



## Clinical trial results:

**NASH EXploratory Single and COmbination Treatment (NEXSCOT): An open label, multicenter, platform study to evaluate the safety, tolerability, pharmacokinetics and efficacy of various single and combination treatments in patients with non-alcoholic fatty liver disease (NAFLD) who manifest a non-alcoholic steatohepatitis (NASH)-like biomarker phenotype.**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2019-000440-10  |
| Trial protocol           | DE              |
| Global end of trial date | 06 January 2022 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v2 (current)     |
| This version publication date  | 14 February 2023 |
| First version publication date | 15 December 2022 |
| Version creation reason        |                  |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | CADPT02A12001 |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04147195 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Pharma AG  |
| Sponsor organisation address | Novartis Campus, Basel, Switzerland,  |
| Public contact               | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com |
| Scientific contact           | Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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                       | 06 January 2022 |
| Is this the analysis of the primary completion data? | No              |

|                                  |                 |
|----------------------------------|-----------------|
| Global end of trial reached?     | Yes             |
| Global end of trial date         | 06 January 2022 |
| Was the trial ended prematurely? | Yes             |

Notes:

## General information about the trial

Main objective of the trial:

To determine the safety and tolerability of single or combination therapy during 12 weeks of treatment

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 04 June 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 | Argentina: 2      |
| Country: Number of subjects enrolled | Germany: 3        |
| Country: Number of subjects enrolled | United States: 36 |
| Worldwide total number of subjects   | 41                |
| EEA total number of subjects         | 3                 |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 38 |
| From 65 to 84 years                       | 3  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Participants were recruited from 10 sites in 3 countries.

### Pre-assignment

Screening details:

Participants underwent a Screening period of up to 33 days followed by a Baseline assessment period of up to 27 days.

### Period 1

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

### Arms

|                              |        |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes    |
| <b>Arm title</b>             | LYS006 |

Arm description:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | LYS006       |
| Investigational medicinal product code | LYS006       |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | LYS006 + LNJ452 |
|------------------|-----------------|

Arm description:

LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LNJ452 200ug administered orally once daily for 12 weeks

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | LNJ452       |
| Investigational medicinal product code | LNJ452       |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

LNJ452 200ug administered orally once daily for 12 weeks

|  |          |
|--|----------|
| Investigational medicinal product name | LYS006   |
| Investigational medicinal product code | LYS006   |
| Other name                             |          |
| Pharmaceutical forms                   | Capsule  |
| Routes of administration               | Oral use |

Dosage and administration details:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

| <b>Number of subjects in period 1</b> | LYS006 | LYS006 + LJN452 |
|---------------------------------------|--------|-----------------|
| Started                               | 20     | 21              |
| PD analysis set                       | 20     | 17              |
| Completed                             | 16     | 15              |
| Not completed                         | 4      | 6               |
| Consent withdrawn by subject          | -      | 1               |
| Adverse event, non-fatal              | -      | 3               |
| Study Terminated by Sponsor           | 4      | 2               |

## Baseline characteristics

### Reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | LYS006          |
| Reporting group description:<br>LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks  |                 |
| Reporting group title  | LYS006 + LJN452 |
| Reporting group description:<br>LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks |                 |

| Reporting group values                                | LYS006 | LYS006 + LJN452 | Total |
|---|--------|-----------------|-------|
| Number of subjects                                    | 20     | 21              | 41    |
| Age categorical<br>Units: Subjects                    |        |                 |       |
| In utero  | 0      | 0               | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0      | 0               | 0     |
| Newborns (0-27 days)                                  | 0      | 0               | 0     |
| Infants and toddlers (28 days-23<br>months)           | 0      | 0               | 0     |
| Children (2-11 years)                                 | 0      | 0               | 0     |
| Adolescents (12-17 years)                             | 0      | 0               | 0     |
| Adults (18-64 years)                                  | 19     | 19              | 38    |
| From 65-84 years                                      | 1      | 2               | 3     |
| 85 years and over                                     | 0      | 0               | 0     |
| Age Continuous<br>Units: Year                         |        |                 |       |
| arithmetic mean                                       | 52.0   | 54.9            |       |
| standard deviation                                    | ± 9.23 | ± 8.36          | -     |
| Sex: Female, Male<br>Units: Participants              |        |                 |       |
| Female  | 11     | 11              | 22    |
| Male  | 9      | 10              | 19    |
| Race (NIH/OMB)<br>Units: Subjects                     |        |                 |       |
| American Indian or Alaska Native                      | 0      | 0               | 0     |
| Asian   | 0      | 1               | 1     |
| Native Hawaiian or Other Pacific<br>Islander          | 0      | 1               | 1     |
| Black or African American                             | 1      | 1               | 2     |
| White   | 19     | 17              | 36    |
| More than one race                                    | 0      | 1               | 1     |
| Unknown or Not Reported                               | 0      | 0               | 0     |

## End points

### End points reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | LYS006          |
| Reporting group description:<br>LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks  |                 |
| Reporting group title  | LYS006 + LJN452 |
| Reporting group description:<br>LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks |                 |

### Primary: Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs)

|   |   |
|---|---|
| End point title   | Number of Participants with Adverse Events (AEs) and Serious Adverse Events (SAEs) <sup>[1]</sup> |
| End point description:<br>Number of participants with AEs and SAEs including significant changes from baseline in vital signs, electrocardiograms and laboratory parameters qualifying and reported as AEs. The number of participants in each category is reported in the table. |   |
| End point type  | Primary   |
| End point timeframe:<br>From the start of treatment to 28 days after end of treatment, assessed up to maximum duration of 113 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 statistical analysis were planned for this endpoint.                           |   |

| End point values                                  | LYS006          | LYS006 + LJN452 |  |  |
|---|-----------------|-----------------|--|--|
| Subject group type                                | Reporting group | Reporting group |  |  |
| Number of subjects analysed                       | 20              | 21              |  |  |
| Units: Participants                               |                 |                 |  |  |
| AEs   | 14              | 17              |  |  |
| Treatment-related AEs                             | 2               | 15              |  |  |
| SAEs  | 0               | 0               |  |  |
| AEs leading to discontinuation of study treatment | 0               | 3               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score

|   |  |
|---|--|
| End point title   | Change From Baseline in Non-invasive Markers of Hepatic Fibrosis: Enhanced Liver Fibrosis Test (ELF) Score |
| End point description:<br>The markers of fibrosis assessed in this test comprised hyaluronic acid (HA), tissue inhibitor of |  |

metalloproteinase (TIMP1) and procollagen III N-terminal peptide (PIIINP); these are components of the extracellular matrix and basement sinusoidal membrane of the liver and are elevated during fibrogenesis as a result of activation of the hepatic stellate cell. The ELF test is a composite score: < 7.7: no to mild fibrosis;  $\geq 7.7$  - < 9.8: Moderate fibrosis;  $\geq 9.8$  - < 11.3: Severe fibrosis;  $\geq 11.3$ : Cirrhosis.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates decreased fibrosis.

|  |           |
|--|-----------|
| End point type                             | Secondary |
| End point timeframe:                       |           |
| Baseline and Days 57, 85 and EOS (Day 113) |           |

| End point values                     | LYS006               | LYS006 + LYN452     |  |  |
|--------------------------------------|----------------------|---------------------|--|--|
| Subject group type                   | Reporting group      | Reporting group     |  |  |
| Number of subjects analysed          | 20                   | 17                  |  |  |
| Units: Scores on a scale             |                      |                     |  |  |
| arithmetic mean (standard deviation) |                      |                     |  |  |
| Day 57                               | -0.25 ( $\pm$ 0.564) | 0.29 ( $\pm$ 0.286) |  |  |
| Day 85                               | -0.12 ( $\pm$ 0.780) | 0.18 ( $\pm$ 0.687) |  |  |
| EOS                                  | 0.01 ( $\pm$ 0.713)  | 0.09 ( $\pm$ 0.461) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Cholesterol: fasting lipid profile endpoint

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Cholesterol: fasting lipid profile endpoint |
|-----------------|---|

End point description:

Fasting lipid profile (total cholesterol) was examined as a cardiometabolic risk parameter. Total cholesterol was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates cardiovascular risk.

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:                                   |           |
| Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113) |           |



| End point values                     | LYS006            | LYS006 + LJN452  |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 20                | 17               |  |  |
| Units: mmol / L                      |                   |                  |  |  |
| arithmetic mean (standard deviation) |                   |                  |  |  |
| Day 15                               | -0.025 (± 0.5814) | 0.086 (± 0.8825) |  |  |
| Day 29                               | -0.058 (± 0.6058) | 0.431 (± 1.0688) |  |  |
| Day 43                               | -0.109 (± 0.6758) | 0.474 (± 1.0364) |  |  |
| Day 57                               | -0.246 (± 0.6341) | 0.463 (± 1.3026) |  |  |
| Day 85                               | 0.001 (± 0.8558)  | 0.754 (± 0.9915) |  |  |
| EOS                                  | -0.283 (± 1.1182) | 0.249 (± 0.5175) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in percent liver fat at day 85

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in percent liver fat at day 85 |
|-----------------|---|

End point description:

Percent (%) Liver fat was measured by Magnetic Resonance Imaging Proton Density Liver Fat Fraction (MRIPDFF). Participants underwent magnetic resonance imaging twice during the course of the study (baseline and end of treatment) to quantitate liver fat.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in a component of NAFLD.

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

End point timeframe:

Baseline and Day 85

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 14              | 11              |  |  |
| Units: Percentage of Liver Fat       |                 |                 |  |  |
| arithmetic mean (standard deviation) | -3.74 (± 3.470) | -7.52 (± 5.846) |  |  |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline in Total Body Weight

|                 |   |
|-----------------|---|
| End point title | Change From Baseline in Total Body Weight |
|-----------------|---|

End point description:

Body weight (to the nearest 0.1 kilogram [kg]) was measured on a calibrated scale. The measurement was performed with the study participant in underwear and without shoes; or while wearing minimal indoor clothing.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in obesity.

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

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

| End point values                     | LYS006          | LYS006 + LYN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 20              | 17              |  |  |
| Units: kg                            |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Day 15                               | -0.21 (± 1.412) | -1.09 (± 2.030) |  |  |
| Day 29                               | -0.27 (± 1.513) | -1.17 (± 2.455) |  |  |
| Day 43                               | -0.24 (± 1.664) | -1.94 (± 2.780) |  |  |
| Day 57                               | -0.48 (± 1.548) | -2.97 (± 3.144) |  |  |
| Day 85                               | -0.54 (± 2.334) | -3.33 (± 2.892) |  |  |
| EOS                                  | 0.17 (± 2.753)  | -2.56 (± 2.789) |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from Baseline in Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) at Day 85

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) at Day 85 |
|-----------------|--|

End point description:

HOMA-IR is a test that uses a simultaneous fasting blood glucose test and fasting insulin test to accurately estimate the degree of insulin resistance (IR) and  $\beta$ -cell function (the cells of the pancreas that produce insulin). HOMA-IR scores are classified as follows: Insulin sensitive is considered less than 1.0, Healthy is considered 0.5-1.4, Above 1.8 is early insulin resistance and Above 2.7 is considered significant insulin resistance

$$\text{HOMA-IR} = [\text{Fasting glucose (mmol/L)} \times (\text{fasting insulin (pmol/L)} / 6)] / 22.5$$

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in insulin sensitivity.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Baseline and Day 85  |           |

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 14              | 9               |  |  |
| Units: HOMA-IR score                 |                 |                 |  |  |
| arithmetic mean (standard deviation) | -3.74 (± 9.865) | 1.67 (± 7.741)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in Fasting Glucose

|                 |   |
|-----------------|---|
| End point title | Change from baseline in Fasting Glucose |
|-----------------|---|

End point description:

Fasting Glucose was examined as a cardiometabolic risk parameter. Total fasting glucose was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in glycemic control.

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

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 20              | 17              |  |  |
| Units: mmol / L                      |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Day 15                               | 0.26 (± 2.609)  | 0.26 (± 2.402)  |  |  |
| Day 29                               | -0.04 (± 3.541) | 0.61 (± 2.362)  |  |  |
| Day 43                               | -0.53 (± 3.655) | 1.05 (± 2.449)  |  |  |
| Day 57                               | -0.82 (± 3.176) | 0.84 (± 1.960)  |  |  |
| Day 85                               | -1.74 (± 3.810) | 0.41 (± 2.023)  |  |  |
| EOS                                  | -1.01 (± 3.627) | -0.40 (± 1.563) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Fasting Insulin at Day 85

|                 |   |
|-----------------|---|
| End point title | Change from Baseline in Fasting Insulin at Day 85 |
|-----------------|---|

End point description:

Fasting insulin was examined as a cardiometabolic risk parameter. Total fasting insulin was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in insulin sensitivity.

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

End point timeframe:

Baseline and Day 85

| End point values                     | LYS006            | LYS006 + LJN452  |  |  |
|--------------------------------------|-------------------|------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group  |  |  |
| Number of subjects analysed          | 14                | 9                |  |  |
| Units: pmol / L                      |                   |                  |  |  |
| arithmetic mean (standard deviation) | -28.36 (± 139.23) | 14.23 (± 63.875) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in Hemoglobin A1c (HbA1c)

|                 |  |
|-----------------|--|
| End point title | Change from baseline in Hemoglobin A1c (HbA1c) |
|-----------------|--|

End point description:

HbA1c was examined as a cardiometabolic risk parameter. HbA1c was measured on blood samples under fasted conditions and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates improvement in glycemic control.

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

End point timeframe:

Baseline and Days 15, 29, 43, 57, 85 and EOS (Day 113)

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 20              | 17              |  |  |
| Units: Percentage                    |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Day 15                               | 0.10 (± 0.194)  | 0.08 (± 0.338)  |  |  |
| Day 29                               | 0.03 (± 0.431)  | 0.21 (± 0.487)  |  |  |
| Day 43                               | -0.02 (± 0.544) | 0.31 (± 0.884)  |  |  |
| Day 57                               | -0.11 (± 0.730) | 0.36 (± 0.680)  |  |  |
| Day 85                               | -0.48 (± 0.834) | -0.03 (± 0.863) |  |  |
| EOS                                  | -0.59 (± 0.961) | 0.34 (± 0.359)  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change from Baseline in Alanine aminotransferase (ALT)

|                 |  |
|-----------------|--|
| End point title | Change from Baseline in Alanine aminotransferase (ALT) |
|-----------------|--|

End point description:

Alanine aminotransferase (ALT) is an enzyme found primarily in the liver. ALT is increased with liver damage. In this study, the blood levels of ALT was used to detect liver inflammation.

Baseline is defined as the mean of the last 2 non-missing measurements taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in liver inflammation.

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

End point timeframe:

Baseline and days 15, 29, 43, 57, 85 and EOS (Day 113)

| End point values                     | LYS006            | LYS006 + LJN452   |  |  |
|--------------------------------------|-------------------|-------------------|--|--|
| Subject group type                   | Reporting group   | Reporting group   |  |  |
| Number of subjects analysed          | 20                | 17                |  |  |
| Units: U / L                         |                   |                   |  |  |
| arithmetic mean (standard deviation) |                   |                   |  |  |
| Day 15                               | 0.97 (± 18.255)   | -19.75 (± 25.617) |  |  |
| Day 29                               | -6.92 (± 22.166)  | -9.63 (± 13.774)  |  |  |
| Day 43                               | -11.13 (± 21.624) | -8.68 (± 14.573)  |  |  |

|        |                   |                   |  |  |
|--------|-------------------|-------------------|--|--|
| Day 57 | -12.09 (± 25.401) | -17.04 (± 12.841) |  |  |
| Day 85 | -7.21 (± 34.702)  | -11.14 (± 26.318) |  |  |
| EOS    | -14.50 (± 29.619) | -8.05 (± 14.570)  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in High-sensitivity C-reactive Protein (hsCRP)

|                 |   |
|-----------------|---|
| End point title | Change from baseline in High-sensitivity C-reactive Protein (hsCRP) |
|-----------------|---|

End point description:

High-sensitivity C-reactive protein is a blood test marker for inflammation in the body. HsCRP was measured from a blood sample and analyzed at a central laboratory.

Baseline is defined as the last non-missing measurement taken at the Screening and Baseline visits (prior to the first dose of study drug administered at the Day 1). A negative change from Baseline indicates a reduction in liver inflammation.

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

End point timeframe:

Baseline and Days 57, 85 and EOS (Day 113)

| End point values                     | LYS006          | LYS006 + LJN452  |  |  |
|--------------------------------------|-----------------|------------------|--|--|
| Subject group type                   | Reporting group | Reporting group  |  |  |
| Number of subjects analysed          | 20              | 17               |  |  |
| Units: mg / L                        |                 |                  |  |  |
| arithmetic mean (standard deviation) |                 |                  |  |  |
| Day 57                               | -0.32 (± 2.192) | -7.78 (± 27.500) |  |  |
| Day 85                               | -0.62 (± 2.180) | 0.24 (± 1.692)   |  |  |
| EOS                                  | 0.19 (± 3.432)  | 0.05 (± 1.015)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: LYS006 plasma concentration

|                 |                             |
|-----------------|-----------------------------|
| End point title | LYS006 plasma concentration |
|-----------------|-----------------------------|

End point description:

LYS006 plasma concentrations were determined by a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) method. No methods for imputation of missing data were used.

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

End point timeframe:

pre-dose at Days 1, 29, 57 and 85 and post-dose (1, 2, 3 and 4 hours) at Days 29 and 57

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 20              | 21              |  |  |
| Units: ng / mL                       |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Day 1 (0 h)                          | 0.162 (± 0.648) | 0.00 (± 0.00)   |  |  |
| Day 29 (0 h)                         | 78.9 (± 74.0)   | 53.5 (± 74.9)   |  |  |
| Day 29 (1 h)                         | 174 (± 89.6)    | 169 (± 105)     |  |  |
| Day 29 (2 h)                         | 224 (± 113)     | 189 (± 105)     |  |  |
| Day 29 (3 h)                         | 188 (± 89.8)    | 145 (± 54.9)    |  |  |
| Day 29 (4 h)                         | 149 (± 73.6)    | 110 (± 31.8)    |  |  |
| Day 57 (0 h)                         | 58.0 (± 57.2)   | 24.0 (± 21.4)   |  |  |
| Day 57 (1 h)                         | 200 (± 118)     | 123 (± 123)     |  |  |
| Day 57 (2 h)                         | 222 (± 80.3)    | 198 (± 88.7)    |  |  |
| Day 57 (3 h)                         | 188 (± 74.3)    | 156 (± 59.2)    |  |  |
| Day 57 (4 h)                         | 140 (± 83.3)    | 126 (± 54.1)    |  |  |
| Day 85 (0 h)                         | 15.2 (± 17.6)   | 10.2 (± 18.7)   |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Maximum observed plasma concentration (C<sub>max</sub>) of LYS006

|                 |   |
|-----------------|---|
| End point title | Maximum observed plasma concentration (C <sub>max</sub> ) of LYS006 |
|-----------------|---|

End point description:

LYS006 plasma concentrations were determined by a validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) method. C<sub>max</sub> of LYS006 was determined with Phoenix WinNonlin (Version 8.0 or higher). No methods for imputation of missing data were used.

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

End point timeframe:

pre-dose and post-dose (1, 2, 3 and 4 hours) at Days 29 and 57

| End point values                     | LYS006          | LYS006 + LJN452 |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 20              | 21              |  |  |
| Units: ng / mL                       |                 |                 |  |  |
| arithmetic mean (standard deviation) |                 |                 |  |  |
| Day 29                               | 264 (± 87.7)    | 215 (± 98.8)    |  |  |
| Day 57                               | 271 (± 71.1)    | 228 (± 88.1)    |  |  |

## **Statistical analyses**

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No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events

Adverse event reporting additional description:

Any sign or symptom that occurs during the study treatment plus the 28 days post treatment

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |        |
|-----------------------|--------|
| Reporting group title | LYS006 |
|-----------------------|--------|

Reporting group description:

LYS006 20 mg was administered orally twice per day (b.i.d) for 12 weeks

|                       |       |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

Total

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | LYS006 + LJN452 |
|-----------------------|-----------------|

Reporting group description:

LYS006 20 mg was administered orally twice per day (b.i.d) in addition to LJN452 200ug administered orally once daily for 12 weeks

| Serious adverse events                            | LYS006         | Total          | LYS006 + LJN452 |
|---|----------------|----------------|-----------------|
| Total subjects affected by serious adverse events |                |                |                 |
| subjects affected / exposed                       | 0 / 20 (0.00%) | 0 / 41 (0.00%) | 0 / 21 (0.00%)  |
| number of deaths (all causes)                     | 0              | 0              | 0               |
| number of deaths resulting from adverse events    | 0              | 0              | 0               |

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

| Non-serious adverse events                            | LYS006          | Total            | LYS006 + LJN452  |
|---|-----------------|------------------|------------------|
| Total subjects affected by non-serious adverse events |                 |                  |                  |
| subjects affected / exposed                           | 9 / 20 (45.00%) | 24 / 41 (58.54%) | 15 / 21 (71.43%) |
| Investigations  |                 |                  |                  |
| Aspartate aminotransferase increased                  |                 |                  |                  |
| subjects affected / exposed                           | 0 / 20 (0.00%)  | 2 / 41 (4.88%)   | 2 / 21 (9.52%)   |
| occurrences (all)                                     | 0               | 3                | 3                |
| Alanine aminotransferase increased                    |                 |                  |                  |

|  |                      |                        |                        |
|--|----------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 20 (0.00%)<br>0  | 2 / 41 (4.88%)<br>2    | 2 / 21 (9.52%)<br>2    |
| Blood alkaline phosphatase increased<br>subjects affected / exposed<br>occurrences (all) | 0 / 20 (0.00%)<br>0  | 3 / 41 (7.32%)<br>3    | 3 / 21 (14.29%)<br>3   |
| Nervous system disorders   |                      |                        |                        |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)                            | 2 / 20 (10.00%)<br>2 | 2 / 41 (4.88%)<br>2    | 0 / 21 (0.00%)<br>0    |
| Headache<br>subjects affected / exposed<br>occurrences (all)                             | 4 / 20 (20.00%)<br>4 | 8 / 41 (19.51%)<br>8   | 4 / 21 (19.05%)<br>4   |
| Gastrointestinal disorders   |                      |                        |                        |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 20 (5.00%)<br>1  | 3 / 41 (7.32%)<br>3    | 2 / 21 (9.52%)<br>2    |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                            | 3 / 20 (15.00%)<br>3 | 3 / 41 (7.32%)<br>3    | 0 / 21 (0.00%)<br>0    |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                               | 3 / 20 (15.00%)<br>3 | 5 / 41 (12.20%)<br>5   | 2 / 21 (9.52%)<br>2    |
| Skin and subcutaneous tissue disorders   |                      |                        |                        |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 20 (0.00%)<br>0  | 13 / 41 (31.71%)<br>14 | 13 / 21 (61.90%)<br>14 |
| Rash<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 20 (0.00%)<br>0  | 2 / 41 (4.88%)<br>2    | 2 / 21 (9.52%)<br>2    |
| Psychiatric disorders  |                      |                        |                        |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)                             | 0 / 20 (0.00%)<br>0  | 2 / 41 (4.88%)<br>2    | 2 / 21 (9.52%)<br>2    |
| Metabolism and nutrition disorders   |                      |                        |                        |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)                       | 1 / 20 (5.00%)<br>1  | 4 / 41 (9.76%)<br>4    | 3 / 21 (14.29%)<br>3   |



## 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? Yes

| Date             | Interruption   | Restart date |
|------------------|--|--------------|
| 10 December 2021 | The study was terminated based upon an ongoing review of the study data, which showed a low likelihood of achieving required efficacy in either treatment arm. | -            |

Notes:

### Limitations and caveats

None reported