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Supplementary information

The landscape for radioligand therapies in oncology

In the format provided by the authors and unedited

Database assembly and analysis

We assembled a comprehensive database of 69 radioligand therapies (RLTs) in commercial clinical development as of March 2025.

Core source. We compiled our initial set of assets using the EvaluatePharma database. To identify relevant assets, we filtered the database based on keywords ("Radiation", "Radionuclide", "Radiopharmaceuticals") in the "Mechanism of Action", "Pharmacological Class", or "Therapeutic Subcategory" data fields in the overall EvaluatePharma database.

Validation. We manually cross-checked the resulting database against company websites, company presentations, and academic publications to classify the asset as an RLT. Radiopharmaceutical assets that did not meet our criteria for RLTs were excluded. Exclusion criteria included lack of systemic administration, absence of a distinct ligand-based targeting moiety (for example, Xofigo/Radium-223, nanoparticle- or liposome-only based formulations), or use for diagnostic purposes only.

Stage of development. Approved assets are currently approved. Clinical-stage assets are currently in phase I–III clinical trials as established using the company website and/or ClinicalTrials.gov. Assets in combined, seamless trials (for example, phase I/II or phase I/III) were assigned to a specific phase based on information from company disclosures or by assessing the current point in time relative to trial start and end dates. Assets under regulatory review were counted under phase III.

Radioisotope. Radioisotopes of RLT assets were identified based on information from company websites and disclosures. Radioisotopes were classified based on the more novel or clinically relevant particle emitted during its nuclear decay chain. Radioisotopes presented in Figure 1 exclude those that are used in previous generations of clinically validated RLTs and other radiopharmaceuticals (Iodine-123, Iodine-131, Yttrium-90); the full breakdown of clinical-stage RLTs by radioisotope is presented in Supplementary Figure 1.

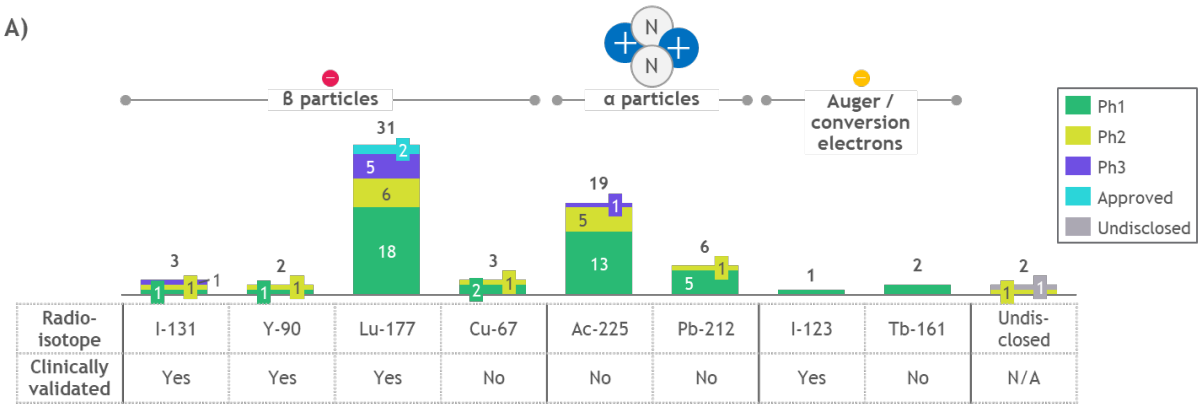
Targeting moiety. Targeting moieties were determined based on explicit classifications provided in company websites or publications. For assets without the targeting moiety type specified, the chemical structure of the asset was evaluated, if available. Peptide-based targeting moieties were identified based on clearly defined structures of multiple peptide bonds and amino acids, in contrast to non-peptide small molecule targeting moieties. Conventional antibodies refer to antibodies without further engineering or modifications specified. Engineered protein and antibody derivatives include heavy-chain-only antibodies, single-domain antibodies, antigen-binding fragments (Fabs), nanobodies, miniproteins, bispecifics and antibody tetramers.

Target. Targets of RLT assets were identified based on information from company websites and disclosures. Targets were categorized into validated for RLTs, validated in other modalities (via the presence of an approved therapy), and exploratory targets (not yet validated in any approved therapy) based on a review of FDA approvals.

Tumour type. Tumour types targeted by each RLT asset were identified using information from company websites and ClinicalTrials.gov. For early-stage phase I assets, tumour types were further determined by reviewing the inclusion criteria of the corresponding active trial listing (note: many phase I assets are in basket trials with multiple tumour types being studied). In cases where the targeted tumour type is based on a biomarker (for example, SSTR2+ tumors, FAP+ tumors) without further indicating the exact tumor type, the "Unspecified" label was used. Where feasible, tumor types were grouped into broader categories (for example, "Melanoma and skin" includes melanoma, Merkel cell carcinoma, uveal melanoma).

Assessment of next-generation technology. Early-generation RLTs were defined as those approved in the 2000s (Zevalin; ibritumomab tiuxetan and Bexxar; tositumomab and I-131 tositumomab); current-generation RLTs represent recently approved and commercially available RLTs (Lutathera; Lu-177 dotatate and Pluvicto; Lu-177 vipivotide tetraxetan); and next-generation RLTs were categorized as clinical-stage assets in development. The potential impact and challenges of the different technologies were evaluated based on a review of the scientific literature.

A)



Radio-isotope	I-131	Y-90	Lu-177	Cu-67	Ac-225	Pb-212	I-123	Tb-161	Undis-closed
Clinically validated	Yes	Yes	Yes	No	No	No	Yes	No	N/A

B)

Radioisotope	Particles emitted	Decay chain
Lu-177	1x β	Lu-177 6.7 d → (β⁻) Hf-177 Stable
Cu-67	1x β	Cu-67 2.6 d → (β⁻) Zn-67 Stable
Ac-225	4x α 2x β	Ac-225 9.9 d → (α) Fr-221 5 m → (α) At-217 32 ms → (α) Bi-213 46 m → (β⁻) Po-213 4 µs → (α) Po-209 3 h → (β⁻) Bi-209 Stable; Bi-213 46 m → (α) Tl-209 2 m → (β⁻) Po-209 3 h
Pb-212	1x α 2x β	Pb-212 11 h → (β⁻) Bi-212 1 h → (β⁻) Po-212 0.3 µs → (α) Pb-208 Stable; Bi-212 1 h → (α) Tl-208 3 m → (β⁻) Pb-208 Stable
Tb-161	1x β Multiple Auger / conversion electrons	Tb-161 6.9 d → (β⁻) Dy-161 Stable Auger / conversion electrons

Supplementary Figure 1 | **Clinical-stage RLTs by radioisotope. A**, Radioisotopes used in clinical-stage RLTs, organized by class of particle emission and by clinical validation in an approved radiopharmaceutical (I-131, Y-90 and I-123 are used in non-targeted radiotherapeutics or radiodiagnostics). **B**, Particles emitted and decay chains of main novel radioisotopes in clinical-stage RLTs. Half-lives are shown for each radioisotope (µs = microsecond, ms = millisecond, s = second, h = hour, d = day).

Supplementary Table 1 | Commercial clinical-stage RLTs

Company	Asset	Radioisotope	Targeting moiety	Target	Tumour type	Phase
Abdera Therapeutics	ABD-147	Ac-225	Engineered Ab / protein	DLL3	Lung (neuroendocrine)	I
Actinium	Iomab-B	I-131	Conv. Ab	CD45	Bone-marrow conditioning	III
Actinium	Actimab-A	Ac-225	Conv. Ab	CD33	AML	II
AdvanCell	ADVC001	Pb-212	Non-peptide small molecule	PSMA	Prostate	I
Aktis	AKY-1189	Ac-225	Engineered Ab / protein	Nectin-4	Bladder, breast, lung (NSCLC), colorectal, cervical	I
Ariceum	SS0110 (Lu-177)	Lu-177	Peptide	SSTR2	Lung (neuroendocrine)	I
Ariceum	SS0110 (Ac-225)	Ac-225	Peptide	SSTR2	Lung (neuroendocrine), melanoma & skin	I
Ariceum	ATT001	I-123	Non-peptide small molecule	PARPi	Glioblastoma	I
ArtBio	AB001	Pb-212	Non-peptide small molecule	PSMA	Prostate	I
AstraZeneca	FPI-1434	Ac-225	Conv. Ab	IGF-1R	Endometrial, cervical, ovarian, breast, head & neck, melanoma & skin	I
AstraZeneca	FPI-2068	Ac-225	Engineered Ab / protein	EGFR/cMET	Head & neck, lung (NSCLC), colorectal, pancreatic	I
AstraZeneca	FPI-2265	Ac-225	Non-peptide small molecule	PSMA	Prostate	II
Bayer	BAY3546828	Ac-225	Conv. Ab	PSMA	Prostate	I
Bayer	BAY3563254	Ac-225	Non-peptide small molecule	PSMA	Prostate	I
Bivision	JH020002 (JH02)	Lu-177	Peptide	PSMA	Prostate	I
Blue Earth Therapeutics	177 Lu-rhPSMA-10.1	Lu-177	Non-peptide small molecule	PSMA	Prostate	I
Bristol Myers Squibb	RYZ801	Ac-225	Peptide	GPC3	Liver	I
Bristol Myers Squibb	RYZ101	Ac-225	Peptide	SSTR2	GEP-NETs, lung (neuroendocrine), breast	III
Cancer Targeted Technology	CTT1403	Lu-177	Non-peptide small molecule	PSMA	Prostate	I
CellBion	177Lu-PSMA-DGUL	Lu-177	Non-peptide small molecule	PSMA	Prostate	II
Clarity	67 Cu-SAR-bisPSMA	Cu-67	Non-peptide small molecule	PSMA	Prostate	II
Clarity	67 Cu-SAR-Bombesin	Cu-67	Peptide	GRPR	Prostate	I
Clarity	67 Cu-SARTATE	Cu-67	Peptide	SSTR2	Neuroblastoma	I
Convergent Therapeutics	CONV01-α	Ac-225	Conv. Ab	PSMA	Prostate	II
Curium	177Lu-PSMA I&T	Lu-177	Non-peptide small molecule	PSMA	Prostate	III
Eli Lilly	PNT2001	Ac-225	Non-peptide small molecule	PSMA	Prostate	I
Eli Lilly	PNT6555	Lu-177	Peptide	FAP	Pancreatic, sarcoma, esophageal, colorectal, melanoma, head & neck, bile duct)	I
FutureChem	177Lu-FC705 (Ludotadipep)	Lu-177	Molecule	PSMA	Prostate	II
GlyTherix	177 Lu-Miltuximab	Lu-177	Conv. Ab	GPC-1	Prostate, Bladder	I
HengRui	HRS-4357	Undisc.	Undisc.	PSMA	Prostate	II
ITM	ITM-11	Lu-177	Peptide	SSTR2	GEP-NETs	III
ITM	ITM-23	Tb-161	Non-peptide small molecule	PSMA	Prostate	I
ITM	ITM-63	Tb-161	Peptide	SSTR2	GEP-NETs	I
ITM	ITM-31	Lu-177	Engineered Ab / protein	CAXII	Glioblastoma	I
ITM	ITM-91	Lu-177	Peptide	CAIX	Kidney, pancreatic, colorectal	I
J&J	JNJ-69086420	Ac-225	Conv. Ab	hK2	Prostate	I

Lantheus	PNT2002	Lu-177	Non-peptide small molecule	PSMA	Prostate	III
Lantheus	PNT2003	Lu-177	Peptide	SSTR2	GEP-NETs	III (Filed)
Modulation	MTI-201	Ac-225	Undisc.	MC1R	Melanoma & skin	I
Molecular Targeting Technologies	177 Lu-EBTATE	Lu-177	Peptide	SSTR2	GEP-NETs, lung (neuroendocrine), thyroid, head & neck	II
Monopar	MNPR-101-Lu	Lu-177	Conv. Ab	uPAR	Bladder, breast, lung (neuroendocrine, NSCLC), colorectal, ovarian, pancreatic	I
Novartis	Pluvicto	Lu-177	Non-peptide small molecule	PSMA	Prostate	Marketed
Novartis	Lutathera	Lu-177	Peptide	SSTR2	GEP-NETs	Marketed
Novartis	AAA817 (Ac-PSMA-617)	Ac-225	Non-peptide small molecule	PSMA	Prostate	II
Novartis	AAA603 (177Lu-NeoB)	Lu-177	Peptide	GRPR	Breast, glioblastoma	II
Novartis	FXX489 (Lu-NNS309)	Lu-177	Undisc.	Undisc.	Pancreatic, lung (NSCLC), breast, colorectal	I
Novartis	AAA614 (Lu-FAP-2286)	Lu-177	Peptide	FAP	Lung (NSCLC), pancreatic, breast	I
Novartis	GIZ943 (Lu-EVS-459)	Lu-177	Undisc.	FRα	Ovarian, NSCLC	I
Novartis	AAA802 (225Ac-PSMA-R2)	Ac-225	Non-peptide small molecule	PSMA	Prostate	II
Orano Med	AlphaMedix	Pb-212	Peptide	SSTR2	GEP-NETs	II
Orano Med	212 Pb-GRPR	Pb-212	Peptide	GRPR	Prostate, breast	I
PentixaPharm	PentixaTher PT-002 (Lu-177)	Lu-177	Peptide	CXCR4	Leukemia	I
PentixaPharm	PentixaTher PT-002 (Y-90)	Y-90	Peptide	CXCR4	Lymphoma, multiple myeloma	I
Perspective Therapeutics	212pb-VMT-α-NET	Pb-212	Peptide	SSTR2	GEP-NETs	I
Perspective Therapeutics	VMT01	Pb-212	Peptide	MC1R	Melanoma & skin	I
Philogen	OncoFAP	Lu-177	Non-peptide small molecule	FAP	FAP+ solid tumors	I
Precirix	CAM-H2	I-131	Engineered Ab / protein	HER2	Breast, gastric, GEJ	I
Radiopharm Theranostics	RAD204	Lu-177	Engineered Ab / protein	PD-L1	Lung (NSCLC)	I
Ratio Therapeutics	N/A	Ac-225	Non-peptide small molecule	FAP	Sarcoma	I
Sinotau	XTR008 (177Lu Oxodotreotide)	Lu-177	Peptide	SSTR2	Neuroendocrine neoplasms other than grade G1/G2 GEP-NETs	II
Sinotau	XTR010	Undisc.	Undisclosed	Undisc.	Prostate	Undisc.
Sinotau	XTR017 / XT-117	Lu-177	Undisclosed	FAP	Unspecified	I
Telix	TLX591	Lu-177	Conv. Ab	PSMA	Prostate	III
Telix	TLX250	Lu-177	Conv. Ab	CAIX	Kidney cancer	II
Telix	TLX101	I-131	Non-peptide small molecule	LAT-1	Glioblastoma	II
Telix	TLX592	Ac-225	Conv. Ab	PSMA	Prostate	I
Telix	TLX66	Y-90	Conv. Ab	CD66	Bone-marrow conditioning	II
Y-mAbs	GD2-SADA	Lu-177	Engineered Ab / protein	GD2	Lung (neuroendocrine), melanoma & skin, sarcoma, neuroblastoma	I
Y-mAbs	CD38-SADA	Lu-177	Engineered Ab / protein	CD38	Non-Hodgkin lymphoma	I