



## Clinical trial results:

**An International Multicentre, Open-Label First in Human Phase I/II study to evaluate the safety, tolerability, biodistribution and antitumour activity of 177Lu-3BP-227 for the treatment of subjects with solid tumours expressing neurotensin receptor 1**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-001263-20 |
| Trial protocol           | BE NL          |
| Global end of trial date | 28 April 2021  |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 08 May 2022  |
| First version publication date | 08 May 2022  |

### Trial information

#### Trial identification

|                       |                |
|-----------------------|----------------|
| Sponsor protocol code | D-FR-01087-001 |
|-----------------------|----------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03525392 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Ipsen Pharma SAS  |
| Sponsor organisation address | 65, quai Georges Gorse, Boulogne-Billancourt, France, 92100   |
| Public contact               | Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.com |
| Scientific contact           | Medical Director, Ipsen Pharma SAS, clinical.trials@ipsen.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                       | 28 April 2021 |
| Is this the analysis of the primary completion data? | No            |

|                                  |               |
|----------------------------------|---------------|
| Global end of trial reached?     | Yes           |
| Global end of trial date         | 28 April 2021 |
| Was the trial ended prematurely? | Yes           |

Notes:

## General information about the trial

Main objective of the trial:

Phase 1: To establish the safety and tolerability of fractionated intravenous (IV) administrations of 177Lu-3BP-227 in participants with unresectable, locally advanced or metastatic cancers expressing neurotensin receptor 1 (NTSR1).

Phase 2: To estimate objective response rate (ORR) of fractionated IV administrations of 177Lu-3BP-227 in participants with unresectable, locally advanced or metastatic cancers expressing NTSR1.

Protection of trial subjects:

The study was conducted under the provisions of the Declaration of Helsinki and in accordance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Consolidated Guideline on Good Clinical Practice and in compliance with Independent Ethics Committees/Institutional Review Boards and informed consent regulations.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 03 May 2018      |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety, Efficacy |
| Long term follow-up duration                              | 5 Years          |
| Independent data monitoring committee (IDMC) involvement? | Yes              |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                  |
|--------------------------------------|------------------|
| Country: Number of subjects enrolled | France: 10       |
| Country: Number of subjects enrolled | Switzerland: 1   |
| Country: Number of subjects enrolled | United States: 3 |
| Worldwide total number of subjects   | 14               |
| EEA total number of subjects         | 10               |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23          | 0 |

|                           |   |
|---------------------------|---|
| months)                   |   |
| Children (2-11 years)     | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years)      | 5 |
| From 65 to 84 years       | 9 |
| 85 years and over         | 0 |

## Subject disposition

### Recruitment

Recruitment details:

This Phase 1/2 first in human study was conducted in participants with unresectable, locally advanced or metastatic solid tumors expressing NTSR1 at 9 investigational sites. The sponsor terminated the study early during Cohort 5 in phase 1 dose escalation; phase 1 dose expansion and phase 2 were not started.

### Pre-assignment

Screening details:

For phase 1, core trial was up to 19 weeks and comprised of 2 treatment cycles. If a participant had clinical benefit, they could receive up to 4 additional cycles after end of core trial (EOCT). Due to early termination, only results of core trial are presented. 14 participants received a therapeutic dose of 177Lu-3BP-227 in phase 1 of the study.

### Period 1

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

### Arms

|                              |                                 |
|------------------------------|---------------------------------|
| Are arms mutually exclusive? | Yes                             |
| <b>Arm title</b>             | Cohort 1: 177Lu-3BP-227 2.5 GBq |

Arm description:

Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | 177Lu-3BP-227         |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study medication formulation consisted of 2.5 GBq of 177Lu-3BP-227 in a total volume of 20 milliliter (mL) that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Cohort 2: 177Lu-3BP-227 4.0 GBq |
|------------------|---------------------------------|

Arm description:

Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | 177Lu-3BP-227         |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study medication formulation consisted of 4.0 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|------------------|---------------------------------|

Arm description:

Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5

weeks during the core trial period.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | 177Lu-3BP-227         |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study medication formulation consisted of 5.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Cohort 4: 177Lu-3BP-227 6.5 GBq |
|------------------|---------------------------------|

Arm description:

Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | 177Lu-3BP-227         |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study medication formulation consisted of 6.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

|                  |                                 |
|------------------|---------------------------------|
| <b>Arm title</b> | Cohort 5: 177Lu-3BP-227 7.5 GBq |
|------------------|---------------------------------|

Arm description:

Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|  |                       |
|--|-----------------------|
| Arm type                               | Experimental          |
| Investigational medicinal product name | 177Lu-3BP-227         |
| Investigational medicinal product code |                       |
| Other name                             |                       |
| Pharmaceutical forms                   | Solution for infusion |
| Routes of administration               | Intravenous use       |

Dosage and administration details:

The study medication formulation consisted of 7.5 GBq of 177Lu-3BP-227 in a total volume of 20 mL that was administered by IV infusion over 20 minutes. If infusion reactions were observed, the infusion rate was to be slowed to around 30 minutes or stopped if the reaction was severe.

| <b>Number of subjects in period 1</b> | Cohort 1: 177Lu-3BP-227 2.5 GBq | Cohort 2: 177Lu-3BP-227 4.0 GBq | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|---------------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Started                               | 2                               | 3                               | 5                               |
| Completed                             | 1                               | 2                               | 2                               |
| Not completed                         | 1                               | 1                               | 3                               |
| Adverse event, non-fatal              | 1                               | -                               | 2                               |
| Progressive disease                   | -                               | 1                               | 1                               |

| <b>Number of subjects in period 1</b> | Cohort 4: 177Lu-3BP-227 6.5 GBq | Cohort 5: 177Lu-3BP-227 7.5 GBq |
|---------------------------------------|---------------------------------|---------------------------------|
|---------------------------------------|---------------------------------|---------------------------------|

|                          |   |   |
|--------------------------|---|---|
| Started                  | 3 | 1 |
| Completed                | 0 | 0 |
| Not completed            | 3 | 1 |
| Adverse event, non-fatal | - | - |
| Progressive disease      | 3 | 1 |

## Baseline characteristics

### Reporting groups

|  |                                 |
|--|---------------------------------|
| Reporting group title  | Cohort 1: 177Lu-3BP-227 2.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period. |                                 |
| Reporting group title  | Cohort 2: 177Lu-3BP-227 4.0 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                 |                                 |
| Reporting group title  | Cohort 3: 177Lu-3BP-227 5.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                 |                                 |
| Reporting group title  | Cohort 4: 177Lu-3BP-227 6.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                 |                                 |
| Reporting group title  | Cohort 5: 177Lu-3BP-227 7.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                 |                                 |

| Reporting group values             | Cohort 1: 177Lu-3BP-227 2.5 GBq | Cohort 2: 177Lu-3BP-227 4.0 GBq | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|------------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Number of subjects                 | 2                               | 3                               | 5                               |
| Age categorical<br>Units: Subjects |                                 |                                 |                                 |

|   |       |        |       |
|---|-------|--------|-------|
| Age continuous  |       |        |       |
| 99999 = Standard deviation cannot be calculated when only 1 participant analyzed. |       |        |       |
| Units: years  |       |        |       |
| arithmetic mean   | 70.0  | 64.3   | 64.0  |
| standard deviation  | ± 4.2 | ± 16.2 | ± 7.2 |
| Gender categorical<br>Units: Subjects   |       |        |       |
| Female  | 0     | 1      | 1     |
| Male  | 2     | 2      | 4     |
| Race<br>Units: Subjects   |       |        |       |
| Not Collected   | 2     | 3      | 5     |
| White   | 0     | 0      | 0     |
| Asian   | 0     | 0      | 0     |
| Black / African American  | 0     | 0      | 0     |
| Native Hawaiian / Other Pacific Islander  | 0     | 0      | 0     |
| American Indian / Alaska Native   | 0     | 0      | 0     |
| Other   | 0     | 0      | 0     |
| Ethnicity<br>Units: Subjects  |       |        |       |

|                        |   |   |   |
|------------------------|---|---|---|
| Hispanic or Latino     | 0 | 0 | 0 |
| Not Hispanic or Latino | 2 | 3 | 5 |

| Reporting group values             | Cohort 4: 177Lu-3BP-227 6.5 GBq | Cohort 5: 177Lu-3BP-227 7.5 GBq | Total |
|------------------------------------|---------------------------------|---------------------------------|-------|
| Number of subjects                 | 3                               | 1                               | 14    |
| Age categorical<br>Units: Subjects |                                 |                                 |       |

|   |       |         |    |
|---|-------|---------|----|
| Age continuous  |       |         |    |
| 99999 = Standard deviation cannot be calculated when only 1 participant analyzed. |       |         |    |
| Units: years  |       |         |    |
| arithmetic mean   | 66.3  | 77.0    |    |
| standard deviation  | ± 9.1 | ± 99999 | -  |
| Gender categorical<br>Units: Subjects   |       |         |    |
| Female  | 2     | 0       | 4  |
| Male  | 1     | 1       | 10 |
| Race<br>Units: Subjects   |       |         |    |
| Not Collected   | 0     | 0       | 10 |
| White   | 3     | 1       | 4  |
| Asian   | 0     | 0       | 0  |
| Black / African American  | 0     | 0       | 0  |
| Native Hawaiian / Other Pacific Islander  | 0     | 0       | 0  |
| American Indian / Alaska Native   | 0     | 0       | 0  |
| Other   | 0     | 0       | 0  |
| Ethnicity<br>Units: Subjects  |       |         |    |
| Hispanic or Latino  | 0     | 0       | 0  |
| Not Hispanic or Latino  | 3     | 1       | 14 |



## End points

### End points reporting groups

|  |                                 |
|--|---------------------------------|
| Reporting group title  | Cohort 1: 177Lu-3BP-227 2.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 2.5 Gigabecquerel (GBq) fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.           |                                 |
| Reporting group title  | Cohort 2: 177Lu-3BP-227 4.0 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                           |                                 |
| Reporting group title  | Cohort 3: 177Lu-3BP-227 5.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                           |                                 |
| Reporting group title  | Cohort 4: 177Lu-3BP-227 6.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                           |                                 |
| Reporting group title  | Cohort 5: 177Lu-3BP-227 7.5 GBq |
| Reporting group description:<br>Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.                           |                                 |
| Subject analysis set title   | All Participants                |
| Subject analysis set type  | Full analysis                   |
| Subject analysis set description:<br>Participants received 177Lu-3BP-227 dose range of 2.5 to 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period. |                                 |

### Primary: Phase 1: Number of Participants With Dose-Limiting Toxicities (DLT)

|  |  |
|--|--|
| End point title  | Phase 1: Number of Participants With Dose-Limiting Toxicities (DLT) <sup>[1]</sup> |
| End point description:<br>DLTs were defined for a list of predefined study medication-related adverse events (AEs) as specified in the protocol, according to the National Cancer Institute – Common Terminology Criteria for Adverse Events scale version 5.0 (CTCAE v5.0) that occurred during the defined DLT assessment period (during Cycle 1 or 2). Safety population contained all participants who received at least 1 dose of study medication. |  |
| End point type   | Primary  |
| End point timeframe:<br>From the start of the first study medication (Cycle 1 Day 1) up to EOCT, maximum of 16 weeks.  |  |
| 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: Only descriptive statistical analysis was performed for the primary endpoint.  |  |

| End point values            | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed | 2                                     | 3                                     | 5                                     | 3                                     |
| Units: participants         | 0                                     | 0                                     | 0                                     | 0                                     |

|                             |                                       |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>     | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 1                                     |  |  |  |
| Units: participants         | 0                                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1: Maximum Uptake (%) of 177Lu-3BP-227 at Target Lesions and Discernible Organs

|                 |   |
|-----------------|---|
| End point title | Phase 1: Maximum Uptake (%) of 177Lu-3BP-227 at Target Lesions and Discernible Organs |
|-----------------|---|

End point description:

177Lu-3BP-227 uptake in organs and lesions was evaluated centrally, using nuclear medicine images, as part of the dosimetry workflow. Uptake activity for organs of interest (i.e., body, bone marrow, left kidney, right kidney, healthy liver, and spleen) was determined. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n = number of observations for both cycles.

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

End point timeframe:

Measurements were performed at 0 to 1 hours, 2 to 4 hours, 16 to 24 hours, 40 to 48 hours, 72 to 96 hours post infusion in each treatment cycle.

|                                    |                        |  |  |  |
|------------------------------------|------------------------|--|--|--|
| <b>End point values</b>            | All Participants       |  |  |  |
| Subject group type                 | Subject analysis set   |  |  |  |
| Number of subjects analysed        | 14                     |  |  |  |
| Units: percentage of 177Lu-3BP-227 |                        |  |  |  |
| median (full range (min-max))      |                        |  |  |  |
| All cycles: Body (n= 21)           | 99.7 (99.2 to 100)     |  |  |  |
| All cycles: Bone marrow (n= 20)    | 1.10 (0.560 to 1.98)   |  |  |  |
| All cycles: Left kidney (n= 25)    | 0.247 (0.130 to 0.409) |  |  |  |
| All cycles: Right kidney (n= 25)   | 0.227 (0.129 to 0.452) |  |  |  |
| All cycles: Healthy liver (n= 20)  | 1.01 (0.0760 to 1.84)  |  |  |  |
| All cycles: Spleen (n= 17)         | 0.280 (0.110 to 0.770) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Maximal Concentration (Cmax) of 177Lu-3BP-227

|                 |  |
|-----------------|--|
| End point title | Phase 1: Maximal Concentration (Cmax) of 177Lu-3BP-227 |
|-----------------|--|

End point description:

The pharmacokinetic (PK) sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood and organs/lesions were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

| End point values                     | All Participants     |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[2]</sup>     |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[2] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Time Post Injection to Achieve Cmax of 177Lu-3BP-227

|                 |   |
|-----------------|---|
| End point title | Phase 1: Time Post Injection to Achieve Cmax of 177Lu-3BP-227 |
|-----------------|---|

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

| End point values              | All Participants     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 0 <sup>[3]</sup>     |  |  |  |
| Units: not applicable         |                      |  |  |  |
| median (full range (min-max)) | ( to )               |  |  |  |

Notes:

[3] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Area Under the Plasma Concentration Versus Time Curve (AUC) of 177Lu-3BP-227

|                 |   |
|-----------------|---|
| End point title | Phase 1: Area Under the Plasma Concentration Versus Time Curve (AUC) of 177Lu-3BP-227 |
|-----------------|---|

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| End point values                     | All Participants     |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[4]</sup>     |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ()                   |  |  |  |

Notes:

[4] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Half-life (t<sub>1/2</sub>) of 177Lu-3BP-227

|                 |   |
|-----------------|---|
| End point title | Phase 1: Half-life (t <sub>1/2</sub> ) of 177Lu-3BP-227 |
|-----------------|---|

End point description:

The PK sampling was performed from Day 1 to Day 5 post infusion for each treatment cycle. Due to the early termination of the study, 177Lu-3BP-227 PK parameters in blood, urine and organs/lesions were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 24 hours, 48 hours and 72 to 96 hours post infusion in each treatment cycle.

| End point values              | All Participants     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 0 <sup>[5]</sup>     |  |  |  |
| Units: not applicable         |                      |  |  |  |
| median (full range (min-max)) | ( to )               |  |  |  |

Notes:

[5] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1: Number of Participants With Highest Absorbed Dose of 177Lu-3BP-227 to Each Discernible Organ

|                 |  |
|-----------------|--|
| End point title | Phase 1: Number of Participants With Highest Absorbed Dose of 177Lu- 3BP-227 to Each Discernible Organ |
|-----------------|--|

End point description:

The absorbed dose to the target lesions and discernible organs (i.e., organs showing uptake) was evaluated by image-based analysis. The organs considered for 177Lu-3BP-227 image-based dosimetry assessment included: healthy liver, total liver, bone marrow, left kidney, right kidney, intestine (large and small), spleen, pancreas, stomach wall, right ovary, left ovary, uterus, right testis, left testis, thymus, right thyroid gland, left thyroid gland, prostate gland and total body. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n= number of participants analyzed for each specific organ/cycle.

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

End point timeframe:

From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.

| End point values                 | All Participants     |  |  |  |
|----------------------------------|----------------------|--|--|--|
| Subject group type               | Subject analysis set |  |  |  |
| Number of subjects analysed      | 14                   |  |  |  |
| Units: participants              |                      |  |  |  |
| Cycle 1: Right kidney (n= 14)    | 4                    |  |  |  |
| Cycle 1: Left kidney (n= 14)     | 3                    |  |  |  |
| Cycle 1: Large intestine (n= 14) | 5                    |  |  |  |
| Cycle 1: Bladder (n= 14)         | 2                    |  |  |  |
| Cycle 1: Lymph node (n= 14)      | 0                    |  |  |  |
| Cycle 2: Right kidney (n= 11)    | 2                    |  |  |  |
| Cycle 2: Left kidney (n= 11)     | 2                    |  |  |  |
| Cycle 2: Large intestine (n= 11) | 4                    |  |  |  |
| Cycle 2: Bladder (n= 11)         | 2                    |  |  |  |
| Cycle 2: Lymph node (n= 11)      | 1                    |  |  |  |

## Statistical analyses

No statistical analyses for this end point

**Secondary: Phase 1: Specific Absorbed Dose to the Target Lesions of 177Lu-3BP-227**

|  |  |
|--|--|
| End point title  | Phase 1: Specific Absorbed Dose to the Target Lesions of 177Lu-3BP-227 |
| End point description:<br>The specific absorbed dose to the target lesions was evaluated by image-based analysis. Results for all studied diseases (pancreatic ductal adenocarcinoma and colorectal carcinoma) at all anatomical locations (cervical, intrapelvic, liver, lung, lymphnode, and pancreas) for all cycles (Cycle 1 and 2) are reported. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. |  |
| End point type   | Secondary  |
| End point timeframe:<br>From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.  |  |

|                               |                        |  |  |  |
|-------------------------------|------------------------|--|--|--|
| <b>End point values</b>       | All Participants       |  |  |  |
| Subject group type            | Subject analysis set   |  |  |  |
| Number of subjects analysed   | 14 <sup>[6]</sup>      |  |  |  |
| Units: Gray/GBq               |                        |  |  |  |
| median (full range (min-max)) | 0.183 (0.0551 to 1.21) |  |  |  |

Notes:

[6] - 47 Lesions.

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Phase 1: Specific Absorbed Dose Per Organ of 177Lu-3BP-227**

|  |  |
|--|--|
| End point title  | Phase 1: Specific Absorbed Dose Per Organ of 177Lu-3BP-227 |
| End point description:<br>The specific absorbed dose per organ was evaluated by image-based analysis. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Here, n = number of observations for both cycles. |  |
| End point type   | Secondary  |
| End point timeframe:<br>From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.  |  |

|                                   |                           |  |  |  |
|-----------------------------------|---------------------------|--|--|--|
| <b>End point values</b>           | All Participants          |  |  |  |
| Subject group type                | Subject analysis set      |  |  |  |
| Number of subjects analysed       | 14                        |  |  |  |
| Units: Gray/GBq                   |                           |  |  |  |
| median (full range (min-max))     |                           |  |  |  |
| All cycles: Bone marrow (n= 25)   | 0.0636 (0.0346 to 0.0943) |  |  |  |
| All cycles: Healthy liver (n= 25) | 0.0515 (0.0263 to 0.0811) |  |  |  |

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| All cycles: Left kidney (n= 25)  | 0.255 (0.102 to 1.05)  |  |  |  |
| All cycles: Right kidney (n= 25) | 0.242 (0.118 to 0.943) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Cumulative Absorbed Organ Doses of 177Lu-3BP-227

|                 |   |
|-----------------|---|
| End point title | Phase 1: Cumulative Absorbed Organ Doses of 177Lu-3BP-227 |
|-----------------|---|

End point description:

The cumulative absorbed dose to the discernible organs (i.e., organs showing uptake) was evaluated by image-based analysis. Dosimetry population included all participants with organ dosimetry data and with no major protocol deviations with an impact on dosimetry analysis. Cumulative absorbed doses on Cycles 1 and 2 are only presented for participants who have performed the 2 cycles.

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

End point timeframe:

From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.

| End point values              | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|-------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type            | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed   | 1                                     | 3                                     | 3                                     | 3                                     |
| Units: Gray                   |                                       |                                       |                                       |                                       |
| median (full range (min-max)) |                                       |                                       |                                       |                                       |
| Cycle 2: Bone marrow          | 0.326 (0.326 to 0.326)                | 0.604 (0.304 to 0.645)                | 0.680 (0.391 to 0.837)                | 0.820 (0.628 to 1.11)                 |
| Cycle 2: Healthy liver        | 0.254 (0.254 to 0.254)                | 0.353 (0.271 to 0.415)                | 0.530 (0.428 to 0.637)                | 0.714 (0.469 to 0.927)                |
| Cycle 2: Left kidney          | 2.17 (2.17 to 2.17)                   | 4.19 (1.38 to 6.21)                   | 3.33 (1.90 to 5.12)                   | 3.44 (1.90 to 3.48)                   |
| Cycle 2: Right kidney         | 2.38 (2.38 to 2.38)                   | 3.39 (1.53 to 5.51)                   | 2.97 (2.14 to 5.74)                   | 3.01 (2.00 to 4.67)                   |

| End point values              | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
|-------------------------------|---------------------------------------|--|--|--|
| Subject group type            | Reporting group                       |  |  |  |
| Number of subjects analysed   | 1                                     |  |  |  |
| Units: Gray                   |                                       |  |  |  |
| median (full range (min-max)) |                                       |  |  |  |
| Cycle 2: Bone marrow          | 0.694 (0.694 to 0.694)                |  |  |  |
| Cycle 2: Healthy liver        | 0.571 (0.571 to 0.571)                |  |  |  |
| Cycle 2: Left kidney          | 2.95 (2.95 to 2.95)                   |  |  |  |

|                       |                     |  |  |  |
|-----------------------|---------------------|--|--|--|
| Cycle 2: Right kidney | 2.92 (2.92 to 2.92) |  |  |  |
|-----------------------|---------------------|--|--|--|

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Cmax of 3BP-227

|                 |                          |
|-----------------|--------------------------|
| End point title | Phase 1: Cmax of 3BP-227 |
|-----------------|--------------------------|

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | All Participants     |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[7]</sup>     |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[7] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: AUC of 3BP-227

|                 |                         |
|-----------------|-------------------------|
| End point title | Phase 1: AUC of 3BP-227 |
|-----------------|-------------------------|

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.



| End point values                     | All Participants     |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[8]</sup>     |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[8] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: t1/2 of 3BP-227

|                 |                          |
|-----------------|--------------------------|
| End point title | Phase 1: t1/2 of 3BP-227 |
|-----------------|--------------------------|

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

| End point values              | All Participants     |  |  |  |
|-------------------------------|----------------------|--|--|--|
| Subject group type            | Subject analysis set |  |  |  |
| Number of subjects analysed   | 0 <sup>[9]</sup>     |  |  |  |
| Units: not applicable         |                      |  |  |  |
| median (full range (min-max)) | ( to )               |  |  |  |

Notes:

[9] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Clearance of 3BP-227

|                 |                               |
|-----------------|-------------------------------|
| End point title | Phase 1: Clearance of 3BP-227 |
|-----------------|-------------------------------|

End point description:

The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.

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

End point timeframe:

Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.

| End point values                     | All Participants     |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[10]</sup>    |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[10] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Volume of Distribution of 3BP-227

|  |  |
|--|--|
| End point title  | Phase 1: Volume of Distribution of 3BP-227 |
| End point description:<br>The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced. |  |
| End point type   | Secondary                                  |
| End point timeframe:<br>Pre-infusion and at the end of infusion, and 5 minutes, 30 minutes, 90 minutes, 4 hours, 6 hours, 8 hours, 24 hours and 48 hours post infusion of 177Lu-3BP-227 in Cycle 1.  |  |

| End point values                     | All Participants     |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[11]</sup>    |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[11] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Cumulative Amount of Unchanged 3BP-227 Excreted Into the Urine

|  |   |
|--|---|
| End point title  | Phase 1: Cumulative Amount of Unchanged 3BP-227 Excreted Into the Urine |
| End point description:<br>The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 in Cycle 1. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated and related PK summary tables were not produced.     |   |
| End point type   | Secondary   |
| End point timeframe:<br>For other sites, from the start of the infusion to 6 hours, 6 to 12 hours, 12 to 24 hours, and 24 to 48 hours post infusion of 177Lu-3BP-227 in Cycle 1; For USA sites, from the start of the infusion to 6 hours post infusion of 177Lu-3BP-227 in Cycle 1. |   |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | All Participants     |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[12]</sup>    |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[12] - Early termination of the study.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Renal Clearance of 3BP-227 From Plasma

|                 |   |
|-----------------|---|
| End point title | Phase 1: Renal Clearance of 3BP-227 From Plasma |
|-----------------|---|

End point description:

The CLR of 3BP-227 was evaluated. The PK sampling was performed from Day 1 to Day 3 post infusion of 177Lu-3BP-227 for each treatment cycle. Due to the early termination of the study, 3BP-227 PK parameters in plasma and urine were not calculated.

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

End point timeframe:

For other sites, from the start of the infusion to 6 hours, 6 to 12 hours, 12 to 24 hours, and 24 to 48 hours post infusion of 177Lu-3BP-227 in Cycle 1; For USA sites, from the start of the infusion to 6 hours post infusion of 177Lu-3BP-227 in Cycle 1.

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | All Participants     |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[13]</sup>    |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[13] - Early termination of the study.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Number of Participants With ORR

|                 |  |
|-----------------|--|
| End point title | Phase 1: Number of Participants With ORR |
|-----------------|--|

End point description:

The ORR was defined as number of participants with a best overall response (BOR) characterized as either a complete response (CR) or partial response (PR) according to Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) relative to the total number of evaluable participants. Primary Pharmacodynamic population (for tumor response) included all participants who received at least 2 therapeutic doses of 177Lu-3BP-227 and reached the end of Cycle 2 or EOCT visit with available postbaseline tumor assessment based on RECIST 1.1 and with no major protocol deviations with an impact on the analysis.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks. |           |

| End point values            | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed | 1                                     | 1                                     | 2                                     | 1                                     |
| Units: participants         | 0                                     | 1                                     | 0                                     | 0                                     |

| End point values            | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 1                                     |  |  |  |
| Units: participants         | 0                                     |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Number of Participants With Disease Control Rate (DCR)

|                 |   |
|-----------------|---|
| End point title | Phase 1: Number of Participants With Disease Control Rate (DCR) |
|-----------------|---|

End point description:

The DCR was defined as number of participants with a BOR characterized as CR, PR or stable disease according to RECIST 1.1 relative to the total number of evaluable participants. Primary Pharmacodynamic population (for tumor response) included all participants who received at least 2 therapeutic doses of 177Lu-3BP-227 and reached the end of Cycle 2 or EOCT visit with available postbaseline tumor assessment based on RECIST 1.1 and with no major protocol deviations with an impact on the analysis.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks. |           |

| End point values            | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed | 1                                     | 1                                     | 2                                     | 1                                     |
| Units: participants         | 0                                     | 1                                     | 0                                     | 0                                     |

|                             |                                       |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>     | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 1                                     |  |  |  |
| Units: participants         | 0                                     |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1: Progression-Free Survival (PFS)

|   |  |
|---|--|
| End point title   | Phase 1: Progression-Free Survival (PFS) |
| End point description:<br>The PFS was defined as the time from date of first study medication administration until progression, according to RECIST 1.1. Due to the early termination of the study, survival analysis on PFS was not performed. |  |
| End point type  | Secondary                                |
| End point timeframe:<br>From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.   |  |

|                             |                                       |                                       |                                       |                                       |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| <b>End point values</b>     | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed | 0 <sup>[14]</sup>                     | 0 <sup>[15]</sup>                     | 0 <sup>[16]</sup>                     | 0 <sup>[17]</sup>                     |
| Units: participants         |                                       |                                       |                                       |                                       |

Notes:

[14] - Early termination of the study.

[15] - Early termination of the study.

[16] - Early termination of the study.

[17] - Early termination of the study.

|                             |                                       |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>     | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 0 <sup>[18]</sup>                     |  |  |  |
| Units: participants         |                                       |  |  |  |

Notes:

[18] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Overall Survival (OS)

|   |                                |
|---|--------------------------------|
| End point title   | Phase 1: Overall Survival (OS) |
| End point description:<br>The OS was defined from first study medication administration until death, according to RECIST 1.1. Due to the early termination of the study, survival analysis on OS was not performed. |                                |
| End point type  | Secondary                      |
| End point timeframe:<br>From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.   |                                |

|                             |                                       |                                       |                                       |                                       |
|-----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| <b>End point values</b>     | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
| Subject group type          | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed | 0 <sup>[19]</sup>                     | 0 <sup>[20]</sup>                     | 0 <sup>[21]</sup>                     | 0 <sup>[22]</sup>                     |
| Units: participants         |                                       |                                       |                                       |                                       |

Notes:

[19] - Early termination of the study.

[20] - Early termination of the study.

[21] - Early termination of the study.

[22] - Early termination of the study.

|                             |                                       |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| <b>End point values</b>     | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 0 <sup>[23]</sup>                     |  |  |  |
| Units: participants         |                                       |  |  |  |

Notes:

[23] - Early termination of the study.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Phase 1: Metabolic Tumor Response Using Positron Emission Tomography (PET) Response Criteria In Solid Tumors (PERCIST) Version 1.0 or Practical PERCIST

|   |   |
|---|---|
| End point title   | Phase 1: Metabolic Tumor Response Using Positron Emission Tomography (PET) Response Criteria In Solid Tumors (PERCIST) Version 1.0 or Practical PERCIST |
| End point description:<br>Tumor response assessments were planned to perform by the site investigator (local) for the phase 1 and dose escalation part and by independent reader (central) for the phase 2. All fluorine-18 fluorodeoxyglucose-PET images were used for the metabolic tumor response assessments as described in PERCIST version 1.0 by the Investigator and/or independent readers. Due to the early termination of the study, metabolic tumor response was not performed. |   |
| End point type  | Secondary   |
| End point timeframe:<br>From the start of the first study medication (Day 1) up to EOCT, maximum of 16 weeks.   |   |

|                                      |                      |  |  |  |
|--------------------------------------|----------------------|--|--|--|
| <b>End point values</b>              | All Participants     |  |  |  |
| Subject group type                   | Subject analysis set |  |  |  |
| Number of subjects analysed          | 0 <sup>[24]</sup>    |  |  |  |
| Units: not applicable                |                      |  |  |  |
| arithmetic mean (standard deviation) | ( )                  |  |  |  |

Notes:

[24] - Early termination of the study.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1: Tumor Marker Levels in Serum - Cancer Antigen 19-9

|                 |   |
|-----------------|---|
| End point title | Phase 1: Tumor Marker Levels in Serum - Cancer Antigen 19-9 |
|-----------------|---|

End point description:

Changes in tumor markers in serum relevant and specific to the underlying tumor disease was determined. Pharmacodynamic population included all participants who received at least 1 therapeutic dose and with available post-baseline pharmacodynamics/efficacy data. Here, n = number of participants analyzed at each specific time point, 99999 = no participants analyzed and 9999 = standard deviation cannot be calculated when only 1 participant analyzed.

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

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, EOCT (maximum of 16 weeks) and early withdrawal.

| <b>End point values</b>               | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type                    | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed           | 2                                     | 3                                     | 5                                     | 3                                     |
| Units: international units/milliliter |                                       |                                       |                                       |                                       |
| arithmetic mean (standard deviation)  |                                       |                                       |                                       |                                       |
| Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)      | 50019.00 (± 70683.81)                 | 13.00 (± 9999)                        | 20939.54 (± 46482.66)                 | 1455.50 (± 78.49)                     |
| Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)      | 66.00 (± 9999)                        | 456.33 (± 753.23)                     | 277.90 (± 239.71)                     | 18420.33 (± 27442.99)                 |
| EOCT (n= 1, 2, 1, 1, 1)               | 112.00 (± 9999)                       | 928.00 (± 1294.01)                    | 1166.90 (± 9999)                      | 3532.00 (± 9999)                      |
| Early withdrawal (n= 0, 0, 2, 1, 0)   | 99999 (± 99999)                       | 99999 (± 99999)                       | 64.90 (± 86.41)                       | 8398.00 (± 9999)                      |

| <b>End point values</b>     | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 1                                     |  |  |  |

|                                       |                 |  |  |  |
|---------------------------------------|-----------------|--|--|--|
| Units: international units/milliliter |                 |  |  |  |
| arithmetic mean (standard deviation)  |                 |  |  |  |
| Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)      | 314.70 (± 9999) |  |  |  |
| Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)      | 490.50 (± 9999) |  |  |  |
| EOCT (n= 1, 2, 1, 1, 1)               | 629.90 (± 9999) |  |  |  |
| Early withdrawal (n= 0, 0, 2, 1, 0)   | 99999 (± 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Phase 1: Tumor Marker Levels in Serum - Carcinoembryonic Antigen

|   |  |
|---|--|
| End point title   | Phase 1: Tumor Marker Levels in Serum - Carcinoembryonic Antigen |
| End point description:  |  |
| Changes in tumor markers in serum relevant and specific to the underlying tumor disease was determined. Pharmacodynamic population included all participants who received at least 1 therapeutic dose and with available post-baseline pharmacodynamics/efficacy data. Here, n = number of participants analyzed at each specific time point, 99999 = no participants analyzed and 9999 = standard deviation cannot be calculated when only 1 participant analyzed. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Cycle 1 Day 1, Cycle 2 Day 1, EOCT (maximum of 16 weeks) and early withdrawal.  |  |

| End point values                     | Cohort 1:<br>177Lu-3BP-227<br>2.5 GBq | Cohort 2:<br>177Lu-3BP-227<br>4.0 GBq | Cohort 3:<br>177Lu-3BP-227<br>5.5 GBq | Cohort 4:<br>177Lu-3BP-227<br>6.5 GBq |
|--------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|
| Subject group type                   | Reporting group                       | Reporting group                       | Reporting group                       | Reporting group                       |
| Number of subjects analysed          | 2                                     | 3                                     | 5                                     | 3                                     |
| Units: microgram per liter           |                                       |                                       |                                       |                                       |
| arithmetic mean (standard deviation) |                                       |                                       |                                       |                                       |
| Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)     | 857.95 (± 1209.22)                    | 117.40 (± 9999)                       | 112.38 (± 94.41)                      | 6.65 (± 7.14)                         |
| Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)     | 3.20 (± 9999)                         | 37.93 (± 41.01)                       | 210.97 (± 213.86)                     | 47.87 (± 62.85)                       |
| EOCT (n= 1, 2, 1, 1, 1)              | 4.30 (± 9999)                         | 75.50 (± 47.09)                       | 321.20 (± 9999)                       | 184.00 (± 9999)                       |
| Early withdrawal (n= 0, 0, 2, 1, 0)  | 99999 (± 99999)                       | 99999 (± 99999)                       | 53.75 (± 23.83)                       | 29.60 (± 9999)                        |

| End point values            | Cohort 5:<br>177Lu-3BP-227<br>7.5 GBq |  |  |  |
|-----------------------------|---------------------------------------|--|--|--|
| Subject group type          | Reporting group                       |  |  |  |
| Number of subjects analysed | 1                                     |  |  |  |



|                                      |                 |  |  |  |
|--------------------------------------|-----------------|--|--|--|
| Units: microgram per liter           |                 |  |  |  |
| arithmetic mean (standard deviation) |                 |  |  |  |
| Cycle 1 Day 1 (n= 2, 1, 5, 2, 1)     | 3.50 (± 9999)   |  |  |  |
| Cycle 2 Day 1 (n= 1, 3, 3, 3, 1)     | 4.60 (± 9999)   |  |  |  |
| EOCT (n= 1, 2, 1, 1, 1)              | 5.10 (± 9999)   |  |  |  |
| Early withdrawal (n= 0, 0, 2, 1, 0)  | 99999 (± 99999) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent AEs are reported for participants who received the therapeutic dose of 177Lu-32P-227 during the core trial (Cycle 1 Day 1 up to EOCT); maximum of 16 weeks.

Adverse event reporting additional description:

Safety population contained all participants who received at least 1 dose of study medication.

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

### Dictionary used

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

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

### Reporting groups

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Cohort 1: 177Lu-3BP-227 2.5 GBq |
|-----------------------|---------------------------------|

Reporting group description:

Participants received 177Lu-3BP-227 2.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Cohort 2: 177Lu-3BP-227 4.0 GBq |
|-----------------------|---------------------------------|

Reporting group description:

Participants received 177Lu-3BP-227 4.0 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|-----------------------|---------------------------------|

Reporting group description:

Participants received 177Lu-3BP-227 5.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Cohort 4: 177Lu-3BP-227 6.5 GBq |
|-----------------------|---------------------------------|

Reporting group description:

Participants received 177Lu-3BP-227 6.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

|                       |                                 |
|-----------------------|---------------------------------|
| Reporting group title | Cohort 5: 177Lu-3BP-227 7.5 GBq |
|-----------------------|---------------------------------|

Reporting group description:

Participants received 177Lu-3BP-227 7.5 GBq fractionated into 2 IV administrations separated by 4 to 5 weeks during the core trial period.

| Serious adverse events                            | Cohort 1: 177Lu-3BP-227 2.5 GBq | Cohort 2: 177Lu-3BP-227 4.0 GBq | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|---|---------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by serious adverse events |                                 |                                 |                                 |
| subjects affected / exposed                       | 2 / 2 (100.00%)                 | 2 / 3 (66.67%)                  | 5 / 5 (100.00%)                 |
| number of deaths (all causes)                     | 1                               | 0                               | 2                               |
| number of deaths resulting from adverse events    | 1                               | 0                               | 2                               |
| Injury, poisoning and procedural complications    |                                 |                                 |                                 |
| Subdural haematoma                                |                                 |                                 |                                 |
| subjects affected / exposed                       | 1 / 2 (50.00%)                  | 0 / 3 (0.00%)                   | 0 / 5 (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                           |
| Blood and lymphatic system disorders              |                                 |                                 |                                 |

|  |                |               |                |
|--|----------------|---------------|----------------|
| Anaemia  |                |               |                |
| subjects affected / exposed                          | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 2 / 5 (40.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 4          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 0          |
| General disorders and administration site conditions |                |               |                |
| Disease progression                                  |                |               |                |
| subjects affected / exposed                          | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 3 / 5 (60.00%) |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0         | 0 / 3          |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0         | 0 / 2          |
| General physical health deterioration                |                |               |                |
| subjects affected / exposed                          | 1 / 2 (50.00%) | 0 / 3 (0.00%) | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0         | 0 / 1          |
| deaths causally related to treatment / all           | 0 / 1          | 0 / 0         | 0 / 0          |
| Immune system disorders                              |                |               |                |
| Drug hypersensitivity                                |                |               |                |
| subjects affected / exposed                          | 1 / 2 (50.00%) | 0 / 3 (0.00%) | 0 / 5 (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                           |                |               |                |
| Abdominal pain                                       |                |               |                |
| subjects affected / exposed                          | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 5 (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          |
| Constipation   |                |               |                |
| subjects affected / exposed                          | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 5 (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          |
| Enterocolitis  |                |               |                |
| subjects affected / exposed                          | 0 / 2 (0.00%)  | 0 / 3 (0.00%) | 0 / 5 (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          |
| Large intestinal obstruction                         |                |               |                |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Nausea  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 5 (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          |
| Oesophageal varices haemorrhage                 |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Small intestinal obstruction                    |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 5 (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          |
| Subileus  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Vomiting  |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 5 (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 |               |                |                |
| Pulmonary embolism                              |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                     |               |                |                |
| Acute kidney injury                             |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          | 0 / 0          |

|   |               |               |               |
|---|---------------|---------------|---------------|
| Musculoskeletal and connective tissue disorders |               |               |               |
| Back pain                                       |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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                     |               |               |               |
| Hepatic infection                               |               |               |               |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%) | 0 / 5 (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>                        | Cohort 4: 177Lu-3BP-227 6.5 GBq | Cohort 5: 177Lu-3BP-227 7.5 GBq |  |
| Total subjects affected by serious adverse events    |                                 |                                 |  |
| subjects affected / exposed                          | 3 / 3 (100.00%)                 | 0 / 1 (0.00%)                   |  |
| number of deaths (all causes)                        | 0                               | 0                               |  |
| number of deaths resulting from adverse events       | 0                               | 0                               |  |
| Injury, poisoning and procedural complications       |                                 |                                 |  |
| Subdural haematoma                                   |                                 |                                 |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)                   | 0 / 1 (0.00%)                   |  |
| occurrences causally related to treatment / all      | 0 / 0                           | 0 / 0                           |  |
| deaths causally related to treatment / all           | 0 / 0                           | 0 / 0                           |  |
| Blood and lymphatic system disorders                 |                                 |                                 |  |
| Anaemia  |                                 |                                 |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)                   | 0 / 1 (0.00%)                   |  |
| occurrences causally related to treatment / all      | 0 / 0                           | 0 / 0                           |  |
| deaths causally related to treatment / all           | 0 / 0                           | 0 / 0                           |  |
| General disorders and administration site conditions |                                 |                                 |  |
| Disease progression                                  |                                 |                                 |  |
| subjects affected / exposed                          | 0 / 3 (0.00%)                   | 0 / 1 (0.00%)                   |  |
| occurrences causally related to treatment / all      | 0 / 0                           | 0 / 0                           |  |
| deaths causally related to treatment / all           | 0 / 0                           | 0 / 0                           |  |
| General physical health deterioration                |                                 |                                 |  |
| subjects affected / exposed                          | 1 / 3 (33.33%)                  | 0 / 1 (0.00%)                   |  |
| occurrences causally related to treatment / all      | 0 / 1                           | 0 / 0                           |  |
| deaths causally related to treatment / all           | 0 / 0                           | 0 / 0                           |  |

|   |                |               |  |
|---|----------------|---------------|--|
| Immune system disorders                         |                |               |  |
| Drug hypersensitivity                           |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Gastrointestinal disorders                      |                |               |  |
| Abdominal pain                                  |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Constipation                                    |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Enterocolitis                                   |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Large intestinal obstruction                    |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Nausea  |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Oesophageal varices haemorrhage                 |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Small intestinal obstruction                    |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |

|   |                |               |  |
|---|----------------|---------------|--|
| Subileus  |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Vomiting  |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |                |               |  |
| Pulmonary embolism                              |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Renal and urinary disorders                     |                |               |  |
| Acute kidney injury                             |                |               |  |
| subjects affected / exposed                     | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Musculoskeletal and connective tissue disorders |                |               |  |
| Back pain                                       |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Infections and infestations                     |                |               |  |
| Hepatic infection                               |                |               |  |
| subjects affected / exposed                     | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |

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

| <b>Non-serious adverse events</b>                                   | Cohort 1: 177Lu-3BP-227 2.5 GBq | Cohort 2: 177Lu-3BP-227 4.0 GBq | Cohort 3: 177Lu-3BP-227 5.5 GBq |
|---|---------------------------------|---------------------------------|---------------------------------|
| Total subjects affected by non-serious adverse events               |                                 |                                 |                                 |
| subjects affected / exposed   | 2 / 2 (100.00%)                 | 3 / 3 (100.00%)                 | 5 / 5 (100.00%)                 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |                                 |                                 |
| Cancer pain   |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 0 / 5 (0.00%)                   |
| occurrences (all)   | 0                               | 0                               | 0                               |
| Vascular disorders  |                                 |                                 |                                 |
| Deep vein thrombosis  |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 1 / 3 (33.33%)                  | 0 / 5 (0.00%)                   |
| occurrences (all)   | 0                               | 1                               | 0                               |
| Venous thrombosis   |                                 |                                 |                                 |
| subjects affected / exposed   | 1 / 2 (50.00%)                  | 0 / 3 (0.00%)                   | 0 / 5 (0.00%)                   |
| occurrences (all)   | 1                               | 0                               | 0                               |
| General disorders and administration site conditions                |                                 |                                 |                                 |
| Asthenia  |                                 |                                 |                                 |
| subjects affected / exposed   | 1 / 2 (50.00%)                  | 0 / 3 (0.00%)                   | 1 / 5 (20.00%)                  |
| occurrences (all)   | 1                               | 0                               | 2                               |
| Chest pain  |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 1 / 5 (20.00%)                  |
| occurrences (all)   | 0                               | 0                               | 1                               |
| Fatigue   |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 1 / 3 (33.33%)                  | 2 / 5 (40.00%)                  |
| occurrences (all)   | 0                               | 1                               | 2                               |
| General physical health deterioration                               |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 2 / 5 (40.00%)                  |
| occurrences (all)   | 0                               | 0                               | 2                               |
| Non-cardiac chest pain  |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 0 / 5 (0.00%)                   |
| occurrences (all)   | 0                               | 0                               | 0                               |
| Oedema peripheral   |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 1 / 5 (20.00%)                  |
| occurrences (all)   | 0                               | 0                               | 1                               |
| Pyrexia   |                                 |                                 |                                 |
| subjects affected / exposed   | 0 / 2 (0.00%)                   | 0 / 3 (0.00%)                   | 1 / 5 (20.00%)                  |
| occurrences (all)   | 0                               | 0                               | 1                               |



|   |                |                |                |
|---|----------------|----------------|----------------|
| Respiratory, thoracic and mediastinal disorders |                |                |                |
| Dyspnoea  |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 0              | 0              |
| Psychiatric disorders                           |                |                |                |
| Anxiety   |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 1              | 0              | 1              |
| Illusion  |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0              | 0              | 1              |
| Sleep disorder                                  |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 2 / 5 (40.00%) |
| occurrences (all)                               | 0              | 0              | 2              |
| Investigations                                  |                |                |                |
| Aspartate aminotransferase increased            |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0              | 1              | 0              |
| Blood alkaline phosphatase increased            |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 2 / 3 (66.67%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1              | 4              | 0              |
| Blood bicarbonate decreased                     |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Blood bilirubin increased                       |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1              | 0              | 0              |
| Blood cholesterol increased                     |                |                |                |
| subjects affected / exposed                     | 1 / 2 (50.00%) | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)                               | 1              | 1              | 0              |
| Blood creatinine increased                      |                |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0              | 0              | 3              |
| Blood lactate dehydrogenase increased           |                |                |                |

|                                     |                |                |                |
|-------------------------------------|----------------|----------------|----------------|
| subjects affected / exposed         | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)                   | 0              | 1              | 0              |
| Blood urea increased                |                |                |                |
| subjects affected / exposed         | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                   | 0              | 0              | 3              |
| C-reactive protein increased        |                |                |                |
| subjects affected / exposed         | 0 / 2 (0.00%)  | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                   | 0              | 0              | 1              |
| Gamma-glutamyltransferase increased |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 2 / 3 (66.67%) | 0 / 5 (0.00%)  |
| occurrences (all)                   | 2              | 4              | 0              |
| Haematocrit decreased               |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                   | 2              | 0              | 0              |
| Lymphocyte count decreased          |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 2 / 3 (66.67%) | 1 / 5 (20.00%) |
| occurrences (all)                   | 2              | 7              | 1              |
| Neutrophil count decreased          |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                   | 1              | 0              | 1              |
| Platelet count decreased            |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 1 / 3 (33.33%) | 1 / 5 (20.00%) |
| occurrences (all)                   | 1              | 1              | 1              |
| Protein total increased             |                |                |                |
| subjects affected / exposed         | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)                   | 0              | 1              | 0              |
| Red blood cell count decreased      |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                   | 2              | 0              | 0              |
| Weight decreased                    |                |                |                |
| subjects affected / exposed         | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 4 / 5 (80.00%) |
| occurrences (all)                   | 0              | 1              | 5              |
| White blood cell count decreased    |                |                |                |
| subjects affected / exposed         | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                   | 4              | 0              | 1              |

|   |                     |                     |                     |
|---|---------------------|---------------------|---------------------|
| Injury, poisoning and procedural complications<br>Product prescribing error<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)  | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 2 (50.00%)<br>1 | 2 / 3 (66.67%)<br>4 | 3 / 5 (60.00%)<br>6 |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 2 (50.00%)<br>1 | 1 / 3 (33.33%)<br>1 | 2 / 5 (40.00%)<br>3 |
| Anal haemorrhage<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Ascites<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 2 / 5 (40.00%)<br>2 |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Haemorrhoids  |                     |                     |                     |

|  |                     |                     |                     |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 2 / 5 (40.00%)<br>2 |
| Ileus<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Small intestinal obstruction<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 | 2 / 5 (40.00%)<br>3 |
| Hepatobiliary disorders<br>Cholestasis<br>subjects affected / exposed<br>occurrences (all)                 | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Jaundice<br>subjects affected / exposed<br>occurrences (all)   | 1 / 2 (50.00%)<br>1 | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Skin and subcutaneous tissue disorders<br>Pain of skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 2 (0.00%)<br>0  | 1 / 3 (33.33%)<br>1 | 0 / 5 (0.00%)<br>0  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Renal and urinary disorders<br>Acute kidney injury<br>subjects affected / exposed<br>occurrences (all)     | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 1 / 5 (20.00%)<br>1 |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 2 (0.00%)<br>0  | 0 / 3 (0.00%)<br>0  | 0 / 5 (0.00%)<br>0  |
| Pollakiuria  |                     |                     |                     |

|   |               |                |                |
|---|---------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Proteinuria                                     |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Musculoskeletal and connective tissue disorders |               |                |                |
| Arthralgia                                      |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 2 / 5 (40.00%) |
| occurrences (all)                               | 0             | 0              | 2              |
| Back pain                                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 1 / 3 (33.33%) | 2 / 5 (40.00%) |
| occurrences (all)                               | 0             | 1              | 3              |
| Musculoskeletal stiffness                       |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Myalgia   |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Pain in extremity                               |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Polyarthrititis                                 |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)                               | 0             | 0              | 1              |
| Infections and infestations                     |               |                |                |
| Oral candidiasis                                |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Urinary tract infection                         |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)                               | 0             | 0              | 0              |
| Metabolism and nutrition disorders              |               |                |                |
| Decreased appetite                              |               |                |                |
| subjects affected / exposed                     | 0 / 2 (0.00%) | 0 / 3 (0.00%)  | 2 / 5 (40.00%) |
| occurrences (all)                               | 0             | 0              | 2              |
| Hypercalcaemia                                  |               |                |                |

|                             |                |                |                |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 3              | 0              |
| Hyperglycaemia              |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)           | 2              | 0              | 1              |
| Hyperkalaemia               |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 4 / 5 (80.00%) |
| occurrences (all)           | 0              | 1              | 8              |
| Hypernatraemia              |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 1              | 0              |
| Hypertriglyceridaemia       |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 1              | 0              |
| Hyperuricaemia              |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 1 / 5 (20.00%) |
| occurrences (all)           | 0              | 1              | 2              |
| Hypoalbuminaemia            |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 2              | 0              |
| Hypocalcaemia               |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 0 / 5 (0.00%)  |
| occurrences (all)           | 1              | 0              | 0              |
| Hypoglycaemia               |                |                |                |
| subjects affected / exposed | 0 / 2 (0.00%)  | 1 / 3 (33.33%) | 0 / 5 (0.00%)  |
| occurrences (all)           | 0              | 2              | 0              |
| Hypokalaemia                |                |                |                |
| subjects affected / exposed | 1 / 2 (50.00%) | 0 / 3 (0.00%)  | 1 / 5 (20.00%) |
| occurrences (all)           | 1              | 0              | 3              |

| Non-serious adverse events  | Cohort 4: 177Lu-3BP-227 6.5 GBq | Cohort 5: 177Lu-3BP-227 7.5 GBq |  |
|---|---------------------------------|---------------------------------|--|
| Total subjects affected by non-serious adverse events               |                                 |                                 |  |
| subjects affected / exposed   | 3 / 3 (100.00%)                 | 0 / 1 (0.00%)                   |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                 |                                 |  |

|   |                     |                    |  |
|---|---------------------|--------------------|--|
| Cancer pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Vascular disorders<br>Deep vein thrombosis<br>subjects affected / exposed<br>occurrences (all)                          | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Venous thrombosis<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| General physical health deterioration<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Non-cardiac chest pain<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)      | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |

|                                       |               |               |  |
|---------------------------------------|---------------|---------------|--|
| Psychiatric disorders                 |               |               |  |
| Anxiety                               |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Illusion                              |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Sleep disorder                        |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Investigations                        |               |               |  |
| Aspartate aminotransferase increased  |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood alkaline phosphatase increased  |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood bicarbonate decreased           |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood bilirubin increased             |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood cholesterol increased           |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood creatinine increased            |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood lactate dehydrogenase increased |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| Blood urea increased                  |               |               |  |
| subjects affected / exposed           | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                     | 0             | 0             |  |
| C-reactive protein increased          |               |               |  |



|  |               |               |  |
|--|---------------|---------------|--|
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Gamma-glutamyltransferase increased            |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Haematocrit decreased                          |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Lymphocyte count decreased                     |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Neutrophil count decreased                     |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Platelet count decreased                       |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Protein total increased                        |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Red blood cell count decreased                 |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Weight decreased                               |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| White blood cell count decreased               |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Injury, poisoning and procedural complications |               |               |  |
| Product prescribing error                      |               |               |  |
| subjects affected / exposed                    | 0 / 3 (0.00%) | 0 / 1 (0.00%) |  |
| occurrences (all)                              | 0             | 0             |  |
| Nervous system disorders                       |               |               |  |

|  |                     |                    |  |
|--|---------------------|--------------------|--|
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)    | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Gastrointestinal disorders<br>Abdominal discomfort<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)                                     | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Anal haemorrhage<br>subjects affected / exposed<br>occurrences (all)                                   | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Ascites<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Haemorrhoids<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Ileus<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Nausea   |                     |                    |  |

|  |                     |                    |  |
|--|---------------------|--------------------|--|
| subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Small intestinal obstruction<br>subjects affected / exposed<br>occurrences (all)                           | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)   | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Hepatobiliary disorders<br>Cholestasis<br>subjects affected / exposed<br>occurrences (all)                 | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Jaundice<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Skin and subcutaneous tissue disorders<br>Pain of skin<br>subjects affected / exposed<br>occurrences (all) | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)   | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Renal and urinary disorders<br>Acute kidney injury<br>subjects affected / exposed<br>occurrences (all)     | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Dysuria<br>subjects affected / exposed<br>occurrences (all)  | 1 / 3 (33.33%)<br>1 | 0 / 1 (0.00%)<br>0 |  |
| Pollakiuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Proteinuria<br>subjects affected / exposed<br>occurrences (all)  | 0 / 3 (0.00%)<br>0  | 0 / 1 (0.00%)<br>0 |  |
| Musculoskeletal and connective tissue disorders  |                     |                    |  |

|                                    |                |               |  |
|------------------------------------|----------------|---------------|--|
| Arthralgia                         |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Back pain                          |                |               |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 1              | 0             |  |
| Musculoskeletal stiffness          |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Myalgia                            |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Pain in extremity                  |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Polyarthrititis                    |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Infections and infestations        |                |               |  |
| Oral candidiasis                   |                |               |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 1              | 0             |  |
| Urinary tract infection            |                |               |  |
| subjects affected / exposed        | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 1              | 0             |  |
| Metabolism and nutrition disorders |                |               |  |
| Decreased appetite                 |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Hypercalcaemia                     |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Hyperglycaemia                     |                |               |  |
| subjects affected / exposed        | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)                  | 0              | 0             |  |
| Hyperkalaemia                      |                |               |  |

|                             |                |               |  |
|-----------------------------|----------------|---------------|--|
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypernatraemia              |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypertriglyceridaemia       |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hyperuricaemia              |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypoalbuminaemia            |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypocalcaemia               |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypoglycaemia               |                |               |  |
| subjects affected / exposed | 0 / 3 (0.00%)  | 0 / 1 (0.00%) |  |
| occurrences (all)           | 0              | 0             |  |
| Hypokalaemia                |                |               |  |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 1 (0.00%) |  |
| occurrences (all)           | 1              | 0             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 16 October 2017  | The protocol was amended to update tumor biopsy inclusion criteria as per review by the Ethical Committee in France.   |
| 09 November 2017 | The protocol was amended to incorporate changes to inclusion criteria, dose escalation part, physical examination and electrocardiogram assessments as per review by the Health Authorities in France.   |
| 06 December 2017 | The protocol was amended to include Ewing sarcoma as an additional indication in the phase 1/2 study and to provide updated information regarding the study medication.  |
| 02 March 2018    | The protocol was amended to give precision on the calculation of the tumor growth rate, information about drug-drug interactions, clarification of discontinuation process, information about infusion rate in response to AEs and increase time for use of contraception for females in the inclusion criteria from 30 days to 6 months, as well as information about spillages.  |
| 17 July 2018     | The protocol was amended to improve the determination of the biokinetics of <sup>177</sup> Lu-3BP-227 and perform an absolute quantification of radioactivity in target organs. Whole body scans (planar scintigraphy) were added to single photon emission computed tomography during treatment period. Whole body scans would allow the calculation of whole-body time-integrated activity coefficient ("residence time") that was needed for dosimetry analysis, as it accounts for nonspecific activity in the body. Inclusion criterion was updated to enable the recruitment of participants who did not have a compelling standard-of-care option.  |
| 20 June 2019     | <p>The protocol was amended to update personnel (the sponsor-authorized protocol approver and sponsor medical monitor), to update the background information, especially new nonclinical toxicology data, to update the number of participants receiving screening and therapeutic dose, to remove tumor growth rate and add genomic alterations in circulating cell-free DNA and gene mutation status as exploratory objectives and endpoints, to change pharmacokinetic timepoints to improve the clinical feasibility, to specify the biopsy conditions and put them as optional assessments, to remove tumor markers assessments for gastric cancer (serum cancer antigen 72-4) and squamous-cell carcinoma of head and neck (tissue polypeptide antigen), to refine the exclusion criteria regarding body weight, to clarify discontinuation rules, to clarify the duration of the safety follow-up period after the study medication screening dose administration and the reporting of AE collection after the last study medication administration, to specify that death due to disease progression will be reported as an SAE, to specify details on the preparation of the clinical study report, and to add schedule of assessments for screen failure participants. In addition, the recording of safety laboratory test results was changed from recording "any AEs according to National Cancer Institute-CTCAE" to "abnormalities in laboratory test values should only be reported as AEs if any of the following apply:</p> <ul style="list-style-type: none"><li>• They resulted in a change in study medication schedule of administration (change in dosage, delay in administration, study medication discontinuation).</li><li>• They required intervention or a diagnosis evaluation to assess the risk to the participant.</li><li>• They were considered as clinically significant by the Investigator, or the laboratory test abnormality suggested a disease and/or organ toxicity that was new or had worsened from baseline based on sponsor review.</li></ul> |

|              |  |
|--------------|--|
| 12 June 2020 | <p>The protocol was amended to update the following:</p> <ul style="list-style-type: none"> <li>• Clarify the inclusion criteria for participant selection as follows: <ul style="list-style-type: none"> <li>- To clearly state nonresectable locally advanced disease.</li> <li>- To clearly state that no further suitable treatment options were available for participants eligible for the study.</li> </ul> </li> <li>• Allow participants screened and found positive for NTSR1 in the 111In-IPN01087 phase 1 diagnostic study to take part in this study without having the diagnostic dose of 177Lu-3BP-227 during the Screening phase.</li> <li>• Extend the long-term follow-up period from 2 years to a maximum of 5 years or until lost to follow-up, withdrawal of consent or death, whichever occurred first.</li> <li>• Revise the DLT criteria to adequately describe the grading as stated in the CTCAE v5.0 dictionary.</li> <li>• Revise the participant discontinuation rules so if there were life-threatening toxicities outside of the DLT period, treatment was discontinued.</li> <li>• Optimize the dosimetry evaluation through adaptation of the imaging schedule.</li> <li>• Clarify biopsy collection.</li> <li>• Clarify about COVID-19 added following the recent pandemic.</li> <li>• Remove the exploratory endpoint of DNA-double strand breaks in peripheral lymphocytes.</li> </ul> |
|--------------|--|

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

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

The sponsor terminated the study early and phase 1 dose expansion and phase 2 were not started. The decision to terminate the study was not due to any safety or tolerability concern, or any event associated with the use of 177Lu-3BP-227.

Notes: