



## Clinical trial results:

### A Randomized, Double-Blind, Parallel Group, Vehicle-Controlled Phase 2 Study to Evaluate the Safety and Efficacy of Topical ATx201 OINTMENT in Adolescents and Adults with Mild to Moderate Atopic Dermatitis

#### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2019-002771-33  |
| Trial protocol           | DK PL BG        |
| Global end of trial date | 22 October 2020 |

#### Results information

|                                   |   |
|-----------------------------------|---|
| Result version number             | v1 (current)  |
| This version publication date     | 26 November 2021  |
| First version publication date    | 26 November 2021  |
| Summary attachment (see zip file) | ATx201-207 CTR Synopsis for EudraCT (ATx201-207 CTR synopsis for EudraCT.pdf) |

#### Trial information

##### Trial identification

|                       |            |
|-----------------------|------------|
| Sponsor protocol code | ATX201-207 |
|-----------------------|------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04339985 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Union Therapeutics A/S  |
| Sponsor organisation address | Tuborg Havnevej 18, 2900 Hellerup, Denmark,   |
| Public contact               | Union Therapeutics A/S, Union Therapeutics A/S, +45 61777435, clinicaltrials@uniontherapeutics.com  |
| Scientific contact           | Union Therapeutics A/S, Union Therapeutics A/S, +45 61777435, rclinicaltrials@uniontherapeutics.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                       | 22 October 2020 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 22 October 2020 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 22 October 2020 |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

Evaluate clinical efficacy of ATx201 in subjects with mild to moderate atopic dermatitis.

Protection of trial subjects:

This study was performed according to the principles of the current edition of the Declaration of Helsinki, all applicable legislation and regulation, and to Good Clinical Practice (GCP) as denoted in the International Council for Harmonisation (ICH) of Technical Requirements for Pharmaceuticals for Human Use E6 requirements for GCP. The Investigator conducted all aspects of this study in accordance with applicable national, state, and local laws of the pertinent regulatory authorities. Personal data of investigators and subjects were collected, stored, and processed in accordance with the General Data Protection Regulation (GDPR); appropriate organizational measures were taken to protect these data by preventing their disclosure to unauthorized third parties.

Background therapy:

-

Evidence for comparator:

-

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 16 September 2019 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |               |
|--------------------------------------|---------------|
| Country: Number of subjects enrolled | Poland: 26    |
| Country: Number of subjects enrolled | Bulgaria: 184 |
| Country: Number of subjects enrolled | Denmark: 2    |
| Worldwide total number of subjects   | 212           |
| EEA total number of subjects         | 212           |

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) | 20  |
| Adults (18-64 years)      | 192 |
| From 65 to 84 years       | 0   |
| 85 years and over         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The first subject was enrolled on 05 November 2019.

### Pre-assignment

Screening details:

Subjects (age  $\geq 12$  and  $< 60$  years) with a diagnosis of atopic dermatitis (AD) per the protocol were included. Subjects with actively infected AD or acute exacerbation or flare as defined in the protocol were excluded.

### Period 1

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

Blinding implementation details:

In the main study, the study medications were double-blinded. The blinding codes were available to the investigator in a secured manner.

### Arms

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

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | ATx201 OINTMENT 4% |
|------------------|--------------------|

Arm description:

ATx201; 4% OINTMENT; topical application 2 mg/cm<sup>2</sup>, twice daily to treatable area

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | ATx201 OINTMENT |
| Investigational medicinal product code | ATx201          |
| Other name                             | niclosamide     |
| Pharmaceutical forms                   | Ointment        |
| Routes of administration               | Topical use     |

Dosage and administration details:

ATx201 4% OINTMENT, dermal topical application, apply 2 mg/cm<sup>2</sup> twice daily to treatable area.

|                  |                    |
|------------------|--------------------|
| <b>Arm title</b> | ATx201 OINTMENT 7% |
|------------------|--------------------|

Arm description:

ATx201 7% OINTMENT, topical application, 2 mg/cm<sup>2</sup> twice daily to treatable area

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | ATx201 OINTMENT |
| Investigational medicinal product code | ATx201          |
| Other name                             | niclosamide     |
| Pharmaceutical forms                   | Ointment        |
| Routes of administration               | Topical use     |

Dosage and administration details:

ATx201 7% OINTMENT, dermal topical application, apply 2 mg/cm<sup>2</sup> twice daily to treatable area.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | OINTMENT vehicle |
|------------------|------------------|

Arm description:

Placebo, OINTMENT 0% (vehicle), topical application, 2 mg/cm<sup>2</sup> twice daily to treatable area

|          |         |
|----------|---------|
| Arm type | Placebo |
|----------|---------|

|  |                  |
|--|------------------|
| Investigational medicinal product name | Placebo          |
| Investigational medicinal product code | OINTMENT vehicle |
| Other name                             |                  |
| Pharmaceutical forms                   | Ointment         |
| Routes of administration               | Topical          |

Dosage and administration details:

OINTMENT vehicle, 0% vehicle, 2 mg/cm<sup>2</sup> twice daily to treatable area

| <b>Number of subjects in period 1</b> | ATx201 OINTMENT<br>4% | ATx201 OINTMENT<br>7% | OINTMENT vehicle |
|---------------------------------------|-----------------------|-----------------------|------------------|
| Started                               | 70                    | 70                    | 72               |
| Completed                             | 65                    | 63                    | 68               |
| Not completed                         | 5                     | 7                     | 4                |
| Consent withdrawn by subject          | 3                     | 5                     | -                |
| Adverse event, non-fatal              | 2                     | 1                     | 2                |
| Patient decision to resign from study | -                     | -                     | 1                |
| Lack of efficacy                      | -                     | 1                     | 1                |

## Baseline characteristics

### Reporting groups

|   |                    |
|---|--------------------|
| Reporting group title   | ATx201 OINTMENT 4% |
| Reporting group description:<br>ATx201; 4% OINTMENT; topical application 2 mg/cm <sup>2</sup> , twice daily to treatable area           |                    |
| Reporting group title   | ATx201 OINTMENT 7% |
| Reporting group description:<br>ATx201 7% OINTMENT, topical application, 2 mg/cm <sup>2</sup> twice daily to treatable area             |                    |
| Reporting group title   | OINTMENT vehicle   |
| Reporting group description:<br>Placebo, OINTMENT 0% (vehicle), topical application, 2 mg/cm <sup>2</sup> twice daily to treatable area |                    |

| Reporting group values      | ATx201 OINTMENT 4% | ATx201 OINTMENT 7% | OINTMENT vehicle |
|-----------------------------|--------------------|--------------------|------------------|
| Number of subjects          | 70                 | 70                 | 72               |
| Age categorical             |                    |                    |                  |
| <18 years                   |                    |                    |                  |
| Units: Subjects             |                    |                    |                  |
| Adolescents (12-17 years)   | 5                  | 7                  | 8                |
| Adults (18-59 years)        | 65                 | 63                 | 64               |
| Age continuous              |                    |                    |                  |
| Units: years                |                    |                    |                  |
| arithmetic mean             | 38                 | 38                 | 35               |
| standard deviation          | ± 13               | ± 14               | ± 13             |
| Gender categorical          |                    |                    |                  |
| Units: Subjects             |                    |                    |                  |
| Female                      | 45                 | 42                 | 46               |
| Male                        | 25                 | 28                 | 26               |
| Race                        |                    |                    |                  |
| Units: Subjects             |                    |                    |                  |
| Caucasian                   | 70                 | 70                 | 72               |
| Treatable Body Surface Area |                    |                    |                  |
| Units: percent              |                    |                    |                  |
| arithmetic mean             | 12                 | 13                 | 14               |
| standard deviation          | ± 7                | ± 6                | ± 8              |
| Baseline IGA                |                    |                    |                  |
| Units: Score                |                    |                    |                  |
| arithmetic mean             | 2.30               | 2.31               | 2.38             |
| standard deviation          | ± 0.46             | ± 0.47             | ± 0.49           |
| Baseline EASI Score         |                    |                    |                  |
| Units: Score                |                    |                    |                  |
| arithmetic mean             | 5.41               | 5.79               | 5.63             |
| standard deviation          | ± 3.68             | ± 4.48             | ± 3.32           |
| Reporting group values      | Total              |                    |                  |
| Number of subjects          | 212                |                    |                  |

|                             |     |  |  |
|-----------------------------|-----|--|--|
| Age categorical             |     |  |  |
| <18 years                   |     |  |  |
| Units: Subjects             |     |  |  |
| Adolescents (12-17 years)   | 20  |  |  |
| Adults (18-59 years)        | 192 |  |  |
| Age continuous              |     |  |  |
| Units: years                |     |  |  |
| arithmetic mean             |     |  |  |
| standard deviation          | -   |  |  |
| Gender categorical          |     |  |  |
| Units: Subjects             |     |  |  |
| Female                      | 133 |  |  |
| Male                        | 79  |  |  |
| Race                        |     |  |  |
| Units: Subjects             |     |  |  |
| Caucasian                   | 212 |  |  |
| Treatable Body Surface Area |     |  |  |
| Units: percent              |     |  |  |
| arithmetic mean             |     |  |  |
| standard deviation          | -   |  |  |
| Baseline IGA                |     |  |  |
| Units: Score                |     |  |  |
| arithmetic mean             |     |  |  |
| standard deviation          | -   |  |  |
| Baseline EASI Score         |     |  |  |
| Units: Score                |     |  |  |
| arithmetic mean             |     |  |  |
| standard deviation          | -   |  |  |

### Subject analysis sets

|   |                            |
|---|----------------------------|
| Subject analysis set title  | Safety Population          |
| Subject analysis set type   | Safety analysis            |
| Subject analysis set description:   |                            |
| The Safety population included all enrolled subjects who received any amount of the IMP.  |                            |
| Subject analysis set title  | Intent-to-Treat Population |
| Subject analysis set type   | Intention-to-treat         |
| Subject analysis set description:   |                            |
| The Intent to Treat Analysis Set included data from all randomized subjects regardless of whether IMP was administered (not including open-label PK sub-study). |                            |

| Reporting group values    | Safety Population | Intent-to-Treat Population |  |
|---------------------------|-------------------|----------------------------|--|
| Number of subjects        | 212               | 212                        |  |
| Age categorical           |                   |                            |  |
| <18 years                 |                   |                            |  |
| Units: Subjects           |                   |                            |  |
| Adolescents (12-17 years) | 20                | 20                         |  |
| Adults (18-59 years)      | 192               | 192                        |  |
| Age continuous            |                   |                            |  |
| Units: years              |                   |                            |  |
| arithmetic mean           | 37                | 37                         |  |

|                    |          |          |  |
|--------------------|----------|----------|--|
| standard deviation | $\pm 13$ | $\pm 13$ |  |
|--------------------|----------|----------|--|

|   |         |         |  |
|---|---------|---------|--|
| Gender categorical<br>Units: Subjects         |         |         |  |
| Female  | 133     | 133     |  |
| Male  | 79      | 79      |  |
| Race<br>Units: Subjects                       |         |         |  |
| Caucasian                                     | 212     | 212     |  |
| Treatable Body Surface Area<br>Units: percent |         |         |  |
| arithmetic mean                               | 13      | 13      |  |
| standard deviation                            | $\pm 7$ | $\pm 7$ |  |
| Baseline IGA<br>Units: Score                  |         |         |  |
| arithmetic mean                               |         |         |  |
| standard deviation                            | $\pm$   | $\pm$   |  |
| Baseline EASI Score<br>Units: Score           |         |         |  |
| arithmetic mean                               |         |         |  |
| standard deviation                            | $\pm$   | $\pm$   |  |



## End points

### End points reporting groups

|                                   |   |
|-----------------------------------|---|
| Reporting group title             | ATx201 OINTMENT 4%  |
| Reporting group description:      | ATx201; 4% OINTMENT; topical application 2 mg/cm <sup>2</sup> , twice daily to treatable area   |
| Reporting group title             | ATx201 OINTMENT 7%  |
| Reporting group description:      | ATx201 7% OINTMENT, topical application, 2 mg/cm <sup>2</sup> twice daily to treatable area   |
| Reporting group title             | OINTMENT vehicle  |
| Reporting group description:      | Placebo, OINTMENT 0% (vehicle), topical application, 2 mg/cm <sup>2</sup> twice daily to treatable area   |
| Subject analysis set title        | Safety Population   |
| Subject analysis set type         | Safety analysis   |
| Subject analysis set description: | The Safety population included all enrolled subjects who received any amount of the IMP.  |
| Subject analysis set title        | Intent-to-Treat Population  |
| Subject analysis set type         | Intention-to-treat  |
| Subject analysis set description: | The Intent to Treat Analysis Set included data from all randomized subjects regardless of whether IMP was administered (not including open-label PK sub-study). |

### Primary: EASI mean change from baseline at Week 6

|                        |  |
|------------------------|--|
| End point title        | EASI mean change from baseline at Week 6 |
| End point description: |  |
| End point type         | Primary                                  |
| End point timeframe:   | Baseline to Week 6                       |

| End point values                     | ATx201 OINTMENT 4% | ATx201 OINTMENT 7% | OINTMENT vehicle | Intent-to-Treat Population |
|--------------------------------------|--------------------|--------------------|------------------|----------------------------|
| Subject group type                   | Reporting group    | Reporting group    | Reporting group  | Subject analysis set       |
| Number of subjects analysed          | 70                 | 70                 | 72               | 0 <sup>[1]</sup>           |
| Units: score                         |                    |                    |                  |                            |
| arithmetic mean (standard deviation) | -3.38 (± 3.55)     | -2.86 (± 3.22)     | -2.95 (± 4.67)   | ()                         |

Notes:

[1] - Overall not analysed

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | EASI Mean Change from Baseline ANCOVA Analysis/EASI mean |
|-----------------------------------|--|

### Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | ANCOVA   |
| Comparison groups                 | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |

|   |                    |
|---|--------------------|
| Number of subjects included in analysis | 212                |
| Analysis specification                  | Pre-specified      |
| Analysis type                           | other              |
| P-value                                 | < 0.05             |
| Method                                  | ANCOVA             |
| Parameter estimate                      | Least squares mean |
| Confidence interval                     |                    |
| level                                   | 95 %               |

### Secondary: EASI-50 at Week 6

|                        |                   |
|------------------------|-------------------|
| End point title        | EASI-50 at Week 6 |
| End point description: |                   |
| End point type         | Secondary         |
| End point timeframe:   |                   |
| Up to Week 6           |                   |

| End point values            | ATx201<br>OINTMENT 4% | ATx201<br>OINTMENT 7% | OINTMENT<br>vehicle | Intent-to-Treat<br>Population |
|-----------------------------|-----------------------|-----------------------|---------------------|-------------------------------|
| Subject group type          | Reporting group       | Reporting group       | Reporting group     | Subject analysis set          |
| Number of subjects analysed | 70                    | 70                    | 72                  | 212                           |
| Units: percent              |                       |                       |                     |                               |
| number (not applicable)     | 45                    | 40                    | 45                  | 130                           |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | CMH Statistics for EASI-50/CMH Statistics for EASI-50 -ITT |
|-----------------------------------|--|

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Cohran-Mantel-Haenszel Test                                |
| Comparison groups                       | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |
| Number of subjects included in analysis | 212  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| P-value                                 | < 0.05   |
| Method                                  | Cochran-Mantel-Haenszel                                    |

### Secondary: EASI-75 at Week 6

|                        |                   |
|------------------------|-------------------|
| End point title        | EASI-75 at Week 6 |
| End point description: |                   |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to Week 6         |           |

| End point values            | ATx201<br>OINTMENT 4% | ATx201<br>OINTMENT 7% | OINTMENT<br>vehicle | Intent-to-Treat<br>Population |
|-----------------------------|-----------------------|-----------------------|---------------------|-------------------------------|
| Subject group type          | Reporting group       | Reporting group       | Reporting group     | Subject analysis set          |
| Number of subjects analysed | 70                    | 70                    | 72                  | 212                           |
| Units: percent              |                       |                       |                     |                               |
| number (not applicable)     | 31                    | 21                    | 33                  | 85                            |

|                                   |   |
|-----------------------------------|---|
| <b>Attachments (see zip file)</b> | CMH Statistics for EASI-75/CMH Statistics for EASI-75.pdf |
|-----------------------------------|---|

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Cohran-Mantel-Haenszel Test                                |
| Comparison groups                       | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |
| Number of subjects included in analysis | 212  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| P-value                                 | < 0.05   |
| Method                                  | Cochran-Mantel-Haenszel                                    |

### Secondary: IGA success at Week 6

|                        |                       |
|------------------------|-----------------------|
| End point title        | IGA success at Week 6 |
| End point description: |                       |

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to Week 6         |           |

| End point values            | ATx201<br>OINTMENT 4% | ATx201<br>OINTMENT 7% | OINTMENT<br>vehicle | Intent-to-Treat<br>Population |
|-----------------------------|-----------------------|-----------------------|---------------------|-------------------------------|
| Subject group type          | Reporting group       | Reporting group       | Reporting group     | Subject analysis set          |
| Number of subjects analysed | 70                    | 70                    | 72                  | 212                           |
| Units: subjects             | 20                    | 16                    | 23                  | 59                            |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | CMH Statistics for IGA Success/CMH Statistics for IGA Success. |
|-----------------------------------|--|

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Cohran-Mantel-Haenszel Test                                |
| Comparison groups                       | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |
| Number of subjects included in analysis | 212  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| P-value                                 | < 0.05   |
| Method                                  | Cochran-Mantel-Haenszel                                    |

## Secondary: Distribution of IGA scores at change from baseline at Week 6

|                        |  |
|------------------------|--|
| End point title        | Distribution of IGA scores at change from baseline at Week 6 |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Up to Week 6           |  |

| End point values              | ATx201 OINTMENT 4% | ATx201 OINTMENT 7% | OINTMENT vehicle | Intent-to-Treat Population |
|-------------------------------|--------------------|--------------------|------------------|----------------------------|
| Subject group type            | Reporting group    | Reporting group    | Reporting group  | Subject analysis set       |
| Number of subjects analysed   | 70                 | 70                 | 72               | 212                        |
| Units: Frequency distribution |                    |                    |                  |                            |
| IGA score 0                   | 10                 | 8                  | 13               | 31                         |
| IGA Score 1                   | 29                 | 26                 | 22               | 77                         |
| IGA Score 2                   | 27                 | 30                 | 27               | 84                         |
| IGA Score 3                   | 4                  | 6                  | 10               | 20                         |
| IGA Score 4                   | 0                  | 0                  | 0                | 0                          |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | CMH Statistics for IGA scores based on ridit score/CMH |
|-----------------------------------|--|

## Statistical analyses

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Cohran-Mantel-Haenszel Test                                |
| Comparison groups                 | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |

|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 212                     |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | other                   |
| P-value                                 | < 0.05                  |
| Method                                  | Cochran-Mantel-Haenszel |

### Secondary: Proportion of subjects with a treatable BSA <5% at Week 6

|                        |   |
|------------------------|---|
| End point title        | Proportion of subjects with a treatable BSA <5% at Week 6 |
| End point description: |   |
| End point type         | Secondary   |
| End point timeframe:   |   |
| Up to Week 6           |   |

| End point values            | ATx201<br>OINTMENT 4% | ATx201<br>OINTMENT 7% | OINTMENT<br>vehicle | Intent-to-Treat<br>Population |
|-----------------------------|-----------------------|-----------------------|---------------------|-------------------------------|
| Subject group type          | Reporting group       | Reporting group       | Reporting group     | Subject analysis set          |
| Number of subjects analysed | 70                    | 70                    | 72                  | 212                           |
| Units: Subjects             | 27                    | 21                    | 25                  | 73                            |

|                                   |  |
|-----------------------------------|--|
| <b>Attachments (see zip file)</b> | CMH Statistics for BSA less than 5%/CMH Statistics for BSA |
|-----------------------------------|--|

### Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Cohran-Mantel-Haenszel Test                                |
| Comparison groups                       | ATx201 OINTMENT 4% v ATx201 OINTMENT 7% v OINTMENT vehicle |
| Number of subjects included in analysis | 212  |
| Analysis specification                  | Pre-specified  |
| Analysis type                           | other  |
| P-value                                 | < 0.05   |
| Method                                  | Cochran-Mantel-Haenszel                                    |

### Secondary: Target lesion Total Sign Score mean change from baseline at Week 6

|                        |  |
|------------------------|--|
| End point title        | Target lesion Total Sign Score mean change from baseline at Week 6 |
| End point description: |  |
| End point type         | Secondary  |
| End point timeframe:   |  |
| Up to Week 6           |  |

| <b>End point values</b>              | ATx201<br>OINTMENT 4% | ATx201<br>OINTMENT 7% | OINTMENT<br>vehicle | Intent-to-Treat<br>Population |
|--------------------------------------|-----------------------|-----------------------|---------------------|-------------------------------|
| Subject group type                   | Reporting group       | Reporting group       | Reporting group     | Subject analysis set          |
| Number of subjects analysed          | 70                    | 70                    | 72                  | 0 <sup>[2]</sup>              |
| Units: Score                         |                       |                       |                     |                               |
| arithmetic mean (standard deviation) | -3.16 (± 1.95)        | -2.97 (± 2.2)         | -3.17 (± 2.37)      | ( )                           |

Notes:

[2] - Overall not analysed

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to Week 6

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

### Dictionary used

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

|                    |    |
|--------------------|----|
| Dictionary version | 22 |
|--------------------|----|

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | ATx201 OINTMENT 4% |
|-----------------------|--------------------|

Reporting group description:

ATx201; 4% ointment; topical application 2 mg/cm<sup>2</sup>, twice daily to treatable area

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | ATx201 OINTMENT 7% |
|-----------------------|--------------------|

Reporting group description:

ATx201 7% OINTMENT, topical application, 2 mg/cm<sup>2</sup> twice daily to treatable area

|                       |                  |
|-----------------------|------------------|
| Reporting group title | OINTMENT vehicle |
|-----------------------|------------------|

Reporting group description:

Placebo, OINTMENT 0% (vehicle), topical application, 2 mg/cm<sup>2</sup> twice daily to treatable area

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

Reporting group description:

Total for all study groups combined

| Serious adverse events                            | ATx201 OINTMENT 4% | ATx201 OINTMENT 7% | OINTMENT vehicle |
|---|--------------------|--------------------|------------------|
| Total subjects affected by serious adverse events |                    |                    |                  |
| subjects affected / exposed                       | 0 / 71 (0.00%)     | 0 / 69 (0.00%)     | 0 / 72 (0.00%)   |
| number of deaths (all causes)                     | 0                  | 0                  | 0                |
| number of deaths resulting from adverse events    | 0                  | 0                  | 0                |

| Serious adverse events                            | Overall Study   |  |  |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events |                 |  |  |
| subjects affected / exposed                       | 0 / 212 (0.00%) |  |  |
| number of deaths (all causes)                     | 0               |  |  |
| number of deaths resulting from adverse events    | 0               |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| <b>Non-serious adverse events</b>                           | <b>ATx201 OINTMENT<br/>4%</b> | <b>ATx201 OINTMENT<br/>7%</b> | <b>OINTMENT vehicle</b> |
|---|-------------------------------|-------------------------------|-------------------------|
| Total subjects affected by non-serious adverse events       |                               |                               |                         |
| subjects affected / exposed                                 | 22 / 71 (30.99%)              | 18 / 69 (26.09%)              | 14 / 72 (19.44%)        |
| <b>Vascular disorders</b>                                   |                               |                               |                         |
| Flushing  |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 0 / 69 (0.00%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 1                             | 0                             | 0                       |
| Vein collapse   |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 1 / 69 (1.45%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 1                             | 1                             | 0                       |
| <b>General disorders and administration site conditions</b> |                               |                               |                         |
| Drug intolerance  |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 2 / 69 (2.90%)                | 2 / 72 (2.78%)          |
| occurrences (all)   | 1                             | 2                             | 2                       |
| Influenza like illness                                      |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 0 / 69 (0.00%)                | 1 / 72 (1.39%)          |
| occurrences (all)   | 1                             | 0                             | 1                       |
| <b>Reproductive system and breast disorders</b>             |                               |                               |                         |
| Dysmenorrhoea   |                               |                               |                         |
| subjects affected / exposed                                 | 0 / 71 (0.00%)                | 1 / 69 (1.45%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 0                             | 1                             | 0                       |
| <b>Respiratory, thoracic and mediastinal disorders</b>      |                               |                               |                         |
| Rhinorrhoea   |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 0 / 69 (0.00%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 1                             | 0                             | 0                       |
| <b>Investigations</b>                                       |                               |                               |                         |
| Blood creatinine increased                                  |                               |                               |                         |
| subjects affected / exposed                                 | 1 / 71 (1.41%)                | 0 / 69 (0.00%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 1                             | 0                             | 0                       |
| Blood iron decreased  |                               |                               |                         |
| subjects affected / exposed                                 | 0 / 71 (0.00%)                | 0 / 69 (0.00%)                | 1 / 72 (1.39%)          |
| occurrences (all)   | 0                             | 0                             | 1                       |
| <b>Injury, poisoning and procedural complications</b>       |                               |                               |                         |
| Arthropod bite  |                               |                               |                         |
| subjects affected / exposed                                 | 0 / 71 (0.00%)                | 1 / 69 (1.45%)                | 0 / 72 (0.00%)          |
| occurrences (all)   | 0                             | 1                             | 0                       |



|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Arthropod sting<br>subjects affected / exposed<br>occurrences (all)                                       | 1 / 71 (1.41%)<br>1 | 0 / 69 (0.00%)<br>0 | 0 / 72 (0.00%)<br>0 |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 71 (1.41%)<br>2 | 1 / 69 (1.45%)<br>1 | 0 / 72 (0.00%)<br>0 |
| Headache<br>subjects affected / exposed<br>occurrences (all)  | 2 / 71 (2.82%)<br>2 | 2 / 69 (2.90%)<br>2 | 2 / 72 (2.78%)<br>2 |
| Eye disorders<br>Eyelid irritation<br>subjects affected / exposed<br>occurrences (all)                    | 1 / 71 (1.41%)<br>1 | 0 / 69 (0.00%)<br>0 | 0 / 72 (0.00%)<br>0 |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)          | 0 / 71 (0.00%)<br>0 | 1 / 69 (1.45%)<br>1 | 0 / 72 (0.00%)<br>0 |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                                  | 1 / 71 (1.41%)<br>1 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 71 (0.00%)<br>0 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |
| Toothache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 71 (0.00%)<br>0 | 1 / 69 (1.45%)<br>1 | 0 / 72 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Dermal cyst<br>subjects affected / exposed<br>occurrences (all) | 0 / 71 (0.00%)<br>0 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |
| Dermatitis atopic<br>subjects affected / exposed<br>occurrences (all)                                     | 2 / 71 (2.82%)<br>2 | 1 / 69 (1.45%)<br>1 | 2 / 72 (2.78%)<br>2 |
| Dermatitis contact<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 71 (0.00%)<br>0 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Dry skin  |                |                |                |
| subjects affected / exposed                     | 3 / 71 (4.23%) | 3 / 69 (4.35%) | 1 / 72 (1.39%) |
| occurrences (all)                               | 3              | 3              | 2              |
| Perioral dermatitis                             |                |                |                |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 69 (1.45%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Pruritus  |                |                |                |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 69 (1.45%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Seborrhoeic dermatitis                          |                |                |                |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 69 (1.45%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Skin irritation                                 |                |                |                |
| subjects affected / exposed                     | 3 / 71 (4.23%) | 6 / 69 (8.70%) | 3 / 72 (4.17%) |
| occurrences (all)                               | 3              | 6              | 3              |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Intervertebral disc protrusion                  |                |                |                |
| subjects affected / exposed                     | 0 / 71 (0.00%) | 1 / 69 (1.45%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 0              | 1              | 0              |
| Infections and infestations                     |                |                |                |
| Corona virus infection                          |                |                |                |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 69 (0.00%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Folliculitis                                    |                |                |                |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 69 (0.00%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Influenza                                       |                |                |                |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 69 (0.00%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Nasopharyngitis                                 |                |                |                |
| subjects affected / exposed                     | 2 / 71 (2.82%) | 0 / 69 (0.00%) | 1 / 72 (1.39%) |
| occurrences (all)                               | 2              | 0              | 1              |
| Oral herpes                                     |                |                |                |
| subjects affected / exposed                     | 1 / 71 (1.41%) | 0 / 69 (0.00%) | 0 / 72 (0.00%) |
| occurrences (all)                               | 1              | 0              | 0              |
| Rhinitis  |                |                |                |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 71 (0.00%)<br>0 | 1 / 69 (1.45%)<br>1 | 0 / 72 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                     | 0 / 71 (0.00%)<br>0 | 1 / 69 (1.45%)<br>1 | 0 / 72 (0.00%)<br>0 |
| Metabolism and nutrition disorders<br>Fluid retention<br>subjects affected / exposed<br>occurrences (all) | 0 / 71 (0.00%)<br>0 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |
| Vitamin D deficiency<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 71 (0.00%)<br>0 | 0 / 69 (0.00%)<br>0 | 1 / 72 (1.39%)<br>1 |

| <b>Non-serious adverse events</b>  | Overall Study        |  |  |
|--|----------------------|--|--|
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed   | 54 / 212 (25.47%)    |  |  |
| Vascular disorders<br>Flushing<br>subjects affected / exposed<br>occurrences (all)   | 1 / 212 (0.47%)<br>1 |  |  |
| Vein collapse<br>subjects affected / exposed<br>occurrences (all)  | 2 / 212 (0.94%)<br>2 |  |  |
| General disorders and administration site conditions<br>Drug intolerance<br>subjects affected / exposed<br>occurrences (all) | 5 / 212 (2.36%)<br>5 |  |  |
| Influenza like illness<br>subjects affected / exposed<br>occurrences (all)   | 2 / 212 (0.94%)<br>2 |  |  |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all)                | 1 / 212 (0.47%)<br>1 |  |  |
| Respiratory, thoracic and mediastinal disorders  |                      |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)  | 1 / 212 (0.47%)<br>1 |  |  |
| Investigations<br>Blood creatinine increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 212 (0.47%)<br>1 |  |  |
| Blood iron decreased<br>subjects affected / exposed<br>occurrences (all)   | 1 / 212 (0.47%)<br>1 |  |  |
| Injury, poisoning and procedural complications<br>Arthropod bite<br>subjects affected / exposed<br>occurrences (all) | 1 / 212 (0.47%)<br>1 |  |  |
| Arthropod sting<br>subjects affected / exposed<br>occurrences (all)  | 1 / 212 (0.47%)<br>1 |  |  |
| Nervous system disorders<br>Dizziness<br>subjects affected / exposed<br>occurrences (all)                            | 2 / 212 (0.94%)<br>3 |  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 6 / 212 (2.83%)<br>6 |  |  |
| Eye disorders<br>Eyelid irritation<br>subjects affected / exposed<br>occurrences (all)                               | 1 / 212 (0.47%)<br>1 |  |  |
| Gastrointestinal disorders<br>Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 212 (0.47%)<br>1 |  |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)   | 2 / 212 (0.94%)<br>2 |  |  |
| Constipation   |                      |  |  |

|   |                  |  |  |
|---|------------------|--|--|
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Toothache                                       |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Skin and subcutaneous tissue disorders          |                  |  |  |
| Dermal cyst                                     |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Dermatitis atopic                               |                  |  |  |
| subjects affected / exposed                     | 5 / 212 (2.36%)  |  |  |
| occurrences (all)                               | 5                |  |  |
| Dermatitis contact                              |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Dry skin  |                  |  |  |
| subjects affected / exposed                     | 7 / 212 (3.30%)  |  |  |
| occurrences (all)                               | 8                |  |  |
| Perioral dermatitis                             |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Pruritus  |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Seborrhoeic dermatitis                          |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Skin irritation                                 |                  |  |  |
| subjects affected / exposed                     | 12 / 212 (5.66%) |  |  |
| occurrences (all)                               | 12               |  |  |
| Musculoskeletal and connective tissue disorders |                  |  |  |
| Intervertebral disc protrusion                  |                  |  |  |
| subjects affected / exposed                     | 1 / 212 (0.47%)  |  |  |
| occurrences (all)                               | 1                |  |  |
| Infections and infestations                     |                  |  |  |

|                                    |                 |  |  |
|------------------------------------|-----------------|--|--|
| Corona virus infection             |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Folliculitis                       |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Influenza                          |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Nasopharyngitis                    |                 |  |  |
| subjects affected / exposed        | 3 / 212 (1.42%) |  |  |
| occurrences (all)                  | 3               |  |  |
| Oral herpes                        |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Rhinitis                           |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Upper respiratory tract infection  |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Metabolism and nutrition disorders |                 |  |  |
| Fluid retention                    |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |
| Vitamin D deficiency               |                 |  |  |
| subjects affected / exposed        | 1 / 212 (0.47%) |  |  |
| occurrences (all)                  | 1               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 26 July 2019     | <p>Clinical Study Protocol Version 2.0 made the following changes:</p> <ul style="list-style-type: none"><li>-Corrected discrepancies regarding what procedures could be performed either at day -1 or day 1 (this was correctly assigned in the appendix E Schedule of Study Procedures, but erroneously described in the protocol text sections 7.2 and 7.7). This was for clarification.</li><li>-Corrected an error in sections 7.1 and 7.2 that erroneously put the hematology and serum chemistry at the baseline visit, rather than at the screening visit. The same error was also in sections 7.7.1 and 7.7.2 for the PK Sub-study.</li><li>-Simplified Appendix B re. microbiological sampling to not include a description of the processing of the samples. Discussion with the local laboratories, who will perform the sampling revealed that procedures and preferred materials varied slightly from country to country. It was deemed to be preferable to capture these procedures in the laboratory protocols instead of the study protocol, to allow for local variations and thus allow laboratories to use their current standard operating procedures and supplies that they are already trained in using and that have been validated on site.</li></ul>   |
| 30 October 2019  | <p>Clinical Study Protocol Version 3.0 made the following changes:</p> <ul style="list-style-type: none"><li>-Changed the process for weighing of returned kits (Sections 6.5 and 7.3-7.7), so weighing happens at each visit as opposed to all returned kits from one subject being weighed at the end of study (for that subject). Monitoring the actual dosing of subjects continuously during the study allows the investigators to intervene in cases where subjects are dosing much higher or lower than expected and by doing so hopefully adjust the dosing in order for the study results to reflect 'normal' dosing of an ointment.</li><li>-Added a triplicate set of ECGs to be taken 1 hour after application of IMP at the Day 1 (Section 7.7.2) and Week 2 (Section 7.7.4) visits in addition to the ECGs already planned at those Visits 2, 4, and 12 hours after application. (This change only impacted the PK substudy.) Adding an additional set of ECGs will strengthen the data collected on cardiac safety. Adding a set of ECGs 1 hour after application ensures that in the case that maximum systemic exposure (C<sub>max</sub>) occurs before 2 hours after application, the study will still produce the desired data on cardiac safety at C<sub>max</sub>.</li><li>-Added a list of Adverse Events of Special Interest (AESIs) in Section 8.1 to require additional and prompt reporting if such AEs arose.</li></ul> |
| 19 February 2020 | <p>Clinical Study Protocol Version 4.0 made the following changes:</p> <ul style="list-style-type: none"><li>-Allowed the use of emollient in lesional areas, if subjects develop dry skin in the areas treated by IMP and if so authorized on a case-by-case basis based on the medical judgment of the investigator (Previously the use of emollient was only allowed in areas around, but not overlapping, the treatable areas.) Feedback has been received from investigators in the study that some patients, while showing improvement of redness, developed skin dryness. Following discussion with the investigators, it was concluded that the use of an emollient on such areas would be beneficial for subject comfort and compliance with study procedures.</li><li>-Removed collection of full body photo documentation at the Week 2 and 4 visits (was still collected at Day -1/1 [baseline] and Week 6 [end-of-treatment] visits). The image procedure is challenging and takes a lot of time for both subjects and study staff. Therefore it was decided to limit the photo requirements to the 2 timepoints most important for efficacy assessment, baseline and end-of-treatment.</li><li>-Clarification added that IP application is not performed during Week 6 visit.</li></ul>  |

|              |   |
|--------------|---|
| 02 June 2020 | <p>Clinical Study Protocol Version 5.0 made the following changes:</p> <ul style="list-style-type: none"> <li>-Changed the estimated date for the completion of the last subject from June 2020 to November 2020. Recruitment of new subjects was not possible during the months where societies have been closed down due to COVID-19.</li> <li>-Added interim analysis based on the 89/210 subjects that have been randomized and completed or dropped-out of the study by end-of-May. Due to COVID-19 restrictions making recruitment and visit attendance difficult, it was decided to assess an early stop of the study, either for futility or efficacy.</li> <li>-Removed an erroneous statement specifying that the trough level PK sample at the Week 6 visit should be collected "prior to morning or evening application."</li> <li>-Clarification added to Appendix C Assessment Measurements (Local Tolerability Score) that Severe Irritation should also be reported as adverse event. By mistake severe irritation was not marked as requiring reporting as adverse event.</li> </ul> |
|--------------|---|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported