Zorevunersen demonstrates disease-modifying potential in patients with Dravet syndrome with improvements in seizure burden, quality of life, and overall clinical status

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Speaker disclosures: Biocodex, Vitaflo, GW Pharmaceuticals / Jazz, Zogenix/UCB, Stoke Therapeutics, Encoded, Servier, Neuraxpharm, Harmony Biosciences, GRIN Therapeutics, Ultragenyx, Lundbeck Advisory board and clinical investigator, all monies to department

These studies were supported by Stoke Therapeutics. Medical writing and editorial assistance for this presentation were funded by Stoke Therapeutics and Biogen and were provided by Porterhouse Medical US according to Good Publication Practice guidelines. Data have been updated since abstract acceptance.

Dravet syndrome: A severe genetic developmental and epileptic encephalopathy

>90% of DS cases are caused by ***SCN1A* gene variants →**
reduced functional $Na_V1.1$ expression[1–4]

1 out of ~16,000 babies are born with DS[5]

Patients experience refractory seizures, including GTC and focal-to-BTC seizures, and **significant cognitive and behavioural deficits**[6]

Current ASMs only target seizures; **up to 57% of patients fail to achieve ≥50% reduction in seizure frequency**[7–13]

No approved treatments for non-seizure symptoms[10–13]

Cognition **Communication** **Behaviour** **Movement**

Natural history data show widening gaps in adaptive functioning and neurodevelopment vs. population norms[6]

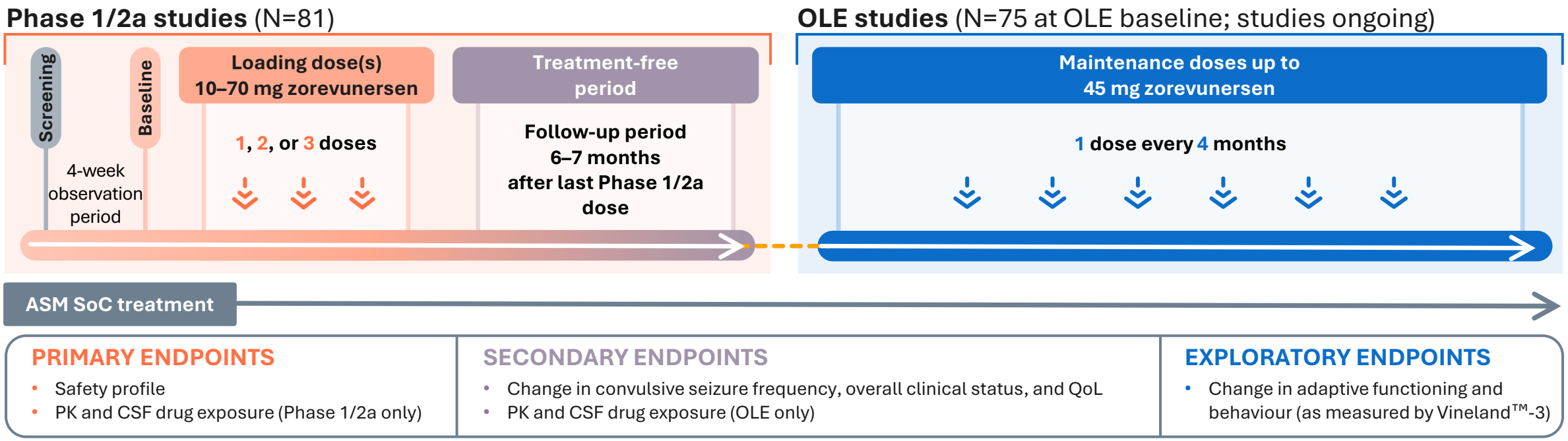
Urgent need for **disease-modifying therapies addressing the underlying genetic cause of DS** to improve both seizure AND non-seizure symptoms[10]

Zorevunersen is an investigational ASO that is designed to **upregulate $Na_V1.1$ protein expression** via the wild-type copy of the *SCN1A* gene[14,15]

ASM, antiseizure medication; ASO, antisense oligonucleotide; BTC, bilateral tonic-clonic; DS, Dravet syndrome; GTC, generalised tonic-clonic; *SCN1A,* voltage-gated sodium channel alpha subunit 1.

1. Balestrini S *et al. CNS Drugs* 2026; 40 (4): 535–548. 2. Li W *et al. Epilepsia* 2021; 62 (9): 2205–2217. 3. Gertler TS *et al. Seizure* 2020; 75: 1–6. 4. Bechi G *et al. Epilepsia* 2012; 53 (1): 87–100. 5. Wu YW *et al. Pediatrics* 2015; 136 (5): e1310–e1315. 6. Sullivan J *et al. Neurology* 2025; 105 (11): e214388. 7. Devinsky O *et al. N Engl J Med* 2017; 376 (21): 2011–2020. 8. Sullivan J *et al. Epilepsia* 2023; 64 (10): 2653–2666. 9. Guerrini R *et al. Neurol Ther* 2024; 13 (3): 869–884. 10. Wirrell EC *et al. Epilepsia* 2022; 63 (7): 1761–1777. 11. Biocodex, Inc. DIACOMIT – prescribing information; 2026. 12. UCB, Inc. FINTEPLA – prescribing information; 2025. 13. Jazz Pharmaceuticals plc. EPIDIOLEX – prescribing information; 2026. 14. Isom LL *et al. Neurotherapeutics* 2021; 18 (3): 1524–1534. 15. Lim KH *et al. Nat Commun* 2020; 11 (1): 3501.

Phase 1/2a and OLE studies investigating zorevunersen safety, PK, and efficacy in children and adolescents with Dravet syndrome



PRIMARY ENDPOINTS

- Safety profile
- PK and CSF drug exposure (Phase 1/2a only)

SECONDARY ENDPOINTS

- Change in convulsive seizure frequency, overall clinical status, and QoL
- PK and CSF drug exposure (OLE only)

EXPLORATORY ENDPOINTS

- Change in adaptive functioning and behaviour (as measured by Vineland™-3)

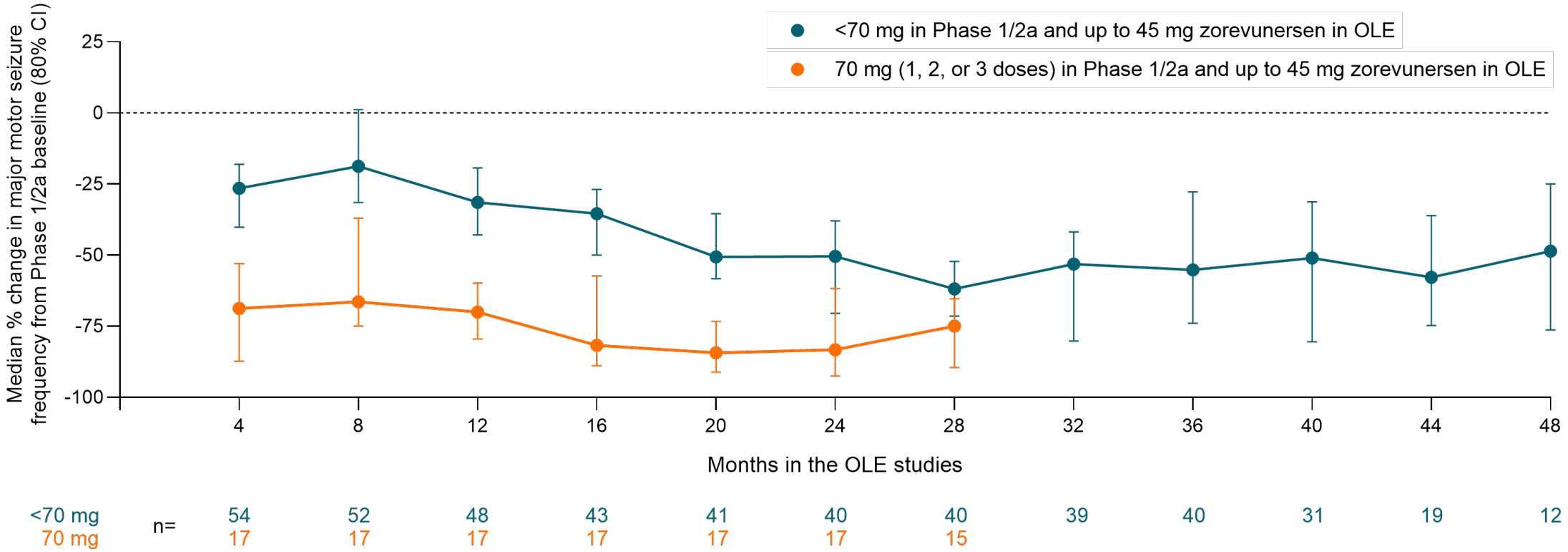
Baseline concomitant ASMs[1]

- **81% patients on ≥3 ASMs; 51% on ≥4 ASMs**
- Most common ASMs: Clobazam (70%), fenfluramine (49%), cannabidiol (44%), and valproate compounds (44%)

Phase 1/2a studies: NCT04442295 (USA) and 2020-006016-24 (UK). OLE studies: NCT04740476 (USA) and 2021-005626-14 (UK). Vineland™ is a trademark of NCS Pearson, Inc. This presentation was prepared by Stoke Therapeutics and Biogen. Stoke Therapeutics and Biogen are not affiliated with, sponsored by, or endorsed by Pearson, and Pearson has not reviewed or approved this presentation.
ASM, antiseizure medication; CSF, cerebrospinal fluid; OLE, open-label extension; PK, pharmacokinetics; QoL, quality of life; SoC, standard of care; Vineland-3, Vineland Adaptive Behavior Scales – Third Edition.
1. Laux L *et al. N Engl J Med* 2026; 394 (10): 969–982.

Reductions in major motor seizure frequency were maintained through 4 years of treatment with zorevunersen on top of SoC in the OLE studies

Most substantial seizure reductions seen in patients who received 70 mg Phase 1/2a regimens



At baseline, 81% of patients were on ≥3 ASMs; 51% were on ≥4 ASMs[1]

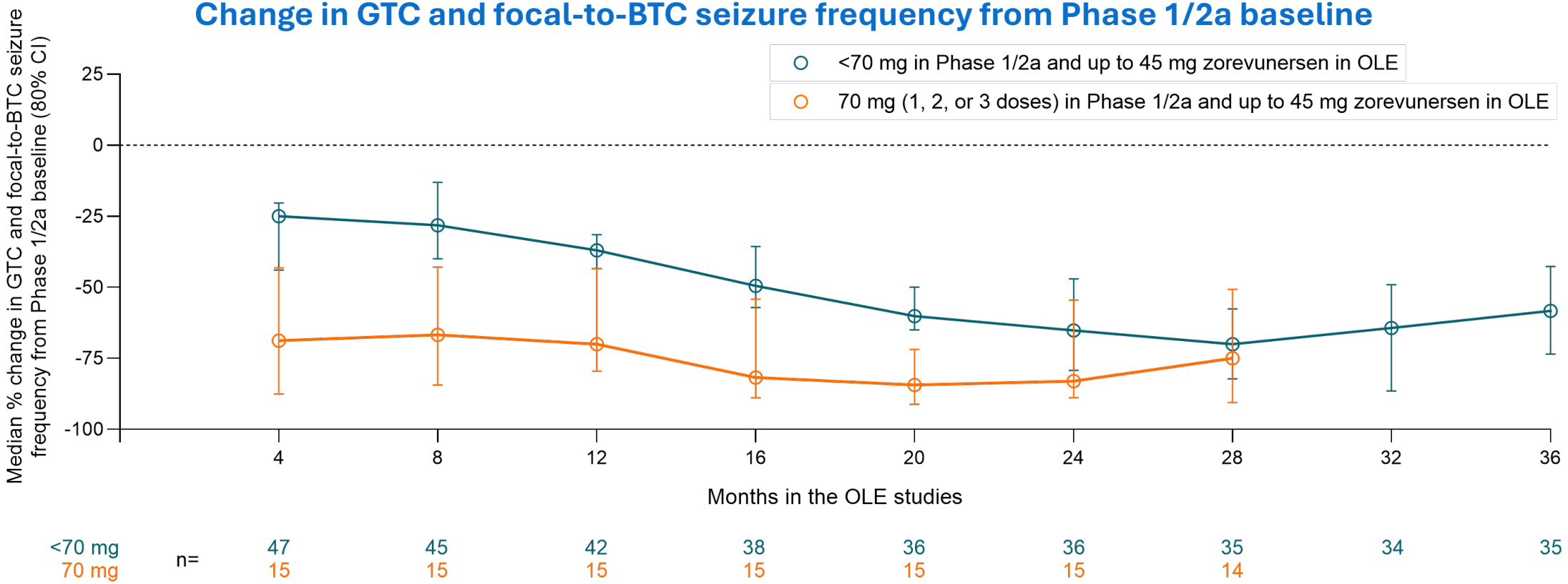
Data cut date: 19 February 2026. Analysis performed using available data from patients in the seizure evaluable set of the SWALLOWTAIL and LONGWING OLE studies (N=71), with n=12 to 54 patients in the <70 mg group and n=15 to 17 patients in the 70 mg (1, 2, or 3 doses) group having evaluable percent change-from-baseline data across visits. 1 month = 4 weeks. Major motor seizures are defined as hemiclonic, focal with motor signs, focal-to-bilateral tonic–clonic convulsion, generalized tonic–clonic convulsion, tonic, tonic/atonic (drop attacks), and clonic. Reported data show changes in major motor seizure frequency per 28 days from Phase 1/2a baseline.

ASM, antiseizure medication; CI, confidence interval; OLE, open-label extension; SoC, standard of care.

1. Laux L *et al. N Engl J Med* 2026; 394 (10): 969–982.

Frequency of the most severe seizure types was reduced following treatment with zorevunersen in the OLE studies

Change in GTC and focal-to-BTC seizure frequency from Phase 1/2a baseline

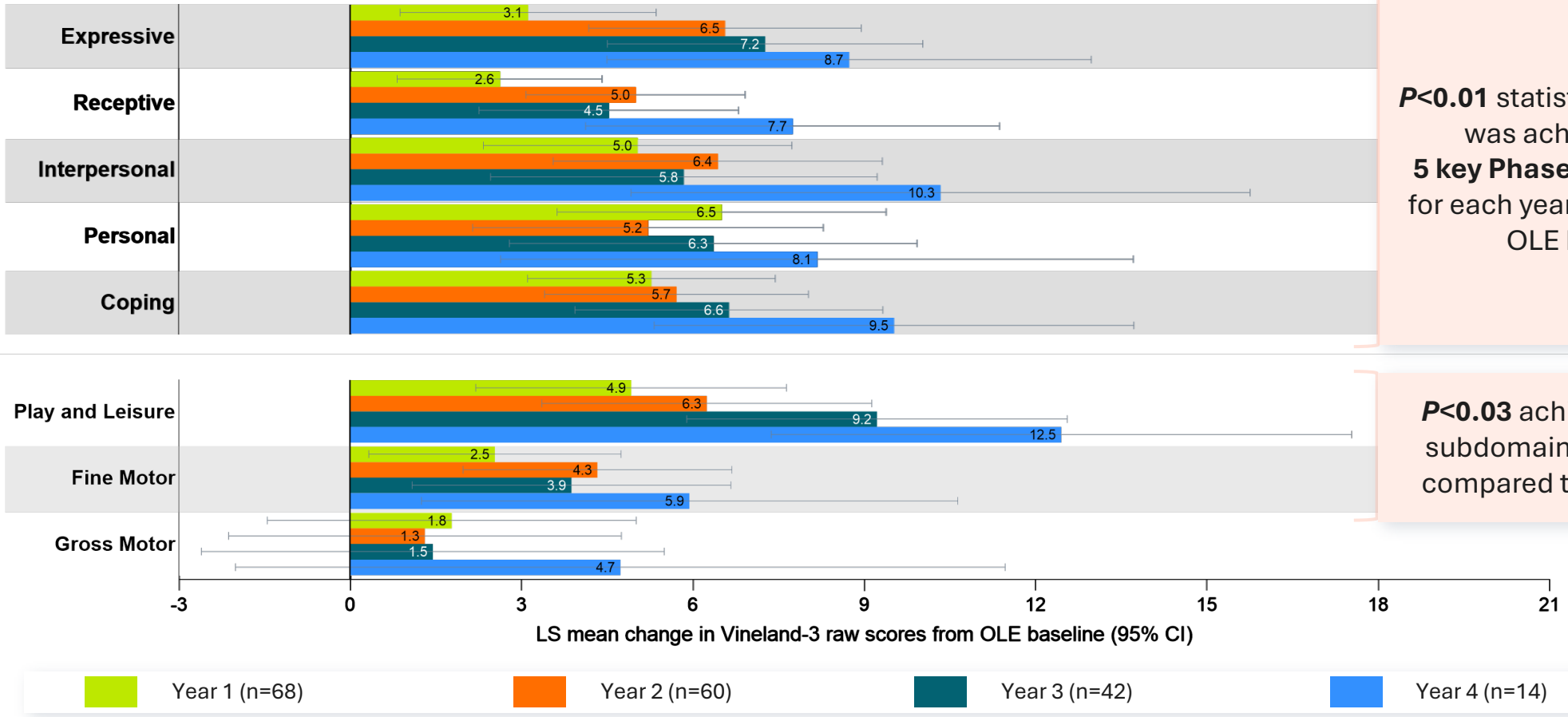


These severe seizure types are the leading risk factor for SUDEP (≥3 GTC seizures per year OR: 15.46)[1–3]

Data cut date: 19 February 2026. Analysis performed using available data from patients in the seizure evaluable set of the SWALLOWTAIL and LONGWING OLE studies (N=71), with n=34 to 47 patients in the <70 mg group and n=14 to 15 patients in the 70 mg (1, 2, or 3 doses) group having evaluable percent change-from-baseline data across visits. 1 month = 4 weeks. Reported data show changes in GTC and focal-to-BTC seizure frequency per 28 days from Phase 1/2a baseline.
BTC, bilateral tonic–clonic; CI, confidence interval; GTC, generalised tonic–clonic; OLE, open-label extension; OR, odds ratio; SUDEP, sudden unexpected death in epilepsy.
1. Harden C *et al. Neurology* 2017; 88 (17): 1674–1680. 2. Devinsky O *et al. Lancet Neurol* 2016; 15:1075–1088. 3. Hesdorffer DC *et al. Epilepsia* 2011; 52 (6): 1150–1159.

Clinically meaningful improvements[1] in adaptive functioning and behaviour continuing through 4 years of treatment in the OLE studies

Change in Vineland-3 subdomain scores from OLE baseline



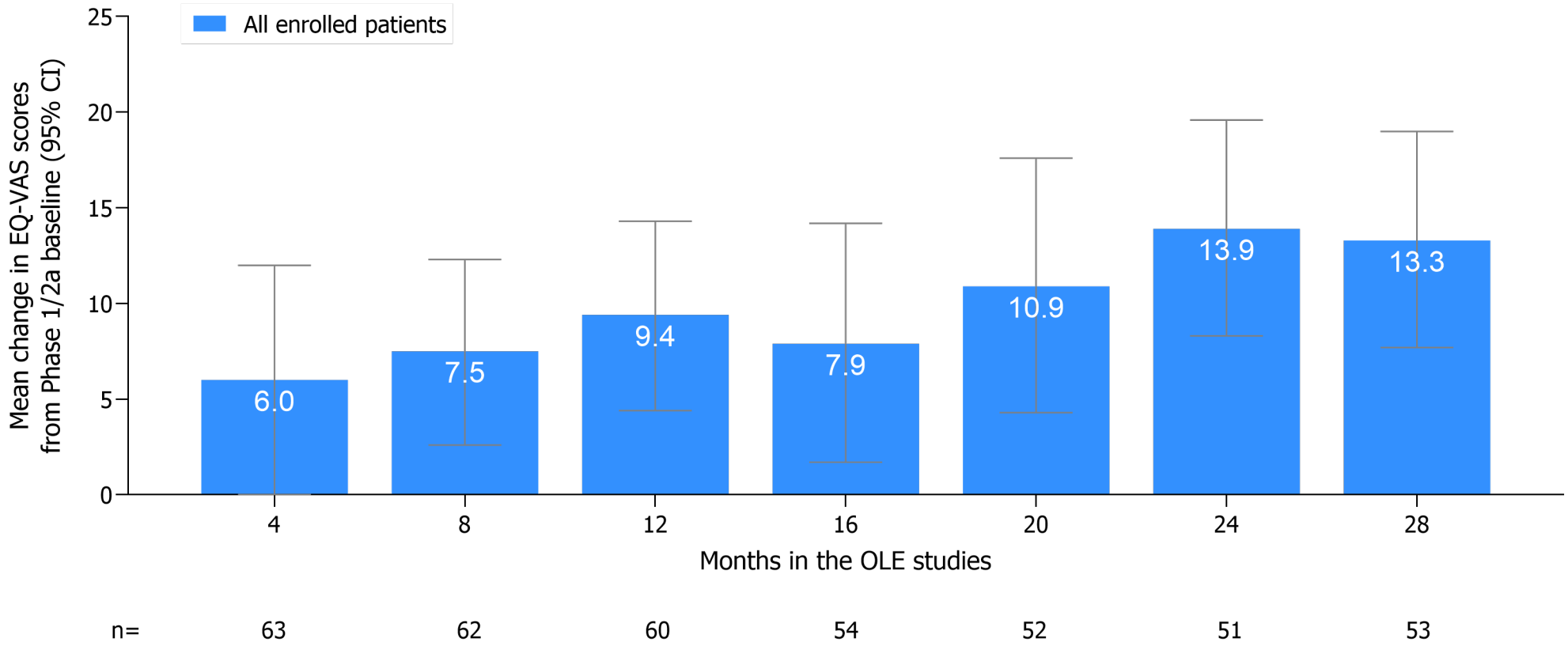
***P*<0.01** statistical significance was achieved in the **5 key Phase 3 subdomains** for each year compared with OLE baseline

***P*<0.03** achieved in 2 other subdomains for each year compared to OLE baseline

Data cut date: 19 February 2026. Mixed-effects models for repeated measures (MMRMs) for each subdomain were fit using available data from patients with baseline and at least one post baseline assessment in the SWALLOWTAIL and LONGWING OLE studies, with n representing the number of completed patient visits at each timepoint shown. Statistical analyses are post-hoc and exploratory. 1 year = 48 weeks.
CI, confidence interval; LS, least squares; OLE, open-label extension; Vineland-3, Vineland Adaptive Behavior Scales – Third Edition.
1. Condon C *et al. Epilepsy Behav* 2025; 167: 110381.

Improvements in quality of life following treatment with zorevunersen

Change in EQ-VAS scores from Phase 1/2a baseline



Substantial increases in quality of life were observed in addition to reductions in seizure frequency and improvements in adaptive functioning and behaviour

Data cut date: 19 February 2026. Analysis performed using available data from patients enrolled in the SWALLOWTAIL and LONGWING OLE studies (N=75), with n=51 to 63 patients having evaluable change-from-baseline data across visits. EQ-VAS is a validated visual analogue scale ranging from 0 to 100 (worst to best imaginable health). 1 month = 4 weeks.
CI, confidence interval; EQ-VAS, EuroQol visual analogue scale; OLE, open-label extension.

The safety profile of zorevunersen with long-term dosing

Phase 1/2a studies (N=81)[1]

- **30%** (24/81) of patients experienced a study drug–related TEAE
  - Most common: CSF protein elevations (14%) and procedural vomiting (5%)
- **22%** (18/81) of patients experienced a TESAE
  - TESAEs for 17/18 patients were assessed as unrelated to study drug
  - 1 patient had study drug-related SUSARs
- 1 patient died because of SUDEP, **unrelated to study drug**

OLE studies (N=75)

- **56%** (42/75) of patients experienced a study drug–related TEAE
- **31%** (23/75) of patients experienced a TESAE; all unrelated to study drug
- **CSF protein elevation*** occurred in **94%** (68/72) of patients and was **classified as a TEAE in 59%** (40/68)
  - No serious or severe clinical manifestations associated with CSF protein elevation were observed
  - 1 patient discontinued treatment because of CSF protein elevation
- 1 patient died because of SUDEP and 1 because of malnutrition; both **unrelated to study drug**

Phase 1/2a data cut: 12 December 2023 (after End of Study). OLE data cut: 19 February 2026.
*≥1 CSF protein value >50 mg/dL. Percentage based on 72/75 patients who had ≥1 post-baseline CSF protein value in the OLE studies.
CSF, cerebrospinal fluid; OLE, open-label extension; SUDEP, sudden unexpected death in epilepsy; SUSAR, suspected unexpected serious adverse reaction; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.
1. Laux L *et al. N Engl J Med* 2026; 394 (10): 969–982.

Long-term dosing of zorevunersen has now extended past 5 years

Phase 1/2a (N=81) and OLE (N=75) studies

Parameter	Result
Median treatment days per patient	1,255
Median doses per patient	11
Total exposure, patient-years	260.7
Maximum duration of years	5.33
Patients on treatment at data cutoff*	58

>930 doses administered in the Phase 1/2a and OLE studies as of 31 July 2026

Phase 1/2a data cut: 12 December 2023 (after End of Study). OLE data cut: 19 February 2026.
*As of the 19 February 2026 data cut, 58/75 (77%) of patients remained in the OLEs. Most discontinuations were in the lower dose groups.
OLE, open-label extension.

Key findings

- Patients receiving zorevunersen on top of SoC **experienced substantial reductions in major motor seizure frequency** through 4 years of treatment in the OLEs

- Patients receiving zorevunersen in the OLEs experienced substantial reductions in the frequency of **the most severe seizure types, the leading risk factor for SUDEP**

- **Adaptive functioning and behaviour were significantly improved** from the OLE baseline in patients receiving zorevunersen through 4 years of treatment

- **Substantial increases in QoL** accompanied the improvements in seizure frequency, adaptive functioning, and behaviour, highlighting the disease-modifying potential of zorevunersen in DS

- Treatment with **zorevunersen has been generally well tolerated** over more than 260 total patient-years of exposure and some patients have been treated for more than 5 years

- **Zorevunersen is being investigated in a global, Phase 3, double-blind, randomised, sham-controlled study** to assess the efficacy, safety profile, and tolerability among children and adolescents with DS

Acknowledgements: We thank the patients, caregivers, investigators, healthcare providers, and research staff who participated in the Phase 1/2a and OLE studies.

Phase 3 Study EU CT: 2024-519555-28-00; NCT06872125. DS, Dravet syndrome; OLE, open-label extension; QoL, quality of life; SoC, standard of care; SUDEP, sudden unexpected death in epilepsy.