

Table 1
Summary of ECHO Measures by Visit

Time Point	Parameter	n (%)	Mean (std)	Median	Min	Max
V1 - Screening	LV EF Single Plane 2D	23 (100)	64.8 (5.11)	64.27	57.4	76.4
V11 - Month 6	LV EF Single Plane 2D	2 (8.7)	62.8 (0.49)	62.82	62.5	63.2

Table 14.1.1: Patient Disposition (All Patients)

	Screen Failures	1.1E14 vg/kg
Screen Failures	6	
Patients Screened		23
Patients in the Enrolled Set		23
Patients in the ITT Set		22 (95.7)
Patients in the Safety Analysis Set		23 (100.0)
Patients in the Efficacy Completer Analysis Set		0
Patients Completed the Study		0
Patients Discontinued from the Study		1 (4.3)
Reason for discontinuation		
Death		1 (4.3)

Note: Percentages are based on the number of patients enrolled.
Program Name: t_sf_ds_sum.sas

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Table 14.1.2: Demographics and Baseline Characteristics (Safety Population)

Parameter	Statistics	1.1E14 vg/kg (N = 23)
Gestational age at birth (weeks)	n	22
	Mean (SD)	39.3 (1.04)
	Median	39
	Min, Max	37, 41
Birth Weight (kg)	n	23
	Mean (SD)	3.5 (0.52)
	Median	3
	Min, Max	3, 5
Birth length/height (cm)	n	15
	Mean (SD)	52.1 (2.14)
	Median	52
	Min, Max	48, 56
Head circumference at birth (cm)	n	13
	Mean (SD)	34.2 (1.39)
	Median	34
	Min, Max	32, 37

Note: cm = centimeters, kg = kilograms, SD = standard deviation, SMA = spinal muscular atrophy.

* Age = (dose date - date of birth + 1).

Percentages are based on number of patients in Safety population for presented cohort.

Program Name: t_sf_dm_sum.sas

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Table 14.1.2: Demographics and Baseline Characteristics (Safety Population)

Parameter	Statistics	1.1E14 vg/kg (N = 23)
Age at Baseline (days)*	n	23
	Mean (SD)	112.5 (38.85)
	Median	105
	Min, Max	58, 188
Age at Baseline (days)*	n	23
28 Days - 23 Months	n (%)	23 (100)
Weight at Baseline (kg)	n	23
	Mean (SD)	5.8 (1.13)
	Median	6
	Min, Max	4, 8
Length/height at Baseline (cm)	n	23
	Mean (SD)	61.9 (3.34)
	Median	62
	Min, Max	55, 68
Gender	n	23
Female	n (%)	13 (56.5)
Male	n (%)	10 (43.5)

Note: cm = centimeters, kg = kilograms, SD = standard deviation, SMA = spinal muscular atrophy.

* Age = (dose date - date of birth + 1).

Percentages are based on number of patients in Safety population for presented cohort.

Program Name: t_sf_dm_sum.sas

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Table 14.1.2: Demographics and Baseline Characteristics (Safety Population)

Parameter	Statistics	1.1E14 vg/kg (N = 23)
Familial history of SMA including affected siblings or parent carriers	n	23
Missing	n (%)	3 (13.0)
No	n (%)	19 (82.6)
Yes	n (%)	1 (4.3)
Parental history of SMA	n	1
No Parental History Of Sma	n (%)	1 (4.3)
Siblings affected by SMA	n	1
Siblings Affected	n (%)	1 (4.3)
Patient reported hospitalizations since birth	n	23
No	n (%)	11 (47.8)
Yes	n (%)	12 (52.2)

Note: cm = centimeters, kg = kilograms, SD = standard deviation, SMA = spinal muscular atrophy.

* Age = (dose date - date of birth + 1).

Percentages are based on number of patients in Safety population for presented cohort.

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Cut-off Date: 08 March 2019

Table 14.2.1.1: Proportion of Patients Demonstrating Sitting without support (WHO-MGRS) at any Point up to 18 Months of Age (ITT Population)

	Statistics	1.1E14 vg/kg (N = 22)
Independent sitting for at least 30 seconds	n (%)	1 (4.5)
	97.5% CI	(0.7430, 0.9994)
	p-value	<.0001
Age when milestone was first demonstrated (months)	n	1
	Mean (SD)	8.60
	Median	8.60
	Min, Max	8.6, 8.6
Duration of milestone (days)*	n	1
	Mean (SD)	101.00
	Median	101.00
	Min, Max	101.0, 101.0

Note: A one-sided exact binomial test was used to test the null hypothesis at significance level of 0.025.

The corresponding 97.5% confidence interval was estimated by the exact method for binomial proportions.

*Duration is calculated as (days since first demonstrating milestone to the date of the 18 months of age visit or cut-off date (if patient is continuing in study and did not reach 18 months of age visit yet). For patients who demonstrate the milestone but prematurely withdraw from the study prior to the 18 months of age visit, duration is calculated as (date of premature withdrawal - date milestone was first demonstrated + 1 day).

Program Name: t_ef_qs_sum_01.sas

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Table 14.2.4.1: Proportion of Patients Demonstrating achievement of Developmental Milestones by month (ITT Population)

Visit	Milestone	Statistics	1.1E14 vg/kg (N = 22)
Month 1	Head Control	n (%)	1 (4.5)
Month 2	Head Control	n (%)	2 (9.1)
	Sits Without Support	n (%)	1 (4.5)
Month 3	Head Control	n (%)	1 (4.5)
	Sits Without Support	n (%)	1 (4.5)
	WHO Sitting without support	n (%)	1 (4.5)

Note: Motor milestones assessed by WHO-MGRS criteria at any visit up to and including the 18 months of age visit.

Program Name: t_ef_vid_sum_03.sas

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Table 14.3.1.1: Treatment Emergent Adverse Events that code to the SOC of Cardiac Disorders and Investigations (Safety Population)

MedDRA v21.0 System Organ Class Preferred Term	1.1E14 vg/kg (N = 23) n (%) [m]
Any TEAE	4 (17.4) [19]
Cardiac disorders	1 (4.3) [3]
Bradycardia	1 (4.3) [2]
Tachycardia	1 (4.3) [1]
Investigations	4 (17.4) [16]
Alanine aminotransferase increased	1 (4.3) [1]
Aspartate aminotransferase increased	1 (4.3) [1]
Blood phosphorus decreased	1 (4.3) [1]
Body temperature increased	1 (4.3) [1]
Haemoglobin decreased	1 (4.3) [1]
Haemophilus test positive	1 (4.3) [1]
Oxygen saturation decreased	2 (8.7) [2]
Platelet count decreased	1 (4.3) [1]
Respiratory syncytial virus test positive	2 (8.7) [3]
Respirovirus test positive	1 (4.3) [1]
Staphylococcus test positive	1 (4.3) [1]
Transaminases increased	2 (8.7) [2]

n = Number of subjects, m = Number of events
Program Name: t_sf_ae_sum_01.sas

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Table 14.3.4.1.2: Laboratory - Chemistry: CK-MB (Safety Population)

1.1E14 vg/kg (N = 23)

Lab Parameter (unit)	Visit	Observed Values						Change from Baseline Values					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
CK-MB Creatine Kinase MB (ug/L)	Baseline	23	24.98	11.887	26.90	4.3	49.4						
	V3 - Day 7	20	23.36	15.968	18.75	2.7	84.0	20	-2.61	12.026	-2.35	-21.5	34.6
	V6 - Month 1	20	16.12	7.460	14.30	4.2	32.4	20	-7.95	8.906	-7.25	-23.9	7.5
	V7 - Month 2	19	16.13	6.069	16.30	6.5	28.1	19	-10.61	8.860	-10.10	-27.1	5.0
	V11 - Month 6	2	35.80	13.718	35.80	26.1	45.5	2	9.90	12.304	9.90	1.2	18.6

Table 14.3.4.9.1: Summary of 12-Lead ECG (Safety Population)

1.1E14 vg/kg (N = 23)

ECG Parameter (unit)	Visit	Observed Values						Change from Baseline Values					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
ECG Mean Ventricular Rate (beats/min)	Baseline	23	143.17	14.531	143.00	121.0	172.0						
	V2 - Day 2	22	143.73	12.699	142.00	117.0	167.0	22	-0.27	13.024	-1.00	-28.0	21.0
	Unscheduled 27/Feb/2019	1	151.00		151.00	151.0	151.0	1	30.00		30.00	30.0	30.0
	V11 - Month 6	2	142.00	4.243	142.00	139.0	145.0	2	9.00	9.899	9.00	2.0	16.0
PR Interval, Single Beat (msec)	Baseline	23	101.35	14.396	100.00	79.0	132.0						
	V2 - Day 2	22	101.77	15.684	96.50	79.0	156.0	22	1.14	12.544	1.50	-27.0	32.0
	Unscheduled 27/Feb/2019	1	131.00		131.00	131.0	131.0	1	7.00		7.00	7.0	7.0
	V11 - Month 6	2	112.50	7.778	112.50	107.0	118.0	2	-1.50	33.234	-1.50	-25.0	22.0
QRS Duration, Single Beat (msec)	Baseline	23	67.39	7.739	66.00	56.0	86.0						
	V2 - Day 2	22	66.27	7.330	65.00	55.0	78.0	22	-0.86	5.792	0.00	-15.0	10.0
	Unscheduled 27/Feb/2019	1	61.00		61.00	61.0	61.0	1	-5.00		-5.00	-5.0	-5.0
	V11 - Month 6	2	75.00	5.657	75.00	71.0	79.0	2	8.50	3.536	8.50	6.0	11.0

Table 14.3.4.9.1: Summary of 12-Lead ECG (Safety Population)

1.1E14 vg/kg (N = 23)

ECG Parameter (unit)	Visit	Observed Values						Change from Baseline Values					
		n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
QTcF Interval, Single Beat (msec)	Baseline	23	370.61	17.984	372.00	332.0	410.0						
	V2 - Day 2	22	364.32	13.541	363.50	338.0	397.0	22	-6.18	20.306	-3.50	-49.0	32.0
	Unscheduled 27/Feb/2019	1	360.00		360.00	360.0	360.0	1	-25.00		-25.00	-25.0	-25.0
	V11 - Month 6	2	372.00	14.142	372.00	362.0	382.0	2	2.00	5.657	2.00	-2.0	6.0
QT Interval, Single Beat (msec)	Baseline	23	278.30	19.373	281.00	237.0	323.0						
	V2 - Day 2	22	272.82	13.358	277.50	245.0	298.0	22	-4.86	18.072	-1.50	-45.0	29.0
	Unscheduled 27/Feb/2019	1	265.00		265.00	265.0	265.0	1	-40.00		-40.00	-40.0	-40.0
	V11 - Month 6	2	279.50	13.435	279.50	270.0	289.0	2	-5.00	2.828	-5.00	-7.0	-3.0
RR Interval, Aggregate (msec)	Baseline	23	423.35	42.139	420.00	350.0	497.0						
	V2 - Day 2	22	420.23	36.974	422.50	360.0	511.0	22	-0.55	37.688	2.50	-60.0	72.0
	Unscheduled 27/Feb/2019	1	398.00		398.00	398.0	398.0	1	-99.00		-99.00	-99.0	-99.0
	V11 - Month 6	2	422.00	12.728	422.00	413.0	431.0	2	-31.00	33.941	-31.00	-55.0	-7.0

Table 14.3.4.9.2: Summary of Patients Meeting Criteria for Potentially Clinically Significant ECG Values (Safety Population)

Visit / Time Point	ECG Parameter (unit)	PCS Criteria	1.1E14 vg/kg (N = 23)
V2 - Day 2	QTcF Interval, Single Beat (msec)	Change (increase) from Baseline $\geq$ 30 msec	1/22 (4.5)

Nobs is number of patients with non-missing value for respective parameter at respective time point.
Percentages are calculated using Nobs as denominator.
Program Name: t_sf_eg_sum_02.sas

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Pages 13 to 954 of CSR Appendix 16.2 have been removed as per Health Canada Guidance on Public Release of Clinical Information (Patient data listings).

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