



## Clinical trial results:

**An open-label, non-randomized, single dose, exploratory Phase II trial of FG001 (an imaging agent) for localization of biopsy-proven primary non-small cell lung cancer (NSCLC)**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-004389-37 |
| Trial protocol           | DK             |
| Global end of trial date | 02 June 2023   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 31 May 2024  |
| First version publication date | 31 May 2024  |

### Trial information

#### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | FG001-CT-002 |
|-----------------------|--------------|

#### Additional study identifiers

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

Notes:

### Sponsors

|                              |                                                               |
|------------------------------|---------------------------------------------------------------|
| Sponsor organisation name    | Fluoguide A/S                                                 |
| Sponsor organisation address | Ole Maaløes vej 3, København N, Denmark, 2200                 |
| Public contact               | Director Regulatory Affairs, FluoGuide A/S, alk@fluoguide.com |
| Scientific contact           | Director Regulatory Affairs, FluoGuide A/S, alk@fluoguide.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                       | 02 June 2023 |
| Is this the analysis of the primary completion data? | Yes          |
| Primary completion date                              | 02 June 2023 |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 02 June 2023 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate FG001 for the detection of NSCLC

Protection of trial subjects:

The trial was conducted, in compliance with the protocol, regulatory requirements, Good Clinical Practice (GCP) and the ethical principles of the latest revision of the Declaration of Helsinki as adopted by the World Medical Association. All subjects provided written informed consent to participate in the trial prior to being screened. All subjects received written and verbal information regarding the trial. The given information emphasized that participation in the trial was voluntary and that the subjects could withdraw from the trial at any time and for any reason. All subjects were given the opportunity to ask questions about the trial and were given sufficient time to decide whether to participate in the trial.

A subject was discontinued from the trial at any time if the subject, the Investigator, or the FluoGuide A/S evaluated that it was not in the subject's best interest to continue. The following were possible reasons for trial treatment discontinuation:

- Subject withdrawal of consent.
- Subject was not compliant with trial procedures.
- AE that in the opinion of the Investigator was in the best interest of the subject to discontinue trial participation.
- Protocol violation requiring discontinuation.
- Lost to follow-up.
- FluoGuide A/S request for early termination of trial.
- Subject death.

All subjects could withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. Reasonable attempts were made by the Investigator to provide a reason for the subject's withdrawal. The reason for the subject's withdrawal from the trial was specified in the subject's journal and the eCRF. If a subject was withdrawn from treatment due to an AE, the subject was followed and treated by the Investigator until the abnormal parameter or symptom has resolved or stabilized. Although subjects could withdraw from the trial at any time and for any reason, subject withdrawal was avoided to the extent possible.

Background therapy:

None

Evidence for comparator:

None

|                                                           |             |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment                          | 24 May 2022 |
| Long term follow-up planned                               | No          |
| Independent data monitoring committee (IDMC) involvement? | No          |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 18 |
| Worldwide total number of subjects   | 18          |
| EEA total number of subjects         | 18          |

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)                      | 3  |
| From 65 to 84 years                       | 15 |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

This study was conducted at Copenhagen University Hospital, Rigshospitalet, Denmark. A total of 18 subjects were screened, 17 subjects received trial drug as a 36 mg single administration, 1 subject withdrew before dosing.

### Pre-assignment

Screening details:

At the screening visit the subject's medical history and concomitant illnesses were obtained, and the previous and concomitant medication documented.

### Period 1

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

Blinding implementation details:

The trial was not blinded.

### Arms

|                              |          |
|------------------------------|----------|
| Are arms mutually exclusive? | Yes      |
| <b>Arm title</b>             | Cohort 1 |

Arm description:

36 mg of FG001, administered day before surgery

|                                        |                                   |
|----------------------------------------|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | FG001                             |
| Investigational medicinal product code | FG001                             |
| Other name                             |                                   |
| Pharmaceutical forms                   | Powder for solution for injection |
| Routes of administration               | Injection                         |

Dosage and administration details:

36 mg of FG001, slow intravenous infusion

|                  |          |
|------------------|----------|
| <b>Arm title</b> | Cohort 2 |
|------------------|----------|

Arm description:

36 mg of FG001, administered 2 days prior to surgery

|                                        |                                   |
|----------------------------------------|-----------------------------------|
| Arm type                               | Experimental                      |
| Investigational medicinal product name | FG001                             |
| Investigational medicinal product code | FG001                             |
| Other name                             |                                   |
| Pharmaceutical forms                   | Powder for solution for injection |
| Routes of administration               | Injection                         |

Dosage and administration details:

36 mg of FG001, slow intravenous infusion

| Number of subjects in period<br>1 <sup>[1]</sup> | Cohort 1 | Cohort 2 |
|--------------------------------------------------|----------|----------|
|                                                  |          |          |
| Started                                          | 9        | 8        |
| Completed                                        | 8        | 8        |
| Not completed                                    | 1        | 0        |
| Adverse event, serious fatal                     | 1        | -        |

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The disparity is due to 1 screening failure (withdrawal of consent) - a total of 18 subjects underwent screening, and a total of 17 subjects received trial drug (Cohort 1: N=9; Cohort 2: N=8). One subject in Cohort 1 died during the trial. This subject had a fatal TEAE of arterial rupture that was considered not related to the trial drug. 16 subjects completed the trial.

## Baseline characteristics

### Reporting groups

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

Reporting group description: -

| Reporting group values                                | Overall period | Total |  |
|-------------------------------------------------------|----------------|-------|--|
| Number of subjects                                    | 17             | 17    |  |
| Age categorical                                       |                |       |  |
| Units: Subjects                                       |                |       |  |
| In utero                                              |                | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |                | 0     |  |
| Newborns (0-27 days)                                  |                | 0     |  |
| Infants and toddlers (28 days-23<br>months)           |                | 0     |  |
| Children (2-11 years)                                 |                | 0     |  |
| Adolescents (12-17 years)                             |                | 0     |  |
| Adults (18-64 years)                                  |                | 0     |  |
| From 65-84 years                                      |                | 0     |  |
| 85 years and over                                     |                | 0     |  |
| Age continuous                                        |                |       |  |
| Units: years                                          |                |       |  |
| median                                                | 72             |       |  |
| full range (min-max)                                  | 58 to 83       | -     |  |
| Gender categorical                                    |                |       |  |
| Units: Subjects                                       |                |       |  |
| Female                                                | 9              | 9     |  |
| Male                                                  | 8              | 8     |  |
| Fertility Status                                      |                |       |  |
| Units: Subjects                                       |                |       |  |
| Post-menopausal                                       | 9              | 9     |  |
| NA                                                    | 8              | 8     |  |
| Ethnicity                                             |                |       |  |
| Units: Subjects                                       |                |       |  |
| White                                                 | 17             | 17    |  |
| Tumor location                                        |                |       |  |
| Units: Subjects                                       |                |       |  |
| Peripheral                                            | 17             | 17    |  |
| Tumor size                                            |                |       |  |
| (cm, longest diameter)                                |                |       |  |
| Units: centimetre                                     |                |       |  |
| arithmetic mean                                       | 3.84           |       |  |
| standard deviation                                    | ± 1.337        | -     |  |

### Subject analysis sets

|                            |                         |
|----------------------------|-------------------------|
| Subject analysis set title | Full Analysis Set (FAS) |
|----------------------------|-------------------------|

|                           |                    |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

Full Analysis Set (FAS) or Intent-to-Treat Population: All subjects who were exposed to trial drug irrespective of their compliance to the planned course of treatment. All enrolled subjects dosed with FG001 and with any valid imaging information were included in the FAS.

Note: The FAS/ITT Population was removed from the analysis in a post database lock statistical analysis plan (SAP) addendum.

|                            |                       |
|----------------------------|-----------------------|
| Subject analysis set title | Per-Protocol (PP) Set |
| Subject analysis set type  | Per protocol          |

Subject analysis set description:

Per-Protocol (PP) Set: The set of FAS subjects who had at least 80% of the trial drug administered, and who did not have any major protocol violations that may affect the assessment of efficacy endpoints.

Note: The PP Set was redefined as a subset of the Safety Analysis Set in a post database lock SAP addendum.

|                            |                     |
|----------------------------|---------------------|
| Subject analysis set title | Safety Analysis Set |
| Subject analysis set type  | Safety analysis     |

Subject analysis set description:

Safety Analysis Set: All subjects who received trial drug.

| Reporting group values                                                                                                                                                                                                                                    | Full Analysis Set (FAS) | Per-Protocol (PP) Set | Safety Analysis Set |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|-----------------------|---------------------|
| Number of subjects                                                                                                                                                                                                                                        | 17                      | 17                    | 17                  |
| Age categorical<br>Units: Subjects                                                                                                                                                                                                                        |                         |                       |                     |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                         |                       |                     |
| Age continuous<br>Units: years                                                                                                                                                                                                                            |                         |                       |                     |
| median                                                                                                                                                                                                                                                    | 72                      | 72                    | 72                  |
| full range (min-max)                                                                                                                                                                                                                                      | 58 to 83                | 58 to 83              | 58 to 83            |
| Gender categorical<br>Units: Subjects                                                                                                                                                                                                                     |                         |                       |                     |
| Female                                                                                                                                                                                                                                                    | 9                       | 9                     | 9                   |
| Male                                                                                                                                                                                                                                                      | 8                       | 8                     | 8                   |
| Fertility Status<br>Units: Subjects                                                                                                                                                                                                                       |                         |                       |                     |
| Post-menopausal                                                                                                                                                                                                                                           | 9                       | 9                     | 9                   |
| NA                                                                                                                                                                                                                                                        | 8                       | 8                     | 8                   |
| Ethnicity<br>Units: Subjects                                                                                                                                                                                                                              |                         |                       |                     |
| White                                                                                                                                                                                                                                                     | 17                      | 17                    | 17                  |
| Tumor location<br>Units: Subjects                                                                                                                                                                                                                         |                         |                       |                     |
| Peripheral                                                                                                                                                                                                                                                | 17                      | 17                    | 17                  |

|                        |         |         |         |
|------------------------|---------|---------|---------|
| Tumor size             |         |         |         |
| (cm, longest diameter) |         |         |         |
| Units: centimetre      |         |         |         |
| arithmetic mean        | 3.84    | 3.84    | 3.84    |
| standard deviation     | ± 1.337 | ± 1.337 | ± 1.337 |

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## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                | Cohort 1                |
| Reporting group description:<br>36 mg of FG001, administered day before surgery                                                                                                                                                                                                                                                                                                                                                                      |                         |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                | Cohort 2                |
| Reporting group description:<br>36 mg of FG001, administered 2 days prior to surgery                                                                                                                                                                                                                                                                                                                                                                 |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                           | Full Analysis Set (FAS) |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                            | Intention-to-treat      |
| Subject analysis set description:<br>Full Analysis Set (FAS) or Intent-to-Treat Population: All subjects who were exposed to trial drug irrespective of their compliance to the planned course of treatment. All enrolled subjects dosed with FG001 and with any valid imaging information were included in the FAS.<br>Note: The FAS/ITT Population was removed from the analysis in a post database lock statistical analysis plan (SAP) addendum. |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                           | Per-Protocol (PP) Set   |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                            | Per protocol            |
| Subject analysis set description:<br>Per-Protocol (PP) Set: The set of FAS subjects who had at least 80% of the trial drug administered, and who did not have any major protocol violations that may affect the assessment of efficacy endpoints.<br>Note: The PP Set was redefined as a subset of the Safety Analysis Set in a post database lock SAP addendum.                                                                                     |                         |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                           | Safety Analysis Set     |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                            | Safety analysis         |
| Subject analysis set description:<br>Safety Analysis Set: All subjects who received trial drug.                                                                                                                                                                                                                                                                                                                                                      |                         |

### Primary: Sensitivity for detection of NSCLC

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                   |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Sensitivity for detection of NSCLC <sup>[1]</sup> |
| End point description:<br>The primary efficacy endpoint (sensitivity measured as the proportion of biopsies encompassing active tumor tissue that were fluorescent and TBR values based on in vivo and ex vivo images) was challenging to achieve as the fluorescence signal was weak, resulting in mean TBR values between 1 and 2. Consequently, the surgeon could not be guided by the fluorescent light to sample the biopsies, and this is why these biopsies were not evaluated for fluorescence on the back table. A subjective evaluation of in vivo and ex vivo images was performed by the Sponsor team and identified that 11/15 subjects had a tumor that was fluorescent with FG001. |                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Primary                                           |
| End point timeframe:<br>Duration of the trial                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                   |
| 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: The primary efficacy endpoint (sensitivity measured as the proportion of biopsies encompassing active tumor tissue that were fluorescent and TBR values based on in vivo and ex vivo images) was challenging to achieve as the fluorescence signal was weak. Subjective evaluation of in vivo and ex vivo images was performed by the Sponsor team and no statistical analyses were thus performed.                                                                                               |                                                   |

|                                                 |                       |  |  |  |
|-------------------------------------------------|-----------------------|--|--|--|
| <b>End point values</b>                         | Per-Protocol (PP) Set |  |  |  |
| Subject group type                              | Subject analysis set  |  |  |  |
| Number of subjects analysed                     | 15                    |  |  |  |
| Units: tumours that were fluorescent with FG001 | 11                    |  |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Duration of the trial

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 25.1 |
|--------------------|------|

### Reporting groups

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Safety Analysis Set |
|-----------------------|---------------------|

Reporting group description:

Safety Analysis Set: All subjects who received trial drug.

All subjects in the Safety Analysis Set received a 36.0 mL administration of trial drug

| Serious adverse events                            | Safety Analysis Set                                                  |  |  |
|---------------------------------------------------|----------------------------------------------------------------------|--|--|
| Total subjects affected by serious adverse events |                                                                      |  |  |
| subjects affected / exposed                       | 2 / 17 (11.76%)                                                      |  |  |
| number of deaths (all causes)                     | 1                                                                    |  |  |
| number of deaths resulting from adverse events    | 0                                                                    |  |  |
| Vascular disorders                                |                                                                      |  |  |
| Arterial rupture                                  | Additional description: Arterial rupture and bleeding during surgery |  |  |
| subjects affected / exposed                       | 1 / 17 (5.88%)                                                       |  |  |
| occurrences causally related to treatment / all   | 0 / 1                                                                |  |  |
| deaths causally related to treatment / all        | 0 / 1                                                                |  |  |
| Respiratory, thoracic and mediastinal disorders   |                                                                      |  |  |
| Hemothorax                                        |                                                                      |  |  |
| subjects affected / exposed                       | 1 / 17 (5.88%)                                                       |  |  |
| occurrences causally related to treatment / all   | 0 / 1                                                                |  |  |
| deaths causally related to treatment / all        | 0 / 0                                                                |  |  |

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

| Non-serious adverse events                            | Safety Analysis Set |  |  |
|-------------------------------------------------------|---------------------|--|--|
| Total subjects affected by non-serious adverse events |                     |  |  |
| subjects affected / exposed                           | 1 / 17 (5.88%)      |  |  |
| Investigations                                        |                     |  |  |

|                                      |                |  |  |
|--------------------------------------|----------------|--|--|
| Alanine aminotransferase increased   |                |  |  |
| subjects affected / exposed          | 1 / 17 (5.88%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Aspartate aminotransferase increased |                |  |  |
| subjects affected / exposed          | 1 / 17 (5.88%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Blood alkaline phosphatase increased |                |  |  |
| subjects affected / exposed          | 1 / 17 (5.88%) |  |  |
| occurrences (all)                    | 1              |  |  |
| Gamma-glutamyltransferase increased  |                |  |  |
| subjects affected / exposed          | 1 / 17 (5.88%) |  |  |
| occurrences (all)                    | 1              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 27 June 2022     | Protocol Version 2.0:<br>Removed "single site" wording throughout.<br>Update to inclusion criterion 1 to include subjects with squamous-cell carcinoma.<br>Update to inclusion criterion 3 to include subjects with tumor size $\geq 1.5$ cm.<br>Update the time window for PK sample collection at +44 hours post FG001 administration.<br>Add new section describing financial aspects of the study including site payments.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| 23 November 2022 | Protocol version 3.0:<br>GCP statement was removed.<br>Study visit structure updated to include an EoT visit at Day 4 from FG001 administration.<br>Risk assessment information updated.<br>Secondary efficacy endpoints were separated for Cohorts 1 and 2 and updated to include "Demonstrate exposure of FG001 after 1 hour and prior to surgery" for Cohort 2.<br>Exploratory endpoint was updated to "To evaluate the correlation between the normalized FG001 intensities and the uPAR expression as determined by IHC".<br>Exploratory endpoint was added "To explore the impact on normalized intensity level for surrounding benign tissue such as but not constrained to anthracosis and atelectasis".<br>Correction to exclusion criterion 4.<br>Planned number of subjects changed from "20 to 24" to "16 up to 44".<br>Study design revised to allow up to 5 cohorts each including 8 subjects, with FG001 administration 2 days prior to surgery.<br>Details of safety monitoring updated.<br>PK sample timing updated, with an updated PK sampling schedule for Cohort 2.<br>Vital signs timing updated.<br>Sample size calculation updated. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported