Introduction

✓ **NS Pharma, Inc.** (Sponsor) is a wholly-owned, US subsidiary of Nippon Shinyaku Co., Ltd. (Kyoto, Japan)
  - National Center of Neurology and Psychiatry (Tokyo, Japan) is a co-inventor of NS-065/NCNP-01

✓ **PharmaLex Development Services, LLC (PDS)** is a regulatory affairs and drug development consultancy.

✓ **CINRG Network** and **TRiNDS**
  - Dr. Paula Clemens is the Phase 2 Study Chair and CINRG Medical Director
  - TRiNDS, overseen by Lauren Morgenroth, is responsible for clinical trial project management with the CINRG clinical sites
Nippon Shinyaku and NS Pharma Offices

Head Office & Discovery Research Labs. in Kyoto

Tajima Shokuhin Kogyo Co., Ltd.

Sioe Pharmaceutical Co., Ltd.

Discovery Research Labs. in Tsukuba

Odagawa Central Factory <Japanese GMP, ISO 14001>

Offices

Subsidiaries

NS Pharma Inc.(US)

Beijing Office

London Office
Study Organization

Study Sponsor

NS Pharma, Inc.

Regulatory/Strategic Consulting
PHARMALEX

Clinical Project Management
TRiNDS

CINRG Clinical Study Sites
Clinical Study: NS-065/NCNP-01-201

Latest Updates

A Phase 2, Dose Finding Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of NS-065/NCNP-01 in Boys with Duchenne Muscular Dystrophy (DMD)
Clinical Sites

Planned or Possible Anticipated Sites

UC Davis
Sacramento
Soon

Washington Univ
St. Louis
Recruiting

Lurie Children’s Hospital Chicago
Recruiting

Children’s Hospital
Richmond
Soon

Duke Univ
Durham

Children’s Healthcare
Atlanta

Univ Florida
Gainesville
Soon

For updated information, please visit at ClinicalTrials.gov
Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto City; President, Shigenobu Maekawa) announced today that the first patient dosed in the phase 2 clinical trial of NS-065/NCNP-01 in patients with Duchenne muscular dystrophy (DMD) amenable to exon 53 skipping.

A phase 2 clinical study in the US and a phase 1/2 study in Japan began recruitment in December 2016 and July 2016, respectively. NS-065/NCNP-01 was registered as "SAKIGAKE designation(Japanese version of Breakthrough Therapy Designation) " of the Ministry of Health, Labour and Welfare in Japan in October 2015.

For more information:

Phase 2 design

- All patients will receive NS-065/NCNP-01 40 or 80mg/kg
- Muscle biopsy is conducted twice during the study
- 80mg/kg cohort will be initiated after safety of 40mg/kg is confirmed (at week 5)
Approximately 16 patients (4 - <10 years of age) with DMD amenable to exon 53 skipping
Summary of Inclusion Criteria

✓ Patient has a confirmed DMD mutation(s) in the dystrophin gene that is amenable to skipping of exon 53

✓ Patient is ≥ 4 years and <10 years of age

✓ Patient is able to walk independently without assistive devices

✓ Patient is able to complete strength and function tests

✓ Patient must be on a stable dose of glucocorticoid for at least 3 months prior to study entry
Summary of Exclusion Criteria

- Patient has evidence of symptomatic cardiomyopathy
- Patient has an allergy or hypersensitivity to the study medication
- Patient is taking any other investigational drug currently or within 3 months prior to the start of study treatment
- Patient has had surgery within the 3 months prior to the first anticipated administration of study medication
- Patient has positive test results for HB antigen, HCV antibody or HIV antibody
Study Assessments

- Muscle biopsy (Biceps) (at Screening and Week25)
- Strength and function test (at Screening, Wk13, Wk25)
- Blood draw 11 visits
- Urine collection 11 visits
- Vital signs Every visit (27 visits)
- Physical exam 11 visits
NS-065/NCNP-01

- Antisense oligonucleotide with a novel morpholino backbone and molecule size
- Originated in Nippon Shinyaku jointly with National Center of Neurology and Psychiatry (NCNP)
- Exon 53 skipping agent (Mechanism of Action)
- IV infusion, once weekly
Mechanism of Action

Dystrophin mRNA

Normal

DMD

DMD + NS-065

Exon 53 skipping

Partly functional protein
Target Exon of NS-065/NCNP-01

NS-065/NCNP-01 is targeted to skip Exon 53

<table>
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<th>Target Exon</th>
<th>Deleted Exon</th>
<th>Patient % out of DMD $^{1}$</th>
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</tr>
<tr>
<td>52</td>
<td>51, 53, 53-55</td>
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</tr>
</tbody>
</table>

Investigator-Initiated Phase 1 Study

Design: Open label, Escalating dose, Safety, Efficacy (dystrophin recovery) and PK

# of patients: 10 DMD boys

Dosing: Once weekly IV infusion for 12 weeks

Study site: National Center of Neurology and Psychiatry (1 site)

Cohort 1
- 1.25 mg/kg IV (n=3) for 12 weeks

Cohort 2
- 5.0 mg/kg IV (n=3) for 12 weeks

Cohort 3
- 20 mg/kg IV (n=4) for 12 weeks
An Investigator-Initiated Clinical Trial of NS-065/NCNP-01 for the Treatment of Duchenne Muscular Dystrophy Has Been Completed

Early analysis by NCNP detected dystrophin mRNA with the amino acid reading frame restored by exon 53 skipping in every dose group. Furthermore, the expression of dystrophin protein which appeared to have been translated from such a mRNA was detected in the high-dose group. On the basis of these results, NS-065/NCNP-01 is expected to have therapeutic efficacy in DMD.

In addition, no serious adverse events were observed throughout the study, and no subjects discontinued administration. Anemia and a slight effect on renal function have been reported as general adverse events.

For more information:

Review of several new FDA designations granted to the program

IMPORTANT FDA DEVELOPMENTS
FDA Grants **Fast Track Designation** to **NS-065/NCNP-01** for the Treatment of **Duchenne Muscular Dystrophy**

Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto City; President, Shigenobu Maekawa) announced today that the Food and Drug Administration (FDA) has granted Fast Track Designation to NS-065/NCNP-01 for the treatment of Duchenne Muscular Dystrophy (DMD). Fast Track is a process designed to expedite the review of drugs which will be highly effective to treat intractable diseases. NS-065/NCNP-01 is the first antisense oligonucleotide discovered in Japan to be granted Fast Track Designation from the FDA.

For more information:


http://www.nippon-shinyaku.co.jp/english/company_profile/offices.php
FDA Grants **Orphan Drug Designation** to NS-065/NCNP-01 for the Treatment of Duchenne Muscular Dystrophy

Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto City; President, Shigenobu Maekawa) announced today that the Food and Drug Administration (FDA) has granted Orphan Drug Designation to NS-065/NCNP-01 which is being developed for the treatment of Duchenne Muscular Dystrophy (DMD) in patients who are amenable to exon 53 skipping in the United States (US). The Orphan Drug Designation is issued to drugs which are intended for rare diseases that affect fewer than 200,000 people in the US, or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug.

For more information:

FDA Grants Rare Pediatric Disease Designation to NS-065/NCNP-01 for the Treatment of Duchenne Muscular Dystrophy

Nippon Shinyaku Co., Ltd. (Nippon Shinyaku; Headquarters, Kyoto City; President, Shigenobu Maekawa) announced today that the Food and Drug Administration (FDA) has granted Rare Pediatric Disease Designation to NS-065/NCNP-01 which is being developed for the treatment of Duchenne Muscular Dystrophy (DMD). The Rare Pediatric Disease is defined as a disease that affects fewer than 200,000 persons in the US, primarily aged from birth to 18 years. Under this designation, when an approval is granted for NS-065/NCNP-01, Nippon Shinyaku may be eligible to obtain priority review for a subsequent marketing application for a different product.

For more information:

Reimbursement for Travel

Participants in the study will receive reimbursement to support their travel for participation in the clinical trial. **Greenphire** is a company working on behalf of NS Pharma to support this reimbursement process.

- Fast, easy way to make payments
- Site visit payments by visit description
- Manual payments
- Travel Reimbursements
- Travel Arrangements
- Opt-in patient messaging strategy
Patient Advocate

For more information, please contact Lauren Morgenroth (trialinfo@nspharma.com) or visit at ClinicalTrials.gov (NCT02740972).