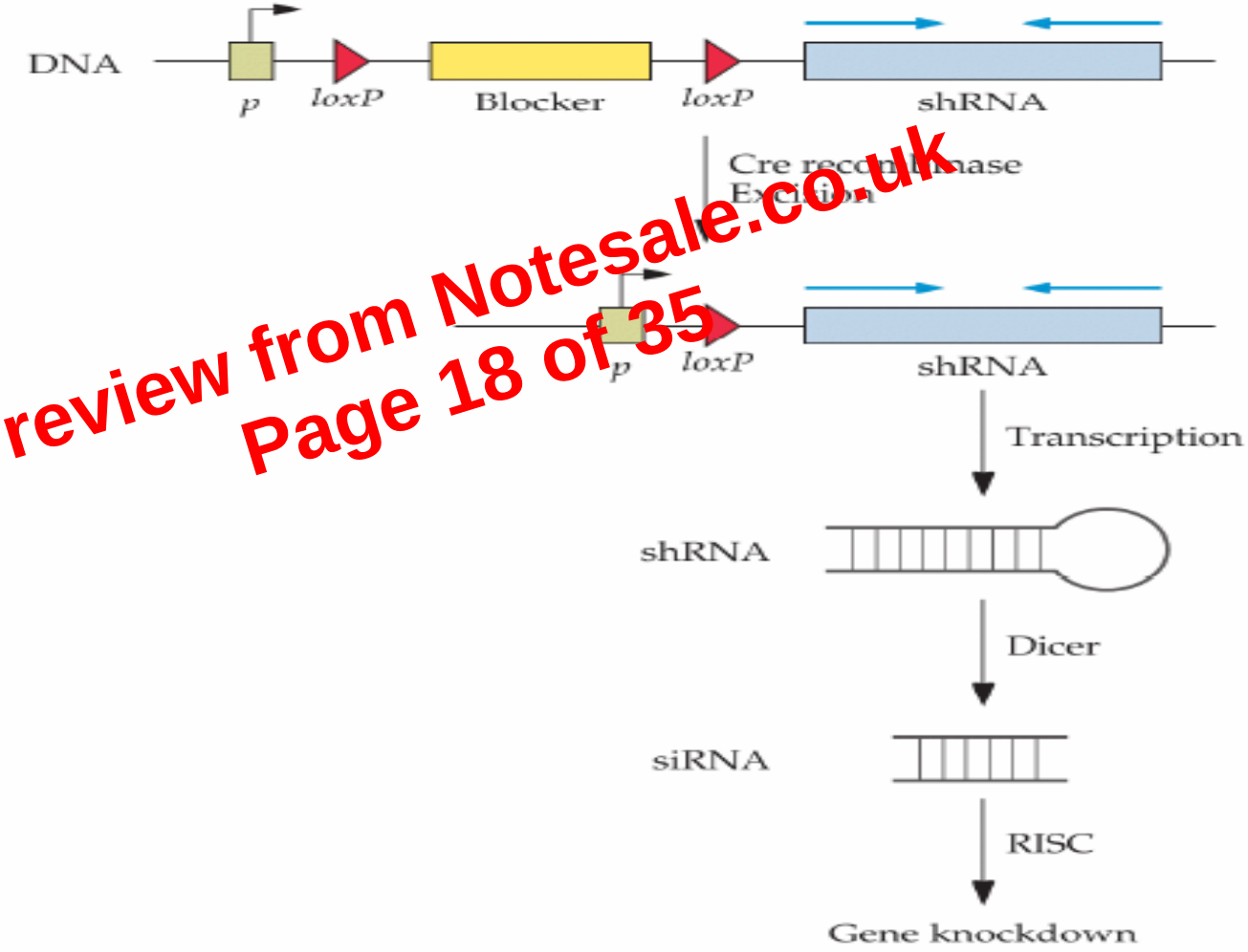

FIGURE 21.14 Conditional knockdown of target gene expression using RNAi. A blocking sequence, flanked by *loxP* sites in the same orientation, is inserted between the sequence encoding the shRNA and the promoter that controls expression of the hairpin RNA (*p*). Cre recombinase-mediated recombination between *loxP* sites excises the blocking sequence and restores expression of the hairpin RNA.

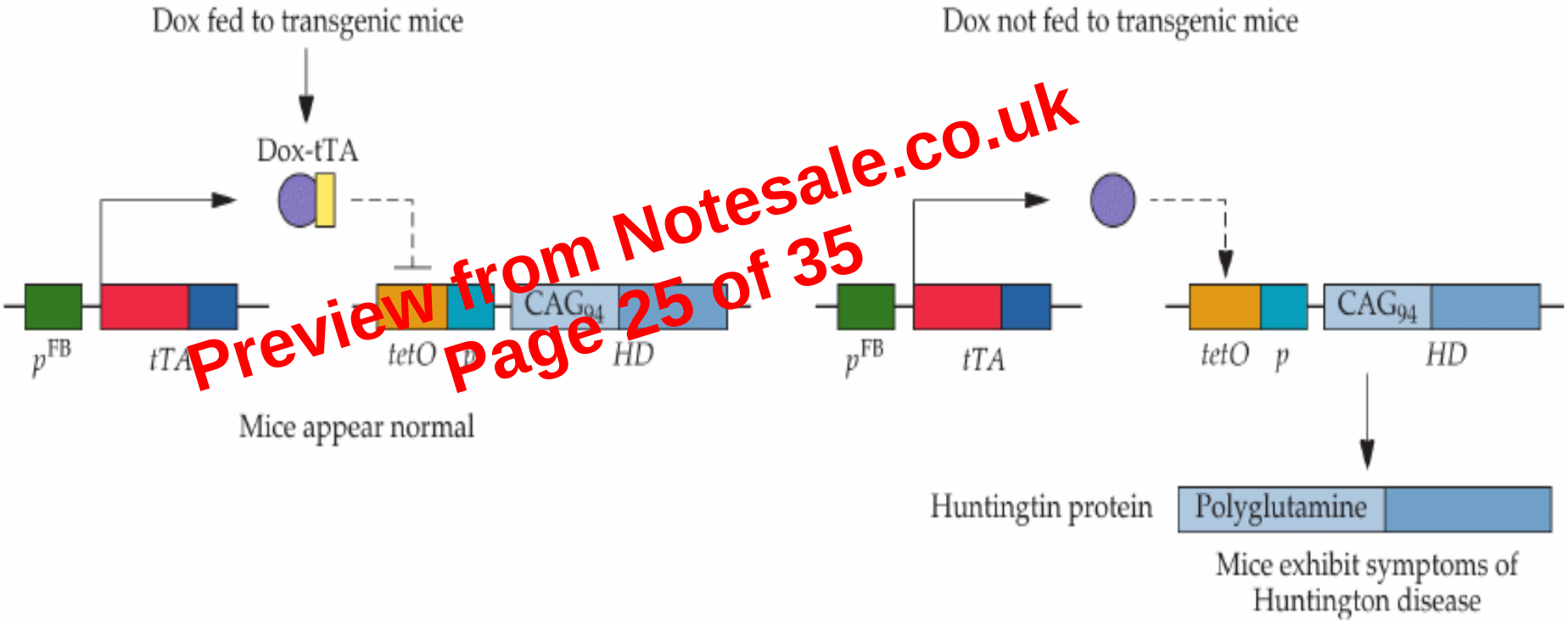

FIGURE 21.20 A transgenic mouse model of Huntington disease carrying a mutant form of the *HD* gene encoding the huntingtin protein expressed under the control of the tet-off system. CAG_{94} indicates a sequence of 94 CAG repeats in exon 1 of the mutant *HD* transgene that encode polyglutamine. p^{FB}, forebrain-specific promoter; tTA, tetracycline transactivator; *tetO*, tetracycline operator; *p*, promoter.

Transgenic Livestock

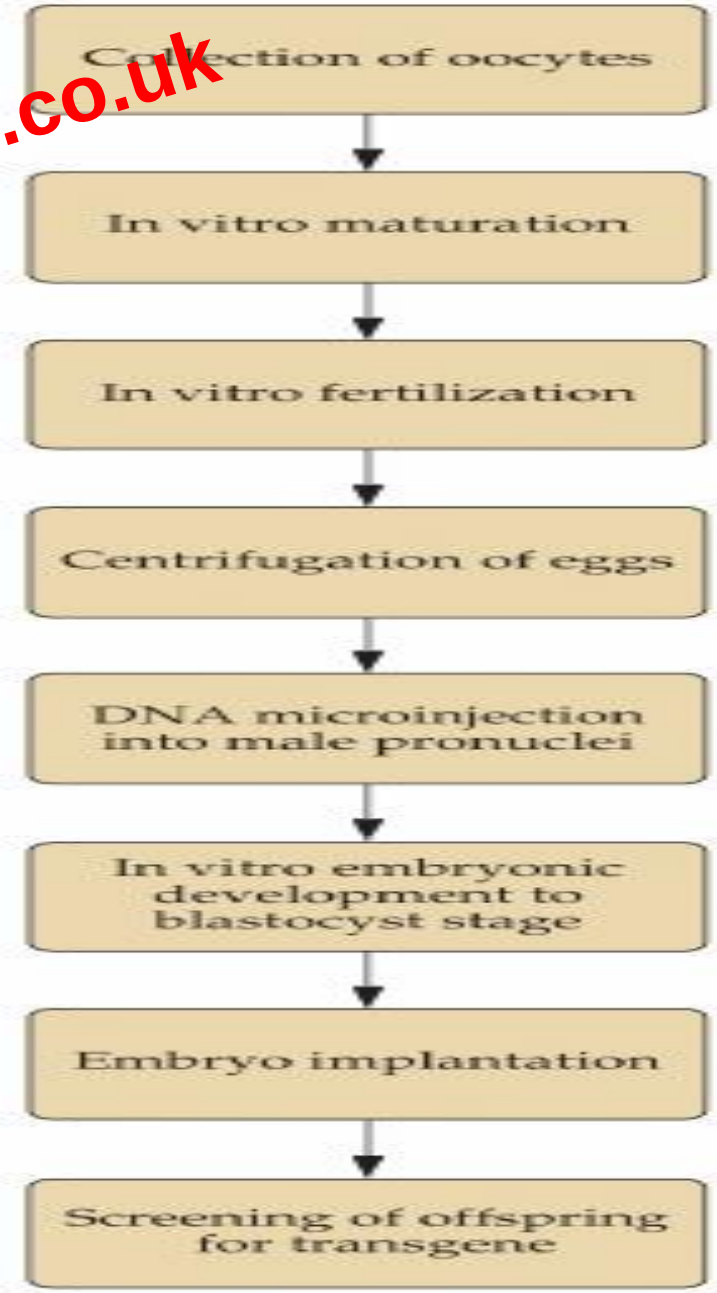

FIGURE 21.23 Steps in the development of transgenic cattle.

Production of Pharmaceuticals

Much of the research with transgenic livestock has been devoted to developing the mammary glands of these animals as bioreactors for the production of pharmaceutical proteins. For example, large quantities of the authentic cystic fibrosis transmembrane regulator (CFTR) protein are needed to study its function and to formulate potential therapies for treating cystic fibrosis, a prevalent genetic disease. A faulty in CFTR proteins disrupted the proper flow of chloride ions into and out of cells, resulting into accumulation of mucus in the ducts of several organs preventing its normal functioning and also mucus accumulating areas becomes the site of a bacterial infection that is difficult to control with antibiotics.

FIGURE 21.24 Goat β-casein gene–CFTR cDNA expression construct. The full-length cDNA for CFTR was cloned between exon 2 (EX2) and exon 7 (EX7) of the goat β-casein gene. The promoter *(p)* and transcription termination *(t)* sequences and exons 1, 8, and 9 (EX1, EX8, and EX9) of the β-casein gene were retained.