

# **Viltolarsen (NS-065/NCNP-01)**

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## **Exon 53 Skipping for DMD**

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**Vice President, Medical Affairs**

**NS Pharma, Inc.**

# Forward-Looking Statements

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# NS Pharma and Nippon Shinyaku

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## **NS Pharma, Inc.** (Paramus, NJ, USA)

- Wholly-owned, US subsidiary of Nippon Shinyaku Co., Ltd (Kyoto, Japan)
- Sponsor of the North American Phase 2 trials
- Focus area: Orphan Rare Disease

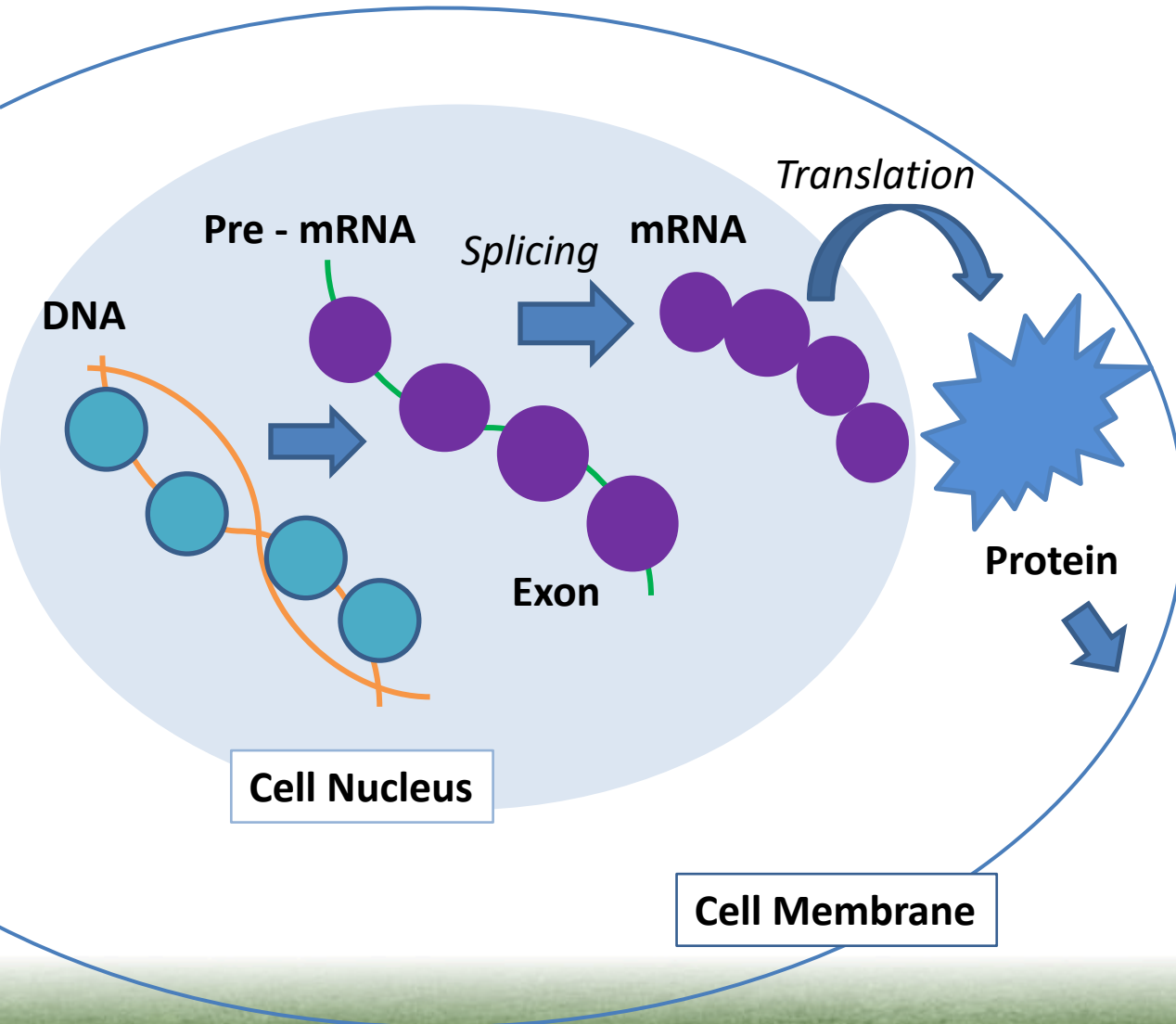


## **Nippon Shinyaku** (Kyoto, Japan)

- Parent company of NS Pharma, Inc.
- Founded in 1919
- Four focus areas are: drugs for rare diseases, urological diseases, hematology, and gynecology.



# Overview: How Protein is Made



**Step 1: Make the message**

**Step 2: Trim the message**

**Step 3: Make the protein**

**Step 4: Utilize the protein**

# Exon Skipping Strategy

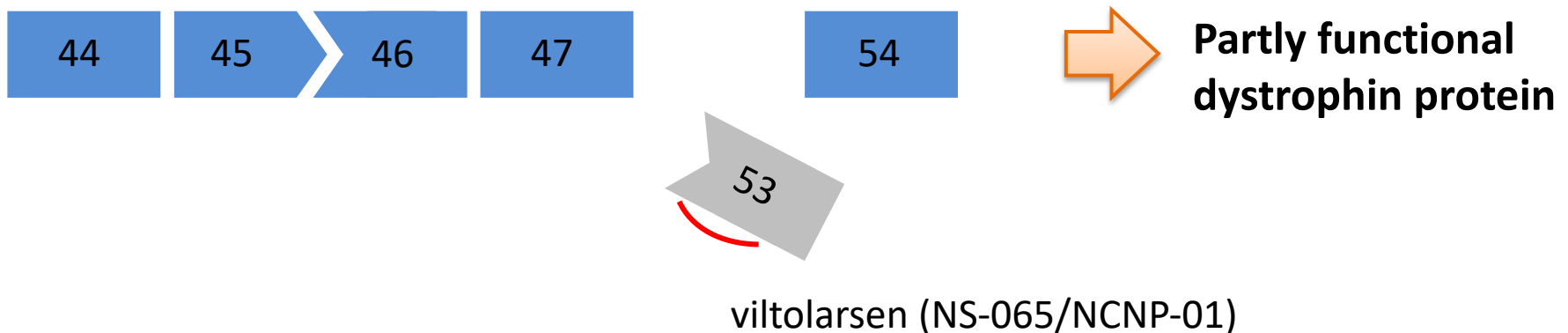
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Example of a deletion that disrupts the dystrophin mRNA reading frame that is restored to in-frame by exon 53 skipping

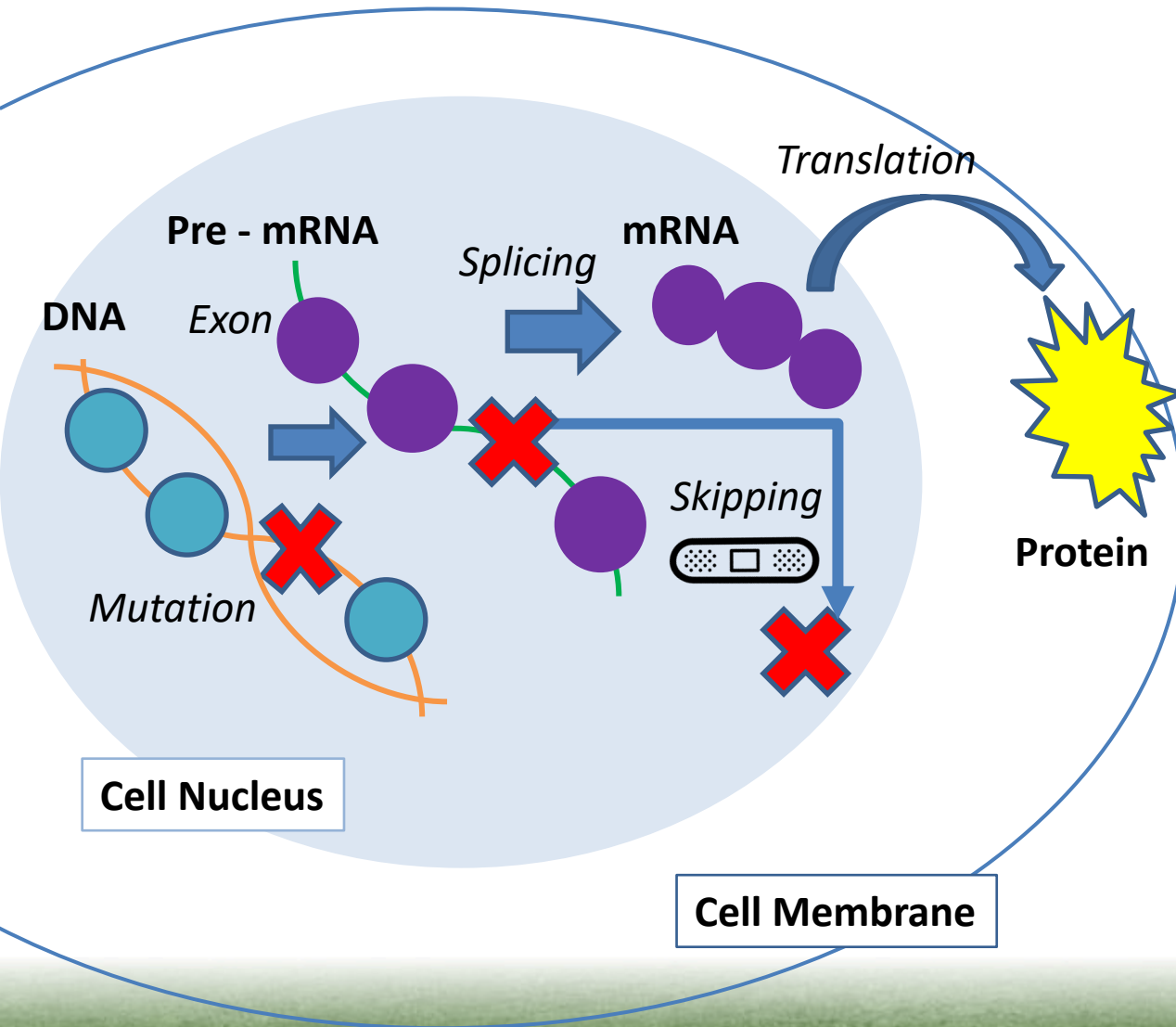
Exon 48-52 deletion: disrupts reading frame



Exon 53 skipping by viltolarsen (NS-065/NCNP-01): restores reading frame



# Exon Skipping Overview



**Step 1: Make the message**

**Step 2: Trim the message**

**Step 3: Make the protein**

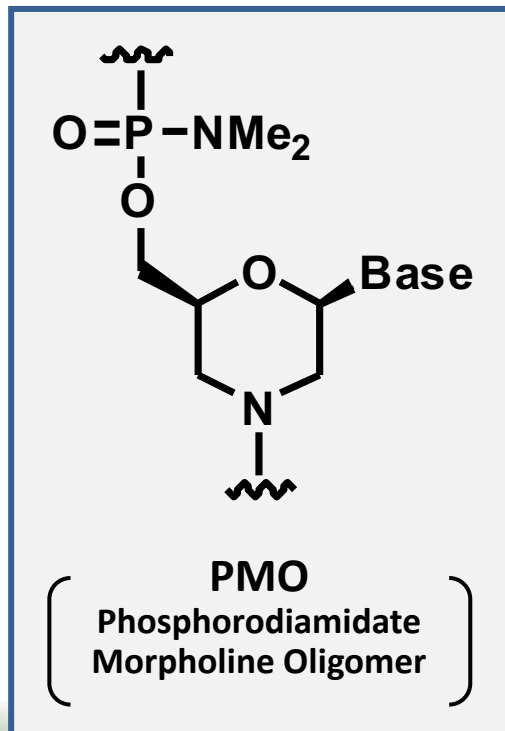
**Step 4: Utilize the protein**

# Viltolarsen (NS-065/NCNP-01)

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**Origin** Nippon Shinyaku jointly with National Center of Neurology and Psychiatry (NCNP)

**Mechanism** Exon 53 skipping



## Characteristics

- Antisense oligonucleotide with a morpholino backbone and a neutral charge
- Demonstrated exon 53 skipping activity
- Demonstrated dystrophin production across multiple models
- I.V. administration, once weekly

# Viltolarsen (NS-065/NCNP-01)

## Clinical Program

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NS Pharma, Inc.

**Phase II** Dose finding study (NORTH AMERICA)  
40, 80mg/kg for 24 weeks

**Phase II** Extension study (NORTH AMERICA)  
40, 80mg/kg, ongoing



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Nippon Shinyaku  
jointly with  
National Center of Neurology  
and Psychiatry (NCNP)

**Phase I** Investigator Initiated study (JAPAN)  
1.25, 5, 20 mg/kg for 12 weeks

**Phase I/II** Dose finding study (JAPAN)  
40, 80 mg/kg for 24 weeks





# Phase 3 study

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- Most phase 3 clinical trials have a larger number of patients and longer than phase 1 and 2 studies.
- We are planning to start Phase 3 study in 3Q/4Q, 2019. Details will be found in [www.clinicaltrials.gov](http://www.clinicaltrials.gov) in the future.

# Viltolarsen (NS-065/NCNP-01) Community Announcement



140 East Ridgewood Avenue, Suite 2805  
Paramus, NJ 07652, USA

## NS Pharma Community Letter

Dear Friends,

NS Pharma is pleased to announce that we have initiated submission of a rolling New Drug Application (NDA) seeking accelerated approval for viltolarsen (NS-065/NCNP-01), an investigational drug for the treatment of Duchenne Muscular Dystrophy (DMD) in patients amenable to exon 53 skipping. While this is the first step towards the US regulatory approval, we wanted to share our news with the DMD community.

As you may know, NS Pharma has completed a Phase 2 study in North America, and its parent company, Nippon Shinyaku Co., Ltd. (Headquarters, Kyoto, Japan; President, Shigenobu Maekawa) completed a Phase 1/2 study in Japan. The scientists, investigators, and families all made great efforts to collect data about the safety and efficacy of viltolarsen (NS-065/NCNP-01) in clinical trials. Viltolarsen (NS-065/NCNP-01) is not approved in any country for use outside clinical trials.

Working together to analyze the data, we have decided to move forward to seek regulatory approval. We have submitted the first portion of the data and reports to the US Food and Drug Administration (FDA) under rolling review pathway. Under that pathway, the sponsor is allowed to start submission with completed portions of the application for review by FDA rather than waiting until every portion is completed. NS Pharma plans to complete the NDA submission in September 2019.

Finally, we would like to take this moment to thank all the researchers, clinical trial staff, and families around the world who have made this step possible. We deeply appreciate everyone's hard work and dedication, and thank you for your continued support.

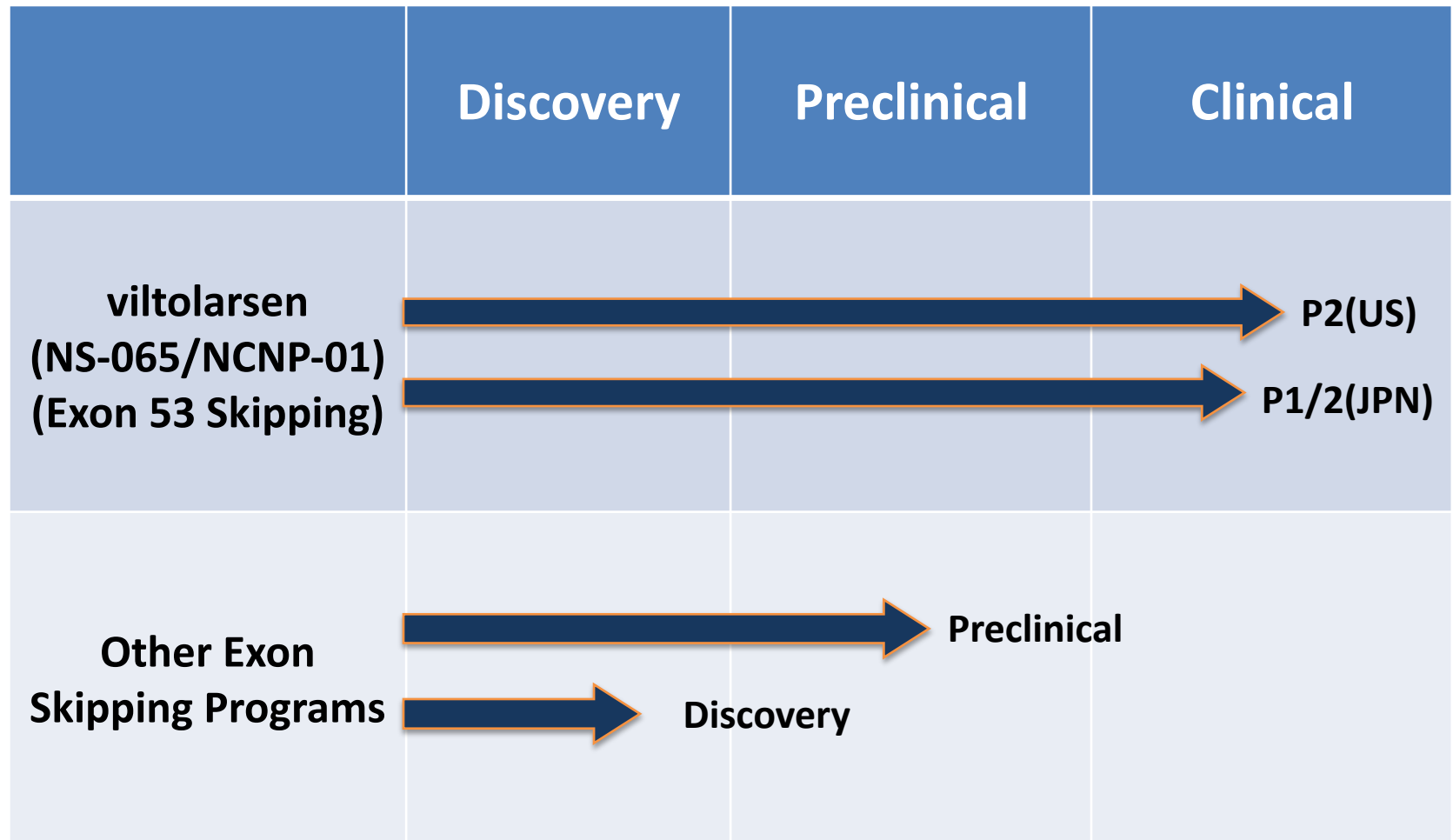
Thank you,  
Tsugio Tanaka  
President, NS Pharma, Inc.

For family or community questions: Email [dmdresearch@nspharma.com](mailto:dmdresearch@nspharma.com)

To learn more about viltolarsen (NS -065/NCNP-01): Please visit [www.nspharma.com](http://www.nspharma.com)

- Initiation of rolling NDA submission for viltolarsen was done by Nippon Shinyaku to the FDA.
- NS Pharma and Nippon Shinyaku plan to complete the NDA submission in September of 2019.
- It has been granted Rare Pediatric Disease Designation, Orphan Drug Designation, Fast Track Designation, and Accelerated Approval process.

# DMD Pipeline



# Acknowledgement

## North American Phase II study

### Site Investigators

- Vamshi Rao, Lurie Children's Hospital, Chicago, IL
- Anne Connolly, Washington University, St. Louis, MO
- Amy Harper, Children's Hospital of Richmond, Richmond, VA
- Jean Mah, Alberta Children's Hospital, Calgary, Alberta, Canada
- Edward Smith, Duke Children's Hospital, Durham, NC
- Craig McDonald, University of California, Davis, Sacramento, CA
- Barry Byrne, University of Florida, Gainesville, FL

### AGADA Biosciences

Eric Hoffman

### TRiNDS

Lauren Morgenroth

### PharmaLex

**Sponsor: NS Pharma, Inc.**

## Japan Phase I/II Study

### Site Investigators

- Yasuhiro Takeshima, Hyogo College of Medicine
- Tsuyoshi Matsumura, Toneyama National Hospital
- Shiro Ozasa, Kumamoto University Hospital
- Michinori Funato, Nagara Medical Center
- Hirofumi Komaki, National Center of Neurology and Psychiatry (NCNP)

### Medical Advisor

Shin'ichi Takeda, National Center of Neurology and Psychiatry (NCNP)

**Sponsor: Nippon Shinyaku Co., Ltd.**

**Thank you to all the patients and families who made these studies possible!**