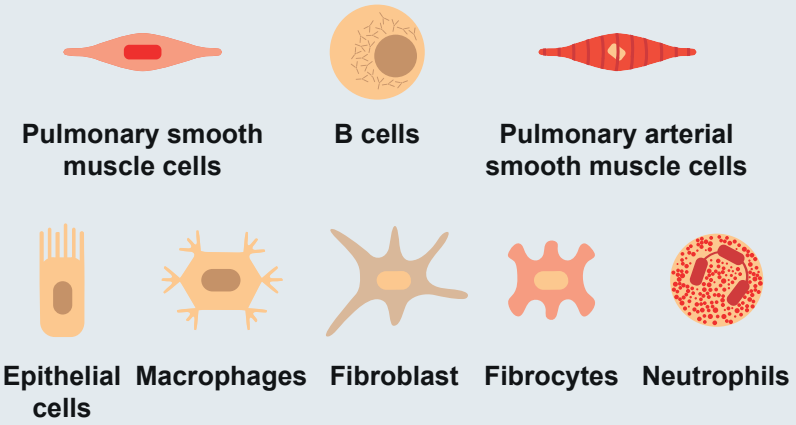
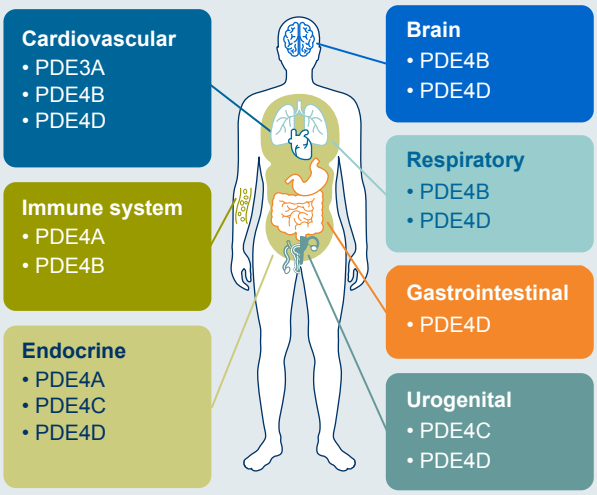
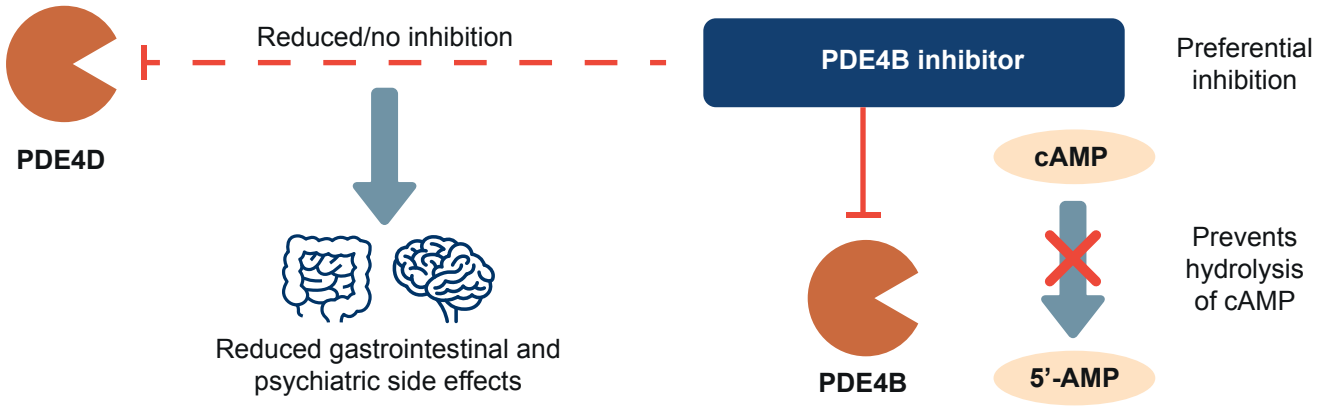
PDE4B INHIBITION: A POTENTIAL NOVEL STRATEGY FOR TREATING PULMONARY FIBROSIS

PDE4/PDE4B expression in different tissues[1-4]





Role of cAMP and targeting PDE4B[5]



PDE4B

Targets PDE4B expressed in lungs and immune cells

Reduces class-associated adverse events

Antifibrotic effects
- ↓ Fibroblast proliferation
- ↓ Fibroblast function
- ↓ Extracellular matrix protein synthesis

Anti-inflammatory effects
- ↓ Pro-inflammatory mediators from neutrophils
- ↓ Eosinophil infiltration into lungs
- ↓ Macrophage activity

PDE4B inhibitor clinical development

✓ Preclinical[5]
- Reduced emesis in animal models
- Reduced pro-inflammatory mediators
- Inhibition of myofibroblasts and extracellular matrix proteins

✓ Phase 1[6]
- Most adverse events either mild or moderate
- Gastrointestinal adverse events were the most common

✓ Phase 2[7]
- Stabilised pulmonary function in patients with IPF following 12 weeks of treatment
- Tolerability was acceptable, with diarrhoea the most common adverse event

Kolb M, et al. *European Respiratory Review* 2022

References: 1. Azevedo MF, et al. Endocr Rev 2014;35(2):195-233; 2. Bender AT, et al. Pharmacol Rev 2006;58(3):488-520; 3. Francis SH, et al. Physiol Rev 2011;91(2):651-90; 4. Maurice DH, et al. Nat Rev Drug Discov 2014;13(4):290-314; 5. Herrmann FE, et al. Front Pharmacol 2022;13:838449; 6. Maher TM et al. ERJ Open Research 2022;8(4):00240-20227; 7. Richeldi L, et al. New Engl J Med 2022;386(23):2178-87.