*Single-dose AAV9-*CLN6 *gene transfer stabilizes motor and language function in variant late infantile neuronal ceroid lipofuscinosis 6 (vLINCL6) disease: interim results from the first clinical gene therapy trial*

Emily de los Reyes,[1] Kathrin Meyer,[2] Lenora Lehwald,[1] Charles Albright,[1] David L. Rogers,[1] Jeff Castelli,[3] Hai Jiang,[3] Allen Reha,[3] Jay A. Barth[3]

[1]Nationwide Children's Hospital, Columbus, OH, USA, [2]Nationwide Children's Hospital and Department of Pediatrics, Ohio State University, Columbus, OH, USA; [3]Amicus Therapeutics, Inc., Cranbury, NJ, USA

Disclosures

- Dr. Emily de los Reyes received grants and consulting fees from Amicus and Biomarin
- This study was funded by Amicus Therapeutics, Inc.
- This presentation shares information about an investigational drug, which has not yet been approved by the FDA

Background and Objectives

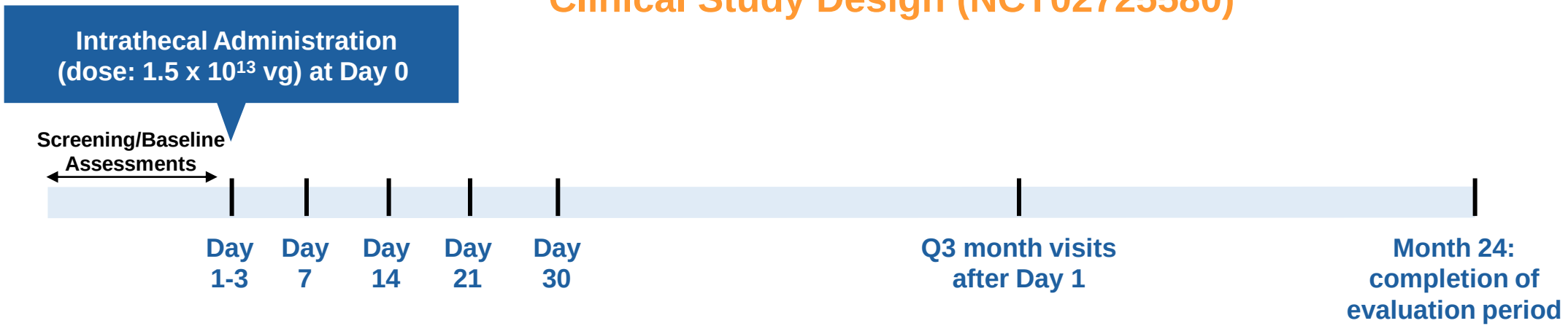
- Variant late infantile neuronal ceroid lipofuscinosis 6 (vLINCL6), or CLN6 Batten disease, is a fatal neurodegenerative disorder for which there is no treatment[1,2]
- Affected children experience language delay, motor regression, intractable epilepsy, and vision loss, leading to early death in childhood[1,2]
- The objectives of the study are to evaluate safety and efficacy of a single intrathecal injection of AT-GTX-501, a non-replicating, recombinant, self-complementary AAV9 vector containing the human *CLN6* gene, into the lumbar spinal cord for the treatment of CLN6 Batten disease

AAV9=adeno-associated virus serotype 9.

1. Schultz A et al. *Biochem Biophys Acta.* 2013;1832(11):1801-1806. 2. Mink J et al. *J Child Neurol*. 2013;28(9):1101-1105.

Methods

Clinical Study Design (NCT02725580)



Hamburg Motor & Language (HML) Scale

Score	Motor Function	Language Function
3	Normal	Normal (individual best performance)
2	Frequent falls, obvious clumsiness	Recognizably abnormal
1	No unaided walking or crawling only	Hardly understandable
0	Immobile, mostly bedridden	Unintelligible or no language

Q3=every 3; vg=viral genomes.

Wyrwich KW et al. *J Inborn Error Metab Screening*. 2018;6:1-7.

Results – Primary Efficacy Analysis

Rate of Decline in the HML Aggregate Score

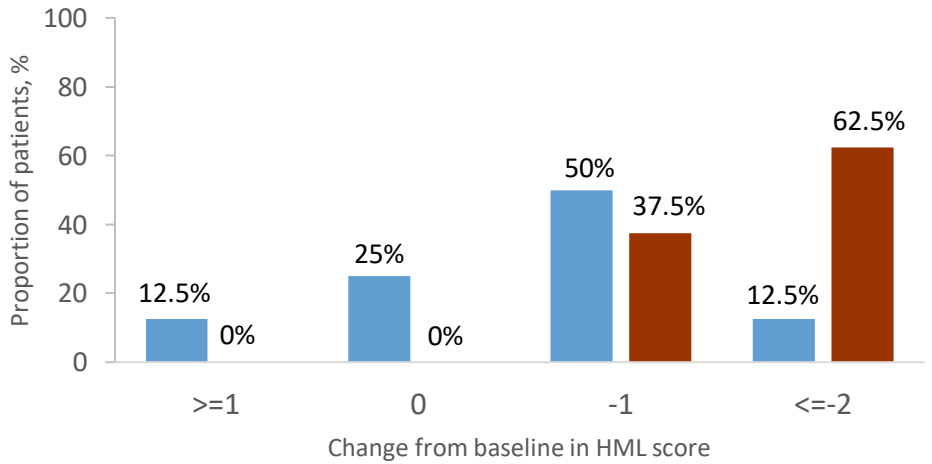
Parameter	Statistics	12 months		24 months	
		AT-GTX-501-treated Subjects n=12[a]	Natural History Subjects n=16[b]	AT-GTX-501-treated Subjects n=8[c]	Natural History Subjects n=16[b]
Rate of decline*	Mean ± SD	0.4 ± 0.82	1.2 ± 0.40	0.6 ± 0.91	2.4 ± 0.79
	Range	-1.3, 2.0	0.8, 2.0	−1.0, 2.0	1.5, 4.0
Difference between groups	Mean ± SE	-0.8 (0.26)	–	−1.8 (0.36)	–
	95% CI of Mean	(-1.4, -0.3)	–	(−2.6, −1.1)	–
	p-value	<0.01	–	<0.0001	–

*Positive number indicates decline; negative number indicates improvement.

CI=confidence interval; SD=standard deviation; SE=standard error.
[a]The efficacy analysis included all patients with 12-month HML data (12 of 13 treated patients in the study). [b]12- and 24-month HML data are available for 16 of 17 patients in the natural history cohort derived from a retrospective CLN6 natural history study conducted by Emily de los Reyes, MD (ClinicalTrials.gov Identifier: NCT03285425). [c]The efficacy analysis included all patients with 24-month HML data (8 of 13 treated patients in the study).
Data cutoff March 13, 2020.

Results – Secondary Efficacy Analyses

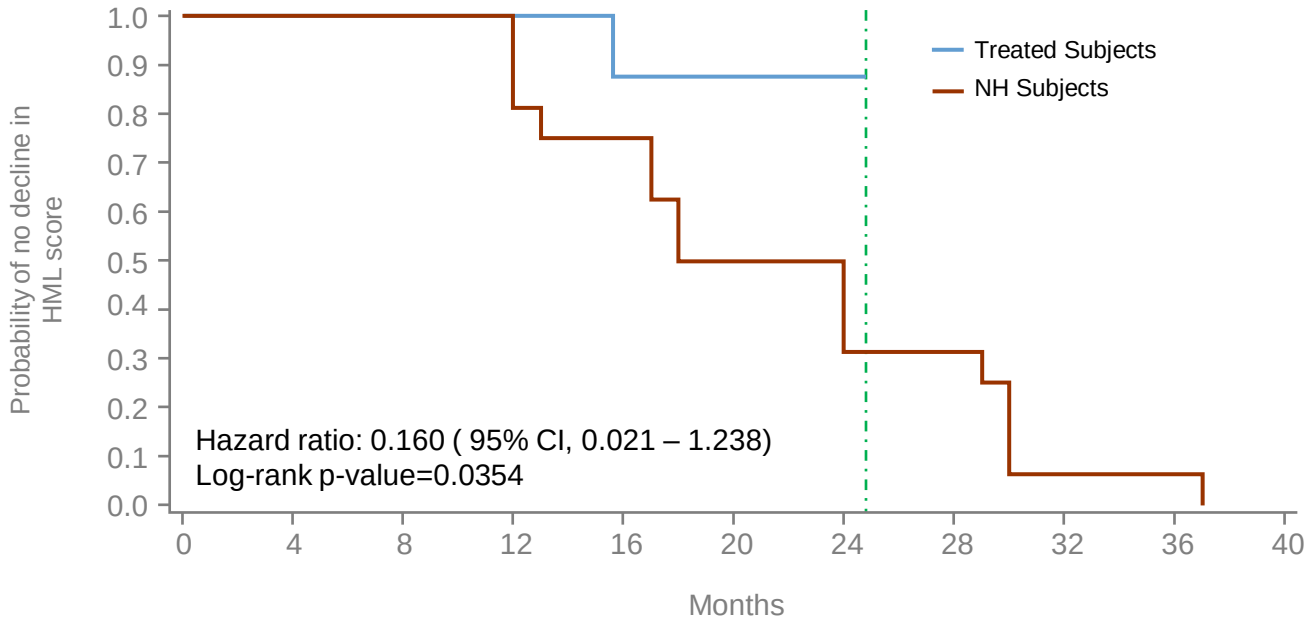
Proportion of Patients with a Change in the HML Aggregate Score at Month 24[a,b]



Treated Subjects Natural History Subjects

Difference in risk of unreversed 2-point decline:
−50% (95% CI, −77.5%, −3.6%)
Exact p-value=0.0335

Time to Unreversed 2-point Decline in the HML Aggregate Score



Treated Subjects	8					7				7	
NH Subjects	16			13	12		10	8		5	4	1		0

M+L, motor and language. NH, natural history.
[a]The efficacy analysis included all patients with 24-month HML data (8 of 13 treated patients in the study). [b]24-month HML data are available for 16 of 17 patients in the natural history cohort derived from a retrospective CLN6 natural history study conducted by Emily de los Reyes, MD (ClinicalTrials.gov Identifier: NCT03285425).
Data cutoff March 13, 2020.

Conclusions

- Interim safety data (n=13) show that AT-GTX-501 was generally well tolerated
  - 11 Grade 3 (severe) serious adverse events reported in 5 patients and 4 were considered possibly related to treatment: vomiting (2), fever (1); upper abdominal pain (1); patients recovered in all 4 cases
  - No pattern of adverse events related to AAV9 or *CLN6* immunogenicity
- Interim efficacy data on AT-GTX-501 appear to demonstrate a statistically significant and meaningful treatment effect in slowing disease progression of vLINCL6 at 24 months
  - Mean rate of decline was 0.4 vs 1.2 points over 12 months in treated subjects (n=12) vs subjects from the natural history cohort (n=16) (p-value<0.01)
  - Mean rate of decline was 0.6 vs 2.4 points over 24 months in treated subjects (n=8) vs subjects from the natural history cohort (n=16) (p-value<0.0001)