Stoke Therapeutics

Edward M. Kaye MD
CEO

January 15, 2025

Forward-Looking Statements and Other Legal Notices

This presentation has been prepared by Stoke Therapeutics, Inc. ("Stoke" or "us") for informational purposes only and not for any other purpose. Nothing contained in this presentation is, or should be construed as, a recommendation, promise or representation by the presenter(s) or Stoke or any officer, director, employee, agent or advisor of Stoke. This presentation does not purport to be all-inclusive or to contain all of the information you may desire. Information provided in this presentation speaks only as of the date hereof. Stoke assumes no obligation to publicly update any information or forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments, subsequent events, or circumstances after the date hereof, or to reflect the occurrence of unanticipated events.

This presentation contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to: the ability of zorevunersen (STK-001) to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in behavior or cognition at the indicated dosing levels or at all; the design, timing and results of the Phase 3 study, data readouts, regulatory decisions and other presentations for zorevunersen; the potential for zorevunersen to be the first disease-modifying therapy for Dravet syndrome; the timing of regulatory interactions or the outcomes thereof; our expectations, plans, aspirations and goals, including those related to the potential of zorevunersen; and the anticipated market for zorevunersen. Statements including words such as "anticipate," "believe," "hope," "plan," "will," "continue," expect," "ongoing," or "potential" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they prove incorrect or do not fully materialize, could cause our results to differ materially from those expressed or implied by such forward-looking statements, including, but not limited to, risks and uncertainties related to: our ability to advance, obtain regulatory approval of, and ultimately commercialize our product candidates, including zorevunersen; the timing of data readouts and interim and final results of nonclinical and clinical studies; nonclinical and clinical data are voluminous and detailed, and regulatory authorities may interpret or weigh the importance of data differently and reach different conclusions than us or others, request additional information, have additional recommendations or change their guidance or requirements before or after approval; receiving Breakthrough Therapy Designation may not lead to a faster development or regulatory review or approval and does not mean zorevunersen will receive marketing approval; our ability to fund development activities and achieve development goals; our ability to protect our intellectual property; global business, political and macroeconomic conditions, including inflation, interest rate volatility, cybersecurity events, uncertainty with respect to the federal budget, instability in the global banking system and volatile market conditions, and global events, including public health crises and ongoing geopolitical conflicts, such as the conflicts in Ukraine and the Middle East; and other risks and uncertainties described under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2023, our quarterly reports on Form 10-Q and the other documentation we file from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this presentation, and we undertake no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

By attending or receiving this presentation you acknowledge that you are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date such statements are made, you will be solely responsible for your own assessment of the market and our market position, and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of Stoke.

Certain information contained in or that may orally accompany this presentation relate to or are based on studies, research, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, research, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently verified, and we make no representation as to the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources.

This presentation discusses product candidates, including zorevunersen, that have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory agency.

OUR GOAL

Restore protein expression by harnessing the body's potential with RNA medicine

Stoke's pipeline offers potential first-in-class disease modifying new medicines for diseases caused by protein insufficiency

zorevunersen for Dravet syndrome	STK-002 for Autosomal Dominant Optic Atrophy (ADOA)	Rett syndrome, SYNGAP1	And beyond…
A severe genetic developmental epileptic encephalopathy	The most common inherited optic nerve disorder	Severe and rare genetic neurodevelopmental diseases	~6,500 add'l genes with TANGO target signatures

STOKE THERAPEUTICS

Compelling Clinical Data and Key Stakeholder Engagement Underscore the Potential for Zorevunersen

Clinical Data

Substantial and durable reductions in **seizure frequency** and continuing improvements across **multiple measures of cognition and behavior** are evidence of disease modification

Breakthrough Therapy Designation

FDA

Indicates that zorevunersen may demonstrate **substantial improvement over available therapy**

The Right Team

An **experienced team** that is ready to take zorevunersen into Phase 3

KEY TAKEAWAYS

First-ever Phase 3 study of a potential disease-modifying medicine for **Dravet syndrome**

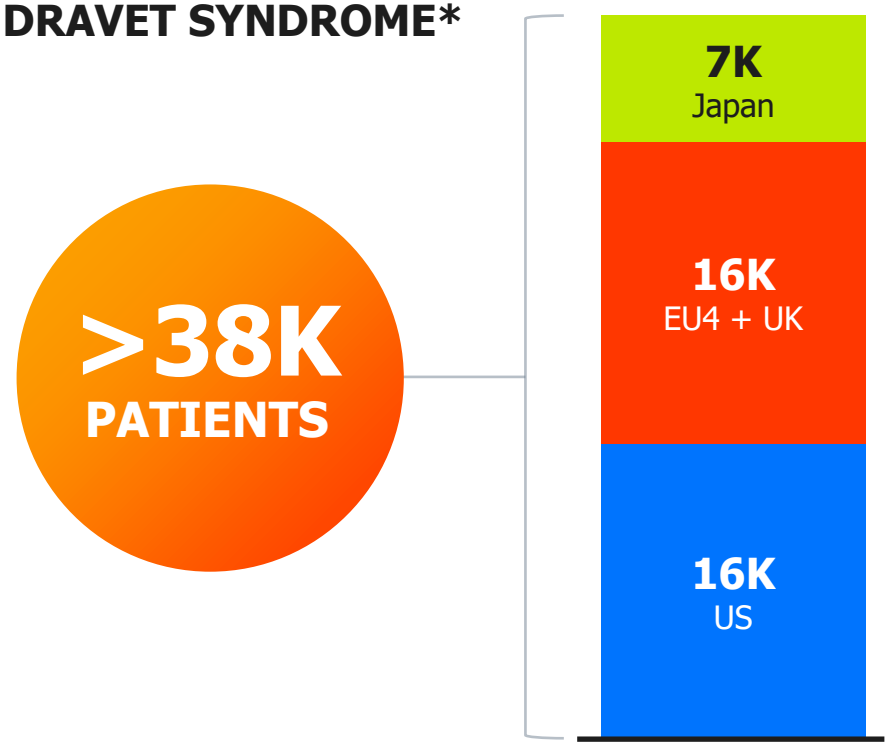
Disease modification would represent a **major step forward in the treatment** of Dravet syndrome – fundamental shift in the treatment

**Breakthrough Therapy Designation is not the same as drug approval. Zorevunersen is an investigational drug candidate.*

Substantial Patient Population

More than 38K patients with Dravet syndrome across 7 major markets

PREVALENCE OF DRAVET SYNDROME*



SIGNIFICANT UNMET NEED DESPITE ANTI-SEIZURE MEDICINES

No disease modifying medicines are currently available

Seizures are inadequately controlled in 90% of patients

- **Mean 14.3 seizures per 28 days** while receiving an average of 3.5 ASMs at baseline

Developmental delays and cognitive impairment are persistent and cannot be treated today

- Patients with Dravet syndrome **fall further and further behind** their neurotypical peers

**Numbers may not add up due to rounding. EU4: Germany, France, Italy and Spain; ASMs: anti-seizure medications*

Wu. Pediatrics. 2015; UN World Population Prospects 2022; World Bank Open Data 2021; WHO Life Tables 2019; Physician Interviews; ClearView Analysis. Sullivan, J. et al., 24-Month Analysis of BUTTERFLY. AES 2023. Lagae et al., Developmental Medicine & Child Neurology, 2017; 2018 Health Advances Report; Dravet Syndrome Foundation Voice of the Patient Report

Current Treatments For Dravet Aim to Reduce Seizures Leaving a Significant Gap in Treatment of the Syndrome

MULTIPLE MEDICINES available for Seizure Management

- Bromide
- Cannabinoid
- Clobazam
- Diazepam
- Fenfluramine
- Levetiracetam
- Stiripentol
- Topiramate
- Valproate
- Zonisamide

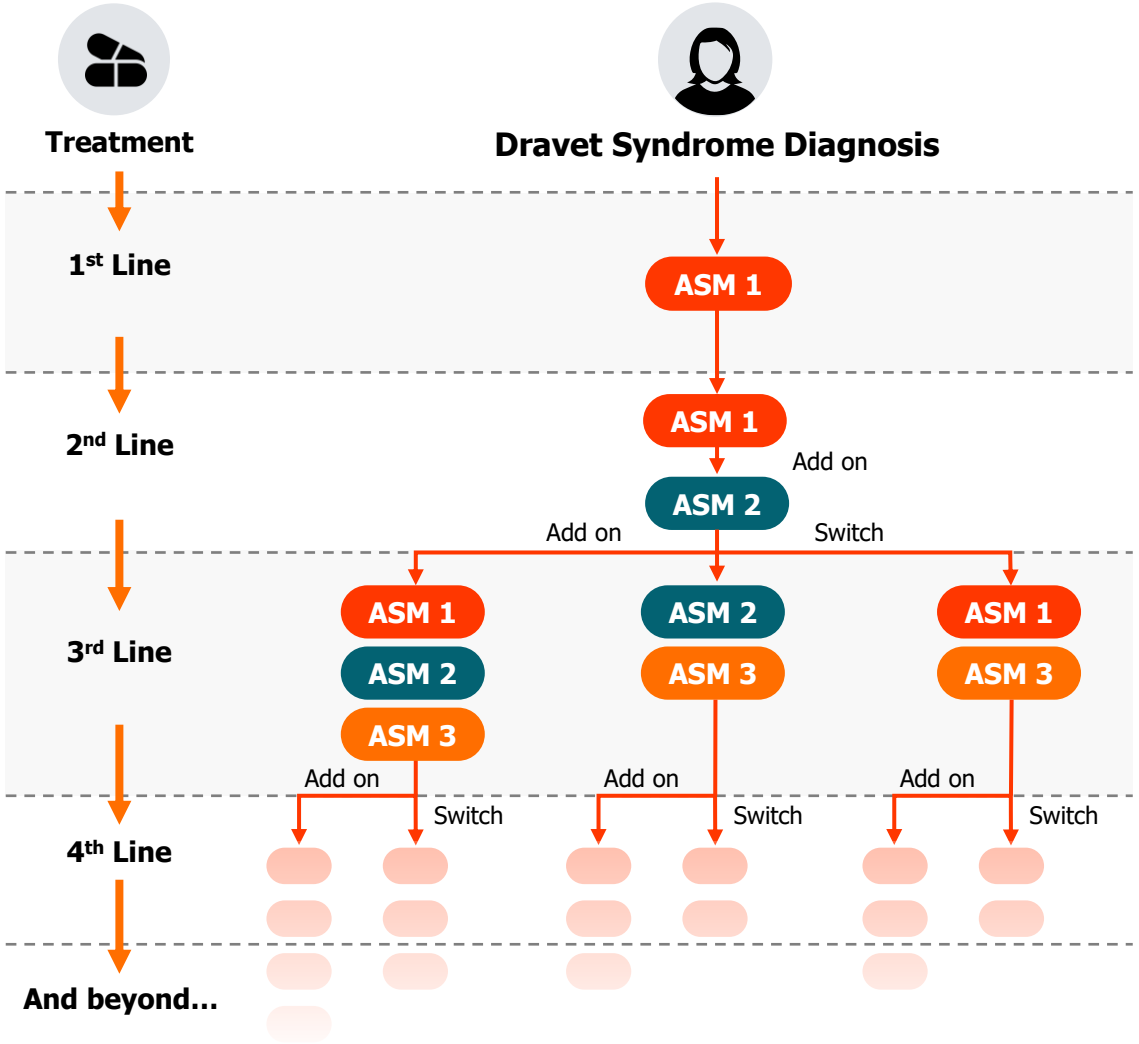
Currently **NO MEDICINES** available for Syndrome Management

ASM, antiseizure medication; DS, Dravet syndrome; SOC, standard of care.

1. Lagae L, et al. Dev Med Child Neurol 2018; 60 (1): 63–72. Appendix S4. 2. Lagae L, et al. Dev Med Child Neurol 2018; 60 (1): 63–72.

Once Diagnosed, the Current Treatment Paradigm is Burdensome and Ineffective

Most patients are on ≥3 anti-seizure medicines



CLINICIAN PERSPECTIVES ON CURRENT TREATMENT OPTIONS

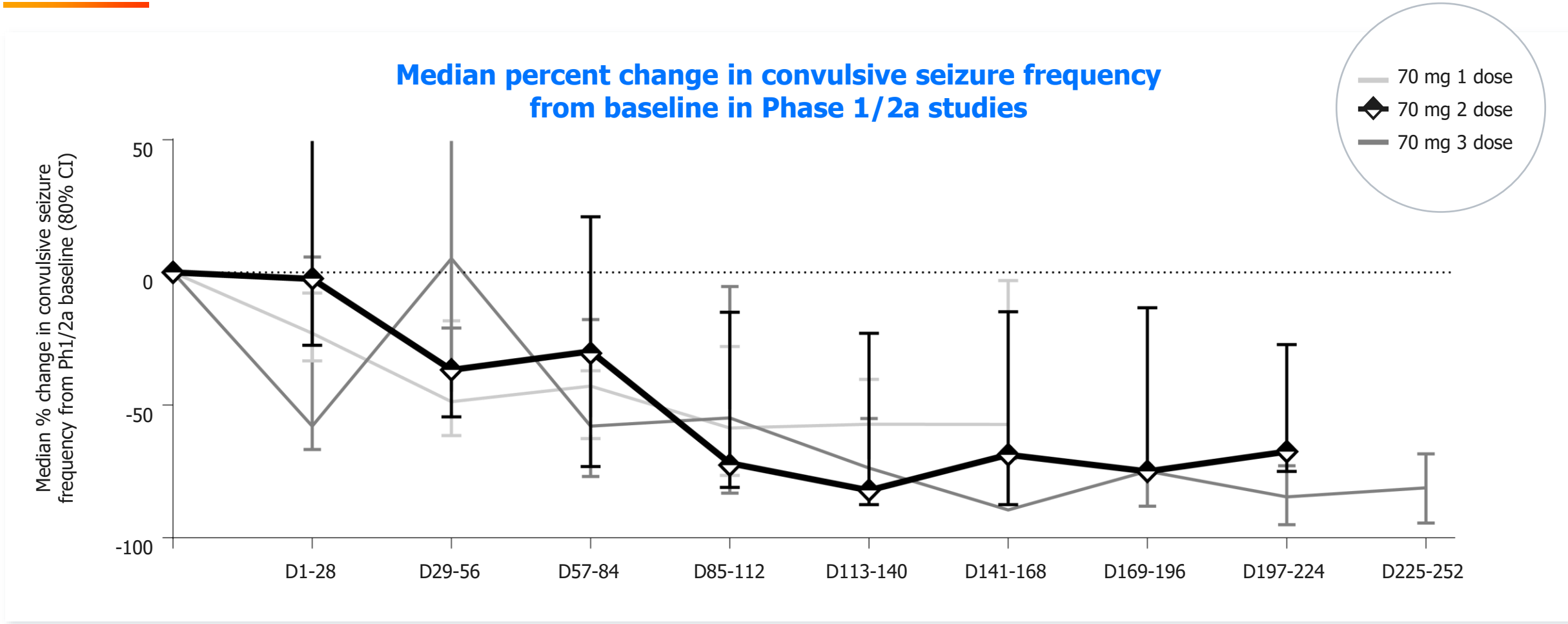
"We have 20–25 ASMs but there is no magic pill. We **need something that addresses the root cause**."

"A lot of these patients end up being **sedated around the clock** between the meds and the disease."

"We need to improve **seizure** control given patients can **still experience 20 seizures in a week while on many medications**."

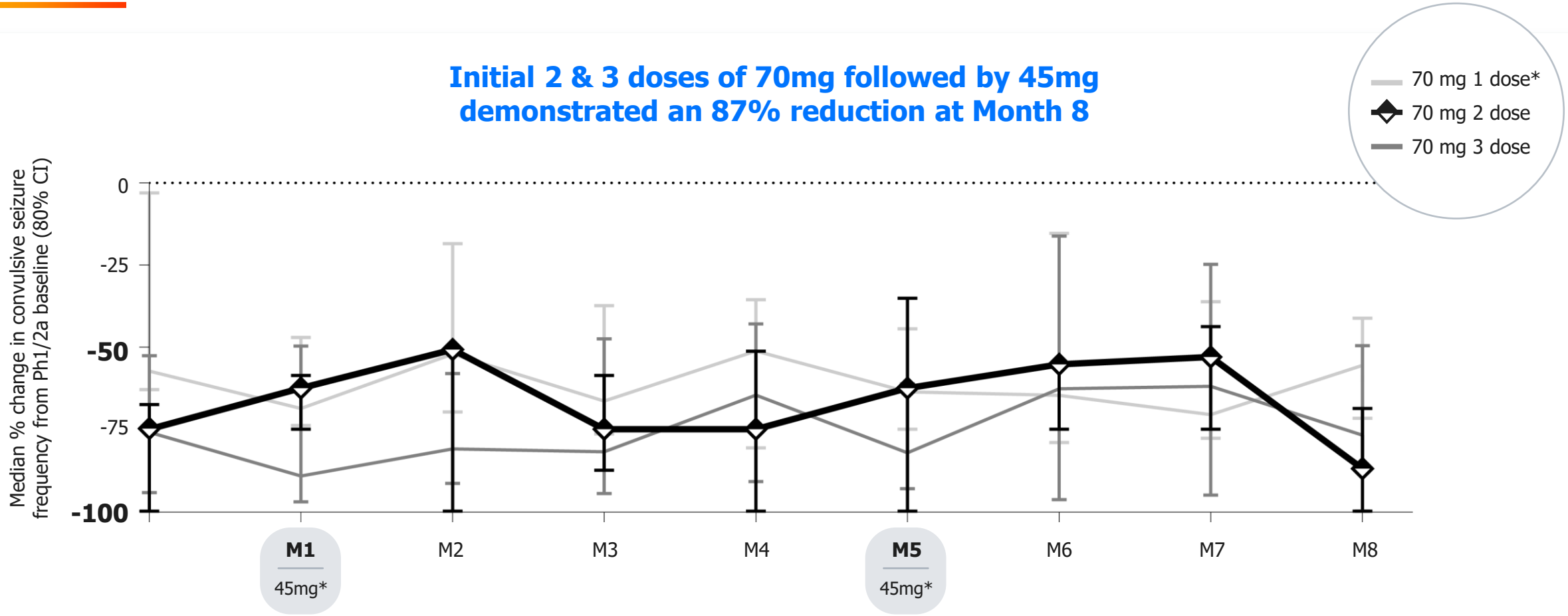
Adapted from Wirrell et al. International consensus on diagnosis and management of Dravet syndrome. May 2022.
Comments extracted from company sponsored interviews using a Product X profile based on MONARCH and ADMIRAL study results.

Initial 70mg Doses of Zorevunersen Demonstrated Substantial and Sustained Reductions in Convulsive Seizure Frequency



Ongoing Treatment Demonstrated Substantial and Durable Reductions in Convulsive Seizure Frequency

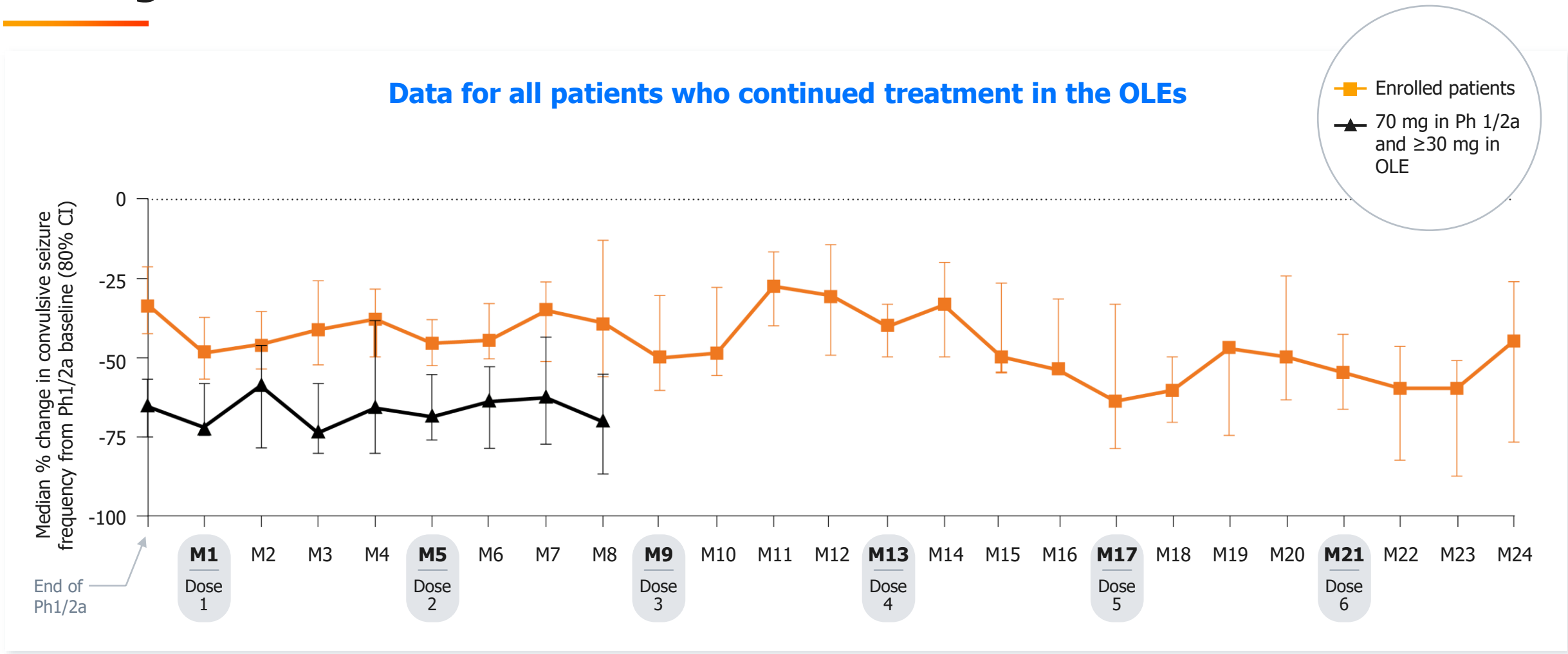
Initial 2 & 3 doses of 70mg followed by 45mg demonstrated an 87% reduction at Month 8



Patients from the single dose 70mg cohort received 30mg doses at M1 and M5.

Patients with Dravet syndrome in open-label extension studies of zorevunersen (STK-001) have durable reductions in seizure frequency and ongoing improvements in cognition and behavior. AES 2024

Durable, Substantial Reductions in Seizures on Top of SOC Observed Through Two Years of Treatment with Zorevunersen



Orange: Enrolled Patients (n=70 M1 and 17 at M24 based on study progression)

Black: 70mg Cohorts from Ph1/2a who received ≥30 mg in OLE (n=16 – 17 at each timepoint)

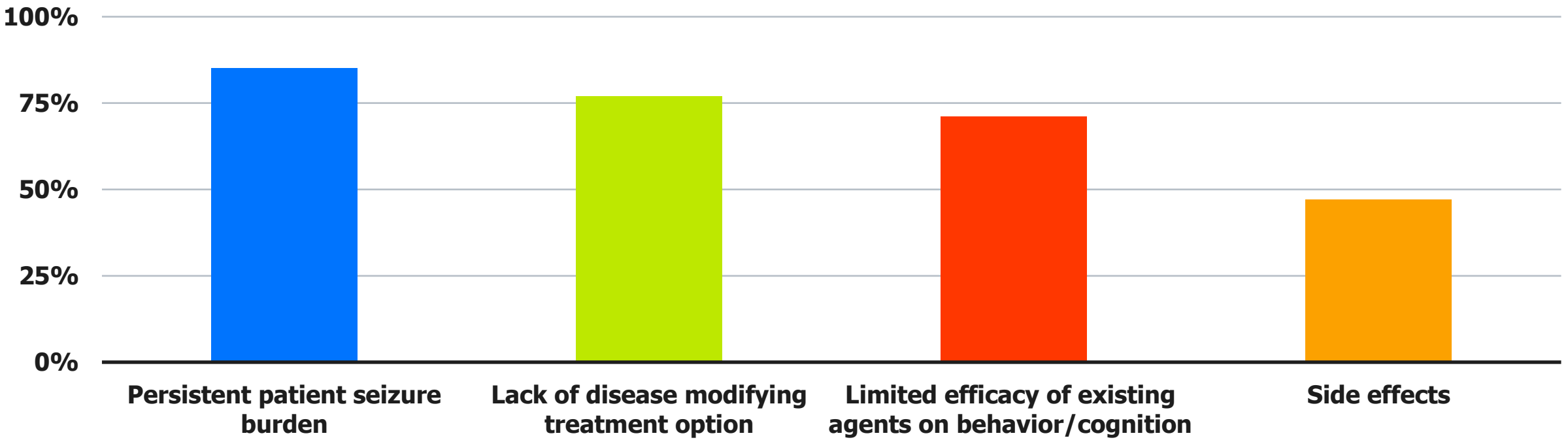
Ph1/2a End of Study results.; OLE data cut: June 28, 2024.

Sullivan, J et al. Patients with Dravet syndrome in open-label extension studies of zorevunersen (STK-001) have durable reductions in seizure frequency and ongoing improvements in cognition and behavior (poster). American Epilepsy Society Annual Meeting, December 6-10, 2024 (Los Angeles, USA).

Approximately 90% of HCPs See a Significant Unmet Need for Patients with Dravet Syndrome

Most pressing unmet needs identified by HCPs*

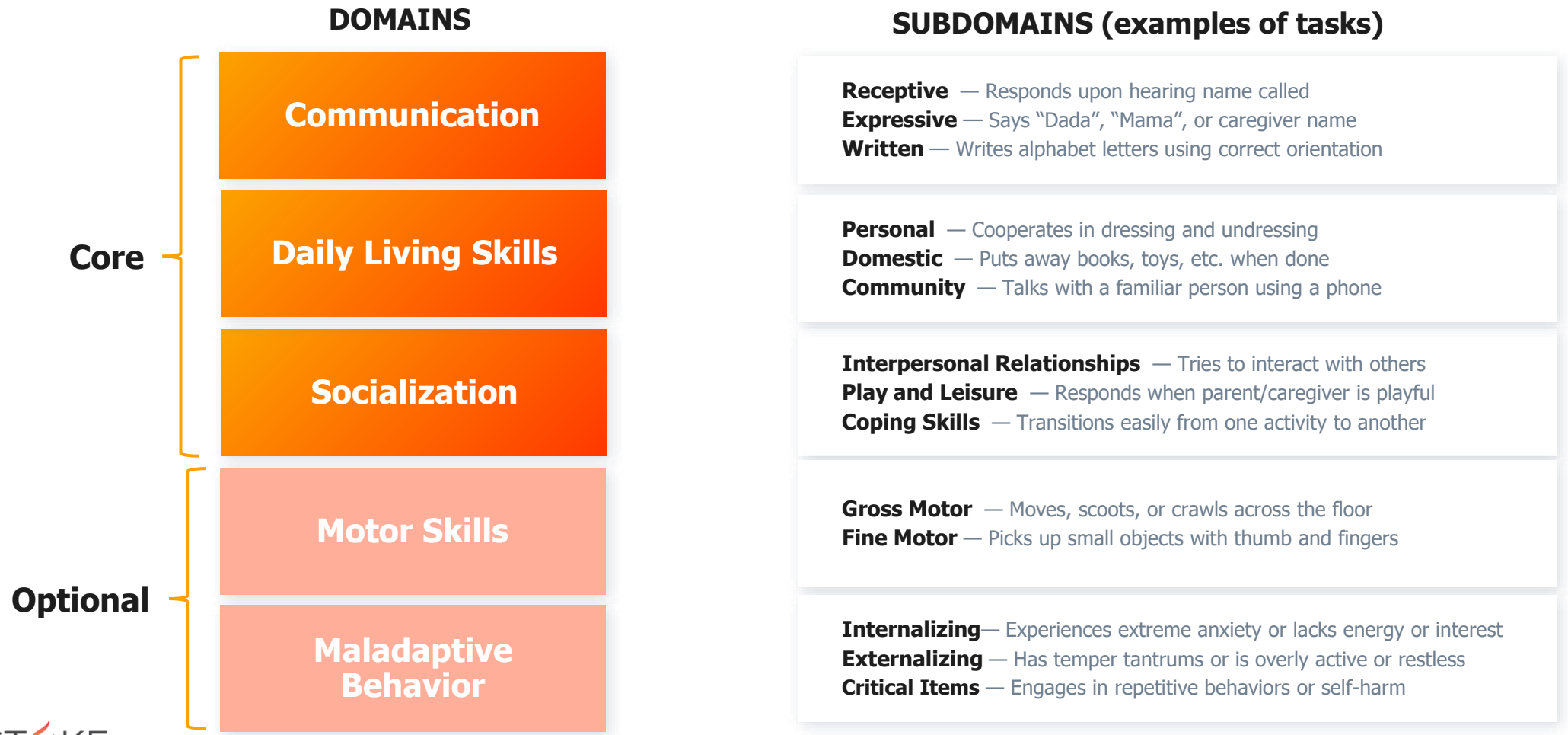
Percent of respondents



*Based on Stoke quantitative market research with 135 HCP participants who treat Dravet syndrome in the US and EU in 2024.

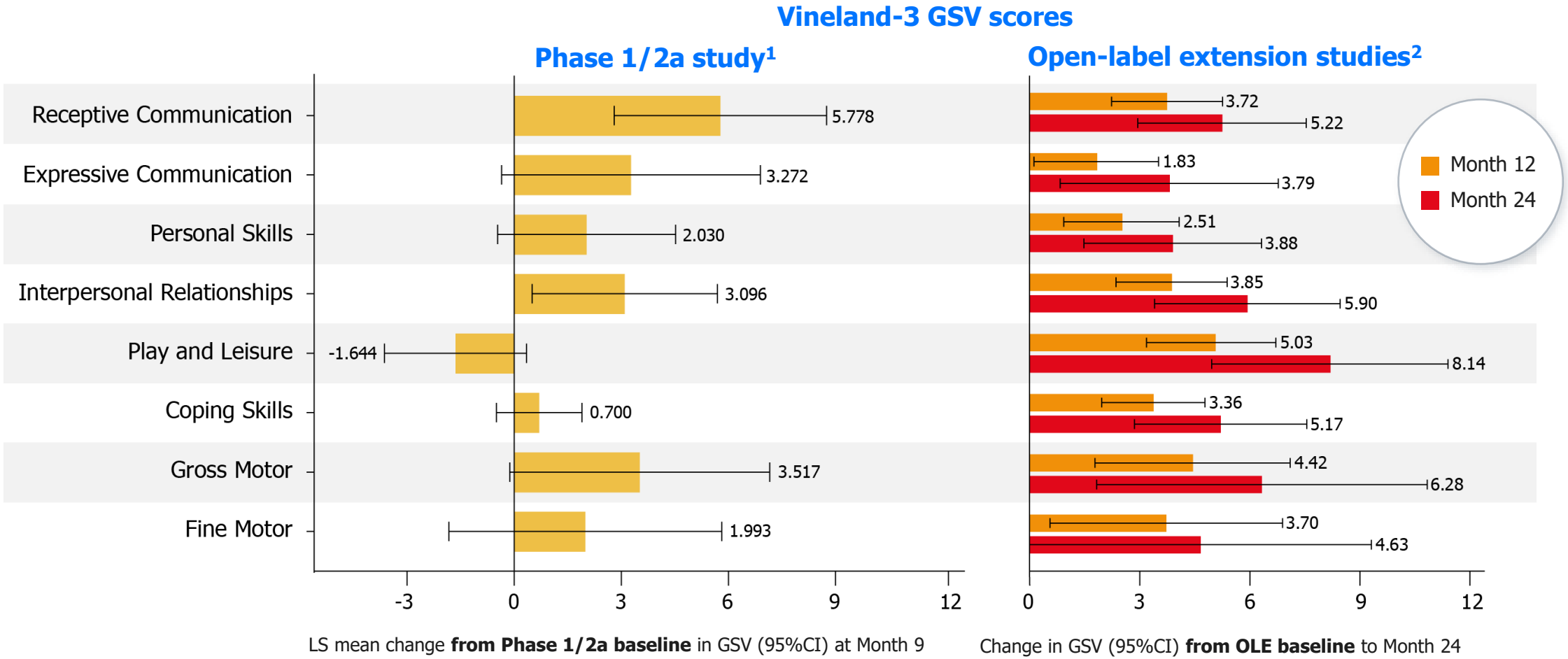
Vineland-3 is Commonly Used to Assess Cognitive & Developmental Outcomes

Vineland-3 Adaptive Behavior Scales – Overview



STOKE THERAPEUTICS

Improvements in Cognition and Behavior Within 9 Months Continuing Improvements Throughout the OLEs



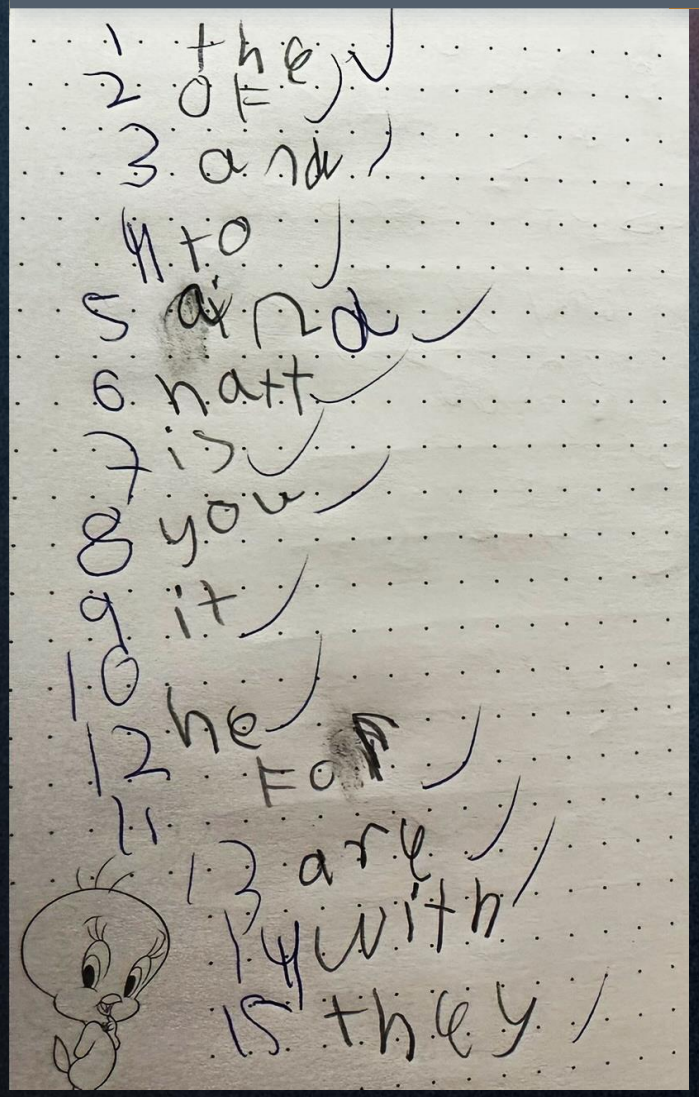
[1] *Machine learning model constructed using data from EOS Ph1/2a ADMIRAL (all dose cohorts) and data through Month 4 visit in LONGWING OLE (as of Nov. 2023)*

[2] *Mixed-effects model for repeated measures constructed using data through Month 24 from enrolled patients in OLE studies. Data cutoff 28 June 2024.*

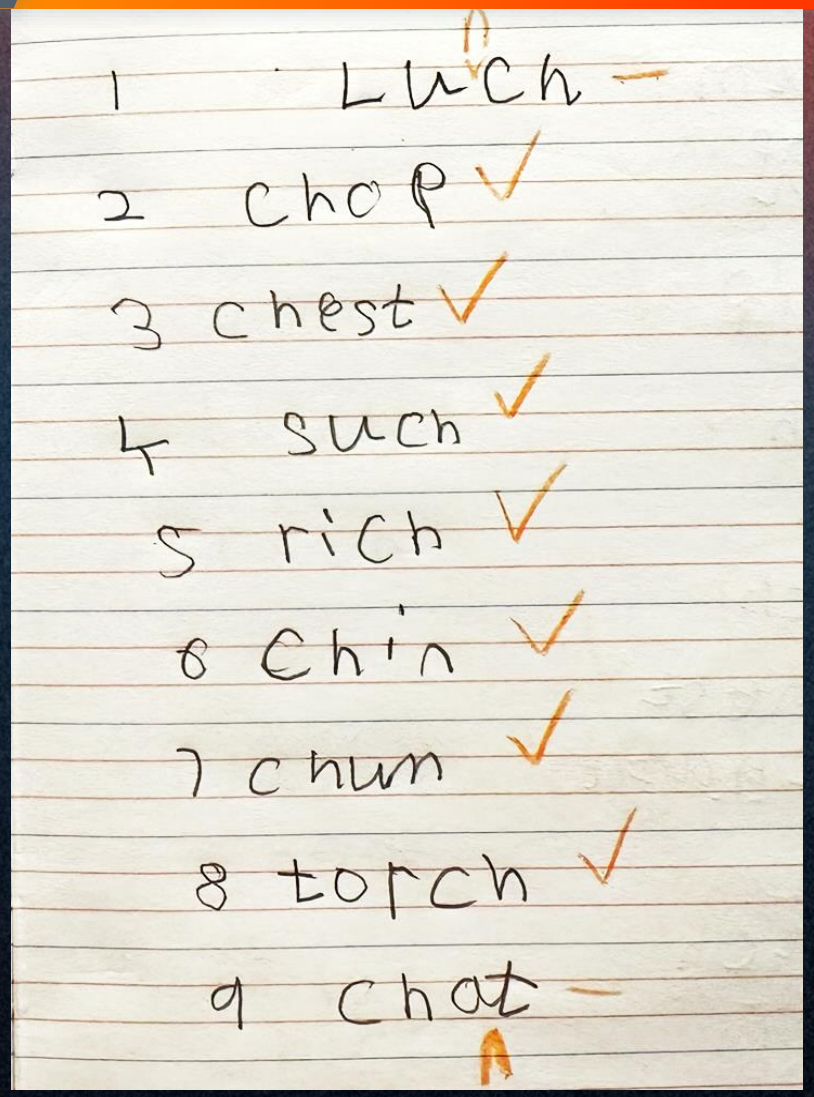
Handwriting from a 12 year-old before and after treatment with zorevunersen*

Each patient experience is unique and not representative of the patient population as a whole. This patient's experience is not intended to depict what other patients may experience.

BEFORE Treatment
November 2022



AFTER 9mo of Treatment
November 2023



Images captured during the Phase 1/2a ADMIRAL study independently by the investigator.
Brunklaus A, et al, British Paediatric Neurology Association Conference (scheduled January 9, 2025).
**Zorevunersen is an investigational drug candidate and has not been approved for marketing by the FDA or any other regulatory authorities.*

Zorevunersen Generally Well-Tolerated Across Studies

Phase 1/2a studies

(n=81)

TEAEs

- **30% of patients** experienced a study drug-related TEAE
- Most common: **CSF protein elevations** (13.6%) and **procedural vomiting** (4.9%)

TESAEs

- **22% of patients** experienced a TESAE
- All were **unrelated to study drug** except for 1 patient with SUSARs

OLE studies

(n=74)

Findings consistent with Ph1/2, with the exception of a higher incidence of CSF protein elevation

- **79% (56/71*)** of patients in the OLEs had at least 1 CSF protein value >50 mg/dL
- **No clinical manifestations** have been observed in these patients
- One patient discontinued treatment due to elevated CSF protein levels

To date,

>600 doses of zorevunersen†

have been administered; 3 years of treatment in some patients

End of Phase 1/2a study data. Datacut June 28, 2024, for OLEs.

**71/74 patients had ≥1 post-baseline CSF protein value in the OLEs*

†Number of doses to date includes doses administered after the June 28, 2024, safety datacut for the OLEs.

CSF, cerebrospinal fluid; OLE, open-label extension; SUSAR, suspected unexpected serious adverse reaction; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

STOKE THERAPEUTICS

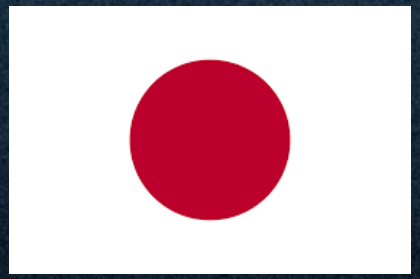
Strong Regulatory Alignment

FDA

EMA

Global Alignment FOR EMPEROR Phase 3 Protocol

PMDA

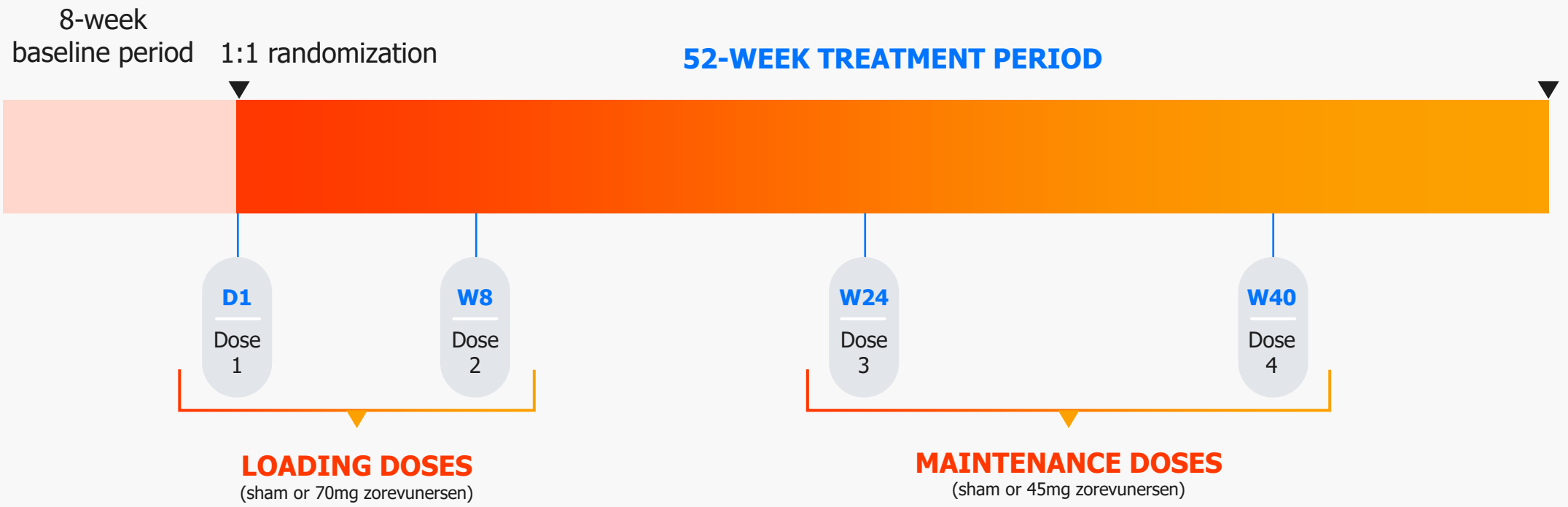


Regulatory discussions ongoing

Emperor Clinical Study Design

First Phase 3 study of a potential disease-modifying medicine for Dravet syndrome

TOTAL STUDY DURATION: 60 WEEKS



EMPEROR Phase 3 Study Overview

Planned Study Parameters

Primary endpoint

Seizures

Percent change from baseline in major motor seizure frequency in patients receiving zorevunersen as compared to sham

Key secondaries

Durability of effect on major motor seizure frequency

Improvements in behavior & cognition measured by Vineland-3 subdomains

Other Endpoints

Safety, CGI-C, CaGI-C, BSID-IV, and others

Study Design: Sham-controlled, 1:1 randomization

Dosing Regimen: 2x70mg + 2x45mg

Study Start: Mid-2025

Population: 2 to <18 years with a confirmed variant in the *SCN1A* gene not associated with gain of function

Number of Patients Randomized: ~150

Sites: ~60 across the US, UK, EU and Japan

Treatment Duration: 52 weeks

Data Anticipated: YE 2027

Regulatory discussions ongoing

Zorevunersen is Positioned to Change the Treatment of Dravet Syndrome, Representing Blockbuster Potential

SIGNIFICANT NEED

Current treatments focus on reducing seizure frequency. There is nothing available to treat the entire syndrome.

CLINICAL DATA

Substantial and durable reductions in seizures and continuing improvements in cognition and behavior on top of standard of care anti-seizure medicines.

STAKEHOLDER SUPPORT

HCPs and caregivers have had an overwhelming positive reaction to the zorevunersen profile as a disease-modifying medicine.

The option of a treatment, such as zorevunersen, that could not only potentially reduce or eliminate seizures, as well as offer some level of disease reversal, would **represent a profound breakthrough for individuals living with Dravet syndrome**. It could change Dravet syndrome from a profoundly life-altering and debilitating condition into a more manageable challenge, providing the **opportunity for patients to live a more fulfilling and independent life**.

Mary Anne Meskis, Executive Director, Dravet Syndrome Foundation

STOKE THERAPEUTICS

OUR GOAL

Restore protein expression by harnessing the body's potential with RNA medicine

Stoke's pipeline offers potential first-in-class disease modifying new medicines for diseases caused by protein insufficiency

zorevunersen for Dravet syndrome	STK-002 for Autosomal Dominant Optic Atrophy (ADOA)	Rett syndrome, SYNGAP1	And beyond…
A severe genetic developmental epileptic encephalopathy	The most common inherited optic nerve disorder	Severe and rare genetic neurodevelopmental diseases	~6,500 add'l genes with TANGO target signatures

STOKE THERAPEUTICS

Q&A