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): March 25, 2024

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** **(Address of Principal Executive Offices)**		**01730** **(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 March 25, 2024, Stoke Therapeutics, Inc. (the "Company") issued a press release announcing new data from two Phase 1/2a studies and two open-label extension studies of children and adolescents ages 2 to 18 with Dravet syndrome who were treated with STK-001. The Company also released an investor presentation with information about these data.

A copy of each of press release and the presentation regarding the data announcement is furnished as Exhibit 99.1 and 99.2, respectively, to this Current Report on Form 8-K and incorporated by reference herein.

The information furnished under this Item 7.01, 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 9.01 Financial Statements and Exhibits.

Exhibit Number	Description
99.1	Press Release dated March 25, 2024
99.2	Presentation, dated as of March 2024
104	Cover Page Interactive Data File (the cover page XBRL tags are embedded within the inline XBRL document).

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: March 25, 2024

By: /s/ Stephen J. Tulipano
Stephen J. Tulipano
Chief Financial Officer

Exhibit 99.1

Stoke Therapeutics Announces Landmark New Data That Support the Potential for STK-001 to be the First Disease-Modifying Medicine for the Treatment of Patients with Dravet Syndrome

– Phase 1/2a End of Study Data: 70mg doses demonstrated substantial and sustained reductions in convulsive seizure frequency on top of the best available anti-seizure medicines; Median reductions of 85% (n=10) at 3 months and 74% (n=9) at 6 months after last dose –

– Open Label Extension Studies: Durable reductions in seizures and clinically meaningful improvements in multiple measures of cognition and behavior were maintained over 12 months with continued dosing at 30mg and 45mg –

– STK-001 generally well-tolerated –

– Company to meet with regulatory agencies to discuss registrational study design with initial doses of 70mg followed by continued dosing at 45mg –

– Webcast and conference call for analysts and investors at 4:30 p.m. Eastern Time today –

BEDFORD, Mass., March 25, 2024 – Stoke Therapeutics, Inc. (Nasdaq: STOK), a biotechnology company dedicated to addressing the underlying cause of severe diseases by upregulating protein expression with RNA-based medicines, today announced landmark new data from two open-label Phase 1/2a studies and two open-label extension (OLE) studies of children and adolescents ages 2 to 18 with Dravet syndrome who were treated with STK-001. Data from these studies showed clinically meaningful effects, including substantial and durable reductions in convulsive seizure frequency and improvements in multiple measures of cognition and behavior that support the potential for disease modification. These improvements were observed among a highly refractory group of patients who were already taking the best available anti-seizure medicines. STK-001 has been generally well-tolerated in studies to date.

Today, the Company also announced clearance from the U.S. Food and Drug Administration (FDA) that allows patients to receive three doses of 70mg followed by continued dosing at 45mg. Based on this regulatory update and these data, the Company plans to meet with regulatory agencies to discuss a registrational study that includes initial doses of 70mg followed by continued dosing at 45mg.

“The totality of these data provide compelling evidence that support the potential for STK-001 to be a disease-modifying medicine for patients with Dravet syndrome by treating the underlying cause of the disease, rather than just the symptoms,” said Edward M. Kaye, M.D., Chief Executive Officer of Stoke Therapeutics. “STK-001 is the first medicine in development to demonstrate substantial and durable reductions in seizure frequency and improvements in multiple measures of cognition and behavior. These effects were observed in patients who were already taking the best available anti-seizure medicines, which confirms our highly differentiated mechanism of action and approach to treating this disease. We look forward to meeting with regulatory agencies to discuss our plans for a randomized, controlled registrational study and to providing an update coming out of those discussions later in 2024.”

“For decades, the primary goal of treating Dravet syndrome has been to control the frequency and severity of seizures, but, as we can now see from natural history data, many patients still experience high rates of seizure frequency and fall further and further behind in their neurodevelopment,” said Joseph Sullivan, M.D., FAES, Professor of Neurology and Pediatrics and Director of the Pediatric Epilepsy Center of Excellence at the University of California San Francisco, and a prominent researcher in Dravet syndrome. “A 50% reduction in seizures is an important measure of clinical efficacy, so an 80% reduction on top of any benefit patients may already be getting from their baseline anti-seizure regimen is profound. The further evidence of improvements in skills like communication, behavior, socialization and movement distinguish this approach from anything we have seen to date and mark our entry into a new era in the treatment of Dravet syndrome.”

Phase 1/2a Study Results: Substantial and Sustained Reductions in Convulsive Seizure Frequency

The Phase 1/2a studies were multi-center and included children and adolescents who have an established diagnosis of Dravet syndrome. Patients enrolled in these studies were highly refractory to treatment and taking the best available anti-seizure medicines: 85% of patients were taking at least three and 54% were taking at least four medicines to control seizures. Half the patients in the studies were taking concomitant fenfluramine.

New data from a combined analysis of 19 clinically evaluable patients who were treated with one, two or three doses of 70mg demonstrated substantial reductions in convulsive seizure frequency compared to baseline at 3 months and at 6 months after the last dose, one of several secondary endpoints in each study.

Observed Reductions in Convulsive Seizure Frequency Among Patients Treated with 70mg Doses of STK-001 in the Phase 1/2a Studies

Median % Reduction from Baseline in Convulsive Seizure Frequency	70mg (1 dose, n=8)	70mg (2 or 3 doses, n=11)
At 3 Months After Last Dose	43% (n=8)	85% (n=10†)
At 6 Months After Last Dose	57% (n=7*)	74% (n=9†)

* Seizure data excluded from month 5-6 for 1 patient because >50% seizure diary was missing

† Seizure data excluded for 2 patients (1 patient prior to 3m after last dose, 1 prior to 6m after last dose) following a change in background antiseizure medicines

Open Label Extension Studies: Durable reductions in seizures and clinically meaningful improvements in multiple measures of cognition and behavior over 12 months with continued dosing at 30mg and 45mg

Eligible patients who completed treatment in the Phase 1/2a studies continued treatment with STK-001 in one of two OLEs. At the time of the analysis, 92% (68/74) of eligible patients had enrolled in the OLEs and 84% (57/68) remained in the studies.

Durable reductions in convulsive seizure frequency were observed throughout the course of treatment. This analysis only included patients who received ≥30mg of STK-001 in the Phase 1/2a studies and then continued treatment with STK-001 (30mg or 45mg) every four months in the OLEs. Clinically meaningful improvements from baseline through 12 months were observed in multiple measures of cognition and behavior, including multiple sub-domains of the Vineland Adaptive Behavior Scale (VINELAND-3).

These improvements are in stark contrast to recent natural history study data that showed that, on average, patients with Dravet syndrome experienced no meaningful improvement in convulsive seizure frequency and exhibited widening gaps in cognition and behavior compared to neurotypical peers, despite treatment with the best available anti-seizure medicines.

Key Safety Findings

At the time of the analyses, 81 patients had been treated with STK-001. Safety findings are summarized below.

- STK-001 was generally well-tolerated across the Phase 1/2a and OLE studies.
- In the Phase 1/2a studies:
  - 30% (24/81) of patients experienced a treatment-emergent adverse event (TEAE) that was related to study drug. The most common were CSF protein elevations and procedural vomiting; and
  - 22% (18/81) of patients had a treatment-emergent serious adverse event. These events were assessed as unrelated to study drug except for the previously reported case of one patient who experienced Suspected Unexpected Serious Adverse Reactions (SUSARs).
- A greater incidence of CSF protein elevation was observed in the OLEs. 74% (50/68) of patients in the OLEs had at least 1 CSF protein value >50 mg/dL. No clinical manifestations have been observed in these patients.
- Across the studies, one patient discontinued treatment due to study drug. As previously reported, this patient discontinued treatment in the OLE due to elevated CSF protein.

Stoke Webcast and Conference Call for Analysts and Investors

Stoke will host a webcast and conference call for analysts and investors at 4:30 p.m. Eastern Time on March 25, 2024, to present landmark new data from two Phase 1/2a studies and two ongoing open-label extension (OLE) studies in children and adolescents ages 2 to 18 with Dravet syndrome. The webcast will be broadcast live on the Investors & News section of Stoke's website at https://investor.stoketherapeutics.com/. Participants who want to join the call and ask a question may register here to receive the dial-in numbers and unique PIN to seamlessly access the call. Otherwise please access the listen-only webcast by clicking here. An archived replay of the webcast will be available for at least 90 days following the event.

About Dravet Syndrome

Dravet syndrome is a severe and progressive genetic epilepsy characterized by frequent, prolonged and refractory seizures, beginning within the first year of life. 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. The effects of the disease go beyond seizures and 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. The disease is classified as a developmental and epileptic encephalopathy due to the developmental delays and cognitive impairment associated with the disease. 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 out of 16,000 babies are born with Dravet syndrome, which is not concentrated in a particular geographic area or ethnic group.

About STK-001

STK-001 is an investigational new medicine for the treatment of Dravet syndrome currently being evaluated in ongoing clinical trials. Stoke believes that STK-001, a proprietary antisense oligonucleotide (ASO), has the potential to be the first disease-modifying therapy to address the genetic cause of Dravet syndrome. STK-001 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. STK-001 has been granted orphan drug designation by the FDA and the EMA, and rare pediatric disease designation by the FDA as a potential new treatment for Dravet syndrome.

About the U.S. Studies: MONARCH (Phase 1/2a) and SWALLOWTAIL (OLE)

The MONARCH study was a Phase 1/2a open-label study of children and adolescents ages 2 to 18 who have an established diagnosis of Dravet syndrome and have evidence of a genetic mutation in the *SCN1A* gene. The primary objectives for the study were to assess the safety and tolerability of STK-001, as well as to determine the pharmacokinetics in plasma and exposure in cerebrospinal fluid. A secondary objective was to assess the efficacy as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency.

Following completion of MONARCH, patients who met study entry criteria were eligible to continue treatment in SWALLOWTAIL, an open-label extension (OLE) study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001. The study is also evaluating the long-term effects of STK-001 on convulsive seizure frequency and on behavior, cognition and overall quality of life. Dosing in SWALLOWTAIL is ongoing.

About the UK Studies: ADMIRAL (Phase 1/2a) and LONGWING (OLE)

The ADMIRAL study was a Phase 1/2a open-label study of children and adolescents ages 2 to <18 who have an established diagnosis of Dravet syndrome and have evidence of a genetic mutation in the *SCN1A* gene. The primary objectives for the study were to assess the safety and tolerability

of multiple doses of STK-001, as well as to determine the pharmacokinetics in plasma and exposure in cerebrospinal fluid. A secondary objective was to assess the effect of multiple doses of STK-001 as an adjunctive antiepileptic treatment with respect to the percentage change from baseline in convulsive seizure frequency. Overall clinical status and quality of life were secondary endpoints of ADMIRAL.

Following completion of ADMIRAL, patients who met study entry criteria were eligible to continue treatment in LONGWING, an open-label extension (OLE) study designed to evaluate the long-term safety and tolerability of repeat doses of STK-001. The study is also evaluating the long-term effects of STK-001 on convulsive seizure frequency and on behavior, cognition and overall quality of life. Dosing in LONGWING is ongoing.

About the BUTTERFLY Observational Study

The BUTTERFLY study was a multicenter, longitudinal, prospective, observational study of children and adolescents ages 2 to 18 who have been diagnosed with Dravet syndrome as a result of an *SCN1A* gene mutation. This study was designed to evaluate neurodevelopmental status and change from baseline to 24 months. Secondary and exploratory endpoints in the study evaluated changes in other disease measures, including seizures and additional non-seizure comorbidities. No investigational medications or other treatments were provided. Participants continued to receive their usual care, including anti-seizure medications, and were observed for up to two years. The study was conducted at approximately 20 sites in the United States. Two-year results were presented at the American Epilepsy Society in December 2023 and showed that, on average, patients experienced no meaningful improvement in convulsive seizure frequency and exhibited widening gaps in cognition and behavior compared to neurotypical peers, despite treatment with the best available anti-seizure medicines.

About Stoke Therapeutics

Stoke Therapeutics (Nasdaq: STOK), is a biotechnology company dedicated to addressing the underlying cause of severe diseases by upregulating protein expression with RNA-based medicines. 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, 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 STK-001 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, and the timing and expected progress of clinical trials, 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 of, and ultimately commercialize its product candidates, including STK-001; 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 into 2025; 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.

Stoke Media & Investor Contacts:

Dawn Kalmar
Chief Communications Officer
dkalmar@stoketherapeutics.com
781-303-8302

Eric Rojas
Vice President, Investor Relations
IR@stoketherapeutics.com
617-312-2754

Exhibit 99.2

Analysis of STK-001 for the Treatment of Dravet Syndrome

Stoke Therapeutics

March 25, 2024

Agenda

- **Introduction**
  Eric Rojas, Head of Investor Relations
- **Introductory Remarks**
  Edward M. Kaye, M.D., Chief Executive Officer
- **Analysis of Phase 1/2a and Open-Label Extension (OLE) Studies of STK-001**
  Barry Ticho, M.D., Ph.D., Chief Medical Officer
  Kimberly Parkerson, M.D., Ph.D., Head of Neurology Clinical Development
- **Closing Remarks**
  Edward M. Kaye, M.D., Chief Executive Officer
- **Q&A (to include additional Stoke leadership)**
  Shamim Ruff, Chief Regulatory Officer

Forward Looking Statements

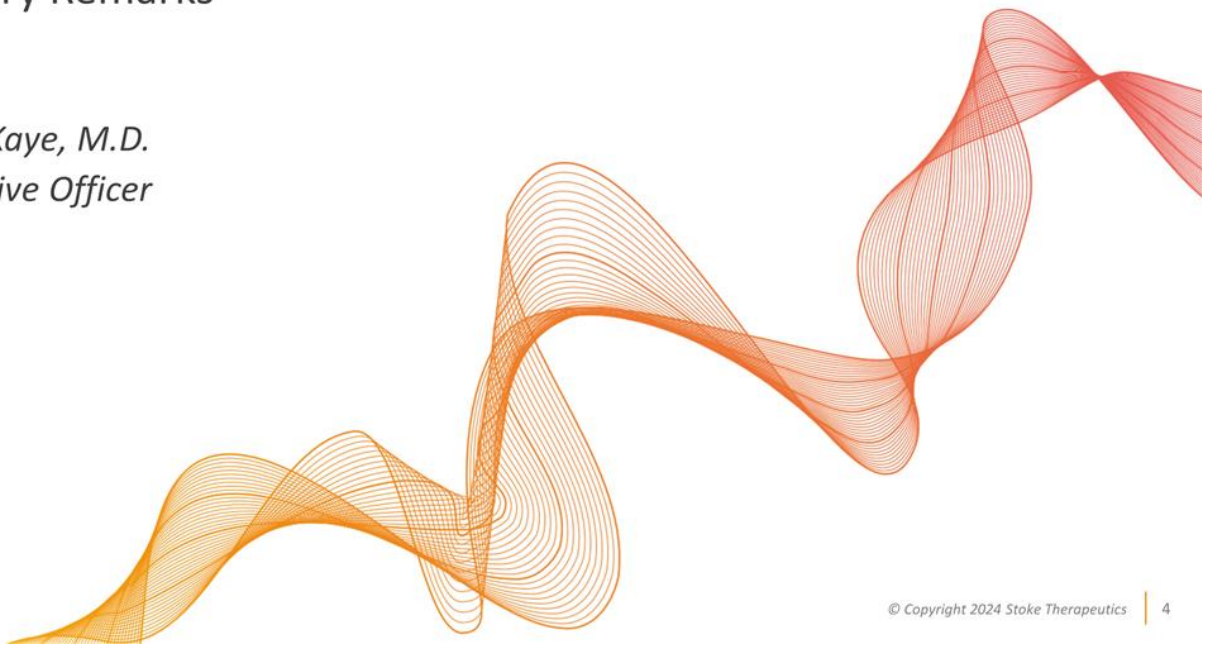
This presentation has been prepared by Stoke Therapeutics, Inc. ("Stoke" or "we") for informational purposes only and for no other purpose. Nothing contained in this presentation is, or should be construed as, a recommendation, promise or representation by the presenter or Stoke or any officer, director, 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.

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 STK-001 to treat the underlying causes of Dravet syndrome and reduce seizures or show improvements in cognition or behavior at the indicated dosing levels or at all, and the timing and expected progress of clinical trials, data readouts, regulatory meetings, regulatory decisions and other presentations. Statements including words such as "anticipate," "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: our ability to advance, obtain regulatory approval of, and ultimately commercialize our product candidates, including STK-001; 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; our ability to fund development activities and achieve development goals into 2025; our ability to protect our 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 our Annual Report on Form 10-K for the year ended December 31, 2023, our quarterly reports on Form 10-Q, and the other documents 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.

Introductory Remarks

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



Landmark New Data Support the Potential for STK-001 to be The First Medicine to Treat the Underlying Cause of Dravet Syndrome

Reductions in seizures **and** improvements in cognition and behavior that support the potential for disease modification

Phase 1/2a Study Data: 70mg doses demonstrated **substantial & sustained** reductions in convulsive seizure frequency of:

85% at 3 months (n=10)

&

74% at 6 months (n=9)

on top of the best available anti-seizure medicines

OLE Studies (30mg, 45mg): Clinically meaningful, durable **reductions in seizures** and **improvements in multiple measures of cognition & behavior** over 12 months

Recent FDA clearance for 3 doses of 70mg and continued dosing at 45mg

Next Steps: Meet with regulatory agencies to discuss registrational study of 70mg followed by 45mg

OLE: Open-Label Extension Study

Cause of Dravet Syndrome

of Dravet cases caused by a **HAPLOINSUFFICIENCY** of the *SCN1A* gene

Resulting in

$Na_V1.1$ protein expression

Source: Nabbout et al., Orphanet Journal of Rare Diseases, 2013

Our Goal

Deliver the first disease modifying-medicine for Dravet syndrome

Our Approach

Leverage the wild-type *SCN1A* allele to boost the production of full-length, fully-functional $Na_V1.1$ protein to treat the underlying cause of Dravet syndrome

STK-001 is on Track to be the First Disease-Modifying Medicine to Treat the Underlying Cause of Dravet Syndrome

Multiple medicines available for

Seizure management

Despite these treatments, seizures are not adequately controlled in 90% of patients with Dravet syndrome

Available medicines used to control seizures:

- Acetazolamide
- Benzodiazepines
- Brivaracetam
- Cannabidiol
- Carbamazepine
- Clobazam
- Ethosuximide
- Felbamate
- Fenfluramine
- Lamotrigine
- Levetiracetam
- Mesuximide
- Oxcarbazepine
- Phenytoin
- Rufinamide
- Stiripentol
- Topiramate
- Valproate products
- Zonisamide

No medicines currently available for

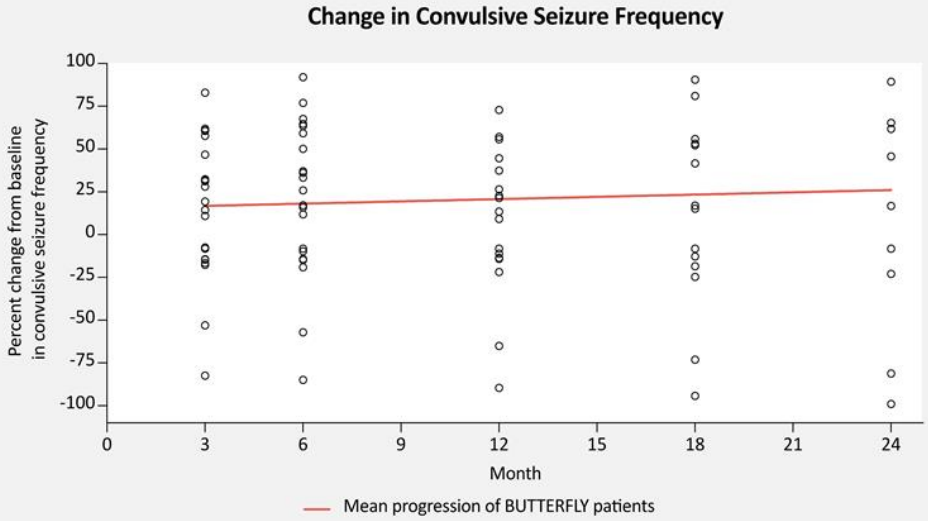
Dravet syndrome management

STK-001

The first potential disease-modifying approach to address the genetic cause of Dravet syndrome

Source: Lagae et al., Developmental Medicine & Child Neurology, 2017

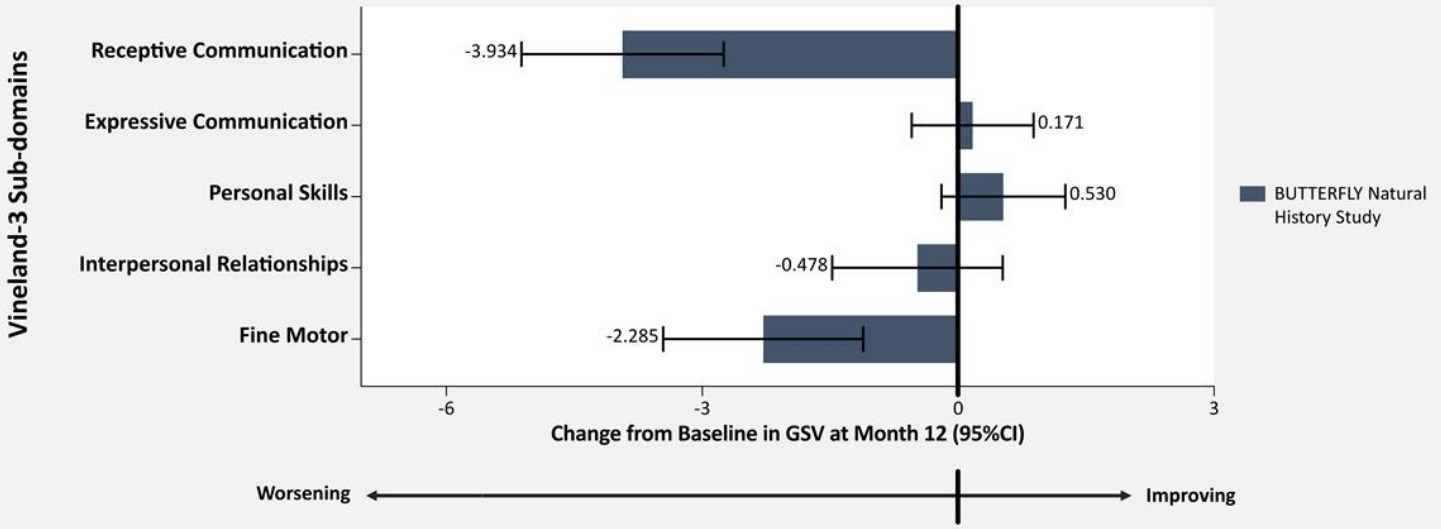
Natural History Data: Despite Standard Anti-Seizure Medicines, No Meaningful Improvement in Convulsive Seizure Frequency



Patients were treated with the best available anti-seizure medicines	
Median baseline convulsive seizure frequency per 28 days (95% CI), n=26	
10.0 (5.50, 15.5)	
Most common ongoing anti-seizure medicines, n (%)	
Clobazam	25 (69.4%)
Fenfluramine	16 (44.4%)
Stiripentol	14 (38.9%)
Valproic Acid	14 (38.9%)
Cannabidiol	12 (33.3%)
Levetiracetam	8 (22.2%)

Source: 24-Month Analysis of BUTTERFLY: A Prospective, Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome (DS), AES 2023.

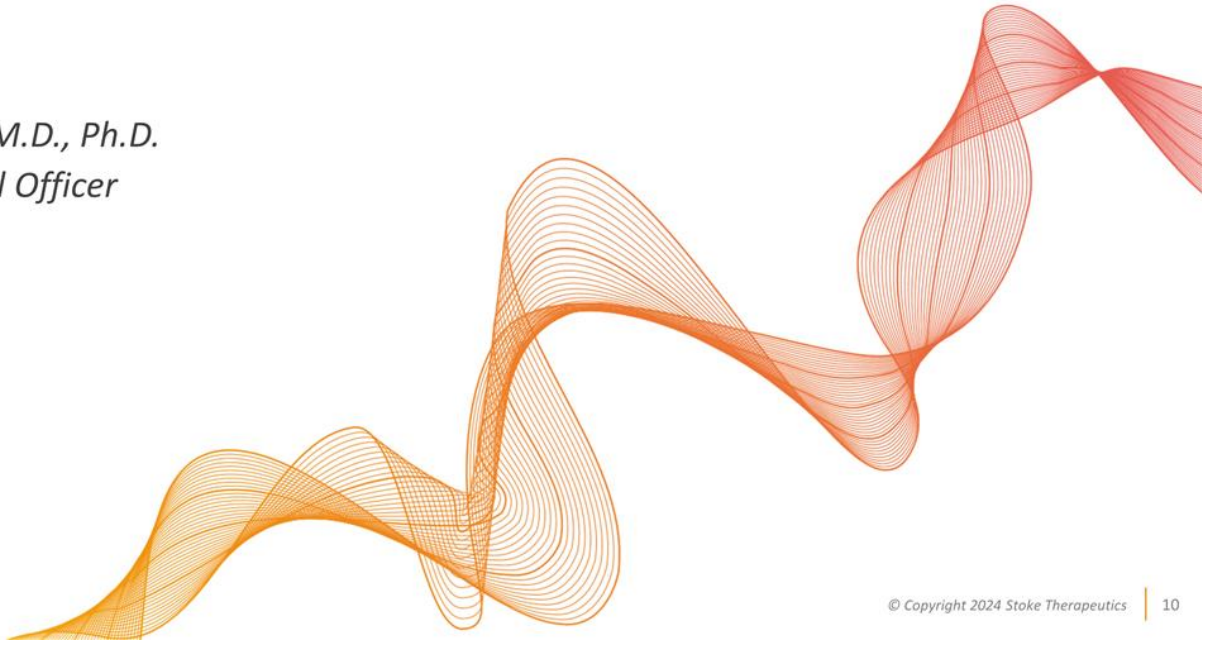
Natural History Data: Despite Best Available Anti-Seizure Medicines, No Improvement in Cognition and Behavior



Note: Analysis based on data from BUTTERFLY through Month 24 analyzed with Machine Learning.
Vineland-3: The Vineland Adaptive Behavior Scales, Third Edition. GSV = Growth Scale Value.

Analysis of Data from Studies of STK-001

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



81 Patients Treated to Date with STK-001

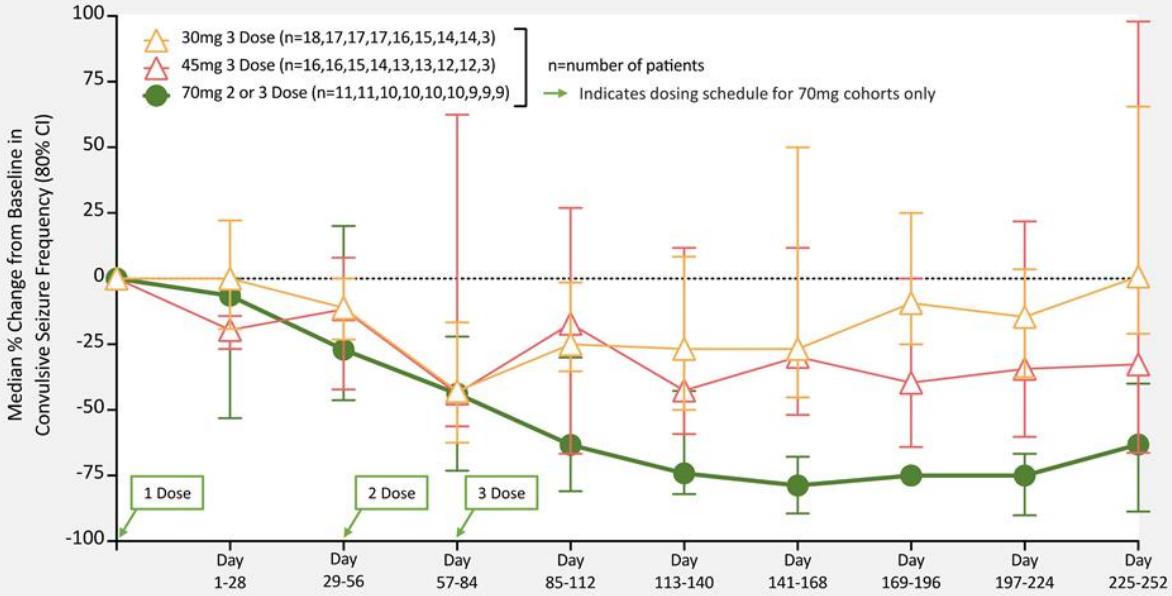
- Ages 2-18
- Highly refractory to standard treatment

Patient Demographics at Phase 1/2a Study Initiation

	Total, n (%)
N	81
Age at Screening	
Mean (SD)	9.9 years (5.05)
Number of Concomitant Anti-Seizure Medications	
≥3	69 (85%)
≥4	44 (54%)
Concomitant Fenfluramine	
Yes	40 (49%)
Baseline Convulsive Seizure Frequency per 28 days (n = 77)	
Median (min, max)	17 (4.0, 2335)

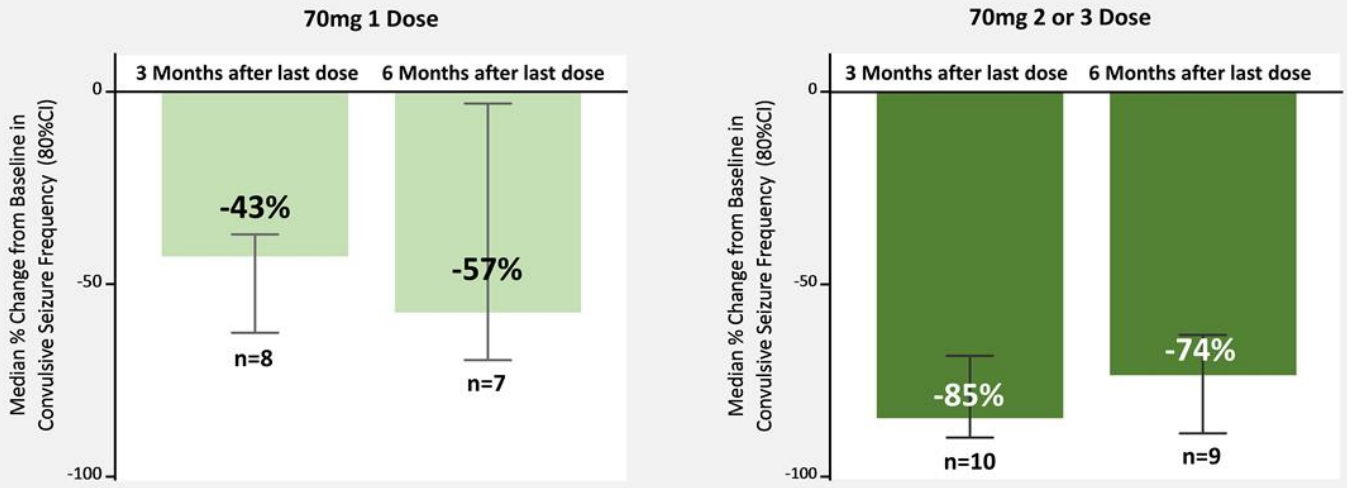
Data cutoff dates: Phase 1/2a Studies 12DEC2023; OLE Studies 01NOV2023

70mg Doses of STK-001 Demonstrated the Most Substantial Reductions in Seizure Frequency on Top of Standard of Care Medicines



Substantial Reductions in Seizure Frequency **at** 3 and Sustained **at** 6 Months after Last Dose with 1, 2 or 3 Doses of STK-001 (70mg)

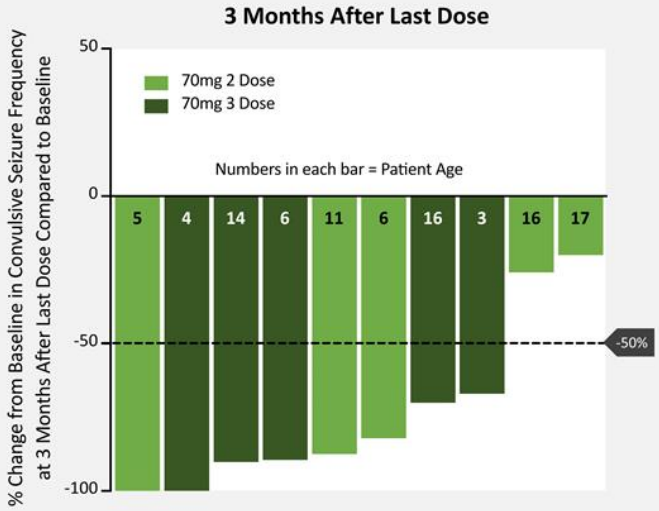
Benefits observed across highly refractory patients already taking best available anti-seizure medicines

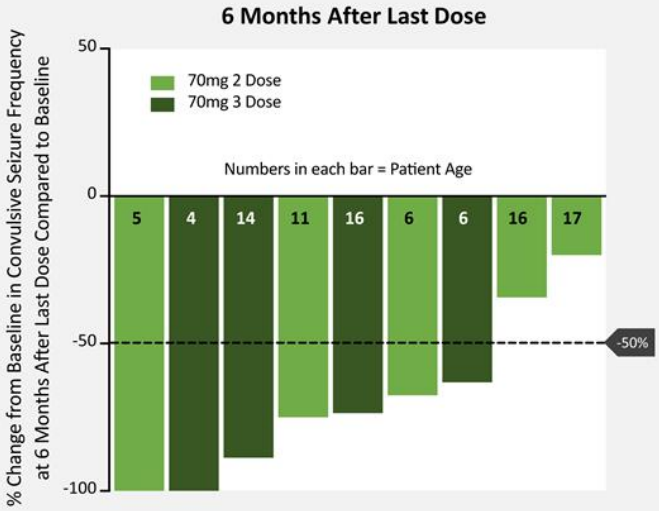


1 dose data is from the U.S. MONARCH study, 2 and 3 dose data is from UK ADMIRAL study

~80% of Patients Treated with 2 or 3 Doses of STK-001 (70mg) Experienced >50% Reduction in Seizures

A 50% responder rate is an important measure of efficacy





Note: 3 months after last dose refers to D113 to D140 (2 dose MAD) and D141 to D168 (3 dose MAD) and 6 months after last dose refers to D197 to D224 (2 dose MAD) and D225 to D252 (3 dose MAD)

2 and 3 dose data is from UK ADMIRAL study

Phase 1/2a Data Support a Potential 70mg Loading Dose Regimen in a Registrational Study

The most substantial reductions in seizures observed with 2 and 3 doses of 70mg

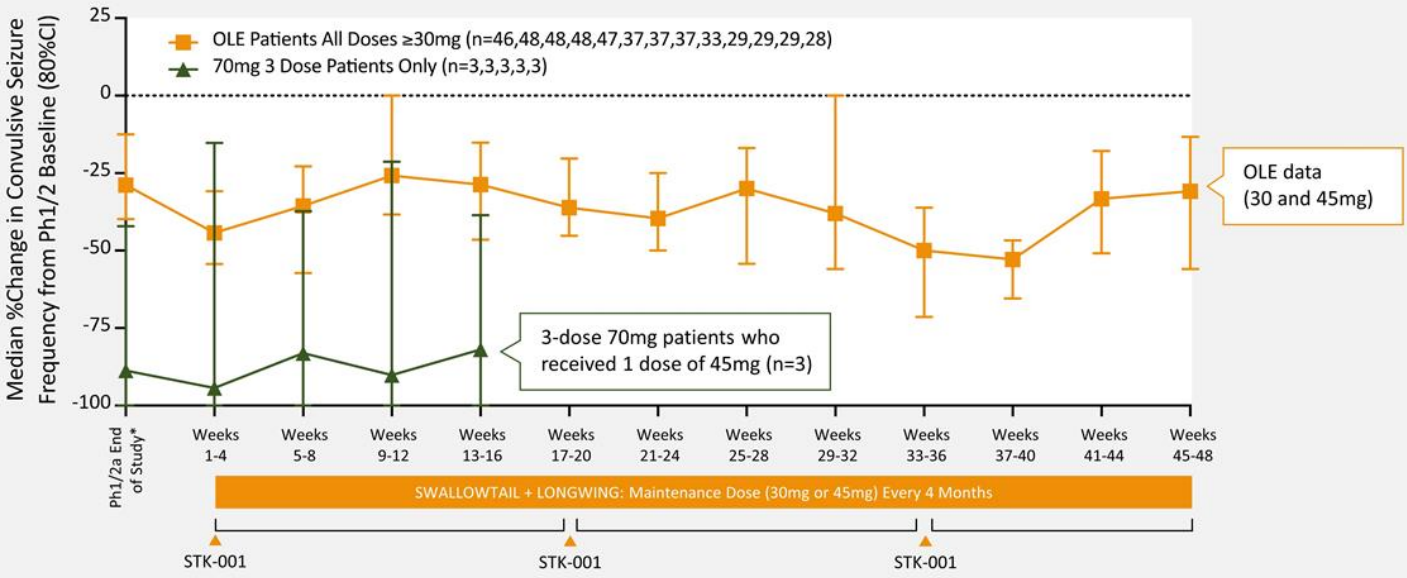
- 85% at 3 months and 74% at 6 months post last dose
- ~80% of patients experienced >50% reduction in convulsive seizure frequency

Patient Progression Through Studies

Ph 1/2a Studies (n=81)	6 Month Follow Up Period	Open Label Extension Studies (n=68)	Status*
Single or multiple doses of STK-001 up to 70mg	ASM regimen continues	Continued treatment with STK-001 at 30mg or 45mg every 4 months	84% (57/68) remained on study
1, 2 or 3 doses of STK-001 administered on top of existing anti-seizure regimen	No STK-001 is administered	STK-001 administered on top of anti-seizure regimen	10 patients have received up to 10 doses of STK-001
	74 patients eligible for OLE		

Data cutoff dates: Phase 1/2a Studies 12DEC2023; OLE Studies 01NOV2023

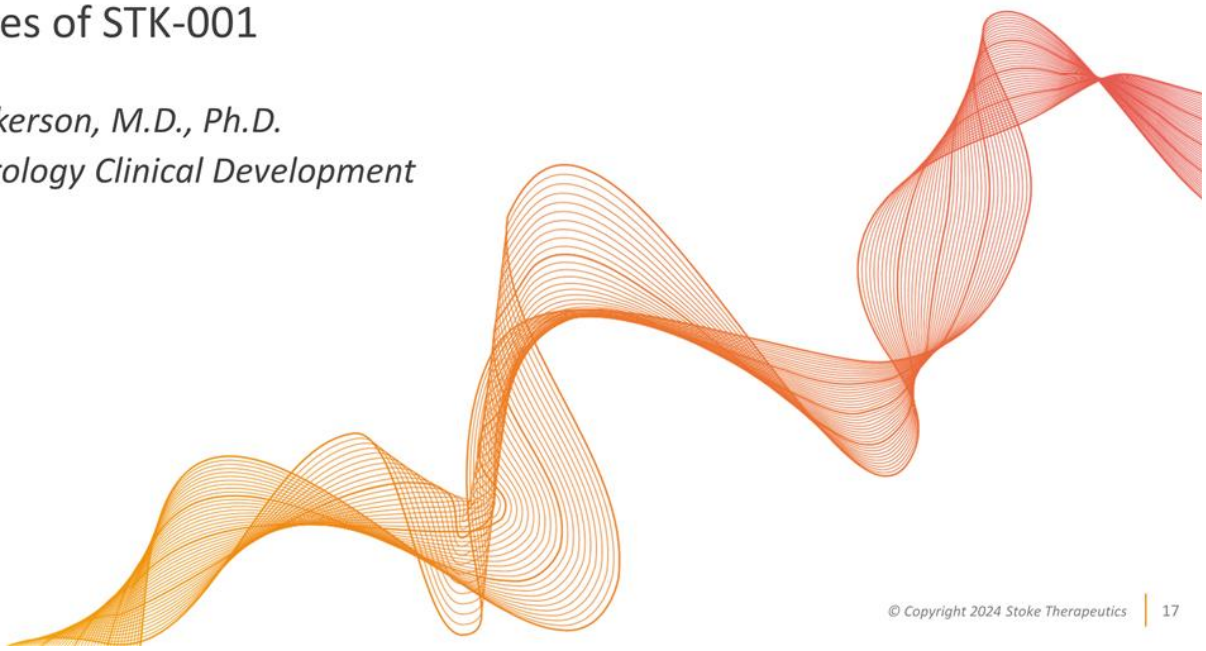
Durable Reductions in Seizure Frequency Observed with Continued Treatment with STK-001 in OLE Studies



*End of Study = 24 Weeks After Last Dose in Phase 1/2 Study

Analysis of Safety, Cognition and Behavior from Studies of STK-001

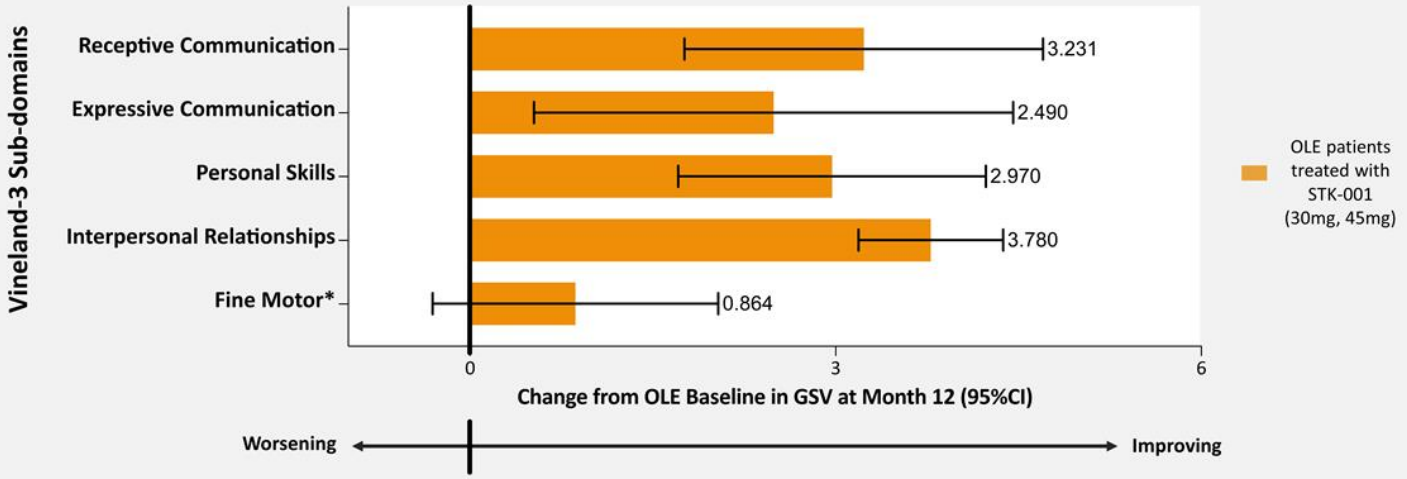
Kimberly Parkerson, M.D., Ph.D.
Head of Neurology Clinical Development



Clinically Meaningful Improvements in Cognition and Behavior Over 12 Months with Continued Treatment with STK-001 (30mg, 45mg)

STOKE THERAPEUTICS

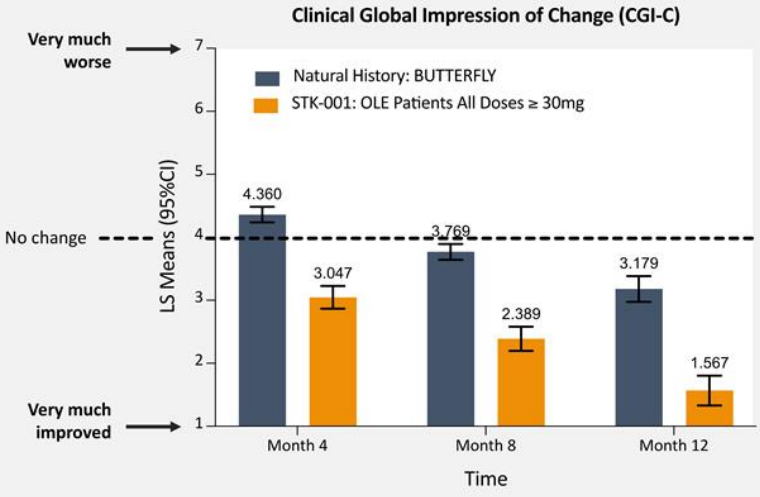
Improvements are in stark contrast to natural history study data

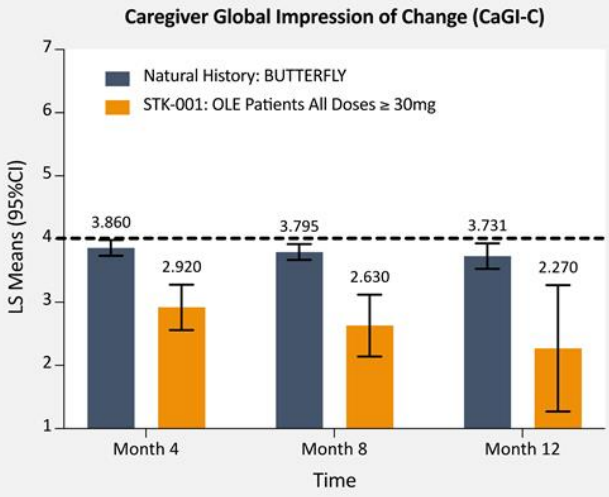


Note: Analysis based on a mixed-effects model for repeated measures (MMRM).
**Fine motor did not meet the threshold of clinically meaningful change.*
Vineland-3: The Vineland Adaptive Behavior Scales, Third Edition. GSV = Growth Scale Value.

Clinically Meaningful Improvements in Overall Condition Over 12 Months with Continued Treatment with STK-001 (30mg, 45mg)

Consistency across clinician and caregiver assessments of improvements observed in the OLEs





Note: Analysis based on a mixed-effects model for repeated measures (MMRM). Data from BUTTERFLY through Month 24 from start of study analyzed with machine learning. Due to differences between trials, cross-study comparisons may provide limited information on the efficacy or safety of a drug.

OLE Data Support a Potential 45mg Maintenance Dosing Regimen in a Registrational Study

Effects observed on cognition and behavior indicate potential for disease modification

Clinically meaningful improvements in cognition and behavior over 12 months

Improvements are in contrast to 2-year natural history study data that show widening gaps in cognition and behavior compared to neurotypical peers

Improvements in multiple measures of cognition and behavior:

- Receptive communication
- Expressive communication
- Personal skills
- Interpersonal relationships
- Fine motor skills

Consistency of improvements observed by caregivers and clinicians provide confidence in these findings

At the time of this analysis, 28 patients had reached one year of treatment in the OLE's

Single & Multiple Doses Up To 70mg Were Generally Well-Tolerated

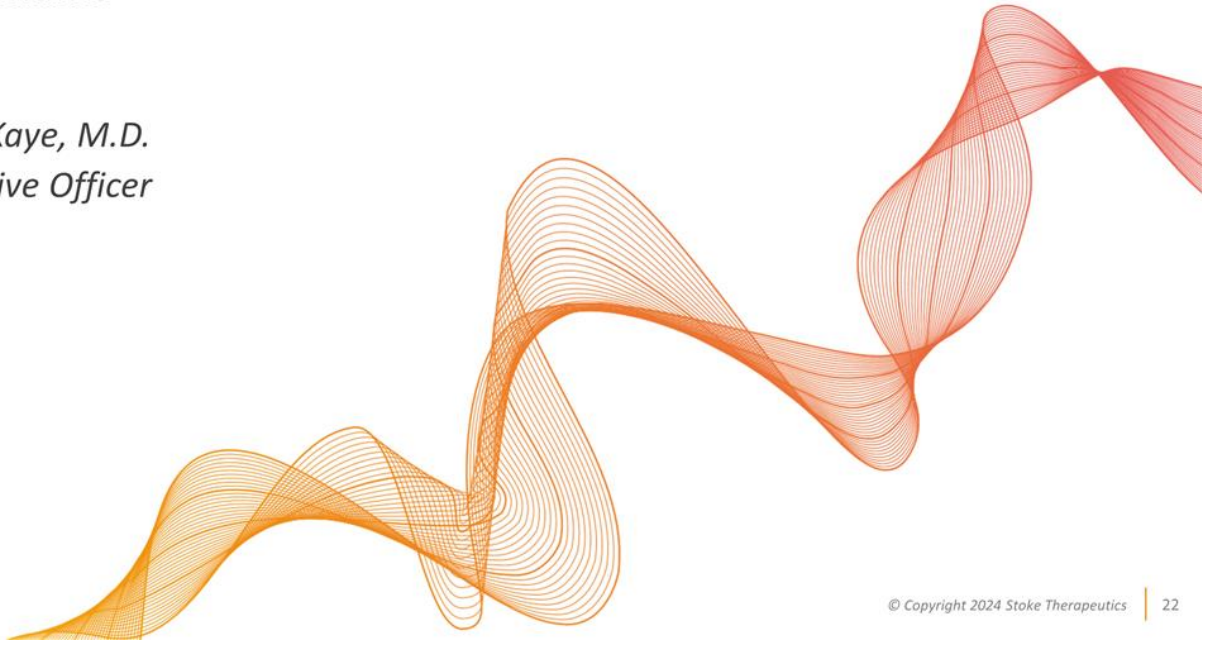
No new safety findings related to study drug

Phase 1/2a Studies (n=81)	**30%** had a TEAE related to study drug. CSF protein elevations and procedural vomiting were the most common **22%** had a TESAE. These events were assessed as unrelated to study drug except for the previously reported case of one patient who experienced SUSARs
OLE Studies (n=68)	**74%** had CSF protein elevations*. No clinical manifestations have been observed in patients with elevated CSF protein levels. 1 patient discontinued treatment due to elevated CSF protein

** >1 CSF protein value >50mg/dL*
TEAE: treatment-emergent adverse event.
TESAE: treatment-emergent serious adverse event
SUSARs: Suspected Unexpected Serious Adverse Reactions

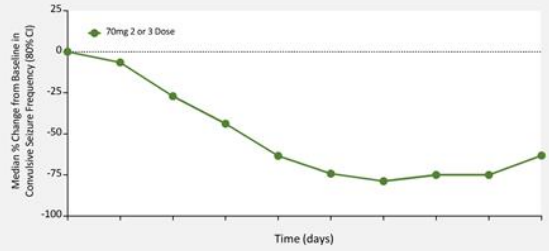
Closing Remarks

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

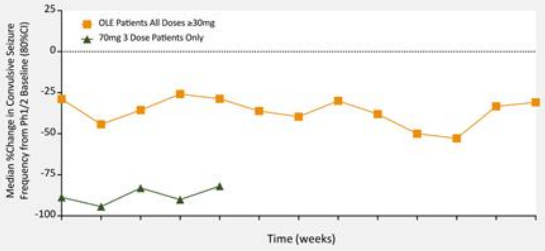


Landmark New Data Support the Potential for STK-001 to be the First Medicine to Treat the Underlying Cause of Dravet Syndrome

Phase 1/2a (2 and 3 doses of 70mg):
Substantial & sustained reductions in seizure frequency

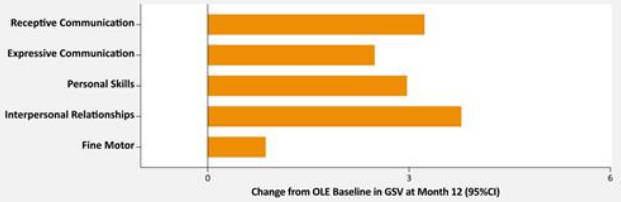


Open-Label Extensions (30mg, 45mg):
Durable reductions in seizures with dosing every 4 months



Company to meet with regulatory agencies to discuss registrational study design: 70mg loading doses followed by 45mg maintenance doses

OLE (30mg, 45mg): Clinically meaningful improvements
in multiple measures of **cognition & behavior** over 12 months



Q&A