Muscular Dystrophy Association – 2021 MDA virtual

Roche Analyst Audio Webcast

Basel, 19 March 2021

This presentation contains certain forward-looking statements. These forward-looking statements may be identified by words such as ‘believes’, ‘expects’, ‘anticipates’, ‘projects’, ‘intends’, ‘should’, ‘seeks’, ‘estimates’, ‘future’ or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this presentation, among others:

1 pricing and product initiatives of competitors;
2 legislative and regulatory developments and economic conditions;
3 delay or inability in obtaining regulatory approvals or bringing products to market;
4 fluctuations in currency exchange rates and general financial market conditions;
5 uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side-effects of pipeline or marketed products;
6 increased government pricing pressures;
7 interruptions in production;
8 loss of or inability to obtain adequate protection for intellectual property rights;
9 litigation;
10 loss of key executives or other employees; and
11 adverse publicity and news coverage.

Any statements regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche’s earnings or earnings per share for this year or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

For marketed products discussed in this presentation, please see full prescribing information on our website www.roche.com

Agenda

Welcome
Karl Mahler, Head of Investor Relations and Group Business Planning

Phase II/III SUNFISH part 2: 24-month efficacy and safety of risdiplam in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA)
Paulo Fontoura, M.D. Ph.D., Global Head Neuroscience and Rare Diseases Clinical Development

Roche Neuroscience and Rare Disease franchise update
Simona Skerjanec, Therapeutic Area Head Neuroscience and Rare Diseases, Global Product Strategy

Q&A
Karl Mahler, Head of Investor Relations and Group Business Planning

Welcome

Karl Mahler

Head of Investor Relations and Group Business Planning

Rich newsflow ahead – expect mostly virtual analyst events in 2021

	Compound	Indication	Milestone
Phase III / pivotal readouts*	**faricimab**	nAMD	Ph III TENAYA/LUCERNE ✓
	casirivimab/imdevimab	SARS-CoV-2 Outpatient	Ph III Study 2067
	casirivimab/imdevimab	SARS-CoV-2 Post-exposure prophylaxis	Ph III Study 2069
	Tecentriq	Adjuvant NSCLC	Ph III IMpower010
	Evrysdi	SMA type 1/2/3 in previously treated patients	Ph II JEWELFISH
	Polivy + R-CHP	1L DLBCL	Ph III POLARIX
	Tecentriq + chemo	Adjuvant SCCHN	Ph III IMvoke010
	mosunetuzumab	3L+ FL	Ph Ib GO29781
	glofitamab	3L+ DLBCL	Ph Ib NP30179

Virtual Event Angiogenesis ✓	*Virtual Event MDA*	*Virtual Event Diagnostics Day*	*Virtual Event ASCO*	*Roche Pharma Day*
Tuesday, 16 February 16:30 to 17:30 CEST	**Friday, 19 March 14:00 to 15:00 CEST**	**Tuesday, 23 March 14:00 to 16:00 CEST**	**8 June, TBC**	**14 September, TBC**

* Outcome studies are event-driven: timelines may change

Roche commitment in neuroscience and rare diseases

The challenge

- >600 diseases of the nervous system
- 700 million cases of neurological disorders each year
- $789B annual cost of HC in the US*, €800B in Europe

Our commitment

- – 3 recently launched first in class medicines
  – 14 pipeline assets
  – 115 clinical trials
- 60 years in neuroscience – from Valium and Madopar to Ocrevus, Enspryng and Evrysdi
- >4,000 scientists dedicated to discovery and development

*Contribution of nine of the most common neurological disorders to annual cost of healthcare in 2017

SUNFISH part 2 data: 24 month efficacy and safety of risdiplam in patients with type 2 or type 3 SMA

Paulo Fontoura, M.D. Ph.D.

Global Head Neuroscience and Rare Diseases Clinical Development

SUNFISH Part 2: 24-month efficacy and safety of risdiplam in patients with Type 2 or non-ambulant Type 3 spinal muscular atrophy (SMA)

Maryam Oskoui,[1]* John W Day,[2] Nicolas Deconinck,[3,4] Elena Mazzone,[5] Andres Nascimento,[6] Kayoko Saito,[7] Carole Vuillerot,[8,9] Giovanni Baranello,[10,11] Odile Boespflug-Tanguy,[12,13] Nathalie Goemans,[14] Janbernd Kirschner,[15,16] Anna Kostera- Pruszczyk,[17] Laurent Servais,[12,18,19] Marianne Gerber,[20] Ksenija Gorni,[21] Heidemarie Kletzl,[22] Carmen Martin,[23] Renata S Scalco,[24] Hannah Staunton,[23] Wai Yin Yeung,[23] Eugenio Mercuri;[5] on behalf of the SUNFISH Working Group

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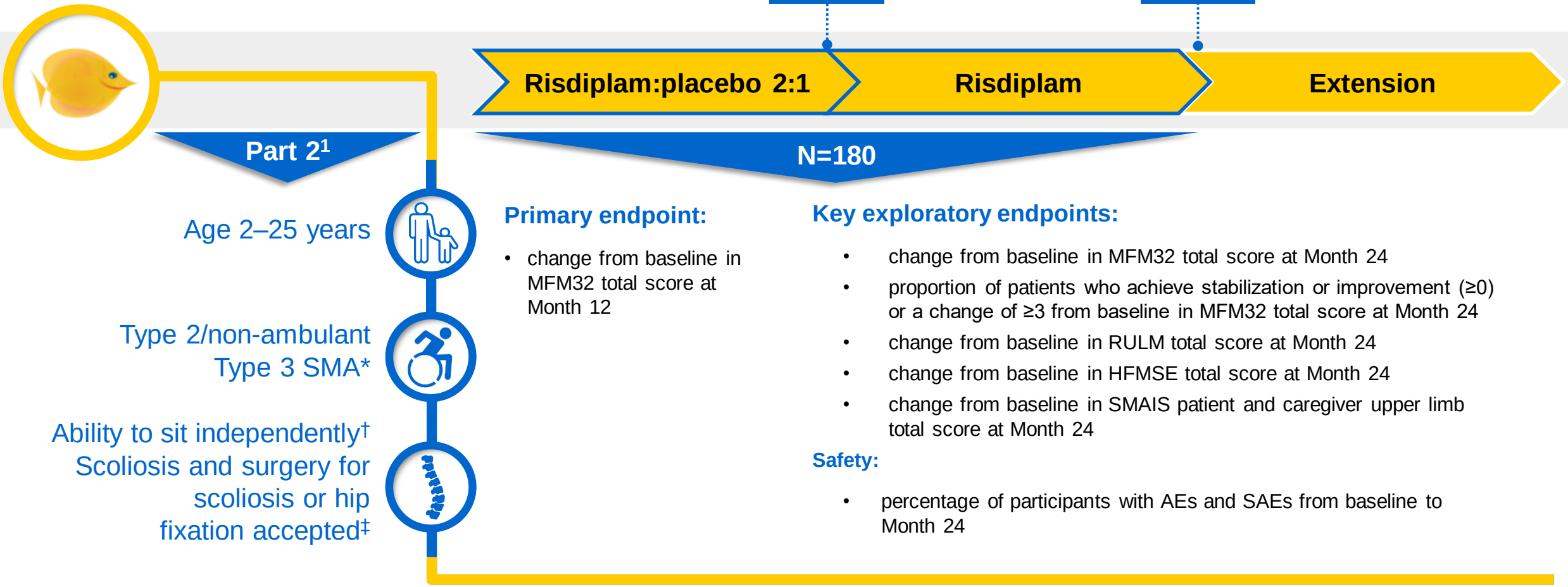
Disclosures

- MO is a PI of SMA studies for F. Hoffmann-La Roche and Biogen
- JWD reports grants from: AMO Pharmaceuticals, aTyr, AveXis, Biogen, Bristol Meyers Squibb, Cytokinetics, Ionis Pharmaceuticals, Roche Pharmaceuticals, Sanofi-Genzyme, and Sarepta Therapeutics; He has served as a consultant for: AMO Pharmaceuticals, AveXis, Biogen, Cytokinetics, Ionis Pharmaceuticals, Roche Pharmaceuticals, Pfizer, Sarepta Therapeutics, Santhera Pharmaceuticals; He has patents licensed to Athena Diagnostics for genetic testing of myotonic dystrophy type 2 (US patent 7442782) and spinocerebellar ataxia type 5 (US patent 7527931)
- ND is a PI of SMA studies for F. Hoffmann-La Roche, Novartis, Biogen and AveXis. He has received consultancy fees from F. Hoffmann-La Roche, Biogen and AveXis
- EMa is a Master trainer for SMA studies and receives consultancy fees from Avexis, Biogen, F. Hoffmann-La Roche and Scholar Rock
- AN is a PI of SMA studies for F. Hoffmann-La Roche, Biogen and Scholar Rock. He has received consultancy fees from F. Hoffmann-La Roche, Biogen, Scholar Rock and AveXis
- KS has attended advisory boards for Biogen, Novartis Pharma, and Roche/Chugai. She is a consultant for AveXis and has received research funding from AveXis/Novartis, Biogen, and Roche/Chugai for research consultation for execution of clinical trial projects, and from Ionis Pharmaceuticals for execution of clinical trial projects
- CV is a PI of SMA studies for F. Hoffmann-La Roche. She has attended SAB of Roche, Biogen and AveXis and received consultancy fees from F. Hoffmann-La Roche
- GB has received speaker and consultancy honoraria from AveXis, Inc., Roche, PTC, and Sarepta Therapeutics
- OBT is a PI of studies for F. Hoffmann-La Roche, AveXis, Santhera, Italfarmaco, Ultragenyx and Metfora. She is a DSMB member for Inventiva and Minoryx Therapeutics
- NG is a PI of SMA studies for F. Hoffmann-La Roche. She has received consultancy fees from F. Hoffmann-La Roche, Biogen and AveXis
- JK has received honoraria for clinical research and/or consultancy activities from Biogen, Novartis Gene Therapies, Roche, and Scholar Rock
- AKP is a PI of SMA studies for F. Hoffmann-La Roche. She has attended advisory boards of Biogen, PTC Therapeutics and AveXis, received speaker honoraria from Biogen and PTC Therapeutics and grant support from Biogen
- LS is a principal investigator of SMA studies for F. Hoffmann-La Roche Ltd, Biogen, and AveXis; he has attended SAB of F. Hoffmann-La Roche Ltd, Biogen, and AveXis and received consultancy fees from Biogen; he serves on the board for Cytokinetics. He is co-inventor in the patent 20190029605 (Method for estimating physical activity of the upper limb) from which he has not perceived any financial interest.
- MG, KG, HK, CM, RSS, HS and WYY are employees of, and hold shares in, F. Hoffmann-La Roche
- EM receives fees from AveXis, Biogen and F. Hoffmann-La Roche

A randomized, placebo-controlled, double-blind study with broad inclusion criteria and a large dataset



*Non-ambulant is defined as not having the ability to walk unassisted for ≥10m; †RULM entry item A (Brooke score) ≥2; ability to sit independently (≥1 on item 9 of the MFM32). ‡Except in the 1 year preceding screening or planned within the next 18 months.
AE, adverse event; HFMSE; Hammersmith Functional Motor Score – Expanded; MFM32, 32-item Motor Function Measure; RULM, Revised Upper Limb Module; SAE, serious AE; SMA, spinal muscular atrophy; SMAIS; SMA Independence Scale.
1. Clinicaltrials.gov. NCT02908685 (Accessed Mar 2021).

Roche in collaboration with SMA FOUNDATION and PTC THERAPEUTICS

Overall baseline demographics were balanced between risdiplam and placebo/risdiplam groups

	Risdiplam (n=120)	Placebo/risdiplam* (n=60)	Total (N=180)
Age at screening, years, median (range)	9 (2–25)	9 (2–24)	9 (2–25)
Age group, years, n (%)			
2–5	37 (30.8)	18 (30.0)	55 (30.6)
6–11	39 (32.5)	18 (30.0)	57 (31.7)
12–17	30 (25.0)	16 (26.7)	46 (25.6)
18–25	14 (11.7)	8 (13.3)	22 (12.2)
Gender, n (%)			
Female	61 (50.8)	30 (50.0)	91 (50.6)
Male	59 (49.2)	30 (50.0)	89 (49.4)
SMA type, n (%)			
2	84 (70.0)	44 (73.3)	128 (71.1)
3	36 (30.0)	16 (26.7)	52 (28.9)
SMN2 copy number, n (%)			
2	3 (2.5)	1 (1.7)	4 (2.2)
3	107 (89.2)	51 (85.0)	158 (87.8)
4	10 (8.3)	8 (13.3)	18 (10)

*Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months.
Based on enrollment criteria, at least 56% of patients in SUNFISH Part 2 would have been ineligible for the CHERISH trial (CHERISH inclusion criteria included: age 2 to 12 years, baseline HFMSE score ≥10; and exclusion criteria included: severe scoliosis [>40 degrees curvature]). This percentage does not take into consideration patients with severe contractures [CHERISH exclusion criteria included any contracture that, according to the investigator, could interfere with HFMSE])[1] Intent to treat patients. Data cut-off: 30 Sep 2020.
HFMSE, Expanded Hammersmith Functional Motor Scale – Expanded; SMA, spinal muscular atrophy; SMN, survival of motor neuron.
1. Mercuri E, et al. N Engl J Med 2018; 378:625–635.

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Overall baseline disease characteristics were balanced between risdiplam and placebo/risdiplam groups

	Risdiplam (n=120)	Placebo/risdiplam* (n=60)	Total (N=180)
Age at onset of symptoms, months, mean (SD)	14.1 (8.4)	18.5 (21.1)	15.5 (14.1)
Scoliosis, n (%)			
Yes	76 (63.3)	44 (73.3)	120 (66.7)
>40 degrees curvature	34 (28.3)	23 (38.3)	57 (31.7)
Surgery for scoliosis before screening, n (%)†			
Yes	29 (24.2)	17 (28.3)	46 (25.6)
No	63 (52.5)	33 (55.0)	96 (53.3)
Not recorded	28 (23.3)	10 (16.7)	38 (21.1)
MFM32 total score, mean (SD)	45.48 (12.09)‡	47.35 (10.12)§	46.11 (11.46)‖
RULM total score, mean (SD)	19.65 (7.22)¶	20.91 (6.41)**	20.06 (6.97)††
HFMSE total score, mean (SD)	16.10 (12.46)	16.62 (12.09)	16.27 (12.30)

*Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. †Surgery before screening is not a compulsory question and therefore some data are not available. ‡n=115. §n=59. ‖n=174. ¶n=119. **n=58. ††n=177.
Based on enrollment criteria, at least 56% of patients in SUNFISH Part 2 would have been ineligible for the CHERISH trial (CHERISH inclusion criteria included: age 2 to 12 years, baseline HFMSE score ≥10; and exclusion criteria included: severe scoliosis [>40 degrees curvature]). This percentage does not take into consideration patients with severe contractures [CHERISH exclusion criteria included any contracture that, according to the investigator, could interfere with HFMSE]).[1] Intent to treat patients. Data cut-off: 30 Sep 2020.
HFMSE, Hammersmith Functional Motor Scale – Expanded; MFM32, 32-item Motor Function Measure; RULM, Revised Upper Limb Module; SD, standard deviation.
1. Mercuri E, et al. N Engl J Med 2018; 378:625–635.

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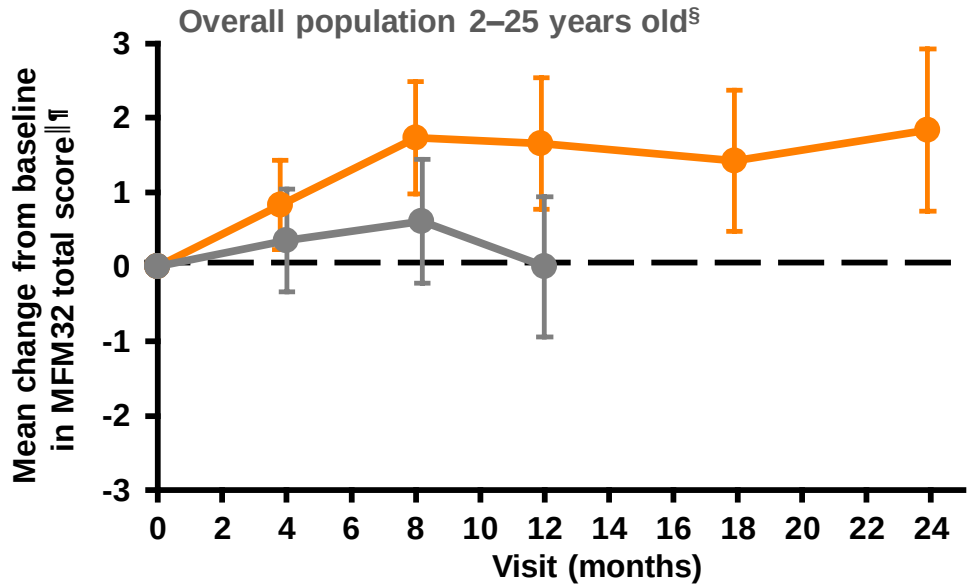
The increase in MFM32 total score from baseline was maintained between Month 12 and 24 in the risdiplam treatment arm; an overall decline was seen in natural history

SUNFISH Part 2: Patients treated with risdiplam over 24 months versus patients in placebo arm who received placebo for 12 months

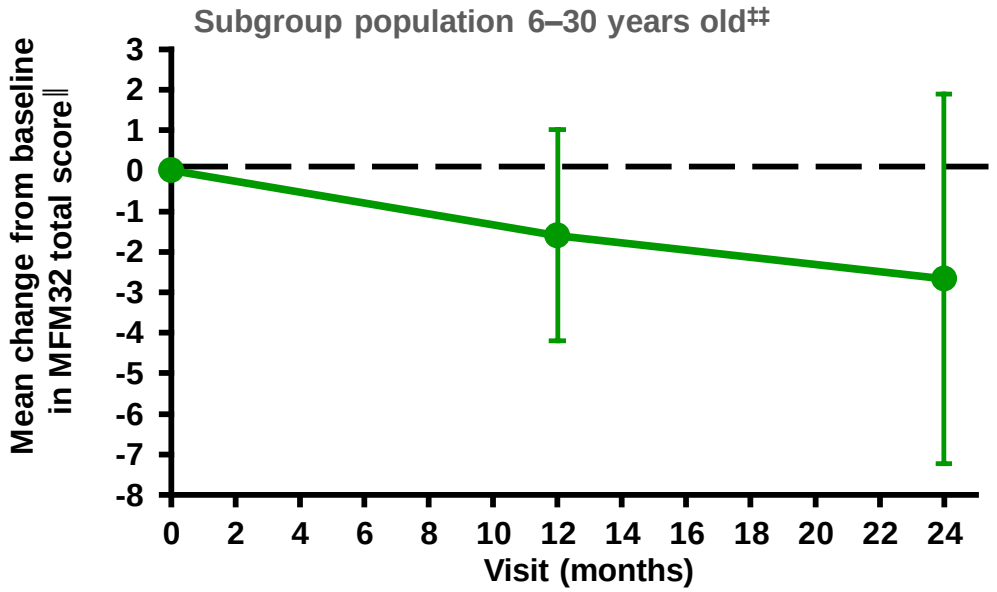
Risdiplam arm* (Months 0–24) **Placebo arm/placebo†‡** (Months 0–12)



Risdiplam (n)**	115	113	113	112	107	103
Placebo arm/ placebo (n)**	59	57	58	58		

NatHis-SMA††: Natural history study in sitters with Type 2 SMA and patients with non-ambulant Type 3 SMA over 24 months[1]

Sitters with Type 2 SMA and non-ambulant patients with Type 3 SMA



Sitters with Type 2 SMA and patients with non-ambulant Type 3 SMA (n)**	20	15	9

*Data cut-off: 30 Sep 2020. †Data cut-off: 6 Sep 2019. ‡Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. Risdiplam period not shown in this graph. §31% (55/180) of the SUNFISH intent-to-treat population were 2–5 years old at baseline. ‖+/- 95% CI. ¶Baseline is the last measurement prior to the first dose of risdiplam or placebo. **Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients. ††The NatHis-SMA study (NCT02391831) included nine study sites in Europe and 81 patients aged 2–30 years with Types 2 and 3 SMA.‡‡Patients aged 2–5 years old in the NatHis-SMA study were assessed using the MFM20 and were therefore not included in the data shown.
AIM, Association Institut de Myology; CI, confidence interval; MFM32, 32-item Motor Function Measure; NatHis, natural history; SMA, spinal muscular atrophy.
1. Roche data on file; courtesy of AIM.

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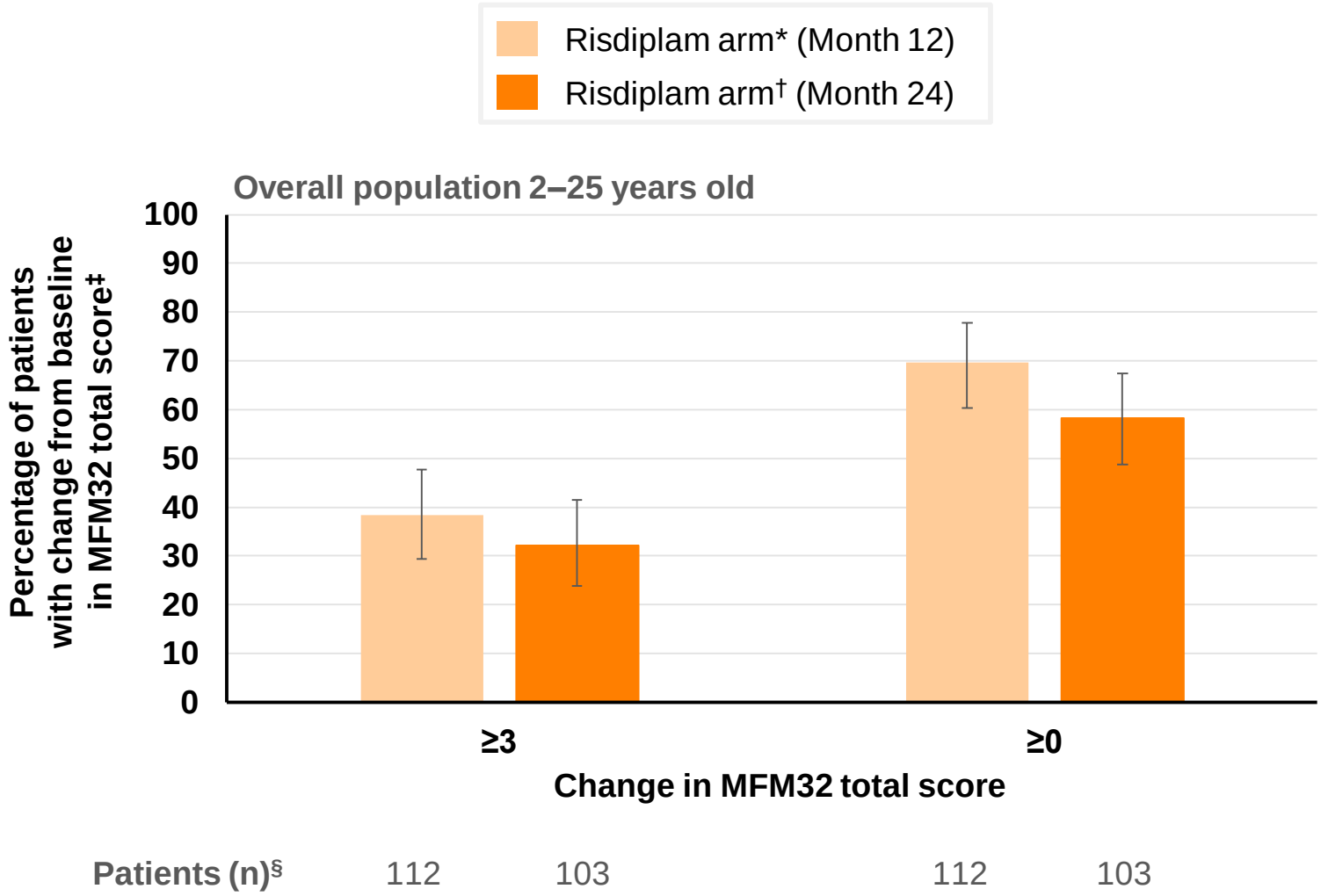
The percentage of patients improving or stabilizing from baseline in MFM32 score was similar between Month 12 and 24



*Data cut-off: 6 Sep 2019. †Data cut-off: 30 Sep 2020. ‡+/- 95% CI. **The percentage of patients is calculated by using the number of valid total scores at baseline as a denominator**. §Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients.
CI, confidence interval; MFM32, 32-item Motor Function Measure.

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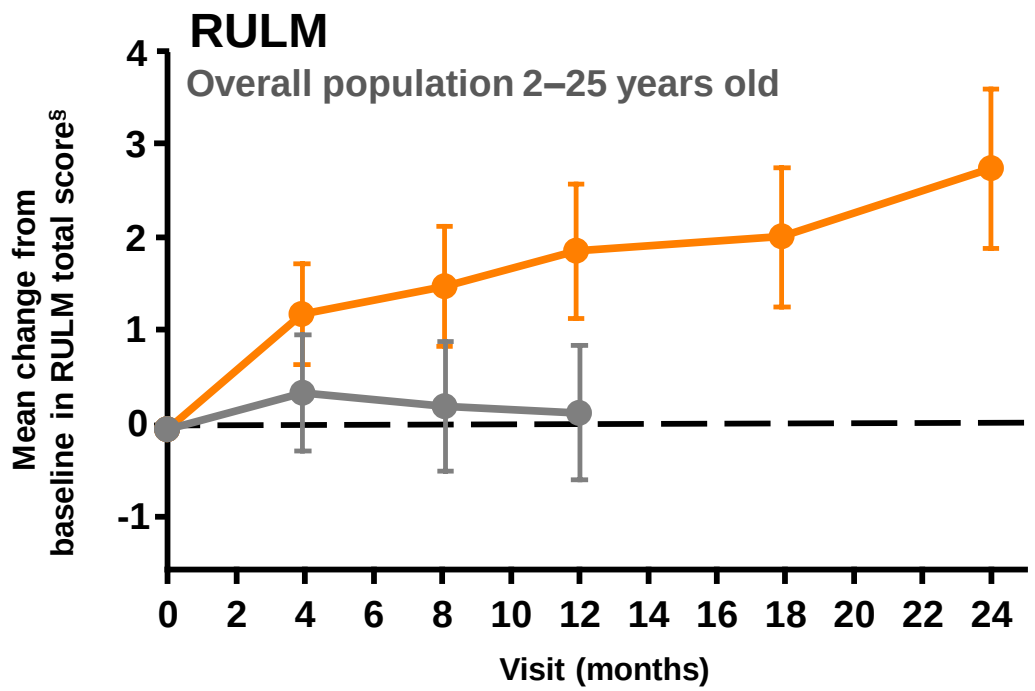
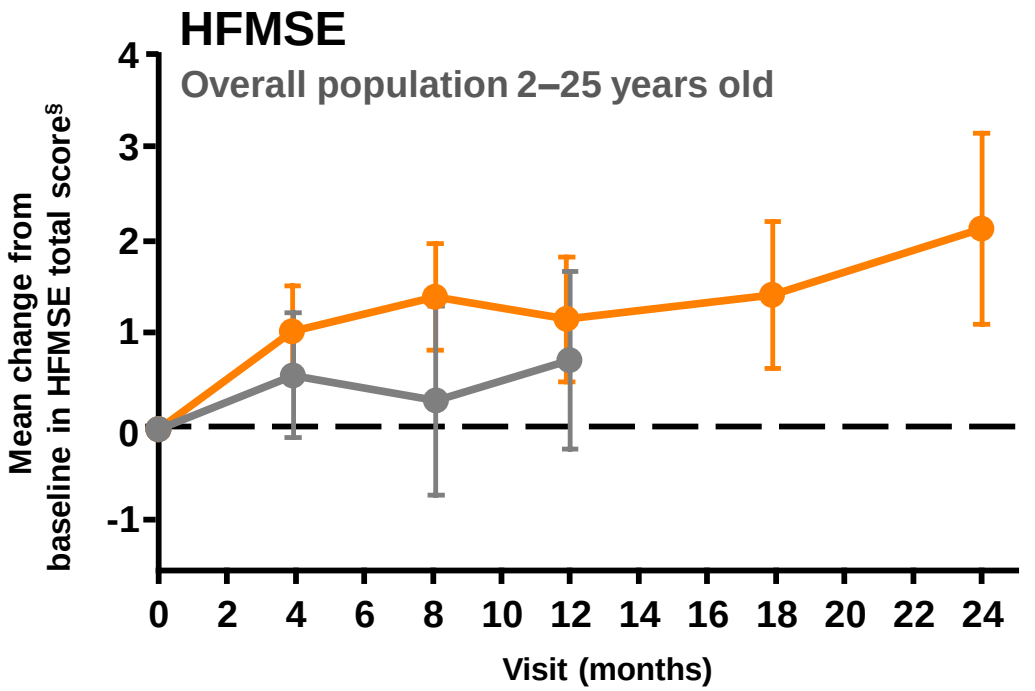
RULM and HFMSE total score change from baseline increased in patients receiving risdiplam for 24 months

Without treatment, patients with Types 2 and 3 SMA show a decline in RULM and HFMSE scores over time[1,2]

Risdiplam arm* (Months 0–24) **Placebo arm/placebo†‡** (Months 0–12)



Risdiplam (n)‖	119	119	117	116	108	105
Placebo arm/ placebo (n)‖	58	57	56	56		



Risdiplam (n)‖	120	120	119	117	109	106
Placebo arm/ placebo (n)‖	60	60	58	58		

*Data cut-off: 30 Sep 2020. †Data cut-off: 6 Sep 2019. ‡Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. Risdiplam period not shown in this graph. §+/- 95% CI. Baseline is the last measurement prior to the first dose of risdiplam or placebo. ‖Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients.
CI, confidence interval; HFMSE, Expanded Hammersmith Functional Motor Scale – Expanded; RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy.
1. Pera MC, et al. Muscle Nerve. 2019; 59:426–430; 2. Kaufmann P, et al. Neurology. 2012; 79:1889–1897.

Roche in collaboration with SMA FOUNDATION and PTC THERAPEUTICS

The SMAIS was developed to measure self-reported and caregiver-reported independence

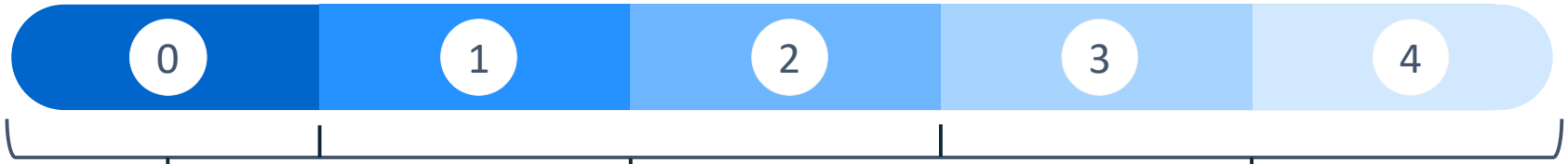
- The SMAIS is a scale developed with patients by Roche that measures the level of help patients with SMA need to carry out daily activities
- The SMAIS measures 29 items of daily living
  - The upper limb total score includes 22 of these items

The scale has been developed to incorporate both self-reported and caregiver-reported independence

Self reporting for individuals with SMA aged ≥12 years

Caregiver reporting on behalf of individuals with SMA aged ≥2 years

For each item of the 22-item upper limb total score, individuals/caregivers rated the level of help on a 0–4 scale, which was rescored to a 0–2 scale based on validation analyses



0

Individual not able to put on a shirt/jacket without help from another person

1

Individual needs help a lot or a moderate amount of help (e.g. putting arms into shirt jacket

2

Individual only needs a small amount of help (e.g. with buttons) or no help

The **SMAIS total score** combines the **22 items** into a single summary score ranging from 0–44

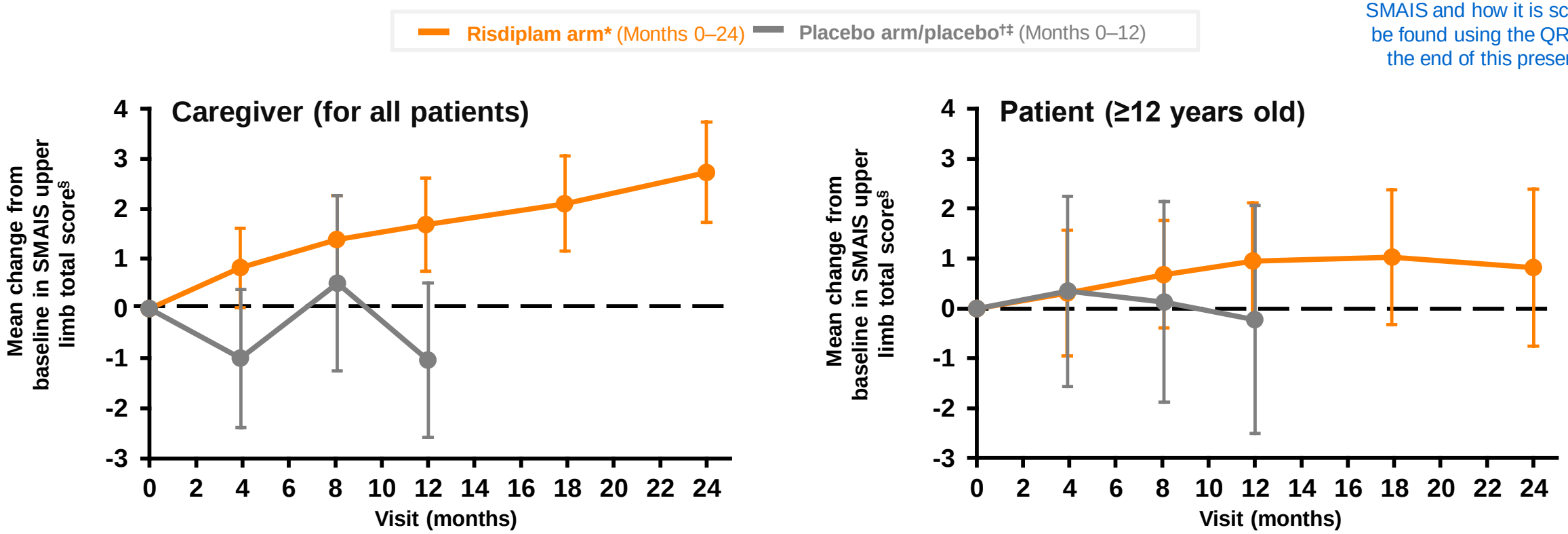
SMA, spinal muscular atrophy; SMAIS, SMA Independence Scale.

Trundell D, et al. J Neurol Sci 2020.

Roche in collaboration with SMA FOUNDATION and PTC THERAPEUTICS

Caregivers and patients reported continuous improvements or stabilization in the SMAIS upper limb total score change from baseline with risdiplam treatment over 24 months

Additional information on the SMAIS and how it is scored can be found using the QR code at the end of this presentation



Risdiplam (n)‖	116	114	114	112	108	103
Placebo arm/ placebo (n)‖	60	60	59	58		

Risdiplam (n)‖	43	42	41	43	39	39
Placebo arm/ placebo (n)‖	23	23	23	23		

*Data cut-off: 30 Sep 2020. †Data cut-off: 6 Sep 2019. ‡Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. Risdiplam period not shown in this graph. §+/- 95% CI. Baseline is the last measurement prior to the first dose of risdiplam or placebo. ‖Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients.
CI, confidence interval; SMA, spinal muscular atrophy; SMAIS, SMA Independence Scale.

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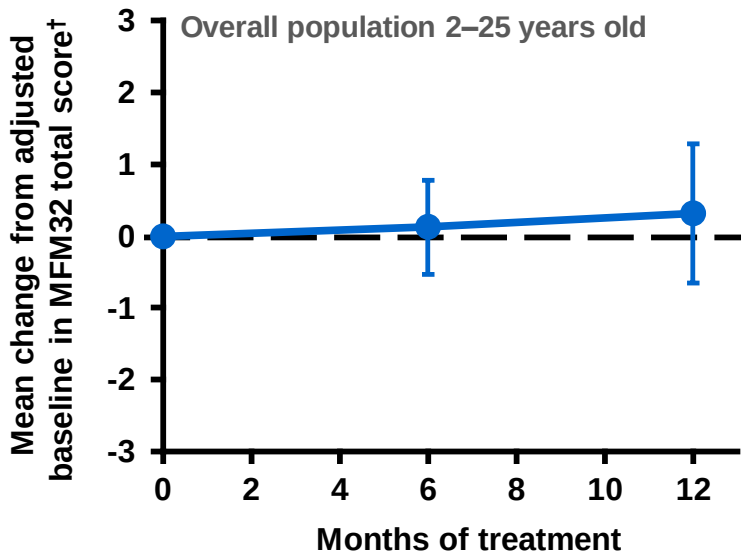
MFM32, RULM and HFMSE total score change from adjusted baseline was stable over 12 months in patients who switched from placebo to risdiplam

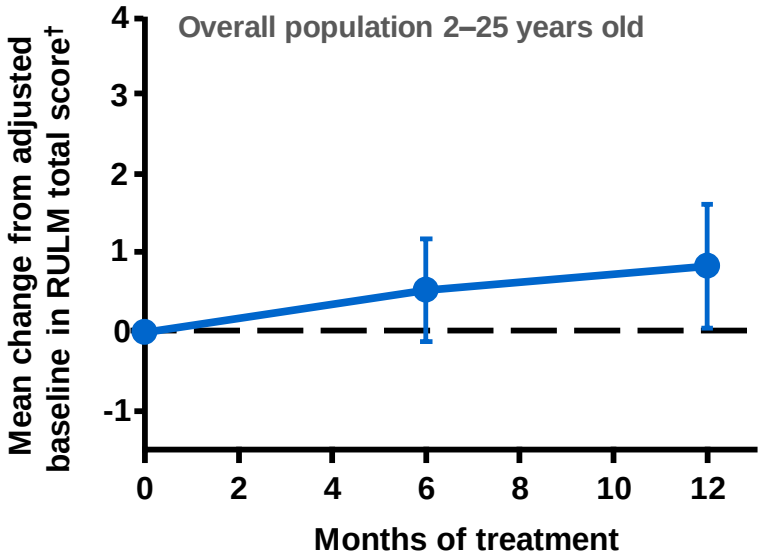
Without treatment, patients with Types 2 and 3 SMA show a decline in MFM, RULM and HFMSE scores over time[1-3]

Placebo arm switched to risdiplam, Months 12–24*

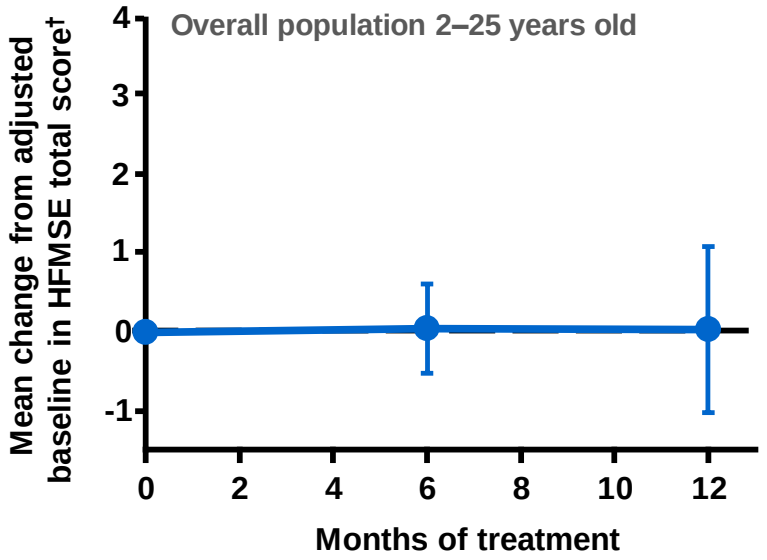
MFM32



RULM



HFMSE



Patients (n)‡									
	59	59	53	59	59	53	59	57	49

*Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. Placebo period not shown in this graph. †+/- 95% CI. Baseline is the last measurement prior to the first dose of risdiplam. ‡Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients. Data cut-off: 30 Sep 2020.

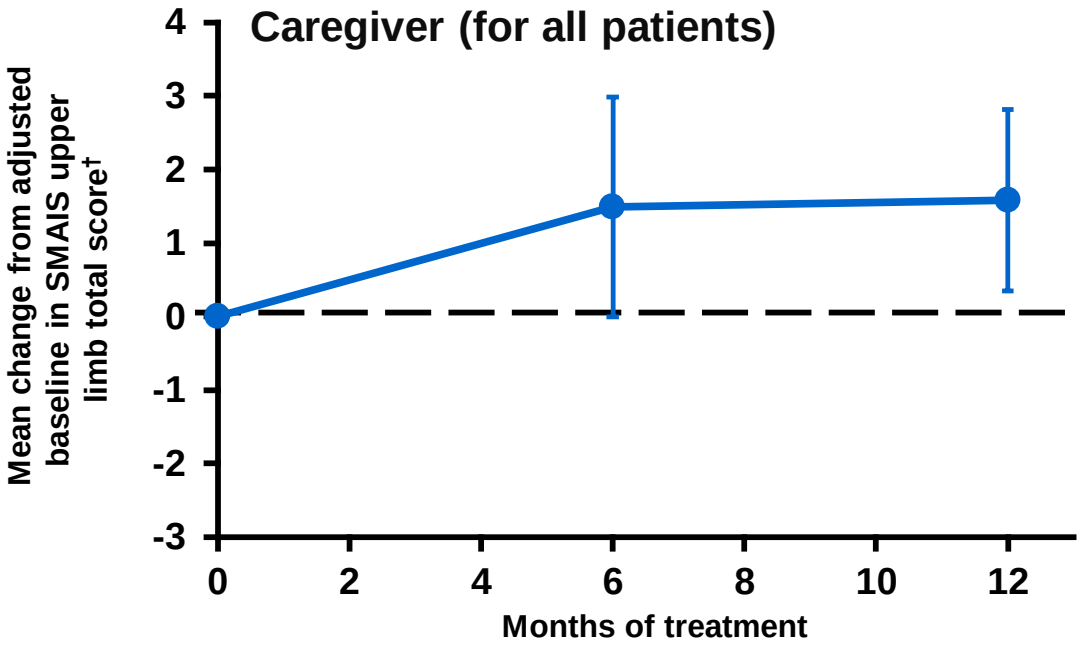
CI, confidence interval; HFMSE, Expanded Hammersmith Functional Motor Scale – Expanded; MFM32, 32-item motor function measure; RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy.

1. Annoussamy M, et al. Ann Clin Transl Neurol 2020; 8:359–373; 2. Pera MC, et al. Muscle Nerve. 2019; 59:426–430; 3. Kaufmann P, et al. Neurology. 2012; 79:1889–1897.

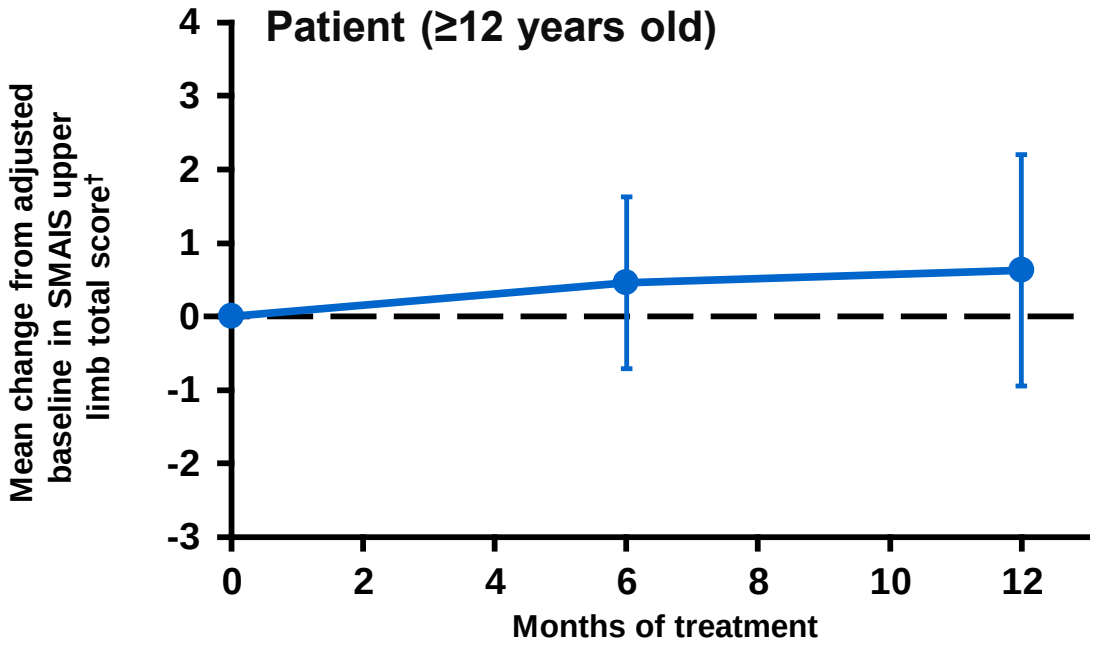
Roche in collaboration with SMA FOUNDATION and PTC THERAPEUTICS

SMAIS upper limb total score change from adjusted baseline increased or stabilized over 12 months in patients who switched from placebo to risdiplam

Placebo arm switched to risdiplam, Months 12–24*



Patients (n)‡	59	59	53



Patients (n)‡	24	24	24

*Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months. Placebo period not shown in this graph. †+/- 95% CI. Baseline is the last measurement prior to the first dose of risdiplam. ‡Number of patients with valid results = number of patients with an available total score (result) at respective time points. Intent to treat patients. SMA, spinal muscular atrophy; SMAIS, SMA Independence Scale. Data cut-off: 30 Sep 2020.

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The observed AE profile was reflective of underlying disease

		Risdiplam arm 0–12 months (n=120)*	Risdiplam arm 12–24 months (n=120)†	Placebo arm/placebo 0–12 months (n=60)*‡	Placebo arm/risdiplam 12–24 months (n=60)†‡
Most common AEs, n (number of patients [%])	Upper respiratory tract infection	38 (31.7)	19 (15.8)	18 (30.0)	6 (10.0)
	Nasopharyngitis	31 (25.8)	26 (21.7)	15 (25.0)	10 (16.7)
	Pyrexia	25 (20.8)	16 (13.3)	10 (16.7)	6 (10.0)
	Headache	24 (20.0)	12 (10.0)	10 (16.7)	10 (16.7)
	Diarrhea	20 (16.7)	9 (7.5)	5 (8.3)	6 (10.0)
	Vomiting	17 (14.2)	14 (11.7)	14 (23.3)	8 (13.3)
	Cough	17 (14.2)	12 (10.0)	12 (20.0)	5 (8.3)
Most common SAEs, n (number of patients [%])	Pneumonia	9 (7.5)	8 (6.7)	1 (1.7)	0 (0)
	Influenza	2 (1.7)	1 (0.8)	0 (0)	0 (0)

- Decreases in AEs, Grade 3–5 AEs, and treatment-related AEs were observed in both arms during 12–24 months compared with 0–12 months§
- There have been no treatment-related AEs leading to withdrawal or treatment discontinuation
- Ophthalmologic monitoring has not shown any evidence in humans of the retinal findings seen in preclinical monkey studies
- Hematologic parameters have remained stable over time and no drug-induced skin findings have been observed

*Data cut-off: 6 Sep 2019. †Data cut-off: 30 Sep 2020. ‡Patients in the placebo arm received placebo for 12 months followed by risdiplam treatment for 12 months.. §One patient withdrew from treatment after the CCOD due to an AE of transaminitis initially reported as related to risdiplam, which was reassessed after discontinuation as unrelated to risdiplam. Safety-evaluable patients.
AE, adverse event; CCOD, clinical cut-off date; SAE, serious AE.

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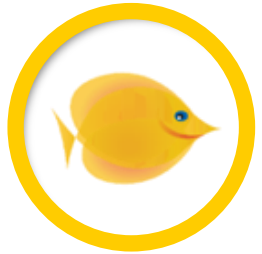
Conclusions from SUNFISH Part 2 at 24 months



Roche

Motor function was stable or showed continued improvement during the second year of treatment with risdiplam (as measured by change in MFM32, RULM and HFMSE)

Continuous improvement or stabilization in the level of help needed for activities in daily living beyond the first year was reported using the SMAIS measure

MFM32, RULM, HFMSE and SMAIS change was stable over 12 months in patients who switched from placebo to risdiplam treatment

A decrease in AEs was observed during the second year in both risdiplam and placebo/risdiplam arms

The gains observed with risdiplam treatment at Month 12 were maintained or improved upon at Month 24

These results are an important milestone confirming longer-term efficacy and safety of risdiplam in a broad population of individuals with Type 2 and non-ambulant Type 3 SMA

AE, adverse event; HFMSE, Expanded Hammersmith Functional Motor Scale – Expanded; MFM32, 32-item Motor Function Measure; RULM, Revised Upper Limb Module; SAE, serious AE; SMA, spinal muscular atrophy; SMAIS, SMA Independence Scale.
Please scan using your QR reader application to access the graphs and data presented in this presentation.
NB: there may be associated costs for downloading data. These costs may be high if you are using your smartphone abroad. Please check your mobile data tariff or contact your service provider for more details. Alternatively this can be accessed at: https://bit.ly/3pdYfyI.

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Acknowledgments

Many thanks to all the patients who participate in these studies and their families, healthcare professionals and the support of patient groups throughout the world

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Roche Neuroscience and Rare Disease franchise update

Simona Skerjanec

Therapeutic Area Head Neuroscience and Rare Diseases, Global Product Strategy

Roche: Broad pipeline leading the way to first in class medicines in neuroscience and rare diseases

NeuroImmunology

Multiple Sclerosis
Ocrevus

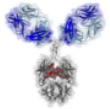
First B-cell targeted therapy

NMOSD
Enspryng

First recycable IL6-mAb, SC q4w dosing

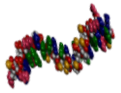
NeuroDegeneration

Alzheimer disease
gantenerumab



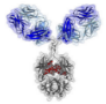
First anti-Aβ mAb, SC convenience

Huntington's disease
HTT-ASO



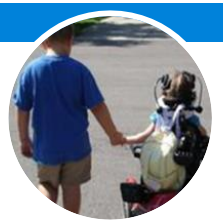
First antisense drug to reduce toxic mHTT

Parkinsons's disease
prasinezumab

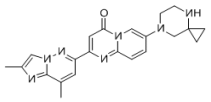


First mAB targeting pathogenic α-synuclein

NeuroMuscular



SMA
Evrysdi



First and only oral DMT in SMA T1/2/3

DMD
SRP-9001
(Sarepta)

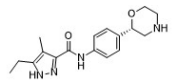
First micro-dystrophin gene therapy to express potentially functional protein

NeuroDevelopment & Psychiatry

Angelman syndrome
UBE3A LNA

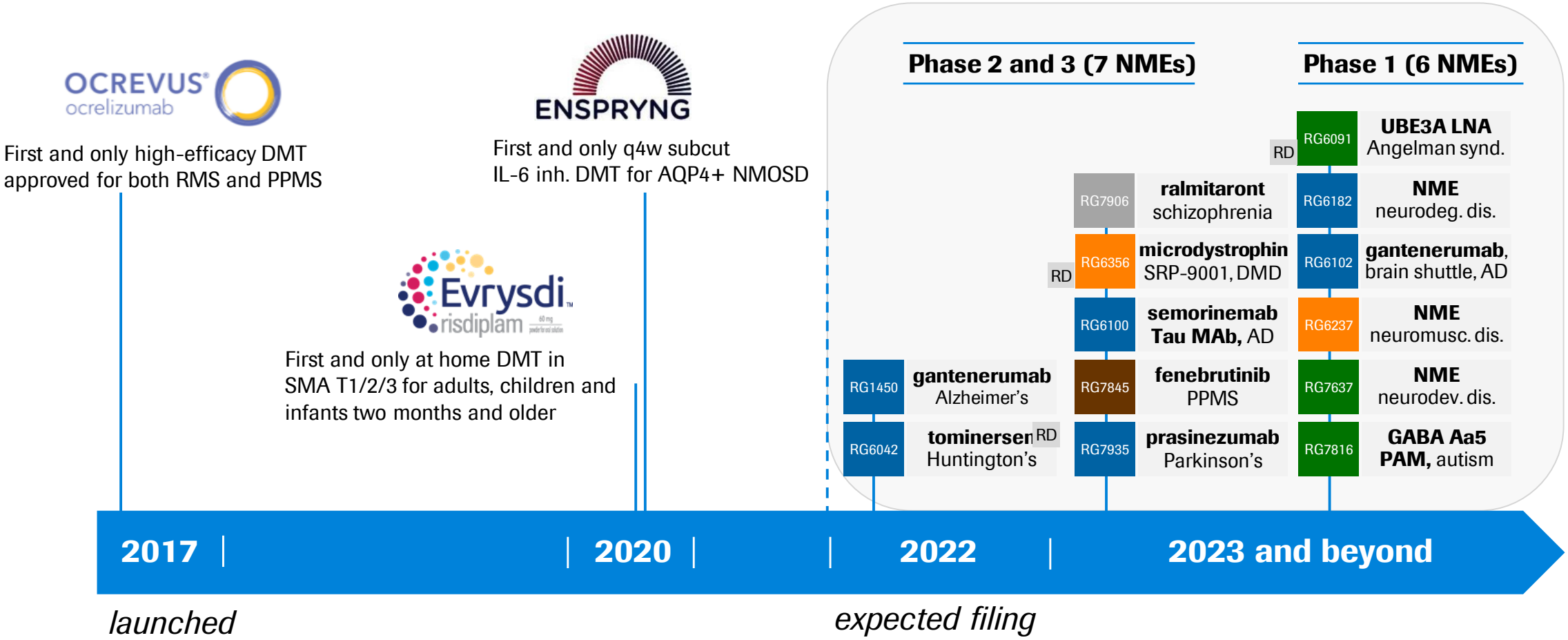
First in class antisense oligonucleotide activating paternal gene to produce functional protein

Schizophrenia
ralmitaront



First state-dependent modulator of monoaminergic neurotransmission

Roche: Strong momentum with successful launches in MS, SMA and NMOSD



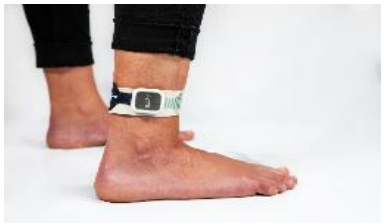
Neuro-immunologic disorders | Neuro-degenerative disorders | Neuro-developmental disorders | Neuro-muscular disorders | Psychiatric disorders

RD = Rare Diseases

Roche: Better decision making using digital technology

Continuous and longitudinal measurements to capture episodic and rare events

Duchenne muscular dystrophy: First-of-its-kind endpoint* for digital health tech qualified by EMA

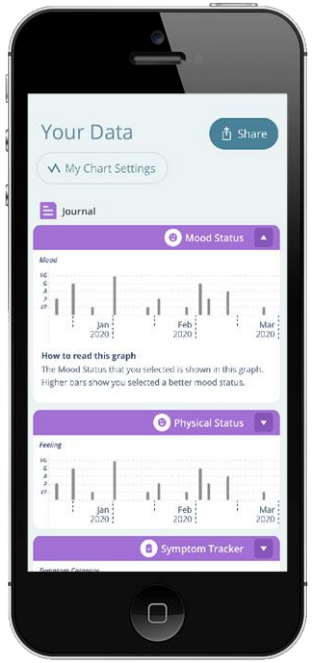


sysnav
NAVIGATION TECHNOLOGIES

- Traditional outcome measures for DMD limited by patient motivation
- First wearable qualified by EMA as a sensitive, precise, and objective measure of a patient's ability to ambulate at home
- Disease-agnostic technology allows for broad portfolio deployment
- Partnership with SYSNAV

Launch of Floodlight MS: Seeing beyond the surface of living with MS

floodlight ms



- Captures impact on function between clinic visits that might otherwise go unobserved
- Collects objective data across 3 key neurological domains; app easily accessible on a smartphone
- Complements the clinical interview with objective documentation and may inform HCP decisions
- 2021 launch in 10+ countries

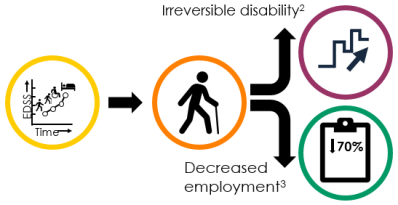
*Stride Velocity 95th Centile (SV95C): qualified novel endpoint for remote real-world monitoring of how well a patient can ambulate.

MS franchise: Ocrevus shifting the standard of care

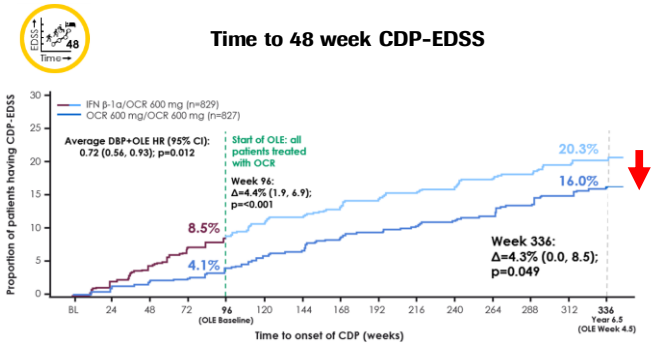
>200,000 patients treated globally

Robust, consistent, sustained impact on slowing disability

RMS: Ph III (OPERA) 6.5-year follow-up

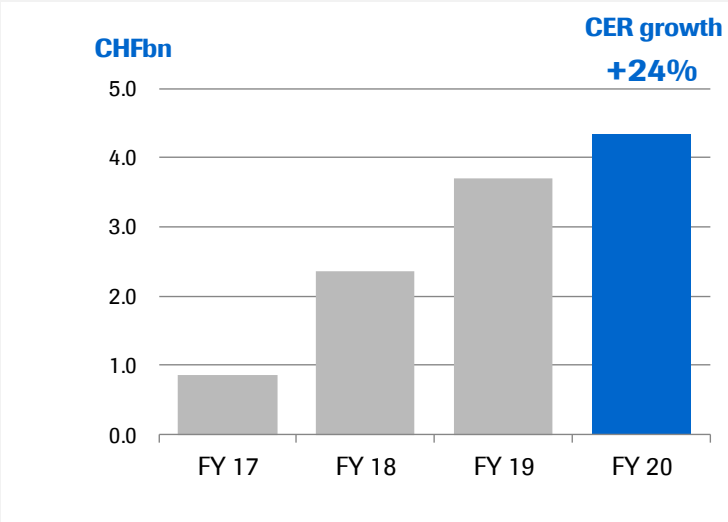


Reaching EDSS score ≥6.0, a key clinical disability milestone representing the requirement of a walking aid, which is associated with increased patient and societal burden



- RMS patients on Ocrevus over 6.5 yrs had a 46% reduction in the risk of needing a walking aid vs those who switched over from IFN β-1α treatment at the end of the double-blind period (p=0.004)

2020 global sales: CHF 4,326m

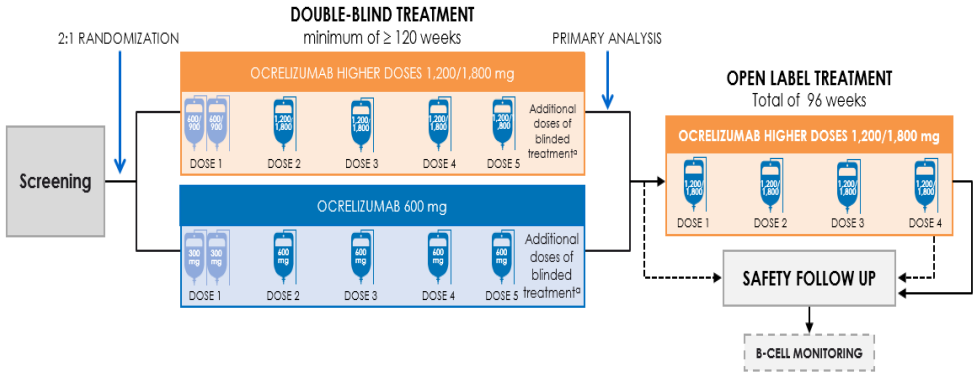


- Ocrevus with 25% total US market share
- US new patient share remains ~40%
- Q4 growth despite COVID-19 and carry over from Q2 (1st wave)
- Expect growth to continue in 2021
- Launches in EU and International ongoing

MS franchise: Changing the course of the disease

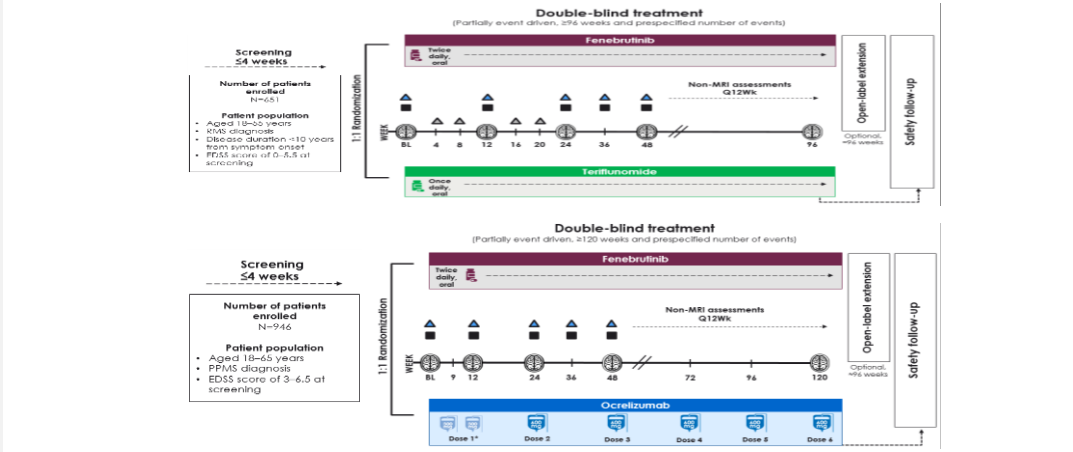
Extensive clinical development ongoing in RMS and PPMS

Ocrevus Ph III higher-dose studies in RMS and PPMS



- Exposure/response analysis suggests a higher dose could further lower the risk of disability progression without compromising safety
- Two double-blind, randomized Ph III studies MUSETTE in RMS and GAVOTTE in PPMS started in 2020

Fenebrutinib Ph III program in RMS and PPMS



- Highly differentiated and potentially best-in-class BTKi in MS
- Ph III FENtrepid in PPMS FPI Q4 2020
- Ph III studies FENHance I & II in RMS FPI expected Q1 2021
- Primary endpoint is composite Confirmed Disability Progression 12 (cCDP12); co-primary endpoint in RMS is ARR

Hauser S.L. et al, ACTRIMS-ECTRIMS 2020; 24W-CDP=24 week confirmed disability progression; AAR=annual relapse rate; MRI=magnetic resonance imaging; RMS=relapsing multiple sclerosis; PPMS=primary progressive MS; OLE=open label extension

NMOSD: Enspryng launched in 16 countries to date

Differentiated profile for a rare and debilitating autoimmune CNS disease

ENSPRYNG is the first and only approved treatment designed to target and inhibit the IL-6 receptor activity

~5	Per 100,000
1/2	Blind within 5 years Require wheelchair
9/1	Female/male prevalence

IL-6 is a key driver in the pathogenesis of NMOSD

Highly effective
Robust efficacy, significant reduction of the risk of relapse across a broad patient population

Flexible and convenient
Q4w SC dosing at home
Studied as monotherapy or combination with immunosuppressants

Well tolerated safety profile
No black box warning; lower rate of infections incl. serious infections than placebo group

Competitively priced
Priced 72% below eculizumab and 27% below inebilizumab after first year (US)

US Launch performance to date

- US launch ongoing as planned with over >130 patient enrollments* to date
- Favorable payer coverage with ~60% of lives covered 1L
- ENSPRYNG efficacy and flexible SC dosing garners positive feedback from advocates and patients ratings: 4.5/5 or better**

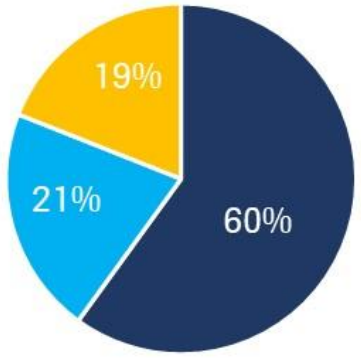
AQP4=aquaporin 4; MOA=mechanism of action, **Genentech Access Solutions enrollments, **Genentech internal data on file*

SMA: Leading genetic cause of death and disability in children

Majority of patients untreated today despite treatment options

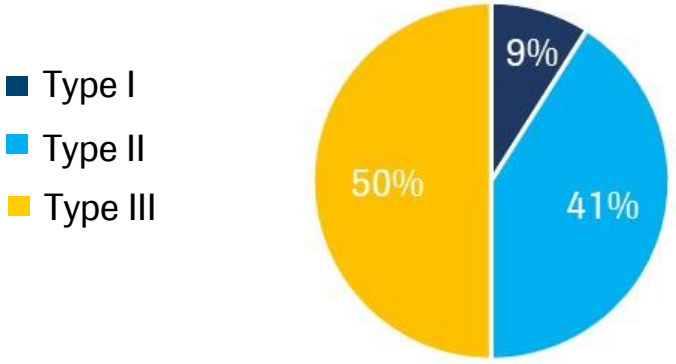
- Autosomal recessive neuromuscular disorder (SMN1 gene)
- ~1:11,000 live births; ~18,000 patients in EU & US*
- Prevalence likely to increase as treatments become available

Type I: highest incidence.



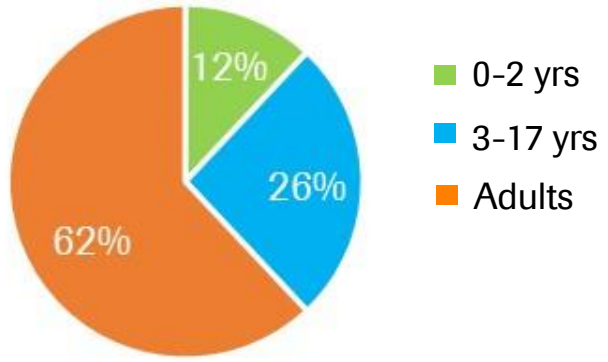
SMA incidence by Type

Type II & III: >90% of overall prevalence.



SMA prevalence by Type

Adults: >60% of patients



SMA incidence by Age

*Incidence and prevalence data from Verhaart et al. Orphanet Journal of Rare Diseases (2017) 12:124.

SMA: Significant unmet needs remain despite current treatments

Key barriers to treatment most pronounced in adults

Population	0–2 years	3–17 years	18+ years
Disease severity			
Body of evidence			
Access to treatment			

High unmet need Medium unmet need Low unmet need

Evrysdi in Type 1/2/3 SMA		
Clinically meaningful efficacy	2mo -2 years	✓
	3–17 years	✓
	18+ years	✓
Breadth of data *Heterogenous population studied*		✓
Sustained benefit *Sustainable elevation of SMN protein*		✓
SMN protein increased *throughout CNS and in peripheral tissues*		✓
At home administration *Low burden on patients, caregivers and health care system*		✓

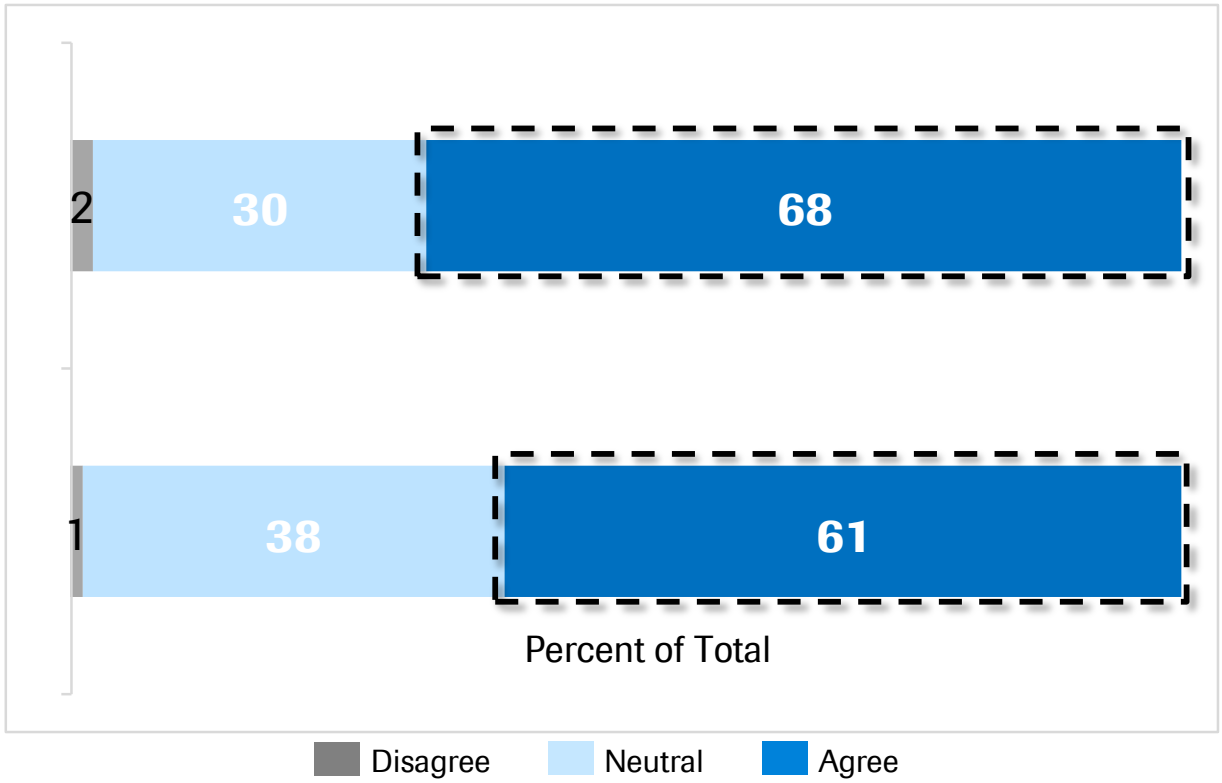
Evrysdi has demonstrated a compelling benefit/risk profile in infants, children and adults

Source: Roche internal estimates

Two thirds of neurologists believe in the importance of targeting SMN protein throughout the CNS as well as the periphery

Evrysdi durably increases SMN protein throughout the CNS and in peripheral tissues

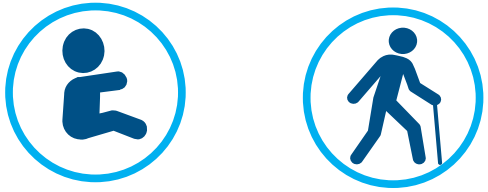
Neurologist attitudes toward need for SMA treatment to impact SMN in periphery



Source: Q1 2021 SMA Partnership & Perception Monitor Study, n = 237 neurologists in US, EU5, Brazil, Canada and China
Question: To what extent do you agree with the following statements?

Evrysdi – potential to be preferred SMA treatment option for patients, doctors and payers

Patients



Appropriate for a broad range of SMA patients
Clinical studies included Types 1, 2 and 3

Broad range of ages
2m old infants to 70+ year old adults

Oral (liquid) at home formulation
Easy at-home administration from first dose

Doctors (neurologists, HCPs)

Compelling benefit / risk profile
Proven across SMA Types, varying disease severity & ages

Real-world spectrum of SMA patients
Including severe scoliosis, contractures, etc.

Well tolerated across trials
No treatment-related safety findings have led to withdrawal in any study

Payers

Clear value proposition
Shown across broad patient segments

Responsible pricing
Supporting broad access

No administration costs
Oral administration, no need for in hospital administration, anesthesia or hospitalization

Launches on track and moving at pace around the globe

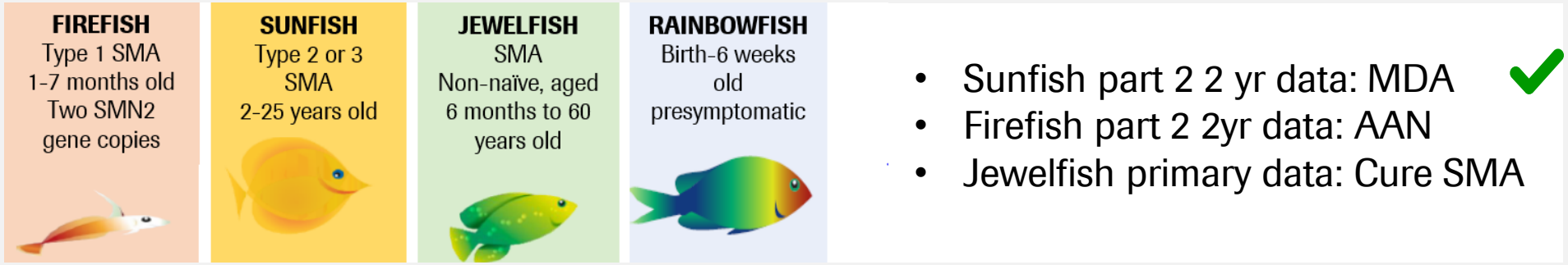
Important data milestones to be presented throughout 2021

- FDA approved since Aug 2020; >1000 SMA patients treated, i.e. >10% total share within first 6 months
- Patients treated with all SMA types - 25% type 1, 50% type 2, 25% type 3
- Fastest uptake of a DMT in SMA
- >2500 patients treated worldwide between clinical trials, commercial, and compassionate use program

- CHMP positive opinion received 25 Feb 2021; on track for EMA approval H1 2021

- China approval expected H1 2021

Upcoming data presentations:



- Sunfish part 2 2 yr data: MDA ✔
- Firefish part 2 2yr data: AAN
- Jewelfish primary data: Cure SMA

Doing now what patients need next

Multiple motor function endpoints included in SUNFISH Part 2

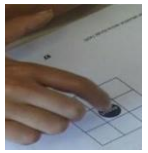
MFM32: selected as **primary endpoint** due to its expected sensitivity for a broad SMA population

- Validated, reliable, and easy-to-conduct test to measure motor function in SMA.
- 32 items classified into 3 domains with a total score of 0–100; higher scores indicate greater motor function.

Domain 1:
standing, transfers and ambulation

Domain 2:
axial and proximal motor function

Domain 3:
distal motor function



RULM (Revised Upper Limb Module): **Secondary EP**

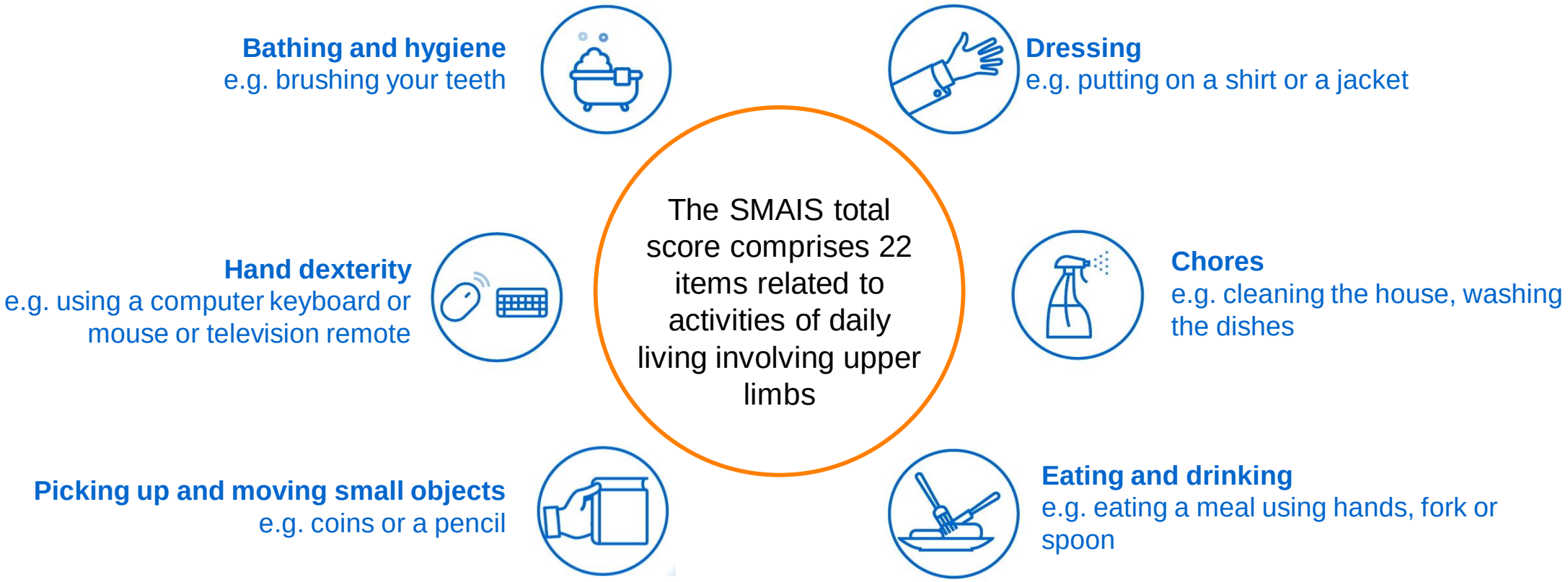
- Next most important endpoint in SUNFISH SAP (after MFM32) due to its focus on upper limb function – especially relevant for a non-ambulant population.
- 19 items scored in a total score of 0-37; higher scores indicate greater upper limb function.
- Items assessed include moving hands from lap to table, bringing a cup to the mouth, as well as items involving weighted objects.

HFMSE (Expanded Hammersmith Functional Motor Scale): **Secondary EP**

- Third ranked endpoint in SUNFISH SAP due to its anticipated lower sensitivity in weaker patients.
- 33 items resulting in a total score of 0 – 66; higher scores indicate greater motor function.
- Items assessed include sitting, rolling, crawling, standing, walking, squatting, jumping and going up and down stairs.

EP= End Point; SAP=statistical analysis plan

The SMAIS was developed to measure self-reported and caregiver-reported independence



SMA, spinal muscular atrophy; SMAIS, SMA Independence Scale.