



## Clinical trial results:

### An Eighteen-Month, Two-Arm, Randomized, Double- Masked, Multi-center, Phase III Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Macular Edema secondary to Branch Retinal Vein Occlusion (RAPTOR)

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2018-001842-33       |
| Trial protocol           | DE AT DK ES GB IT CZ |
| Global end of trial date | 26 July 2021         |

#### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 28 July 2022 |
| First version publication date | 28 July 2022 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | CRTH258C2301 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03802630 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |                                                                                           |
|------------------------------|-------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Novartis Pharma AG                                                                        |
| Sponsor organisation address | Novartis Campus, Basel, Switzerland,                                                      |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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                       | 26 July 2021 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 26 July 2021 |
| Was the trial ended prematurely? | Yes          |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate that brolucizumab is non-inferior to aflibercept with respect to the change in BCVA from baseline up to Month 6

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

At the investigator's discretion, treatment with macular laser photocoagulation (focal or grid) for the study eye from Week 24 onwards was allowed in case macular edema worsened, resulting in a  $\geq 10$ -letter loss in BCVA at 2 consecutive visits, or in a  $\geq 15$ -letter loss in BCVA at 1 visit in the study eye, compared to best previous measurement, and the study eye BCVA value was not better than the baseline value.

Background therapy: -

Evidence for comparator: -

|                                                           |              |
|-----------------------------------------------------------|--------------|
| Actual start date of recruitment                          | 02 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 | Austria: 3             |
| Country: Number of subjects enrolled | Canada: 15             |
| Country: Number of subjects enrolled | China: 85              |
| Country: Number of subjects enrolled | Czechia: 5             |
| Country: Number of subjects enrolled | Denmark: 3             |
| Country: Number of subjects enrolled | France: 31             |
| Country: Number of subjects enrolled | Germany: 37            |
| Country: Number of subjects enrolled | Hong Kong: 10          |
| Country: Number of subjects enrolled | Israel: 14             |
| Country: Number of subjects enrolled | Italy: 21              |
| Country: Number of subjects enrolled | Japan: 17              |
| Country: Number of subjects enrolled | Russian Federation: 14 |
| Country: Number of subjects enrolled | Slovakia: 15           |
| Country: Number of subjects enrolled | Spain: 28              |
| Country: Number of subjects enrolled | Switzerland: 10        |
| Country: Number of subjects enrolled | Taiwan: 10             |

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 13 |
| Country: Number of subjects enrolled | United States: 119 |
| Worldwide total number of subjects   | 450                |
| EEA total number of subjects         | 143                |

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)                      | 214 |
| From 65 to 84 years                       | 220 |
| 85 years and over                         | 16  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from 103 sites in 18 countries

### Pre-assignment

Screening details:

The study comprised a screening period of 28 days

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |                   |
|------------------|-------------------|
| <b>Arm title</b> | Brolucizumab 6 mg |
|------------------|-------------------|

Arm description:

1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT)

|                                        |                  |
|----------------------------------------|------------------|
| Arm type                               | Experimental     |
| Investigational medicinal product name | Brolucizumab     |
| Investigational medicinal product code | RTH258           |
| Other name                             |                  |
| Pharmaceutical forms                   | Injection        |
| Routes of administration               | Intravitreal use |

Dosage and administration details:

Brolucizumab 6 mg intravitreal injection.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Aflibercept 2 mg |
|------------------|------------------|

Arm description:

1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT)

|                                        |                   |
|----------------------------------------|-------------------|
| Arm type                               | Active comparator |
| Investigational medicinal product name | Aflibercept       |
| Investigational medicinal product code |                   |
| Other name                             |                   |
| Pharmaceutical forms                   | Injection         |
| Routes of administration               | Intravitreal use  |

Dosage and administration details:

Aflibercept 2 mg intravitreal injection

| <b>Number of subjects in period 1</b> | Brolucizumab 6 mg | Aflibercept 2 mg |
|---------------------------------------|-------------------|------------------|
| Started                               | 226               | 224              |
| Completed                             | 73                | 76               |
| Not completed                         | 153               | 148              |
| Adverse event, serious fatal          | -                 | 2                |
| Physician decision                    | 2                 | -                |
| Adverse event, non-fatal              | 3                 | 1                |
| Subject decision                      | 16                | 9                |
| Study terminated by sponsor           | 130               | 134              |
| Lost to follow-up                     | 2                 | 2                |

## Baseline characteristics

### Reporting groups

|                                                                                                                                                                     |                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                                                                               | Brolucizumab 6 mg |
| Reporting group description:<br>1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT) |                   |
| Reporting group title                                                                                                                                               | Aflibercept 2 mg  |
| Reporting group description:<br>1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT) |                   |

| Reporting group values                             | Brolucizumab 6 mg | Aflibercept 2 mg | Total |
|----------------------------------------------------|-------------------|------------------|-------|
| Number of subjects                                 | 226               | 224              | 450   |
| Age categorical<br>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)                          | 0                 | 0                | 0     |
| Adults (18-64 years)                               | 106               | 108              | 214   |
| From 65-84 years                                   | 113               | 107              | 220   |
| 85 years and over                                  | 7                 | 9                | 16    |
| Age Continuous<br>Units: Years                     |                   |                  |       |
| arithmetic mean                                    | 65.4              | 65.0             |       |
| standard deviation                                 | ± 11.05           | ± 10.92          | -     |
| Sex: Female, Male<br>Units: Participants           |                   |                  |       |
| Female                                             | 117               | 125              | 242   |
| Male                                               | 109               | 99               | 208   |
| Race/Ethnicity, Customized<br>Units: Subjects      |                   |                  |       |
| White                                              | 153               | 153              | 306   |
| Black or African American                          | 7                 | 4                | 11    |
| Asian                                              | 65                | 67               | 132   |
| White/Black or African American                    | 1                 | 0                | 1     |

## End points

### End points reporting groups

|                                                                                                                                                                     |                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|
| Reporting group title                                                                                                                                               | Brolucizumab 6 mg |
| Reporting group description:<br>1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT) |                   |
| Reporting group title                                                                                                                                               | Aflibercept 2 mg  |
| Reporting group description:<br>1 intravitreal injection every 4 weeks for a total of 6 injections, followed by 48 weeks of individualized flexible treatment (IFT) |                   |

### Primary: Change from baseline in best-corrected visual acuity (BCVA) at Week 24

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Change from baseline in best-corrected visual acuity (BCVA) at Week 24 |
| End point description:<br>BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at an initial testing distance of 4 meters.<br><br>Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.<br><br>Missing and censored BCVA values were imputed by Last observation carried forward (LOCF) as the primary approach. Observed values from both scheduled and unscheduled post-baseline visits were used for the LOCF imputation. For subjects with no post-baseline BCVA value, the baseline value was carried forward. |                                                                        |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Primary                                                                |
| End point timeframe:<br>Baseline, Week 24                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                        |

| End point values                    | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|-------------------------------------|-------------------|------------------|--|--|
| Subject group type                  | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed         | 226               | 224              |  |  |
| Units: Letters read                 |                   |                  |  |  |
| least squares mean (standard error) | 13.1 (± 0.71)     | 15.0 (± 0.71)    |  |  |

### Statistical analyses

|                            |                                      |
|----------------------------|--------------------------------------|
| Statistical analysis title | Change from BCVA at week 24          |
| Comparison groups          | Brolucizumab 6 mg v Aflibercept 2 mg |

|                                         |                                |
|-----------------------------------------|--------------------------------|
| Number of subjects included in analysis | 450                            |
| Analysis specification                  | Pre-specified                  |
| Analysis type                           | non-inferiority <sup>[1]</sup> |
| P-value                                 | = 0.018                        |
| Method                                  | ANOVA                          |
| Parameter estimate                      | Least Square Mean Difference   |
| Point estimate                          | -1.9                           |
| Confidence interval                     |                                |
| level                                   | 95 %                           |
| sides                                   | 2-sided                        |
| lower limit                             | -3.9                           |
| upper limit                             | 0.1                            |
| Variability estimate                    | Standard error of the mean     |
| Dispersion value                        | 1.01                           |

Notes:

[1] - Non-inferiority was considered established if the lower limit of the corresponding 95% CI for the estimated between group difference (brolucizumab vs. aflibercept) on change from baseline in BCVA at Week 24 is greater than -4 letters.

### Secondary: Change from baseline in BCVA averaged over Week 40 to Week 52

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change from baseline in BCVA averaged over Week 40 to Week 52 |
|-----------------|---------------------------------------------------------------|

End point description:

An average BCVA over week 40 to week 52 was calculated.

BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at an initial testing distance of 4 meters.

Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.

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

End point timeframe:

Baseline, Week 40 to Week 52

| End point values                     | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 123               | 132              |  |  |
| Units: Letters read                  |                   |                  |  |  |
| arithmetic mean (standard deviation) | 12.9 (± 12.81)    | 16.9 (± 10.63)   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in BCVA averaged over Week 64 to Week 76

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change from baseline in BCVA averaged over Week 64 to Week 76 |
|-----------------|---------------------------------------------------------------|

End point description:

An average BCVA over week 64 to week 76 was calculated.

BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study

(ETDRS) visual acuity testing charts at an initial testing distance of 4 meters.

Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.

|                              |           |
|------------------------------|-----------|
| End point type               | Secondary |
| End point timeframe:         |           |
| Baseline, Week 64 to Week 76 |           |

| End point values                     | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 110               | 121              |  |  |
| Units: Letters read                  |                   |                  |  |  |
| arithmetic mean (standard deviation) | 13.7 (± 13.33)    | 17.9 (± 10.65)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in BCVA by visit up to Week 76

|                                                                                                                                                                                      |                                                     |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title                                                                                                                                                                      | Change from baseline in BCVA by visit up to Week 76 |
| End point description:                                                                                                                                                               |                                                     |
| BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at an initial testing distance of 4 meters. |                                                     |
| Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.                                                                |                                                     |
| End point type                                                                                                                                                                       | Secondary                                           |
| End point timeframe:                                                                                                                                                                 |                                                     |
| Baseline and every 4 weeks from baseline up to Week 76                                                                                                                               |                                                     |

| End point values                     | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 226               | 224              |  |  |
| Units: Letters read                  |                   |                  |  |  |
| arithmetic mean (standard deviation) |                   |                  |  |  |
| Week 4 (n=223, 217)                  | 9.2 (± 8.22)      | 10.3 (± 10.13)   |  |  |
| Week 8 (n=204, 199)                  | 11.9 (± 10.68)    | 12.8 (± 10.84)   |  |  |
| Week 12 (n=185, 182)                 | 13.2 (± 10.22)    | 14.8 (± 11.23)   |  |  |
| Week 16 (n=160, 160)                 | 12.2 (± 12.59)    | 16.3 (± 11.58)   |  |  |
| Week 20 (n=144, 149)                 | 13.5 (± 10.83)    | 16.3 (± 12.15)   |  |  |
| Week 24 (n=147, 144)                 | 12.7 (± 12.36)    | 16.6 (± 11.35)   |  |  |
| Week 28 (n=135, 136)                 | 12.1 (± 13.88)    | 16.4 (± 10.62)   |  |  |
| Week 32 (n=124, 128)                 | 12.2 (± 13.24)    | 15.7 (± 10.94)   |  |  |
| Week 36 (n=123, 125)                 | 11.8 (± 14.75)    | 16.9 (± 10.95)   |  |  |
| Week 40 (n=119, 124)                 | 12.7 (± 12.89)    | 16.9 (± 10.74)   |  |  |

|                      |                |                |  |  |
|----------------------|----------------|----------------|--|--|
| Week 44 (n=116, 120) | 13.5 (± 13.28) | 17.2 (± 11.37) |  |  |
| Week 48 (n=114, 120) | 13.3 (± 13.38) | 17.7 (± 10.79) |  |  |
| Week 52 (n=106, 125) | 13.5 (± 13.42) | 17.2 (± 10.46) |  |  |
| Week 56 (n=106, 122) | 14.9 (± 10.86) | 17.7 (± 10.62) |  |  |
| Week 60 (n=105, 123) | 13.7 (± 13.67) | 17.7 (± 10.33) |  |  |
| Week 64 (n=102, 117) | 14.1 (± 13.72) | 18.0 (± 10.54) |  |  |
| Week 68 (n=94, 110)  | 13.9 (± 13.83) | 17.7 (± 10.75) |  |  |
| Week 72 (n=83, 92)   | 13.9 (± 13.38) | 18.4 (± 11.44) |  |  |
| Week 76 (n=68, 74)   | 14.4 (± 13.72) | 18.1 (± 11.19) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of participants with a gain ≥ 5, 10 and 15 letters in BCVA by visit compared to baseline

|                 |                                                                                                     |
|-----------------|-----------------------------------------------------------------------------------------------------|
| End point title | Proportion of participants with a gain ≥ 5, 10 and 15 letters in BCVA by visit compared to baseline |
|-----------------|-----------------------------------------------------------------------------------------------------|

End point description:

The summary by visit was conducted based on the BCVA observed from each of the corresponding visits. BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at an initial testing distance of 4 meters.

Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.

Every 5 letters represents 1 line of vision on the reading chart.

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

End point timeframe:

Baseline and every 4 weeks from baseline up to Week 76

| End point values                                 | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|--------------------------------------------------|-------------------|------------------|--|--|
| Subject group type                               | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed                      | 226               | 224              |  |  |
| Units: Participants                              |                   |                  |  |  |
| Week 4; BCVA gain from baseline ≥5 (n=223, 217)  | 154               | 150              |  |  |
| Week 4; BCVA gain from baseline ≥10 (n=223, 217) | 102               | 110              |  |  |
| Week4; BCVA gain from baseline ≥15(n=223, 217)   | 64                | 79               |  |  |
| Week8; BCVA gain from baseline ≥5(n=204, 199)    | 158               | 155              |  |  |
| Week8; BCVA gain from baseline ≥10(n=204, 199)   | 117               | 118              |  |  |
| Week8; BCVA gain from baseline ≥15(n=204, 199)   | 92                | 93               |  |  |
| Week 12; BCVA gain from baseline ≥5(n=185, 182)  | 156               | 156              |  |  |
| Week 12; BCVA gain from baseline ≥10(n=185, 182) | 114               | 125              |  |  |

|                                                     |     |     |  |  |
|-----------------------------------------------------|-----|-----|--|--|
| Week 12; BCVA gain from baseline<br>≥15(n=185, 182) | 90  | 102 |  |  |
| Week 16; BCVA gain from baseline<br>≥5(n=160, 160)  | 127 | 143 |  |  |
| Week 16; BCVA gain from baseline<br>≥10(n=160, 160) | 95  | 118 |  |  |
| Week 16; BCVA gain from baseline<br>≥15(n=160, 160) | 73  | 100 |  |  |
| Week 20; BCVA gain from baseline<br>≥5(n=144, 149)  | 119 | 131 |  |  |
| Week 20; BCVA gain from baseline<br>≥10(n=144, 149) | 96  | 108 |  |  |
| Week20; BCVA gain from baseline ≥15<br>(n=144, 149) | 74  | 92  |  |  |
| Week24; BCVA gain from baseline ≥5<br>(n=147, 144)  | 122 | 126 |  |  |
| Week24; BCVA gain from baseline ≥10<br>(n=147, 144) | 90  | 109 |  |  |
| Week24; BCVA gain from baseline ≥15<br>(n=147, 144) | 75  | 91  |  |  |
| Week28; BCVA gain from baseline ≥5<br>(n=135, 136)  | 108 | 121 |  |  |
| Week28; BCVA gain from baseline ≥10<br>(n=135, 136) | 89  | 107 |  |  |
| Week28; BCVA gain from baseline ≥15<br>(n=135, 136) | 75  | 87  |  |  |
| Week32; BCVA gain from baseline ≥5<br>(n=124, 128)  | 97  | 110 |  |  |
| Week32; BCVA gain from baseline ≥10<br>(n=124, 128) | 79  | 94  |  |  |
| Week32; BCVA gain from baseline ≥15<br>(n=124, 128) | 60  | 78  |  |  |
| Week36; BCVA gain from baseline ≥5<br>(n=123, 125)  | 100 | 112 |  |  |
| Week36; BCVA gain from baseline ≥10<br>(n=123, 125) | 81  | 98  |  |  |
| Week36; BCVA gain from baseline ≥15<br>(n=123, 125) | 62  | 83  |  |  |
| Week40; BCVA gain from baseline ≥5<br>(n=119, 124)  | 96  | 114 |  |  |
| Week40; BCVA gain from baseline ≥10<br>(n=119, 124) | 79  | 98  |  |  |
| Week40; BCVA gain from baseline ≥15<br>(n=119, 124) | 65  | 85  |  |  |
| Week44; BCVA gain from baseline ≥5<br>(n=116, 120)  | 94  | 111 |  |  |
| Week44; BCVA gain from baseline ≥10<br>(n=116, 120) | 78  | 97  |  |  |
| Week44; BCVA gain from baseline ≥15<br>(n=116, 120) | 64  | 88  |  |  |
| Week48; BCVA gain from baseline ≥5<br>(n=114, 120)  | 92  | 112 |  |  |
| Week48; BCVA gain from baseline ≥10<br>(n=114, 120) | 76  | 95  |  |  |
| Week48; BCVA gain from baseline ≥15<br>(n=114, 120) | 61  | 80  |  |  |
| Week52; BCVA gain from baseline ≥5<br>(n=106, 125)  | 87  | 117 |  |  |
| Week52; BCVA gain from baseline ≥10<br>(n=106, 125) | 75  | 99  |  |  |
| Week52; BCVA gain from baseline ≥15<br>(n=106, 125) | 64  | 87  |  |  |

|                                                           |    |     |  |  |
|-----------------------------------------------------------|----|-----|--|--|
| Week56; BCVA gain from baseline $\geq 5$<br>(n=106, 122)  | 90 | 113 |  |  |
| Week56; BCVA gain from baseline $\geq 10$<br>(n=106, 122) | 76 | 106 |  |  |
| Week56; BCVA gain from baseline $\geq 15$<br>(n=106, 122) | 58 | 84  |  |  |
| Week60; BCVA gain from baseline $\geq 5$<br>(n=105, 123)  | 86 | 116 |  |  |
| Week60; BCVA gain from baseline $\geq 10$<br>(n=105, 123) | 71 | 104 |  |  |
| Week60; BCVA gain from baseline $\geq 15$<br>(n=105, 123) | 62 | 88  |  |  |
| Week64; BCVA gain from baseline $\geq 5$<br>(n=102, 117)  | 86 | 112 |  |  |
| Week64; BCVA gain from baseline $\geq 10$<br>(n=102, 117) | 74 | 98  |  |  |
| Week64; BCVA gain from baseline $\geq 15$<br>(n=102, 117) | 58 | 82  |  |  |
| Week68; BCVA gain from baseline $\geq 5$<br>(n=94, 110)   | 79 | 103 |  |  |
| Week68; BCVA gain from baseline $\geq 10$<br>(n=94, 110)  | 67 | 88  |  |  |
| Week68; BCVA gain from baseline $\geq 15$<br>(n=94, 110)  | 55 | 76  |  |  |
| Week72; BCVA gain from baseline $\geq 5$<br>(n=83, 92)    | 68 | 89  |  |  |
| Week72; BCVA gain from baseline $\geq 10$<br>(n=83, 92)   | 56 | 75  |  |  |
| Week72; BCVA gain from baseline $\geq 15$<br>(n=83, 92)   | 45 | 63  |  |  |
| Week76; BCVA gain from baseline $\geq 5$<br>(n=68, 74)    | 62 | 67  |  |  |
| Week76; BCVA gain from baseline $\geq 10$<br>(n=68, 74)   | 52 | 61  |  |  |
| Week76; BCVA gain from baseline $\geq 15$<br>(n=68, 74)   | 43 | 53  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of participants with a loss $\geq 5$ , 10 and 15 letters in BCVA by visit compared to baseline

|                 |                                                                                                           |
|-----------------|-----------------------------------------------------------------------------------------------------------|
| End point title | Proportion of participants with a loss $\geq 5$ , 10 and 15 letters in BCVA by visit compared to baseline |
|-----------------|-----------------------------------------------------------------------------------------------------------|

End point description:

The summary by visit was conducted based on the BCVA observed from each of the corresponding visit. BCVA measurements were taken in a sitting position using Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity testing charts at an initial testing distance of 4 meters.

Min and max possible scores are 0-100 letters read respectively. A higher score represents better visual functioning.

Every 5 letters represents 1 line of vision on the reading chart.

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

End point timeframe:

Baseline and every 4 weeks from baseline up to Week 76

| End point values                                          | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|-----------------------------------------------------------|-------------------|------------------|--|--|
| Subject group type                                        | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed                               | 226               | 224              |  |  |
| Units: Participants                                       |                   |                  |  |  |
| Week4; BCVA loss from baseline $\geq 5$<br>(n=223, 217)   | 6                 | 7                |  |  |
| Week4; BCVA loss from baseline $\geq 10$<br>(n=223, 217)  | 1                 | 3                |  |  |
| Week4; BCVA loss from baseline $\geq 15$<br>(n=223, 217)  | 0                 | 0                |  |  |
| Week8; BCVA loss from baseline $\geq 5$<br>(n=204, 199)   | 2                 | 4                |  |  |
| Week8; BCVA loss from baseline $\geq 10$<br>(n=204, 199)  | 1                 | 2                |  |  |
| Week8; BCVA loss from baseline $\geq 15$<br>(n=204, 199)  | 1                 | 0                |  |  |
| Week12; BCVA loss from baseline $\geq 5$<br>(n=185,182 )  | 3                 | 2                |  |  |
| Week12; BCVA loss from baseline $\geq 10$<br>(n=185,182 ) | 2                 | 1                |  |  |
| Week12; BCVA loss from baseline $\geq 15$<br>(n=185,182 ) | 1                 | 0                |  |  |
| Week16; BCVA loss from baseline $\geq 5$<br>(n=160,160 )  | 9                 | 4                |  |  |
| Week16; BCVA loss from baseline $\geq 10$<br>(n=160,160 ) | 5                 | 2                |  |  |
| Week16; BCVA loss from baseline $\geq 15$<br>(n=160,160 ) | 3                 | 2                |  |  |
| Week20; BCVA loss from baseline $\geq 5$<br>(n=144,149 )  | 6                 | 4                |  |  |
| Week20; BCVA loss from baseline $\geq 10$<br>(n=144,149 ) | 2                 | 3                |  |  |
| Week20; BCVA loss from baseline $\geq 15$<br>(n=144,149 ) | 2                 | 1                |  |  |
| Week24; BCVA loss from baseline $\geq 5$<br>(n=147,144 )  | 8                 | 3                |  |  |
| Week24; BCVA loss from baseline $\geq 10$<br>(n=147,144 ) | 3                 | 3                |  |  |
| Week24; BCVA loss from baseline $\geq 15$<br>(n=147,144 ) | 3                 | 1                |  |  |
| Week28; BCVA loss from baseline $\geq 5$<br>(n=135,136 )  | 9                 | 2                |  |  |
| Week28; BCVA loss from baseline $\geq 10$<br>(n=135,136 ) | 6                 | 1                |  |  |
| Week28; BCVA loss from baseline $\geq 15$<br>(n=135,136 ) | 6                 | 1                |  |  |
| Week32; BCVA loss from baseline $\geq 5$<br>(n=124,128 )  | 8                 | 3                |  |  |
| Week32; BCVA loss from baseline $\geq 10$<br>(n=124,128 ) | 5                 | 2                |  |  |
| Week32; BCVA loss from baseline $\geq 15$<br>(n=124,128 ) | 3                 | 0                |  |  |
| Week36; BCVA loss from baseline $\geq 5$<br>(n=123,125 )  | 9                 | 2                |  |  |
| Week36; BCVA loss from baseline $\geq 10$<br>(n=123,125 ) | 7                 | 1                |  |  |

|                                                           |   |   |  |  |
|-----------------------------------------------------------|---|---|--|--|
| Week36; BCVA loss from baseline $\geq 15$<br>(n=123,125 ) | 5 | 1 |  |  |
| Week40; BCVA loss from baseline $\geq 5$<br>(n=119,124)   | 5 | 4 |  |  |
| Week40; BCVA loss from baseline $\geq 10$<br>(n=119,124)  | 4 | 1 |  |  |
| Week40; BCVA loss from baseline $\geq 15$<br>(n=119,124)  | 2 | 1 |  |  |
| Week44; BCVA loss from baseline $\geq 5$<br>(n=116,120)   | 4 | 5 |  |  |
| Week44; BCVA loss from baseline $\geq 10$<br>(n=116,120)  | 3 | 3 |  |  |
| Week44; BCVA loss from baseline $\geq 15$<br>(n=116,120)  | 2 | 2 |  |  |
| Week48; BCVA loss from baseline $\geq 5$<br>(n=114,120)   | 5 | 3 |  |  |
| Week48; BCVA loss from baseline $\geq 10$<br>(n=114,120)  | 3 | 1 |  |  |
| Week48; BCVA loss from baseline $\geq 15$<br>(n=114,120)  | 1 | 1 |  |  |
| Week52; BCVA loss from baseline $\geq 5$<br>(n=106,125)   | 5 | 2 |  |  |
| Week52; BCVA loss from baseline $\geq 10$<br>(n=106,125)  | 3 | 1 |  |  |
| Week52; BCVA loss from baseline $\geq 15$<br>(n=106,125)  | 2 | 1 |  |  |
| Week56; BCVA loss from baseline $\geq 5$<br>(n=106,122)   | 3 | 3 |  |  |
| Week56; BCVA loss from baseline $\geq 10$<br>(n=106,122)  | 1 | 1 |  |  |
| Week56; BCVA loss from baseline $\geq 15$<br>(n=106,122)  | 0 | 0 |  |  |
| Week60; BCVA loss from baseline $\geq 5$<br>(n=105, 123)  | 7 | 2 |  |  |
| Week60; BCVA loss from baseline $\geq 10$<br>(n=105, 123) | 3 | 0 |  |  |
| Week60; BCVA loss from baseline $\geq 15$<br>(n=105, 123) | 1 | 0 |  |  |
| Week64; BCVA loss from baseline $\geq 5$<br>(n=102, 117)  | 5 | 2 |  |  |
| Week64; BCVA loss from baseline $\geq 10$<br>(n=102, 117) | 1 | 1 |  |  |
| Week64; BCVA loss from baseline $\geq 15$<br>(n=102, 117) | 1 | 1 |  |  |
| Week68; BCVA loss from baseline $\geq 5$<br>(n=94, 110)   | 6 | 3 |  |  |
| Week68; BCVA loss from baseline $\geq 10$<br>(n=94, 110)  | 3 | 1 |  |  |
| Week68; BCVA loss from baseline $\geq 15$<br>(n=94, 110)  | 1 | 0 |  |  |
| Week72; BCVA loss from baseline $\geq 5$<br>(n=83, 92)    | 1 | 2 |  |  |
| Week72; BCVA loss from baseline $\geq 10$<br>(n=83, 92)   | 1 | 2 |  |  |
| Week72; BCVA loss from baseline $\geq 15$<br>(n=83, 92)   | 1 | 1 |  |  |
| Week76; BCVA loss from baseline $\geq 5$<br>(n=68, 74)    | 2 | 2 |  |  |
| Week76; BCVA loss from baseline $\geq 10$<br>(n=68, 74)   | 1 | 0 |  |  |
| Week76; BCVA loss from baseline $\geq 15$<br>(n=68, 74)   | 1 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in CSFT averaged over Week 40 to Week 52

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change from baseline in CSFT averaged over Week 40 to Week 52 |
|-----------------|---------------------------------------------------------------|

End point description:

Change from baseline in central subfield thickness (CSFT) averaged over Week 40 to Week 52 , measured in  $\mu\text{m}$  by Spectral Domain Optical Coherence Tomography (SD-OCT)

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

End point timeframe:

Baseline, Week 40 to Week 52

|                                      |                        |                        |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| <b>End point values</b>              | Brolucizumab 6 mg      | Aflibercept 2 mg       |  |  |
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 123                    | 132                    |  |  |
| Units: $\mu\text{m}$                 |                        |                        |  |  |
| arithmetic mean (standard deviation) | -231.8 ( $\pm$ 188.97) | -259.2 ( $\pm$ 190.69) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in CSFT averaged over Week 64 to Week 76

|                 |                                                               |
|-----------------|---------------------------------------------------------------|
| End point title | Change from baseline in CSFT averaged over Week 64 to Week 76 |
|-----------------|---------------------------------------------------------------|

End point description:

Change from baseline in central subfield thickness (CSFT) averaged over Week 64 to Week 76, measured in  $\mu\text{m}$  by Spectral Domain Optical Coherence Tomography (SD-OCT)

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

End point timeframe:

Baseline, Week 64 to Week 76

| End point values                     | Brolucizumab 6 mg      | Aflibercept 2 mg       |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 110                    | 121                    |  |  |
| Units: $\mu\text{m}$                 |                        |                        |  |  |
| arithmetic mean (standard deviation) | -243.6 ( $\pm$ 201.61) | -272.6 ( $\pm$ 194.29) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in CSFT by visit up to Week 76

|                                                                                                                                                                        |                                                     |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------|
| End point title                                                                                                                                                        | Change from baseline in CSFT by visit up to Week 76 |
| End point description:<br>Change from baseline in central subfield thickness (CSFT) measured in $\mu\text{m}$ by Spectral Domain Optical Coherence Tomography (SD-OCT) |                                                     |
| End point type                                                                                                                                                         | Secondary                                           |
| End point timeframe:<br>Baseline, and every 4 weeks from baseline up to Week 76                                                                                        |                                                     |

| End point values                     | Brolucizumab 6 mg      | Aflibercept 2 mg       |  |  |
|--------------------------------------|------------------------|------------------------|--|--|
| Subject group type                   | Reporting group        | Reporting group        |  |  |
| Number of subjects analysed          | 226                    | 224                    |  |  |
| Units: $\mu\text{m}$                 |                        |                        |  |  |
| arithmetic mean (standard deviation) |                        |                        |  |  |
| Week 4 (n=223, 217)                  | -247.1 ( $\pm$ 197.99) | -259.4 ( $\pm$ 185.11) |  |  |
| Week 8 (n=203, 201)                  | -255.9 ( $\pm$ 206.00) | -270.7 ( $\pm$ 195.49) |  |  |
| Week 12 (n=184, 182)                 | -264.5 ( $\pm$ 208.70) | -271.9 ( $\pm$ 194.99) |  |  |
| Week 16 (n=161, 160)                 | -271.1 ( $\pm$ 209.38) | -276.1 ( $\pm$ 209.70) |  |  |
| Week 20 (n=143, 147)                 | -257.1 ( $\pm$ 197.31) | -285.2 ( $\pm$ 210.32) |  |  |
| Week 24 (n=147, 143)                 | -254.9 ( $\pm$ 203.29) | -286.6 ( $\pm$ 207.67) |  |  |
| Week 28 (n=134, 136)                 | -245.4 ( $\pm$ 197.62) | -263.6 ( $\pm$ 197.11) |  |  |
| Week 32 (n=124, 128)                 | -231.1 ( $\pm$ 208.02) | -262.1 ( $\pm$ 193.80) |  |  |
| Week 36 (n=123, 125)                 | -234.1 ( $\pm$ 199.02) | -260.8 ( $\pm$ 195.03) |  |  |
| Week 40 (n=119, 124)                 | -224.7 ( $\pm$ 190.50) | -259.0 ( $\pm$ 189.01) |  |  |
| Week 44 (n=116, 120)                 | -242.8 ( $\pm$ 197.34) | -264.1 ( $\pm$ 192.06) |  |  |
| Week 48 (n=114, 120)                 | -237.1 ( $\pm$ 200.64) | -279.4 ( $\pm$ 193.41) |  |  |

|                      |                   |                   |  |  |
|----------------------|-------------------|-------------------|--|--|
| Week 52 (n=106, 125) | -243.0 (± 203.87) | -263.4 (± 190.36) |  |  |
| Week 56 (n=106, 122) | -249.2 (± 206.54) | -271.4 (± 198.09) |  |  |
| Week 60 (n=105, 123) | -238.3 (± 185.78) | -265.3 (± 187.29) |  |  |
| Week 64 (n=102, 117) | -249.8 (± 207.86) | -266.1 (± 199.79) |  |  |
| Week 68 (n=93, 110)  | -247.5 (± 217.61) | -261.1 (± 192.30) |  |  |
| Week 72 (n=83, 92)   | -253.4 (± 211.06) | -279.4 (± 185.21) |  |  |
| Week 76 (n=68, 74)   | -255.6 (± 184.22) | -283.7 (± 197.29) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Proportion of subjects with presence of retinal fluid (intra- and/or subretinal fluid) in the study eye by visit up to Week 76

|                 |                                                                                                                                |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Proportion of subjects with presence of retinal fluid (intra- and/or subretinal fluid) in the study eye by visit up to Week 76 |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

Presence of retinal fluid (intra- and/or subretinal fluid) assessed by Spectral Domain Optical Coherence Tomography (SD-OCT)

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

End point timeframe:

Every 4 weeks from baseline up to Week 76

| End point values            | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|-----------------------------|-------------------|------------------|--|--|
| Subject group type          | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed | 226               | 224              |  |  |
| Units: Participants         |                   |                  |  |  |
| Week 4 (n=223, 217)         | 83                | 101              |  |  |
| Week 8 (n=204, 201)         | 56                | 68               |  |  |
| Week 12 (n=184, 182)        | 41                | 49               |  |  |
| Week 16 (n=161, 160)        | 34                | 50               |  |  |
| Week 20 (n=144, 149)        | 33                | 45               |  |  |
| Week 24 (n=147, 143)        | 35                | 42               |  |  |
| Week 28 (n=134, 136)        | 47                | 56               |  |  |
| Week 32 (n=124, 128)        | 58                | 50               |  |  |
| Week 36 (n=123, 125)        | 48                | 57               |  |  |
| Week 40 (n=119, 124)        | 42                | 56               |  |  |
| Week 44 (n=116, 120)        | 43                | 54               |  |  |
| Week 48 (n=114, 120)        | 44                | 49               |  |  |
| Week 52 (n=106, 125)        | 34                | 57               |  |  |
| Week 56 (n=106, 122)        | 34                | 54               |  |  |
| Week 60 (n=105, 123)        | 39                | 63               |  |  |

|                      |    |    |  |  |
|----------------------|----|----|--|--|
| Week 64 (n=102, 117) | 31 | 52 |  |  |
| Week 68 (n=93, 110)  | 34 | 52 |  |  |
| Week 72 (n=83, 92)   | 33 | 39 |  |  |
| Week 76 (n=68, 74)   | 16 | 38 |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Proportion of subjects with a CSFT < 300 µm for the study eye by visit up to Week 76

|                 |                                                                                      |
|-----------------|--------------------------------------------------------------------------------------|
| End point title | Proportion of subjects with a CSFT < 300 µm for the study eye by visit up to Week 76 |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

Central subfield thickness (CSFT) is measured in µm by Spectral Domain Optical Coherence Tomography (SD-OCT)

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

End point timeframe:

Every 4 weeks from Week 4 up to Week 76

| End point values            | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|-----------------------------|-------------------|------------------|--|--|
| Subject group type          | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed | 226               | 224              |  |  |
| Units: Participants         |                   |                  |  |  |
| Week 4 (n=223, 217)         | 167               | 153              |  |  |
| Week 8 (n=203, 201)         | 172               | 166              |  |  |
| Week 12 (n=184, 182)        | 156               | 155              |  |  |
| Week 16 (n=161, 160)        | 137               | 131              |  |  |
| Week 20 (n=143, 147)        | 120               | 118              |  |  |
| Week 24 (n=147, 143)        | 127               | 114              |  |  |
| Week 28 (n=134, 136)        | 109               | 103              |  |  |
| Week 32 (n=124, 128)        | 92                | 97               |  |  |
| Week 36 (n=123, 125)        | 96                | 91               |  |  |
| Week 40 (n=119, 124)        | 94                | 92               |  |  |
| Week 44 (n=116, 120)        | 95                | 93               |  |  |
| Week 48 (n=114, 120)        | 89                | 97               |  |  |
| Week 52 (n=106, 125)        | 86                | 95               |  |  |
| Week 56 (n=106, 122)        | 86                | 91               |  |  |
| Week 60 (n=105, 123)        | 83                | 90               |  |  |
| Week 64 (n=102, 117)        | 85                | 90               |  |  |
| Week 68 (n=93, 110)         | 82                | 79               |  |  |
| Week 72 (n=83, 92)          | 70                | 76               |  |  |
| Week 76 (n=68, 74)          | 59                | 59               |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of injections between Week 24 and Week 52 and between Week 24 and Week 72

|                 |                                                                                  |
|-----------------|----------------------------------------------------------------------------------|
| End point title | Number of injections between Week 24 and Week 52 and between Week 24 and Week 72 |
|-----------------|----------------------------------------------------------------------------------|

End point description:

Number of administered injections during the individualized flexible treatment (IFT) period, between Week 24 and Week 52 and between Week 24 and Week 72 are presented

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

End point timeframe:

Week 24 to Week 52 and Week 24 to Week 72

| End point values                         | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|------------------------------------------|-------------------|------------------|--|--|
| Subject group type                       | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed              | 111               | 126              |  |  |
| Units: Injections                        |                   |                  |  |  |
| arithmetic mean (standard deviation)     |                   |                  |  |  |
| Between Week 24 and Week 52 (n=111, 126) | 2.2 (± 1.69)      | 2.5 (± 2.17)     |  |  |
| Between Week 24 and Week 72 (n=65, 75)   | 3.2 (± 2.54)      | 4.0 (± 3.28)     |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to recurrence after Week 20 and up to Week 76

|                 |                                                    |
|-----------------|----------------------------------------------------|
| End point title | Time to recurrence after Week 20 and up to Week 76 |
|-----------------|----------------------------------------------------|

End point description:

Recurrence is defined as the need for injection while showing a lack of disease stability for the first time after Week 20 and up to Week 76.

For subjects with recurrence after the Week 20 visit, time-to-event is calculated as (first time with the lack of disease stability – the injection date on Week 20 visit + 1). For subjects without recurrence after Week 20, the censoring time will be calculated as (last visit with disease stability assessment – the injection date on Week 20 visit + 1).

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

End point timeframe:

Week 20 to Week 76

| End point values                 | Brolucizumab 6 mg   | Aflibercept 2 mg    |  |  |
|----------------------------------|---------------------|---------------------|--|--|
| Subject group type               | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed      | 157                 | 159                 |  |  |
| Units: Weeks                     |                     |                     |  |  |
| median (confidence interval 95%) | 12.9 (12.1 to 14.4) | 13.1 (11.3 to 17.4) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with ocular and non-ocular AEs up to Week 52 and Week 76

|                        |                                                                                 |
|------------------------|---------------------------------------------------------------------------------|
| End point title        | Number of subjects with ocular and non-ocular AEs up to Week 52 and Week 76     |
| End point description: | Number of subjects with at least one ocular or non-ocular Adverse Events (AEs). |
| End point type         | Secondary                                                                       |
| End point timeframe:   | Baseline to Week 76                                                             |

| End point values             | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|------------------------------|-------------------|------------------|--|--|
| Subject group type           | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed  | 226               | 224              |  |  |
| Units: Participants          |                   |                  |  |  |
| Ocular AEs up to week 52     | 93                | 72               |  |  |
| Non-Ocular AEs up to week 52 | 94                | 112              |  |  |
| Ocular AEs up to week 76     | 98                | 75               |  |  |
| Non-Ocular AEs up to week 76 | 103               | 120              |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in patient reported outcomes (NEI VFQ-25) at Week 24, Week 52 and Week 76

|                        |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title        | Change from baseline in patient reported outcomes (NEI VFQ-25) at Week 24, Week 52 and Week 76                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| End point description: | <p>The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) measures a patient's subjective assessment of vision-related Quality of Life (QoL).</p> <p>The 11 subscales in the VFQ-25 are general vision, ocular pain, near activities, distance activities, social functioning, mental health, role difficulties, dependency, driving, color vision, and peripheral vision. The scores on the subscales were added together for a total score, which ranged from 0 to 100. A higher score indicated better vision-related quality of life.</p> |

|                                        |           |
|----------------------------------------|-----------|
| End point type                         | Secondary |
| End point timeframe:                   |           |
| Baseline, Week 24, Week 52 and Week 76 |           |

| End point values                     | Brolucizumab 6 mg | Aflibercept 2 mg |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 226               | 224              |  |  |
| Units: score on a scale              |                   |                  |  |  |
| arithmetic mean (standard deviation) |                   |                  |  |  |
| Week 24 (n=193, 192)                 | 5.6 (± 11.51)     | 6.4 (± 11.92)    |  |  |
| Week 52 (n=119, 125)                 | 6.9 (± 13.21)     | 7.6 (± 10.47)    |  |  |
| Week 76 (n=95, 114)                  | 8.6 (± 13.89)     | 7.5 (± 11.55)    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects according to their Anti-drug antibody (ADA) titer at screening and Week 4, Week 12, Week 24, Week 36, Week 52 and Week 76

|                 |                                                                                                                                                             |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of subjects according to their Anti-drug antibody (ADA) titer at screening and Week 4, Week 12, Week 24, Week 36, Week 52 and Week 76 <sup>[2]</sup> |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Anti-drug antibodies (ADA) levels were assessed from subjects assigned to brolucizumab treatment only.

|                                                                  |           |
|------------------------------------------------------------------|-----------|
| End point type                                                   | Secondary |
| End point timeframe:                                             |           |
| Baseline, Week 4, Week 12, Week 24, Week 36, Week 52 and Week 76 |           |

Notes:

[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: No statistical analysis was planned for this secondary outcome

| End point values            | Brolucizumab 6 mg |  |  |  |
|-----------------------------|-------------------|--|--|--|
| Subject group type          | Reporting group   |  |  |  |
| Number of subjects analysed | 226               |  |  |  |
| Units: Participants         |                   |  |  |  |
| Baseline Negative (n=219)   | 67                |  |  |  |
| Week 4 Negative (n=208)     | 76                |  |  |  |
| Week 12 Negative (n=170)    | 58                |  |  |  |
| Week 24 Negative (n=134)    | 44                |  |  |  |
| Week 36 Negative (n=114)    | 33                |  |  |  |
| Week 52 Negative (n=101)    | 28                |  |  |  |
| Week 76 Negative (n=68)     | 17                |  |  |  |
| Baseline 40 (n=219)         | 29                |  |  |  |
| Week 4 40 (n=208)           | 29                |  |  |  |

|                        |    |  |  |  |
|------------------------|----|--|--|--|
| Week 12 40 (n=170)     | 17 |  |  |  |
| Week 24 40 (n=134)     | 14 |  |  |  |
| Week 36 40 (n=114)     | 18 |  |  |  |
| Week 52 40 (n=101)     | 18 |  |  |  |
| Week 76 40 (n=68)      | 6  |  |  |  |
| Baseline 120 (n=219)   | 33 |  |  |  |
| Week 4 120 (n=208)     | 31 |  |  |  |
| Week 12 120 (n=170)    | 31 |  |  |  |
| Week 24 120 (n=134)    | 23 |  |  |  |
| Week 36 120 (n=114)    | 19 |  |  |  |
| Week 52 120 (n=101)    | 19 |  |  |  |
| Week 76 120 (n=68)     | 18 |  |  |  |
| Baseline 360 (n=219)   | 37 |  |  |  |
| Week 4 360 (n=208)     | 28 |  |  |  |
| Week 12 360 (n=170)    | 25 |  |  |  |
| Week 24 360 (n=134)    | 17 |  |  |  |
| Week 36 360 (n=114)    | 17 |  |  |  |
| Week 52 360 (n=101)    | 16 |  |  |  |
| Week 76 360 (n=68)     | 14 |  |  |  |
| Baseline 1080 (n=219)  | 31 |  |  |  |
| Week 4 1080 (n=208)    | 27 |  |  |  |
| Week 12 1080 (n=170)   | 19 |  |  |  |
| Week 24 1080 (n=134)   | 19 |  |  |  |
| Week 36 1080 (n=114)   | 17 |  |  |  |
| Week 52 1080 (n=101)   | 14 |  |  |  |
| Week 76 1080 (n=68)    | 10 |  |  |  |
| Baseline 3240 (n=219)  | 15 |  |  |  |
| Week 4 3240 (n=208)    | 9  |  |  |  |
| Week 12 3240 (n=170)   | 11 |  |  |  |
| Week 24 3240 (n=134)   | 11 |  |  |  |
| Week 36 3240 (n=114)   | 8  |  |  |  |
| Week 52 3240 (n=101)   | 5  |  |  |  |
| Week 76 3240 (n=68)    | 2  |  |  |  |
| Baseline 9720 (n=219)  | 1  |  |  |  |
| Week 4 9720 (n=208)    | 6  |  |  |  |
| Week 12 9720 (n=170)   | 7  |  |  |  |
| Week 24 9720 (n=134)   | 5  |  |  |  |
| Week 36 9720 (n=114)   | 1  |  |  |  |
| Week 52 9720 (n=101)   | 1  |  |  |  |
| Week 76 9720 (n=68)    | 1  |  |  |  |
| Baseline 29200 (n=219) | 6  |  |  |  |
| Week 4 29200 (n=208)   | 2  |  |  |  |
| Week 12 29200 (n=170)  | 2  |  |  |  |
| Week 24 29200 (n=134)  | 1  |  |  |  |
| Week 36 29200 (n=114)  | 1  |  |  |  |
| Week 52 29200 (n=101)  | 0  |  |  |  |
| Week 76 29200 (n=68)   | 0  |  |  |  |

## Statistical analyses



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 4 weeks post treatment, up to maximum duration of 76 weeks

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious adverse events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Brolucizumab 6mg |
|-----------------------|------------------|

Reporting group description:

Brolucizumab 6mg

|                       |         |
|-----------------------|---------|
| Reporting group title | Overall |
|-----------------------|---------|

Reporting group description:

Overall

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Aflibercept 2mg |
|-----------------------|-----------------|

Reporting group description:

Aflibercept 2mg

| Serious adverse events                                              | Brolucizumab 6mg  | Overall           | Aflibercept 2mg  |
|---------------------------------------------------------------------|-------------------|-------------------|------------------|
| Total subjects affected by serious adverse events                   |                   |                   |                  |
| subjects affected / exposed                                         | 32 / 226 (14.16%) | 48 / 450 (10.67%) | 16 / 224 (7.14%) |
| number of deaths (all causes)                                       | 0                 | 2                 | 2                |
| number of deaths resulting from adverse events                      | 0                 | 0                 | 0                |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |                   |                  |
| Bladder neoplasm                                                    |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 226 (0.00%)   | 1 / 450 (0.22%)   | 1 / 224 (0.45%)  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1             | 0 / 1            |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             | 0 / 0            |
| Eyelid seborrhoeic keratosis - Fellow eye                           |                   |                   |                  |
| subjects affected / exposed                                         | 0 / 226 (0.00%)   | 1 / 450 (0.22%)   | 1 / 224 (0.45%)  |
| occurrences causally related to treatment / all                     | 0 / 0             | 0 / 1             | 0 / 1            |
| deaths causally related to treatment / all                          | 0 / 0             | 0 / 0             | 0 / 0            |
| Prostate cancer                                                     |                   |                   |                  |

|                                                      |                 |                 |                 |
|------------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                          | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 2           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Vascular disorders                                   |                 |                 |                 |
| Aortic stenosis                                      |                 |                 |                 |
| subjects affected / exposed                          | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Vasospasm                                            |                 |                 |                 |
| subjects affected / exposed                          | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| General disorders and administration site conditions |                 |                 |                 |
| Chest pain                                           |                 |                 |                 |
| subjects affected / exposed                          | 1 / 226 (0.44%) | 2 / 450 (0.44%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 3           | 0 / 2           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders             |                 |                 |                 |
| Benign prostatic hyperplasia                         |                 |                 |                 |
| subjects affected / exposed                          | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                 |                 |                 |
| Pleural mass                                         |                 |                 |                 |
| subjects affected / exposed                          | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Psychiatric disorders                                |                 |                 |                 |
| Depression                                           |                 |                 |                 |
| subjects affected / exposed                          | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0           | 0 / 0           | 0 / 0           |
| Product issues                                       |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Device dislocation                              |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 3           | 0 / 3           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Investigations                                  |                 |                 |                 |
| Weight increased                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Dislocation of vertebra                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Fall                                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Subdural haemorrhage                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Congenital, familial and genetic disorders      |                 |                 |                 |
| Atrial septal defect                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac disorders                               |                 |                 |                 |
| Angina pectoris                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Atrial fibrillation                             |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac arrest                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1           |
| Cardiac failure                                 |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac failure congestive                      |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cardiac valve disease                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Myocardial infarction                           |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Palpitations                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Cerebral infarction                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cerebrovascular accident                        |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 1           | 0 / 1           |
| Ischaemic stroke                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Syncope                                         |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Transient ischaemic attack                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Blood and lymphatic system disorders            |                 |                 |                 |
| Anaemia                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ear and labyrinth disorders                     |                 |                 |                 |
| Vertigo                                         |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Eye disorders                                   |                 |                 |                 |
| Cataract - Fellow eye                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Cataract - Study eye                            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Glaucoma - Study eye                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Glaucoma - Fellow eye                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Iridocyclitis - Study eye                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal aneurysm - Study eye                    |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal artery occlusion - Fellow eye           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal artery occlusion - Study eye            |                 |                 |                 |
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal detachment - Study eye                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal occlusive vasculitis - Study eye        |                 |                 |                 |
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 2 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal vasculitis - Study eye                  |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2           | 2 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Retinal vascular occlusion - Study eye          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Uveitis - Study eye                             |                 |                 |                 |
| subjects affected / exposed                     | 3 / 226 (1.33%) | 3 / 450 (0.67%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 2 / 3           | 2 / 3           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vitreous haemorrhage - Study eye                |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vitreous opacities - Study eye                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Vitritis - Study eye                            |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Mallory-Weiss syndrome                          |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pancreatitis acute                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Hepatobiliary disorders                         |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Cholecystitis acute                             |                 |                 |                 |
| subjects affected / exposed                     | 0 / 226 (0.00%) | 1 / 450 (0.22%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Renal and urinary disorders                     |                 |                 |                 |
| Urinary retention                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Osteoarthritis                                  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 2 / 450 (0.44%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Muscular weakness                               |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| COVID-19                                        |                 |                 |                 |
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Bronchitis                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 2 / 450 (0.44%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 2           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| COVID-19 pneumonia                              |                 |                 |                 |
| subjects affected / exposed                     | 1 / 226 (0.44%) | 1 / 450 (0.22%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Endophthalmitis - Study eye                     |                 |                 |                 |

|                                                 |                 |                 |                 |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 2 / 226 (0.88%) | 2 / 450 (0.44%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2           | 1 / 2           | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

Frequency threshold for reporting non-serious adverse events: 2 %

| <b>Non-serious adverse events</b>                     | Brolucizumab 6mg   | Overall            | Aflibercept 2mg   |
|-------------------------------------------------------|--------------------|--------------------|-------------------|
| Total subjects affected by non-serious adverse events |                    |                    |                   |
| subjects affected / exposed                           | 109 / 226 (48.23%) | 204 / 450 (45.33%) | 95 / 224 (42.41%) |
| Investigations                                        |                    |                    |                   |
| Intraocular pressure increased - Fellow eye           |                    |                    |                   |
| subjects affected / exposed                           | 3 / 226 (1.33%)    | 9 / 450 (2.00%)    | 6 / 224 (2.68%)   |
| occurrences (all)                                     | 3                  | 10                 | 7                 |
| Intraocular pressure increased - Study eye            |                    |                    |                   |
| subjects affected / exposed                           | 4 / 226 (1.77%)    | 12 / 450 (2.67%)   | 8 / 224 (3.57%)   |
| occurrences (all)                                     | 4                  | 25                 | 21                |
| Injury, poisoning and procedural complications        |                    |                    |                   |
| Fall                                                  |                    |                    |                   |
| subjects affected / exposed                           | 3 / 226 (1.33%)    | 8 / 450 (1.78%)    | 5 / 224 (2.23%)   |
| occurrences (all)                                     | 4                  | 10                 | 6                 |
| Vascular disorders                                    |                    |                    |                   |
| Hypertension                                          |                    |                    |                   |
| subjects affected / exposed                           | 26 / 226 (11.50%)  | 45 / 450 (10.00%)  | 19 / 224 (8.48%)  |
| occurrences (all)                                     | 28                 | 48                 | 20                |
| Nervous system disorders                              |                    |                    |                   |
| Dizziness                                             |                    |                    |                   |
| subjects affected / exposed                           | 4 / 226 (1.77%)    | 11 / 450 (2.44%)   | 7 / 224 (3.13%)   |
| occurrences (all)                                     | 4                  | 13                 | 9                 |
| Eye disorders                                         |                    |                    |                   |
| Cataract - Study eye                                  |                    |                    |                   |
| subjects affected / exposed                           | 9 / 226 (3.98%)    | 11 / 450 (2.44%)   | 2 / 224 (0.89%)   |
| occurrences (all)                                     | 9                  | 11                 | 2                 |
| Dry eye - Fellow eye                                  |                    |                    |                   |
| subjects affected / exposed                           | 5 / 226 (2.21%)    | 14 / 450 (3.11%)   | 9 / 224 (4.02%)   |
| occurrences (all)                                     | 5                  | 14                 | 9                 |
| Dry eye - Study eye                                   |                    |                    |                   |

|                                            |                  |                  |                  |
|--------------------------------------------|------------------|------------------|------------------|
| subjects affected / exposed                | 6 / 226 (2.65%)  | 15 / 450 (3.33%) | 9 / 224 (4.02%)  |
| occurrences (all)                          | 8                | 17               | 9                |
| Eye pain - Study eye                       |                  |                  |                  |
| subjects affected / exposed                | 4 / 226 (1.77%)  | 15 / 450 (3.33%) | 11 / 224 (4.91%) |
| occurrences (all)                          | 6                | 23               | 17               |
| Conjunctival haemorrhage - Study eye       |                  |                  |                  |
| subjects affected / exposed                | 11 / 226 (4.87%) | 23 / 450 (5.11%) | 12 / 224 (5.36%) |
| occurrences (all)                          | 11               | 27               | 16               |
| Macular oedema - Study eye                 |                  |                  |                  |
| subjects affected / exposed                | 15 / 226 (6.64%) | 25 / 450 (5.56%) | 10 / 224 (4.46%) |
| occurrences (all)                          | 25               | 38               | 13               |
| Foreign body sensation in eyes - Study eye |                  |                  |                  |
| subjects affected / exposed                | 5 / 226 (2.21%)  | 6 / 450 (1.33%)  | 1 / 224 (0.45%)  |
| occurrences (all)                          | 5                | 6                | 1                |
| Retinal haemorrhage - Study eye            |                  |                  |                  |
| subjects affected / exposed                | 2 / 226 (0.88%)  | 10 / 450 (2.22%) | 8 / 224 (3.57%)  |
| occurrences (all)                          | 2                | 10               | 8                |
| Uveitis - Study eye                        |                  |                  |                  |
| subjects affected / exposed                | 5 / 226 (2.21%)  | 5 / 450 (1.11%)  | 0 / 224 (0.00%)  |
| occurrences (all)                          | 6                | 6                | 0                |
| Visual acuity reduced - Study eye          |                  |                  |                  |
| subjects affected / exposed                | 15 / 226 (6.64%) | 27 / 450 (6.00%) | 12 / 224 (5.36%) |
| occurrences (all)                          | 19               | 33               | 14               |
| Retinal exudates - Study eye               |                  |                  |                  |
| subjects affected / exposed                | 5 / 226 (2.21%)  | 13 / 450 (2.89%) | 8 / 224 (3.57%)  |
| occurrences (all)                          | 5                | 13               | 8                |
| Vitreous detachment - Study eye            |                  |                  |                  |
| subjects affected / exposed                | 5 / 226 (2.21%)  | 10 / 450 (2.22%) | 5 / 224 (2.23%)  |
| occurrences (all)                          | 5                | 12               | 7                |
| Vitreous floaters - Study eye              |                  |                  |                  |
| subjects affected / exposed                | 11 / 226 (4.87%) | 16 / 450 (3.56%) | 5 / 224 (2.23%)  |
| occurrences (all)                          | 12               | 18               | 6                |
| Vitritis - Study eye                       |                  |                  |                  |

|                                                                                                                       |                      |                        |                      |
|-----------------------------------------------------------------------------------------------------------------------|----------------------|------------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)                                                                      | 5 / 226 (2.21%)<br>5 | 5 / 450 (1.11%)<br>5   | 0 / 224 (0.00%)<br>0 |
| Vitreous opacities - Study eye<br>subjects affected / exposed<br>occurrences (all)                                    | 5 / 226 (2.21%)<br>5 | 6 / 450 (1.33%)<br>6   | 1 / 224 (0.45%)<br>1 |
| Gastrointestinal disorders<br>Toothache<br>subjects affected / exposed<br>occurrences (all)                           | 5 / 226 (2.21%)<br>7 | 8 / 450 (1.78%)<br>10  | 3 / 224 (1.34%)<br>3 |
| Musculoskeletal and connective tissue disorders<br>Osteoarthritis<br>subjects affected / exposed<br>occurrences (all) | 6 / 226 (2.65%)<br>7 | 8 / 450 (1.78%)<br>10  | 2 / 224 (0.89%)<br>3 |
| Back pain<br>subjects affected / exposed<br>occurrences (all)                                                         | 2 / 226 (0.88%)<br>2 | 9 / 450 (2.00%)<br>9   | 7 / 224 (3.13%)<br>7 |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)                                                        | 2 / 226 (0.88%)<br>2 | 8 / 450 (1.78%)<br>9   | 6 / 224 (2.68%)<br>7 |
| Infections and infestations<br>Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)            | 5 / 226 (2.21%)<br>5 | 11 / 450 (2.44%)<br>12 | 6 / 224 (2.68%)<br>7 |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)                                                          | 7 / 226 (3.10%)<br>7 | 14 / 450 (3.11%)<br>14 | 7 / 224 (3.13%)<br>7 |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                                   | 6 / 226 (2.65%)<br>6 | 13 / 450 (2.89%)<br>14 | 7 / 224 (3.13%)<br>8 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                                 | 2 / 226 (0.88%)<br>2 | 9 / 450 (2.00%)<br>11  | 7 / 224 (3.13%)<br>9 |
| Metabolism and nutrition disorders<br>Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all)       | 5 / 226 (2.21%)<br>5 | 8 / 450 (1.78%)<br>8   | 3 / 224 (1.34%)<br>3 |

|                                                                              |                      |                      |                      |
|------------------------------------------------------------------------------|----------------------|----------------------|----------------------|
| Type 2 diabetes mellitus<br>subjects affected / exposed<br>occurrences (all) | 5 / 226 (2.21%)<br>5 | 5 / 450 (1.11%)<br>5 | 0 / 224 (0.00%)<br>0 |
|------------------------------------------------------------------------------|----------------------|----------------------|----------------------|

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|--------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 08 June 2020 | The main purpose of the amendment was to provide clarification and guidance on safety assessments in accordance to the urgent safety measure regarding the postmarketing reports with brolocizumab in the treatment of nAMD, which were identified as retinal vasculitis and/or retinal vascular occlusion, typically in the presence of IOI, that may result in severe vision loss. In addition, the amendment included modifications (exclusion criteria, prohibited medications/procedures, informed consent procedures, visit schedule and assessments, safety, laboratory evaluations, data analysis and statistical methods) due to the COVID-19 pandemic. |

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.

Study was terminated by sponsor due to increased incidences of AEs of special interest (intraocular inflammation including retinal vasculitis and retinal vascular occlusion), in patients dosed brolocizumab 6mg every 4 weeks beyond 3 initial doses

Notes: