

Antimicrobial Research and Optimisation Workflow

A DimiCare Biotech® Brand

Services in Microbiology (BSL-2 laboratory)

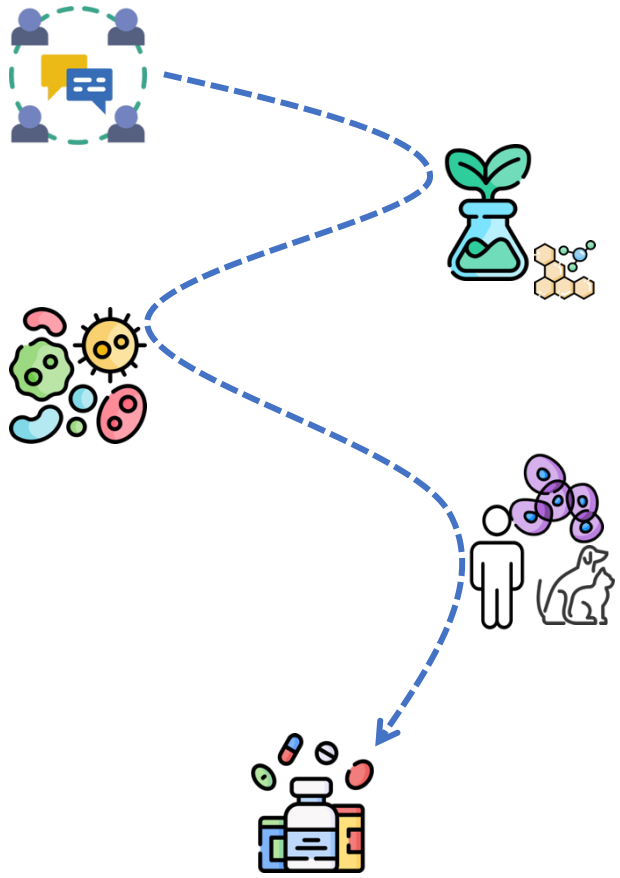
In vitro Pharmacodynamics and ADMET

Efficacy in vitro
- Screening mono-concentration (Biostatic activity)
- 2-steps Screening mono-concentration (Biostatic vs Biocide activity)
- Screening anti-biofilm mono-concentration (formation inhibition)

Potency in vitro
- Minimum Inhibitory Concentration (MIC) (5 doses)
- Minimum Bactericidal/Fungicidal/Parasiticidal Concentration (MBC/MFC/MPC) (5 doses)
- Time-Killing Curve (TKC) (3 doses)
- Time-Inhibiting Curve (TIC) and Fetal Bovine Serum (FBS) impact (3 doses)
- Intra-biofilm activity (MIC) (5 doses)

Resistance to treatment
- Resistance/Mutation Rate (RMR) - single step (4-8xMIC)
- RMR - multiple step (Dose-Response – 30-50 days)

In vitro ADMET
- LDH release/AlamarBlue (IC50) (5 doses)
- Hemolytic assay (IC50) (5 doses)
- CYP450 transcription regulation (qPCR) (5 doses)



Our models : Clinical Pathogens & Cell types

Bacteria (Gram-positive)
- *Staphylococcus sp. (S. aureus; S. epidermidis; S. pseudintermedius…etc.)*
- *Bacillus sp. (B. cereus; B. thuringiensis; B. paranthracis…Etc.)*
- *Enterococcus faecium/faecalis*
- *Streptococcus pyogenes/pneumoniae*
- *Cutibacterium acnes*

Bacteria (Gram-negative)
- *Escherichia coli*
- *Pseudomonas aeruginosa*
- *Klebsiella pneumoniae*
- *Acinetobacter baumannii*
- *Salmonella typhimurium*

Yeasts
- *Candida sp. (C. albicans; C. auris; C. tropicalis…etc.)*
- *Cryptococcus neoformans*

Filamentous fungi
- *Trichophyton rubrum*
- *Aspergillus fumigatus*

Parasites
- *Leishmania infantum/major*

Cell types – immortal cells
- Human Hepatocytes (HepG2)
- Human Neurons (SH-SY5Y)
- Human Neuro-endocrine kidney cells (HEK293T)
- Human Immune cells – pre-monocytes (THP1)
- Dog immune cells – macrophage-like (DH82)
- Human Kidney cells (HK-2) (on demand)

Ex vivo models - on demand
- Human Peripheral blood mononuclear cells (hPBMC)
- Murine Bone Marrow Derived Macrophages (mBMDM)
- Primary murine hepatocytes (PmH)

In vivo (murine) models – on demand
- ABSSSI (*S. aureus*)
- Bacteremia (*E. coli* / *S. aureus*)
- Infection-derived inflammatory diseases (in progress)
- Osteoarticular infection /Osteomyelitis (in progress)

Read-outs
- Survival
- Blood & Organs CFU/ml
- Bioluminescence *in vivo* following (just few bacterial strains or on demand)
- Weight changes & Organ size
- Biomarkers – cytokines (ELISA), Hepatic and Kidney toxicity…

ARROW platform

Hit identification

- Rational **Medicinal Chemistry** / *in silico* target-based **design**
- Compounds' **synth.** and **characterization**
- **Antimicrobial** testing (clinical pathogens)
- **Cytotoxicity** assays (~10 cell types)

Hit-to-lead

- **SAR** analys. & *in silico* **ADMET** prediction
- **Plasma prot. binding & activity impact**
- **Metabolism & DDI** (CYP450 qPCR)
- **Inflamm. profiling** (Cytok. qPCR)

Lead-Optimization

- **Preformulation** (IV, PO, SC & Topical)
- **Preliminary comparative PK** (Cmax, Tmax, T ½ ...)
- **Resistance develop.** (Spontaneous & serial passaging...)
- **Preliminary comparative PD** Peritonitis / ABSSSI

BD / Biotech POC

- **Market Study** (Competitors, market size, regul. strategy)
- **Preclinical POC** (efficacy in adapted preclinical model)
- Regulatory and Business **strategy**
- **Final TPP** (target product, reg. roadmap...etc.)

ARROW platform – internal services

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ARROW platform – early-stage valorization services

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ARROW platform – in collaboration services

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DCB001 – our first proof-of-concept (*in vivo* efficacy)

300 new chemical activities
(ICN, UMR7272 **CNRS**)

Clinical isolates
(C3M, U1065 **INSERM**)

DCB001
New chemical structure

Antibacterial activity *in vitro*

Clinical Staphylococcus MDR

Veterinary Staphylococcus MDR

Positive early Pharmacology studies

Efficacy *in vivo*

Preclinical model (murine)

Efficacy against MRSA

Safe at maximal tested doses



Accelerating discovery & optimisation through targeted scientific expertise