



## Clinical trial results:

### Combined Randomized, Double-Blind, Dose-Confirming Phase 3a Study in Parallel Design to Assess the Efficacy and Safety of Topical 4-Week Treatment With 1% GPB Cream vs Placebo and Open-Label Phase 3b Study to Assess Long-Term Efficacy and Safety in Patients With Primary Axillary Hyperhidrosis Treated With 1% GPB Cream

#### Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2017-004534-28       |
| Trial protocol           | DE SE GB AT HU DK PL |
| Global end of trial date | 02 November 2021     |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1               |
| This version publication date  | 25 December 2022 |
| First version publication date | 25 December 2022 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | Hyp1-18/2016 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03658616 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Dr. August Wolff GmbH & Co. KG Arzneimittel   |
| Sponsor organisation address | Sudbrackstr. 56, Bielefeld, Germany, 33611  |
| Public contact               | Clinical Trial Disclosures Office, Dr. August Wolff GmbH & Co. KG Arzneimittel, ClinicalTrialDisclosures@drwolffgroup.com |
| Scientific contact           | Clinical Trial Disclosures Office, Dr. August Wolff GmbH & Co. KG Arzneimittel, ClinicalTrialDisclosures@drwolffgroup.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                       | 17 February 2022 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 02 November 2021 |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 02 November 2021 |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

The assessment of efficacy and safety of topical administration of 1% GPB or placebo cream in patients with primary axillary hyperhidrosis, and the assessment of long-term efficacy and safety of topical administration of 1% GPB cream in patients with primary axillary hyperhidrosis.

Protection of trial subjects:

This study was in compliance with the ethical principles of current applicable regulations, International Council for Harmonisation (ICH) of Good Clinical Practice, the principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements. All regulatory requirements relevant to the safety of the study participants were followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 01 May 2018      |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 17 Months        |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Poland: 72         |
| Country: Number of subjects enrolled | Sweden: 116        |
| Country: Number of subjects enrolled | United Kingdom: 17 |
| Country: Number of subjects enrolled | Denmark: 15        |
| Country: Number of subjects enrolled | Germany: 273       |
| Country: Number of subjects enrolled | Hungary: 35        |
| Worldwide total number of subjects   | 528                |
| EEA total number of subjects         | 511                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|  |     |
|--|-----|
| Infants and toddlers (28 days-23 months) | 0   |
| Children (2-11 years)                    | 0   |
| Adolescents (12-17 years)                | 0   |
| Adults (18-64 years)                     | 526 |
| From 65 to 84 years                      | 2   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Men and woman between 18 to 65 years with a body mass index of 18-32 kg/m<sup>2</sup> that were diagnosed with severe primary axillary hyperhidrosis scoring a 3 or 4 in hyperhidrosis disease severity were recruited for the study. Recruitment took place for the dose-confirming part (3a) and subsequently for the long-term part (3b).

### Pre-assignment

Screening details:

For part 3a, 171 out of 272 screened patients fulfilled the criteria of at least 50 mg sweat production in each axilla after a 14-day washout phase of previously used antiperspirants. For part 3b, 161 patients rolled over from part 3a and 357 out of 566 newly screened patients were also recruited fulfilling the selection criteria.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Dose-confirming part (Phase 3a)                 |
| Is this the baseline period? | Yes   |
| Allocation method            | Randomised - controlled                         |
| Blinding used                | Double blind                                    |
| Roles blinded                | Subject, Investigator, Monitor, Carer, Assessor |

Blinding implementation details:

To maintain the blind, GPB and placebo cream had identical appearance, texture, smell, as well as identical labeling and packaging. To minimize the potential for bias, treatment randomization information was kept confidential by the responsible sponsor personnel and was disclosed to the investigator, other study center personnel, the sponsor or its designee, and clinical research associate until after database lock.

### Arms

|                              |                                       |
|------------------------------|---------------------------------------|
| Are arms mutually exclusive? | Yes                                   |
| <b>Arm title</b>             | 1% glycopyrronium bromide (GPB) cream |

Arm description:

In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | 1% GPB cream |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Cream        |
| Routes of administration               | Topical use  |

Dosage and administration details:

Topical administration to both axillae, once daily for 4 weeks starting on Day 1a. After Week 4 topical administration as needed (at least twice per week and at most once daily).

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

Arm description:

The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance.

|  |             |
|--|-------------|
| Arm type                               | Placebo     |
| Investigational medicinal product name | Placebo     |
| Investigational medicinal product code |             |
| Other name                             |             |
| Pharmaceutical forms                   | Cream       |
| Routes of administration               | Topical use |

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**Dosage and administration details:**

Topical administration to both axillae, once daily for 4 weeks starting on Day 1a.

| <b>Number of subjects in period 1<sup>[1]</sup></b> | <b>1% glycopyrronium bromide (GPB) cream</b> | <b>Placebo cream</b> |
|---|--|----------------------|
| Started   | 87   | 84                   |
| Completed   | 84   | 82                   |
| Not completed                                       | 3  | 2                    |
| Consent withdrawn by subject                        | 1  | -                    |
| Lost to follow-up                                   | 1  | 1                    |
| Lack of efficacy                                    | 1  | 1                    |

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**Notes:**

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The study consists of part 3a and 3b. Part 3a includes 171 patients and part 3b includes 357 newly recruited patients, for a total of 528 patients. Part 3a and 3b each has a baseline (Day 1a and Day 1b). For technical reasons, we only can report one baseline period.

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**Period 2**

|                              |                             |
|------------------------------|-----------------------------|
| Period 2 title               | Long-term part (Phase 3b)   |
| Is this the baseline period? | No                          |
| Allocation method            | Non-randomised - controlled |
| Blinding used                | Not blinded                 |

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**Blinding implementation details:**

The long-term part of the study was open-label; thus, no randomization or blinding was done.

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**Arms**

|                  |                                       |
|------------------|---------------------------------------|
| <b>Arm title</b> | 1% glycopyrronium bromide (GPB) cream |
|------------------|---------------------------------------|

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**Arm description:**

During the Phase 3b part, patients were treated with 1% GPB cream for up to 72 weeks. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice per week but at most once daily) up to Week 72/EOTb, followed by a 4-week safety follow-up.

|  |                           |
|--|---------------------------|
| Arm type                               | Experimental              |
| Investigational medicinal product name | 1% glycopyrronium bromide |
| Investigational medicinal product code | 1% GPB cream              |
| Other name                             |                           |
| Pharmaceutical forms                   | Cream                     |
| Routes of administration               | Topical use               |

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**Dosage and administration details:**

Topical administration to both axillae. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice a week, but at most once daily) up to Week 72.

| <b>Number of subjects in period 2<sup>[2]</sup></b> | 1% glycopyrronium bromide (GPB) cream   |
|---|---|
| Started   | 161   |
| Completed   | 368   |
| Not completed                                       | 150   |
| Adverse event, non-fatal                            | 15  |
| Death   | 1   |
| Other reasons                                       | 36  |
| Lost to follow-up                                   | 43  |
| Consent withdrawn by subject                        | 55  |
| Joined  | 357   |
| Late recruitment                                    | 357   |
| Late recruitment reason                             | To achieve the planned total of 500 patients for the long-term 3b part of the study (including roll-over patients from Phase 3a), 357 additional patients were enrolled at Visit 3b (Baseline of long-term part). |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The study consists of part 3a and 3b. Part 3a includes 171 patients and part 3b includes 357 newly recruited patients, for a total of 528 patients. Part 3a and 3b each has a baseline (Day 1a and Day 1b). For technical reasons, we only can report one baseline period.

## Baseline characteristics

### Reporting groups

|   |                                       |
|---|---------------------------------------|
| Reporting group title   | 1% glycopyrronium bromide (GPB) cream |
| Reporting group description:<br>In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.       |                                       |
| Reporting group title   | Placebo cream                         |
| Reporting group description:<br>The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance. |                                       |

| Reporting group values                             | 1% glycopyrronium bromide (GPB) cream | Placebo cream | Total |
|--|---------------------------------------|---------------|-------|
| Number of subjects                                 | 87                                    | 84            | 171   |
| 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)                               | 0                                     | 0             | 0     |
| From 65-84 years                                   | 0                                     | 0             | 0     |
| 85 years and over                                  | 0                                     | 0             | 0     |
| Adults (18-65 years)                               | 87                                    | 84            | 171   |
| Age continuous<br>Units: years                     |                                       |               |       |
| arithmetic mean                                    | 37.4                                  | 37.8          |       |
| standard deviation                                 | ± 11.9                                | ± 12.3        | -     |
| Gender categorical<br>Units: Subjects              |                                       |               |       |
| Female   | 43                                    | 41            | 84    |
| Male   | 44                                    | 43            | 87    |

### Subject analysis sets

|   |                 |
|---|-----------------|
| Subject analysis set title  | 1% GPB (SAFa)   |
| Subject analysis set type   | Safety analysis |
| Subject analysis set description:<br>The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a. |                 |
| Subject analysis set title  | 1% GPB (FASa)   |
| Subject analysis set type   | Full analysis   |
| Subject analysis set description:<br>The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The       |                 |

FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | 1% GPB (PPSa) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | Placebo (SAFa)  |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.

|                            |                |
|----------------------------|----------------|
| Subject analysis set title | Placebo (FASa) |
| Subject analysis set type  | Full analysis  |

Subject analysis set description:

The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.

|                            |                |
|----------------------------|----------------|
| Subject analysis set title | Placebo (PPSa) |
| Subject analysis set type  | Per protocol   |

Subject analysis set description:

The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.

|                            |                 |
|----------------------------|-----------------|
| Subject analysis set title | 1% GPB (SAFb)   |
| Subject analysis set type  | Safety analysis |

Subject analysis set description:

The SAFb includes all patients treated at least once with IMP in the Phase 3b part of the study (ie, roll-over patients from the Phase 3a and patients newly recruited to the Phase 3b part) and was used for all safety analyses of Phase 3b.

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | 1% GPB (FASb) |
| Subject analysis set type  | Full analysis |

Subject analysis set description:

The FASb includes all patients of the SAFb

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | 1% GPB (FASnewb) |
| Subject analysis set type  | Full analysis    |

Subject analysis set description:

The FASnewb includes all patients newly recruited to the Phase 3b part who were treated at least once with IMP. This set is a subset of the FASb and was used for the evaluation of the primary and all secondary endpoints regarding only newly recruited patients. The FASb was used for all other secondary endpoint analyses.

|                            |               |
|----------------------------|---------------|
| Subject analysis set title | 1% GPB (PPSb) |
| Subject analysis set type  | Per protocol  |

Subject analysis set description:

The PPSb or PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28. No analyses using the PPSb or PPSnewb were planned after Week 28. Protocol deviations were reviewed during a DRM held before the final data base lock to identify major deviations leading to the exclusion of patients from the PPSb or PPSnewb.

|                            |                  |
|----------------------------|------------------|
| Subject analysis set title | 1% GPB (PPSnewb) |
| Subject analysis set type  | Per protocol     |

Subject analysis set description:

1% GPB PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28



| Reporting group values                             | 1% GPB (SAFa) | 1% GPB (FASa) | 1% GPB (PPSa) |
|--|---------------|---------------|---------------|
| Number of subjects                                 | 87            | 87            | 69            |
| Age categorical                                    |               |               |               |
| Units: Subjects                                    |               |               |               |
| In utero   | 0             | 0             | 0             |
| Preterm newborn infants (gestational age < 37 wks) | 0             | 0             | 0             |
| Newborns (0-27 days)                               | 0             | 0             | 0             |
| Infants and toddlers (28 days-23 months)           | 0             | 0             | 0             |
| Children (2-11 years)                              | 0             | 0             | 0             |
| Adolescents (12-17 years)                          | 0             | 0             | 0             |
| Adults (18-64 years)                               | 0             | 0             | 0             |
| From 65-84 years                                   | 0             | 0             | 0             |
| 85 years and over                                  | 0             | 0             | 0             |
| Adults (18-65 years)                               | 87            | 87            | 69            |
| Age continuous                                     |               |               |               |
| Units: years                                       |               |               |               |
| arithmetic mean                                    |               | 37.4          |               |
| standard deviation                                 | ±             | ± 11.9        | ±             |
| Gender categorical                                 |               |               |               |
| Units: Subjects                                    |               |               |               |
| Female   |               | 43            |               |
| Male   |               | 44            |               |

| Reporting group values                             | Placebo (SAFa) | Placebo (FASa) | Placebo (PPSa) |
|--|----------------|----------------|----------------|
| Number of subjects                                 | 84             | 84             | 58             |
| Age categorical                                    |                |                |                |
| Units: Subjects                                    |                |                |                |
| In utero   | 0              | 0              | 0              |
| Preterm newborn infants (gestational age < 37 wks) | 0              | 0              | 0              |
| Newborns (0-27 days)                               | 0              | 0              | 0              |
| Infants and toddlers (28 days-23 months)           | 0              | 0              | 0              |
| Children (2-11 years)                              | 0              | 0              | 0              |
| Adolescents (12-17 years)                          | 0              | 0              | 0              |
| Adults (18-64 years)                               | 0              | 0              | 0              |
| From 65-84 years                                   | 0              | 0              | 0              |
| 85 years and over                                  | 0              | 0              | 0              |
| Adults (18-65 years)                               | 84             | 84             | 58             |
| Age continuous                                     |                |                |                |
| Units: years                                       |                |                |                |
| arithmetic mean                                    |                | 37.8           |                |
| standard deviation                                 | ±              | ± 12.3         | ±              |
| Gender categorical                                 |                |                |                |
| Units: Subjects                                    |                |                |                |
| Female   |                | 41             |                |
| Male   |                | 43             |                |

| Reporting group values | 1% GPB (SAFb) | 1% GPB (FASb) | 1% GPB (FASnewb) |
|------------------------|---------------|---------------|------------------|
| Number of subjects     | 518           | 518           | 357              |

|   |   |   |   |
|---|---|---|---|
| Age categorical<br>Units: Subjects  |   |   |   |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over<br>Adults (18-65 years) |   |   |   |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ± | ± | ± |
| Gender categorical<br>Units: Subjects   |   |   |   |
| Female<br>Male  |   |   |   |

| <b>Reporting group values</b>   | 1% GPB (PPSb) | 1% GPB (PPSnewb) |  |
|---|---------------|------------------|--|
| Number of subjects  | 326           | 205              |  |
| Age categorical<br>Units: Subjects  |               |                  |  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over<br>Adults (18-65 years) |               |                  |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation   | ±             | ±                |  |
| Gender categorical<br>Units: Subjects   |               |                  |  |
| Female<br>Male  |               |                  |  |

## End points

### End points reporting groups

|  |                                       |
|--|---------------------------------------|
| Reporting group title  | 1% glycopyrronium bromide (GPB) cream |
| Reporting group description:<br>In the dose-confirming Phase 3a part, 171 patients were randomized in a 1:1 ratio to once-daily treatment with 1% GPB cream (87 patients) or placebo cream (84 patients) for 4 weeks.  |                                       |
| Reporting group title  | Placebo cream                         |
| Reporting group description:<br>The placebo cream was used in the Phase 3a part only and was identical to the GPB cream in terms of appearance, constitution of excipients, and packaging but was lacking active substance.  |                                       |
| Reporting group title  | 1% glycopyrronium bromide (GPB) cream |
| Reporting group description:<br>During the Phase 3b part, patients were treated with 1% GPB cream for up to 72 weeks. Newly recruited patients applied 1% GPB cream once daily for the first 4 weeks (analogous to the treatment applied during Phase 3a). After the first 4 weeks of treatment (ie, after completion of Week 4), all patients (including those who rolled-over from the Phase 3a part) applied 1% GPB cream as needed (at least twice per week but at most once daily) up to Week 72/EOTb, followed by a 4-week safety follow-up. |                                       |
| Subject analysis set title   | 1% GPB (SAFa)                         |
| Subject analysis set type  | Safety analysis                       |
| Subject analysis set description:<br>The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.  |                                       |
| Subject analysis set title   | 1% GPB (FASa)                         |
| Subject analysis set type  | Full analysis                         |
| Subject analysis set description:<br>The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.  |                                       |
| Subject analysis set title   | 1% GPB (PPSa)                         |
| Subject analysis set type  | Per protocol                          |
| Subject analysis set description:<br>The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.  |                                       |
| Subject analysis set title   | Placebo (SAFa)                        |
| Subject analysis set type  | Safety analysis                       |
| Subject analysis set description:<br>The SAFa includes all patients who received at least 1 dose of IMP in Phase 3a. The assignment of patients to the treatment groups was as actually treated. The SAFa was used for all safety analyses of Phase 3a.  |                                       |
| Subject analysis set title   | Placebo (FASa)                        |
| Subject analysis set type  | Full analysis                         |
| Subject analysis set description:<br>The FASa includes all patients randomized and treated at least once with IMP in Phase 3a. As per the intention-to-treat principle, the assignment of patients to the treatment groups was as randomized. The FASa was used for the evaluation of all efficacy endpoints of Phase 3a.  |                                       |
| Subject analysis set title   | Placebo (PPSa)                        |
| Subject analysis set type  | Per protocol                          |
| Subject analysis set description:<br>The PPSa includes all patients of the FASa without any major protocol deviations in Phase 3a. The assignment of patients to the treatment groups was as actually treated. Protocol deviations were reviewed during a blind data review meeting (BDRM) held before the data base lock and unblinding of the Phase 3a part data to identify major deviations leading to the exclusion of patients from the PPSa.  |                                       |

|  |                  |
|--|------------------|
| Subject analysis set title   | 1% GPB (SAFb)    |
| Subject analysis set type  | Safety analysis  |
| Subject analysis set description:  |                  |
| The SAFb includes all patients treated at least once with IMP in the Phase 3b part of the study (ie, roll-over patients from the Phase 3a and patients newly recruited to the Phase 3b part) and was used for all safety analyses of Phase 3b.   |                  |
| Subject analysis set title   | 1% GPB (FASb)    |
| Subject analysis set type  | Full analysis    |
| Subject analysis set description:  |                  |
| The FASb includes all patients of the SAFb   |                  |
| Subject analysis set title   | 1% GPB (FASnewb) |
| Subject analysis set type  | Full analysis    |
| Subject analysis set description:  |                  |
| The FASnewb includes all patients newly recruited to the Phase 3b part who were treated at least once with IMP. This set is a subset of the FASb and was used for the evaluation of the primary and all secondary endpoints regarding only newly recruited patients. The FASb was used for all other secondary endpoint analyses.                                      |                  |
| Subject analysis set title   | 1% GPB (PPSb)    |
| Subject analysis set type  | Per protocol     |
| Subject analysis set description:  |                  |
| The PPSb or PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28. No analyses using the PPSb or PPSnewb were planned after Week 28. Protocol deviations were reviewed during a DRM held before the final data base lock to identify major deviations leading to the exclusion of patients from the PPSb or PPSnewb. |                  |
| Subject analysis set title   | 1% GPB (PPSnewb) |
| Subject analysis set type  | Per protocol     |
| Subject analysis set description:  |                  |
| 1% GPB PPSnewb includes all patients of the FASb or FASnewb who had no major protocol deviations until Week 28   |                  |

**Primary: 3a: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1a) to Day 29**

|   |   |
|---|---|
| End point title   | 3a: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1a) to Day 29 |
| End point description:  |   |
| Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1a) to Day 29 in the 1% GPB group compared to the placebo group. For the dose-confirming part (Phase 3a), the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a). |   |
| End point type  | Primary   |
| End point timeframe:  |   |
| Baseline (Day 1a) to Day 29   |   |

| End point values              | 1% GPB (FASa)        | 1% GPB (PPSa)        | Placebo (FASa)       | Placebo (PPSa)       |
|-------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed   | 77                   | 65                   | 78                   | 55                   |
| Units: mg/ 5 min              |                      |                      |                      |                      |
| log mean (standard deviation) | -1.58 (± 1.87)       | -1.40 (± 1.57)       | -0.72 (± 1.55)       | -0.53 (± 1.21)       |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Absolute change in total sweat production from Bas |
| Statistical analysis description:<br>A mixed effects model was used with treatment and logarithmic baseline values as fixed effects and center as random effect to test the primary hypothesis on a significance level of 5% ( $\alpha=0.05$ ; 2-sided). |  |
| Comparison groups  | 1% GPB (FASa) v Placebo (FASa)                     |
| Number of subjects included in analysis  | 155  |
| Analysis specification   | Pre-specified                                      |
| Analysis type  | superiority  |
| P-value  | < 0.05   |
| Method   | Mixed models analysis                              |

### Primary: 3b: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1b) to Week 12

|  |  |
|--|--|
| End point title  | 3b: Primary efficacy endpoint: Absolute change in total sweat production from Baseline (Day 1b) to Week 12 |
| End point description:<br>Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1b) to Day 29 in the 1% GPB group compared to the placebo group. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12. |  |
| End point type   | Primary  |
| End point timeframe:<br>Baseline (Day 1b) to Week 12   |  |

| End point values              | 1% GPB (FASnewb)      | 1% GPB (PPSnewb)      |  |  |
|-------------------------------|-----------------------|-----------------------|--|--|
| Subject group type            | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed   | 316                   | 198                   |  |  |
| Units: mg/ 5 min              |                       |                       |  |  |
| log mean (standard deviation) | -1.529 ( $\pm$ 2.107) | -1.579 ( $\pm$ 2.112) |  |  |

## Statistical analyses

|   |                                     |
|---|-------------------------------------|
| <b>Statistical analysis title</b>   | Titel Endpunkt                      |
| Statistical analysis description:<br>A mixed effects model will be used with mean centered logarithmic baseline values as fixed effects and center as random effect to test the primary hypothesis on a significance level of 2.94% ( $\alpha=0.0294$ ; 2-sided). |                                     |
| Comparison groups   | 1% GPB (FASnewb) v 1% GPB (PPSnewb) |

|   |                       |
|---|-----------------------|
| Number of subjects included in analysis | 514                   |
| Analysis specification                  | Pre-specified         |
| Analysis type                           | other <sup>[1]</sup>  |
| P-value                                 | < 0.0294              |
| Method                                  | Mixed models analysis |

Notes:

[1] - Absolute change from Baseline was analysed

### Secondary: 3a: First key secondary endpoint: Percentage of HDSS responders at Day 29

|                 |   |
|-----------------|---|
| End point title | 3a: First key secondary endpoint: Percentage of HDSS responders at Day 29 |
|-----------------|---|

End point description:

Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively.

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

End point timeframe:

Day 29

| End point values              | 1% GPB (FASa)        | 1% GPB (PPSa)        | Placebo (FASa)       | Placebo (PPSa)       |
|-------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed   | 87                   | 69                   | 84                   | 58                   |
| Units: percentage of patients |                      |                      |                      |                      |
| number (not applicable)       | 23.0                 | 27.5                 | 11.9                 | 12.1                 |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Second key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 29

|                 |   |
|-----------------|---|
| End point title | 3a: Second key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 29 |
|-----------------|---|

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

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

End point timeframe:

Baseline (Day 1a) to Day 29

| End point values              | 1% GPB (FASa)        | 1% GPB (PPSa)        | Placebo (FASa)       | Placebo (PPSa)       |
|-------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type            | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed   | 84                   | 69                   | 79                   | 56                   |
| Units: Total score            |                      |                      |                      |                      |
| median (full range (min-max)) |                      |                      |                      |                      |
| Total score                   | -6 (-36 to 6)        | -6 (-36 to 6)        | -1 (-35 to 4)        | -1 (-35 to 4)        |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: First key secondary endpoint: Percentage of responders assessed by the HDSS ( $\geq 2$ -point improvement from Baseline) at Week 12 ( $> 25\%$ )

|                        |   |
|------------------------|---|
| End point title        | 3b: First key secondary endpoint: Percentage of responders assessed by the HDSS ( $\geq 2$ -point improvement from Baseline) at Week 12 ( $> 25\%$ )  |
| End point description: | Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Week 12                |   |

| End point values              | 1% GPB (FASb)        | 1% GPB (PPSb)        |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed   | 518                  | 326                  |  |  |
| Units: percentage of patients |                      |                      |  |  |
| number (not applicable)       | 28.0                 | 31.6                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Second key secondary endpoint: Percentage of responders assessed by the HDSS ( $\geq 2$ -point improvement from Baseline) at Week 28 ( $> 25\%$ )

|                        |   |
|------------------------|---|
| End point title        | 3b: Second key secondary endpoint: Percentage of responders assessed by the HDSS ( $\geq 2$ -point improvement from Baseline) at Week 28 ( $> 25\%$ )   |
| End point description: | Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |
| End point type         | Secondary   |

End point timeframe:

Week 28

| End point values              | 1% GPB (FASb)        | 1% GPB (PPSb)        |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed   | 518                  | 326                  |  |  |
| Units: percentage of patients |                      |                      |  |  |
| number (not applicable)       | 29.3                 | 35.6                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Third key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Week 12

|                 |   |
|-----------------|---|
| End point title | 3b: Third key secondary endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Week 12 |
|-----------------|---|

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

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

End point timeframe:

Baseline (Day 1b) to Week 12

| End point values                 | 1% GPB (FASb)        | 1% GPB (PPSb)        |  |  |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed      | 468                  | 321                  |  |  |
| Units: Total score               |                      |                      |  |  |
| median (confidence interval 95%) |                      |                      |  |  |
| Total score                      | -11 (-13 to -10)     | -12 (-13 to -10)     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Secondary efficacy endpoint: Absolute change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

|                 |  |
|-----------------|--|
| End point title | 3a: Secondary efficacy endpoint: Absolute change in sweat production assessed by GM from Baseline (Day 1a) to Day 29 |
|-----------------|--|



End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1a) to Day 29 by treatment group. For the dose-confirming part (Phase 3a), the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a).

End point type Secondary

End point timeframe:

Baseline (Day 1a) to Day 29

| End point values                   | 1% GPB (FASa)          | Placebo (FASa)         |  |  |
|------------------------------------|------------------------|------------------------|--|--|
| Subject group type                 | Subject analysis set   | Subject analysis set   |  |  |
| Number of subjects analysed        | 77                     | 78                     |  |  |
| Units: mg                          |                        |                        |  |  |
| log mean (confidence interval 95%) | -1.58 (-2.01 to -1.16) | -0.72 (-1.07 to -0.37) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Secondary efficacy endpoint: Percentage change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point title 3a: Secondary efficacy endpoint: Percentage change in sweat production assessed by GM from Baseline (Day 1a) to Day 29

End point description:

Percentage change of total sweat production from Baseline (Day 1a) to Day 29 by treatment group and in the 1% GPB group compared with the placebo group.

End point type Secondary

End point timeframe:

Baseline (Day 1a) to Day 29

| End point values                 | 1% GPB (FASa)             | 1% GPB (FASb)            |  |  |
|----------------------------------|---------------------------|--------------------------|--|--|
| Subject group type               | Subject analysis set      | Subject analysis set     |  |  |
| Number of subjects analysed      | 77                        | 78                       |  |  |
| Units: percent                   |                           |                          |  |  |
| median (confidence interval 95%) | -64.63 (-73.13 to -51.75) | -34.32 (-49.71 to -2.67) |  |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: 3a: Secondary efficacy endpoint: Percentage of responders assessed by GM on Day 29**

|  |  |
|--|--|
| End point title  | 3a: Secondary efficacy endpoint: Percentage of responders assessed by GM on Day 29 |
| End point description:<br>Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessed by gravimetric measurement (GM) compared to Baseline. For this dose-confirming part, the GM of sweat production was performed at the Screening Visit 2a, on Day 1a, and on Day 29/EOTa (Visit 5a). |  |
| End point type   | Secondary  |
| End point timeframe:<br>Day 29   |  |

| End point values                  | 1% GPB (FASa)        | Placebo (FASa)       |  |  |
|-----------------------------------|----------------------|----------------------|--|--|
| Subject group type                | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed       | 87                   | 84                   |  |  |
| Units: percentage of patients     |                      |                      |  |  |
| number (not applicable)           |                      |                      |  |  |
| 1. sweat reduction of $\geq 50\%$ | 57.5                 | 34.5                 |  |  |
| 2. sweat reduction of $\geq 75\%$ | 32.2                 | 16.7                 |  |  |
| 3. sweat reduction of $\geq 90\%$ | 23.0                 | 9.5                  |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: 3a: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1a) to Day 15 and Day 29**

|   |  |
|---|--|
| End point title   | 3a: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1a) to Day 15 and Day 29 |
| End point description:<br>Change of the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline (Day 1a) to Day 15 and to Day 29   |  |

| End point values                 | 1% GPB (FASa)        | Placebo (FASa)       |  |  |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed      | 87 <sup>[2]</sup>    | 84 <sup>[3]</sup>    |  |  |
| Units: score                     |                      |                      |  |  |
| median (confidence interval 95%) |                      |                      |  |  |
| Day 15                           | -1 (-1 to 0)         | 0 (0 to 0)           |  |  |
| Day 29                           | 0 (-1 to 0)          | 0 (0 to 0)           |  |  |

Notes:

[2] - Day 15: N=84

Day 29: N=83

[3] - Day 15: N=79

Day 29: N=80

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS on Day 15

|   |  |
|---|--|
| End point title   | 3a: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS on Day 15 |
| End point description:<br>Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Day 15  |  |

| End point values              | 1% GPB (FASa)        | Placebo (FASa)       |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed   | 87                   | 84                   |  |  |
| Units: percentage of patients |                      |                      |  |  |
| number (not applicable)       | 25.3                 | 9.5                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 15 and Day 29

|   |  |
|---|--|
| End point title   | 3a: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1a) to Day 15 and Day 29 |
| End point description:<br>The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Baseline (Day 1a) to Day 15 and Day 29  |  |

| End point values                 | 1% GPB (FASa)        | Placebo (FASa)       |  |  |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed      | 87 <sup>[4]</sup>    | 79                   |  |  |
| Units: Total score               |                      |                      |  |  |
| median (confidence interval 95%) |                      |                      |  |  |
| Day 15                           | -5 (-8 to -2)        | -1 (-2 to -1)        |  |  |
| Day 29                           | -6 (-9 to -4)        | -1 (-2 to -1)        |  |  |

Notes:

[4] - Day 15: N=85

Day 29: N=84

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3a: Secondary efficacy endpoint: Absolute change in the DLQI from Baseline (Day 1a) to Day 15 and Day 29

|                 |  |
|-----------------|--|
| End point title | 3a: Secondary efficacy endpoint: Absolute change in the DLQI from Baseline (Day 1a) to Day 15 and Day 29 |
|-----------------|--|

End point description:

The Dermatology Life Quality Index [DLQI] is scored on a 4-point scale: 'very much' = 3, 'a lot' = 2, 'a little' = 1, 'not at all' or 'question not relevant' = 0. It is calculated as sum score of all questions resulting in a total score between 0 and 30. The higher the score, the more the quality of life is impaired.

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

End point timeframe:

Baseline (Day 1a) to Day 15 and Day 29

| End point values                 | 1% GPB (FASa)        | Placebo (FASa)       |  |  |
|----------------------------------|----------------------|----------------------|--|--|
| Subject group type               | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed      | 87 <sup>[5]</sup>    | 79                   |  |  |
| Units: score                     |                      |                      |  |  |
| median (confidence interval 95%) |                      |                      |  |  |
| Day 15                           | -5 (-7 to -2)        | -2 (-3 to -1)        |  |  |
| Day 29                           | -5 (-8 to -4)        | -3 (-4 to -1)        |  |  |

Notes:

[5] - Day 15: N=85

Day 29: N=84

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Percentage change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4 and Week 12

|                 |  |
|-----------------|--|
| End point title | 3b: Secondary efficacy endpoint: Percentage change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4 and Week 12 |
|-----------------|--|

End point description:

Percentage change in total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1b) to Week 4 and Week 12 in the 1% GPB group. For the long-term part of the study (Phase 3b),

the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

|   |           |
|---|-----------|
| End point type                          | Secondary |
| End point timeframe:                    |           |
| Baseline (Day 1b) to Week 4 and Week 12 |           |

| End point values              | 1% GPB (FASnewb)          |  |  |  |
|-------------------------------|---------------------------|--|--|--|
| Subject group type            | Subject analysis set      |  |  |  |
| Number of subjects analysed   | 357 <sup>[6]</sup>        |  |  |  |
| Units: percent                |                           |  |  |  |
| median (full range (min-max)) |                           |  |  |  |
| Week 4                        | -68.270 (-99.97 to 2100)  |  |  |  |
| Week 12                       | -65.630 (-99.97 to 17050) |  |  |  |

Notes:

[6] - Week 4: N=313

Week 12: N= 316

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Absolute change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4

|                 |  |
|-----------------|--|
| End point title | 3b: Secondary efficacy endpoint: Absolute change in total sweat production assessed by GM from Baseline (Day 1b) to Week 4 |
|-----------------|--|

End point description:

Absolute change in logarithmic values of total sweat production assessed by gravimetric measurement (GM) from Baseline (Day 1b) to Week 4 in the 1% GPB group. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

|                             |           |
|-----------------------------|-----------|
| End point type              | Secondary |
| End point timeframe:        |           |
| Baseline (Day 1b) to Week 4 |           |

| End point values              | 1% GPB (FASnewb)     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 313                  |  |  |  |
| Units: mg                     |                      |  |  |  |
| log mean (standard deviation) | -1.642 (± 2.132)     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 4

|                 |  |
|-----------------|--|
| End point title | 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 4 |
|-----------------|--|

End point description:

Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessed by gravimetric measurement (GM) compared to Baseline. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

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

End point timeframe:

Week 4

| End point values              | 1% GPB (FASnewb)     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 357                  |  |  |  |
| Units: percentage of patients |                      |  |  |  |
| number (not applicable)       |                      |  |  |  |
| ≥50%                          | 55.5                 |  |  |  |
| ≥75%                          | 38.9                 |  |  |  |
| ≥90%                          | 21.8                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 12

|                 |   |
|-----------------|---|
| End point title | 3b: Secondary efficacy endpoint: Percentage of responders assessed by GM at Week 12 |
|-----------------|---|

End point description:

Responders are defined as patients with at least 50%, 75%, and 90% sweat reduction assessed by gravimetric measurement (GM) compared to Baseline. For the long-term part of the study (Phase 3b), the GM was only performed for newly recruited patients, and was performed at Screening Visit 2b, Day 1b, Week 4, and Week 12.

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

End point timeframe:

Week 12

| End point values              | 1% GPB (FASnewb)     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 357                  |  |  |  |
| Units: percentage of patients |                      |  |  |  |
| number (not applicable)       |                      |  |  |  |
| ≥50%                          | 54.1                 |  |  |  |
| ≥75%                          | 36.4                 |  |  |  |
| ≥90%                          | 21.6                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Weeks 4, 8, 52, and 72 (unequal 25%)

|                        |   |
|------------------------|---|
| End point title        | 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Weeks 4, 8, 52, and 72 (unequal 25%)   |
| End point description: | Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |
| End point type         | Secondary   |
| End point timeframe:   | Weeks 4, 8, 52, 72  |

| End point values              | 1% GPB (FASb)        |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 518 <sup>[7]</sup>   |  |  |  |
| Units: percentage of patients |                      |  |  |  |
| number (not applicable)       |                      |  |  |  |
| Week 4                        | 20.7                 |  |  |  |
| Week 8                        | 26.6                 |  |  |  |
| Week 52                       | 30.1                 |  |  |  |
| Week 72                       | 32.0                 |  |  |  |

Notes:

[7] - Week 4: N=357 (newly recruited patients only)

Week 8: N=518

Week 52: N=518

Week 72: N=518

## Statistical analyses

No statistical analyses for this end point

## Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS (≥2-point improvement from Baseline) at Week 12 (unequal 50%)

|   |  |
|---|--|
| End point title   | 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HDSS ( $\geq 2$ -point improvement from Baseline) at Week 12 (unequal 50%) |
| End point description:<br>Responders are defined as patients with at least 2-point improvement (= reduction) on the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Week 12   |  |

| End point values              | 1% GPB (FASb)        | 1% GPB (PPSb)        |  |  |
|-------------------------------|----------------------|----------------------|--|--|
| Subject group type            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed   | 518                  | 326                  |  |  |
| Units: percentage of patients |                      |                      |  |  |
| number (not applicable)       | 28.0                 | 31.6                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

|   |   |
|---|---|
| End point title   | 3b: Secondary efficacy endpoint: Absolute change in the HDSS from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72 |
| End point description:<br>Change of the Hyperhidrosis Disease Severity Scale [HDSS] compared to Baseline. This 4-point scale was completed at each visit of both study parts (Phase 3a and 3b) starting with the Screening Visit, respectively. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Weeks 4, 8, 12, 28, 52, and 72  |   |

| End point values              | 1% GPB (FASb)        |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   |                      |  |  |  |
| Units: score                  |                      |  |  |  |
| median (full range (min-max)) |                      |  |  |  |
| Week 4                        | -1 (-3 to 1)         |  |  |  |
| Week 8                        | -1 (-3 to 1)         |  |  |  |
| Week 12                       | -1 (-3 to 1)         |  |  |  |
| Week 28                       | -1 (-3 to 1)         |  |  |  |
| Week 52                       | -1 (-3 to 1)         |  |  |  |
| Week 72                       | -1 (-3 to 1)         |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Weeks 4, 8, 28, 52, and 72

|                 |   |
|-----------------|---|
| End point title | 3b: Secondary efficacy endpoint: Absolute change in the HidroQoL from Baseline (Day 1b) to Weeks 4, 8, 28, 52, and 72 |
|-----------------|---|

End point description:

The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated.

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

End point timeframe:

Baseline (Day 1 b) to Weeks 4, 8, 28, 52, and 72

| End point values              | 1% GPB (FASb)        |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 518 <sup>[8]</sup>   |  |  |  |
| Units: Score                  |                      |  |  |  |
| median (full range (min-max)) |                      |  |  |  |
| Week 4                        | -7.0 (-36.0 to 6.0)  |  |  |  |
| Week 8                        | -10.0 (-36.0 to 5.0) |  |  |  |
| Week 28                       | -13.0 (-36.0 to 6.0) |  |  |  |
| Week 52                       | -16.0 (-36.0 to 6.0) |  |  |  |
| Week 72                       | -17.0 (-36.0 to 9.0) |  |  |  |

Notes:

[8] - Week 4: N=332

Week 8: N=474

Week 28: N=430

Week 52: N=383

Week 72: N=369

## Statistical analyses

No statistical analyses for this end point

### Secondary: 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HidroQoL (≥4-point improvement from Baseline (Day 1b)) at Weeks 4, 8, 12, 28, 52, and 72

|   |  |
|---|--|
| End point title   | 3b: Secondary efficacy endpoint: Percentage of responders assessed by the HidroQoL ( $\geq 4$ -point improvement from Baseline (Day 1b)) at Weeks 4, 8, 12, 28, 52, and 72 |
| End point description:<br>The Hyperhidrosis Quality of Life index [HidroQoL] consists of 18 items divided into 2 domains: a daily life activities domain (items 1 to 6) and a psychosocial domain (items 7 to 18). The answers are scored on a 3-point scale as follows: 'no, not at all' = 0, 'a little' = 1, and 'very much' = 2. A total score was calculated. |  |
| End point type  | Secondary  |
| End point timeframe:<br>Weeks 4, 8, 12, 28, 52, and 72  |  |

| End point values            | 1% GPB (FASb)        |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 518 <sup>[9]</sup>   |  |  |  |
| Units: percent              |                      |  |  |  |
| number (not applicable)     |                      |  |  |  |
| Week 4                      | 64.7                 |  |  |  |
| Week 8                      | 72.4                 |  |  |  |
| Week 12                     | 76.1                 |  |  |  |
| Week 28                     | 72.2                 |  |  |  |
| Week 52                     | 65.6                 |  |  |  |
| Week 72                     | 64.9                 |  |  |  |

Notes:

[9] - Week 4: N=357

Week 8, 12, 28, 52 and 72: N=518

## Statistical analyses

No statistical analyses for this end point

## Secondary: 3b: Secondary efficacy endpoint: Absolute change in the DLQI questionnaire from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

|  |   |
|--|---|
| End point title  | 3b: Secondary efficacy endpoint: Absolute change in the DLQI questionnaire from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72 |
| End point description:<br>The Dermatology Life Quality Index [DLQI] is scored on a 4-point scale: 'very much' = 3, 'a lot' = 2, 'a little' = 1, 'not at all' or 'question not relevant' = 0. It is calculated as sum score of all questions resulting in a total score between 0 and 30. The higher the score, the more the quality of life is impaired. |   |
| End point type   | Secondary   |
| End point timeframe:<br>Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72  |   |

| End point values              | 1% GPB (FASb)        |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 518 <sup>[10]</sup>  |  |  |  |
| Units: Score                  |                      |  |  |  |
| median (full range (min-max)) |                      |  |  |  |
| Week 4                        | -6 (-30 to 13)       |  |  |  |
| Week 8                        | -7 (-30 to 19)       |  |  |  |
| Week 12                       | -7 (-30 to 21)       |  |  |  |
| Week 28                       | -8 (-28 to 21)       |  |  |  |
| Week 52                       | -9 (-28 to 12)       |  |  |  |
| Week 72                       | -10 (-27 to 8)       |  |  |  |

Notes:

[10] - Week 4: N=331

Week 8: N=472

Week 12: N=468

Week 28: N=430

Week 52: N=383

Week 72: N=369

## Statistical analyses

No statistical analyses for this end point

## Secondary: 3b: Secondary efficacy endpoint: Absolute change in patient-rated hyperhidrosis severity from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72

|                 |   |
|-----------------|---|
| End point title | 3b: Secondary efficacy endpoint: Absolute change in patient-rated hyperhidrosis severity from Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72 |
|-----------------|---|

End point description:

The patient-rated hyperhidrosis severity was assessed by asking the following question: "How did you perceive your underarm sweating in the past 24 hours?" and is rated on a scale from 0 (no sweating at all) to 10 (worst sweating that you ever had).

|                      |   |
|----------------------|---|
| End point type       | Secondary   |
| End point timeframe: | Baseline (Day 1b) to Weeks 4, 8, 12, 28, 52, and 72 |

| End point values              | 1% GPB (FASb)        |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 518 <sup>[11]</sup>  |  |  |  |
| Units: Score                  |                      |  |  |  |
| median (full range (min-max)) |                      |  |  |  |
| Week 4                        | -3 (-10 to 2)        |  |  |  |
| Week 8                        | -3 (-10 to 3)        |  |  |  |
| Week 12                       | -3 (-10 to 5)        |  |  |  |
| Week 28                       | -3 (-10 to 3)        |  |  |  |
| Week 52                       | -4 (-10 to 2)        |  |  |  |
| Week 72                       | -4 (-10 to 3)        |  |  |  |

Notes:

[11] - Week 4: N=217

Week 8: N=211

Week 12: N=210

Week 28: N=189

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline (BL) to Week 72

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 21.1 |
|--------------------|------|

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Phase 3a: 1% GPB (SAFa) |
|-----------------------|-------------------------|

Reporting group description:

Phase 3a: Treatment-emergent adverse events which started up to and including Day 29 or Week 4; patients self-administered the 1% GPB cream once daily in this period (SAFa, N=171)

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Phase 3a: Placebo (SAFa) |
|-----------------------|--------------------------|

Reporting group description:

Phase 3a: Treatment-emergent adverse events which started up to and including Day 29 or Week 4; patients self-administered the placebo cream once daily in this period (SAFa, N=171)

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb) |
|-----------------------|---|

Reporting group description:

Phase 3b: Treatment-emergent adverse events which started up to and including Day 29 or Week 4; Phase 3a (1% GPB only; N=81) PLUS Phase 3b (patients newly recruited to Phase 3b; N=357); patients self-administered the 1% GPB cream once daily in this period (SAFb, N=518)

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 3b: After Day 29/Week 4 to Week 72 (SAFb) |
|-----------------------|---|

Reporting group description:

Phase 3b: Treatment-emergent adverse events which started after Day 29 or Week 4 until Week 72 (EOTb): patients administered the 1% GPB cream as needed (at least twice per week and at most once daily) in this period (SAFb, N=518)

|                       |   |
|-----------------------|---|
| Reporting group title | Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb) |
|-----------------------|---|

Reporting group description:

Phase 3b: Treatment-emergent adverse events which started up to Week 72 (without AEs of Placebo patients during Phase 3a): all patients in the long-term part (SAFb, N=518)

|                       |  |
|-----------------------|--|
| Reporting group title | Phase 3b: BL to Week 72 - 1% GPB patients only (SAF) |
|-----------------------|--|

Reporting group description:

Phase 3b: Treatment-emergent adverse events which started up to Week 72 (without AEs of Placebo patients during Phase 3a): all patients in the safety analysis set who received GPB (SAF, N=528)

| Serious adverse events                            | Phase 3a: 1% GPB (SAFa) | Phase 3a: Placebo (SAFa) | Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb) |
|---|-------------------------|--------------------------|---|
| Total subjects affected by serious adverse events |                         |                          |   |
| subjects affected / exposed                       | 1 / 87 (1.15%)          | 0 / 84 (0.00%)           | 1 / 438 (0.23%)   |
| number of deaths (all causes)                     | 0                       | 0                        | 0   |
| number of deaths resulting from adverse events    | 0                       | 0                        | 0   |
| Surgical and medical procedures                   |                         |                          |   |
| Ovarian operation                                 |                         |                          |   |

|  |                |                |                 |
|--|----------------|----------------|-----------------|
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Sinus operation                                      |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| General disorders and administration site conditions |                |                |                 |
| Death  |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Gait disturbance                                     |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Reproductive system and breast disorders             |                |                |                 |
| Asthma   |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders      |                |                |                 |
| Tonsillar hypertrophy                                |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Psychiatric disorders                                |                |                |                 |
| Chronic idiopathic pain syndrome                     |                |                |                 |
| subjects affected / exposed                          | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          | 0 / 0           |
| Depression   |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Injury, poisoning and procedural complications  |                |                |                 |
| Electric shock                                  |                |                |                 |
| subjects affected / exposed                     | 1 / 87 (1.15%) | 0 / 84 (0.00%) | 1 / 438 (0.23%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Ankle fracture                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Concussion                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Humerus fracture                                |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Congenital, familial and genetic disorders      |                |                |                 |
| Micrognathia                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Nervous system disorders                        |                |                |                 |
| Relapsing-remitting multiple sclerosis          |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Ear and labyrinth disorders                     |                |                |                 |
| Tympanic membrane perforation                   |                |                |                 |

|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Eye disorders                                   |                |                |                 |
| Mydriasis                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Pupils unequal                                  |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Scleritis                                       |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Gastrointestinal disorders                      |                |                |                 |
| Crohn's disease                                 |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Umbilical hernia                                |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                |                |                 |
| Arthralgia                                      |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Infections and infestations                     |                |                |                 |
| Appendicitis                                    |                |                |                 |



|   |                |                |                 |
|---|----------------|----------------|-----------------|
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Corona virus infection                          |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Otitis media                                    |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |
| Vestibular neuronitis                           |                |                |                 |
| subjects affected / exposed                     | 0 / 87 (0.00%) | 0 / 84 (0.00%) | 0 / 438 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0           |

| <b>Serious adverse events</b>                        | Phase 3b: After Day 29/Week 4 to Week 72 (SAFb) | Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb) | Phase 3b: BL to Week 72 - 1% GPB patients only (SAF) |
|--|---|---|--|
| Total subjects affected by serious adverse events    |   |   |  |
| subjects affected / exposed                          | 22 / 518 (4.25%)                                | 23 / 518 (4.44%)                                      | 23 / 528 (4.36%)                                     |
| number of deaths (all causes)                        | 1   | 1   | 1  |
| number of deaths resulting from adverse events       | 0   | 0   | 0  |
| Surgical and medical procedures                      |   |   |  |
| Ovarian operation                                    |   |   |  |
| subjects affected / exposed                          | 1 / 518 (0.19%)                                 | 1 / 518 (0.19%)                                       | 1 / 528 (0.19%)                                      |
| occurrences causally related to treatment / all      | 0 / 1   | 0 / 1   | 0 / 1  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   | 0 / 0  |
| Sinus operation                                      |   |   |  |
| subjects affected / exposed                          | 1 / 518 (0.19%)                                 | 1 / 518 (0.19%)                                       | 1 / 528 (0.19%)                                      |
| occurrences causally related to treatment / all      | 0 / 1   | 0 / 1   | 0 / 1  |
| deaths causally related to treatment / all           | 0 / 0   | 0 / 0   | 0 / 0  |
| General disorders and administration site conditions |   |   |  |
| Death  |   |   |  |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 1           | 0 / 1           | 0 / 1           |
| Gait disturbance                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Reproductive system and breast disorders        |                 |                 |                 |
| Asthma  |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Respiratory, thoracic and mediastinal disorders |                 |                 |                 |
| Tonsillar hypertrophy                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Psychiatric disorders                           |                 |                 |                 |
| Chronic idiopathic pain syndrome                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Depression                                      |                 |                 |                 |
| subjects affected / exposed                     | 2 / 518 (0.39%) | 2 / 518 (0.39%) | 2 / 528 (0.38%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Injury, poisoning and procedural complications  |                 |                 |                 |
| Electric shock                                  |                 |                 |                 |
| subjects affected / exposed                     | 0 / 518 (0.00%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ankle fracture                                  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Concussion                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Humerus fracture                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Congenital, familial and genetic disorders      |                 |                 |                 |
| Micrognathia                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Nervous system disorders                        |                 |                 |                 |
| Relapsing-remitting multiple sclerosis          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Ear and labyrinth disorders                     |                 |                 |                 |
| Tympanic membrane perforation                   |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Eye disorders                                   |                 |                 |                 |
| Mydriasis                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Pupils unequal                                  |                 |                 |                 |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 1 / 1           | 1 / 1           | 1 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Scleritis                                       |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Gastrointestinal disorders                      |                 |                 |                 |
| Crohn's disease                                 |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Umbilical hernia                                |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Musculoskeletal and connective tissue disorders |                 |                 |                 |
| Arthralgia                                      |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                 |                 |                 |
| Appendicitis                                    |                 |                 |                 |
| subjects affected / exposed                     | 2 / 518 (0.39%) | 2 / 518 (0.39%) | 2 / 528 (0.38%) |
| occurrences causally related to treatment / all | 0 / 2           | 0 / 2           | 0 / 2           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Corona virus infection                          |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |
| Otitis media                                    |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0           | 0 / 0           |

|   |                 |                 |                 |
|---|-----------------|-----------------|-----------------|
| Vestibular neuronitis                           |                 |                 |                 |
| subjects affected / exposed                     | 1 / 518 (0.19%) | 1 / 518 (0.19%) | 1 / 528 (0.19%) |
| occurrences causally related to treatment / all | 0 / 1           | 0 / 1           | 0 / 1           |
| 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>                     | Phase 3a: 1% GPB (SAFa) | Phase 3a: Placebo (SAFa) | Phase 3b: BL to Day 29/Week 4 - 1% GPB patients only (SAFb) |
|---|-------------------------|--------------------------|---|
| Total subjects affected by non-serious adverse events |                         |                          |   |
| subjects affected / exposed                           | 43 / 87 (49.43%)        | 37 / 84 (44.05%)         | 179 / 438 (40.87%)  |
| Vascular disorders                                    |                         |                          |   |
| Hypertension  |                         |                          |   |
| subjects affected / exposed                           | 0 / 87 (0.00%)          | 2 / 84 (2.38%)           | 0 / 438 (0.00%)   |
| occurrences (all)                                     | 0                       | 2                        | 0   |
| Nervous system disorders                              |                         |                          |   |
| Headache  |                         |                          |   |
| subjects affected / exposed                           | 9 / 87 (10.34%)         | 8 / 84 (9.52%)           | 28 / 438 (6.39%)  |
| occurrences (all)                                     | 11                      | 10                       | 38  |
| Migraine  |                         |                          |   |
| subjects affected / exposed                           | 1 / 87 (1.15%)          | 0 / 84 (0.00%)           | 1 / 438 (0.23%)   |
| occurrences (all)                                     | 1                       | 0                        | 1   |
| Dizziness   |                         |                          |   |
| subjects affected / exposed                           | 1 / 87 (1.15%)          | 2 / 84 (2.38%)           | 1 / 438 (0.23%)   |
| occurrences (all)                                     | 1                       | 2                        | 1   |
| General disorders and administration site conditions  |                         |                          |   |
| Application site erythema                             |                         |                          |   |
| subjects affected / exposed                           | 5 / 87 (5.75%)          | 4 / 84 (4.76%)           | 13 / 438 (2.97%)  |
| occurrences (all)                                     | 5                       | 4                        | 13  |
| Application site irritation                           |                         |                          |   |
| subjects affected / exposed                           | 0 / 87 (0.00%)          | 0 / 84 (0.00%)           | 5 / 438 (1.14%)   |
| occurrences (all)                                     | 0                       | 0                        | 5   |
| Application site pain                                 |                         |                          |   |
| subjects affected / exposed                           | 1 / 87 (1.15%)          | 1 / 84 (1.19%)           | 4 / 438 (0.91%)   |
| occurrences (all)                                     | 1                       | 1                        | 4   |
| Application site papules                              |                         |                          |   |

|   |                        |                     |                        |
|---|------------------------|---------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                              | 2 / 87 (2.30%)<br>3    | 0 / 84 (0.00%)<br>0 | 2 / 438 (0.46%)<br>3   |
| Application site pruritus<br>subjects affected / exposed<br>occurrences (all) | 1 / 87 (1.15%)<br>3    | 1 / 84 (1.19%)<br>1 | 4 / 438 (0.91%)<br>7   |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                   | 0 / 87 (0.00%)<br>0    | 0 / 84 (0.00%)<br>0 | 1 / 438 (0.23%)<br>1   |
| Eye disorders   |                        |                     |                        |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 87 (1.15%)<br>1    | 1 / 84 (1.19%)<br>1 | 6 / 438 (1.37%)<br>6   |
| Ocular hyperaemia<br>subjects affected / exposed<br>occurrences (all)         | 2 / 87 (2.30%)<br>2    | 0 / 84 (0.00%)<br>0 | 2 / 438 (0.46%)<br>2   |
| Gastrointestinal disorders  |                        |                     |                        |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)      | 1 / 87 (1.15%)<br>1    | 0 / 84 (0.00%)<br>0 | 4 / 438 (0.91%)<br>5   |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 87 (0.00%)<br>0    | 1 / 84 (1.19%)<br>1 | 2 / 438 (0.46%)<br>2   |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)                 | 16 / 87 (18.39%)<br>16 | 4 / 84 (4.76%)<br>4 | 43 / 438 (9.82%)<br>45 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 87 (0.00%)<br>0    | 1 / 84 (1.19%)<br>2 | 4 / 438 (0.91%)<br>4   |
| Gastritis<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 87 (0.00%)<br>0    | 2 / 84 (2.38%)<br>2 | 0 / 438 (0.00%)<br>0   |
| Respiratory, thoracic and mediastinal disorders                               |                        |                     |                        |
| Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)        | 0 / 87 (0.00%)<br>0    | 2 / 84 (2.38%)<br>2 | 7 / 438 (1.60%)<br>7   |
| Nasal dryness   |                        |                     |                        |

|  |                        |                        |                         |
|--|------------------------|------------------------|-------------------------|
| subjects affected / exposed<br>occurrences (all)   | 2 / 87 (2.30%)<br>2    | 0 / 84 (0.00%)<br>0    | 5 / 438 (1.14%)<br>5    |
| Skin and subcutaneous tissue disorders<br>Eczema<br>subjects affected / exposed<br>occurrences (all)             | 1 / 87 (1.15%)<br>1    | 0 / 84 (0.00%)<br>0    | 3 / 438 (0.68%)<br>3    |
| Rash papular<br>subjects affected / exposed<br>occurrences (all)   | 0 / 87 (0.00%)<br>0    | 2 / 84 (2.38%)<br>2    | 0 / 438 (0.00%)<br>0    |
| Musculoskeletal and connective tissue disorders<br>Back pain<br>subjects affected / exposed<br>occurrences (all) | 1 / 87 (1.15%)<br>1    | 1 / 84 (1.19%)<br>2    | 4 / 438 (0.91%)<br>4    |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)               | 10 / 87 (11.49%)<br>11 | 14 / 84 (16.67%)<br>14 | 50 / 438 (11.42%)<br>54 |
| Corona virus infection<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 87 (0.00%)<br>0    | 0 / 84 (0.00%)<br>0    | 0 / 438 (0.00%)<br>0    |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 87 (2.30%)<br>2    | 0 / 84 (0.00%)<br>0    | 2 / 438 (0.46%)<br>2    |

| <b>Non-serious adverse events</b>  | Phase 3b: After Day 29/Week 4 to Week 72 (SAFb) | Phase 3b: BL to Week 72 - 1% GPB patients only (SAFb) | Phase 3b: BL to Week 72 - 1% GPB patients only (SAF) |
|--|---|---|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed     | 346 / 518 (66.80%)                              | 378 / 518 (72.97%)                                    | 379 / 528 (71.78%)                                   |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 3 / 518 (0.58%)<br>3                            | 3 / 518 (0.58%)<br>3                                  | 3 / 528 (0.57%)<br>3                                 |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all) | 68 / 518 (13.13%)<br>168                        | 85 / 518 (16.41%)<br>206                              | 85 / 528 (16.10%)<br>206                             |
| Migraine   |   |   |  |

|   |                        |                        |                        |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)                                | 13 / 518 (2.51%)<br>27 | 14 / 518 (2.70%)<br>28 | 14 / 528 (2.65%)<br>28 |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                   | 1 / 518 (0.19%)<br>1   | 2 / 518 (0.39%)<br>2   | 2 / 528 (0.38%)<br>2   |
| General disorders and administration<br>site conditions                         |                        |                        |                        |
| Application site erythema<br>subjects affected / exposed<br>occurrences (all)   | 34 / 518 (6.56%)<br>67 | 44 / 518 (8.49%)<br>80 | 44 / 528 (8.33%)<br>80 |
| Application site irritation<br>subjects affected / exposed<br>occurrences (all) | 7 / 518 (1.35%)<br>21  | 11 / 518 (2.12%)<br>26 | 11 / 528 (2.08%)<br>26 |
| Application site pain<br>subjects affected / exposed<br>occurrences (all)       | 7 / 518 (1.35%)<br>19  | 11 / 518 (2.12%)<br>23 | 11 / 528 (2.08%)<br>23 |
| Application site papules<br>subjects affected / exposed<br>occurrences (all)    | 10 / 518 (1.93%)<br>20 | 12 / 518 (2.32%)<br>23 | 12 / 528 (2.27%)<br>23 |
| Application site pruritus<br>subjects affected / exposed<br>occurrences (all)   | 16 / 518 (3.09%)<br>32 | 19 / 518 (3.67%)<br>39 | 19 / 528 (3.60%)<br>39 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                     | 10 / 518 (1.93%)<br>11 | 11 / 518 (2.12%)<br>12 | 11 / 528 (2.08%)<br>12 |
| Eye disorders   |                        |                        |                        |
| Dry eye<br>subjects affected / exposed<br>occurrences (all)                     | 19 / 518 (3.67%)<br>20 | 25 / 518 (4.83%)<br>26 | 25 / 528 (4.73%)<br>26 |
| Ocular hyperaemia<br>subjects affected / exposed<br>occurrences (all)           | 1 / 518 (0.19%)<br>1   | 3 / 518 (0.58%)<br>3   | 3 / 528 (0.57%)<br>3   |
| Gastrointestinal disorders  |                        |                        |                        |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)        | 9 / 518 (1.74%)<br>15  | 13 / 518 (2.51%)<br>20 | 13 / 528 (2.46%)<br>20 |
| Diarrhoea   |                        |                        |                        |



|   |                    |                    |                    |
|---|--------------------|--------------------|--------------------|
| subjects affected / exposed                     | 9 / 518 (1.74%)    | 11 / 518 (2.12%)   | 11 / 528 (2.08%)   |
| occurrences (all)                               | 10                 | 12                 | 12                 |
| Dry mouth                                       |                    |                    |                    |
| subjects affected / exposed                     | 32 / 518 (6.18%)   | 63 / 518 (12.16%)  | 64 / 528 (12.12%)  |
| occurrences (all)                               | 54                 | 99                 | 100                |
| Nausea  |                    |                    |                    |
| subjects affected / exposed                     | 8 / 518 (1.54%)    | 12 / 518 (2.32%)   | 12 / 528 (2.27%)   |
| occurrences (all)                               | 8                  | 12                 | 12                 |
| Gastritis                                       |                    |                    |                    |
| subjects affected / exposed                     | 9 / 518 (1.74%)    | 9 / 518 (1.74%)    | 9 / 528 (1.70%)    |
| occurrences (all)                               | 10                 | 10                 | 10                 |
| Respiratory, thoracic and mediastinal disorders |                    |                    |                    |
| Oropharyngeal pain                              |                    |                    |                    |
| subjects affected / exposed                     | 22 / 518 (4.25%)   | 29 / 518 (5.60%)   | 29 / 528 (5.49%)   |
| occurrences (all)                               | 25                 | 32                 | 32                 |
| Nasal dryness                                   |                    |                    |                    |
| subjects affected / exposed                     | 2 / 518 (0.39%)    | 7 / 518 (1.35%)    | 7 / 528 (1.33%)    |
| occurrences (all)                               | 2                  | 7                  | 7                  |
| Skin and subcutaneous tissue disorders          |                    |                    |                    |
| Eczema  |                    |                    |                    |
| subjects affected / exposed                     | 12 / 518 (2.32%)   | 15 / 518 (2.90%)   | 15 / 528 (2.84%)   |
| occurrences (all)                               | 16                 | 19                 | 19                 |
| Rash papular                                    |                    |                    |                    |
| subjects affected / exposed                     | 0 / 518 (0.00%)    | 0 / 518 (0.00%)    | 0 / 528 (0.00%)    |
| occurrences (all)                               | 0                  | 0                  | 0                  |
| Musculoskeletal and connective tissue disorders |                    |                    |                    |
| Back pain                                       |                    |                    |                    |
| subjects affected / exposed                     | 20 / 518 (3.86%)   | 23 / 518 (4.44%)   | 23 / 528 (4.36%)   |
| occurrences (all)                               | 26                 | 30                 | 30                 |
| Infections and infestations                     |                    |                    |                    |
| Nasopharyngitis                                 |                    |                    |                    |
| subjects affected / exposed                     | 140 / 518 (27.03%) | 168 / 518 (32.43%) | 168 / 528 (31.82%) |
| occurrences (all)                               | 202                | 256                | 256                |
| Corona virus infection                          |                    |                    |                    |
| subjects affected / exposed                     | 20 / 518 (3.86%)   | 20 / 518 (3.86%)   | 20 / 528 (3.79%)   |
| occurrences (all)                               | 20                 | 20                 | 20                 |

|   |                      |                      |                      |
|---|----------------------|----------------------|----------------------|
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all) | 4 / 518 (0.77%)<br>6 | 6 / 518 (1.16%)<br>8 | 6 / 528 (1.14%)<br>8 |
|---|----------------------|----------------------|----------------------|

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment   |
|---------------|---|
| 26 July 2019  | Version 2.0 of the protocol, dated 26-Jul-2019:<br>All changes implemented in country-specific amendments; Addition of assessment of patient-rated severity; Addition of documentation of previous hyperhidrosis treatment; Addition of option for re-screening; Update of the number of planned study centers; Clarification of anticholinergic side effects to be potentially related to the IMP; Clarification of 2 exclusion criteria (Exclusion Criteria 12 and 14); Deletion of 1 exclusion criterion (Exclusion Criterion 13); Addition of 1 exclusion criterion (Exclusion Criterion 30); Update on use of aluminum-free deodorants and recording of deodorant use in patient diary; Update of general restrictions and precautions; Update of handling of missing data; Removal of time window for Visits 3a and 3b; Change of reporting of immediately reportable events to reporting via the eCRF. |
| 08 April 2020 | Amendment 1.0 to protocol Version 2.0, dated 08-Apr-2020: Addition of a DMC to ensure the preservation of trial integrity during the time of the COVID-19 pandemic restrictions; Change in IMP dispensing during the COVID-19 pandemic; Change of some center visits to telephone visits during the COVID-19 pandemic; Temporary change of consent procedure to this amendment during the COVID 19 pandemic.  |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported