The goal of the joint research:

Challenge of a novel siRNA drug development against cancer
February 24, 2015

✔ **siRNA Joint Research Agreement with Chugai Pharmaceutical Co., Ltd.**
✔ **Third-party Allotment of Shares to Chugai**

**Summary of the Joint Research Agreement**

- Two companies will collaborate to create innovative, first-in-class cancer drug by combining antibodies and siRNA which Chugai designs with NanoCarrier’s active-type NanoFect™ technology by using such sensor delivering to the target cells.

- The agreement includes the option for Chugai to have a priority right in acquiring agreement for exclusive use of NanoCarrier’s patents if Chugai wishes to utilize NanoCarrier’s patents or deliverables of this partnership to create new drugs and businesses. In return for the option, NanoCarrier will receive a certain amount of payment from Chugai.

**Summary of the Third-party Allotment of Shares**

Chugai Pharmaceutical invests in shares of NanoCarrier for 500 million yen to further strengthen relationship between two companies and enhance the partnership.
Challenge for the anti-cancer siRNA drug

**challenge**

We aim for discovery of the unprecedented novel active-targeting siRNA drug against cancer

~ To establish the new market ~

Creating a first-in-class anti-cancer drug

Launched Nucleic Acid Medicines in the World

- Fomiviren (Vitravene®, ISIS Pharmaceuticals, antisense)
  CMV retinitis in patients with AIDS (withdrawn by commercial reason)
- Pegaptanib (Macugen®, Gilead Sciences, aptamer)
  Wet age related macular degeneration
- Mipomersen sodium (Kynamro®, ISIS Pharmaceuticals, antisense)
  patients with homozygous familial hypercholesterolemia (HoFH)
- Rintatolimod (Ampligen®, HemispheRx Biopharma, double stranded RNA)
  Chronic fatigue syndrome (Pre-registration)
Overview of joint research

Discovery of innovative pharmaceutical products by combination of active-type NanoFect™ technology of NanoCarrier and rich experiences of Chugai Pharmaceutical

**The main role of the two companies**

NanoCarrier: *active-type NanoFect™ technology to efficiently and selectively deliver nucleic acid medicines such as siRNA to cancer cells*

Chugai Pharmaceutical: *candidate of siRNA drug*

Cancer cell-specific sensor (Such as antibody drugs)

**Expected outcome**

Cancer cell-specific sensor

*First-in-class pharmaceutical product*

*The leading company of antibody drugs in Japan*

*Rich experiences in anticancer drug*
Micellar nanoparticles  next-generation DDS*

NanoCarrier's platform technology
for innovative pharmaceutical products

- Carrier technology for nucleic acid medicine by micellar nanoparticles
  NanoFect™
- Enhanced targeting performance by antibody as a sensor
  ADCM (Antibody/Drug-Conjugated Micelle)

The breakthrough carrier technology in nucleic acid medicine

active-type NanoFect™

Next-generation delivery system that combines the targeting performance and controlled release of drug

*DDS = Drug Delivery System
The mechanism of action of next-generation DDS

1. Stably encapsulate a large amount of drug
2. Active and selective delivery to the target cells by antibody
   - Example) Active-targeting micelles (green) encapsulating siRNA were attached to the surface of cancer cell
3. Internalize to the cell (Endocytosis)
   - Example) Micelles were subject to endocytosis (yellow) after 30 mins
4. Release active compounds
5. Exert anticancer effect
   - Example) siRNA (red) was successfully released to cytoplasm after 75 mins

We will vigorously promote joint research collaborations with companies that have candidates of antibody and/or drug (nucleic medicine and anti-cancer drug) and enrich the pipeline based on our next-generation DDS technology