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# ANTAGONIST OF THE NUCLEAR HORMONE RECEPTOR PPARγ FOR SEPSIS THERAPY

## Technology Offer

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**Branch**
drug therapy, sepsis, intensive care

**Patent Situation**
EP patent application filed

**Offer**
license or co-development

**Key Words**
PPARγ antagonism, sepsis


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### Introduction

Sepsis and septic shock in response to infection are life threatening complications and among the leading causes of death in industrial society. Sepsis is characterized by a hyper-inflammatory phase followed by a hypo-inflammatory phase, known also as "immune paralysis". Here T cells of the adaptive immune system undergo apoptosis and stasis with loss of host defence. Current approaches to treatment focus on inhibition of the hyper-inflammatory phase of the disease in order to suppress disease progression. However, despite recent major advances, the incidence of and mortality due to sepsis continue to increase. There is, therefore, a need for new methods for the prevention and treatment of sepsis.

### Invention

The present invention pertains to a new compound (MTTB) and its derivatives. The compounds are selective, competitive peroxisome proliferator-activated receptor gamma (PPARγ) antagonists indicated for the treatment of immune related diseases such as systemic inflammation, sepsis and septic shock. The advantage of PPARγ antagonism is the inhibition of T cell apoptosis and the prevention of "immune paralysis". The compounds of the invention, in contrast to available agents, are competitive inhibitors, thus facilitating control of parenteral dosing The new compounds permit careful timing of sepsis therapy to target hypo- rather than hyper-inflammation during sepsis.

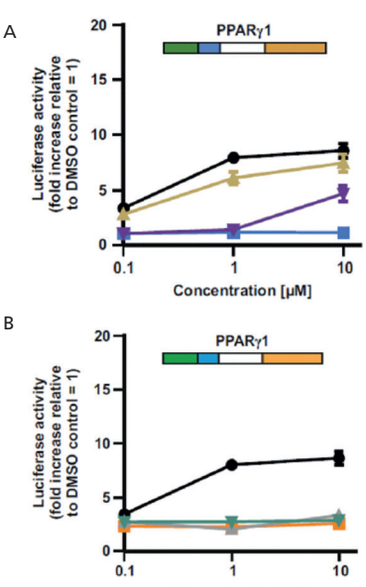
### Market Potential

Commercial applications:

- therapy of immune paralysis during sepsis
- adjuvant therapy of viral and neurodege nerative diseases associated with excessive apoptosis

### Development Status

The therapy approach has been shown to be effective in a mouse model of sepsis.




Shift of the dose response curve to the PPARγ agonist rosiglitazone by MTTB (A) and GW9662 (B) at concentrations of 1 and 10 µM (triangles) in comparison to inhibitor alone (squares).
The test system was a full PPARγ protein-induced transactivation assay using a luciferase reporter gene in HEK293T cells. MTTB showed competitive and GW9662 irreversible antagonist properties.