CorA as an effective therapeutic agent

Natural product for the treatment of dirofilariasis

Invention
Dirofilariasis is caused by Dirofilaria immitis and D. repens, parasitic nematodes transmitted by mosquitoes. The heartworms harbour the bacterial endosymbionts Wolbachia, which are essential for worm development, fecundity and survival. Corallopyronin A (CorA) has efficacy against the intracellular Wolbachia of filarial nematodes. Experiments in mice and jirds show that all worms were depleted of their Wolbachia by more than 98%, resulting in blocked larval development and phenotypically altered worms. The results indicate the potential of CorA to effectively kill filarial nematodes in the larval stages as well as adult worms. Thus, this antibiotic is a good option for prophylactic as well as therapeutic treatment.

No toxicity against eukaryotic cells or the treated rodents was detected. Pharmacokinetic data show that the antibiotic is amenable to oral administration. Based on the present results CorA will be administered once a day for two to a maximum of four weeks. CorA is a non-competitive inhibitor of bacterial DNA-dependent RNA polymerase. Detrimental drug-drug interactions are not expected, since CorA does not induce expression or activation of CYP450.

Commercial Opportunities
Heartworm disease is endemic in all states of the USA, especially in the South. Prophylactically, the macrocyclic lactone (ML) ivermectin is given for prevention of infection. If pets are infected, Melarsomine is administered by injection, to clear the adult worms. In recent years loss-of-efficacy in infected dogs treated with ivermectin has been reported, indicating a resistance to ML. Melarsomine may cause severe side effects – one of the reasons why Melarsomine is not used for humans. One advantage of CorA is that formation of resistance is significantly reduced. As a therapeutic agent with adulticidal activity, CorA would prevent potential pulmonary thromboembolism after the death of the heartworm because the worms are killed slowly, thus avoiding a strong inflammatory reaction.

On behalf of the University of Bonn, PROvendis offers an access to rights for commercial use of this invention and the opportunity for further co-development.

Current Status
US patent granted (US 9 168 244). An EP and a second US patent application are pending. Data of in vitro and in vivo experiments are available.

Competitive Advantages
- Effective control of dirofilarial infections
- High efficacy against the bacteria Wolbachia – potential for killing larvae as well as adult worms
- Oral administration is probable
- Slow worm death prevents potential pulmonary thromboembolism
- Is likely to be well tolerated and could be used in all dog races, e.g. Collies
- Will probably be suitable for the treatment of pregnant dogs

Contact:
Ref. No. 2838
Kordula Kruber
PROvendis GmbH
Schloßstr. 11-15
45468 Mülheim an der Ruhr
Germany
Phone: +49 (0) 208 94 105 30
Fax: +49 (0) 208 94 105 50
E-Mail: kk@provendis.info
Web: www.provendis.info

An invention of the Rheinische-Friedrich-Wilhelms Universität Bonn (UniBonn).