

Sanofi	AVE0847
Mechanism of Action	<p>Peroxisome proliferator-activated receptor α/γ (PPARα/γ)/nuclear receptor 1C1/1C3 (NR1C1/1C3) agonist http://iuphar-db.org/DATABASE/ObjectDisplayForward?objectId=593&familyId=86 http://iuphar-db.org/DATABASE/ObjectDisplayForward?familyId=86&objectId=595 http://www.ncbi.nlm.nih.gov/gene/5465; http://www.ncbi.nlm.nih.gov/gene/5468</p>
Overview	<p>AVE0847 is an orally active, novel potent PPARα/γ agonist intended for the treatment of type 2 diabetes/insulin resistance and mixed dyslipidemia.</p>
Safety/Tolerability	<p>AVE0847 showed severe rhabdomyolysis at the maximum tolerated dose 0.5 mg, however, this dose was at least ten times above the dose that had maximum and strong triglyceride (TG)-lowering effects. The compatibility with statins with regards to rhabdomyolysis would have to be taken into account, requiring an early interaction program with statins.</p> <p>AVE0847 did not show free fatty acid (FFA)-lowering activity better than fenofibrate, which seems needed to lower blood glucose.</p>
Additional Information	<p>The target indication for AVE0847 is type 2 diabetes (T2DM). Preclinical results from animal models of T2DM demonstrated reductions of free fatty acids, blood glucose and HbA1c.</p> <p>The clinical relevance of PPARα agonists for glycemic control has not been demonstrated for any PPARα agonist so far. The relevance of the target remains to be shown.</p>
Suitable for and Exclusions	<p>The treatment in T2DM is chronic, requiring demonstration of chronic use safety. Carcinogenicity will have to be completed before the start of Phase 3.</p>
Clinical Trials	<p>Studies have been conducted in healthy volunteers only. Key results of single and multiple escalating dose, and food interaction studies were available since February 2005. AVE0847 was a back-up for AVE8134.</p>
Publications	<p>None</p>