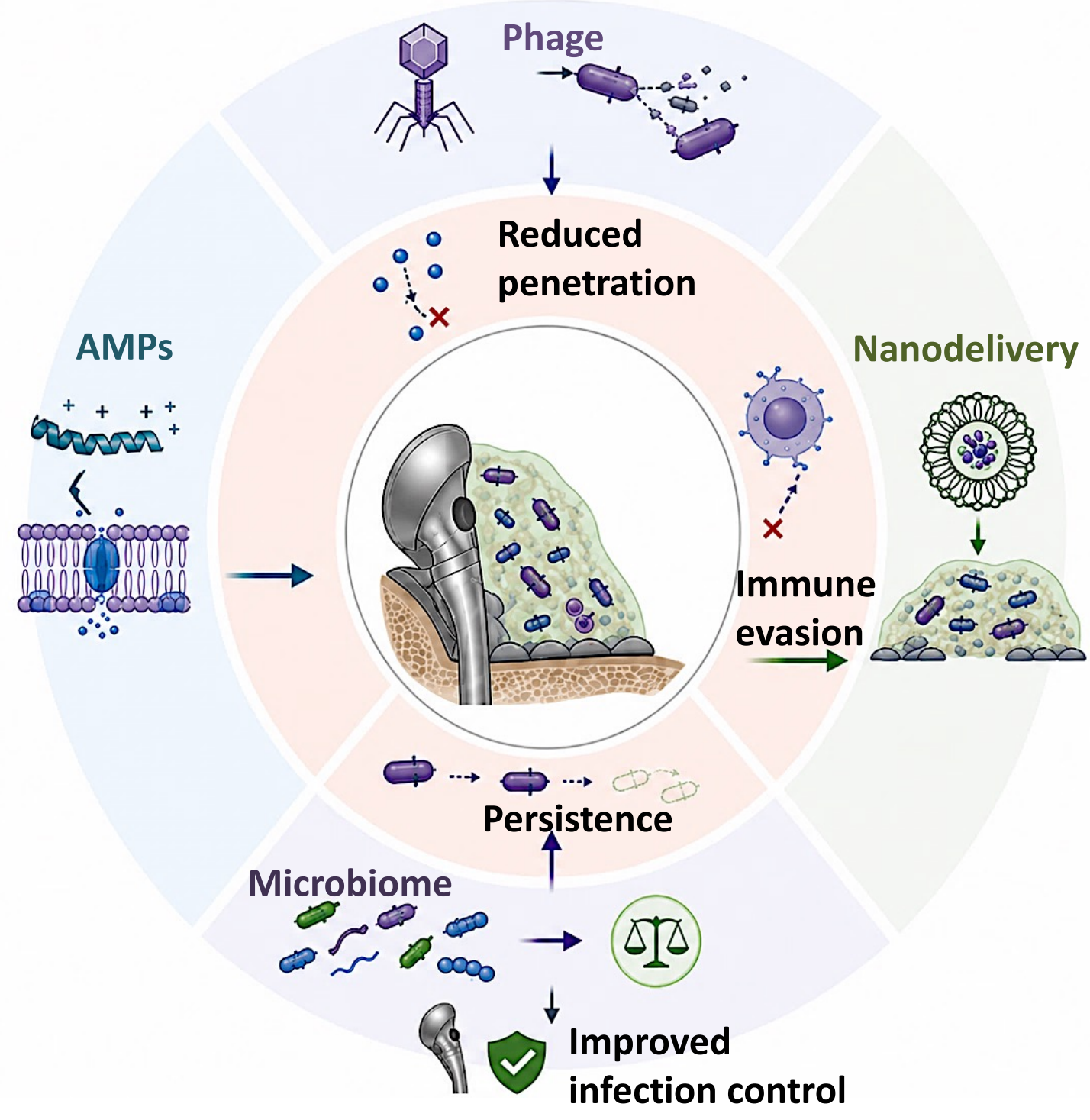


1. Introduction

Why Are Musculoskeletal Infections Difficult to Treat?



- Biofilm protects bacteria**
Biofilm matrix restricts antimicrobial penetration and shields bacteria from immune clearance.
- Pathogens persist in protected niches**
Implant surfaces, bone, necrotic tissue, and intracellular reservoirs can sustain infection.
- Standard care has limits**
Surgery and antibiotics remain essential, but recurrence can occur when biofilm persists.
- New therapies must target mechanisms**
Match the intervention to the specific biofilm barrier and clinical context.

2. Review Question & Methods

- Which emerging biofilm-targeted and precision-enabling strategies offer the greatest potential beyond conventional antibiotics, and how close are they to clinical implementation?
- Narrative review of clinical, translational, and preclinical evidence across emerging biofilm-targeted, host-directed, diagnostic, and drug-delivery strategies.

3. Therapeutic Framework

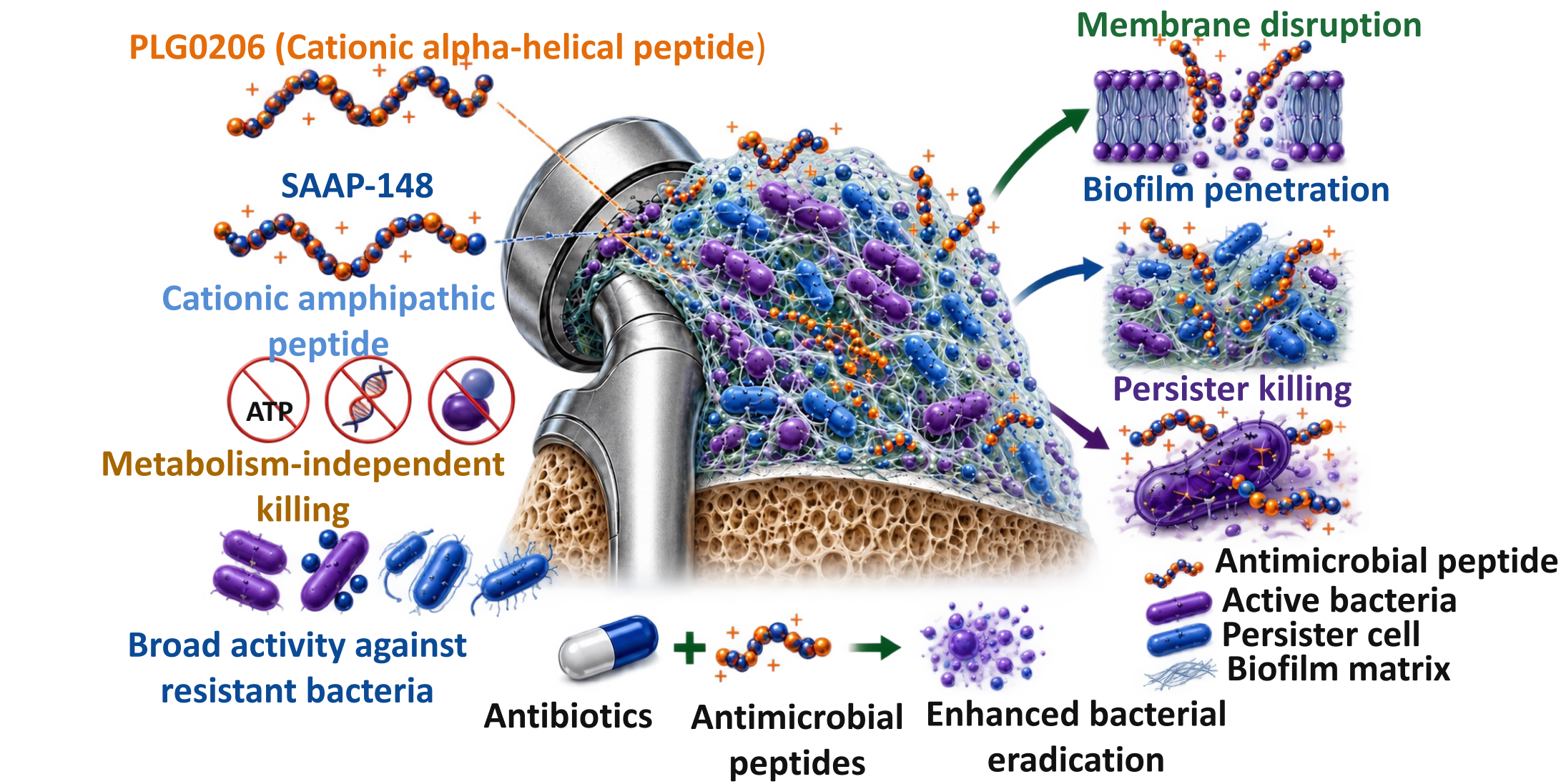
HOST / PREVENTION / DELIVERY
Microbiome • Probiotics • Immunomodulation • Nanotechnology

PRECISION GUIDANCE
Molecular diagnostics

DIRECT ANTIBIOFILM THERAPY
Phage • AMPs • Afabacin • QS inhibition / dispersal

EARLY CLINICAL

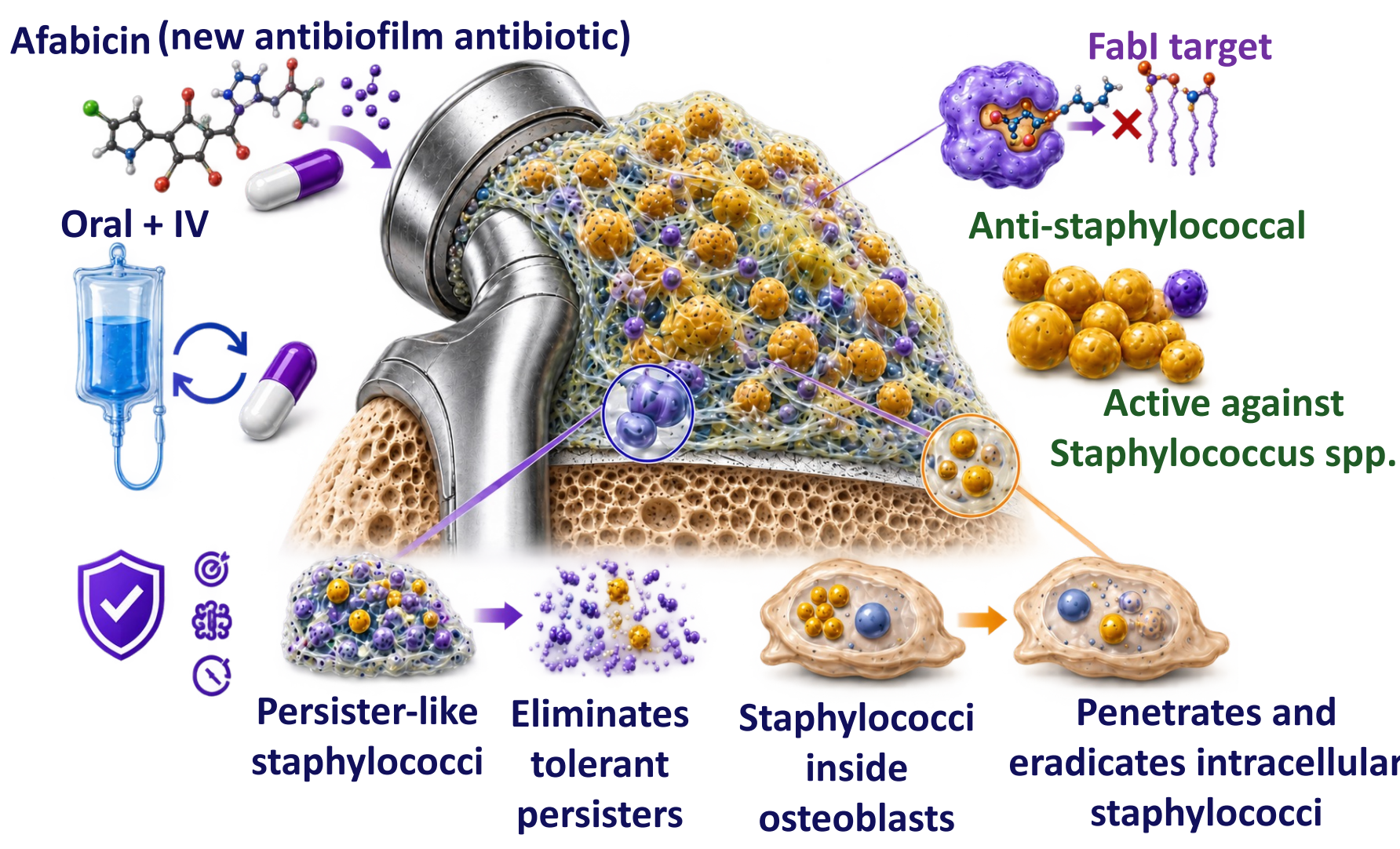
Bacteriophage Therapy



Target: Biofilm-associated bacteria
Mechanism: Pathogen-specific lysis + biofilm disruption
Clinical position: MOST CLINICALLY ADVANCED
Role: Adjunct to surgery + antibiotics

PRECLINICAL →
EARLY CLINICAL

Antimicrobial Peptides



Target: Resistant and biofilm-associated organisms
Mechanism: Rapid membrane disruption + activity against persisters
Clinical position: STRONG TRANSLATIONAL PROMISE

Other Emerging Strategies

AFABICIN
FabI inhibition
• anti-staphylococcal activity
EARLY CLINICAL

PHAGE-DERIVED ENZYMES
Endolysins + depolymerases
Cell-wall lysis + matrix degradation
EARLY TRANSLATIONAL

MICROBIOME / PROBIOTICS
Ecological prevention + host modulation
INVESTIGATIONAL

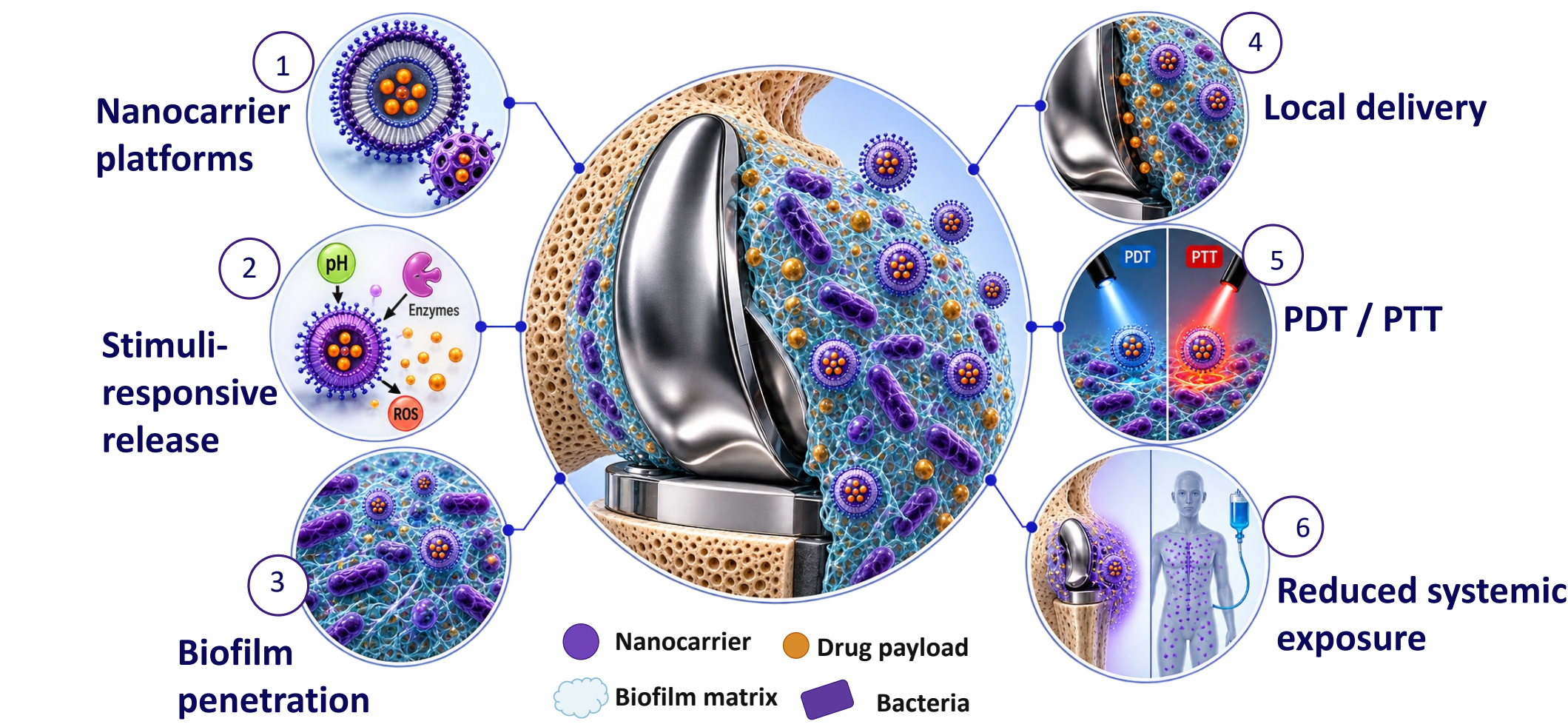
IMMUNOMODULATION
Restore effective host defence
EXPERIMENTAL

QS INHIBITION / DISPERSAL
Disrupt signalling + weaken biofilm structure
PRECLINICAL

LOCAL DRUG DELIVERY
High local exposure
• reduced systemic exposure
EARLY CLINICAL

PREDOMINANTLY
PRECLINICAL

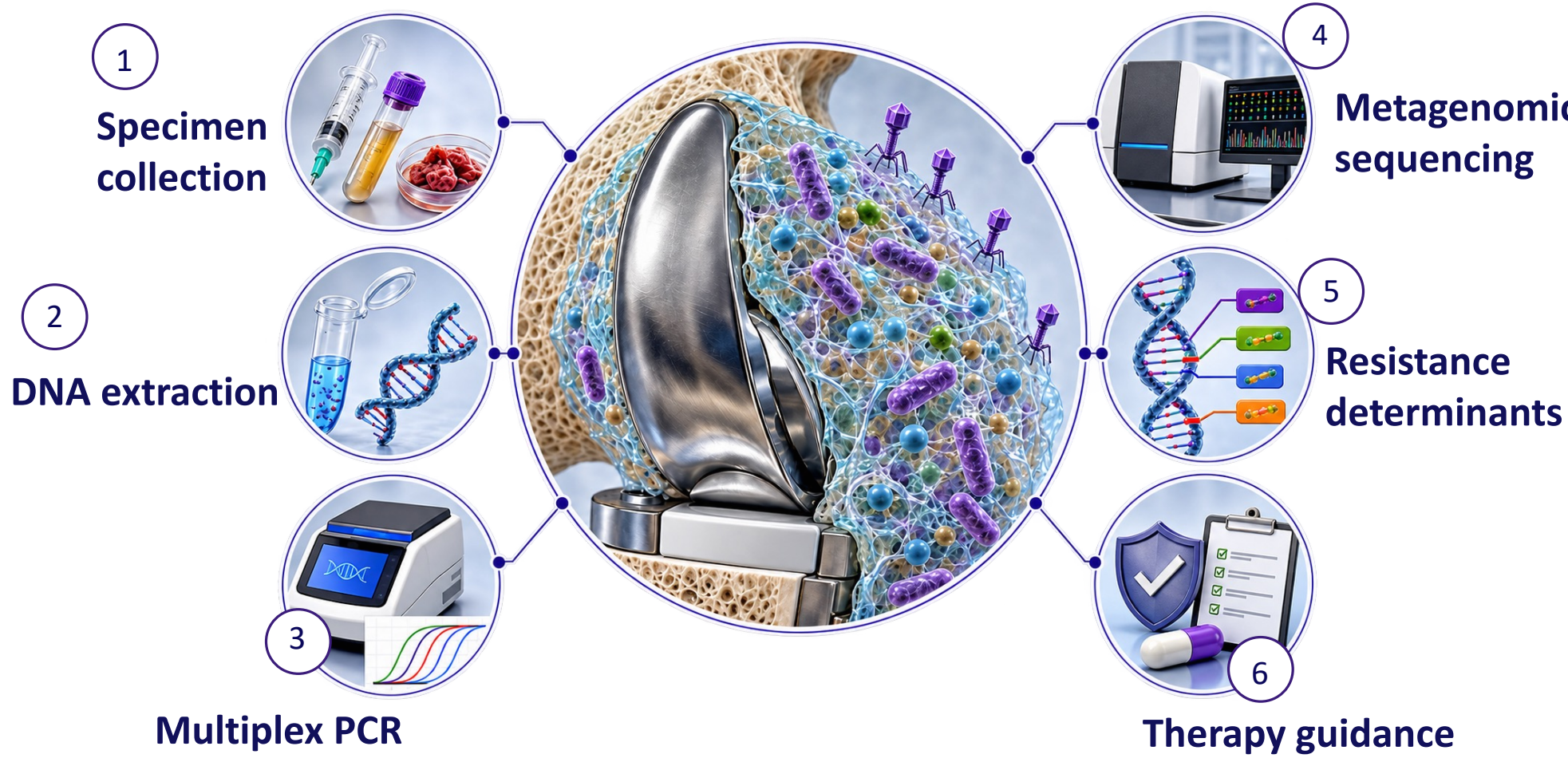
Nanotechnology-Based Delivery



Target: Biofilm-protected niches
Mechanism: Enhanced penetration + controlled local delivery
Clinical position: PREDOMINANTLY PRECLINICAL

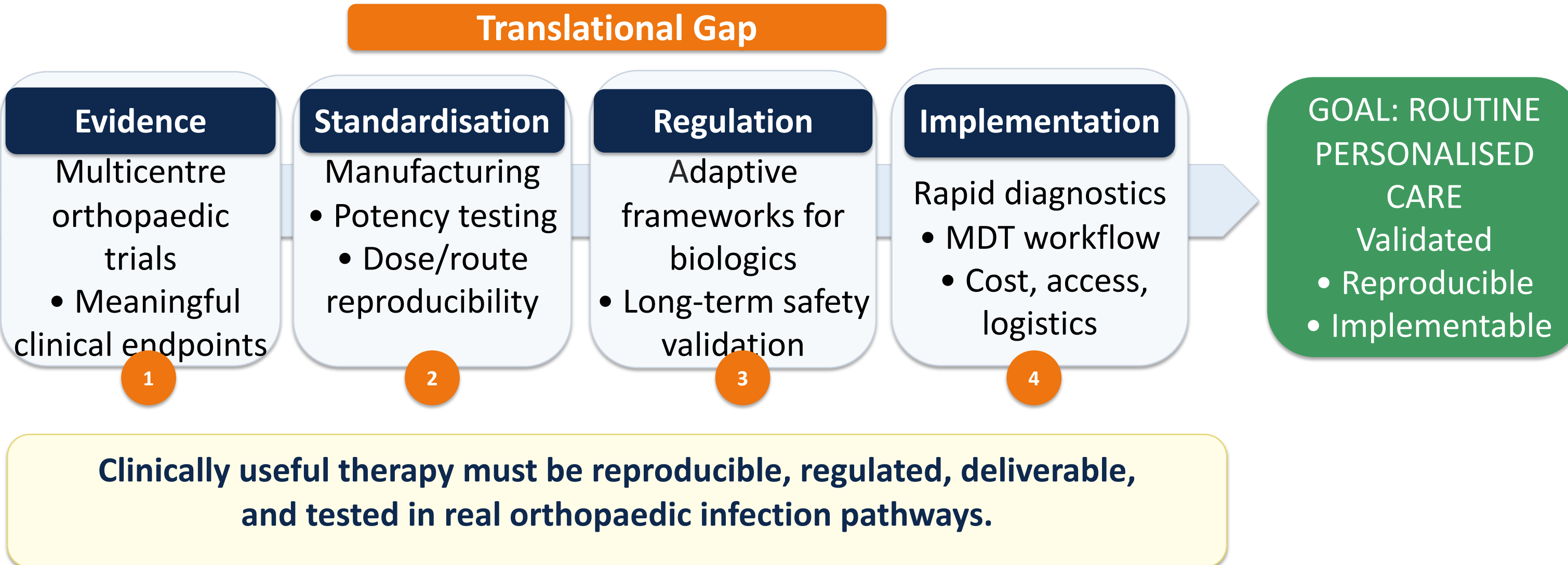
PRECISION ENABLER

Molecular Diagnostics

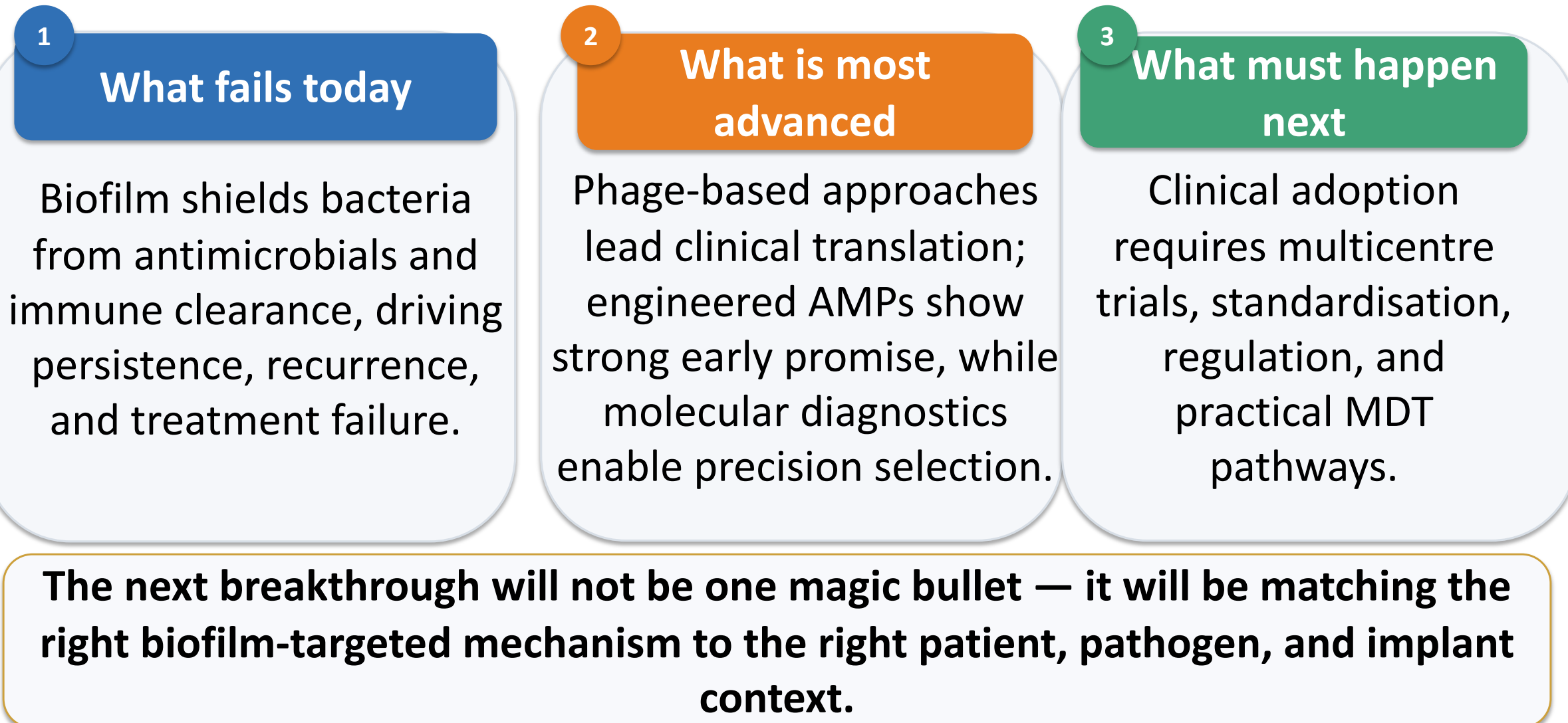


Role: Culture-independent pathogen identification
Value: Detects pathogens + selected resistance determinants
Clinical relevance: Supports targeted treatment selection, especially in culture-negative or polymicrobial infections.

4. From Promise to Practice



5. Conclusion



6. References

- Muthukrishnan G, et al. Biofilm Workgroup Summary. *J Orthop Res*. 2026;44(1):e70130.
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- Oleary F, et al. Diagnostic accuracy of molecular methods in periprosthetic joint infection: systematic review and meta-analysis. *Clin Microbiol Infect*. 2025;31(7):1115–1125.
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