



## Clinical trial results:

**A multi-center, open-label, single-arm Phase I dose-escalation and Phase II dose-expansion study to evaluate the safety, tolerability, PK characteristics and anti-tumor activity of FCN-159 in adult and pediatric participants with neurofibromatosis type 1**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2021-001572-42    |
| Trial protocol           | ES IT PL          |
| Global end of trial date | 23 September 2024 |

### Results information

|                                |                  |
|--------------------------------|------------------|
| Result version number          | v1 (current)     |
| This version publication date  | 20 February 2026 |
| First version publication date | 20 February 2026 |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | FCN-159-002 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04954001 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Shanghai Fosun Pharmaceutical Development Co., Ltd.   |
| Sponsor organisation address | No. 1289, Yishan Road, Xuhui District, Shanghai, China, 200233  |
| Public contact               | Project Management, Shanghai Fosun Pharmaceutical Development Co., Ltd., +86 21- 33987558, chenleilei@fosunpharma.com |
| Scientific contact           | Project Management, Shanghai Fosun Pharmaceutical Development Co., Ltd., +86 21- 33987558, chenleilei@fosunpharma.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                       | 11 June 2025      |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 23 September 2024 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

Phase I:

-To evaluate the safety and tolerability of FCN-159 administered PO daily.

-To determine the maximum tolerated dose (MTD) and recommended Phase II dose (RP2D).

Phase II:

-To assess the efficacy of FCN-159 per REiNS criteria.

Protection of trial subjects:

The clinical study protocol, ICF, eCRF, and other relevant materials for this study were approved by the IEC before the start of the study. IEC strictly followed the requirements of relevant laws and regulations to review these materials and issue approval files after approval. The entire trial process of this study complied with relevant laws and regulations, Good Clinical Practice, and the principles of the Declaration of Helsinki (2013). The ICF must be signed and dated by patients or their legal representatives, and the investigator who performs the informed consent process or the representative before any drug administration.

Background therapy:

The commonly used concomitant medications were supportive care for the target disease, corrective medications for adverse events, and treatment of medical history, including dermatological antibiotics and chemotherapy drugs, anti-inflammatory and anti-rheumatic drugs, and systemic anti-bacterial drugs, analgesics and systemic antihistamines, etc.

Evidence for comparator:

Not applicable

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 16 March 2021    |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy, Safety |
| Long term follow-up duration                              | 35 Months        |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | China: 82        |
| Country: Number of subjects enrolled | United States: 3 |
| Country: Number of subjects enrolled | Spain: 1         |
| Worldwide total number of subjects   | 86               |
| EEA total number of subjects         | 1                |

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)                      | 86 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Phase I: a total of 19 Chinese patients (3 in the 4 mg dose group, 4 in the 6 mg dose group, 8 in the 8 mg dose group, and 4 in the 12 mg dose group) and 1 U.S. patient (8 mg dose group); Phase II: 63 Chinese patients and 3 non-Chinese patients (2 U.S. patients and 1 Spanish patient).

### Pre-assignment

Screening details:

Adult patients diagnosed with symptomatic Neurofibromatosis type 1 with Plexiform neurofibroma (NF1 with PN) with PNs that was inoperable or had postoperative residual/recurrence.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Treatment period - Phase I and Phase II (overall period) |
| Is this the baseline period? | Yes  |
| Allocation method            | Not applicable   |
| Blinding used                | Not blinded  |

Blinding implementation details:

This is an open-label study

### Arms

|                              |                        |
|------------------------------|------------------------|
| Are arms mutually exclusive? | Yes                    |
| <b>Arm title</b>             | Phase I - 4 mg FCN-159 |

Arm description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 4 mg FCN-159.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | FCN-159      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

4 mg FCN-159 tablets were orally administered once daily, for continuous use, with 28 days as a cycle.

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Phase I - 6 mg FCN-159 |
|------------------|------------------------|

Arm description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 6 mg FCN-159.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | FCN-159      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

6 mg FCN-159 tablets were orally administered once daily, for continuous use, with 28 days as a cycle.

|                  |                        |
|------------------|------------------------|
| <b>Arm title</b> | Phase I - 8 mg FCN-159 |
|------------------|------------------------|

Arm description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 8 mg FCN-159.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |          |
|--|----------|
| Investigational medicinal product name | FCN-159  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

8 mg FCN-159 tablets were orally administered once daily, for continuous use, with 28 days as a cycle.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Phase I - 12 mg FCN-159 |
|------------------|-------------------------|

Arm description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 12 mg FCN-159.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | FCN-159      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

12 mg FCN-159 tablets were orally administered once daily, for continuous use, with 28 days as a cycle.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Phase II - 8 mg FCN-159 |
|------------------|-------------------------|

Arm description:

Participants enrolled in Phase II dose-expansion clinical trial assigned to receive Recommended Phase II dose (RP2D) of 8 mg FCN-159.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | FCN-159      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

8 mg FCN-159 tablets were orally administered once daily, for continuous use, with 28 days as a cycle.

| <b>Number of subjects in period 1</b> | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 |
|---------------------------------------|------------------------|------------------------|------------------------|
| Started                               | 3                      | 4                      | 9                      |
| Completed                             | 3                      | 4                      | 9                      |
| Not completed                         | 0                      | 0                      | 0                      |
| Consent withdrawn by subject          | -                      | -                      | -                      |
| Adverse event, non-fatal              | -                      | -                      | -                      |
| Other                                 | -                      | -                      | -                      |
| Death                                 | -                      | -                      | -                      |

| <b>Number of subjects in period 1</b> | Phase I - 12 mg FCN-159 | Phase II - 8 mg FCN-159 |
|---------------------------------------|-------------------------|-------------------------|
| Started                               | 4                       | 66                      |
| Completed                             | 3                       | 54                      |
| Not completed                         | 1                       | 12                      |
| Consent withdrawn by subject          | -                       | 8                       |

|                          |   |   |
|--------------------------|---|---|
| Adverse event, non-fatal | 1 | 1 |
| Other                    | - | 2 |
| Death                    | - | 1 |

## Baseline characteristics

### Reporting groups

|   |                         |
|---|-------------------------|
| Reporting group title   | Phase I - 4 mg FCN-159  |
| Reporting group description:  |                         |
| Participants enrolled in Phase I dose-finding clinical trial assigned to receive 4 mg FCN-159.  |                         |
| Reporting group title   | Phase I - 6 mg FCN-159  |
| Reporting group description:  |                         |
| Participants enrolled in Phase I dose-finding clinical trial assigned to receive 6 mg FCN-159.  |                         |
| Reporting group title   | Phase I - 8 mg FCN-159  |
| Reporting group description:  |                         |
| Participants enrolled in Phase I dose-finding clinical trial assigned to receive 8 mg FCN-159.  |                         |
| Reporting group title   | Phase I - 12 mg FCN-159 |
| Reporting group description:  |                         |
| Participants enrolled in Phase I dose-finding clinical trial assigned to receive 12 mg FCN-159.                                       |                         |
| Reporting group title   | Phase II - 8 mg FCN-159 |
| Reporting group description:  |                         |
| Participants enrolled in Phase II dose-expansion clinical trial assigned to receive Recommended Phase II dose (RP2D) of 8 mg FCN-159. |                         |

| Reporting group values | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 |
|------------------------|------------------------|------------------------|------------------------|
| Number of subjects     | 3                      | 4                      | 9                      |
| Age categorical        |                        |                        |                        |
| Units: Subjects        |                        |                        |                        |
| Adults (18-64 years)   | 3                      | 4                      | 9                      |
| Gender categorical     |                        |                        |                        |
| Units: Subjects        |                        |                        |                        |
| Female                 | 0                      | 0                      | 6                      |
| Male                   | 3                      | 4                      | 3                      |

| Reporting group values | Phase I - 12 mg FCN-159 | Phase II - 8 mg FCN-159 | Total |
|------------------------|-------------------------|-------------------------|-------|
| Number of subjects     | 4                       | 66                      | 86    |
| Age categorical        |                         |                         |       |
| Units: Subjects        |                         |                         |       |
| Adults (18-64 years)   | 4                       | 66                      | 86    |
| Gender categorical     |                         |                         |       |
| Units: Subjects        |                         |                         |       |
| Female                 | 3                       | 28                      | 37    |
| Male                   | 1                       | 38                      | 49    |

## End points

### End points reporting groups

|   |                                   |
|---|-----------------------------------|
| Reporting group title   | Phase I - 4 mg FCN-159            |
| Reporting group description:<br>Participants enrolled in Phase I dose-finding clinical trial assigned to receive 4 mg FCN-159.  |                                   |
| Reporting group title   | Phase I - 6 mg FCN-159            |
| Reporting group description:<br>Participants enrolled in Phase I dose-finding clinical trial assigned to receive 6 mg FCN-159.  |                                   |
| Reporting group title   | Phase I - 8 mg FCN-159            |
| Reporting group description:<br>Participants enrolled in Phase I dose-finding clinical trial assigned to receive 8 mg FCN-159.  |                                   |
| Reporting group title   | Phase I - 12 mg FCN-159           |
| Reporting group description:<br>Participants enrolled in Phase I dose-finding clinical trial assigned to receive 12 mg FCN-159.   |                                   |
| Reporting group title   | Phase II - 8 mg FCN-159           |
| Reporting group description:<br>Participants enrolled in Phase II dose-expansion clinical trial assigned to receive Recommended Phase II dose (RP2D) of 8 mg FCN-159.                 |                                   |
| Subject analysis set title  | Phase II - 8 mg FCN-159 - ITT set |
| Subject analysis set type   | Intention-to-treat                |
| Subject analysis set description:<br>Intent-to-treat (ITT) set: It included patients who signed the informed consent form (ICF) and had received at least one dose of FCN-159 Tablets |                                   |

### Primary: Phase I - The occurrence of dose-limiting toxicity (DLT)

|   |  |
|---|--|
| End point title   | Phase I - The occurrence of dose-limiting toxicity (DLT) <sup>[1][2]</sup> |
| End point description:<br>DLT analysis set: All patients who met the DLT evaluation criteria enrolled in the dose escalation part, regardless of whether DLT occurred during the DLT observation period.<br>DLT = Dose-Limited Toxicity<br>* The results present information only for Chinese participants.   |  |
| End point type  | Primary  |
| End point timeframe:<br>28 days after the dose of FCN-159   |  |
| 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 was done for this end point<br>[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.<br>Justification: This end point is applicable only for arms in Phase I. |  |

| End point values             | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 | Phase I - 12 mg FCN-159 |
|------------------------------|------------------------|------------------------|------------------------|-------------------------|
| Subject group type           | Reporting group        | Reporting group        | Reporting group        | Reporting group         |
| Number of subjects analysed  | 3                      | 3                      | 6                      | 3                       |
| Units: number                |                        |                        |                        |                         |
| Subjects with any TEAE       | 0                      | 0                      | 1                      | 3                       |
| DLT of Grade 3: folliculitis | 0                      | 0                      | 1                      | 3                       |



## Statistical analyses

No statistical analyses for this end point

### Primary: Phase I - Maximum tolerated dose and recommended Phase II dose (RP2D) in clinical practice

|                 |  |
|-----------------|--|
| End point title | Phase I - Maximum tolerated dose and recommended Phase II dose (RP2D) in clinical practice <sup>[3][4]</sup> |
|-----------------|--|

End point description:

MTD is defined as the maximum dose level with a DLT incidence rate of < 33% (0/3 or 1/6 cases). After integrating the Phase I PK, PD, efficacy, and safety data, it was decided to set the adult RP2D at 8 mg after full discussion at the Safety Management Committee (SMC) meeting.

\* The results present information only for Chinese participants.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Approximately 6-9 months for MTD and RP2D (phase I duration)

Notes:

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

Justification: No statistical analysis was done for this end point

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: This end point is applicable only for arms in Phase I.

| End point values            | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 | Phase I - 12 mg FCN-159 |
|-----------------------------|------------------------|------------------------|------------------------|-------------------------|
| Subject group type          | Reporting group        | Reporting group        | Reporting group        | Reporting group         |
| Number of subjects analysed | 3                      | 3                      | 6                      | 3                       |
| Units: percent              |                        |                        |                        |                         |
| number (not applicable)     |                        |                        |                        |                         |
| Subjects with any TEAE      | 0                      | 0                      | 16.7                   | 100                     |

## Statistical analyses

No statistical analyses for this end point

### Primary: Phase II - ORR assessed by the investigator: Best overall response

|                 |   |
|-----------------|---|
| End point title | Phase II - ORR assessed by the investigator: Best overall response <sup>[5]</sup> |
|-----------------|---|

End point description:

Objective response rate (ORR) is defined as Proportion of patients achieving confirmed disease response (Complete response (CR) or Partial response (PR)). CR is defined as the disappearance of the target lesion. PR is defined as a  $\geq 20\%$  reduction in the volume of the target PN from baseline. Both CR and PR were confirmed by reassessment over at least 3 months.

\* The results present information only for Chinese participants.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Through study completion, an average of 2 years

Notes:

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

Justification: No statistical analysis was done for this end point

|                                     |                                   |  |  |  |
|-------------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>             | Phase II - 8 mg FCN-159 - ITT set |  |  |  |
| Subject group type                  | Subject analysis set              |  |  |  |
| Number of subjects analysed         | 63                                |  |  |  |
| Units: percent                      |                                   |  |  |  |
| number (not applicable)             |                                   |  |  |  |
| Complete response (CR)              | 0                                 |  |  |  |
| Partial response (PR)               | 42.9                              |  |  |  |
| Stable disease (SD)                 | 52.4                              |  |  |  |
| Stable disease (SD) $\geq$ 6 months | 41.3                              |  |  |  |
| Progressive disease (PD)            | 0                                 |  |  |  |
| Not evaluable (NE)                  | 4.8                               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: Phase II - ORR assessed by the investigator

|                 |  |
|-----------------|--|
| End point title | Phase II - ORR assessed by the investigator <sup>[6]</sup> |
|-----------------|--|

End point description:

Objective response rate (ORR), defined as the proportion of patients with disease response (Responsive Disease, RD) confirmed using volumetric MRI analysis.

Clinical benefit rate (CBR), defined as assessments including CR, PR, and SD lasting over 6 months.

Disease control rate (DCR), defined as the percentage of cases with best response (PR or CR) and stable disease (SD) after treatment to the number of evaluable cases.

Data includes subject of Intent-to-treat (ITT) set: It included patients who signed the informed consent form (ICF) and had received at least one dose of FCN-159 Tablets.

\* The results present information only for Chinese participants.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Through study completion, an average of 2 years

Notes:

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

Justification: No statistical analysis was done for this end point

|                                  |                                   |  |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| <b>End point values</b>          | Phase II - 8 mg FCN-159 - ITT set |  |  |  |
| Subject group type               | Subject analysis set              |  |  |  |
| Number of subjects analysed      | 63                                |  |  |  |
| Units: percent                   |                                   |  |  |  |
| number (confidence interval 95%) |                                   |  |  |  |
| Objective Response Rate (ORR)    | 42.9 (30.5 to 56.0)               |  |  |  |

|                             |                     |  |  |  |
|-----------------------------|---------------------|--|--|--|
| Clinical benefit rate (CBR) | 84.1 (72.7 to 92.1) |  |  |  |
| Disease control rate (DCR)  | 95.2 (86.7 to 99.0) |  |  |  |

## Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Since the first administered dose till the end of safety follow up period (30 days of the last dose)

Adverse event reporting additional description:

\*The results present information only for Chinese participants.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.0 |
|--------------------|------|

### Reporting groups

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Phase I - 4 mg FCN-159 |
|-----------------------|------------------------|

Reporting group description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 4 mg FCN-159.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Phase I - 6 mg FCN-159 |
|-----------------------|------------------------|

Reporting group description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 6 mg FCN-159.

|                       |                        |
|-----------------------|------------------------|
| Reporting group title | Phase I - 8 mg FCN-159 |
|-----------------------|------------------------|

Reporting group description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 8 mg FCN-159.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Phase I - 12 mg FCN-159 |
|-----------------------|-------------------------|

Reporting group description:

Participants enrolled in Phase I dose-finding clinical trial assigned to receive 12 mg FCN-159.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Phase II - 8 mg FCN-159 |
|-----------------------|-------------------------|

Reporting group description:

Participants enrolled in Phase II dose-expansion clinical trial assigned to receive Recommended Phase II dose (RP2D) of 8 mg FCN-159.

| Serious adverse events                            | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 |
|---|------------------------|------------------------|------------------------|
| Total subjects affected by serious adverse events |                        |                        |                        |
| subjects affected / exposed                       | 1 / 3 (33.33%)         | 0 / 4 (0.00%)          | 0 / 8 (0.00%)          |
| number of deaths (all causes)                     | 0                      | 0                      | 0                      |
| number of deaths resulting from adverse events    | 0                      | 0                      | 0                      |
| Injury, poisoning and procedural complications    |                        |                        |                        |
| Head injury                                       |                        |                        |                        |
| subjects affected / exposed                       | 0 / 3 (0.00%)          | 0 / 4 (0.00%)          | 0 / 8 (0.00%)          |
| occurrences causally related to treatment / all   | 0 / 0                  | 0 / 0                  | 0 / 0                  |
| deaths causally related to treatment / all        | 0 / 0                  | 0 / 0                  | 0 / 0                  |
| Spinal compression fracture                       |                        |                        |                        |

|   |                |               |               |
|---|----------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Scapula fracture                                |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Ankle fracture                                  |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Cardiac disorders                               |                |               |               |
| Atrial fibrillation                             |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Nervous system disorders                        |                |               |               |
| Vertebrobasilar artery dissection               |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Blood and lymphatic system disorders            |                |               |               |
| Hemolytic anemia                                |                |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Eye disorders                                   |                |               |               |
| Rhegmatogenous retinal detachment               |                |               |               |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 0         |
| Gastrointestinal disorders                      |                |               |               |
| Duodenal ulcer                                  |                |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Haemorrhoidal haemorrhage                       |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Hepatobiliary disorders                         |               |               |               |
| Drug-induced liver injury                       |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Respiratory, thoracic and mediastinal disorders |               |               |               |
| Pneumothorax spontaneous                        |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Renal and urinary disorders                     |               |               |               |
| IgA nephropathy                                 |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Infections and infestations                     |               |               |               |
| Soft tissue infection                           |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| COVID-19  |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Upper respiratory tract infection               |               |               |               |

|   |               |               |               |
|---|---------------|---------------|---------------|
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |
| Pulmonary tuberculosis                          |               |               |               |
| subjects affected / exposed                     | 0 / 3 (0.00%) | 0 / 4 (0.00%) | 0 / 8 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0         | 0 / 0         |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0         | 0 / 0         |

| <b>Serious adverse events</b>                     | Phase I - 12 mg<br>FCN-159 | Phase II - 8 mg<br>FCN-159 |  |
|---|----------------------------|----------------------------|--|
| Total subjects affected by serious adverse events |                            |                            |  |
| subjects affected / exposed                       | 1 / 4 (25.00%)             | 13 / 63 (20.63%)           |  |
| number of deaths (all causes)                     | 0                          | 1                          |  |
| number of deaths resulting from adverse events    | 0                          | 0                          |  |
| Injury, poisoning and procedural complications    |                            |                            |  |
| Head injury                                       |                            |                            |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)              | 1 / 63 (1.59%)             |  |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1                      |  |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0                      |  |
| Spinal compression fracture                       |                            |                            |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)              | 1 / 63 (1.59%)             |  |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1                      |  |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0                      |  |
| Scapula fracture                                  |                            |                            |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)              | 1 / 63 (1.59%)             |  |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1                      |  |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0                      |  |
| Ankle fracture                                    |                            |                            |  |
| subjects affected / exposed                       | 0 / 4 (0.00%)              | 1 / 63 (1.59%)             |  |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1                      |  |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0                      |  |
| Cardiac disorders                                 |                            |                            |  |
| Atrial fibrillation                               |                            |                            |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Vertebrobasilar artery dissection               |                |                |  |
| subjects affected / exposed                     | 1 / 4 (25.00%) | 0 / 63 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Blood and lymphatic system disorders            |                |                |  |
| Hemolytic anemia                                |                |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Eye disorders                                   |                |                |  |
| Rhegmatogenous retinal detachment               |                |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 0 / 63 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                      |                |                |  |
| Duodenal ulcer                                  |                |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Haemorrhoidal haemorrhage                       |                |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hepatobiliary disorders                         |                |                |  |
| Drug-induced liver injury                       |                |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)  | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders |                |                |  |
| Pneumothorax spontaneous                        |                |                |  |



|   |               |                |  |
|---|---------------|----------------|--|
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Renal and urinary disorders                     |               |                |  |
| IgA nephropathy                                 |               |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Infections and infestations                     |               |                |  |
| Soft tissue infection                           |               |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 2 / 63 (3.17%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| COVID-19  |               |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Upper respiratory tract infection               |               |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 63 (1.59%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Pulmonary tuberculosis                          |               |                |  |
| subjects affected / exposed                     | 0 / 4 (0.00%) | 1 / 63 (1.59%) |  |
| 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 %

| Non-serious adverse events                            | Phase I - 4 mg FCN-159 | Phase I - 6 mg FCN-159 | Phase I - 8 mg FCN-159 |
|---|------------------------|------------------------|------------------------|
| Total subjects affected by non-serious adverse events |                        |                        |                        |
| subjects affected / exposed                           | 0 / 3 (0.00%)          | 4 / 4 (100.00%)        | 8 / 8 (100.00%)        |
| Investigations  |                        |                        |                        |
| Blood creatine phosphokinase increased                |                        |                        |                        |

|                                       |               |                |                |
|---------------------------------------|---------------|----------------|----------------|
| subjects affected / exposed           | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 5 / 8 (62.50%) |
| occurrences (all)                     | 0             | 3              | 5              |
| Blood lactate dehydrogenase increased |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 1 / 8 (12.50%) |
| occurrences (all)                     | 0             | 2              | 1              |
| Aspartate aminotransferase increased  |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0             | 2              | 0              |
| Urinary occult blood positive         |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 3 / 8 (37.50%) |
| occurrences (all)                     | 0             | 1              | 3              |
| Weight increased                      |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 3 / 8 (37.50%) |
| occurrences (all)                     | 0             | 1              | 3              |
| Blood alkaline phosphatase increased  |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 4 / 8 (50.00%) |
| occurrences (all)                     | 0             | 1              | 4              |
| Alanine aminotransferase increased    |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 1 / 8 (12.50%) |
| occurrences (all)                     | 0             | 2              | 1              |
| Blood fibrinogen increased            |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0             | 0              | 0              |
| Protein urine present                 |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 3 / 8 (37.50%) |
| occurrences (all)                     | 0             | 3              | 3              |
| Electrocardiogram T wave abnormal     |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                     | 0             | 1              | 0              |
| Blood uric acid increased             |               |                |                |
| subjects affected / exposed           | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 2 / 8 (25.00%) |
| occurrences (all)                     | 0             | 3              | 2              |
| pH urine decreased                    |               |                |                |

|                                  |               |                |                |
|----------------------------------|---------------|----------------|----------------|
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 4 / 8 (50.00%) |
| occurrences (all)                | 0             | 3              | 4              |
| Specific gravity urine increased |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 4 / 8 (50.00%) |
| occurrences (all)                | 0             | 3              | 4              |
| Bile acids increased             |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 0 / 8 (0.00%)  |
| occurrences (all)                | 0             | 2              | 0              |
| Blood urea increased             |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 3              | 2              |
| Urobilinogen urine increased     |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 3              | 2              |
| QRS axis abnormal                |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 1 / 8 (12.50%) |
| occurrences (all)                | 0             | 1              | 1              |
| Urine ketone body present        |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 3 / 8 (37.50%) |
| occurrences (all)                | 0             | 1              | 3              |
| pH urine increased               |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 1 / 8 (12.50%) |
| occurrences (all)                | 0             | 2              | 1              |
| Blood bilirubin increased        |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 3              | 2              |
| Immunoglobulins increased        |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 1              | 2              |
| Prealbumin decreased             |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 0              | 2              |
| White blood cells urine positive |               |                |                |
| subjects affected / exposed      | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 2 / 8 (25.00%) |
| occurrences (all)                | 0             | 1              | 2              |
| Cardiac disorders                |               |                |                |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| Tricuspid valve incompetence<br>subjects affected / exposed<br>occurrences (all)                                 | 0 / 3 (0.00%)<br>0 | 3 / 4 (75.00%)<br>3 | 3 / 8 (37.50%)<br>3 |
| Mitral valve incompetence<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 3 (0.00%)<br>0 | 3 / 4 (75.00%)<br>3 | 2 / 8 (25.00%)<br>2 |
| Sinus arrhythmia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 1 / 4 (25.00%)<br>1 | 2 / 8 (25.00%)<br>2 |
| Blood and lymphatic system disorders<br>Anemia<br>subjects affected / exposed<br>occurrences (all)               | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 2 / 8 (25.00%)<br>2 |
| Gastrointestinal disorders<br>Mouth ulceration<br>subjects affected / exposed<br>occurrences (all)               | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 2 / 4 (50.00%)<br>2 | 3 / 8 (37.50%)<br>3 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 4 / 8 (50.00%)<br>4 |
| Stomatitis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 2 / 4 (50.00%)<br>2 | 5 / 8 (62.50%)<br>5 |
| Respiratory, thoracic and mediastinal disorders<br>Epistaxis<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 1 / 8 (12.50%)<br>1 |
| Cough<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Pulmonary mass<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0 | 3 / 4 (75.00%)<br>3 | 0 / 8 (0.00%)<br>0  |

|  |               |                |                |
|--|---------------|----------------|----------------|
| Skin and subcutaneous tissue disorders |               |                |                |
| Folliculitis                           |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 4 / 8 (50.00%) |
| occurrences (all)                      | 0             | 1              | 4              |
| Paronychia                             |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 3 / 8 (37.50%) |
| occurrences (all)                      | 0             | 2              | 3              |
| Dermatitis                             |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Alopecia                               |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 1 / 4 (25.00%) | 4 / 8 (50.00%) |
| occurrences (all)                      | 0             | 1              | 4              |
| Urticaria                              |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 0 / 8 (0.00%)  |
| occurrences (all)                      | 0             | 0              | 0              |
| Dry skin                               |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 1 / 8 (12.50%) |
| occurrences (all)                      | 0             | 0              | 1              |
| Pruritus                               |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 0 / 4 (0.00%)  | 2 / 8 (25.00%) |
| occurrences (all)                      | 0             | 0              | 2              |
| Rash                                   |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 2 / 8 (25.00%) |
| occurrences (all)                      | 0             | 2              | 2              |
| Drug eruption                          |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 2 / 8 (25.00%) |
| occurrences (all)                      | 0             | 2              | 2              |
| Infections and infestations            |               |                |                |
| Upper respiratory tract infection      |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 2 / 4 (50.00%) | 1 / 8 (12.50%) |
| occurrences (all)                      | 0             | 2              | 1              |
| COVID-19                               |               |                |                |
| subjects affected / exposed            | 0 / 3 (0.00%) | 3 / 4 (75.00%) | 2 / 8 (25.00%) |
| occurrences (all)                      | 0             | 3              | 2              |
| Pharyngitis                            |               |                |                |

|  |                    |                     |                     |
|--|--------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Metabolism and nutrition disorders               |                    |                     |                     |
| Hypercholesterolemia                             |                    |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0  | 0 / 8 (0.00%)<br>0  |
| Dyslipidaemia                                    |                    |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 2 / 4 (50.00%)<br>2 | 2 / 8 (25.00%)<br>2 |
| Hypophosphataemia                                |                    |                     |                     |
| subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0 | 2 / 4 (50.00%)<br>2 | 1 / 8 (12.50%)<br>1 |

| <b>Non-serious adverse events</b>                        | Phase I - 12 mg<br>FCN-159 | Phase II - 8 mg<br>FCN-159 |  |
|--|----------------------------|----------------------------|--|
| Total subjects affected by non-serious<br>adverse events |                            |                            |  |
| subjects affected / exposed                              | 4 / 4 (100.00%)            | 63 / 63 (100.00%)          |  |
| Investigations   |                            |                            |  |
| Blood creatine phosphokinase<br>increased                |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 0 / 4 (0.00%)<br>0         | 25 / 63 (39.68%)<br>25     |  |
| Blood lactate dehydrogenase<br>increased                 |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 3 / 4 (75.00%)<br>3        | 25 / 63 (39.68%)<br>25     |  |
| Aspartate aminotransferase<br>increased                  |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 1 / 4 (25.00%)<br>1        | 28 / 63 (44.44%)<br>28     |  |
| Urinary occult blood positive                            |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 1 / 4 (25.00%)<br>1        | 20 / 63 (31.75%)<br>20     |  |
| Weight increased   |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 3 / 4 (75.00%)<br>3        | 17 / 63 (26.98%)<br>17     |  |
| Blood alkaline phosphatase increased                     |                            |                            |  |
| subjects affected / exposed<br>occurrences (all)         | 2 / 4 (50.00%)<br>2        | 18 / 63 (28.57%)<br>18     |  |

|  |                      |                        |
|--|----------------------|------------------------|
| Alanine aminotransferase increased<br>subjects affected / exposed<br>occurrences (all) | 1 / 4 (25.00%)<br>1  | 17 / 63 (26.98%)<br>17 |
| Blood fibrinogen increased<br>subjects affected / exposed<br>occurrences (all)         | 4 / 4 (100.00%)<br>4 | 18 / 63 (28.57%)<br>18 |
| Protein urine present<br>subjects affected / exposed<br>occurrences (all)              | 1 / 4 (25.00%)<br>1  | 13 / 63 (20.63%)<br>13 |
| Electrocardiogram T wave abnormal<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0   | 14 / 63 (22.22%)<br>14 |
| Blood uric acid increased<br>subjects affected / exposed<br>occurrences (all)          | 0 / 4 (0.00%)<br>0   | 10 / 63 (15.87%)<br>10 |
| pH urine decreased<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 4 (0.00%)<br>0   | 5 / 63 (7.94%)<br>5    |
| Specific gravity urine increased<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0   | 5 / 63 (7.94%)<br>5    |
| Bile acids increased<br>subjects affected / exposed<br>occurrences (all)               | 1 / 4 (25.00%)<br>1  | 9 / 63 (14.29%)<br>9   |
| Blood urea increased<br>subjects affected / exposed<br>occurrences (all)               | 0 / 4 (0.00%)<br>0   | 8 / 63 (12.70%)<br>8   |
| Urobilinogen urine increased<br>subjects affected / exposed<br>occurrences (all)       | 0 / 4 (0.00%)<br>0   | 5 / 63 (7.94%)<br>5    |
| QRS axis abnormal<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 4 (75.00%)<br>3  | 5 / 63 (7.94%)<br>5    |
| Urine ketone body present<br>subjects affected / exposed<br>occurrences (all)          | 2 / 4 (50.00%)<br>2  | 3 / 63 (4.76%)<br>3    |

|   |                     |                        |  |
|---|---------------------|------------------------|--|
| pH urine increased<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 4 (0.00%)<br>0  | 5 / 63 (7.94%)<br>5    |  |
| Blood bilirubin increased<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 2 / 63 (3.17%)<br>2    |  |
| Immunoglobulins increased<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 2 / 63 (3.17%)<br>2    |  |
| Prealbumin decreased<br>subjects affected / exposed<br>occurrences (all)                              | 0 / 4 (0.00%)<br>0  | 3 / 63 (4.76%)<br>3    |  |
| White blood cells urine positive<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 4 (0.00%)<br>0  | 1 / 63 (1.59%)<br>1    |  |
| Cardiac disorders<br>Tricuspid valve incompetence<br>subjects affected / exposed<br>occurrences (all) | 0 / 4 (0.00%)<br>0  | 12 / 63 (19.05%)<br>12 |  |
| Mitral valve incompetence<br>subjects affected / exposed<br>occurrences (all)                         | 0 / 4 (0.00%)<br>0  | 11 / 63 (17.46%)<br>11 |  |
| Sinus arrhythmia<br>subjects affected / exposed<br>occurrences (all)                                  | 0 / 4 (0.00%)<br>0  | 8 / 63 (12.70%)<br>8   |  |
| Blood and lymphatic system disorders<br>Anemia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 4 (0.00%)<br>0  | 13 / 63 (20.63%)<br>13 |  |
| Gastrointestinal disorders<br>Mouth ulceration<br>subjects affected / exposed<br>occurrences (all)    | 3 / 4 (75.00%)<br>3 | 37 / 63 (58.73%)<br>37 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 2 / 4 (50.00%)<br>2 | 28 / 63 (44.44%)<br>28 |  |
| Constipation  |                     |                        |  |



|   |                 |                  |  |
|---|-----------------|------------------|--|
| subjects affected / exposed                     | 2 / 4 (50.00%)  | 11 / 63 (17.46%) |  |
| occurrences (all)                               | 2               | 11               |  |
| Stomatitis                                      |                 |                  |  |
| subjects affected / exposed                     | 0 / 4 (0.00%)   | 5 / 63 (7.94%)   |  |
| occurrences (all)                               | 0               | 5                |  |
| Respiratory, thoracic and mediastinal disorders |                 |                  |  |
| Epistaxis                                       |                 |                  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%)  | 15 / 63 (23.81%) |  |
| occurrences (all)                               | 1               | 15               |  |
| Cough   |                 |                  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%)  | 13 / 63 (20.63%) |  |
| occurrences (all)                               | 1               | 13               |  |
| Pulmonary mass                                  |                 |                  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%)  | 6 / 63 (9.52%)   |  |
| occurrences (all)                               | 1               | 6                |  |
| Skin and subcutaneous tissue disorders          |                 |                  |  |
| Folliculitis                                    |                 |                  |  |
| subjects affected / exposed                     | 4 / 4 (100.00%) | 49 / 63 (77.78%) |  |
| occurrences (all)                               | 4               | 49               |  |
| Paronychia                                      |                 |                  |  |
| subjects affected / exposed                     | 3 / 4 (75.00%)  | 35 / 63 (55.56%) |  |
| occurrences (all)                               | 3               | 35               |  |
| Dermatitis                                      |                 |                  |  |
| subjects affected / exposed                     | 3 / 4 (75.00%)  | 25 / 63 (39.68%) |  |
| occurrences (all)                               | 3               | 25               |  |
| Alopecia  |                 |                  |  |
| subjects affected / exposed                     | 3 / 4 (75.00%)  | 20 / 63 (31.75%) |  |
| occurrences (all)                               | 3               | 20               |  |
| Urticaria                                       |                 |                  |  |
| subjects affected / exposed                     | 1 / 4 (25.00%)  | 18 / 63 (28.57%) |  |
| occurrences (all)                               | 1               | 18               |  |
| Dry skin  |                 |                  |  |
| subjects affected / exposed                     | 2 / 4 (50.00%)  | 14 / 63 (22.22%) |  |
| occurrences (all)                               | 2               | 14               |  |
| Pruritus  |                 |                  |  |

|  |                     |                        |  |
|--|---------------------|------------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 2 / 4 (50.00%)<br>2 | 10 / 63 (15.87%)<br>10 |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 4 / 63 (6.35%)<br>4    |  |
| Drug eruption<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 3 / 63 (4.76%)<br>3    |  |
| Infections and infestations<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 3 / 4 (75.00%)<br>3 | 37 / 63 (58.73%)<br>37 |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)   | 0 / 4 (0.00%)<br>0  | 17 / 63 (26.98%)<br>17 |  |
| Pharyngitis<br>subjects affected / exposed<br>occurrences (all)  | 2 / 4 (50.00%)<br>2 | 13 / 63 (20.63%)<br>13 |  |
| Metabolism and nutrition disorders<br>Hypercholesterolemia<br>subjects affected / exposed<br>occurrences (all)       | 1 / 4 (25.00%)<br>1 | 13 / 63 (20.63%)<br>13 |  |
| Dyslipidaemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 5 / 63 (7.94%)<br>5    |  |
| Hypophosphataemia<br>subjects affected / exposed<br>occurrences (all)  | 0 / 4 (0.00%)<br>0  | 1 / 63 (1.59%)<br>1    |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 10 December 2020 | Protocol, Version 2.1 <ul style="list-style-type: none"><li>• Data summary from the first-in-human study of FCN-159 in patients with melanoma (including clinical PK and safety data for 0.2 mg-6 mg) was added as the basis for FCN-159 dose bridging in patients with NF1</li><li>• The starting dose was increased from 1 mg to 4 mg based on updated FCN-159 data in patients with melanoma</li><li>• The last 13 lung cancer-specific questions were deleted from the EORTC QLQ-C30 (V3.0) quality-of-life scale in Attachment 12.</li></ul>   |
| 19 February 2021 | Protocol, Version 3.0 <ul style="list-style-type: none"><li>• Patient numbers were increased (42 adults in Phase I, 55 adults in Phase II)</li><li>• Study sites were expanded (~10 sites for Phase I, ~30 sites for Phase II)</li><li>• CYP2C9 enzyme polymorphism testing was added.</li><li>• Treatment duration was modified to "the administration of FCN-159 Tablets was continued until progressive disease or other criteria for termination of treatment were met"</li><li>• Tumor assessment frequency was adjusted from "every 3 cycles in the first year, every 6 cycles thereafter" to "every 4 cycles in the first 2 years, every 6 cycles thereafter"</li><li>• Functional scales were added</li></ul> |
| 19 March 2021    | Protocol, Version 3.1 <ul style="list-style-type: none"><li>• Safety Management Committee (SMC) was added</li><li>• Management and prevention of adverse events (e.g., skin toxicity, hepatotoxicity, gastrointestinal events, LVEF, ocular toxicity) were refined</li></ul>  |
| 22 May 2021      | Protocol, Version 3.2 <ul style="list-style-type: none"><li>• PD testing was added in Phase I to better analyze dose-response relationships and determine the optimal recommended phase II dose</li><li>• The patient age range was revised to "&gt;18 and ≤70 years</li><li>• Both Phase I and II enrollment populations were revised to "patients with symptomatic plexiform fibroma"</li><li>• Strong CYP2C8 and CYP2C9 inhibitors or inducers (including moderate inducers) as prohibited drugs were added</li><li>• PK sampling times were adjusted based on tumor assessment cycles</li><li>• It was specified that efficacy assessment would follow REINS criteria</li></ul>                                   |
| 13 October 2021  | Protocol, Version 4.0 <ul style="list-style-type: none"><li>• 3D laser scanning for NF1 with PNs evaluation was deleted</li><li>• The adult RP2D of 8 mg was confirmed by the SMC meeting based on Phase I data, and this information was added</li><li>• Specific ophthalmologic examination items were added to avoid inconsistent items in eye examination of each site</li><li>• A single ECG was changed to three ECGs, and ECG frequency was reduced in Phase II</li></ul>  |

|                  |   |
|------------------|---|
| 11 June 2022     | Protocol, Version 5.0 <ul style="list-style-type: none"> <li>• The administration under fasting was adjusted to not requiring fasting state based on the food effect test.</li> <li>• Family history of sudden cardiac death, acute neurological events, and concurrent use of anticoagulants were added as exclusion criteria.</li> <li>• Pharmacokinetic blood collection time points were updated.</li> <li>• ERK phosphorylation inhibition assessment was updated.</li> <li>• Amylase testing was replaced with lipase testing during the screening/baseline period.</li> <li>• Ophthalmologic function and airway function evaluations for orbital PN were deleted.</li> <li>• Delete impulse concussion pulmonary function method Impulse oscillometry was deleted.</li> <li>• Assessments for plexiform neurofibromas affecting speech/swallowing were deleted</li> </ul> |
| 29 December 2023 | Protocol, Version 6.2 <ul style="list-style-type: none"> <li>• The investigator-assessed ORR was adjusted to the primary endpoint, while the IRC-assessed ORR was adjusted to a secondary endpoint</li> </ul>   |

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported

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## Online references

<http://www.ncbi.nlm.nih.gov/pubmed/37400844>