

PPAR-alpha/gamma AGONISTS

DESCRIPTION OF THE TECHNOLOGY

Peroxisome proliferator activating receptors (PPAR) are considered powerful therapeutic tools for the control of different pathologies, such as type 2 diabetes (T2D), obesity, hyperlipidaemia, cardiovascular disorders, inflammation and neurodegenerative diseases. In addition, PPARs are involved in the control of inflammatory processes, so they can regulate inflammation, vascular function, and vascular remodelling.

Although PPAR α agonists (e.g. fenofibrate and WY-14643) and PPAR γ agonists (e.g. rosiglitazone and pioglitazone) has shown clinical efficacy for the treatment of hypertriglyceridemia and T2D treatment, respectively, most of them have been removed from the market based on toxicity issues.

On the other hand, single compounds able to activate both PPAR α and PPAR γ receptors are considered a potentially one-for-all treatment of metabolic disorders and their associate cardiovascular disease. However, most dual agonists, such as farglitazar, muraglitazar, ragaglitazar and tesaglitazar have been removed from market due to their adverse events.

In summary, there is a need to develop new PPAR α and/or PPAR γ agonists of greater efficacy and lower toxicity. For this reason, researchers from INCLIVA has synthesised a novel family of drug candidates with dual PPAR α/γ activity. This compounds are characterized by their improvement of lipid and glycaemic parameters in plasma, as well as their anti-inflammatory effect with a low or almost absent toxicity.

MARKET APPLICATION SECTORS

Pharmaceutical companies willing to increase their pipeline of drugs in development in the field of cardiovascular disease and metabolic disorders.

In addition, these compounds may be suitable for the treatment of neurodegenerative disorders such as, Parkinson disease, Alzheimer disease or amyotrophic lateral sclerosis (ALS).

TECHNICAL ADVANTAGES AND BUSINESS BENEFITS

- Powerful dual PPAR α/γ agonist activity.
- A single-compound for the simultaneous treatment of metabolic and cardiovascular disease.
- Low toxicity.

CURRENT STATE OF DEVELOPMENT

Discovery phase of lead optimization.

The following toxicity studies have been carried out:

- MTT assay.
- Flow cytometry cell viability assay.
- Human neutrophils and HUVEC.
- Transaminase (ALT/AST) activity assays.

INTELLECTUAL PROPERTY RIGHTS

Priority patent application filed in December 2017.

COLLABORATION SOUGHT

- Pharmaceutical companies interested in in-licensing these drug candidates.
- A collaboration for the preclinical development of this drug candidates is also sought.

CONTACT

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