



## Clinical trial results:

### A 3-Year, Multi-Center, Long-Term Safety (LTS) Study to Evaluate the Safety and Tolerability of TD-1473 in Subjects with Ulcerative Colitis (UC)

#### Summary

|                          |                                  |
|--------------------------|----------------------------------|
| EudraCT number           | 2018-002135-19                   |
| Trial protocol           | HU DE PT SK FR PL ES GR BG IT RO |
| Global end of trial date | 27 October 2021                  |

#### Results information

|                                |                 |
|--------------------------------|-----------------|
| Result version number          | v1 (current)    |
| This version publication date  | 26 October 2022 |
| First version publication date | 26 October 2022 |

#### Trial information

##### Trial identification

|                       |      |
|-----------------------|------|
| Sponsor protocol code | 0164 |
|-----------------------|------|

##### Additional study identifiers

|                                    |                       |
|------------------------------------|-----------------------|
| ISRCTN number                      | -                     |
| ClinicalTrials.gov id (NCT number) | NCT03920254           |
| WHO universal trial number (UTN)   | -                     |
| Other trial identifiers            | US IND Number: 128299 |

Notes:

#### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Theravance Biopharma Ireland Limited   |
| Sponsor organisation address | 10 Earlsfort Terrace, Dublin, Ireland, D04 C5Y6  |
| Public contact               | Medical Monitor, Theravance Biopharma Ireland Limited, +1 855 633 8479, medinfo@theravance.com |
| Scientific contact           | Medical Monitor, Theravance Biopharma Ireland Limited, +1 855 633 8479, medinfo@theravance.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                       | 27 October 2021 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 27 October 2021 |
| Was the trial ended prematurely? | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety and tolerability of TD-1473 administered up to 3 years in participants with moderate to severe UC after participation in the Maintenance Study of Protocol 0157 (EudraCT number: 2018-002136-24).

Protection of trial subjects:

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the International Conference on Harmonization Harmonised Tripartite Guideline.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 23 July 2020 |
| 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: 9        |
| Country: Number of subjects enrolled | Portugal: 2      |
| Country: Number of subjects enrolled | Slovakia: 1      |
| Country: Number of subjects enrolled | Spain: 1         |
| Country: Number of subjects enrolled | Bulgaria: 5      |
| Country: Number of subjects enrolled | France: 1        |
| Country: Number of subjects enrolled | Germany: 1       |
| Country: Number of subjects enrolled | Italy: 1         |
| Country: Number of subjects enrolled | Ukraine: 8       |
| Country: Number of subjects enrolled | Japan: 5         |
| Country: Number of subjects enrolled | Serbia: 5        |
| Country: Number of subjects enrolled | United States: 4 |
| Country: Number of subjects enrolled | Australia: 2     |
| Country: Number of subjects enrolled | Georgia: 1       |
| Worldwide total number of subjects   | 46               |
| EEA total number of subjects         | 21               |

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)                      | 40 |
| From 65 to 84 years                       | 6  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 46 out of the planned 500 participants were enrolled and received study drug between 23 July 2020 and 27 October 2021.

### Period 1

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

### Arms

|                              |              |
|------------------------------|--------------|
| Are arms mutually exclusive? | Yes          |
| <b>Arm title</b>             | TD-1473 20mg |

Arm description:

Participants received TD-1473 orally at a dose of 20mg once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | TD-1473      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Received orally.

|                  |              |
|------------------|--------------|
| <b>Arm title</b> | TD-1473 80mg |
|------------------|--------------|

Arm description:

Participants received TD-1473 orally at a dose of 80mg once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | TD-1473      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Received orally.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | TD-1473 200mg |
|------------------|---------------|

Arm description:

Participants received TD-1473 orally at a dose of 200mg once daily.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | TD-1473      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

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Dosage and administration details:

Received orally.

| <b>Number of subjects in period 1</b> | TD-1473 20mg | TD-1473 80mg | TD-1473 200mg |
|---------------------------------------|--------------|--------------|---------------|
| Started                               | 13           | 18           | 15            |
| Completed                             | 0            | 0            | 0             |
| Not completed                         | 13           | 18           | 15            |
| Physician decision                    | -            | 1            | 2             |
| Consent withdrawn by subject          | -            | -            | 1             |
| Adverse event, non-fatal              | 1            | -            | -             |
| Study Terminated By Sponsor           | 12           | 17           | 12            |

## Baseline characteristics

### Reporting groups

|   |               |
|---|---------------|
| Reporting group title   | TD-1473 20mg  |
| Reporting group description:  |               |
| Participants received TD-1473 orally at a dose of 20mg once daily.  |               |
| Reporting group title   | TD-1473 80mg  |
| Reporting group description:  |               |
| Participants received TD-1473 orally at a dose of 80mg once daily.  |               |
| Reporting group title   | TD-1473 200mg |
| Reporting group description:  |               |
| Participants received TD-1473 orally at a dose of 200mg once daily. |               |

| Reporting group values | TD-1473 20mg | TD-1473 80mg | TD-1473 200mg |
|------------------------|--------------|--------------|---------------|
| Number of subjects     | 13           | 18           | 15            |
| Age categorical        |              |              |               |
| Units: Subjects        |              |              |               |

|                         |          |          |          |
|-------------------------|----------|----------|----------|
| Age continuous          |          |          |          |
| Units: years            |          |          |          |
| arithmetic mean         | 46.31    | 43.22    | 46.13    |
| standard deviation      | ± 17.375 | ± 15.869 | ± 13.432 |
| Gender categorical      |          |          |          |
| Units: Subjects         |          |          |          |
| Female                  | 8        | 7        | 7        |
| Male                    | 5        | 11       | 8        |
| Ethnicity (NIH/OMB)     |          |          |          |
| Units: Subjects         |          |          |          |
| Hispanic or Latino      | 1        | 1        | 0        |
| Not Hispanic or Latino  | 12       | 17       | 15       |
| Unknown or Not Reported | 0        | 0        | 0        |
| Race (NIH/OMB)          |          |          |          |
| Units: Subjects         |          |          |          |
| Asian                   | 1        | 3        | 1        |
| White                   | 12       | 15       | 13       |
| Unknown or Not Reported | 0        | 0        | 1        |

| Reporting group values | Total |  |  |
|------------------------|-------|--|--|
| Number of subjects     | 46    |  |  |
| Age categorical        |       |  |  |
| Units: Subjects        |       |  |  |

|                    |   |  |  |
|--------------------|---|--|--|
| Age continuous     |   |  |  |
| Units: years       |   |  |  |
| arithmetic mean    |   |  |  |
| standard deviation | - |  |  |

|                         |    |  |  |
|-------------------------|----|--|--|
| Gender categorical      |    |  |  |
| Units: Subjects         |    |  |  |
| Female                  | 22 |  |  |
| Male                    | 24 |  |  |
| Ethnicity (NIH/OMB)     |    |  |  |
| Units: Subjects         |    |  |  |
| Hispanic or Latino      | 2  |  |  |
| Not Hispanic or Latino  | 44 |  |  |
| Unknown or Not Reported | 0  |  |  |
| Race (NIH/OMB)          |    |  |  |
| Units: Subjects         |    |  |  |
| Asian                   | 5  |  |  |
| White                   | 40 |  |  |
| Unknown or Not Reported | 1  |  |  |

## End points

### End points reporting groups

|   |               |
|---|---------------|
| Reporting group title   | TD-1473 20mg  |
| Reporting group description:<br>Participants received TD-1473 orally at a dose of 20mg once daily.  |               |
| Reporting group title   | TD-1473 80mg  |
| Reporting group description:<br>Participants received TD-1473 orally at a dose of 80mg once daily.  |               |
| Reporting group title   | TD-1473 200mg |
| Reporting group description:<br>Participants received TD-1473 orally at a dose of 200mg once daily. |               |

### Primary: Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE)

|   |   |
|---|---|
| End point title   | Number of Participants Who Experienced a Treatment-emergent Adverse Event (TEAE) <sup>[1]</sup> |
| End point description:<br>A TEAE was defined as any AE with a recorded start date on or after the date of the first dose of study drug up through 4 weeks after the last dose of study drug. Any clinically significant changes in laboratory safety tests, electrocardiograms (ECGs) and vital signs, were also recorded as TEAEs. Includes all participants from the Safety Analysis Set. |   |
| End point type  | Primary   |
| End point timeframe:<br>Day 1 up to 4 weeks after last dose of study drug (median treatment duration was: TD-1473 20 mg - 142 days; TD-1473 80 mg - 180 days; TD-1473 200 mg - 158 days)  |   |
| Notes:<br>[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.<br>Justification: No additional statistical analyses were pre-specified for this endpoint.  |   |

| End point values            | TD-1473 20mg    | TD-1473 80mg    | TD-1473 200mg   |  |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed | 13              | 18              | 15              |  |
| Units: participants         | 4               | 5               | 6               |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Day 1 up to 4 weeks after last dose of study drug (median treatment duration was: TD-1473 20 mg - 142 days; TD-1473 80 mg - 180 days; TD-1473 200 mg - 158 days)

Adverse event reporting additional description:

Includes all participants from the Safety Analysis Set.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | TD-1473 20mg |
|-----------------------|--------------|

Reporting group description:

Participants received TD-1473 orally at a dose of 20mg once daily.

|                       |              |
|-----------------------|--------------|
| Reporting group title | TD-1473 80mg |
|-----------------------|--------------|

Reporting group description:

Participants received TD-1473 orally at a dose of 80mg once daily.

|                       |               |
|-----------------------|---------------|
| Reporting group title | TD-1473 200mg |
|-----------------------|---------------|

Reporting group description:

Participants received TD-1473 orally at a dose of 200mg once daily.

| Serious adverse events                            | TD-1473 20mg   | TD-1473 80mg   | TD-1473 200mg  |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events |                |                |                |
| subjects affected / exposed                       | 0 / 13 (0.00%) | 0 / 18 (0.00%) | 1 / 15 (6.67%) |
| number of deaths (all causes)                     | 0              | 0              | 0              |
| number of deaths resulting from adverse events    | 0              | 0              | 0              |
| Blood and lymphatic system disorders              |                |                |                |
| Anaemia of chronic disease                        |                |                |                |
| subjects affected / exposed                       | 0 / 13 (0.00%) | 0 / 18 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |

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

| Non-serious adverse events  | TD-1473 20mg    | TD-1473 80mg    | TD-1473 200mg   |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by non-serious adverse events               |                 |                 |                 |
| subjects affected / exposed   | 4 / 13 (30.77%) | 5 / 18 (27.78%) | 5 / 15 (33.33%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                 |                 |                 |

|  |  |   |  |
|--|--|---|--|
| Skin papilloma<br>subjects affected / exposed<br>occurrences (all)   | 0 / 13 (0.00%)<br>0                            | 1 / 18 (5.56%)<br>1                             | 0 / 15 (0.00%)<br>0                            |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)   | 1 / 13 (7.69%)<br>1                            | 0 / 18 (0.00%)<br>0                             | 0 / 15 (0.00%)<br>0                            |
| General disorders and administration<br>site conditions<br>Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 2 / 13 (15.38%)<br>2                           | 0 / 18 (0.00%)<br>0                             | 0 / 15 (0.00%)<br>0                            |
| Gastrointestinal disorders<br>Colitis ulcerative<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)              | 1 / 13 (7.69%)<br>1<br><br>1 / 13 (7.69%)<br>2 | 3 / 18 (16.67%)<br>3<br><br>0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1<br><br>0 / 15 (0.00%)<br>0 |
| Reproductive system and breast<br>disorders<br>Endometriosis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 13 (0.00%)<br>0                            | 0 / 18 (0.00%)<br>0                             | 1 / 15 (6.67%)<br>1                            |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all)<br><br>Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all) | 1 / 13 (7.69%)<br>1<br><br>1 / 13 (7.69%)<br>1 | 0 / 18 (0.00%)<br>0<br><br>0 / 18 (0.00%)<br>0  | 0 / 15 (0.00%)<br>0<br><br>0 / 15 (0.00%)<br>0 |
| Skin and subcutaneous tissue disorders<br>Eczema asteatotic<br>subjects affected / exposed<br>occurrences (all)  | 0 / 13 (0.00%)<br>0                            | 1 / 18 (5.56%)<br>1                             | 0 / 15 (0.00%)<br>0                            |
| Psychiatric disorders<br>Depression  |  |   |  |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 13 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders<br>Myalgia<br>subjects affected / exposed<br>occurrences (all)     | 1 / 13 (7.69%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)                        | 0 / 13 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Chlamydial infection<br>subjects affected / exposed<br>occurrences (all)   | 0 / 13 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Clostridium difficile infection<br>subjects affected / exposed<br>occurrences (all)                                | 1 / 13 (7.69%)<br>1 | 0 / 18 (0.00%)<br>0 | 0 / 15 (0.00%)<br>0 |
| Tinea pedis<br>subjects affected / exposed<br>occurrences (all)  | 0 / 13 (0.00%)<br>0 | 1 / 18 (5.56%)<br>1 | 0 / 15 (0.00%)<br>0 |
| Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 13 (0.00%)<br>0 | 1 / 18 (5.56%)<br>2 | 0 / 15 (0.00%)<br>0 |
| Urinary tract infection<br>subjects affected / exposed<br>occurrences (all)  | 0 / 13 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |
| Metabolism and nutrition disorders<br>Type 2 diabetes mellitus<br>subjects affected / exposed<br>occurrences (all) | 0 / 13 (0.00%)<br>0 | 0 / 18 (0.00%)<br>0 | 1 / 15 (6.67%)<br>1 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 07 November 2018 | This protocol was amended to correct incorrect formatting , correct incorrect spelling, correct incorrect references to sections within the protocol, delete duplicated information, add updated information throughout, clarify wording, add updated results of a completed study, include minor administration changes.                            |
| 15 February 2021 | This protocol was amended to clarify some key points related to the inclusion and exclusion criteria. Additionally, some administrative updates were made along with some additional clarifications to provide operational guidance to sites on the appropriate implementation of key study activities. Lastly, typographical errors were corrected. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date          | Interruption   | Restart date  |
|---------------|--|---------------|
| 18 March 2020 | The Sponsor notified all global clinical research sites in writing that screening of new participants was suspended initially for a period of 4 weeks (18 March 2020 to 17 April 2020) with planned reassessment thereafter. Participants already enrolled in the study screening period at the time of this notification could progress to randomization if they met safety criteria as specified by the Medical Director or per the study-specific COVID-19 mitigation plan. | 17 April 2020 |

Notes:

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study 0164 was terminated early because Study 0157 was terminated early and participation in Study 0164 was predicated on participation in Study 0157.

Notes: