

# BX-101

**Nipavir** — an oral fusion (F) glycoprotein inhibitor for Nipah virus infection.

Nipah virus kills between 40% and 75% of the people it infects, transmits from person to person, and has no approved treatment or vaccine anywhere in the world. It is a Risk Group 4 pathogen handled only at biosafety level 4.

|                    |                                                                                                                                    |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------|
| Indication         | Nipah virus infection, including henipavirus encephalitis and acute respiratory syndrome. Secondary activity against Hendra virus. |
| Modality           | Oral small-molecule inhibitor of the henipavirus fusion (F) glycoprotein                                                           |
| Target             | Prefusion conformation of the Nipah F trimer                                                                                       |
| Route and schedule | Oral. Regimen under study: 400 mg loading dose, then 200 mg twice daily for 14 days                                                |
| Development stage  | Phase 1, healthy volunteers                                                                                                        |
| Current study      | SENTINEL-1 (NCT-BX0101-01) — randomised, double-blind, placebo-controlled single and multiple ascending dose                       |
| Containment        | BSL-4 for all live-virus work; Risk Group 4 pathogen                                                                               |
| Regulatory pathway | FDA Animal Rule, 21 CFR 314 Subpart I                                                                                              |

## Mechanism of action

Nipah virus enters a cell using two surface proteins working together. The attachment glycoprotein G binds ephrin-B2 and ephrin-B3 receptors, which are abundant on neurons and on endothelium. That binding triggers the fusion glycoprotein F, a metastable trimer held in a spring-loaded prefusion state, to refold into a six-helix bundle. The refolding is what drags the viral envelope into the host membrane and opens a pore.

BX-101 binds a hydrophobic pocket within the prefusion F trimer and holds it in that state. The refolding transition cannot proceed, so the envelope never fuses and the genome is never delivered. The same block prevents fusion between an infected cell and its neighbours, which is significant because syncytium formation is the mechanism by which Nipah destroys the endothelium of small cerebral vessels and produces the encephalitis that kills most patients.

The pocket is conserved across the genus. In vitro activity is retained against both the Bangladesh and Malaysia genotypes of Nipah virus and against Hendra virus, which matters for a family whose next member has probably not been characterised yet.

### Why brain penetration decided the candidate

Several analogues in the series were more potent in cell culture. We selected BX-101 over them on an unbound brain-to-plasma ratio of 0.42, because Nipah is fundamentally an encephalitis and a molecule that cannot cross into the central nervous system cannot treat it, however good the assay numbers look.

## Why this disease

Nipah virus is a paramyxovirus whose natural reservoir is the *Pteropus* fruit bat. It reaches people by three routes: drinking raw date-palm sap contaminated by bats, contact with infected intermediate livestock, and directly from another infected person. The third route is why Nipah is treated as an epidemic threat rather than a rare zoonosis; caregivers and healthcare workers are repeatedly infected in the recurring Bangladesh and Indian outbreaks.

Clinically it begins with fever, headache and myalgia, and progresses over days to encephalitis with reduced consciousness, seizures and brainstem signs, or to an acute respiratory syndrome. Survivors are not reliably out of danger: relapsing and late-onset encephalitis has been described months to years after apparent recovery, and a substantial proportion of survivors are left with persistent neurological deficit.

| Feature           | Nipah virus                                             | Why it matters                                                              |
|-------------------|---------------------------------------------------------|-----------------------------------------------------------------------------|
| Case fatality     | 40–75% typical; up to ~90% in some Bangladesh outbreaks | A modest treatment effect would still translate into large absolute benefit |
| Reservoir         | <i>Pteropus</i> fruit bats                              | Spillover is recurrent and cannot be eliminated                             |
| Transmission      | Date-palm sap, livestock, person to person              | Human-to-human spread makes containment a race                              |
| Incubation        | Typically 4–14 days                                     | A window in which post-exposure prophylaxis is plausible                    |
| Available therapy | None approved                                           | Care is supportive only                                                     |
| Biosafety         | Risk Group 4, BSL-4                                     | Very few laboratories can do the work at all                                |
| Status            | WHO priority pathogen                                   | Recognised as an epidemic threat requiring urgent R&D                       |

Epidemiological figures quoted in this document are the ranges reported in published World Health Organization and United States Centers for Disease Control and Prevention outbreak summaries. Case fatality varies widely with outbreak size, virus strain, and the supportive care available.

## Preclinical evidence

- Prefusion stabilisation confirmed by differential scanning fluorimetry and by cryo-electron microscopy of the drug-bound trimer.
- Neutralisation of authentic Nipah virus (Bangladesh and Malaysia genotypes) and Hendra virus in BSL-4 culture, with low-nanomolar potency.
- Complete inhibition of syncytium formation in primary human brain microvascular endothelial cells.
- Resistance selection by serial passage under drug pressure; escape substitutions map to the F pocket and carry a measurable fitness cost.
- Survival benefit in the Syrian hamster challenge model with treatment initiated after the onset of viraemia, not before it.
- African green monkey studies ongoing, with delayed treatment start, as the pivotal Animal Rule efficacy package.

- Unbound brain-to-plasma ratio 0.42; cerebrospinal fluid exposure exceeding the in vitro EC90 across the anticipated dosing interval.
- No genotoxic signal; no cardiovascular liability at the exposures tested; IND-enabling toxicology completed in two species.

## Clinical development — SENTINEL-1

|                   |                                                                                                        |
|-------------------|--------------------------------------------------------------------------------------------------------|
| Design            | Randomised, double-blind, placebo-controlled single ascending dose followed by multiple ascending dose |
| Population        | Healthy adult volunteers aged 18–55. No participant is exposed to Nipah virus at any point.            |
| Sites             | Four, United States                                                                                    |
| Enrolment         | 31 of 48 as of 31 July 2026                                                                            |
| Doses studied     | 50 mg to 800 mg once daily; 10-day courses in the multiple-dose cohorts                                |
| Primary objective | Safety and tolerability                                                                                |
| Key secondary     | Pharmacokinetics; cerebrospinal fluid exposure in a dedicated sub-study; food effect; QT assessment    |
| Status            | Recruiting; single ascending dose cohorts 1–4 complete                                                 |

### Safety observed to date

Adverse events have been predominantly grade 1 to 2: headache, nausea and fatigue. Grade 3 or higher events occurred in 8% of participants, comprising ALT elevation and lipase elevation, all reversible. No dose-limiting toxicity has been observed to 800 mg and no participant has discontinued for a treatment-related event.

### Why a healthy volunteer study

Nipah outbreaks are small, remote and over within weeks. A conventional efficacy trial cannot be enrolled in that window. Safety, tolerability and exposure are therefore established in volunteers now, efficacy is carried by animal models under the Animal Rule, and an outbreak-response protocol is held pre-approved and ready to activate.

## Development milestones

| Date     | Milestone                                  | Status   |
|----------|--------------------------------------------|----------|
| Nov 2025 | IND cleared by the FDA                     | Complete |
| Aug 2026 | First subject dosed in SENTINEL-1          | Complete |
| Aug 2026 | Single ascending dose cohorts 1–4 complete | Complete |

| Date    | Milestone                                                | Status  |
|---------|----------------------------------------------------------|---------|
| Q4 2026 | Cerebrospinal fluid exposure sub-study readout           | Planned |
| Q1 2027 | Multiple ascending dose start                            | Planned |
| Q2 2027 | Non-human primate pivotal efficacy readout               | Planned |
| 2027    | End-of-Phase-1 meeting and Animal Rule package alignment | Planned |

## Regulatory status and pathway

**FDA status.** Investigational New Drug application cleared in November 2025. There is no approval of any kind in any jurisdiction.

**Efficacy pathway.** Human efficacy trials in Nipah virus infection are neither ethical nor feasible, so the intended route is 21 CFR 314 Subpart I, the Animal Rule. That requires a well-understood mechanism of pathogenesis, demonstrated effect in more than one animal species, an endpoint clearly related to the benefit sought in humans, and pharmacokinetic data sufficient to select a human dose. All four requirements are being addressed in parallel with the Phase 1 programme.

**Designations.** Orphan drug designation and a request for a material threat medical countermeasure priority review voucher have been discussed with the agency. Designations are not approvals and none has yet been granted.

**Oversight.** The study operates under an FDA-cleared protocol with institutional review board approval at every site. Dose escalation decisions are made by a safety review committee that meets after each cohort. Live virus work is conducted under federal select agent registration.

## Biosafety and handling

Nipah virus is a Risk Group 4 pathogen. All work with replication-competent virus is performed in a maximum-containment suit laboratory: negative pressure cascade, air-fed positive-pressure protective suits, chemical shower on exit, double HEPA filtration on exhaust, and thermal inactivation of all effluent. Pseudovirus, structural and medicinal chemistry work involves no infectious material and is performed at BSL-2.

The investigational product itself is not infectious and presents no biohazard. Clinical supplies are manufactured in ordinary pharmaceutical facilities.

Further detail is published at [baxtra.pages.dev/biocontainment.html](https://baxtra.pages.dev/biocontainment.html).

## Information for clinicians and patients

### For clinicians

Suspect Nipah virus infection in a patient with fever and encephalitis or acute respiratory illness who has, within the previous three weeks, travelled to an area with known Nipah activity, consumed raw date-palm sap, had contact with pigs or bats, or cared for a similar patient. Isolate immediately using contact, droplet and airborne

precautions, notify your public health authority before sending samples, and do not ship specimens without prior arrangement with the receiving reference laboratory.

BX-101 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](https://baxtra.pages.dev/patients.html).

### For volunteers in SENTINEL-1

- No participant is exposed to Nipah virus or to any infectious material at any point.
- Screening includes medical history, examination, laboratory tests and an electrocardiogram.
- Participation involves a residential period, serial blood sampling, and for one sub-study an optional lumbar puncture with separate consent.
- 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.** This 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 a promotional communication, and not guidance for handling infectious material. Suspected high-consequence infectious disease must be isolated and notified to the public health authority immediately.

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