



## Clinical trial results:

**A phase III, double-blind, randomized, placebo-controlled multicentre clinical trial to assess the efficacy and safety of VPM1002 in reducing healthcare professionals' absenteeism in the SARS-CoV-2 pandemic by modulating the immune system**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-001376-15 |
| Trial protocol           | DE             |
| Global end of trial date | 28 April 2021  |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 06 November 2021 |
| First version publication date | 06 November 2021 |

### Trial information

#### Trial identification

|                       |                    |
|-----------------------|--------------------|
| Sponsor protocol code | VPM1002-DE-3.06CoV |
|-----------------------|--------------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04387409 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Vakzine Projekt Management GmbH  |
| Sponsor organisation address | Mellendorfer Str. 9, Hannover, Germany, 30625  |
| Public contact               | Clinical Trial Information, Vakzine Projekt Management GmbH, +49 5111699080, info@vakzine-manager.de |
| Scientific contact           | Clinical Trial Information, Vakzine Projekt Management GmbH, +49 5111699080, info@vakzine-manager.de |

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 June 2021  |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 28 April 2021 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 28 April 2021 |
| Was the trial ended prematurely?                     | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

To assess the reduction of absenteeism among healthcare professionals with direct patient contacts during the pandemic phase of COVID-19

Protection of trial subjects:

The trial was conducted in accordance with GCP ICH-E6(R2) , GCP-V, EU Directives 2005/28/EC and 2001/20/EC, the ethical principles set forth in the Declaration of Helsinki, and local regulatory requirements. Each participating investigator/institution was responsible for assuring that the protocol, the associated informed consent documents, and trial-related documents were reviewed and approved by a local independent ethics committee (IEC) prior to the implementation of the protocol.

Prior to any trial-related screening procedures being performed, informed consent was obtained from each subject before enrollment in the trial. The procedures to explain the meaning of informed consent to the subject to obtain their consent complied with current IEC and legal requirements, the ICH-GCP Guidelines and the ethical principles in the Declaration of Helsinki. Consent for processing personal data was also obtained from the caretaker of the study subject.

Subjects were informed that their participation was voluntary and that they had the right to withdraw from the trial at any time and for any reason without any disadvantages.

Only subjects that met all inclusion criteria and none of the exclusion criteria were enrolled in the study.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 25 May 2020 |
| 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 | Germany: 59 |
| Worldwide total number of subjects   | 59          |
| EEA total number of subjects         | 59          |

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          | 0 |

|                           |    |
|---------------------------|----|
| months)                   |    |
| Children (2-11 years)     | 0  |
| Adolescents (12-17 years) | 0  |
| Adults (18-64 years)      | 57 |
| From 65 to 84 years       | 2  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at 2 study centers in Germany. The first subject signed the informed consent on 25-May-2020 and the last subject completed the trial on 28-Apr-2021. Enrolment stop was on 17-Sep-2020.

### Pre-assignment

Screening details:

At 2 centers, 59 subjects were randomized, 29 to treatment with VPM1002 and 30 to treatment with placebo.

### 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:

The vaccine preparation was done by designated unblinded personnel who did not participate in any of the clinical trial evaluations. The administration was done by blinded trial staff. The unblinded pharmacist, or other qualified site staff, prepared the vaccine out of view of the subject and the site staff who administered the vaccine. The syringes were masked with a colored translucent wrapping before administration.

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | VPM1002 |

Arm description:

The subjects received a single intradermal injection of VPM1002.

|  |                      |
|--|----------------------|
| Arm type                               | Experimental         |
| Investigational medicinal product name | VPM1002              |
| Investigational medicinal product code |                      |
| Other name                             |                      |
| Pharmaceutical forms                   | Powder for injection |
| Routes of administration               | Intradermal use      |

Dosage and administration details:

The subjects received an intradermal injection of 0.1 mL VPM1002 containing 2-8 x 10e5 colony forming units. The active ingredient of VPM1002 is Mycobacterium bovis rBCGΔureC::hly.

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

Arm description:

The subjects received a single intradermal injection of placebo.

|  |                        |
|--|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | Placebo                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intradermal use        |

Dosage and administration details:

The subjects received an intradermal injection of 0.1 mL of placebo consisting of physiological saline.

| <b>Number of subjects in period 1</b> | VPM1002 | Placebo |
|---------------------------------------|---------|---------|
| Started                               | 29      | 30      |
| Completed                             | 27      | 30      |
| Not completed                         | 2       | 0       |
| Lost to follow-up                     | 2       | -       |

## Baseline characteristics

### Reporting groups

|  |         |
|--|---------|
| Reporting group title  | VPM1002 |
| Reporting group description:                                     |         |
| The subjects received a single intradermal injection of VPM1002. |         |
| Reporting group title  | Placebo |
| Reporting group description:                                     |         |
| The subjects received a single intradermal injection of placebo. |         |

| Reporting group values | VPM1002 | Placebo | Total |
|------------------------|---------|---------|-------|
| Number of subjects     | 29      | 30      | 59    |
| Age categorical        |         |         |       |
| Units: Subjects        |         |         |       |

|                      |          |          |    |
|----------------------|----------|----------|----|
| Age continuous       |          |          |    |
| Units: years         |          |          |    |
| median               | 47.0     | 52.5     |    |
| full range (min-max) | 21 to 62 | 27 to 68 | -  |
| Gender categorical   |          |          |    |
| Units: Subjects      |          |          |    |
| Female               | 16       | 17       | 33 |
| Male                 | 13       | 13       | 26 |

## End points

### End points reporting groups

|                              |  |
|------------------------------|--|
| Reporting group title        | VPM1002  |
| Reporting group description: | The subjects received a single intradermal injection of VPM1002. |
| Reporting group title        | Placebo  |
| Reporting group description: | The subjects received a single intradermal injection of placebo. |

### Primary: Number of days absent from work due to respiratory disease (with or without documented SARS-CoV-2 infection)

|                 |   |
|-----------------|---|
| End point title | Number of days absent from work due to respiratory disease (with or without documented SARS-CoV-2 infection) <sup>[1]</sup> |
|-----------------|---|

End point description:

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

End point timeframe:

240 days

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: No statistical analysis was done, because the trial was prematurely terminated.

| End point values                     | VPM1002         | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 29              | 30              |  |  |
| Units: days                          |                 |                 |  |  |
| arithmetic mean (standard deviation) | 1.4 (± 3.6)     | 1.1 (± 2.8)     |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

On or after the date of the investigational medicinal product (IMP) administration until 240 days after administration.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | VPM1002 |
|-----------------------|---------|

Reporting group description:

The subjects received a single intradermal injection of VPM1002.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

The subjects received a single intradermal injection of placebo.

| <b>Serious adverse events</b>                     | VPM1002        | Placebo        |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 29 (0.00%) | 1 / 30 (3.33%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |
| Nervous system disorders                          |                |                |  |
| Neuralgic amyotrophy                              |                |                |  |
| subjects affected / exposed                       | 0 / 29 (0.00%) | 1 / 30 (3.33%) |  |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | VPM1002          | Placebo          |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 26 / 29 (89.66%) | 24 / 30 (80.00%) |  |
| Injury, poisoning and procedural complications        |                  |                  |  |
| Vaccination complication                              |                  |                  |  |
| subjects affected / exposed                           | 3 / 29 (10.34%)  | 7 / 30 (23.33%)  |  |
| occurrences (all)                                     | 3                | 18               |  |
| Nervous system disorders                              |                  |                  |  |

|  |                  |                 |  |
|--|------------------|-----------------|--|
| Dizziness  |                  |                 |  |
| subjects affected / exposed                          | 1 / 29 (3.45%)   | 2 / 30 (6.67%)  |  |
| occurrences (all)                                    | 1                | 2               |  |
| Headache   |                  |                 |  |
| subjects affected / exposed                          | 6 / 29 (20.69%)  | 9 / 30 (30.00%) |  |
| occurrences (all)                                    | 8                | 12              |  |
| Migraine   |                  |                 |  |
| subjects affected / exposed                          | 1 / 29 (3.45%)   | 2 / 30 (6.67%)  |  |
| occurrences (all)                                    | 3                | 6               |  |
| General disorders and administration site conditions |                  |                 |  |
| Influenza like illness                               |                  |                 |  |
| subjects affected / exposed                          | 2 / 29 (6.90%)   | 1 / 30 (3.33%)  |  |
| occurrences (all)                                    | 2                | 1               |  |
| Injection site erythema                              |                  |                 |  |
| subjects affected / exposed                          | 14 / 29 (48.28%) | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 18               | 0               |  |
| Injection site induration                            |                  |                 |  |
| subjects affected / exposed                          | 6 / 29 (20.69%)  | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 6                | 0               |  |
| Injection site inflammation                          |                  |                 |  |
| subjects affected / exposed                          | 2 / 29 (6.90%)   | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 3                | 0               |  |
| Injection site pain                                  |                  |                 |  |
| subjects affected / exposed                          | 10 / 29 (34.48%) | 1 / 30 (3.33%)  |  |
| occurrences (all)                                    | 10               | 1               |  |
| Injection site pruritus                              |                  |                 |  |
| subjects affected / exposed                          | 5 / 29 (17.24%)  | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 5                | 0               |  |
| Injection site reaction                              |                  |                 |  |
| subjects affected / exposed                          | 2 / 29 (6.90%)   | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 2                | 0               |  |
| Injection site swelling                              |                  |                 |  |
| subjects affected / exposed                          | 9 / 29 (31.03%)  | 0 / 30 (0.00%)  |  |
| occurrences (all)                                    | 10               | 0               |  |
| Injection site vesicles                              |                  |                 |  |

|   |                      |                       |  |
|---|----------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)                          | 2 / 29 (6.90%)<br>2  | 0 / 30 (0.00%)<br>0   |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)               | 2 / 29 (6.90%)<br>2  | 2 / 30 (6.67%)<br>2   |  |
| Vaccination site pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 29 (0.00%)<br>0  | 3 / 30 (10.00%)<br>3  |  |
| Gastrointestinal disorders  |                      |                       |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)             | 2 / 29 (6.90%)<br>3  | 5 / 30 (16.67%)<br>6  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                | 1 / 29 (3.45%)<br>1  | 4 / 30 (13.33%)<br>6  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)              | 0 / 29 (0.00%)<br>0  | 2 / 30 (6.67%)<br>2   |  |
| Respiratory, thoracic and mediastinal disorders                           |                      |                       |  |
| Cough<br>subjects affected / exposed<br>occurrences (all)                 | 3 / 29 (10.34%)<br>3 | 4 / 30 (13.33%)<br>4  |  |
| Dyspnoea<br>subjects affected / exposed<br>occurrences (all)              | 0 / 29 (0.00%)<br>0  | 2 / 30 (6.67%)<br>2   |  |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)    | 4 / 29 (13.79%)<br>5 | 6 / 30 (20.00%)<br>14 |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)           | 2 / 29 (6.90%)<br>2  | 0 / 30 (0.00%)<br>0   |  |
| Musculoskeletal and connective tissue disorders                           |                      |                       |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)             | 2 / 29 (6.90%)<br>3  | 6 / 30 (20.00%)<br>6  |  |
| Myalgia   |                      |                       |  |

|   |                      |                      |  |
|---|----------------------|----------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 0 / 29 (0.00%)<br>0  | 2 / 30 (6.67%)<br>2  |  |
| Neck pain<br>subjects affected / exposed<br>occurrences (all)                               | 2 / 29 (6.90%)<br>3  | 1 / 30 (3.33%)<br>2  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)                       | 2 / 29 (6.90%)<br>2  | 3 / 30 (10.00%)<br>3 |  |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all) | 2 / 29 (6.90%)<br>2  | 3 / 30 (10.00%)<br>3 |  |
| Injection site abscess<br>subjects affected / exposed<br>occurrences (all)                  | 6 / 29 (20.69%)<br>6 | 0 / 30 (0.00%)<br>0  |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                         | 5 / 29 (17.24%)<br>7 | 4 / 30 (13.33%)<br>5 |  |
| Rhinitis<br>subjects affected / exposed<br>occurrences (all)                                | 3 / 29 (10.34%)<br>3 | 5 / 30 (16.67%)<br>5 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment   |
|----------------|---|
| 02 June 2020   | Relevant changes introduced in protocol Version 4.0 dated 02-Jun-2020 compared with Version 3.0 (first protocol version under which subjects were enrolled, dated 06-May-2020) were: <ul style="list-style-type: none"><li>• The inclusion criterion "hospital personnel with expected high SARS-CoV-2 exposure" was changed to "healthcare professionals taking care of potentially SARS-CoV-2-infected patients".</li><li>• The exclusion criterion "Participation of subject in another study within 30 days before screening and during this study" was changed to "Participation of subject in another interventional study within 30 days before screening".</li><li>• The exclusion criterion "employed to the hospital &lt;22 hours per week" was changed to "employment of less than 50% of a full-time equivalent".</li><li>• A per-protocol analysis set was defined and added for the sensitivity analysis of the primary endpoint.</li></ul> |
| 11 August 2020 | Relevant changes introduced in Version 5.0 dated 11-Aug-2020 compared with Version 4.0 included: <ul style="list-style-type: none"><li>• Added that subjects who dropped out before IMP administration would be replaced</li><li>• Clarified that documentation of body temperature, adverse events, and concomitant medications in a daily diary was optional</li></ul>  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to an insufficient recruitment rate and premature termination of the trial, only 59 of the originally planned 1200 subjects were analyzed. Therefore, no meaningful conclusions can be drawn for the efficacy of VPM1002 vaccination.

Notes: