Viltepso®
(viltolarsen) injection

**For the treatment of DMD in patients amenable to exon 53 skipping**

# VILTEPSO increases dystrophin, a key protein for supporting muscle health[1]

## The first and only exon 53-skipping therapy to demonstrate an increase in dystrophin in children as young as 4 years[1]

- Patients taking VILTEPSO showed a mean increase in dystrophin expression from 0.6% at baseline to 5.9% of normal after 20 to 24 weeks of treatment[1]

## Indication

VILTEPSO is 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.

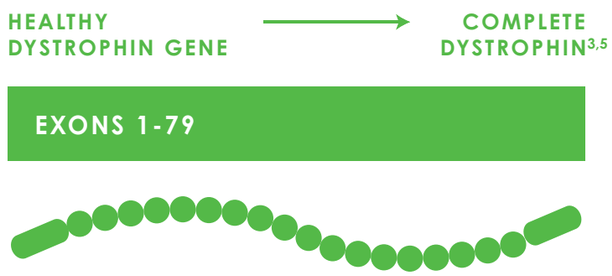
## Important Safety Information

**Warnings and Precautions:** In clinical studies, no patients experienced kidney toxicity during treatment with VILTEPSO. However, kidney toxicity from drugs like VILTEPSO may be possible. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting and during treatment with VILTEPSO. Consider measuring GFR before starting VILTEPSO.

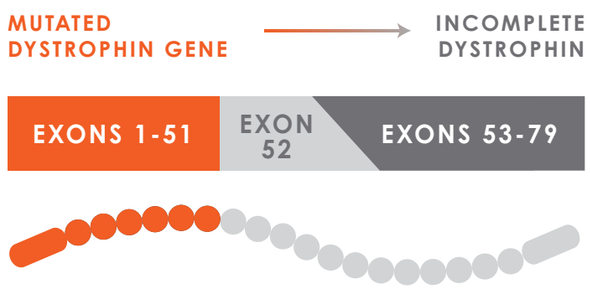
**Please see Important Safety Information throughout. For more information about VILTEPSO, see accompanying full Prescribing Information.**

# Lack of dystrophin (dystrophinopathy) causes a progressive loss of muscle strength and motor function[2,3]

Duchenne muscular dystrophy (DMD) is caused by mutations in the dystrophin gene, which leads to a lack of dystrophin production.[4]




Patients with DMD experience progressive muscle weakness, with symptom onset as early as 2 years.[6]




**EARLY DIAGNOSIS** is instrumental to inform the management of progressive muscle weakness and function decline in patients with DMD.[7,8]

## Important Safety Information

**Adverse Reactions:** The most common adverse reactions include upper respiratory tract infection, injection site reaction, cough, and pyrexia.



# VILTEPSO is the first and only exon 53-skipping therapy to demonstrate an increase in dystrophin in children as young as 4 years[1]

VILTEPSO is designed to bind to and induce **skipping of exon 53 of the dystrophin pre-mRNA,** resulting in the production of a shortened dystrophin protein that contains essential functional portions[1]

An estimated **10% of patients** with DMD would be amenable to exon 53 skipping[9]*

VILTEPSO was discovered through an **innovative triple-screening approach** designed to identify antisense oligonucleotides with the highest possible exon-skipping efficiency[10]

*Common dystrophin gene mutations eligible for exon 53 skipping include deletions in exons 45-52, 47-52, 48-52, 49-52, 50-52, and 52.[9]

mRNA=messenger RNA.

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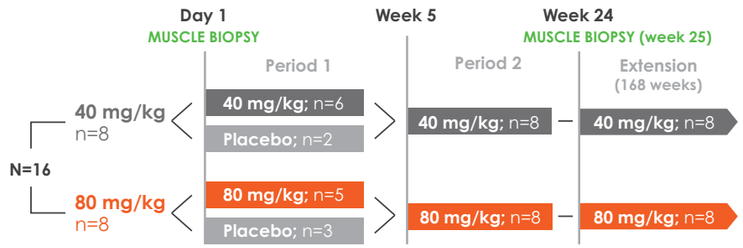
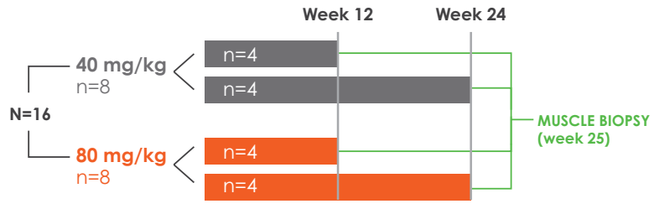
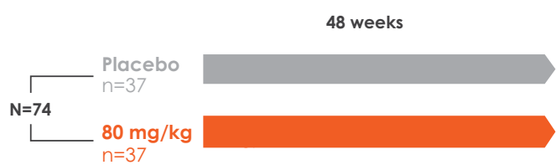
# The safety and efficacy of VILTEPSO have been studied in an ongoing clinical trial program[1,5,11,12]

| | | Study endpoints | Description |
|---|---|---|---|
| **Study 1** (Phase II) |  <br>80 MG/KG/WK IS THE APPROVED RECOMMENDED DOSE FOR VILTEPSO | **Primary:** Safety, tolerability, dystrophin protein production (Western blot)<br>**Secondary:** Other dystrophin measures (RT-PCR, MS, IFS), motor function tests (6MWT, TTCLIMB, TTRW, TTSTAND), NSAA, QMT | A 2-period, North American dose-finding study with ambulant males aged 4 to <10 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping who were receiving a stable dose of corticosteroids for ≥3 months (N=16)[1,5,11]<br>**24 weeks, followed by a 168-week extension study** |
| **Study 2** (Phase I/II) |  <br>80 MG/KG/WK IS THE APPROVED RECOMMENDED DOSE FOR VILTEPSO | **Primary:** Dystrophin measures (Western blot, IFS, RT-PCR)<br>**Secondary:** Safety, pharmacokinetics, motor function tests (6MWT, TTRW, TTSTAND, Timed Up & Go test), muscle strength, serum CK levels | A multicenter, parallel-group, open-label, dose-finding study conducted in Japan in ambulant and nonambulant* males aged 5 to <18 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping (N=16)[1,5]<br>**24 weeks** |
| **RACER53** (Phase III) (recruiting) |  | **Primary:** TTSTAND<br>**Secondary:** TTRW, TTCLIMB, 6MWT, NSAA, muscle strength | A global, multicenter, randomized, double-blind, placebo-controlled study in ambulant males aged 4 to <8 years with a confirmed mutation of the DMD gene amenable to exon 53 skipping who were receiving a stable dose of corticosteroids for ≥3 months (N=74)[12]<br>**48 weeks** |

As part of the accelerated approval of VILTEPSO, NS Pharma is conducting a **CONFIRMATORY STUDY**, begun in October 2019, to further evaluate the functional benefit of treatment.

*Defined as patients with a 6MWT distance of <75 meters.

CK=creatine kinase; IFS=immunofluorescence staining; MS=mass spectrometry; NSAA=North Star Ambulatory Assessment; QMT=Quantitative Muscle Testing; RT-PCR=reverse transcriptase-polymerase chain reaction; 6MWT=6-Minute Walk Test; TTCLIMB=Time to Climb 4 Stairs; TTRW=Time to Run/Walk 10 Meters; TTSTAND=Time to Stand from Supine.

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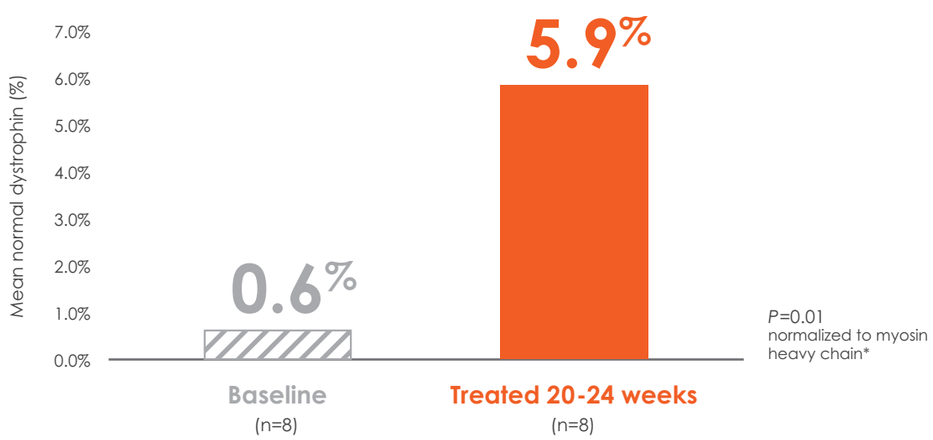
# VILTEPSO provided significant improvements in dystrophin expression[9]

In Study 1 the efficacy of 20-24 weeks of VILTEPSO was evaluated in ambulant males aged 4 to <10 years.[9]

## Study 1: Mean increase in dystrophin expression to nearly 6% of normal with VILTEPSO (80 mg/kg/wk) vs 0.6% at baseline[1,9]




*P-value for change from baseline at week 25 was statistically significant.[9]

**DYSTROPHIN WHERE IT MATTERS:** Immunofluorescence staining showed VILTEPSO-induced increases in dystrophin levels were correctly localized to the muscle cell membrane.[5,9]

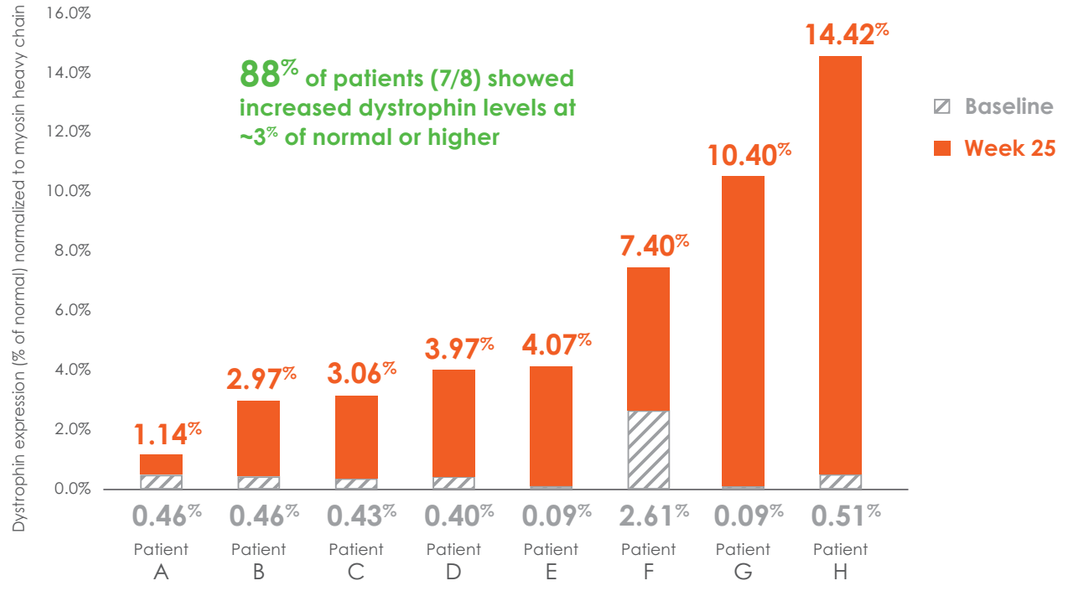
## Important Safety Information

**Adverse Reactions:** The most common adverse reactions include upper respiratory tract infection, injection site reaction, cough, and pyrexia.



# 100% of patients showed an increase in dystrophin levels with VILTEPSO[1]

## Study 1: Dystrophin levels at 25 weeks vs baseline[5]




Exon 53 skipping was observed, on average, in **43.9%** of dystrophin mRNA molecules in patients treated with VILTEPSO (80 mg/kg/wk), as measured by RT-PCR[5]

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# Safety profile evaluated in two 24-week clinical studies[1,5]

**Adverse reactions reported in ≥10% of DMD patients treated with VILTEPSO 80 mg/kg once weekly (pooled Studies 1 and 2)[1,5]**

| Adverse reaction | VILTEPSO (80 mg/kg once weekly) (N=16); n (%) |
|---|---|
| Upper respiratory tract infection* | 10 (63%) |
| Injection site reaction† | 4 (25%) |
| Cough | 3 (19%) |
| Pyrexia | 3 (19%) |
| Contusion | 2 (13%) |
| Arthralgia | 2 (13%) |
| Diarrhea | 2 (13%) |
| Vomiting | 2 (13%) |
| Abdominal pain | 2 (13%) |
| Ejection fraction decreased | 2 (13%) |
| Urticaria | 2 (13%) |

*Upper respiratory tract infection includes the following terms: upper respiratory tract infection, nasopharyngitis, sinusitis, and rhinorrhea.

†Injection site reaction includes the following terms: injection site bruising, injection site erythema, injection site reaction, and injection site swelling.



# VILTEPSO offers a choice of treatment location—at home or at a treatment center

VILTEPSO is given as an 80-mg/kg weekly **intravenous infusion**[1]

The **appropriate dose** of VILTEPSO is calculated based upon patient weight, at a recommended weekly dose of 80 mg/kg[1]

VILTEPSO is infused for **60 minutes** by a healthcare professional at home or at a treatment center[1]

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# Comprehensive care coordination and support from NS Pharma

At NS Support we are dedicated to being a committed partner to the families coping with DMD. We stand ready to provide optimal access support and resources—every step of the way—for patients, their caregivers, and healthcare professionals.

## FOR HEALTHCARE PROFESSIONALS

NS Support will:

- Acknowledge receipt of the completed Patient Start Form within 2 hours
- Verify insurance benefits
- Provide support for prior authorizations, exceptions, and appeals process
- Support streamlined product acquisition options

## FOR PATIENTS

NS Support will:

- Provide a personal case manager who will offer individualized care and support throughout the process
  - Explain insurance benefits and out-of-pocket cost support options
  - Discuss alternative and supplemental sources of financial assistance
  - Provide information about national and local advocacy organizations offering support for patients with DMD

**CONNECT WITH NS SUPPORT** **833-NSSUPRT (833-677-8778)**

Monday–Friday, 8 AM–8 PM ET



# Indication and Important Safety Information

## Indication

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**For more information about VILTEPSO, see accompanying full Prescribing Information.**

**References: 1.** Viltepso [prescribing information]. Paramus, NJ: NS Pharma, Inc.; 2020. **2.** Hoffman EP, Brown RH Jr, Kunkel LM. Dystrophin: the protein product of the Duchenne muscular dystrophy locus. *Cell*. 1987;51(6):919-928. doi:10.1016/0092-8674(87)90579-4 **3.** Niks EH, Aartsma-Rus A. Exon skipping: a first in class strategy for Duchenne muscular dystrophy. *Expert Opin Biol Ther.* 2017;17(2):225-236. doi:10.1080/14712598.2017.1271872 **4.** Birnkrant DJ, Bushby K, Bann CM, et al; for the DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17(3):251-267. doi.org/10.1016/S1474-4422(18)30024-3 **5.** Data on file, NS Pharma, Inc. **6.** Blake DJ, Weir A, Newey SE, Davies KE. Function and genetics of dystrophin and dystrophin-related proteins in muscle. *Physiol Rev*. 2002;82(2):291-329. doi:10.1152/physrev.00028.2001 **7.** US Food and Drug Administration. Duchenne muscular dystrophy and related dystrophinopathies: developing drugs for treatment guidance for industry. Accessed May 27, 2020. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/duchenne-muscular-dystrophy-and-related-dystrophinopathies-developing-drugs-treatment-guidance **8.** Institute for Clinical and Economic Review. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: effectiveness and value. Accessed May 27, 2020. https://icer-review.org/wp-content/uploads/2018/12/ICER_DMD_Draft_Scope_011119-1.pdf **9.** Clemens PR, Rao VK, Connolly AM, et al; for the CINRG DNHS Investigators. Safety, tolerability, and efficacy of viltolarsen in boys with Duchenne muscular dystrophy amenable to exon 53 skipping: a phase 2 randomized clinical trial [published online ahead of print May 26, 2020]. *JAMA Neurology*. doi:10.1001/jamaneurol.2020.1264 **10.** Watanabe N, Nagata T, Satou Y, et al. NS-065/NCNP-01: an antisense oligonucleotide for potential treatment of exon 53 skipping in Duchenne muscular dystrophy. *Mol Ther Nucleic Acids*. 2018;13:442-449. doi:10.1016/j.omtn.2018.09.017 **11.** US National Library of Medicine. Extension study of NS-065/NCNP-01 in boys with Duchenne muscular dystrophy (DMD). ClinicalTrials.gov Identifier: NCT03167255 **12.** US National Library of Medicine. Study to assess the efficacy and safety of viltolarsen in ambulant boys with DMD (RACER53). ClinicalTrials.gov Identifier: NCT04060199

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For the treatment of DMD in patients amenable to exon 53 skipping

# VILTEPSO provided a mean increase in dystrophin to nearly 6% of normal[1]

**100%** of patients who received VILTEPSO showed an **increase in dystrophin** levels from baseline[1]

**Safety profile** evaluated in two 24-week clinical studies[1,5]

IV infusion can be administered by a healthcare professional **at home or at a treatment center**

**Sign up for updates at VILTEPSO.com to learn more about the potential benefits of treatment**

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