



Rediscovering Potential of Liposome in Advanced Drug Discovery in Oncology

Susumu Shimoyama

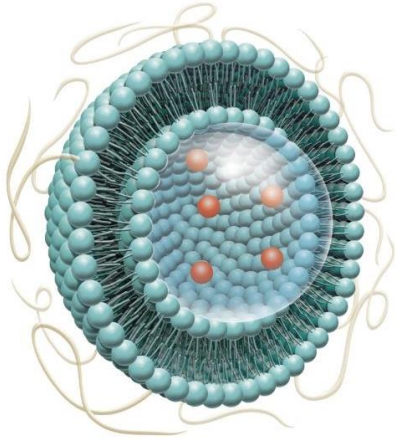
President

FUJIFILM Pharmaceuticals U.S.A., Inc.

FUJIFILM
Value from Innovation

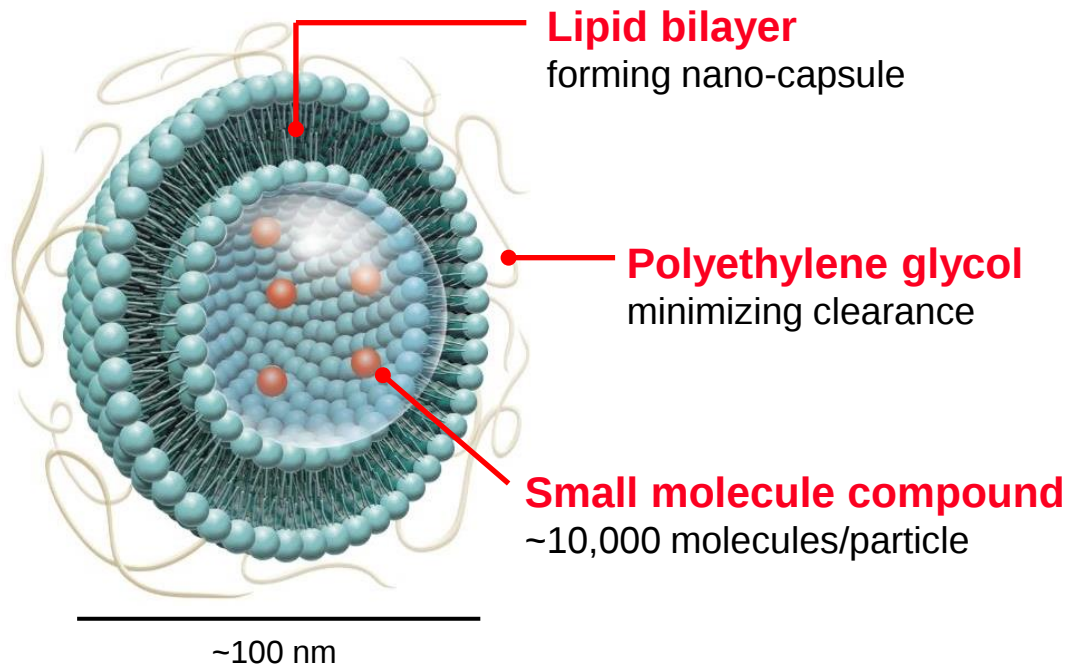


Take Home Message



- Liposome is a clinically proven drug delivery technology using lipid-based nanoparticle encapsulating small molecule compounds
- Liposome can be an option to address challenges in PK, safety, and efficacy profiles

What Is Liposome?



Liposome formulation is expected to provide

- Prolonged plasma half-life
- Preferential distribution to tumor and inflamed tissues
- Improvement of safety and efficacy

Clinically proven modality

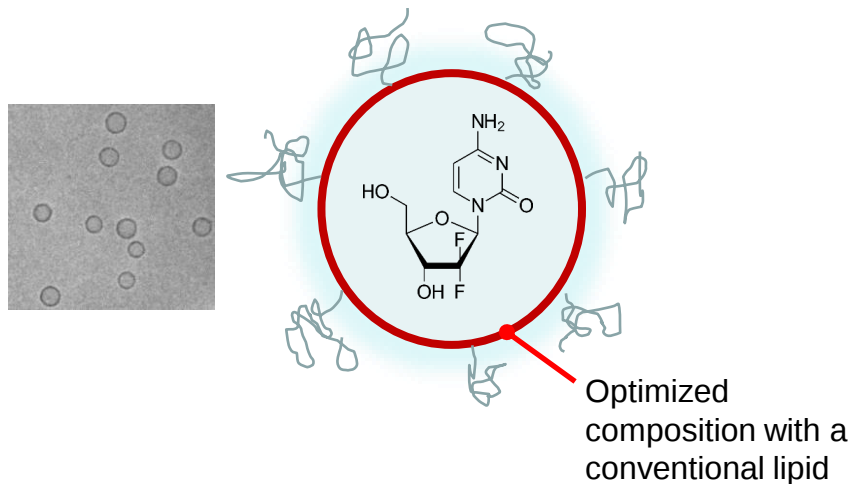
- 15 approved drugs mainly in oncology field
- Served as standard therapies
 - Onivyde for pancreatic cancer (1st line)
 - Vyxeos for some types of AML (1st line)
 - Doxil for platinum-resistant ovarian cancer

Type	Name	API
Cancer therapy (Drug formulation)	Doxil®/Caelyx™	Doxorubicin
	DaunoXome®	Daunorubicin
	Onivyde®	Irinotecan hydrochloride trihydrate
	Myocet®	Doxorubicin
	Mepact®	Mifamurtide
	Marqibo®	Vineristine
	Vyxeos®	Daunorubicin+cytarabine
	Zolsketil®	Doxorubicin
	AmBisome®	Amphotericin B
	DepoCyt®	Cytarabine
Other application (Drug formulation)	Visudyne®	Verteporphin
	DepoDur®	Morphine sulfate
	Arikayce®	Amikacin
	Exparel®	Bupivacaine

Fujifilm's Liposome Project as a Showcase

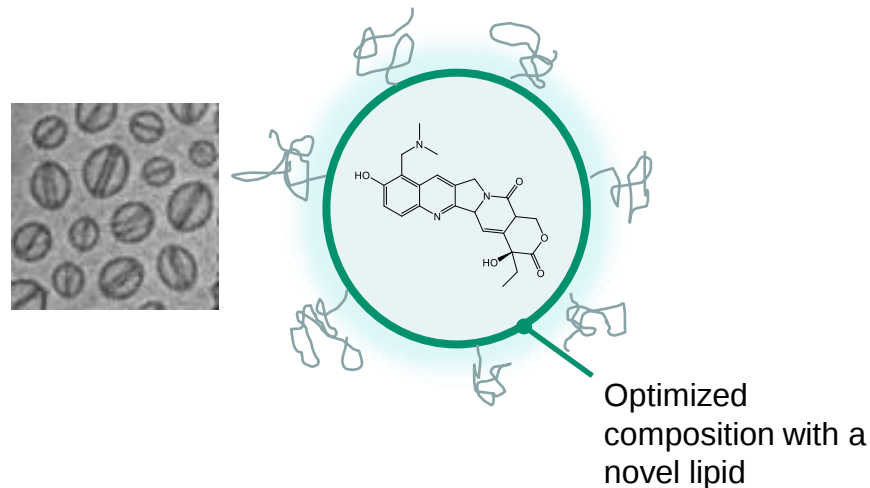
FF-10832 (liposomal gemcitabine)

- Phase 2a in the US
- FDA orphan drug designation for biliary tract cancer
- Liquid solution for intravenous dosing
- 3.5 years stability at the refrigerated condition



FF-10850 (liposomal topotecan)

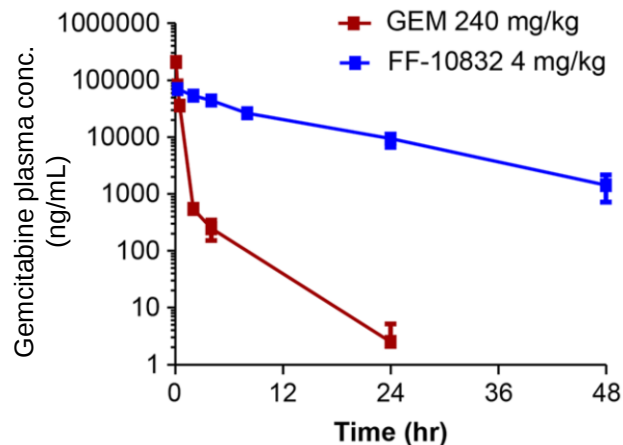
- Phase 1 expansion part in the US
- FDA orphan drug designation for Merkel cell carcinoma
- Liquid solution for intravenous dosing
- 3 years stability at the refrigerated condition



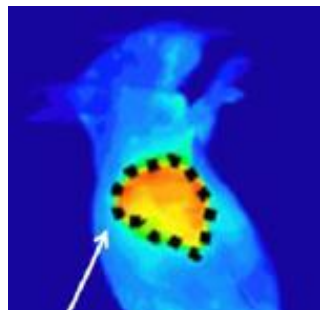
Non-clinical Data of Liposomal Gemcitabine (FF-10832)

- Prolonged Plasma Half-life and Preferential Tumor Exposure

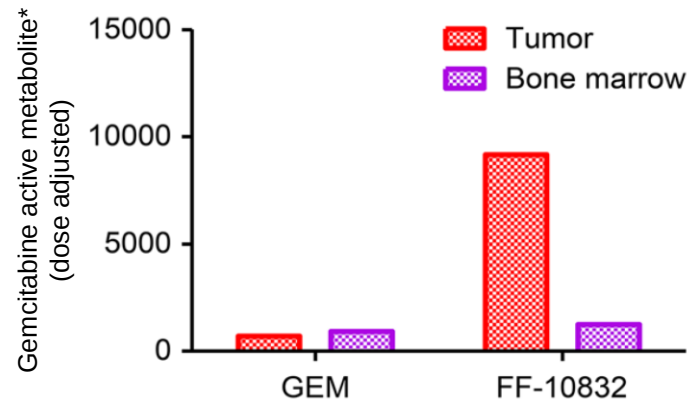
Murine plasma PK



Preferential tumor exposure in mice



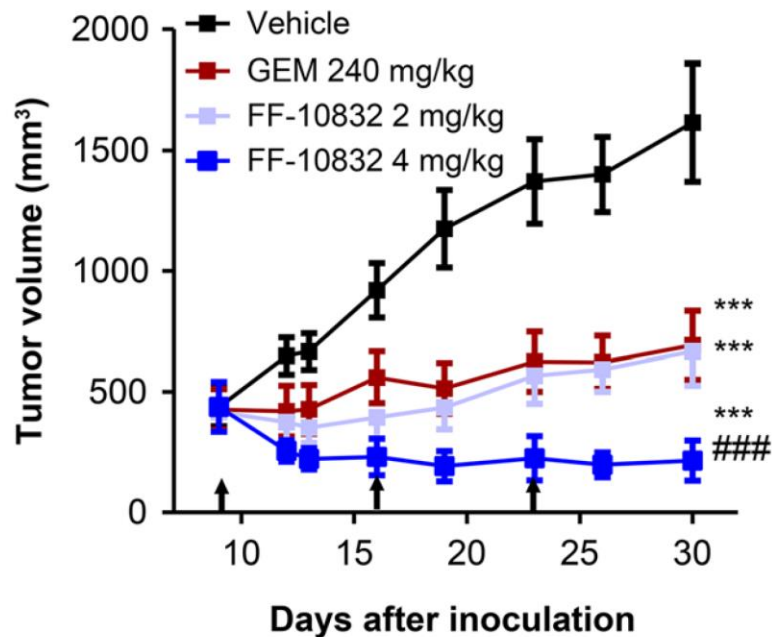
72 h after iv dosing of fluorescent-labeled FF-10832



*AUC/dose of dFdCTP, active metabolite of gemcitabine (ng*hr/g)/(mg/kg)

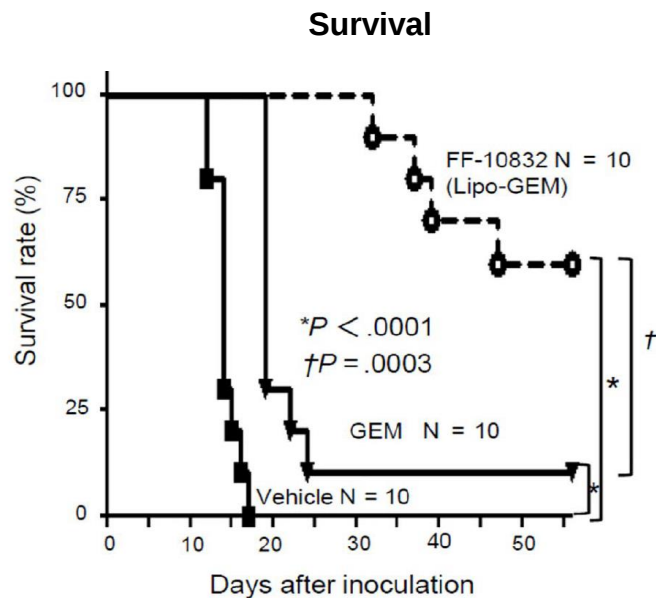
Non-Clinical Data of Liposomal Gemcitabine (FF-10832) - Superior Anti-tumor Activity to Gemcitabine with Much Less Dose

Capan-1 subcutaneous model

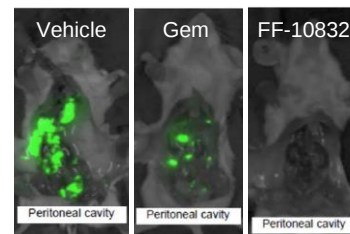


Pharm Res. 2021, 38,1093–1106.

Intraperitoneal disseminated model (Luciferized Colon26 model)



Tumor cell imaging



Cancer Sci. 2019, 110 (9), 2933–40

FDA Granted Orphan Drug Designations to Fujifilm's Liposomes



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**Liposomal gemcitabine (FF-10832)
for biliary tract cancer**

This week the [#FDA](#) has granted orphan drug designation to Fujifilm's FF-10832 — an investigational liposomal formulation of gemcitabine — for the treatment of biliary tract cancers (BTC).



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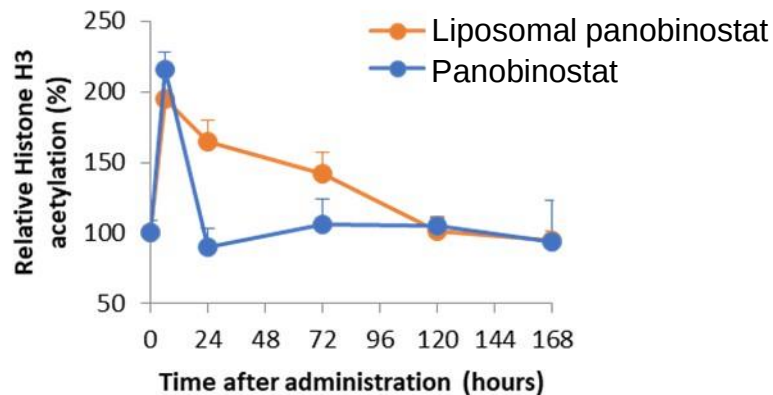
**Liposomal topotecan (FF-10850)
for Merkel cell carcinoma**

We are really excited to announce that FF-10850, liposomal topotecan, has been granted the FDA orphan drug designation for Merkel cell carcinoma, which is a highly aggressive skin cancer. We are actively enrolling Merkel cell carcinoma cohort in the expansion part of phase 1 study (NCT04047251).

Liposome Not Only for Chemo But Also for Molecular Targeted Drugs

Fujifilm internal experiences

- Liposomal panobinostat (pre-clinical candidate)
- Liposomal BET inhibitor (pre-clinical candidate)



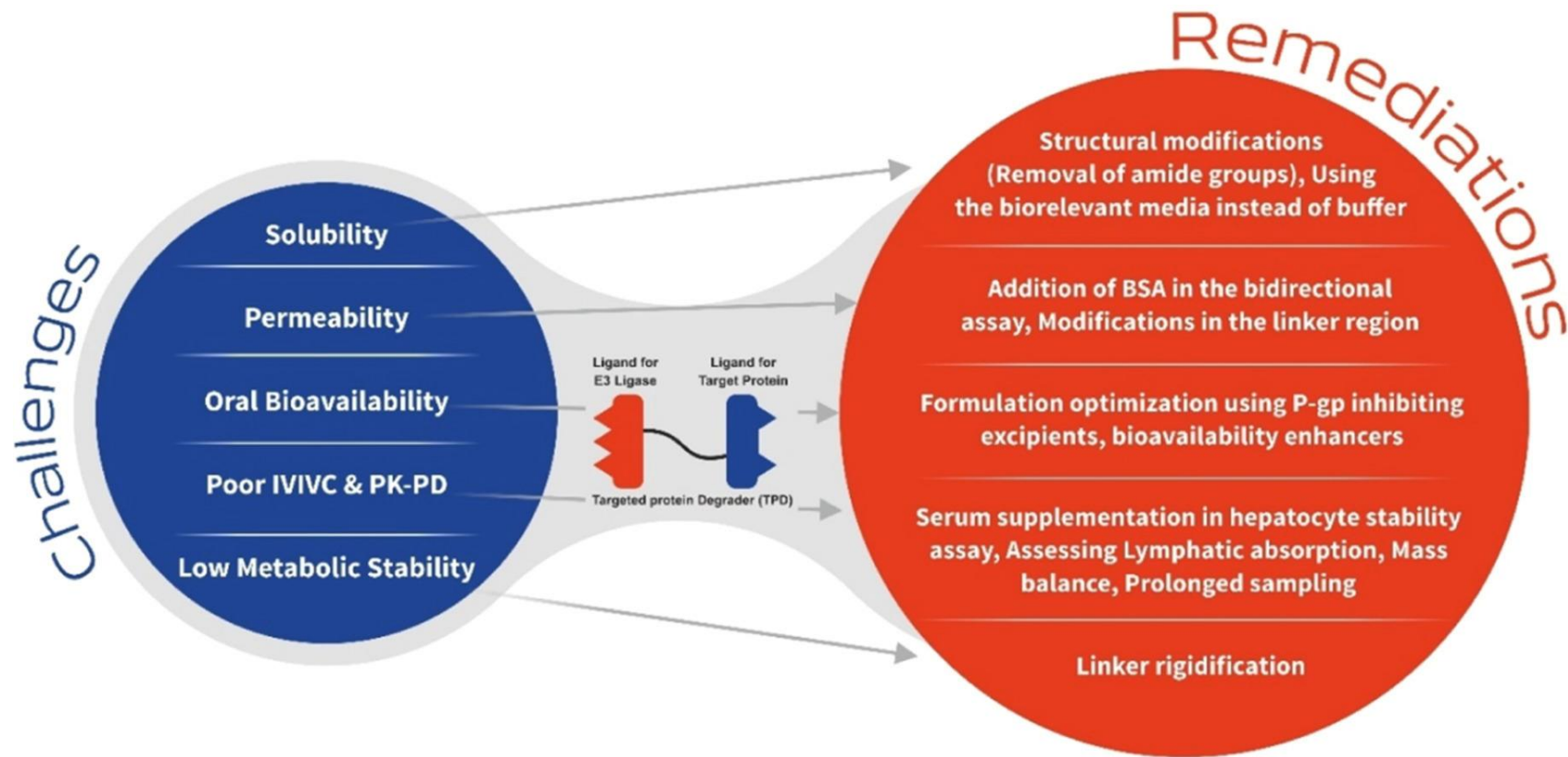
3rd party pipeline

- SMP-3124 (liposomal CHK1 inhibitor)

Origin	in-house	 Sumitomo Pharma Innovation today, healthier tomorrows
Formulation	injection (Liposomal Nanomedicine)	
Development stage	Solid tumors: Phase 1/2 in the U.S. and Japan	

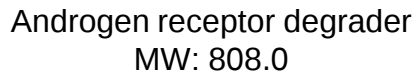
SMP-3124 is an injection, a liposomally encapsulated CHK1 (checkpoint kinase 1) inhibitor. CHK1 is activated by DNA damage response, then arrests the cell cycle, and induces DNA repair via serine-threonine kinase. CHK1 inhibition leads cancer cell with high replication stress to apoptosis by inducing further DNA damages. SMP-3124 is expected to strengthen the anti-tumor activity and weaken side effects by changing pharmacokinetics of the compound with liposomal nanomedicinal encapsulation.

Liposome Can Be an Option to Address ADMET Issues of TPDs

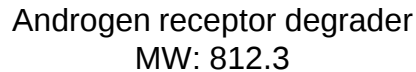


TPD test set

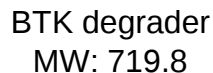
- # ARV-766



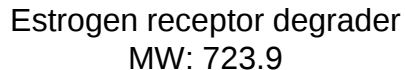
ARV-110



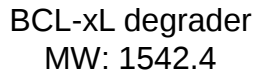
NX-2127



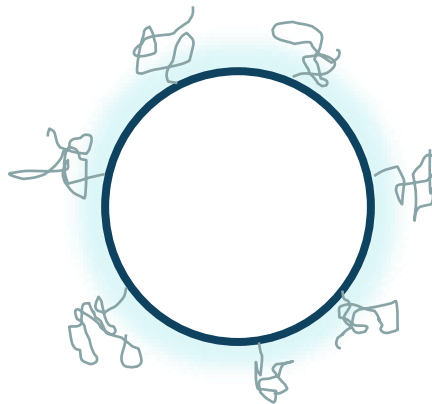
ARV-471



DT2216

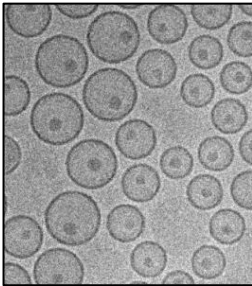
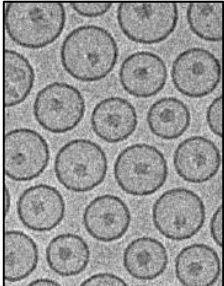
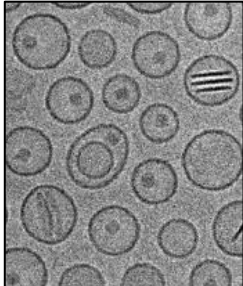
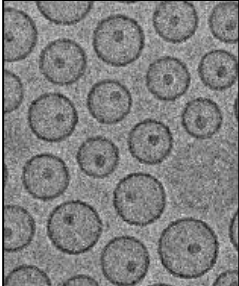
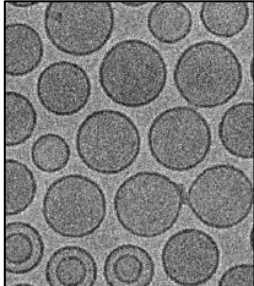


Fujifilm's proprietary versatile liposome formulation



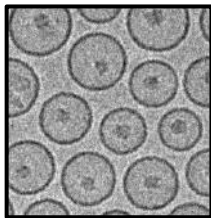
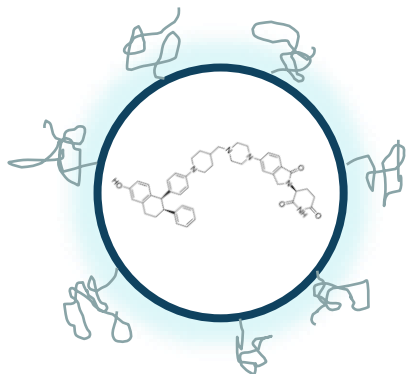
Fujifilm's established conditions for encapsulation

YES! - TPDs Can Be Encapsulated by Liposome

	ARV-110	ARV-471	ARV-766	NX-2127	DT2216
Molecular weight	812.3	723.9	808.0	719.8	1542.4
Yield	98%	96%	99%	>99%	46%
Encapsulation ratio	>99%	99%	99%	91%	88%
Particle size	108 nm	99 nm	105 nm	110 nm	118 nm
Morphology (TEM)					

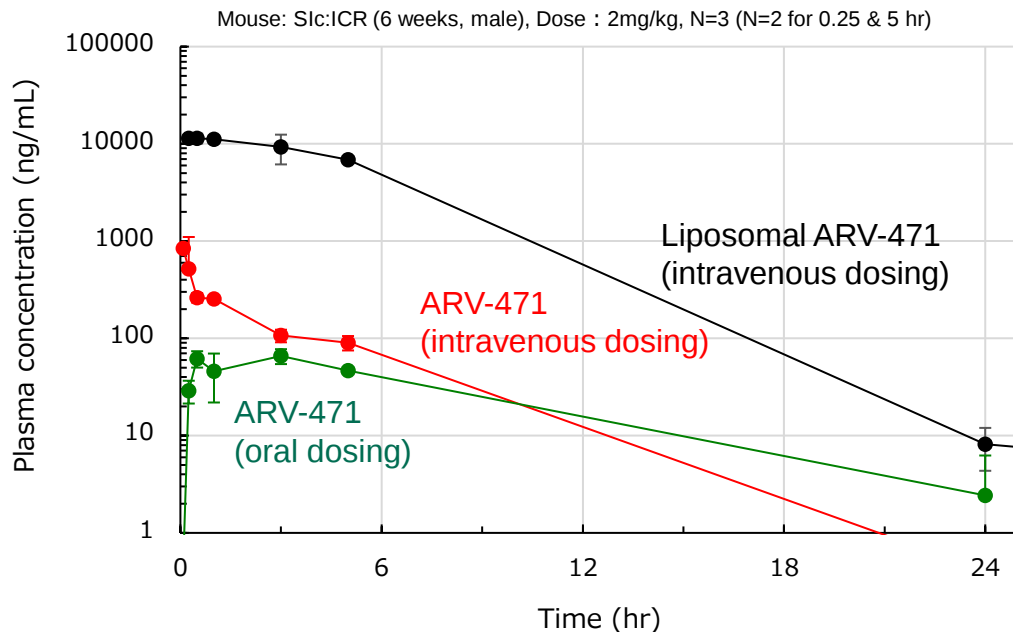
Improved Plasma Exposure of ARV-471 by Liposomal Formulation

Liposomal ARV-471



Particle size: 99 nm
API concentration: 0.50 mg/mL
Encapsulation efficiency: 99%
Yield: 96%

Mouse pharmacokinetics



- Animal efficacy study is ongoing. Please stay tuned!

One-stop Services for Liposome Design and Manufacturing

Through the internal liposome R&D and manufacturing experiences, Fujifilm has

- Proprietary versatile liposomal formulation
- Established analytical methods, manufacturing process, supply chain, GMP facilities and QMS
- Capable and experienced formulation scientists, analytical scientists, and manufacturing staffs



Toyama

Feasibility

- Proprietary formulation

Optimization

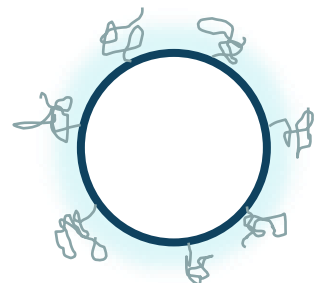
- Formulation
- Analysis

Development

- Processes
- Methods

CTM Preparation

Commercialization



Versatile platform formulation



BSEL, Fujifilm R&D Center
Formulation design & Analysis



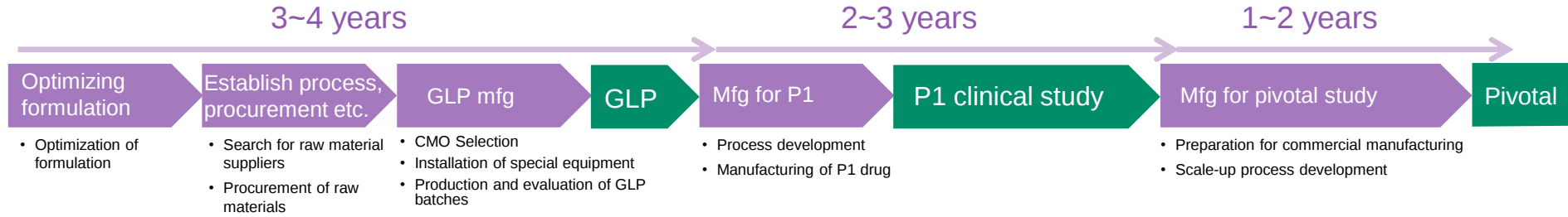
TRD, Pharmaceuticals R&D Center
Development & Tech Transfer



701&702, GMP manufacturing factories
CTM & commercial scale manufacturing

Minimized Timeline from Feasibility Study to Commercial Manufacturing

General timeline for liposomal drugs from scratch

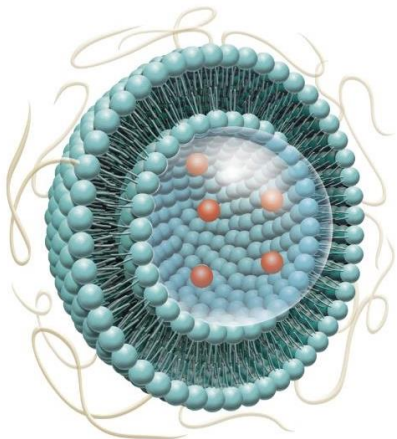


Timeline with Fujifilm's liposome CDMO service

- Minimize timeline and resources leveraging Fujifilm's established liposome formulation, capabilities, knowledge, facilities and equipment
- Initial feasibility study can be done in 1 month



Take Home Message



- Liposome is a clinically proven drug delivery technology using lipid-based nanoparticle encapsulating small molecule compounds
- Liposome can be an option to address challenges in PK, safety, and efficacy profiles

Please visit our booth (#7) for further discussion!

E-mail: susumu.shimoyama@fujifilm.com

Webpage



Fujifilm Group's Purpose

Giving our world more smiles

We bring diverse ideas, unique capabilities,
and extraordinary people together to change the world.

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Value from Innovation