Company Overview

Nanocarrier
LEADING-EDGE NANOTECHNOLOGY

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Japan

Tokyo Stock Exchange
4571
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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

- Keeps on evolving
- Robust oncology pipelines
- New research
- Other Opportunities
NanoCarrier Keeps on Evolving

- Antibody
- Nucleic acid
- Protein Peptide
- Small molecule
- ADCM
- Active NanoFect™ siRNA
- Skin Essence
- Nano medicine
- Nano cosmetics
- Vaccine, Intracellular antibody therapy
- New generation of CNS drug
- Hair growth tonic

BBB-penetrating ligand

Nano medicine

NanoFect™

Skin

NanoFect™

Hair growth tonic

NanoFect™

Skin

NanoFect™

Skin

NanoFect™

Skin
Enhanced solubility
Dissolve the hydrophobic drug in water

<table>
<thead>
<tr>
<th>Drug (mg/mL)</th>
<th>Itraconazole</th>
<th>Paclitaxel</th>
</tr>
</thead>
<tbody>
<tr>
<td>water</td>
<td>&lt;0.001</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Micelle</td>
<td>&gt;2</td>
<td>&gt;50</td>
</tr>
<tr>
<td>Solubility (Micelle/water)</td>
<td>2000 times or more</td>
<td>500 times or more</td>
</tr>
</tbody>
</table>

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 vs. Cancerous tissue

Drug (mg/mL)
- Itraconazole
- Paclitaxel

Solubility (Micelle/water)
- 2000 times or more
- 500 times or more

Enhanced solubility

Nanomicelle: Conventional drugs

NanoCarrier - All in One Delivery Technology
## Advantage of NanoCarrier - Competitive Technology

<table>
<thead>
<tr>
<th>NanoCarrier Type</th>
<th>Controlled release</th>
<th>Targeting</th>
<th>Bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin nanoparticle (Abraxane, etc.)</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>liposome (Doxil, ONIVYDE, Lipodox etc.)</td>
<td>Low</td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td>PEG-PLA (Genoxol-PM, etc.)</td>
<td>Medium</td>
<td>Low</td>
<td>Medium</td>
</tr>
<tr>
<td>Passive Micelle (NC-6004, NC-6300 etc.)</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Active PEG-PLA (BIND-014, etc.)</td>
<td>Medium</td>
<td>Very high</td>
<td>High</td>
</tr>
<tr>
<td>Active Micelle, ADCM (NC-6201, etc.)</td>
<td>High</td>
<td>Very high</td>
<td>Very high</td>
</tr>
</tbody>
</table>
Conventional Anti-cancer Drugs

- Spread to the whole body
- Accumulate at the cancerous tissue

**Disadvantages of conventional anti-cancer drugs:**
- Severe side effects
  - Pre/post medication and hospitalization are needed*
  - Difficulty to continue treatment

NanoCarrier Anti-cancer Drugs

- NC-6004 Micellar Nanoparticles Anticancer Drugs under development in-house

**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

**Merits by NannoCarrier Technology**

- Increase efficacy
- Reduced adverse reactions
- Improve usability and QoL
- Reduce treatment cost
NanoCarrier Highlights

- Keeps on evolving
- Robust oncology pipelines
- New research
- Other Opportunities

Japan Technology Micellar Nanoparticle Highlights Other Opportunities
# Current Status of Pipelines

<table>
<thead>
<tr>
<th>Product</th>
<th>Encapsulation drug</th>
<th>Cancer Indication</th>
<th>BR</th>
<th>PC</th>
<th>ph1</th>
<th>ph2</th>
<th>ph3</th>
<th>Develop Area</th>
<th>Alliance Partner</th>
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<tbody>
<tr>
<td>NC-6004</td>
<td>Cisplatin</td>
<td>Pancreatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Co-Development</td>
<td>Japan/Asia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lung (NSCL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House Development</td>
<td>USA/EU</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bladder</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House</td>
<td>USA/EU Asia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bile duct</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Co-Development</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Head and neck</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House</td>
<td></td>
</tr>
<tr>
<td>NC-4016</td>
<td>Dach-platinum</td>
<td>Solid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House</td>
<td>USA</td>
</tr>
<tr>
<td>NC-6300</td>
<td>Epirubicin</td>
<td>Solid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House</td>
<td>USA</td>
</tr>
<tr>
<td>NC-6201</td>
<td>E7974 (in-licensed)</td>
<td>Solid</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>In-House</td>
<td>USA (Planned)</td>
</tr>
<tr>
<td>Active NanoFect</td>
<td>siRNA</td>
<td>Solid</td>
<td>Co-Research</td>
<td>In-House</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NK105</td>
<td>Paclitaxel</td>
<td>Breast Gastric</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Out-Licensed</td>
<td>Japan</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solid</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
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.
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.
Safety: Renal Function

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

Figure 4. Change in CrCl Over Treatment Duration

Creatinine clearance

Worse

NCI CTCAE Grade 3 (severe)
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
More than 70 ADCs are under clinical developments (PI 46, PII 26, PIII 5) and markets (3) worldwide.

- 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

<table>
<thead>
<tr>
<th>ADC</th>
<th>ADCM</th>
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</table>
| **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  
($IC_{50}: 10^{-10}$-$10^{-11}$ 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 |
Experimental results of ADCM

<table>
<thead>
<tr>
<th>Study</th>
<th>ADC* vs. ADCM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustainable drug release in the plasma</td>
<td>ADC &lt; ADCM</td>
</tr>
<tr>
<td>Drug distribution in the tumor **</td>
<td>ADC &lt; ADCM</td>
</tr>
<tr>
<td>Anti-tumor activity**</td>
<td>ADC &lt; ADCM</td>
</tr>
<tr>
<td>Mab internalization</td>
<td>Mab &lt; ADCM</td>
</tr>
</tbody>
</table>

*ADC: Mab-Drug was originated by NanoCarrier

**Studies were performed in triple-negative human breast cancer xenograft models.
Preclinical studies of NC-6201 are on-going for IND in US.
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
Glioblastoma multiform: one of the most intractable human malignancy still remains

Nanomicelle can be used as a platform of all-in-one type of cancer vaccine
More Opportunities by NanoCarrier

- Approved drugs
- Compounds hold in clinical trials
- ADC products
- New drug targets

Enhances:
- Target specificity
- Safety
- Activity
- Solubility

Reprofiling

Innovative Drug
Increase QOL of patients

Simplifying and accelerating drug discovery

New drugs to meet high UMN

Increase QOL of patients
NanoCarrier Highlights

Keeps on evolving

Robust oncology pipelines

New research

Other Opportunities

Japan Technology Micellar Nanoparticle Highlights Other Opportunities
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

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

2014
Overseas expansion
Increasing refill type

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

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

Growing reputation in health care industry
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

NanoCarrier®

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