Australian Government
Department of Health, Disability and Ageing
Therapeutic Goods Administration

# Australian Public Assessment Report for Kavigale

## Active ingredient: Sipavibart

## Sponsor: AstraZeneca Pty Ltd

April 2026

OFFICIAL

# About the Therapeutic Goods Administration (TGA)

- The Therapeutic Goods Administration (TGA) is part of the Australian Government Department of Health, Disability and Ageing and is responsible for regulating therapeutic goods, including medicines, medical devices, and biologicals.
- The TGA administers the *Therapeutic Goods Act 1989* (the Act), applying a risk management approach designed to ensure therapeutic goods supplied in Australia meet acceptable standards of quality, safety, and efficacy.
- The work of the TGA is based on applying scientific and clinical expertise to decision-making, to ensure that the benefits to the Australian public outweigh any risks associated with the use of therapeutic goods.
- The TGA relies on the public, healthcare professionals and industry to report problems with therapeutic goods. The TGA investigates reports received to determine any necessary regulatory action.
- To report a problem with a therapeutic good, please see the information on the TGA website.

# About AusPARs

- The Australian Public Assessment Report (AusPAR) provides information about the evaluation of a prescription medicine and the considerations that led the TGA to approve or not approve a prescription medicine submission. Further information can be found in Australian Public Assessment Report (AusPAR) guidance.
- AusPARs are prepared and published by the TGA.
- AusPARs are static documents that provide information that relates to a submission at a particular point in time. The publication of an AusPAR is an important part of the transparency of the TGA's decision-making process.
- A new AusPAR may be provided to reflect changes to indications or major variations to a prescription medicine subject to evaluation by the TGA.

# Contents

# List of abbreviations

| Abbreviation | Meaning |
|---|---|
| ACE2 | Angiotensin-converting enzyme 2 |
| ADA | Anti-drug antibody |
| ADE | Antibody-dependent enhancement |
| Adj | Adjusted |
| AE | Adverse event |
| AESI | Adverse event of special interest |
| AIC | Akaike information criterion |
| AIDS | Acquired immune deficiency syndrome |
| ALT | Alanine aminotransferase |
| ANCOVA | Analysis of covariance |
| ARDS | Acute respiratory distress syndrome |
| AST | Aspartate aminotransferase |
| AUC | Area under the serum concentration-time curve |
| $AUC_{0\text{-}180day}$ | Area under the serum concentration-time curve from time zero to Day 180 |
| $AUC_{0\text{-}90day}$ | Area under the serum concentration-time curve from time zero to Day 90 |
| $AUC_{inf}$ | Area under the serum concentration-time curve from time zero to infinity |
| AZD3152 | sipavibart |
| AZD5156 | Sipavibart and cilgavimab |
| AZD7442 | EVUSHELD, combination of tixagevimab and cilgavimab |
| B-hCG | Beta-human chorionic gonadotropin |
| BIC | Bayesian information criterion |
| BLQ | Below limit of quantification |
| BMI | Body mass index |
| BP | Blood pressure |
| BSA | Body surface area |
| C1q | Complement component 1q |
| CAD | Coronary artery disease |
| CDC | Centers for Disease Control and Prevention |
| CHF | Chronic heart failure |
| CI | Confidence interval |

| Abbreviation | Meaning |
|---|---|
| CKD | Chronic kidney disease |
| CL | Total body clearance |
| CL/F | Apparent total body clearance of drug from serum after extravascular administration |
| $C_{max}$ | Maximum serum concentration |
| CMT | Compartment |
| COVID-19 | Coronavirus disease 2019 |
| CTCAE | Common Terminology Criteria for Adverse Events |
| CV | Coefficient of variation |
| CV | Cardiovascular |
| CWRES | Conditional weighted residuals |
| DCO | Data cut-off |
| DV | Dependent variable |
| DVT | Deep vein thrombosis |
| ECG | Electrocardiogram |
| EDV | Early discontinuation visit |
| eGFR | Estimated glomerular filtration rate |
| EMA | European Medicines Agency |
| EU | European Union |
| Exp | Exposure |
| FAS | Full analysis set |
| Fc | Fraction crystallizable |
| FcγR | Fc gamma receptor |
| FcRn | Neonatal Fc receptor |
| FIM | Absolute bioavailability following intramuscular administration |
| FOCE | First order conditional estimation method of NONMEM |
| GCP | Good clinical practice |
| GCV | Geometric coefficient of variation |
| Geomean | Geometric mean serum concentration |
| GMFR | Geometric mean fold rise |
| GMT | Geometric mean titre |
| gSD | Geometric standard deviation |
| h | Hour |

| Abbreviation | Meaning |
|---|---|
| HIV | Human immunodeficiency virus |
| HR | Hazard ratio |
| IC | Immunocompromised |
| IC50 | 50% inhibitory concentration |
| IC80 | 80% inhibitory concentration |
| ICH | International Council for Harmonisation |
| ICU | Intensive care unit |
| I/E | Inclusion/Exclusion |
| Ig | Immunoglobulin |
| IgG | Immunoglobulin G |
| IIV | Inter-individual variability |
| IL-D | Illness visit – Day |
| IM | Intramuscular |
| IMP | Investigational medicinal product |
| INN | International non-proprietary name |
| IPRED | Individual predictions |
| IRT | Interactive response technology |
| IV | Intravenous |
| ka | Absorption rate constant |
| kg | Kilogram |
| LLOQ | Lower limit of quantification |
| MAAE | Medically attended adverse event |
| mAb | Monoclonal antibody |
| Max | Maximum |
| MDV | Missing dependent variable |
| MedDRA | Medical Dictionary for Regulatory Affairs |
| MHRA | Medicines and Healthcare Products Regulatory Agency |
| Min | Minimum |
| N | Number of participants per group |
| n | Number of participants with no missing data for continuous variables and number of participants per category for categorical variables (unless otherwise defined in table or figure legend) |
| NA | Not applicable |
| nAb | Neutralising antibody |

| Abbreviation | Meaning |
|---|---|
| NC | Not calculable |
| NNT | Number needed to treat |
| NONMEM | Nonlinear mixed-effects modelling software |
| NP | Nasopharyngeal |
| NQ | Not quantifiable |
| OFV | Objective function value as calculated in NONMEM software. In non-linear mixed effects, this is the -2 times the log-likelihood of the parameters under the observed data. |
| ORF | Open reading frame |
| PBMC | Peripheral blood mononuclear cell |
| pcVPC | Prediction corrected visual predictive check |
| PD | Pharmacodynamic |
| PDMP | Protocol Deviations Management Plan |
| PI | Prediction interval |
| PK | Pharmacokinetic |
| popPK | Population pharmacokinetics |
| PRED | Population predictions |
| PT | Preferred term |
| PVD | Peripheral venous disease |
| PY | Participant-years |
| Q | Intercompartmental clearance |
| QTL | Quality tolerance limits |
| Q1 | First quartile |
| Q2 | Second quartile |
| Q3 | Third quartile |
| Q4 | Fourth quartile |
| RBD | Receptor binding domain |
| ROW | Rest of world |
| RSE | Relative standard error |
| RT-PCR | Reverse transcription polymerase chain reaction |
| RTSM | Randomisation and Trial Supply Management |
| SAE | Serious adverse event |
| SEAM | Stochastic approximation expectation maximisation |
| SAP | Statistical Analysis Plan |

| Abbreviation | Meaning |
|---|---|
| SARS-CoV-2 | Severe acute respiratory syndrome coronavirus 2 |
| SC | Subcutaneous |
| SD | Standard deviation |
| SOC | System organ class |
| SMQ | Standardised MedDRA Query |
| SN | SUPERNOVA study |
| $t_{½}$ | Terminal elimination half-life |
| T2DM | Type 2 diabetes mellitus |
| TE-ADA | Treatment emergent anti-drug antibody |
| TM | L234F/L235E/P331S substitutions in the immunoglobulin heavy chain to reduce Fc receptor and C1q binding |
| $T_{max}$ | Time to reach maximum observed concentration |
| ULN | Upper limit of normal |
| ULOQ | Upper limit of quantification |
| US | United States of America |
| V | Volume of distribution |
| $V_c$ | Central volume of distribution |
| $V_p$ | Peripheral volume of distribution |
| VPC | Visual predictive check |
| $V_{ss}$ | Volume of distribution at steady state |
| $V_z$ | Volume of distribution based on terminal phase |
| $V_z/F$ | Apparent volume of distribution based on terminal phase |
| WHO | World Health Organisation |
| WOCBP | Women of childbearing potential |
| w/v | Weight per volume |
| YTE | M252Y/S254T/T256E substitutions in the immunoglobulin heavy chain to increase FcRn affinity that results in the increased half-life of an antibody |

# Product submission

## Submission details

| | |
|---|---|
| *Type of submission:* | New chemical entity – Type A application |
| *Product name:* | Kavigale, sipavibart, 300 mg in 2 mL (150 mg/mL), Solution for injection/infusion vial |
| *Active ingredient:* | Sipavibart |
| *Decision:* | Approved |
| *Date of decision:* | 20 May 2025 |
| *Date of entry into ARTG:* | 22 May 2025 |
| *ARTG number:* | 459773 |
| ▼*Black Triangle Scheme for the current submission:* | Yes |
| *Sponsor's name and address:* | AstraZeneca Pty Ltd<br><br>PO Box 131,<br>NORTH RYDE,<br>NSW, 1670<br>Australia |
| *Dose form:* | Solution for injection/infusion vial |
| *Strength:* | 300 mg in 2 mL (150 mg/mL) |
| *Container:* | Vial – Glass Type I Clear |
| *Pack size:* | Each pack contains 1 vial |
| *Approved therapeutic use for the current submission:* | *Kavigale is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.*<br><br>*Kavigale is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.* |
| *Route of administration:* | Intramuscular or intravenous |
| *Dosage:* | The dosage in adults and adolescents aged 12 years and older weighing at least 40 kg is 300 mg of KAVIGALE administered as an intramuscular injection or intravenous infusion. Subsequent doses of 300 mg KAVIGALE administered as an intramuscular injection or intravenous infusion may be given every 3 months until no longer required.<br><br>For further information regarding dosage, such as dosage modifications to manage adverse reactions, refer to the Product Information (PI) document. |
| *Pregnancy category:* | Category B2 |

Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

The use of any medicine during pregnancy requires careful consideration of both risks and benefits by the treating health professional. The pregnancy database must not be used as the sole basis of decision making in the use of medicines during pregnancy. The TGA does not provide advice on the use of medicines in pregnancy for specific cases. More information is available from obstetric drug information services in your state or territory.

# Product background

This AusPAR describes the submission by AstraZeneca (the sponsor) to register Kavigale for the following proposed indication:[1]

> *KAVIGALE is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.*

Kavigale is a recombinant IgG1 antibody that binds to the receptor binding domain (RBD) of COVID-19 virus of the BA.2 linage. BA.2 is a subvariant of Omicron COVID-19 that emerged in 2021 but is no longer the dominant circulating strain, having been displaced by JN.1 and its descendent strains.

Kavigale is similar to Evusheld, a product manufactured by the sponsor and registered in 2022 to provide passive immunity against then circulating Delta and early Omicron strains of COVID-19.

The antibody contains amino acid substitutions to reduce clearance and therefore increase the duration of effect. It is intended that Kavigale is administered by infusion every 3 months.

This application is based mainly on the phase III SUPERNOVA study, supported by population pharmacokinetic and safety analyses of data in this study.

## COVID-19

COVID-19 is a clinical syndrome caused by the SARS-CoV-2 virus, which emerged in 2019 to become a pandemic outbreak from 2020-2024. COVID-19 remains endemic in Australia and over the course of the pandemic new immunotypes of the virus have regularly emerged. COVID-19 is spread by respiratory aerosol and droplets, and is characterised by fever, cough, fatigue and shortness of breath. Severe cases can develop viral pneumonitis requiring supplemental oxygen or ventilatory support and leading, in a minority of cases, to respiratory failure. Extrapulmonary manifestations of COVID-19 include gastroenteritis, clotting and acute cardiac injury. Disease is

[1] This is the original indication proposed by the sponsor when the TGA commenced the evaluation of this submission. It may differ to the final indication approved by the TGA and registered in the Australian Register of Therapeutic Goods.

more severe in older patients, and in those with concomitant illness such as diabetes, heart failure, renal impairment or chronic pulmonary disease.

## Current treatment options

Moderate to severe cases of COVID-19 are treated with antivirals (remdesivir, nirmatrelvir/ritonavir or remdesivir) and with supportive care. The mainstay of COVID-19 management is prevention, either through vaccination or passive immunisation using immunoglobulins. Vaccination and immunoglobulin treatments reduce the incidence of COVID-19 infection, but also the severity of breakthrough infections.

## Clinical rationale

The clinical rationale, as stated by the Sponsor, is outlined below.

SARS-CoV-2, a coronavirus, is the causative agent of COVID-19. Most coronaviruses cause mild disease in humans and animals. However, SARS-CoV-2 can replicate in the lower respiratory tract to cause acute respiratory distress syndrome and fatal pneumonia. Advanced age and underlying medical conditions such as immunocompromise, cardiovascular disease, diabetes, chronic respiratory disease, obesity, or cancer are associated with severe outcomes of COVID-19.

There is a clear unmet medical need to protect the most vulnerable individuals, who do not mount an adequate response to vaccination or cannot receive a vaccine, from developing COVID-19. The immunocompromised are disproportionally hospitalised due to COVID-19, resulting in an increased burden on the health system as well as delays in treatment for the underlying diseases, which result in the immunocompromised condition and reduced overall survival. Neutralising monoclonal antibodies such as EVUSHELD were demonstrated to be effective in preventing development of symptomatic COVID-19 and subsequent hospitalisation when used as pre-exposure prophylaxis.

The emergence of the Omicron lineage resulted in loss of neutralization by antibodies developed early in the pandemic, necessitating the development of new monoclonal antibodies (mAbs).

Sipavibart represents a new therapeutic entity, isolated from a donor following recovery from COVID-19, and binds to a unique epitope on the RBD. Sipavibart utilizes the same platform (i.e., mechanism of action and critical half-life extension technologies) that enabled its predecessor antibody EVUSHELD to demonstrate efficacy against COVID-19 in this same population. As the variant landscape has evolved, so has the need to develop new mAbs that, while built on the same platform, are further tailored to address new variants.

The potential for sipavibart to address the unmet medical need in high-risk populations is of major interest to public health. Enabling rapid access to sipavibart for vulnerable populations is necessary to protect these individuals and reduce burden of disease and hospitalisation.

# Regulatory status at the time of assessment

## Australian regulatory status

This product is considered a new biological entity for Australian regulatory purposes.

## International regulatory status

Similar applications have been approved in Japan (27 December 2024), the European Union (inc EEA) (20 January 2025) and Canada (21 March 2025). Applications were voluntarily withdrawn from the UK and Switzerland.

The sponsor has indicated that the application to the United States (24 January 2024) was for an Emergency Use Authorization (EUA), which is an emergency provision rather than a standard regulatory approval, this application is currently on hold.

# Registration timeline

The following table captures the key steps and dates for this submission.

This submission was evaluated under the priority registration process.

**Table 1: Timeline for Submission PM-2024-03590-1-2**

| Description | Date |
|---|---|
| Submission dossier accepted and first round evaluation commenced | 10 September 2024 |
| Evaluation completed (End of round 2) | 10 February 2025 |
| Registration decision (Outcome) | 20 May 2025 |
| Registration in the ARTG completed | 22 May 2025 |
| Number of working days from submission dossier acceptance to registration decision* | 125 days |

*Statutory timeframe for standard submissions is 255 working days

# Assessment overview

A summary of the TGA's assessment for this submission is provided below.

## Quality evaluation summary

Sipavibart is a glycosylated IgG lambda monoclonal antibody that selectively binds to the receptor binding domain (RBD) of the SARS-CoV-2 spike protein. The molecular weight is approximately 148kD comprising two heavy chain molecules and two light chain molecules.

The active ingredient was produced using recombinant DNA technology. Information about the manufacturing, storage and control facilities for the active substance has been provided in the dossier. GMP compliance for the manufacturers has been demonstrated.

The overall quality of the active substance was demonstrated via adequate control of the starting material, control of critical steps and intermediates, process validation, extensive characterisation using orthogonal and state-of-the-art analytical methods, control of impurities and contaminants, generation of robust reference materials and batch analyses that covered multiple manufacturing campaigns.

Stability data have been generated under stressed and real time conditions to characterise the stability profile of the product. Following evaluation, the recommended storage condition is 2 years when stored at 2-8°C.

In-use stability data have also been submitted. The recommended shelf life and storage conditions for the opened product are the total time from vial puncture to administration not to exceed either:

- *24 hours in a refrigerator at 2°C to 8°C*

  OR

- *4 hours at room temperature up to 25°C.*

Stability studies have been conducted in accordance with relevant ICH guidelines.

The quality evaluator had no objections to the approval of Kavigale from a quality perspective.

# Non-clinical evaluation summary

The non-clinical evaluator concluded the following.

- *In vitro* pharmacology results suggest efficacy against currently circulating variants and variants of concern/interest. However, it does not retain *in vitro* neutralisation activity against XBB subvariants harbouring T415I, K458E, and F456L mutations.
- Efficacy studies in animal models support the prevention and treatment indication for Kavigale.
- Kavigale is not expected to affect antibody responses to COVID-19 adenovirus-based vaccination.
- No toxicity was observed in a repeat-dose toxicity study in monkeys at high exposures. However, in the absence of in vivo pharmacology and tissue–cross-reactivity studies in monkeys, the pharmacological responsiveness to sipavibart and appropriateness of the selected species cannot be commented upon. Therefore, the repeat-dose toxicity study is considered of limited value.
- There are no objections on nonclinical grounds to the registration of Kavigale for the proposed indication.

The non-clinical evaluator recommended amendments to the PI.

# Clinical evaluation summary

## Summary of clinical studies

The dossier comprised the following.

- Two clinical studies that provided evaluable efficacy data, including one pivotal study and one other efficacy study.
  - Pivotal Phase III study: Study D7000C0001 – SUPERNOVA Parent Study (main cohort)
  - Other efficacy study: Study D7000C00001 – SUPERNOVA Substudy
- Clinical pharmacology study: Study D7000C00004 – Little DIPPER

- Study evaluable for safety only: SUPERNOVA Sentinel Study
- Pharmacometric studies:
  - Population Pharmacokinetic Analysis for Sipavibart (AZD3152) in Pre-exposure Prophylaxis of COVID-19
  - Exposure-response analysis

In addition to the clinical studies there was a clinical overview, summaries of clinical safety, efficacy and clinical pharmacology, and a Risk Management Plan.

# Pharmacology

The pharmacokinetics of Kavigale were determined from the population PK model developed using data from the SUPERNOVA and Little Dipper studies.

In brief, bioavailability was estimated to be 81% and 62% when administered IM in the thigh and gluteus respectively. Volume of distribution was 4.59L, with a clearance of 0.44L/day giving a median half -life 81 days (range 42.9-125.8 days).

There was no significant effect of liver or renal function on pharmacokinetics. There was no data submitted on pharmacokinetics in children <12years or pregnant women.

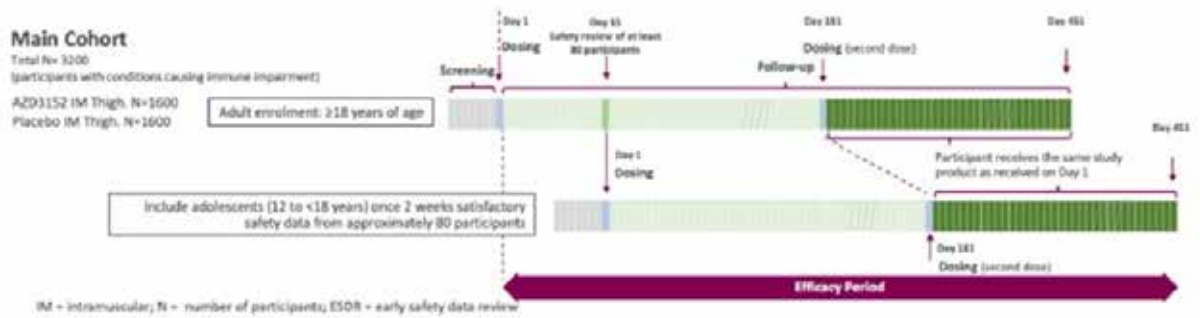
Exposure-response analyses for Kavigale were mainly explored in vitro. The clinical evaluator has noted that there was no strong relationship between dose and effect, and higher doses produced poorer responses. COVID-19 vaccination appeared to be complimentary to the effect of Kavigale, supporting the continued use of active immunisation even where Kavigale is added to a patient's treatment.

# Efficacy evaluation

## Pivotal study D7000C0001 – SUPERNOVA

SUPERNOVA was an ongoing phase I/III placebo-controlled study that examined the safety and efficacy of Kavigale, for which twelve-month data was presented. The study was divided into two cohorts: a Sentinel Safety Cohort that examined safety in healthy participants, and the Main Cohort which compared Kavigale with Evushield in patients with diminished immunity to COVID-19.

**Figure 1: Study Design – Main Cohort SUPERNOVA**




Dosing was staggered, so that no adolescent participants were dosed in the Main Cohort until Day 15 safety data for at least 80 adult Main Cohort participants (including at least 40 participants who received sipavibart) were reviewed.
The placebo arm includes participants that were dosed with EVUSHELD prior to the implementation of CSP version 7.0.

The trial enrolled a total of 3711 participants randomised 1:1 active:comparator. The participants were 12 years of age or older, had a negative RAT test prior to dosing and weight >40kg at screening. They had at least one risk factor for diminished immunity to COVID-19 including receiving immunosuppressive therapy (74.3%), having a haematological malignancy, or having a primary immunodeficiency. Pregnant women were excluded from the trial.

Participants received either:

- Kavigale 300mg IM in the thigh (active)
- Evusheld 600mg IM x2 in the thigh (comparator) or
- saline placebo (comparator).

A second dose of treatment was administered at day 181 if participants met prespecified criteria.

The Main Cohort initially used Evusheld as a comparator, but this was changed to saline placebo during the study. This means that the comparator arm includes both participants who received saline placebo as dose 1 and 2, and participants who received Evusheld (AZD7442) at dose 1 and placebo at dose 2.

The co-primary efficacy outcomes of SUPERNOVA were:

- prevention of symptomatic COVID-19 up to day 181 from infusion
- prevention of symptomatic COVID-19 due to matched variants up to day 361 from infusion.

**Table 3: Patient disposition in the SUPERNOVA trial. AZD3152 is Kavigale and AZD7442 is Evusheld**

| Disposition | Planned intervention (Day 1/Day 181) | | | Comparator [a] n (%) | Total n (%) |
|---|---|---|---|---|---|
| | AZD3152/AZD3152 n (%) | AZD7442/Placebo n (%) | Placebo/Placebo n (%) | | |
| Screened | - | - | - | - | 3711 |
| Not randomized | - | - | - | - | 362 |
| Randomized | 1674 | 1111 | 564 | 1675 | 3349 |
| Randomized, not treated | 5 | 6 | 3 | 9 | 14 |
| Treated | 1669 (100) | 1105 (100) | 561 (100) | 1666 (100) | 3335 (100) |
| Received 1st dose | 1669 (100) | 1105 (100) | 561 (100) | 1666 (100) | 3335 (100) |
| Received 2nd dose | 887 (53.1) | 787 (71.2) | 94 (16.8) | 881 (52.9) | 1768 (53.0) |
| Study ongoing | 1569 (94.0) | 1012 (91.6) | 548 (97.7) | 1560 (93.6) | 3129 (93.8) |
| Completed study | 0 | 0 | 0 | 0 | 0 |
| Withdrawn from study | 100 (6.0) | 93 (8.4) | 13 (2.3) | 106 (6.4) | 206 (6.2) |
| Adverse Event | 2 (0.1) | 1 (< 0.1) | 0 | 1 (< 0.1) | 3 (< 0.1) |
| Death | 19 (1.1) | 11 (1.0) | 2 (0.4) | 13 (0.8) | 32 (1.0) |
| Failure to Meet Inclusion/Exclusion Criteria | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-Up | 17 (1.0) | 19 (1.7) | 1 (0.2) | 20 (1.2) | 37 (1.1) |
| Physician Decision | 5 (0.3) | 6 (0.5) | 0 | 6 (0.4) | 11 (0.3) |
| Withdrawal by Subject | 52 (3.1) | 51 (4.6) | 9 (1.6) | 60 (3.6) | 112 (3.4) |
| Other | 5 (0.3) | 5 (0.5) | 1 (0.2) | 6 (0.4) | 11 (0.3) |

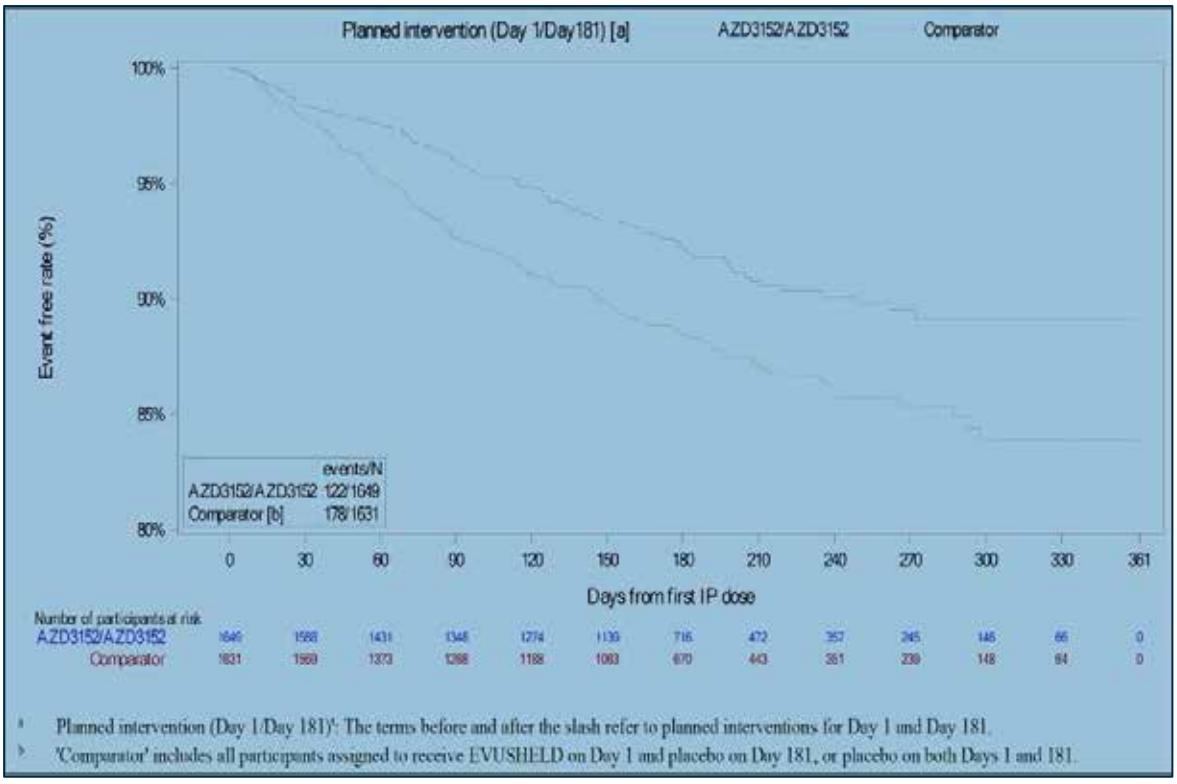
[a] 'Comparator' includes all participants who were assigned to receive EVUSHELD and/or placebo.
Screened participants are those who signed informed consent.
Percentages are based on the number of participants who received treatment.

The study population had slightly more women (57%) than men (43%). There were few participants aged 12-18 years of age (n=15), and the majority (63%) were aged between 18 and 65 years of age.

**Table 4: Baseline participant characteristics (AZD3152 is Kavigale and AZD7442 is Evusheld)**

| Category | Statistic | Planned intervention (Day 1/Day 181) | | | Comparator [a] | Total |
|---|---|---|---|---|---|---|
| | | AZD3152/AZD3152 N = 1669 | AZD7442/Placebo N = 1104 | Placebo/Placebo N = 561 | N = 1665 | N = 3334 |
| **Age (years)** | n | 1669 | 1104 | 561 | 1665 | 3334 |
| | Mean | 58.1 | 58.6 | 57.7 | 58.3 | 58.2 |
| | SD | 13.9 | 13.7 | 13.2 | 13.5 | 13.7 |
| | Min | 12 | 12 | 18 | 12 | 12 |
| | Median | 60.0 | 60.0 | 58.0 | 60.0 | 60.0 |
| | Max | 92 | 89 | 91 | 91 | 92 |
| **Age group (years)** | | | | | | |
| ≥ 12 to < 18 | n (%) | 8 (0.5) | 7 (0.6) | 0 | 7 (0.4) | 15 (0.4) |
| ≥ 18 to < 65 | n (%) | 1055 (63.2) | 680 (61.6) | 375 (66.8) | 1055 (63.4) | 2110 (63.3) |
| ≥ 65 | n (%) | 606 (36.3) | 417 (37.8) | 186 (33.2) | 603 (36.2) | 1209 (36.3) |
| **Sex** | | | | | | |
| Male | n (%) | 715 (42.8) | 494 (44.7) | 232 (41.4) | 726 (43.6) | 1441 (43.2) |
| Female | n (%) | 954 (57.2) | 610 (55.3) | 329 (58.6) | 939 (56.4) | 1893 (56.8) |
| **Hispanic/Latino** | | | | | | |
| Yes | n (%) | 354 (21.2) | 237 (21.5) | 125 (22.3) | 362 (21.7) | 716 (21.5) |
| No | n (%) | 1240 (74.3) | 841 (76.2) | 386 (68.8) | 1227 (73.7) | 2467 (74.0) |
| Not reported | n (%) | 75 (4.5) | 26 (2.4) | 50 (8.9) | 76 (4.6) | 151 (4.5) |
| **Race** | | | | | | |
| Black or African American | n (%) | 202 (12.1) | 122 (11.1) | 78 (13.9) | 200 (12.0) | 402 (12.1) |
| Native Hawaiian or Other Pacific Islander | n (%) | 5 (0.3) | 2 (0.2) | 0 | 2 (0.1) | 7 (0.2) |

**Figure 2: Incidence of symptomatic COVID-19 infection (any variant) in Kavigale (AZD3152) or comparator treatment to 361 days from first dose**




For any COVID-19 variant there were 122 (7.4%) infections in the Kavigale and 178 (10.9%) infections in the comparator group up to day 361 (Figure 2). This indicated a relative risk reduction of 34.9% (95%CI 17.8-48.4) from Kavigale, which was a highly significant difference

from comparator treatment (p<0.001). The clinical evaluator has noted that the absolute risk reduction was only 3.5%.

There was a relative risk reduction for all the variants observed, but this was lower for JN.1 and F456L variants, for which statistical significance was not demonstrated (Table 5). The Delegate notes that this indicates Kavigale appears to have efficacy against current strains of COVID-19, but at a lower level than the BA.2 strain to which the product is targeted.

The clinical evaluator has noted that the efficacy of Kavigale was greater in participants who had received COVID-19 vaccine within 6 months of treatment, producing a relative risk reduction of 50% compared to 31.9% in the incidence of infections.

Additionally, the clinical evaluator has noted there was no difference in hospitalisation or severe COVID-19 rates between treatments (non-primary endpoints), but the study was not adequately powered to detect this.

**Table 5: Incidence of symptomatic COVID-19 cases up to day 361 for specific variants**

| | Planned intervention (Day 1/Day 181) | | | |
|---|---|---|---|---|
| | AZD3152/AZD3152 N = 1649 | Comparator [a] N = 1631 | Relative risk reduction (%) [b] | 95% CI (%) |
| Variant | n (%) | n (%) | | |
| Any (sequenced) | 101 (6.1) | 154 (9.4) | 37.6 | 19.6, 51.6 |
| Matched | 54 (3.3) | 90 (5.5) | 42.9 | 19.9, 59.3 |
| BA.2.86 + subvariants | 1 (0.1) | 10 (0.6) | 90.9 | 27.4, 98.9 |
| XBB + subvariants | 6 (0.4) | 20 (1.2) | 71.6 | 29.0, 88.7 |
| JN.1 + subvariants | 47 (2.9) | 60 (3.7) | 25.1 | -9.7, 48.8 |
| F456L (sequenced) [c] | 47 (2.9) | 64 (3.9) | 30.4 | -1.8, 52.5 |

[a] 'Comparator' includes all participants assigned to receive EVUSHELD on Day 1 and placebo on Day 181, or placebo on both Day 1 and Day 181.

[b] Relative risk reduction was defined as 1 - relative risk of sipavibart/sipavibart versus comparator, where relative risk was evaluated with a Poisson regression with robust variance, which includes study intervention and the randomization stratification factors as covariates and adjusts for follow-up time.

[c] F456L (sequenced) includes all events with the F456L mutation in the sequence regardless of assigned variant.

P-values and CIs are 2-sided unless otherwise specified.

Only participants with non-missing covariates are included in the analysis.

# Safety evaluation

There were no pivotal studies examining safety in the proposed treatment group as a sole outcome.

Safety data was specifically examined in the Sentinel Safety Cohort of SUPERNOVA, the phase I element of this study that examined the PK and immunogenicity of Evusheld and Kavigale in healthy volunteers.

Safety data in the proposed patient population was provided by the SUPERNOVA Main Cohort.

**Table 6: Duration of follow-up of patients in the Main Cohort of SUPERNOVA study**

| Duration (days) | Statistic | Planned intervention (Day 1/Day 181) | | | Comparator [a] | Total |
|---|---|---|---|---|---|---|
| | | AZD3152/AZD3152 N = 1669 | AZD7442/Placebo N = 1104 | Placebo/Placebo N = 561 | N = 1665 | N = 3334 |
| On-study follow-up [b] | n | 1669 | 1104 | 561 | 1665 | 3334 |
| | Mean | 209.2 | 231.9 | 163.6 | 208.9 | 209.0 |
| | SD | 62.05 | 63.72 | 20.28 | 62.24 | 62.14 |
| | Median | 191.0 | 229.0 | 162.0 | 191.0 | 191.0 |
| | Min | 8 | 5 | 22 | 5 | 5 |
| | Max | 360 | 360 | 207 | 360 | 360 |
| Safety follow-up [c] | n | 1669 | 1104 | 561 | 1665 | 3334 |
| | Mean | 137.2 | 166.7 | 74.8 | 135.8 | 136.5 |
| | SD | 82.65 | 69.50 | 70.12 | 82.12 | 82.38 |
| | Median | 183.0 | 190.0 | 58.0 | 183.0 | 183.0 |
| | Min | 1 | 1 | 1 | 1 | 1 |
| | Max | 335 | 359 | 207 | 359 | 359 |
| Post-second IMP dose [d] | n | 887 | 787 | 94 | 881 | 1768 |
| | Mean | 69.2 | 75.9 | 7.4 | 68.6 | 68.9 |
| | SD | 49.77 | 47.83 | 5.46 | 49.94 | 49.84 |
| | Median | 65.0 | 68.0 | 5.0 | 61.0 | 61.0 |
| | Min | 1 | 2 | 1 | 1 | 1 |
| | Max | 180 | 180 | 24 | 180 | 180 |

[a] 'Comparator' includes all participants assigned to EVUSHELD and/or placebo.

[b] On-study follow-up: From the first IMP dose until the earliest of data cutoff, study discontinuation, last follow-up, death, or study completion date.

[c] Safety follow-up: From the first IMP dose to either the data cutoff date or the date of the last safety assessment (ie, scheduled site visit), whichever occurs first.

[d] Post-second IP dose: From the second IMP dose until the earliest of data cutoff, study discontinuation, last follow-up, death, or study completion date.

The rate of adverse events (AEs) in SUPERNOVA was similar for Kavigale as for comparator groups. AEs were reported in 49.9% of participants treated with Kavigale compared to 53.3% when treated with Evusheld and 48.1% when treated with placebo (Table 7).

**Table 7: Overall summary of adverse events up to day 91 after first dose in SUPERNOVA Main Cohort**

| Category | Received intervention (Day 1) | | | | | | Comparator [a] N = 1663 | |
|---|---|---|---|---|---|---|---|---|
| | AZD3152 N = 1671 | | AZD7442 N = 1102 | | Placebo N = 561 | | | |
| | n (%) | 95% CI (%) | n (%) | 95% CI (%) | n (%) | 95% CI (%) | n (%) | 95% CI (%) |
| AEs | 833 (49.9) | (47.43, 52.28) | 587 (53.3) | (50.27, 56.25) | 270 (48.1) | (43.92, 52.35) | 857 (51.5) | (49.10, 53.96) |
| AE ≥ CTCAE Grade 3 | 115 (6.9) | (5.72, 8.20) | 91 (8.3) | (6.70, 10.04) | 38 (6.8) | (4.84, 9.18) | 129 (7.8) | (6.52, 9.15) |
| Related AEs [b] | 123 (7.4) | (6.15, 8.72) | 115 (10.4) | (8.69, 12.39) | 34 (6.1) | (4.23, 8.37) | 149 (9.0) | (7.63, 10.44) |
| Related AEs ≥ CTCAE Grade 3 [b] | 3 (0.2) | (0.04, 0.52) | 4 (0.4) | (0.10, 0.93) | 1 (0.2) | (0, 0.99) | 5 (0.3) | (0.10, 0.70) |
| Immediate AEs [c] | 51 (3.1) | (2.28, 3.99) | 39 (3.5) | (2.53, 4.81) | 10 (1.8) | (0.86, 3.25) | 49 (2.9) | (2.19, 3.88) |
| COVID-19-related AEs [b] | 100 (6.0) | (4.90, 7.23) | 79 (7.2) | (5.72, 8.85) | 66 (11.8) | (9.22, 14.72) | 145 (8.7) | (7.41, 10.18) |
| AESIs [d] | 18 (1.1) | (0.64, 1.70) | 2 (0.2) | (0.02, 0.65) | 5 (0.9) | (0.29, 2.07) | 7 (0.4) | (0.17, 0.87) |
| Related AESIs [b, d] | 0 | - | 1 (0.1) | (0, 0.50) | 2 (0.4) | (0.04, 1.28) | 3 (0.2) | (0.04, 0.53) |
| MAAEs | 536 (32.1) | (29.84, 34.37) | 364 (33.0) | (30.26, 35.90) | 163 (29.1) | (25.33, 33.00) | 527 (31.7) | (29.46, 33.99) |
| Related MAAEs [b] | 7 (0.4) | (0.17, 0.86) | 7 (0.6) | (0.26, 1.30) | 3 (0.5) | (0.11, 1.55) | 10 (0.6) | (0.29, 1.10) |
| SAEs leading to death | 7 (0.4) | (0.17, 0.86) | 4 (0.4) | (0.10, 0.93) | 1 (0.2) | (0, 0.99) | 5 (0.3) | (0.10, 0.70) |
| Related SAEs leading to death [b] | 0 | - | 0 | - | 0 | - | 0 | - |
| SAEs | 120 (7.2) | (5.99, 8.53) | 85 (7.7) | (6.21, 9.45) | 37 (6.6) | (4.69, 8.98) | 122 (7.3) | (6.13, 8.70) |
| Related SAEs [b] | 2 (0.1) | (0.01, 0.43) | 3 (0.3) | (0.06, 0.79) | 2 (0.4) | (0.04, 1.28) | 5 (0.3) | (0.10, 0.70) |
| Serious AESIs [d] | 14 (0.8) | (0.46, 1.40) | 1 (0.1) | (0, 0.50) | 5 (0.9) | (0.29, 2.07) | 6 (0.4) | (0.13, 0.78) |
| Related serious AESIs [b, d] | 0 | - | 1 (0.1) | (0, 0.50) | 2 (0.4) | (0.04, 1.28) | 3 (0.2) | (0.04, 0.53) |
| AEs leading to study DC | 1 (0.1) | (0, 0.33) | 1 (0.1) | (0, 0.50) | 0 | - | 1 (0.1) | (0, 0.33) |
| Related AEs leading to study DC [b] | 0 | - | 0 | - | 0 | - | 0 | - |
| SAEs leading to study DC | 1 (0.1) | (0, 0.33) | 0 | - | 0 | - | 0 | - |
| Related SAEs leading to study DC [b] | 0 | - | 0 | - | 0 | - | 0 | - |
| AEs leading to treatment DC | 3 (0.2) | (0.04, 0.52) | 5 (0.5) | (0.15, 1.06) | 2 (0.4) | (0.04, 1.28) | 7 (0.4) | (0.17, 0.87) |
| Related AEs leading to treatment DC [b] | 2 (0.1) | (0.01, 0.43) | 3 (0.3) | (0.06, 0.79) | 2 (0.4) | (0.04, 1.28) | 5 (0.3) | (0.10, 0.70) |
| SAEs leading to treatment DC | 2 (0.1) | (0.01, 0.43) | 3 (0.3) | (0.06, 0.79) | 1 (0.2) | (0, 0.99) | 4 (0.2) | (0.07, 0.61) |
| Related SAEs leading to treatment DC [b] | 1 (0.1) | (0, 0.33) | 2 (0.2) | (0.02, 0.65) | 1 (0.2) | (0, 0.99) | 3 (0.2) | (0.04, 0.53) |

[a] 'Comparator' includes all participants who received EVUSHELD or placebo.
[b] Possibly related is the reasonable possibility that the AE was caused by an IMP, as assessed by the Investigator.
[c] AEs occurring within one hour following IMP administration.
[d] AESI includes events for serious hypersensitivity reactions, including anaphylaxis, immune complex disease, and CV and thrombotic events as defined in the SAP.

The table includes AEs that started, worsened, or became serious on or after the IMP dosing date up to and including 103 days following the first dosing date. Participants with multiple occurrences in the same category are counted once per category, regardless of the number of occurrences.
The 95% CI for proportions is calculated using the Clopper-Pearson method. The CIs are not presented for categories where the incidence rate is zero (n = 0).

Serious AEs (SAEs) were reported in 7.2%, 7.7% and 6.6% of Kavigale, Evusheld and placebo-treated patients respectively (Table 8). The most commonly reported SAE was pneumonia, which occurred in 0.6%, 0.5% and 0.2% of the Kavigale, Evusheld and placebo groups respectively.

There were 7 deaths (0.4%) in Kavigale treated patients, 4 (0.4%) among Evusheld treated patients and 1 in a placebo treated patient. None of the deaths was attributed to study treatment.

**Table 8: Serious Adverse Events (SAEs) up to day 91 by preferred term in SUPERNOVA Main Cohort**

| Preferred term (MedDRA Version 26.1) | Received intervention (Day 1) | | | Comparator [a] N = 1663 |
|---|---|---|---|---|
| | AZD3152 N = 1671 | AZD7442 N = 1102 | Placebo N = 561 | |
| | n (%) | n (%) | n (%) | n (%) |
| Any SAEs | 120 (7.2) | 85 (7.7) | 37 (6.6) | 122 (7.3) |
| Pneumonia | 10 (0.6) | 5 (0.5) | 1 (0.2) | 6 (0.4) |
| Acute myocardial infarction | 8 (0.5) | 2 (0.2) | 2 (0.4) | 4 (0.2) |
| Cardiac failure acute | 6 (0.4) | 0 | 1 (0.2) | 1 (0.1) |
| Atrial fibrillation | 5 (0.3) | 2 (0.2) | 1 (0.2) | 3 (0.2) |
| COVID-19 | 5 (0.3) | 2 (0.2) | 1 (0.2) | 3 (0.2) |
| Influenza | 5 (0.3) | 0 | 0 | 0 |
| Acute respiratory failure | 4 (0.2) | 4 (0.4) | 1 (0.2) | 5 (0.3) |
| Hypervolaemia | 4 (0.2) | 2 (0.2) | 0 | 2 (0.1) |
| Hypotension | 4 (0.2) | 0 | 0 | 0 |
| Sepsis | 4 (0.2) | 1 (0.1) | 1 (0.2) | 2 (0.1) |
| Septic shock | 4 (0.2) | 2 (0.2) | 1 (0.2) | 3 (0.2) |
| Cardiac failure congestive | 3 (0.2) | 2 (0.2) | 2 (0.4) | 4 (0.2) |
| Dyspnoea | 3 (0.2) | 0 | 0 | 0 |
| Hypertensive emergency | 3 (0.2) | 3 (0.3) | 0 | 3 (0.2) |
| Syncope | 3 (0.2) | 0 | 0 | 0 |
| Urinary tract infection | 3 (0.2) | 2 (0.2) | 1 (0.2) | 3 (0.2) |
| Acute kidney injury | 2 (0.1) | 4 (0.4) | 0 | 4 (0.2) |
| Hypertensive urgency | 1 (0.1) | 1 (0.1) | 2 (0.4) | 3 (0.2) |

[a] 'Comparator' includes all participants who receive EVUSHELD or placebo.

The table includes AEs that started, worsened, or became serious on or after the first IMP dosing date up to and including 103 days following the first dosing date.

Participants with multiple occurrences are counted once per SOC regardless of the number of occurrences.

This table includes PTs occurring in ≥ 3 participants in either the sipavibart or comparator groups and is ordered by descending frequency in the sipavibart group.

In the SUPERNOVA Main Cohort, treatment emergent anti-drug antibodies (ADAs) were detected in 4 patients treated with two doses of Kavigale (in 1 patient who received 1 dose of Kavigale and 3 patients who received Evusheld).

**Table 9: Rates of ADA detection and treatment-emergent ADAs in SUPERNOVA Main Cohort**

| ADA category | Statistic | Received Intervention (Day 1/Day 181)[a] | | |
|---|---|---|---|---|
| | | AZD3152/AZD3152 (N = 545) | AZD3152/- (N = 59) | AZD7442 (N = 597) |
| ADA-positive at any visit (ADA prevalence) | n (%) | 28 (5.1) | 1 (1.7) | 47 (7.9) |
| | Median of maximum titer | 200.0 | 200.0 | 80 |
| | Min of maximum titer, max | 100, 800 | 200, 200 | 40, 20480 |
| | Q1, Q3 | 100.0, 400.0 | 200.0, 200.0 | 40, 160 |
| TE-ADA-positive (ADA incidence) | n (%) | 4 (0.7) | 1 (1.7) | 3 (0.5) |
| | Median of maximum titer | 200.0 | 200.0 | 160 |
| | Min of maximum titer, max | 200, 400 | 200, 200 | 160, 640 |
| | Q1, Q3 | 200.0, 300.0 | 200.0, 200.0 | 160, 640 |
| Non-TE-ADA-positive | n (%) | 24 (4.4) | 0 (0) | 44 (7.4) |
| | Median of maximum titer | 200.0 | NA | 80 |
| | Min of maximum titer, max | 100, 1600 | NA | 40, 20480 |
| | Q1, Q3 | 100.0, 400.0 | NA | 40, 80 |

[a] 'Received intervention (Day 1/Day 181)': The terms before and after the slash refer to actually received interventions for Day 1 and Day 181. '-' signifies that the participant had not received a second dose of sipavibart as of the data cutoff. ADA categories are defined in the SAP.

Summary statistics are calculated based on the maximum post-baseline titers for each ADA-positive participant within each group, except for the following categories: 'ADA-positive at baseline and not detected post-baseline' is based on the maximum titer at baseline only, and 'Non-TE-ADA-positive' is based on the maximum titer at baseline or post-baseline.

Post-baseline assessments include assessments after the first dose of IMP. Baseline is the last non-missing measurement taken on or before the first dose of IMP.

The clinical evaluator has noted the absence of safety information in children below the age of 12 years or pregnant women. The Delegate notes the small number of children aged 12-18 enrolled in the SUPERNOVA study, indicating a general lack of robust paediatric safety data.

## Risk management plan evaluation

The summary of safety concerns and their associated risk monitoring and mitigation strategies are summarised in Table 9.

The TGA may request an updated Risk management plan (RMP) at any stage of a product's life cycle, during both the pre-approval and post-approval phases. Further information regarding the TGA's risk management approach can be found in risk management plans for medicines and biologicals and the TGA's risk management approach. Information on the Australia-specific annex (ASA) can be found on the TGA website.

**Table 10: Summary of safety concerns**

| Summary of safety concerns | | Pharmacovigilance | | Risk minimisation | |
|---|---|---|---|---|---|
| | | Routine | Additional | Routine | Additional |
| **Important identified risks** | None | – | – | – | – |
| **Important potential risks** | None | – | – | – | – |
| **Missing information** | Use in pregnancy | ✓ | ✓* | ✓ | – |

*PASS (D7000R00017)

The RMP evaluator noted the following.

- The summary of safety concerns in the ASA aligns with the EU-RMP and is satisfactory.
- Routine and additional pharmacovigilance activities are proposed. The additional pharmacovigilance activity is a PASS which will provide information regarding Missing Information 'use in pregnancy'. The pharmacovigilance plan is acceptable.
- Routine risk minimisation activities only are proposed, which is adequate to manage the proposed safety concerns.

# Risk-benefit analysis

## Delegate's considerations

Kavigale is a targeted antibody therapy for pre-exposure prophylaxis against COVID-19. This class of agents has been in use for several years but, as with vaccines, evolution of circulating COVID-19 strains has required new products to be formulated to maintain efficacy. This dossier has provided good evidence that Kavigale, at least in the period 2023-2024 that SUPERNOVA was conducted, provided protection against symptomatic COVID-19 disease in an immunosuppressed population. The trial did not provide evidence of a reduction in the severity of COVID-19 cases, but a lowered incidence of infection is a reasonable clinical endpoint. The Sponsor examined this across several strains of COVID-19 and there was protection against contemporary (e.g. JN1) strains.

Generally, Kavigale is well tolerated with the spectrum of adverse events reported consistent with antibody therapy, and experience with other products of this class.

The clinical evaluator has noted that the efficacy of Kavigale was higher in patients who had been vaccinated in the 6 months prior to SUPERNOVA than in those who had not. The relative risk reduction for vaccinated patients was 50.0 (95% CI 6.7-73.2) compared to 31.9 (95% CI 12.6-47.0). The clinical evaluator has proposed that this was due to a synergistic effect between COVID-19 infection and Kavigale.

The Delegate notes that COVID-19 vaccination independently reduces the incidence of COVID-19 infections and so it is not entirely surprising that the incidence of disease was lower in patients who received vaccination and Kavigale when compared to those treated with Kavigale alone.

This is a clinically additive effect, but the Delegate does not conclude that it implies a pharmacological synergy. Synergy implies that the effects of Kavigale and vaccination together were greater than the sum of the effects of each treatment alone, such as the synergy between penicillin and clavulanic acid. This doesn't seem to be the case, and indeed the difference between vaccinated and non-vaccinated patients was not statistically significant.

The CE has raised concerns regarding the optimal timing of Kavigale treatment after COVID-19 vaccination. In SUPERNOVA patients had to have not received COVID-19 vaccine within 3 months of the first dose of Kavigale, which the Delegate concludes is a reasonable exclusion to baseline the trial population. A second dose of Kavigale could be given within 14 days of COVID-19 vaccination, and the CE proposes that this exclusion also be included in any approved labelling.

The Delegate notes that there was no requirement to be vaccinated prior to enrolment in SUPERNOVA. If the Sponsor had maintained a 3-month exclusion during the trial it would have made it very difficult for unvaccinated participants to get vaccinated, but a short exclusion period would be necessary to baseline adverse events (such as fatigue, headache, injection pain) which are common in both vaccination and Kavigale. There is no good evidence that administering Kavigale less than 14 days after vaccination reduces the efficacy of either treatment, or that it increases the rates of adverse events from that attendant on each treatment alone. Immunoglobulins and vaccines are often administered together, albeit at separate sites (e.g. measles vaccine and immunoglobulin for post-exposure prophylaxis).

The Delegate notes, however, that the trend to greater efficacy in vaccinated patients does highlight the importance of Kavigale (and passive immunity generally) not being used in place of vaccination but together with it. The Delegate notes that the labelling for Evusheld, a very similar product from the same Sponsor, contained a definitive statement to this effect in section 4.1 of the labelling:

> *Evusheld is no recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.*

The Delegate notes that while SUPERNOVA was nominally a study in patients 12 years and older, only 15 patients between the ages of 12-18 were actually enrolled. This does not amount to a robust examination of the safety and efficacy of this age group. While the Delegate is not minded to exclude these patients from the Kavigale indication, the Delegate has concluded that the lack of data in this population should be outlined in the Prescribing Information.

## Proposed action

The Delegate intends to approve Kavigale for the amended indication:

> *KAVIGALE is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.*
>
> ***KAVIGALE is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.***

The PI will be amended from that provided in response to the round 2 clinical evaluation as follows:

- The statements identified by comment numbers RG1 and RG2 will be removed.

- The 'Paediatric use' statement will read:

  *The safety and efficacy of sipavibart in children <12 years of age has not been studied and no data is available. There is limited clinical trial evidence supporting the safety and efficacy of sipavibart in children 12-18 years of age due to the low number of trial participants in this age group (See SUPERNOVA study in Clinical Trials)*

# Assessment outcome

Based on a review of quality, safety, and efficacy, the TGA decided to register Kavigale for the following indication:

*Kavigale is indicated for the pre-exposure prophylaxis of COVID-19 in adults and adolescents aged 12 years and older weighing at least 40 kg who are immunocompromised due to a medical condition or receipt of immunosuppressive medications or treatments.*

*Kavigale is not recommended as a substitute for vaccination in individuals for whom COVID-19 vaccination is recommended.*

# Specific conditions of registration

- Kavigale (sipavibart) is to be included in the Black Triangle Scheme. The PI and CMI for Kavigale must include the black triangle symbol and mandatory accompanying text for five years, which starts from the date of first supply of the product.
- The KAVIGALE EU-Risk Management Plan (RMP) (version 1.0 succession number 2.0, dated 8 October 2024, data lock point 29 March 2024), with Australia-Specific Annex (ASA) (version 1.0 succession number 2.0, dated 13 November 2024), included with submission PM-2024-03590-1-2, and any subsequent revisions, as agreed with the TGA will be implemented in Australia.
- An obligatory component of risk management plans is routine pharmacovigilance. Routine pharmacovigilance includes the submission of periodic safety update reports (PSURs).
  - Unless agreed separately between the supplier who is the recipient of the approval and the TGA, the first report must be submitted to TGA no later than 15 calendar months after the date of this approval letter. The subsequent reports must be submitted no less frequently than annually from the date of the first submitted report until the period covered by such reports is not less than three years from the date of this approval letter. The annual submission may be made up of two PSURs each covering six months. If the sponsor wishes, the six-monthly reports may be submitted separately as they become available.
  - If the product is approved in the EU during the three years period, reports can be provided in line with the published list of EU reference dates no less frequently than annually from the date of the first submitted report until the period covered by such reports is not less than three years from the date of this approval letter. The reports are to at least meet the requirements for PSURs as described in the European Medicines Agency's Guideline on good pharmacovigilance practices (GVP) Module VII-periodic safety update report (Rev 1), Part VII.B Structures and processes. Note that submission of a PSUR does not constitute an application to vary the registration. Each report must be submitted within ninety calendar days of the data lock point for that report.
- Laboratory testing & compliance with Certified Product Details (CPD)

  - i. All batches of KAVIGALE sipavibart 300 mg in 2mL (150 mg/mL) solution for injection vial supplied in Australia must comply with the product details and specifications approved during evaluation and detailed in the Certified Product Details (CPD).
  - ii. When requested by the TGA, the Sponsor should be prepared to provide product samples, specified reference materials and documentary evidence to enable the TGA to conduct laboratory testing on the Product. Outcomes of laboratory testing are published biannually in the TGA Database of Laboratory Testing Results http://www.tga.gov.au/ws-labs-index and periodically in testing reports on the TGA website.

- Certified Product Details
  - The Certified Product Details (CPD), as described in Guidance 7: Certified Product Details of the Australian Regulatory Guidelines for Prescription Medicines (ARGPM), in PDF format, for the above products should be provided upon registration of these therapeutic goods. In addition, an updated CPD should be provided when changes to finished product specifications and test methods are approved in a Category 3 application or notified through a self-assessable change.
  - A template for preparation of CPD for biological prescription medicines can be obtained from the TGA website:
    - [for the form] https://www.tga.gov.au/form/certified-product-details-cpd-biologicalprescription-medicines
    - [for the CPD guidance] https://www.tga.gov.au/guidance-7-certified-product-details

## Product Information and Consumer Medicine Information

For the most recent Product Information (PI) and Consumer Medicine Information (CMI), please refer to the TGA PI/CMI search facility.

**Therapeutic Goods Administration**

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