

## CorA as anthelmintic

### Natural product as antibiotic for the treatment of filariasis

#### Invention

Human filariasis (elephantiasis and river blindness) is caused by the nematodes *W. bancrofti* and *O. volvulus*, transmitted via blood sucking insects. The worms harbour the bacterial endosymbiont



Infections with filarial nematodes can develop into lymphoedema, which may further develop into the severe disease elephantiasis

worms are long lived and fecund for most of their lifespan, populations in endemic regions must be treated for many years. Suboptimal responders are observed, indicating possible resistance development. Further, severe adverse effects may develop. A promising approach is to target the *Wolbachia* using doxycycline or rifampicin. However, an impediment to their use is the contraindication for children and possible formation of resistance, respectively. Rifampicin is given as a standard drug against tuberculosis. Thus, there is a clear benefit by avoiding the use of rifampicin for other indications to minimize the risk of developing resistance in *M. tuberculosis*. CorA is a beneficial alternative to rifampicin for treating filariasis. 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.

#### Relevant Publications

A. Schiefer et al. (2012), *JID*, 206:249-57.  
A. Hoerauf et al. (2011), *CMI*, 17:977-85.

An invention of the University of Bonn.

*Wolbachia*, which is essential for embryogenesis, larval development and adult worm survival. Coralopyronin A (CorA) has efficacy against the intracellular *Wolbachia* of filarial nematodes. Experiments in mice show that all worms were depleted of more than 98% of their *Wolbachia*, resulting in blocked larval development and phenotypically altered worms. The results indicate the potential of CorA to effectively eliminate filarial disease by killing larvae as well as adult worms with one (maximum of two) treatment regimens. No toxicity against eukaryotic cells was detected. Preliminary pharmacokinetic data show that the antibiotic is amenable to oral administration. CorA is a non-competitive inhibitor of bacterial DNA-dependent RNA polymerase, with a different mode of action from rifampicin.

#### Commercial Opportunities

The current treatment approach targets the worm itself. The drugs, e.g. diethylcarbamazine and ivermectin, mainly kill larvae. Because adult

#### Competitive Advantages

- Effective control of dirofilarial infections
- Kills larvae as well as adult worms
- Requires fewer treatment cycles in logistically difficult regions
- Treatment of children is probable
- Oral administration is possible
- Alternative mode of action avoids selection for rifampicin cross-resistant *M. tuberculosis*

#### Technology Readiness Level

1 2 3 4 5 6 7 8

Technology validated in relevant environment

#### Industries

- Pharmaceutical Industry
- Veterinary Medicine

#### Ref. No.

2838

#### Contact

Kordula Kruber

E-Mail: [kk@provendis.info](mailto:kk@provendis.info)

Phone: +49(0)208-94105-30

