37th Annual J.P. Morgan Healthcare Conference

Company Overview

Tokyo Stock Exchange, Mothers 4571

NanoCarrier®

Leading-Edge Nanotechnology

Ichiro Nakatomi, Ph.D.
President & CEO
NanoCarrier Co.,Ltd.
Japan

January 9, 2019

Disclaimer

This presentation contains "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the U.S. Securities Exchange Act of 1934, as amended. These statements appear in a number of places in this presentation and include statements regarding the intent, belief or current expectations of the management of NanoCarrier Co., Ltd. (the "Company") with respect to the Company's business, results of operations and financial condition. In many cases, but not all, such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "outlook," "plan," "probability," "project," "risk," "seek," "should," "target," "will" and similar expressions are used here in relation to the Company or its management to identify forward-looking statements. You can also identify forward-looking statements by discussions of strategies, plans or intentions. These statements reflect the Company's current views with respect to future events and are subject to risks, uncertainties and assumptions. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, the company's actual results may vary materially from those the Company currently anticipates. The Company disclaims any obligation to update, or to announce publicly any revision to, any of the forward-looking statements contained in this presentation to reflect future actual events or developments except as required by applicable law.

Highlights

Company Overview

Core Technology

Clinical Pipeline

Next Generation and Next Application

Business Development

NanoCarrier Co., Ltd.

MISSION We develop new drug products by using nanotechnology and contribute to improvement of human healthcare and quality of life.

VISION We aim to become "FIRST ONE", an oncology-focused innovative pharmaceutical company

2000 : Establishment of research activity in Kashiwa-city
2008 : Listing at Tokyo Stock Exchange (TSE) Mothers Market
2010: Commencement of cosmetic business
2018 : Clinical trials of own projects involving global phase III trials

Company Profile

Founded	June 14, 1996	
Listed market	Listed on the Mothers Section of the Tokyo Stock Exchange on March 5, 2005	
Location	Head Office and Lab Wakashiba, Kashiwa, Chiba Prefecture Tokyo Office Kyobashi, Chuo-ku, Tokyo iCONM Lab Tonomachi, Kawasaki, Kanagawa Prefecture	
Subsidiaries	NanoCarrier U S Medford, MA	
Capital	1,115million yen as of Aug. 31, 2018	
Total issued stocks	46,193,584 shares as of Aug. 31, 2018	
Employees and Management	58	
Directors	President and CEO	Ichiro Nakatomi, Ph.D.
	CSFO	Tetsuhito Matsuyama
	Outside Directors	Teruo Okano, Ph.D. (Professor, Tokyo Women's Medical University)
		Akira Ohashi, MD, Ph.D. (Clinical Doctor)
Auditors		Kanshiro Noguchi
		Tadashi Morishima (Representative, Morishima CPA Office)
		Mieko Nakayama (Partner, Haruka Sogo Law Firm)
Scientific Advisor	Kazunori Kataoka, Ph.D. (Director General, iCONM/ Project Professor, The University of Tokyo)	
	Yukio Nagasaki, Ph.D. (Professor, University of Tsukuba)	
	Nobuhiro Nishiyama, Ph.D. (Professor, Tokyo Institute of Technology)	

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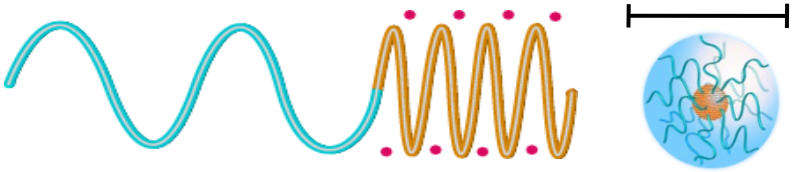
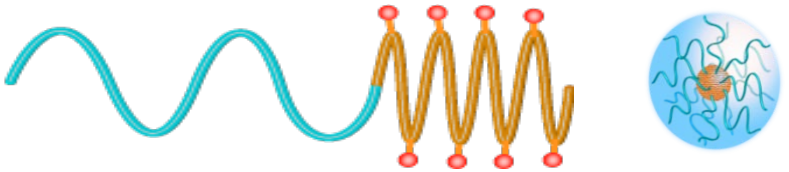
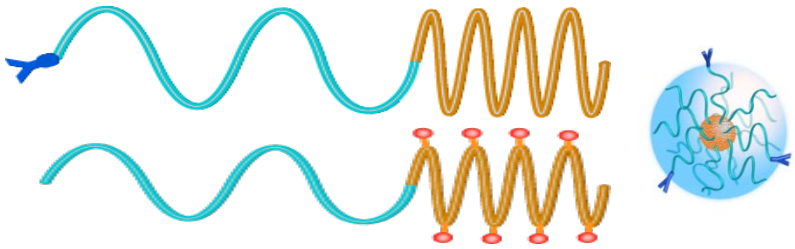
Drug Design System

	Characteristics	Structure
NanoCap™ ➢ Physical entrapment NK105(Paclitaxel) cosmetics ➢ Electrostatic bonding Protein,siRNA	Improves drug's solubility and retention in blood stream	**Polyethylene Glycol** (Hydrophilic, outside of micelle) / **Polyamino acid** (Hydrophobic, inside micelle) / Average particle diameter 30-100nm 
Medicelle™ ➢ Chemical conjugation NC-6004 (Cisplatin) NC-4016 (DACH-Platinum) NC-6300 (Epirubicin)	Improves drug's retention in bloodstream	
ADCM (Antibody/Drug-Conjugated Micelle) ➢ Sensor drug-conjugated micelle (Active Targeting) Sensor:antibody, peptide etc.	Enhances amount of drugs effectively targeted to specific locus	

NanoCarrier - All in One Delivery Technology

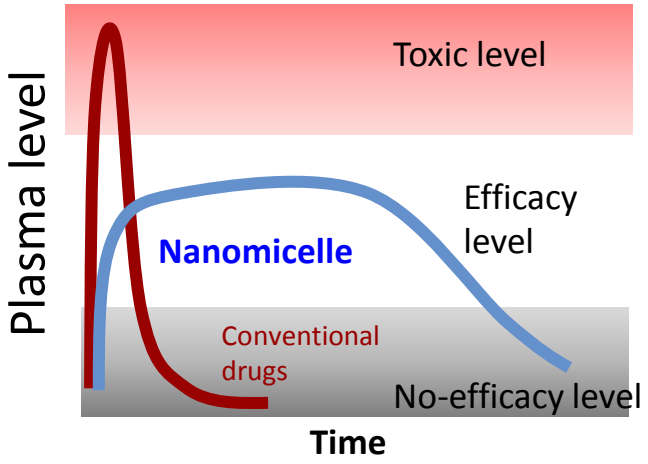
Enhanced solubility

Dissolve the hydrophobic drug in water

Drug (mg/mL)	Itraconazole	Paclitaxel
water	<0.001	<0.1
Micelle	>2	>50
Solubility (Micelle/water)	2000 times or more	500 times or more

Controlled release

Superior controlled release (improved stability and safety) and improved retention in bloodstream

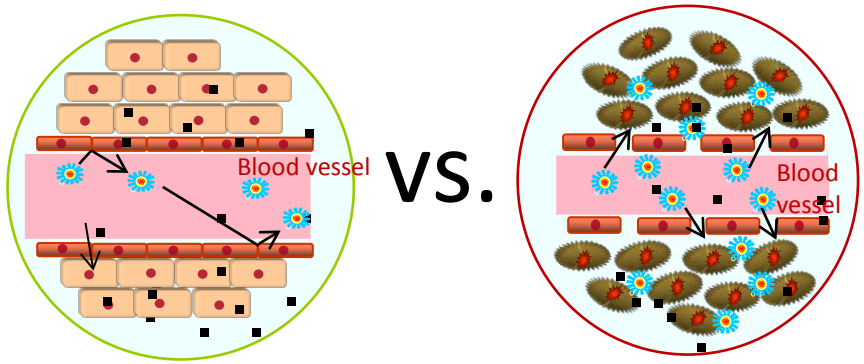


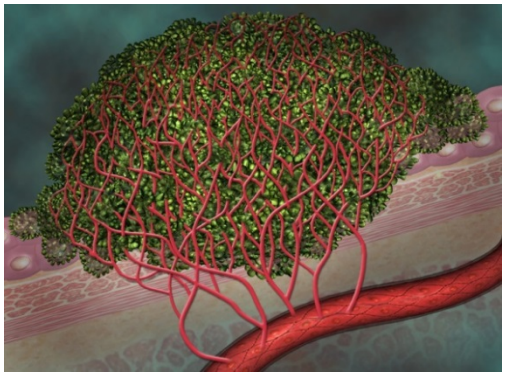
Enhanced Targeting

Nanomicelles accumulate in cancerous tissue by taking advantage of characteristics of cancer cells

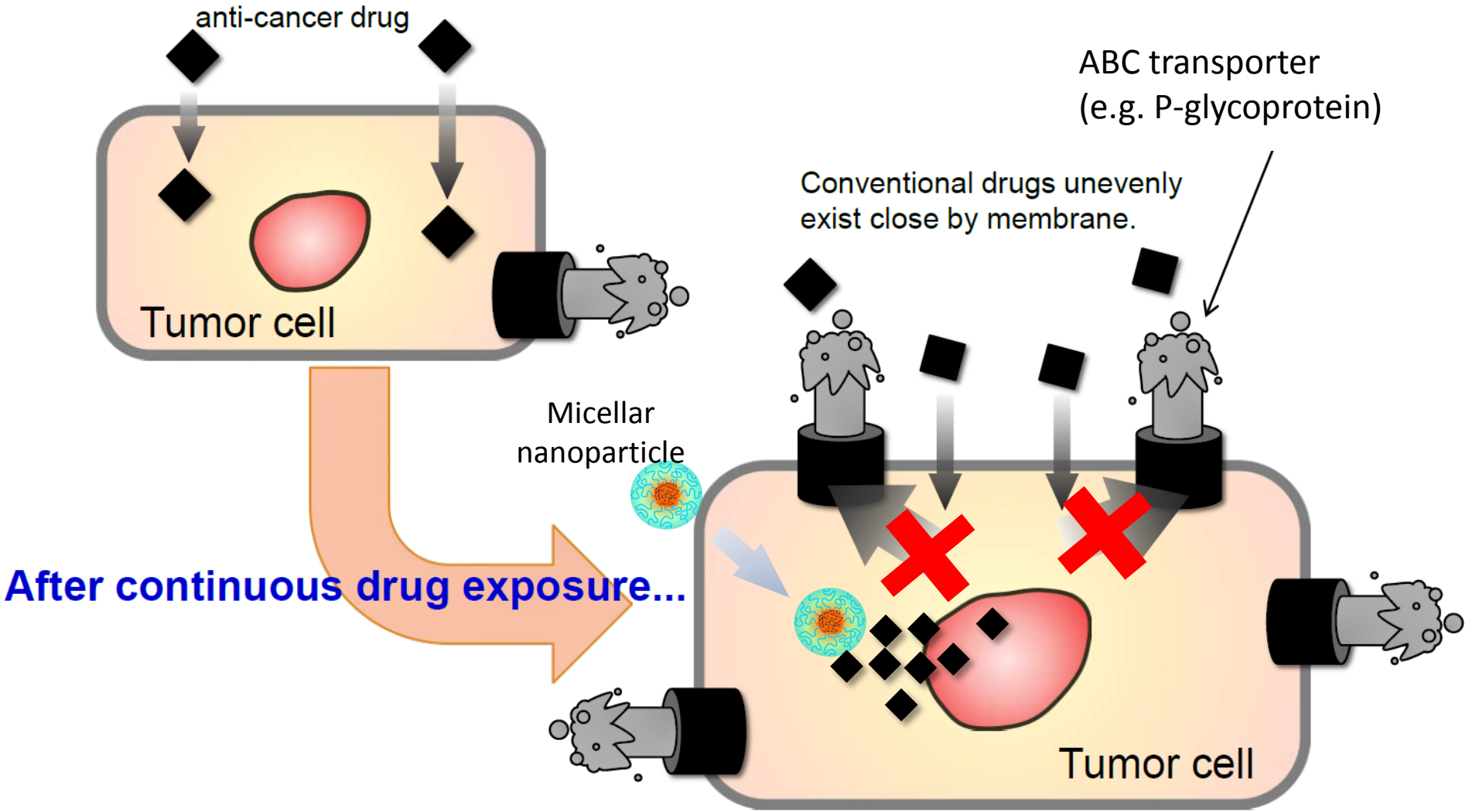
Normal tissue **Cancerous tissue**

●: Conventional drugs
: Nanomicelle





Mechanism of Overcoming Multi-drug Resistance



Advantages of Micellar Nanoparticle Anti-cancer Agents

Development of high added value drugs

- Controlled released

  Drug release is controlled

- Targeting

  Drug is delivered to site of lesions

- Improved bioavailability[1]

  Solubility of poorly soluble drugs is enhanced

Improvement of patient QOL

- Greater therapeutic effect

  Drug is delivered to target cells

- Reduction of adverse reactions

  Toxicity is reduced through controlled drug release

- Greater convenience

  No need for hospitalization, fewer adverse drug reactions and lower medical costs

Note: [1]Bioavailability: Index that shows fraction of drug that enters systemic circulation and its efficacy

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Product	Indication	BR	PC	ph1	ph2	ph3	Develop Area	Alliance Partner
NC-6004 Cisplatin micelle	Pancreatic cancer	Co-Development					Japan/Asia	友華股份有限公司 Orient Europharma Co., Ltd.
	Lung (NSCL), Bladder, Biliary tract cancer	In-House Development					USA/EU	
	Head and neck cancer	Co-Development					USA/EU /Asia	友華股份有限公司 Orient Europharma Co., Ltd.
NC-6300 Epirubicin micelle	Soft tissue sarcoma	In-House					USA	
NC-4016 Dach-platinum micelle	Solid cancer	In-House					USA	
NK105 (Out-Licensed) Paclitaxel micelle	Breast cancer Gastric cancer	Out-Licensed					Japan	Global "sukima" ideas NIPPON KAYAKU
VB-111 (In-Licensed) Non-replicating Adeno 5 vectors	Development in Japan under examination	In-Licensed	Operation by VBL				Japan	VBL therapeutics
ENT product	ENT	Co-Development					Japan	CEOLIA

Development of Major Clinical Pipeline

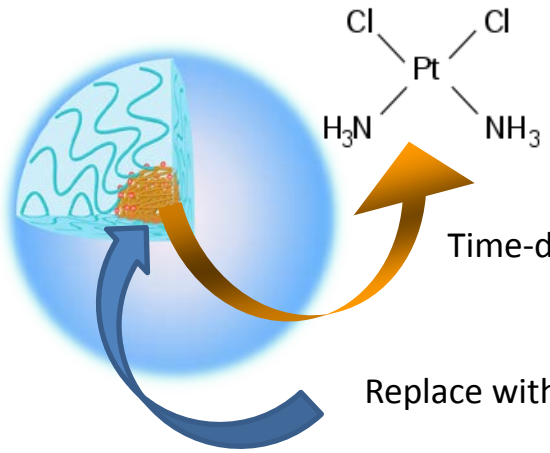
NC-6004

- Phase III: Pancreatic cancer
  - ✓ Resumed patient enrolment (August 2017)
- Phase II: Basket design trial (biliary tract, NSCLC, bladder)
  - ✓ Granted orphan drug designation from the US FDA for the indication of biliary tract cancer
  - ✓ Completed the enrolment for biliary tract cancer
- Phase II: Head and neck cancer
  - ✓ In combination with the immune checkpoint inhibitor (KEYTRUDA®)
  - ✓ Prepared to start the multinational clinical trial in the US, EU and Asia
  - ✓ Filed IND application (US) (October 2018)

NC-6300

- Phase I/II: Soft tissue sarcoma
  - ✓ Granted orphan drug designation from the US FDA.
  - ✓ Completed Phase I part
  - ✓ Ongoing the preparation of Phase II part

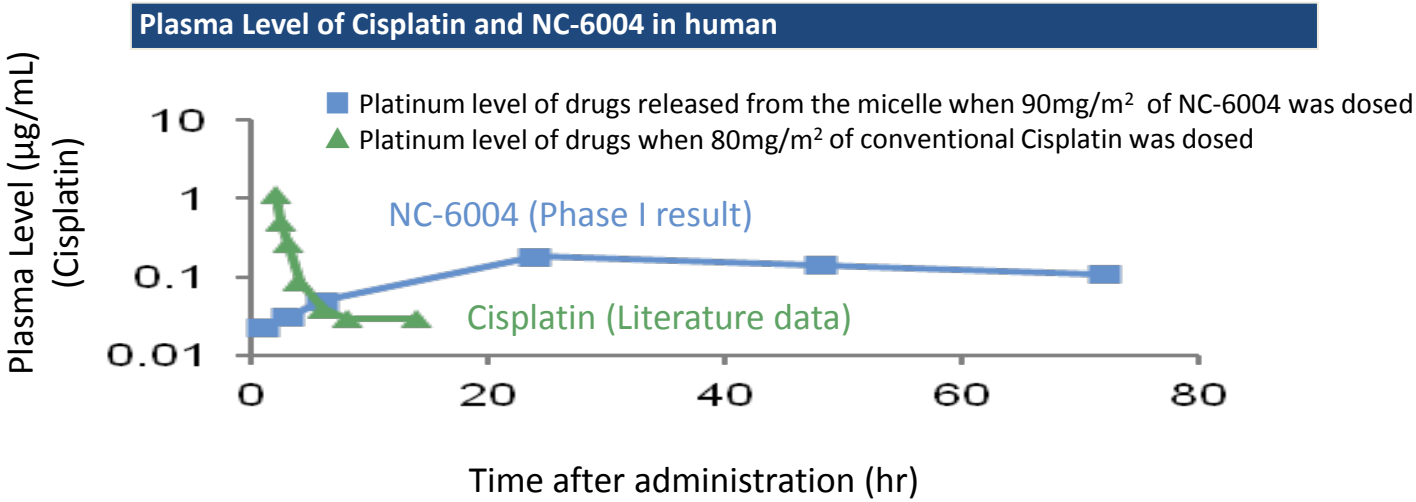
NC-6004 (Cisplatin Micelle)



- Sustained Rerelease of Drugs in Blood
- Enhance Efficacy
- Reduce Side Effect
- Improve Accessibiiy

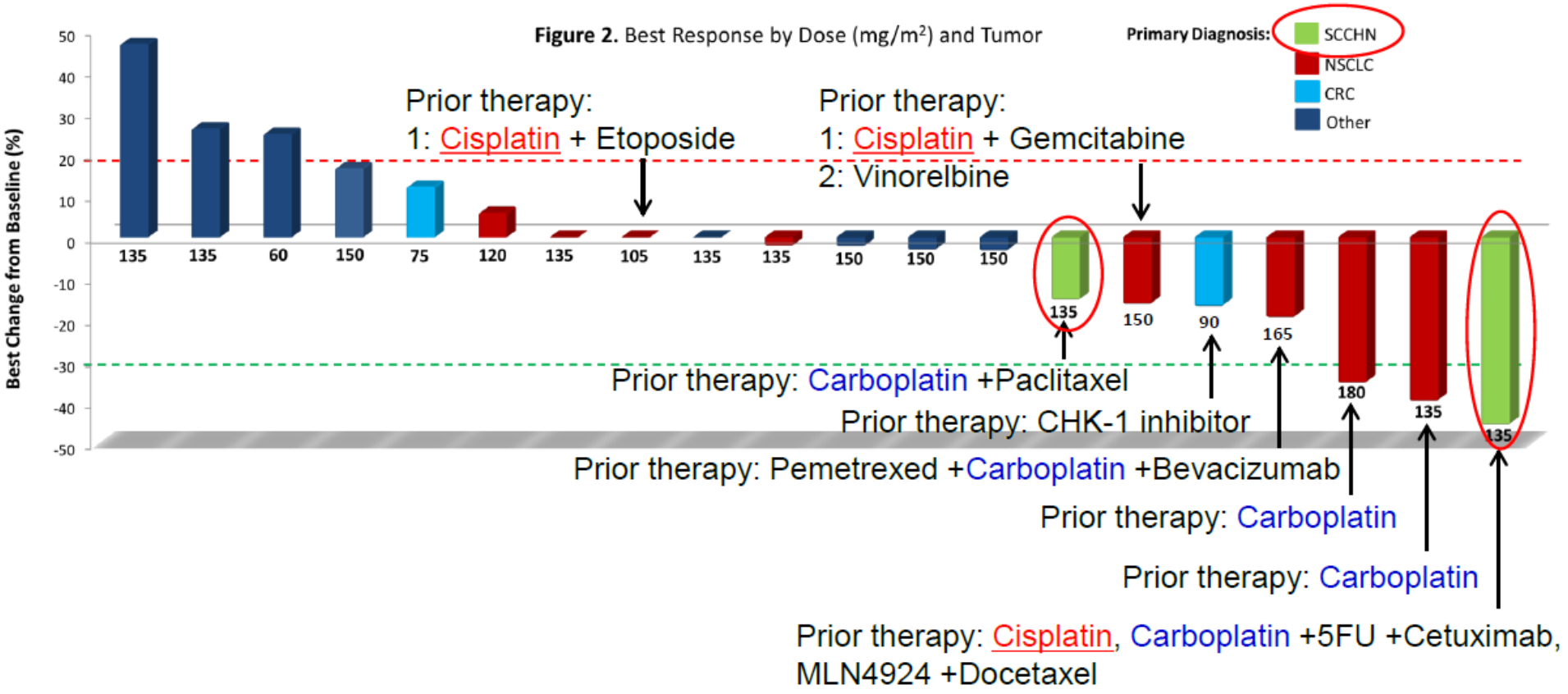
Phase I

➢ Reduced Cisplatin specific side effects (nephrotoxicity, nausea & vomiting)



Efficacy of NC-6004 in Phase Ib

- H&N responded to NC-6004
- NC-6004 was efficacious to platinum treated patients

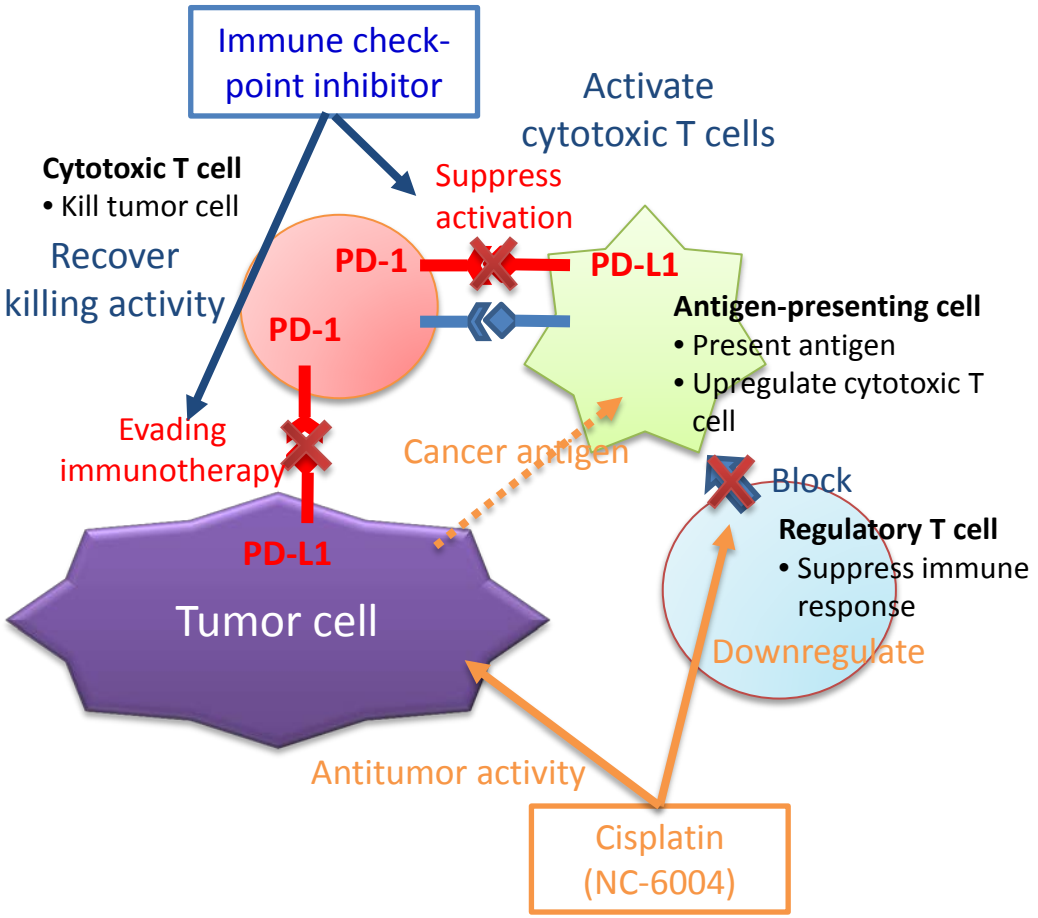


A New Clinical Study for Head & Neck Cancer

1. Anti-cancer activity to patients with Head and Neck Cancer was observed in Phase I study conducted in US and Taiwan
2. Immune checkpoint inhibitors were already approved for Head and Neck Cancer (monotherapy)
3. Efficacy of the combination therapy of cisplatin with immune checkpoint inhibitor was approved for NSCLC in the US.
4. Possibly effective on patients with recurrent/refractory to platinum-based treatment

<u>Anticipate Probability of Success, Development Speed and Marketability</u>

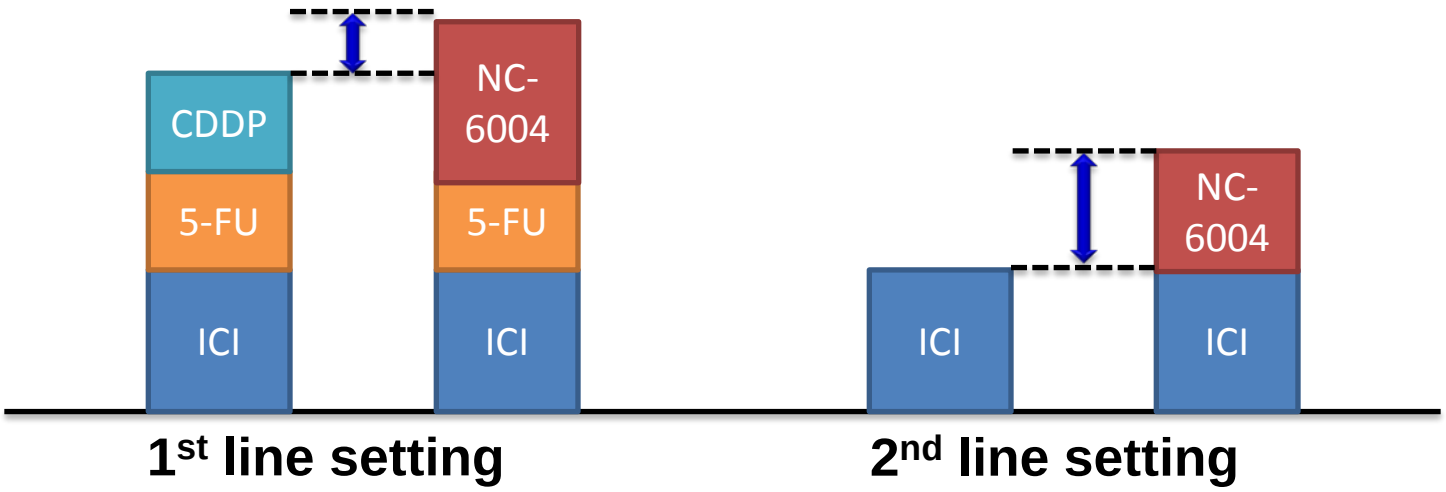
Mechanism of potential synergistic effect of NC-6004 in combination with immune checkpoint inhibitor
(Cancelation of suppression/evasion of cancer immunotherapy)

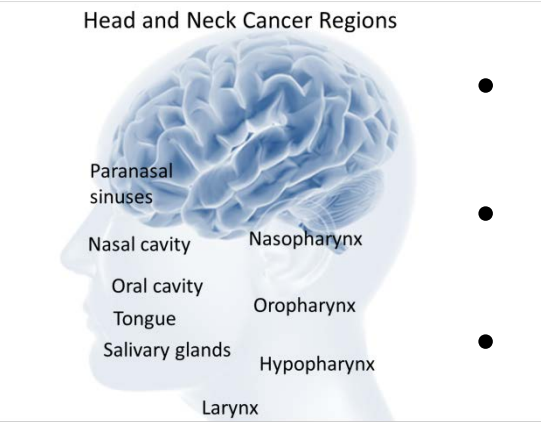


※Immune checkpoint inhibitors

Tasuku Honjo, distinguished professor at Kyoto University, has won the 2018 Nobel Prize in physiology and medicine. Professor Honjo has discovered a protein named PD-1 which brakes immune activity. Immunecheck point inhibitor, which shows anti-cancer activity by removing such immune suppression by PD-1 pathway, has been spotlighted as novel immune-oncology therapy and has been developed actively in worldwide.

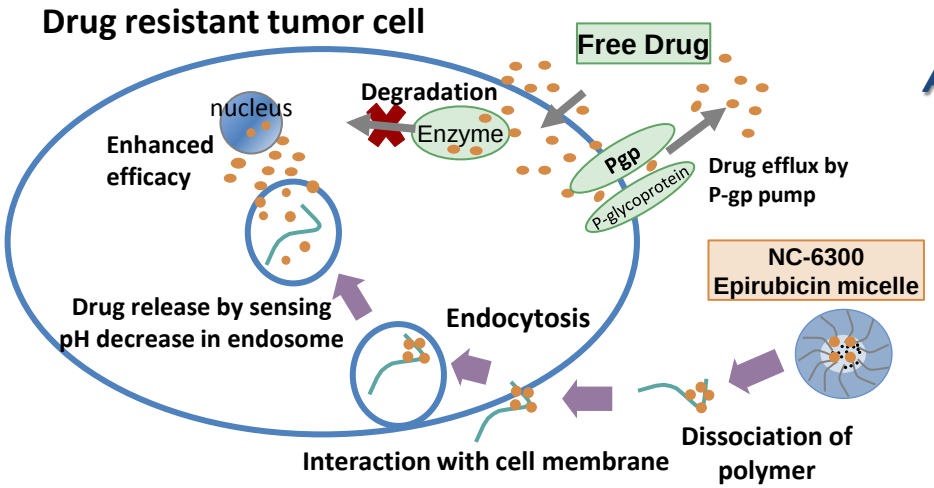
Strategy Selecting 2nd Line Treatment for H&N Cancer





- **Difference of the effect size (↕) in add-on study is expected to be larger than head-to-head study.**
- **Larger difference of effect size decreases sample size of the study and enables to get the result faster.**
- **The Result of 1st line ICI study is presently not available.**

NC-6300（Epirubicin Micelle）



Application of System to Enhance Functionality

- Sustained Release by Sensing Intracellular pH
- Enhance Efficacy
- Reduce Side Effect
- Improve Accessibiiy

Endocytosis: energy-using process by which cells absorb molecules (such as foreign matters, proteins, nutrition) by engulfing them
Endosome: Membrane-bound compartment created by endocytosis

- **Results of First-in Human Study of NC-6300 in Japan**
  - The recommended dose ：170 mg/m^2（used in standard of care, i.e., 60 mg/m^2 or 100 mg/m^2 ）
  - Major adverse events of epirubicin, such as vomiting and Myelosuppression, had a tendency to decrease
  - No clinically significant decrease in cardiac function was observed even in cases who were received NC-6300 administration for more than 12 months
  - No cardiac failure was observed in 4 cases treated with 900 mg/m2 in Phase I data in Japan, which is the maximum accumulated dose of conventional epirubicin in lifetime to avoid risks of cardiac failure.
- **<u>Phase I/II Clinical Study Undergoing in US (PI part completed)</u>**
  - ✓ Granted orphan drug designation from the US FDA.

Summary of Phase I in US

Phase I Part

No. of Patients: 29
Indication : Advanced solid tumors, including soft tissue sarcoma

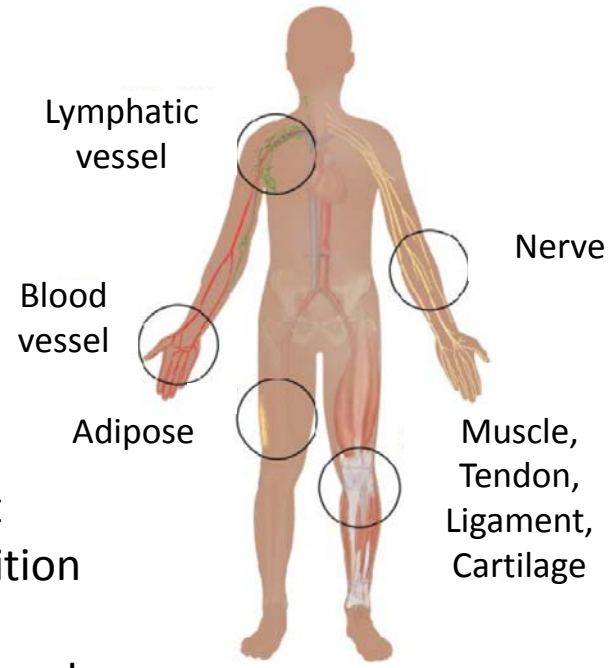
1. Maximum tolerated dose of NC-6300 monotherapy was determined to be 185 mg/m^2.
2. Observed adverse events were similar to the conventional epirubicin.
3. Incidence rate or severity of adverse events are lower or milder than conventional epirubicin.
4. No clinically significant cardiac toxicity was observed.
5. Enrolled 2 angiosarcoma subjects responded to NC-6300.
6. Long SD was observe in a melanoma subject who was refractory to anti-PD-1 mAb and anti-PD-1 mAb +anti-CTLA-4 treatments.

NC-6300 Clinical Study for Soft Tissue Sarcoma

Considering indication for Phase II Part

Soft tissue sarcoma

- Malignant tumor that develops in the soft tissue such as the subcutaneous tissue or muscle
- Orphan drug (US: 12,000 pts per year)
- Development of new drugs is desired, as treatment options are limited.



Aims of development

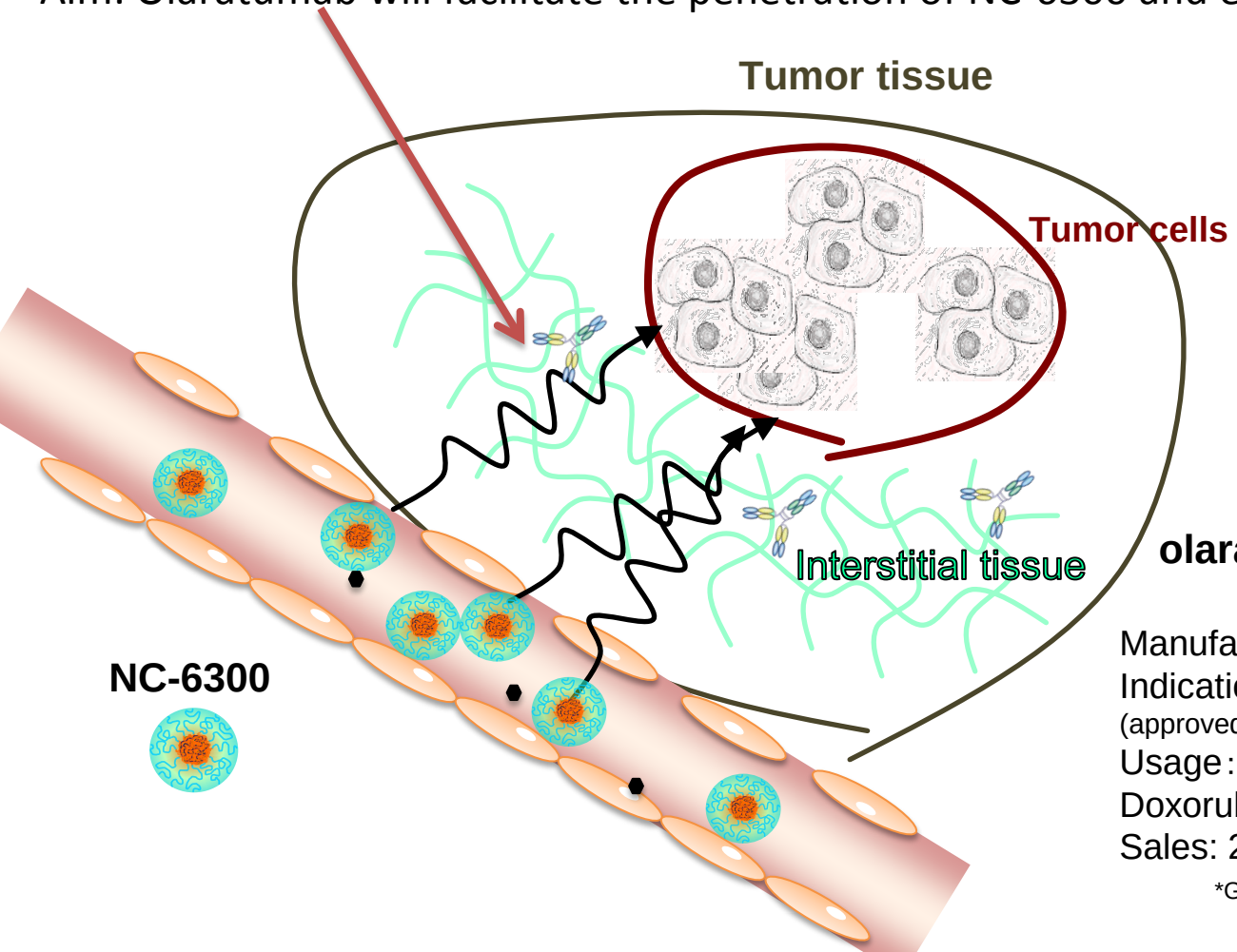
1. Epirubicin is approved anthracycline anticancer agent
2. Not many drug candidates and relatively less competition (Efficacy of immune checkpoint inhibitors is limited)
3. Possibility of application of the FDA Accelerated Approval Program

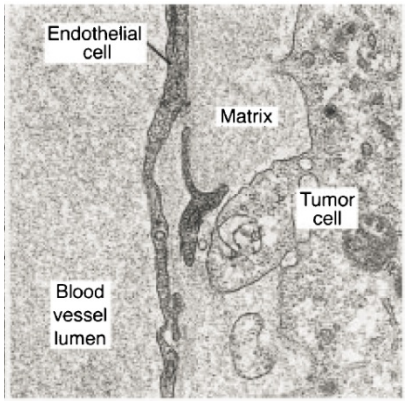
NC-6300 in combination with Olaratumab

In combination with Olaratumab (Lartruvo™)

Olaratumab: Antibody therapeutic approved for the treatment of soft tissue sarcoma in 2016
Blocks PDGF-alpha receptors and improves tumor microenvironment

Aim: Olaratumab will facilitate the penetration of NC-6300 and enhance its antitumor activity





Cancer and Metastasis Reviews, 2010, 19, 109-120

olaratumab

Manufacturer: Eli Lilly
Indication: Malignant soft tissue tumors
(approved October 2016)
Usage：Used in combination with Doxorubicin
Sales: 22.9 billion JPY (2017 forecast)*

*Global antibody therapeutics market size 2018
(TPC Marketing Research Corp.)

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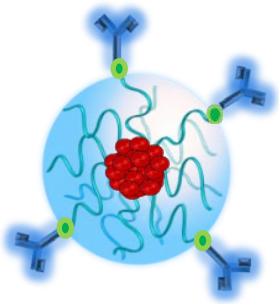
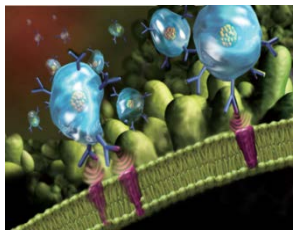
Next Generation of our Technology

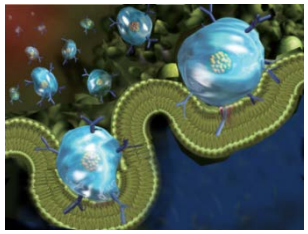
ADCM （Antibody-Drug Conjugated Micelle）

A large quantity of payload can be delivered to target cells.

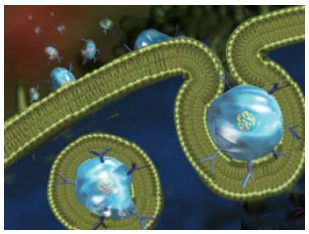




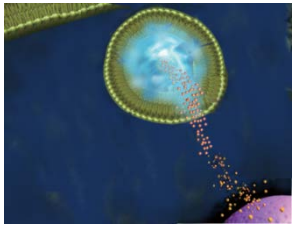
Recognition of target cells



Adhesion to the cell membrane



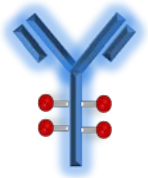
Intracellular incorporation



Intracellular drug release

Advantages of ADCM

1. ADCM can carry 100-300 molecules of payload per Mab.
2. ADCM is equal or more active for sensitive tumors.
3. ADCM is significantly active for resistant tumors.
4. ADCM is more effectively internalized in the tumors.
5. ADCM shows a continuous drug release in the tumors.



ADC

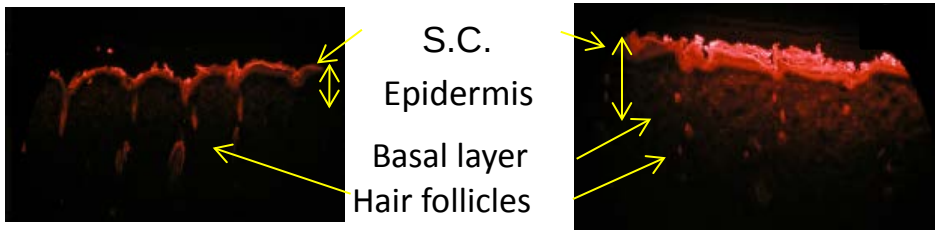
Antibody-Drug Conjugates

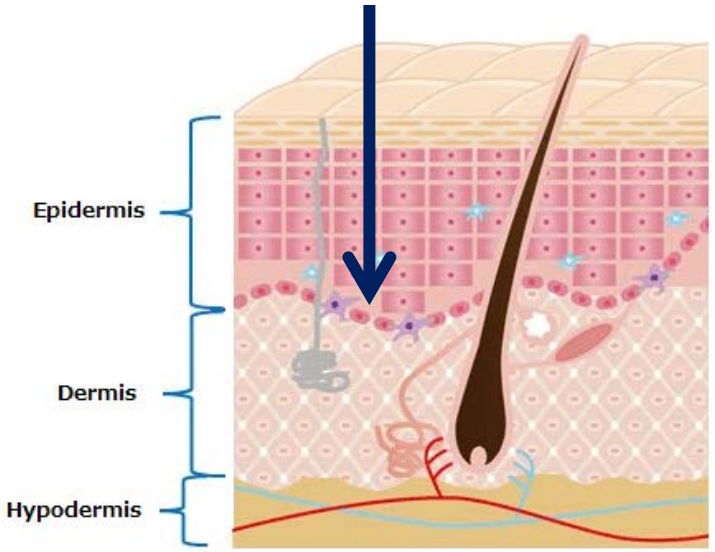
Application of Dermatology

The drug was found to be localized in epidermis *in vivo* permeation study.

Control
（Fluorescent in water）

Encapsulated Fluorescent in micellar nanoparticles





A Track Record of Cosmetic Products

2010
e'clafutur-W essence:
own development/
own marketing

2013
eclafutur:
co-development with ALBION
marketing by ALBION

2016
EXCIA AL:
co-development with ALBION
marketing by ALBION

2016
Depth:
hair growth set
for men

2017
Depth for share:
hair growth set
for women

co-development with ALBION
marketing by NanoCarrier

2018
eclafutur d :
co-development with ALBION
marketing by ALBION

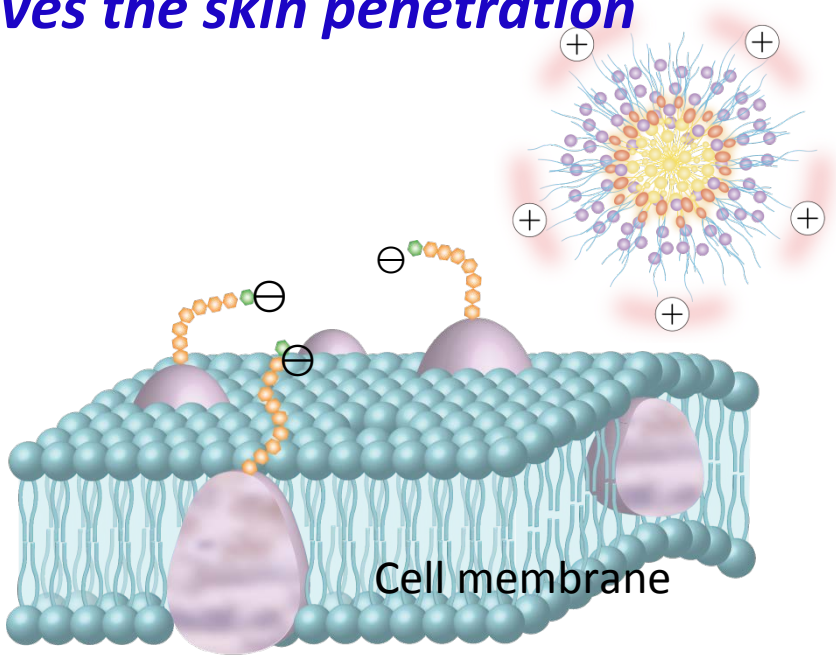
Cosmetics Business

Nanocesta, a micellar nanoparticle for delivering cosmetic ingredients, is powered up through the electrostatic interaction.

Positively charges the nanoparticle surface

binds negatively charged cell membrane

Improves the skin penetration



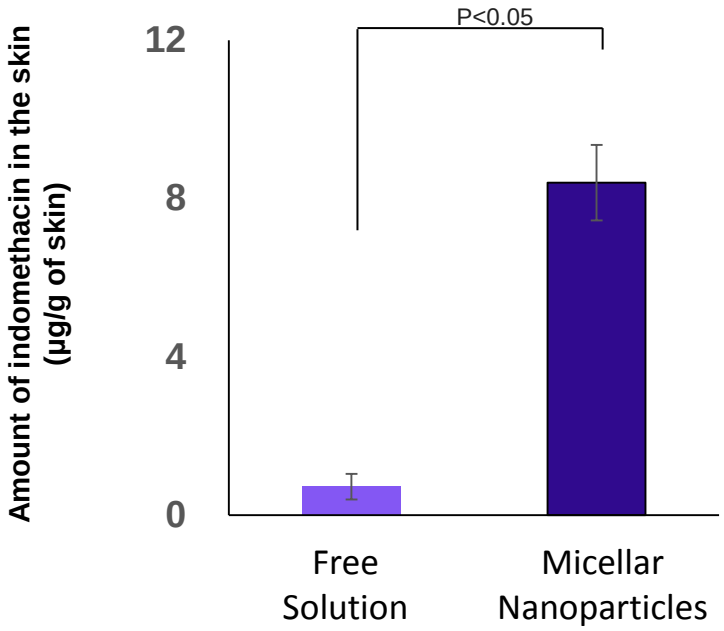
New *eclafatur d* ®

Launched in department stores and beauty salon on October 18, 2018

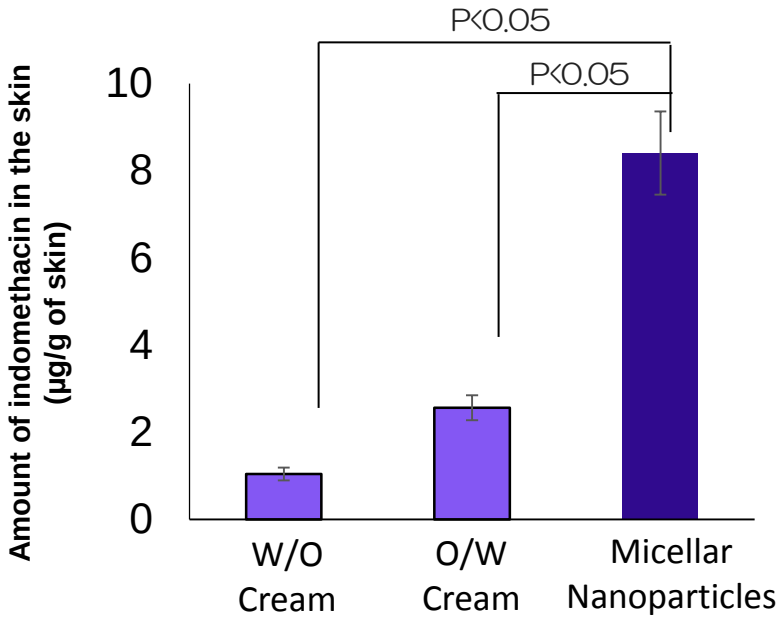
High Permeation of Hydrophobic Drug in Skin

30-40% of total applied drug was penetrated into the skin

Free Solution
vs
Micellar Nanoparticles



Oil-based Formulation
vs
Micellar Nanoparticles



Indomethacin: 100μg/g

Kensuke Yotsumoto, et al, Int J Pharm. 553 (2018)

Dermatological Advantage of Technology

- ✓ **Improves the skin permeability of hydrophobic compounds**
- ✓ **Improves the water solubility of hydrophobic compounds**
- ✓ **Improves the thermal and light stabilities of hydrophobic compounds**
- ✓ **Improves the sustainability of compound activity**

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Business Developments

License and Joint development for our Pipeline

Orient Europharma	NC-6004
Nippon Kayaku	NK105

Joint research of ADCM Technology

TPG Biologics	Optimization of sensor molecules
JCR Pharmaceuticals	Brain delivery Combination of ACDM with J-Brain cargo®
Gene Techno Science	Exploration of new sensor molecules, *etc.*

License-in cancer filed and Joint development in other field

Enhancement of the late stage pipeline for early generation of revenue

VBL Therapeutics	Introduction of systemically administered gene therapy in Japan
Ceolia Pharma	Moves to acquire joint development and sales network for pharmaceuticals in ENT field

Unique Drug Delivery Technology Opening Up for New Possibility of Therapy

Discovery of any compounds to meet unmet needs

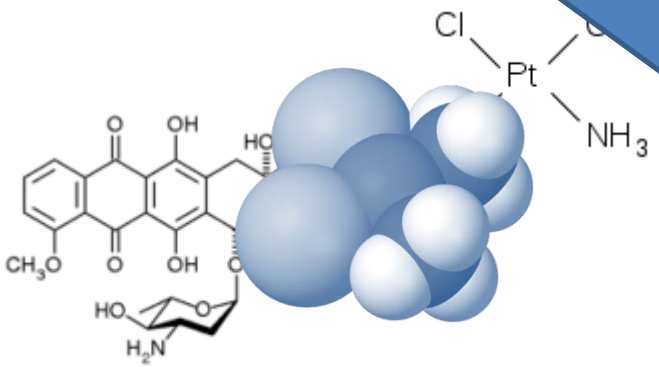
Partners

NanoCarrier®

- Existing drugs
- New drug candidates
- Compounds abandoned at development stage
- Cosmetic products

Seeking to enhance performance through unique formulation technologies

- Sustainability
- Solubility
- Pharmacodynamics
- Stability



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Initiatives Ongoing

Future on NanoCarrier

- ✓ **Develop new products by using *NANOTECHNOLOGY* and contribute to improvement of human healthcare and *QOL***
- ✓ **Aim to become "*FIRST ONE*", as for the innovative company**
- ✓ **Moving towards a *SPECIALITY PHARMA* for new drugs with high unmet needs**

Thank you very much

Contact
NanoCarrier Co.,Ltd.
CEO Office
E-mail: info@nanocarrier.co.jp