STS101 (Dihydroergotamine Nasal Powder) Shows Pain Relief in Difficult to Treat Migraine Attacks: Results From the Phase 3 Double-Blind, Randomized, Placebo-Controlled SUMMIT Study

Jessica Ailani, MD¹, Shannon Strom, PhD², Detlef Albrecht, MD², Alan Rapoport, MD³

¹Department of Neurology, Georgetown University, Washington DC, USA; ²Satsuma Pharmaceuticals, Inc., Durham, NC, USA; ³David Geffen School of Medicine, University of California Los Angeles, Los Angeles, CA, USA

Introduction

- Dihydroergotamine mesylate (DHE) is a recommended first-line treatment option for the acute treatment of moderate or severe migraine attacks, with or without aura.1
- STS101 is a novel investigational DHE product that combines a mucoadhesive nasal powder formulation liquid nasal sprays.2 delivered with an easy-to-use, easy-to-carry, pre-filled, single-use nasal delivery device (Figure
- The STS101 advanced nasal powder and device technology maximizes deposition of DHE on the nasal mucosa, enhancing DHE absorption, increasing drug exposure and reducing pharmacokinetic variability in comparison with DHE
 - STS101 is the only DHE-containing product with double-blind, placebo-controlled phase 3 efficacy data using current state of the art clinical trial endpoints recommended by the FDA³ and the International Headache Society.4

Objective

• To compare the pain relief capabilities of STS101 with placebo in difficult-to-treat episodic migraine attacks in a double-blind, randomized, placebo-controlled phase 3 study (SUMMIT)

Methods

Study Design and Treatment Intervention

- SUMMIT (NCT04940390) was a double-blind, randomized, placebo-controlled phase 3 trial in adults with a history of 2–8 moderate or severe migraine attacks and fewer than 15 headache days per month.
- After establishing eligibility, the study participants self-administered a single 5.2-mg dose of STS101 or placebo to treat one migraine attack of moderate or severe pain intensity.

Participants

- Study participants must have had ≥1-year history of migraine (with or without aura) according to the International Classification of Headache Disorders 3rd edition,⁵ including:
- Migraine onset before the age of 50 years 2–8 migraine attacks/month with moderate or severe pain each month
- <15 headache days/month</p>
- Those with a non-migraine headache diagnosis, history of cerebrovascular disease, ≥2 cardiovascula risk factors (hypertension, hypercholesteremia obesity, diabetes mellitus, history of premature coronary artery disease, postmenopausal females, o males >46 years of age), and current (at screening) use of >1 migraine prevention treatment were excluded.

Outcomes and Analyses

- Headache pain relief through 48 hours post-dose
- Pain was assessed from 15 minutes through 48 hours after study treatment on a 4-point scale where 0=no pain, 1=mild pain, 2=moderate pain, and 3=severe pain
- Pain relief was defined as a reduction from moderate (2) or severe (3) headache pain to mild (1) or no (0) headache pain with no prior use of any rescue medication or second dose of study
- Analysis groups: modified intent-to-treat (mITT) population, subgroup with baseline allodynia, and subgroup with menstruation-related migraine
- The mITT population was defined as all migraine attack, received the study medication and had efficacy data in ≥1 post-treatment e-Diary entry through an analysis that treats missing data as a non-responder
- Allodynia status was defined as present if a participant had ≥2 "yes" responses to the 6-question allodynia questionnaire^{6,7}
- If the participant treated a migraine attack on Day 1 (± 2) of menstruation, then the participant was considered as having a menstruation-related migraine attack
- Participants who did not have evaluable assessments at the 2-hour time point, or who received rescue medication prior to the 2-hour time point, were considered non-responders

Results

- Of 1,591 randomized participants, 1,424 were evaluable for efficacy analysis.
- The treated attacks showed high rates of severe pain (38%), nausea (69%), photophobia (96%),
- STS101 demonstrated a statistically significant response rate for relief from headache pain at 2 hours post-dose compared to placebo (53.0% vs 44.6%; nominal *p*<0.01) (**Figure 2**).

phonophobia (91%), and allodynia (63%) (Table

- STS101 significantly improved headache pain relief at 2 hours through 48 hours post-dose.
- In participants with baseline allodynia, STS101 demonstrated a higher and significant response rate for pain relief at 2 hours post-dose vs placebo (50.2% vs 43.5%, respectively; nominal *p*<0.05) (Table 2), which was similar to the response rate in participants without baseline allodynia (57.5% vs 46.6%, respectively; nominal p<0.05).
- STS101 exhibited efficacy in participants with (Table 3) or without menstruation-related migraine attacks (with: 50.0% STS101 vs 39.6% placebo; without: 50.0% STS101 vs 60.4% placebo).
- In participants with Headache Impact Test (HIT)-6 scores indicating severe impact (>60), STS101 demonstrated a higher response rate compared with placebo with nominal significance (p<0.001) a 2 hours post-dose (52.5% vs 42.8%, respectively).

p*<0.01, *p*<0.001.

1. Ailani J, et al. *Headache*. 2021;61(7):1021-39.

3. FDA Acute Migraine Guidance, 2018.

2. Lipton R, et al. *Headache*. 2024;64(3):266-75.

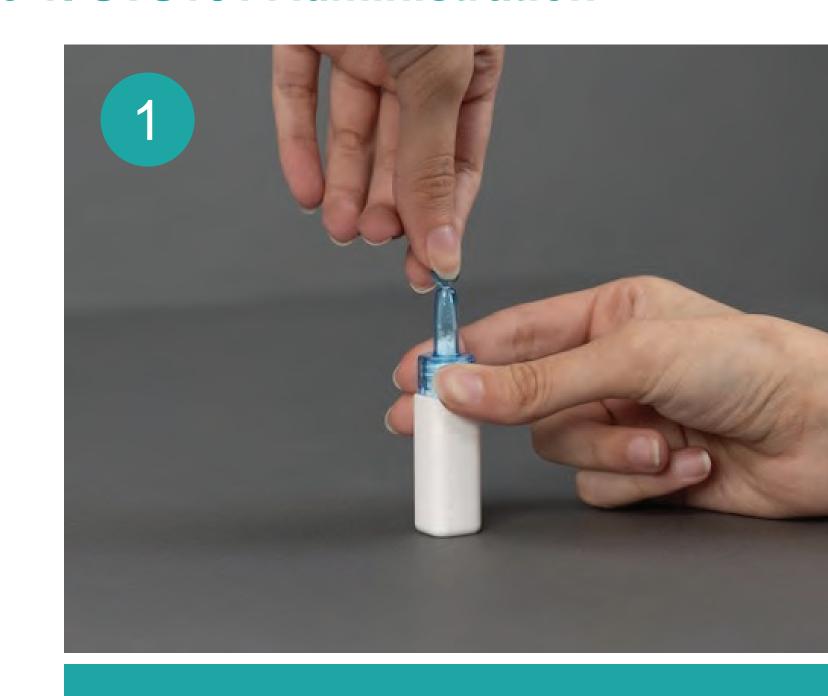
4. Diener HC, et al. *Cephalalgia*. 2019;39(6):687-710.

ICHD-3. Cephalalgia. 2018;38(1):1-211.

6. Ashkenazi A, et al. Cephalalgia. 2007:27(4):325-9.

Tepper S, et al. *Headache*. 2012;52:37-47.

Figure 1. STS101 Administration



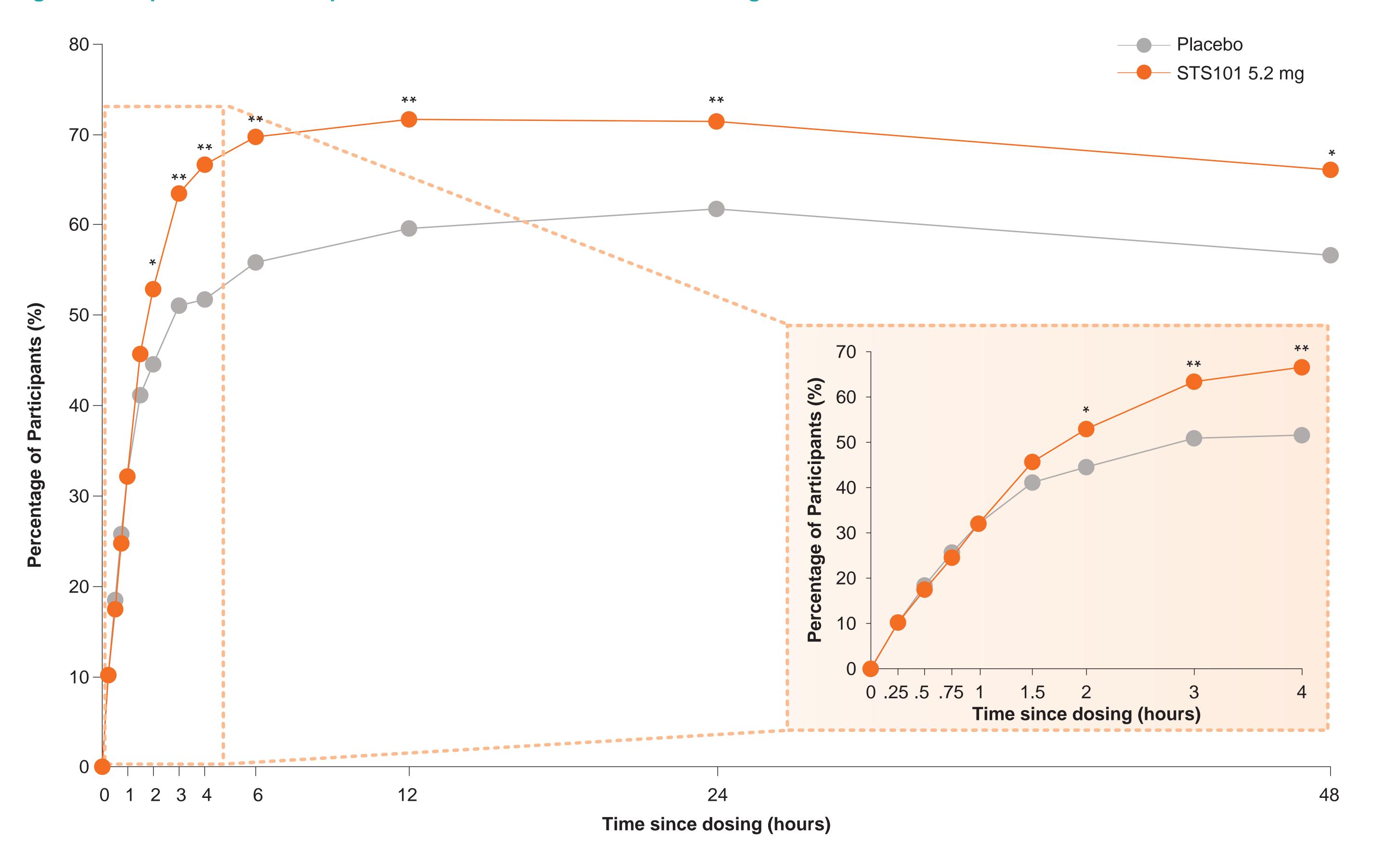
FOLD OFF TAB





SQUEEZE TO DELIVER

Figure 2. Proportion of Participants With Headache Pain Relief Through 48 Hours Post-Dose



Dr. Ailani has been a consultant for Allergan/AbbVie, Amgen, Dr. Reddy, Eli Lilly, Eneura, GlaxoSmithKline, Gore, Ipsen, Linpharma,

Lundbeck, Merz, Neurolief, Pfizer, Satsuma, Scilex, and Theranica; has participated on a scientific advisory or data safety monitoring

and Headache Reports and Medscape; and has received research support (to institution) from Ipsen, Parema, and Satsuma.

Table 1. Demographics and Baseline Characteristics

	STS101 5.2 mg n=716	Placebo n=708
Age, mean (SD)	38.2 (11.4)	38.9 (11.5)
Sex, % male/female	21/79	20/80
Race, %		
White	82.5	81.4
African American	12.0	13.7
Asian	3.5	3.4
Other	1.0	0.7
Years since onset, mean (SD)	16.2 (11.3)	16.9 (1.7)
Monthly migraines or headache days reported before screening, n (%)		
Moderate or severe	4.5 (1.7)	4.5 (1.7)
Headache days	6.9 (2.7)	6.9 (3.0)
Participants on migraine prevention medication at randomization, %	10.2	10.2
Mean HIT-6 score (% of participants with severe impact [>60])	64.2 (88.1)	64.1 (86.4)
Data are for the modified intent-to-treat population. HIT-6, 6-item Headache Impact Test; SD, standard deviation.		

Table 2. Proportion of Participants With Headache Pain Relief Through 48 Hours Post-Dose in Attacks With Allodynia

	STS101 5.2 mg n=716	Placebo n=708	<i>p</i> -value
Allodynia at baseline, n	450	444	
1 hour post-dose responders, n (%)	133 (29.6)	146 (32.9)	0.283
2 hours post-dose responders, n (%)	226 (50.2)	193 (43.5)	< 0.05
3 hours post-dose responders, n (%)	273 (60.7)	227 (51.1)	<0.01
4 hours post-dose responders, n (%)	285 (63.3)	230 (51.8)	<0.001
6 hours post-dose responders, n (%)	306 (68.0)	249 (56.1)	<0.001
12 hours post-dose responders, n (%)	313 (69.6)	280 (63.1)	< 0.05
24 hours post-dose responders, n (%)	314 (69.8)	287 (64.6)	0.102
48 hours post-dose responders, n (%)	294 (65.3)	268 (60.4)	0.124

Table 3. Proportion of Participants With Headache Pain Relief Through 48 Hours Post-Dose in Menstruation-Related Migraine **Attacks**

	STS101 5.2 mg n=716	Placebo n=708	<i>p</i> -value
Menstruation-related migraine at baseline, n	100	106	
1 hour post-dose responders, n (%)	33 (33.0)	29 (27.4)	0.378
2 hours post-dose responders, n (%)	50 (50.0)	42 (39.6)	0.134
3 hours post-dose responders, n (%)	61 (61.0)	48 (45.3)	< 0.05
4 hours post-dose responders, n (%)	67 (67.0)	51 (48.1)	<0.01
6 hours post-dose responders, n (%)	65 (65.0)	55 (51.9)	0.057
12 hours post-dose responders, n (%)	66 (66.0)	64 (60.4)	0.403
24 hours post-dose responders, n (%)	65 (65.0)	62 (58.5)	0.337
48 hours post-dose responders, n (%)	67 (67.0)	59 (55.7)	0.095

Dr. Rapoport is an advisor for AbbVie, Amgen, Biohaven, Cala Health, Satsuma, Teva Pharmaceutical, Theranica, Xoc, and Zosano; is on the speakers bureau of AbbVie, Amgen, Biohaven, Lundbeck, and Teva Pharmaceutical; and is an Editor-in-Chief of Neurology Reviews.

Conclusions

- The results of the SUMMIT study show that STS101 had significant effects versus placebo on headache pain relief starting at 2 through 48 hours post-treatment.
- Single-dose STS101 demonstrated significant effects on headache pain relief versus placebo in difficult-to-treat episodic migraine attacks such as migraine with allodynia, and menstruation-related migraine.



This study and medical writing support were funded by Satsuma Pharmaceuticals. Inc. (Durham, NC, USA). Medical writing support was provided by The Medicine Group, LLC (New Hope, PA, USA) in accordance with Good Publication Practice guidelines.

board for Allergan/AbbVie, Aeon, Eli Lilly, and Linpharma; is an editor, associate editor, or editorial advisory board member of Current Pain Dr. Albrecht was an employee and stockholder of Satsuma Pharmaceuticals at the time of study conduct and is now a consultant for

and stockholder for Satsuma Pharmaceuticals.

Dr. Strom is an employee of Satsuma Pharmaceuticals and was a stockholder at the time of study conduct.