Novel inhibitor of mutated IDH1 in cancer therapy

Reference Number: 15-00302

Challenge
Mutated Isocitrate Dehydrogenase 1 (IDH1) has been described as a key mutation in several types of cancer, especially in most forms of advanced stage Glioblastoma, and 8% of Acute Myeloid Leukemias (AML). Specifically, IDH1 mutations lead to a gain of function resulting in a new enzyme metabolite which ultimately leads to defects in DNA repair, chromatin remodelling and genome methylation. With an incidence of 2-3 per 100,000 both AML and Glioblastoma are rare diseases but both are associated with severely high mortality rates (AML, 80% after 5 years and Glioblastoma, 97% after 5 years). Hence, there is an urgent need for new treatment options for these diseases.

Technology
The technology comprises the use of the substance HMS-101 as an inhibitor of mutated IDH1 for the treatment of cancer. HMS-101 is a commercially available substance, distributed by a variety of manufacturers but has not yet been recognized for the application in cancer therapy. Experiments have shown a significantly higher affinity of HMS-101 for mutated IDH1 than for the wild type enzyme, resulting in stronger growth inhibition in cells carrying the mutation. These findings make HMS-101 a highly promising substance for use in targeted cancer therapy.

Commercial Opportunity
In-licensing or collaboration for further development is possible.

Developmental Status
In-vitro inhibition assays of mutated IDH1 and first in vivo sensitivity tests have been performed. Further studies revealed a promising in vivo activity and a prolonged survival in an established mouse model with IDH1 mutation.

Patent Situation

Further Reading
Chaturvedi A et al. 2013. Mutant IDH1 promotes leukemogenesis in vivo and can be specifically targeted in human AML. Blood. 122: 2877-87