WARF THERAPEUTICS
Invest-Develop-Partner

Radiopharmaceutical for CA9+ cancers

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PCC WT-7695 radiopharmaceutical for CA9+ cancers

Best-in-class profile

- Superior off-rate translated to greater *in vivo* tumor uptake, retention and efficacy
- 55% IA/g delivered to tumor at 24 hours
- 18% IA/g retained in tumor at 7 days
- WT-7695 delivers 8X more radiation to tumors vs. DPI-4452

Partnering opportunity for CA9 targeting radiopharmaceutical

Program PCC WT-7695

- **Target:** Carbonic Anhydrase 9 (CA9)
- **Primary indications:** non small cell lung cancer and metastatic clear cell renal cell carcinoma
- **Unmet need:** Low survival rates and high patient populations for both primary indications

	5-year relative survival	United States Incidence for CA9+	Worldwide Incidence for CA9+	Worldwide Market 2023
NSCLC	28%	54,636	411,400	$31.5B
Metastatic ccRCC	18%	11,398	47,769	$10.1B

  - Secondary indications include prostate, bladder, breast, ovarian, pancreatic, and head and neck cancers
- **Modality:** Small molecule radiolabeled with a beta-emitter (Lu-177)
- **Development stage:** Lead optimization
- **Progress to date:** Single dose, efficacy study in ccRCC mouse model to be complete in July

Radiopharmaceuticals are the future for metastatic ccRCC therapy

Radiopharmaceuticals programs in development for ccRCC

Company	Name	Compound	Stage	Mechanism of Action	Indication
WARF Therapeutics	PCC WT-7695	Small molecule with radiation emitter	Preclinical	Radiation emitter	ccRCC
DebioPharm	Debio 0228	Peptide with Lu	Phase II	Radiation emitter	Metastatic ccRCC
RayzeBio	RAYZ-15710	Small molecule with radiation emitter	Preclinical	Radiation emitter	ccRCC

PCC WT-7695 is highly potent and selective for CA9

PCC WT-7695 demonstrated

- **Excellent CA9 binding affinity** with **long residence times**
- **> 100-fold selectivity** vs. other CAs
- Excellent *in vitro* and *in vivo* mouse PK profile

Mouse PK

PK parameters	Unit	7695 Mean
Cl_obs	mL/min/kg	8.42
$T_{1/2}$	h	1.45
C_0	umol/L	4.71
AUC_{Inf}	h*umol/L	1.90
V_{ss}_obs	L/kg	0.315

Biophysical Profile:

SPR KD (nM) / $t_{1/2}$ (min)	7695
CA9	**0.03 / 490**
CA4	11 / 10
CA12	9 / 31
CA14	4 / 15

Cell Membrane Binding (nM):

CA9 (nM) (CaSki)	0.8
CA12 (nM) (A498)	32
SK-RC-52 (nM)	0.2

Solubility and in vitro DMPK:

Solubility (μM)	300
logD	-1.1
Mouse PPB (%)	77
Mouse microsomal CL (ml/min/kg)	0

WT vs. Debiopharm and RayzeBio

WT candidates have comparable selectivity with superior off-rates, greater tumor uptake, longer tumor retention and improved dosimetry (~3 Gy/MBq)

Compound	CA9 potency (nM) / off-rate (min)	CA12 selectivity / off-rate (min)	% of dose in tumor		^{177}Lu therapeutic dose (mCi)
			24 h	7 d	
PCC WT-7695	0.03 / 490	300 / 31	**55%**	**18%**	0.5
DPI-4452	0.25 / 99	NR	**10% (4 h)**	**NR**	3.0
RAYZ-15710	0.09 / 27	1500 / NR	6%	**<3%**	3.0

PCC WT-7695 has best in class potential

NR: Not reported

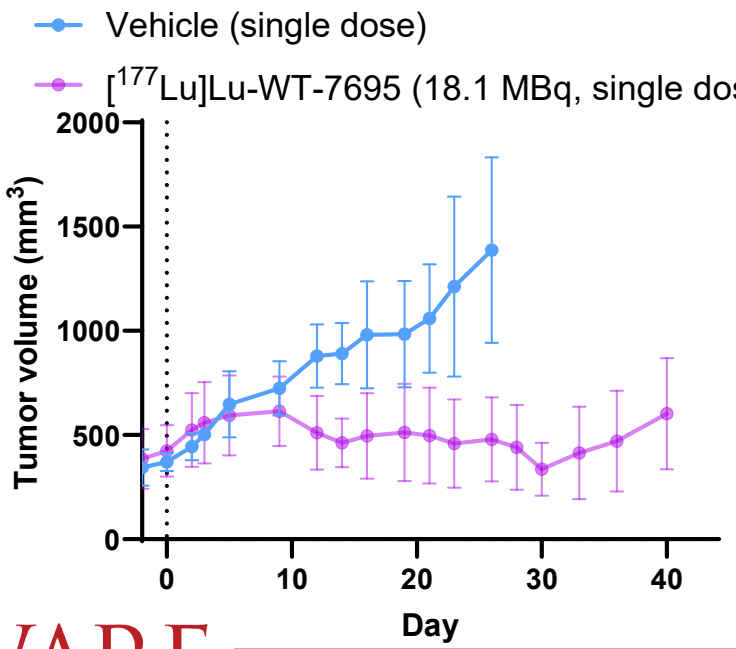
Animal proof of concept for PCC WT-7695

- 8 cohorts of 5 mice per cohort
  - 3 conditions
  - All cohorts will be repeated with 5 additional mice
- Implant tumors in mice on day 1
- Allow tumors to grow for 14 days
- Divide mice into treatment (Lu177) and placebo groups and give a single dose on day 15
- Monitor tumor size, survival (out 120 days), and treatment related toxicity
- PCC-WT-7695 dosed on January 10, 2024

PCC WT-7695 requires 80% less ^{177}Lu than DPI-4452 to achieve comparable efficacy

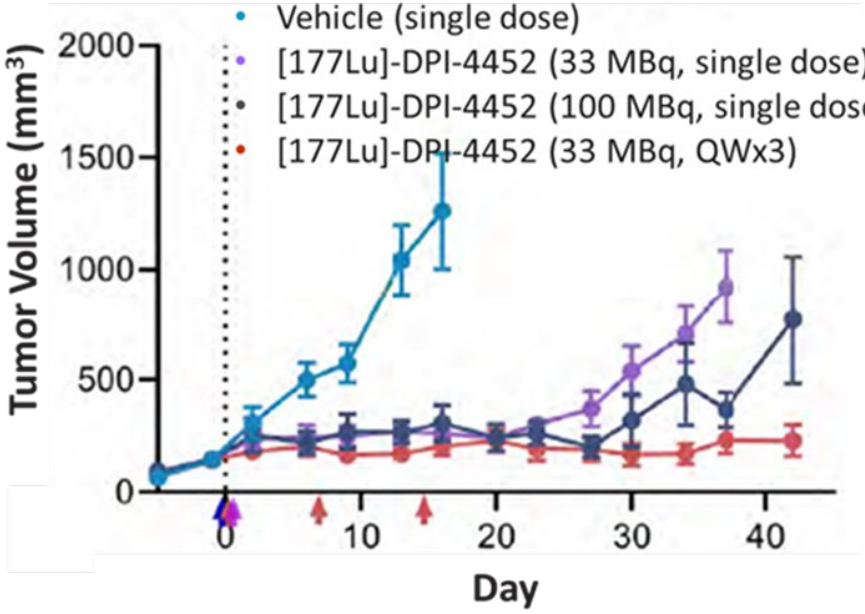
PCC WT-7695

- Mice treated with WT-7695 showed tumor **regression starting on day 9-12**
- **Statistical significance was achieved at day 12-16** after dosing
- Survival tracking ongoing



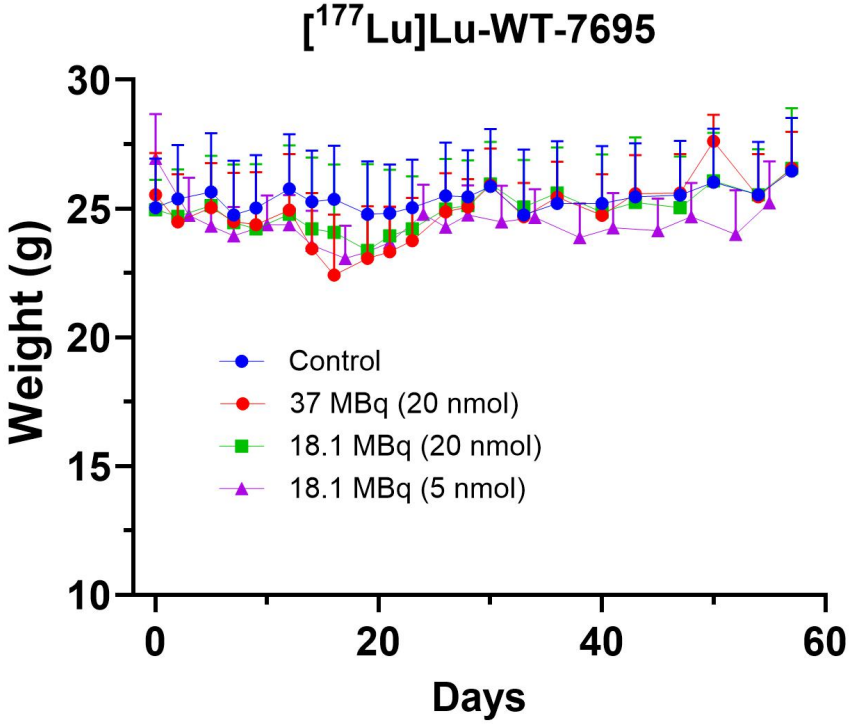
DPI-4452

- Mice given 3 mCi of DPI-4452 **(6X higher than 7695)** achieved only **temporary tumor response**
- **Tumors progressed after day 20** at the same initial growth rate
- To improve response multiple injections of ^{177}Lu were required



Mice body weights were unaffected by the treatments

Dosimetry data estimates that ~90 Gy of radiation can be safely delivered to the tumor without off target effects in the stomach



- *Mouse 3 @ 1.0mCi 7695 group excluded from every measurement/dataset (tumor not visible from day 12 to day 26)*
- *Mouse 1 @ 0.5mCi cG250 group excluded from every measurement/dataset (mouse died on 01/29/24 @ day 17)*
- *Group 0.5mCi 729 sick with visible C. Bovis on 01/19/24 @ day 9*

Next steps

- ccRCC model
  - Dose & schedule optimization
  - Isotope exploration
- Toxicology in normal mice
- Non-human primate biodistribution imaging
- Initiate NSCLC tumor models
- GMP production and IND enabling studies

CA9 radiopharmaceutical opportunity

- **NSCLC and metastatic ccRCC are large indications with high unmet need**
  - Upside potential with multiple secondary indications
- **PCC WT-7695 shows best in class potential**
  - Single dose, mouse efficacy study demonstrates **superior efficacy** vs. the competition
  - Candidates have comparable selectivity with **superior off-rates, greater tumor uptake, longer tumor retention and improved dosimetry** vs. the competition
- **Single dose, efficacy data in mice will be complete by 2Q 2024**
- **WT is seeking a partner to continue the development and commercialize this asset**
  - Worldwide, exclusive rights are available
  - We are open to various deal structures such as licensing, co-development, build to buy or startup formation
- For more information contact John Nagel at **jnagel@warf.org** or Mike Partsch at **mpartsch@warf.org**