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

Archana Desurkar[1], M. Scott Perry[2], Joseph Sullivan[3], Andreas Brunklaus[4], Linda Laux[5], J Helen Cross[6], Orrin Devinsky[7], Kelly G. Knupp[8], Matt Lallas[9], Steven Phillips[10], John Schreiber[11], Colin Roberts[12], Javier Avendano[13], Charlene Brathwaite[13], Carrie Condon[13], Dana Fitzpatrick[13], Jessie Lynch[13], James Stutely[13], Fei Wang[13], Kimberly A. Parkerson[13], Barry Ticho[13]

[1]Sheffield Hospital, [2]Cook Children's; [3]University of California San Francisco; [4]Royal Hospital for Children; [5]Children's Hospital of Chicago; [6]Great Ormond Street Hospital for Children; [7]New York University Langone; [8]Children's Hospital Colorado; [9]Nicklaus Children's Hospital; [10]Mary Bridge Children's; [11]Children's National Hospital; [12]Oregon Health & Sciences University; [13]Stoke Therapeutics

DS is a severe and progressive epilepsy

- DS is characterized by frequent, prolonged, and refractory seizures, typically beginning within the first year (y) of life
- DS includes comorbidities including intellectual disability, ataxia/motor abnormalities, behavioral problems, speech impairment, sleep disturbances, and a high risk for sudden unexpected death
- In approximately 85% of cases, DS is caused by spontaneous, heterozygous loss of function mutations in the *SCN1A* gene, which encodes the voltage-gated sodium channel type 1 α subunit ($Na_v1.1$) protein
- In DS, patients have one wild type copy and one mutated copy, resulting in half as much $Na_v1.1$ protein as needed to maintain health
- Upregulating $Na_v1.1$ protein may restore functioning neurons and prevent seizures and reduce non-seizure related comorbidities in DS

STK-001 is designed to address the genetic cause of DS

- STK-001 is an investigational antisense oligonucleotide designed to upregulate $Na_v1.1$ protein expression by leveraging the non-mutant (wild type) copy of *SCN1A* to restore physiological $Na_v1.1$ protein levels

SWALLOWTAIL and LONGWING are ongoing OLE studies of STK-001

- OLE studies conducted at 18 sites in the US (NCT04740476; SWALLOWTAIL) and 3 sites in the UK (2021-005626-14; LONGWING)
- Patients enroll following completion of MONARCH (NCT04442295) or ADMIRAL (2020-006016-24)
- Patients currently receive intrathecal (IT) doses of STK-001, once every 4 months at 30 mg/dose in SWALLOWTAIL and 45 mg/dose in LONGWING

Data cutoff in SWALLOWTAIL and LONGWING: 05May2023 except Clinical Assessment Data from SWALLOWTAIL: 24Mar2023

~90% of patients enrolled in OLEs following completion of an STK-001 Ph1/2a study

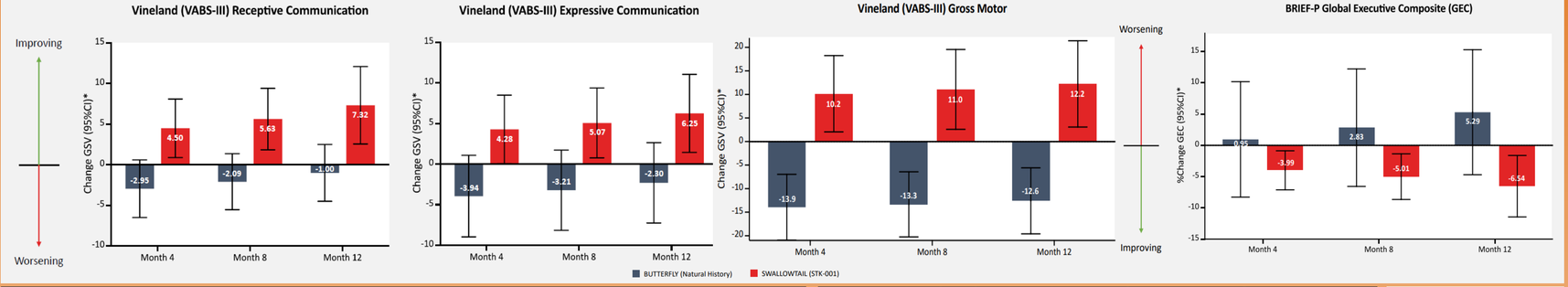
Demographics (N=58; N=48 from SWALLOWTAIL and N=10 from LONGWING)	
Age at Screening, y	
Mean (SD)	10.4 (5.19)
Median (min, max)	11.0 (0, 19)**
Age Group, n (%)	
2–12y	31 (53.4)
13y and older	27 (46.6)
Sex	
Female, n (%)	30 (51.7)
Male, n (%)	28 (48.3)
Race, n (%)*	
Asian	4 (6.90)
Black or African American	4 (6.90)
White	50 (86.2)
Prefer not to answer	4 (6.90)
Ethnicity, n (%)	
Not Hispanic/Latino	49 (84.5)

*Able to choose more than 1 option; **Min age of 0y was data entry error and corrected after data cutoff

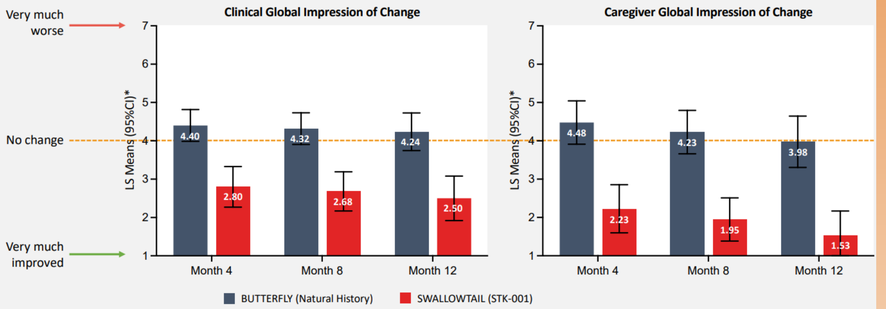
Patients have received up to 8 doses of STK-001 administered every 4 months ranging from 10-45 mg/dose

STK-001 doses administered in SWALLOWTAIL or LONGWING	
10 mg	10
20 mg	14
30 mg	94
45 mg	53
Total All Doses	171

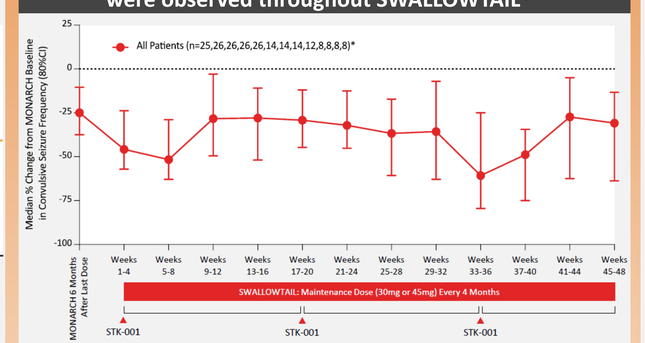
Substantial improvements were evident in multiple measures of cognition and behavior assessed by the VABS-III and BRIEF-P*



Clinicians and caregivers rated improvements in overall clinical status similarly*



Sustained reductions in convulsive seizure frequency were observed throughout SWALLOWTAIL*



*Clinical assessment and convulsive seizure frequency analyses not yet available from LONGWING; current analyses included patients completing MONARCH who received only doses of 30 or 45 mg in SWALLOWTAIL. Vineland Adaptive Behavior Scales-III (VABS-III) and Behavior Rating Inventory of Executive Function Preschool (BRIEF-P) analyzed in mixed model repeated measures with AR(1) covariance structure. Baseline covariates in BUTTERFLY matched to SWALLOWTAIL. BUTTERFLY sample size: n=36 at screening and n=27 for VABS-III and n=30 for BRIEF-P at Month 12; SWALLOWTAIL sample size: n=24 for VABS-III and n=25 for BRIEF-P at screening; n=9 at Week 48 and n=5 at Week 64. GSV=Growth Scale Value.

Multiple doses up to 45 mg have been generally well-tolerated in SWALLOWTAIL and LONGWING

Number (N (%)) of Patients with	2-12y N=31	13-18y N=27	Total N=58
TEAEs	19 (61.3)	24 (88.9)	43 (74.1)
TEAEs related to study drug (all mild or moderate)*	6 (19.4)	12 (44.4)	18 (31.0)
TEAEs related to CSF or study drug administration	6 (19.4)	12 (44.4)	18 (31.0)
≥Grade 3 TEAEs	1 (3.22)	2 (7.41)	3 (5.17)
≥Grade 3 TEAEs related to study drug	0	0	0
Serious TEAEs	5 (16.1)	4 (14.8)	9 (15.5)
Serious TEAE related to study drug	0	0	0

*Only Treatment-Related TEAE in >1 patient was CSF protein increased: 14/58 (24.1%) patients

TEAEs Reported in >10% Patients	
Preferred Term	N (%)
CSF protein increased	14 (24.1)
COVID-19	13 (22.4)
Pyrexia	10 (17.2)
Seizure	9 (15.5)
Post lumbar puncture syndrome	7 (12.1)
Headache	6 (10.3)
Upper respiratory tract infection	6 (10.3)
Vomiting	6 (10.3)

OLE study data support STK-001 as the first potential disease-modifying therapy for DS

- Multiple doses of STK-001 up to 45 mg per dose given every 4 months intrathecally were generally well-tolerated
- Clinical effects were observed in patients treated with the best available medicines for DS
- In addition to durable reductions in convulsive seizure frequency throughout the course of treatment, data indicated substantial improvements in multiple assessments of cognition and behavior over 12 months
- Totality of data from these ongoing studies suggest the potential for STK-001 as syndrome management for DS
- Poster #1.276 reports MONARCH and ADMIRAL study results

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