# A Study of 177Lu-FAP-2286 in Advanced Solid Tumors

Last Update: May 02, 2025
LuMIERE: A Phase 1/2, Multicenter, Open-label, Non-randomized Study to Investigate Safety and Tolerability, Pharmacokinetics, Dosimetry, and Preliminary Activity of 177Lu-FAP-2286 in Patients With an Advanced Solid Tumor
ClinicalTrials.gov Identifier:
NCT04939610
Novartis Reference Number:CO-2286-114
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All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

## Study Description

Fibroblast activation protein (FAP) is a cell surface protein that is highly expressed on the surface of cancer-associated fibroblasts (CAFs) present in the tumor microenvironment of most epithelial cancers, whereas limited expression of FAP is observed in normal tissues. In some cancers of mesenchymal origin, notably sarcoma and mesothelioma, FAP expression has also been observed on the tumor cells themselves. Given the restricted expression profile, FAP is a promising target for peptide-targeted radionuclide imaging and therapeutic agents.

Phase 1 of this study is designed to evaluate the safety and establish the recommended intravenous (IV) Phase 2 dose (RP2D) for \[177Lu\]Lu FAP 2286 monotherapy in participants with FAP expressing solid tumors.

Phase 2 is designed to evaluate the safety and efficacy of \[177Lu\]Lu FAP 2286 as monotherapy in participants with pancreatic ductal adenocarcinoma (PDAC), non-small cell lung cancer (NSCLC), and breast cancer (BC) and in combination with chemotherapy in participants with untreated PDAC or relapsed NSCLC.

Participants in both Phase 1 and 2 will be selected for treatment with \[177Lu\]Lu FAP 2286 based on \[68Ga\]Ga FAP 2286 imaging for determining tumor FAP expression. Screening Period:

All participants will undergo screening assessments including disease assessments per CT or MRI per RECIST v1.1 criteria prior to administration of \[68Ga\]Ga FAP 2286. Each participant must provide informed consent and agree to provide an archival tumor tissue sample, if available, and blood samples for biomarker assessment. Participants must meet all entry criteria as specified in the protocol.

In Phase 1 only, participants will also undergo FDG-PET imaging. In the Phase 2 part, \[177Lu\]Lu FAP 2286 will be investigated in monotherapy and in combination with chemotherapy. All participants in the combination group may begin chemotherapy prior to \[177Lu\]Lu FAP 2286.

Participants meeting entry criteria will be enrolled and participants who have not had prior PET/CT imaging

with \[68Ga\]Ga FAP 2286 in the previous 3 months (applicable only to Phase 1) will undergo PET imaging with \[68Ga\]Ga FAP prior to initiating treatment with \[177Lu\]Lu FAP 2286. Participants must have a positive \[68Ga\]Ga FAP PET/CT scan, as described in the criteria for continuation to \[177Lu\]Lu FAP 2286 therapy, in order to be treated with \[177Lu\]Lu FAP 2286.

Treatment Period:

A single IV dose of \[177Lu\]Lu FAP 2286 will be initially administered every 6 weeks (window of - 1 to + 7 days) up to a maximum of 6 doses in Phase 1. In Phase 2, \[177Lu\]Lu FAP 2286 will be administered every 4 weeks (28 days ± 3 days).

All participants will be monitored for safety throughout the Treatment Period. All participants will be assessed for disease status per RECIST v1.1 every 6 weeks (42 days). Participants will receive \[177Lu\]Lu FAP 2286 until the maximum doses allowed are administered, confirmed radiographic disease progression assessed by investigator based on RECIST v1.1 criteria, unequivocal clinical disease progression, unacceptable toxicity or inability to tolerate further treatment, loss to follow-up, or withdrawal of consent.

Safety data will be periodically reviewed by the DCRC during dose escalation and by a Data Monitoring Committee (DMC) during dose expansion.

End of Treatment (EOT) Visit:

In Phase 1, participants will have an EOT Visit 6 to 8 weeks after the last dose of \[177Lu\]Lu FAP 2286 except in cases of participant death, loss to follow up, or withdrawal of consent for further follow up. Participants in Phase 2 will have an EOT visit within 28 days from the last dose of study treatment except in case of participant death, loss to follow-up, or withdrawal of consent for further follow-up.

Post treatment safety follow-up:

In Phase 2, after discontinuation of study treatment for any reason, all participants will have safety follow-up for 6 weeks (+/- 1 week) after their last study treatment administration, except in case of death, loss to follow-up or withdrawal of consent as per the schedule of assessments.

Long-term Follow-up (LFTU) Period:

Upon completion of the EOT Visit, participants will enter the LTFU Period. The LTFU Period will include safety, disease, and survival assessments, as applicable.

* Safety assessments will be performed every 12 weeks (+/- 1 week) for 2 years, then every 6 months until 5 years.
* Disease assessments will be performed for all participants who complete the EOT for a reason other than radiographic disease progression. Participants should continue to have tumor scans performed until radiographic disease progression, death, loss to follow-up, withdrawal from study, study closure or initiation of subsequent anticancer treatment.
* Survival assessments will be performed for all participants.

Condition
Solid Tumor
Phase
Phase1, Phase2
Overall Status
Recruiting

Number of Participants
222
Start Date
Jul 30, 2021
Completion Date
Jun 30, 2028
Gender
All
Age(s)
18 Years - (Adult, Older Adult)

# Interventions

Drug

### 177Lu-FAP-2286

Phase 1: Patients with positive uptake of 68Ga-FAP- 2286 will receive a fixed dose of 177Lu-FAP-2286 IV administered every 6 weeks for a maximum of 6 doses. Doses range between 3.7 and 9.25 GBq (100-250 mCi). Phase 2: Monotherapy: Patients with positive uptake of 68Ga FAP 2286 will receive a fixed dose of 177Lu FAP 2286 IV administered at the RP2D determined in Phase 1 dose escalation in every 4 weeks. Combination therapy: Patients with positive uptake of 68Ga FAP 2286 will receive 177Lu-FAP-2286 based on dose escalation (starting with dose level 1) followed by dose expansion at selected dose.
Drug

### 68Ga-FAP-2286

68Ga-FAP-2286 IV administered as imaging agent for PET scan.

# Eligibility Criteria

Inclusion Criteria:

Eligible participants must meet the following inclusion criteria. The criteria below apply to participants enrolling in Phase 1 and Phase 2, unless otherwise specified.

1. Have signed and dated an Institutional Review Board (IRB)/Independent Ethics Committee (IEC)-approved Informed Consent Form (ICF) prior to any study-specific evaluation.
2. Be ≥ 18 years of age at the time the ICF is signed.
3. Have consented to submission of fresh or archival tumor tissue, if available.
4. Have adequate organ function confirmed by the following laboratory values obtained within the Screening Period prior to administration of \[68Ga\]Ga FAP 2286 and prior to first cycle of chemotherapy in the combination groups:

a. Bone Marrow Function (independent of transfusion or growth factor support within 21 days prior to planned first administration of \[177Lu\]Lu FAP 2286): i. Absolute neutrophil count (ANC) ≥ 1.5 × 109/L; ii. Platelets \> 100 × 109/L; and iii.Hemoglobin ≥ 9 g/dL. b. Hepatic Function: i. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3 × institutional upper limit of normal (ULN); if liver metastases, then ≤ 5 × the institutional ULN; ii. Serum Bilirubin ≤ 1.5 × institutional ULN or if known Gilbert's syndrome then ≤ 3 ×

institutional ULN; iii. Serum albumin ≥ 30 g/L (3 g/dL) and iv. INR ≤ 1.5 x ULN and activated partial thromboplastin time (aPTT)≤1.5 x ULN. This applies to participants who are not receiving therapeutic anticoagulation, participants receiving therapeutic anticoagulation should be on a stable dose.

c. Renal Function: i. Estimated glomerular filtration rate (eGFR) ≥ 60 mL/min using the Cockcroft Gault formula.
5. Have an Eastern Oncology Group (ECOG) performance status of 0 or 1.
6. Have a life expectancy of ≥ 6 months.
7. Have measurable disease per RECIST v1.1 meeting the following criteria:

1. At least 1 lesion of ≥ 10 mm in the longest diameter for a non lymph node or ≥ 15 mm in the short axis diameter for a lymph node that is serially measurable according to RECIST v1.1 using conventional CT and/or MRI.

• Lesions that have had external beam radiotherapy or loco-regional therapies such as radiofrequency ablation must show subsequent evidence of substantial size increase to be deemed a target lesion.

For Phase 1 only:
8. Have a histologically and/or cytologically confirmed advanced/metastatic solid tumor not amenable to treatment with curative intent:

a. Tumor must be refractory to or have progressed following prior treatment and have no satisfactory alternative treatment options.

For Phase 2 only:
9. Have cytologically or histologically and radiologically confirmed recurrent or metastatic disease as outlined below:

a. Pancreatic Cancer monotherapy group: i. Pancreatic ductal adenocarcinoma (ductal adenocarcinoma and related subtypes eligible; endocrine and neuroendocrine tumors excluded) ii. Participants must have progressed after at least 1, but no more than two prior chemotherapy regimens for locally advanced unresectable or metastatic disease.

Criteria b through h removed during Protocol amendment 7. i. Pancreatic Cancer combination group (with mFOLFIRINOX) i. Pancreatic ductal adenocarcinoma (ductal adenocarcinoma and related subtypes eligible; endocrine and neuroendocrine tumors excluded); ii. Participants have not received prior systemic therapy for metastatic disease.

j. Non-small cell lung cancer monotherapy group i. Non-small cell lung cancer (adenocarcinoma and squamous eligible; endocrine, neuroendocrine and small cell tumors are excluded) ii. Participants must have progressed after at least 1 but not more than 2 prior systemic regimens including chemotherapy and immunotherapy, if eligible.

iii. Participants who have received adjuvant or neoadjuvant platinum-doublet chemotherapy (after surgery and/or radiation therapy) and an immune checkpoint inhibitor and developed recurrent or metastatic disease while on or within 12 months of completing therapy are eligible iv. Participants with recurrent disease \> 12 months after adjuvant or neoadjuvant platinum-based chemotherapy, who also subsequently progressed during or after a platinum-doublet regimen and an immune checkpoint inhibitor (given either together or sequentially to treat the recurrence), are eligible v. Participants must have received platinum-based chemotherapy for advanced or metastatic disease and immune checkpoint inhibitor either together (in the same line of treatment) or sequentially (two different lines of treatment) and then progressed.

k. Non small cell lung cancer combination group i. Non-small cell lung cancer (adenocarcinoma and squamous eligible; endocrine, neuroendocrine and small cell tumors are excluded) ii. Participants must have progressed after at least 1 but not more than 2 prior systemic regimens including chemotherapy and immunotherapy, if eligible.

iii. Participants who have received adjuvant or neoadjuvant platinum-doublet chemotherapy (after surgery and/or radiation therapy) and an immune checkpoint inhibitor and developed recurrent or metastatic disease while on or within 12 months of completing therapy are eligible iv. Participants with recurrent disease \> 12 months after adjuvant or neoadjuvant platinum-based chemotherapy, who also subsequently progressed during or after a platinum-doublet regimen and an immune checkpoint inhibitor (given either together or sequentially to treat the recurrence), are eligible v. Participants must not have received prior taxane therapy either as monotherapy or in combination.

l. Breast cancer monotherapy group i. HR positive HER2 negative

• Participant has a histologically and/or cytologically documented diagnosis of HR positive HER2 negative metastatic breast cancer (based on the most recently analyzed tissue sample tested by a local laboratory).
* Participants must have progressed on at least one line of hormone-based therapy (either alone or in combination) and at least one, but not more than two lines of chemotherapy (including cytotoxic, targeted and/or anti-drug conjugate therapies) for metastatic disease.

ii. HER2 positive

• Participant has a histologically and/or cytologically documented diagnosis of HER2 positive metastatic breast cancer (based on the most recently analyzed tissue sample tested by a local laboratory).

• Participant must have progressed on at least two lines of HER2 targeted therapy for metastatic disease.

iii. Triple negative breast cancer (TNBC)

• Participant has a histologically and/or cytologically documented diagnosis of TNBC (based on the most recently analyzed tissue sample tested by a local laboratory).
* Participants must have progressed on at least two lines of cytotoxic chemotherapy (including cytotoxic, anti-drug conjugate, targeted therapies and/or IO) for metastatic disease.

Key Exclusion Criteria:

Participants who meet any of the following criteria will be excluded from the study. The criteria below apply to participants enrolling in Phase 1 or Phase 2.

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1. Active malignancy except for the specific cancer under investigation in this study, ie, participant known to have potentially fatal cancer present for which he/she may be (but not necessarily) currently receiving treatment with the following exceptions:

1. History of second malignancy that has been successfully treated, with no evidence of active cancer for 3 years prior to enrollment;
2. Surgically cured low-risk tumors, such as early-stage cervical or endometrial cancer, any cancer in situ, or non-melanoma skin cancers; and
3. Prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen.

2. Symptomatic and/or untreated CNS metastases or leptomeningeal disease or with primary tumor of CNS origin.

a. Participants with asymptomatic, previously treated CNS metastases are eligible provided they have been clinically stable for at least 4 weeks and have completed RT\> 2 weeks prior to treatment. Participants may be on corticosteroids if on a stable dose equivalent to prednisone 10 mg daily or less.
3. Received anticancer treatment with chemotherapy, antibody therapy or other immunotherapy, gene therapy, vaccine therapy, angiogenesis inhibitors, or experimental drugs ≤ 14 days prior (≤ 28 days prior in case of checkpoint inhibitor therapy and other antibody therapies) to the administration of \[177Lu\]Lu FAP 2286.
4. Received prior radiopharmaceutical therapy (eg, radium 223 223Ra-dichloride, \[177Lu\]Lu-DOTA-TATE, \[177Lu\]Lu-prostate-specific membrane antigen (PSMA)-617, actinium 225 \[225Ac\]Ac PSMA-617, etc.) or prior EBRT to more than 25% of the bone marrow or received any prior EBRT directly to kidney, or received any EBRT within 2 weeks prior to administration of \[177Lu\]Lu FAP 2286.

* Prior administration of a radiopharmaceutical unless 10 or more half-lives have elapsed before injection/infusion of \[68Ga\]Ga-FAP-2286 or \[177Lu\]Lu FAP 2286.
5. Ongoing adverse effects from anticancer treatment NCI-CTCAE v5.0 (or higher) Grade 1, with the exception for alopecia and vitiligo.

Exclusion criteria 6 and 7 are removed with Protocol Amendment 7. 8. Impaired cardiac function or clinically significant cardiac diseases, including any of the following:

1. Clinically significant and/or uncontrolled cardiac disease such as congestive heart failure requiring treatment (New York Heart Association \> Class 2), uncontrolled hypertension, clinically significant arrhythmia, or congenital prolonged QT syndrome;
2. Corrected QT interval (Fridericia's formula) \> 450 msec for males or \> 470 msec for females at Screening; or
3. Acute coronary syndrome or acute myocardial infarction ≤ 6 months prior to administration of \[177Lu\]Lu FAP 2286.

9. Active severe urinary incontinence, severe voiding dysfunction, or urinary obstruction requiring an indwelling/condom catheter that, in the judgment of the investigator, could prevent adhering to radiation safety instructions.

10. Severe chronic or active HIV infection:

a. Participants on effective antiretroviral therapy with undetectable viral load within 6 months prior to the first dose of \[177Lu\]Lu FAP 2286 are eligible.

Exclusion criteria 11 and 12 are removed with Protocol Amendment 7. 13. Non-study-related minor surgical procedure ≤ 5 days, or major surgical procedure ≤ 21 days, prior to the administration of \[177Lu\]Lu FAP 2286; in all cases, the participant must be sufficiently recovered and stable before treatment administration.

14. The following are exclusion criteria, as applicable:

a. Female participants of childbearing potential: i. Refusal to use a highly effective method of contraception or to practice true abstinence during treatment and for 6 months following the last dose of investigational product; ii. Pregnant, suspected pregnancy, or breast feeding; iii. Planning on getting pregnant during treatment and for 6 months following the last dose of investigational product.

b. Male participants with female partners of childbearing potential: i. Refusal to use a highly effective method of contraception or to practice true abstinence during treatment and for 6 months following the last dose of

investigational product.

c. All male participants: i. Refusal to use condoms during sex. ii. Planning to make semen donations during treatment and for 6 months following the last dose of investigational product.

15. Significant weight loss (\> 10% of body weight) within 28 days prior to providing informed consent for this study.

16. Presence of any other condition that may increase the risk associated with study participation or interfere with the interpretation of study results, and, in the opinion of the investigator, would make the participant inappropriate for entry into the study.

17. Inability to complete the needed investigational and standard imaging examinations due to any reason (e.g., severe claustrophobia, inability to lie still for the entire imaging time).

18. Participants with known hypersensitivity to the active agent or excipients. 19. Severe chronic or active infections (including active tuberculosis, HBV, or HCV infection) requiring systemic antibacterial, antifungal or antiviral therapy within 2 weeks before enrollment.

Note: Antiviral therapy is permitted for participants with chronic HBV or HCV infection. Participants receiving antivirals at Screening should have been treated for \> 2 weeks before enrollment. Inactive hepatitis B surface antigen (HbsAg) carriers treated and stable hepatitis B participants (HBV DNA \< 500 IU/mL or \< 2500 copies/mL) can be enrolled. Participants with detectable hepatitis B surface antigen (HbsAg) or detectable HBV DNA should be managed per treatment guidelines. Participants positive for HCV antibody are eligible only if PCR is negative for HCV RNA.

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Recruiting

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**University of Texas MD Anderson Cancer Center**

Recruiting

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If the location of your choosing does not feature any contact detail, please reach out using the information below.

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