SUPPLEMENTAL DATA

Materials & Equipment.

All cell lines were originally purchased from ATCC (Manassas, VA). Cell culture media including RPMI-1640, and DMEM were purchased from GIBCO. 200-proof ethanol was purchased from Decon Labs, Inc. (King of Prussia, PA). All other cell culture reagents such as 2 mM glutamine, penicillin-streptomycin, and fetal bovine serum (FBS) were purchased from Life Technologies. Common cell culture materials such as syringes and culture flasks were acquired from VWR (Chicago, IL). Sterile BD insulin syringes were purchased from ADW® Diabetes (Pompano Beach, FL). Amine-coated 24-well cultureware plates were purchased from BD Biosciences (San Jose, CA). DOTA-NHS ester was purchased from Macrocyclics. acetic acid, DTPA, L-methionine, TEA, DIPEA, DCM, DMF, DMSO, TFA, EtOH, MeOH, and ACN were purchased from Sigma-Aldrich (St. Louis, MO). Commercial reagents and solvents were all used without additional purification. Purifications were performed as indicated either by flash chromatography (Combi-Flash RF, Teledyne) or RP-HPLC (Agilent 1200 Instrument) with an XBridge OBD preparative column (19 x 150 mm, 5 μm) purchased from Waters (Milford, MA). NMR was performed with a Bruker 500 and 125 MHz NMR spectrometer equipped with a TXI cryoprobe. LC-MS was performed with an Agilent 1220 Infinity LC with a reverse-phase XBridge Shield RP18 column (3.0 x 50 mm, 3.5 μm). Radio-HPLC analysis was performed with an Agilent 1260 Infinity II equipped with a reverse-phase XBridge Shield RP18 column (.0 x 50 mm, 3.5 μm) and a Flow-RAM detector purchased from LabLogic (Brandon, FL). Radiolabeling was accomplished using a Fisherbrand Isotemp Digital Dry Bath/Block Heater (Waltham, MA). SPECT/CT scans were acquired with a VECTor/CT system with a clustered multi-pinhole high-energy collimator (MILabs, Utrecht, The Netherlands). All radioactive binding and biodistribution study samples were measured with a Hidex Automatic Gamma Counter (Hidex Oy, Turku, Finland).

ABBREVIATION.

CAF, cancer-associated fibroblast; TME: tumor micro environment, FAP, fibroblast activation protein; RLT, radioligand therapy; FDA, Food and Drug Administration, AUC , area under the curve; ; Kd, equilibrium dissociation constant; SPECT, single photon emission computed tomography; MBq, megabecquerels; mGy, milligray; Gy, gray; PEG, polyethylene glycol; FBS, fetal bovine serum; NIDC, National Isotope Development Center; U.S. DOE, United States

Department of Energy; %ID/g, percentage of injected dose per gram; CPM, counts per minute; p.i., post-injection; SE, standard error;.

Analysis of FAP ligand affinity and specificity.

FAPα (catalog number: 3715-SE), PREP (catalog number: 4308-SE) and DPP4 (catalog number: 9168-SE-010) recombinant human enzymes were purchased from R&D Systems and enzyme buffer was obtained from BPS Bioscience. H-Gly-Pro-AMC and Z-Gly-Pro-AMC were purchased from Bachem Americas, Inc. Increasing concentrations of FAP8 ligand (2) or FAP8-PEG_3-IP-DOTA conjugate (**3**) were mixed with the appropriate fluorescent substrates for FAP, PREP (Z-Gly-Pro-AMC) or DPP-IV (H-Gly-Pro-AMC) in enzyme buffer prior to addition of the desired enzyme (FAP, PREP or DPP-IV) and subsequent incubation at room temperature for 60 min. Fluorescence was then measured using a Cary Eclipse Fluorescence Spectrophotometer at an excitation wavelength of 380 nm and emission wavelength of 450 nm. All assays were performed in triplicate.

In vitro fluorescence and radioligand binding assays.

HEK-hFAP cells (200,000/ well) were seeded into amine-coated 24 well plates to ensure cell adherence. Following the formation of monolayers, the cells were incubated at 4ºC for 1h with increasing concentrations of FAP8-PEG_3-FITC or ^{177}Lu-labelled FAP8-PEG_3-IP-DOTA in the presence or absence of excess unlabeled FAP8 ligand. Cells were then washed 3x with PBS to remove unbound fluorescence or radioactivity and then dissolved in 300 µl of 1% SDS. The resulting solutions were then transferred into 96 well black plates for quantitation of FAP8-PEG_3-FITC fluorescence or gamma counter tubes for ^{177}Lu-labelled FAP8-PEG_3-IP-DOTA counting. Fluorescence was measured using a fluorescence NeO2 Plate Reader (ʎex= 488 nm and ʎem= 520 nm), while radioactivity was counted using a HidexAMG gamma counter. Cell-bound fluorescence or radioactivity was plotted against corresponding concentrations of conjugate, and the apparent Kd values were determined using a one-site binding (hyperbola) curve fitting program in GraphPad Prism9. All experiments were performed in triplicate.

Animal Husbandry

Mice were provided normal rodent chow and water ad *libitum* and maintained on a standard 12-hour light-dark cycle. All animal procedures were approved by the Purdue Animal Care and Use Committee.

Tumor models

Balb/c mice were inoculated on their shoulders with 1 x 10^5 4T1 cells, whereas nu/nu mice were inoculated on their shoulders with 5 x 10^6 cells HT29, KB, MDA-MB-231 or HEK-hFAP cells.

Radiolabeling

FAP8-PEG$_3$-DOTA or FAP8-PEG$_3$-IP-DOTA was dissolved in ammonium acetate buffer (NH_4OAc) (1.0 M, pH 7.0) and labeled with [^{111}In]$InCl_3$ (BWMX Canada) or [^{177}Lu]$LuCl_3$ (National Isotope Development Center (NIDC), Oak Ridge National Laboratory) to obtain a specific activity of ≤ 3 MBq/nmol or ≤7.4 MBq/nmol, respectively. The resulting solutions were heated at 90ºC for 5 minutes and the radiopurities of the products were analyzed by radio-HPLC, (radio-HPLC method: a linear gradient from 5% B (acetonitrile) and 95% A (20 mM ammonium bicarbonate buffer) to 95% B over 15 minutes (see Fig. S21). Radio purities exceeded >95% in all studies. Then DTPA (5 mM, pH 7.0) was added at a final concentration of 0.2 mM to chelate any unreacted traces of radionuclide. Followed by radiolabeled products were then formulated in 5% ethanol in PBS (v/v) containing 0.5% L-methionine (w/v) and 10% sodium ascorbate (w/v) and used without further purification for all studies.

***Ex vivo* radioligand biodistribution**

Mice implanted with 4T1 or HEK-hFAP tumors were intravenously injected with different doses (0.3 nmol/mouse, 1.0 nmol/mouse and 5 nmol/mouse) of FAP8-PEG$_3$-IP-DOTA conjugate chelated with fixed amount of [^{177}Lu]$LuCl_3$ (7.4 MBq/mouse). At the indicated times (1h, 4h, 24h, 72h, 120h and 168h post injection, n = 4 mice/time point), mice were euthanized by CO_2 asphyxiation and organs of interest were harvested, rinsed, dried, weighed, and then measured by gamma counting. After correcting for decay, the results were plotted as the percentage of the injected dose per gram of tissue (%ID/g).

Dosimetry analysis:

From the biodistribution data, the total absorbed radiation doses (mGy/MBq) were calculated using OLINDA 2.2.3 software. Dose estimates for healthy organs such as blood, heart, lungs, liver, spleen, kidneys, and bone marrow were calculated assuming a 25 g mouse phantom, whereas tumor dose estimates were calculated with the sphere model(*2,3*). Time-activity curves were fitted to the biodistribution data of each organ individually with exponential functions.

SPECT/CT scans

Two different tumor-bearing mice (HT29 and KB, n = 2) were injected intravenously with FAP8-PEG_3-IP-DOTA conjugate (5nmol/mouse) radiolabeled with ~14.8 MBq/mouse of [^{111}In]$InCl_3$. At the indicated times, mice were anesthetized and scanned using a MILabs VECTor/CT instrument. The SPECT scans were captured at a scan time of 20-60 minutes with a 0.35 mm pinhole (mouse whole body) collimator, with 15-60 second acquisitions per bed position across 50 bed positions. CT scans were captured with an X-ray source set at 615 μA and 60 kV. The SPECT images were reconstructed with U-SPECT II software using ^{111}In γ-energy windows of 171 and 241 keV. The CT images were reconstructed using NRecon software as described recently(*3*). A POS-EM algorithm was used with 16 subsets and 4 iterations on a 0.8 mm voxel grid. A 3.0 median filter was applied to all scans while background remover was only applied to remove low levels of noise seen outside the bodies of mice. To allow better tumor visualization the bladders uptakes were masked as needed for scans taken for the first time points at 4h and 24h post injection. No background remover was applied at any time points.

Radiotherapy

4T1 (n =5/group), HT29 (n = 5/group), KB (n= 3/group), and MDA-MB231(n = 5/group) tumor-bearing mice were randomly divided into control and treatment groups to ensure similar average starting tumor volumes. Each cohort received a single intravenous injection of saline or [^{177}Lu] Lu-FAP8-PEG_3-IP-DOTA (37 MBq/mouse in case of HT29, KB and MDA-MB231 tumor bearing mice and 9.25, 18.5 and 37 MBq/mouse in case of 4T1 tumor bearing mice) chelated with 5nmol/mouse of conjugate (FAP8-PEG_3-IP-DOTA) on day 0, as indicated. Tumors were measured with a caliper in two perpendicular directions every other day, and mice were euthanized when

body weight loss reached 20% or tumor volume exceeded 1500 mm^3, according to Institutional Animal Care and Use Committee (IACUC) regulations.

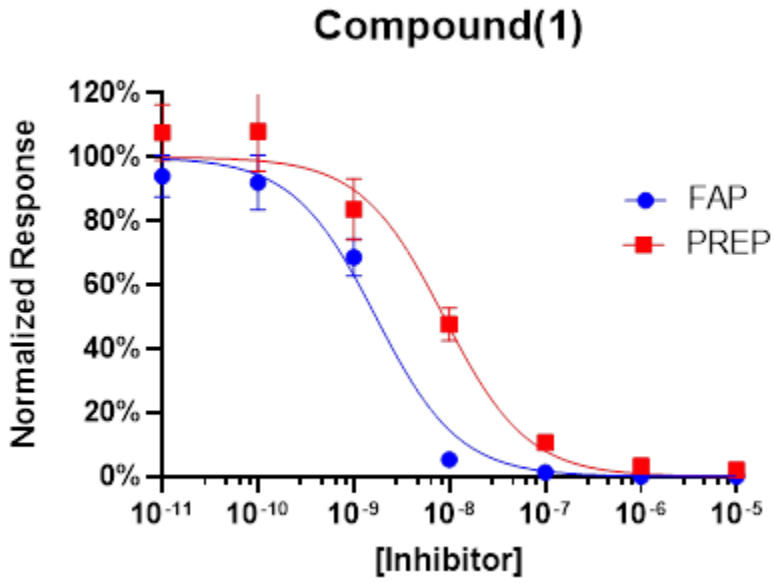
Statistical Analysis

Data was analyzed using GraphPad Prism 9 unless otherwise stated. All results are presented as mean ± SE. Statistical significance in tumor size was calculated using unpaired student's t-test (*P < 0.05, **P < 0.01, ***P < 0.001 and ****P<0.0001. Survival rates were determined by Kaplan Meier estimator analysis.

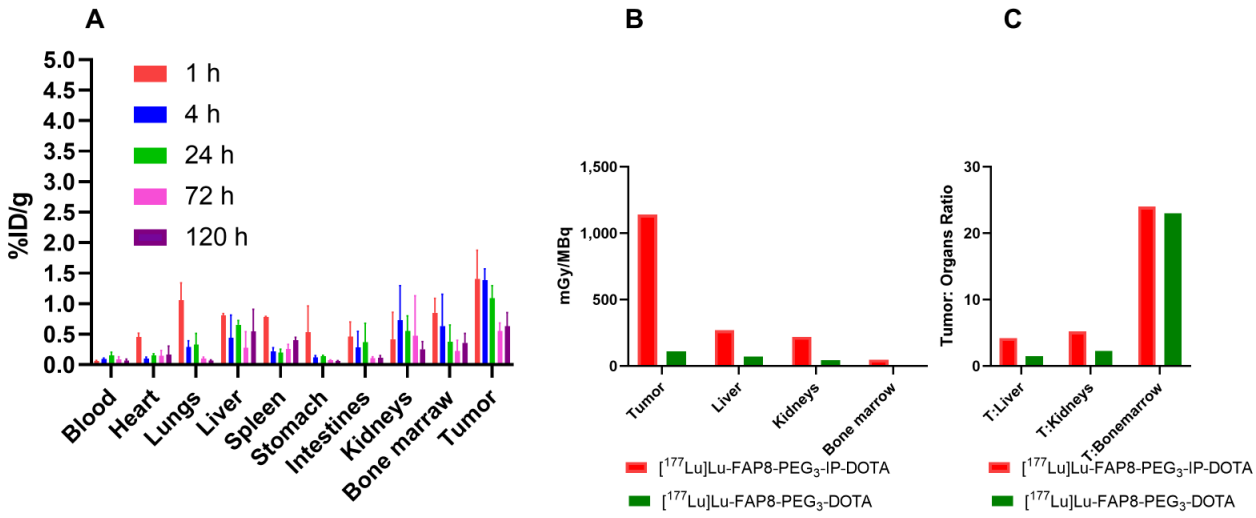
Supplemental Table 1. Inhibition of FAP, PREP and DPP-IV by compounds 1, 2 & 3.

	IC50 (nM)			[a]FAP selectivity	
Compound	FAP	PREP	DPP-IV	FAP: PREP	FAP: DPPIV
1[b]	0.089[b]	0.2[b]	>3000[b]	2.2[b]	>34000[b]
1[c]	1.7[c]	8.7[c]	n.d	5.1[c]	n.d
2	0.76	13	>3000	16.5	>3500
3	1.6	14	860	8.7	537

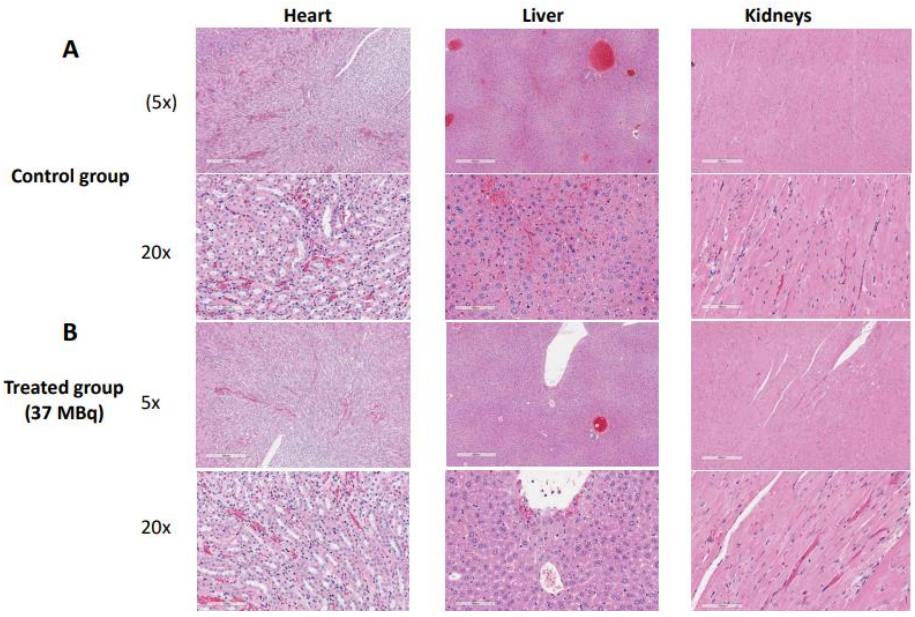
[a] FAP selectivity is calculated from the ratio IC_{50}(PREP)/IC_{50}(FAP) and IC_{50}(DPP-IV)/IC_{50} (FAP). [b] The compound **1** data are obtained from reference (*1*).[c] The compound **1** data were determined experimentally as described in Methods and shown in Supplemental Fig. S1.



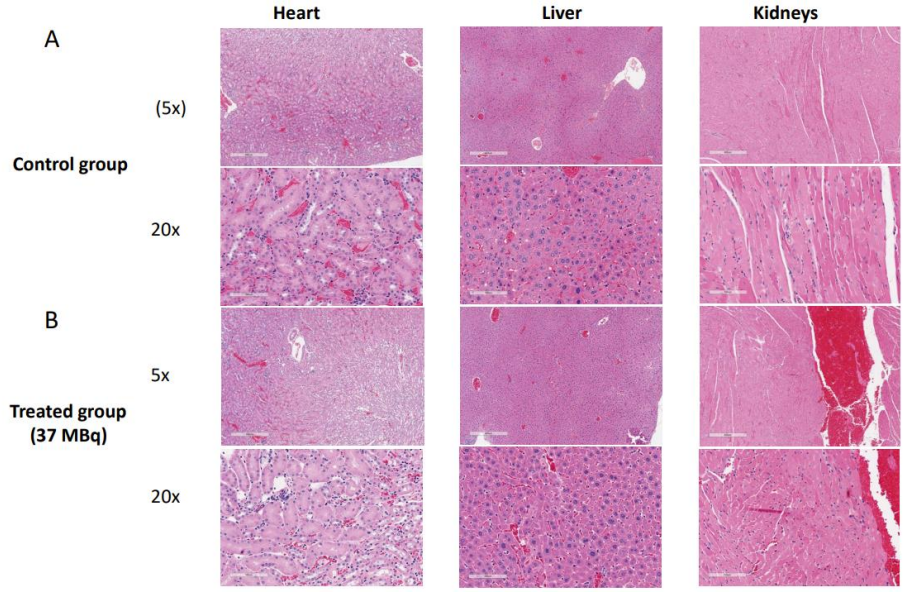
Supplemental Figure 1. Repeating the inhibition measurements of the catalytic activity for FAP, PREP by compound (**1**) as reported by Simkova et al.(*1*)



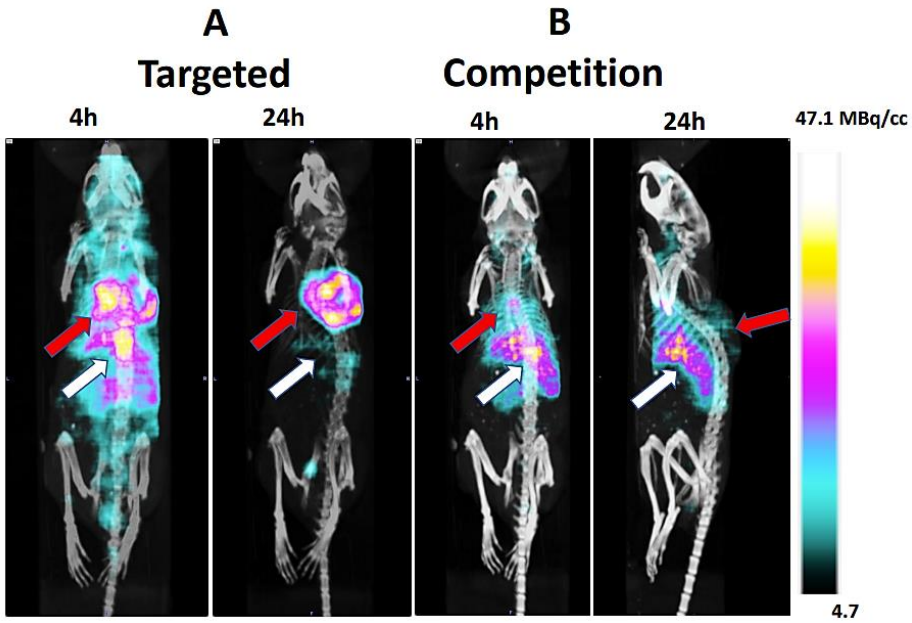
Supplemental Figure 2. (A) Biodistribution analysis of [^{177}Lu] Lu-FAP8-PEG$_3$-DOTA in 4T1 tumor-bearing mice (n = 4) at different times post-injection, injected with 5 nmol/mouse. (**B**) Comparison of the total absorbed radiation doses (AUC) of [^{177}Lu]Lu-FAP8-PEG$_3$-IP-DOTA (red bar) and [^{177}Lu]Lu-FAP8-PEG$_3$-DOTA (green bar) in the selected organs (Tumor, liver, kidneys and bone marrow) data calculated from time course biodistribution data from manuscript **Fig 3C** and **Supplemental Figure 2A.** (**D**) Calculated tumor to healthy tissues ratios from the data in **Supplemental Figure 2B**.



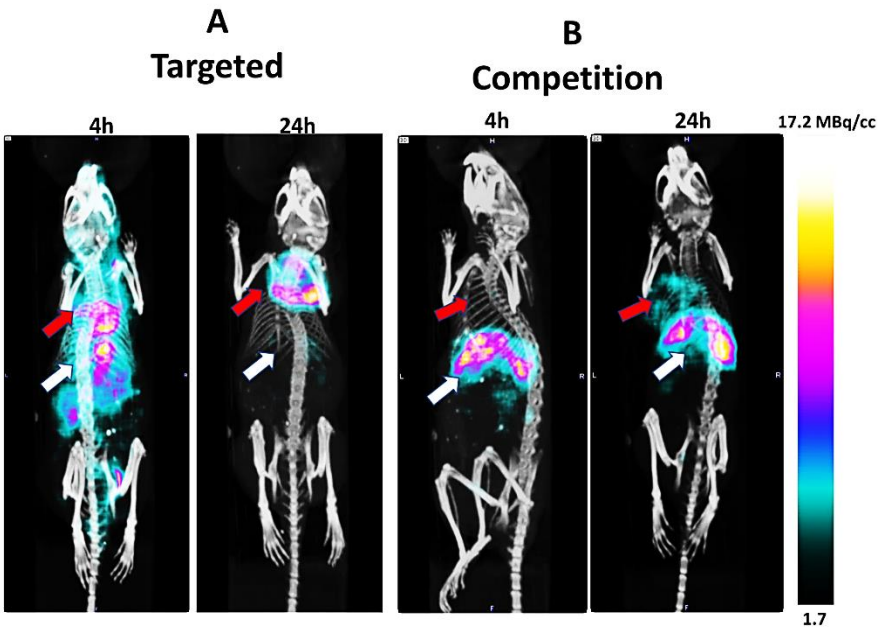
Supplemental Figure 3. Representative photomicrographs of 4 µm sections of mouse heart, liver, and kidney tissue following radiotherapy treatments of [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA from **Fig 6A** treated with 37 MBq in athymic nu/nu mice bearing MDA-MB-231 tumors stained with H&E.



Supplemental Figure 4. Representative photomicrographs of 4 µm sections of mouse heart, liver, and kidney tissue following radiotherapy treatments of [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA from **Fig 6C** treated with 37 MBq in athymic nu/nu mice bearing KB tumors stained with H&E.



Supplemental Figure 5. SPECT/CT imaging of [^{111}In]In-FAP8-PEG$_3$-IP-DOTA in human colorectal (HT29) tumor bearing mice at 4 and 24h post injection (A). Red arrow indicates tumor, white arrow indicates liver. SPECT/CT imaging of [^{111}In]In-FAP8-PEG$_3$-IP-DOTA in human colorectal (HT29) tumor bearing mice with 100-fold excess of unlabeled FAP8-PEG$_3$-IP-DOTA conjugate at 4h and 24h postinjection (B).



Supplemental Figure 6. SPECT/CT imaging of [^{111}In]In-FAP8-PEG$_3$-IP-DOTA in human cervical (KB) tumor bearing mice at 4 and 24h post injection (A). Red arrow indicates tumor, white arrow indicates liver. SPECT/CT imaging of [^{111}In]In-FAP8-PEG$_3$-IP-DOTA in human cervical (KB) tumor bearing mice with 100-fold excess of unlabeled FAP8-PEG3-IP-DOTA conjugate at 4h and 24h postinjection (B).

Supplemental Table 2: Biodistribution analysis of [^{177}Lu]Lu-FAP8-PEG$_3$-IP-DOTA in 4T1 tumor bearing mice injected with 0.3 nmol/mouse.

Tissue (%ID/g)	1h (n=4)	4h (n =4)	24h (n=4)	72h (n =4)	120h (n =4)	168h (n= 4)
Blood	25.42±3.72	10.35±4.64	4.28±1.46	1.48±0.12	0.23±0.90	0.4±0.1
Heart	5.03±3.16	2.72±1.53	1.63±1.02	2.08±0.28	1.07±0.30	0.8±0.5
Lungs	5.73±1.54	4.96±3.24	2.12±0.76	2.30±1.00	1.53±1.52	0.5±0.2
Liver	7.05±2.01	5.79±0.12	5.88±2.38	6.39±2.65	3.62±1.59	4.93±0.49
Spleen	4.12±1.79	3.48±1.64	2.07±1.11	2.85±1.28	2.22±0.28	3.13±0.98
Stomach	1.50±0.78	0.73±0.09	0.91±0.25	0.67±0.135	0.54±0.22	0.46±0.05
Intestine	1.92±0.411	1.26±0.64	0.65±0.15	0.88±0.27	0.68±0.37	0.6±0.2
Kidneys	4.86±3.29	3.48±2.54	2.09±2.44	1.52±0.59	2.12±0.88	1.33±1.02
Bone marrow	6.70±4.92	4.32±2.99	1.49±1.4	1.20±2.08	0.85±5.57	1.76±1.72
Tumor	5.79±3.38	5.24±1.91	5.94±2.18	5.12±1.34	3.32±2.49	3.43±0.98
Tumor/Blood	0.17±0.06	0.53±0.31	1.35±1.45	3.41±0.55	3.99±2.45	8.4±0.94
Tumor/Kidneys	1.19±0.23	1.02±0.23	1.36±8.95	4.09±2.30	1.62±0.63	3.55±2.09
Tumor/ Bone marrow	1.08±0.77	1.25±0.85	2.54±87.50	1.69±0.0	3.03±1.91	4.77±4.55

Values (% ID/g) represent the mean ± SE of data obtained from four animals per cohort.

Supplemental Table 3. Biodistribution analysis of [^{177}Lu]Lu-FAP8-PEG$_3$-IP-DOTA in 4T1 tumor bearing mice injected with 1.0 nmol/mouse.

Tissue (%ID/g)	1h (n=4)	4h (n =4)	24h (n=4)	72h (n =4)	120h (n =4)	168h (n= 4)
Blood	16.3±6.47	10.16±8.11	4.66±1.32	1.48±0.06	0.88±0.13	0.5±0.1
Heart	2.00±1.08	1.89±0.31	1.04±0.32	1.26±0.58	0.56±0.18	1.16±0.15
Lungs	1.97±1.67	3.16±2.58	0.92±0.52	0.99±0.50	1.29±0.54	0.7±0.51
Liver	5.23±0.52	5±1.00	4.6±1.40	4.90±1.61	6.36±1.2	2.43±0.40
Spleen	2.66±0.69	2.28±0.71	1.93±0.09	1.98±0.19	2.97±0.59	1.9±0.45
Stomach	1.13±0.77	0.95±0.47	0.51±0.101	0.86±0.35	0.40±0.12	0.33±0.05
Intestine	1.67±1.53	1.51±1.15	0.89±0.37	0.79±0.19	0.42±0.18	0.46±0.15
Kidneys	3.51±0.22	7.89±1.58	4.4±0.79	1.19±0.02	1.36±0.67	1.56±0.73
Bone marrow	1.46±1.05	0.63±0.44	2.26±1.06	0.13±0.22	1.02±0.67	0.33±0.30
Tumor	4.59±1.59	9.19±4.39	6.93±1.10	6.99±1.70	4.68±0.85	5±1.57
Tumor/Blood	0.22±0.06	0.93±0.14	1.15±0.04	4.74±1.07	5.29±0.27	11.22±4.12
Tumor/Kidneys	1.15±0.40	1.49±0.14	1.38±0.33	5.88±1.22	3.93±1.23	3.60±1.29
Tumor/ Bone marrow	7.53±8.14	15.60±3.49	2.27±0.10	16.96±0.1	5.80±2.27	11.38±2.95

Values (% ID/g) represent the mean ± SE of data obtained from four animals per cohort.

Supplemental Table 4. Biodistribution analysis of [^{177}Lu]Lu-FAP8-PEG$_3$-IP-DOTA in 4T1 tumor bearing mice (5.0 nmol).

Tissue (%ID/g)	1h (n=4)	4h (n =4)	24h (n=4)	72h (n =4)	120h (n =4)	168h (n= 4)
Blood	28.96±12.08	4.65±1.32	6.12±4.78	1.1775±0.38	0.73±0.25	0.34±0.27
Heart	2.46±1.42	1.79±0.79	0.72±0.68	0.22±0.08	0.67±0.40	0.48±0.31
Lungs	3.90±0.62	2.66±0.71	2.07±1.38	0.67± 0.50	0.36 ±0.17	0.92±0.26
Liver	5.32±0.90	3.09±0.66	2.99 ± 1.46	2.42±0.63	1.74±0.68	1.42±1.00
Spleen	2.27±1.76	1.37±1.15	1.13±0.456	1.54±0.74	0.84±0.78	0.74±0.29
Stomach	1.35±0.32	1.97±0.31	1.17±1.13	0.45±0.17	0.45±0.26	0.25±0.13
Intestine	1.38±0.30	1.67±0.42	1.30±0.72	0.62±0.26	0.69±0.20	0.26±0.15
Kidneys	4.83±2.4	4.94±2.88	1.53±1.17	1.48±0.57	0.40±0.09	0.302±0.39
Bone marrow	1.15±0.38	1.50±0.717	0.46±0.34	0.44±0.31	0.66±0.74	0.63±0.75
Tumor	9.6±4.95	10.97±1.43	6.13±2.89	6.36±0.96	3.71±1.59	2.2±0.3
Tumor/Blood	0.33±0.08	2.54±0.76	2.16±1.97	6.31±2.73	4.39±1.39	7.08±4.78
Tumor/Kidneys	2.09±0.92	2.67±1.00	5.82±2.82	5.02±1.79	7.54±3.45	5.95±2.92
Tumor/ Bone marrow	8.54±318	8.24±2.53	21.03±11.54	20.78±9.88	11.04±9.17	3.07±1.35

Values (% ID/g) represent the mean ± SE of data obtained from four animals per cohort.

Supplemental Table 5. Biodistribution analysis of [^{177}Lu]Lu-FAP8-PEG$_3$-IP-DOTA in HEK-hFAP tumor bearing mice injected with 5.0 nmol/mouse.

Tissue (%ID/g)	1h (n=4)	4h (n =4)	24h (n=4)	72h (n =4)	120h (n =4)	168h (n= 4)
Blood	21.69±4.75	14.19±2.67	4.23±1.81	1.22±0.51	0.29±0.07	0.22±0.05
Heart	1.16±0.32	0.5±0.26	0.54±0.32	0.54±0.31	0.30±0.14	0.42±0.22
Lungs	1.79±0.65	1.54±1.08	0.58±0.17	0.63±0.44	0.335±0.17	0.67±0.25
Liver	8.39±1.48	4.37±1.31	3.98±0.96	3.73±1.25	2.37±0.88	2.3±0.81
Spleen	4.21±1.23	1.44±0.48	1.59±0.55	4.46±2.52	2.50±0.71	1.82±0.61
Stomach	0.75±0.12	0.15±0.07	0.37±0.16	0.26±0.10	0.127±0.02	0.15±0.05
Intestine	1.14±0.48	0.23±0.26	0.62±0.35	0.29±0.10	0.195±0.05	0.15±0.05
Kidneys	5.61±2.08	3.35±1.93	1.54±1.08	1.42±0.51	1.425±1.01	0.62±0.26
Bone marrow	0.63±0.39	1.07±0.80	0.56±0.39	1.31±0.88	0.922±1.07	1.825±0.6
Tumor	7.79±1.32	10.13±1.7	13.99±4.61	21.89±13.2	13.48±3.24	14.05±5.15
Tumor/Blood	0.34±0.04	0.70±0.04	3.63±1.16	13.03±4.45	43.42±20.68	55.10±18.20
Tumor/Kidneys	1.5±0.31	3.37±1.78	12.76±6.73	13.23±6.51	11.78±7.78	22.40±10.87
Tumor/ Bone marrow	30.29±35.11	22.34±20.76	33.58±19.14	12.69±6.67	30.40±25.91	8.35±2.00

Values (% ID/g) represent the mean ± SE of data obtained from four animals per cohort.

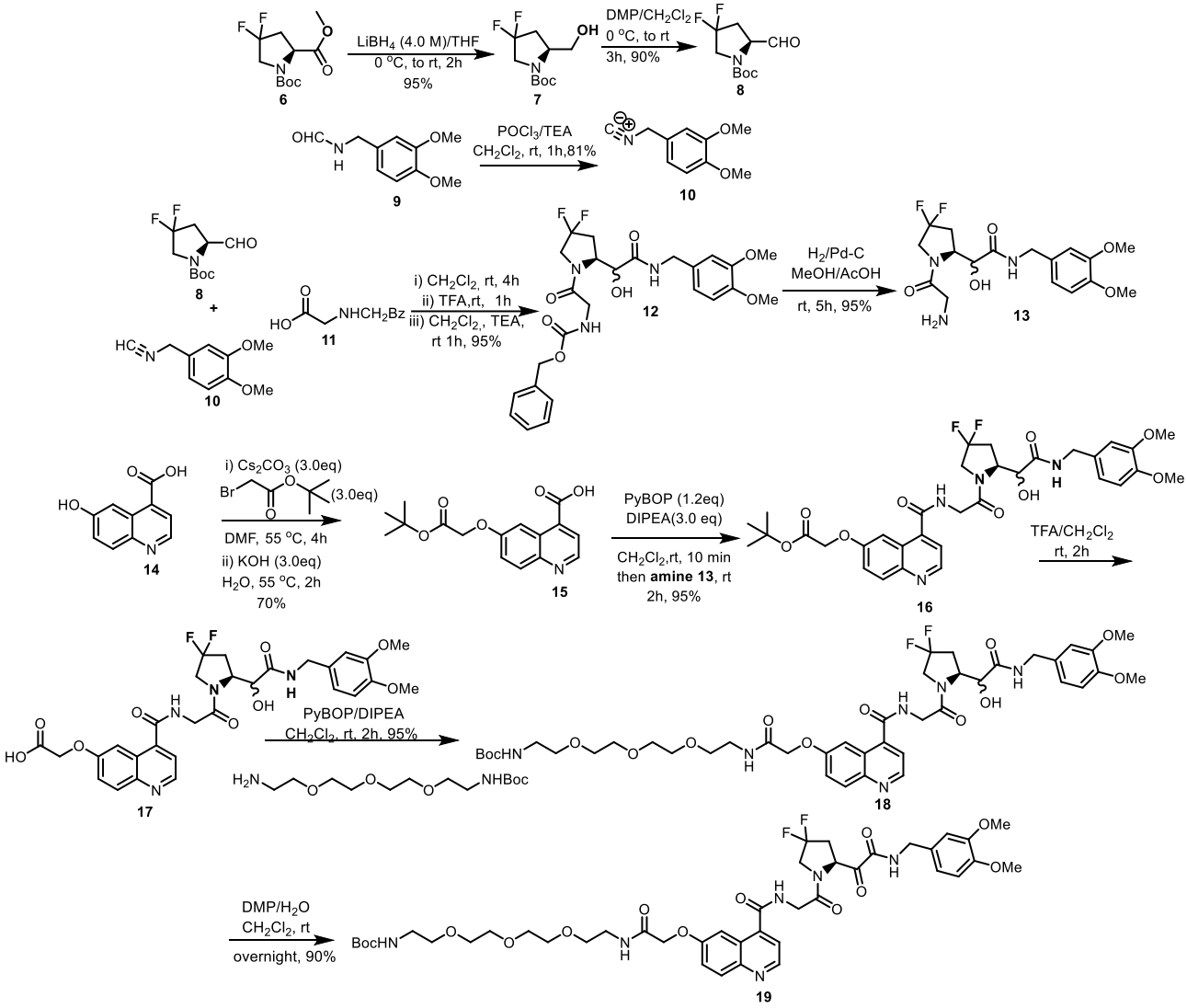
Supplemental Table 6. [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA dosimetry analysis using OLINDA software.

[^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA (0.3nmol/mouse) in 4T1tumor			[^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA (1.0 nmol/mouse) in 4T1 tumor		
Organs	Kinetics value [MBq-hr/MBq]	Organ doses [mGy/MBq]	Organs	Kinetics value [MBq-hr/MBq]	Organ doses [mGy/MBq]
Blood	4.48E-1	2.38E02	Blood	5.84E-1	2.95E02
Heart	5.62E-01	4.14E02	Heart	2.39E-1	1.76E02
Lung	9.69E-1	2.84E02	Lung	5.16E-1	1.36E02
Liver	5.77E0	5.67E02	Liver	8.19E0	8.90E02
Spleen	9.20E+0	1.46E03	Spleen	3.23E+0	4.13E02
Stomach	1.81E-1	8.58E01	Stomach	2.08E-1	6.44E-03
Intestines	1.76E-1	9.23E01	Intestines	2.22E-1	1.46E02
Kidneys	1.22E0	3.57E02	Kidneys	9.99E-01	2.94E02
Bone Marrow	8.84E-02	3.382E02	Bone Marrow	3.5E-02	1.14E02
Tumor	9.500E02	9.04E02	Tumor	8.95E0	9.94E02

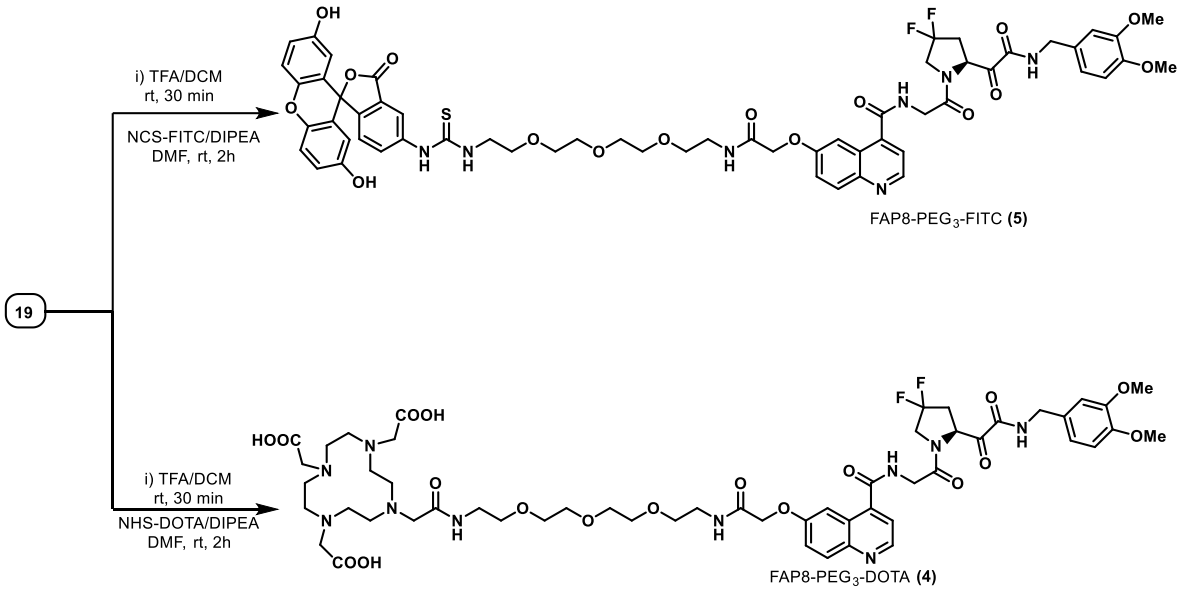
Supplemental Table 7. [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA dosimetry analysis using OLINDA software.

[^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA (5nmol/mouse) in 4T1tumor			[^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA(5nmol/mouse) in HEK-hFAP tumor		
Organ	Kinetics value [MBq-h/MBq]	Organ doses [mGy/MBq]	Organs	Kinetics value [MBq-h/MBq]	Organ doses [mGy/MBq]
Blood	3.27E-01	3.49E02	Blood	4.26E-1	2.70E02
Heart	6.34E-002	4.55E01	Heart	1.05E-1	7.18E01
Lung	2.93E-01	8.15E01	Lung	1.56E-1	5.73E01
Liver	3.55E0	2.70E02	Liver	4.44E0	4.41E02
Spleen	7.30E-1	1.10E02	Spleen	4.17E-1	3.08E02
Stomach	1.38E-1	4.27E-03	Stomach	5.81E-2	4.13E01
Intestines	1.83E-1	9.04E01	Intestines	1.20E-1	7.32E01
Kidneys	8.89E-01	2.20E02	Kidneys	4.46E-01	2.34E02
Bone Marrow	1.99E-02	4.81E01	Bone Marrow	6.27E-02	1.36E02
Tumor	6.43E0	1.14E03	Tumor	1.34E01	2.27E03

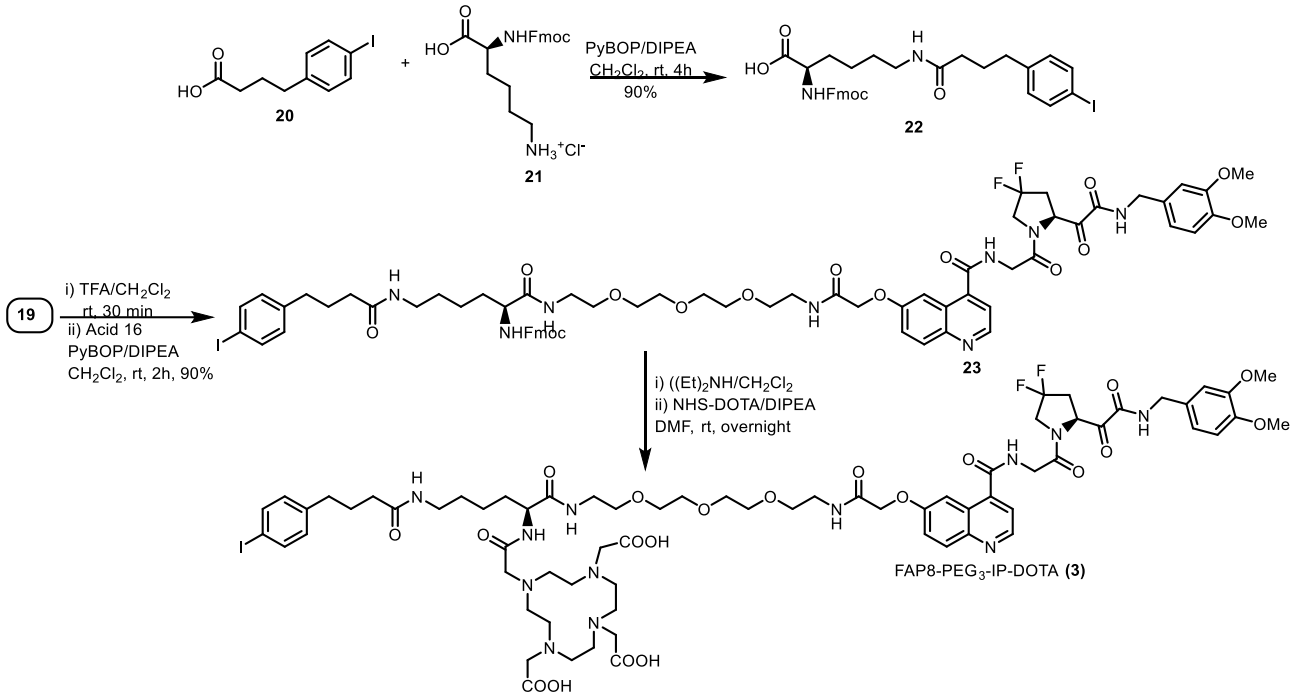
Synthetic schemes for FAP8 (2), FAP8-PEG$_3$-IP-DOTA (3), FAP8-PEG$_3$-DOTA (4) and FAP8-PEG$_3$-FITC (5) conjugates.



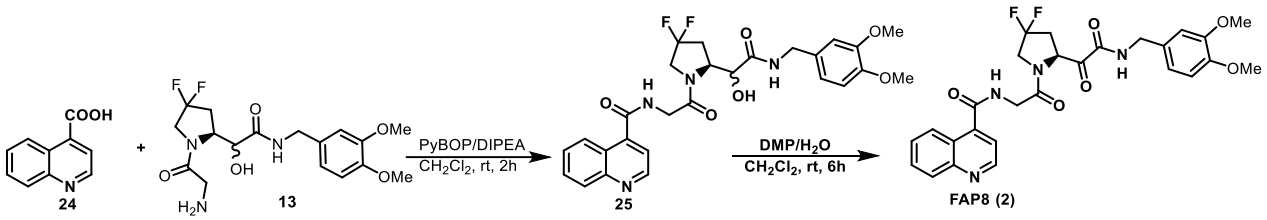
Supplemental Scheme 1: Synthesis of FAP8 base ligand (19).



Supplemental Scheme 2: Synthesis of FAP8-PE$_3$-DOTA (**4**) and FAP8-PEG$_3$-FITC (**5**) conjugates.



Supplemental Scheme 3: Synthesis of FAP8-PEG$_3$-IP-DOTA (3) conjugate.



Supplemental Scheme 4. Synthesis of FAP8 (2) base ligand.

Experimental section.

Synthesis of tert-butyl (S)-4,4-difluoro-2-formylpyrrolidine-1-carboxylate (8):

Step-i:

To a stirred solution of 1-(tert-butyl) 2-methyl (S)-4,4-difluoropyrrolidine-1,2-dicarboxylate (**6**) (1g, 3.77 mmol) in THF (10 mL) at 0 ºC was added $LiBH_4$ (1.1 eq, 4M in THF) slowly dropwise. The reaction mixture was further transferred to room temperature and continued stirring there for 1h. reaction mixture was evaporated under vacuum and obtained residue was redissolved in CH_2Cl_2 (100 mL) followed extracted by saturated aqueous sodium bicarbonate solution (50 mL), organic layer was separated and evaporated under vacuum, then obtained crude residue was purified by column chromatography using ethyl acetate hexanes as mobile offered desired compound (**7**) 850 mg, 95% as white gummy liquid.

Step-ii:

Dess-Martin periodinane (4.92 g, 11.60 mmol) was added portion wise to a solution of tert-butyl 4,4-difluoro-2-(hydroxymethyl) pyrrolidine-l-carboxylate (**7**) (2.5 g, 10.55 mmol) in DCM (30 mL) at 0 °C. After complete addition the reaction was warmed to rt and stirred for 2 h. Saturated $NaHCO_3$ was added, and the layers separated using a phase separator. The DCM was removed in vacuo to give a clear oil which was purified by combi flash using ethyl acetate and hexanes as mobile phase provided the desired aldehyde **8** (2.25g, 90%) as white solid.

Synthesis of 4-(isocyanomethyl)-1,2-dimethoxybenzene (10).

For the synthesis of compound **10** followed the literature procedure (*4*). Briefly, to a stirred solution of compound **9** (0.5g, 2.56mmol) in dry DCM (1.5 mL) at 0 ºC was added Et_3N (5.0 eq, 12.82 mmol, 1.68 mL), followed by $POCl_3$ (1.5 eq, 3.84 mmol, 0.24 mL) and continued the reaction mixture at same temperature for 1h, progress of the reaction was monitored by TLC, after completion of starting materials as indicated on TLC plates, reaction mixture was further diluted with CH_2Cl_2 then absorbed on silica-gel cartridge and purified using ethylacetae+hexanes as mobile phase provided the desired compound **10** (750mg, 81%) as light yellow liquid and it was slowly converted to light yellow solid upon storage.

Synthesis of compound (13):

To a mixture of N-Boc-L-prolinal (**8**) (1 eq. 200 mg, 0.851 mmol), N-protected glycine (**11**) (1 eq, 161mg, 0.851mmol) and isocyanide (**10**) (1 eq, 162 mg, 0.851 mmol.) were dissolved in anhydrous CH_2Cl_2 (10.0 mL) and stirred for 4 hours at room temperature. After complete conversion (LC-MS) of starting materials, trifluoroacetic acid (2.0 mL) was added and the mixture was stirred for an additional one hour. The volatiles were evaporated under reduced pressure. The oily residue was redissolved in anhydrous DCM and cooled down to 0° C with an ice bath. Triethylamine (2.0 mL) was added dropwise, and the stirring continued till the full conversion (LC-MS), usually less than 2 hours. The liquids were evaporated under reduced pressure, the mixture was redissolved in DCM and washed 3 times with water. Organic phase was washed with brine, dried over sodium sulfate and the solvent was evaporated under reduced pressure and obtained crude residue was purified by using combiflash with hexanes + ethyl acetate as mobile phase provided desired α-hydroxyamide (**12**)(*1*).

^{1}H-NMR (500 MHz, $CDCl_3$) δ:7.35 (s, 5H); 7.21 (t, J = 5.9 Hz, 1H); 6.93-6.57 (m, 3H); 5.76-5.37 (m, 1H); 5.12 (s, 2H); 5.10-4.98 (m, 1H); 4.62-4.20 (m,4H); 4.04-3.40 (m, 10H); 3.15-2.77 (m 1H); 2.67-2.39 (m,1H) ppm. **^{13}C-NMR (125 MHz, $CDCl_3$) δ:** 170.49, 170.35, 156.40, 149.17, 148.62, 136.06, 130.50, 128.59, 128.25, 128.00, 120.33, 119.90, 111.41, 111.27, 72.33, 72.19, 67.32, 60.17, 56.05, 55.96, 55.90, 43.72, 43.57, 43.15, 42.73 ppm. LC-MS for **12**. [M+H] calcd for $C_{25}H_{30}F_2N_3O_7$ found 522.19736 g/mol.

The product was then used in the next step by dissolving in MeOH +AcOH (1:1) and added 10%Pd-C (100 mg for 1g of starting material), then stirred under hydrogen atmosphere for 6h, the reaction mixture was filtered thorough celite pad and filtrate was evaporated under reduced pressure and obtained crude residue was azeotrope with EtOH then purified by combiflash using MeOH +DCM gave the amine **13** as orange color solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ: 7.38 (q, J = 6.1 Hz,1H); 6.80-6.63 (m, 3H); 5.29 (s, 1H); 4.68-4.19 (m, 4H); 3.86 (m, 6H); 3.78-3.65 (m, 3H); 3.54-3.21 (m, 2H); 3.10-2.65 (m, 1H); 2.61-2.36 (m, 1H) ppm. **^{13}C-NMR (125 MHz, $CDCl_3$) δ:** 173.8, 171.2, 171.00, 149.19, 148.60, 130.39, 120.17, 119.94, 111.29, 73.07, 60.18, 55.97, 55.93, 44.11, 42.99, 42.71 ppm. LC-MS for **13**. [M+H] calcd for $C_{17}H_{24}F_2N_3O_5$ found 388.16058 g/mol.

Synthesis of compound (15)

To a solution of compound **14** (500 mg, 2.64mmol) in DMF (10. mL) was added Cs_2CO_3 (2.65 gm, 7.93 mmol) then tertiary-butyl bromo acetate (7.93 mmol), the stirred the reaction mixture at 55 ºC, for 4h, then (KOH, 7.93 mmol) +H_2O (5.0 mL) were added to the same reaction mixture and continued stirring there for additional 2h, progress of the reaction was monitored by LC-MS, reaction mixture carefully neutralized with 1N HCl, the purified by using reversphase combi flash using (20 mM, pH = 7.0 ammonium acetate buffer) and acetonitrile as mobile phase gave desired acid **15** as white solid upon lypolization (650 mg 70%).

^{1}H-NMR (500 MHz, CD_3OD) δ: 8.85-8.68 (m, 1H); 8.19 (dt, J = 6.2, 2.7 Hz, 1H); 8.05-7.97 (m, 1H); 7.96-7.86 (m, 1H); 7.45 (dq, J =9.1, 2.6 Hz, 1H); 4.63 (s, 2H); 1.45 (s, 9H) ppm. ^{13}C-NMR (125 MHz, CD_3OD) δ: 167.90, 157.09, 147.21, 145.23, 130.83, 126.70, 122.95, 122.65, 104.95, 82.86, 65.73, 22.91 ppm. LC-MS for **15**. [M+H] calcd for $C_{16}H_{18}NO_5$ found 304.11067g/mol.

Synthesis of compound (16):

To a stirred solution of compound **15** (200 mg, 0.66 mmol) in anhydrous CH_2Cl_2 (10.0 mL) were added PyBOP (411 mg, 0.792 mmol) and DIPEA (0.22 mL, 1.32 mmol), then continued stirring there for 10 minutes, then amine **13** (0.66 mmol) was added to the above reaction mixture and continued stirring there for additional 2h. reaction mixture was diluted with water, then extracted into CH_2Cl_2 (2x20 mL), the combined organic extracts were dried over anhydrous sodium sulphate, filtered and filtrate was evaporated under reduced pressure, then obtained crude residue was purified by combiflash using MeOH+DCM as mobile phase provided the compound **16** as white solid.

Synthesis of compound (19):

To a solution of compound **16** (200.0 mg, 0.297mmol) in CH_2Cl_2 (5 mL) was added TFA (2.0 mL) the stirred at rt for 2h, then reaction mixture was evaporated under reduced pressure and purified by combiflash with 0-20% methanol in dichloromethane as mobile phase for 25 minutes provides the compound **17** as light yellow solid. **^{1}H-NMR (500 MHz, CD_3OD) δ:** 8.79 (t, J = 4.8 Hz, 1H); 8.02 (m, 2H); 7.64 (d, J = 4.5 Hz, 1H); 7.58 (ddt, J = 12.4, 9.2, 2.8 Hz, 1H); 6.95 (d, J = 2.0 Hz, 1H); 6.91 (t, J = 2.0 Hz, 1H); 6.90 -6.81 (m, 2H); 4.85 (s, 1H); 4.42-4.15 (m, 3H); 3.18-3.70 (m,

5H) ppm. **^{13}C-NMR (125 MHz, CD_3OD) δ:** 173.38, 172.15, 170.82, 170.55, 168.78, 168.54, 168.08, 167.49, 157.38, 156.95, 149.04, 148.45, 148.38, 146.65, 143.28, 142.35, 131.73, 131.46, 129.02, 125.92, 123.65, 120.35, 119.99, 119.32, 119.22, 119.94, 111.57, 104.68, 104.61, 72.45, 72.07, 68.99, 68.82, 67.79, 64.8, 44.09, 55.06, 54.95, 42.86, 42.61, 42.34, 42.22, 42.06, 41.44, 41.26, 22.07, 21.07 ppm. LC-MS for **17**. [M+H] calcd for $C_{29}H_{31}F_2N_4O_9$ found 617.57481g/mol.

To a stirred solution of compound **17** in CH_2Cl_2 (10.0 mL), were added PyBOP (1.2 eq) + DIPEA (5.0eq) and $BocNH(PEG)_3NH_2$ (1.2 eq) and continued stirring there for additional 2h, then reaction mixture was diluted with water, followed by extracted into CH_2Cl_2 (2x20 mL), organic extracts were dried over anhydrous sodium sulphate, evaporated under reduced pressure and obtained crude residue was purified by combiflash provided compound **18** as white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ: 8.76 (t, J = 4.7Hz, 1H); 7.98 (dd, J = 9.3, 4.2 Hz, 1H); 7.93 (t, J = 6.1 Hz, 1H); 7.71 (d, J =2.8 Hz, 1H); 7.65 (t, J = 6.0 Hz, 1H); 7.45 (d, J = 4.4 Hz, 1H); 7.42 (d, J = 4.4 Hz, 1H); 7.42 (d, J = 4.4 Hz, 1H); 7.39 (ddd, J = 9.3, 2.9, 1.6 1H); 6.85-6.70 (m, 4H); 5.17-4.97 (m, 1H); 4.78 (d, J = 15.1 Hz, 1H); 4.72-4.56 (m, 3H); 4.52-4.42 (m, 1H); 4.42-4.30 (m, 1H); 4.33-4.12 (m, 3H); 3.87-3.79 (m, 6H); 3.79-3.73 (m, 3H); 3.63-3.39 (m, 19H); 3.09 (td, J = 6.7, 3.6 Hz, 7H); 2.27-2.25 (m, 5H); 1.83-1.69(m, 6H); 1.39 (s, 9H); **^{13}C-NMR (125 MHz, $CDCl_3$) δ:** 171.5, 171.3, 168.8, 168.5, 167.82, 156.3, 155.9, 149.07, 148.9, 148.5, 147.9, 145.00, 140.43, 131.53, 131.02, 130.76, 125.41, 125.15, 122.7, 120.27, 120.16, 119.7, 119.24, 111.76, 111.45, 111.22, 104.25, 71.11, 70.27, 70.16, 70.03, 67.48, 67.26, 56.29, 56.26, 42.86, 42.43, 40.25, 38.95, 28.36, 26.42, 26.36 ppm. LC-MS for **18**. [M+H] calcd for $C_{42}H_{57}F_2N_6O_{13}$ found 891.38734g/mol.

Finally, compound **18** (1.0 eq) dissolved in CH_2Cl_2 followed by Dess-Martin periodinane (DMP) (3.0 eq) the water (10. eq) was added to reaction mixture and stirred at room temperature overnight. Rection mixture was further diluted saturated sodium bicarbonate solution and extracted into DCM (2x30 mL), the combined organic extracts were dried over anhydrous sodium sulphate, filtered and filtrate was evaporated under reduced pressure, then the obtained crude residue was purified by combiflash using MeOH +DCM as mobile phase provided the desired keto compound **19** as white solid. **^{1}H-NMR (500 MHz, $CDCl_3$) δ:** 8.88-8.80 (m, 1H); 8.67 (bs, 1H), 8.07 (dd, J = 17.8, 9.3 Hz, 1H); 7.73-7.62 (m, 1H); 7.52-7.39 (m, 2H); 7.10 (bs, 1H); 6.93-6.53 (m, 2H); 4.73-4.39 (m, 4H); 4.35-4.08 (m, 3H); 4.08-3.92 (m, 2H); 3.92-3.69 (m, 5H); 3.68-3.30 (m, 25H); 3.00-2.53 (m, 1H); 2.45 (td, J = 14.0, 7.0 Hz, 1H); 1.42 (s, 9H); ^{13}C-NMR (125 MHz, CDCl3) δ: 192.2,

168.15, 167.25, 159.85, 156.00, 155.85, 149.26, 148.8, 148.3, 147.94, 132.77, 131.61, 130.03, 125.2, 122.8, 120.8, 120.02, 112.5, 111.20, 104.26, 70.56, 70.32, 70.19, 69.6, 67.02, 60.49, 42.97, 41.96, 40.34, 38.91, 28.42ppm. LC-MS for **19**. [M+H] calcd for $C_{42}H_{55}F_2N_6O_{13}$ found 889.37169g/mol.

Synthesis of FAP8-PEG$_3$-DOTA (4) and FAP8-PEG$_3$-FITC (5) Conjugates

To a stirred solution of compound **19** (100 mg, 0.1126 mmol) in DCM (1.0 mL) was added TFA (0.5 mL) and continued stirring there for 30 min, reaction mixture was evaporated under reduced pressure provided the free amine of compound **19** as brown color gummy solid, and this amine was used for further steps without purification. To a stirred solution of amine from compound **19** (20 mg, 0.0253 mmol) in DMF (500 µl) DIPEA (0.11mmol) followed by NHS-DOTA (16.0 mg) were added and stirring continued at rt for additional 6h. reaction mixture was diluted with water and purified by u-HPLC using (A = Ammonium acetate (10 mM, pH = 7.0), B = Acetonitrile for 60 min using 5-35 method and obtained desired fractions are quickly freeze using liquid nitrogen and lyophilized for 48h provided the desired compound FAP8-PEG$_3$-DOTA (**4)** as white solid (20 mg, 68%), LC-MS for **4.** LC-MS (m/z): [M+K] calcd for $C_{53}H_{72}F_2N_{10}O_{18}$ found 1214.2078 g/mol.

Similarly, to a stirred solution of free amine from compound **19** (1.0 eq) in DMF (500 ul for 20 mg) were added DIPEA (3.0 eq) followed by Fluorescein 5-isothiocyanate (1.0) then continued stirrering under conditions for 30 minutes, reaction mixture was further diluted with water and purified by u-HPLC using (A = Ammonium acetate (10 mM, pH = 7.0), B = Acetonitrile for 60 min using 5-35 method and obtained desired fractions are quickly freeze using liquid nitrogen and lyophilized for 48h provided the desired compound FAP8-PEG$_3$-FITC (**5)** as Yellow solid in quantitative yield. LC-MS for **5**. [M+H] calcd for $C_{58}H_{58}F_2N_7O_{16}S$ found 1178.35506 g/mol.

Synthesis of FAP8-PEG$_3$-IP-DOTA conjugate (3).

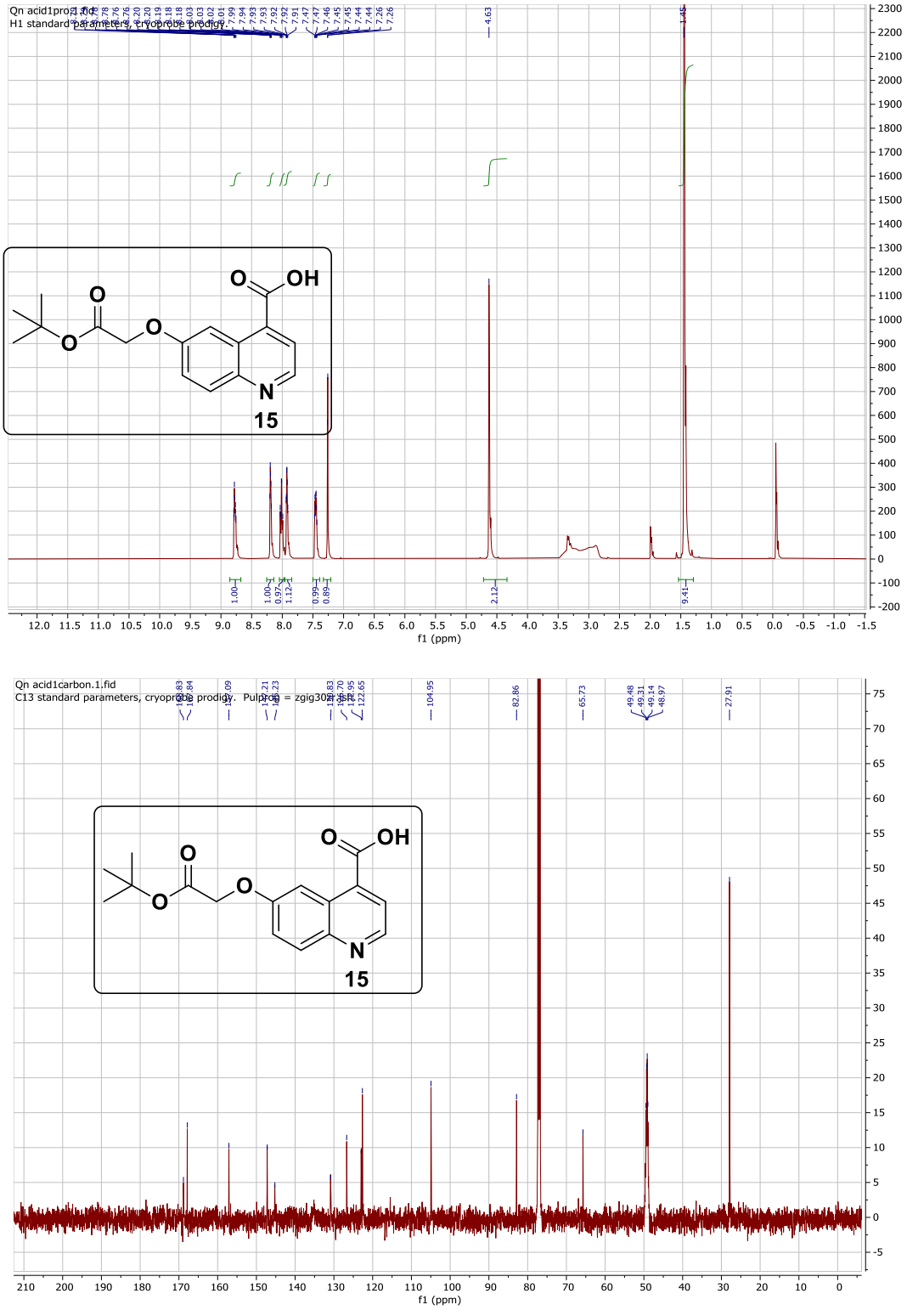
To a stirred solution of 4-(4-iodophenyl)butanoic acid (**20)** (1g, 3.460 mmol) in DCM (15 mL) were added PyBOP (1.2 eq) then DIPEA (2.0 eq) continued stirring rt for 10 min, then the (S)-5-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5-carboxypentan-1-aminium chloride **21** (1.39 gm, 3.460 mmol) and DIPEA (2.0eq) were added to the above reaction mixture and continued stirring there for additional 4h, progress of the reaction was monitored by LC-MS. Reaction mixture was diluted with water and extracted into DCM (2X30 mL) and then combined organic extracts were

evaporated under reduced pressure and obtained crude residue was purified by using combiflash with CH_2Cl_2 +MeOH as mobile phase gave the desired compound coupled product **22** (2.0 gm, 90%) as white solid. **^{1}H-NMR (500 MHz, $CDCl_3$) δ:** 7.76 (d, J = 7.6 Hz, 2H); 7.60 (dd, J = 9.1, 7.4 Hz, 2H); 7.55 (d, J = 7.9 Hz, 2H); 7.40 (t, J = 7.5 Hz, 2H); 7.34-7.28 (m, 2H); 6.87(d, J = 7.9 Hz, 2H); 4.70-4.24(m, 3H); 4.23-4.05 (m, 1H); 3.24 (t, J = 13.3, 6.5 Hz, 2H); 2.54 (t, J = 7.5 Hz, 2H); 2.15 (t, J = 7.5 Hz, 2H); 1.92 (q, J = 7.5 Hz, 2H); 1.79 (bs, 1H); 1.53 (t, J = 7.2Hz, 2H); 1.48-1.38 (m, 2H) ppm. **^{13}C-NMR (125 MHz, $CDCl_3$) δ:** 174.97, 173.71, 156.36, 143.88, 141.29, 140.95, 137.43, 130.58, 127.77, 127.11, 125.16, 120.02, 91.02, 67.11, 53.53, 47.13, 39.10, 35.68, 31.79, 28.92, 26.81, 22.17 ppm. LC-MS for **22.** LC-MS (m/z): [M+H] calcd for $C_{31}H_{33}IN_2O_5$ found 640.14342 g/mol.

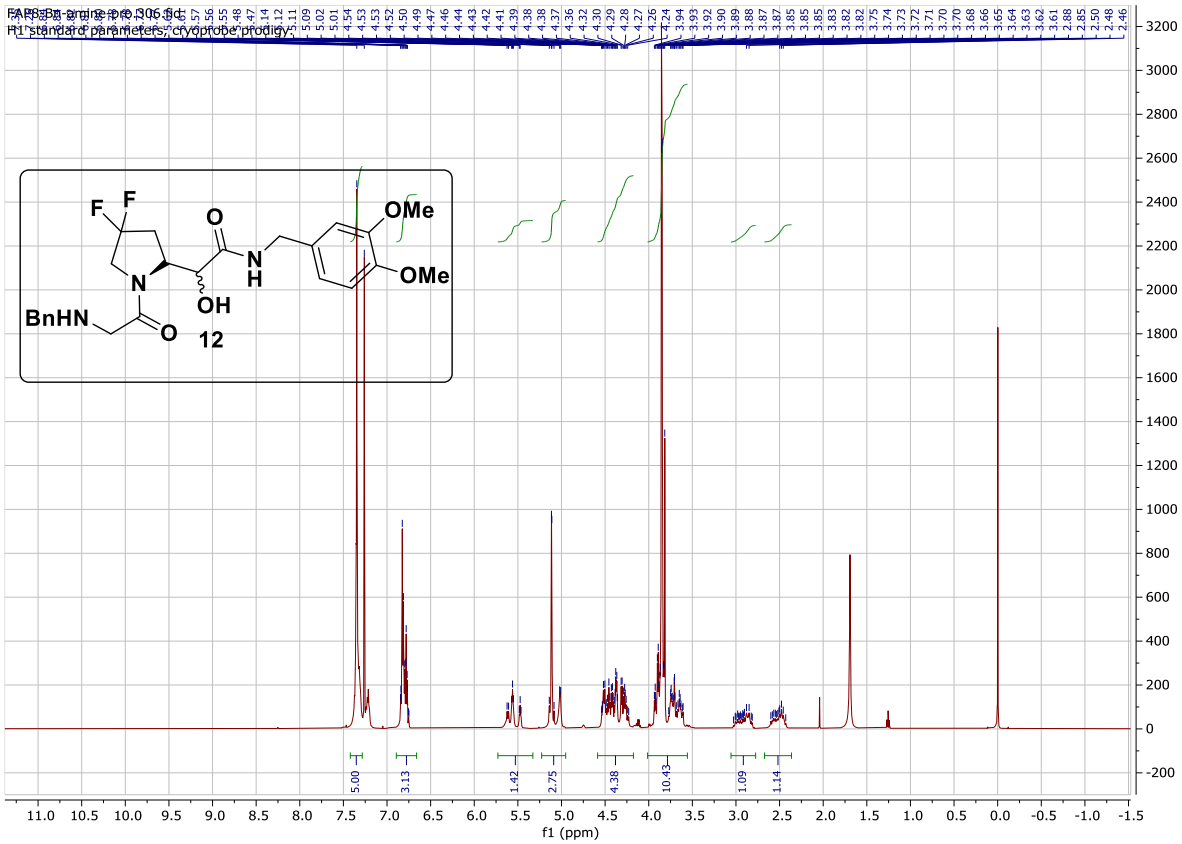
Finally, to a stirred solution of acid **22** (50 mg, 0.0781 mmol), in CH_2Cl_2 (2.0 mL) was added PyBOP (1.2 eq), DIPEA (2.0 eq) and stirred there for 10 min. then free amine (from compound-**19**) (0.0781 mmol) was added to the above reaction mixture and continued stirring for additional 2h, reaction mixture was diluted with water (20 mL) the extracted into CH2Cl2 (2x 20 mL) and the combined organic extracts were evaporated under reduced pressure, then obtained crude residue was purified by combiflash using MeOH+DCM as mobile phase provided the compound **23** as white solid. Then the compound **23** (50.0 mg, 0.035mmol) was dissolved in DCM (500 µLmL) + diethylamine (500 µl) and stirred at rt for 1 h. reaction mixture was evaporated under reduced pressure and obtained crude residue washed with diethyl ether, dried under reduced pressure and re-dissolved in DMF (1.0 mL) followed by DIPEA (5.0 eq), NHS-DOTA (1.0 eq) were added, stirred the reaction mixture at rt for 6h, reaction mixture was further diluted with water and purified by u-HPLC using (A = Ammonium acetate (10 mM, pH = 7.0), B = Acetonitrile for 60 min using 5-35 method and obtained desired fractions are quickly freeze using liquid nitrogen and lyophilized for 48h provided the desired compound FAP8-PEG_3-IP-DOTA (**3)** as white solid.

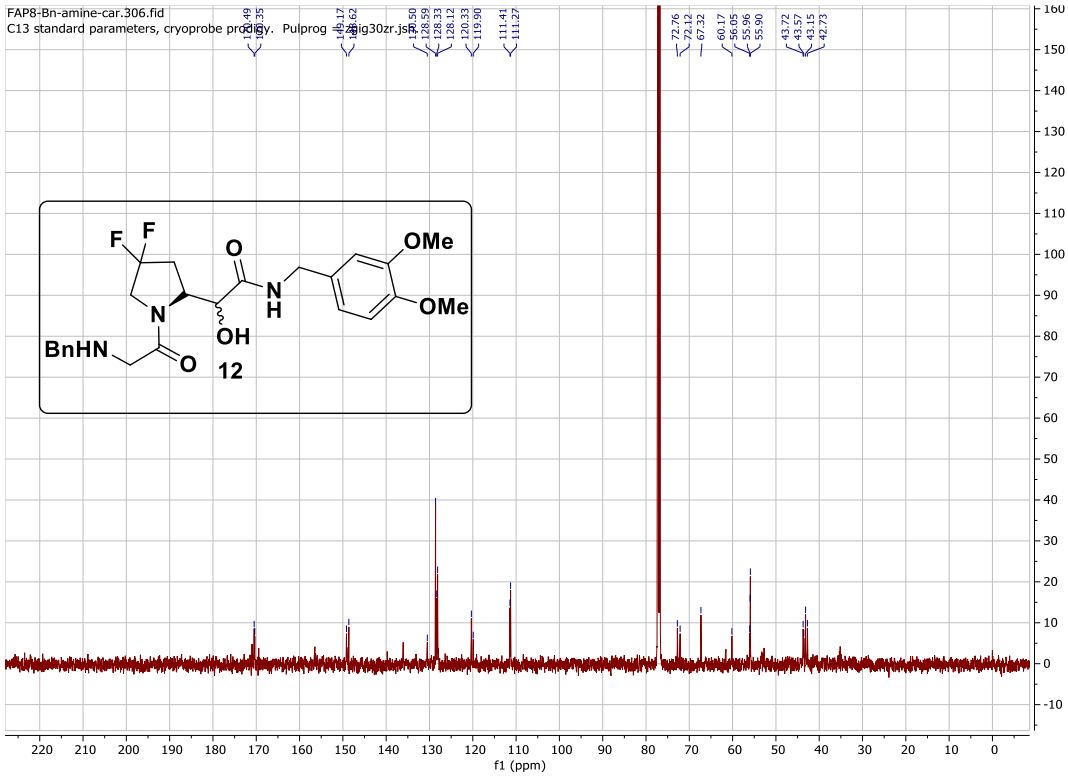
^{1}H-NMR (500 MHz, CD_3OD) δ: 8.84 (d, J = 4.4 Hz, 1H); 8.80 (q, J = 4.6 Hz, 2H); 8.24 (bs, 2H); 8.04 (d, J = 15.3 Hz, 9.2 Hz, 3H); 7.96-7.83 (m, 1H); 7.73-7.74 (m, 10 H); 4.79-4.51 (m, 4H); 4.50-4.18 (m, 12H); 4.12-3.62 (m, 21H); 3.59-3.51 (m, 32H); 2.56(t, J = 7.7 Hz, 6H); 2.17 (t, J = 7.6 Hz, 5H);1.86 (dd, J = 8.7, 6.5 Hz, 5H); 1.84-1.73 (m, 2H); 1.64 (d, J = 8.7Hz, 2H); 1.56-133 (m, 7H) ppm. **^{13}C-NMR (125 MHz, CD_3OD**) δ: 173.89; 172.40; 141.60; 137.73; 130.44; 119.91; 111.59; 89.41; 70.11; 69.81; 69.57; 68.93; 67.25; 55.09; 54.22; 53.24; 50.83; 38.66; 35.06; 34.34;

28.50; 27.18; 22.83 ppm. LC-MS for **3.** LC-MS (m/z): [M+39] calcd for $C_{69}H_{92}F_2IN_{12}O_{20}K$ found 1613.2 g/mol.

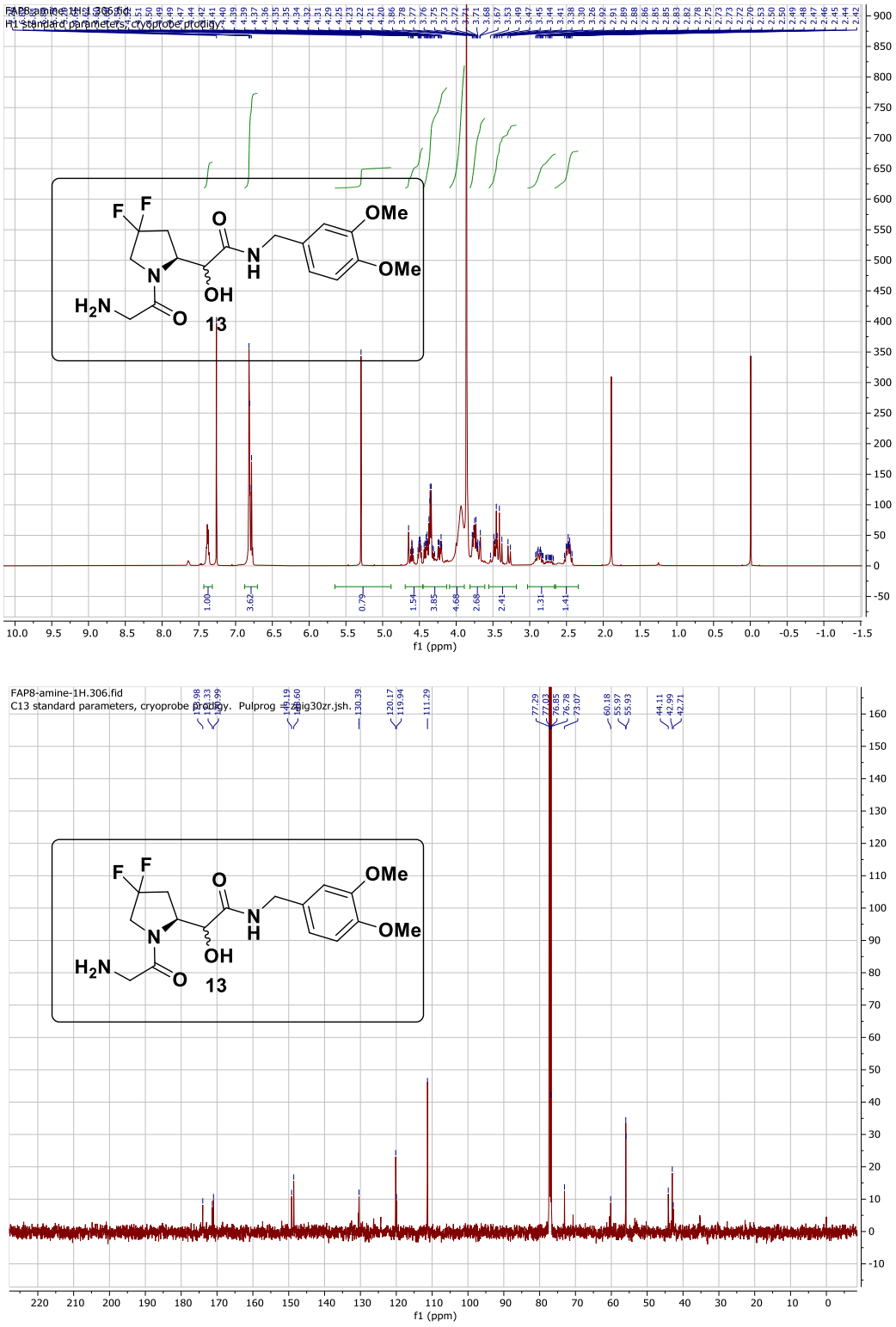


Supplemental Figure 7. ^{1}H &^{13}C NMR of Compound 15

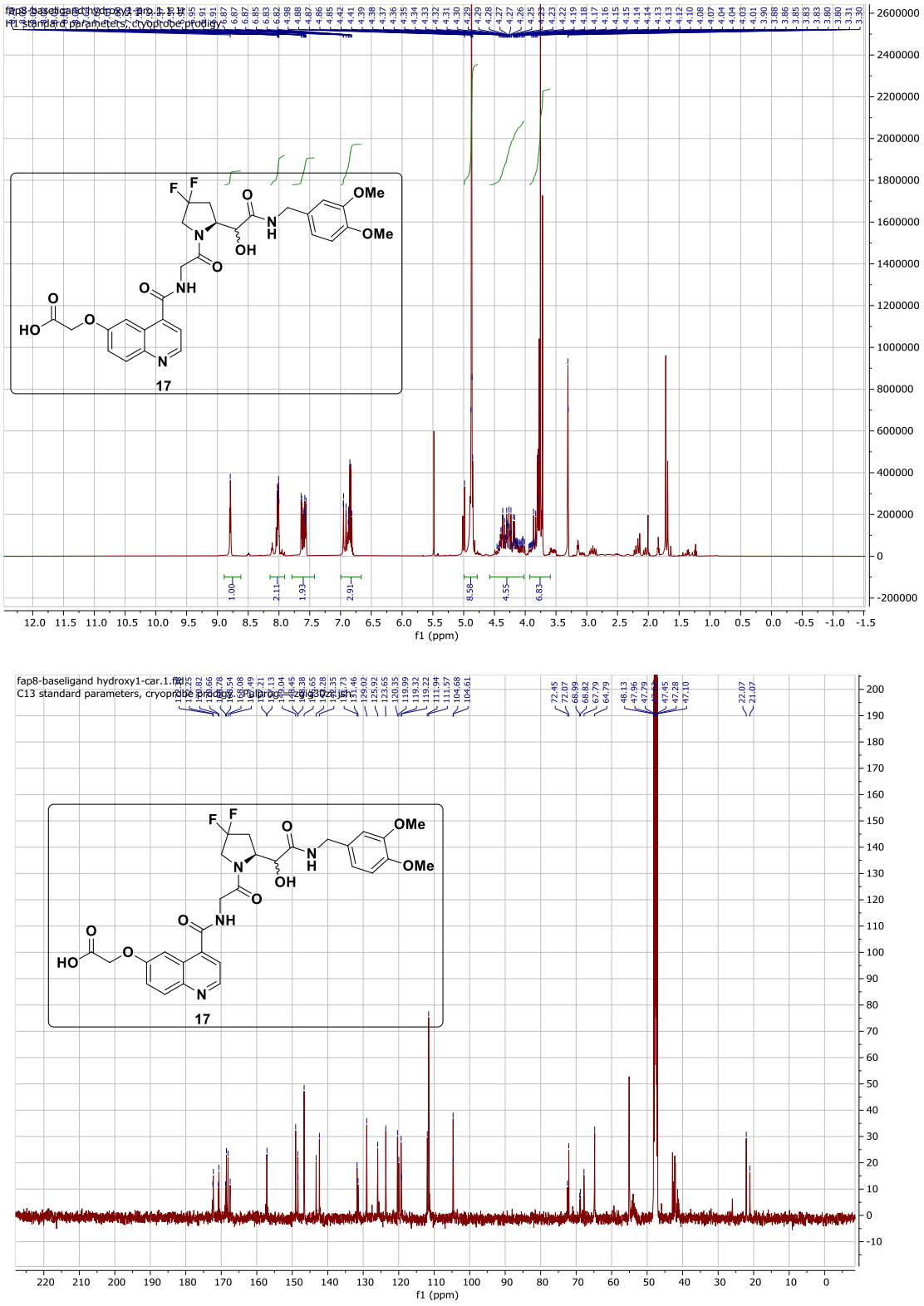




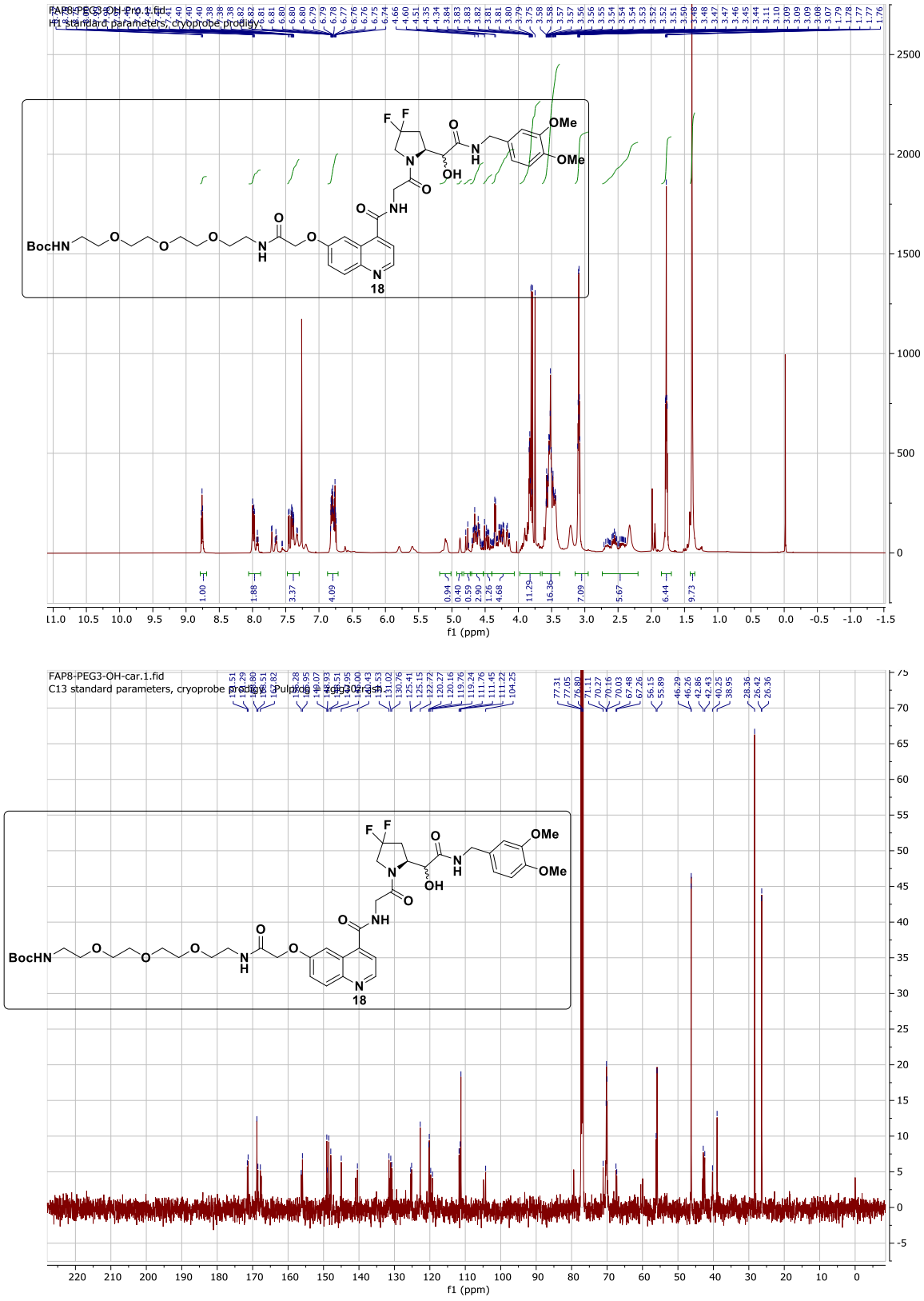
Supplemental Figure 8. ^{1}H &^{13}C NMR of Compound 12



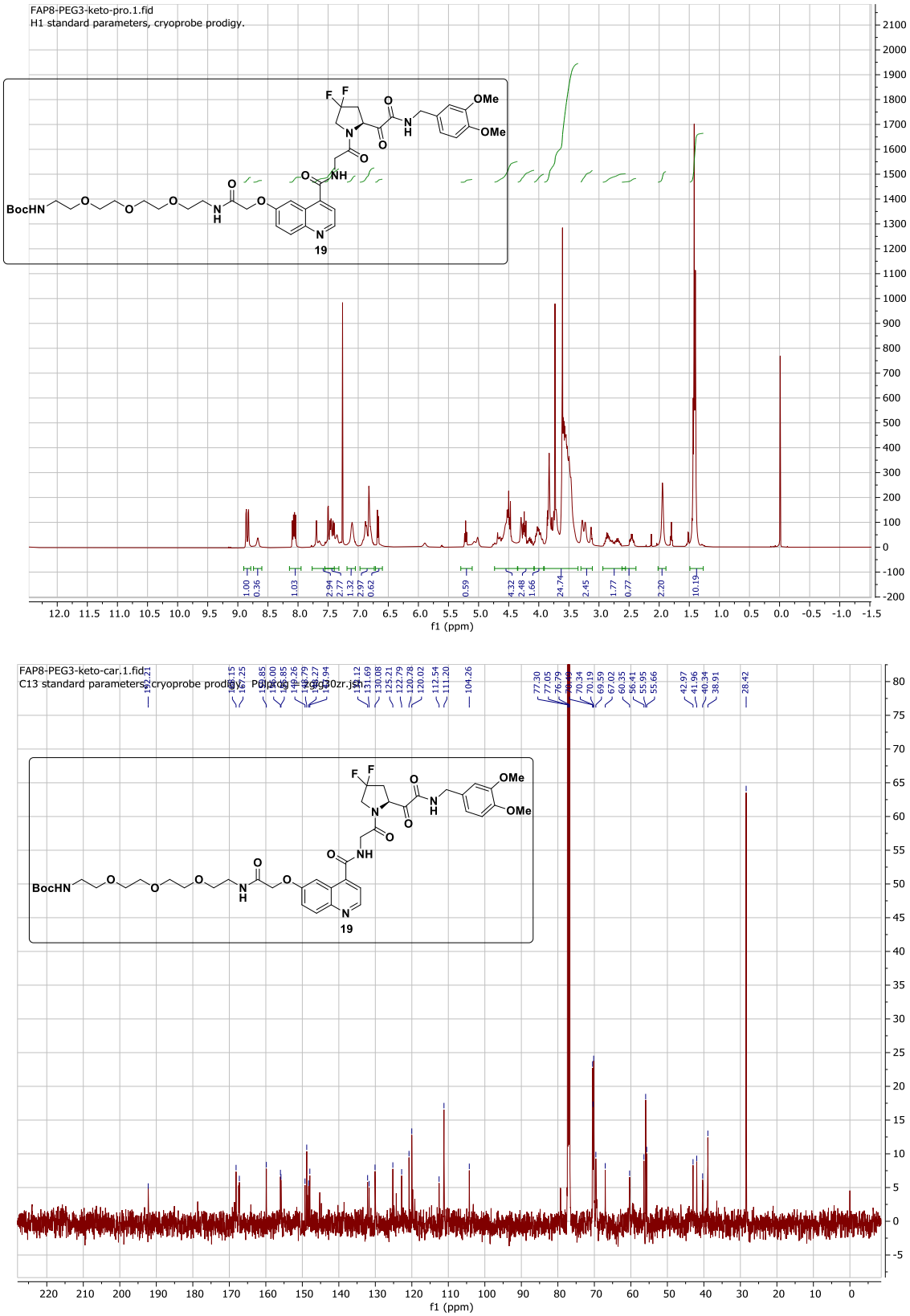
Supplemental Figure 9. ^{1}H &^{13}C NMR of Compound 13.



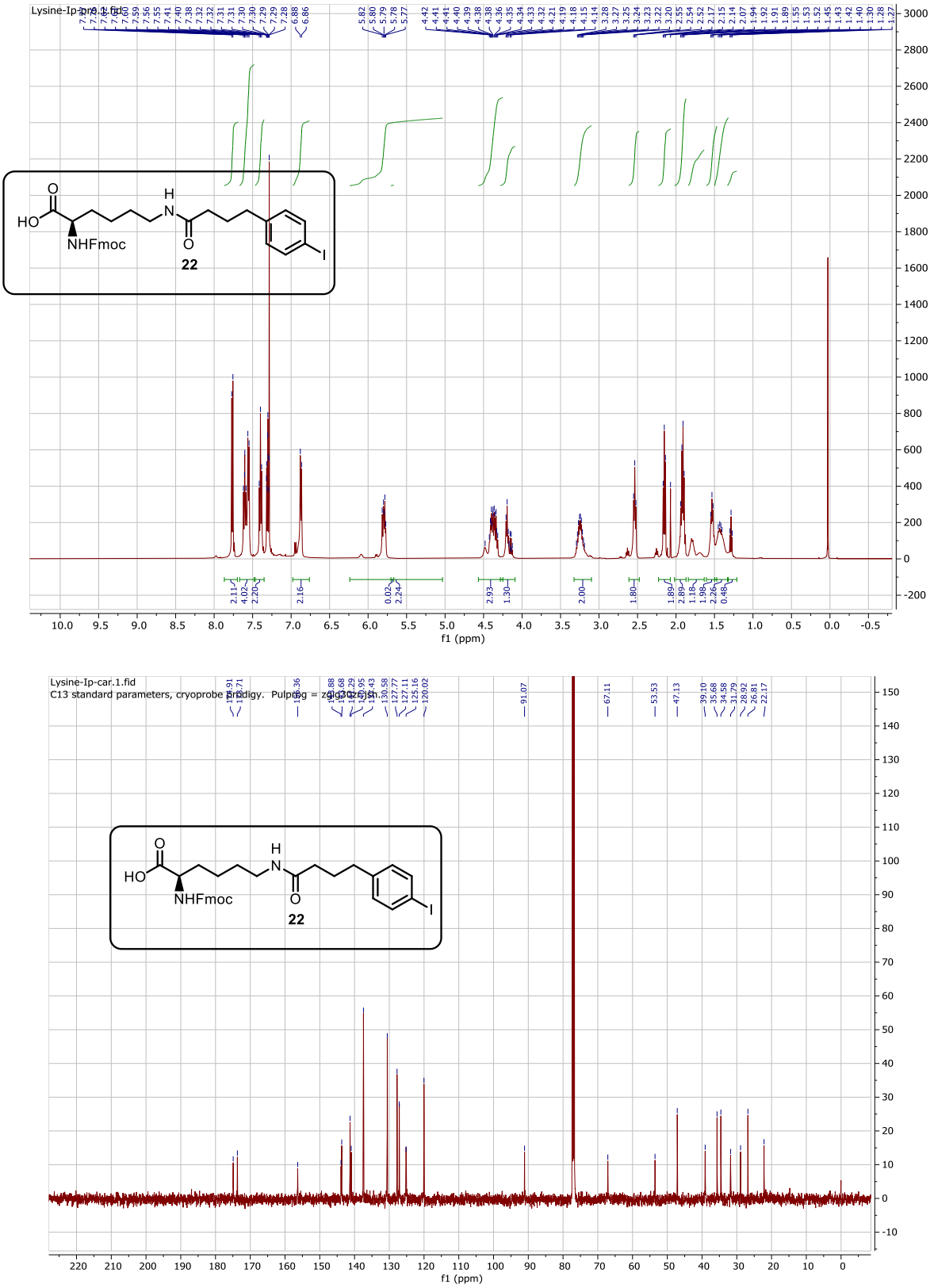
Supplemental Figure 10. ^{1}H &^{13}C-NMR of Compound 17



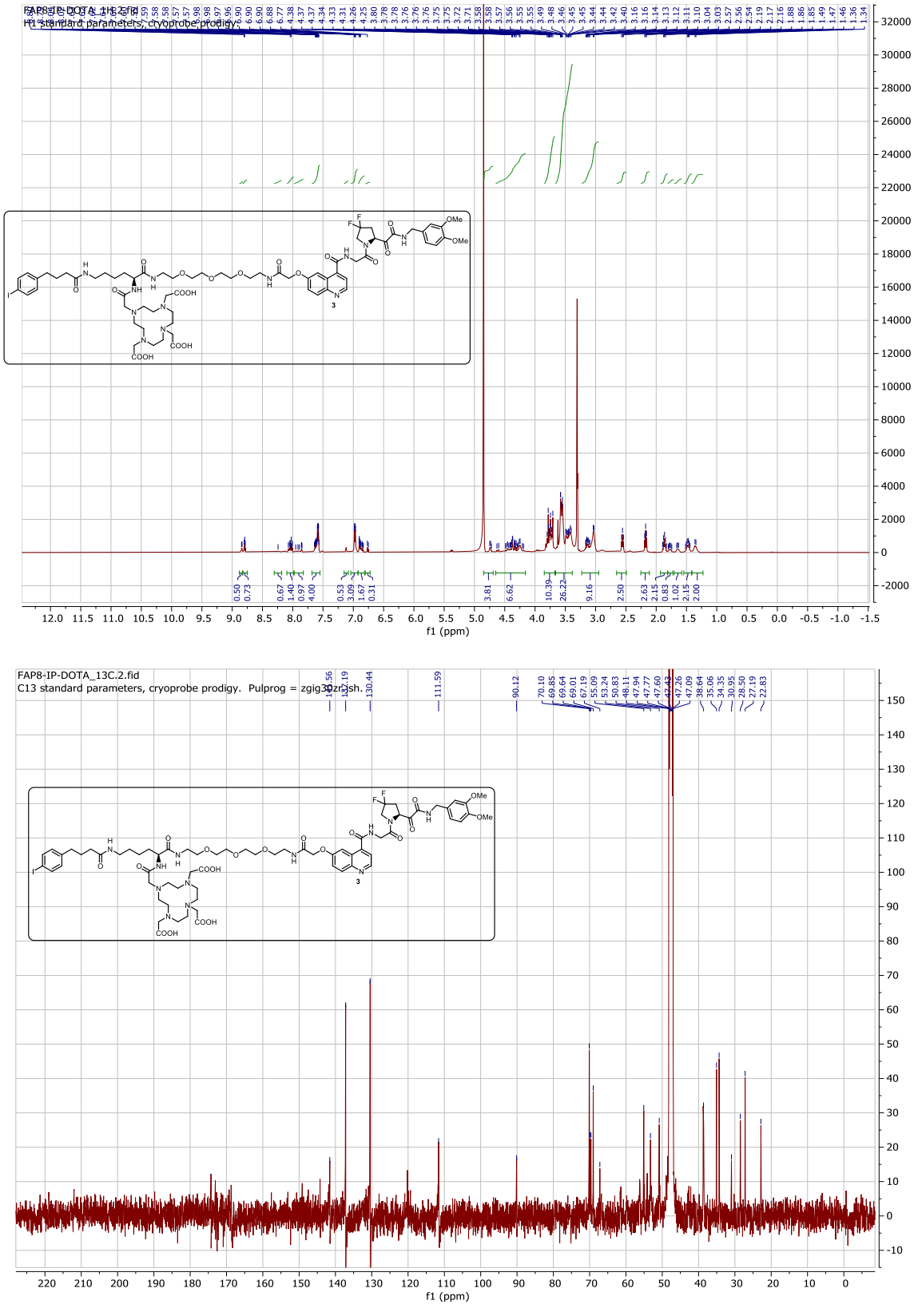
Supplemental Figure 11: ^{1}H &^{13}C-NMR of Compound 18.



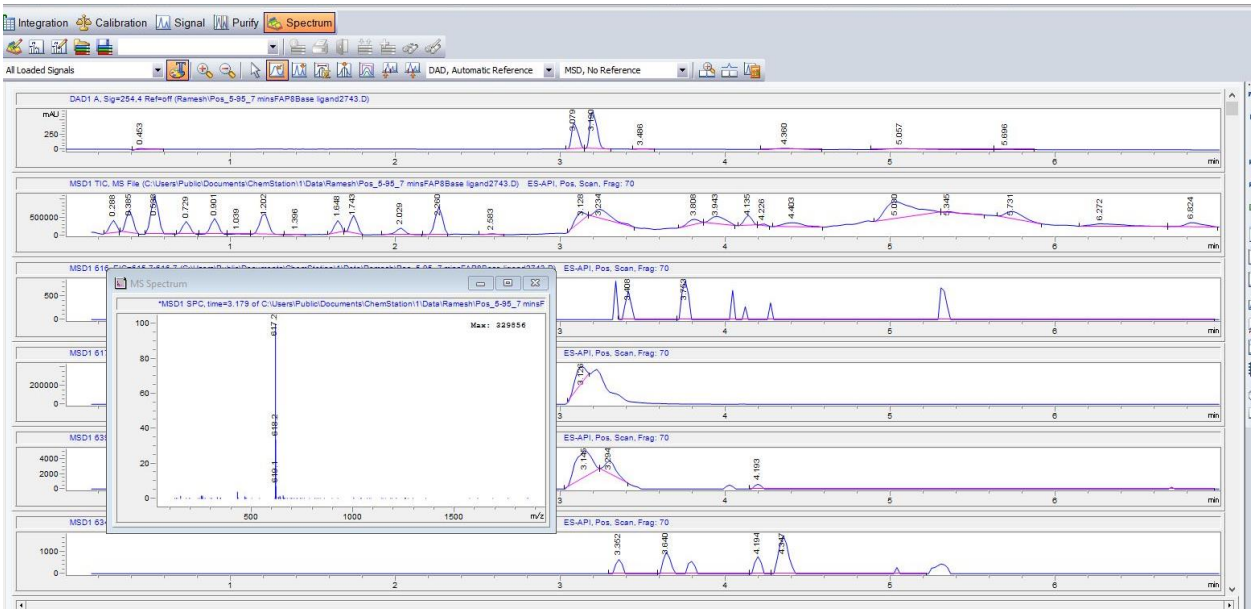
Supplemental Figure 12. ^{1}H &^{13}C-NMR of Compound 19.



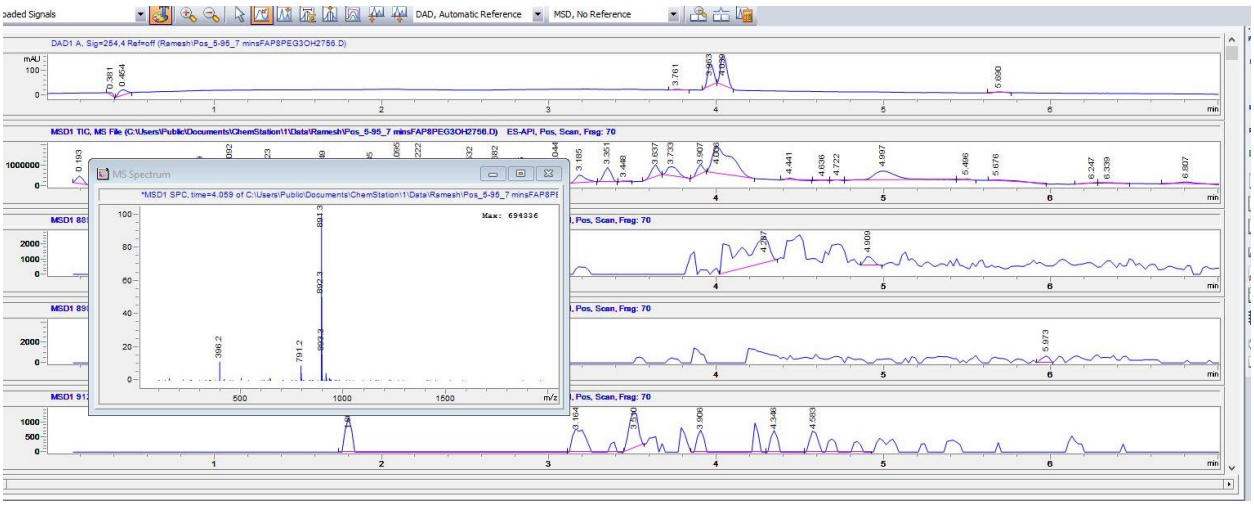
Supplemental Figure 13. ^{1}H &^{13}C-NMR of Compound 22.



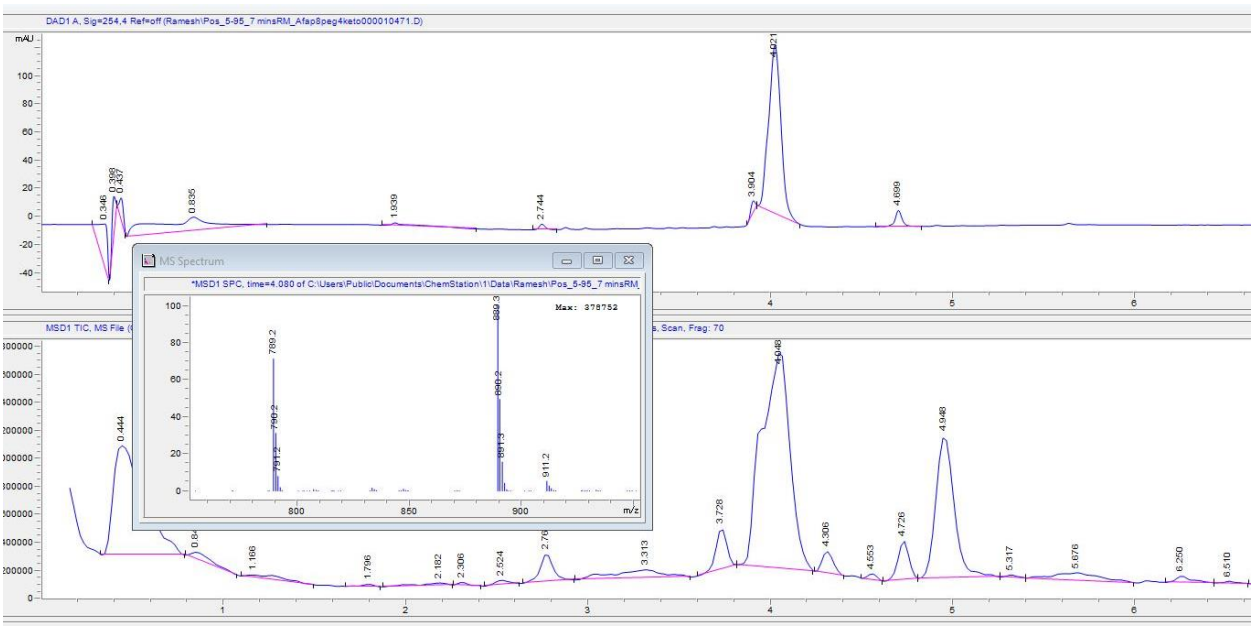
Supplemental Figure 14. ^{1}H &^{13}C-NMR of Compound 3.



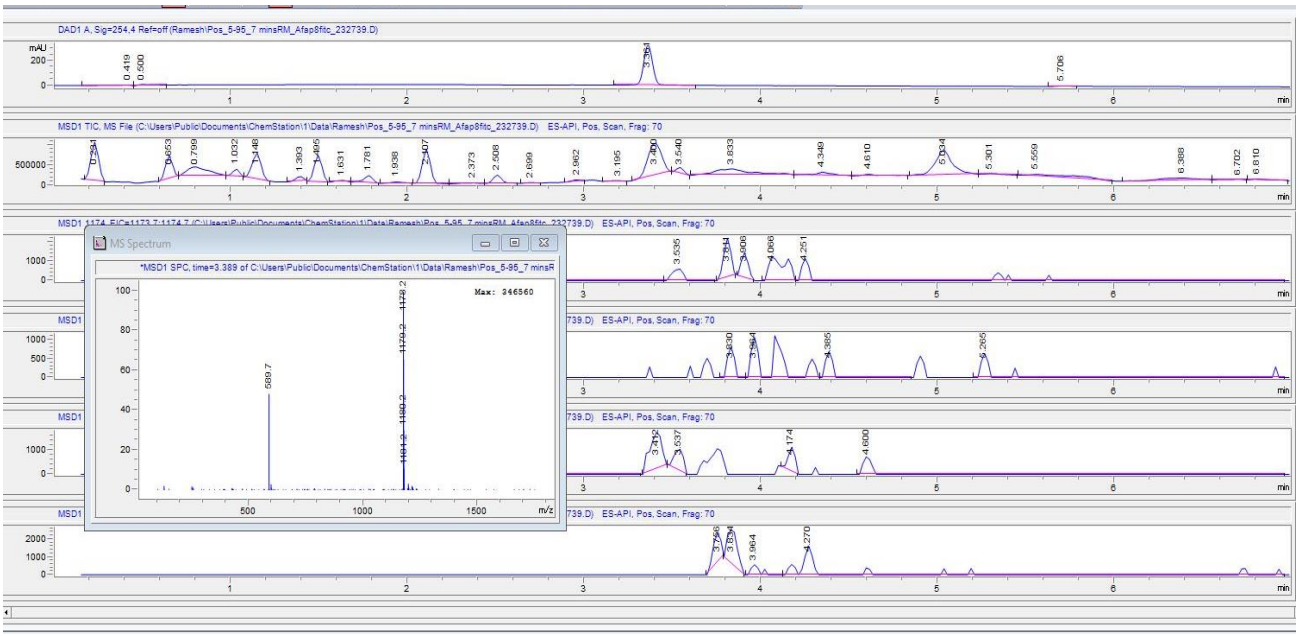
Supplemental Figure 15. LC-MS of Compound 17.



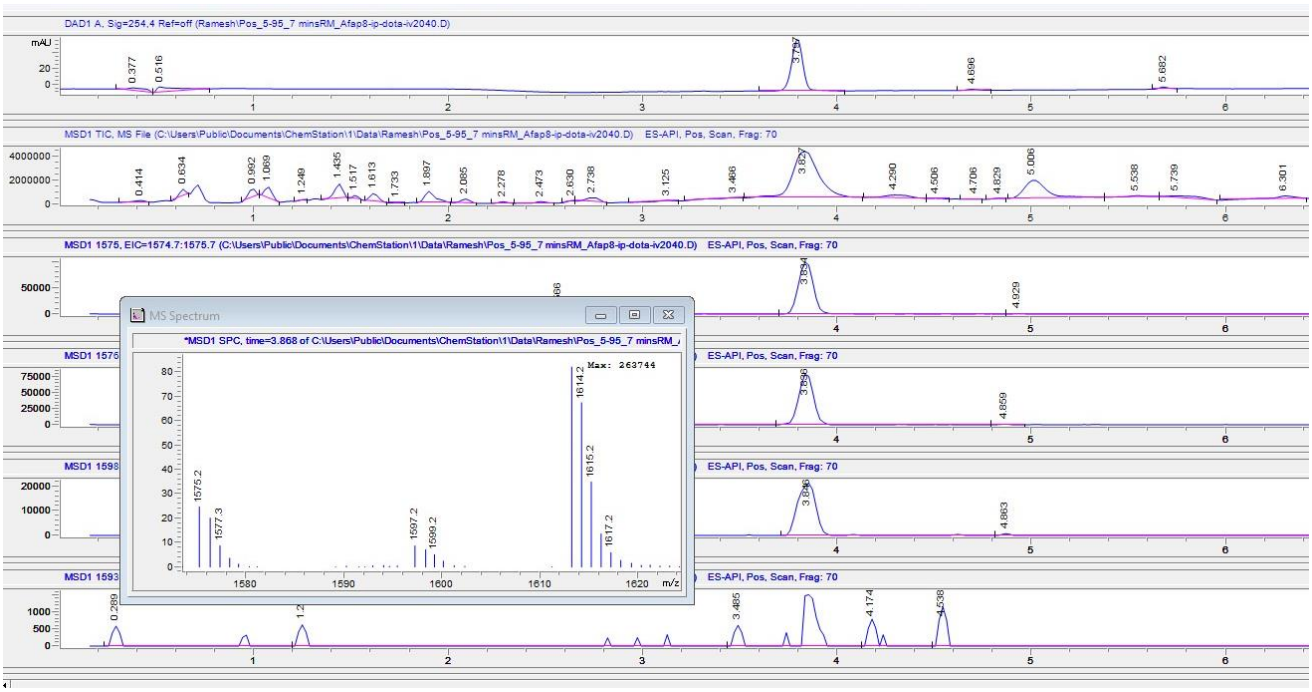
Supplemental Figure 16. LC-MS of Compound 18



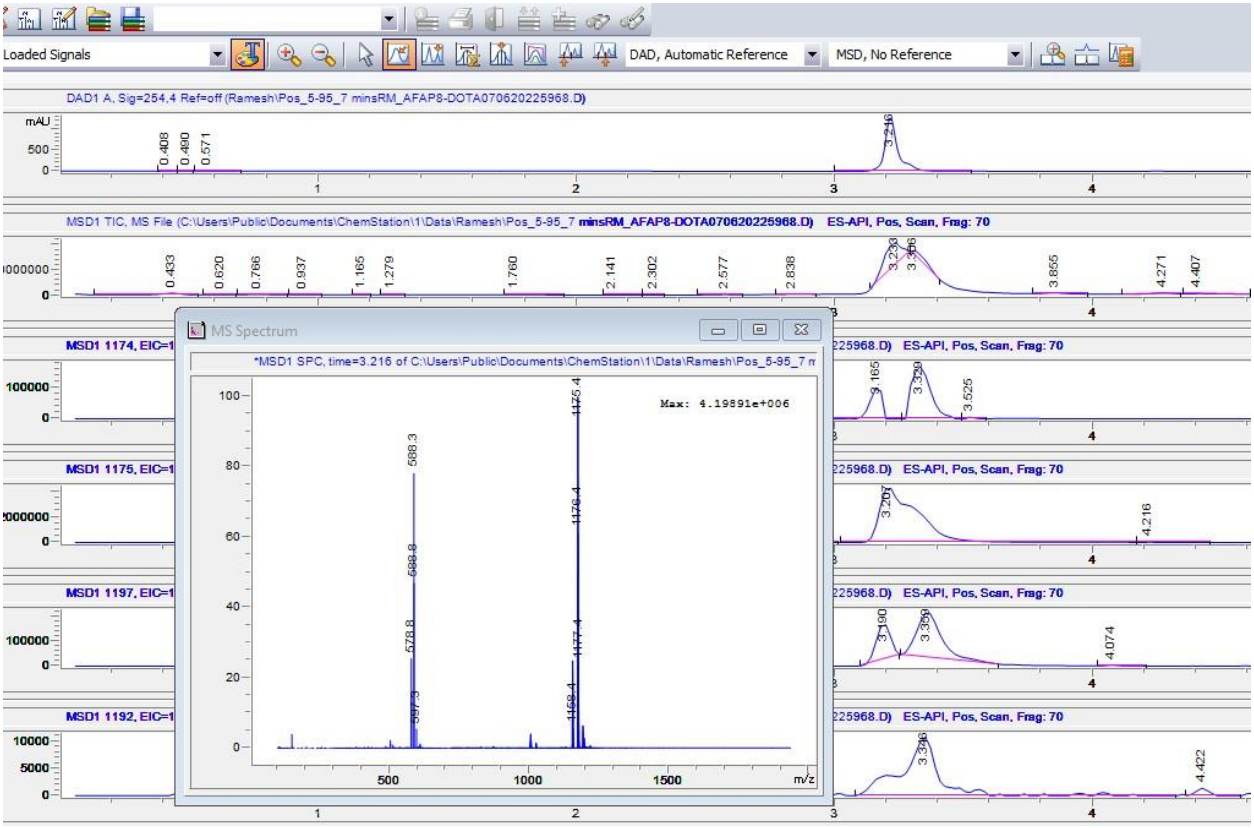
Supplemental Figure 17. LC-MS of Compound **19**



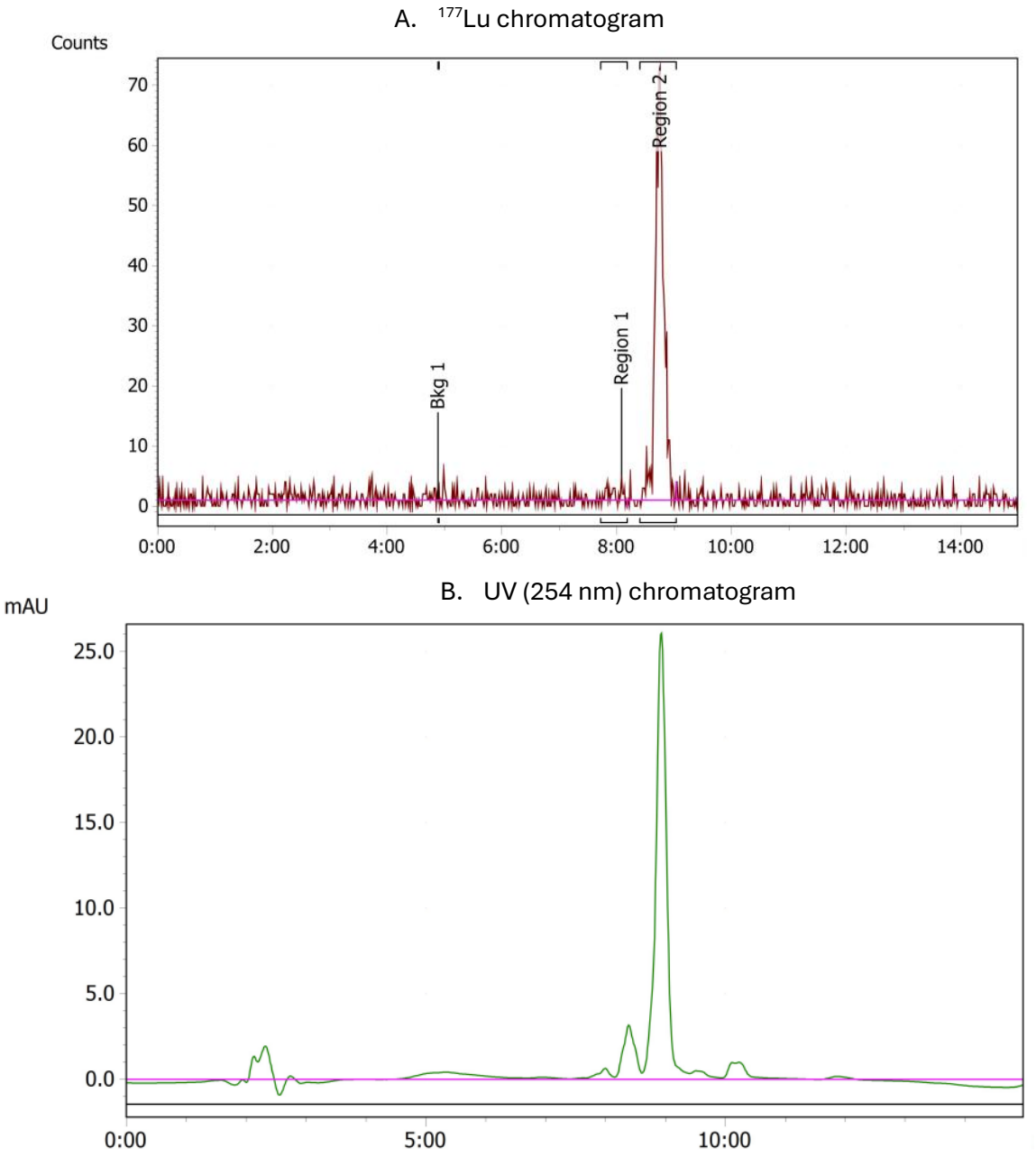
Supplemental Figure 18. LC-MS of FAP8-PEG$_3$-FITC (**5**).



Supplemental Figure 19. LC-MS of FAP8-PEG$_3$-IP-DOTA **(3).**



Supplemental Figure 20. LC-MS of FAP8-PEG$_3$-DOTA **(4).**



Supplemental Figure 21. Radiochromatogram of [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA (A). UV chromatogram of [^{177}Lu] Lu-FAP8-PEG$_3$-IP-DOTA (B). Radio-HPLC conditions: gradient = 0.5 min 5% B → 4.5 min 95% B → 10.0 min 95% B → 11.0 min 5% B → 14.0 min 5% B → 15.0 min 5% B [A = 20 mM pH 7 NH_4HCO_3, B = ACN]; flow rate = 0.75 mL/min; λ = 254 nm extracted.

References

1. Šimková A, Ormsby T, Sidej N, et al. Structure-activity relationship and biochemical evaluation of novel fibroblast activation protein and prolyl endopeptidase inhibitors with α-ketoamide warheads. *Eur J. Med Chem.* 2021;224:113717.
2. Guillaume PN, Rosalba M, Lisa M, et al. Biodistribution, Pharmacokinetics, and Dosimetry of ¹⁷⁷Lu-, ⁹⁰Y-, and ¹¹¹In-Labeled Somatostatin Receptor Antagonist OPS201 in Comparison to the Agonist ¹⁷⁷Lu-DOTATATE: The Mass Effect. *J Nucl Med* 2017;58:1435.
3. Spencer DL, Ramesh M, Autumn H, et al. Fibroblast Activation Protein–Targeted Radioligand Therapy for Treatment of Solid Tumors. *J Nucl Med.* 2023;64:759.
4. Patil P, Ahmadian-Moghaddam M, Dömling A. Isocyanide 2.0. *Green Chemistry.* 2020;22:6902-6911.