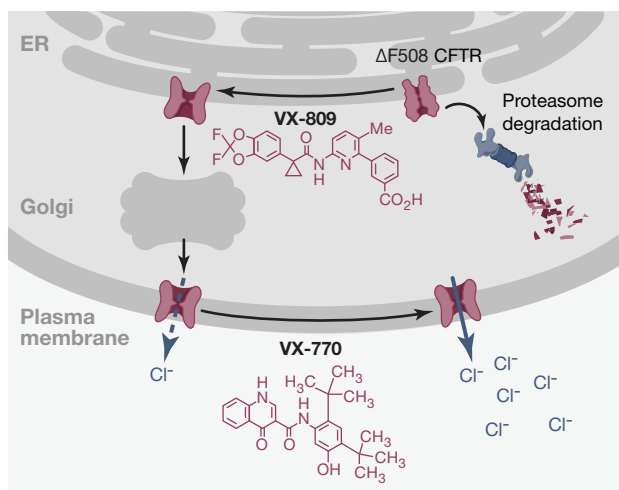


A Combination Therapy for Cystic Fibrosis

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NAME

Orkambi, a combination of VX-809 (Lumacaftor) and VX-770 (Ivacaftor)

APPROVED FOR

Cystic fibrosis (CF) in patients older than 12 with two copies of the $\Delta F508$ CFTR gene

TYPE

Small-molecules

MOLECULAR TARGETS

CFTR, an anion channel in the ATP binding cassette transporter family

CELLULAR TARGETS

Various epithelial tissues in which CFTR regulates chloride, bicarbonate, and fluid secretion

EFFECTS ON TARGETS

Lumacaftor corrects mutant CFTR folding, and Ivacaftor potentiates CFTR channel activity. Restored CFTR trafficking and activity counters the fluid secretion defects in pancreas, intestine, sweat glands, and lung, where it improves airway surface liquid formation and productive mucus and microbe clearance.

DEVELOPED BY

Vertex Pharmaceuticals and Cystic Fibrosis Foundation Therapeutics

The most prevalent form of cystic fibrosis arises from an amino acid deletion in the cystic fibrosis transmembrane conductance regulator, CFTR. A recently approved treatment for individuals homozygous for this mutation combines a chemical corrector, which helps CFTR fold, and a potentiator that increases CFTR channel activity.

Lumacaftor rescues

30%

from degradation

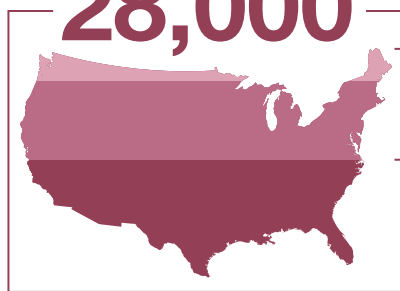
Ivacaftor

2-fold

increase in channel activity

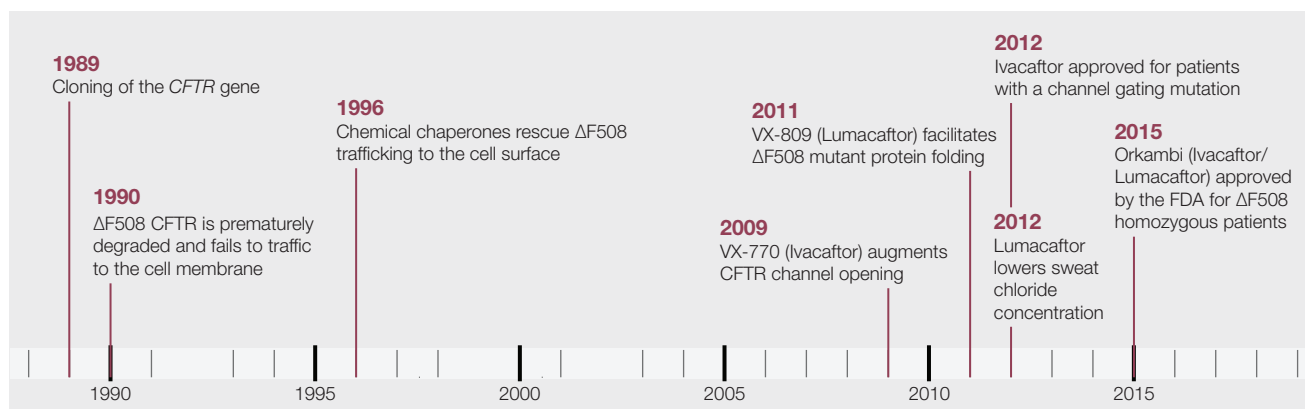
Individuals with cystic fibrosis

28,000



5% have benefited from Ivacaftor

50% may benefit from Orkambi



References for further reading are available with this article online: [www.cell.com/cell/abstract/S0092-8674\(15\)01123-X](http://www.cell.com/cell/abstract/S0092-8674(15)01123-X)

