Filarial Diseases: Unmet Medical Needs

- Unmet medical needs:
  - IVM is microfilaricidal (repeated application)
  - No macrofilaricidal treatment available
  - *Loa-loa* coinfections with risk of serious adverse events

- Major feasibility concerns
  - *Loa loa* coinfection (areas w/o treatment)
  - Political and economical situations
  - Recrudescence / Parasites adapt
  - Resistance

- Alternative therapy for:
  - case management / morbidity management
  - “mop-up” campaigns to contribute to elimination as public health problem
  - Test and Treat (TNT) approaches
  - Potentially safe treatment in *Loa loa* coendemic regions
### Possible mode of actions: direct vs indirect

<table>
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<tr>
<th>Direct acting drugs: Emodepside, Oxfendazole</th>
<th>Indirect-acting drugs (anti-wolbachial): TylAMac</th>
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| **PoC:**
  Macrofil. (Oncho-Loa coinfected areas)
  Macrofil. + microfil. (Oncho only areas)* |
  **Advantage:**
  Proven MoA in veterinary medicine
  Fast-killing, morbidity management*
  Potentially used for multiple nematodes |
  **Disadvantage:**
  Risk of AE due to microfil. activity (Emod.) |
  **Possible:** Combination treatments |
| **PoC:**
  Macrofil. (Oncho-Loa coinfected areas) |
  **Advantage:**
  slow-killing, MoA well known,
  Reduction of inflammation due to removal of *Wolbachia* |
  No side effects in loiasis infected individuals |
| **Disadvantage:**
  long time to death of the adult parasite |
| **Possible:** Combination treatments |

**High attrition rates: need for a variety of candidates**
**Pursue both approaches are valuable and build up the anti-filarial tool-kit**
Clinical Trials

- **Aim:**
  - Determine the maximum tolerated dose (MTD) of the new treatment
  - MTD is found by escalating the treatment dose until dose-limiting toxicity (DLT) is reached

- **First in Human:**
  - SAD: single ascending dose
  - MAD: multiple ascending dose
  - Food Effect
  - Relative bioavailability

- **Proof of concept:**
  - Multicenter Trial
  - Safety: UHAS (N. Opoku)
  - Safety and Efficacy: DNDi HAT Platform
Thanks to all of you for being our partner

- Improving the Onchocerciasis Network to get the job done
  - Increase connectivity
  - Increase visibility of the network
  - Share resources and know-how across the countries
  - Create sustainability beyond onchocerciasis in clinical trials in Africa
Find new tools for elimination and case management

**Discovery programs = New Clinical Entities**

**Long-term projects**
- Research
- AbbVie (anti-Wolbachia), Celgene (lead optimization macrofilaricide)
- Filarial Clinical Trial and Research Platform

**Medium-term projects**
- Translation
- Repurposing of veterinary: Emodepside (Bayer), oxfendazole
- Based on known mode of action: TylAMac (AbbVie)
- Fingerprint studies

**Supportive Activities**
- Development
- AbbVie (anti-Wolbachia), Celgene (lead optimization macrofilaricide)
- Filarial Clinical Trial and Research Platform

**Short-term projects**
- Implementation
- Explore pediatric IVM
- Modelling of distribution/morbidity to address the patients needs
- Modelling of CT endpoints
- Surrogate Biomarker