

BX-204

Marburavir — an IV and oral L-polymerase inhibitor for Marburg virus disease.

Marburg virus disease has a reported case fatality of 24 to 88 per cent across outbreaks. There is no licensed vaccine or therapeutic. Marburavir is an investigational nucleoside analogue with intravenous loading and oral step-down under evaluation in CORDON-1.

Indication	Marburg virus disease and Ravn virus disease, with secondary activity against Zaire and Sudan ebolaviruses.
Modality	IV + oral L-polymerase inhibitor (nucleoside analogue)
Target	Filovirus L-protein RNA-dependent RNA polymerase catalytic site
Route and schedule	Intravenous loading and once-daily infusion followed by oral step-down; several 5- and 14-day courses are under study
Development stage	Phase 1, healthy volunteers
Current study	CORDON-1 (NCT-BX0204-01) — randomised, double-blind, placebo-controlled single and multiple ascending dose study with intravenous-to-oral step-down cohorts
Containment	BSL-4 for all live-virus work; Risk Group 4 pathogen; federal select agent registration
Regulatory pathway	FDA Animal Rule, 21 CFR 314 Subpart I

Mechanism of action

Marburavir is a 4'-modified nucleoside analogue that is phosphorylated intracellularly to an active triphosphate. The triphosphate is accepted by the filovirus L protein RNA-dependent RNA polymerase in place of the natural nucleoside substrate. Incorporation causes delayed chain termination three to five nucleotides downstream and, at sustained exposure, increases the number of copying errors in the negative-sense genome. The intended pharmacological consequence is loss of a viable replication programme, although no clinical efficacy has been established. The polymerase catalytic site is more conserved across filoviruses than their surface glycoproteins, so the development hypothesis includes Marburg, Ravn, Zaire and Sudan viruses. This breadth is operationally relevant: an outbreak may be recognised before the species is confirmed, and intravenous loading is intended for a patient already in an isolation unit while oral step-down could reduce the burden of prolonged infusion care.

Why this disease

Marburg virus and Ravn virus are filoviruses in the family Filoviridae. Their natural reservoir is the Egyptian rousette bat, and spillover is followed by person-to-person transmission through blood and body fluids. Outbreaks are often amplified in hospitals, where clinicians and family members are exposed before the diagnosis is recognised. Severe disease includes fever, gastrointestinal symptoms, rash, vascular injury and haemorrhage; supportive care must be delivered in an isolation unit with full encapsulating personal protective equipment.

The recorded case-fatality range of 24 to 88 per cent reflects differences among outbreaks, access to supportive care and the speed of recognition, not a benign end of the disease spectrum. Survivors may have persistent virus in immune-privileged sites, including semen, ocular fluid and cerebrospinal fluid. That persistence matters for follow-up and for infection-control decisions after apparent clinical recovery.

There is no licensed vaccine or therapeutic for Marburg virus disease. Candidate countermeasures developed for one filovirus species cannot be assumed to cover another, and an outbreak may require treatment before species confirmation is available. CORDON-1 therefore measures exposure, intracellular activation and tolerability across an IV-to-oral regimen; it is a Phase 1 study in healthy volunteers, not a treatment study in infected people.

The disease at a glance

Feature	Detail	Why it matters
Reservoir	Egyptian rousette bat; spillover is zoonotic	Surveillance and safe handling must extend beyond hospitals.
Transmission	Contact with blood and body fluids; healthcare-associated spread is documented	Barrier precautions and isolation are central to care.
Geography	Recorded outbreaks have occurred in sub-Saharan Africa	Local diagnostic and containment capacity determines response speed.
Clinical course	Acute febrile illness can progress to gastrointestinal, vascular and haemorrhagic disease	Supportive care and isolation decisions cannot wait for every laboratory result.
Case fatality	24–88% across recorded outbreaks	A wide range does not make an individual case predictable.
Persistence	Virus may remain in immune-privileged sites after recovery	A negative clinical assessment is not proof of clearance from every compartment.
Prevention	No licensed vaccine or therapeutic	The countermeasure gap remains material during an outbreak.
Pathogen status	Risk Group 4; Category A infectious substance for transport	Live-virus work requires maximum containment and specialised procedures.

Preclinical and pharmacology package

- Cell-based polymerase assays measure delayed chain termination and error accumulation across Marburg, Ravn, Zaire and Sudan virus polymerase systems.
- Intracellular phosphorylation and triphosphate persistence are measured in primary human monocytes, hepatocytes and endothelial cells rather than inferred from plasma concentration alone.
- The pharmacokinetic package includes renal clearance, infusion exposure, oral bioavailability, food effect and the exposure relationship between IV loading and oral step-down.
- Non-human-primate studies are planned under maximum containment to define treatment timing, exposure margins and virological sampling; no animal result is a substitute for clinical efficacy evidence.
- Resistance surveillance sequences the polymerase coding region from breakthrough cell-culture populations and tests substitutions individually against the parent compound.
- Safety pharmacology covers renal, hepatic, haematological, cardiac repolarisation and infusion-related findings, with special attention to the intended use in critically ill patients.

Clinical development — CORDON-1

Design	Randomised, double-blind, placebo-controlled single and multiple ascending dose study with intravenous-to-oral step-down cohorts
Population	Healthy adult volunteers aged 18–55. No participant is exposed to Marburg virus, Ravn virus, an ebolavirus or any infectious material at any point.
Sites	Three, United States
Enrolment	24 of 36 as of 31 August 2026
Doses studied	Intravenous 100, 300 and 600 mg once daily over 30 minutes; oral 200, 400 and 800 mg once daily; 5-day and 14-day courses
Primary objective	Safety and tolerability, including renal and infusion-related events
Key secondary	Pharmacokinetics and intracellular triphosphate exposure; viral-polymerase target engagement in cell-based assays; renal clearance; QT interval and laboratory safety markers
Status	Recruiting; intravenous and oral dose bands open; 24 of 36 participants enrolled

Safety observed to date

Most frequent ($\geq 20\%$): nausea, infusion site reaction, headache. Grade ≥ 3 observed in 9 per cent: neutropenia, creatinine increased. One participant discontinued for asymptomatic grade 3 lipase elevation.

Warnings and monitoring in the protocol

Investigational agent. Renal function must be assessed before each infusion; dose adjustment is required below an estimated glomerular filtration rate of 50 mL/min. Infusion-related reactions occurred in 6 per cent of participants and resolved with rate reduction. Not to be used outside a clinical trial or an authorised emergency framework. Viral persistence in immune-privileged sites after clinical recovery is well documented for filoviruses; completion of therapy does not establish clearance from semen, ocular fluid or cerebrospinal fluid.

Development milestones

Date	Milestone	Status
Q4 2025	Marburg and Ravn polymerase series nominated; IV and oral formulation work opened	Complete
Q1 2026	CORDON-1 IND cleared and first US site activated	Complete
Q2 2026	Single-ascending-dose cohorts and IV-to-oral bridging cohort completed	Complete
Q3 2026	CORDON-1 enrolment reached 24 of 36 participants	Current
Q4 2026	Multiple-ascending-dose readout and triphosphate exposure analysis	Planned
2027	Non-human-primate treatment-timing study and End-of-Phase-1 meeting	Planned

Regulatory status and pathway

Marburavir is being developed under a cleared US Investigational New Drug application. The intended regulatory route is the FDA Animal Rule (21 CFR 314 Subpart I), because controlled human challenge is neither ethical nor feasible for Marburg virus disease. The programme must establish a defined relationship between exposure, pharmacodynamic measures and outcomes in relevant animal models, together with human safety and pharmacokinetic data. CORDON-1 remains a Phase 1 healthy-volunteer study. No efficacy, marketing authorisation or availability on prescription is claimed; Marburavir has not been approved by any regulatory authority.

Biosafety and handling

Live Marburg, Ravn and ebolavirus work is conducted only in registered maximum-containment facilities under BSL-4 procedures, with positive-pressure suits, dedicated decontamination and select-agent controls. CORDON-1 does not expose volunteers to virus or infectious material. The 29 August 2026 public statement, 'Statement on a containment failure' (ref BXRA-PS-2026-08), confirms only that an event occurred, was found by Baxtra's own staff, that work stopped, an independent review is open, and authorities were notified. It declines to name the programme, suite, material, quantities, dates or individuals, and states there is no identified risk outside the facility. Please do not write to ask.

For volunteers in CORDON-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-204 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-204 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.

Cleared for external publication by the Disclosure Review Board · DRB-2026-0204 · public revision 3 of 12 · issued 31 August 2026. Queries to disclosure@baxtra.pages.dev.