2025年10月22日原子力委員会説明
リンクメッド株式会社取り組み

令和7年第36回原子力委員会
資料第1号

Link for Life

^{64}Cuを用いた見えるがん治療薬開発
Develpoment of Visible Cancer Radiotherapeutics with ^{64}Cu

吉井　幸恵　リンクメッド株式会社

Yukie Yoshii, PhD　LinqMed Inc.

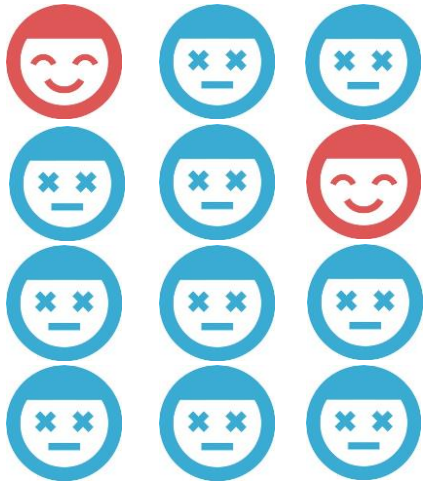
Problem

CANCER is still a major cause of death worldwide, despite development of many new therapies.

Why?

"True Theranostics" is missing.
= Combination of Therapy + Diagnostics using one drug

Predict efficacy and toxicity



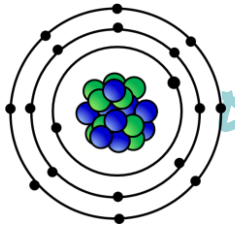
Monitor to adjust treatment regimes

We can find the best treatment for each patient based on evidence.

Before treatment → During treatment

“Visible” cancer radiotherapeutics with Copper-64 (^{64}Cu) to provide true theranostics for intractable cancers

^{64}Cu



Positron

β-

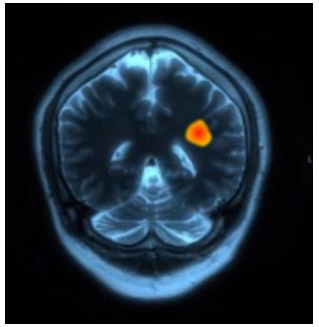
Auger

Precise Diagnostics

Only One

Effective Therapy

PET

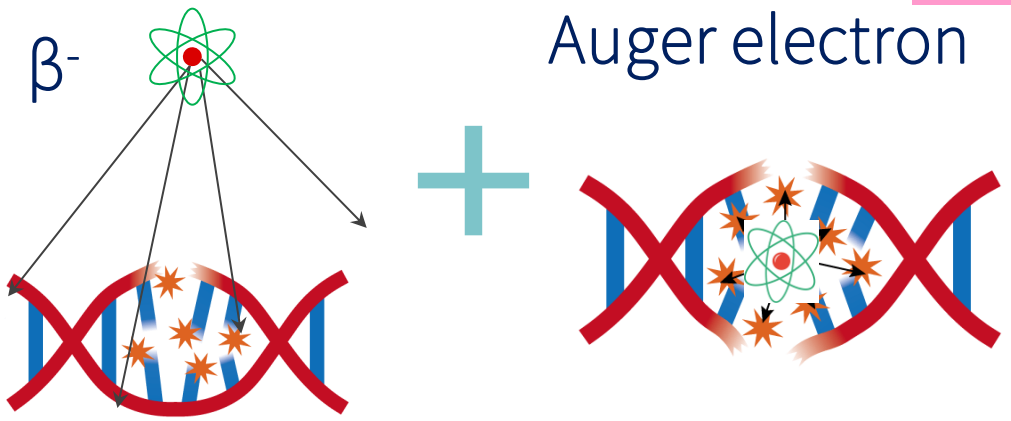


Efficacy prediction
Toxicity prediction
Therapy monitoring

New

β-

Auger electron



Mixed irradiation

^{64}Cu true theranostics for “intractable” cancers

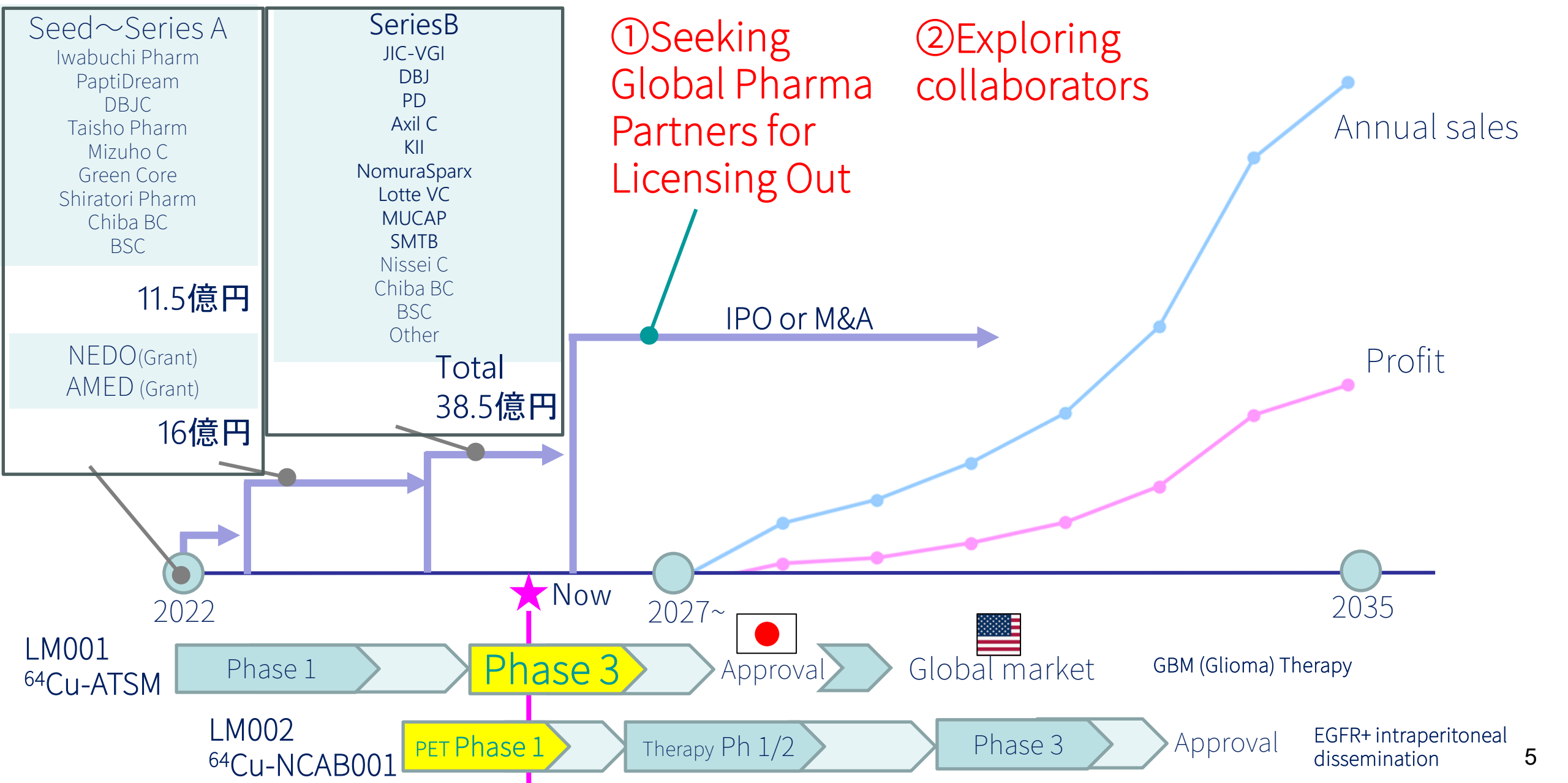
	Population	5-year survival
Prostate cancer	80,000	99%
Breast cancer	90,000	92%
Brain tumor (Glioblastoma)	2,000	10%
Pancreatic cancer	40,000	10%
Lung cancer	170,000	30% (47%)

https://ganjoho.jp/

Intractable Cancers

= Cancers hard to treat

Summary: We are developing anti-cancer ^{64}Cu radiotherapeutics



Closely-linked team with experience & expertise

Link for Life

Management

CEO, Founder Ph.D.
Yukie Yoshii

- Researcher with a 20-year career
- Developed "Visible" Cancer Radiotherapeutics
- Founded LinqMed in 2022

CFO, Accountant
Shin Nakamura

- Worked at RESONA bank
- Accountant at EY Japan
- Achieved IPO at Modalis
- LinqMed from 2023

CSO, R & D, Pharmacist
Yoshiyuki Shibasaki

- Clinical development and medical affairs in oncology at Pfizer
- LinqMed from 2024

BD Lead
Shuichi Isoyama

- BD for radioactive pharmaceuticals at Bayer
- BD at Oncolys BioPharma
- LinqMed from 2024

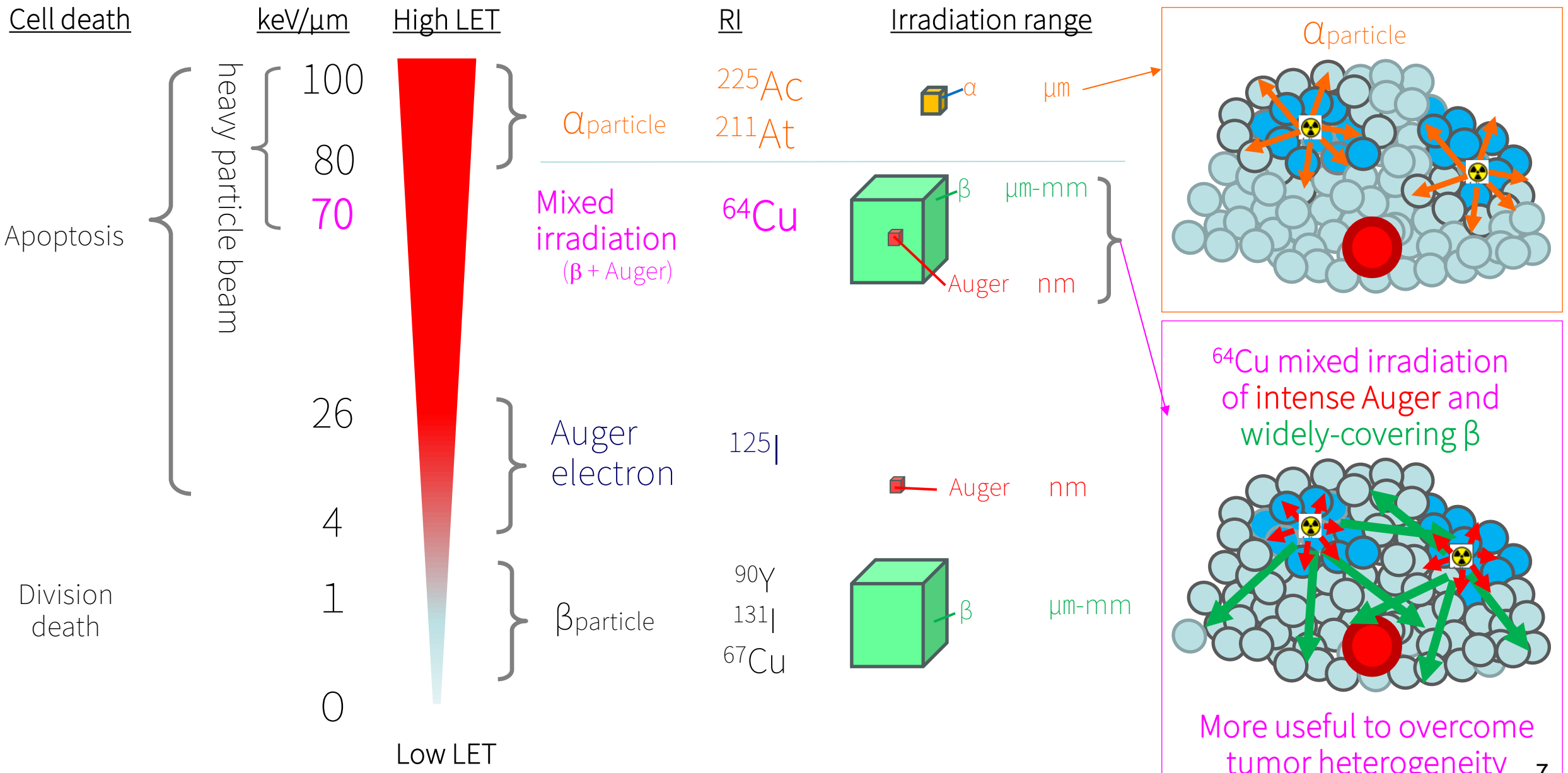
Manufacturing Lead
Yasuharu Sato

- GMP facility manager

He manufactured radiopharmaceuticals

- LinqMed from 2024

^{64}Cu (Auger + β) : Auger (intense) + β (wide coverage)



^{64}Cu: High safety profile

^{64}Cu

Radioactive

^{64}Cu

Single-step decay generates only **stable** nuclides

Auger

β

^{64}Ni

Stable

^{64}Zn

Stable

No Renal Toxicity
No Liver Toxicity
No Hair Loss

^{225}Ac

Radioactive

^{225}Ac

α

^{221}Fr

α

β

^{217}At

^{217}Rn

α

α

^{213}Bi

^{213}Po

α

α

^{209}Tl

^{209}Pb

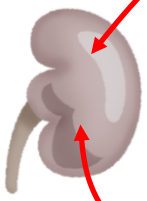
^{209}Bi

Stable

β

β

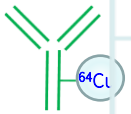
Multiple-step decay generates **toxic** daughter nuclides

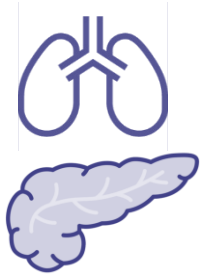


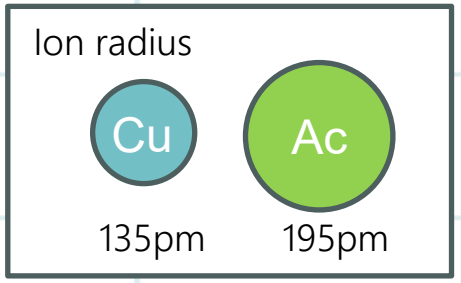
Causing Renal Toxicity

Pipeline: Easy drug design with ^{64}Cu small ion radius & easy labeling

Modality	Disease	Basic	Non-clinical	Clinical Ph1/2	Clinical Ph3
^{64}Cu-ATSM Small Molecule	Recurrent Glioblastoma	→	→	→	→
	Primary Glioblastoma	→	→	→	
	Brain metastasis PCNSL Meningioma	→	→	→	
	Lung cancer	→	→	→	
Anti-EGFR anti body	Pancreatic cancer (Diagnosis)	→	→	→	
	Pancreatic cancer (Therapy)	→	→		
	Breast cancer	→	→		
Small Molecule	Bile duct cancer	→	→		

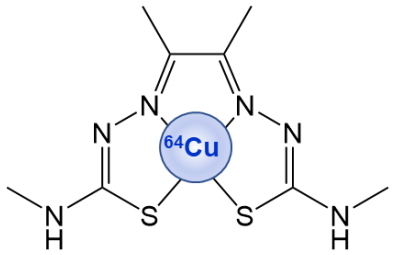






Product Summary of ^{64}Cu-ATSM: LM001

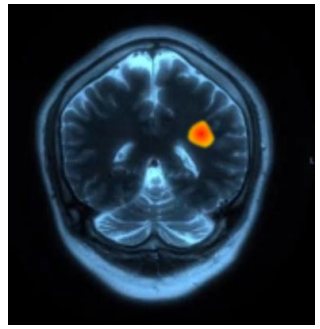
Fujibayashi et al. JNM 1997
Obata et al. NMB 2001
Yoshii et al. NMB 2012



LM001

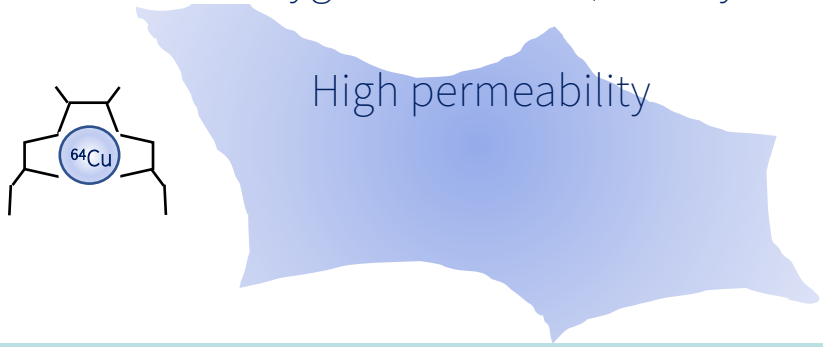
Feature

- Designed to accumulate in various cancers by targeting tumor-specific characteristic: "hypoxia"

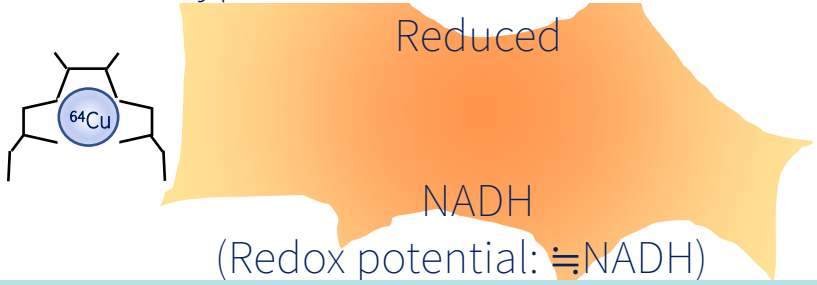


Mechanism

Normal oxygen condition (healthy cells)



Hypoxic condition (cancer cells)

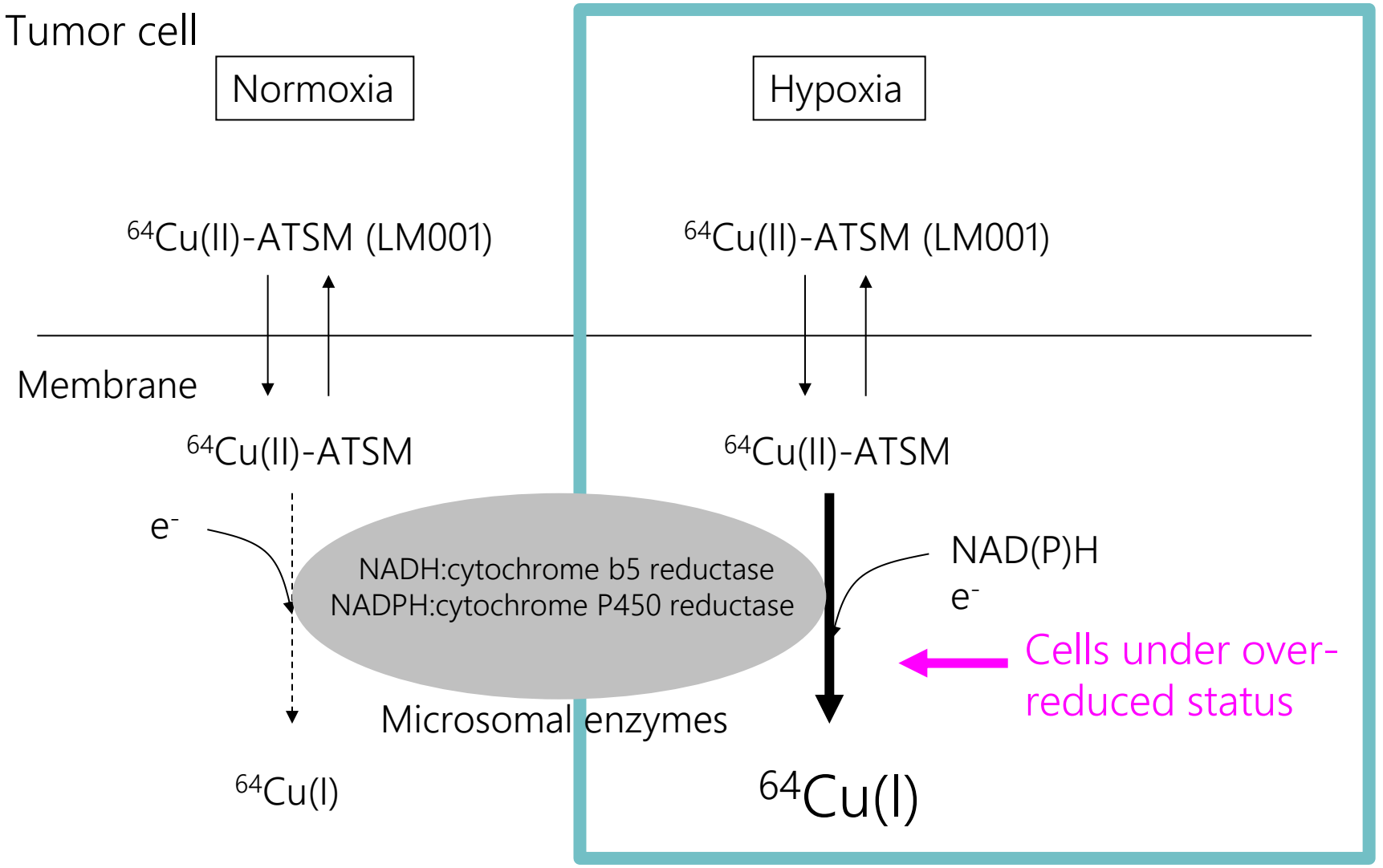


Reaching brain tumors

LM001 reaches to the brain through blood-brain barrier via intravenous injection

Mechanism of ^{64}Cu-ATSM accumulation in hypoxia

Fujibayashi et al. JNM 1997
Obata et al. NMB 2001
Yoshii et al. NMB 2012



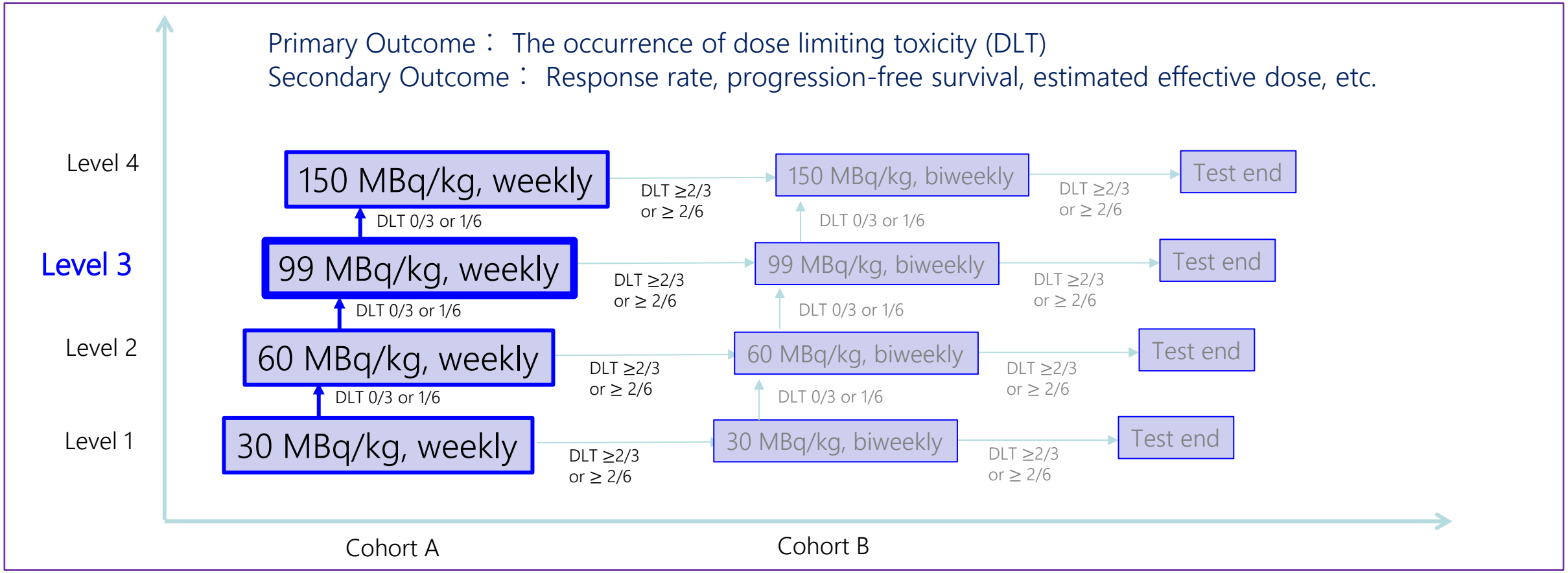
Under highly reduced intracellular conditions such as hypoxia, Cu(II) in Cu-ATSM is reduced to Cu(I), instantly released from the ATSM ligand and trapped in tumor cells.

Phase 1 clinical trial (STAR-64)

Supported by AMED

Target: Recurrent cases of Glioblastoma, Grade III glioma, primary central nervous system lymphoma, or malignant meningioma (Grade II/ III)

@National Cancer Center Hospital
@ Kanagawa Cancer Center
^{64}Cu-ATSM synthesis: QST, NCCH



Summary

- No toxicity other than lymphopenia (grade 3).
- Recommended dose: 99 MBq/kg 4 times every 7 days, intravenously.

^{64}Cu-ATSM therapy Phase 1 clinical trial

Kurihara et al. J Clin Oncol 42, 2024 (suppl 16; abstr 2052)
Presentation in ASCO 2024

Histological classifications	N (FAS/SAS/REG)	% in FAS (N=18)
Anaplastic astrocytoma	4 / 4 / 4	22.2
Anaplastic oligodendroglioma	1 / 2 / 2	5.6
Glioblastoma	9 / 9 / 9	50.0
Primary central nervous system lymphoma (PCNLS)	0 / 0 / 0	0.0
Malignant meningioma (WHO grade II)	2 / 2 / 2	11.1
Malignant meningioma (WHO grade III)	0 / 0 / 0	0.0
Metastatic brain tumor	2 / 2 / 3	11.1

REG: Registration

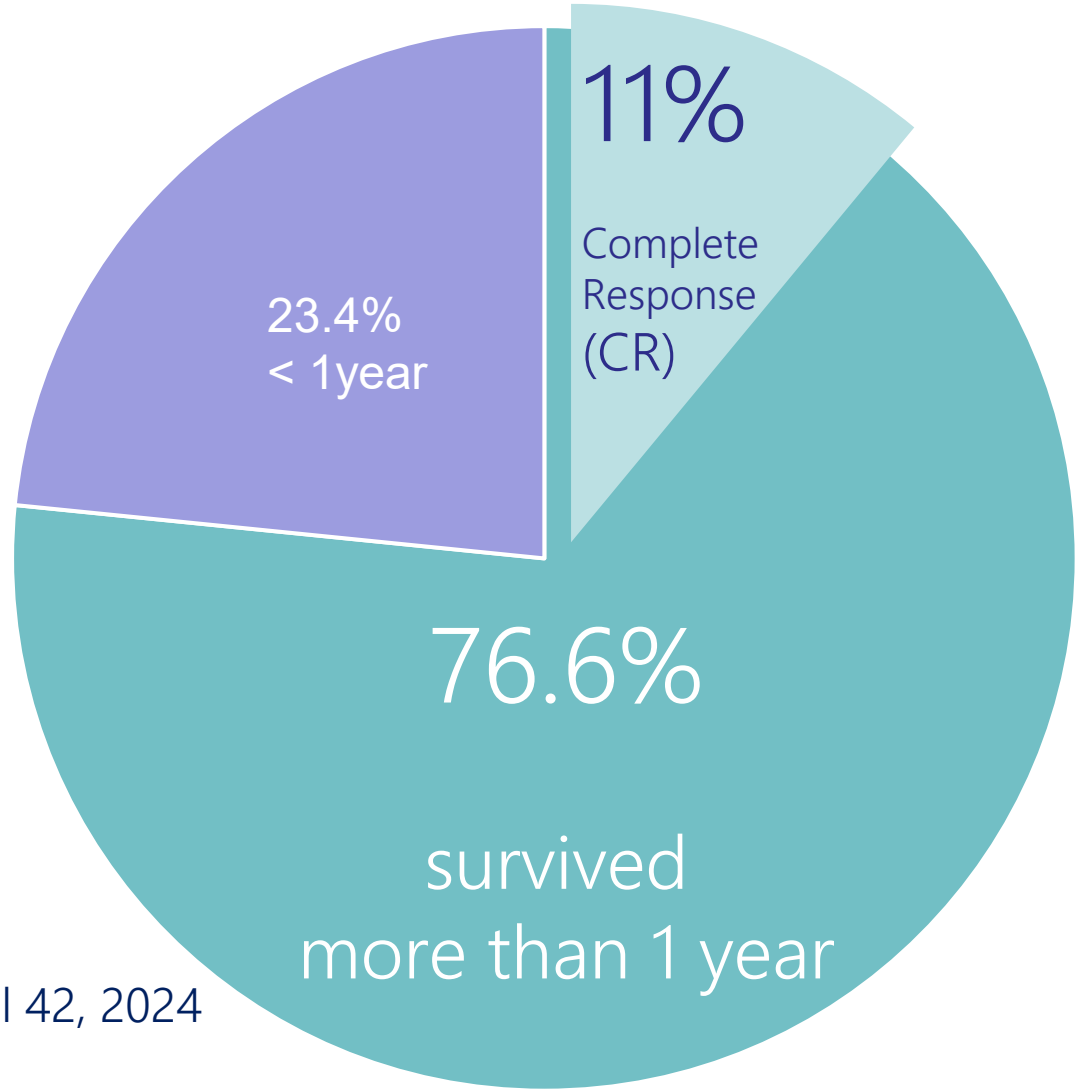
^{64}Cu-ATSM therapy Phase 1 DLT in each dose cohorts (N=18)

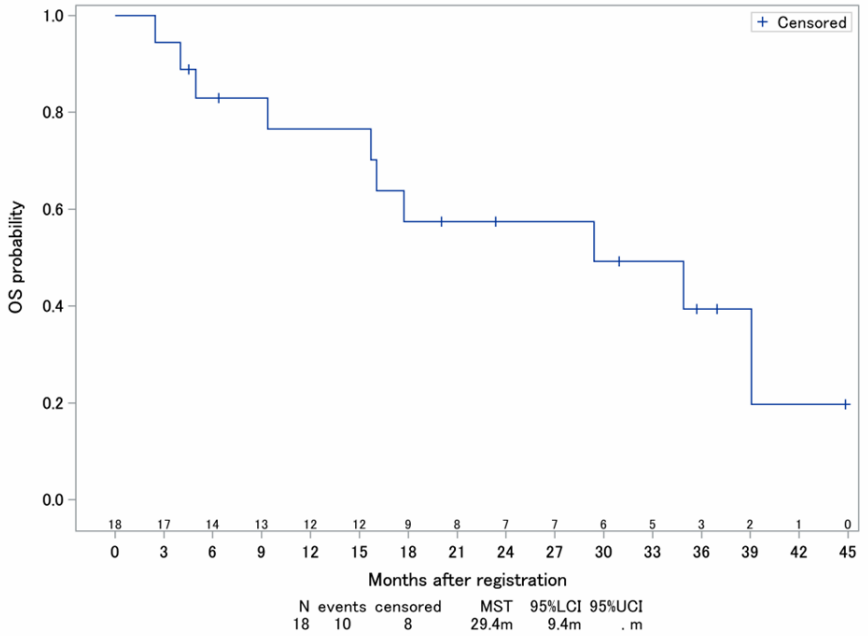
Kurihara et al. J Clin Oncol 42, 2024 (suppl 16; abstr 2052)
Presentation in ASCO 2024

Cohort level	Diagnosis	DLT	Expression rate (95% CI)
1 (30 MBq/kg)	Glioblastoma	-	0.0 % (0.0% - 70.8%)
	Glioblastoma	-	
	Anaplastic astrocytoma	-	
2 (60 MBq/kg)	Anaplastic oligodendroglioma	-	16.7 % (0.4% – 64.1 %)
	Glioblastoma	Lymphopenia G3	
	Anaplastic astrocytoma	-	
	Glioblastoma	-	
	Anaplastic astrocytoma	-	
	Malignant meningioma grade II	-	
3 (99 MBq/kg)	Meta. (breast ca.)	-	16.7 % (0.4% – 64.1 %)
	Meta. (NSCLC)	Lymphopenia G3	
	Malignant meningioma grade II	-	
	Glioblastoma	-	
	Glioblastoma	-	
	Anaplastic astrocytoma	-	
4 (150 MBq/kg)	Glioblastoma	-	66.7 % (9.4% – 99.2 %)
	Glioblastoma	Lymphopenia G3	
	Glioblastoma	Lymphopenia G3	
Analysis set for evaluating DLT (n=18)			22.2 % (6.4% – 47.6 %)

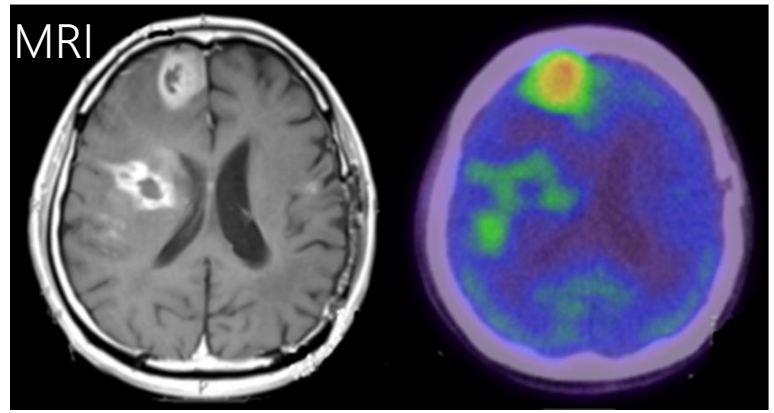
^{64}Cu-ATSM therapy: Promising Phase 1 outcome

18 Recurrent Brain Tumor Patients:
9 Glioblastoma
5 Glioma (Grade III)
2 Malignant meningioma
2 Metastatic brain tumor





Glioblastoma patient in Phase 1

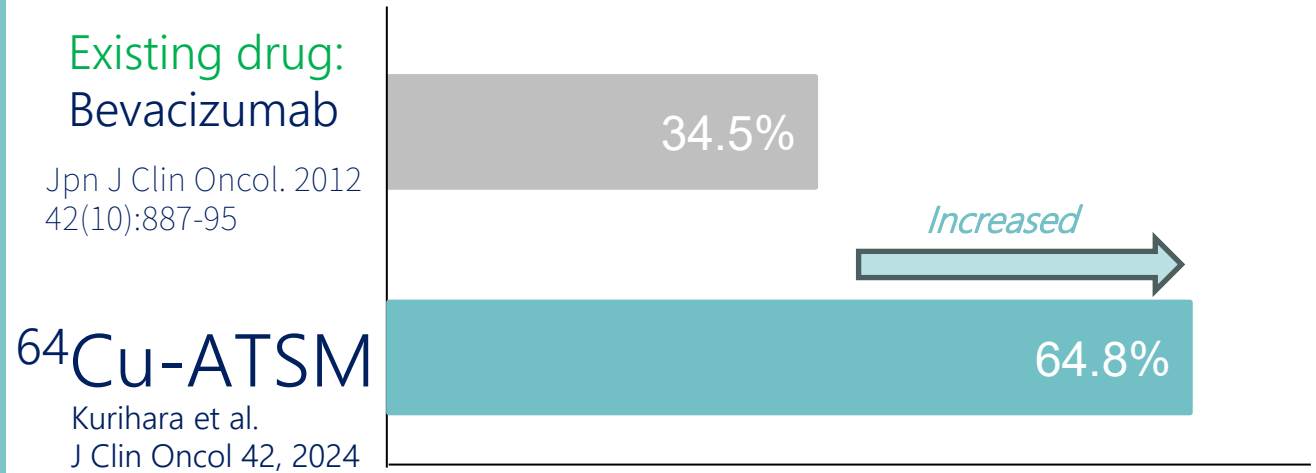


Kurihara et al. J Clin Oncol 42, 2024 (suppl 16; abstr 2052)
Presentation in ASCO 2024

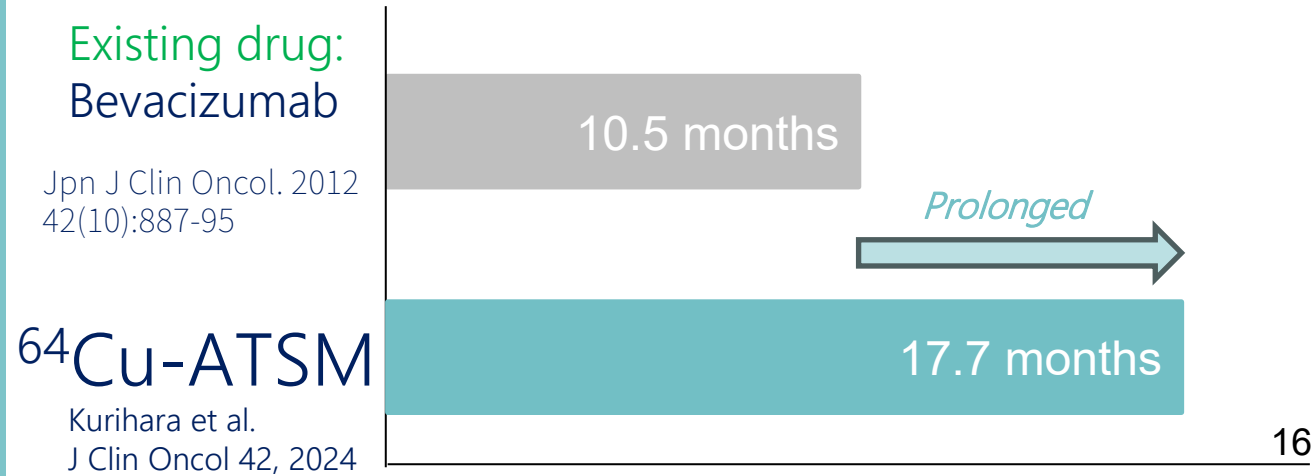
Recurrent Glioblastoma

^{64}Cu-ATSM therapy Phase 1

1-year survival rate:



Median overall survival:



^{64}Cu-ATSM therapy Phase 1: Response rate determined by facility

Kurihara et al. J Clin Oncol 42, 2024 (suppl 16; abstr 2052)
Presentation in ASCO 2024

Histology	N	CR	PR	SD	PD	NE	N of responders	Response rate (95% CI)
Anaplastic astrocytoma	4	0	0	4	0	0	0	0.0% (0.0% – 60.2%)
Anaplastic oligodendroglioma	1	1	0	0	0	0	1	100% (2.5% – 100%)
Glioblastoma	9	1	0	4	4	0	1	11.1% (0.3% – 48.3%)
PCNLS	0	-	-	-	-	-	-	-
Malignant meningioma grade II	2	0	0	0	2	0	0	0.0% (0.0% – 84.2%)
Malignant meningioma grade III	0	-	-	-	-	-	-	-
Metastatic brain tumor	2	0	0	1	1	0	0	0.0% (0.0% – 84.2%)
FAS	18	2	0	9	7	0	2	11.1% (1.4% – 34.7%)

^{64}Cu-ATSM therapy Phase 1 : OS, PFS

Kurihara et al. J Clin Oncol 42, 2024 (suppl 16; abstr 2052)
Presentation in ASCO 2024

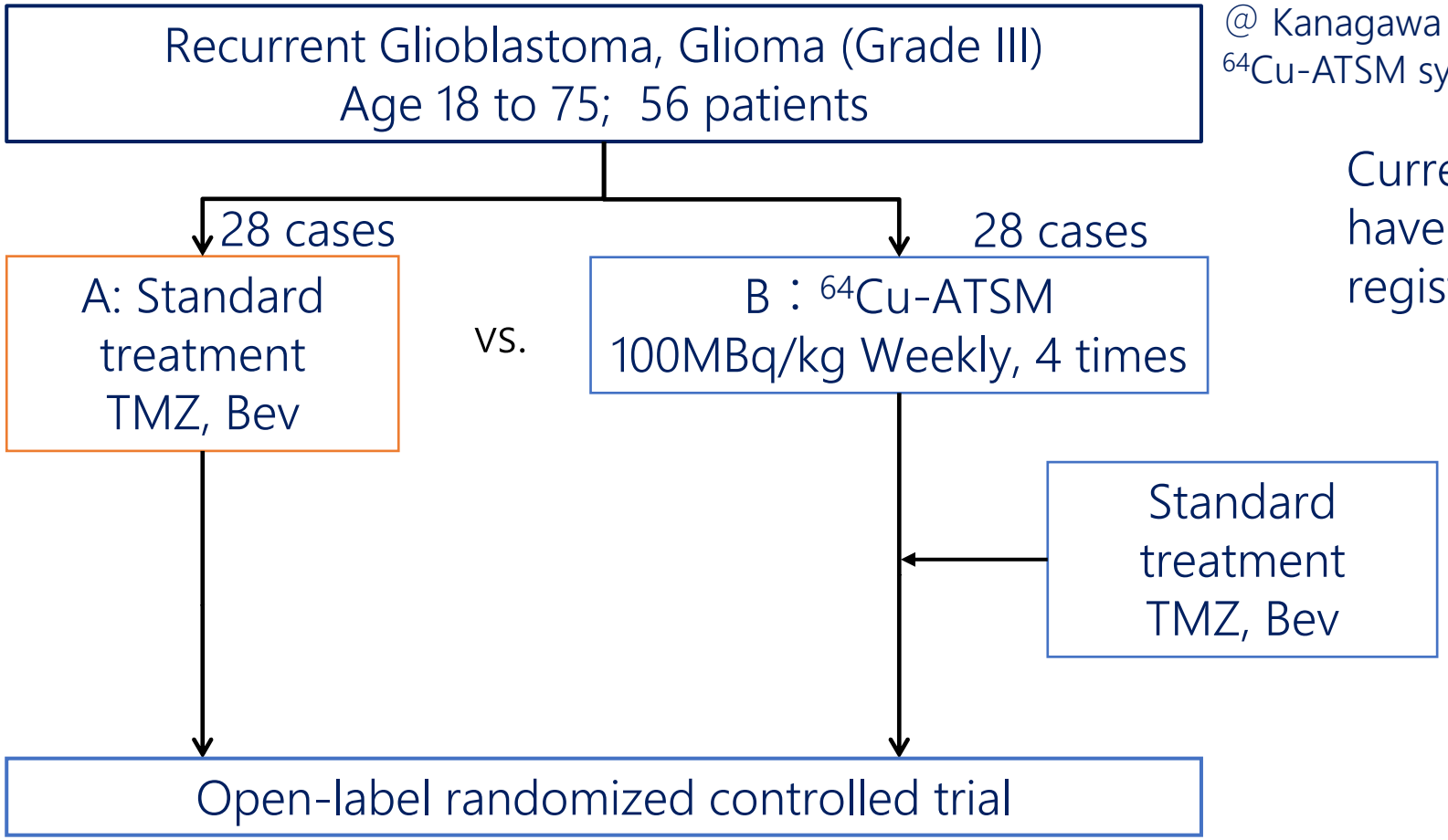
	1year-OS (95%CI)	1year-PFS (95%CI)	6month-PFS (95%CI)	medianOS (95%CI)	medianPFS (95%CI)
FAS (N=18)	76.6% (48.8% - 90.6%)	19.0% (4.8% - 40.3%)	38.1% (16.6% - 59.5%)	29.4 M (9.4 - NE)	3.8 M (1.1 - 9.9)
N of events	-	-	-	10	17
glioblastoma (N=9)	64.8% (25.3% - 87.2%)	14.8% (0.8% - 46.8%)	44.4% (13.6% - 71.9%)	17.7 M (2.5 - NE)	3.8 M (0.4 - 9.9)
N of events	-	-	-	4	8
vs Bevacizumab	34.5%		33.9%	10.5M	3.3M

Jpn J Clin Oncol. 2012;42(10):887-95

On-going Phase III Pivotal comparative clinical trial: ^{64}Cu-ATSM

jRCT2031240090

@National Cancer Center Hospital
@ Kanagawa Cancer Center
^{64}Cu-ATSM synthesis: LM, NCCH



Currently, 20% have already been registered.

Primary endpoint: 1-year overall survival

Secondary endpoints: Response rate, progression-free survival, overall survival, adverse events
Enrollment period: 2.5 years
Observation period: 1 year after completion of treatment

Global Expansion Strategy: ^{64}Cu-ATSM

Indication	~2023	2024	2025	2026	2027	2028	2029	2030-

Brain tumors

IND@JPN

Launch

Phase 3 | Observation | Apply → JPN Approval

Fast Track
Orphan

Phase 3 | Apply → FDA Approval

Lung cancer

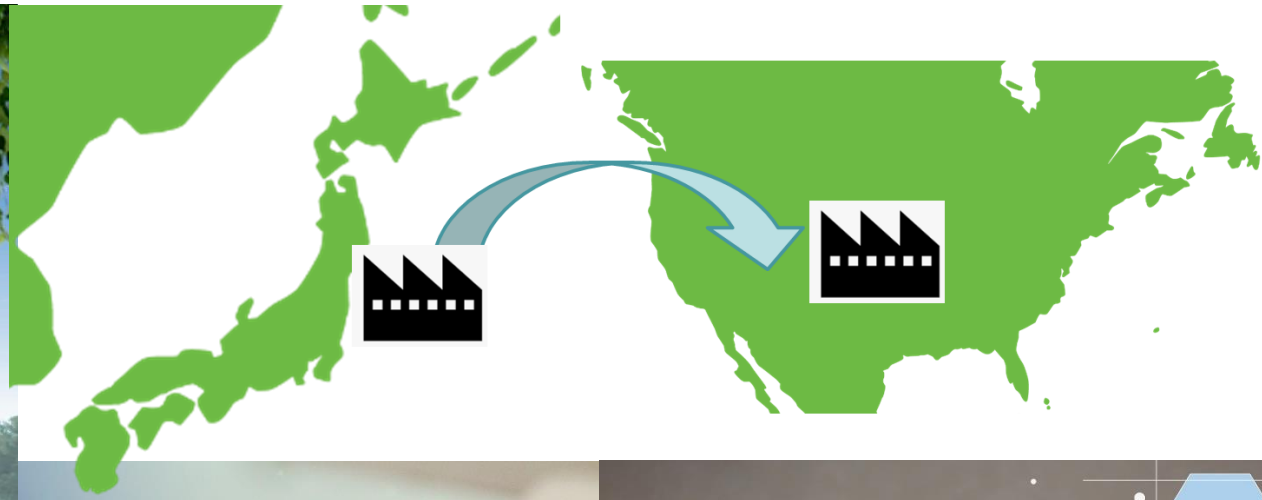
Phase 1/2 global trial @ Japan
Multiple races to apply FDA

P3
Lung cancer

→ FDA Approval

^{64}Cu manufacturing site being constructed covering JP market (completed in autumn 2025)

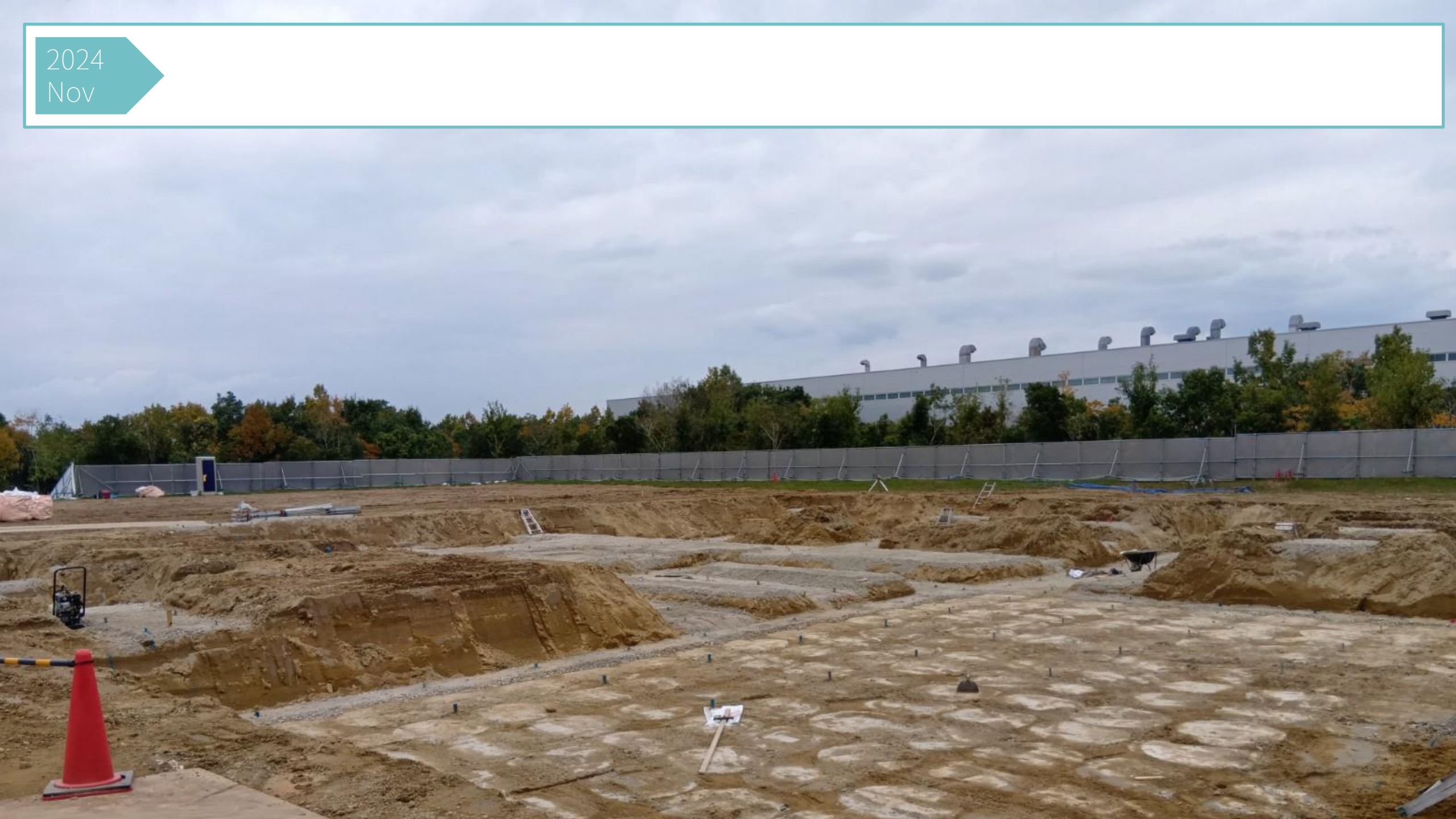
Supported by NEDO



Short-term tech-transfer to global partners is possible

^{64}Cu Manufacturing Plant Construction Project @ Chiba, Japan

2024
Nov



2024
Nov

2024
Dec

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Nov

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Jan

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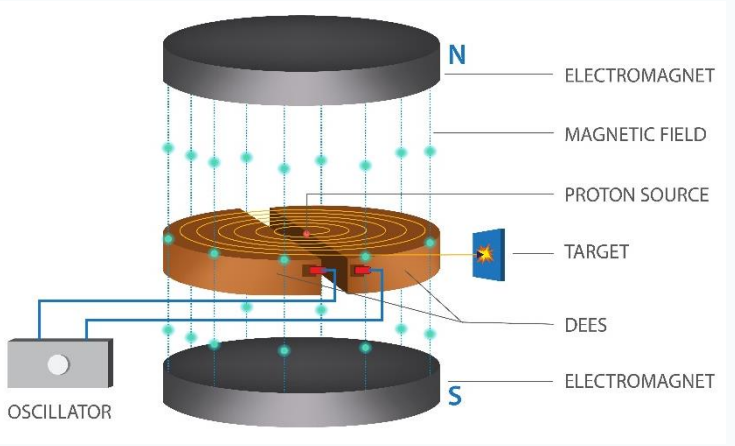
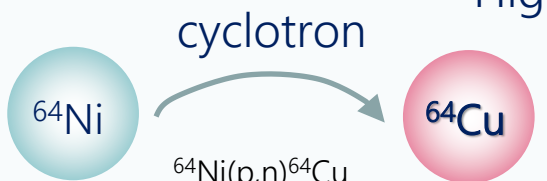
2024 Nov → 2024 Dec → 2025 Jan → 2025 Feb → 2025 March → 2025 April → 2025 May → 2025 June → 2025 July

Production of ^{64}Cu





High-purity ^{64}Cu

2024 Nov → 2024 Dec → 2025 Jan → 2025 Feb → 2025 March → 2025 April → 2025 May → 2025 June → 2025 July → 2025 Aug

2024 Nov → 2024 Dec → 2025 Jan → 2025 Feb → 2025 March → 2025 April → 2025 May → 2025 June → 2025 July → 2025 Aug

2025
Sep

Complete


2025
Sep
Complete

We Make Patients Happy with

Link for Life

LinqMed Inc.

Acknowledgements

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