

Study Eligibility Criteria

Key Inclusion Criteria:^{6,#}



Non-congenital DM1
(≥ 50 CTG repeats in 1 allele on molecular testing)



Part A: 18 to 50 years of age
Part B: 10 to 50 years of age



Walk independently for at least 10 meters at screening



Part A only: Pacemakers and/or cardioverter-defibrillator (ICD)

Key Exclusion Criteria:^{6,#}



Neutralizing antibodies against AAV.SAN011 capsid



Left ventricular ejection fraction (LVEF) <50%



Percent predicted FVC <50%



Contraindications to corticosteroids



Active malignancies or active infections; Liver, renal or biliary disease

#A full list of inclusion and exclusion criteria are available on www.clinicaltrials.gov (NCT06844214).

References

1. Pascual-Gilbert M, et al. *Drug Discov Today*. 2021;26(7):1765-1772.
2. Pettersson OJ, et al. *Nucleic Acids Res*. 2015;43(4):2433-41.
3. Johnson NE, et al. *Neurology*. 2021;96(7):e1045-e1053.
4. Visconti VV, et al. *Int J Mol Sci*. 2021;22(22):12594.
5. Nakamori M, et al. *Ann Neurol*. 2013;74(6): 862-72.
6. NCT06844214. Available at [Study Details | A Study to Investigate the Safety, Tolerability, and Efficacy of SAR446268, an Adeno-associated Viral Vector-mediated Gene Therapy in Participants Aged 10 to 50 Years of Age With Non-congenital Myotonic Dystrophy Type 1](#) | [ClinicalTrials.gov](#). Accessed on 4 August, 2025.

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MAT-US-2511218 v1.0 - P | Expiration date: 09/25/2027

BrAAVe

Phase 1/Phase 2
clinical trial in DM1

Introduction

- Myotonic Dystrophy Type 1 (DM1) is a progressive genetic disease with a wide range of muscle and systemic manifestations characterized by life-threatening muscle weakness and myotonia, impaired respiratory function and cardiac conduction abnormalities¹⁻³
- DM1 is an autosomal-dominant disorder caused by a cytosine-thymine-guanine (CTG) repeat expansion (>50) in the 3' untranslated region (UTR) of the dystrophin myotonia protein kinase (DMPK) gene.
- The CTG repeats leads to abnormal DMPK messenger ribonucleic acid (mRNA) hairpin structures that form insoluble ribonuclear foci, sequestering RNA-binding proteins causing mis-splicing of many genes involved in various critical functions leading to multisystemic organ dysfunction¹⁻⁵

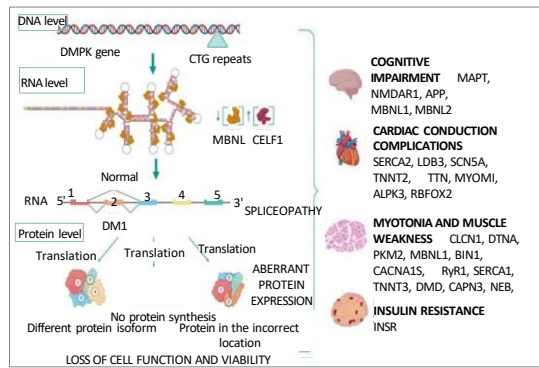
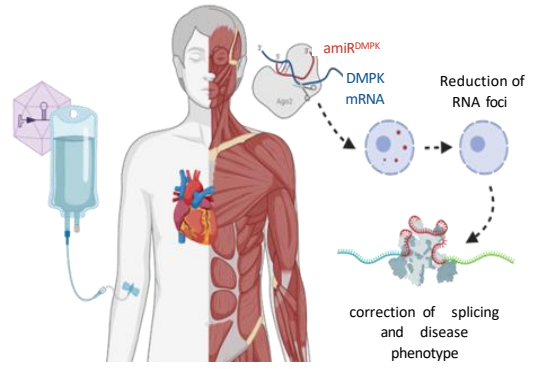


Figure from López-Martínez A, et al. Genes (Basel). 2020;11(9):1109 (no modification), CCBY license (<http://creativecommons.org/licenses/by/4.0/>)

Therapeutic Strategy of SAR446268

- SAR446268 is an investigational muscle-directed gene transfer therapeutic modality with a non-replicating AAV-based vector (AAV.SAN011) carrying a muscle-tropic promoter that delivers an engineered miRNA to downregulate DMPK mRNA
- It is administered as a single intravenous infusion being investigated to determine if it will reduce DMPK mRNA levels and restore splicing levels towards wild type levels.



ClinicalTrials.gov ID: NCT06844214

BrAAVe is an ongoing multicentre, Phase 1/2, single arm study aimed at determining the safety, tolerability, and efficacy of SAR446268 in downregulating DMPK mRNA levels in 32 participants (aged 10 to 50 years) with non-congenital DM1

Study Design

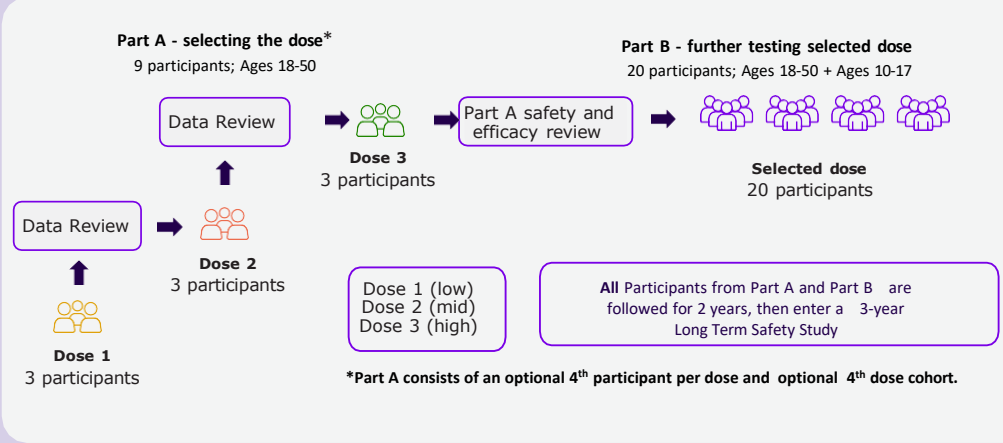
This Phase I/Phase 2 study will be conducted in two parts⁶

Part A (Dose escalation)

- Single ascending doses of SAR446268 evaluated in 3 distinct cohorts*

Part B (Dose expansion)

- Selected dose will be administered to 20 participants



Study Endpoints⁶

Primary endpoints

Part A and B

- Incidence of treatment-emergent adverse events (TEAEs) at Week 52

Part B

- Proportion of participants with ≥40% DMPK mRNA knockdown in muscle biopsy at Weeks 12 and 52

Secondary endpoints

Part A

- Proportion of participants with ≥40% DMPK mRNA knockdown in muscle biopsy at Weeks 12 and 52

Part A and B

- Change in 10-meter walk-run test, myotonia, and bilateral hand grip test from baseline to Weeks 26
- Change in DMPK mRNA levels and RNA splicing index in muscle biopsy from baseline to Weeks 12 and 52
- Assessment of the duration of AAV vector shedding of SAR446268 in sampling of urine, saliva, and semen at baseline, Weeks 4, 8, and 12