

BX-1140

Poxavir — a second-generation p37 envelope inhibitor for clade I mpox and orthopoxvirus disease.

The one orally available orthopoxvirus antiviral in wide use did not beat placebo on lesion resolution in the PALM007 trial in the Democratic Republic of the Congo, and resistance-conferring substitutions in the p37 gene have now been reported in treated patients. A second molecule against the same validated target, chosen for a different resistance profile, is not a luxury.

Indication	Orthopoxvirus disease, including clade I and clade II mpox, and treatment of complications of smallpox vaccination; retained activity against p37 variants associated with reduced susceptibility to first-generation inhibitors.
Modality	Oral small-molecule inhibitor of the p37 envelope wrapping protein, with an intravenous formulation
Target	p37 (F13L gene product), the phospholipase-like envelope wrapping protein
Route and schedule	600 mg orally twice daily with food for 14 days; intravenous formulation for patients unable to swallow
Development stage	Phase 1, healthy volunteers
Current study	MERIDIAN-1 (NCT-BX1140-01) — randomised, double-blind, placebo-controlled single and multiple ascending dose study with a food-effect cohort and an intravenous bridging cohort
Containment	BSL-3 for variola-surrogate work; monkeypox virus and cowpox virus at BSL-3; no variola virus is held or handled by Baxtra at any site
Regulatory pathway	FDA Animal Rule for smallpox, 21 CFR 314 Subpart I; conventional randomised controlled trial route for clade I mpox

Mechanism of action

Orthopoxviruses replicate in the cytoplasm and produce two infectious forms. The mature virion accounts for most of the infectivity within a lysed cell; the extracellular enveloped virion is what leaves the cell intact and spreads the infection through the host and to other hosts. The wrapping step that produces it depends on p37, the F13L gene product, a palmitoylated phospholipase-like protein that recruits trans-Golgi and endosomal membranes around the mature virion. Inhibiting p37 does not stop replication and does not reduce lesion virus titre in the first instance; it stops dissemination, which is why the target is validated and also why the endpoint has to be chosen carefully. BX-1140 binds the p37 hydrophobic groove at a position offset from the site engaged by first-generation inhibitors. The practical consequence is the point of the programme: p37 substitutions reported in treated patients — including the alterations most frequently seen at codons associated with reduced susceptibility — retain full sensitivity to BX-1140 in plaque reduction assay, while the parent-compound-resistant phenotype is preserved as a control. Activity extends across monkeypox clade Ia, clade Ib and clade II, cowpox virus, and vaccinia virus, the latter being the relevant agent for progressive vaccinia after immunisation.

Why this disease

Smallpox was eradicated in 1980 and routine vaccination stopped, which means that most people alive today have no orthopoxvirus immunity at all. That is the background condition against which every other statement about this virus family should be read. Mpox, previously a sporadic zoonosis of Central and West Africa, has moved into sustained human-to-human transmission twice in four years.

Clade I, the more virulent lineage, drove the emergency declared in August 2024, spreading from the Democratic Republic of the Congo into neighbouring countries with a new sexually-transmitted sublineage, clade Ib. Reported case fatality has been between 1.4 and 3.3 per cent overall, and considerably worse in young children and in people with advanced, untreated HIV — a population in which the disease becomes necrotic, disseminated and frequently fatal, and in which any antiviral is under the greatest pressure to select resistance.

The PALM007 randomised trial in the Democratic Republic of the Congo reported that the first-generation p37 inhibitor did not shorten time to lesion resolution compared with placebo, in a well-conducted trial with good supportive care. Separately, p37 substitutions conferring reduced susceptibility have been identified in treated, immunocompromised patients in the United States and Europe. The target is validated by decades of virology; the single available molecule against it is not enough.

The disease at a glance

Feature	Detail	Why it matters
Case fatality	1.4–3.3% (clade I); higher in children and advanced HIV	Lower than the filoviruses, but the case count is orders of magnitude larger
Emergency status	WHO public health emergency of international concern, August 2024	Sustained human-to-human transmission of clade I
Population immunity	Absent in anyone born after ~1980	Routine smallpox vaccination ended after eradication
First-line antiviral	One oral p37 inhibitor; no benefit over placebo in PALM007	Clinical benefit of the existing option is unproven
Resistance	p37 substitutions reported in treated immunocompromised patients	A single-molecule target is a fragile position
Highest-risk group	Advanced untreated HIV; children under 5	Prolonged replication and the greatest resistance pressure
Transmission	Close contact, sexual contact, household, nosocomial	Interruptible, but only with a treatment that works
Biosafety	Monkeypox virus Risk Group 3; variola virus RG4, held at two WHO repositories only	Baxtra holds no variola virus at any site

Preclinical and pharmacology package

- Oral bioavailability 43 per cent with a high-fat meal and 12 per cent fasted; the food requirement is a labelled design feature, not an inconvenience to be worked around.
- Terminal half-life 19 hours; steady state reached by day 4 on twice-daily dosing.
- Intravenous-to-oral bridging established, giving a route for patients with severe oropharyngeal or gastrointestinal lesions who cannot reliably swallow — a group the first-generation oral-only product cannot serve.

- Plaque reduction EC50 retained within 2-fold against a panel of eight p37 variants selected for reduced susceptibility to the first-generation inhibitor, including the substitutions most frequently reported clinically.
- Activity confirmed against monkeypox clade Ia, clade Ib and clade II, cowpox virus and vaccinia virus.
- Efficacy demonstrated in the intranasal cowpox mouse model and the intravenous monkeypox virus cynomolgus macaque model, with treatment started after lesion onset.
- No genotoxic signal; QT assessment negative to 900 mg twice daily; 28-day toxicology complete in rat and dog.

Clinical development — MERIDIAN-1

Design	Randomised, double-blind, placebo-controlled single and multiple ascending dose study with a food-effect cohort and an intravenous bridging cohort
Population	Healthy adult volunteers aged 18–55.
Sites	Four, United States
Enrolment	34 of 56 as of 31 July 2026
Doses studied	100 mg to 900 mg orally twice daily, 14-day courses; 200 mg and 400 mg intravenously
Primary objective	Safety and tolerability
Key secondary	Pharmacokinetics with and without food; intravenous-to-oral bridging; QT assessment; ex vivo plaque reduction against monkeypox clade Ia, Ib and clade II and against a panel of p37 variants
Status	Recruiting; oral cohorts 1–6 complete, intravenous bridging cohort open

Safety observed to date

Most frequent ($\geq 20\%$): headache, nausea, diarrhoea. Grade ≥ 3 observed in 5 per cent of participants: ALT increased at the highest dose level. No dose-limiting toxicity observed at or below 600 mg twice daily.

Warnings and monitoring in the protocol

Investigational agent. Observed events in dose escalation have been grade 1 to 2 headache, nausea and abdominal discomfort. Transaminase elevation was seen at 900 mg twice daily and that dose was not carried forward. Weekly hepatic monitoring through day 28. Not to be used outside a clinical trial or an authorised expanded access or emergency use framework. Monotherapy in a severely immunocompromised patient risks selecting resistance, and the protocol and any expanded access arrangement require resistance monitoring of sequential lesion samples in that population.

Development milestones

Date	Milestone	Status
Q4 2026	MERIDIAN-1 intravenous bridging cohort completion	Planned
Q4 2026	Antiretroviral drug–drug interaction sub-study	Planned
Q1 2027	Non-human primate monkeypox efficacy readout, post-lesion treatment	Planned

Date	Milestone	Status
Q2 2027	Phase 2 protocol for clade I mpox with Central African investigators	Planned
Q4 2027	Animal Rule package alignment for the smallpox indication	Planned
2028	Randomised controlled Phase 2 in confirmed clade I mpox	Planned

Regulatory status and pathway

Investigational New Drug application cleared in April 2026. There is no approval of any kind in any jurisdiction. The programme has two regulatory routes because it has two indications. For clade I mpox, a randomised controlled trial with a time-to-lesion-resolution and mortality endpoint is feasible and is the intended route; PALM007 demonstrated that such trials can be run well in the Democratic Republic of the Congo, and its negative result is the clearest argument for running another one. For smallpox, human efficacy trials are impossible and the route is 21 CFR 314 Subpart I. Orphan drug designation and material threat medical countermeasure status have been discussed with the agency. Designations are not approvals and none has yet been granted.

Biosafety and handling

Monkeypox virus, cowpox virus and vaccinia virus are handled at BSL-3 under federal select agent registration where applicable, with staff vaccinated against orthopoxvirus and titre-monitored. Baxtra does not hold and has never held variola virus; the only authorised repositories are the two WHO collaborating centres, and any statement to the contrary about this programme is false. Clinical sites handle no infectious material. Clinicians managing a suspected mpox case should apply contact and droplet precautions with attention to lesion exudate and bedding, and should discuss any request for investigational therapy through the medical information route rather than the trial sites.

For volunteers in MERIDIAN-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-1140 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-1140 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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