

BX-1620

Meliovex — an efflux-inhibitor-potentiated beta-lactam for melioidosis.

Melioidosis is estimated to cause around 165,000 cases and 89,000 deaths a year, mostly in South and Southeast Asia and northern Australia, and it is diagnosed in a small fraction of them. Treatment takes weeks of intravenous therapy followed by months of oral eradication, and it still relapses. *Burkholderia pseudomallei* is also a Tier 1 select agent.

Indication	Melioidosis (<i>Burkholderia pseudomallei</i> infection), including bacteraemic and pneumonic disease, for intensive-phase therapy and oral eradication; secondary activity against <i>Burkholderia mallei</i> .
Modality	Fixed-combination beta-lactam with a small-molecule resistance-nodulation-division efflux pump inhibitor, intravenous and oral
Target	Penicillin-binding protein 3 of <i>B. pseudomallei</i> , with concurrent inhibition of the AmrAB-OprA and BpeEF-OprC efflux systems
Route and schedule	2 g/500 mg intravenously every 8 hours for 14 days (intensive phase), then 500 mg/125 mg orally twice daily for 12 weeks (eradication phase)
Development stage	Phase 1, healthy volunteers
Current study	REDLAND-1 (NCT-BX1620-01) — randomised, double-blind, placebo-controlled single and multiple ascending dose study with a food-effect cohort, a renal-impairment cohort and an intravenous-to-oral bridging cohort
Containment	BSL-3 for all culture work; Tier 1 select agent; federal registration and personnel reliability programme
Regulatory pathway	Conventional randomised controlled trial route, with non-inferiority against ceftazidime or meropenem

Mechanism of action

Burkholderia pseudomallei is difficult to treat for two reasons that compound each other. It survives intracellularly, which slows killing and protects a reservoir from which relapse occurs, and it carries a formidable set of resistance-nodulation-division efflux pumps — principally AmrAB-OprA and BpeEF-OprC — that export a wide range of antibacterial agents, including several that would otherwise be active, and that are readily upregulated under therapy. The organism's intrinsic PenA beta-lactamase adds a second layer, and mutations in it during prolonged treatment are a recognised cause of emergent ceftazidime resistance. BX-1620 pairs a ceftazidime-class beta-lactam, which binds penicillin-binding protein 3 and is the anchor of current standard therapy, with a small-molecule efflux pump inhibitor that blocks the periplasmic adaptor interface of both principal RND systems. The inhibitor has no intrinsic antibacterial activity; its entire function is to keep the beta-lactam inside the cell. In checkerboard assay against clinical isolates the combination reduced the beta-lactam minimum inhibitory concentration by four to sixteen-fold, restored activity against isolates with upregulated BpeEF-OprC, and — the result that matters most clinically — reduced the frequency of resistant mutant selection at therapeutic exposure by more than two orders of magnitude. Melioidosis relapses because sub-inhibitory exposure inside cells selects for resistance over a twelve-week course. Raising intracellular concentration and closing the efflux route addresses that mechanism directly.

Why this disease

Melioidosis is caused by a bacterium that lives in wet soil and surface water and infects people who work in it — rice farmers, above all, plus construction workers, and anyone caught in a flood or a storm. Modelled estimates put the annual burden at approximately 165,000 cases and 89,000 deaths, which would make it comparable to measles or dengue in mortality. Recorded cases are a small fraction of that, because diagnosis requires culture, culture requires a laboratory, and the organism is regularly misidentified as a contaminant by automated systems.

Diabetes is the dominant risk factor, present in roughly half of cases, and the two epidemics are expanding together across exactly the same geography. The clinical picture ranges from a localised abscess to fulminant septicaemic pneumonia, and it has a habit of presenting years after exposure, which has earned it the name 'the great mimicker'. Untreated septicaemic melioidosis has a case fatality above 70 per cent; with optimal modern care in northern Australia it is around 10 per cent, and in most endemic settings it sits far above that.

Treatment is long and it is fragile. Two weeks or more of intravenous ceftazidime or meropenem, then twelve weeks of oral trimethoprim-sulfamethoxazole for eradication, with relapse in around 5 to 10 per cent even when the course is completed — and adherence to twelve weeks of an antibiotic with a real side-effect burden is not universal. Emergent ceftazidime resistance through PenA mutation during therapy is documented. *B. pseudomallei* is additionally a Tier 1 select agent, and *Burkholderia mallei*, its close relative, has a history of deliberate use, which is why this programme sits inside a biocontainment company rather than a conventional antibacterial portfolio.

The disease at a glance

Feature	Detail	Why it matters
Estimated burden	~165,000 cases and ~89,000 deaths a year	Comparable to major recognised killers; diagnosed in a small fraction
Case fatality	>70% untreated septicaemic; ~10% with optimal modern care	The gap between those two numbers is almost entirely access and diagnosis
Dominant risk factor	Diabetes, present in ~half of cases	Both epidemics are growing across the same geography
Exposure	Wet soil and surface water; rice farming; flooding and storms	Occupational and environmental; not controllable by behaviour alone
Current therapy	2+ weeks IV ceftazidime or meropenem, then 12 weeks oral eradication	Long, poorly adhered to, and still followed by relapse in 5–10%
Resistance	Intrinsic RND efflux pumps; PenA mutation emergent under therapy	The failure mechanism is known and is directly addressable
Latency	Can present years after exposure	Known as 'the great mimicker'; frequently misdiagnosed
Biothreat status	<i>B. pseudomallei</i> Tier 1 select agent; <i>B. mallei</i> historically weaponised	Countermeasure development has a dual public health and preparedness rationale
Biosafety	Risk Group 3; laboratory-acquired infection documented	Culture work restricted to registered BSL-3 facilities

Preclinical and pharmacology package

- Efflux inhibitor has no intrinsic antibacterial activity at any concentration tested, confirming that the observed effect is potentiation rather than additive killing.
- Beta-lactam minimum inhibitory concentration reduced 4- to 16-fold across 84 clinical *B. pseudomallei* isolates, including 11 with upregulated BpeEF-OprC and 4 with PenA substitutions.
- Frequency of resistant mutant selection at therapeutic exposure reduced by more than 100-fold compared with the beta-lactam alone — the primary translational objective of the programme.
- Epithelial lining fluid penetration 0.48 of unbound plasma for the beta-lactam and 0.41 for the inhibitor; pneumonic melioidosis is the commonest severe presentation, so lung exposure was a gating criterion.
- Intracellular accumulation in infected macrophages increased 6-fold with the inhibitor present, addressing the intracellular reservoir from which relapse is believed to arise.
- Oral bioavailability 61 per cent (beta-lactam prodrug ester) and 78 per cent (inhibitor), with the component ratio maintained within 1.4-fold across the dosing interval — the technical requirement for a twelve-week fixed-combination oral eradication phase.
- Renal-impairment cohort in progress; dose adjustment bands prespecified by creatinine clearance because beta-lactam neurotoxicity in renal failure is a known and avoidable harm.
- Efficacy demonstrated in the BALB/c mouse acute inhalational model and a chronic relapse model, with relapse at 60 days after treatment cessation reduced from 9 of 12 to 2 of 12.

Clinical development — REDLAND-1

Design	Randomised, double-blind, placebo-controlled single and multiple ascending dose study with a food-effect cohort, a renal-impairment cohort and an intravenous-to-oral bridging cohort
Population	Healthy adult volunteers aged 18–65, including a cohort with mild to moderate renal impairment. No participant is exposed to <i>B. pseudomallei</i> at any point.
Sites	Four, United States
Enrolment	41 of 72 as of 31 July 2026
Doses studied	Intravenous 500 mg/125 mg to 3 g/750 mg every 8 hours; oral 125 mg/32 mg to 750 mg/188 mg twice daily; 10-day courses in the multiple-dose cohorts
Primary objective	Safety and tolerability of the fixed combination
Key secondary	Pharmacokinetics of both components including the ratio maintained across the dosing interval; renal-impairment dose adjustment; intravenous-to-oral bridging; epithelial lining fluid penetration; ex vivo potentiation against clinical <i>B. pseudomallei</i> isolates
Status	Recruiting; intravenous cohorts 1–5 and oral cohorts 1–4 complete, renal cohort open

Safety observed to date

Most frequent ($\geq 20\%$): diarrhoea, nausea, headache, infusion-site reaction. Grade ≥ 3 observed in 7 per cent of participants: ALT increased, and one case of neutropenia at the highest intravenous dose which resolved on discontinuation. No seizure, no anaphylaxis and no *C. difficile* infection occurred in the programme to date.

Warnings and monitoring in the protocol

Investigational agent. Observed events in dose escalation have been grade 1 to 2 diarrhoea, nausea, infusion-site reaction and transient transaminase elevation. Beta-lactam class effects apply: hypersensitivity including anaphylaxis, *Clostridioides difficile*-associated diarrhoea, and neurotoxicity with seizure at high exposure in renal impairment, which is why a dedicated renal cohort is part of Phase 1 rather than a post-approval commitment. Coombs-positive haemolytic anaemia has been reported for the beta-lactam class. Not to be used outside a clinical trial or an authorised expanded access or emergency use framework. Handling of *B. pseudomallei* cultures is restricted to registered BSL-3 facilities; this product is not a substitute for laboratory containment, and laboratory-acquired infection from sniffing plates or bench aerosols remains a documented hazard.

Development milestones

Date	Milestone	Status
Q4 2026	REDLAND-1 renal-impairment cohort completion and dosing bands	Planned
Q1 2027	Intravenous-to-oral bridging and epithelial lining fluid sub-study readout	Planned
Q2 2027	Non-human primate inhalational melioidosis efficacy study	Planned
Q3 2027	Phase 2 protocol with Thai and northern Australian investigators	Planned
Q4 2027	End-of-Phase-1 meeting; non-inferiority design agreement	Planned
2028	Randomised controlled Phase 2 in culture-confirmed melioidosis	Planned

Regulatory status and pathway

Investigational New Drug application cleared in May 2026 as a fixed combination. There is no approval of any kind in any jurisdiction. Melioidosis is the one programme in this portfolio that can be developed entirely conventionally: there are tens of thousands of culture-confirmed cases a year at identified referral centres in Thailand, Malaysia and northern Australia, and a randomised non-inferiority trial against ceftazidime or meropenem with a relapse-free-survival endpoint is straightforwardly feasible. The programme is being developed under 505(b)(1) with Qualified Infectious Disease Product designation requested, which would carry priority review and an additional exclusivity period. A separate Animal Rule package is being assembled for the inhalational biothreat indication, which cannot be studied in humans. Orphan drug designation has been requested. Designations are not approvals and none has yet been granted.

Biosafety and handling

Burkholderia pseudomallei is a Risk Group 3 organism and a United States Tier 1 select agent, which places it under the most stringent registration regime in the programme alongside the Risk Group 4 viruses: personnel reliability screening, two-person access control, and inventory accountability for every vial. All culture, susceptibility, efflux and animal work is performed at BSL-3 under federal registration. Clinical sites handle no infectious material. Laboratory-acquired melioidosis is documented and is usually the result of routine bacteriology performed on an organism nobody expected: any clinical laboratory in an endemic area that grows an oxidase-positive, bipolar-staining Gram-negative rod with a wrinkled colony should stop bench work and move to a containment cabinet before proceeding.

For volunteers in REDLAND-1

- No participant is exposed to the target pathogen or to any infectious material at any point.

- Screening includes medical history, physical examination, laboratory tests and an electrocardiogram.
- Participation involves scheduled clinic visits or a residential period, and serial blood sampling.
- A safety follow-up visit takes place approximately 30 days after the last dose.
- Taking part is voluntary; a participant may withdraw at any time, for any reason or none.
- All study procedures and study medicine are provided at no cost, and reasonable travel expenses are reimbursed.
- Suspected side effects can also be reported directly to the FDA through MedWatch.

Important. BX-1620 is an investigational medical countermeasure. It has not been approved by any regulatory authority, and its safety and efficacy have not been established. This document is for information only. It is not medical advice, not biosafety guidance, not an offer to sell or a solicitation to buy securities, and not a promise that this programme will succeed. BX-1620 is not available on prescription. Requests for expanded access or emergency use in a confirmed or strongly suspected case can be made by a treating physician through the medical information route at baxtra.pages.dev/patients.html.

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Queries to disclosure@baxtra.pages.dev.