AURIGENE
PHARMACEUTICAL SERVICES

Case Study

Anti-infective drug discovery

Objective & Challenges:

Objective was to identify an optimized anti-bacterial lead molecule with *in vivo* efficacy in relevant infection models an acceptable safety profile, and a patentable series.

Challenge was to develop a more efficacious compound than the reference standard.

Study design:

- Compounds were designed and synthesized with variation.
- 232 compounds were generated from 8 different series.
- 3 molecules were identified from different series meeting the early lead criteria & 148 compounds were generated from 3 series.
- 2 patentable leads were identified from structurally diverse series out which AU-XXX was nominated as candidate molecule.

Outcome:

- Improved potency (1-4x) with expanded spectrum of activity was observed.
- *In vitro* to *in vivo* translation.
- Favourable DMPK properties – Metabolically stable (MLM, RLM, PHLM) with good solubility and low serum protein binding.
- No CYP liability.
- Probe toxicity studies indicate better safety profile than the reference compound.

Results:

- AU-XXX exhibited Minimum Inhibitory Concentration (MIC) of 1-2 µg/mL against different phenotypes of Gram-positive pathogens *S. aureus*, *E. faecalis* and *E. faecium*.
- AU-XXX exhibited good *in vitro* antibacterial activity against respiratory pathogens *S. pneumoniae*, *H. influenzae*, and *M. cattarrhalis*.
- AU-XXX was evaluated in murine systemic and lung infection models and it demonstrated *in vivo* efficacy better than comparator reference drug.
- Absorption, distribution, metabolism and excretion (ADME) of AU-XXX in mouse, rat and dog was favourable in support of preclinical safety studies and clinical development.
- Toxicity studies were conducted in rats with dosage 200 mg/kg/day for 14 days. The incidence and severity observed was less compared to the reference compound.

Microbiology capabilities:

- Anti-infective research and development is a core research facility.
- Key resources are fully dedicated to enable multiple anti-infectives research programs to be conducted to proof of concept.
- Ability to reproduce and setup in-house assays rapidly.
- Best/first in class medicinal chemistry expertise.
- Full toxicology back-up to achieve IND optimally.

Thank You

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https://www.aurigeneservices.com/

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