



## Innovative treatment of Leishmaniasis

### New immunostimulatory synthetic compounds for the treatment of Leishmaniasis and Tuberculosis

#### FOCUS INDICATIONS

- ▶ Tuberculosis
- ▶ Leishmaniasis

#### PROJECT KEY WORDS

- ▶ Immune response
- ▶ Synthetic immunostimulator
- ▶ Intracellular Infections
- ▶ Leishmaniasis
- ▶ Tuberculosis

#### DEVELOPMENT STATUS

- ▶ POC
- ▶ *In-vitro* tests on human NKT cells
- ▶ *In-vivo* tests on mice
- ▶ Compound administration studies ongoing

#### PATENT PROCEDURE STATUS

- ▶ Patent application filed

#### POTENTIAL FOR COOPERATION

- ▶ R&D Cooperation
- ▶ Transfer of rights
- ▶ Licensing

#### Innovation & Customer benefit

Inadequate immune response leads to an insufficient elimination of pathogens in intracellular infective diseases.

Current treatment options involve the supportive stimulation of the immune system by administering immune activators like  $\alpha$ GalCer. Experience has shown that treatment with  $\alpha$ GalCer can lead to undesirable side effects due to an unspecific induction of cytokines.

We are presenting novel immunostimulatory compounds based on active glycolipids, EhLPPG analogues, isolated from *Entamoeba histolytica*. These synthetic immune activators are characterized by:

- ▶ Efficient stimulation of the immune response
- ▶ Reliable induction of favourable cytokines
- ▶ Better performance and less side effects than current treatment options

#### Potential Applications

To date the novel synthetic activators have been successfully tested with regard to their anti-infective activity *in vivo* in mice (ongoing) and *in vitro* with murine and human macrophages.

Therapeutical indications are intracellular infections such as:

Tuberculosis: latent and active forms, as combination with antituberculosis therapy

Leishmaniasis: cutaneous and visceral

The current treatment options are insufficient due to long, systemic treatment durations, toxic side effects and high treatment costs. Moreover, they bear the risk of the induction of resistances.

New well-tolerated and effective compounds are needed which are able to activate or re-stimulate the otherwise insufficient immune response in patients.

#### Technical Description

Synthetic EhLPPG derivatives answer the need for good availability and purity in an actually complex extraction process.

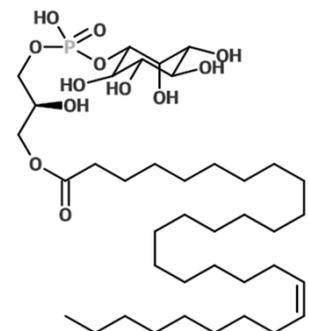
The stimulation activity of EhLPPG is linked to its active Phosphatidylinositol (PI) anchor. As stimulators of the immune system, they are a valuable tool to fight resistance problems of current treatments.

Our invention covers different synthetic PI anchor analogues and derivatives.

EhLPPG activates the immune response through a cascade reaction involving the stimulation of infected antigen presenting cells (APCs) and Natural Killer T (NKT) cells.

The application of EhLPPG analogues allows an increased expression of IL-12p35, IL1 $\beta$  and NOS2 in infected and treated APCs and a favourable cytokine profile in NKT cells (IFN $\gamma$ ; IL-4) and lead to a reliable anti-infective effect. Furthermore unlike in  $\alpha$ GalCer treatments, the production of TNF $\alpha$  and IL-17 is minimized and the putative related side effects will be reduced.

Tests on compound administration using nanocarriers are ongoing.



Molecular structure of an EhLPPG analogue (C30-EhPla-cis)

Ref: BNI002