Supplementary Table 1. Published studies

Crossover study
- 38 patients with COPD
- Administration of 500 mg roflumilast or placebo once daily for 4 weeks
- Collection of sputum samples before and after 2 and 4 weeks of treatment
- Determination of differential and absolute cell counts in whole sputum samples
- Determination of markers of inflammation in sputum supernatants and blood
- Implementation of spirometry weekly

14 studies
- State the relationship between COPD and levels of CRP, fibrinogen, leucocytes, TNF-a and interleukins 6 and 8.

2 placebo-controlled, double-blind, multicentre trials
- 2 different populations
- Patients with COPD >40 years old, with - severe airflow limitation
  - bronchitic symptoms
  - history of exacerbations
- 1 Randomised - oral roflumilast 500 μg once per day
  - placebo for 52 weeks
- Primary endpoints - change in prebronchodilator forced expiratory volume in 1 s (FEV1)
  - moderate or severe rate of exacerbations