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Healthcare Conference

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NanoCarrier[®]

LEADING-EDGE NANOTECHNOLOGY

Tokyo Stock Exchange
4571

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Company Overview



Forward-Looking Statements

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.





Company Overview

- **NanoCarrier is a leading player in Nanomedicine leveraging proprietary platform technology.**
- **Four (4) oncology-product candidates are undergoing 8 clinical trials globally, including Phase III trials.**
- **Various new projects such as ADCM, RNAi and other candidates beyond oncology are under development.**
- **We already have enough fund for accelerated R&D activities, supply of API and maintenance of company's operation.**





2016 Highlights

1

Accelerated Clinical Trials to Increase Probability of Success

- **NC-6004:**
 - Expanded clinical studies in US to EU
 - ✓ Moved to PII for NSCL, bladder cancer, and biliary tract cancer
 - ✓ Moved to PI for head and neck cancer
- **NC-6300:**
 - Started PI/PII for soft tissue sarcoma (rare cancer) in US

2

Investment for New Technology

- Promoted preclinical studies for the first ADCM (NC-6201) for IND
- Accelerated the research to establish nucleic acid delivery technology
- Investment and license-out of NanoCarrier technologies to AccuRna

3

Expansion of Cosmetics Products with ALBION

- Started collaboration for new product
- Launched hair growth tonic for men
- Launched new skin essence

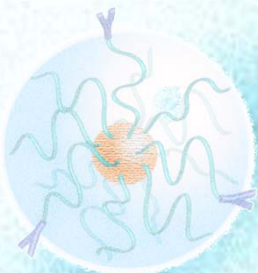




NanoCarrier Highlights

Japan
Technology

Micellar
Nanoparticle



Keeps on evolving

Robust oncology pipelines

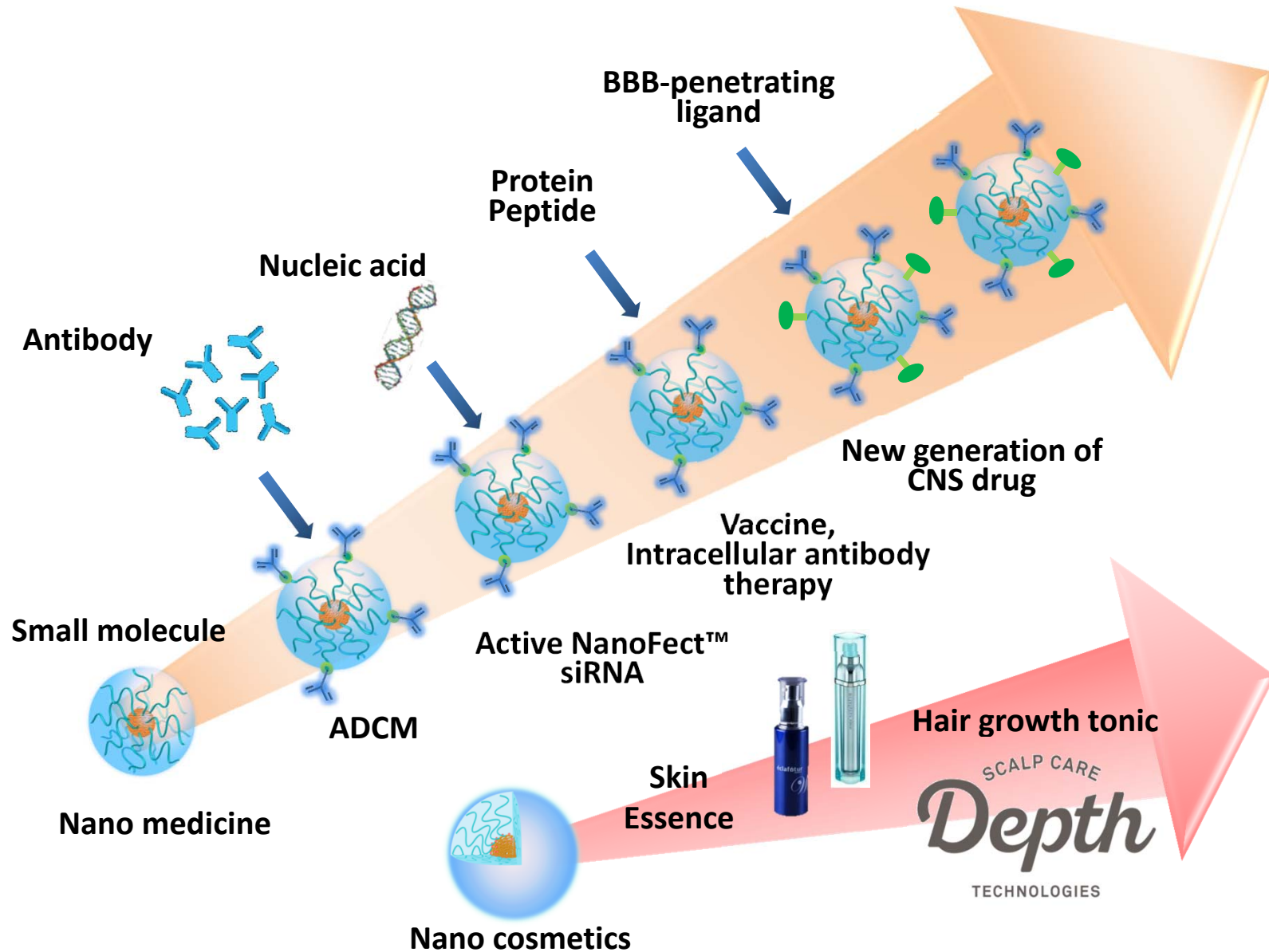
New research

Other Opportunities





NanoCarrier Keeps on Evolving





NanoCarrier - All in One Delivery Technology

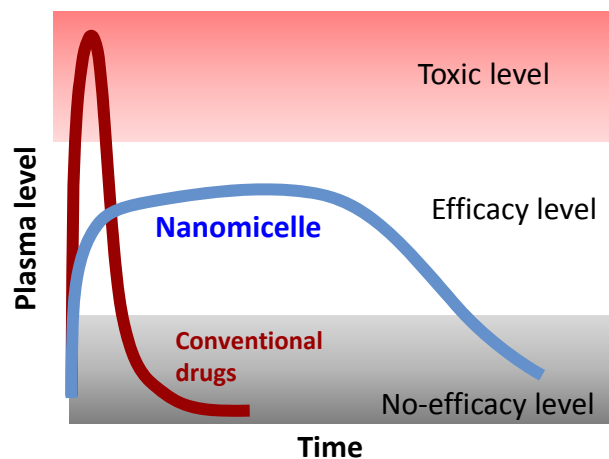
Enhanced solubility

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



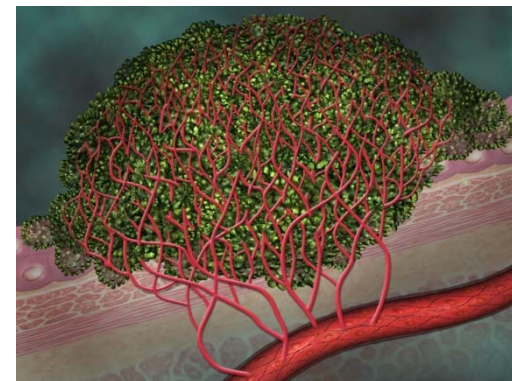
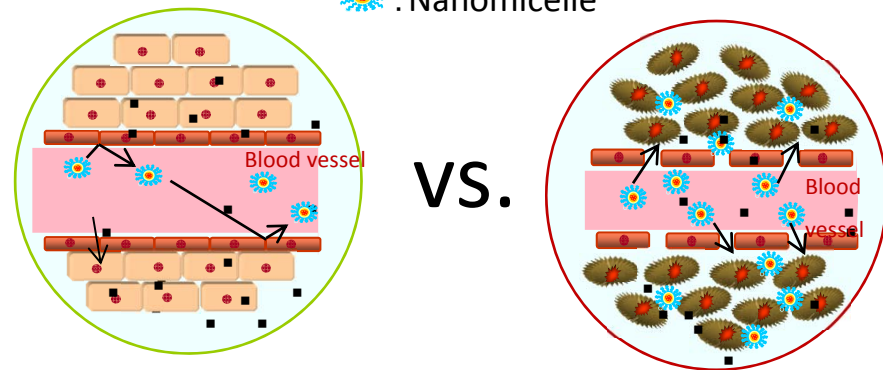
Enhanced Targeting

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

Normal tissue

Cancerous tissue

■ : Conventional drugs
☼ : Nanomicelle



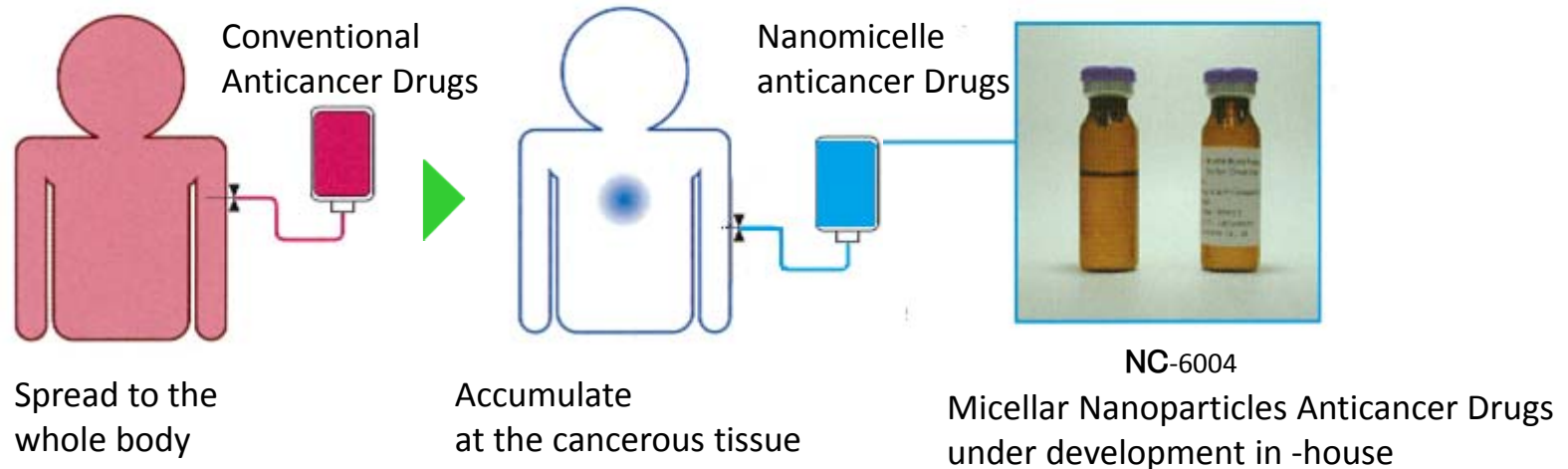


Advantage of NanoCarrier - Competitive Technology

		Controlled release	Targeting	Bioavailability
Passive	Albumin nanoparticle (Abraxane, etc.)	Low	Low	Low
	liposome (Doxil, ONIVYDE, Lipodox etc.)	Low	High	Medium
	PEG-PLA (Genoxol-PM, etc.)	Medium	Low	Medium
	Passive Micelle (NC-6004, NC-6300 etc.)	High	High	High
Active	Active PEG-PLA (BIND-014, etc.)	Medium	Very high	High
	Active Micelle, ADCM (NC-6201, etc.)	High	Very high	Very high



Merits by NannoCarrier Technology



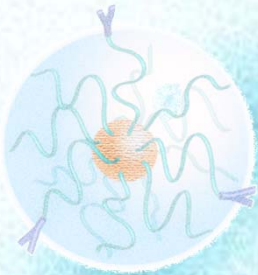
Disadvantages of conventional anticancer drugs:
Severe side effects
→ Pre/post medication and Hospitalization are needed*
→ Difficult to continue treatment

Advantages of NanoCarrier anti-cancer drugs:
More effective but less toxic
→ No hospitalization

*Hydration or other medication is required before/after the infusion to reduce adverse reactions



NanoCarrier Highlights



Keeps on evolving

Robust oncology pipelines





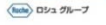

New research

Other Opportunities





Current Status of Pipelines

Product	Encapsulation drug	Cancer Indication	BR	PC	ph1	ph2	ph3	Develop Area	Alliance Partner	
NC-6004	Cisplatin	Pancreatic	Co-Development						Japan/Asia	 友華股份有限公司 Orient Europharma Co., Ltd.
		Lung (NSCL)	In-House Development						USA/EU	
		Bladder	In-House Development						USA/EU	
		bile duct	In-House Development						USA/EU	
		Head and neck	In-House		Co-Development			USA/EU Asia	 友華股份有限公司 Orient Europharma Co., Ltd.	
NC-4016	Dach-platinum	Solid	In-House					USA		
NC-6300	Epirubicin	Solid	In-House					USA		
NC-6201	E7974 (in-licensed)	Solid	In-House					USA (Planned)	 Eisai	
Active NanoFect	siRNA	Solid	Co-Research		In-House			—	 CHUGAI <small>すべての笑顔は君さんのために</small>  ロシュグループ	
NK105	Paclitaxel	Breast Gastric Solid	Out-Licensed					Japan	Global "sukima" ideas  NIPPON KAYAKU	





Results of Phase I Study of NC-6004 in Japan

Combination Therapy of NC-6004 with Gemcitabin

Abstract for 2016 ASCO Annual Meeting on June 10, 2016

- Recommended dose of NC-6004 in combination with GEM: 90 mg/m² in Japanese patients with advanced solid tumors
- Neutropenia and thrombocytopenia were common toxicities. No grade 3 or higher nausea/vomiting was observed without antiemetic premedication.
- The disease control rate: 81.8%.
- Cisplatin is reported to cause acute kidney injury in almost 70% of patients but NC-6004 causes it in 30% of patients based on PK/PD simulation.

Based on these results, PIII for pancreatic cancer is on-going in Japan/Asia.



Results of Phase Ib Clinical Study of NC-6004 in US

Combination Therapy of NC-6004 with Gemcitabin

Poster presentation for European Society for Medical Oncology (ESMO) 2016 Congress on Oct. 10, 2016

Abstract

- RD of NC-6004 in combination with GEM is determined to be 135 mg/m² with advanced solid tumors in US.
- No clinically significant adverse events which occur in patients treated with cisplatin (e.g. neurotoxicity, ototoxicity, and nephrotoxicity) were observed even at 1.5 times higher dose than the standard dose of cisplatin.
- NC-6004 was well tolerated and showed efficacy in patients who had previously received platinum-based chemotherapy including cisplatin.

Based on these results, PII for basket design (NSCL, bladder cancer, and biliary tract cancer) is on-going in US/EU.



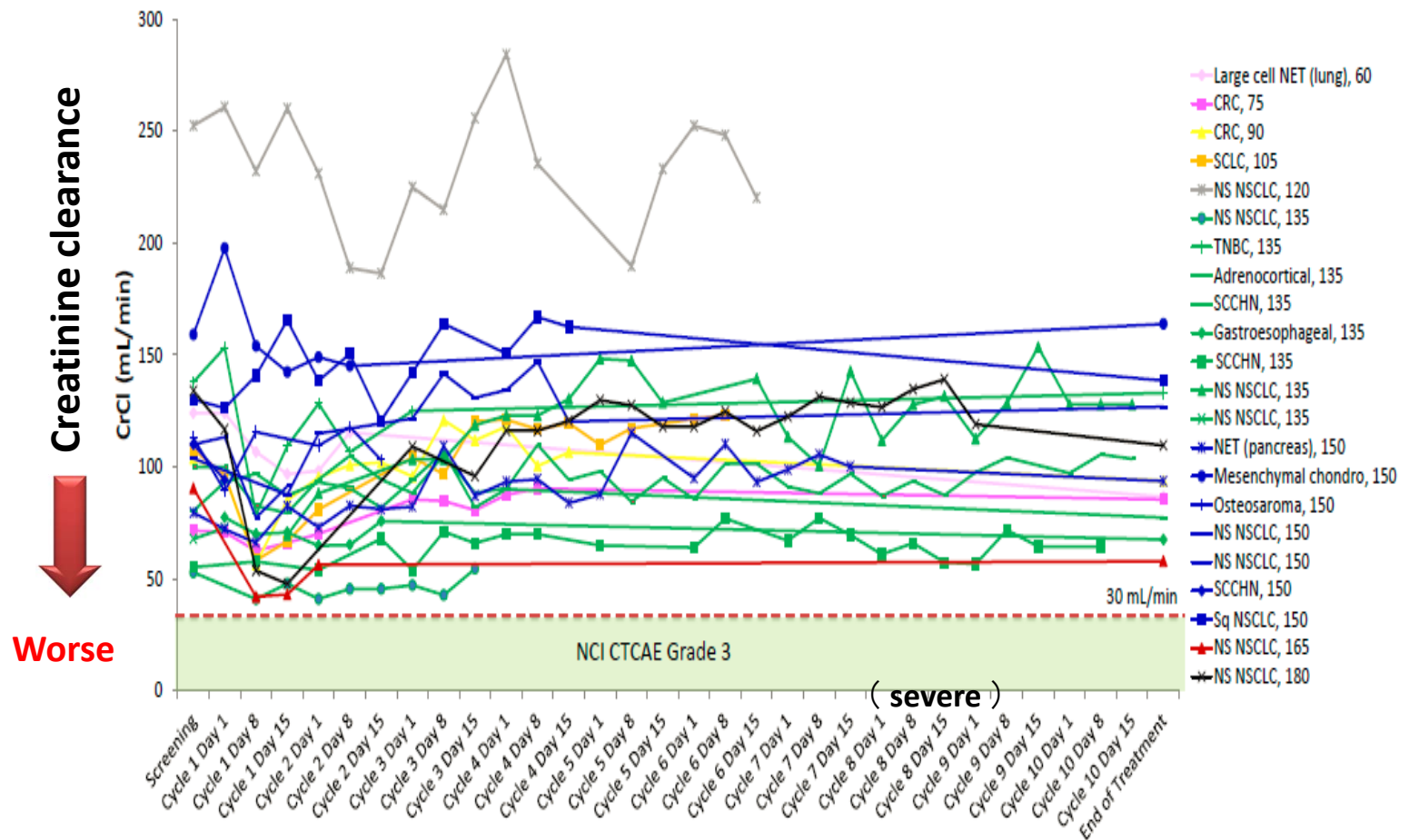


Results of Phase Ib Clinical Study of NC-6004 in US (I)

Safety: Renal Function

- No subjects with severe decrease of renal function index were observed.

Figure 4. Change in CrCl Over Treatment Duration

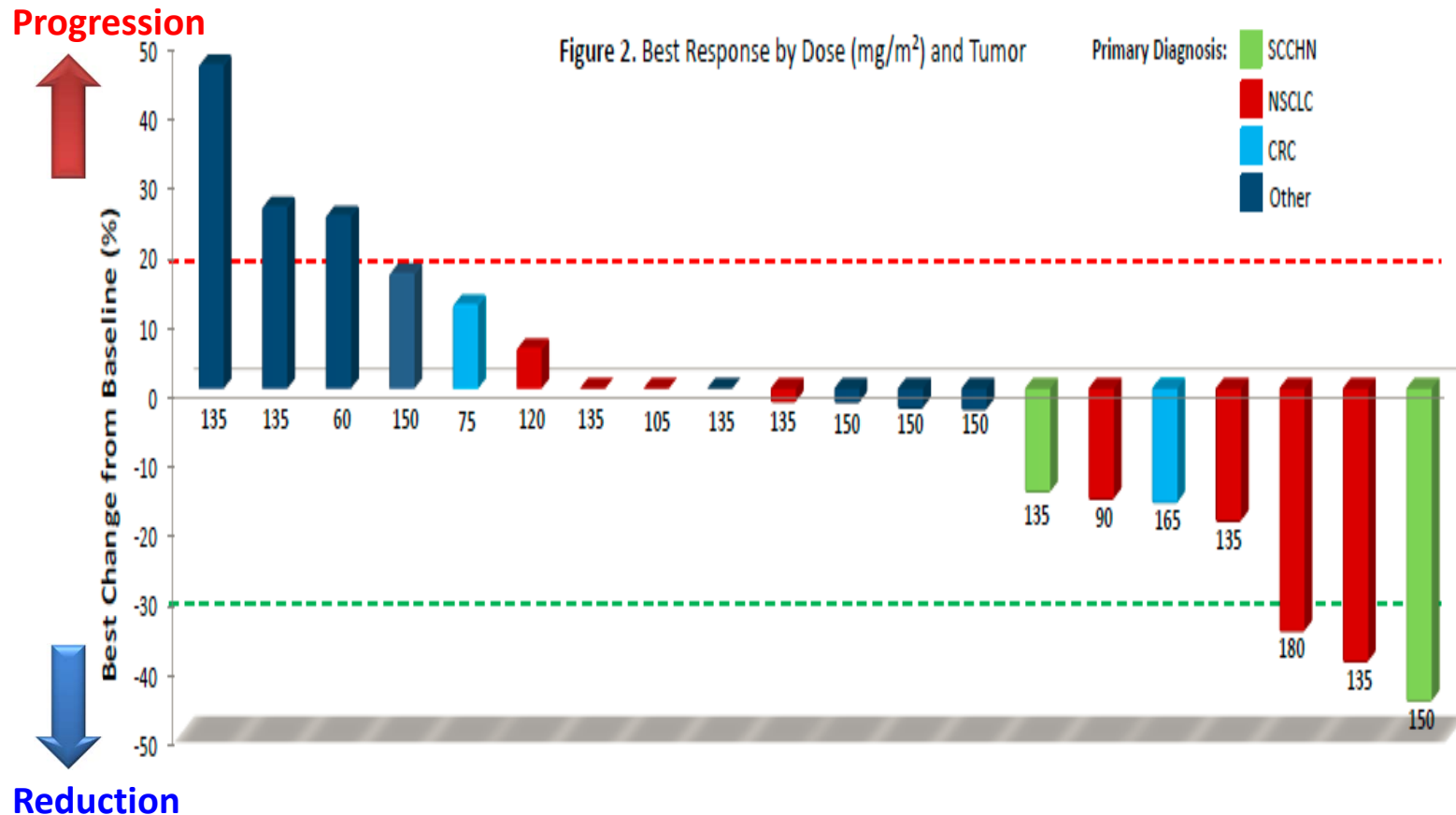




Results of Phase Ib Clinical Study of NC-6004 in US (II)

Anti-Tumor Effect

- The disease control rate: 85.0% (SD: 14/20pts, PR: 3/20pts)
- Unconfirmed PRs in 3pts (1 who failed prior anti-PD1)





NC-6300: Encapsulating pH-sensitive release of epirubicin

Phase I: Completed in Japan

- Promising results of Phase I study was obtained in Japan.
 - Reduction of the characteristic adverse reactions of epirubicin, including vomiting and bone marrow toxicity
 - Higher-dose administration than epirubicin alone
 - Administrations of more than 12 months without decrease of cardiac function

- NanoCarrier accelerates the development of NC-6300
 - Forward-looking to rapid approval by using expedited review programs of US FDA for malignant tumors without standard therapy, etc.

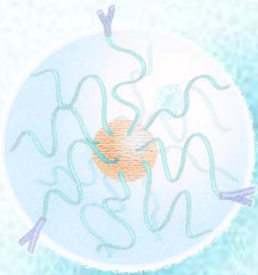
Current Status:

Submitted IND to US FDA for Phase I/II of soft tissue sarcoma





NanoCarrier Highlights



Keeps on evolving

Robust oncology pipelines

New research

Other Opportunities





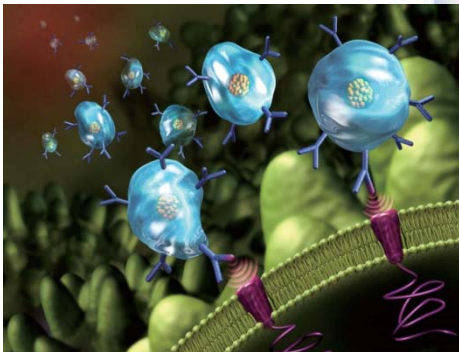
Next Generation of Active Targeting System

ex. More than 70 ADCs are under clinical developments (PI 46, PII 26, PIII 5) and markets (3) world wide.

- Has limits of use on Mabs and payloads
- Has limits of use for indications

NanoCarrier provides the solution by enabling to use many kinds of targeting sensors and payloads.

ex. Antibody/Drug-Conjugated Micelle (ADCM)

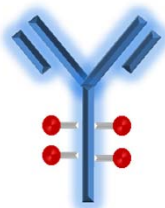


Expands the market opportunity

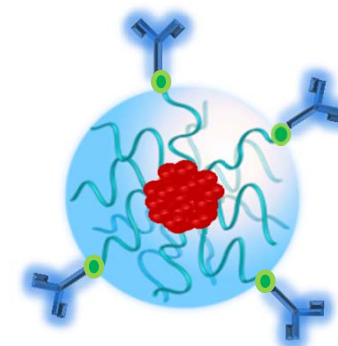


Differences in Key Requirements

ADC



ADCM



ADC

ADCM

Sensor molecule

- Incompatible with Fab and scFv
- Internalization required

- Fab and scFv applicable
- Protein, peptide, and small molecule also applicable
- Internalization preferable

Drug

- Highly potent agents (IC_{50} : $10^{-10} \sim 10^{-11}$ M)
- Low Ab-drug ratio

- Moderately potent agents (IC_{50} : $\sim 10^{-9}$ M)
- High Ab-drug ratio

Linker

- Must be stable in plasma to avoid premature release of the drug

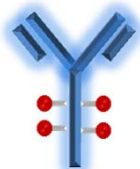
- Enable slow release of payload in plasma



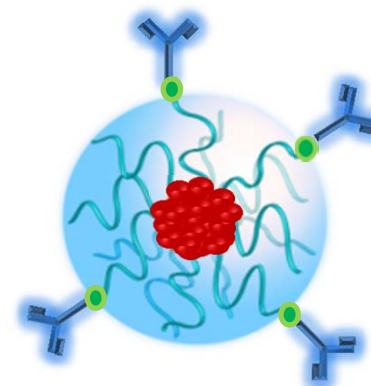


Advantages of ADCM

ADC



ADCM



Experimental results of ADCM

Study	ADC* vs. ADCM
Sustainable drug release in the plasma	ADC < ADCM
Drug distribution in the tumor **	ADC < ADCM
Anti-tumor activity**	ADC < ADCM
Mab internalization	Mab < ADCM

*ADC: Mab-Drug was originated by NanoCarrier

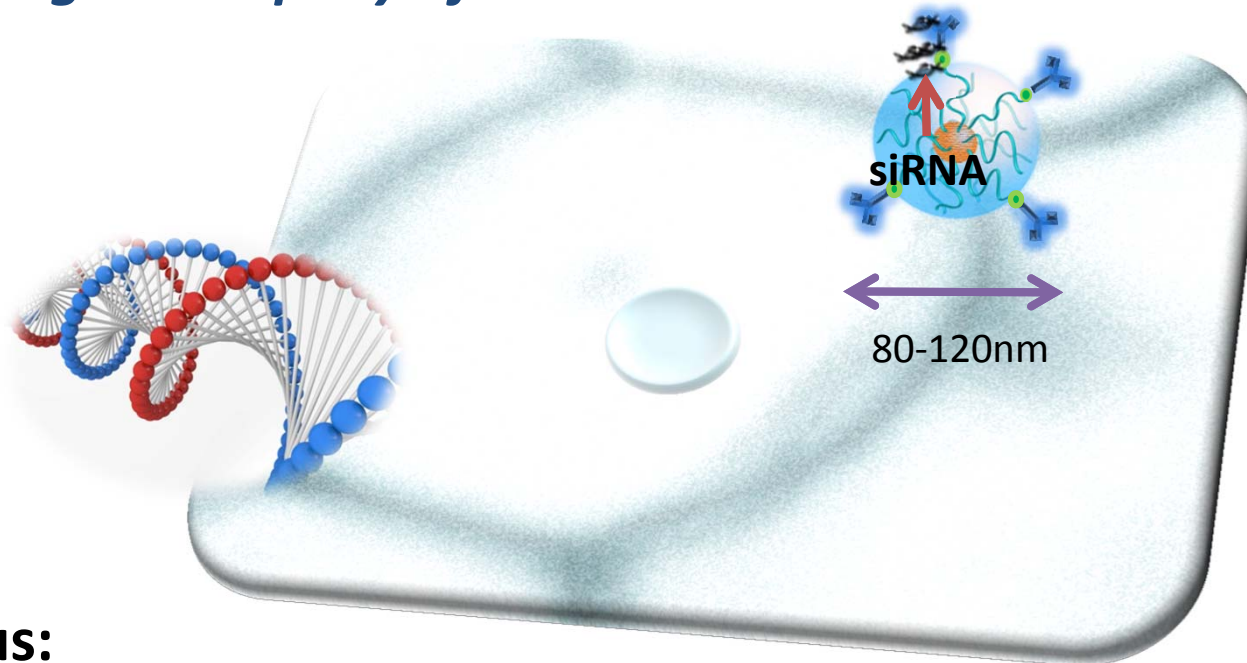
**Studies were performed in triple-negative human breast cancer xenograft models.





Active-Type NanoFect™ siRNA

For effective nucleic acid medicines such as siRNAs, well-designed delivery system must be mandate because they degrade rapidly after administered.



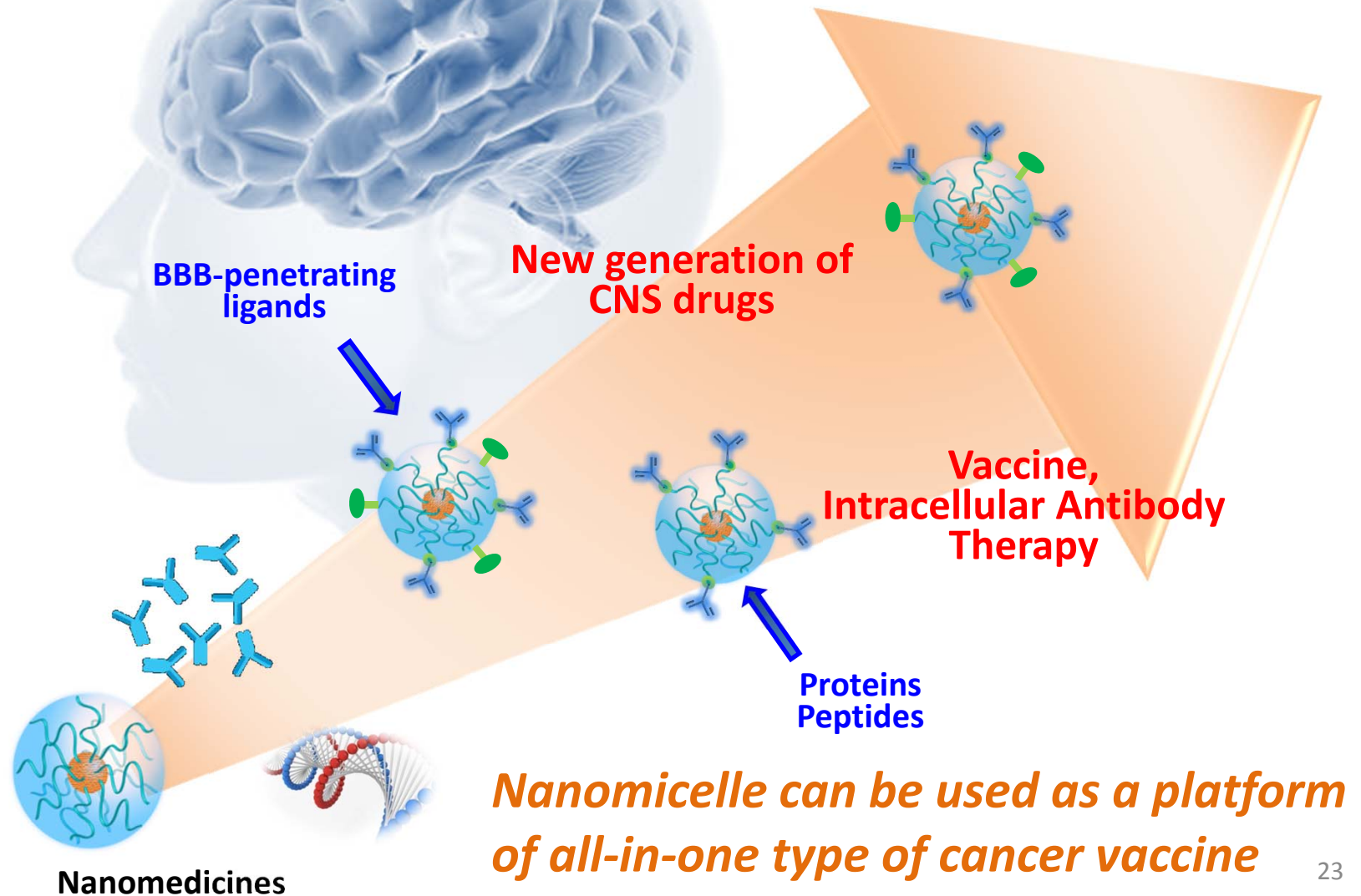
Current Status:

- **Joint Research Collaboration with Chugai**
Discovery of innovative pharmaceutical products by combination of active-type NanoFect™ technology of NanoCarrier and rich experiences of Chugai



Be Continued to Challenge

Glioblastoma multiforme: one of the most intractable human malignancy still remains





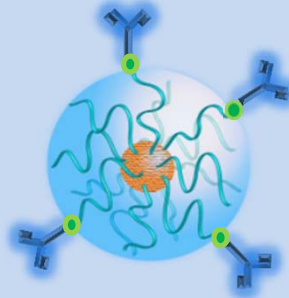
More Opportunities by NanoCarrier



- Approved drugs
- Compounds hold in clinical trials

- ADC products

- New drug targets



Enhances:

- Target specificity
- Safety
- Activity
- Solubility

Reprofiling



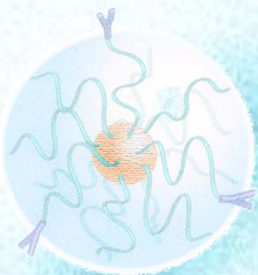
Simplifying and accelerating drug discovery

New drugs to meet high UMN





NanoCarrier Highlights



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Cosmetics Business

Growing reputation in health care industry

Micellar nanoparticle established a track record as cosmetic technology by co-development with luxury cosmetics maker.

2013
eclafutur:
Co-development with ALBION
Marketing by ALBION



2014
Overseas expansion
Increasing refill type



2010
e'clafutur-W Lotion:
Self-development/
marketing



2016
EXCIA AL:
Co-development with ALBION
Marketing by ALBION



SCALP CARE
Depth
TECHNOLOGIES

2016
Hair growth lotion
Co-development with ALBION
Marketing by NanoCarrier





FY 2017 Goal

1

Clinical PoC Establishment

NC-6004:

- Continuation of Phase III for panc. cancer in Japan/Asia
- Completion of Phase II for basket design in USA/EU

NC-6300:

- Accelerating Phase I/II in USA

2

Initiation of New Clinical Trial for the 1st ADCM pipeline

- Starting Phase I of NC-6201 in US

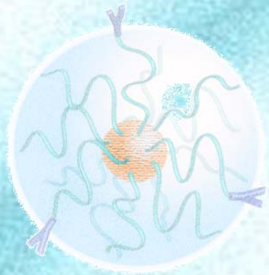
3

Promote Research Alliance, Licensing, and Investment



Thank you very much

We put on the market a new drug based on
a proprietary platform technology



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