Stoke Therapeutics

NASDAQ: STOK

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Chief Executive Officer

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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 non-seizure comorbidities at the indicated dosing levels or at all, the ability of STK-002 to treat the underlying causes of Autosomal Dominant Optic Atrophy (ADOA), and the timing and expected progress of clinical trials, data readouts and presentations for STK-001 and STK-002. Statements including words such as "anticipate," "plan," "will," "continue," "expect," or "ongoing" and statements in the future tens 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: Stoke's ability to advance, obtain regulatory approval of, and ultimately commercialize its produce candidates; the timing of data readouts and interim and final results of preclinical and clinical trials; 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; preliminary interim data readouts of ongoing trials may show results that change when such trials are completed; Stoke's ability to fund development activities and achieve development goals into 2025; Stoke's ability to protect its intellectual property; the direct and indirect impacts of the ongoing COVID-19 pandemic and its variants on Stoke's business; and other risks and uncertainties described under the heading "Risk Factors" in Stoke's Annual Report on Form 10-K for the year ended December 31, 2021, its quarterly reports on Form 10-Q and the other documentation Stoke files 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.

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OUR GOAL:

Upregulate protein expression to treat the underlying cause of severe genetic diseases

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

STK-001 for Dravet syndrome

A severe and progressive genetic epilepsy

STK-002 for Autosomal Dominant Optic Atrophy (ADOA)

The most common inherited optic nerve disorder

Rett syndrome, Syngap1 syndrome

Severe and rare genetic neurodevelopmental diseases

And beyond…

~6,500 additional genes with TANGO target signatures

Advantages of Stoke's Approach vs. Other Genetic Approaches

Selectively boosts expression only in tissues where the protein is normally expressed

No observed unwanted off-target genetic effects

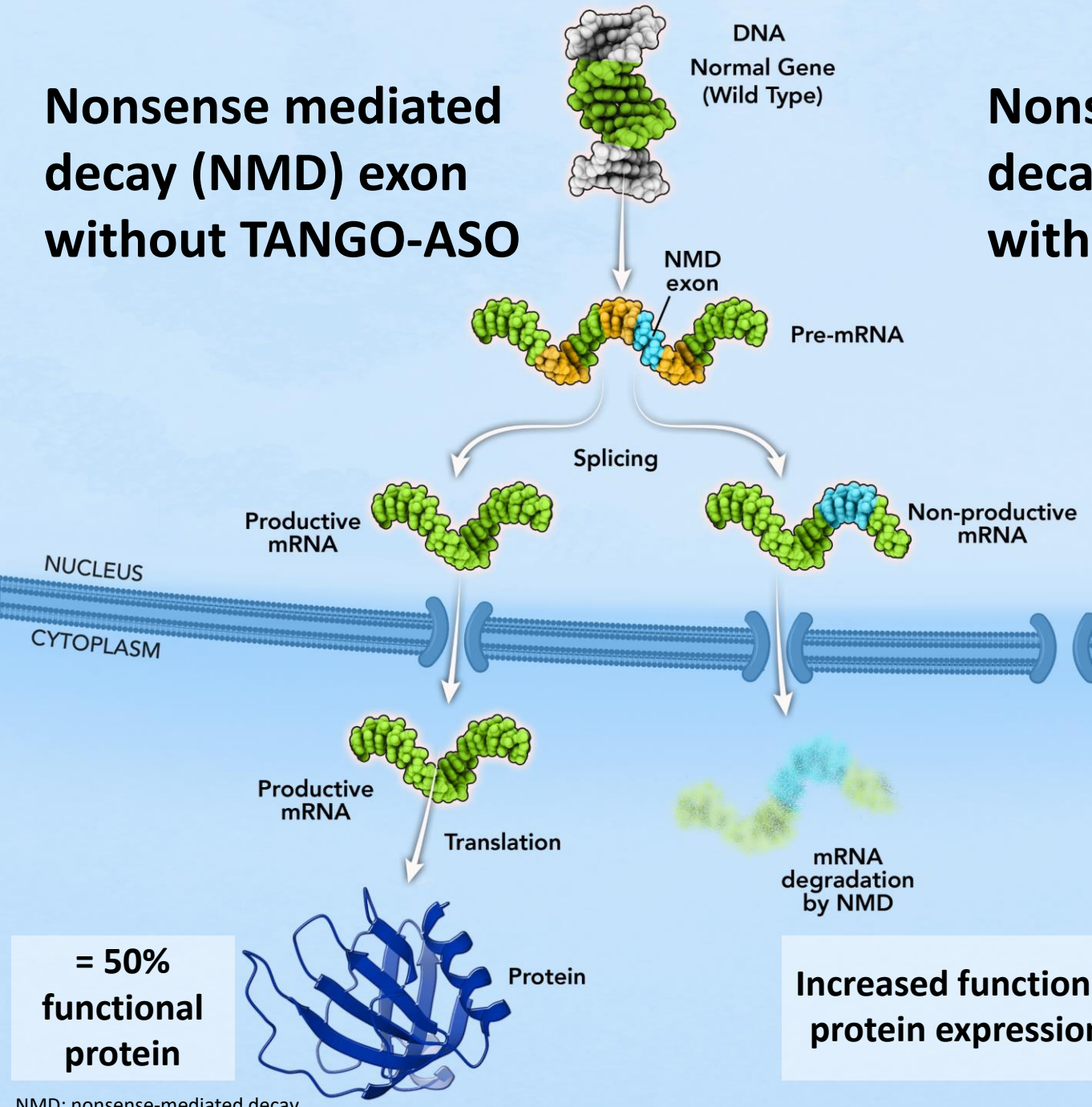
Utility across small and large gene targets and mutations

Does not alter DNA

Ability to control dose level and duration

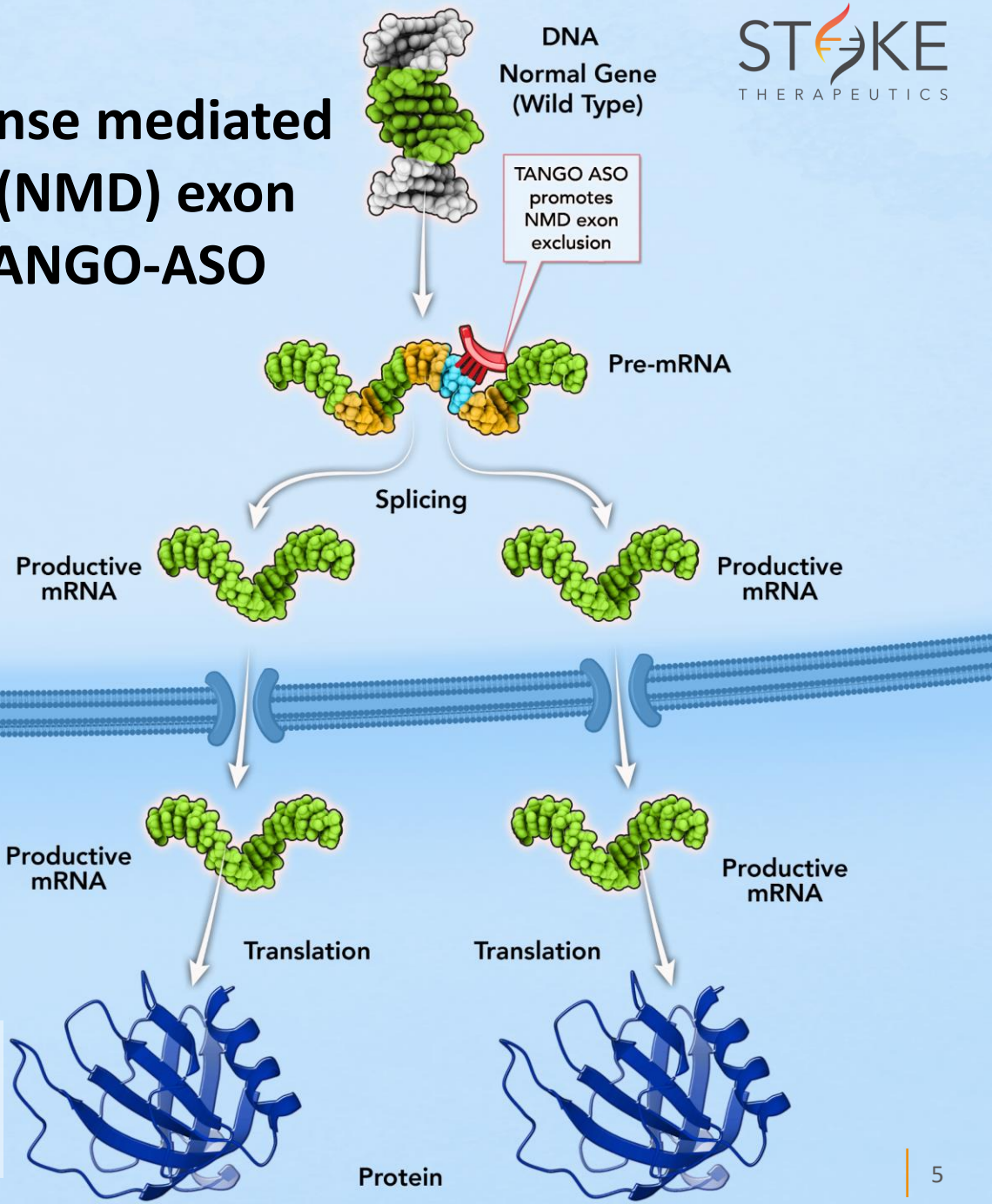
Simple and scalable manufacturing

Nonsense mediated decay (NMD) exon without TANGO-ASO



= 50% functional protein

Nonsense mediated decay (NMD) exon with TANGO-ASO



Increased functional protein expression

NMD: nonsense-mediated decay

Dravet Syndrome: A Severe, Progressive Genetic Epilepsy

85%
of cases caused by a **HAPLOINSUFFICIENCY** of the *SCN1A* gene

RESULTING in

50%
$Na_V1.1$ protein expression

1 out of 16,000
babies are born with Dravet syndrome

Up to 20%
of children and adolescents with Dravet syndrome die before adulthood, due to SUDEP[1], prolonged seizures, seizure-related accidents or infections

Seizures are not adequately controlled in **90%** of people with Dravet syndrome

~35,000
people affected in the U.S., Canada, Japan, Germany, France and the UK

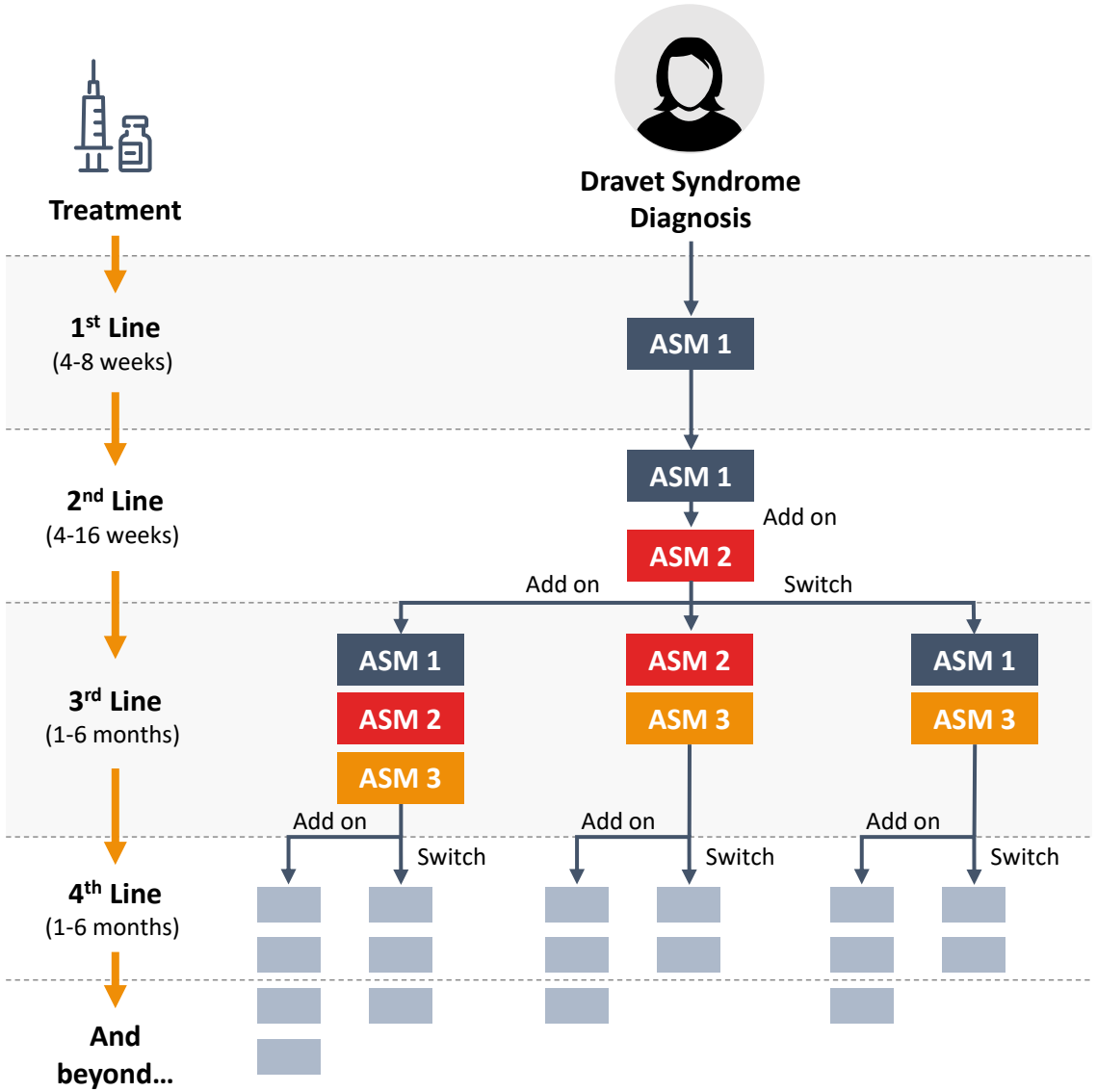
Dravet syndrome is not concentrated in a particular geographic area or ethnic group

[1] Sudden Unexpected Death in Epilepsy

Sources: *2018 Health Advances Report*; Djémié et al., *Molecular Genetics & Genomic Medicine,* 2016; Lagae et al., *Developmental Medicine & Child Neurology,* 2017; Nabbout et al., *Orphanet Journal of Rare Diseases,* 2013

Current Treatment Paradigm is Burdensome and Ineffective

Most patients end up on 3 or more anti-seizure medicines (ASM)



Clinician perspectives on current treatment options

"Eliminating seizures is not possible. We strive for balance between seizure frequency, duration, and quality of life. Parents tolerate more seizures if it enables normal social activity."

"Patients are never well-controlled on one drug. After a month or two establishing efficacy, dosing, and comfort, we always add at least a second."

"ASMs are notorious for side effects, which is a big reason we switch drugs so frequently."

Our Goal: Transform the Treatment of Dravet Syndrome by Targeting the Underlying Cause of the Disease, Not Just the Seizures

Multiple medicines available for

Seizure management

No medicines available for

Syndrome management

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

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

STK-001

The only potential disease-modifying approach currently in the clinic

“Our entire life has been impacted by this diagnosis. Our family has been disrupted. Our livelihood has been impacted. Our future is unknown, and the unknown can be so consuming.”

– Jennifer MK., Mom of Daughter with Dravet syndrome

Voice of the Patient Report Published by the Dravet Syndrome Foundation, May 2022

Dravet Syndrome is More Than “Just Seizures”

Intellectual Disability & Developmental Delays

*“Over time, we have seen **slow, steady decline** in all areas, from speech, to mobility, endurance, loss of energy, tolerance for stimulation, stamina, etc.”*

Movement & Balance

*“We're disappointed when [our son’s] physical activity is limited and the short walk or visit that we plan with his grandmothers must now be changed to a longer **wheelchair ride**.”*

Language & Speech Disturbances

*“At age 19, [our son] stopped talking, seemingly **losing his capacity for speech** overnight. Most days he is silent, and though he can understand simple conversation he is largely **unable to express himself**.”*

Sleep Abnormalities

*“Every single night, he has **seizures in his sleep**. In addition to all of the other comorbidities of DS, he's **robbed of the basic human necessity** of getting a good night's sleep. This impacts our entire family, as it is hard to function on **so little sleep day after day**."*

Source: Voice of the Patient Report Published by the Dravet Syndrome Foundation, May 2022

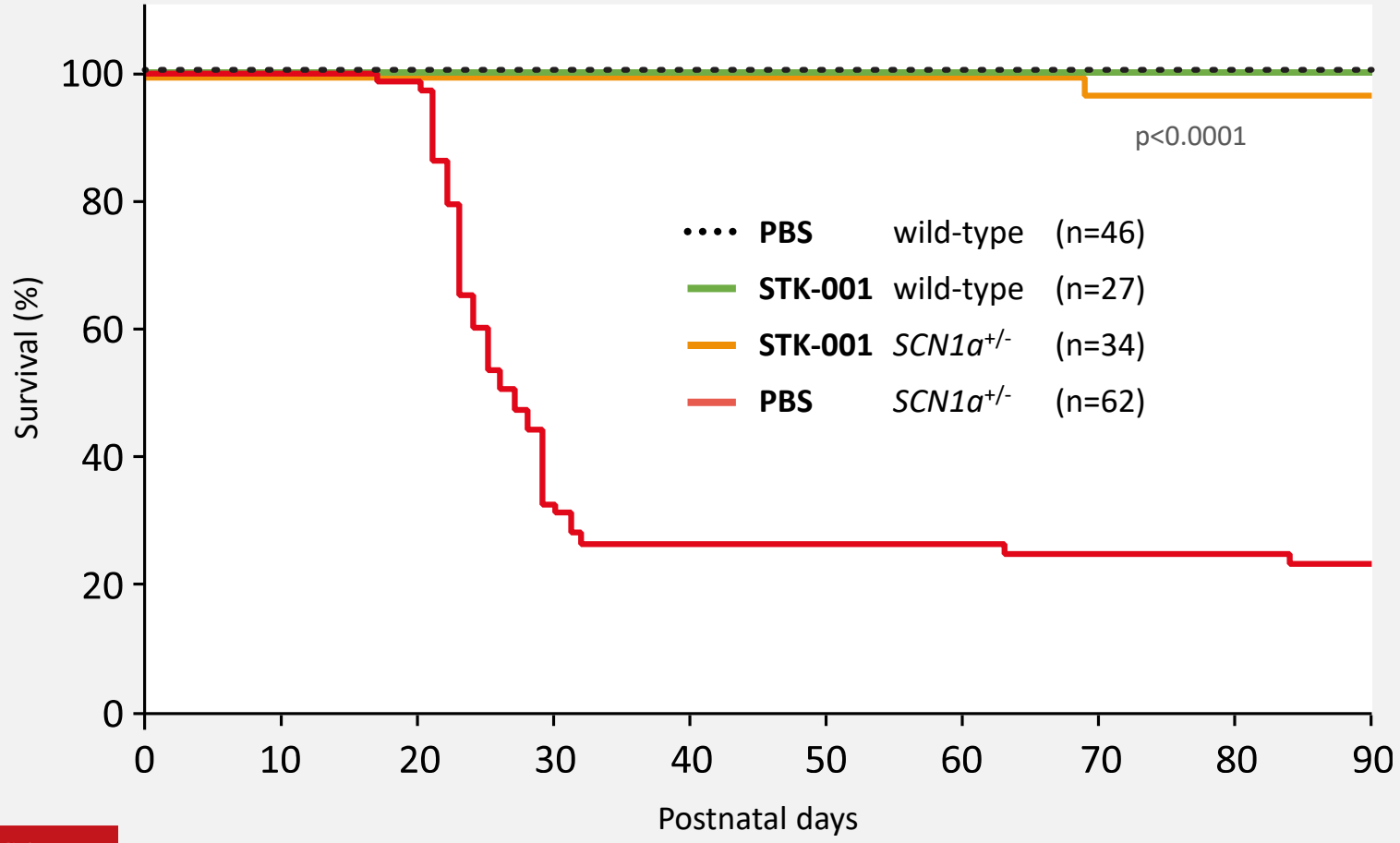
“Potential disease-modifying gene therapies in SCN1A-positive Dravet syndrome….include antisense oligonucleotide (STK-001)…are positioned to improve not only seizure control, but by targeting the underlying cause and restoring native gene expression, could also address the equally important comorbidities that so often negatively impact patients living with epilepsy.”

– Joseph E. Sullivan, M.D., 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 into Dravet syndrome

Genetic Testing in Patients With Epilepsy May Impact Treatments and Improve Outcomes, Sullivan, JAMA Neurology, 2022

Preclinical Findings Support Disease Modifying Potential of STK-001

Significant reductions in premature mortality and seizure frequency in DS mice after a single dose

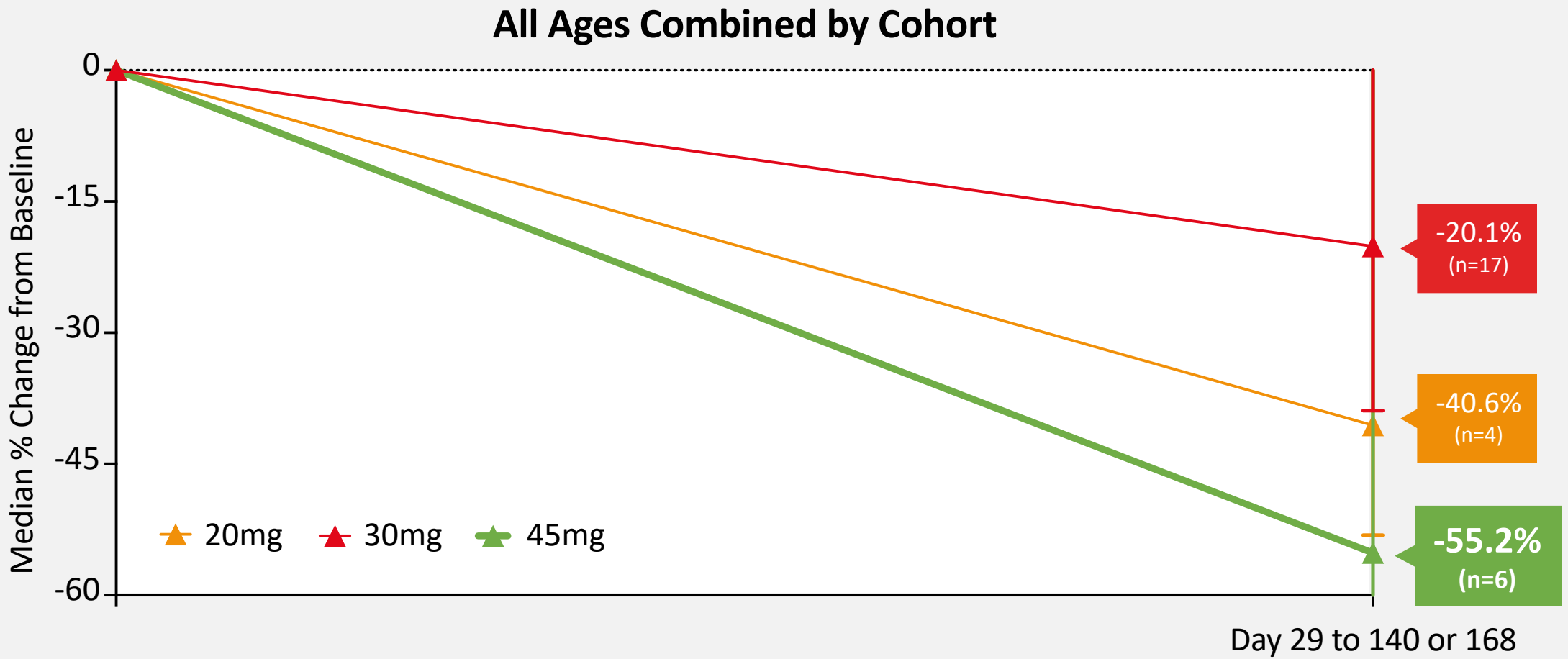


- ✓ Single dose restores $Na_V1.1$ to near-normal levels for >3 months in DS mice
- ✓ Achieves broad distribution and increases $Na_V1.1$ protein expression in NHPs
- ✓ NHP toxicology studies support current clinical dosing

Science Translational Medicine AAAS

Sources: Antisense oligonucleotides increase Scn1a expression and reduce seizures and SUDEP incidence in a mouse model of Dravet syndrome. *Sci. Transl. Med.* 12, eaaz6100 (2020). Targeted Augmentation of Nuclear Gene Output (TANGO) of SCN1A reduces seizures and rescues parvalbumin positive interneuron firing frequency in a mouse model of Dravet syndrome (AES 2020). TANGO oligonucleotides for the treatment of Dravet Syndrome: Safety, biodistribution and pharmacology in the non-human primate (AES 2019).

Reductions in Convulsive Seizure Frequency Observed in Patients Treated With STK-001 On Top of Multiple Anti-Seizure Medicines

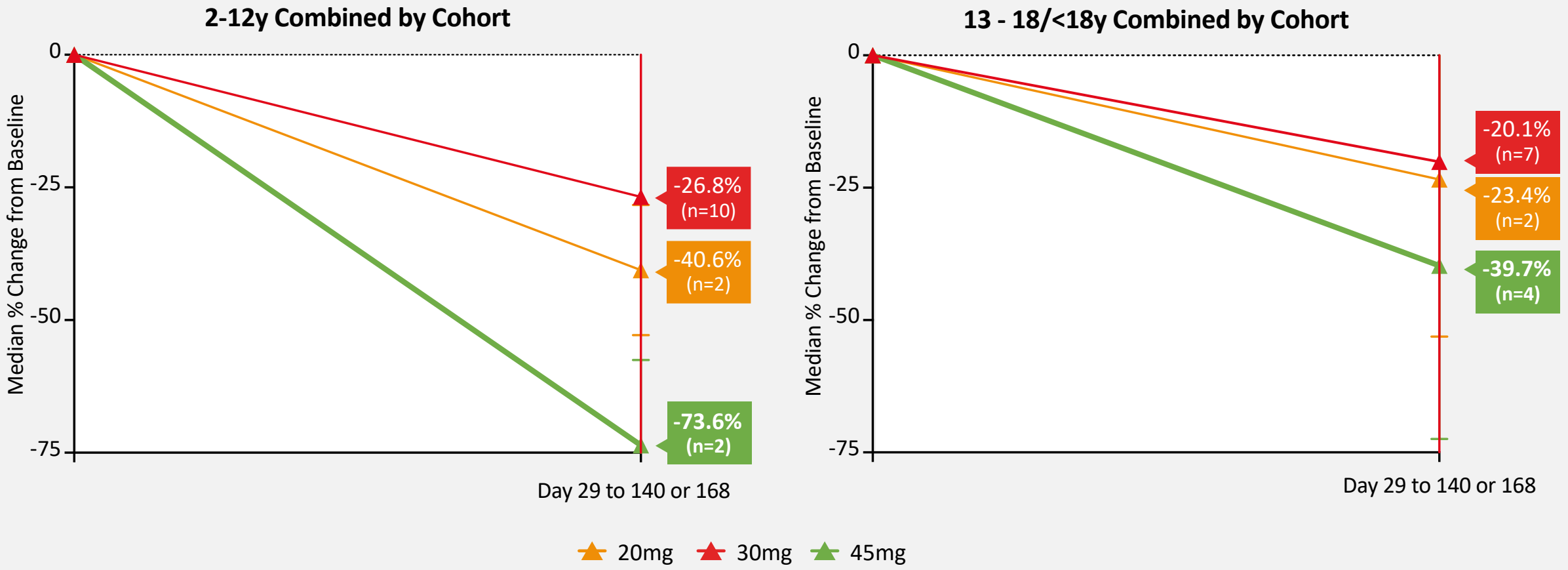


>50% of patients were taking concomitant fenfluramine

Source: MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS) (AES 2022).

Reductions in Convulsive Seizure Frequency Observed Across Age Groups Taking Multiple Doses of STK-001

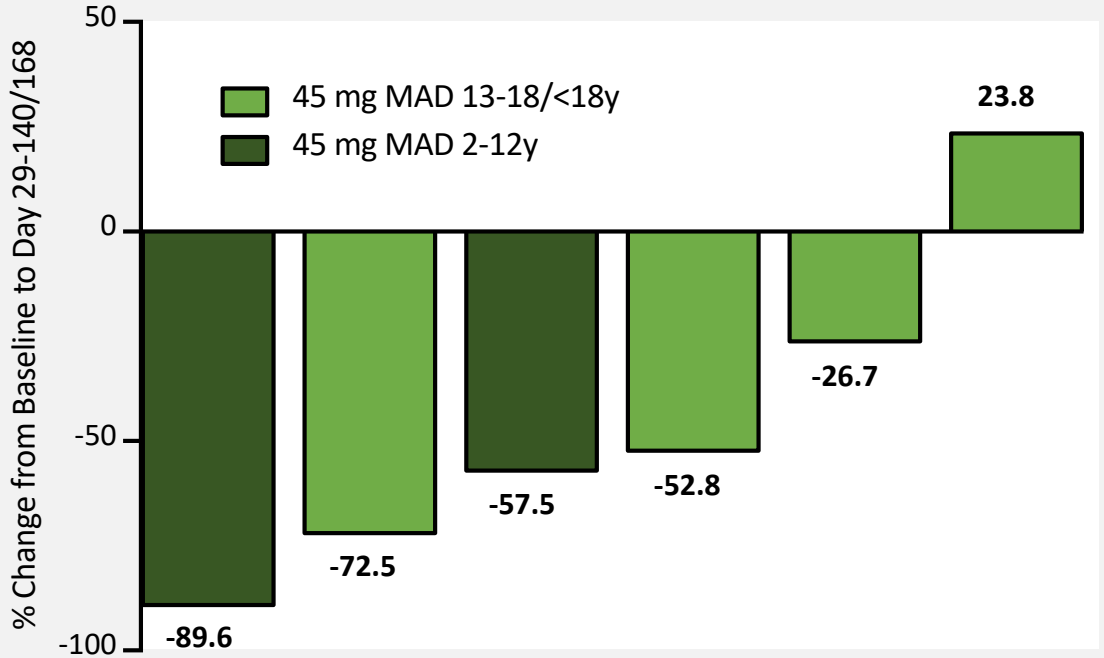
74% Median seizure reduction observed in younger patients



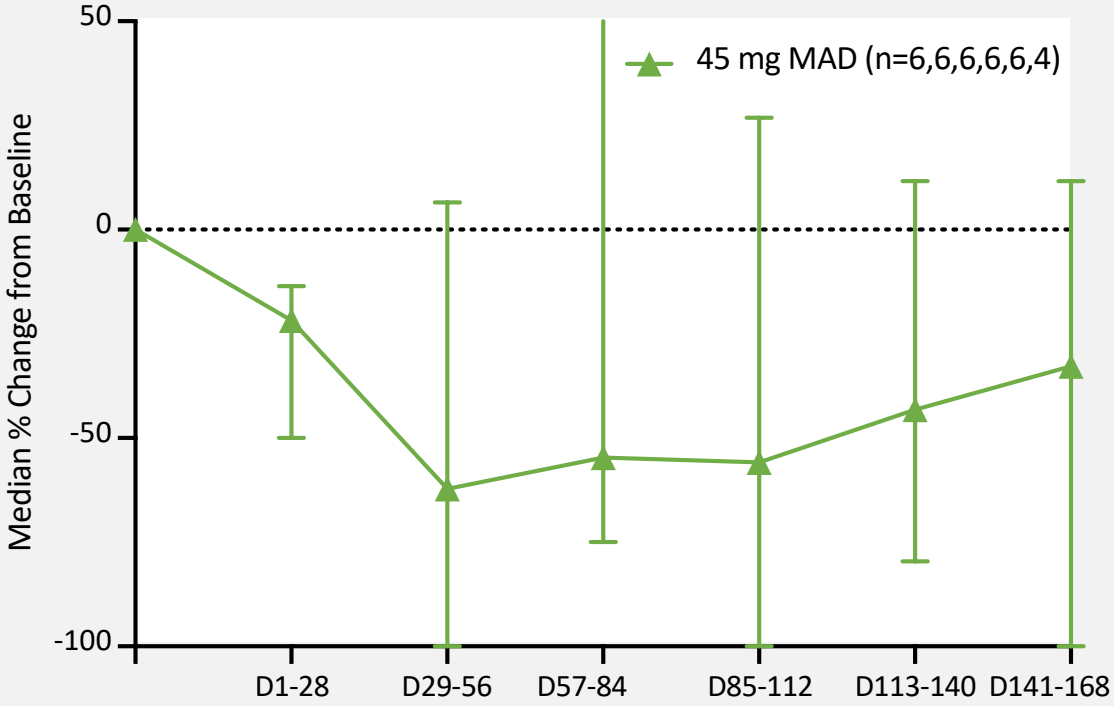
Source: MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS) (AES 2022).

67% (4/6) Patients Experienced >50% Reduction in Convulsive Seizure Frequency with Three Doses of STK-001 (45mg)

Reductions began after the first dose and continued with additional treatment



4/6 patients were taking concomitant fenfluramine

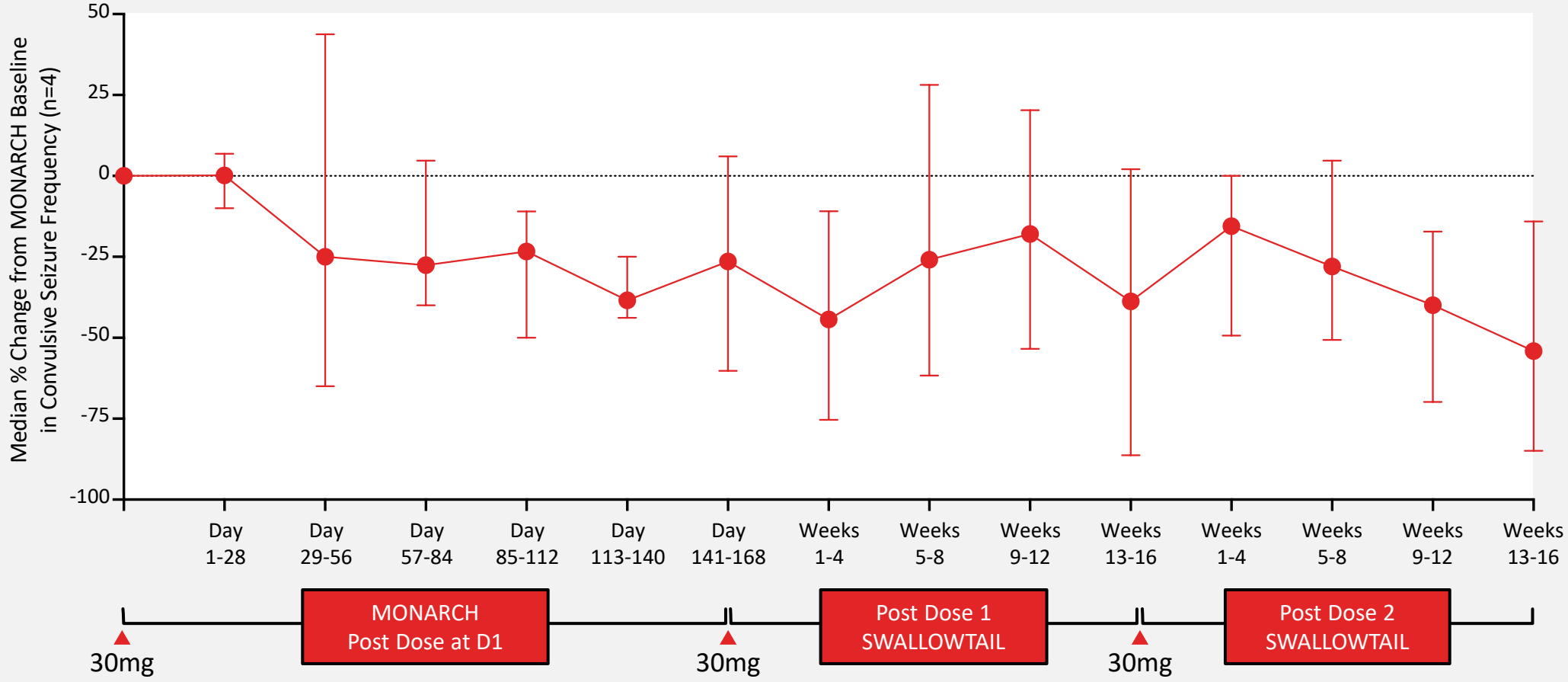


Convulsive Seizure Frequency All Ages

Source: MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS) (AES 2022).

Reductions in Seizure Frequency Were Maintained with Ongoing STK-001 Treatment

Convulsive Seizure Frequency

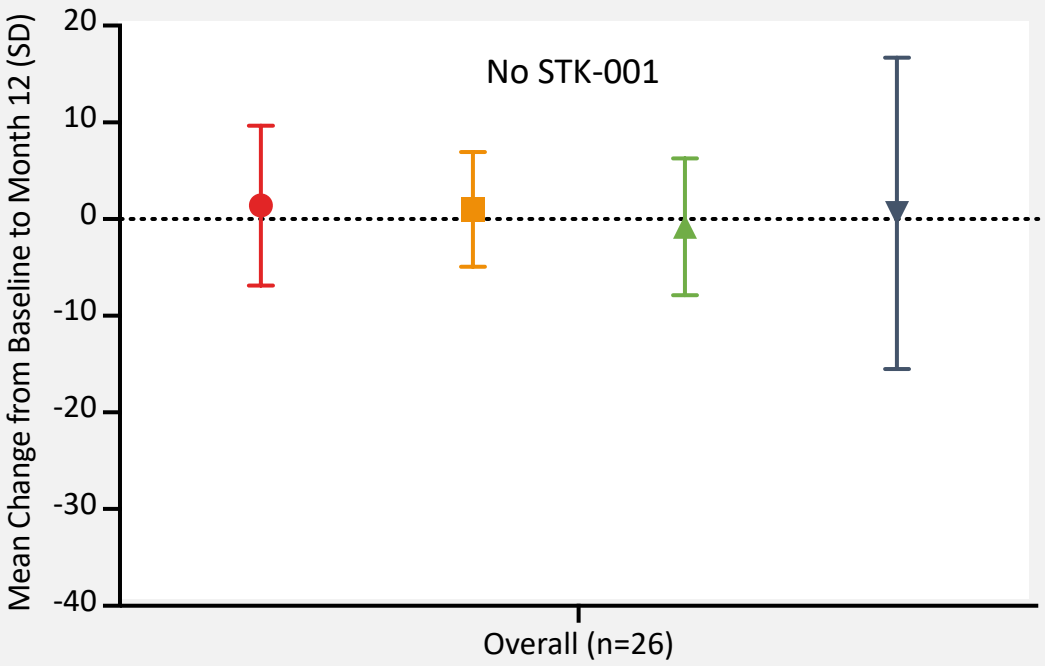


No exclusions for AED modification

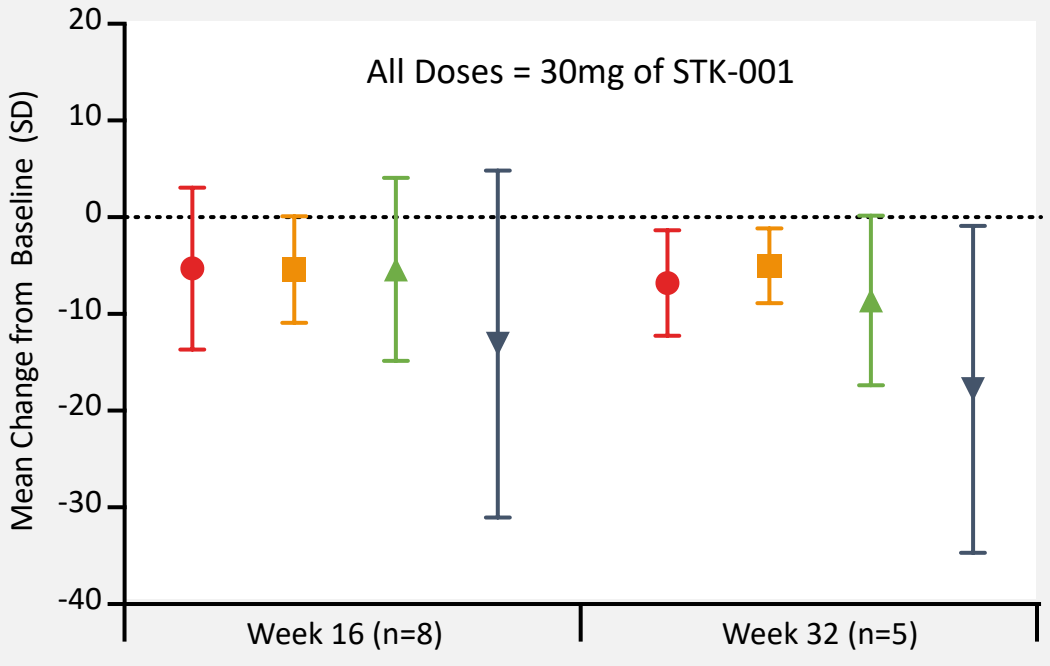
Source: SWALLOWTAIL: An Open-Label Extension (OLE) Study for Children and Adolescents with Dravet Syndrome (DS) who Previously Participated in a Study of Antisense Oligonucleotide (ASO) STK-001 (AES 2022).

Improvements in Non-Seizure Comorbidities Measured by the BRIEF-P Indicate the Potential for Disease Modification

BUTTERFLY
An observational study of Dravet Syndrome patients



swallowtail
A DRAVET SYNDROME EXTENSION STUDY



ISCI (Inhibit + Emotional Control) FI (Shift + Emotional Control) EMI (Working Memory + Plan/Organize) Global Executive Composite

As measured by Behavior Rating Inventory of Executive Function–Preschool Version, an assessment of pediatric executive function.

Sources: Twelve-month Analysis of BUTTERFLY: An Observational Study to Investigate Cognition and Other Non-seizure Comorbidities in Children and Adolescents with Dravet Syndrome (DS) (AES 2022). SWALLOWTAIL: An Open-Label Extension (OLE) Study for Children and Adolescents with Dravet Syndrome (DS) who Previously Participated in a Study of Antisense Oligonucleotide (ASO) STK-001 (AES 2022).

STK-001 Has Potential to Address the Genetic Cause of Dravet Syndrome

Summary of Key Ph1/2a Interim Data

- ✓ Single and multiple doses of STK-001 up to 45mg were well-tolerated
- ✓ 55% median reduction in convulsive seizure frequency observed in patients treated with three doses of STK-001 (45mg)
- ✓ Reductions in seizure frequency were maintained with ongoing treatment
- ✓ Early indication of improvements in non-seizure comorbidities as measured by BRIEF-P*

*Behavior Rating Inventory of Executive Function–Preschool Version, an assessment of pediatric executive function

Sources: MONARCH and ADMIRAL Interim Analyses: Phase 1/2a Studies Investigating Safety and Drug Exposure of STK-001, an Antisense Oligonucleotide (ASO), in Children and Adolescents with Dravet Syndrome (DS) (AES 2022). SWALLOWTAIL: An Open-Label Extension (OLE) Study for Children and Adolescents with Dravet Syndrome (DS) who Previously Participated in a Study of Antisense Oligonucleotide (ASO) STK-001 (AES 2022).

Our Pipeline of First-in-Class Disease Modifying Potential Medicines

PROGRAM	TARGET	DISCOVERY & PRECLINICAL	PHASE 1/2	PHASE 3	PARTNER
Central Nervous System					
Dravet Syndrome	*SCN1A*		STK-001		100% Stoke Global
SYNGAP1 Syndrome	*SYNGAP1*				Stoke : Acadia 50:50
Rett Syndrome	*MECP2*				Acadia Worldwide License
Undisclosed	*Undisclosed*				Acadia Worldwide License
Ophthalmology					
ADOA	*OPA1*	STK-002			100% Stoke Global

ADOA: Autosomal dominant optic atrophy

2023 Priorities

Advance STK-001 for Dravet Syndrome to Pivotal

- 45mg clinical data anticipated in mid-2023
- 70mg clinical data anticipated in second half of 2023
- Complete Phase 1/2a in 2023 to enable a Phase 3 program in 2024

Advance STK-002 for ADOA

- Submit CTA in the UK in the first half of 2023 to enable Phase 1/2 start in 2024

Develop & Expand Pipeline

- Expand TANGO ASOs as a first-in-class disease-modifying approach for additional genetic diseases
- Execute on collaboration with Acadia to advance Rett syndrome and Syngap1 syndrome programs

ADOA: Autosomal dominant optic atrophy

Current Liquidity Anticipated to Fund Operations into 2025

$252.2M

Cash, Cash Equivalents, Marketable Securities, and Restricted Cash

as of 9/30/2022

39.4M

Common Shares Outstanding

as of 9/30/2022

OUR DAUGHTER WILL BE THREE YEARS OLD IN DECEMBER. IT IS HER **FULL LIFE** THAT WE ARE **FIGHTING FOR**. IT IS HER FULL LIFE **YOU** ARE FIGHTING FOR.

– AMY, DRAVET PARENT

STOKE THERAPEUTICS

Q&A