CDMO services for Liposome formulation

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FUJIFILM
Value from Innovation

CDMO services for Liposome

Fujifilm assets

- ❑ The Established manufacturing process, facility, and analytical lab used for developing liposome formulations, CTM mfg., and batch release.
- ❑ The Established platform liposome cargo potentially utilize for costumer's APIs: DHSM-based liposome *(Shown on the left panel)*
- ❑ The experienced scientists with hands-on knowledge of liposome CMC and related regulations for preclinical and clinical development in the U.S.

Providing a full package of Liposome CDMO services could significantly shorten the timeline for FIH clinical trials compared to a DIY in-house development.

Fujifilm Liposome Track record on U.S. Clinical trials

A Phase 1 Dose-escalation Study of FF-10832 for Treatment of Solid Tumors - ClinicalTrials.gov

Dose-escalation Phase: Eligible patients will receive FF-10832 in 28 day or 21 day cycles. Dosing will continue until progression of disease, observation of unacceptable adverse events, intercurrent illness, or changes in the patient's condition that prevents further study participation after discussion between the Investigator and the Medical Monitor.

NCT03440450

A Study of FF-10850 Topotecan Liposome Injection in Advanced Solid Tumors - Full Text View - ClinicalTrials.gov

Inclusion Criteria: Patients must meet all the following criteria to participate in the study: Males and females ≥ 18 years of age; Dose-escalation phase: Histologically or cytologically confirmed metastatic and/or unresectable solid tumor, relapsed or refractory to standard therapy, or for which no standard therapy is available that is expected to improve survival by at least 3 months

NCT04047251

A Study to Evaluate Safety, Efficacy of FF-10832 in Combination With Pembrolizumab in Solid Tumors - ClinicalTrials.gov

This is a Phase 2a, open label clinical trial evaluating FF-10832 in combination with pembrolizumab and as monotherapy. The trial will begin with a safety run-in phase of 10 patients receiving combination therapy with pembrolizumab: FF-10832 will be dosed at 40 mg/m2 with a fixed dose of pembrolizumab (200 mg).

NCT05318573

INVESTIGATIONAL USE ONLY:
NOT FOR SALE IN THE US

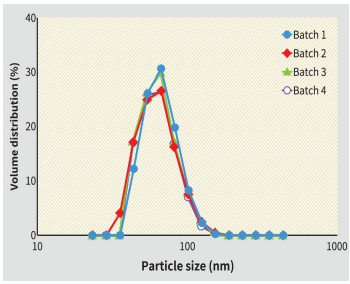
✓**Liposomal formulation design, preclinical toxicity, PK, and efficacy studies, CTM manufacturing, and phase 1 clinical trials in the U.S. were fully conducted by Fujifilm.**
✓**Fujifilm is the CDMO that possesses the hands-on knowledge required for liposome formulation and development**

The manufacturing facility

- ✓*GMP production of LNPs and liposomes*
- ✓*Compliant with US, EU, JP GMP*
- ✓*LNP / Liposome NxGen™ Microfluidic mixer (0.2 – 100L)*
- ✓*Highly potent APIs handling area*
- ✓*KrosFlo® KMPi and Mobius Flex Ready® from mL scale to ~100 L*
- ✓ *Vial filling system 3000 vials/hour*



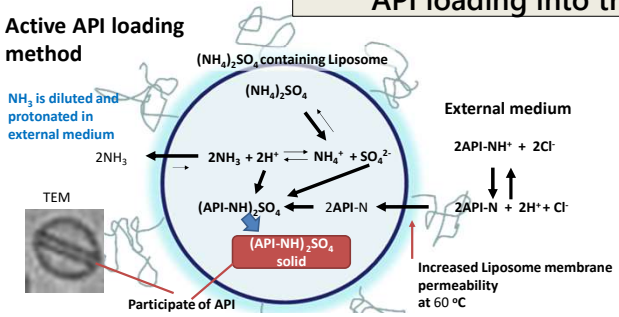
Manufacturing of Empty Liposome

Produce Empty Liposome by the dispersing system with high reproductivity

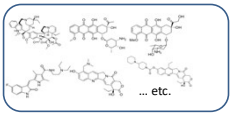
API loading into the DHSM Based liposome

Active API loading method



✓ **Protonation of API within the internal phase of preformed liposome leads to the formation of insoluble sulfate API precipitate, effectively trapping it within the liposomal core.**
✓ **This process is widely applicable to APIs with weak basic groups**

Market available APIs



Dozens of APSs Thrown into Active loading trial

~ 75% of APIs tested showed high loading efficiency

Mouse PK study (IV)

API-Loaded liposome

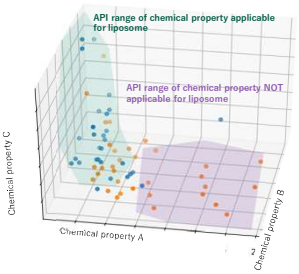
Mice pk study (IV)

Liposome Formulation		T1/2	AUC∞(1mpk)	
API	Lipid	hr	ng/mL*h	DHSM/HSPC
A	**HSPC**/Chol/mPEG-DSPE	15.2	433691	x 1.2
	DHSM/Chol/mPEG-DSPE	17.4	506246	
B	**HSPC**/Chol/mPEG-DSPE	1.0	24695	x 3.3
	DHSM/Chol/mPEG-DSPE	3.3	82122	
C	**HSPC**/Chol/mPEG-DSPE	3.5	89195	x 1.8
	DHSM/Chol/mPEG-DSPE	9.9	148189	
D	**HSPC**/Chol/mPEG-DSPE	0.5	6453	x 5.8
	DHSM/Chol/mPEG-DSPE	0.7	37661	
E	**HSPC**/Chol/mPEG-DSPE	2.4	86692	x 1.4
	DHSM/Chol/mPEG-DSPE	9.0	227177	

Data generated in-house

DHSM Liposome showed higher AUC for various types of APIs

Computation prediction of loading efficiency



Fee free prediction application

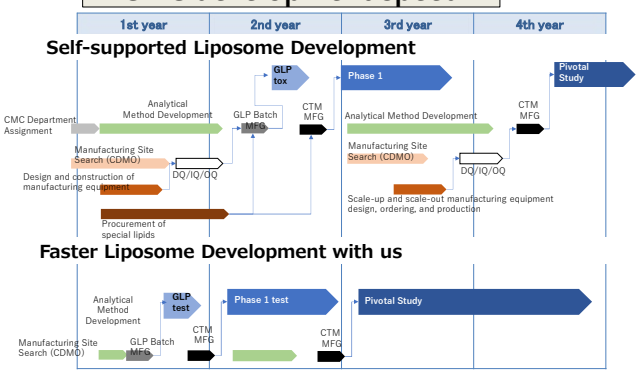
Success rate can be predicted in silico before moving on actual experiment

Analytical method and Spec Devs.

- ✓*In vitro release test method development*
- ✓*Assay encapsulated and unencapsulated API*
- ✓*HPLC method development for lipids and API with quantification and validation of ICH guidelines*
- ✓*Size and distribution by DLS*
- ✓*Zeta potential, pH, osmolality, Particle matter*
- ✓*Residual solvent analysis by GC (FID)*
- ✓*Sterility*
- ✓*Spectroscopy (UV, IR) and others*

Fujifilm provide a full range of analytical services for Liposome

CMC development speed



Locations