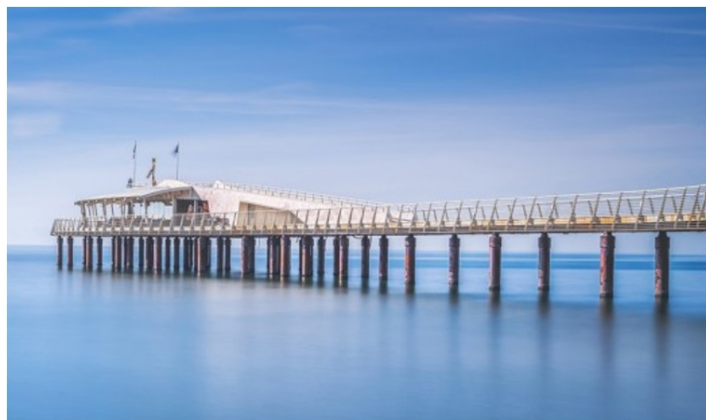




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S6.6 GY971, a new anti-inflammatory agent for the treatment of Cystic Fibrosis lung disease

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In *Cystic Fibrosis* (CF), chronic lung inflammation and progressive pulmonary damage persist despite the use of *highly effective CFTR modulator therapy* (HEMT). For this reason, there is an urgent need for innovative anti-inflammatory agents to be administered via the pulmonary route to people with CF (pwCF), working through novel mechanisms and maintaining an acceptable side effect profile. GY971 is a new synthetic furocoumarin derivative developed to inhibit NF- κ B/DNA complexes and characterized by anti-inflammatory action, at nanomolar concentrations, based on the regulation of neutrophil chemotaxis mediators in CF bronchial epithelial cells *in vitro* and murine lungs *in vivo*. The study was focused on the analysis of GY971 in CF bronchial epithelial cell lines exposed to *P.aeruginosa* (PAO-1) or TNF- α *in vitro*, and in mouse models of *P.aeruginosa* lung infection *in vivo*. The anti-inflammatory effect of GY971 was also validated in primary HBE (Human Bronchial Epithelial) cells and HNE (Human Nasale Epithelial) cells derived from pwCF.

Thanks to the promising results obtained, GY971 was recently approved by the *European Medicines Agency* (EMA) as orphan drug for CF. Ongoing research aims to consolidate its efficacy and safety profile, bringing it closer to clinical application as an innovative anti-inflammatory treatment for CF lung disease.