

SOFIE

From start to clinic

Fibroblast Activation Protein (FAP)- a target for Imaging and Therapy

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FAP (Fibroblast Activation Protein)

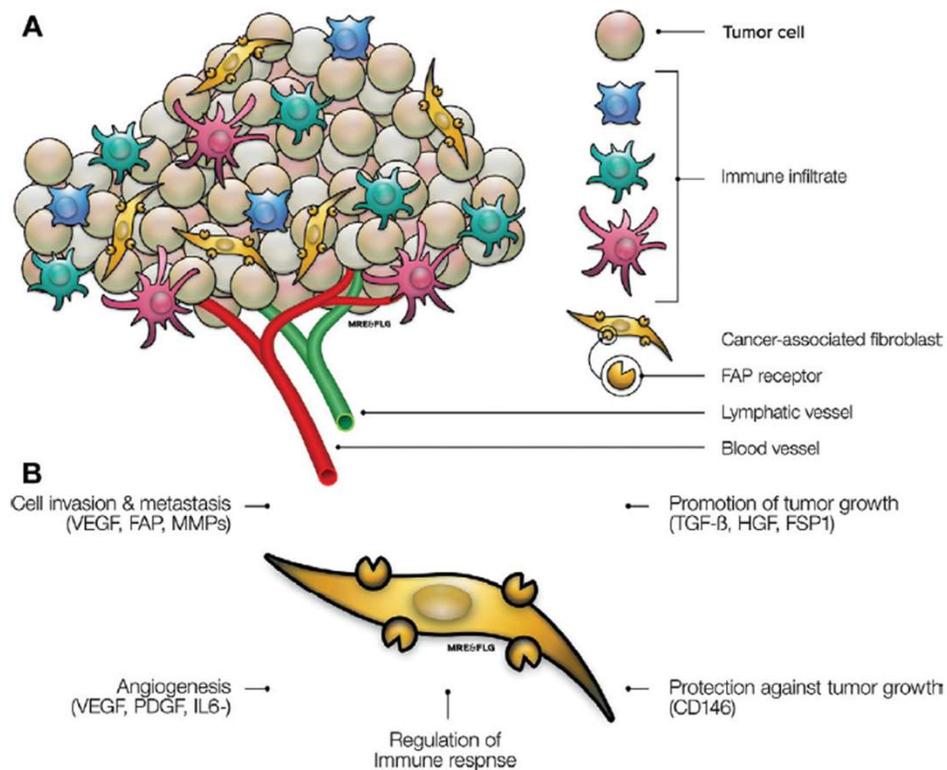
Activated Fibroblasts express high levels of FAP

Fibroblasts become activated during wound repair and regeneration. Malignant tumors are recognized as “wounds that do not heal”

Among all the stromal cells, **cancer-associated fibroblasts (CAFs)** are dominant populations in the tumor microenvironment

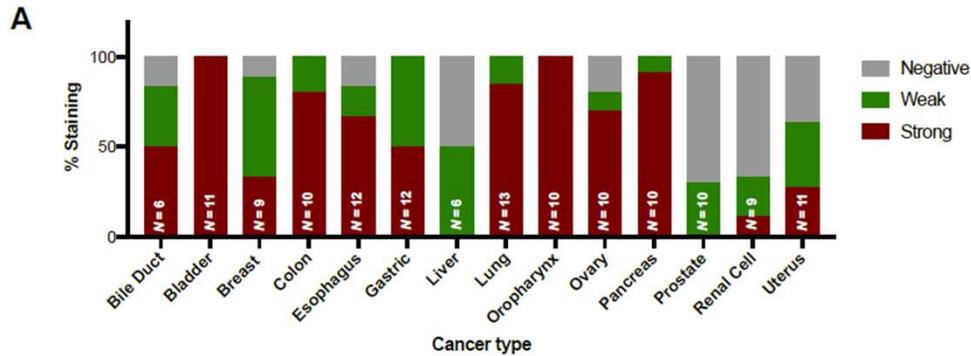
FAP is highly expressed on the surface of CAFs

FAP is a great target due to its overexpression in most of the cancer types (90%)

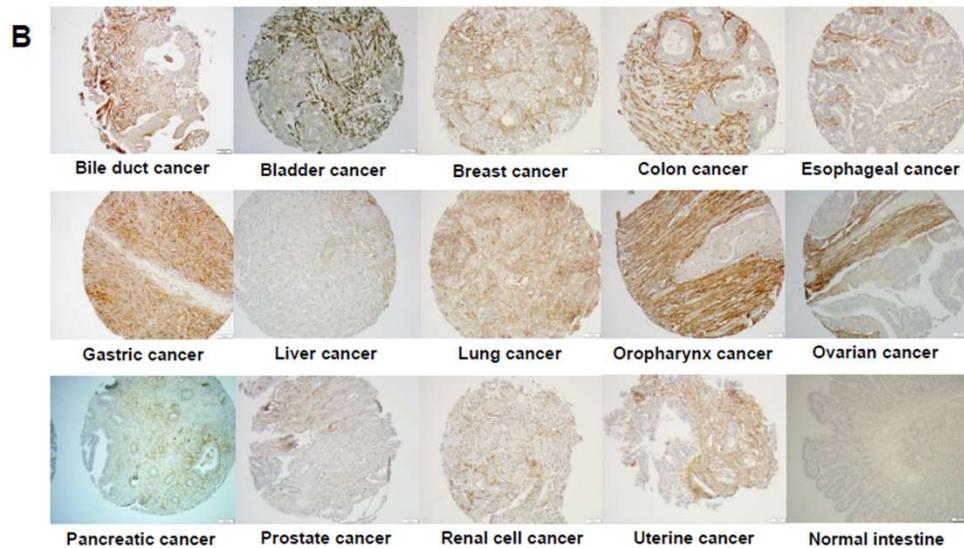


Mori Y, Dendl K, Cardinale J, Kratochwil C, Giesel FL, Haberkorn U. FAPI PET: Fibroblast Activation Protein Inhibitor Use in Oncologic and Nononcologic Disease. *Radiology*. 2023 Jan 3:220749. doi: 10.1148/radiol.220749. Epub ahead of print. PMID: 36594838.

FAP protein expression in oncology



- FAP is highly expressed in the microenvironment of an array of different cancers
- Sarcomas are one cancer group where FAP expression is detected in the tumor cells.



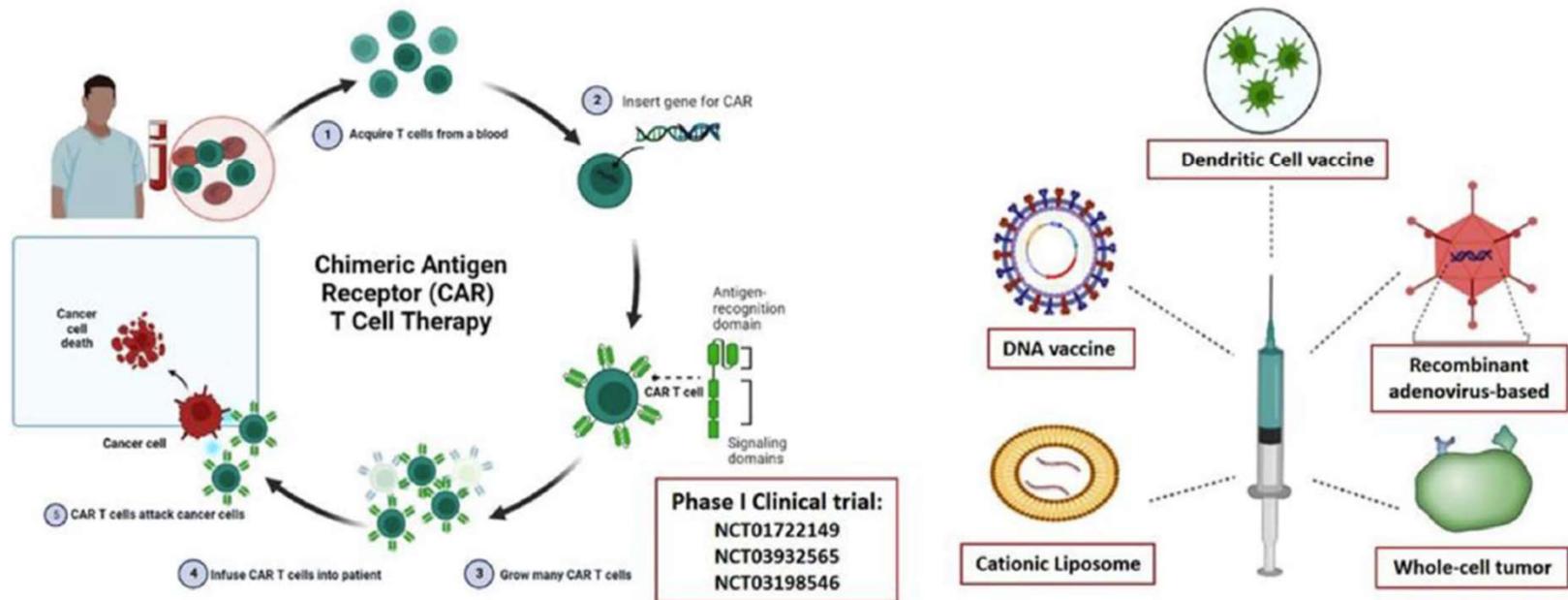
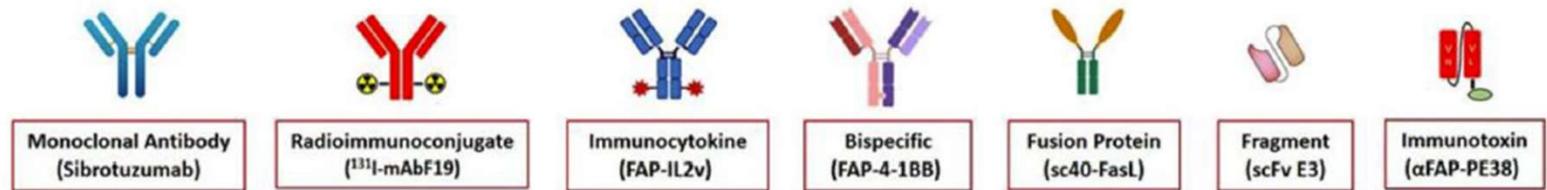
Note: FAP expression levels can vary based on sample size, sample location, sub-type of disease and stage of disease.

Mona et al. doi: 10.2967/jnumed.121.262426

FAP targeting approaches

- Small Molecule Inhibitors (Talabostat & Linagliptin)
- Pro-Drug (AVA-6000)
- **Immune therapy**

Shahvali et. al. 2023 <https://doi.org/10.1007/s13346-023-01308-9>



Active FAP targeting therapeutic trials (non RLT)

| NCT Number | Sponsor | Interventions | Conditions | Phase |
|-------------|--------------------------|--|--|-----------------|
| NCT04053283 | Akamis Bio | BIOLOGICAL: NG-641 | Metastatic Cancer Epithelial Tumor | Phase 1 |
| NCT04830592 | Akamis Bio | BIOLOGICAL: NG-641 BIOLOGICAL: Pembrolizumab | Squamous Cell Carcinoma of the Head and Neck | Phase 1 |
| NCT05043714 | Akamis Bio | BIOLOGICAL: NG-641 in combination with Nivolumab | Metastatic Cancer Epithelial Tumor | Phase 1 |
| NCT04826003 | Hoffmann-La Roche | DRUG: RO7122290 DRUG: Cibisatamab DRUG: Obinutuzumab | Metastatic Colorectal Cancer | Phase 1/Phase 2 |
| NCT04857138 | Hoffmann-La Roche | DRUG: RO7300490 DRUG: Atezolizumab | Solid Tumors | Phase 1 |
| NCT05098405 | Molecular Partners AG | DRUG: MP0317, a tri-specific fibroblast activation protein (FAP) x CD40 DARPIn [®] drug candidate | Advanced Malignant Solid Tumor | Phase 1 |
| NCT04969835 | Avacta Life Sciences Ltd | DRUG: AVA6000 | Pancreatic Cancer Colorectal Cancer Non-small Cell Lung Cancer Head and Neck Cancer Cancer of Unknown Primary Site Ovarian Cancer Breast Cancer Soft Tissue Sarcoma Bladder Cancer Oesophageal Cancer Prostate Cancer Biliary Tract Cancer | Phase 1 |

Data as of 7/12/2023 for "FAP" or "Fibroblast Activation Protein" and actively recruiting in clinicaltrials.gov



Radiopharmaceuticals targeting FAP

Theranostics: Recent Successes

Target: Somatostatin Receptor
Disease: Neuroendocrine Tumors
PET Imaging Probe is ^{68}Ga -DOTATATE
Treatment Probe is ^{177}Lu -DOTATATE

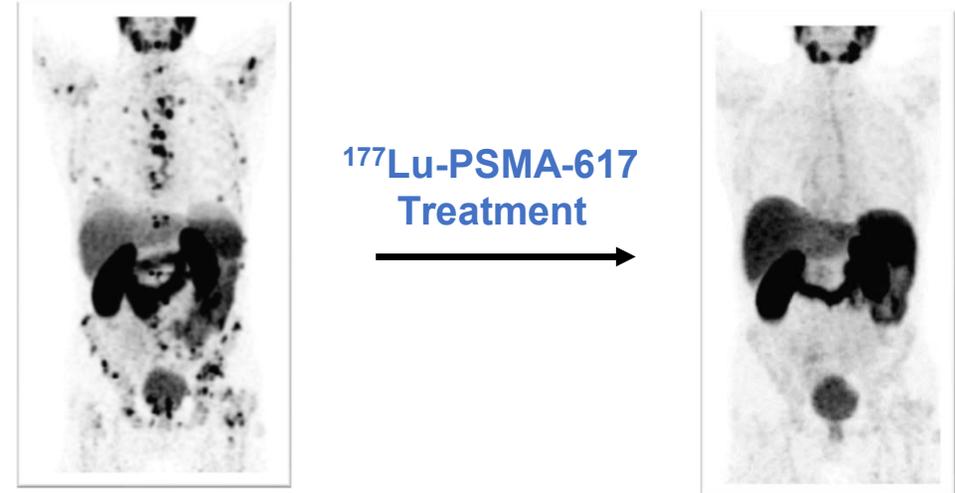


**BEFORE
TREATMENT**

**AFTER
TREATMENT**

F. Giesel (U of Heidelberg), K. Herrmann (U of Essen), W. Fendler (UCLA), J. Czernin (UCLA)

Target: PSMA
Disease: Castration Resistant Prostate Cancer
PET Imaging: ^{68}Ga -PSMA-11
Treatment: ^{177}Lu -PSMA-617



**BEFORE
TREATMENT**
PSA = 2,923 ng/ml

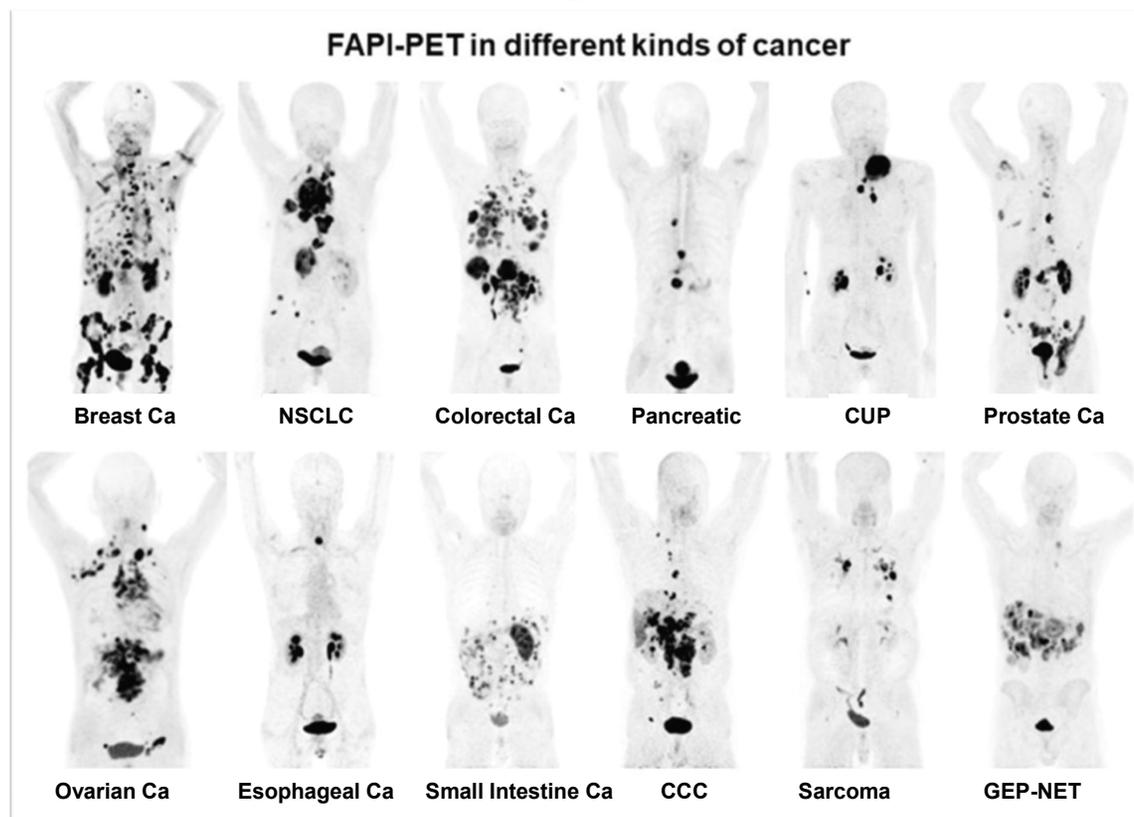
**AFTER
TREATMENT**
PSA < 0.1 ng/ml

F. Giesel (U of Heidelberg), K. Herrmann (U of Essen), W. Fendler (UCLA), J. Czernin (UCLA)

(Fibroblast Activation Protein Inhibitor)-**FAPI** family of compounds

SNMMI Image of the Year 2019

“A single radiotracer can identify nearly 30 types of cancer, allowing for new applications in noninvasive diagnosis, staging and treatment, according to research presented at the 2019 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI). This honor goes to a team of researchers at University Hospital Heidelberg, Germany, showcasing the efficacy of the FAPI radiotracer.”



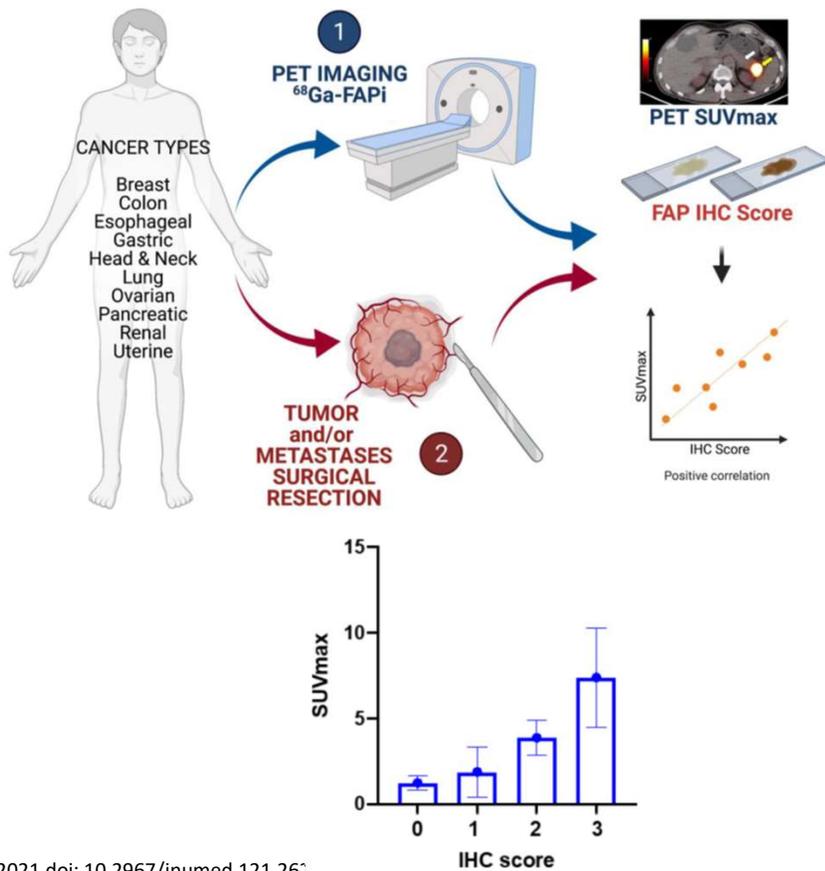
FAP targeting radioligands (with clinical data)

| Affiliation | Product | Diagnostic | Therapy | Clinical.Trials.gov |
|-----------------------|--------------------------|---|---|--|
| SOFIE | FAPI family of compounds | [⁶⁸ Ga]FAPI-46 [¹⁸ F]FAPI-74 | | NCT05262855 Phase 2 (PDAC) NCT05641896 Phase 2 (GI) |
| Heidelberg University | FAPI family of compounds | | FAPI-46 (alpha/beta) | |
| Novartis | FAP-2286 | [⁶⁸ Ga]FAP-2286 | [¹⁷⁷ Lu]FAP-2286 | NCT04939610 Phase 1-2 (Basket) |
| Point Biopharma | PNT6555 | [⁶⁸ Ga]PNT6555 | [¹⁷⁷ Lu]PNT6555 | NCT05432193 Phase 1 (Basket) |
| Yantai LNC Biotech | EB-FAPI/LNC1004 | | [¹⁷⁷ Lu]LNC1004 | |
| Philogen | OncoFAP | [⁶⁸ Ga]OncoFAP | [¹⁷⁷ Lu]OncoFAP | |
| 3BP | | 3BP-3940 | 3BP-3940 | |
| Ratio Therapeutics | RTX-1363S | [⁶⁴ Cu]RTX-1363S | | |
| | SA.FAPI | [⁶⁸ Ga]DOTAGA(SA.FAPI) (variations) | [¹⁷⁷ Lu]DOTAGA(SA.FAPI) (variations) | |

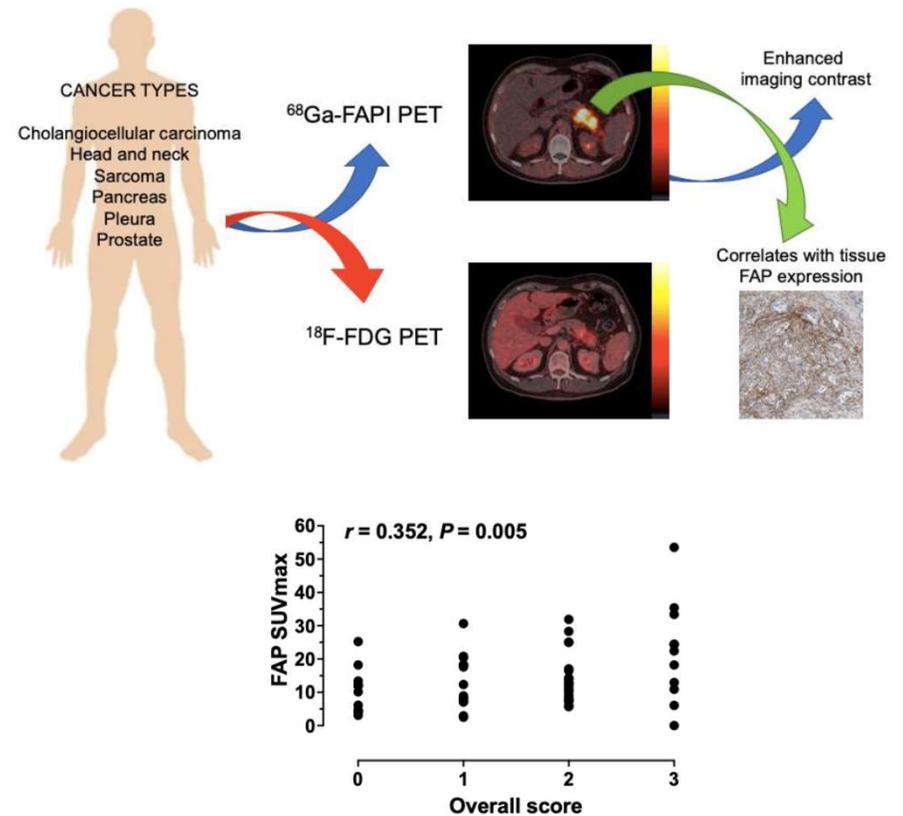
*Note: This represents industry FAP assets in clinical development (clinicaltrials.gov or other published data).
Not a comprehensive list of all FAP assets in pipeline*

FAP IHC and PET signal validation- 2 independent studies for [68Ga]FAPi-46

Correlation between FAP immunohistochemistry score and ⁶⁸Ga-FAPi-46 PET SUVs across cancer and non-cancer tissues



Fibroblast activation protein positron emission tomography and histopathology in a single-center database of 324 patients and 21 tumor entities



FAP Diagnostic

Stand-alone diagnostic

Companion diagnostic- FAP Biomarker

Oncology

Non-oncology

RLT

Non-RLT

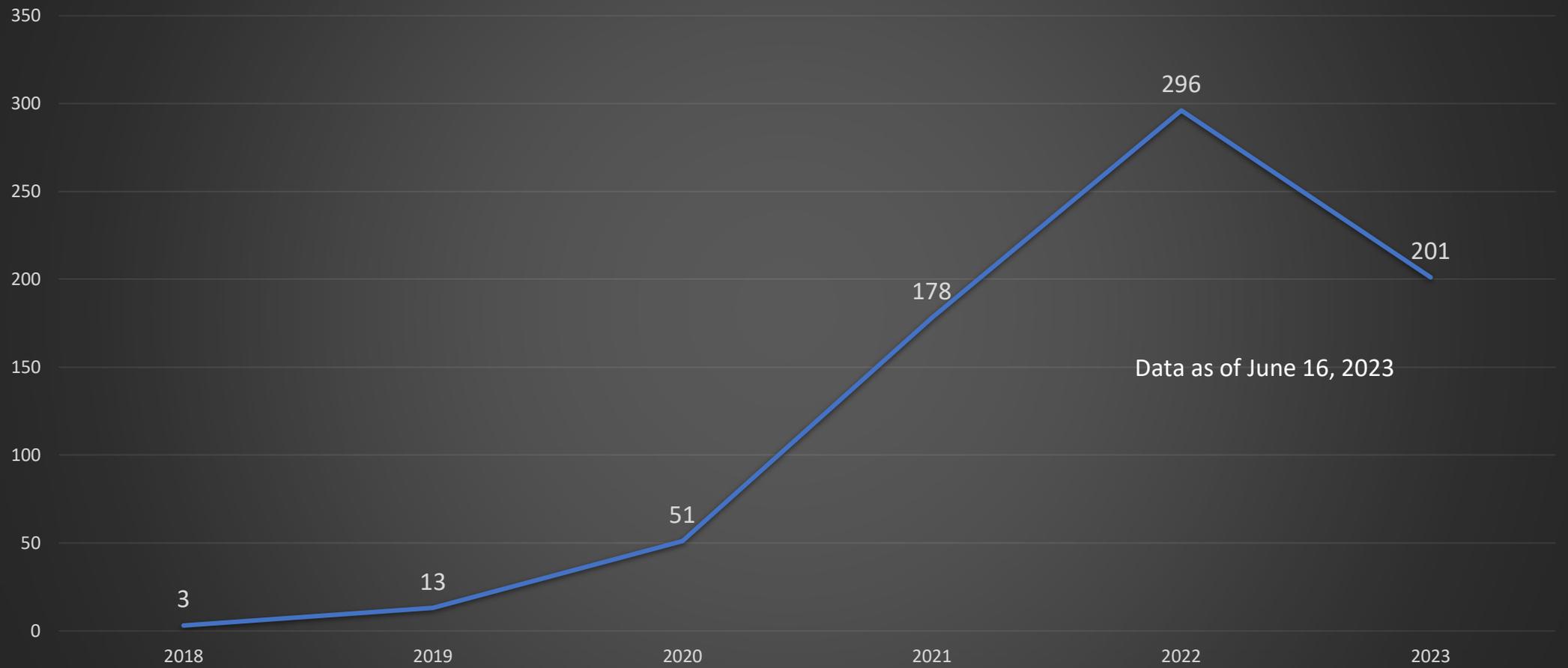
Oncology

Oncology

Non-oncology

Mounting interest and growth in published evidence with FAPI

Publication counts with keywords "FAPI" and "PET"

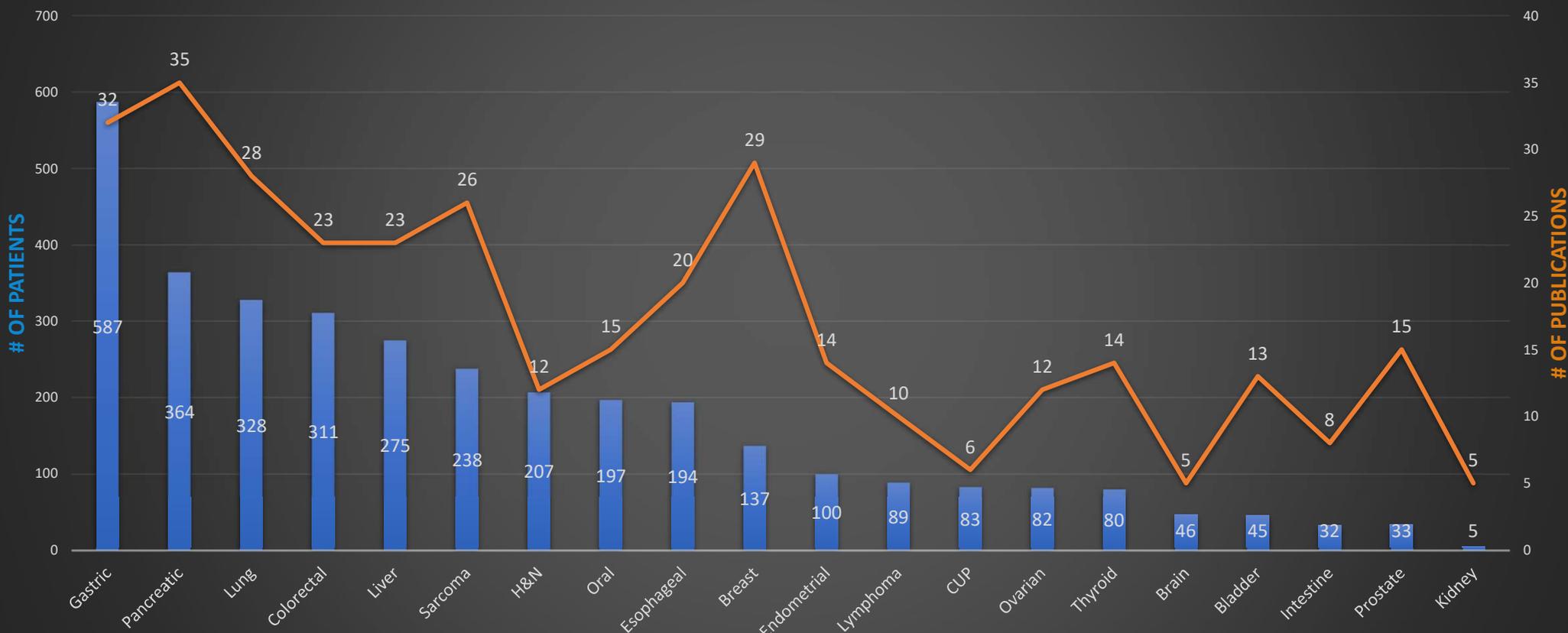


Publication analysis

| | Total Publications/Patients with ALL FAP targeted radiopharmaceuticals | Publications/Patients with FAPI family of compounds | |
|--|--|---|-----|
|  # of patients reported | 5903 | 5321 | 90% |
| | | 4234- Oncology 1087- non-oncology | |
|  # of publications | 464 | 396 | 85% |

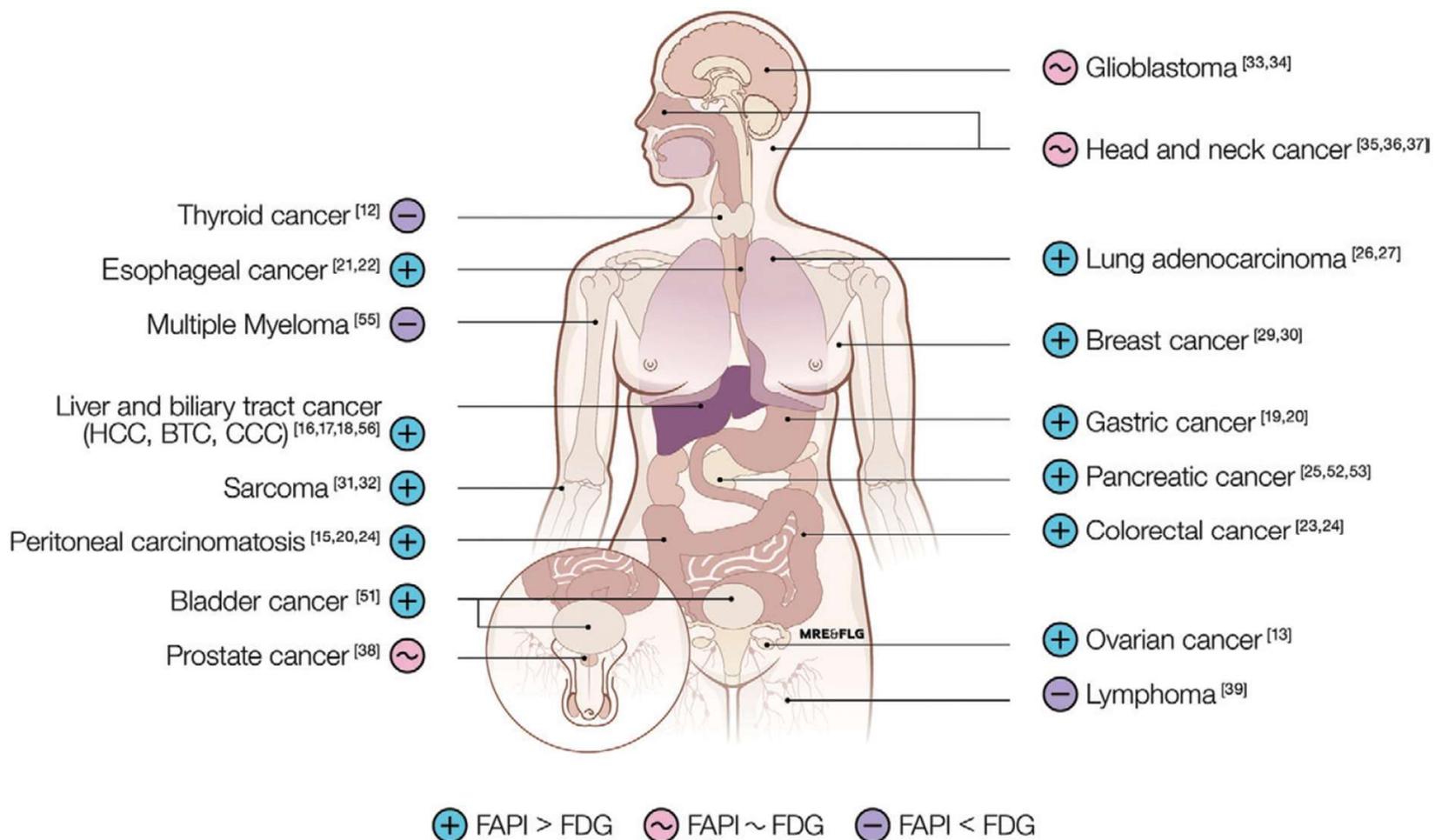
Takeaway: FAPI family of compounds comprise the majority of publications and patient reported data to date (May 2023). *(Review articles are excluded)*

of patients/publications in various oncologic disease



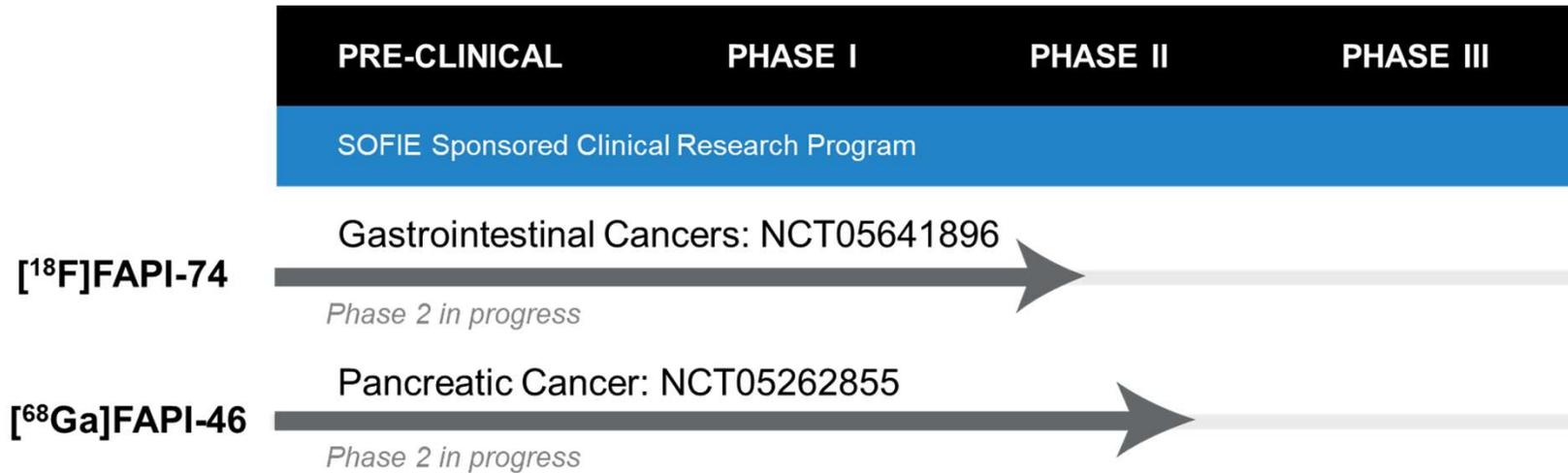
GI cancers encompass majority of the patient numbers reported with FAPI

Comparison of FAPI vs. FDG in oncological PET-imaging



Mori Y, Dendl K, Cardinale J, Kratochwil C, Giesel FL, Haberkorn U. FAPI PET: Fibroblast Activation Protein Inhibitor Use in Oncologic and Nononcologic Disease. Radiology. 2023 Jan 3;220749. doi: 10.1148/radiol.220749. Epub ahead of print. PMID: 36594838.

SOFIE's pipeline-FAPI family of compounds



Licensed by SOFIE from Heidelberg University for Diagnostic and Companion Diagnostic use

Family of compounds



Phase 2 in patients with Pancreatic Ductal Adenocarcinoma (PDAC)



68 minutes half life



4 sites activated

- NYU Langone
- Mayo Clinic
- UCLA
- BAMF Health



60 patients planned
• 22 patients imaged



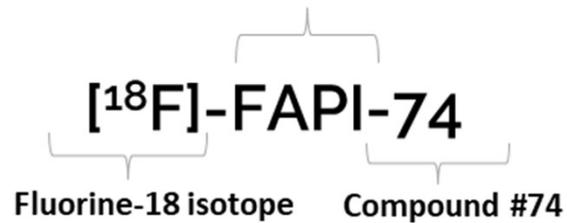
Lead Gallium-68 product

Can be utilized for theranostic use

Study launched May 2022

Companion diagnostic partnerships

Family of compounds



Phase 2 in patients with GI Cancers: hepatocellular carcinoma, gastric cancer, cholangiocarcinoma, colorectal cancer and pancreatic cancer



110 minutes half life



5 sites selected

- MGH activated
- 4 sites in activation process



100 patients planned

- 3 patient imaged

First Patient Imaged in SOFIE's 18F-FAPI Phase II trial

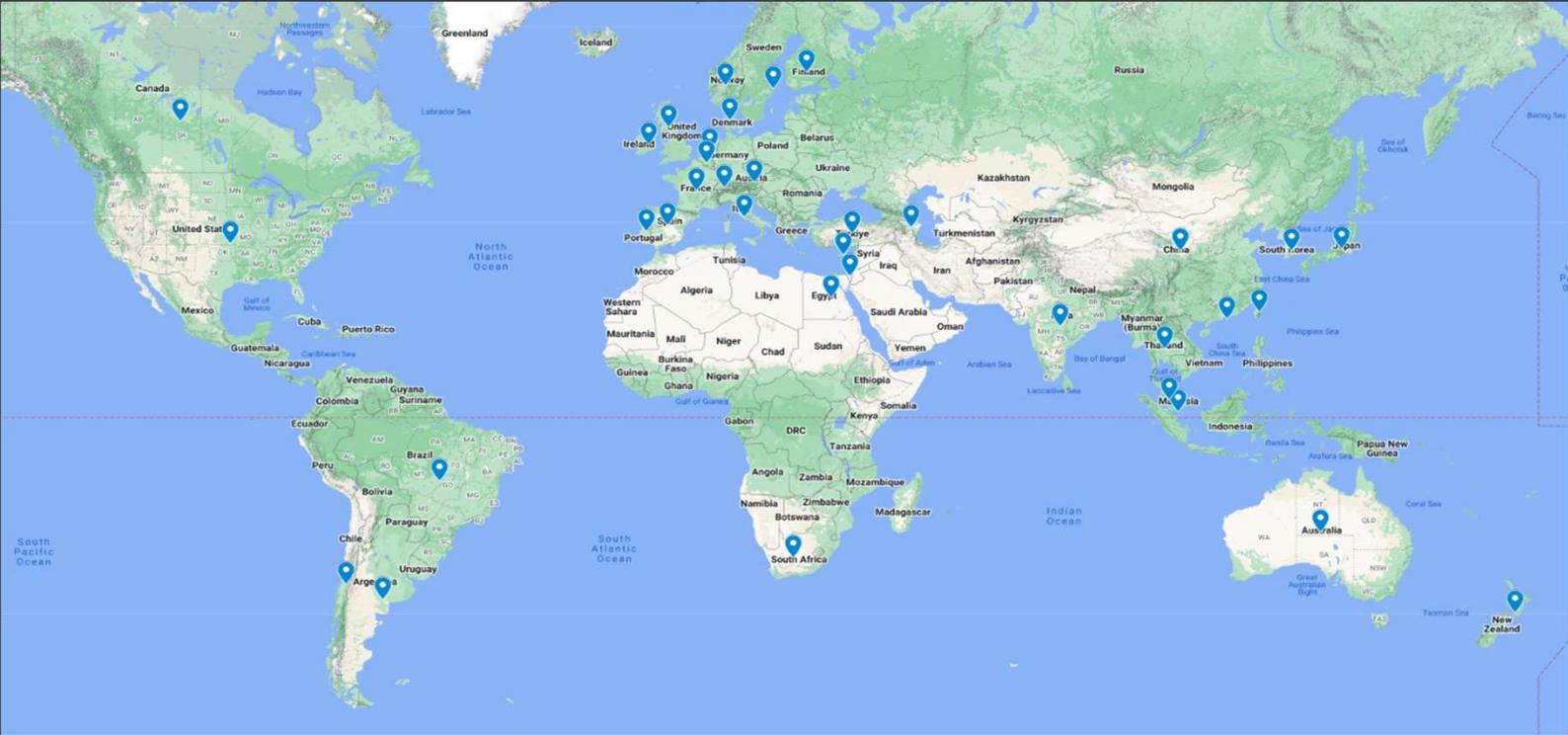
Lead Fluorine-18 product

Study launched May 2023

Automated synthesis and consumables available with Trasis Mini-AIO and AIO

Companion diagnostic partnerships

SOFIE's FAPI Global Outreach Program



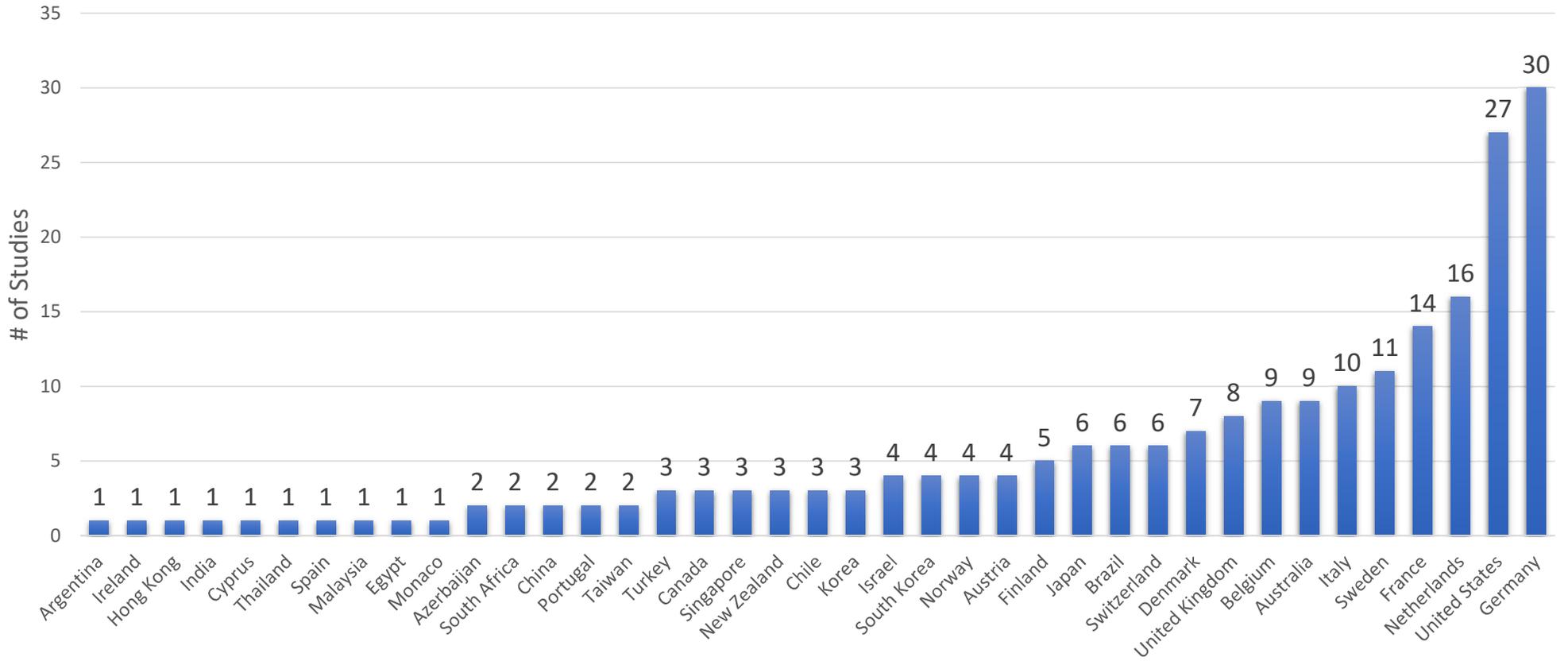
- 39 Countries
- 227 research studies
- 126 unique institutions

Gain access to GMP grade FAPI precursor

Manufacturing and regulatory support

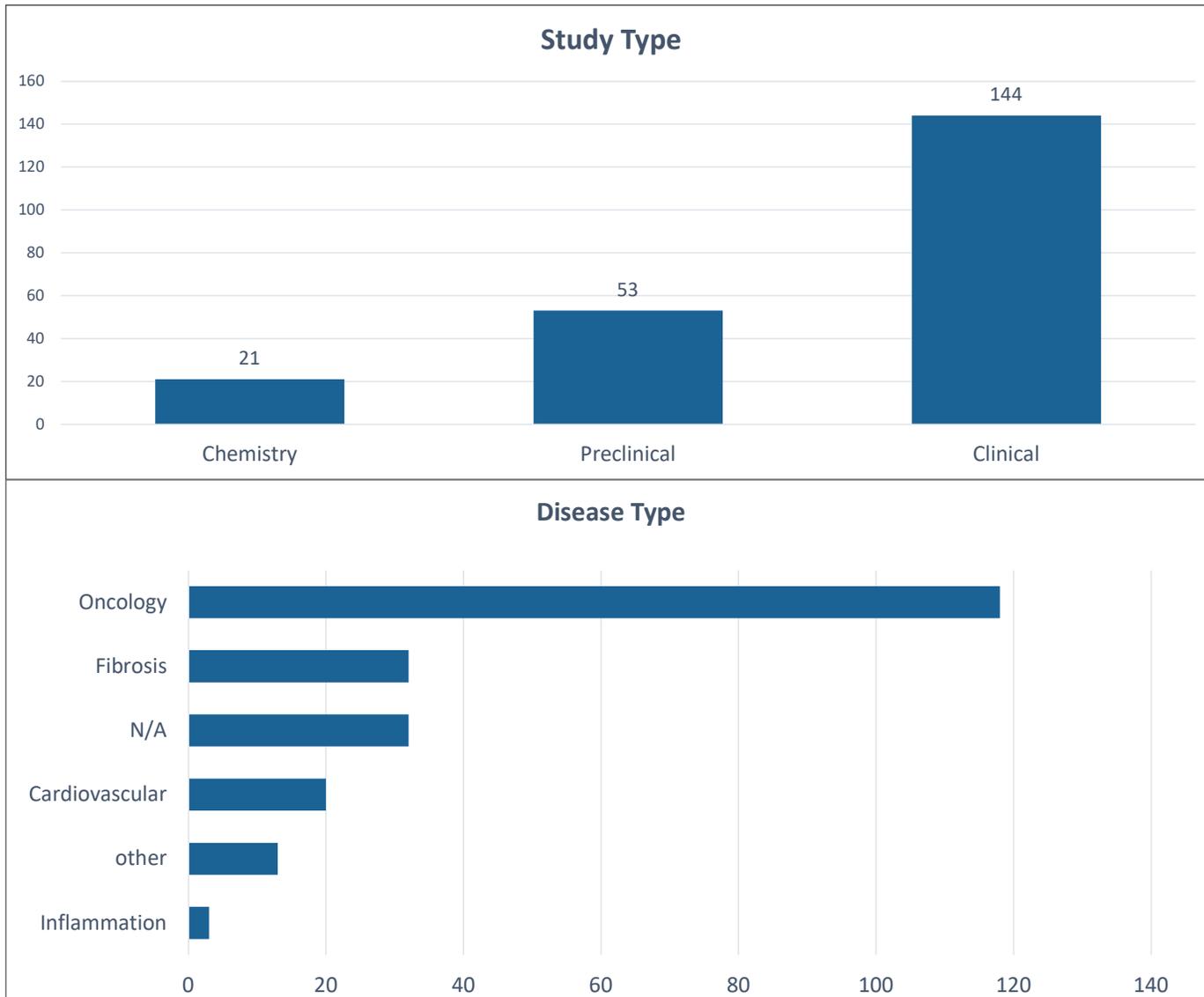
Expand grant and research opportunities

Studies by Country



FAPI studies by country. 39 countries are part of our FAPI Global Outreach Program, conducting studies with FAPI. The countries conducting the highest number of studies in descending order are: Germany (30), United States (27), Netherlands (16), France (14), Sweden (11) and Italy (10).

FAPI Global Outreach Program



- Majority of studies are clinical/investigator initiated

- Majority of studies are in oncology

N/A captures a broad, non disease specific study

FAP Diagnostic

Stand-alone diagnostic

Companion diagnostic- FAP Biomarker

Oncology

Non-oncology

RLT

Non-RLT

Oncology

Oncology

Non-oncology



To improve patient outcomes by developing and delivering molecular diagnostics and therapeutics (theranostics). With our robust radiopharmaceutical production and distribution network, mature contract manufacturing services, and now, high value radiopharmaceutical intellectual property, we are poised to deliver on the promise of radiopharmaceuticals.



Our Pipeline

With over 50 years of passion and dedication for the future of PET, we have taken bold steps to advance the development of next generation radiopharmaceuticals.

[VIEW PIPELINE](#)



Partnership

We offer a range of contract manufacturing services to meet your clinical needs through our network and new Theranostics Center of Excellence.

[VIEW SERVICES](#)



PET Education

We have created a multifaceted approach designed to strengthen the quality of PET programs in your practice and deliver enhanced care to your patients.

[LEARN MORE](#)



Our Network

We have 14 network sites committed to on-time delivery of radiopharmaceuticals to meet our clients' need in diagnosing and treating critical illnesses every day.

[FIND A PHARMACY](#)

Thank you

For any questions regarding FAPI,
please reach out to us at FAPIprogram@sofie.com

