



## Clinical trial results:

### A Phase 2a, Randomized, Double-blind, Placebo-controlled, Parallel-group, Proof of Concept Study to Investigate Efficacy, Safety, Pharmacodynamics and Pharmacokinetics of ASP6294 in the Treatment of Female Subjects With Bladder Pain Syndrome/Interstitial Cystitis

#### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2016-004138-12             |
| Trial protocol           | DE HU CZ GB BE PL NL LV ES |
| Global end of trial date | 21 March 2019              |

#### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 08 February 2020 |
| First version publication date | 08 February 2020 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | 6294-CL-0101 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03282318 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Astellas Pharma Europe B.V.   |
| Sponsor organisation address | Sylviusweg 62, Leiden, Netherlands, 2333 BE   |
| Public contact               | Astellas Pharma Global Development, Inc., Clinical Trial Disclosure, <a href="mailto:astellas.resultsdisclosure@astellas.com">astellas.resultsdisclosure@astellas.com</a> |
| Scientific contact           | Astellas Pharma Global Development, Inc., Clinical Trial Disclosure, <a href="mailto:astellas.resultsdisclosure@astellas.com">astellas.resultsdisclosure@astellas.com</a> |

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                       | 21 March 2019 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 21 March 2019 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

To investigate efficacy, safety, pharmacodynamics, and pharmacokinetics of ASP6294 in the treatment of female participants with bladder pain syndrome/interstitial cystitis (BPS/IC).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 28 September 2017 |
| 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 | Belgium: 3             |
| Country: Number of subjects enrolled | Germany: 6             |
| Country: Number of subjects enrolled | Netherlands: 2         |
| Country: Number of subjects enrolled | Spain: 3               |
| Country: Number of subjects enrolled | United Kingdom: 3      |
| Country: Number of subjects enrolled | Czech Republic: 7      |
| Country: Number of subjects enrolled | Hungary: 15            |
| Country: Number of subjects enrolled | Latvia: 27             |
| Country: Number of subjects enrolled | Poland: 29             |
| Country: Number of subjects enrolled | Russian Federation: 24 |
| Worldwide total number of subjects   | 119                    |
| EEA total number of subjects         | 95                     |

Notes:

| <b>Subjects enrolled per age group</b>    |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 94 |
| From 65 to 84 years                       | 24 |
| 85 years and over                         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

Female participants  $\geq 18$  years of age with BPS/IC were enrolled at 26 sites in the European Union and Russian Federation.

### Pre-assignment

Screening details:

A total of 209 participants signed informed consent. After screening, eligible participants entered a 2-week run-in period, a total of 90 participants discontinued prior to or during the run-in period. Eligible participants who met inclusion criteria and none of the exclusion criteria were enrolled.

### Period 1

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

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | ASP6294 |

Arm description:

Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

|  |                        |
|--|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | ASP6294                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

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

Arm description:

Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

|  |                        |
|--|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | Placebo                |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Subcutaneous use       |

Dosage and administration details:

Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

| <b>Number of subjects in period 1</b> | ASP6294 | Placebo           |
|---------------------------------------|---------|-------------------|
| Started                               | 57      | 62                |
| Treated                               | 56      | 61                |
| Completed Follow-up                   | 51      | 57 <sup>[1]</sup> |
| Completed                             | 51      | 59                |
| Not completed                         | 6       | 3                 |
| Consent withdrawn by subject          | 3       | -                 |
| Adverse Event                         | 1       | 1                 |
| Miscellaneous                         | 2       | 1                 |
| Lost to follow-up                     | -       | 1                 |

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Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: The participants who discontinued treatment could have continued in follow-up.

## Baseline characteristics

### Reporting groups

|   |         |
|---|---------|
| Reporting group title   | ASP6294 |
| Reporting group description:  |         |
| Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.                  |         |
| Reporting group title   | Placebo |
| Reporting group description:  |         |
| Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8. |         |

| Reporting group values   | ASP6294 | Placebo | Total |
|--|---------|---------|-------|
| Number of subjects   | 57      | 62      | 119   |
| Age categorical<br>Units: Subjects   |         |         |       |
| Age continuous<br>Units: years   |         |         |       |
| arithmetic mean  | 49.4    | 52.8    |       |
| standard deviation   | ± 15.6  | ± 16.1  | -     |
| Gender categorical<br>Units: Subjects  |         |         |       |
| Male   | 0       | 0       | 0     |
| Female   | 57      | 62      | 119   |
| Race<br>Units: Subjects  |         |         |       |
| WHITE  | 57      | 62      | 119   |
| Ethnicity<br>Units: Subjects   |         |         |       |
| Hispanic or Latino   | 1       | 0       | 1     |
| Not Hispanic or Latino   | 56      | 61      | 117   |
| Not reported   | 0       | 1       | 1     |
| Hunners Lesion<br>Units: Subjects  |         |         |       |
| Yes  | 5       | 4       | 9     |
| No   | 52      | 58      | 110   |
| Presence of a Nonurological Functional Somatic Syndrome<br>Units: Subjects   |         |         |       |
| Yes  | 6       | 10      | 16    |
| No   | 51      | 52      | 103   |
| Average Mean Daily Bladder Pain (MDP)  |         |         |       |
| Participants recorded their MDP each day in the evening into an e-diary. The MDP was the average pain experienced over the past 24 hours. The average MDP was the mean of daily assessments of MDP in the week prior to the visit with at least 5 recordings in that week. MDP was measured using an 11-point Numerical Rating Scale (NRS) ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain). |         |         |       |
| Units: Units on a scale  |         |         |       |
| arithmetic mean  | 5.58    | 5.61    |       |
| standard deviation   | ± 0.96  | ± 1.25  | -     |

|   |        |        |   |
|---|--------|--------|---|
| Average Worst Daily Bladder Pain (WDP)  |        |        |   |
| Participants recorded their WDP each day in the evening into an e-diary. The WDP was the worst pain experienced over the past 24 hours. The average WDP was the mean of daily assessments of WDP in the week prior to the visit with at least 5 recordings in that week. WDP was measured using an 11-point NRS ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain).   |        |        |   |
| Units: Units on a scale   |        |        |   |
| arithmetic mean   | 6.99   | 7.04   |   |
| standard deviation  | ± 0.96 | ± 1.12 | - |
| Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score   |        |        |   |
| BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over previous 7 days. Question (Q) 1 to Q5 assess urinary symptoms and are rated 0 (never) to 4 (always). Q6 and Q7 assess impact of bladder pain and are rated 0 (not at all) to 4 (a great deal). Q8 assess the worst pain on 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. The BPIC-SS total score is the sum of individual question scores and range from 0 to 38, with higher scores indicating a worse situation. A score of 19 or more represents moderate/severe disease activity. |        |        |   |
| Units: Units on a scale   |        |        |   |
| arithmetic mean   | 26.4   | 26.8   |   |
| standard deviation  | ± 3.8  | ± 3.5  | - |
| Mean Number of Level 3 or 4 Urgency Episodes per 24 hours   |        |        |   |
| For each micturition episode, participants rated the degree of associated urgency severity according to Patient Perception of Intensity of Urgency Scale (PPIUS) on a 5-point categorical scale ranging from 0 to 4, where 0 = no urgency, 1 = mild urgency, 2 = moderate urgency, 3 = severe urgency, and 4 = urge incontinence. Mean number of Level 3 or 4 urgency episodes was the mean of the recordings of Level 3 or 4 urgency episodes in the 3-day electronic micturition diary in the week prior to the visit.  |        |        |   |
| Units: Episodes per 24 hours  |        |        |   |
| arithmetic mean   | 3.87   | 4.14   |   |
| standard deviation  | ± 5.09 | ± 4.35 | - |
| Mean Voiding Frequency per 24 hours   |        |        |   |
| Mean voiding frequency was the mean of the recordings of voiding frequency in the electronic micturition diary in the week prior to the visit with at least 2 days recorded in that week.   |        |        |   |
| Units: Voids per 24 hours   |        |        |   |
| arithmetic mean   | 13.74  | 13.33  |   |
| standard deviation  | ± 4.09 | ± 3.74 | - |
| BPIC-SS Worst Bladder Pain (Question 8) Score   |        |        |   |
| The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Q8 of BPIC-SS assessed the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. For these characteristics, the number of participants analyzed were 53 and 59 in ASP6294 and Placebo arm, respectively.   |        |        |   |
| Units: Units on a scale   |        |        |   |
| log mean  | 7.58   | 7.54   |   |
| standard deviation  | ± 1.36 | ± 1.21 | - |

## End points

### End points reporting groups

|   |         |
|---|---------|
| Reporting group title   | ASP6294 |
| Reporting group description:<br>Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.                  |         |
| Reporting group title   | Placebo |
| Reporting group description:<br>Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8. |         |

### Primary: Change from Baseline in Average Mean Daily Pain (MDP) Score at Week 12

|  |  |
|--|--|
| End point title  | Change from Baseline in Average Mean Daily Pain (MDP) Score at Week 12 |
| End point description:<br>Participants recorded their MDP each day in the evening into an e-diary. The MDP was the average pain experienced over the past 24 hours. The average MDP was the mean of daily assessments of MDP in the week prior to the visit with at least 5 recordings in that week. MDP was measured using an 11-point Numerical Rating Scale (NRS) ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain). A negative change indicates a reduction/improvement from baseline. The analysis population was Full Analysis Set (FAS), which consisted of all randomized participants who received $\geq 1$ injection of double-blind study drug and had nonmissing MDP values at Visit 2/baseline and $\geq 1$ postbaseline visit (i.e., $\geq 5$ recordings in any week postbaseline). FAS participants with available data were included in analysis. |  |
| End point type   | Primary  |
| End point timeframe:<br>Baseline and Week 12   |  |

| End point values                    | ASP6294             | Placebo             |  |  |
|-------------------------------------|---------------------|---------------------|--|--|
| Subject group type                  | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed         | 48                  | 52                  |  |  |
| Units: Units on a scale             |                     |                     |  |  |
| least squares mean (standard error) | -2.34 ( $\pm$ 0.28) | -2.13 ( $\pm$ 0.26) |  |  |

### Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Change from Baseline Analysis at Week 12 |
| Statistical analysis description:<br>Analysis was performed using Mixed-Effect Model Repeated Measures (MMRM) model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no). Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group. |  |
| Comparison groups   | ASP6294 v Placebo                        |



|   |                                    |
|---|------------------------------------|
| Number of subjects included in analysis | 100                                |
| Analysis specification                  | Pre-specified                      |
| Analysis type                           | superiority                        |
| P-value                                 | = 0.591                            |
| Method                                  | MMRM                               |
| Parameter estimate                      | Least-Squares (LS) Mean Difference |
| Point estimate                          | -0.2                               |
| Confidence interval                     |                                    |
| level                                   | 90 %                               |
| sides                                   | 2-sided                            |
| lower limit                             | -0.84                              |
| upper limit                             | 0.43                               |
| Variability estimate                    | Standard error of the mean         |
| Dispersion value                        | 0.38                               |

## Secondary: Change from Baseline in Average Worst Daily Pain (WDP) Score at Week 12

|  |   |
|--|---|
| End point title  | Change from Baseline in Average Worst Daily Pain (WDP) Score at Week 12 |
| End point description:   |   |
| Participants recorded their WDP each day in the evening into an e-diary. The WDP was the worst pain experienced over the past 24 hours. The average WDP was the mean of daily assessments of WDP in the week prior to the visit with at least 5 recordings in that week. WDP was measured using an 11-point NRS ranging from 0 (no bladder pain) to 10 (worst imaginable bladder pain). A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline and Week 12   |   |

| End point values                    | ASP6294         | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 48              | 52              |  |  |
| Units: Units on a scale             |                 |                 |  |  |
| least squares mean (standard error) | -2.22 (± 0.32)  | -2.33 (± 0.30)  |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Change from Baseline Analysis at Week 12 |
| Statistical analysis description:   |  |
| Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no). Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group. |  |
| Comparison groups   | ASP6294 v Placebo                        |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 100                        |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.817                    |
| Method                                  | MMRM                       |
| Parameter estimate                      | LS Mean Difference         |
| Point estimate                          | 0.1                        |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.63                      |
| upper limit                             | 0.84                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.44                       |

## Secondary: Change From Baseline in Mean Voiding Frequency per 24 hours at Week 12

|  |  |
|--|--|
| End point title  | Change From Baseline in Mean Voiding Frequency per 24 hours at Week 12 |
| End point description:   |  |
| Mean voiding frequency was the mean of the recordings of voiding frequency in the electronic micturition diary in the week prior to the visit with at least 2 days recorded in that week. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline and Week 12   |  |

| End point values                    | ASP6294         | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 41              | 39              |  |  |
| Units: Voids per 24 hours           |                 |                 |  |  |
| least squares mean (standard error) | -2.16 (± 0.65)  | -1.15 (± 0.64)  |  |  |

## Statistical analyses

|   |  |
|---|--|
| Statistical analysis title  | Change from Baseline Analysis at Week 12 |
| Statistical analysis description:   |  |
| Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no). Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group. |  |
| Comparison groups   | ASP6294 v Placebo                        |

|   |                            |
|---|----------------------------|
| Number of subjects included in analysis | 80                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.272                    |
| Method                                  | MMRM                       |
| Parameter estimate                      | LS Mean Difference         |
| Point estimate                          | -1.01                      |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -2.54                      |
| upper limit                             | 0.52                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.91                       |

### Secondary: Change From Baseline in Mean Number of Level 3 or 4 Urgency Episodes (Based on Patient Perception of Intensity of Urgency Scale [PPIUS]) per 24 hours at Week 12

|                 |  |
|-----------------|--|
| End point title | Change From Baseline in Mean Number of Level 3 or 4 Urgency Episodes (Based on Patient Perception of Intensity of Urgency Scale [PPIUS]) per 24 hours at Week 12 |
|-----------------|--|

#### End point description:

The perceived level of urinary urgency was measured using PPIUS. For each micturition episode, participant was asked to rate the degree of associated urgency severity according to PPIUS. PPIUS is a 5-point categorical scale ranging from 0 to 4, where 0 = no urgency (participant felt no need to empty the bladder, but did so for other reasons), 1 = mild urgency (participant could postpone voiding as long as necessary, without fear of wetting herself), 2 = moderate urgency (participant could postpone voiding for a short while, without fear of wetting herself), 3 = severe urgency (participant could not postpone voiding, had to rush to the toilet in order not to wet herself), and 4 = urge incontinence (participant leaked before arriving to the toilet). Mean number of Level 3 or 4 urgency episodes was the mean of recordings of Level 3 or 4 urgency episodes in 3-day electronic micturition diary in the week prior to visit. FAS participants with available data were included in analysis.

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

#### End point timeframe:

Baseline and Week 12

| End point values                    | ASP6294         | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 41              | 39              |  |  |
| Units: Episodes per 24 hours        |                 |                 |  |  |
| least squares mean (standard error) | -1.52 (± 0.51)  | -1.84 (± 0.51)  |  |  |

### Statistical analyses

|                            |  |
|----------------------------|--|
| Statistical analysis title | Change from Baseline Analysis at Week 12 |
|----------------------------|--|

#### Statistical analysis description:

Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week

interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).

Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group.

|   |                            |
|---|----------------------------|
| Comparison groups                       | ASP6294 v Placebo          |
| Number of subjects included in analysis | 80                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | superiority                |
| P-value                                 | = 0.664                    |
| Method                                  | MMRM                       |
| Parameter estimate                      | LS Mean Difference         |
| Point estimate                          | 0.31                       |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | -0.89                      |
| upper limit                             | 1.51                       |
| Variability estimate                    | Standard error of the mean |
| Dispersion value                        | 0.72                       |

## Secondary: Change From Baseline in Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score at Week 12

|  |  |
|--|--|
| End point title  | Change From Baseline in Bladder Pain/ Interstitial Cystitis Symptom Score (BPIC-SS) Total Score at Week 12 |
| End point description:   |  |
| <p>The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Question (Q) 1 to Q5 assess urinary symptoms (how often urinated because of pain, need to urinate just after previous urination, urination to avoid pain, pressure in the bladder, and pain in the bladder) and are rated 0 (never) to 4 (always). Q6 and Q7 assess the impact of bladder pain (bothered by frequent urination during daytime and nighttime) and are rated 0 (not at all) to 4 (a great deal). Q8 assess the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. The BPIC-SS total score is the sum of the individual question scores and range from 0 to 38, with higher scores indicating a worse situation. A score of 19 or more represents moderate/severe disease activity. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis.</p> |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline and Week 12   |  |

| End point values                    | ASP6294         | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 49              | 54              |  |  |
| Units: Units on a scale             |                 |                 |  |  |
| least squares mean (standard error) | -7.41 (± 1.13)  | -7.16 (± 1.07)  |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Change from Baseline Analysis at Week 12 |
| Statistical analysis description:  |  |
| Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).<br>Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group. |  |
| Comparison groups  | ASP6294 v Placebo                        |
| Number of subjects included in analysis  | 103                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | superiority                              |
| P-value  | = 0.872                                  |
| Method   | MMRM                                     |
| Parameter estimate   | LS Mean Difference                       |
| Point estimate   | -0.25                                    |
| Confidence interval  |  |
| level  | 90 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -2.84                                    |
| upper limit  | 2.33                                     |
| Variability estimate   | Standard error of the mean               |
| Dispersion value   | 1.56                                     |

### Secondary: Change From Baseline in BPIC-SS Worst Bladder Pain (Question 8) Score at Week 12

|  |  |
|--|--|
| End point title  | Change From Baseline in BPIC-SS Worst Bladder Pain (Question 8) Score at Week 12 |
| End point description:   |  |
| The BPIC-SS is a psychometrically validated and reliable questionnaire with 8 questions concerning bladder pain over the previous 7 days. Q8 of BPIC-SS assess the worst pain on a 0 (no bladder pain) to 10 (worst possible bladder pain) NRS. A negative change indicates a reduction/improvement from baseline. FAS participants with available data were included in analysis. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Baseline and Week 12   |  |

| End point values                    | ASP6294         | Placebo         |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 49              | 54              |  |  |
| Units: Units on a scale             |                 |                 |  |  |
| least squares mean (standard error) | -2.35 (± 0.36)  | -2.38 (± 0.34)  |  |  |

### Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Change from Baseline Analysis at Week 12 |
| Statistical analysis description:  |  |
| Analysis was performed using MMRM model with treatment group, week (as factor), treatment-by-week interaction, baseline value, baseline-by-week interaction, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no).<br>Difference was calculated by subtracting the LS mean of placebo group from the LS mean of ASP6294 group. |  |
| Comparison groups  | ASP6294 v Placebo                        |
| Number of subjects included in analysis  | 103                                      |
| Analysis specification   | Pre-specified                            |
| Analysis type  | superiority                              |
| P-value  | = 0.956                                  |
| Method   | MMRM                                     |
| Parameter estimate   | LS Mean Difference                       |
| Point estimate   | 0.03                                     |
| Confidence interval  |  |
| level  | 90 %                                     |
| sides  | 2-sided                                  |
| lower limit  | -0.79                                    |
| upper limit  | 0.84                                     |
| Variability estimate   | Standard error of the mean               |
| Dispersion value   | 0.49                                     |

### Secondary: Percentage of Participants With Moderately Improved or Better Grade on the Global Response Assessment (GRA) at Week 12

|  |  |
|--|--|
| End point title  | Percentage of Participants With Moderately Improved or Better Grade on the Global Response Assessment (GRA) at Week 12 |
| End point description:   |  |
| A self-reported 7 grade GRA was used to evaluate a participant's clinical condition relative to baseline. The GRA read: As compared to when the participant started the study, how would the participant rate the participant's overall symptoms now? The 7 GRA grades were "markedly worse", "moderately worse", "slightly worse", "no change", "slightly improved", "moderately improved" or "markedly improved". Percentage of participants with a successful GRA response (defined as the response of "moderately improved" or better ["markedly improved"]) are reported. FAS participants with available data were included in analysis. |  |
| End point type   | Secondary  |
| End point timeframe:   |  |
| Week 12  |  |

|                                   |                     |                     |  |  |
|-----------------------------------|---------------------|---------------------|--|--|
| <b>End point values</b>           | ASP6294             | Placebo             |  |  |
| Subject group type                | Reporting group     | Reporting group     |  |  |
| Number of subjects analysed       | 49                  | 54                  |  |  |
| Units: percentage of participants |                     |                     |  |  |
| number (confidence interval 90%)  | 40.6 (29.6 to 52.7) | 32.9 (23.3 to 44.3) |  |  |

## Statistical analyses

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Moderately Improved or Better Grade on GRA |
| Statistical analysis description:  |  |
| Analysis was performed using a logistic regression model with treatment group, region (3 regions), nonurological functional somatic syndrome (yes, no) and Hunner's lesions (yes, no). |  |
| Comparison groups  | ASP6294 v Placebo                          |
| Number of subjects included in analysis  | 103  |
| Analysis specification   | Pre-specified                              |
| Analysis type  | superiority                                |
| P-value  | = 0.426                                    |
| Method   | Regression, Logistic                       |
| Parameter estimate   | Odds ratio (OR)                            |
| Point estimate   | 1.394                                      |
| Confidence interval  |  |
| level  | 90 %                                       |
| sides  | 2-sided                                    |
| lower limit  | 0.702                                      |
| upper limit  | 2.767                                      |

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From the first administration of study drug until Week 18

Adverse event reporting additional description:

Safety analysis set (SAF) consisted of all participants who received  $\geq 1$  injection of double-blind study drug.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | ASP6294 |
|-----------------------|---------|

Reporting group description:

Participants received 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Participants received placebo to match 320 mg ASP6294 subcutaneous injection at 4-week intervals at baseline (Day 1/Week 0), Week 4 and Week 8.

| Serious adverse events  | ASP6294        | Placebo        |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events                   |                |                |  |
| subjects affected / exposed   | 0 / 56 (0.00%) | 3 / 61 (4.92%) |  |
| number of deaths (all causes)                                       | 0              | 0              |  |
| number of deaths resulting from adverse events                      | 0              | 0              |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |  |
| Vaginal cancer  |                |                |  |
| subjects affected / exposed   | 0 / 56 (0.00%) | 1 / 61 (1.64%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Nervous system disorders  |                |                |  |
| Cervicobrachial syndrome  |                |                |  |
| subjects affected / exposed   | 0 / 56 (0.00%) | 1 / 61 (1.64%) |  |
| occurrences causally related to treatment / all                     | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders  |                |                |  |
| Abdominal pain  |                |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 61 (1.64%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Musculoskeletal pain                            |                |                |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 61 (1.64%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Diverticulitis                                  |                |                |  |
| subjects affected / exposed                     | 0 / 56 (0.00%) | 1 / 61 (1.64%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| <b>Non-serious adverse events</b>                     | ASP6294         | Placebo        |  |
|---|-----------------|----------------|--|
| Total subjects affected by non-serious adverse events |                 |                |  |
| subjects affected / exposed                           | 8 / 56 (14.29%) | 5 / 61 (8.20%) |  |
| Nervous system disorders                              |                 |                |  |
| Headache  |                 |                |  |
| subjects affected / exposed                           | 5 / 56 (8.93%)  | 2 / 61 (3.28%) |  |
| occurrences (all)                                     | 9               | 2              |  |
| Musculoskeletal and connective tissue disorders       |                 |                |  |
| Arthralgia  |                 |                |  |
| subjects affected / exposed                           | 4 / 56 (7.14%)  | 2 / 61 (3.28%) |  |
| occurrences (all)                                     | 6               | 4              |  |
| Infections and infestations                           |                 |                |  |
| Nasopharyngitis                                       |                 |                |  |
| subjects affected / exposed                           | 3 / 56 (5.36%)  | 1 / 61 (1.64%) |  |
| occurrences (all)                                     | 4               | 2              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment   |
|--------------|---|
| 06 June 2017 | The changes included:<br>1) Added information for Data Safety Monitoring Board throughout the protocol.<br>2) Addition of inclusion criterion: Participants must have tried 2 previous therapies for BPS/IC with unsatisfactory results, prior to study entry.<br>3) Inclusion criterion number 9 was reworded to participants must agree not to donate ova at screening and throughout the study period. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported