

# Therapeutic drug

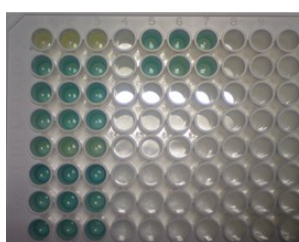
## Chronic obstructive pulmonary disease

### Keywords:

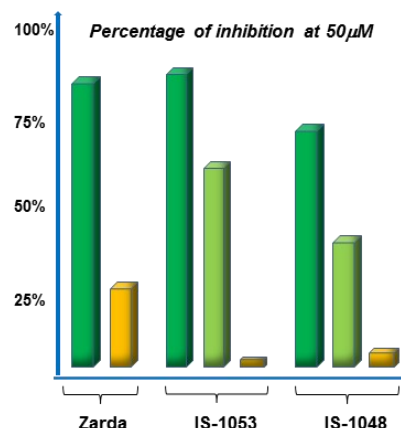
- ◆ COPD
- ◆ Asthma
- ◆ Phosphodiesterases
- ◆ PDE-4 inhibitors

### New molecules (pyridazinones fluorinated) for the treatment of respiratory diseases

Type 4 Phosphodiesterases (PDE-4) are a major subfamilies of PDE enzymes present in inflammatory and immune cells, bronchial smooth muscle and brain. Inhibition of PDE4 activity results in the bronch by anti-inflammatory effects in combination with a relaxation of bronchial smooth muscle. A new family of pyridazinone-type molecules were synthesized, for selective inhibition of PDE4 compared to other isoforms.



■ PDE-4B  
■ PDE-4D  
■ PDE-1



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### ➔ BENEFITS:

- ◆ Obtained by synthesis of new fluorinated pyridazinones
- ◆ The methodology allows, according to a general formula, large number of pharmaco-modulations: structure-activity-selectivity developments
- ◆ The nature of the fluorinated pattern allows the modulation of the selectivity of molecules and limits the known side-effects
- ◆ Activity equal or greater than marketed molecule Roflumilast
- ◆ Selectivity for PDE-4B (bronchi) relative to isoforms (PDE-4D) and subtypes (PDE-1, PDE-7A, PDE-10A).
- ◆ Specific inhibition of subtype PDE-4B reduces the known side-effects related to a non specific inhibition such as headache, nausea, weight loss, depression, etc.

### ➔ APPLICATIONS:

- ◆ Treatment of inflammatory lung diseases
- ◆ COPD (chronic obstructive pulmonary disease) - Asthma
- ◆ Applications to be considered in cystic fibrosis
- ◆ Possible veterinary applications (Asthma)

### ➔ DEVELOPMENT STATUS:

*In vitro* validation of the biological activity on isolated enzymes  
Comparison with reference substances (Zardaverine, Roflumilast and IBMX)

Leads Optimisation ongoing

*Ex vivo* and *in vivo* tests in a mouse model ongoing

### ➔ INTELLECTUAL PROPERTY:

Patent Application No. FR14 / 60501  
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