



## Clinical trial results:

### International Open-Label Extension of the Phase 3 Study CL-503012 with KIACTA™ in Patients with AA Amyloidosis

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2013-004150-16    |
| Trial protocol           | LT GB PL          |
| Global end of trial date | 12 September 2016 |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 12 November 2017 |
| First version publication date | 12 November 2017 |

#### Trial information

##### Trial identification

|                       |           |
|-----------------------|-----------|
| Sponsor protocol code | CL-503015 |
|-----------------------|-----------|

##### Additional study identifiers

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

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | A.T. Development Switzerland SARL   |
| Sponsor organisation address | Rue Saint-Perre 2 , Lausanne Vaud, Switzerland, 1003  |
| Public contact               | Patrick C O'Connor Ph.D, FRCP , Auvén Therapeutics, 954 903 0492, Patrick.OConnor@auventx.com |
| Scientific contact           | Patrick C O'Connor Ph.D, FRCP , Auvén Therapeutics, 954 903 0492, Patrick.OConnor@auventx.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:

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**Results analysis stage**

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|  |                  |
|--|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 19 December 2016 |
| Is this the analysis of the primary completion data? | No               |

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|                                  |                   |
|----------------------------------|-------------------|
| Global end of trial reached?     | Yes               |
| Global end of trial date         | 12 September 2016 |
| Was the trial ended prematurely? | Yes               |

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Notes:

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**General information about the trial**

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Main objective of the trial:

The primary objective of this open-label extension (OLE) study is to provide access to Kiacta (eprodiate disodium) for those patients who have completed the pivotal, randomized, placebo-controlled Phase 3 Study CL-503012.

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Protection of trial subjects:

Institutions, investigators, and contract research organizations, etc., associated with this study have abided by all requirements applicable to the use and disclosure of patients' protected health information (such as the requirements provided for under the Health Insurance Portability and Accountability Act in the United States, the European Union Directive on Data Protection, the Personal Information Protection and Electronic Document Act in Canada and in any other similar regulations or legislation). The study was conducted according to the International Council for Harmonisation harmonised tripartite guideline E6(R1): Good Clinical Practice.

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Background therapy:

There is no standard therapy allowed per protocol (this is an orphan medicine).

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Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 17 December 2014 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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|                                      |                        |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Poland: 16             |
| Country: Number of subjects enrolled | United Kingdom: 3      |
| Country: Number of subjects enrolled | Lithuania: 1           |
| Country: Number of subjects enrolled | Russian Federation: 16 |
| Country: Number of subjects enrolled | Peru: 9                |
| Country: Number of subjects enrolled | Ukraine: 4             |
| Country: Number of subjects enrolled | Tunisia: 3             |
| Worldwide total number of subjects   | 52                     |
| EEA total number of subjects         | 20                     |

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Notes:

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**Subjects enrolled per age group**

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|          |   |
|----------|---|
| In utero | 0 |
|----------|---|

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|   |    |
|---|----|
| 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)                      | 40 |
| From 65 to 84 years                       | 12 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Patients completing Study CL-503012 who fulfilled the selection criteria were offered the opportunity to participate in Study CL-503015. This study was conducted at 11 study centers in 7 countries.

### Pre-assignment

Screening details:

Male or nonpregnant females of at least 18 years of age who completed Study CL-503012 and had undergone all study assessments that could affect the primary endpoint of Study CL-503012.

### Period 1

|                              |   |
|------------------------------|---|
| Period 1 title               | Overall treatment period (overall period) |
| Is this the baseline period? | Yes                                       |
| Allocation method            | Not applicable                            |
| Blinding used                | Not blinded                               |

### Arms

|                  |   |
|------------------|---|
| <b>Arm title</b> | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |
|------------------|---|

Arm description:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Kiacta TM    |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS. The dose regimen will depend on the patient's CrCl as calculated with the Cockcroft-Gault formula. At Baseline, the dose regimen will be based on CrCl of the last Study CL-503012 visit. At subsequent visits the dose regimen will be adjusted based on CrCl. If the dose regimen requires adjustment during the treatment period due to a change in the CrCl range, the change in renal function will be confirmed, and the Investigator will notify the patient of the new dose regimen.

|                                       |   |
|---------------------------------------|---|
| <b>Number of subjects in period 1</b> | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |
| Started                               | 52  |
| Completed                             | 43  |
| Not completed                         | 9   |
| treatment discontinuation             | 9   |

## Baseline characteristics

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### Reporting groups

|                       |                          |
|-----------------------|--------------------------|
| Reporting group title | Overall treatment period |
|-----------------------|--------------------------|

Reporting group description: -

| Reporting group values                | Overall treatment period | Total |  |
|---------------------------------------|--------------------------|-------|--|
| Number of subjects                    | 52                       | 52    |  |
| Age categorical<br>Units: Subjects    |                          |       |  |
| Adults (18-64 years)                  | 40                       | 40    |  |
| From 65-84 years                      | 12                       | 12    |  |
| Gender categorical<br>Units: Subjects |                          |       |  |
| Female                                | 33                       | 33    |  |
| Male                                  | 19                       | 19    |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |
| Reporting group description:<br>This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS. |   |

### Primary: Collection of data on Kiacta slowing renal function decline

|   |  |
|---|--|
| End point title   | Collection of data on Kiacta slowing renal function decline <sup>[1]</sup> |
| End point description:<br>All patients were to receive the study drug for a maximum of 12 months unless Kiacta became commercially available in the specific country. Study CL-503015 was terminated prematurely on 21 Jun 2016 after the efficacy analysis of Study CL-503012 showed that Kiacta did not meet the primary efficacy endpoint in slowing renal function decline. |  |
| End point type  | Primary  |
| End point timeframe:<br>Patients completing Study CL-503012 and fulfilling selection criteria will be offered the opportunity to participate in this OLE study for a maximum 12 months in those countries where the compassionate use program is not applicable.  |  |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analyses were performed. No sample size target was identified. This study planned to include all patients completing Study CL-503012 who fulfilled all selection criteria and who provided their written consent to participate. Data were collected and listings were produced for demography, drug dosage, AEs, clinical laboratory parameters, past and concurrent medical conditions, and concomitant medications. Study CL-503015 was terminated prematurely on 21 Jun 2016.

|                             |   |  |  |  |
|-----------------------------|---|--|--|--|
| <b>End point values</b>     | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |  |  |  |
| Subject group type          | Reporting group                               |  |  |  |
| Number of subjects analysed | 52  |  |  |  |
| Units: not applicable       | 0   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All patients were to receive Kiacta for a maximum of 12 months unless Kiacta became commercially available in the specific country.

Adverse event reporting additional description:

Safety was assessed by the incidence of AEs and SAEs. Adverse events included any clinically significant change or new clinically significant occurrence in laboratory tests, and vital signs when compared with Baseline status.

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

### Dictionary used

|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 19.0   |

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |
|-----------------------|---|

Reporting group description:

This is an OLE of the Study CL-503012. Therefore, all patients will receive Kiacta 400 mg administered orally as 1 to 3 capsules BID starting at Baseline until EOS.

| Serious adverse events                            | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |  |  |
|---|---|--|--|
| Total subjects affected by serious adverse events |   |  |  |
| subjects affected / exposed                       | 4 / 52 (7.69%)                                |  |  |
| number of deaths (all causes)                     | 1   |  |  |
| number of deaths resulting from adverse events    | 0   |  |  |
| Cardiac disorders                                 |   |  |  |
| congestive heart failure                          |   |  |  |
| subjects affected / exposed                       | 1 / 52 (1.92%)                                |  |  |
| occurrences causally related to treatment / all   | 0 / 1   |  |  |
| deaths causally related to treatment / all        | 0 / 0   |  |  |
| Heart failure                                     |   |  |  |
| subjects affected / exposed                       | 1 / 52 (1.92%)                                |  |  |
| occurrences causally related to treatment / all   | 0 / 1   |  |  |
| deaths causally related to treatment / all        | 0 / 0   |  |  |
| Blood and lymphatic system disorders              |   |  |  |
| Meningeal haemorrhage with severe hypertension    |   |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 52 (1.92%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Immune system disorders                         |                |  |  |
| Insufficiency of multiorgan                     |                |  |  |
| subjects affected / exposed                     | 1 / 52 (1.92%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 1          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| infected bronchiectasis                         |                |  |  |
| subjects affected / exposed                     | 1 / 52 (1.92%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| pleural effusion worsening                      |                |  |  |
| subjects affected / exposed                     | 1 / 52 (1.92%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 1 %

|   |   |  |  |
|---|---|--|--|
| <b>Non-serious adverse events</b>                     | Kiacta 400 mg BID, 800 mg BID, or 1200 mg BID |  |  |
| Total subjects affected by non-serious adverse events |   |  |  |
| subjects affected / exposed                           | 7 / 52 (13.46%)                               |  |  |
| Injury, poisoning and procedural complications        |   |  |  |
| Calcaneal spur  |   |  |  |
| subjects affected / exposed                           | 1 / 52 (1.92%)                                |  |  |
| occurrences (all)                                     | 1   |  |  |
| Fracture of the left humerus                          |   |  |  |
| subjects affected / exposed                           | 1 / 52 (1.92%)                                |  |  |
| occurrences (all)                                     | 1   |  |  |
| Cardiac disorders                                     |   |  |  |
| Mitral insufficiency                                  |   |  |  |
| subjects affected / exposed                           | 1 / 52 (1.92%)                                |  |  |
| occurrences (all)                                     | 1   |  |  |



|   |  |  |  |
|---|--|--|--|
| Tachicardia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 52 (1.92%)<br>1                            |  |  |
| Blood and lymphatic system disorders<br>Hypertension worsening<br>subjects affected / exposed<br>occurrences (all)  | 1 / 52 (1.92%)<br>1                            |  |  |
| Gastrointestinal disorders<br>Acute diarrhea<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 52 (1.92%)<br>1<br><br>1 / 52 (1.92%)<br>1 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Infected brochientasis<br>subjects affected / exposed<br>occurrences (all)<br><br>Pleural effusion<br>subjects affected / exposed<br>occurrences (all) | 2 / 52 (3.85%)<br>3<br><br>1 / 52 (1.92%)<br>1 |  |  |
| Skin and subcutaneous tissue disorders<br>Lichen ruber planus<br>subjects affected / exposed<br>occurrences (all)   | 1 / 52 (1.92%)<br>1                            |  |  |
| Psychiatric disorders<br>Depresion<br>subjects affected / exposed<br>occurrences (all)<br><br>Sleep disturbances<br>subjects affected / exposed<br>occurrences (all)                                      | 1 / 52 (1.92%)<br>1<br><br>1 / 52 (1.92%)<br>1 |  |  |
| Musculoskeletal and connective tissue disorders<br>Restless legs syndrome<br>subjects affected / exposed<br>occurrences (all)   | 1 / 52 (1.92%)<br>1                            |  |  |
| Infections and infestations   |  |  |  |

|  |                     |  |  |
|--|---------------------|--|--|
| Herpes zoster of right buttock<br>subjects affected / exposed<br>occurrences (all)     | 1 / 52 (1.92%)<br>1 |  |  |
| Inflammation of skin of left shank<br>subjects affected / exposed<br>occurrences (all) | 1 / 52 (1.92%)<br>1 |  |  |
| Common cold<br>subjects affected / exposed<br>occurrences (all)                        | 1 / 52 (1.92%)<br>1 |  |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported