Positive motor and cardiac function improvements of DMD Base editor, GEN6050X, in early phase I study

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Introduction

Duchenne muscular dystrophy (DMD) is a devastating disease caused by the mutation of DMD gene. Gene editing drug may convert DMD to milder BMD through restoring dystrophin, providing a promising option against DMD. GEN6050X is a one-dose, intravenously administered, dual AAV9-delivered base editor drug targeting DMD patients amenable for exon 50 skipping. GEN6050X received FDA IND approval in Mar 2025. Currently, there is no effective drug for this DMD population.

An investigator-initiated trial (IIT, NCT06392724) has been conducted in Peking Union Medical College Hospital since August 2024. This study is to evaluate the safety and preliminary efficacy of GEN6050X. Three patients have been enrolled for this study. All patients received a single IV dose of 5×10^{13} vg/kg. As of Sept 2025, the first patient has completed 12 months of follow-up, the second patient has completed 6 months, and the third patient has received treatment and is at 3 months of follow-up.

Safety

Table 1. Baseline Demographics of Patients

Characteristic	Patient1	Patient2	Patient3	Mean(SD)
Age, y	10	6.5	7.8	8.1（1.8）
Height, cm	123	112	118	117.7（5.5）
Weight, kg	26.5	20.0	27.35	24.6（4.0）
BMI	17.2	15.9	19.6	17.6（1.9）
DMD mutation	Del E51	Del E51-55	Del E51	NA
Prednisolone, mg	22.5	15	20	NA

Findings: GEN6050X was well tolerated, with only transient and manageable serious adverse events; and no liver toxicity or suspected unexpected serious adverse reaction occurred. **All events resolved within the planned two-week inpatient period**, and no clinically significant symptoms or laboratory abnormalities were observed during follow-up.

Table 2. Safety Overview of GEN6050X

Overview of AEs	D1-D180 （N=3）
Total number of AEs, n	34
Total number of TEAES, n	34
Total number of treatment –related TEAEs, n	28
Patients with any TEAEs ,No.%	3(100)
Patients with any SAEs ,No.%	1(33)
Patients with any TR-TEAEs ,No.%	3(100)
Patients with any TR-SAEs, No.%	1(33)
AEs leading to study discontinuation, No.%	0 (0)
Deaths, No.%	0 (0)

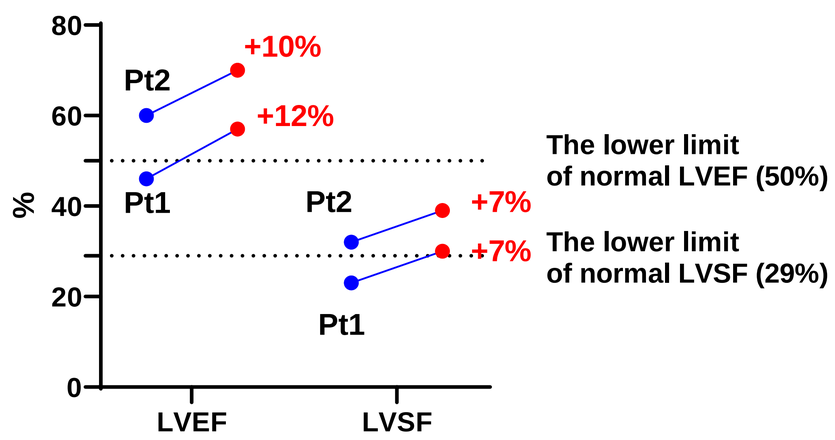
Number of patients with TR-TEAEs, listed by frequency, n (%)		
	D1-2wks	>2wks-52wks
Vomiting	3(100)	0(0)
Thrombocytopenia	3(100)	0(0)
Anorexia	3(100)	0(0)
Decreased appetite	3(100)	0(0)
Proteinuria	3(100)	0(0)
Nausea	2(66.6)	0(0)
Hypoxia	2(66.6)	0(0)
Troponin-I increase	1(33)	0(0)
Gamma-glutamyl transferase increase	0(0)	0(0)

Preliminary Clinical Efficacy

Table 3 Change from baseline to 24 weeks in functional outcomes

Test Item	Patient1		Patient2		Mean (SD) of Change
	Baseline	24W	Baseline	24W	
NSAA	30	31	25	28	2 (1)
PUL2.0	39	42	41	42	2 (1)
Time to stand from supine(s)	2.90	3.36	4.05	4.75	0.58 (0.12)
Time to run/walk 10 m (s)	3.98	3.95	4.74	4.21	-0.28 (0.26)
Time to climb 4 stairs (s)	1.47	1.46	2.26	2.83	0.28 (0.29)
6-Minute walk test (m)	400	509	385.5	377.5	50.5 (58.5)

Fig 1. Cardiac assessment change from baseline to 24 weeks



Muscle Biopsy Outcomes and Pharmacokinetics

Fig 2. Dystrophin restoration at 24 weeks

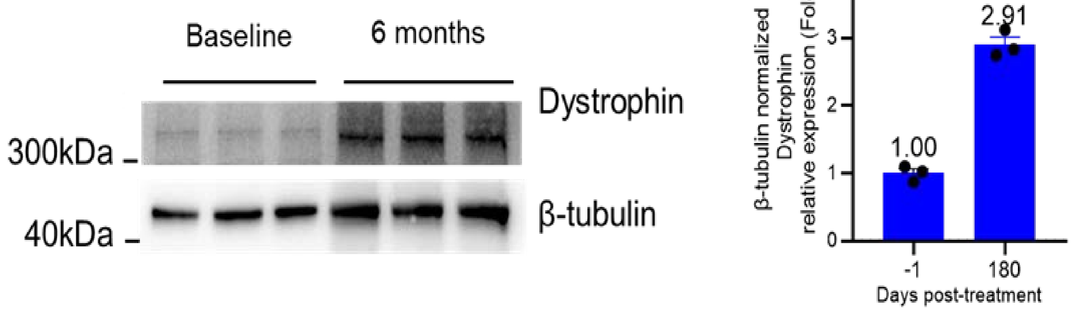
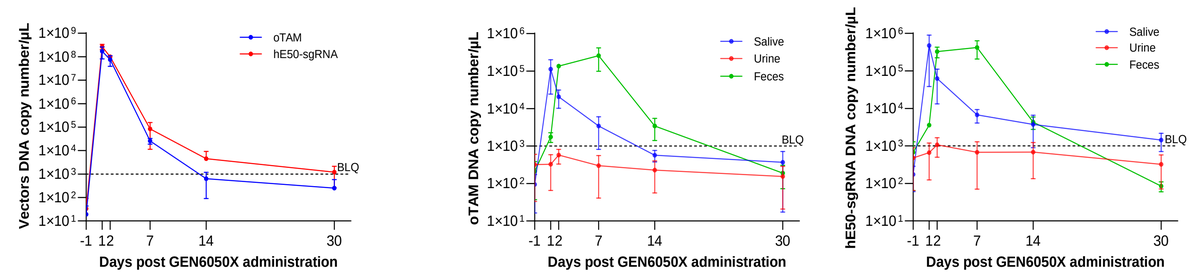


Fig 3. GEN6050X serum PK and shedding



Conclusion and limitations

1. These interim Data from the IIT study indicate that GEN6050X is well tolerated and shows early clinical benefits in DMD patients.
2. The MOA has been proved by effective editing and dystrophin protein restoration. These data reinforce GEN6050X's potential as a transformative base editing therapy for DMD.