Target Product Profile –Therapeutic Product (Gram-Negative Lower Respiratory Infections)

Variable	Minimal Requirement	Ideal Requirement
Product Indication	Treatment for hospital-acquired bacterial pneumonia (HABP) or ventilator-associated bacterial pneumonia (VABP) and associated bacteremias.	Treatment for hospital-acquired bacterial pneumonia (HABP) or ventilator-associated bacterial pneumonia (VABP) and associated bacteremias. **"Nice to have" expansion** to treatment for hospitalized community-acquired pneumonia (hCABP).
Organisms Covered	**Product must target** antibiotic-susceptible and -resistant isolates of **at least** *Pseudomonas aeruginosa* (incl. MDR) **+/-** Enterobacterales spp. (incl. MDR, CRE, and ESBL-producing); *Acinetobacter baumannii* (incl. CRAB), considered a bonus.	**Product must target** antibiotic-susceptible and -resistant isolates of **at least** *Pseudomonas aeruginosa* (incl. MDR) **and/or** Enterobacterales spp. (incl. MDR, CRE, and ESBL-producing); *Acinetobacter baumannii* (incl. CRAB), considered a bonus. **"Nice to have" additional coverage** of antibiotic-susceptible and -resistant isolates of: *Streptococcus pneumoniae* (incl. penicillin non-susceptible); *Staphylococcus aureus* (incl. MRSA); *Haemophilus influenzae* (incl. ampicillin-resistant); *Moraxella catarrhalis*; *Legionella spp.; Mycoplasma pneumoniae; Chlamydophila pneumoniae.*
Patient Population	Adults in a healthcare setting for the treatment of a confirmed serious Gram-negative infection.	Adults and children (>1yr) in a healthcare setting for the treatment of a confirmed serious Gram-negative infection, with the possibility of early discharge with a PO step-down treatment
Treatment Duration	10 – 14 days	5 – 10 days
Delivery Mode	**IV**	**Oral and IV**
Dosage Form	Solution or powder for reconstitution	Tablet, capsule (Oral), solution or powder for reconstitution (IV)
Regimen	Up to 3 doses/day	Up to 3 doses/day for IV treatment, then up to 2 doses/day for oral treatment
Efficacy	Equal to the standard of care for all targeted indications	Greater than or equal to the standard of care for all targeted indications
Risk/Side Effects	**Manageable drug interactions; clean safety profile; minimum safety margin 3X over effective dose**	Manageable drug interactions; clean safety profile; minimum safety margin >5X over effective dose
Stability	At least 3-month solid state stability at 4C	At least 3-month solid state stability at 4C and 25C
Cost	Equivalent to current treatment regimens in HIC	COGs that are compatible with launch in LMICs
Specific Population Claims		
Overall Value Proposition: Effective IV, Oral, or IV/Oral antibiotic active against antibiotic-resistant Gram-negative pathogens enabling timely transition from hospital to outpatient setting		

Target Product Profile – Therapeutic Product (Urinary Tract Infections)

Variable	Minimal Requirement	Ideal Requirement
Product Indication	Treatment of acute UTI or complicated UTI including pyelonephritis and associated bacteremia	Treatment of acute UTI or complicated UTI including pyelonephritis and associated bacteremia
Organisms Covered	*E. coli* and *K. pneumoniae (*including MDR, CRE and ESBL-producing isolates).	*E. coli, K. pneumoniae,* other Enterobacterales and *P. aeruginosa* (including MDR, CRE and ESBL-producing isolates).
Patient Population	Acute UTI in adult women or men with and without signs or symptoms of infection beyond the bladder	Acute UTI in adult women or men with and without signs or symptoms of infection beyond the bladder
Treatment Duration	Up to 5 days for acute UTI confined to the bladder and up to 10 days for pyelonephritis and complicated UTI	Up to 5 days for acute UTI confined to the bladder and up to 10 days for pyelonephritis and complicated UTI
Delivery Mode	Oral, or IV/oral	Oral, or IV/oral
Dosage Form	Tablet, capsule (Oral), solution or powder for reconstitution (IV)	Tablet, capsule (Oral), solution or powder for reconstitution (IV)
Regimen	Up to 3 doses/day for IV treatment, then up to 2 doses/day for oral treatment	Up to 3 doses/day for IV treatment, then up to 2 doses/day for oral treatment
Efficacy	Non-inferior to SOC (e.g. nitrofurantoin, pivmecillinam, fosfomycin, trimethoprim-sulfamethoxazole, quinolones, BL-BLI therapies and cefiderocol)	Non-inferior to SOC (e.g. nitrofurantoin, pivmecillinam, fosfomycin, trimethoprim-sulfamethoxazole, quinolones, BL-BLI therapies and cefiderocol)
Risk/Side Effects	Comparable to current therapies with β-lactams, no toxicity signals in preclinical reproduction toxicity studies; minimum safety margin 3X over effective dose	Comparable to current therapies with β-lactams, no toxicity signals in preclinical reproduction toxicity studies; minimum safety margin >5X over effective dose
Stability	Heat stable, 3-year shelf life	Heat stable, 3-year shelf life
Cost	Equivalent to current treatment regimens	Equivalent to current treatment regimens
Population Claims	Contraindicated in pregnant women, catheterized patients and patients with comorbidities	Safe in pregnant women, catheterized patients and patients with comorbidities
Overall Value Proposition: Safe, effective and affordable therapy against hard-to-treat, antibiotic-resistant UTI infections in HIC and LMICs		

Minimal criteria for portfolio entry*

- Scaffold(s) demonstrated to inhibit a defined target in at least in one relevant assay, has ample chemical space to explore, shows indications of Structure-Activity-Relationships that can be optimized
- Demonstration of expected cell-based antibacterial mechanism of action
- Active upon resynthesis; >90% purity
- Low cytotoxicity against a relevant human cell line which suggests selectivity will be achievable
- Demonstration of direct antibacterial activity against a wild-type pathogen(s) that is relevant to the desired target indication in a broth microdilution (MIC) assay
- For an IV product, appropriate aqueous solubility will be required. For an oral product, molecular properties that portend good oral bioavailability (medium-to-high Caco-2-cell (or equivalent) permeability or if in a later stage of development – positive baseline exposure (at least >10 %F) in appropriate compartments when dosed orally *in vivo*) will be required. Any proposed prodrug strategy must be explicit and well-defined, with baseline demonstration of conversion to the parent drug at a rate consistent with pharmacological efficacy.

*see website for full details of baseline criteria, by stage of development