

BX-806

Sudanavir — a two-antibody cocktail for Sudan ebolavirus disease.

Two monoclonal antibody products are approved for Zaire ebolavirus. Neither works against Sudan ebolavirus, which caused the 2022 Uganda outbreak with a case fatality of 47 per cent. The approved products exist and the gap is species-specific, which is an unusually well-defined problem.

Indication	Sudan ebolavirus disease, with secondary activity against Bundibugyo ebolavirus; post-exposure prophylaxis after recognised high-risk exposure.
Modality	Cocktail of two non-competing human IgG1 monoclonal antibodies, intravenous
Target	The internal fusion loop of Sudan virus GP2 (component BX-806A) and the glycan cap of GP1 (component BX-806B)
Route and schedule	Single intravenous infusion of 50 mg/kg over 90 minutes
Development stage	Phase 1, healthy volunteers
Current study	KEYSTONE-1 (NCT-BX0806-01) — randomised, double-blind, placebo-controlled single ascending dose study in healthy adult volunteers
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, with an outbreak-activated randomised protocol held in reserve

Mechanism of action

Ebolaviruses enter cells through a glycoprotein spike that must first be stripped of its glycan cap by endosomal cathepsins before the receptor-binding site can engage NPC1 in the late endosome, after which the GP2 internal fusion loop inserts into the endosomal membrane and drives fusion. BX-806 attacks both halves of that sequence with two antibodies that do not compete for the same footprint. BX-806A binds the internal fusion loop of GP2, an epitope that is structurally constrained and comparatively conserved across the genus, and blocks membrane insertion after cleavage. BX-806B binds the glycan cap of GP1 and blocks the proteolytic priming step itself, while also recruiting Fc-mediated effector function — antibody-dependent cellular phagocytosis and natural killer cell activity — which contributes materially to filovirus protection in animal models and is not captured by neutralisation assays. The two epitopes are far apart on the trimer, so a single amino acid substitution cannot escape both, and escape variants selected against either component in vitro remained neutralised by the pair. Species coverage was the primary selection criterion rather than potency: the programme exists because of a species gap, and a more potent antibody that covered only one strain of Sudan virus would not have solved it.

Why this disease

There are six known ebolaviruses. Public attention, vaccine development and antibody licensure have concentrated almost entirely on one of them, Zaire ebolavirus, because it caused the 2014–2016 West African epidemic. That work was successful: two monoclonal antibody products and a vaccine are now licensed, and case fatality in a well-run treatment unit has fallen substantially.

None of it works for Sudan ebolavirus. The glycoprotein differs sufficiently that the licensed antibodies do not neutralise it, and the licensed vaccine does not protect against it. When Sudan virus emerged in Mubende, Uganda in September 2022, there was no therapeutic and no vaccine, 164 cases were recorded and 77 people died. Clinicians were, in effect, working in 2013.

Sudan virus has caused eight recorded outbreaks since 1976, with case fatality between 41 and 71 per cent. It is not a hypothetical threat and it is not an exotic one. It is the same disease, in the same treatment units, with the same transmission dynamics — and the countermeasure shelf for it is empty. Filling a species-shaped gap is a narrower scientific problem than most in this portfolio, and it is one of the reasons the programme moved quickly.

The disease at a glance

Feature	Detail	Why it matters
Case fatality	41–71% across recorded outbreaks; 47% in Uganda 2022	Comparable to Zaire ebolavirus before licensed therapy existed
Recorded outbreaks	Eight since 1976, Uganda and Sudan	Recurrent, not hypothetical
Licensed therapy	None for Sudan virus; two products licensed for Zaire virus	The gap is species-specific and precisely defined
Licensed vaccine	None for Sudan virus	Ring vaccination is not currently an option in a Sudan outbreak
Reservoir	Presumed bat, not definitively identified	Spillover cannot be predicted or prevented
Transmission	Body fluids; funerary practice; nosocomial	Healthcare workers are disproportionately affected
Incubation	Typically 2–21 days	Long enough for contact tracing and post-exposure prophylaxis
Biosafety	Risk Group 4, BSL-4, select agent	Live work restricted to registered maximum-containment facilities

Preclinical and pharmacology package

- Terminal half-life 22 days (BX-806A) and 25 days (BX-806B); component ratio remained within 1.3-fold of the formulated ratio through day 56.
- Serum neutralising titre against Sudan virus remained above the in vitro IC90 for 38 days after a single 50 mg/kg dose.
- Neutralisation retained against all four sequenced Sudan virus outbreak lineages and against Bundibugyo ebolavirus; partial activity against Taï Forest ebolavirus; no activity against Marburg virus, which is covered separately by BX-204.
- Escape selection against each component individually produced variants that remained fully neutralised by the cocktail, the specific result the two-epitope design was intended to produce.
- Fc effector function confirmed: antibody-dependent cellular phagocytosis and natural killer cell degranulation both demonstrated for BX-806B with an intact Fc and abolished in an Fc-null variant.
- IND-enabling toxicology completed in the cynomolgus macaque; no target-organ toxicity at 12-fold the anticipated clinical exposure.

Clinical development — KEYSTONE-1

Design	Randomised, double-blind, placebo-controlled single ascending dose study in healthy adult volunteers
Population	Healthy adult volunteers aged 18–60. No participant is exposed to any filovirus at any point.
Sites	Three, United States
Enrolment	27 of 40 as of 31 July 2026
Doses studied	5, 15, 50 and 100 mg/kg single intravenous doses
Primary objective	Safety and tolerability, including infusion-related reactions
Key secondary	Pharmacokinetics of both components and their ratio over time; immunogenicity; ex vivo neutralisation of Sudan, Bundibugyo and Tai Forest ebolaviruses; Fc effector function assays
Status	Recruiting; cohorts 1–3 complete, cohort 4 in screening

Safety observed to date

Most frequent ($\geq 20\%$): headache, infusion-site discomfort, chills during infusion. Grade ≥ 3 observed in 4 per cent of participants: transient lymphocyte count decreased. No participant discontinued for a treatment-related event and no dose-limiting toxicity was observed to 100 mg/kg.

Warnings and monitoring in the protocol

Investigational agent. Infusion-related reactions occurred in 11 per cent of participants, all grade 1 to 2, managed by slowing the infusion. Participants are observed for four hours after infusion with resuscitation equipment immediately available. Not to be used outside a clinical trial or an authorised expanded access or emergency use framework. Handling of Sudan ebolavirus itself is restricted to registered maximum-containment facilities; this product is not a substitute for containment, isolation, safe burial practice or personal protective equipment, and it does not reduce the infectiousness of a patient to their contacts.

Development milestones

Date	Milestone	Status
Q4 2026	KEYSTONE-1 cohort 4 completion and full pharmacokinetic readout	Planned
Q1 2027	Non-human primate pivotal efficacy study, treatment initiated after viraemia	Planned
Q2 2027	Non-human primate post-exposure prophylaxis arm	Planned
Q3 2027	End-of-Phase-1 meeting and Animal Rule package alignment	Planned
2027	Outbreak-activated randomised protocol filed with Ugandan and Kenyan partners	Under discussion
2028	Stockpile-readiness manufacturing at commercial scale	Planned

Regulatory status and pathway

Investigational New Drug application cleared in December 2025. There is no approval of any kind in any jurisdiction. Sudan ebolavirus outbreaks are episodic and short, so a conventional efficacy trial cannot be planned against a calendar. The programme therefore runs two routes in parallel: an Animal Rule package under 21 CFR 314 Subpart I based on non-human primate efficacy, and a pre-written, pre-reviewed randomised controlled protocol held in reserve for activation inside a live outbreak, developed with investigators in Uganda and Kenya. The second route is the scientifically stronger one and it is entirely dependent on being ready before the outbreak rather than after it. Orphan drug designation and a material threat medical countermeasure priority review voucher have been discussed with the agency. Designations are not approvals and none has yet been granted.

Biosafety and handling

Sudan ebolavirus is a Risk Group 4 organism. All live-virus neutralisation, escape selection and non-human primate challenge work is performed inside the Palm Coast maximum-containment suite under federal select agent registration, in positive-pressure suits, behind an airlock, with effluent decontamination and two-person rule. Clinical sites handle no infectious material of any kind. Clinicians managing a suspected case should apply full viral haemorrhagic fever precautions, notify their public health authority before sending samples, and not ship specimens without prior arrangement with the receiving reference laboratory.

For volunteers in KEYSTONE-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-806 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-806 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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