



## Clinical trial results:

### A Phase 2, Double-Blind, Placebo Controlled Study of RV001V in Men with Biochemical Failure following Curatively Intended Therapy for Localized Prostate Cancer

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2019-000951-14    |
| Trial protocol           | DK FI SE DE BE GB |
| Global end of trial date | 02 June 2022      |

#### Results information

|                                   |  |
|-----------------------------------|--|
| Result version number             | v1 (current)   |
| This version publication date     | 06 January 2023  |
| First version publication date    | 06 January 2023  |
| Summary attachment (see zip file) | Abbreviated CSR_Synopsis (20221207 Abbreviated CSR_Synopsis (EudraCT)).pdf |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | RhoVac-002 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03199872 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | RhoVac ApS   |
| Sponsor organisation address | Agern Alle 24, Hørsholm, Denmark, 2970               |
| Public contact               | Malene Weis, RhoVac ApS, +45 53542818, mw@rhovac.com |
| Scientific contact           | Malene Weis, RhoVac ApS, +45 53542818, mw@rhovac.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| 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? | No |

Notes:

## Results analysis stage

|  |                |
|--|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 18 August 2022 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 18 May 2022    |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 02 June 2022   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective is to investigate whether a vaccination regimen with multiple subcutaneous (SC) administrations of RV001 Vaccine 0.1 mg/mL (RV001V) can reduce prostate-specific antigen (PSA) progression compared to the control group.

Protection of trial subjects:

The DMC will be advisory to the Sponsor. The DMC will periodically monitor the accumulating data from the trial, including central laboratory data, and advise the Sponsor regarding the continuing safety of trial subjects and those yet to be recruited to the trial, as well as the continuing validity. The primary charge of the DMC is to monitor the study for participant safety. DMC responsibilities include;

- Protect the safety of the study participants;
- Review and evaluate ad hoc safety issues concerning the study at the request of the sponsor;
- Make recommendations to the sponsor concerning continuation, termination, or other modifications of the study based on the observed beneficial or adverse effects of the study;
- Consider factors external to the study when relevant information becomes available, such as scientific or therapeutic developments that may have an impact on participant safety, scientific integrity, or the ethics of conducting the study

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 01 July 2019 |
| Long term follow-up planned                               | No           |
| Independent data monitoring committee (IDMC) involvement? | Yes          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Sweden: 22        |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | Belgium: 12       |
| Country: Number of subjects enrolled | Denmark: 72       |
| Country: Number of subjects enrolled | Finland: 22       |
| Country: Number of subjects enrolled | Germany: 19       |
| Country: Number of subjects enrolled | United States: 39 |
| Worldwide total number of subjects   | 192               |
| EEA total number of subjects         | 147               |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 43  |
| From 65 to 84 years                       | 146 |
| 85 years and over                         | 3   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of the 257 subjects who signed the written informed consent form (IC), 192 subjects completed the screening and were enrolled in the study. For the 65 patients who were not eligible for participation, the major reason was BCR after the last definitive treatment, distant metastasis or locoregional recurrence.

### Period 1

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

Blinding implementation details:

Investigators, patients, and all study staff with direct patient contact were blinded to assignment to RV001V or placebo. The Interactive web response system IWRS assigned RV001V, or placebo based on a block randomization scheme.

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | RV001V group |

Arm description:

RV001 vaccine 0.1 mg/mL in water-in-oil (w/o) emulsion for injection containing RV001 and the adjuvant Montanide ISA 51 were administered to subjects in the V001V arm at a dose of 0.1 mg RV001

|  |                  |
|--|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | RV001            |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

The dose of RV001 0.1 mg was given as a subcutaneous injection

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe

|  |                  |
|--|------------------|
| Arm type                               | Placebo          |
| Investigational medicinal product name | Placebo vaccine  |
| Investigational medicinal product code |                  |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Subcutaneous use |

Dosage and administration details:

Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe

| <b>Number of subjects in period 1</b>              | RV001V group | Placebo |
|--|--------------|---------|
| Started  | 96           | 96      |
| Completed  | 51           | 48      |
| Not completed                                      | 45           | 48      |
| Consent withdrawn by subject                       | 1            | 1       |
| Physician decision                                 | 2            | -       |
| Adverse event, non-fatal                           | 1            | 2       |
| Death  | 1            | 1       |
| Primary analysis point reached prior to completion | 2            | 6       |
| Sponsor decision                                   | 1            | -       |
| Metastatic disease and/or PSA doubles              | 37           | -       |
| Metastatics disease and/or PSA doubles             | -            | 38      |

## Baseline characteristics

### Reporting groups

|                                |               |
|--------------------------------|---------------|
| Reporting group title          | Overall trial |
| Reporting group description: - |               |

| Reporting group values                             | Overall trial | Total |  |
|--|---------------|-------|--|
| Number of subjects                                 | 192           | 192   |  |
| Age categorical                                    |               |       |  |
| Units: Subjects                                    |               |       |  |
| In utero   |               | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) |               | 0     |  |
| Newborns (0-27 days)                               |               | 0     |  |
| Infants and toddlers (28 days-23 months)           |               | 0     |  |
| Children (2-11 years)                              |               | 0     |  |
| Adolescents (12-17 years)                          |               | 0     |  |
| Adults (18-64 years)                               |               | 0     |  |
| From 65-84 years                                   |               | 0     |  |
| 85 years and over                                  |               | 0     |  |
| Age continuous                                     |               |       |  |
| Units: years                                       |               |       |  |
| median   | 70            |       |  |
| full range (min-max)                               | 56 to 86      | -     |  |
| Gender categorical                                 |               |       |  |
| Units: Subjects                                    |               |       |  |
| Female   | 0             | 0     |  |
| Male   | 192           | 192   |  |

### Subject analysis sets

|                            |                             |
|----------------------------|-----------------------------|
| Subject analysis set title | Primary Analysis            |
| Subject analysis set type  | Modified intention-to-treat |

Subject analysis set description:

Strata combined and based on the primary analysis which were conducted when 88 events had occurred in the modified intention-to-treat (m-ITT) population

| Reporting group values                             | Primary Analysis |  |  |
|--|------------------|--|--|
| Number of subjects                                 | 185              |  |  |
| Age categorical                                    |                  |  |  |
| Units: Subjects                                    |                  |  |  |
| In utero   |                  |  |  |
| Preterm newborn infants (gestational age < 37 wks) |                  |  |  |
| Newborns (0-27 days)                               |                  |  |  |
| Infants and toddlers (28 days-23 months)           |                  |  |  |
| Children (2-11 years)                              |                  |  |  |
| Adolescents (12-17 years)                          |                  |  |  |

|  |     |  |  |
|--|-----|--|--|
| Adults (18-64 years)<br>From 65-84 years<br>85 years and over    |     |  |  |
| Age continuous<br>Units: years<br>median<br>full range (min-max) |     |  |  |
| Gender categorical<br>Units: Subjects                            |     |  |  |
| Female   | 0   |  |  |
| Male   | 185 |  |  |

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## End points

### End points reporting groups

|  |                             |
|--|-----------------------------|
| Reporting group title  | RV001V group                |
| Reporting group description:<br>RV001 vaccine 0.1 mg/mL in water-in-oil (w/o) emulsion for injection containing RV001 and the adjuvant Montanide ISA 51 were administered to subjects in the V001V arm at a dose of 0.1 mg RV001 |                             |
| Reporting group title  | Placebo                     |
| Reporting group description:<br>Placebo vaccine containing 50/50 mixture of adjuvant and sterile acetate buffered saline pH 3.5 in a 1-mL syringe  |                             |
| Subject analysis set title   | Primary Analysis            |
| Subject analysis set type  | Modified intention-to-treat |
| Subject analysis set description:<br>Strata combined and based on the primary analysis which were conducted when 88 events had occurred in the modified intention-to-treat (m-ITT) population                                    |                             |

### Primary: Primary endpoint

|   |                  |
|---|------------------|
| End point title   | Primary endpoint |
| End point description:<br>The primary endpoint was defined as the time from randomization until doubling of PSA from the baseline value, clinical recurrence or death from any cause, whichever occurred first. When the subject reached a primary endpoint, he continued into the extended follow up (E-FU) phase for safety monitoring until the study was terminated 36 months after first subject's first injection. At the time of the primary analysis all subjects who have not yet reached the primary endpoint continued into E-FU for safety until study termination. |                  |
| End point type  | Primary          |
| End point timeframe:<br>The primary endpoint was defined as the time from randomization until doubling of PSA from the baseline value   |                  |

| End point values                 | RV001V group     | Placebo           |  |  |
|----------------------------------|------------------|-------------------|--|--|
| Subject group type               | Reporting group  | Reporting group   |  |  |
| Number of subjects analysed      | 93               | 92                |  |  |
| Units: months                    |                  |                   |  |  |
| median (confidence interval 95%) |                  |                   |  |  |
| PSA doubling time                | 7.5 (5.9 to 9.2) | 9.3 (7.2 to 11.3) |  |  |

### Statistical analyses

|                            |                         |
|----------------------------|-------------------------|
| Statistical analysis title | Cox regression analysis |
| Comparison groups          | RV001V group v Placebo  |



|   |                    |
|---|--------------------|
| Number of subjects included in analysis | 185                |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | equivalence        |
| P-value                                 | = 0.1327           |
| Method                                  | Regression, Cox    |
| Parameter estimate                      | Hazard ratio (HR)  |
| Confidence interval                     |                    |
| level                                   | 95 %               |
| sides                                   | 2-sided            |
| lower limit                             | 0.91               |
| upper limit                             | 2.07               |
| Variability estimate                    | Standard deviation |
| Dispersion value                        | 1.37               |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Overall study period

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

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 25.0 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Safety population |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events                            | Safety population |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events |                   |  |  |
| subjects affected / exposed                       | 12 / 192 (6.25%)  |  |  |
| number of deaths (all causes)                     | 4                 |  |  |
| number of deaths resulting from adverse events    | 2                 |  |  |
| Injury, poisoning and procedural complications    |                   |  |  |
| Craniocerebral injury                             |                   |  |  |
| subjects affected / exposed                       | 1 / 192 (0.52%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 1             |  |  |
| Multiple fractures                                |                   |  |  |
| subjects affected / exposed                       | 1 / 192 (0.52%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |
| Rib fracture                                      |                   |  |  |
| subjects affected / exposed                       | 1 / 192 (0.52%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |
| Vascular disorders                                |                   |  |  |
| Lymphocele  |                   |  |  |
| subjects affected / exposed                       | 1 / 192 (0.52%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 1             |  |  |
| deaths causally related to treatment / all        | 0 / 0             |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Cardiac disorders                               |                 |  |  |
| Arrhythmia                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac arrest                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Nervous system disorders                        |                 |  |  |
| Cerebrovascular accident                        |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Incarcerated inguinal hernia                    |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Pneumonitis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Erysipelas                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonia legionella                            |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Streptococcal sepsis                            |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Metabolism and nutrition disorders              |                 |  |  |
| Diabetes mellitus inadequate control            |                 |  |  |
| subjects affected / exposed                     | 1 / 192 (0.52%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

| <b>Non-serious adverse events</b>                     | Safety population  |  |  |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 171 / 192 (89.06%) |  |  |
| Vascular disorders                                    |                    |  |  |
| Hypertension  |                    |  |  |
| subjects affected / exposed                           | 11 / 192 (5.73%)   |  |  |
| occurrences (all)                                     | 11                 |  |  |
| Nervous system disorders                              |                    |  |  |
| Dizziness   |                    |  |  |
| subjects affected / exposed                           | 18 / 192 (9.38%)   |  |  |
| occurrences (all)                                     | 18                 |  |  |
| Headache  |                    |  |  |
| subjects affected / exposed                           | 41 / 192 (21.35%)  |  |  |
| occurrences (all)                                     | 41                 |  |  |
| General disorders and administration site conditions  |                    |  |  |
| Fatigue   |                    |  |  |
| subjects affected / exposed                           | 47 / 192 (24.48%)  |  |  |
| occurrences (all)                                     | 47                 |  |  |
| Injection site erythema                               |                    |  |  |
| subjects affected / exposed                           | 36 / 192 (18.75%)  |  |  |
| occurrences (all)                                     | 36                 |  |  |
| Injection site mass                                   |                    |  |  |
| subjects affected / exposed                           | 11 / 192 (5.73%)   |  |  |
| occurrences (all)                                     | 11                 |  |  |
| Injection site pain                                   |                    |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| subjects affected / exposed<br>occurrences (all)  | 68 / 192 (35.42%)<br>68 |  |  |
| Injection site pruritus<br>subjects affected / exposed<br>occurrences (all)                                       | 42 / 192 (21.88%)<br>42 |  |  |
| Injection site reaction<br>subjects affected / exposed<br>occurrences (all)                                       | 35 / 192 (18.23%)<br>35 |  |  |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)                                       | 51 / 192 (26.56%)<br>51 |  |  |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                       | 12 / 192 (6.25%)<br>12  |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 11 / 192 (5.73%)<br>11  |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)      | 11 / 192 (5.73%)<br>11  |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 23 / 192 (11.98%)<br>23 |  |  |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 23 / 192 (11.98%)<br>23 |  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)   | 19 / 192 (9.90%)<br>19  |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 12 April 2019    | <p>Revision of protocol from V1.0 to V2.0</p> <ul style="list-style-type: none"><li>- Front page: Short protocol name BRaVac is added to front page</li><li>- Section 2.3 and 7.7.2: Exploratory endpoint C removed from protocol.</li><li>- Section 6.1: Collection of archival tumor slice has been removed from the protocol. This relates to the above reasons re. the exploratory endpoint.</li><li>- Section 6.1: Collection of oncology history including oncotype DX and radiation dose, in case the patient has received radiation therapy as part of previous curative treatment, has been added. This is based on recommendation from FDA received at a recent pre-IND meeting.</li><li>- Section 7.3 and 9.1.1: Specification of collection of AEs/SAEs during follow up and E-follow up. AEs/SAEs are collected for 3 months post End of Treatment visit.</li><li>- Section 9.11.1: Description of Dose Limiting Toxicities (DLTs) has been removed.</li><li>- Section 13.1: Precision of what can be considered source document in accordance with GCP.</li><li>- Section 14: Change in the publication strategy rec</li></ul> |
| 15 May 2019      | <p>Protocol V2.0 to V3.0</p> <ul style="list-style-type: none"><li>- Synopsis: number of sites reduced from 35 to 30</li><li>- Section 4.3; Selection/Enrollment of Patients; Amended to clarify that only inclusion/exclusion data relevant to randomisation in IWRS will be entered in IWRS</li><li>- Section 5.6 Blinding and Unblinding Method; updated to clarify that the investigator can unblind a patient with our first speaking to the Medical Monitor. Where possible the Medical monitor should be consulted.</li><li>- Section 9.1.1 AE Monitoring: updated to clarify that any untoward medical occurrence event that occurs after screening and before the first dose of IP will be recorded as a S(AE)</li><li>- Section 9.1.2 Reporting of Adverse Events; the following text was added;</li><li>- Section 9.2.1 Adverse Events; clarification that surgical procedure (pre-planned) is not considered an AE</li><li>- 9.8 Reporting Serious Adverse Events, the following sentence was deleted;</li></ul>   |
| 13 November 2019 | <p>Protocol V3.0 to V4.0</p> <ul style="list-style-type: none"><li>- Specification of primary end point further with method for calculating PSA doubling</li><li>- Slight revision of secondary and exploratory endpoint</li><li>- Adaption of inclusion criteria</li><li>- Adaption of exclusion criteria</li><li>- Adding a specific benefit-risk assessment section</li><li>- Safety monitorin process updated</li><li>- DMC section updated</li></ul>  |
| 08 July 2020     | <p>Protocol V4.0 to V4.0 with Amendment #1</p> <ul style="list-style-type: none"><li>- Removal of Gleason score from study inclusion criteria and enrolment of patients based on PSA doubling time, to allow for inclusion of additional patients potentially benefitting from treatment</li><li>- Collection of highest historical Gleason score at baseline for each patient added to assessments and procedures</li></ul>   |

|               |  |
|---------------|--|
| 26 March 2021 | Protocol V4.0 with Amendment #1 to V4.0 with Amendments #1 and #2<br>- Correction of incorrect hemoglobin value<br>- COVID-19 vaccination allowed during RV001 priming and maintenance treatment periods with down to 6 days following each injection<br>- COVID-19 vaccination excluded from prohibited medications<br>- Rewording to remove unnecessary restriction of standard diagnostics in tumor assessments<br>- Deletion of Annex 1: Gleason Score, as no longer applicable following amendment #1 to v4.0 |
|---------------|--|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported