

Stoke Therapeutics Third Quarter 2026 Business Update

Webcast for Investors & Analysts

October 29, 2026

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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, statements regarding: the ability of zorevunersen 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 potential benefits, safety and efficacy of zorevunersen; the design, timing and results of clinical studies, enrollment timelines, data readouts, regulatory submissions or decisions and other presentations for zorevunersen and STK-002; our ability to achieve an NDA submission or approval on the expedited timeframe disclosed or at all, and the associated timing, if any, of a potential U.S. commercial launch; the ability of STK-002 to treat the underlying causes of Autosomal Dominant Optic Atrophy (ADOA) and maintain or improve vision; the potential for us to advance and develop our research and development programs; our expectations, plans, aspirations and goals, including those related to the potential of zorevunersen, STK-002 or our other product candidates and our collaborations with Biogen and Acadia; the anticipated market, access, reimbursement and label, if any, for zorevunersen; our future operating results, financial position and cash runway and ability to fund operations through to early 2028. Statements including words such as "anticipate," "believe," "expect," "hope," "plan," "will," "continue," "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 and STK-002; the timing of data readouts and interim and final results of nonclinical and clinical studies; nonclinical and clinical data being 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; 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, 2025, 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.

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This presentation discusses product candidates, including zorevunersen and STK-002, that have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory agency.

Opening Remarks

Ian F. Smith

Chief Executive Officer & Director

Advancing Zorevunersen to Patients

EMPEROR Phase 3 Progress

- ✓ **~110 Patients Through Week 28**
measurement of primary endpoint
- ✓ **~20 Patients Through Week 52**
completion of efficacy treatment period and measurement of key secondary endpoints
- ✓ **All ~20 Continuing into OLE**
- ✓ **No Treatment Discontinuations**

FDA Meeting to Prepare for NDA

- ✓ **Reviewed 5 Years of Clinical Data**
from Phase 1/2 and ongoing OLE studies
- ✓ **Multicomponent Assessment**
will analyze changes in cognition and behavior, a key secondary endpoint in EMPEROR
- ✓ **Active Engagement with FDA**
and planned submission of data throughout H1 2027

Commercial Readiness

- ✓ **~6,000 Patients**
addressable at launch
- ✓ **Strong Awareness and Understanding of Zorevunersen**
among clinicians and caregivers
- ✓ **Field Market Access Team**
built out to support payer engagement and information exchange
- ✓ **New Stakeholder Initiatives**
including American Epilepsy Society's Presidential Task Force

Data Readout in Q3 2027

Completion of NDA in H2 2027

Potential U.S. Launch in Early 2028

Expanding Our Research and Building Our Pipeline

With an Emphasis On

Severe genetic diseases

Caused by haploinsufficiency

Focused on CNS

Phase 1 Study Underway of STK-002 in Patients with ADOA



Rare, genetic disease



Most common optic nerve disorder



Primarily caused by haploinsufficiency of OPA1 protein



No approved treatments

Preclinical data support advancement of OSPREY



Dosing of third cohort underway; completion expected by year-end



Initiation of fourth cohort expected in early 2027



Initial safety and efficacy data anticipated in H1 2027

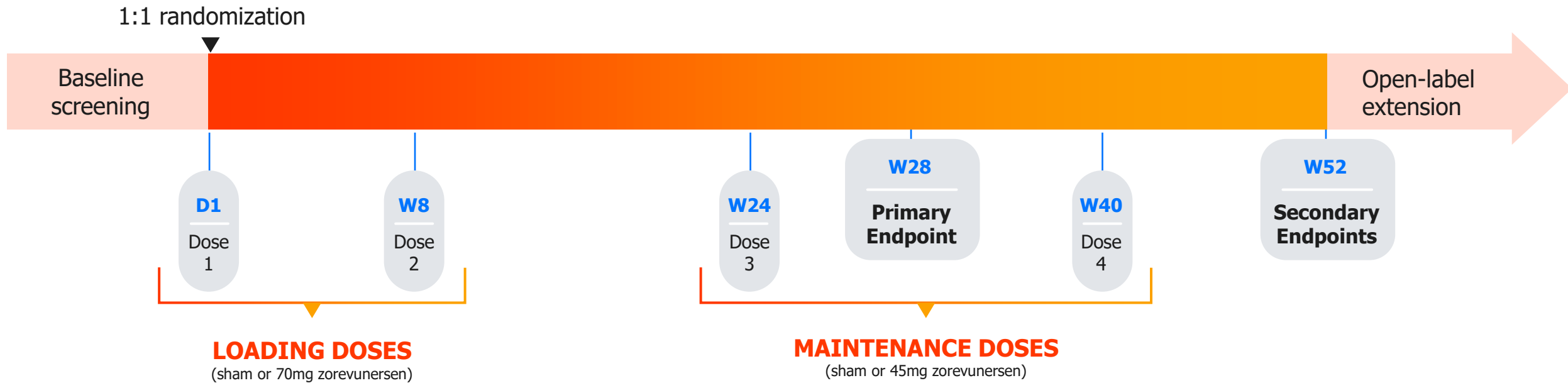
Phase 3 EMPEROR Progress

Barry Ticho, M.D., Ph.D.

Chief Medical Officer

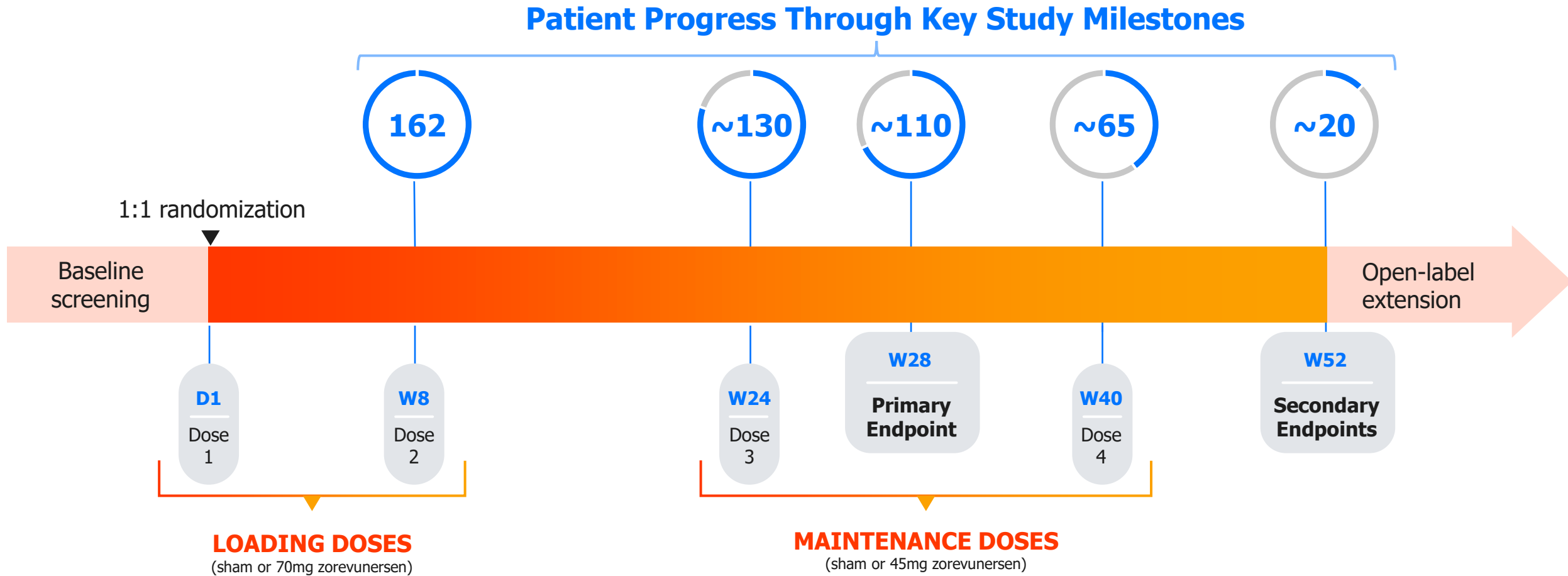
EMPEROR: A Global, Double-Blind, Sham Controlled Phase 3 Study

In patients 2 to <18 years old with a confirmed *SCN1A* gene variant not associated with gain of function



Patient Progression Through Key EMPEROR Timepoints

No Discontinuations to Date



EMPEROR is Designed to Evaluate the Disease-Modifying Potential of Zorevunersen

Study Endpoints

PRIMARY

Percent change from baseline in major motor seizure frequency at Week 28

KEY SECONDARY

Durability of effect on major motor seizure frequency at Week 52

KEY SECONDARY

Change in behavior & cognition measured by multicomponent assessment of four Vineland-3 subdomains at Week 52

Multicomponent Assessment

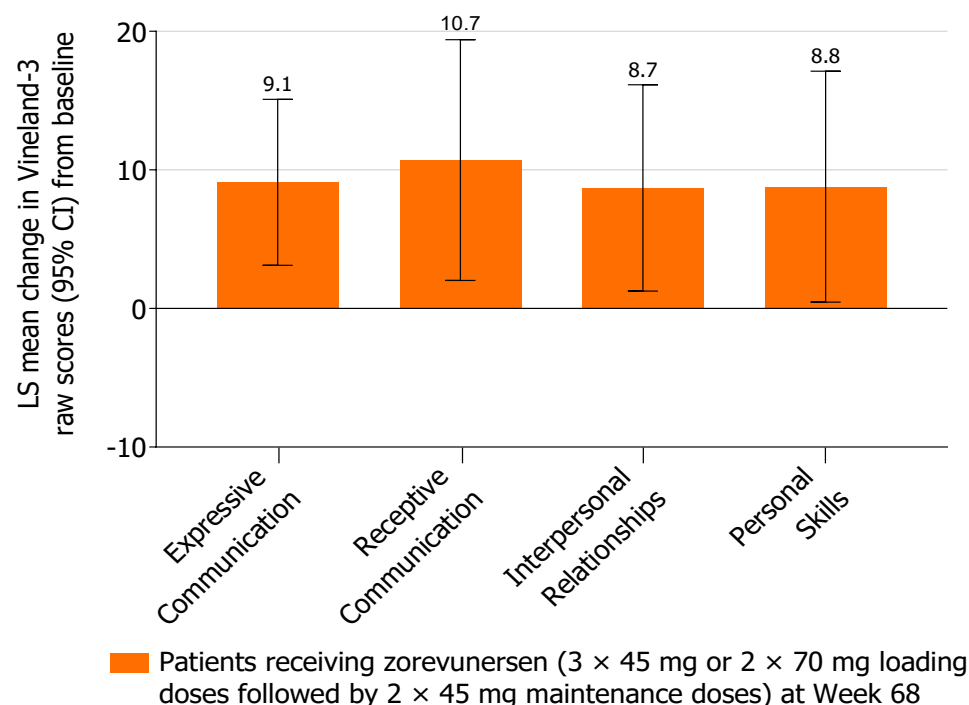
Four Vineland-3 Subdomains:

- Expressive Communication
- Receptive Communication
- Interpersonal Relationships
- Personal Skills

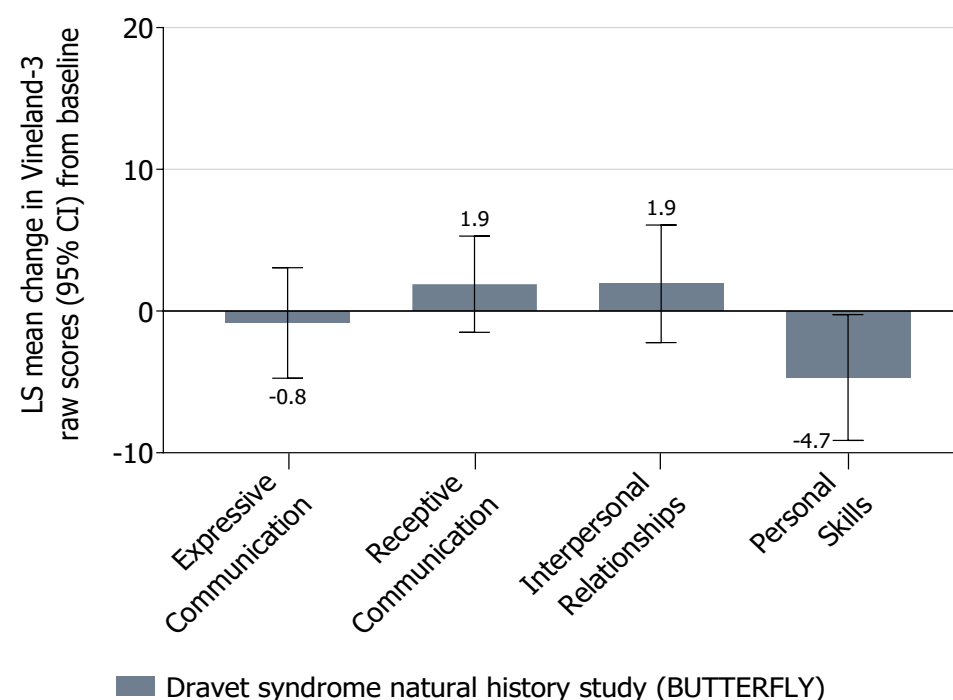
Individual treatment effect for each subdomain is calculated, then all four scores are averaged to produce a **single score** that reflects overall treatment effect

Matching Adjusted Indirect Comparison of Patient Data Supported Phase 3 Selection of Dose and Vineland Subdomains

Patients treated with zorevunersen



Dravet syndrome natural history study patients

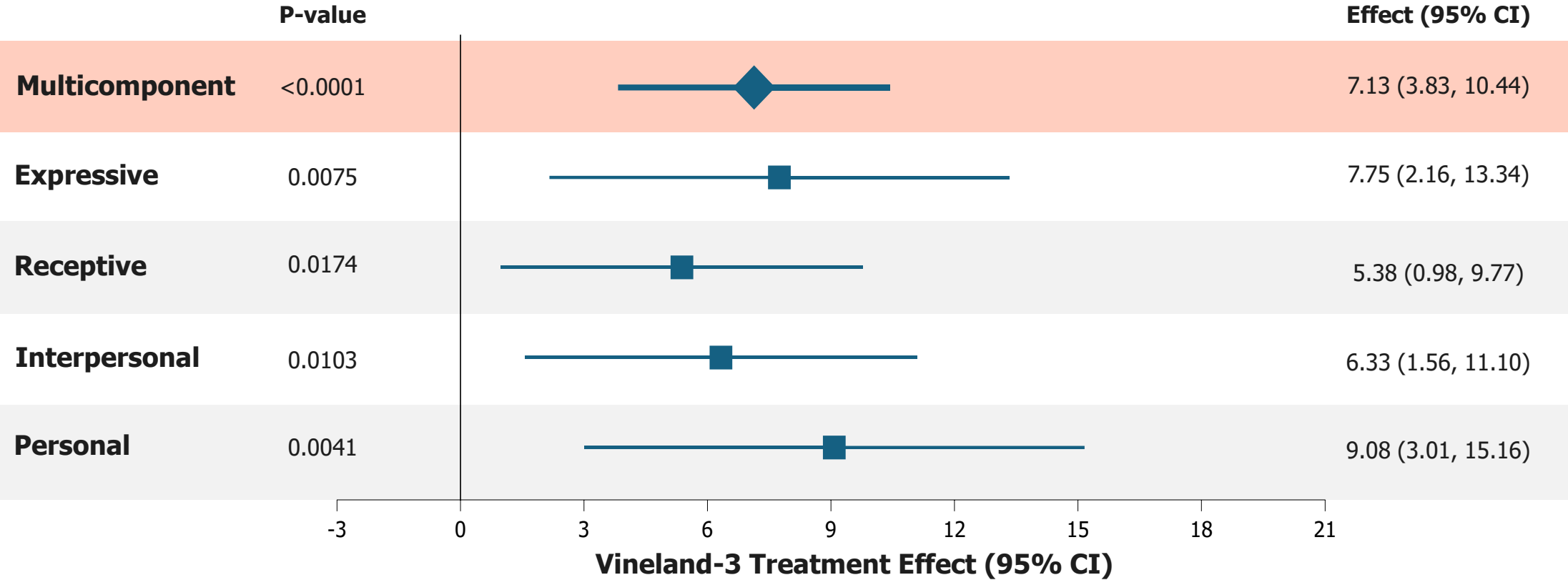


Phase 1/2a data cut: December 12, 2023 (after End of Study); OLE data cut: June 28, 2024. Treatment group (left, n=7 at Week 68) includes patients who received loading doses of 2x70mg or 3x45mg plus two maintenance doses of 45mg. Matching of baseline characteristics was performed using population-adjusted least squares means to allow for cross-trial comparison with the BUTTERFLY natural history study (right, n=36 at baseline, n=26-27 at Month 12, n=22 at Month 18).

LS, least squares; OLE, open-label extension; Vineland-3, Vineland Adaptive Behavior Scales – Third Edition. Brunklaus A, et al. EPNS Congress; July 10, 2025. Due to differences between trials, cross-study comparisons may provide limited information on the efficacy or safety of a drug.

Statistically Significant Improvements in Cognition and Behavior Using a Multicomponent Assessment Support Planned Phase 3 Analysis

Treatment effect in Phase 1/2 and OLE patients who received cumulative doses of zorevunersen consistent with Phase 3, compared to natural history at 18 months



EMPEROR is Powered to Detect Statistically Significant Treatment Effects in Primary and Key Secondary Endpoints

Patient enrollment and progression with no discontinuations, combined with planned multicomponent assessment, enhance statistical power

Endpoints

PRIMARY

Percent change from baseline in major motor seizure frequency at Week 28

KEY SECONDARY

Durability of effect on major motor seizure frequency at Week 52

KEY SECONDARY

Change in behavior & cognition measured by multicomponent assessment of four Vineland-3 subdomains at Week 52

Minimum Detectable Treatment Effect

Modeled with 150 evaluable patients at 90% power

$\alpha=0.05$

$\alpha=0.01$

46%

53%

Relative reduction between treatment arms

1.8

2.1

Difference in raw score points

Advancing STK-002 for ADOA

Barry Ticho, M.D., Ph.D.

Chief Medical Officer

Autosomal Dominant Optic Atrophy (ADOA): A Progressive Vision Disorder Primarily Caused by OPA1 Haploinsufficiency

Disease and Cause

 **65-90%**

of cases caused by mutations in one copy of the *OPA1* gene, most of which lead to **haploinsufficiency**

Resulting in



functional OPA1 protein and disease manifestation

Epidemiology

1 out of 25,000

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

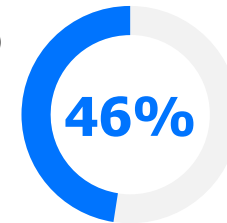
~13,000

people affected in the U.S., UK, EU-4, and Denmark

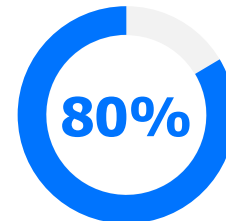


Burden

up to



of patients are registered legally blind



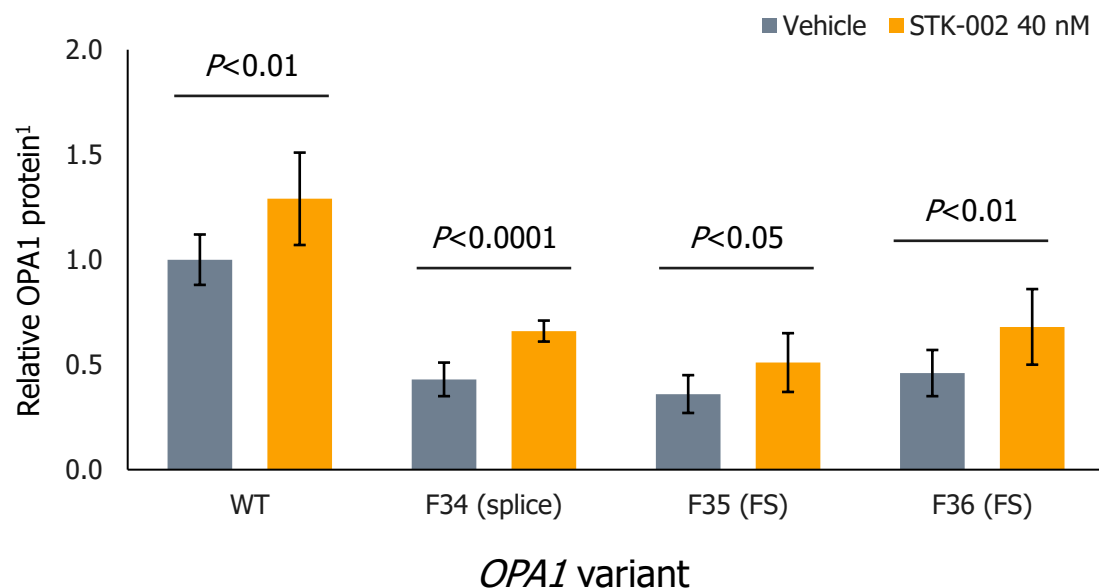
of patients are symptomatic by age 10

>600

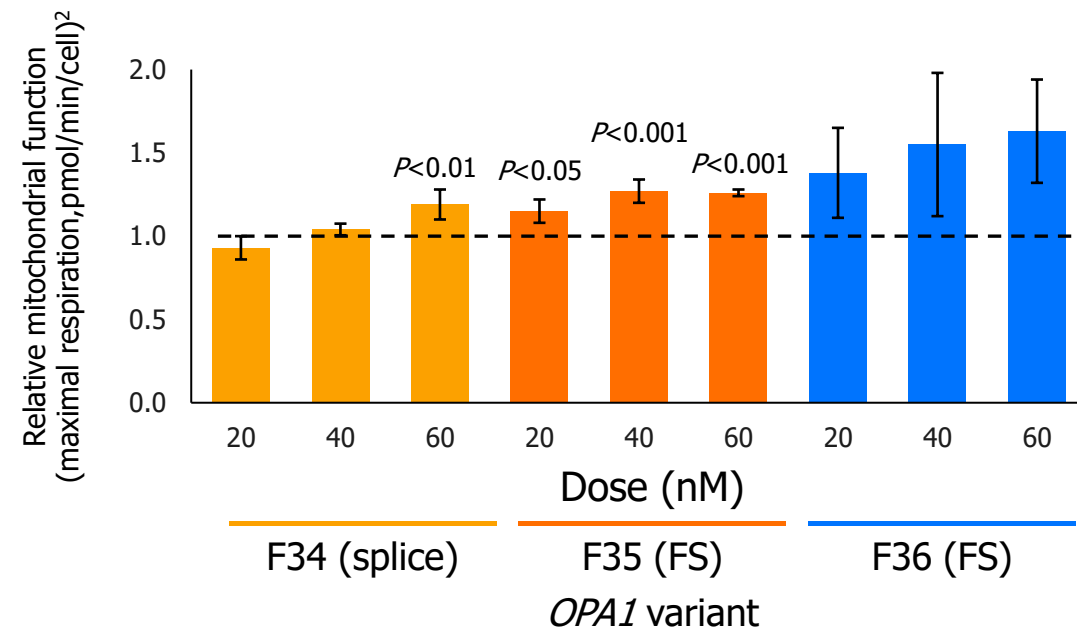
Different *OPA1* mutations reported in ADOA patients

STK-002 Shows Statistically Significant Increases in OPA1 Protein and Improvements in Mitochondrial Function in ADOA Patient-Derived Cells

Increased OPA1 protein expression



Improved mitochondrial function



STK-002 demonstrated activity across cells carrying different *OPA1* variants

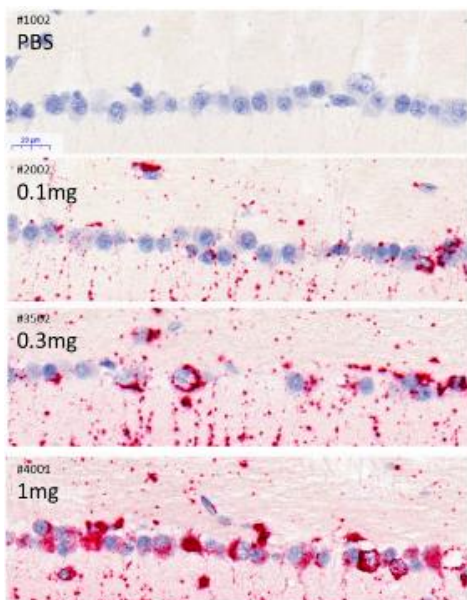
1. Mean (SD) OPA1 protein levels (n=9) plotted relative to WT Vehicle group. Statistical analysis by unpaired t-tests. 2. Mean (SD) maximal respiration determined by OCR (pmol/min/cell) under basal and stress conditions, normalized to cell count (n=3) plotted relative to Vehicle (1.0) for each cell type. Statistical analysis by ordinary one-way ANOVA and Dunnett's multiple comparison test.

ADOA, autosomal dominant optic atrophy; FS, frameshift; mRNA, messenger ribonucleic acid; OCR, oxygen consumption rate; OPA1, OPA1 mitochondrial dynamin like GTPase; SD, standard deviation; WT, wild-type.

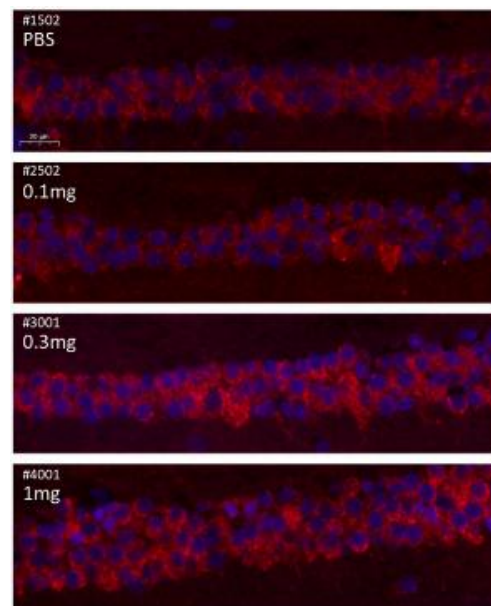
Figures adapted from Venkatesh A et al. *Nucleic Acid Ther* 2024; 34 (5): 221–236. Licensed under CC BY 4.0. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>

A Single Intravitreal Dose of STK-002 Increased Retinal OPA1 Protein by 47% at 4 Weeks in Wild-Type Non-Human Primates Versus Control

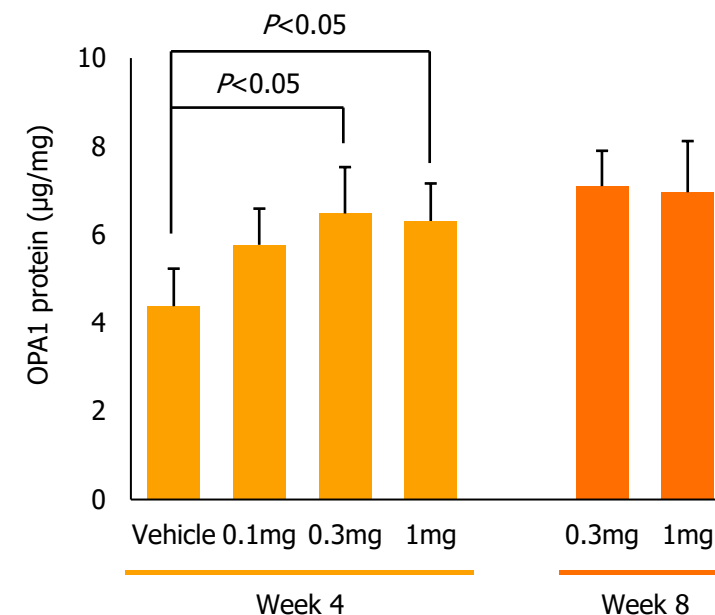
STK-002 detected in RGC layer



OPA1 protein in RGC layer



OPA1 protein in retinal lysates

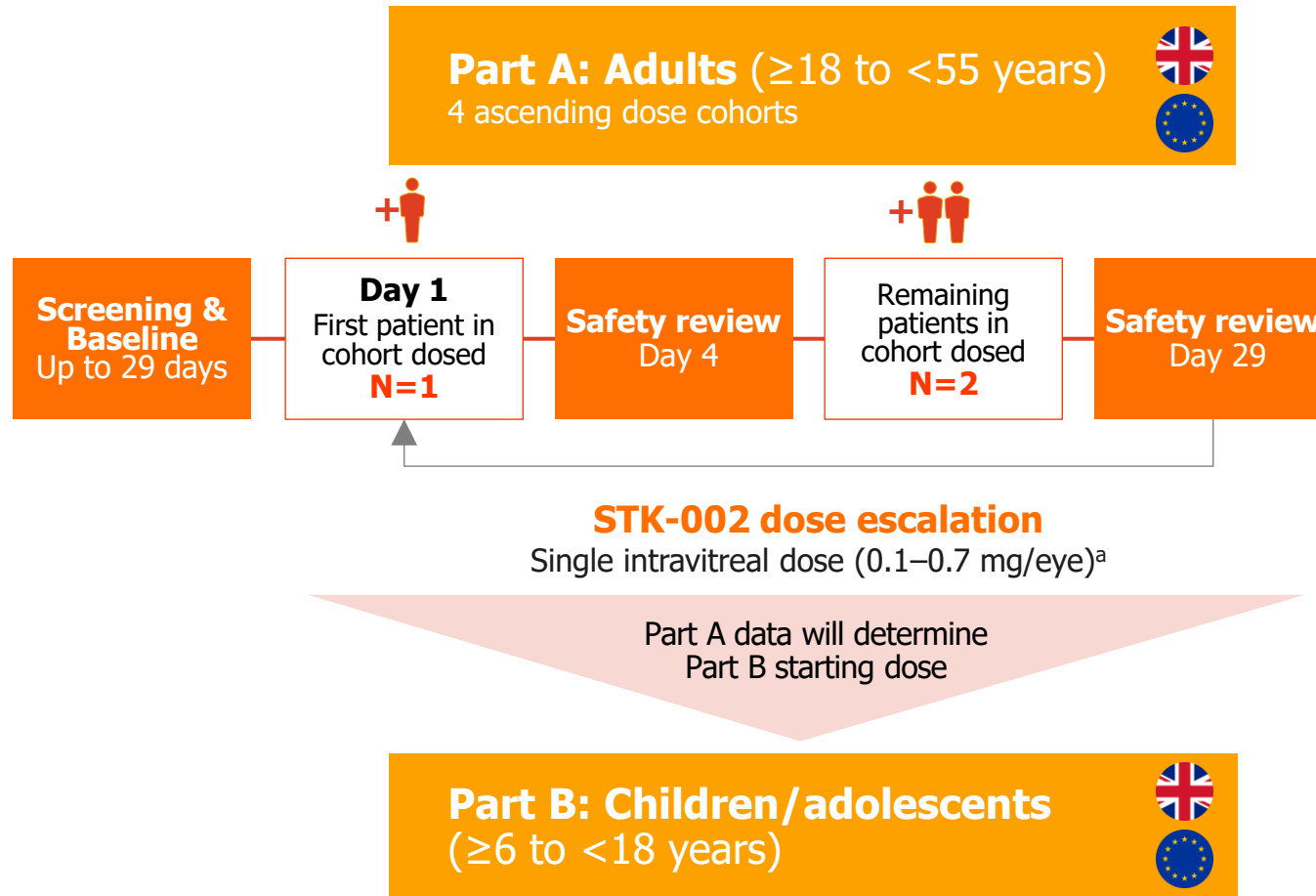


Retinas were collected at 4 or 8 weeks after intravitreal dosing.

OPA1, OPA1 mitochondrial dynamin like GTPase; PBS, phosphate-buffered saline; RGC, retinal ganglion cell.

Figures are adapted from Venkatesh A et al. *Nucleic Acid Ther* 2024; 34 (5): 221–236. Licensed under CC BY 4.0. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>

Phase 1 OSPREY Study of STK-002 in Patients with ADOA



Principal focus

- Safety and tolerability

Other measures

- Visual function – LCVA
- Ocular structure – OCT
- Mitochondrial stress – OcuMet Beacon™ imaging

Recruitment ongoing

OSPREY: Dose Escalation Continuing with Initial Safety & Efficacy Data Expected in H1 2027

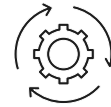
Cohorts 3 and 4 have the potential to reach therapeutic levels of dosing

Significance



May demonstrate whether STK-002's ability to upregulate OPA1 expression translates into measurable effects on visual function

Status



Dosing complete in cohorts #1 and #2

Cohort #3 expected to complete by the end of 2026

Initial data expected in H1 2027

Future



Inform dose selection and future clinical development of this novel RNA-based potentially disease-modifying approach

Preparing for a Potential U.S. Launch

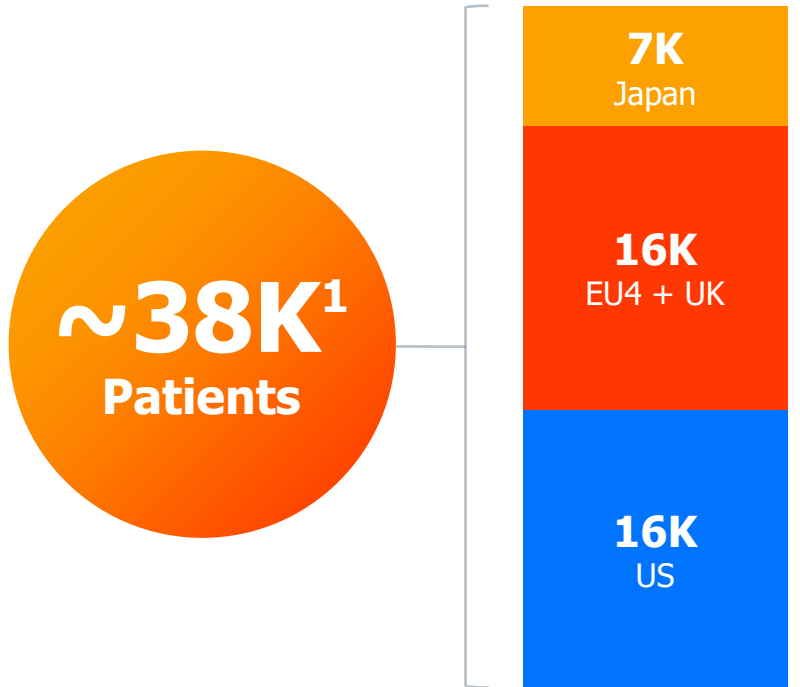
Jason Hoitt

Chief Patient Officer

Significant Market Opportunity

~38K patients with Dravet syndrome across 7 major geographic markets

Prevalence of Dravet Syndrome²



Concentrated U.S. Market

~6,000 patients immediately addressable at launch

- <25 years old and likely in the care of a pediatric provider
- Insights into where ~80% of these patients are being cared for today

ICD10 code established in 2020 will continue to increase patient identification

- **40-50 new patients³** entering claims databases every month

¹ Based on preliminary management estimates, which scaled annual incidence to prevalence using country-specific live birth rates over the past 85 years and adjusted for Dravet-specific mortality. The estimate is based on incidence rates published by Wu et al., *Pediatrics*, 2015; Lagae et al., *Developmental Medicine & Child Neurology*, 2017; 2018 Health Advances Report; Dravet Syndrome Foundation Voice of the Patient Report.

² Numbers may not add up due to rounding. EU4: Germany, France, Italy and Spain

³ De-identified U.S. medical and pharmacy claims database, Oct 2022 – Sep 2026. Patients with a first observed ICD-10 Dravet syndrome code (G40.833/G40.834) per month; observed, unprojected counts.

Established Infrastructure at Key Sites of Care Provides Foundation for Early Adoption



Treating Sites

~50%

of identified U.S. patients are cared for by the top 50 sites



Existing Infrastructure

100%

of top 50 sites have established intrathecal administration infrastructure



Zorevunersen Experience

~50%

of top 50 sites have participated in zorevunersen clinical studies



"We've used Spinraza for years and **we've already established the infrastructure of recurrent intrathecal injections** for these patients. I can't imagine that I'm going to need a completely different infrastructure."

Preparing to Deliver Zorevunersen



Adding Capabilities

Patient Services to
enable timely access

Payer Account Team
to educate medical directors
at insurers



Expanding Education

Continuing engagement
with HCPs

Expansion into broader
neurology community



Collaborative Efforts

Genetic testing
initiatives

Medical society
leadership initiatives

Two additional studies of zorevunersen in adults and infants & toddlers anticipated to initiate by year-end

Financial Summary

Thomas Leggett

Chief Financial Officer

Third Quarter 2026 Financial Summary

\$358.8 Million

Cash, Cash Equivalents, & Marketable Securities
as of September 30, 2026

**Current financial position anticipated to fund
operations through to early 2028**

Q&A
