NEWS RELEASE

NIPPON SHINYAKU CO., LTD.

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Presentation of top line results of Phase I/II study of NS-065/NCNP-01 in Japan, for Duchenne muscular dystrophy

Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto City; President, Shigenobu Maekawa) announced today that top line results of a Phase I/II clinical trial of NS-065/NCNP-01[*1] in Japan were presented at the 2018 New Directions in Biology and Disease of Skeletal Muscle Conference held in New Orleans, LA.

Hirofumi Komaki, MD, PhD, Study Chair, and Director general of Translational Medical Center, National Center of Neurology and Psychiatry (NCNP) made a presentation at the 2018 New Directions in Biology and Disease of Skeletal Muscle Conference on June 27 (CST), reporting partial restoration of dystrophin in skeletal muscle by NS-065/ NCNP-01.

Duchenne muscular dystrophy (DMD) is a debilitating and progressive muscle disease, and is caused by the loss of the dystrophin protein in patient muscle. An approach to restore dystrophin expression in patient muscle is through exon skipping[*2], where nucleic acid drugs are delivered to change the RNA splicing patterns. About 8% of DMD patients have gene mutations that can be rescued by a drug targeting exon 53 for exon skipping.

Nippon Shinyaku is developing NS-065/NCNP-01[*1] in Japan as a new therapy for DMD for patients with dystrophin mutations that are amenable to exon 53 skipping.

A 24-week dose finding study of intravenous NS-065/NCNP-01 (Japic CTI-163291) was conducted in 16 boys, age 5-12 years, equally distributed between 2 dose cohorts, 40 and 80 mg/kg/week. Measurement of dystrophin protein in muscle was done either at week 12 (8 patients) or week 24 (8 patients). Drug-induced increases in dystrophin content of muscle were seen in 14 of 16 patients. Dystrophin expression in 8 patients who were measured at week 24, was on average 1.92% (0.41%-3.91%) of normal level in the 40mg/kg/week cohort (4 patients) and 5.21% (1.05%-8.08%) of normal level in the 80 mg/kg/week cohort (4

patients) respectively. Tendency of dose and dosing period dependency were seen in this study. All adverse events were mild or moderate in this study.

“It is noteworthy that dystrophin rescue in DMD patients was confirmed in this Phase I/II study. I expect that NS-065/NCNP-01 contributes the treatment for DMD patients in Japan which is not established yet, “ said Dr. Hirofumi Komaki, M.D., Study Chair, and Director general of Translational Medical Center, NCNP.

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NOTES:

*1 NS-065/NCNP-01, an exon skipping morpholino nucleic acid drug, is being developed to treat DMD patients with mutations of the dystrophin gene that are amenable to exon 53 skipping. NS-065/NCNP-01 was discovered through a collaborative research of National Center of Neurology and Psychiatry (Kodaira City, Tokyo; President, Hidehiro Mizusawa and Corporate Director, Shin’ichi Takeda)

*2Exon skipping has potential as a therapy for patients with DMD, based on the use of a synthetic oligonucleotide, known as an antisense oligonucleotide, to restore the amino acid reading frame by skipping certain exons of the transcription product (mRNA) to be translated into protein. This approach produces a dystrophin protein that is shorter than normal but still functional, to improve muscle function.