UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 7, 2025

Stoke Therapeutics, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-38938**	**47-1144582**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

45 Wiggins Ave **Bedford, Massachusetts**	**01730**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (781) 430-8200

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	STOK	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD.

On January 7, 2025, Stoke Therapeutics, Inc. (the "Company") issued a press release (the "Press Release") and conducted a virtual event for investors and analysts (the "Webinar Presentation") announcing alignment with global regulatory agencies on plans to initiate a Phase 3 study of zorevunersen as potentially the first disease-modifying medicine for the treatment of Dravet syndrome. The Company is furnishing copies of the Press Release and Webinar Presentation, which are attached hereto as Exhibits 99.1 and 99.2, respectively.

The information furnished with this report, including Exhibits 99.1 and 99.2, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference into any other filing under the Exchange Act or the Securities Act of 1933, as amended, except as expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

The Press Release and Webinar Presentation provide an update related to the design of the Company's Phase 3 study of zorevunersen, including the following:

Phase 3 Study of Zorevunersen

- Following successful interactions with the U.S. Food and Drug Administration (FDA), European Medicines Association (EMA) and Japan's Pharmaceuticals and Medical Devices Agency, the Company has finalized its plans for the EMPEROR Phase 3 protocol.
- The proposed study will evaluate two loading doses of 70mg followed by two maintenance doses of 45mg over 52-weeks compared to sham in children and adolescents ages 2 to <18 with Dravet syndrome.
    - The primary endpoint will be reduction in major motor seizure frequency.
    - Key secondary endpoints will include improvements in cognition and behavior as measured primarily by Vineland-3.
- The Company plans to initiate the Phase 3 study by mid-2025 and data are anticipated by the end of 2027, pending enrollment and study timelines.

Commercial Opportunity

- In connection with the planned initiation of its Phase 3 study, the Company is evaluating the potential commercial opportunity for zorevunersen for more than 38,000 patients with Dravet syndrome in seven major markets.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press Release dated January 7, 2025
99.2	Webinar Presentation dated January 7, 2025
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document)

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995 and other federal securities laws. Any statements contained herein that do not describe historical facts, including, but not limited to the ability of zorevunersen to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in behavior and cognition at the indicated dosing levels or at all; the design, timing and results of the Phase 3 study; and the timing and expected progress of data readouts, regulatory meetings, regulatory decisions and other presentations. Statements including words such as “expect,” “plan,” “will,” “continue” or “ongoing” 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 the Company’s results to differ materially from those expressed or implied by such forward-looking statements, including, but not limited to, risks and uncertainties related to: the Company’s ability to advance, obtain regulatory approval of, and ultimately commercialize its product candidates, including zorevunersen; the timing of data readouts and interim and final results of preclinical and clinical trials; the receipt and timing of potential regulatory decisions; positive results in a clinical trial may not be replicated in subsequent trials or successes in early stage clinical trials may not be predictive of results in later stage trials; the Company’s ability to fund development activities and achieve development goals, including expectations regarding its collaboration with Acadia Pharmaceuticals; the Company’s ability to protect its intellectual property; the direct or indirect impact of 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 the Company’s Annual Report on Form 10-K for the year ended December 31, 2023, its quarterly reports on Form 10-Q, and the other documents it files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

STOKE THERAPEUTICS, INC.

Date: January 7, 2025

By: /s/ Thomas E. Leggett
Thomas E. Leggett
Chief Financial Officer

Stoke Therapeutics Announces Alignment with Global Regulatory Agencies and Plans to Initiate a Phase 3 Study of Zorevunersen as Potentially the First Disease-Modifying Medicine for the Treatment of Dravet Syndrome

– Alignment achieved with U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA) and Japan's Pharmaceuticals and Medical Devices Agency (PMDA) for EMPEROR –

– One-year study of zorevunersen will evaluate reductions in major motor seizure frequency as well as improvements in behavior and cognition in children and adolescents ages 2 to <18 years old –

– FDA Breakthrough Therapy designation positions zorevunersen on efficient development path; Company plans to start Phase 3 in mid-2025 –

– Webcast and conference call for analysts and investors at 8:00AM Eastern Time today –

BEDFORD, Mass., January 7, 2025 – Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to restoring protein expression by harnessing the body's potential with RNA medicine, today announced alignment with global regulatory agencies on the design of the Company's Phase 3 EMPEROR study of zorevunersen as potentially the first disease-modifying medicine for the treatment of Dravet syndrome.

Following successful interactions with the FDA, EMA and PMDA, the Company has finalized its EMPEROR Phase 3 study protocol. The proposed study will evaluate two loading doses of 70mg followed by two maintenance doses of 45mg over 52-weeks compared to sham in children and adolescents ages 2 to <18 with Dravet syndrome. The primary endpoint will be reduction in major motor seizure frequency. Key secondary endpoints will include improvements in cognition and behavior as measured primarily by Vineland-3. The Company plans to initiate the Phase 3 study in mid-2025.

"Alignment around a global Phase 3 study design for zorevunersen puts us one step closer to our goal of delivering the first disease-modifying medicine for the treatment of Dravet syndrome," said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. "The level of attention and enthusiasm from clinicians, patient organizations and regulatory authorities for this study
speaks to the shared understanding that current treatments are inadequate. Their support also underscores a belief in the data from our clinical studies that demonstrated substantial and

durable reductions in seizure frequency and improvements across multiple measures of cognition and behavior, when treated with a similar dosing regimen. We look forward to continuing to work together with a sense of purpose and urgency as we prepare to initiate the EMPEROR study by mid-year."

"I have participated as an investigator in many clinical research studies, nearly all of which have been designed to test the next best anti-seizure medicine," said Dr. Kelly Knupp, M.D., MSCS, Professor of Pediatrics and Neurology at the University of Colorado, Anshutz Medical Campus and the Dravet Program Director and Epilepsy Program Lead at Children's Hospital Colorado. "What families and we as clinicians now want are medicines that go beyond reducing seizures to address the neurodevelopmental issues associated with Dravet syndrome, including giving patients the ability to communicate with the people around them and achieve a certain level of independence, which cannot be achieved with today's standard of care. This is the first Phase 3 study to assess the effects of a disease-modifying medicine on seizures as well as multiple aspects of cognition and behavior, which could lead us into a new era in the treatment of Dravet syndrome."

Zorevunersen was recently granted FDA Breakthrough Therapy Designation, a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically-significant endpoint(s).

Clinical Data Support the Phase 3 Dosing Regimen

The Company recently presented data demonstrating that patients treated with two or three doses of 70mg in the Phase 1/2a study and two doses of 45mg in an open-label extension study (OLE), experienced an 87% median reduction in convulsive seizure frequency at month eight (four months after the second dose of 45mg). Patients experienced continuing improvements in multiple measures of cognition and behavior as measured by the Vineland-3 through 2 years of treatment with ongoing maintenance dosing in the OLEs. Additional improvements were indicated within the first nine months of treatment among patients in the Phase 1/2a study. These effects were observed in patients who were already receiving the best available anti-seizure medicines.

Zorevunersen has been generally well tolerated across the studies. To date, more than 600 doses of zorevunersen have been administered to patients across multiple studies, with some patients remaining on treatment for more than three years.

EMPEROR Pivotal Phase 3 Design Summary

The pivotal Phase 3 study will be a global, randomized, double-blind, sham-controlled trial.

Anticipated Enrollment: Approximately 150 patients with Dravet syndrome between the ages of 2 to <18 years of age.

Diagnosis: A confirmed variant in the *SCN1A* gene not associated with a gain of function.

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

Key Secondary Endpoints: Durability of effect on major motor seizure frequency. Improvements in behavior and cognition as measured by Vineland-3 subdomains, including expressive communication, receptive communication, interpersonal relationships, coping skills and personal skills.

Additional Endpoints: Safety, Clinician Global Impression of Change (CGI-C), Caregiver Global Impression of Change (CaGI-C), and the Bayley Scales of Infant Development (BSID-IV).

Global Participation: The study will be conducted in the UK, US, EU, and Japan.

Duration: 60 weeks (8-week baseline period followed by 52-week treatment period)

Phase 3 Data: Data are anticipated by the end of 2027, pending enrollment and study timelines.

Continuing Treatment: Patients who are eligible will be offered ongoing treatment with zorevunersen as part of an OLE study.

Stoke Webcast and Conference Call for Analysts and Investors

Stoke management will host a webcast and conference call for analysts and investors on Tuesday, January 7, 2025, at 8:00am Eastern Time. The call will focus on the successful alignment with global regulatory agencies related to a Phase 3 study of zorevunersen. The webcast will be available on the Investors & News section of Stoke's website at https://investor.stoketherapeutics.com/. Research analysts who plan to join the call and participate in the Q&A session may register here to receive the dial-in details and a unique PIN. All other participants are invited to access the listen-only webcast by clicking here. A replay of the webcast will be archived and available for at least 90 days following the event.

About Dravet Syndrome

Dravet syndrome is a severe developmental and epileptic encephalopathy (DEE). Dravet syndrome is difficult to treat and has a poor long-term prognosis. Complications of the disease often contribute to a poor quality of life for patients and their caregivers. Dravet syndrome is characterized by frequent, prolonged and refractory seizures, beginning within the first year of life. Beyond seizures, Dravet syndrome is associated with developmental and cognitive impairments that often include intellectual disability, developmental delays, movement and balance issues, language and speech disturbances, growth defects, sleep abnormalities, disruptions of the autonomic nervous system and mood disorders. Compared with the general

epilepsy population, people living with Dravet syndrome have a higher risk of sudden unexpected death in epilepsy, or SUDEP. There are no approved disease-modifying therapies for people living with Dravet syndrome. One in 15,600 babies are born with Dravet syndrome, which is not concentrated in a particular geographic area or ethnic group.

About Zorevunersen

Zorevunersen is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in ongoing clinical trials. Stoke believes that zorevunersen, a proprietary antisense oligonucleotide (ASO), has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome. Zorevunersen is designed to upregulate NaV1.1 protein expression by leveraging the non-mutant (wild-type) copy of the *SCN1A* gene to restore physiological NaV1.1 levels, thereby reducing both occurrence of seizures and significant non-seizure comorbidities. Zorevunersen has been granted orphan drug designation by the FDA and the EMA. The FDA has also granted zorevunersen rare pediatric disease designation and Breakthrough Therapy Designation for the treatment of Dravet syndrome with a confirmed mutation, not associated with gain-of-function, in the *SCN1A* gene.

About Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company dedicated to restoring protein expression by harnessing the body's potential with RNA medicine. Using Stoke's proprietary TANGO (Targeted Augmentation of Nuclear Gene Output) approach, Stoke is developing antisense oligonucleotides (ASOs) to selectively restore protein levels. Stoke's first compound, zorevunersen (STK-001), is in clinical testing for the treatment of Dravet syndrome, a severe and progressive genetic epilepsy. Dravet syndrome is one of many diseases caused by a haploinsufficiency, in which a loss of ~50% of normal protein levels leads to disease. Stoke is pursuing the development of STK-002 for the treatment of autosomal dominant optic atrophy (ADOA), the most common inherited optic nerve disorder. Stoke's initial focus is haploinsufficiencies and diseases of the central nervous system and the eye, although proof of concept has been demonstrated in other organs, tissues, and systems, supporting its belief in the broad potential for its proprietary approach. Stoke is headquartered in Bedford, Massachusetts with offices in Cambridge, Massachusetts. For more information, visit https://www.stoketherapeutics.com/.

Cautionary Note Regarding Forward-Looking Statements

This press release 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 to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in behavior and cognition at the indicated dosing levels or at all;

the design, timing and results of the Phase 3 clinical trial; and the timing and expected progress of data readouts, regulatory meetings, regulatory decisions and other presentations. Statements including words such as “expect,” “plan,” “will,” “continue,” or “ongoing” 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: the Company’s ability to advance, obtain regulatory approval or, and ultimately commercialize its product candidates, including zorevunersen; the timing of data readouts and interim and final results of nonclinical and clinical trials; the receipt and timing of potential regulatory decisions; positive results in a clinical trial may not be replicated in subsequent trials or successes in early state clinical trials may not be predictive of results in later stage trials; the Company’s ability to fund development activities and achieve development goals, including expectations regarding the Company’s collaboration with Acadia Pharmaceuticals; the Company’s ability to protect its intellectual property; the direct or indirect impact of 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, 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 the Company’s Annual Report on Form 10-K for the year ended December 31, 2023, its quarterly reports on Form 10-Q, and the other documents it files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and the Company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

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781-303-8302

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IR@stoketherapeutics.com
508-642-6485

Exhibit 99.2

STOKE THERAPEUTICS

Zorevunersen Regulatory Alignment & Phase 3 Plans

Virtual Event for Investors & Analysts

January 7, 2025

Agenda

CEO Opening Remarks
Edward M. Kaye, M.D., Chief Executive Officer

The Potential for Disease Modification in the Treatment of Dravet Syndrome: Clinical Data and Phase 3 Plan
Barry Ticho, M.D., Ph.D., FACC, Chief Medical Officer
Kimberly Parkerson, M.D., Ph.D., SVP, Head of Neurology Clinical Development

Zorevunersen Commercial Opportunity
Jason Hoitt, Chief Commercial Officer

Q&A

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.

Opening Remarks

Edward M. Kaye, M.D.
Chief Executive Officer

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

A severe genetic developmental epileptic encephalopathy

STK-002 for Autosomal Dominant Optic Atrophy (ADOA)

The most common inherited optic nerve disorder

Rett syndrome, SYNGAP1

Severe and rare genetic neurodevelopmental diseases

And beyond…

~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

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.*

FDA Breakthrough Puts Zorevunersen on an Efficient Path

	Breakthrough Therapy Designation (BTD)
Qualifying Criteria	A drug that is intended to treat a serious condition AND **preliminary clinical evidence indicates that the drug may demonstrate substantial improvement** on a clinically significant endpoint(s) over available therapies
Status	Granted December 2, 2024
Benefits	**All Fast Track Designations** **Intensive Guidance:** Frequent interactions with FDA to support efficient development **Organizational Commitment:** Involvement of Senior FDA staff in the review process **Rolling Review:** Submit portions of the marketing application as they are completed **Eligible for Priority Review:** Faster NDA review time vs standard applications

EMPEROR Phase 3 protocol has been submitted to FDA

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

Zorevunersen Clinical Data

Barry Ticho, M.D., Ph.D.
Chief Medical Officer

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

MULTIPLE MEDICINES available for Seizure Management

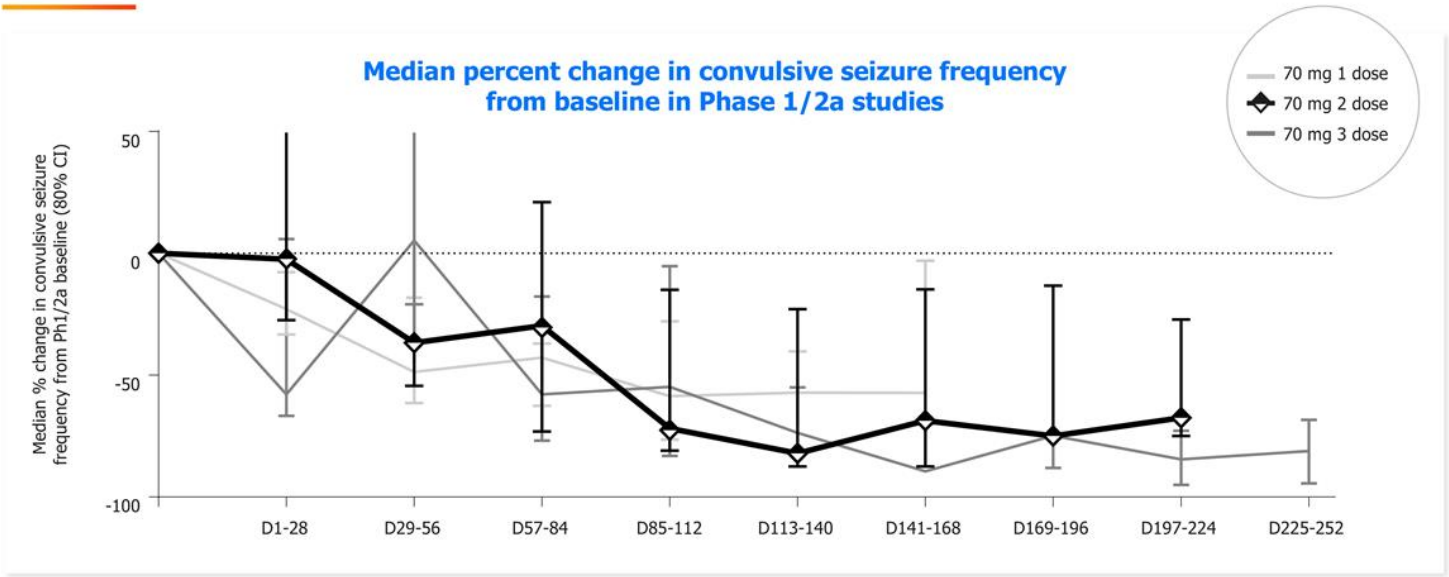
- Bromide
- Cannabinoid
- Clobazam
- Diazepam
- Fenfluramine
- Levetiracetam
- Stiripentol
- Topiramate
- Valproate
- Zonisamide

Currently **NO MEDICINES** available for Syndrome Management

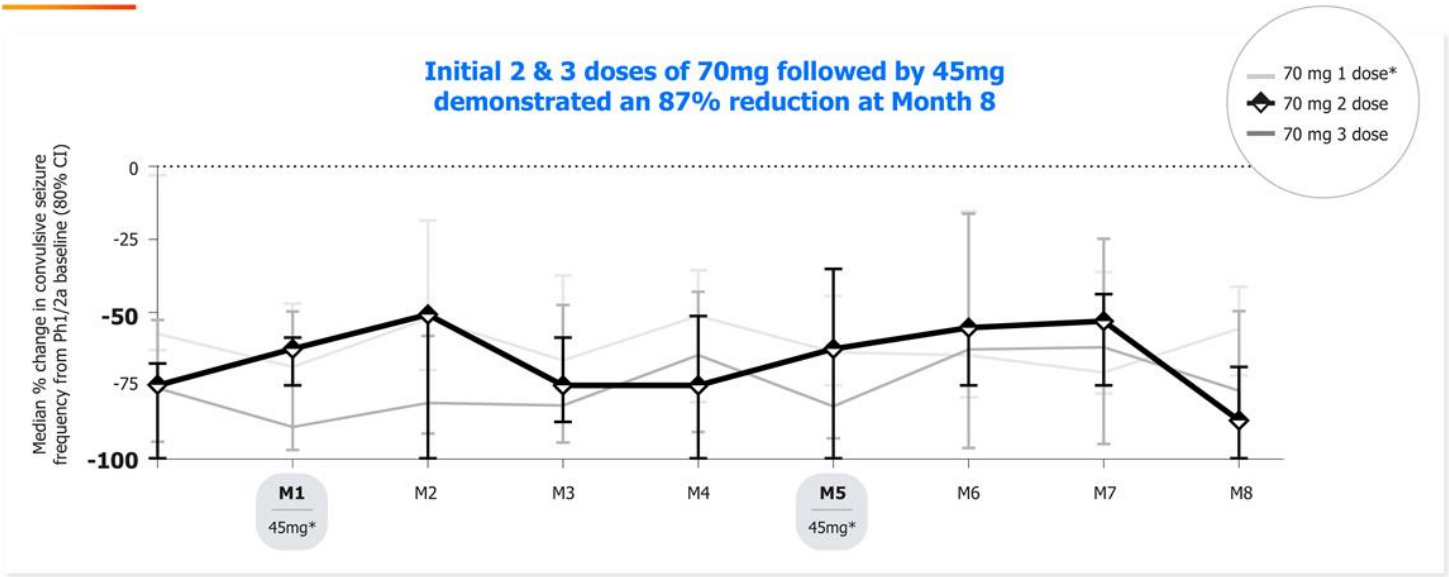
ASM, antiseizure medication; DS, Dravet syndrome; SOC, standard of care.

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.

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



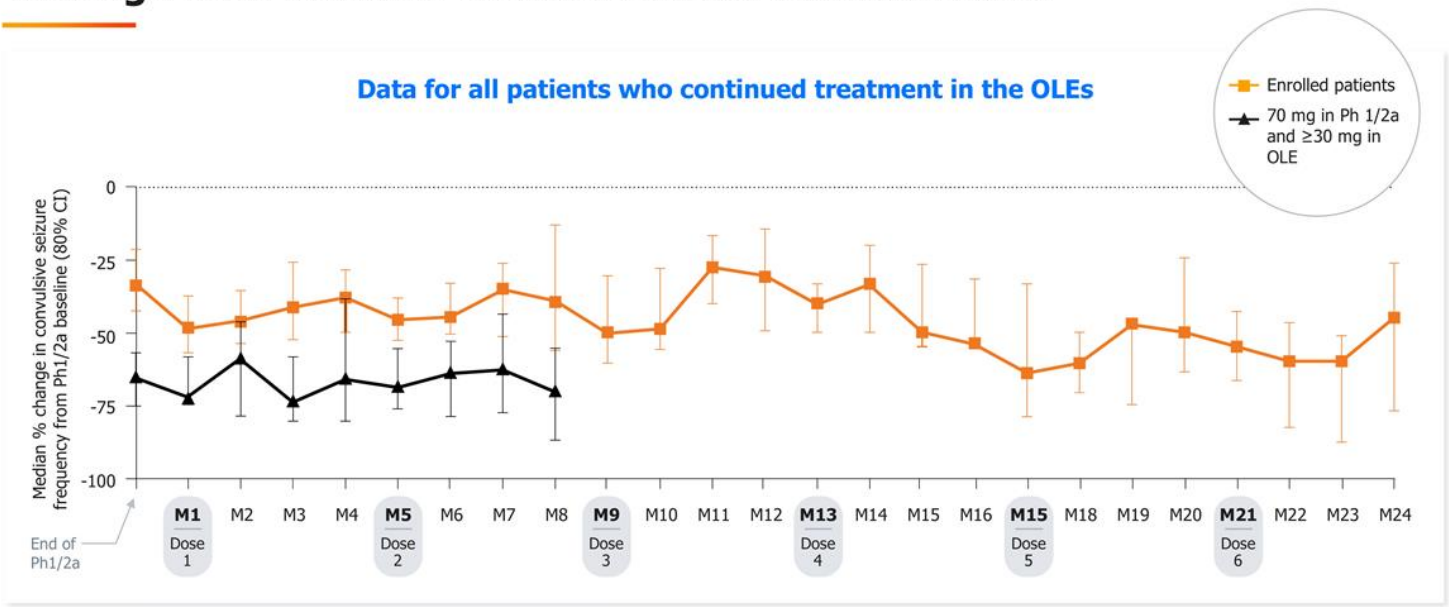
Ongoing Treatment Demonstrated Substantial and Durable Reductions in Convulsive Seizure Frequency



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

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).

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).

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

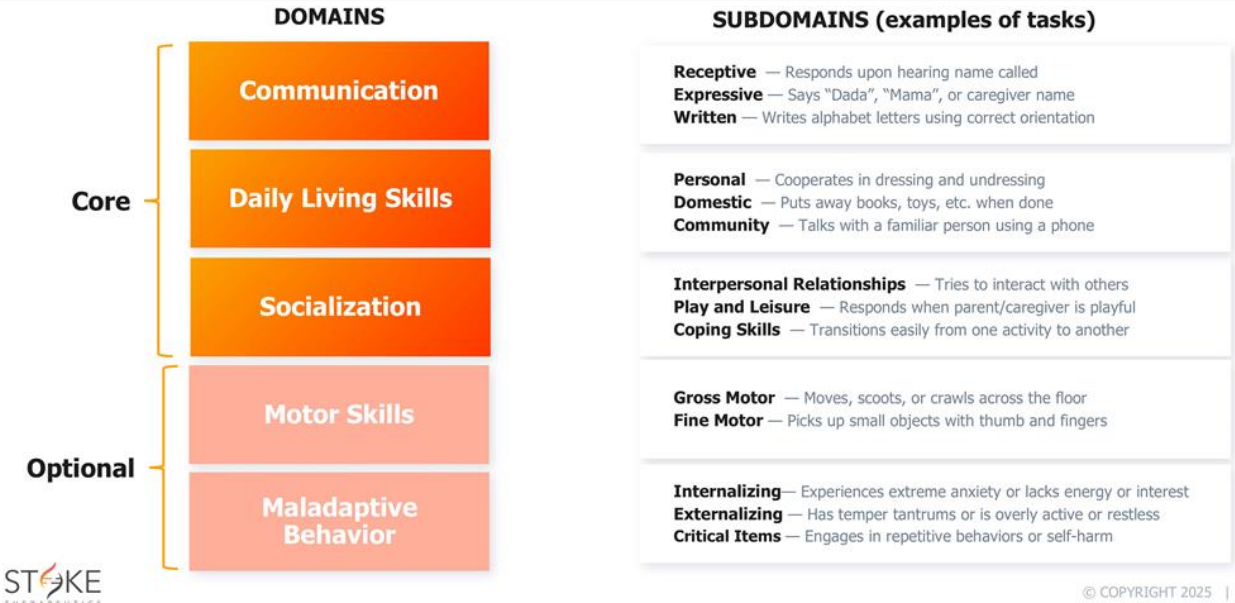
End of Phase 1/2a study data. Datacut June 28, 2024, for OLEs.
**71/74 patients had ≥1 post-baseline CSF protein value in the OLEs*
†Number of doses to date includes doses administered after the June 28, 2024, safety datacut for the OLEs.
CSF, cerebrospinal fluid; OLE, open-label extension; SUSAR, suspected unexpected serious adverse reaction; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Potential for Disease Modification

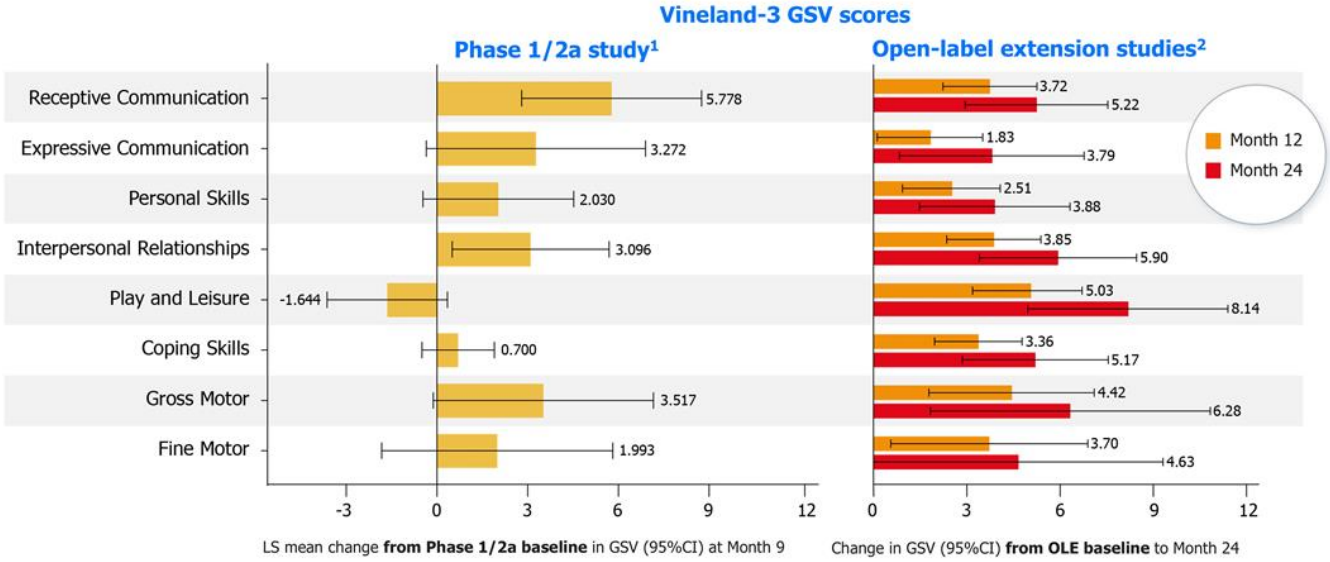
Kimberly Parkerson, M.D., Ph.D.
Head of Neurology Clinical Development

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

Vineland-3 Adaptive Behavior Scales – Overview



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

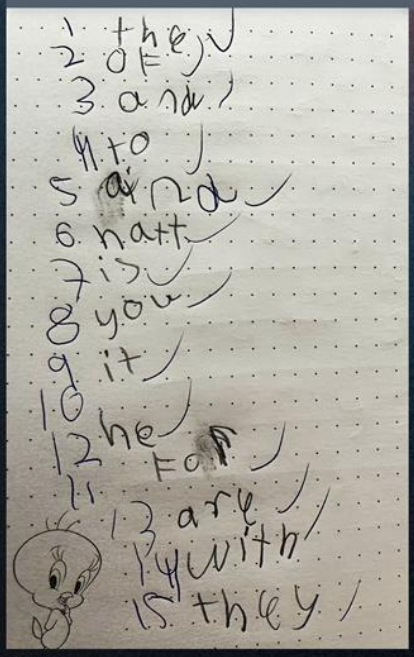


[1] *Machine learning model constructed using data from EOS Ph1/2a ADMIRAL (all dose cohorts) and data through Month 4 visit in LONGWING OLE (as of Nov. 2023)*
[2] *Mixed-effects model for repeated measures constructed using data through Month 24 from enrolled patients in OLE studies. Data cutoff 28 June 2024.*

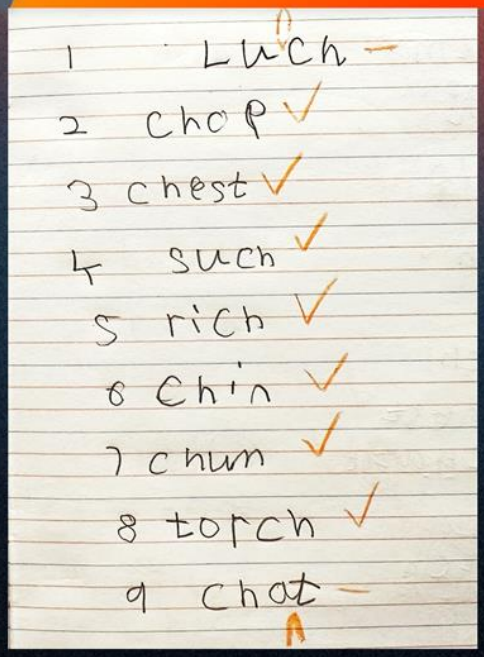
Handwriting from a 12 year-old before and after treatment with zorevunersen*

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

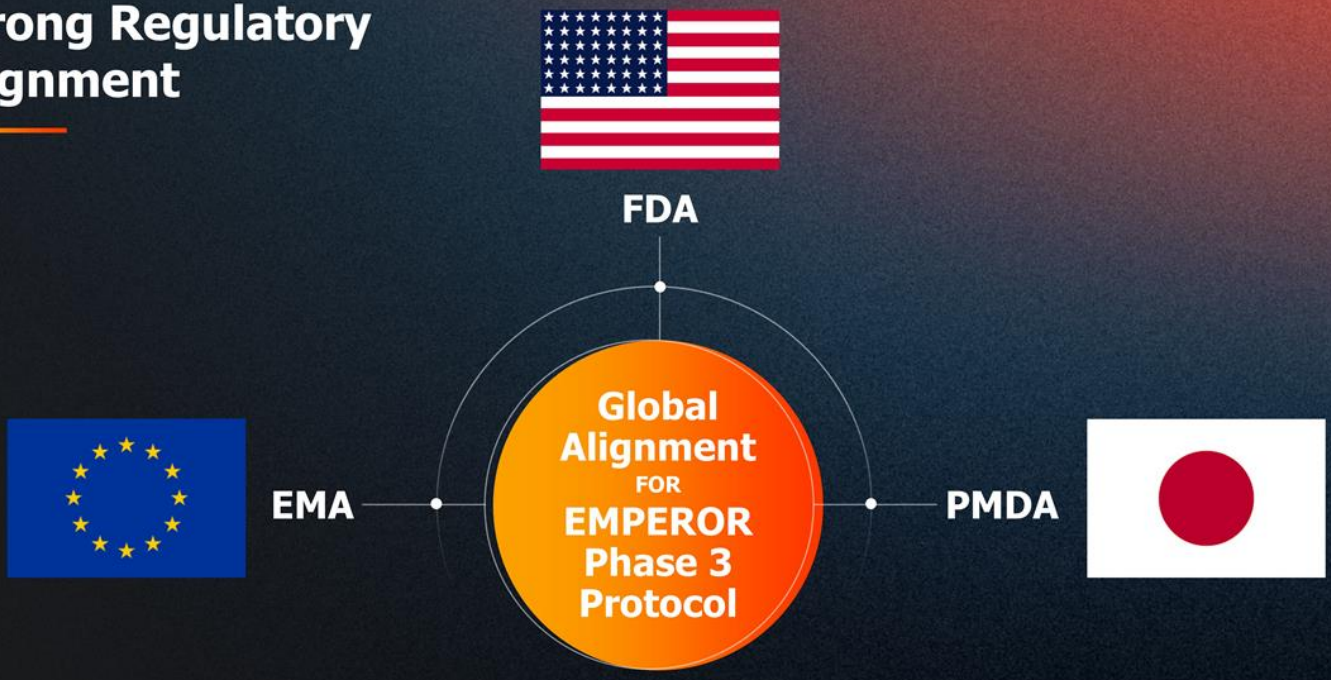


AFTER 9mo of Treatment
November 2023



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.*

Strong Regulatory Alignment

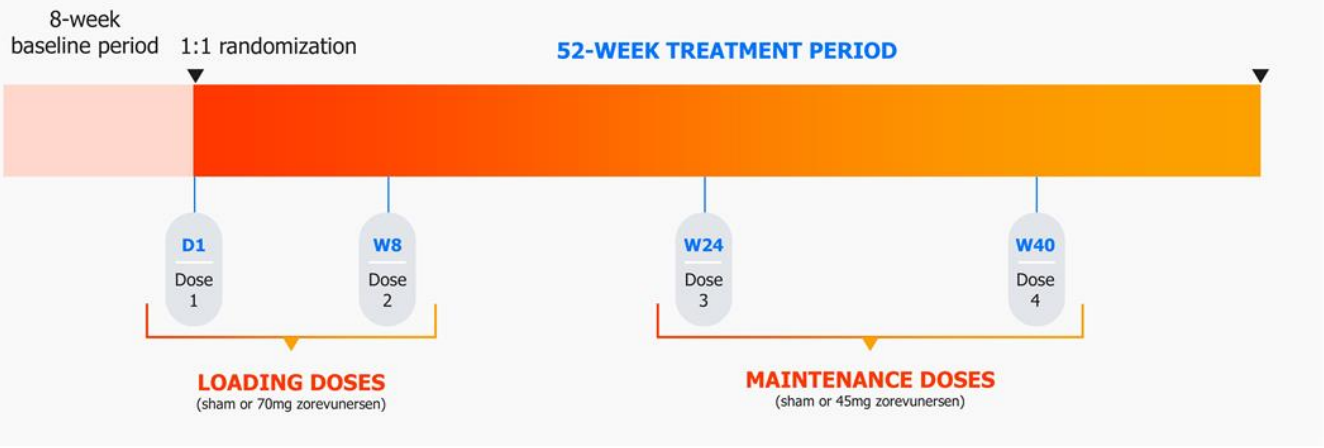


Regulatory discussions ongoing

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

STOKE THERAPEUTICS

Regulatory discussions ongoing

Operational Optimization

Strategies to Drive Efficiency for Emperor Start-Up and Implementation

Speed

- Rapid-start sites identified
- Returning Ph1/2a sites
- Streamlined document submissions to sites
- Pre-screening process to expedite enrollment

Efficiency and Quality

- Site visits to ensure quality and compliance
- Pursue as many centralized IRB sites as possible
- Electronic informed consent

Caregiver and Site Support

- Clinical Trial Educators
- Travel concierge service
- Global patient advocacy education and engagement

HCP Collaboration

- Personalized support for site staff
- Regional study referral programs

Commercial Opportunity

Jason Hoitt
Chief Commercial Officer

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.

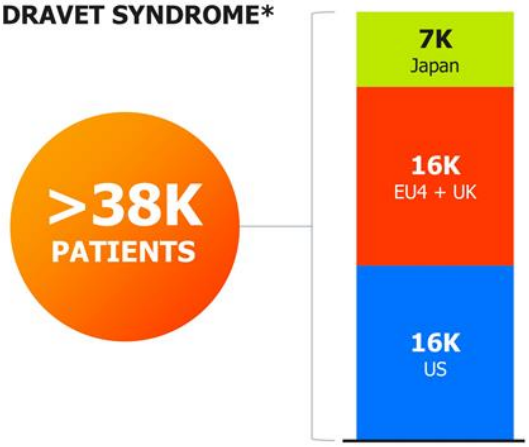
> **The option of a treatment, such as zorevunersen**, that could not only potentially reduce or eliminate seizures, as well as offer some level of disease reversal, would **represent a profound breakthrough for individuals living with Dravet syndrome**. It could change Dravet syndrome from a profoundly 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

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

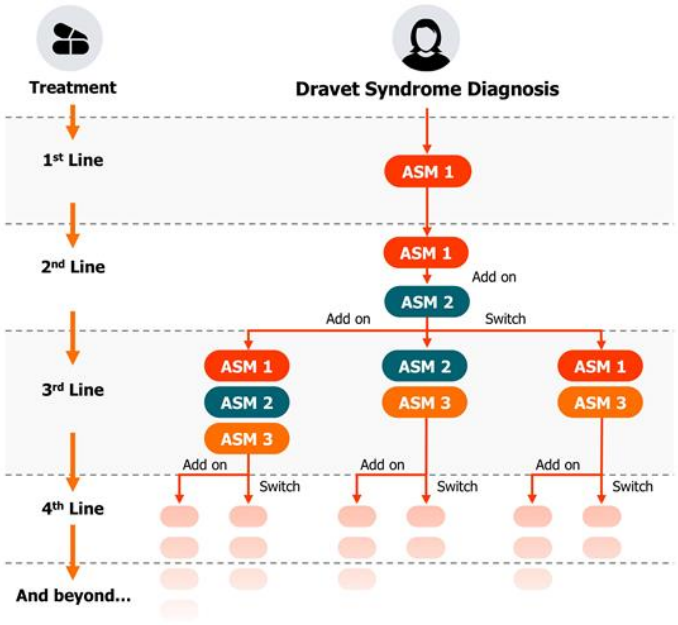
- Patients with Dravet syndrome **fall further and further behind** their neurotypical peers

*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

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."

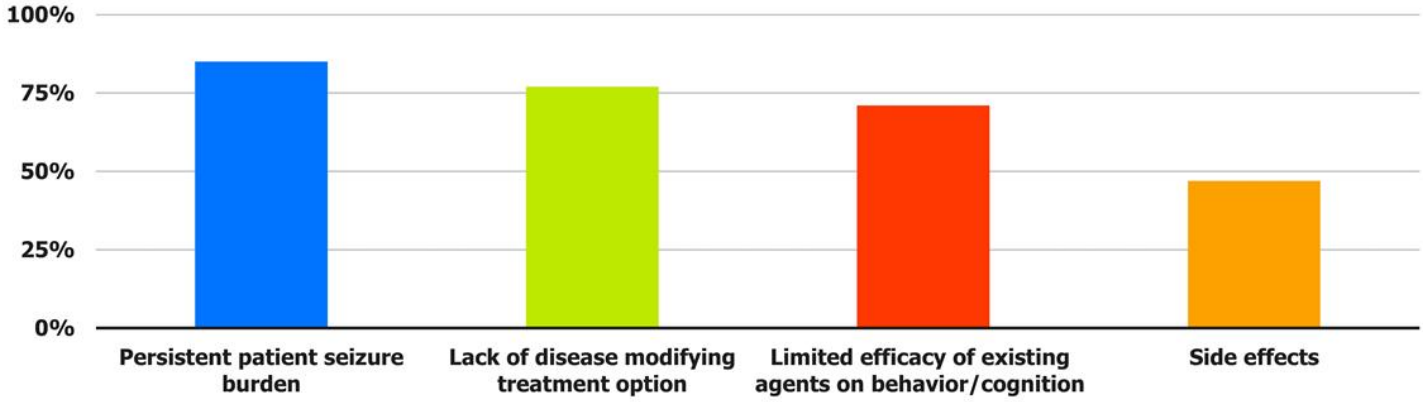
"We need to improve **seizure** control given patients can **still experience 20 seizures in a week while on many medications**."

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.

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.

Support for a Disease Modifying Therapy for Dravet Syndrome

Caregivers & Advocates

My excitement for this product is a 10 out of 7. This gives me hope that there is something that can help my child.

HCPs

No SOC has shown meaningful impact on cognitive improvement. The MOA leads me to believe this will be effective in both reducing seizures and improving cognition and behavior.

Payers

I am happy with the seizure reduction because it is on top of what we consider to be best in class. Behavioral and cognitive benefit is also a helpful endpoint.

ZOREVUNERSEN HAS BLOCKBUSTER POTENTIAL

Based on Company sponsored interviews using a Product X profile based on MONARCH and ADMIRAL study results.
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Closing Remarks

Edward M. Kaye, M.D.
Chief Executive Officer

Q&A

