October 11, 2016

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

We are pleased to announce that on October 10, 2016 local time at the European Society for Medical Oncology (ESMO) 2016 Congress held in Copenhagen (Denmark) from October 7 to 11, 2016, we presented a Phase Ib clinical study results of NC-6004 (cisplatin-encapsulated nanoparticle) conducted in the United States. NC-6004 is a leading pipeline product of NanoCarrier and self-development product by the company in the US and the EU.

We confirmed safety profile and efficacy of NC-6004 in the Phase Ib clinical study conducted in the United States. In terms of the adverse reactions such as neurotoxicity, auditory damage, and nephrotoxicity, which are known to be observed in cisplatin treatment, no clinically significant event of those was observed even when NC-6004 was administered at 1.5 times higher dose than the standard dose of conventional cisplatin. In addition, although the subjects for Phase I clinical study are usually patients who have received standard therapies but have not shown sufficient efficacy, NC-6004 was well tolerable and showed efficacy in patients who had previously received platinum-based chemotherapy including cisplatin.

The Phase II part of this study is currently ongoing as a basket design, expanding the target diseases by adding bladder cancer and biliary tract cancer to non-small cell lung cancer in the EU in addition to the US..

We are also conducting a Phase III clinical study of NC-6004 for pancreatic cancer in Japan and Asian countries, as well as Phase I clinical studies for head and neck cancer in Japan, the US, the EU and Taiwan. We will continue to make efforts to offer a cancer treatment that is expected to improve patients' quality of life, and make a contribution to society.

Please note that this will have no impact on the financial results for the fiscal year ending March 2017. NanoCarrier will move forward steadily with the in-house development of our products around the world to further activities for the practical application of micellar nanoparticle technology, and will accurately disclose the state of progress.

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Please refer to the presentation abstract on the next page for the details.

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October 7 ~ 11, 2016

ESMO2016

http://www.esmo.org/content/download/88721/1622334/file/ESMO-2016-abstracts

398P　October 10, 2016 13:00-14：00 Central Hall

Phase Ib/II trial of NC-6004 (nanoparticle cisplatin) plus gemcitabine (G) in pts with advanced solid tumors

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Background: NC-6004 is a polymeric micelle exhibiting sustained release of cisplatin (CDDP) and selective distribution to tumors, resulting in a lower plasma Cmax and higher AUC. Preclinical data exhibited less neuro- and nephrotoxicity with greater anti-tumor activity versus CDDP. A previous trial evaluated NC-6004 and G defining a RP2D of 90 mg/m2. Escalating doses of NC-6004/G were evaluated in this trial using a Bayesian NCRM.

Methods: Pts with refractory solid tumors were enrolled at 4 US sites. NC-6004 at 60 - 180 mg/m2 IV was given over 1 hr on day 1 with G at 1250 mg/m2 IV over 30 mins on day 1 and day 8 every 3 wks. Escalation of NC-6004 began with a single pt run-in, escalating by 15 mg/m2 until a DLT occurred at 180 mg/m2. Cohorts of 4 pts were then enrolled at each dose predicted by the NCRM model with real time updates. The MTD was defined as the dose with the greatest posterior probability of target toxicity < 25%.

Results: Among 22 pts (10M, 12 F) enrolled, common Grade 3/4 hematologic AEs were leukopenia (67%), thrombocytopenia (55%), neutropenia (55%), lymphopenia (45%) and anemia (23%). All AEs/DLTs were manageable and resolved. Results are presented below (19/22 evaluable for response). Activity was observed in heavily pretreated pts (mean = 2.5 prior lines of therapy): tumor shrinkage in 9/19 (47%), unconfirmed PRs in 3/19 (16%) in H&N and NSCLC pts (1 who failed prior anti-PD1) and SD in 12/19 (63%). The MTD was 135 mg/m2. Of the 8 pts treated at the MTD, the average number of cycles received was 7 (2-17) and none experienced neuro-, oto- or nephrotoxicity. 50% of pts received a prior platinum. Of these, SD was observed in 9 (82%).

Conclusions: The nanoparticle formulation allowed greater CDDP equivalent doses. No clinically significant neuro-, oto- or nephrotoxicity was observed. The NCRM design allowed exploration of the pharmacologic zone of interest and projected a higher MTD versus a 3 + 3. This data demonstrates promising activity and tolerability of NC-6004/G in heavily pretreated pts.