
Dual-vector rAAVrh8 gene therapy for GM2 gangliosidosis: a phase 1/2 trial

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Supplemental Table 1

Total Adverse Events by Dose Cohort				
	Pre-Treatment	Treatment Emergent	Total (including SAEs)	SAEs
Starting Dose	2	22	24	1
Low-Dose	7	52	59	10
Mid-Dose	8	59	67	8
High-Dose	5	20	25	1
Totals	22	153	175	20

Relatedness to Vector by Dose Cohort				
	Possibly Related	Probably Related	Definitely Related	Total
Starting Dose	0	0	0	0
Low Dose	3	1	0	4
Mid Dose	2	3	1	6
High Dose	2	1	2	5
All related AEs were grade 3 or less				

All Adverse Events Related to Vector by Severity and Dose Cohort				
	Grade 1	Grade 2	Grade 3	Total
Starting Dose	0	0	0	0
Low Dose	1	2	1	4
Mid Dose	0	5	1	6
High Dose	1	4	0	5

Relatedness to Neurosurgery by Dose Cohort				
	Possibly Related	Probably Related	Definitely Related	Total
Starting Dose	2	0	0	2
Low Dose	1	1	2	4
Mid Dose	0	2	2	4
High Dose	0	2	4	6
All related AEs were grade 3 or less				

All Adverse Events Related to Neurosurgery by Severity and Dose Cohort				
	Grade 1	Grade 2	Grade 3	Total
Starting Dose	1	1	0	2
Low Dose	1	1	2	4
Mid Dose	0	3	1	4
High Dose	2	4	0	6

Adverse Event Summary:

- There were 155 Non-Serious Treatment Emergent Adverse Events

- There were 20 Serious Adverse Events
- No subjects discontinued treatment due to an adverse event

Serious Adverse Events		
Arm/Group Title	Patients Treated with AXO-AAV-GM2	
	Affected/at Risk (%)	Total Events
Total	8/9 (88.9%)	20
General disorders and administration site conditions		
Pyrexia	1/9 (11.1%)	1
Wound dehiscence	2/9 (22.2%)	2
Infections and infestations		
Aspiration pneumonia	1/9 (11.1%)	1
Clostridium difficile infection†	1/9 (11.1%)	1
Covid-19	2/9 (22.2%)	2
Influenza A	2/9 (22.2%)	2
Pneumonia	3/9 (33.3%)	3
Nervous system disorders		
Death due to disease progression†	1/9 (11.1%)	1
Mental status changes	1/9 (11.1%)	1
Seizures	3/9 (33.3%)	3
Neurological decompensation	1/9 (11.1%)	1
Respiratory, thoracic, and mediastinal disorders		
Bronchiolitis	1/9 (11.1%)	1
Bronchitis	1/9 (11.1%)	1

† Fatal Adverse Events

Treatment Emergent Adverse Events (not including SAEs)	
Arm/Group Title	Patients Treated with AXO-AAV-GM2
	Affected/at Risk (%)
Total	9/9 (100%)
Blood and lymphatic system disorders	
Anemia	4/9 (44.4%)
Neutrophil Count Decreased	1/9 (11.1%)
Cardiac disorders	
Atrial Fibrillation	1/9 (11.1%)
Ear and labyrinth disorders	
Otitis media	1/9 (11.1%)
Eye disorder	
Eyelid Edema	1/9 (11.1%)
Subconjunctival Hemorrhage	1/9 (11.1%)
Gastrointestinal disorders	
Coffee Ground Emesis	1/9 (11.1%)

Constipation	6/9 (66.7%)
Diarrhea	2/9 (22.2%)
Gastrointestinal Reflux	3/9 (33.3%)
Mucositis Oral	4/9 (44.4%)
Vomiting	6/9 (66.7%)
General disorders and administration site conditions	
Edema	1/9 (11.1%)
Pyrexia	4/9 (44.4%)
Rigors	1/9 (11.1%)
Surgery-related Pain	2/9 (22.2%)
Surgical Site Swelling	1/9 (11.1%)
Surgical Wound Drainage	2/9 (22.2%)
Wound Dehiscence	2/9 (22.2%)
Hepatobiliary disorders	
Abnormal Results of Liver Function Studies	5/9 (55.6%)
Immune system disorders	
Allergic Reaction	1/9 (11.1%)
Anti-Capsid immune response by ELISpot	6/9 (66.7%)
Seasonal Allergies	1/9 (11.1%)
Infections and infestations	
Cellulitis	1/9 (11.1%)
Clostridium Difficile Infection	1/9 (11.1%)
Covid-19	3/9 (33.3%)
G-Tube Site Infection	1/9 (11.1%)
Oral Candidiasis	2/9 (22.2%)
Pediculosis Capitis	1/9 (11.1%)
Pneumonia	2/9 (22.2%)
Respiratory syncytial virus infection	1/9 (11.1%)
Sinusitis	2/9 (22.2%)
Upper respiratory tract infection	4/9 (44.4%)
Urinary Tract Infection	2/9 (22.2%)
Vaginal Candidiasis	1/9 (11.1%)
Viral infection	1/9 (11.1%)
Injury, poisoning, and procedural complications	
Catheter Related Complication	1/9 (11.1%)
Metabolism and nutrition disorders	
Hypokalemia	2/9 (22.2%)
Malnutrition	2/9 (22.2%)
Nervous system disorders	
Abnormal Movements	1/9 (11.1%)
Delayed recovery from anesthesia	1/9 (11.1%)

Disease Progression	1/9 (11.1%)
Dystonia [‡]	2/9 (22.2%)
Lethargy	1/9 (11.1%)
Macrocephaly	1/9 (11.1%)
Seizures	4/9 (44.4%)
Tardive dyskinesia	1/9 (11.1%)
Ventriculomegally	1/9 (11.1%)
Weakness	1/9 (11.1%)
Renal and urinary disorders	
Pyuria	1/9 (11.1%)
Urinary retention	1/9 (11.1%)
Respiratory, thoracic, and mediastinal disorders	
Hypersalivation	4/9 (44.4%)
Increased Mucus	1/9 (11.1%)
Laryngospasm	1/9 (11.1%)
Respiratory Failure	1/9 (11.1%)
Upper respiratory tract congestion	1/9 (11.1%)
Skin and subcutaneous tissue disorders	
Alopecia	1/9 (11.1%)
Blister	1/9 (11.1%)
Dermatitis Contact	1/9 (11.1%)
Dermatitis Diaper	1/9 (11.1%)
Dermatitis Due to Adhesive	1/9 (11.1%)
Dermatitis Seborrheic	1/9 (11.1%)
Incision Site Erythema	1/9 (11.1%)
Petechia	1/9 (11.1%)
Scalp Induration	1/9 (11.1%)
Vascular disorders	
Hypertension	1/9 (11.1%)
Perioral Cyanosis	1/9 (11.1%)

‡ 2 TEAEs of Dystonia in juvenile subjects were classified as AEs of Special Interest and led to the decision to only treat infantile subjects to complete the study. This was not seen in infantile subjects.

Pre-Treatment Adverse Events (not including SAEs)	
Arm/Group Title	Patients Treated with AXO-AAV-GM2
	Affected/at Risk (%)
Total	8/9 (88.9%)
Cardiac disorders	
Premature Ventricular Contractions	1/9 (11.1%)
Run of Ventricular Tachycardia	1/9 (11.1%)
Gastrointestinal disorders	

Hiccups	1/9 (11.1%)
Vomiting	2/9 (22.2%)
General disorders and administration site conditions	
Procedure-related Pain	2/9 (22.2%)
Pyrexia	1/9 (11.1%)
Infections and infestations	
Covid-19 Infection	1/9 (11.1%)
Oral Candidiasis	2/9 (22.2%)
Urinary tract infection	1/9 (11.1%)
Respiratory, thoracic, and mediastinal disorders	
Laryngospasm	1/9 (11.1%)
Skin and subcutaneous tissue disorders	
Dermatitis Diaper	1/9 (11.1%)
Infusion Related Rash	7/9 (77.8%)

Supplemental Table 2

Pt 001						
	Week 12	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)	Week 48	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	303	(129-520)	127	(129-520)	176	(74-345)
Homovanillic Acid	648	(294-1115)	376	(294-1115)	268	(233-928)
3-O-methyldopa	32	(<300)	39	(<300)	30	(<150)
Neopterin	20	(7-65)	145	(7-65)	56	(7-65)
Tetrahydrobiopterin	12	(18-58)	13	(18-58)	22	(18-50)

Pt 002		
	Initial	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid		(74-345)
Homovanillic Acid		(233-928)
3-O-methyldopa		(<150)
Neopterin	8	(7-65)
Tetrahydrobiopterin	<5	(18-50)

Pt 004				
	Initial	Normal Range (nmol/l)	Week 12	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	218	(129-520)	188	(129-520)
Homovanillic Acid	514	(294-1115)	298	(294-1115)
3-O-methyldopa	32	(<300)	7	(<300)
Neopterin	10	(7-65)	28	(7-65)
Tetrahydrobiopterin	19	(18-58)	32	(18-58)

Pt 005				
	Initial	Normal Range (nmol/l)	Week 48	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	148	(66-338)	98	(66-338)
Homovanillic Acid	600	(218-852)	413	(218-852)
3-O-methyldopa	28	(<100)	43	(<100)
Neopterin		(7-40)	40	(7-40)
Tetrahydrobiopterin		(9-40)	22	(9-40)

Pt 006								
	Initial	Normal Range (nmol/l)	Week 12	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)	Week 48	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	108	(67-189)	38	(67-189)	64	(67-189)	65	(67-189)
Homovanillic Acid	223	(167-563)	81	(167-563)	104	(167-563)	212	(167-563)
3-O-methyldopa	22	(<100)	11	(<100)	18	(<100)	19	(<100)
Neopterin	13	(8-33)	15	(8-33)	35	(8-33)	43	(8-33)
Tetrahydrobiopterin	15	(9-32)	14	(9-32)	11	(9-32)	12	(9-32)

Pt 007						
	Initial	Normal Range (nmol/l)	Week 12	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	230	(129-520)	283	(129-520)	244	(74-345)
Homovanillic Acid	539	(294-1115)	521	(294-1115)	513	(233-928)
3-O-methyldopa	25	(<300)	11	(<300)	38	(<150)
Neopterin	19	(7-65)	11	(7-65)	24	(7-65)
Tetrahydrobiopterin	14	(18-58)	12	(18-58)	13	(18-50)

Pt 008	
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	Initial	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	272	(129-520)	118	(129-520)
Homovanillic Acid	588	(294-1115)	332	(294-1115)
3-O-methyldopa	39	(<300)	16	(<300)
Neopterin	11	(7-65)	33	(7-65)
Tetrahydrobiopterin	21	(18-58)	16	(18-58)

Pt 010						
	Initial	Normal Range (nmol/l)	Week 12	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	255	(129-520)	105	(129-520)	125	(129-520)
Homovanillic Acid	810	(294-1115)	199	(294-1115)	345	(294-1115)
3-O-methyldopa	30	(<300)	13	(<300)	22	(<300)
Neopterin	10	(7-65)	13	(7-65)	21	(7-65)
Tetrahydrobiopterin	22	(18-58)	16	(18-58)	20	(18-58)

Pt 011						
	Initial	Normal Range (nmol/l)	Week 12	Normal Range (nmol/l)	Week 24	Normal Range (nmol/l)
5-HydroxyIndoleacetic Acid	226	(129-520)	194	(129-520)	133	(129-520)
Homovanillic Acid	486	(294-1115)	358	(294-1115)	318	(294-1115)
3-O-methyldopa	89	(<300)	45	(<300)	14	(<300)
Neopterin	10	(7-65)	23	(7-65)	30	(7-65)
Tetrahydrobiopterin	<5	(18-58)	22	(18-58)	20	(18-58)

Supplemental Table 3. Steroid doses given to patients.

Patient 001		Treated: 1/26/2021			
Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	1/15/2021	-10	1/15/2021	-10
Prednisolone	2 mg/kg	1/16/2021	-9	4/27/2021	92
Prednisolone	1 mg/kg	4/28/2021	93	4/28/2021	93
Prednisolone	2 mg/kg	4/29/2021	94	6/18/2021	144
Prednisolone	1 mg/kg	6/19/2021	145	6/25/2021	151
Prednisolone	0.5 mg/kg	6/26/2021	152	7/2/2021	158
Prednisolone	0.25 mg/kg	7/3/2021	159	7/9/2021	165
Prednisolone	0.125 mg/kg	7/10/2021	166	7/16/2021	172

Patient 002		Treated: 5/25/2021			
Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	5/12/2021	-12	5/12/2021	-12
Prednisolone	2 mg/kg	5/13/2021	-11	7/30/2021	67
Methylprednisolone	10 mg/kg	7/30/2021	67	8/1/2021	69
Prednisolone	2 mg/kg	8/2/2021	70	8/24/2021	92
Prednisolone	1 mg/kg	8/25/2021	93	9/1/2021	100
Prednisolone	0.5 mg/kg	9/2/2021	101	9/8/2021	107
Prednisolone	0.25 mg/kg	9/9/2021	108	9/15/2021	114
Prednisolone	0.125 mg/kg	9/16/2021	115	9/22/2021	121

Patient 004		Treated: 9/21/2021			
Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	9/9/2021	-11	9/9/2021	-11
Prednisolone	2 mg/kg	9/10/2021	-10	10/5/2021	15
Prednisolone	4 mg/kg	10/6/2021	16	10/6/2021	16
Methylprednisolone	10 mg/kg	10/7/2021	17	10/9/2021	19
Prednisolone	2 mg/kg	10/7/2021	17	11/23/2021	64
Prednisolone	1 mg/kg	11/24/2021	65	12/13/2021	84
Prednisolone	0.5 mg/kg	12/14/2021	85	12/20/2021	91
Prednisolone	0.25 mg/kg	12/21/2021	92	12/27/2021	98
Prednisolone	0.125 mg/kg	12/28/2021	99	1/3/2022	105
Prednisolone	0.0625 mg/kg	1/4/2022	106	1/10/2022	112
Prednisolone	0.03125 mg/kg	1/11/2022	113	1/17/2022	119

Patient 005		Treated: 11/30/2021			
Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	11/23/2021	-6	11/23/2021	-6
Prednisolone	1 mg/kg	11/24/2021	-5	12/28/2021	29
Prednisolone	2 mg/kg	12/29/2021	30	1/21/2022	53
Prednisolone	1 mg/kg	1/22/2022	54	2/18/2022	81
Prednisolone	0.5 mg/kg	2/19/2022	82	2/25/2022	88
Prednisolone	0.25 mg/kg	2/26/2022	89	3/4/2022	95
Prednisolone	0.125 mg/kg	3/5/2022	96	3/11/2022	102

Patient 006**Treated: 2/16/2022**

Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	2/4/2022	-11	2/4/2022	-11
Prednisolone	1 mg/kg	2/5/2022	-10	3/11/2022	24
Prednisolone	2 mg/kg	3/12/2022	25	4/4/2022	48
Prednisolone	1 mg/kg	4/5/2022	49	5/10/2022	84
Prednisolone	0.5 mg/kg	5/11/2022	85	5/17/2022	91
Prednisolone	0.25 mg/kg	5/18/2022	92	5/24/2022	98
Prednisolone	0.125 mg/kg	5/25/2022	99	5/31/2022	105

Patient 007**Treated: 5/18/2022**

Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	5/5/2022	-12	5/5/2022	-12
Prednisolone	1 mg/kg	5/6/2022	-11	6/2/2022	16
Prednisolone	2 mg/kg	6/3/2022	17	6/17/2022	31
Methylprednisolone	10 mg/kg	6/8/2022	22	6/10/2022	24
Prednisolone	1 mg/kg	6/18/2022	32	8/1/2022	76
Prednisolone	4 mg/kg	8/2/2022	77	8/11/2022	86
Prednisolone	6 mg/kg	8/12/2022	87	8/18/2022	93
Prednisolone	4 mg/kg	8/19/2022	94	8/23/2022	98
Prednisolone	2 mg/kg	8/24/2022	99	8/28/2022	103
Prednisolone	1 mg/kg	8/29/2022	104	9/2/2022	108
Prednisolone	0.5 mg/kg	9/3/2022	109	9/9/2022	115
Prednisolone	0.25 mg/kg	9/10/2022	116	9/14/2022	120
Prednisolone	2 mg/kg	9/15/2022	121	9/28/2022	134
Prednisolone	1 mg/kg	9/29/2022	135	10/5/2022	141
Prednisolone	0.5 mg/kg	10/6/2022	142	10/12/2022	148
Prednisolone	0.25 mg/kg	10/13/2022	149	10/19/2022	155
Prednisolone	0.125 mg/kg	10/20/2022	156	10/26/2022	162
Prednisolone	0.0625 mg/kg	10/27/2022	163	11/2/2022	169

On very high levels of prednisolone to treat infantile spasms at this time

Patient 008**Treated: 3/1/2023**

Medication	Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	2/16/2023	-12	2/16/2023	-12
Prednisolone	1 mg/kg	2/17/2023	-11	3/9/2023	9
Prednisolone	2 mg/kg	3/10/2023	10	3/23/2023	23
Methylprednisolone	10 mg/kg	3/15/2023	15	3/17/2023	17
Prednisolone	1 mg/kg	3/24/2023	24	5/27/2023	88
Prednisolone	0.5 mg/kg	5/28/2023	89	6/3/2023	95
Prednisolone	0.25 mg/kg	6/4/2023	96	6/10/2023	102
Prednisolone	0.125 mg/kg	6/11/2023	103	6/17/2023	109
Prednisolone	2 mg/kg	7/27/2023	149	8/11/2023	164
Prednisolone	1 mg/kg	8/12/2023	165	8/17/2023	170
Prednisolone	0.5 mg/kg	8/18/2023	171	8/24/2023	177
Prednisolone	0.25 mg/kg	8/25/2023	178	8/31/2023	184

Patient 010**Treated: 9/20/2023**

Medication	Daily Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	9/7/2023	-12	9/7/2023	-12
Prednisolone	1 mg/kg	9/9/2023	-10	10/1/2023	12
Prednisolone	2 mg/kg	10/2/2023	13	11/16/2023	58
Methylprednisolone	10 mg/kg	10/31/2023	42	11/2/2023	44
Prednisolone	4 mg/kg	11/17/2023	59	11/29/2023	71
Prednisolone	2 mg/kg	11/30/2023	72	12/6/2023	78
Prednisolone	1 mg/kg	12/7/2023	79	12/14/2023	86
Prednisolone	0.5 mg/kg	12/15/2023	87	12/27/2023	99
Prednisolone	2 mg/kg	12/28/2023	100	1/8/2024	111
Prednisolone	1 mg/kg	1/9/2024	112	1/23/2024	126
Prednisolone	0.5 mg/kg	1/24/2024	127	3/28/2024	191
Prednisolone	0.25 mg/kg	3/29/2024	192	4/4/2024	198
Prednisolone	0.125 mg/kg	4/5/2024	199	4/11/2024	205
Prednisolone	0.0625 mg/kg	4/12/2024	206	4/18/2024	212

Patient 011**Treated: 12/6/2023**

Medication	Daily Dose	Start Date	Study Day	Stop Date	Study Day
Methylprednisolone	10 mg/kg	11/27/2023	-8	11/27/2023	-8
Prednisolone	1 mg/kg	11/28/2023	-7	12/18/2023	13
Prednisolone	2 mg/kg	12/19/2023	14	1/2/2024	28
Methylprednisolone	10 mg/kg	12/27/2023	22	12/29/2023	24
Prednisolone	4 mg/kg	1/3/2024	29	1/5/2024	31
Prednisolone	2 mg/kg	1/6/2024	32	2/2/2024	59
Prednisolone	1 mg/kg	2/3/2024	60	2/27/2024	84
Prednisolone	0.5 mg/kg	2/28/2024	85	3/12/2024	98
Prednisolone	0.25 mg/kg	3/13/2024	99	3/26/2024	112
Prednisolone	0.125 mg/kg	3/27/2024	113	4/9/2024	126

Supplemental Table 4 Patient C18:0 and C20:0 levels.

Patient #	Visit name	Date	GM2 (18:0) (ng/ml)	GM2 (20:0)		
				CSF (µl)	Area ratio	(ng/ml)
001	Visit A	1/27/2021	199	5	0.06419	64.2
	Week 12	4/21/2021	352	5	0.12411	124.1
	Week 24	8/25/2021	522	5	0.19424	194.2
	Week 48	2/16/2022	1890	5	0.69346	693.5
	Week 72	8/22/2022	2510	5	0.89116	891.2
002	Visit A	4/2/2021	90	5	0.03164	31.6
	Day 1b	5/26/2021	165	5	0.02882	28.8
	Week 8	7/20/2021	86.3	5	0.02134	21.3
003*	Visit A	7/16/2021	53	5	0.01715	17.2
004	Visit A	9/2/2021	460	2	0.10456	261.4
	Day 1b	9/22/2021	1020	5	0.35355	353.6
	Week 12	12/15/2021	875	5	0.29125	291.3
	Week 24	3/30/2022	653	5	0.23774	237.7
	Week 48	8/24/2022	981	5	0.32801	328.0
005	Day 1b	12/1/2021	37.1	5	0.0121	12.1
	Week 24	5/11/2022	39.1	5	0.01555	15.6
	Week 48	10/26/2022	40.8	5	0.0131	13.1
006	Visit A	1/28/2022	64.9	5	0.01982	19.8
	Day 1b	2/17/2022	78.9	5	0.02278	22.8
	Week 12	5/4/2022	39.3	5	0.01135	11.4
	Week 24	8/3/2022	43.2	5	0.01226	12.3
	Week 48	1/11/2023	55.8	5	0.0094	9.4
	Week 120	5/23/2024	51.5	5	0.01299	13.0
007	Visit A	4/29/2022	595	5	0.12306	123.1
	Visit 1b	5/19/2022	489	5	0.11671	116.7
	Week 12	8/10/2022	379	5	0.08574	85.7
	Week 24	11/9/2022	327	5	0.08039	80.4
008	Visit A	2/10/2023	405	5	0.11428	114.3
	Day 1b	3/2/2023	467	5	0.14146	141.5
	Week 12	5/16/2023	413	5	0.10073	100.7
	Week 24	9/13/2023	578	5	0.15237	152.4
010	Visit A	8/24/2023	609	5	0.19695	197.0
	Day 1b	9/21/2023	538	5	0.14746	147.5
	Week 12	12/15/2023	406	5	0.10148	101.5
	Week 24	3/8/2024	442	5	0.11557	115.6
011	Day 1b	12/7/2023	529	5	0.11947	119.5
	Week 12	2/21/2024	547	5	0.1563	156.3
	Week 24	5/24/2024	577	5	0.22662	226.6

Visit A = screening visit for patient enrollment, Day 1b = samples collected before dosing on the day that the patient was treated. *This visit was conducted before the study was put on hold; after the study was resumed, this patient was re-enrolled as Patient 005.

Supplemental Table 5. Statistical analysis using linear mixed model showing fixed effects of treatment and treatment over time for brain, ventricle volumes in the treated GM2 infantile patients compared to untreated patients. The F-statistic and p values are reported along with the magnitude effect in volumetric change. (*NS* – not significant)

Brain						
Effect	<i>F</i>	<i>p</i>	Magnitude effect for each category (+/- ml)			Interpretation
Treatment	14.46	0.002	Treated		-1020.26	Treated group showed a <u>significantly smaller brain volume</u> compared to untreated group
Time	10.24	0.001	Pre-treatment		-1198.82	The pre-treatment and 1 st and 2 nd post-treatment timepoints showed smaller brain volumes compared to the 3 rd post-treatment timepoint
			1 st post-treatment		-819.46	
			2 nd post-treatment		-434.98	
Treatment*Time	5.12	0.016	Treated	Pre-treatment	+861.09	Treated patients at pre-treatment timepoint showed significantly larger brain volume compared to untreated patients
Ventricles						
Effect	<i>F</i>	<i>p</i>	Magnitude effect for each category (+/- ml)			Interpretation
Treatment	0.06	0.816	NS			No time or treatment effects were observed for ventricular volume
Time	1.15	0.362				
Treatment*Time	1.13	0.371				

Supplemental Table 6 Cerebrospinal fluid total nucleated cell (CSF TNC) count and CSF Protein concentration.

Patient 001

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	1	20	
Week 12	1	14	
Week 24	5	28	
Week 48	2	29	

Patient 002

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	0	21	
Day 1a	0	29	
Week 12	1	44	

Patient 004

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	1	26	1550 RBC
Day 1a	1	25	
Week 12	0	22	
Week 24	2	28	
Week 48	2	27	

Patient 005

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	1	26	
Day 1a	0	27	
Week 12	13	600	162, 750 RBC
Week 24	4	38	338 RBC
Week 48	4	29	

Patient 006

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	1	18	904 RBC
Day 1a	1	20	
Week 12	0	18	
Week 24	3	16	
Week 48	3	16	

Patient 007

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	0	10	
Day 1a	0	11	
Week 12	0	11	
Week 24	1	15	

Patient 008

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	0	14	
Day 1a	0	16	
Week 12	2	15	
Week 24	5	16	

Patient 010

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	1	17	
Day 1a	0	17	
Week 12	0	38	703 RBC
Week 24	0	18	

Patient 011

Study Visit	CSF TNC (normal 0–5)	CSF Protein (normal 5–55)	Comments
Screening	147	436	183,750 RBC
Day 1a	1	22	
Week 12	1	25	54 RBC
Week 24	4	21	