



## Clinical trial results:

**A multi-centre, open-label trial evaluating efficacy, safety and pharmacokinetics of nonacog beta pegol when used for treatment and prophylaxis of bleeding episodes in Chinese patients with haemophilia B.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-004947-25 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 11 May 2024    |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 27 November 2024 |
| First version publication date | 27 November 2024 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | NN7999-4670 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |                 |
|------------------------------------|-----------------|
| ISRCTN number                      | -               |
| ClinicalTrials.gov id (NCT number) | NCT05365217     |
| WHO universal trial number (UTN)   | U1111-1260-0438 |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Novo Nordisk A/S   |
| Sponsor organisation address | Novo Alle, Bagsvaerd, Denmark, 2880  |
| Public contact               | Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.com |
| Scientific contact           | Clinical Reporting Office (2834), Novo Nordisk A/S, clinicaltrials@novonordisk.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? | Yes |

Notes:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 28 June 2024 |
| Is this the analysis of the primary completion data? | No           |

|                                  |             |
|----------------------------------|-------------|
| Global end of trial reached?     | Yes         |
| Global end of trial date         | 11 May 2024 |
| Was the trial ended prematurely? | No          |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the clinical efficacy of nonacog beta pegol in haemostasis (treatment of bleeding episodes during on-demand and prophylaxis [PPX]) in Chinese patients aged 12-70 years with moderate to severe haemophilia B.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (Oct 2013) and International Council for Humanization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice, including archiving of essential documents (May 1996) and EN International Organisation for Standardisation (ISO) 14155 Part 1 and 2 and Food and Drug Administration (FDA) 21 US Code of Federal Regulations (CFR) 312.120.

Background therapy:

NA

Evidence for comparator:

NA

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 18 May 2022 |
| 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 | China: 30 |
| Worldwide total number of subjects   | 30        |
| 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)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 5  |
| Adults (18-64 years)                      | 25 |

|                     |   |
|---------------------|---|
| From 65 to 84 years | 0 |
| 85 years and over   | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This trial was conducted at 15 sites that enrolled subjects in 1 country (China mainland).

### Pre-assignment

Screening details:

A total of 30 subjects were exposed to trial products, of which 15 subjects were in Arm A (on demand/Prophylaxis) treatment group and 15 in Arm B (Prophylaxis) treatment group.

### Period 1

|                              |                    |
|------------------------------|--------------------|
| Period 1 title               | Treatment Period 1 |
| Is this the baseline period? | Yes                |
| Allocation method            | Not applicable     |
| Blinding used                | Not blinded        |

### Arms

|                              |                                       |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes                                   |
| <b>Arm title</b>             | Arm A: Nonacog beta pegol (On-demand) |

Arm description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | N9-GP                                      |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder for solution for injection/infusion |
| Routes of administration               | Intravenous use                            |

Dosage and administration details:

Subjects were administered nonacog beta pegol 40 IU/kg for mild or moderate bleeds and 80 IU/kg for severe bleeds.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Arm B: Nonacog beta pegol (Prophylaxis) |
|------------------|---|

Arm description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | N9-GP                                      |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder for solution for injection/infusion |
| Routes of administration               | Intravenous use                            |

Dosage and administration details:

Subjects received prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly.

| Number of subjects in period 1 | Arm A: Nonacog beta pegol (On-demand) | Arm B: Nonacog beta pegol (Prophylaxis) |
|--------------------------------|---------------------------------------|---|
| Started                        | 15                                    | 15                                      |
| Completed                      | 14                                    | 15                                      |
| Not completed                  | 1                                     | 0                                       |
| Consent withdrawn by subject   | 1                                     | -                                       |

## Period 2

|                              |                    |
|------------------------------|--------------------|
| Period 2 title               | Treatment Period 2 |
| Is this the baseline period? | No                 |
| Allocation method            | Not applicable     |
| Blinding used                | Not blinded        |

## Arms

|                              |   |
|------------------------------|---|
| Are arms mutually exclusive? | Yes                                     |
| <b>Arm title</b>             | Arm A: Nonacog beta pegol (Prophylaxis) |

### Arm description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | N9-GP                                      |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder for solution for injection/infusion |
| Routes of administration               | Intravenous use                            |

### Dosage and administration details:

Subjects received nonacog beta pegol weekly intravenous dose of 40 IU/kg to prevent bleeding episodes.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Arm B: Nonacog beta pegol (Prophylaxis) |
|------------------|---|

### Arm description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | N9-GP                                      |
| Investigational medicinal product code |  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder for solution for injection/infusion |
| Routes of administration               | Intravenous use                            |

### Dosage and administration details:

Subjects received prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly.

| <b>Number of subjects in period 2</b> | Arm A: Nonacog<br>beta pegol<br>(Prophylaxis) | Arm B: Nonacog<br>beta pegol<br>(Prophylaxis) |
|---------------------------------------|---|---|
| Started                               | 14  | 15  |
| Completed                             | 14  | 15  |

## Baseline characteristics

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Arm A: Nonacog beta pegol (On-demand) |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled.

|                       |   |
|-----------------------|---|
| Reporting group title | Arm B: Nonacog beta pegol (Prophylaxis) |
|-----------------------|---|

Reporting group description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

| Reporting group values                             | Arm A: Nonacog beta pegol (On-demand) | Arm B: Nonacog beta pegol (Prophylaxis) | Total |
|--|---------------------------------------|---|-------|
| Number of subjects                                 | 15                                    | 15                                      | 30    |
| Age Categorical                                    |                                       |   |       |
| Units: Subjects                                    |                                       |   |       |
| In utero   | 0                                     | 0                                       | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                                     | 0                                       | 0     |
| Newborns (0-27 days)                               | 0                                     | 0                                       | 0     |
| Infants and toddlers (28 days-23 months)           | 0                                     | 0                                       | 0     |
| Children (2-11 years)                              | 0                                     | 0                                       | 0     |
| Adolescents (12-17 years)                          | 1                                     | 4                                       | 5     |
| Adults (18-64 years)                               | 14                                    | 11                                      | 25    |
| From 65-84 years                                   | 0                                     | 0                                       | 0     |
| 85 years and over                                  | 0                                     | 0                                       | 0     |
| Age Continuous                                     |                                       |   |       |
| Units: years                                       |                                       |   |       |
| arithmetic mean                                    | 29.9                                  | 26.9                                    |       |
| standard deviation                                 | ± 7.7                                 | ± 9.7                                   | -     |
| Gender Categorical                                 |                                       |   |       |
| Units: Subjects                                    |                                       |   |       |
| Female   | 0                                     | 0                                       | 0     |
| Male   | 15                                    | 15                                      | 30    |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Arm A: Nonacog beta pegol (On-demand)   |
| Reporting group description:<br>Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 exposure days (EDs) to nonacog beta pegol in the entire trial were fulfilled. |   |
| Reporting group title  | Arm B: Nonacog beta pegol (Prophylaxis) |
| Reporting group description:<br>Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.   |   |
| Reporting group title  | Arm A: Nonacog beta pegol (Prophylaxis) |
| Reporting group description:<br>Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.                 |   |
| Reporting group title  | Arm B: Nonacog beta pegol (Prophylaxis) |
| Reporting group description:<br>Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.   |   |
| Subject analysis set title   | Arm B: Nonacog beta pegol (Prophylaxis) |
| Subject analysis set type  | Full analysis                           |
| Subject analysis set description:<br>Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.  |   |

### Primary: Haemostatic Effect of Nonacog beta pegol when used for Treatment of Bleeding Episodes During on Demand and Prophylaxis (PPX)

|   |  |
|---|--|
| End point title   | Haemostatic Effect of Nonacog beta pegol when used for Treatment of Bleeding Episodes During on Demand and Prophylaxis (PPX) <sup>[1][2]</sup> |
| End point description:<br>Haemostatic effect of N8-GP for treatment of bleeding episodes was assessed by 4-point response scale: none, moderate, good or excellent. Evaluation during trial was done by subject and/or parent(s)/caregiver within approximately 8 hours after a single injection as follows: Excellent: Abrupt pain relief and/or clear improvement in objective signs of bleeding within approximately 8 hrs after a single injection; Good: Definite pain relief and/or improvement in signs of bleeding within approximately 8 hrs after a single injection, but possibly requiring more than one injection for complete resolution; Moderate: Probable or slight beneficial effect within approximately 8 hours after the first injection, but usually requiring more than one injection; None: No improvement, or worsening of symptoms. Results were based on the FAS which included all subjects exposed to N9-GP in this trial. |  |
| End point type  | Primary  |
| End point timeframe:<br>From start of treatment (week 0) until end of treatment (up to week 50)   |  |

#### 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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

[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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

| <b>End point values</b>     | Arm A:<br>Nonacog beta<br>pegol (On-<br>demand) | Arm A:<br>Nonacog beta<br>pegol<br>(Prophylaxis) | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group                                 | Reporting group                                  | Subject analysis set                             |  |
| Number of subjects analysed | 15  | 14   | 15   |  |
| Units: Bleeding Episodes    |   |  |  |  |
| Excellent                   | 195   | 11   | 26   |  |
| Good                        | 8   | 1  | 16   |  |
| Moderate                    | 3   | 0  | 1  |  |
| None                        | 1   | 0  | 0  |  |
| Missing                     | 0   | 0  | 0  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Treated Bleeding Episodes During Prophylaxis (PPX) Treatment (Arm B only)

|                 |   |
|-----------------|---|
| End point title | Number of Treated Bleeding Episodes During Prophylaxis (PPX) Treatment (Arm B only) |
|-----------------|---|

End point description:

Number of bleeding episodes per year data is reported. Annualised bleeding rate (ABR) is the number of bleeding episodes per year. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

| <b>End point values</b>               | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
|---------------------------------------|--|--|--|--|
| Subject group type                    | Subject analysis set                             |  |  |  |
| Number of subjects analysed           | 15   |  |  |  |
| Units: Bleeds per subject per year    |  |  |  |  |
| median (inter-quartile range (Q1-Q3)) | 3.12 (0.00 to 4.23)                              |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: FIX Trough Levels During Prophylaxis (PPX) Treatment (Arm B only)

|                 |   |
|-----------------|---|
| End point title | FIX Trough Levels During Prophylaxis (PPX) Treatment (Arm B only) |
|-----------------|---|

End point description:

Trough levels of FVIII was reported for all participants who received prophylaxis treatment. Chromogenic assay was performed with N8-GP product specific standard (PSS) as a calibrator. The analysis is based on a mixed model on the log transformed plasma FVIII activity with age group as fixed effect and subject as a random effect. The mean trough is presented back-transformed to the natural scale. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

|   |  |  |  |  |
|---|--|--|--|--|
| <b>End point values</b>                         | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
| Subject group type                              | Subject analysis set                             |  |  |  |
| Number of subjects analysed                     | 15   |  |  |  |
| Units: International unit per milliliter(IU/mL) |  |  |  |  |
| arithmetic mean (confidence interval 95%)       | 0.298 (0.260 to 0.341)                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Consumption of Nonacog beta pegol for Prophylaxis (PPX) Treatment (Arm B only)

|                 |  |
|-----------------|--|
| End point title | Consumption of Nonacog beta pegol for Prophylaxis (PPX) Treatment (Arm B only) |
|-----------------|--|

End point description:

The mean consumption of N9-GP for prophylaxis per year per subject was reported and it was measured in international units per kilogram per year (IU/kg/year). Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

|                                      |  |  |  |  |
|--------------------------------------|--|--|--|--|
| <b>End point values</b>              | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
| Subject group type                   | Subject analysis set                             |  |  |  |
| Number of subjects analysed          | 15   |  |  |  |
| Units: IU/kg per year                |  |  |  |  |
| arithmetic mean (standard deviation) | 2212.3 (±  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Consumption of Nonacog beta pegol for Treatment of Bleeding Episodes

|                 |   |
|-----------------|---|
| End point title | Consumption of Nonacog beta pegol for Treatment of Bleeding Episodes <sup>[3]</sup> |
|-----------------|---|

End point description:

The mean number of injections of N9-GP used for treatment of a bleed from start to stop of a bleed was reported and it was measured in international units per kilogram per bleed (IU/kg/bleed). Results were based on the FAS which included all subjects exposed to N8-GP in this trial. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

Notes:

[3] - 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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

| End point values                     | Arm A:<br>Nonacog beta<br>pegol (On-<br>demand) | Arm A:<br>Nonacog beta<br>pegol<br>(Prophylaxis) | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |
|--------------------------------------|---|--|--|--|
| Subject group type                   | Reporting group                                 | Reporting group                                  | Subject analysis set                             |  |
| Number of subjects analysed          | 15  | 14   | 15   |  |
| Units: IU/kg per bleed               |   |  |  |  |
| arithmetic mean (standard deviation) | 42.5 (± 1.0)                                    | 41.4 (± 1.1)                                     | 41.6 (± 0.4)                                     |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Inhibitory Antibodies Against FIX Defined as Titre ≥0.6 Bethesda Units (BU)

|                 |  |
|-----------------|--|
| End point title | Number of Subjects with Inhibitory Antibodies Against FIX Defined as Titre ≥0.6 Bethesda Units (BU) <sup>[4]</sup> |
|-----------------|--|

End point description:

Percentage of subjects who developed inhibitory antibodies (IA) against FVIII was presented. A subject was said to have FVIII-inhibitors if two consecutive tests, preferably within 2 weeks, were positive (greater than or equal to (≥) 0.6 bethesda unit (BU)). For the calculation of the inhibitor rate the numerator was included for all subjects with neutralising antibodies while the denominator was included for all subjects with a minimum of 50 exposures plus any subjects with less than 50 exposures but with neutralising inhibitor. Results were based on the FAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

Notes:

[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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

| End point values                  | Arm A:<br>Nonacog beta<br>pegol (On-<br>demand) | Arm A:<br>Nonacog beta<br>pegol<br>(Prophylaxis) | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                                 | Reporting group                                  | Subject analysis set                             |  |
| Number of subjects analysed       | 15  | 14   | 15   |  |
| Units: Number of subjects with IA | 0   | 0  | 0  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Adverse Events (AEs)

|                 |   |
|-----------------|---|
| End point title | Number of Adverse Events (AEs) <sup>[5]</sup> |
|-----------------|---|

End point description:

An adverse event (AE) was defined as any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a product, whether or not considered related to the product. All presented AEs are treatment-emergent. A treatment-emergent adverse event was defined as an event with onset after first N8-GP administration. Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

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

End point timeframe:

From start of treatment (week 0) until end of treatment (week 50)

Notes:

[5] - 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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

| End point values            | Arm A:<br>Nonacog beta<br>pegol (On-<br>demand) | Arm A:<br>Nonacog beta<br>pegol<br>(Prophylaxis) | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group                                 | Reporting group                                  | Subject analysis set                             |  |
| Number of subjects analysed | 15  | 14   | 15   |  |
| Units: Events               | 16  | 19   | 29   |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Serious Adverse events (SAEs)

|                 |  |
|-----------------|--|
| End point title | Number of Serious Adverse events (SAEs) <sup>[6]</sup> |
|-----------------|--|

**End point description:**

A serious adverse event (SAE) is defined as any untoward medical occurrence that at any dose results in death, or is life-threatening, or requires inpatient hospitalization or causes prolongation of existing hospitalization results in persistent or significant disability/incapacity, or may have caused a congenital anomaly/birth defect, or requires intervention to prevent permanent impairment or damage. All presented SAEs are treatment-emergent (any serious adverse events which occurred after trial product administration). Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

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

**End point timeframe:**

From start of treatment (week 0) until end of treatment (week 50)

**Notes:**

[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: Not all the arms were evaluated for this end point. Data is provided for the arms evaluated for this end point.

| End point values            | Arm A:<br>Nonacog beta<br>pegol (On-<br>demand) | Arm A:<br>Nonacog beta<br>pegol<br>(Prophylaxis) | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Reporting group                                 | Reporting group                                  | Subject analysis set                             |  |
| Number of subjects analysed | 15  | 14   | 15   |  |
| Units: Events               | 0   | 1  | 0  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Incremental Recovery (IR) (Arm B only)**

|                 |  |
|-----------------|--|
| End point title | Incremental Recovery (IR) (Arm B only) |
|-----------------|--|

**End point description:**

The incremental recovery was calculated by subtracting the FVIII activity (IU/mL) measured in plasma at time 0 from that measured at time 30 min after dosing and dividing this difference by the dose injected at time 0 expressed as IU/kg body weight. FVIII activity was measured with a chromogenic assay. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

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

**End point timeframe:**

Single-dose: 30±10 minutes post injection at week 0, Steady-state: 30±10 minutes post injection at week 12

| End point values                                    | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                             |  |  |  |
| Number of subjects analysed                         | 15   |  |  |  |
| Units: (IU/mL)/(IU/kg)                              |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Week 0 (n=14)                                       | 0.0182 (±<br>18.9550)                            |  |  |  |

|                |                         |  |  |  |
|----------------|-------------------------|--|--|--|
| Week 12 (n=15) | 0.0192 ( $\pm$ 17.2668) |  |  |  |
|----------------|-------------------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Terminal Half-life ( $t_{1/2}$ ) (Arm B only)

|                 |   |
|-----------------|---|
| End point title | Terminal Half-life ( $t_{1/2}$ ) (Arm B only) |
|-----------------|---|

End point description:

Terminal half life was calculated as  $\ln(2)/\lambda_z$ ; where  $\lambda_z$  is the terminal elimination rate constant. The terminal elimination rate constant was estimated using linear regression on the terminal part of the log (activity) versus time profile. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

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

End point timeframe:

Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12

|   |  |  |  |  |
|---|--|--|--|--|
| <b>End point values</b>                             | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
| Subject group type                                  | Subject analysis set                             |  |  |  |
| Number of subjects analysed                         | 15   |  |  |  |
| Units: hour   |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Week 0 (n= 13)                                      | 90.868 ( $\pm$ 13.535)                           |  |  |  |
| Week 12 (n=15)                                      | 90.738 ( $\pm$ 21.581)                           |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Clearance (CL) (Arm B only)

|                 |                             |
|-----------------|-----------------------------|
| End point title | Clearance (CL) (Arm B only) |
|-----------------|-----------------------------|

End point description:

Clearance (CL) of drug after intravenous administration was reported. Clearance was calculated using the formula  $CL = \text{Dose} / AUC(0-\text{inf})$  for single dose and  $CL = \text{Dose} / AUC(0-96) \text{ h}$  for steady state. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints.

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

End point timeframe:

Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12

| End point values                                    | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                             |  |  |  |
| Number of subjects analysed                         | 15   |  |  |  |
| Units: mL/h/kg                                      |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Week 0 (n=13)                                       | 0.536 (± 22.143)                                 |  |  |  |
| Week 12 (n=15)                                      | 0.487 (± 26.552)                                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Area Under the Curve (AUC) (Arm B only)

|  |   |
|--|---|
| End point title  | Area Under the Curve (AUC) (Arm B only) |
| End point description:<br>Area under the plasma activity versus time profile from time zero to 168 hours (AUC0-168h) was measured. The PK analysis set included sub-set of subjects from FAS who were included for PK assessments. Number analysed = Number of subjects with available data for specific timepoints. |   |
| End point type   | Secondary                               |
| End point timeframe:<br>Single-dose: 0-168 hours post injection at week 0, Steady-state: 0-168 hours post injection at week 12   |   |

| End point values                                    | Arm B:<br>Nonacog beta<br>pegol<br>(Prophylaxis) |  |  |  |
|---|--|--|--|--|
| Subject group type                                  | Subject analysis set                             |  |  |  |
| Number of subjects analysed                         | 15   |  |  |  |
| Units: h·IU/mL                                      |  |  |  |  |
| geometric mean (geometric coefficient of variation) |  |  |  |  |
| Week 0 (n=14)                                       | 51.856 (± 30.134)                                |  |  |  |
| Week 12 (n=15)                                      | 92.914 (± 21.725)                                |  |  |  |

## Statistical analyses

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From start of treatment (Week 0) until end of trial (Week 54)

Adverse event reporting additional description:

All presented AEs are treatment-emergent adverse events. A TEAE was defined as an event with onset after first N8-GP administration. Results were based on the SAS which included all subjects exposed to N9-GP in this trial.

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 27 |
|--------------------|----|

### Reporting groups

|                       |                                       |
|-----------------------|---------------------------------------|
| Reporting group title | Arm A: Nonacog beta pegol (On-demand) |
|-----------------------|---------------------------------------|

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 international unit per kilogram (IU/kg) for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

|                       |   |
|-----------------------|---|
| Reporting group title | Arm B: Nonacog beta pegol (Prophylaxis) |
|-----------------------|---|

Reporting group description:

Subjects received intravenous injections of 40 IU/kg nonacog beta pegol once weekly (prophylactic treatment with nonacog beta pegol at a dose of 40 IU/kg weekly) until 50 EDs (including treatment of breakthrough bleeds) and 50 weeks in the entire trial were fulfilled.

|                       |   |
|-----------------------|---|
| Reporting group title | Arm A: Nonacog beta pegol (Prophylaxis) |
|-----------------------|---|

Reporting group description:

Subjects received intravenous injections of nonacog beta pegol (on-demand treatment for 28 weeks during treatment period 1, followed by 40 IU/kg for mild or moderate bleeds and 80 IU/kg for severe bleeds, with additional doses as needed if the initial treatment showed no effect during treatment period 2) until 30 EDs to nonacog beta pegol in the entire trial were fulfilled.

| Serious adverse events                            | Arm A: Nonacog beta pegol (On-demand) | Arm B: Nonacog beta pegol (Prophylaxis) | Arm A: Nonacog beta pegol (Prophylaxis) |
|---|---------------------------------------|---|---|
| Total subjects affected by serious adverse events |                                       |   |   |
| subjects affected / exposed                       | 1 / 15 (6.67%)                        | 0 / 15 (0.00%)                          | 0 / 14 (0.00%)                          |
| number of deaths (all causes)                     | 0                                     | 0                                       | 0                                       |
| number of deaths resulting from adverse events    | 0                                     | 0                                       | 0                                       |
| Infections and infestations                       |                                       |   |   |
| Haematoma infection                               |                                       |   |   |
| subjects affected / exposed                       | 1 / 15 (6.67%)                        | 0 / 15 (0.00%)                          | 0 / 14 (0.00%)                          |
| occurrences causally related to treatment / all   | 0 / 1                                 | 0 / 0                                   | 0 / 0                                   |
| deaths causally related to treatment / all        | 0 / 0                                 | 0 / 0                                   | 0 / 0                                   |

| <b>Non-serious adverse events</b>  | Arm A: Nonacog<br>beta pegol (On-<br>demand)  | Arm B: Nonacog<br>beta pegol<br>(Prophylaxis)  | Arm A: Nonacog<br>beta pegol<br>(Prophylaxis)  |
|--|---|--|--|
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 12 / 15 (80.00%)  | 14 / 15 (93.33%)   | 4 / 14 (28.57%)  |
| Vascular disorders<br>Phlebitis superficial<br>subjects affected / exposed<br>occurrences (all)  | 1 / 15 (6.67%)<br>1   | 0 / 15 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |
| General disorders and administration<br>site conditions<br>Chest discomfort<br>subjects affected / exposed<br>occurrences (all)<br><br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)<br><br>Influenza like illness<br>subjects affected / exposed<br>occurrences (all)<br><br>Pain<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0<br><br>2 / 15 (13.33%)<br>2<br><br>1 / 15 (6.67%)<br>1<br><br>1 / 15 (6.67%)<br>1 | 0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1<br><br>0 / 14 (0.00%)<br>0<br><br>0 / 14 (0.00%)<br>0<br><br>0 / 14 (0.00%)<br>0 |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Epistaxis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pulmonary mass<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0                             | 0 / 15 (0.00%)<br>0<br><br>1 / 15 (6.67%)<br>3<br><br>1 / 15 (6.67%)<br>1                            | 0 / 14 (0.00%)<br>0<br><br>0 / 14 (0.00%)<br>0<br><br>0 / 14 (0.00%)<br>0                            |
| Investigations<br>Blood fibrinogen decreased<br>subjects affected / exposed<br>occurrences (all)<br><br>Fibrin D dimer increased   | 1 / 15 (6.67%)<br>1   | 0 / 15 (0.00%)<br>0  | 0 / 14 (0.00%)<br>0  |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Aspartate aminotransferase increased           |                |                |                |
| subjects affected / exposed                    | 0 / 15 (0.00%) | 1 / 15 (6.67%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Blood fibrinogen increased                     |                |                |                |
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| C-reactive protein increased                   |                |                |                |
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Fibrinogen degradation products increased      |                |                |                |
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Procalcitonin increased                        |                |                |                |
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 1              | 0              | 0              |
| Weight increased                               |                |                |                |
| subjects affected / exposed                    | 0 / 15 (0.00%) | 1 / 15 (6.67%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| White blood cell count increased               |                |                |                |
| subjects affected / exposed                    | 1 / 15 (6.67%) | 0 / 15 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 2              | 0              | 0              |
| Injury, poisoning and procedural complications |                |                |                |
| Muscle strain                                  |                |                |                |
| subjects affected / exposed                    | 0 / 15 (0.00%) | 1 / 15 (6.67%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Cardiac disorders                              |                |                |                |
| Atrioventricular block                         |                |                |                |
| subjects affected / exposed                    | 0 / 15 (0.00%) | 1 / 15 (6.67%) | 0 / 14 (0.00%) |
| occurrences (all)                              | 0              | 1              | 0              |
| Nervous system disorders                       |                |                |                |
| Dizziness                                      |                |                |                |
| subjects affected / exposed                    | 0 / 15 (0.00%) | 0 / 15 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all)                              | 0              | 0              | 1              |

|  |                      |                     |                     |
|--|----------------------|---------------------|---------------------|
| Neuritis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Lymphadenitis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Eye disorders<br>Trichiasis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                    | 2 / 15 (13.33%)<br>2 | 0 / 15 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Hepatobiliary disorders<br>Hepatic function abnormal<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Acne<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Rash<br>subjects affected / exposed<br>occurrences (all)   | 1 / 15 (6.67%)<br>1  | 0 / 15 (0.00%)<br>0 | 0 / 14 (0.00%)<br>0 |
| Renal and urinary disorders<br>Proteinuria<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 15 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0 | 1 / 14 (7.14%)<br>1 |
| Musculoskeletal and connective tissue disorders<br>Haemophilic arthropathy<br>subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0  | 1 / 15 (6.67%)<br>1 | 0 / 14 (0.00%)<br>0 |
| Synovitis  |                      |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 15 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 | 1 / 14 (7.14%)<br>1 |
| Infections and infestations                      |                     |                     |                     |
| COVID-19   |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 6 / 15 (40.00%)     | 0 / 14 (0.00%)      |
| occurrences (all)                                | 1                   | 6                   | 0                   |
| Coronavirus infection                            |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 1 / 15 (6.67%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 1                   | 1                   | 0                   |
| Influenza  |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 0 / 15 (0.00%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Rhinitis   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 0 / 15 (0.00%)      | 1 / 14 (7.14%)      |
| occurrences (all)                                | 0                   | 0                   | 1                   |
| Respiratory tract infection                      |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 0 / 15 (0.00%)      | 1 / 14 (7.14%)      |
| occurrences (all)                                | 1                   | 0                   | 1                   |
| Periodontitis                                    |                     |                     |                     |
| subjects affected / exposed                      | 2 / 15 (13.33%)     | 0 / 15 (0.00%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 2                   | 0                   | 0                   |
| Pneumonia  |                     |                     |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 1 / 15 (6.67%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 0                   | 1                   | 0                   |
| Upper respiratory tract infection                |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 4 / 15 (26.67%)     | 0 / 14 (0.00%)      |
| occurrences (all)                                | 1                   | 5                   | 0                   |
| Metabolism and nutrition disorders               |                     |                     |                     |
| Hypoproteinaemia                                 |                     |                     |                     |
| subjects affected / exposed                      | 1 / 15 (6.67%)      | 0 / 15 (0.00%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 1                   | 0                   | 0                   |
| Hyperuricaemia                                   |                     |                     |                     |
| subjects affected / exposed                      | 0 / 15 (0.00%)      | 1 / 15 (6.67%)      | 0 / 14 (0.00%)      |
| occurrences (all)                                | 0                   | 2                   | 0                   |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported