

# **VILTEPSO® (viltolarsen) and NS Pharma Clinical Development Program**

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# Forward-Looking Statements

- This NS Pharma presentation may contain forward-looking statements, including statements regarding future results, unaudited and forward-looking financial information, company performance or achievements, and clinical trial data. These statements are subject to known and unknown risks and uncertainties which may cause our actual results, performance or achievements to be materially different from any future results or performances expressed or implied in this presentation. You should not place undue reliance on the forward-looking statements. NS Pharma cannot and does not guarantee future results, level of activity, FDA Approval, performance or achievements and there is no representation that the actual results achieved will be the same, in whole or in part, as those set out in the forward-looking statements and financial projections.
- Statements that are not historical facts or words such as "believes," "anticipates," "plans," "expects," "will," "intends," "potential," "possible," "goal," "strategy," "may," "should," "project," "estimate," and similar expressions are intended to identify forward-looking statements.
- NS Pharma, Inc. is a wholly owned subsidiary of Nippon Shinyaku Co., Ltd.
- Viltolarsen was co-invented by National Center of Neurology and Psychiatry and Nippon Shinyaku Co., Ltd.

# NS Pharma and Nippon Shinyaku

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

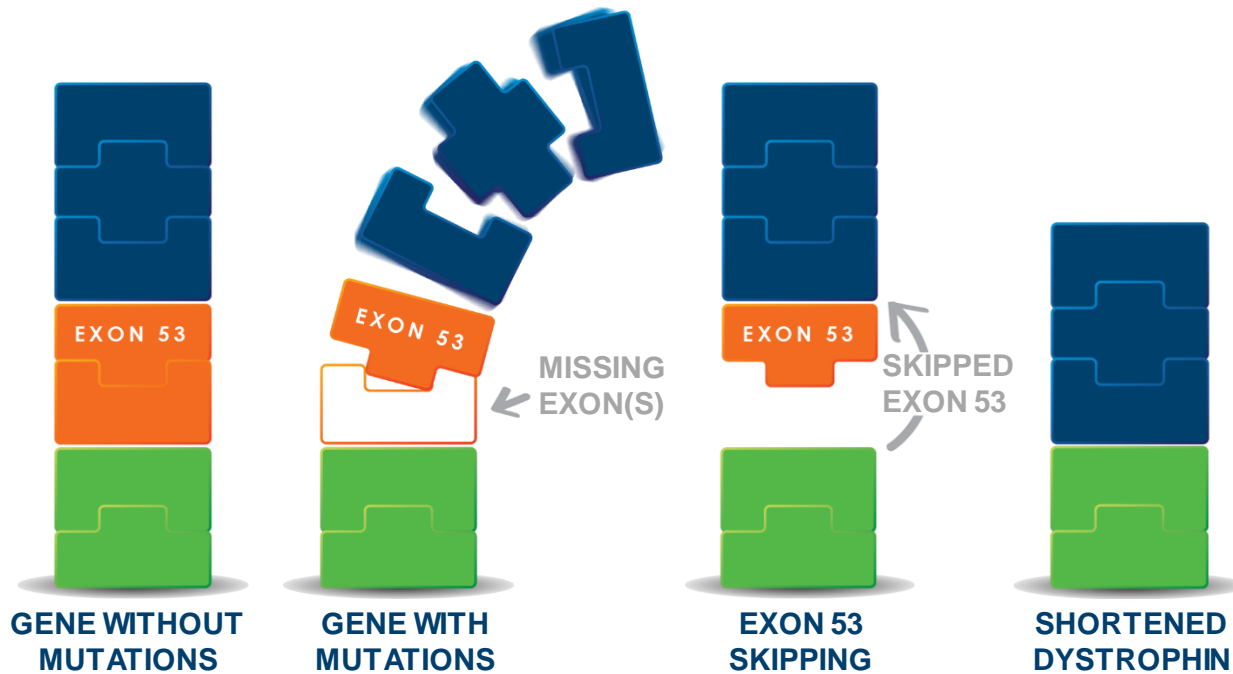
- Wholly-owned, US subsidiary of Nippon Shinyaku Co., Ltd
- Focus areas: rare diseases and hematological oncology
- Sponsor of the N American DMD phase 2 trial
- Sponsor of the global DMD phase 3 trial



## **Nippon Shinyaku Co., Ltd (Kyoto, Japan)**

- Parent company of NS Pharma, Inc.
- Founded in 1919
- Focus areas: drugs for rare diseases, hematological oncology, urology, and gynecology

# VILTEPSO® Is an Exon 53 Skipping, PMO Antisense Oligonucleotide, DMD Disease-Modifying Agent<sup>1,2</sup>



- Common amenable dystrophin gene mutations include exons:
  - 43–52
  - 45–52
  - 47–52
  - 48–52
  - 49–52
  - 50–52
  - 52
  - and others<sup>3</sup>

AON, antisense oligonucleotide; ex, exon; PMO, phosphorodiamidate morpholino oligonucleotide.

1. Watanabe N, et al. *Mol Ther Nucleic Acids*. 2018;13:442-449.

2. Nguyen Q, Yokota T. *Am J Transl Res*. 2019;11(3):1202-1218

3. Komaki H, et al. *Ann Clin Trans Neurol* 2020; 7(12): 2393–2408.

# Indication and Dosing

## Indication

- VILTEPSO<sup>®</sup> (viltolarsen) is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping.
  - This indication is approved under accelerated approval based on an increase in dystrophin production in skeletal muscle observed in patients treated with VILTEPSO. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

## Dosing

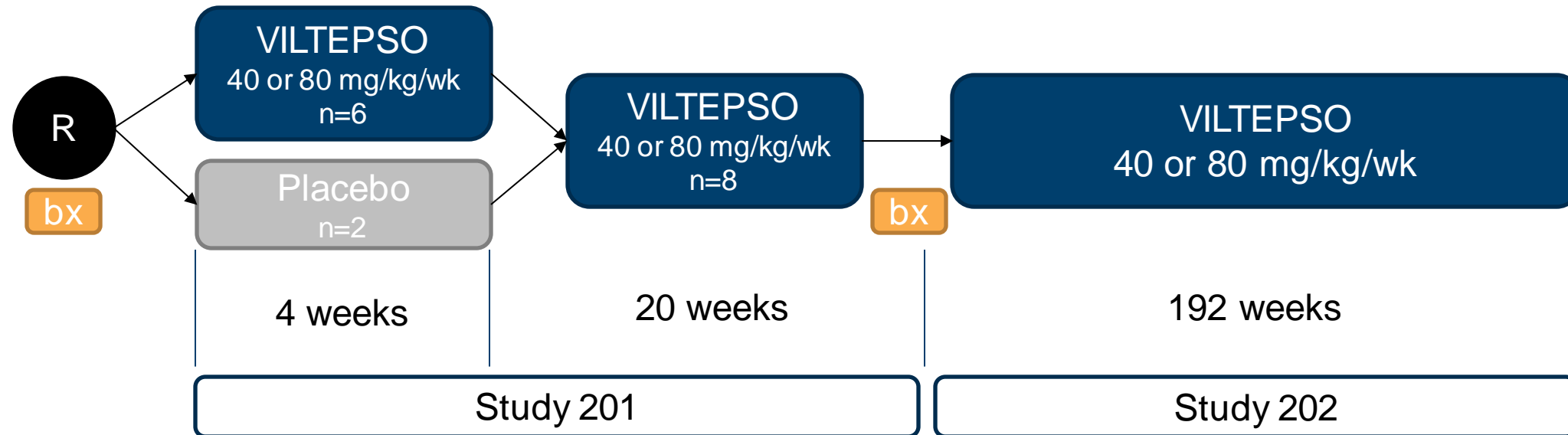
- The recommended dose is 80 mg per kg of body weight administered once weekly as a 60-minute intravenous infusion.
  - If a dose of VILTEPSO is missed, it should be administered as soon as possible after the scheduled dose time

For more information about VILTEPSO, please see Full Prescribing Information at <https://www.vilteps.com/prescribing-information>

# **VILTEPSO Phase 2 Clinical Trial for Boys with DMD Amenable to Exon 53 Skipping**

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# Multicenter, 2-Period Phase 2 and Open Label Extension Studies of VILTEPSO in Boys With DMD<sup>1,2</sup>



bx, biopsy

80 mg/kg/wk is the FDA approved dosing regimen for viltolarsen

- Boys, aged 4 to <10 years (N=16), with DMD were enrolled in a randomized, double-blind, placebo-controlled, 4-week safety period of once-weekly infusion of 40 or 80 mg/kg viltolarsen<sup>1</sup>
- Followed by a 20-week open-label study to assess the efficacy and safety of viltolarsen<sup>1</sup>
- After completion of the 24-week study, patients could enroll in up to a 192-week extension study (216 weeks total). Efficacy assessments were conducted every 12 weeks<sup>2</sup>

# Study Endpoints

## Primary Outcomes

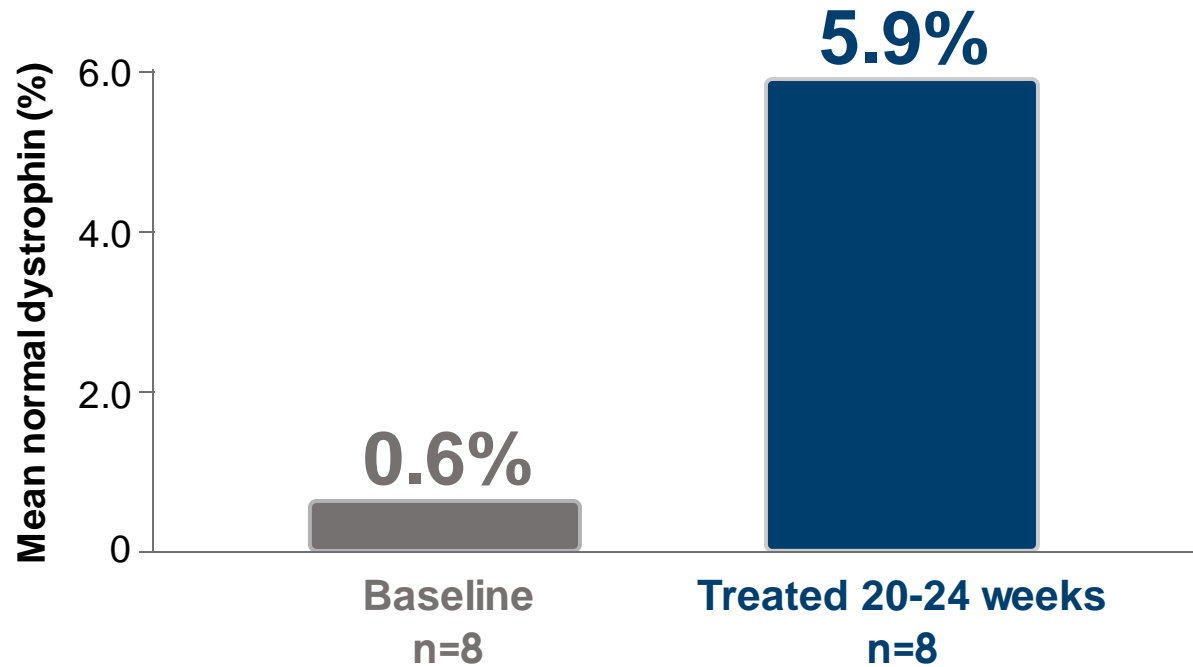
- Dystrophin induction as measured by validated Western blot
- Safety
- Tolerability
- Pharmacokinetics

## Secondary Outcomes

- Dystrophin mRNA splicing by RT-PCR
- Dystrophin localization by immunofluorescence staining
- Dystrophin protein production by mass spectrometry
- Clinical assessments: TTSTAND, TTRW, TTCLIMB, NSAA, 6MWT, QMT



# VILTEPSO<sup>®</sup> Treatment Induced Dystrophin Expression to Nearly 6% of Normal<sup>1</sup>



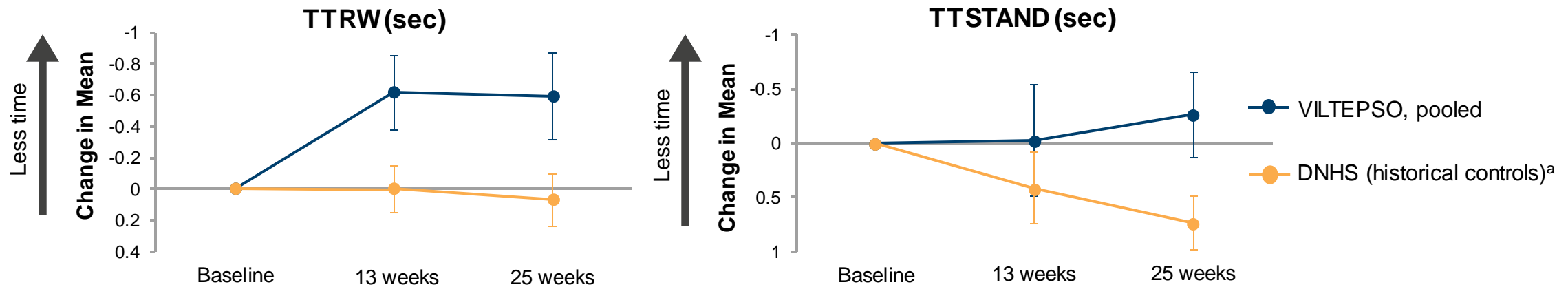
- Mean dystrophin levels increased from 0.6% (SD 0.8) of normal at baseline to 5.9% (SD 4.5) of normal by Week 25
- Mean change in dystrophin of 5.3% (SD 4.5) of normal levels ( $P=0.01$ )
  - Median change from baseline was 3.8%

- The change from baseline was statistically significant for viltolarsen ( $P=0.012$ ), as measured by Western blot
- All patients exhibited an increase in dystrophin levels from baseline

SD, standard deviation

1. Clemens PR, et al. *JAMA Neurology*. 2020;77(8):982-991.

# VILTEPSO<sup>®</sup> Motor Function Test Results at Week 25



- Additional parameters: TTSTAND (velocity), TTCLIMB, and NSAA displayed improvement or stabilization with viltolarsen treatment; differences compared to treatment-matched historical controls did not reach statistical significance.

Functional tests were secondary endpoints of study 201 and were compared to Duchenne natural history data as the control group rather than to placebo. Functional data are not in the USPI therefore definitive conclusions should not be drawn.

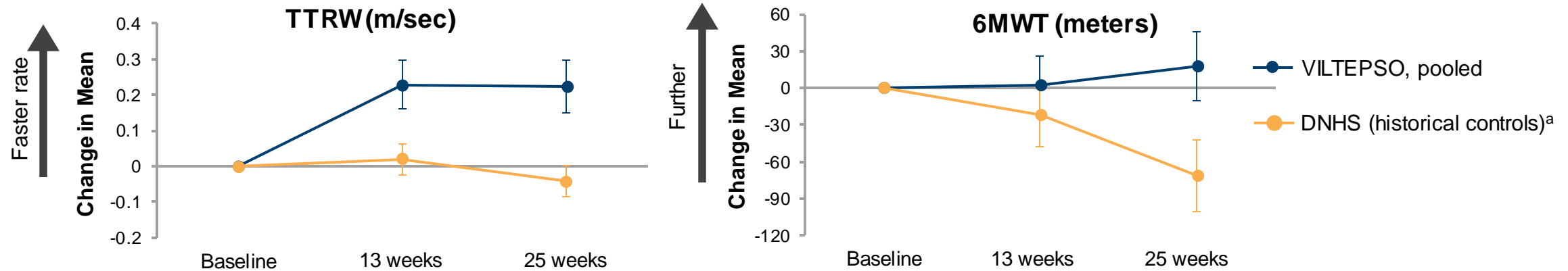
DNHS, Duchenne Natural History Controls.

<sup>a</sup>Observed sample size for DNHS was n=65, n=43, and n=46 for TTSTAND; n=65, n=44, and n=46 for TTRW at baseline, week 13, and week 25, respectively

Continued approval for VILTEPSO<sup>®</sup> may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Clemens PR, et al. *JAMA Neurol.* 2020;77(8):982–991.

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DNHS, Duchenne Natural History Controls.

<sup>a</sup>Observed sample size for DNHS was n=65, n=44, and n=46 for TTRW and n=18, n=14, and n=11 for 6MWT at baseline, week 13, and week 25, respectively

Continued approval for VILTEPSO<sup>®</sup> may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Clemens PR, et al. *JAMA Neurol.* 2020;77(8):982–991.

# Safety Profile of VILTEPSO

## Adverse Reactions Reported in ≥10% of DMD Patients Treated With VILTEPSO 80 mg/kg Once Weekly (Pooled Studies 1 and 2)<sup>1</sup>

Adverse Reaction	VILTEPSO 80 mg/kg Once Weekly (n=16)
Upper respiratory tract infection <sup>a</sup>	63%
Injection site reaction <sup>b</sup>	25%
Cough	19%
Pyrexia	19%
Contusion	13%
Arthralgia	13%
Diarrhea	13%
Vomiting	13%
Abdominal pain	13%
Ejection fraction decreased	13%
Urticaria	13%

No treatment-related SAEs, drug-related TEAEs, discontinuations, or deaths occurred<sup>2,3</sup>

<sup>a</sup>Upper respiratory tract infection includes the following terms: upper respiratory tract infection, nasopharyngitis, and rhinorrhea.

<sup>b</sup>Injection site reaction includes the following terms: injection site bruising, injection site erythema, injection site reaction, and injection site swelling.

AE, adverse event; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

1. Viltepsso [prescribing information]. Paramus, NJ: NS Pharma, Inc. 2021. 2. Clemens PR, et al. *JAMA Neurology*. 2020;77(8):982-991.

3. Komaki H, et al. *Ann Clin Transl Neurol*. 2020;7(12):2393-2408.

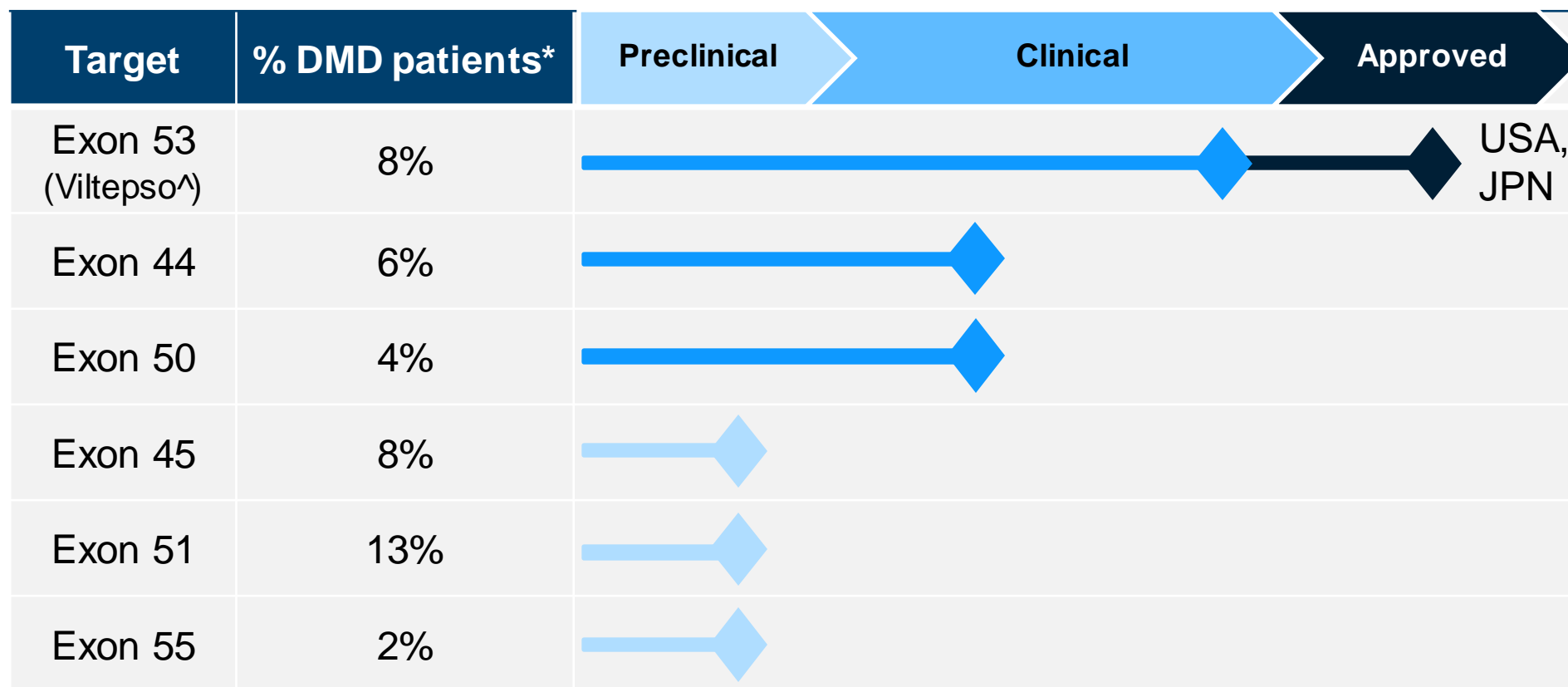
# Important Safety Information

- In clinical studies, no patients experienced kidney toxicity during treatment with VILTEPSO<sup>®</sup>. However, kidney toxicity from drugs like VILTEPSO<sup>®</sup> may be possible. Your doctor may monitor the health of your kidneys before starting and using treatment with VILTEPSO<sup>®</sup>.
- Common side effects include upper respiratory tract infection, injection site reaction, cough, and fever.

**For more information about VILTEPSO, please see Full Prescribing Information at <https://www.viltepsa.com/prescribing-information>**

VILTEPSO [package insert]. Paramus, NJ: NS Pharma, Inc.; 2021.

# NS Pharma Commitment to Duchenne Muscular Dystrophy Treatment



\*Percentage of DMD patient population who may be amenable to exon skipping

- NS-owned DMD pipeline can cover approximately 40% of all DMD patients
- CAP-1002: partnership with Capricor Therapeutics
  - Not mutation dependent and acts by a different mechanism from exon skipping agents
  - Phase 3 HOPE-3 trial in ambulant and non-ambulant patients

<sup>^</sup>Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

**Thank you to all the patients, their dedicated families, and healthcare professionals in the DMD community who make these studies possible!**

**For questions related to VILTEPSO<sup>®</sup>, please call us at:**

**866-NSPHARM (866-677-4276)**

**For questions on our patient support program, please call NS Support at:**

**833-NSSUPRT (833-677-8778)**