The Realisation of Research

DDAH1 Small Molecule Antagonists for the Treatment of Sepsis

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Description:

DDAH1 Small Molecule Antagonists for the Treatment of Sepsis

Available For: Licensing and/or co-development

Summary

Dimethylarginine dimethylaminohydrolase 1 (DDAH1) is an enzyme involved in the regulation of nitric oxide (NO) signalling. Researchers at UCL have developed small molecule inhibitors of DDAH1, which may provide novel therapeutics for the treatment of disease states involving excess NO synthesis, including sepsis.

The Technology and Its Advantages

Nitric oxide signalling plays a role in many biological processes and its implicated in several indications including septic shock - a major cause of mortality in intensive care patients. Researchers at UCL have shown that NO synthesis can be attenuated by selectively inhibiting DDAH1, a tissue-specific enzyme which metabolizes endogenous inhibitors of NO synthesis. Animal studies demonstrate that inhibition or genetic knock out of DDAH1 increases blood pressure and systematic vascular resistance.

Our team has developed a panel of selective small molecule inhibitors of DDAH1. These show efficacy in both in vitro and in vivo models applicable to sepsis. These may prove to be potent therapeutics for treating septic shock, and our lead compound is currently undergoing preclinical development.

Market Opportunity

Sepsis is the tenth leading cause of death in the US and provides a substantial and largely untapped market opportunity, with total annual costs for sepsis treatment estimated at $16.7 billion in the US (Datamonitor, 2006). Analysts have assessed drugs for sepsis as having blockbuster potential. However, Xigris, the only drug currently aimed at the sepsis market, never realised this potential, due in part, to a narrow patient cohort, side effects and high pricing. The small molecules developed at UCL have an inherent competitive advantage over Xigris, avoiding the difficulties and costs associated with recombinant protein therapeutics. As well as treatment of sepsis, inhibition of DDAH1 and resultant tissue specific decrease in NO synthesis could prove beneficial in other indications where excess NO contributes to pathology, including pain and inflammatory disorders.

Further Information

Further Information

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