Table 13: LPAR isoforms tested

Isoform	Polypeptide SEQ ID NO:	cDNA SEQ ID NO:	UniProt
LPAR1	62	1229	Q92633-1
LPAR2	1225	1230	Q9HBW0-1
LPAR3	1226	1231	Q9UBY5

Example 13: Rat pharmacokinetics

The pharmacokinetics of Antibodies 12, 15, 17 and 18 in rats was investigated using method 1.16. A palivizumab biosimilar (SEQ ID NOs: 1227 (VH) and 1228 (VL)) was used as a control isotype antibody. The results are shown in Figure 16A (Antibody 12), Figure 16B (Antibody 15), Figure 16C (Antibody 17), and Figure 16D (Antibody 18).

Upon visual inspection, all 5 antibodies have the same plasma concentration-time profiles after single intravenous administration at 3 mg/kg. For all antibodies, the median tmax was observed at 0.3 hours, i.e. the first blood sampling time after administration. The mean Cmax observed after intravenous administration were between 143.8 µg/mL and 217.5 µg/mL for Antibody 17 and Antibody 12, respectively. Plasma concentrations decrease in a similar way for all antibodies, i.e. a first fast phase and a second slower one with quantifiable plasma concentrations until 504 hours after administration for all antibodies and all animals.

Example 14: SEC-MALS

Size exclusion chromatography using multiangle light scattering was conducted on Antibodies 12, 13, 15, 16, 17 and 18. The results are shown in Figure 17A (Antibody 12), Figure 17B (Antibody 13), Figure 17C (Antibody 15), Figure 17D (Antibody 16), Figure 17E (Antibody 17) and Figure 17F (Antibody 18).

Example 15: Liver histopathology in cynomolgus monkeys

Small-molecule antagonist BMS-986020 showed efficacy in with patients with idiopathic pulmonary fibrosis (IPF) but showed off-target hepatobiliary toxicity. It was confirmed that the observed toxicity was compound-specific due to off-target binding to a number of hepatic bile acid efflux transporters (e.g., BSEP, MRP3 and MRP4) and not mediated via antagonism of LPAR1.

A dose range-finding study was carried out to determine the potential toxicity of Antibody 17 when given by the intravenous (infusion) route to cynomolgus monkeys. The test item, Antibody 17, was administered to 8 animals via intravenous infusion (30 minutes) on Day 1 (Group 1) or on Days 1, 8 and 15 (Groups 2 to 4). Animals were split by sex, allocated into 4 groups and dosed with Antibody 17 at 10, 33 or 100 mg/kg/day.

Table 14: Experimental Design

Group No.	Number of Animals		Dosage Level (mg/kg/day)
	Male	Female	
1	1	1	10