



## Clinical trial results:

### Immunogenicity and Safety of a Purified Vero Rabies Vaccine– Serum Free (VRVg) Assessed with the Institut Pasteur du Cambodge (IPC: 2-2-2-0-0) and the Thai Red Cross (TRC: 2-2-2-0-2) Intradermal Regimens as Simulated Rabies Post-exposure Prophylaxis in Healthy Subjects in Thailand

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2019-004008-36 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 21 July 2022   |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 01 February 2023 |
| First version publication date | 01 February 2023 |

#### Trial information

##### Trial identification

|                       |       |
|-----------------------|-------|
| Sponsor protocol code | VRV09 |
|-----------------------|-------|

##### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT04478084     |
| WHO universal trial number (UTN)   | U1111-1227-4143 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Sanofi Pasteur   |
| Sponsor organisation address | 14 Espace Henry Vallée, Lyon, France, 69007                    |
| Public contact               | Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com |
| Scientific contact           | Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com |

Notes:

#### Paediatric regulatory details

|  |                     |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-002234-PIP01-17 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No                  |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes                 |

Notes:

## Results analysis stage

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 10 September 2022 |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 21 July 2022      |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To describe the immune response induced by purified vero rabies vaccine - serum free vaccine formulation 2 (VRVg-2) and Verorab vaccine at Day 14 (to assess the immune response after 3 doses [2-2-2]) and Day 42 (to assess the immune response after 4 doses [2-2-2-0-2]) when administered as standalone in healthy pediatric population or co-administered with human rabies immunoglobulins (HRIG) (Group 5 and Group 6) at Day 0 in healthy adults.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 04 August 2020 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | No             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |               |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Thailand: 402 |
| Worldwide total number of subjects   | 402           |
| EEA total number of subjects         | 0             |

Notes:

### Subjects enrolled per age group

|   |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 3   |
| Children (2-11 years)                     | 81  |
| Adolescents (12-17 years)                 | 84  |
| Adults (18-64 years)                      | 229 |
| From 65 to 84 years                       | 5   |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 3 active sites in Thailand between 04 August 2020 and 21 July 2022.

### Pre-assignment

Screening details:

A total of 402 subjects were enrolled and randomised in the study. Subjects received vaccination during the active phase of the study on Days 0, 3, 7 and 28 and were followed-up for safety 6-months post-vaccination.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall study (overall period)         |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

|                              |                 |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes             |
| <b>Arm title</b>             | Group 1: VRVg-2 |

Arm description:

Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 millilitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.

|  |   |
|--|---|
| Arm type                               | Experimental                              |
| Investigational medicinal product name | Purified vero rabies vaccine - serum free |
| Investigational medicinal product code |   |
| Other name                             | VRVg-2                                    |
| Pharmaceutical forms                   | Powder for solution for injection         |
| Routes of administration               | Intradermal use                           |

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Group 2: Verorab® |
|------------------|-------------------|

Arm description:

Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.

|  |                                     |
|--|-------------------------------------|
| Arm type                               | Active comparator                   |
| Investigational medicinal product name | Purified inactivated rabies vaccine |
| Investigational medicinal product code |                                     |
| Other name                             | Verorab®                            |
| Pharmaceutical forms                   | Powder for solution for injection   |
| Routes of administration               | Intradermal use                     |

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Group 3: VRVg-2 + ERIG |
|------------------|------------------------|

Arm description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|   |   |
|---|---|
| Investigational medicinal product name  | Purified vero rabies vaccine - serum free |
| Investigational medicinal product code  |   |
| Other name  | VRVg-2                                    |
| Pharmaceutical forms  | Powder for solution for injection         |
| Routes of administration  | Intradermal use                           |
| Dosage and administration details:  |   |
| 6 injections (1 vaccination on each arm) intradermally at Days 0, 3 and 7.  |   |
| Investigational medicinal product name  | Equine rabies immunoglobulins             |
| Investigational medicinal product code  |   |
| Other name  | ERIG                                      |
| Pharmaceutical forms  | Solution for injection in vial            |
| Routes of administration  | Intramuscular use                         |
| Dosage and administration details:  |   |
| Single 0.5 mL IM injection at Day 0.  |   |
| <b>Arm title</b>  | Group 4: Verorab® + ERIG                  |
| Arm description:  |   |
| Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.    |   |
| Arm type  | Active comparator                         |
| Investigational medicinal product name  | Purified inactivated rabies vaccine       |
| Investigational medicinal product code  |   |
| Other name  | Verorab®                                  |
| Pharmaceutical forms  | Powder for solution for injection         |
| Routes of administration  | Intradermal use                           |
| Dosage and administration details:  |   |
| 6 injections (1 vaccination on each arm) intradermally at Days 0, 3 and 7.  |   |
| Investigational medicinal product name  | Equine rabies immunoglobulins             |
| Investigational medicinal product code  |   |
| Other name  | ERIG                                      |
| Pharmaceutical forms  | Solution for injection in vial            |
| Routes of administration  | Intramuscular use                         |
| Dosage and administration details:  |   |
| Single 0.5 mL IM injection at Day 0.  |   |
| <b>Arm title</b>  | Group 5: VRVg-2 + HRIG                    |
| Arm description:  |   |
| Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0. |   |
| Arm type  | Experimental                              |
| Investigational medicinal product name  | Purified vero rabies vaccine - serum free |
| Investigational medicinal product code  |   |
| Other name  | VRVg-2                                    |
| Pharmaceutical forms  | Powder for solution for injection         |
| Routes of administration  | Intradermal use                           |
| Dosage and administration details:  |   |
| 8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.   |   |
| Investigational medicinal product name  | Human rabies immunoglobulins              |
| Investigational medicinal product code  |   |
| Other name  | IMOGAM® Rabies-HT, HRIG                   |
| Pharmaceutical forms  | Solution for injection in vial            |
| Routes of administration  | Intramuscular use                         |
| Dosage and administration details:  |   |
| Single 0.5 mL IM injection at Day 0.  |   |

|   |                                     |
|---|-------------------------------------|
| <b>Arm title</b>  | Group 6: Verorab + HRIG             |
| Arm description:  |                                     |
| Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0. |                                     |
| Arm type  | Active comparator                   |
| Investigational medicinal product name  | Purified inactivated rabies vaccine |
| Investigational medicinal product code  |                                     |
| Other name  | Verorab®                            |
| Pharmaceutical forms  | Powder for solution for injection   |
| Routes of administration  | Intradermal use                     |
| Dosage and administration details:  |                                     |
| 8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.   |                                     |
| Investigational medicinal product name  | Human rabies immunoglobulins        |
| Investigational medicinal product code  |                                     |
| Other name  | IMOGAM® Rabies-HT, HRIG             |
| Pharmaceutical forms  | Solution for injection in vial      |
| Routes of administration  | Intramuscular use                   |
| Dosage and administration details:  |                                     |
| Single 0.5 mL IM injection at Day 0.  |                                     |

| <b>Number of subjects in period 1</b> | Group 1: VRVg-2 | Group 2: Verorab® | Group 3: VRVg-2 + ERIG |
|---------------------------------------|-----------------|-------------------|------------------------|
| Started                               | 112             | 56                | 26                     |
| Vaccination 1 (Day 0)                 | 112             | 56                | 26                     |
| Vaccination 2 (Day 3)                 | 112             | 56                | 23                     |
| Vaccination 3 (Day 7)                 | 112             | 56                | 21                     |
| Vaccination 4 (Day 28)                | 112             | 56                | 0                      |
| Completed                             | 112             | 56                | 0                      |
| Not completed                         | 0               | 0                 | 26                     |
| Adverse event                         | -               | -                 | 6                      |
| Protocol deviation                    | -               | -                 | 20                     |

| <b>Number of subjects in period 1</b> | Group 4: Verorab® + ERIG | Group 5: VRVg-2 + HRIG | Group 6: Verorab + HRIG |
|---------------------------------------|--------------------------|------------------------|-------------------------|
| Started                               | 14                       | 129                    | 65                      |
| Vaccination 1 (Day 0)                 | 14                       | 129                    | 65                      |
| Vaccination 2 (Day 3)                 | 14                       | 129                    | 65                      |
| Vaccination 3 (Day 7)                 | 12                       | 129                    | 65                      |
| Vaccination 4 (Day 28)                | 0                        | 127                    | 64                      |
| Completed                             | 0                        | 114                    | 54                      |
| Not completed                         | 14                       | 15                     | 11                      |
| Adverse event                         | 2                        | -                      | -                       |
| Protocol deviation                    | 12                       | 15                     | 11                      |



## Baseline characteristics

### Reporting groups

|  |                          |
|--|--------------------------|
| Reporting group title  | Group 1: VRVg-2          |
| Reporting group description:<br>Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 millilitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.   |                          |
| Reporting group title  | Group 2: Verorab®        |
| Reporting group description:<br>Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.          |                          |
| Reporting group title  | Group 3: VRVg-2 + ERIG   |
| Reporting group description:<br>Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0. |                          |
| Reporting group title  | Group 4: Verorab® + ERIG |
| Reporting group description:<br>Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.   |                          |
| Reporting group title  | Group 5: VRVg-2 + HRIG   |
| Reporting group description:<br>Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.  |                          |
| Reporting group title  | Group 6: Verorab + HRIG  |
| Reporting group description:<br>Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.  |                          |

| Reporting group values             | Group 1: VRVg-2 | Group 2: Verorab® | Group 3: VRVg-2 + ERIG |
|------------------------------------|-----------------|-------------------|------------------------|
| Number of subjects                 | 112             | 56                | 26                     |
| Age categorical<br>Units: Subjects |                 |                   |                        |

|   |               |               |                |
|---|---------------|---------------|----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 10.1<br>± 4.3 | 10.8<br>± 3.8 | 36.2<br>± 10.4 |
| Gender categorical<br>Units: Subjects                                   |               |               |                |
| Female  | 54            | 24            | 18             |
| Male  | 58            | 32            | 8              |

| Reporting group values             | Group 4: Verorab® + ERIG | Group 5: VRVg-2 + HRIG | Group 6: Verorab + HRIG |
|------------------------------------|--------------------------|------------------------|-------------------------|
| Number of subjects                 | 14                       | 129                    | 65                      |
| Age categorical<br>Units: Subjects |                          |                        |                         |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 37.3<br>± 11.1 | 40.2<br>± 11.1 | 39.2<br>± 10.9 |
| Gender categorical<br>Units: Subjects                                   |                |                |                |
| Female  | 9              | 78             | 39             |
| Male  | 5              | 51             | 26             |

|                                    |       |  |  |
|------------------------------------|-------|--|--|
| <b>Reporting group values</b>      | Total |  |  |
| Number of subjects                 | 402   |  |  |
| Age categorical<br>Units: Subjects |       |  |  |

|   |     |  |  |
|---|-----|--|--|
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -   |  |  |
| Gender categorical<br>Units: Subjects                                   |     |  |  |
| Female  | 222 |  |  |
| Male  | 180 |  |  |

## End points

### End points reporting groups

|  |                          |
|--|--------------------------|
| Reporting group title  | Group 1: VRVg-2          |
| Reporting group description:<br>Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 millilitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.   |                          |
| Reporting group title  | Group 2: Verorab®        |
| Reporting group description:<br>Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.          |                          |
| Reporting group title  | Group 3: VRVg-2 + ERIG   |
| Reporting group description:<br>Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0. |                          |
| Reporting group title  | Group 4: Verorab® + ERIG |
| Reporting group description:<br>Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.   |                          |
| Reporting group title  | Group 5: VRVg-2 + HRIG   |
| Reporting group description:<br>Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.  |                          |
| Reporting group title  | Group 6: Verorab + HRIG  |
| Reporting group description:<br>Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.  |                          |

### Primary: Percentage of Subjects With Rabies Virus Neutralising Antibody (RVNA) Titer Greater Than or Equal to ( $\geq$ ) 0.5 International Units per Millilitres (IU/mL)

|   |   |
|---|---|
| End point title   | Percentage of Subjects With Rabies Virus Neutralising Antibody (RVNA) Titer Greater Than or Equal to ( $\geq$ ) 0.5 International Units per Millilitres (IU/mL) <sup>[1][2]</sup> |
| End point description:<br>RVNA titer against rabies virus was assessed using the Rapid Fluorescent Focus Inhibition test (RFFIT) assay method. Analysis was performed on the per-protocol analysis set (PPAS) that included all subjects who received at least 1 dose of the study vaccine. The subjects who presented protocol deviations and met PPAS exclusion criteria were excluded from PPAS. Here, 'n' = subjects with available data for each specified category. |   |
| End point type  | Primary   |
| End point timeframe:<br>Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)   |   |

#### Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was reported for the endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|----------------------------------|--------------------|----------------------|------------------------------|-------------------------------|
| Subject group type               | Reporting group    | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed      | 98                 | 52                   | 78                           | 37                            |
| Units: percentage of subjects    |                    |                      |                              |                               |
| number (confidence interval 95%) |                    |                      |                              |                               |
| Day 0 (n=98,52,78,37)            | 0.0 (0.0 to 3.7)   | 0.0 (0.0 to 6.8)     | 0.0 (0.0 to 4.6)             | 0.0 (0.0 to 9.5)              |
| Day 14 (n=97,49,74,36)           | 100 (96.3 to 100)  | 98.0 (89.1 to 99.9)  | 59.5 (47.4 to 70.7)          | 52.8 (35.5 to 69.6)           |
| Day 42 (n=98,52,78,37)           | 100 (96.3 to 100)  | 100 (93.2 to 100)    | 96.2 (89.2 to 99.2)          | 100 (90.5 to 100)             |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of Subjects With RVNA Titer $\geq 0.2$ IU/mL (Lower Limit of Quantification [LLOQ])

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With RVNA Titer $\geq 0.2$ IU/mL (Lower Limit of Quantification [LLOQ])[3][4] |
|-----------------|--|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population. Here 'n' = subjects with available data for each specified category.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was reported for the endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|----------------------------------|--------------------|----------------------|------------------------------|-------------------------------|
| Subject group type               | Reporting group    | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed      | 98                 | 52                   | 78                           | 37                            |
| Units: percentage of subjects    |                    |                      |                              |                               |
| number (confidence interval 95%) |                    |                      |                              |                               |
| Day 0 (n=98,52,78,37)            | 0.0 (0.0 to 3.7)   | 0.0 (0.0 to 6.8)     | 0.0 (0.0 to 4.6)             | 0.0 (0.0 to 9.5)              |
| Day 14 (n=97,49,74,36)           | 100 (96.3 to 100)  | 100 (92.7 to 100)    | 85.1 (75.0 to 92.3)          | 83.3 (67.2 to 93.6)           |
| Day 42 (n=98,52,78,37)           | 100 (96.3 to 100)  | 100 (93.2 to 100)    | 98.7 (93.1 to 100)           | 100 (90.5 to 100)             |

## Statistical analyses

No statistical analyses for this end point

### Primary: Geometric Mean Titer Ratios (GMTRs) of Individual RVNA Titers

|  |  |
|--|--|
| End point title  | Geometric Mean Titer Ratios (GMTRs) of Individual RVNA |
| End point description:<br>RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post-vaccination (i.e., on Day 14 and Day 42) and pre-vaccination on Day 0. Analysis was performed on PPAS population. Here, 'n' = subjects with available data for each specified category. |  |
| End point type   | Primary  |
| End point timeframe:<br>Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)  |  |

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistical analysis was reported for the endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                         | Group 1:<br>VRVg-2  | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|--|---------------------|----------------------|------------------------------|-------------------------------|
| Subject group type                       | Reporting group     | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed              | 98                  | 52                   | 78                           | 37                            |
| Units: ratio                             |                     |                      |                              |                               |
| geometric mean (confidence interval 95%) |                     |                      |                              |                               |
| Day 14/ Day 0 (n=97,49,74,36)            | 29.4 (24.8 to 34.9) | 25.3 (19.7 to 32.6)  | 6.77 (5.21 to 8.79)          | 5.39 (3.65 to 7.96)           |
| Day 42/Day 0 (n=98,52,78,37)             | 114 (96.4 to 134)   | 96.2 (79.5 to 116)   | 31.3 (24.9 to 39.2)          | 44.1 (33.1 to 58.7)           |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With RVNA Titer $\geq 0.5$ IU/mL: Group 3 and Group 4

|   |   |
|---|---|
| End point title   | Percentage of Subjects With RVNA Titer $\geq 0.5$ IU/mL: Group 3 and Group 4 <sup>[7]</sup> |
| End point description:<br>RVNA titer against rabies virus was assessed using the RFFIT assay method. Analysis was performed on PPAS population. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Day 0 (pre-vaccination) and Day 14 (post-vaccination)   |   |

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |  |  |
|----------------------------------|---------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group           | Reporting group                |  |  |
| Number of subjects analysed      | 16                        | 9                              |  |  |
| Units: percentage of subjects    |                           |                                |  |  |
| number (confidence interval 95%) |                           |                                |  |  |
| Day 0                            | 0.0 (0.0 to<br>20.6)      | 0.0 (0.0 to<br>33.6)           |  |  |
| Day 14                           | 75.0 (47.6 to<br>92.7)    | 55.6 (21.2 to<br>86.3)         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With RVNA Titer $\geq$ 0.2 IU/mL (LLOQ): Group 3 and Group 4

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With RVNA Titer $\geq$ 0.2 IU/mL (LLOQ): Group 3 and Group 4 <sup>[8]</sup> |
|-----------------|--|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 0 (pre-vaccination) and Day 14 (post-vaccination)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |  |  |
|----------------------------------|---------------------------|--------------------------------|--|--|
| Subject group type               | Reporting group           | Reporting group                |  |  |
| Number of subjects analysed      | 16                        | 9                              |  |  |
| Units: percentage of subjects    |                           |                                |  |  |
| number (confidence interval 95%) |                           |                                |  |  |
| Day 0                            | 0.0 (0.0 to<br>20.6)      | 0.0 (0.0 to<br>33.6)           |  |  |
| Day 14                           | 100 (79.4 to<br>100)      | 77.8 (40.0 to<br>97.2)         |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: GMTRs of Individual RVNA Titers: Group 3 and Group 4

|                 |   |
|-----------------|---|
| End point title | GMTRs of Individual RVNA Titers: Group 3 and Group 4 <sup>[9]</sup> |
|-----------------|---|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post-vaccination (i.e., on Day 14) and pre-vaccination on Day 0. Analysis was performed on PPAS population.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 0 (pre-vaccination) and Day 14 (post-vaccination)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                         | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |  |  |
|--|---------------------------|--------------------------------|--|--|
| Subject group type                       | Reporting group           | Reporting group                |  |  |
| Number of subjects analysed              | 16                        | 9                              |  |  |
| Units: ratio                             |                           |                                |  |  |
| geometric mean (confidence interval 95%) |                           |                                |  |  |
| Day 14/Day 0                             | 10.1 (6.17 to 16.4)       | 13.6 (1.98 to 92.9)            |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With RVNA Titer $\geq 0.5$ IU/mL: Groups 1, 2, 5 and 6

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With RVNA Titer $\geq 0.5$ IU/mL: Groups 1, 2, 5 and 6 <sup>[10]</sup> |
|-----------------|---|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 90 (post-vaccination)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|----------------------------------|--------------------|----------------------|------------------------------|-------------------------------|
| Subject group type               | Reporting group    | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed      | 97                 | 52                   | 76                           | 37                            |
| Units: percentage of subjects    |                    |                      |                              |                               |
| number (confidence interval 95%) | 99.0 (94.4 to 100) | 98.1 (89.7 to 100)   | 75.0 (63.7 to 84.2)          | 78.4 (61.8 to 90.2)           |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With RVNA Titer $\geq$ 0.2 IU/mL (LLOQ): Groups 1, 2, 5 and 6

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects With RVNA Titer $\geq$ 0.2 IU/mL (LLOQ): Groups 1, 2, 5 and 6 <sup>[11]</sup> |
|-----------------|--|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 90 (post-vaccination)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                 | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|----------------------------------|--------------------|----------------------|------------------------------|-------------------------------|
| Subject group type               | Reporting group    | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed      | 97                 | 52                   | 76                           | 37                            |
| Units: percentage of subjects    |                    |                      |                              |                               |
| number (confidence interval 95%) | 100 (96.3 to 100)  | 100 (93.2 to 100)    | 88.2 (78.7 to 94.4)          | 94.6 (81.8 to 99.3)           |

## Statistical analyses

No statistical analyses for this end point

### Secondary: GMTRs of Individual RVNA Titers: Groups 1, 2, 5 and 6

|                 |   |
|-----------------|---|
| End point title | GMTRs of Individual RVNA Titers: Groups 1, 2, 5 and 6 <sup>[12]</sup> |
|-----------------|---|

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post vaccination (i.e., on Day 90) and pre-vaccination on Day 0. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Day 0 (pre-vaccination) and Day (90 post-vaccination)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

| End point values                         | Group 1:<br>VRVg-2  | Group 2:<br>Verorab® | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |
|--|---------------------|----------------------|------------------------------|-------------------------------|
| Subject group type                       | Reporting group     | Reporting group      | Reporting group              | Reporting group               |
| Number of subjects analysed              | 97                  | 52                   | 76                           | 37                            |
| Units: ratio                             |                     |                      |                              |                               |
| geometric mean (confidence interval 95%) |                     |                      |                              |                               |
| Day 90/Day 0                             | 30.3 (25.6 to 36.0) | 22.3 (18.5 to 26.7)  | 7.70 (6.08 to 9.73)          | 9.58 (6.92 to 13.2)           |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)

|                 |   |
|-----------------|---|
| End point title | Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs) |
|-----------------|---|

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study vaccine and does not necessarily had to have a causal relationship with treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset post-vaccination. All subjects were observed for 30 minutes after any vaccination, and any unsolicited AEs occurred during that time were recorded as immediate unsolicited AEs in the CRB. Analysis was performed on the safety analysis set (SafAS) that included subjects who had received at least one dose of the study vaccine and were analysed according to the actual study vaccine they received and after any dose according to the study vaccine received at the first dose. Reported AEs were presented for each arm as pre-specified in the protocol.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Within 30 minutes post-any vaccination

| End point values            | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |
|-----------------------------|--------------------|----------------------|---------------------------|--------------------------------|
| Subject group type          | Reporting group    | Reporting group      | Reporting group           | Reporting group                |
| Number of subjects analysed | 112                | 56                   | 26                        | 14                             |
| Units: subjects             | 0                  | 0                    | 0                         | 0                              |

| End point values | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |  |  |
|------------------|------------------------------|-------------------------------|--|--|
|------------------|------------------------------|-------------------------------|--|--|

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 129             | 65              |  |  |
| Units: subjects             | 0               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Solicited Injection Site Reactions

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Solicited Injection Site Reactions |
|-----------------|--|

End point description:

A solicited reaction (SR) was an expected adverse reaction (AR) observed and reported under conditions (nature and onset) prelisted (i.e., solicited) in the protocol and CRB and considered as related to vaccination (vacc). An AR was all noxious and unintended responses to a medicinal product related to any dose. Solicited injection site reactions included pain, erythema and swelling at and around the injection site. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in the protocol.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Within 7 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])

| End point values                                   | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |
|--|--------------------|----------------------|---------------------------|--------------------------------|
| Subject group type                                 | Reporting group    | Reporting group      | Reporting group           | Reporting group                |
| Number of subjects analysed                        | 112                | 56                   | 26                        | 14                             |
| Units: subjects                                    |                    |                      |                           |                                |
| Pain Post-any vacc.<br>(n=112,56,26,14,129,65)     | 44                 | 23                   | 14                        | 5                              |
| Pain Post-vacc. 1<br>(n=112,56,26,14,129,65)       | 30                 | 19                   | 13                        | 4                              |
| Pain Post-vacc. 2<br>(n=112,56,23,14,129,65)       | 33                 | 16                   | 4                         | 1                              |
| Pain Post-vacc. 3<br>(n=112,56,21,12,129,65)       | 23                 | 6                    | 2                         | 2                              |
| Pain Post-vacc. 4<br>(n=112,56,0,0,127,64)         | 18                 | 8                    | 99999                     | 99999                          |
| Erythema Post-any vacc.<br>(n=112,56,26,14,129,65) | 40                 | 15                   | 0                         | 0                              |
| Erythema Post-vacc. 1<br>(n=112,56,26,14,129,65)   | 20                 | 8                    | 0                         | 0                              |
| Erythema Post-vacc. 2<br>(n=112,56,23,14,129,65)   | 22                 | 10                   | 0                         | 0                              |
| Erythema Post-vacc. 3<br>(n=112,56,21,12,129,65)   | 23                 | 11                   | 0                         | 0                              |
| Erythema Post-vacc. 4<br>(n=112,56,0,0,127,64)     | 31                 | 12                   | 99999                     | 99999                          |
| Swelling Post-any vacc.<br>(n=112,56,26,14,129,65) | 53                 | 27                   | 0                         | 0                              |

|  |    |    |       |       |
|--|----|----|-------|-------|
| Swelling Post-vacc. 1<br>(n=112,56,26,14,129,65) | 28 | 10 | 0     | 0     |
| Swelling Post-vacc. 2<br>(n=112,56,23,14,129,65) | 32 | 18 | 0     | 0     |
| Swelling Post-vacc. 3<br>(n=112,56,21,12,129,65) | 41 | 20 | 0     | 0     |
| Swelling Post-vacc. 4<br>(n=112,56,0,0,127,64)   | 46 | 21 | 99999 | 99999 |

| End point values                                   | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |  |  |
|--|------------------------------|-------------------------------|--|--|
| Subject group type                                 | Reporting group              | Reporting group               |  |  |
| Number of subjects analysed                        | 129                          | 65                            |  |  |
| Units: subjects                                    |                              |                               |  |  |
| Pain Post-any vacc.<br>(n=112,56,26,14,129,65)     | 57                           | 30                            |  |  |
| Pain Post-vacc. 1<br>(n=112,56,26,14,129,65)       | 35                           | 20                            |  |  |
| Pain Post-vacc. 2<br>(n=112,56,23,14,129,65)       | 25                           | 11                            |  |  |
| Pain Post-vacc. 3<br>(n=112,56,21,12,129,65)       | 31                           | 13                            |  |  |
| Pain Post-vacc. 4<br>(n=112,56,0,0,127,64)         | 24                           | 12                            |  |  |
| Erythema Post-any vacc.<br>(n=112,56,26,14,129,65) | 0                            | 2                             |  |  |
| Erythema Post-vacc. 1<br>(n=112,56,26,14,129,65)   | 0                            | 0                             |  |  |
| Erythema Post-vacc. 2<br>(n=112,56,23,14,129,65)   | 0                            | 1                             |  |  |
| Erythema Post-vacc. 3<br>(n=112,56,21,12,129,65)   | 0                            | 0                             |  |  |
| Erythema Post-vacc. 4<br>(n=112,56,0,0,127,64)     | 0                            | 1                             |  |  |
| Swelling Post-any vacc.<br>(n=112,56,26,14,129,65) | 0                            | 0                             |  |  |
| Swelling Post-vacc. 1<br>(n=112,56,26,14,129,65)   | 0                            | 0                             |  |  |
| Swelling Post-vacc. 2<br>(n=112,56,23,14,129,65)   | 0                            | 0                             |  |  |
| Swelling Post-vacc. 3<br>(n=112,56,21,12,129,65)   | 0                            | 0                             |  |  |
| Swelling Post-vacc. 4<br>(n=112,56,0,0,127,64)     | 0                            | 0                             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Solicited Systemic Reactions

|                 |  |
|-----------------|--|
| End point title | Number of Subjects With Solicited Systemic Reactions |
|-----------------|--|

End point description:

SR: expected AR observed and reported under conditions (nature and onset) prelisted (i.e., solicited) in protocol and CRB and considered as related to vaccination. Solicited reactions were collected for different age groups: fever, vomiting, crying abnormal, drowsiness, appetite lost and irritability were collected for subjects aged 12 to 23 months and fever, headache, malaise and myalgia were collected for subjects aged  $\geq 2$  years. Solicited systemic reactions were analysed between each vaccination if vaccinations are separated less than 7 days, and up to 7 days after each vaccination if vaccinations were separated by 7 days or more. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in protocol.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Within 7 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])

| End point values                                  | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |
|---|--------------------|----------------------|---------------------------|--------------------------------|
| Subject group type                                | Reporting group    | Reporting group      | Reporting group           | Reporting group                |
| Number of subjects analysed                       | 112                | 56                   | 26                        | 14                             |
| Units: subjects                                   |                    |                      |                           |                                |
| Fever Post-any Vacc.<br>(n=112,56,26,14,129,65)   | 1                  | 0                    | 2                         | 0                              |
| Fever Post-vacc. 1<br>(n=112,56,26,14,129,65)     | 0                  | 0                    | 0                         | 0                              |
| Fever Post-vacc. 2<br>(n=112,56,23,14,129,65)     | 1                  | 0                    | 0                         | 0                              |
| Fever Post-vacc. 3<br>(n=112,56,21,12,129,65)     | 0                  | 0                    | 2                         | 0                              |
| Fever Post-vacc. 4<br>(n=112,56,0,0,127,64)       | 0                  | 0                    | 99999                     | 99999                          |
| Vomiting Post-any Vacc.<br>(n=2,1,0,0,0,0)        | 0                  | 0                    | 99999                     | 99999                          |
| Vomiting Post-vacc. 1 (n=2,1,0,0,0,0)             | 0                  | 0                    | 99999                     | 99999                          |
| Vomiting Post-vacc. 2 (n=2,1,0,0,0,0)             | 0                  | 0                    | 99999                     | 99999                          |
| Vomiting Post-vacc. 3 (n=2,1,0,0,0,0)             | 0                  | 0                    | 99999                     | 99999                          |
| Vomiting Post-vacc. 4 (n=2,1,0,0,0,0)             | 0                  | 0                    | 99999                     | 99999                          |
| Crying abnormal Post-any Vacc.<br>(n=2,1,0,0,0,0) | 1                  | 0                    | 99999                     | 99999                          |
| Crying abnormal Post-vacc. 1<br>(n=2,1,0,0,0,0)   | 1                  | 0                    | 99999                     | 99999                          |
| Crying abnormal Post-vacc. 2<br>(n=2,1,0,0,0,0)   | 1                  | 0                    | 99999                     | 99999                          |
| Crying abnormal Post-vacc. 3<br>(n=2,1,0,0,0,0)   | 1                  | 0                    | 99999                     | 99999                          |
| Crying abnormal Post-vacc. 4<br>(n=2,1,0,0,0,0)   | 1                  | 0                    | 99999                     | 99999                          |
| Drowsiness Post-any Vacc.<br>(n=2,1,0,0,0,0)      | 0                  | 0                    | 99999                     | 99999                          |
| Drowsiness Post-vacc. 1 (n=2,1,0,0,0,0)           | 0                  | 0                    | 99999                     | 99999                          |
| Drowsiness Post-vacc. 2 (n=2,1,0,0,0,0)           | 0                  | 0                    | 99999                     | 99999                          |
| Drowsiness Post-vacc. 3 (n=2,1,0,0,0,0)           | 0                  | 0                    | 99999                     | 99999                          |
| Drowsiness Post-vacc. 4 (n=2,1,0,0,0,0)           | 0                  | 0                    | 99999                     | 99999                          |
| Appetite lost Post-any Vacc.<br>(n=2,1,0,0,0,0)   | 0                  | 0                    | 99999                     | 99999                          |

|  |    |    |       |       |
|--|----|----|-------|-------|
| Appetite lost Post-vacc. 1<br>(n=2,1,0,0,0,0)      | 0  | 0  | 99999 | 99999 |
| Appetite lost Post-vacc. 2<br>(n=2,1,0,0,0,0)      | 0  | 0  | 99999 | 99999 |
| Appetite lost Post-vacc. 3<br>(n=2,1,0,0,0,0)      | 0  | 0  | 99999 | 99999 |
| Appetite lost Post-vacc. 4<br>(n=2,1,0,0,0,0)      | 0  | 0  | 99999 | 99999 |
| Irritability Post-any Vacc.<br>(n=2,1,0,0,0,0)     | 1  | 0  | 99999 | 99999 |
| Irritability Post-vacc. 1 (n=2,1,0,0,0,0)          | 0  | 0  | 99999 | 99999 |
| Irritability Post-vacc. 2 (n=2,1,0,0,0,0)          | 0  | 0  | 99999 | 99999 |
| Irritability Post-vacc. 3 (n=2,1,0,0,0,0)          | 0  | 0  | 99999 | 99999 |
| Irritability Post-vacc. 4 (n=2,1,0,0,0,0)          | 1  | 0  | 99999 | 99999 |
| Headache Post-any Vacc.<br>(n=110,55,26,14,129,65) | 20 | 10 | 5     | 3     |
| Headache Post-vacc. 1<br>(n=110,55,26,14,129,65)   | 11 | 7  | 4     | 1     |
| Headache Post-vacc. 2<br>(n=109,55,23,14,129,65)   | 8  | 3  | 3     | 2     |
| Headache Post-vacc. 3<br>(n=110,55,21,12,129,65)   | 7  | 4  | 0     | 2     |
| Headache Post-vacc. 4<br>(n=110,55,0,0,127,64)     | 6  | 1  | 99999 | 99999 |
| Malaise Post-any Vacc.<br>(n=110,55,26,14,129,65)  | 18 | 9  | 6     | 5     |
| Malaise Post-vacc. 1<br>(n=110,55,26,14,129,65)    | 13 | 6  | 5     | 4     |
| Malaise Post-vacc. 2<br>(n=108,55,23,14,128,65)    | 8  | 4  | 2     | 1     |
| Malaise Post-vacc. 3<br>(n=109,55,21,12,129,65)    | 3  | 2  | 1     | 1     |
| Malaise Post-vacc. 4<br>(n=110,55,0,0,127,64)      | 6  | 2  | 99999 | 99999 |
| Myalgia Post-any Vacc.<br>(n=110,55,26,14,129,65)  | 26 | 10 | 11    | 8     |
| Myalgia Post-vacc. 1<br>(n=110,55,26,14,129,65)    | 13 | 6  | 11    | 6     |
| Myalgia Post-vacc. 2<br>(n=109,55,23,14,129,65)    | 16 | 6  | 3     | 0     |
| Myalgia Post-vacc. 3<br>(n=108,55,21,12,129,65)    | 5  | 4  | 1     | 2     |
| Myalgia Post-vacc. 4<br>(n=110,55,0,0,127,64)      | 7  | 4  | 99999 | 99999 |

| End point values                                | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |  |  |
|---|------------------------------|-------------------------------|--|--|
| Subject group type                              | Reporting group              | Reporting group               |  |  |
| Number of subjects analysed                     | 129                          | 65                            |  |  |
| Units: subjects                                 |                              |                               |  |  |
| Fever Post-any Vacc.<br>(n=112,56,26,14,129,65) | 2                            | 2                             |  |  |
| Fever Post-vacc. 1<br>(n=112,56,26,14,129,65)   | 0                            | 0                             |  |  |
| Fever Post-vacc. 2<br>(n=112,56,23,14,129,65)   | 0                            | 0                             |  |  |

|  |       |       |  |  |
|--|-------|-------|--|--|
| Fever Post-vacc. 3<br>(n=112,56,21,12,129,65)      | 0     | 0     |  |  |
| Fever Post-vacc. 4<br>(n=112,56,0,0,127,64)        | 2     | 2     |  |  |
| Vomiting Post-any Vacc.<br>(n=2,1,0,0,0,0)         | 99999 | 99999 |  |  |
| Vomiting Post-vacc. 1 (n=2,1,0,0,0,0)              | 99999 | 99999 |  |  |
| Vomiting Post-vacc. 2 (n=2,1,0,0,0,0)              | 99999 | 99999 |  |  |
| Vomiting Post-vacc. 3 (n=2,1,0,0,0,0)              | 99999 | 99999 |  |  |
| Vomiting Post-vacc. 4 (n=2,1,0,0,0,0)              | 99999 | 99999 |  |  |
| Crying abnormal Post-any Vacc.<br>(n=2,1,0,0,0,0)  | 99999 | 99999 |  |  |
| Crying abnormal Post-vacc. 1<br>(n=2,1,0,0,0,0)    | 99999 | 99999 |  |  |
| Crying abnormal Post-vacc. 2<br>(n=2,1,0,0,0,0)    | 99999 | 99999 |  |  |
| Crying abnormal Post-vacc. 3<br>(n=2,1,0,0,0,0)    | 99999 | 99999 |  |  |
| Crying abnormal Post-vacc. 4<br>(n=2,1,0,0,0,0)    | 99999 | 99999 |  |  |
| Drowsiness Post-any Vacc.<br>(n=2,1,0,0,0,0)       | 99999 | 99999 |  |  |
| Drowsiness Post-vacc. 1 (n=2,1,0,0,0,0)            | 99999 | 99999 |  |  |
| Drowsiness Post-vacc. 2 (n=2,1,0,0,0,0)            | 99999 | 99999 |  |  |
| Drowsiness Post-vacc. 3 (n=2,1,0,0,0,0)            | 99999 | 99999 |  |  |
| Drowsiness Post-vacc. 4 (n=2,1,0,0,0,0)            | 99999 | 99999 |  |  |
| Appetite lost Post-any Vacc.<br>(n=2,1,0,0,0,0)    | 99999 | 99999 |  |  |
| Appetite lost Post-vacc. 1<br>(n=2,1,0,0,0,0)      | 99999 | 99999 |  |  |
| Appetite lost Post-vacc. 2<br>(n=2,1,0,0,0,0)      | 99999 | 99999 |  |  |
| Appetite lost Post-vacc. 3<br>(n=2,1,0,0,0,0)      | 99999 | 99999 |  |  |
| Appetite lost Post-vacc. 4<br>(n=2,1,0,0,0,0)      | 99999 | 99999 |  |  |
| Irritability Post-any Vacc.<br>(n=2,1,0,0,0,0)     | 99999 | 99999 |  |  |
| Irritability Post-vacc. 1 (n=2,1,0,0,0,0)          | 99999 | 99999 |  |  |
| Irritability Post-vacc. 2 (n=2,1,0,0,0,0)          | 99999 | 99999 |  |  |
| Irritability Post-vacc. 3 (n=2,1,0,0,0,0)          | 99999 | 99999 |  |  |
| Irritability Post-vacc. 4 (n=2,1,0,0,0,0)          | 99999 | 99999 |  |  |
| Headache Post-any Vacc.<br>(n=110,55,26,14,129,65) | 31    | 11    |  |  |
| Headache Post-vacc. 1<br>(n=110,55,26,14,129,65)   | 19    | 7     |  |  |
| Headache Post-vacc. 2<br>(n=109,55,23,14,129,65)   | 10    | 2     |  |  |
| Headache Post-vacc. 3<br>(n=110,55,21,12,129,65)   | 10    | 3     |  |  |
| Headache Post-vacc. 4<br>(n=110,55,0,0,127,64)     | 8     | 2     |  |  |
| Malaise Post-any Vacc.<br>(n=110,55,26,14,129,65)  | 39    | 13    |  |  |
| Malaise Post-vacc. 1<br>(n=110,55,26,14,129,65)    | 26    | 5     |  |  |
| Malaise Post-vacc. 2<br>(n=108,55,23,14,128,65)    | 17    | 3     |  |  |
| Malaise Post-vacc. 3<br>(n=109,55,21,12,129,65)    | 17    | 5     |  |  |

|   |    |    |  |  |
|---|----|----|--|--|
| Malaise Post-vacc. 4<br>(n=110,55,0,0,127,64)     | 12 | 5  |  |  |
| Myalgia Post-any Vacc.<br>(n=110,55,26,14,129,65) | 61 | 25 |  |  |
| Myalgia Post-vacc. 1<br>(n=110,55,26,14,129,65)   | 44 | 21 |  |  |
| Myalgia Post-vacc. 2<br>(n=109,55,23,14,129,65)   | 25 | 11 |  |  |
| Myalgia Post-vacc. 3<br>(n=108,55,21,12,129,65)   | 21 | 8  |  |  |
| Myalgia Post-vacc. 4<br>(n=110,55,0,0,127,64)     | 20 | 6  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Unsolicited AEs

|  |   |
|--|---|
| End point title  | Number of Subjects With Unsolicited AEs |
| End point description:   |   |
| An AE was defined as any untoward medical occurrence in a subject who received study vaccine and does not necessary had to have a causal relationship with treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in the protocol. |   |
| End point type   | Secondary                               |
| End point timeframe:   |   |
| Within 28 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])  |   |

| End point values                          | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® +<br>ERIG |
|---|--------------------|----------------------|---------------------------|--------------------------------|
| Subject group type                        | Reporting group    | Reporting group      | Reporting group           | Reporting group                |
| Number of subjects analysed               | 112                | 56                   | 26                        | 14                             |
| Units: subjects                           |                    |                      |                           |                                |
| Post-any Vacc.<br>(n=112,56,26,14,129,65) | 22                 | 12                   | 26                        | 12                             |
| Post Vacc. 1 (n=112,56,26,14,129,65)      | 1                  | 1                    | 25                        | 12                             |
| Post Vacc. 2 (n=112,56,23,14,129,65)      | 4                  | 0                    | 3                         | 1                              |
| Post Vacc. 3 (n=112,56,21,12,129,65)      | 12                 | 5                    | 5                         | 2                              |
| Post Vacc. 4 (n=112,56,0,0,127,64)        | 7                  | 7                    | 99999                     | 99999                          |

| End point values | Group 5:<br>VRVg-2 +<br>HRIG | Group 6:<br>Verorab +<br>HRIG |  |  |
|------------------|------------------------------|-------------------------------|--|--|
|------------------|------------------------------|-------------------------------|--|--|

|   |                 |                 |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                        | Reporting group | Reporting group |  |  |
| Number of subjects analysed               | 129             | 65              |  |  |
| Units: subjects                           |                 |                 |  |  |
| Post-any Vacc.<br>(n=112,56,26,14,129,65) | 4               | 2               |  |  |
| Post Vacc. 1 (n=112,56,26,14,129,65)      | 3               | 0               |  |  |
| Post Vacc. 2 (n=112,56,23,14,129,65)      | 0               | 1               |  |  |
| Post Vacc. 3 (n=112,56,21,12,129,65)      | 0               | 0               |  |  |
| Post Vacc. 4 (n=112,56,0,0,127,64)        | 1               | 1               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs)

|   |   |
|---|---|
| End point title   | Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs) |
| End point description:  |   |
| An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required initial or prolonged inpatient hospitalisation, resulted in persistent or significant disability/incapacity, congenital anomaly/birth defect or was a medically important event. An AESI was defined as one of scientific and medical concern specific to the Sponsor's product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate. Relatedness to study vaccine was based on Investigator's discretion. Analysis was performed on SafAS. Reported AEs were presented for each arm as pre-specified in the protocol. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| From Day 0 up to 6 months after last vaccination (i.e., up to Month 7)  |   |

| End point values            | Group 1:<br>VRVg-2 | Group 2:<br>Verorab® | Group 3:<br>VRVg-2 + ERIG | Group 4:<br>Verorab® + ERIG |
|-----------------------------|--------------------|----------------------|---------------------------|-----------------------------|
| Subject group type          | Reporting group    | Reporting group      | Reporting group           | Reporting group             |
| Number of subjects analysed | 112                | 56                   | 26                        | 14                          |
| Units: subjects             |                    |                      |                           |                             |
| SAEs                        | 0                  | 0                    | 1                         | 2                           |
| AESIs                       | 0                  | 0                    | 0                         | 0                           |

| End point values            | Group 5:<br>VRVg-2 + HRIG | Group 6:<br>Verorab + HRIG |  |  |
|-----------------------------|---------------------------|----------------------------|--|--|
| Subject group type          | Reporting group           | Reporting group            |  |  |
| Number of subjects analysed | 129                       | 65                         |  |  |
| Units: subjects             |                           |                            |  |  |
| SAEs                        | 5                         | 3                          |  |  |
| AESIs                       | 0                         | 0                          |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs were collected from Day 0 up to 28 days post any and each vaccination. SR data were collected up to 7 days post any and each vaccination. SAE data were collected from Day 0 up to 6 months post last vaccination (i.e., up to Month 7)

Adverse event reporting additional description:

SR: expected AR observed & reported under conditions (nature and onset) prelisted (i.e., solicited) in protocol & CRB & considered as related vaccination. Unsolicited AE: AE that did not fulfill conditions prelisted (i.e., solicited) in CRB in terms of diagnosis & onset window post-vaccination. SafAS. In AE section, SR fever is reported as pyrexia.

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 25.0   |

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Group 1: VRVg-2 |
|-----------------------|-----------------|

Reporting group description:

Pediatric subjects aged 1 year to < 18 years received 8 injections (1 vaccination on each arm) of 0.5 mL of VRVg-2 intradermally on Days 0, 3, 7 and 28.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Group 2: Verorab |
|-----------------------|------------------|

Reporting group description:

Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Group 3: VRVg-2 + ERIG |
|-----------------------|------------------------|

Reporting group description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Group 4: Verorab + ERIG |
|-----------------------|-------------------------|

Reporting group description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Group 5: VRVg-2 + HRIG |
|-----------------------|------------------------|

Reporting group description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Group 6: Verorab + HRIG |
|-----------------------|-------------------------|

Reporting group description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

| Serious adverse events                            | Group 1: VRVg-2 | Group 2: Verorab | Group 3: VRVg-2 + ERIG |
|---|-----------------|------------------|------------------------|
| Total subjects affected by serious adverse events |                 |                  |                        |
| subjects affected / exposed                       | 0 / 112 (0.00%) | 0 / 56 (0.00%)   | 1 / 26 (3.85%)         |
| number of deaths (all causes)                     | 0               | 0                | 0                      |
| number of deaths resulting from adverse events    |                 |                  |                        |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| Injury, poisoning and procedural complications  |                 |                |                |
| Limb Traumatic Amputation                       |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Surgical and medical procedures                 |                 |                |                |
| Mammoplasty                                     |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Immune system disorders                         |                 |                |                |
| Hypersensitivity                                |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 1 / 26 (3.85%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Gastrointestinal disorders                      |                 |                |                |
| Lower Gastrointestinal Haemorrhage              |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Skin and subcutaneous tissue disorders          |                 |                |                |
| Angioedema                                      |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Hypersensitivity Vasculitis                     |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Infections and infestations                     |                 |                |                |
| Appendicitis Perforated                         |                 |                |                |
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |
| Covid-19  |                 |                |                |

|   |                 |                |                |
|---|-----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 112 (0.00%) | 0 / 56 (0.00%) | 0 / 26 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0          | 0 / 0          |

| <b>Serious adverse events</b>                     | Group 4: Verorab + ERIG | Group 5: VRVg-2 + HRIG | Group 6: Verorab + HRIG |
|---|-------------------------|------------------------|-------------------------|
| Total subjects affected by serious adverse events |                         |                        |                         |
| subjects affected / exposed                       | 2 / 14 (14.29%)         | 5 / 129 (3.88%)        | 3 / 65 (4.62%)          |
| number of deaths (all causes)                     | 0                       | 0                      | 0                       |
| number of deaths resulting from adverse events    |                         |                        |                         |
| Injury, poisoning and procedural complications    |                         |                        |                         |
| Limb Traumatic Amputation                         |                         |                        |                         |
| subjects affected / exposed                       | 0 / 14 (0.00%)          | 1 / 129 (0.78%)        | 0 / 65 (0.00%)          |
| occurrences causally related to treatment / all   | 0 / 0                   | 0 / 1                  | 0 / 0                   |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| Surgical and medical procedures                   |                         |                        |                         |
| Mammoplasty                                       |                         |                        |                         |
| subjects affected / exposed                       | 0 / 14 (0.00%)          | 0 / 129 (0.00%)        | 1 / 65 (1.54%)          |
| occurrences causally related to treatment / all   | 0 / 0                   | 0 / 0                  | 0 / 1                   |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| Immune system disorders                           |                         |                        |                         |
| Hypersensitivity                                  |                         |                        |                         |
| subjects affected / exposed                       | 0 / 14 (0.00%)          | 0 / 129 (0.00%)        | 0 / 65 (0.00%)          |
| occurrences causally related to treatment / all   | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| Gastrointestinal disorders                        |                         |                        |                         |
| Lower Gastrointestinal Haemorrhage                |                         |                        |                         |
| subjects affected / exposed                       | 0 / 14 (0.00%)          | 0 / 129 (0.00%)        | 1 / 65 (1.54%)          |
| occurrences causally related to treatment / all   | 0 / 0                   | 0 / 0                  | 0 / 1                   |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| Skin and subcutaneous tissue disorders            |                         |                        |                         |
| Angioedema  |                         |                        |                         |
| subjects affected / exposed                       | 1 / 14 (7.14%)          | 0 / 129 (0.00%)        | 0 / 65 (0.00%)          |
| occurrences causally related to treatment / all   | 1 / 1                   | 0 / 0                  | 0 / 0                   |
| deaths causally related to treatment / all        | 0 / 0                   | 0 / 0                  | 0 / 0                   |
| Hypersensitivity Vasculitis                       |                         |                        |                         |

|   |                |                 |                |
|---|----------------|-----------------|----------------|
| subjects affected / exposed                     | 1 / 14 (7.14%) | 0 / 129 (0.00%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Infections and infestations</b>              |                |                 |                |
| Appendicitis Perforated                         |                |                 |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 1 / 129 (0.78%) | 0 / 65 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |
| <b>Covid-19</b>                                 |                |                 |                |
| subjects affected / exposed                     | 0 / 14 (0.00%) | 3 / 129 (2.33%) | 1 / 65 (1.54%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3           | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0          |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                           | Group 1: VRVg-2  | Group 2: Verorab | Group 3: VRVg-2 + ERIG |
|---|--|------------------|------------------------|
| Total subjects affected by non-serious adverse events       |  |                  |                        |
| subjects affected / exposed                                 | 85 / 112 (75.89%)  | 42 / 56 (75.00%) | 26 / 26 (100.00%)      |
| <b>Nervous system disorders</b>                             |  |                  |                        |
| Headache  | Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE. |                  |                        |
| subjects affected / exposed                                 | 20 / 112 (17.86%)  | 11 / 56 (19.64%) | 5 / 26 (19.23%)        |
| occurrences (all)   | 34   | 16               | 7                      |
| <b>General disorders and administration site conditions</b> |  |                  |                        |
| Application Site Pain                                       |  |                  |                        |
| subjects affected / exposed                                 | 0 / 112 (0.00%)  | 0 / 56 (0.00%)   | 7 / 26 (26.92%)        |
| occurrences (all)   | 0  | 0                | 7                      |
| Injection Site Erythema                                     |  |                  |                        |
| subjects affected / exposed                                 | 40 / 112 (35.71%)  | 15 / 56 (26.79%) | 0 / 26 (0.00%)         |
| occurrences (all)   | 168  | 76               | 0                      |
| Injection Site Pain   |  |                  |                        |
| subjects affected / exposed                                 | 44 / 112 (39.29%)  | 23 / 56 (41.07%) | 14 / 26 (53.85%)       |
| occurrences (all)   | 177  | 81               | 37                     |
| Injection Site Swelling                                     |  |                  |                        |

|   |   |                  |                  |
|---|---|------------------|------------------|
| subjects affected / exposed                     | 53 / 112 (47.32%)   | 27 / 56 (48.21%) | 0 / 26 (0.00%)   |
| occurrences (all)                               | 243   | 116              | 0                |
| Malaise   |   |                  |                  |
| subjects affected / exposed                     | 18 / 112 (16.07%)   | 9 / 56 (16.07%)  | 6 / 26 (23.08%)  |
| occurrences (all)                               | 30  | 14               | 8                |
| Pyrexia   | Additional description: Pyrexia/Fever events that occurred after 7 days post-vaccination were considered as unsolicited AE. |                  |                  |
| subjects affected / exposed                     | 1 / 112 (0.89%)   | 1 / 56 (1.79%)   | 2 / 26 (7.69%)   |
| occurrences (all)                               | 1   | 1                | 2                |
| Skin and subcutaneous tissue disorders          |   |                  |                  |
| Urticaria                                       |   |                  |                  |
| subjects affected / exposed                     | 1 / 112 (0.89%)   | 0 / 56 (0.00%)   | 7 / 26 (26.92%)  |
| occurrences (all)                               | 1   | 0                | 7                |
| Musculoskeletal and connective tissue disorders |   |                  |                  |
| Myalgia   | Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE.       |                  |                  |
| subjects affected / exposed                     | 26 / 112 (23.21%)   | 10 / 56 (17.86%) | 19 / 26 (73.08%) |
| occurrences (all)                               | 41  | 20               | 33               |
| Infections and infestations                     |   |                  |                  |
| Upper Respiratory Tract Infection               |   |                  |                  |
| subjects affected / exposed                     | 10 / 112 (8.93%)  | 7 / 56 (12.50%)  | 0 / 26 (0.00%)   |
| occurrences (all)                               | 10  | 7                | 0                |

| <b>Non-serious adverse events</b>                     | Group 4: Verorab + ERIG  | Group 5: VRVg-2 + HRIG | Group 6: Verorab + HRIG |
|---|--|------------------------|-------------------------|
| Total subjects affected by non-serious adverse events |  |                        |                         |
| subjects affected / exposed                           | 14 / 14 (100.00%)  | 80 / 129 (62.02%)      | 38 / 65 (58.46%)        |
| Nervous system disorders                              |  |                        |                         |
| Headache  | Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE. |                        |                         |
| subjects affected / exposed                           | 3 / 14 (21.43%)  | 31 / 129 (24.03%)      | 11 / 65 (16.92%)        |
| occurrences (all)                                     | 5  | 47                     | 14                      |
| General disorders and administration site conditions  |  |                        |                         |
| Application Site Pain                                 |  |                        |                         |
| subjects affected / exposed                           | 2 / 14 (14.29%)  | 0 / 129 (0.00%)        | 0 / 65 (0.00%)          |
| occurrences (all)                                     | 2  | 0                      | 0                       |
| Injection Site Erythema                               |  |                        |                         |
| subjects affected / exposed                           | 0 / 14 (0.00%)   | 0 / 129 (0.00%)        | 2 / 65 (3.08%)          |
| occurrences (all)                                     | 0  | 0                      | 2                       |
| Injection Site Pain                                   |  |                        |                         |

|   |   |                   |                  |
|---|---|-------------------|------------------|
| subjects affected / exposed                     | 5 / 14 (35.71%)   | 57 / 129 (44.19%) | 30 / 65 (46.15%) |
| occurrences (all)                               | 11  | 200               | 102              |
| Injection Site Swelling                         |   |                   |                  |
| subjects affected / exposed                     | 0 / 14 (0.00%)  | 0 / 129 (0.00%)   | 0 / 65 (0.00%)   |
| occurrences (all)                               | 0   | 0                 | 0                |
| Malaise   |   |                   |                  |
| subjects affected / exposed                     | 5 / 14 (35.71%)   | 39 / 129 (30.23%) | 13 / 65 (20.00%) |
| occurrences (all)                               | 6   | 72                | 18               |
| Pyrexia   | Additional description: Pyrexia/Fever events that occurred after 7 days post-vaccination were considered as unsolicited AE. |                   |                  |
| subjects affected / exposed                     | 0 / 14 (0.00%)  | 2 / 129 (1.55%)   | 2 / 65 (3.08%)   |
| occurrences (all)                               | 0   | 2                 | 2                |
| Skin and subcutaneous tissue disorders          |   |                   |                  |
| Urticaria                                       |   |                   |                  |
| subjects affected / exposed                     | 2 / 14 (14.29%)   | 0 / 129 (0.00%)   | 0 / 65 (0.00%)   |
| occurrences (all)                               | 2   | 0                 | 0                |
| Musculoskeletal and connective tissue disorders |   |                   |                  |
| Myalgia   | Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE.       |                   |                  |
| subjects affected / exposed                     | 12 / 14 (85.71%)  | 61 / 129 (47.29%) | 25 / 65 (38.46%) |
| occurrences (all)                               | 18  | 113               | 46               |
| Infections and infestations                     |   |                   |                  |
| Upper Respiratory Tract Infection               |   |                   |                  |
| subjects affected / exposed                     | 0 / 14 (0.00%)  | 0 / 129 (0.00%)   | 0 / 65 (0.00%)   |
| occurrences (all)                               | 0   | 0                 | 0                |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 20 November 2019 | Protocol amended for update of Principal investigator.   |
| 22 November 2021 | Following changes were made: Deleted virus complete or incomplete neutralisation endpoint at 1/5 dilution. Wording changed to clarify new sample size calculated. Adult study arm receiving vaccines + ERIG was temporary halt by Sponsor for safety reasons after enrolling 40 subjects, following receipt of cluster of 3 SAEs of hypersensitivity assessed as related to both ERIG and study vaccine by investigator, & assessed as unrelated to study vaccine but related to ERIG by sponsor. Therefore, ERIG administration on Day (D) 0 in adult subjects (Groups 3 and 4) was discontinued and HRIG was then co-administrated on D0 in Groups 5 and 6. Wording changed to clarify: ERIG administration was applied for Groups 3 & 4 & HRIG administration was applied for Groups 5 & 6. Primary immunogenicity objective modified. Additional immunogenicity secondary objective added: Included immunogenicity data analysis for adult subjects in Groups 3 & 4 to evaluate immune response induced by VRVg-2 & Verorab vaccine at D14. Secondary immunogenicity objective on D90 was applied only for adult subjects in Groups 5 and 6 since no immunogenicity data was available at D90 for Groups 3 & 4. Informed that safety profile was described for all groups. Wording changed to clarify the statistical analysis for the new sample size calculated. Wording changed to clarify that ERIG administration was applied only for Groups 3 & 4 & to provide ERIG batch number used until study halt. Deleted "optional, based on Investigator's judgement" since TRC Society ERIG recommended doing positive skin test prior administration. However, it was agreed with the investigators to do the test in all subjects as additional precautionary safety measure. Missing Diary Cards numbers added. Wording changed since the assessment of immediate unsolicited systemic events was recorded in V01, V02, V03 and V05 only. Footnote removed to clarify event reporting at D0. Injection site reaction and systemic AE/AR recorded daily (from V01 to V07). |
| 24 June 2022     | Following changes were made: Modified GSO representative contact details. Modified justification of study design to clarify that after the discontinuation of ERIG, the 40 subjects were withdrawn and excluded from the PPAS for D42 because unable to complete the 4-dose vaccination schedule, and part of the 40 subjects were also excluded from the PPAS for D14 because unable to complete the first 3 doses of the vaccination schedule. Paragraph added to explain the rationale for developing amendment 3. Re-inserted Amendment 1 to provide history of protocol amendments. Per-protocol analysis set for D42 - paragraph modified to clarify PPAS for D42 definition and notably to remove blood sample 2 at D14 from the list of exclusion criteria.  |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported