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 11, 2021

Stoke Therapeutics, Inc.
(Exact Name of Registrant as Specified in its Charter)

Delaware	**001-38938**	**47-114582**
(State or other jurisdiction of incorporation or organization)	**(Commission File Number)**	**(I.R.S. 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

Not Applicable
(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 2.02. Results of Operations and Financial Condition.

On January 11, 2021, Stoke Therapeutics, Inc., a Delaware corporation (the "Company"), plans to present certain preliminary financial and operating information in connection with a presentation (the "Presentation") at the J.P. Morgan Healthcare Conference, including that the Company expects to report that it had cash, cash equivalents and restricted cash of approximately $287.6 million, and 36.6 million shares of common stock outstanding, as of December 31, 2020.

The Company's audited financial statements for the fiscal year ended December 31, 2020 are not yet available. Accordingly, the preliminary financial information included in the Presentation is an estimate subject to the completion of Company's financial closing procedures and any adjustments that may result from the completion of the audit of Company's financial statements. The preliminary financial information may differ materially from the actual results that will be reflected in Company's audited financial statements when they are completed and publicly disclosed.

The information in this Item 2.02 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 2.02 shall not be incorporated by reference into any registration statement or other document filed by the Company with the SEC, whether made before or after the date of this Current Report on Form 8-K, regardless of any general incorporation language in such filing (or any reference to this Current Report on Form 8-K generally), except as shall be expressly set forth by specific reference in such filing.

Item 7.01. Regulation FD.

The Company is furnishing its corporate deck, including the information for the Presentation, a full copy of which is attached hereto as Exhibit 99.1.

The information furnished with this report, including Exhibit 99.1, 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.

In addition, on January 11, 2021, the Company's Presentation will provide a business update with respect to the timing of certain upcoming milestones, including the following:

- First Half of 2021: Initiate Swallowtail Open Label Extension (OLE) study for STK-001;
- Second Half of 2021: Initiate multiple ascending dose (MAD) study of STK-001;
- Second Half of 2021: Preliminary safety and PK data from Phase 1/2a MONARCH study of STK-001;
- Second Half of 2021: Initiate ADOA natural history data collection;
- Year-End of 2021: Complete lead optimization for OPA1 compounds; and
- Year-End of 2021: Demonstrate *in vivo* proof of mechanism and safety for a third program.

The Company also reported that its cash and cash equivalents are expected to fund operations into 2024.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Corporate deck, dated as of January 2021.

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, statements regarding the Company's expected cash, cash equivalents and restricted cash as of December 31, 2020, are forward-looking statements that involve risks and uncertainties that could cause actual results to differ materially from those discussed in such forward-looking statements. Such risks and uncertainties include, among others, the risks identified in the Company's filings with the Securities and Exchange Commission ("SEC"), including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC on November 12, 2020, and subsequent filings with the SEC. Any of these risks and uncertainties could materially and adversely affect the Company's results of operations, which would, in turn, have a significant and adverse impact on the Company's stock price. The Company cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. The Company undertakes no obligation to update publicly any forward-looking statements to reflect new information, events or circumstances after the date they were made or to reflect the occurrence of unanticipated events.

SIGNATURE

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 11, 2021

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

Stoke Therapeutics

NASDAQ: STOK

January 2021

Disclaimer

This presentation has been prepared by Stoke Therapeutics, Inc. ("Stoke" or "our") 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 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 our TANGO platform to design medicines to increase protein production and the expected benefits thereof; the ability of STK-001 to treat the underlying causes of Dravet syndrome; the preclinical data and study results regarding OPA1; our preliminary cash, cash equivalents and restricted cash and shares outstanding as of December 31, 2020; our future operating results, financial position and liquidity; the direct and indirect impact of COVID-19 on our business, financial condition and operations, including on our expenses, supply chain, strategic partners, research and development costs, clinical trials and employees; our expectation about timing and execution of anticipated milestones, responses to regulatory authorities, expected nomination of future product candidates and timing thereof. These forward-looking statements may be accompanied by such words as "aim," "anticipate," "believe," "could," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "potential," "possible," "will," "would," and other words and terms of similar meaning. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such statements, including: our ability to develop, obtain regulatory approval for and commercialize STK-001, OPA1 and future product candidates; the timing and results of preclinical studies and clinical trials; the risk that positive results in a clinical trial may not be replicated in subsequent trials or success in early stage clinical trials may not be predictive of results in later stage clinical trials; risks associated with clinical trials, including our ability to adequately manage clinical activities, unexpected concerns that may arise from additional data or analysis obtained during clinical trials, regulatory authorities may require additional information or further studies, or may fail to approve or may delay approval of our drug candidates; the occurrence of adverse safety events; failure to protect and enforce our intellectual property and other proprietary rights; failure to successfully execute or realize the anticipated benefits of our strategic and growth initiatives; risks relating to technology failures or breaches; our dependence on collaborators and other third parties for the development, regulatory approval, and commercialization of products and other aspects of our business, which are outside of our full control; risks associated with current and potential delays, work stoppages, or supply chain disruptions caused by the coronavirus pandemic; risks associated with current and potential future healthcare reforms; risks relating to attracting and retaining key personnel; failure to comply with legal and regulatory requirements; risks relating to access to capital and credit markets; environmental risks; risks relating to the use of social media for our business; and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the U.S. Securities and Exchange Commission. These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We do not undertake any obligation to publicly update any forward-looking statements.

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.

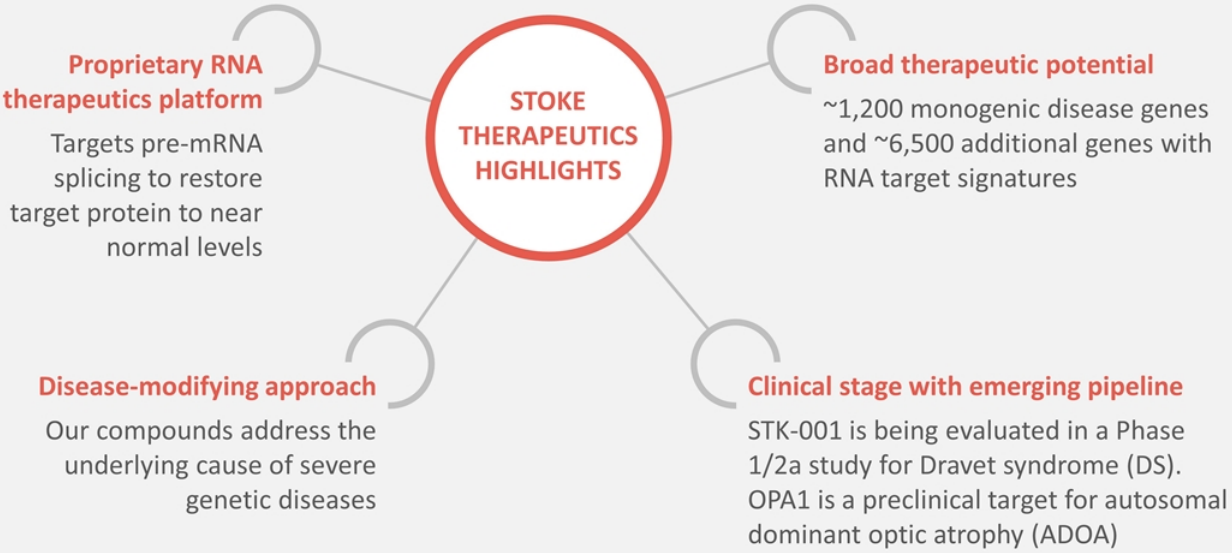
STOKE

STOKE THERAPEUTICS

Boldly Restoring Genetic Health

> Addressing the underlying cause of severe diseases by up-regulating protein expression with RNA-based medicines.

A Differentiated Platform for the Discovery and Development of Novel RNA-based Medicines



Targeted Augmentation of Nuclear Gene Output

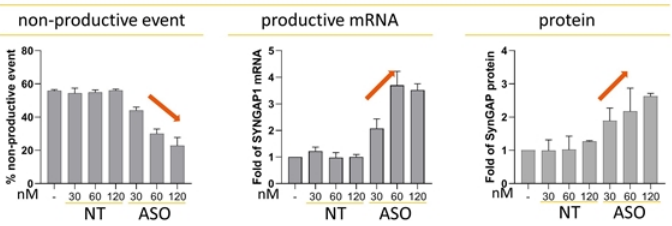
Our compounds aim to restore protein levels by increasing protein production from the functional copy of a gene and:

- Selectively boost expression only in tissues where the protein is normally expressed
- Offer one drug for diseases caused by many different mutations
- Apply to genes of diverse size: can be used to address small or large gene targets

TANGO ASOs Demonstrate Dose-Dependent Increases in Protein Expression Across Targets of Diverse Size, Type and Function

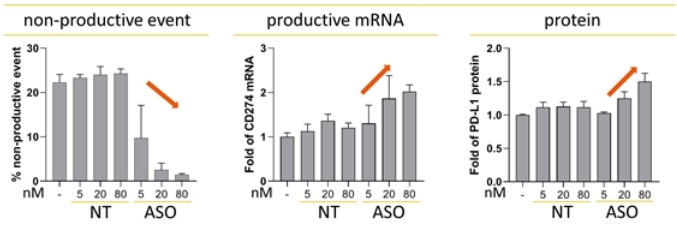
Genetic epilepsy – haploinsufficiency

SYNGAP1



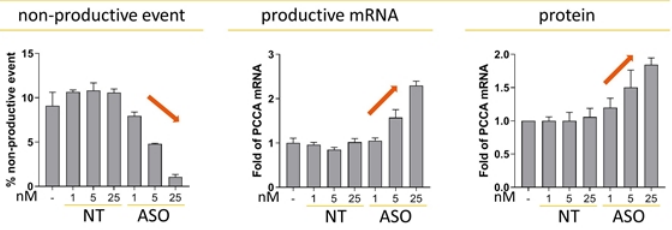
Pathway target – wild-type

CD274 (PD-L1)

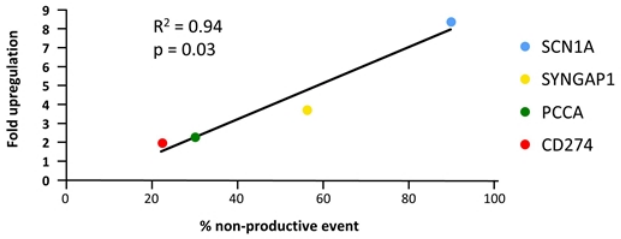


Liver target – autosomal recessive

PCCA



Correlation between event abundance (+CHX) & upregulation



nature communications Lim *et al.*, Nat Comm, 2020

NT: non-targeting ASO control, all experiments n = 3, *in vitro*

Dravet Syndrome: A Severe, Progressive Genetic Epilepsy

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

RESULTS 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

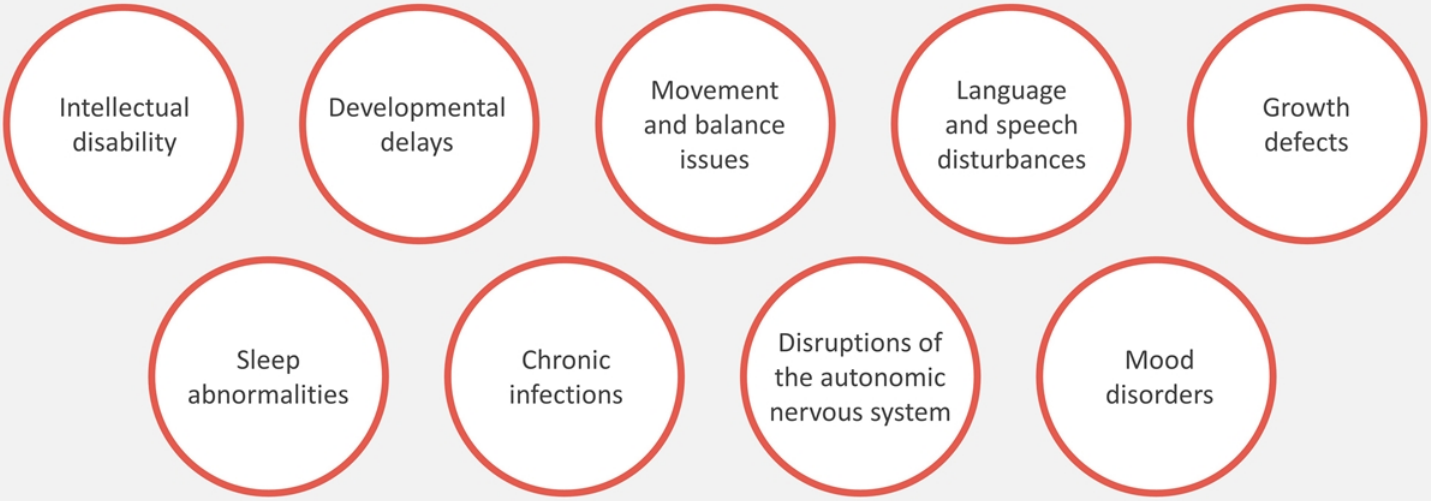
Dravet syndrome is not concentrated in a particular geographic area or ethnic group

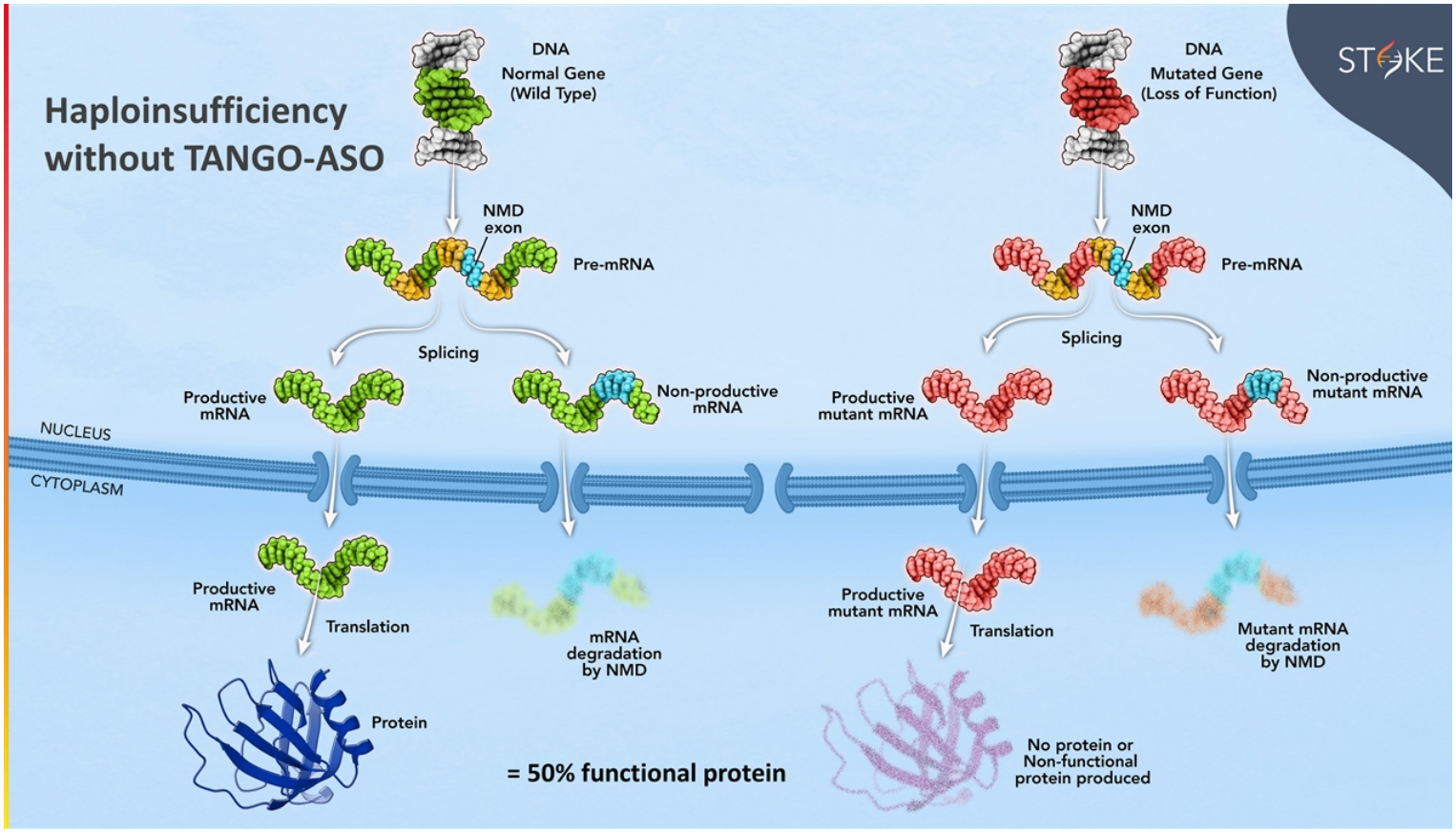
[1] Sudden Unexpected Death in Epilepsy

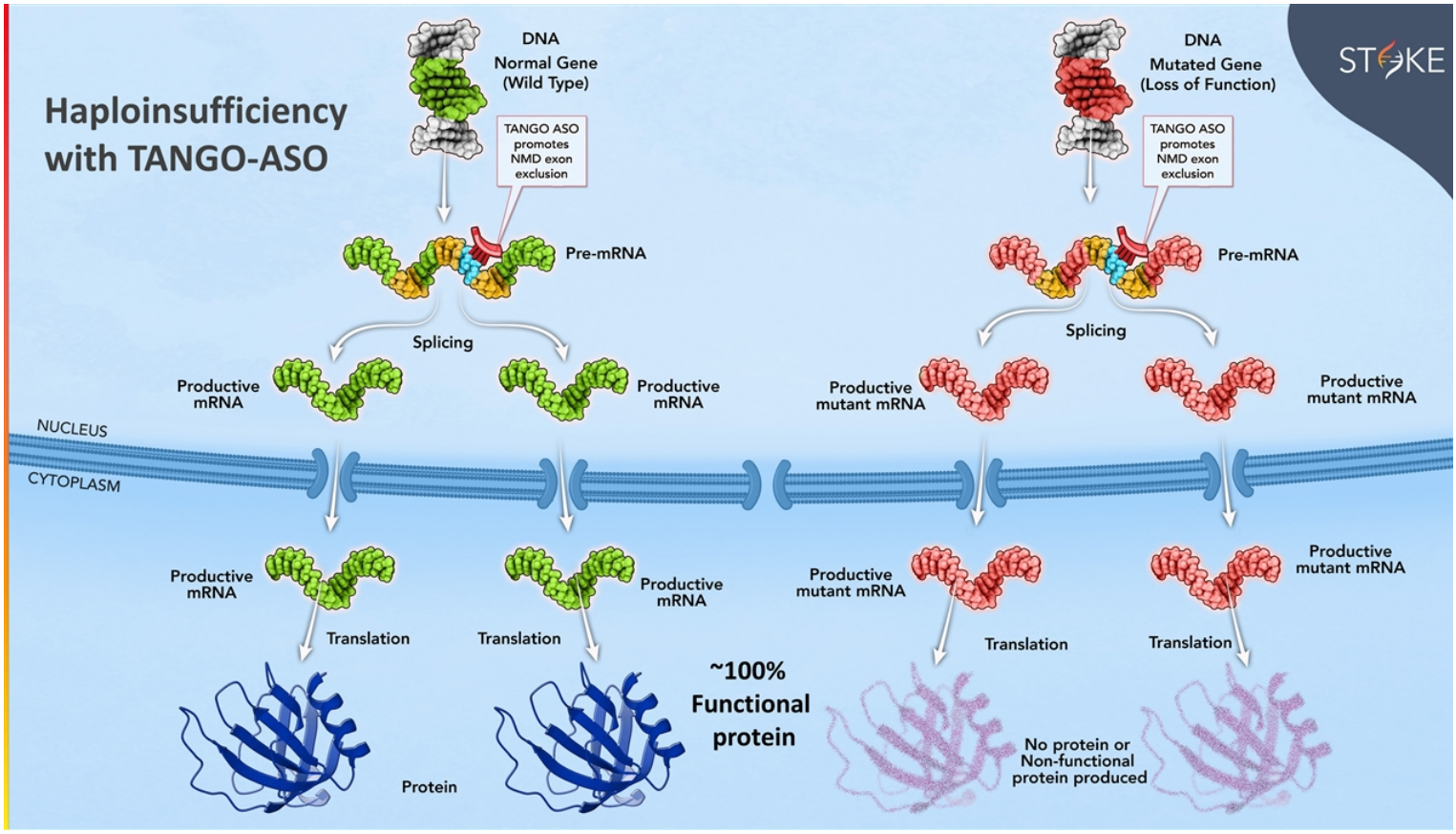
Sources: *2018 Health Advances Report*; Djémié et al., *Molecular Genetics & Genomic Medicine*, 2016; Lagae et al., *Developmental Medicine & Child Neurology*, 2017; Nabbout et al., *Orphanet Journal of Rare Diseases*, 2013

No Approved Disease-Modifying Therapies for Dravet Syndrome

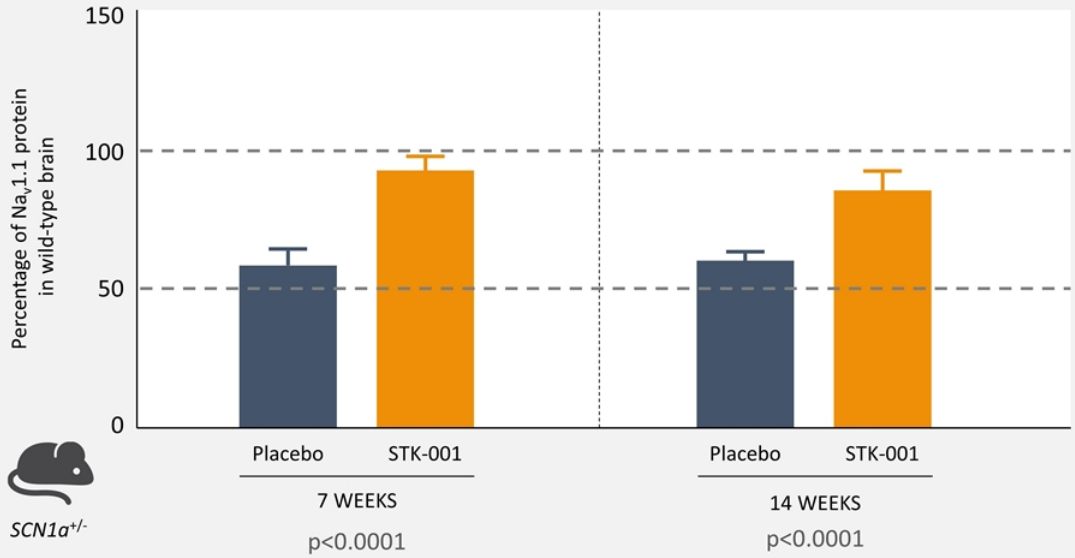
Non-Seizure Comorbidities of Dravet Syndrome Are Not Addressed by Current Therapies




Haploinsufficiency without TANGO-ASO
DNA
Normal Gene (Wild Type)
NMD exon
Pre-mRNA
Splicing
Productive mRNA
Non-productive mRNA
NUCLEUS
CYTOPLASM
Productive mRNA
Translation
Protein
mRNA degradation by NMD
= 50% functional protein
DNA
Mutated Gene (Loss of Function)
NMD exon
Pre-mRNA
Splicing
Productive mutant mRNA
Non-productive mutant mRNA
Productive mutant mRNA
Translation
No protein or Non-functional protein produced
Mutant mRNA degradation by NMD
STOKE


Haploinsufficiency with TANGO-ASO
DNA
Normal Gene
(Wild Type)
TANGO ASO promotes NMD exon exclusion
Pre-mRNA
Splicing
Productive mRNA
Productive mRNA
NUCLEUS
CYTOPLASM
Productive mRNA
Translation
Protein
Productive mRNA
Translation
~100% Functional protein
DNA
Mutated Gene
(Loss of Function)
TANGO ASO promotes NMD exon exclusion
Pre-mRNA
Splicing
Productive mutant mRNA
Productive mutant mRNA
Productive mutant mRNA
Translation
No protein or Non-functional protein produced
Productive mutant mRNA
Translation
STOKE

STK-001 Restores $Na_V1.1$ to Near Normal Levels for >3 Months in Dravet Syndrome (DS) Mice after a Single Dose

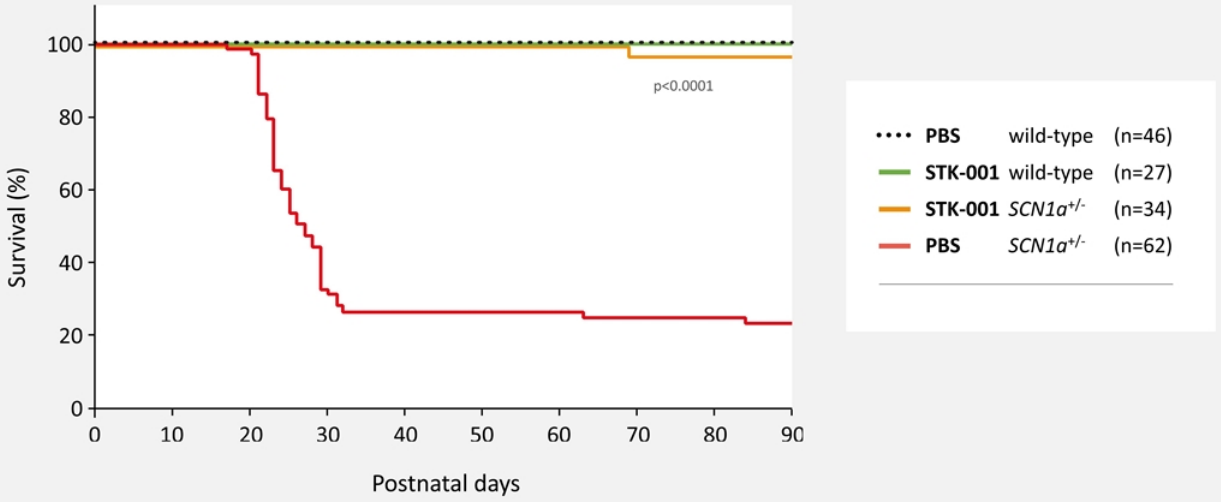


Science Translational Medicine AAAS

Sources: Han *et al.*, Science Trans Med, 2020

STK-001 Significantly Reduces Premature Mortality in DS Mice After a Single Dose

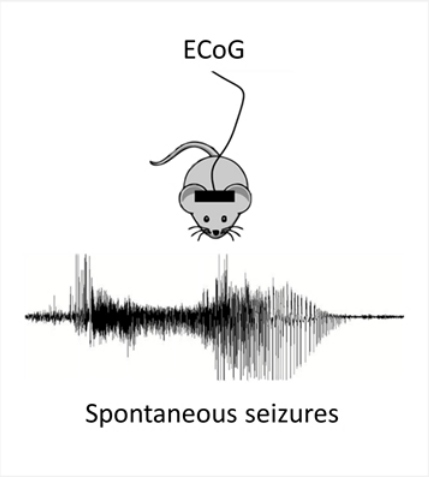
Significant improvements in survival after STK-001 administration at postnatal day 2



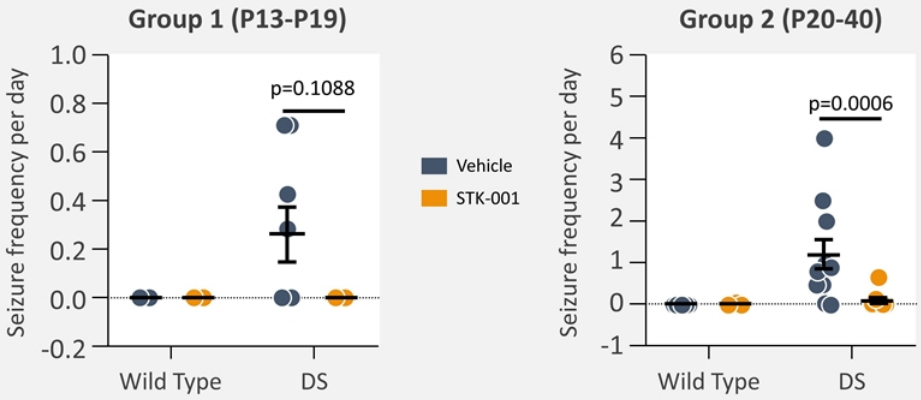
Science Translational Medicine AAAS

Sources: Han *et al.*, Science Trans Med, 2020

STK-001 Administration Reduces Seizure Frequency in DS Mice



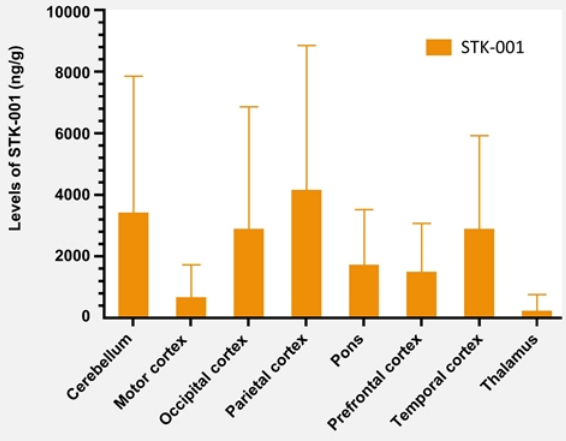
A single dose of STK-001 completely stopped seizure events early (P13-19) and substantially reduced seizure frequency late (P20-40)



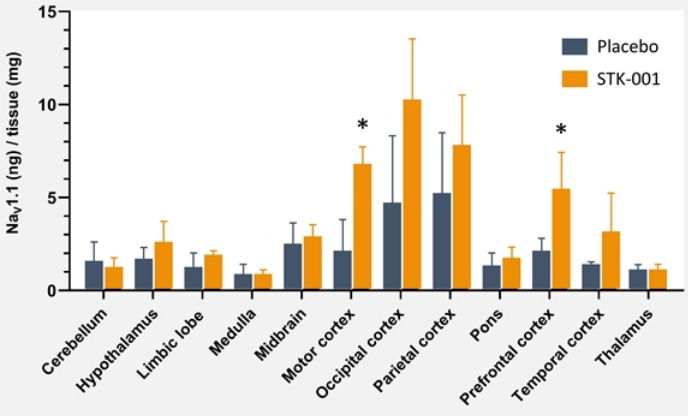
Source: Targeted Augmentation of Nuclear Gene Output (TANGO) of SCN1A reduces seizures and rescues parvalbumin positive interneuron firing frequency in a mouse model of Dravet syndrome (AES 2020)

STK-001 Achieves Broad Distribution and Increases $Na_v1.1$ Protein Expression in NHPs

Study 1: Exposure of STK-001 observed in all brain regions



Study 2: $Na_v1.1$ protein levels increased up to 3-fold



* = p<0.05

NHP = Non-human primate
Source (left graph): Stoke data
Source (right graph) TANGO oligonucleotides for the treatment of Dravet Syndrome: Safety, biodistribution and pharmacology in the non-human primate (AES 2019)

Single and Multiple-Dose Toxicology Studies in NHPs Showed STK-001 Well-Tolerated

Key safety findings from GLP studies*

- No observed adverse events at highest dose tested ✓
- No change in platelet counts or renal/hepatic function ✓
- No adverse histopathology in brain, spinal cord, liver and kidney ✓

*In non-GLP studies in NHPs, at levels above the NOAEL, hind limb paresis was observed; at extremely high dose levels, acute convulsions were observed.

Source: Stoke data

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

- Single dose restores $Na_V1.1$ to near normal levels for >3 months in DS mice
- Significantly reduces mortality and seizure frequency in DS mice
- Achieves broad distribution and increases $Na_V1.1$ protein expression in NHPs
- Well-tolerated as shown in single and multiple-dose toxicology studies in NHPs

Non-Seizure Comorbidities of DS are Progressive and Measurable

Enrollment completed (n=36, 2-18 year-olds). Study ongoing.

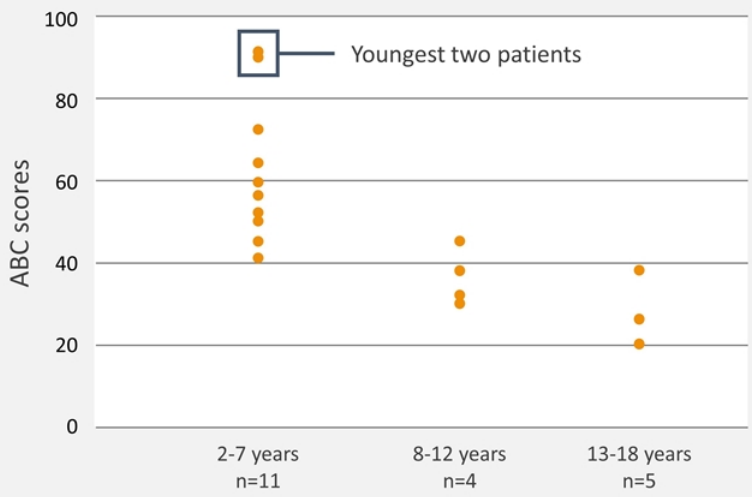
BUTTERFLY

An observational study of Dravet Syndrome patients

Initial findings showed:

- Validation of standard cognitive measures for use in DS patients
- Substantially decreased neurocognitive abilities despite the use of multiple anti-epileptic therapies
- Apparent widening from normal levels in overall intellectual development that increases with age
- A gap in adaptive functioning

Baseline VABS-III Adaptive Behavior Composite (ABC)*



* VABS = Vineland Adaptive Behavior Scales
* ABC score based on Communication, Daily Living, and Socialization domains and expressed relative to normative mean of 100
Source: Observational Study to Investigate Cognition and Quality of Life in Children and Adolescents with Dravet Syndrome: Baseline Analysis of the BUTTERFLY Study (AES 2020)

Enrollment and Dosing in MONARCH Phase 1/2a Trial is Ongoing

Design	Open-label evaluation of single and multiple ascending doses of STK-001 (up to 30mg) • SAD: Currently enrolling • MAD: Planned initiation 2H 2021 *Doses >30mg remain on FDA partial clinical hold*
Target Enrollment	~48 children and adolescents ages 2-18 years old with Dravet syndrome and confirmed *SCN1a* variant
Primary Endpoint	Safety and tolerability of single and multiple ascending dose levels; characterize human pharmacokinetics (PK)
Secondary Endpoint	Change in seizure frequency over 12-weeks, quality of life
Preliminary Data	Initial safety and PK data anticipated in 2021
Open-Label Extension	Planned initiation 1H 2021

monarch
A DRAVET SYNDROME STUDY

swallowtail
A DRAVET SYNDROME EXTENSION STUDY

Source: Safety and Pharmacokinetics of Antisense Oligonucleotide STK-001 in Children and Adolescents with Dravet Syndrome: Single and Multiple Ascending Dose Design for the Open-Label Phase 1/2a MONARCH Study (AES 2020)

Autosomal Dominant Optic Atrophy (ADOA): A Severe, Progressive Optic Nerve Disorder

65-90%
of cases caused by a **HAPLOINSUFFICIENCY** in the *OPA1* gene

RESULTS IN

50%
OPA1 protein expression and disease manifestation

1 out of 30,000
people are affected globally with a higher incidence of ~1 out of 10,000 in Denmark due to a founder effect

>400
Different *OPA1* mutations reported in ADOA patients

Up to 46%
of patients are registered legally blind

80%
of patients are symptomatic by age 10

~18,000
people affected in the U.S., Canada, Japan, Germany, France and the UK

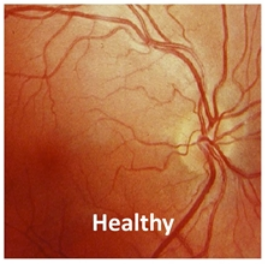
Sources: Yu-Wai-Man P et al. *Ophthalmology*, 2010; Yu-Wai-Man P, Chinnery PF. *Ophthalmology*, 2013; P. Amati-Bonneau P et al. *The International Journal of Biochemistry & Cell Biology*, 2009; Lenaers G, Hamel C, Delettre C, et al. *Orphanet J Rare Dis*, 2012; Chun BY and Rizzo JF III. *Curr Opin Ophthalmol*, 2016; Le Roux B, Lenaers G, Zanlonghi X et al. *Orphanet J Rare Dis*, 2019; "What is ADOA?" Autosomal Dominant Optic Atrophy Association. Accessed May 6, 2020, from https://www.adoaa.org/what-is-adoa;

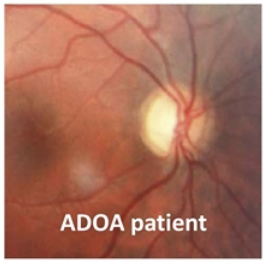
No Approved Disease-Modifying Therapies for ADOA

Healthy Vision

Simulation of Optic Neuropathy

- Most common inherited optic nerve disorder
- Leads to central field defects and reduced color vision in both eyes
- Severity can vary; rate of vision loss difficult to predict
- Supportive services and low-vision aids are offered for patients

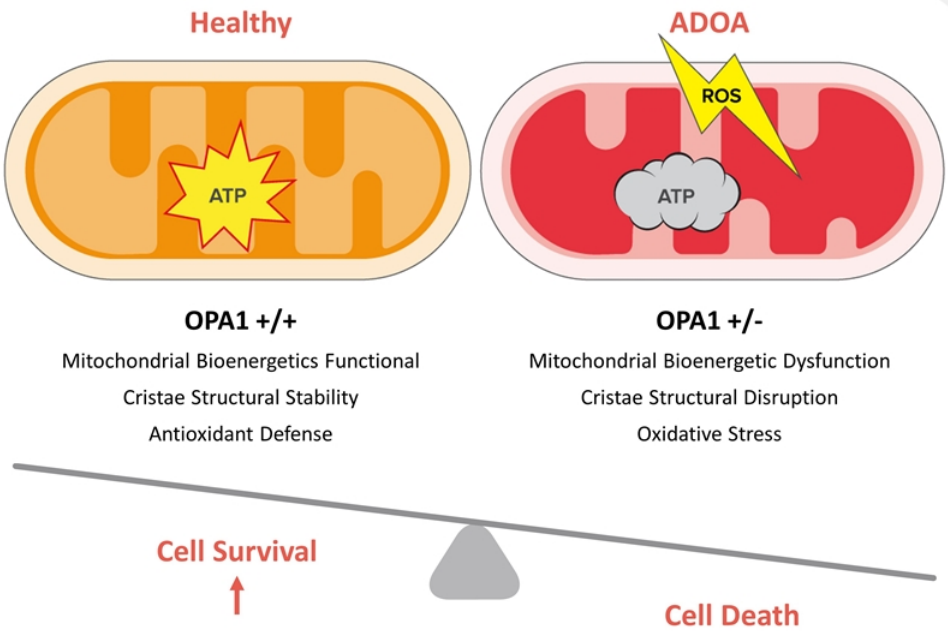




Sources: Yu-Wai-Man P et al. *Ophthalmology*, 2010; Yu-Wai-Man P, Chinnery PF. *Ophthalmology*, 2013; Lenaers G, Hamel C, Delettre C, et al. *Orphanet J Rare Dis*, 2012; Chun BY and Rizzo JF III. *Curr Opin Ophthalmol,* 2016
Image of child sourced from ICR, Ophthalmology Center Barcelona. Accessed Jan. 8, 2021 from https://icrcat.com/en/eye-conditions/leber-hereditary-optic-neuropathy/ Credit: Lhon Eye Society Sweden. Image shown depicts Leber Hereditary Optic Neuropathy, which presents visual effects similar to ADOA.

OPA1 is Critical for Normal Mitochondrial Function and Cellular Metabolism

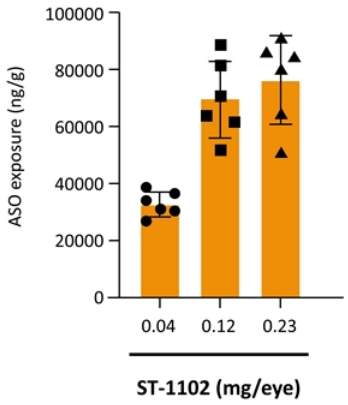
- Retinal ganglion cells have very high energy (ATP) requirements
- Impaired mitochondrial function leads to cell death
- OPA1 is critical for mitochondrial function and energy production



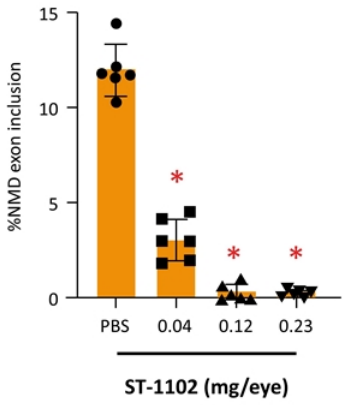
* ROS = Reactive Oxygen Species

TANGO ASO Demonstrates Dose-Dependent OPA1 Protein Increases in Rabbit Retina

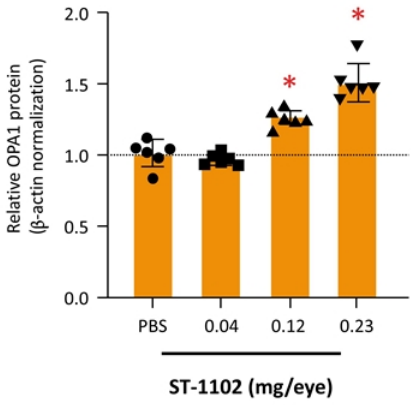
ASO exposure in retina Day 29



Target engagement Day 29



OPA1 protein Day 29

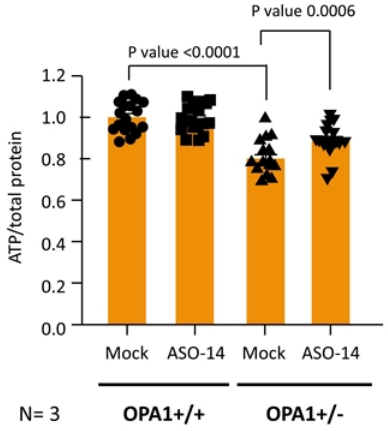


***P*<0.0005 by one-way ANOVA compared to PBS group**

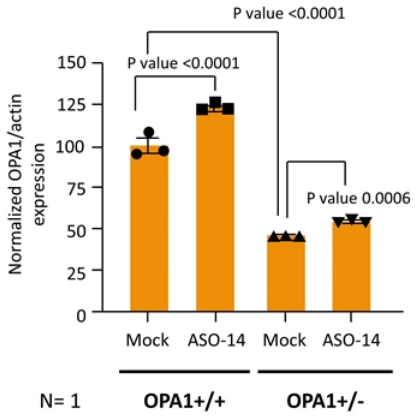
NMD = nonsense mediated decay
Source: TANGO oligonucleotides for the treatment of Dravet Syndrome: Safety, biodistribution and pharmacology in the non-human primate (AES 2019)

TANGO ASO Partially Restores ATP and Protein Levels in Human OPA1 +/- Cells

ASO treatment increased ATP levels in OPA1 deficient cells



ASO treatment increased OPA1 protein levels



*one-way ANOVA
#t-test

Source: Stoke data

TANGO ASOs Have the Potential to Address the Genetic Cause of ADOA

- Dose-dependent increases in OPA1 protein expression in rabbit retina ✓
- Increases ATP and protein levels in human OPA1 +/- cells ✓
- Well tolerated for up to 29 days after intravitreal injection in rabbit ✓

Lead optimization is underway to potentially identify a clinical candidate in 2021

Broad Therapeutic Potential for TANGO

Stoke identified a variety of non-productive alternative-splicing events that lead to mRNA degradation and limit protein production.

10K+
Genetic diseases are caused by mutations in a single gene

5%
Of these diseases are addressed by current therapeutic approaches

~1,200
Monogenic disease genes containing at least one NMD-inducing non-productive event

~6,500
Additional unique genes found by Stoke that contained at least one NMD-inducing non-productive event

nature communications Lim *et al.*, Nat Comm, 2020

2021 Milestones

1H2021	Initiate Swallowtail Open Label Extension (OLE) study of STK-001
2H2021	Initiate multiple ascending dose (MAD) study of STK-001
2H2021	Preliminary safety and PK data from Phase 1/2a MONARCH study of STK-001
2H2021	Initiate ADOA natural history data collection
YE2021	Complete lead optimization for OPA1 compounds
YE2021	Demonstrate *in vivo* proof of mechanism and safety for a third program

Current Financials Anticipated to Fund Operations into 2024

$287.6M

Cash, Cash Equivalents & Restricted Cash

as of 12/31/2020

36.6M

Common Shares Outstanding

as of 12/31/2020

We Are Stoke

United in our mission to address the underlying cause of severe diseases by up-regulating protein expression with RNA-based medicines.