## Accepted Manuscript

Title: *Wolbachia*, doxycycline and macrocyclic lactones: new prospects in the treatment of canine heartworm disease

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PII: S0304-4017(18)30105-5

DOI: https://doi.org/10.1016/j.vetpar.2018.03.005

Reference: VETPAR 8633

To appear in: Veterinary Parasitology

Received date: 1-1-2018 Revised date: 3-3-2018 Accepted date: 5-3-2018

Please cite this article as: Kramer L, Crosara S, Gnudi G, Genchi M, Mangia C, Viglietti A, Quintavalla C, *Wolbachia*, doxycycline and macrocyclic lactones: new prospects in the treatment of canine heartworm disease, *Veterinary Parasitology* (2010), https://doi.org/10.1016/j.vetpar.2018.03.005

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## ACCEPTED MANUSCRIPT

Wolbachia, doxycycline and macrocyclic lactones: new prospects in the treatment of canine heartworm disease

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#### **Highlights**

- Wolbachia is a bacterial endosymbiont essential for heartworm (*Dirofilaria immitis*) development, reproduction and adult worm survival
- Doxycycline alone is adulticidal for heartworm, but when combined with macrocyclic lactones, efficacy increases markedly

#### **Abstract**

Melarsomine dihydrochloride (Immiticide®, Merial) is the only approved adulticidal drug for the treatment of canine heartworm disease (HWD). However, in cases where arsenical therapy is not possible or is contraindicated, a monthly heartworm preventive along with doxycycline for a 4-week period, which targets the bacterial endosymbiont *Wolbachia*, might be considered. There are published reports on the efficacy of ivermectin and doxycycline in both experimentally and naturally infected dogs, but no data on the use of other macrocyclic lactones (MLs) with a similar treatment regime. Preliminary results of studies in dogs show that a topical formulation of

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