CLE-400: Topical α2-adrenergic agonist being developed as a novel mechanism for treating chronic pruritus associated with Notalgia Paresthetica

Orna Goren, PhD, Products Cluster Leader

Sep 2024

Disclaimer

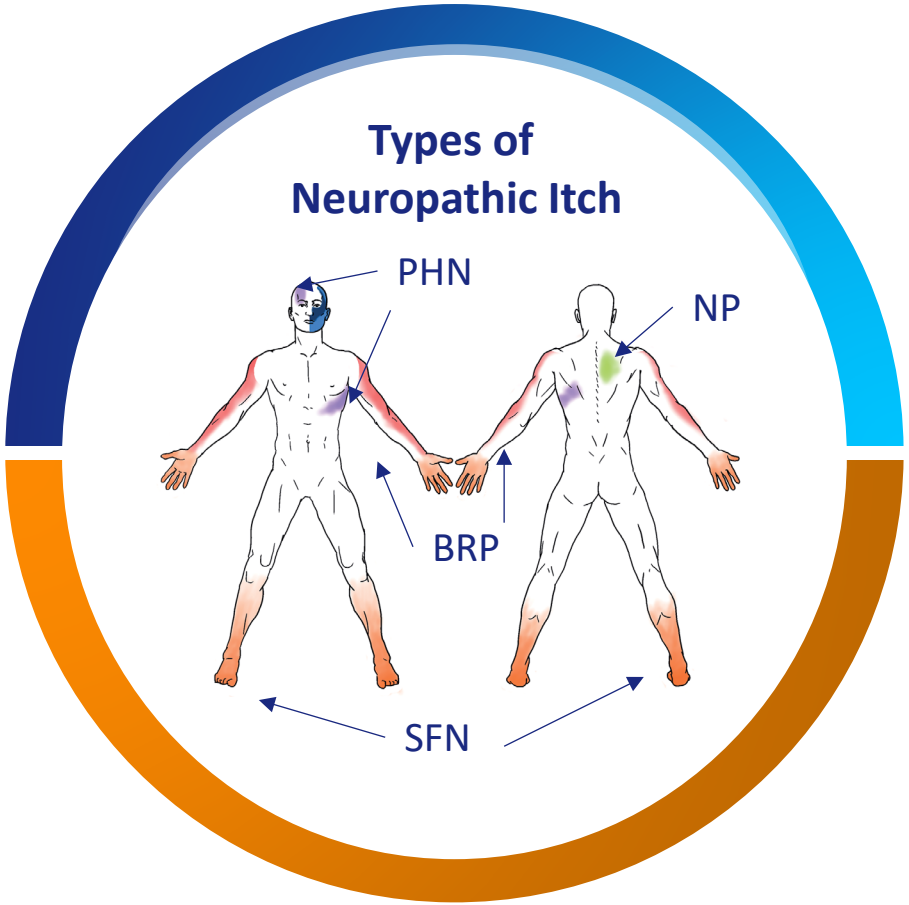
- This presentation includes information about a pharmaceutical product that is currently in clinical development. The data and findings presented are preliminary and subject to further validation through ongoing and future clinical trials. The safety and efficacy of the product have not yet been fully established, and it has not been approved by regulatory authorities for general use.

- The content of this presentation is intended for informational purposes only and should not be construed as medical advice. Healthcare professionals should rely on their own clinical judgment and the most current information available when making treatment decisions.

- Any forward-looking statements regarding the potential benefits, future development, or regulatory approval of the product are based on current expectations and assumptions and are subject to risks and uncertainties. Actual results may differ materially from those expressed or implied in these statements.

Neuropathic itch - an underserved condition

- **Neuropathic itch is caused by neural damage at any point along the afferent sensory pathway of the nervous system**
- **Includes several conditions** such as Notalgia Paresthetica, Brachioradial Pruritus, Post Herpetic Neuralgia, and Small Fiber Neuropathy[1].
- 23-44 million patients in the US suffer from chronic pruritus [2]**. 8-19% suffer from neuropathic itch [2].**
- **No FDA-approved drugs for neuropathic itch,** and limited off-label treatments.



1.Rosen et al. Derm.Clin. 2018;36:213-224
2.Mollanazar, Nicholas K., Savannah Dean Koch, and Gil Yosipovitch. Current Dermatology Reports 4.1 2015: 20-29

BRP=Brachioradial pruritus; NP=Notalgia paresthetica
PHN=Postherpetic neuralgia; SFN= Small fiber neuropathy

Notalgia Paresthetica, a neuropathic itch condition

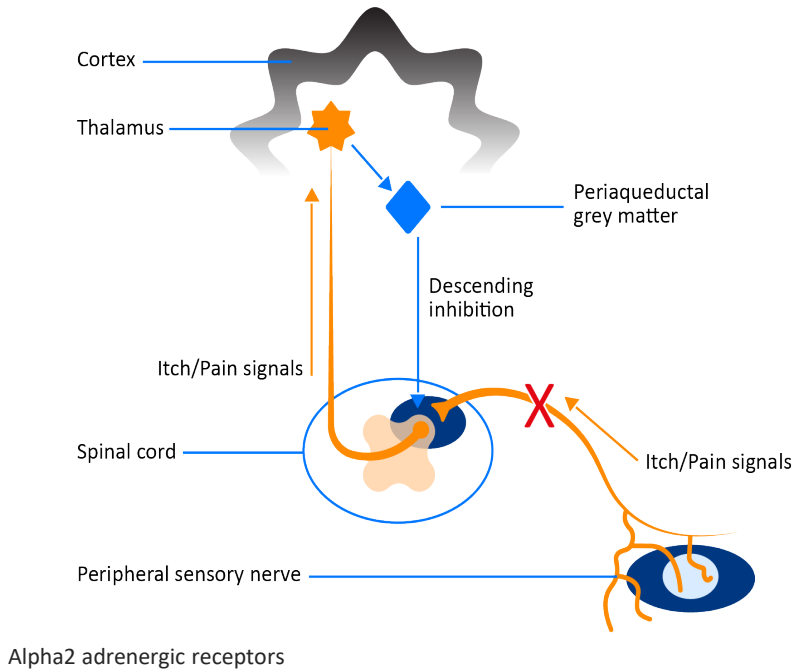
- Notalgia Paresthetica is a chronic neuropathy characterized by localized pruritus and associated dysesthesias, including pain, numbness, and tingling [1]
- Symptoms are typically unilateral and located medial or inferior to the scapula within the middle or upper back
- Believed to be caused by damage to the thoracic nerves (T2-T6) [1]
- May be associated with hyperpigmented skin patches
- Most patients suffer from daily itch [2]
- Estimated prevalence of 2.2M in US, ~600K are treated [3]
- No approved drugs. Topicals are considered as the preferred dosage form

There is a high unmet need for new treatments for Notalgia Paresthetica and neuropathic itch in general

1. Robinson C et al. Clin Pract. 2023 Feb; 13(1): 315–325.
2. Clexio's Market research in the US with 110 dermatologists and according to prescription data

CLE-400*: A topical treatment developed for Notalgia Paresthetica

Pruritus & pain can involve the same type of peripheral sensory neurons
(innervation of C-fibers)



CLE-400 topical application targets α2-adrenergic receptors peripherally

- Detomidine is a potent α2-adrenergic agonist, never approved in human [1]
- Systemically administered α2-adrenergic agonists are approved for analgesia and pain management.
- CLE-400 is a topical gel targeting peripheral α2-adrenergic receptors in the skin. Activation of these receptors could produce **anti pruritic as well as analgesic effects** by inhibiting the excitability and neural signaling from the peripheral nociceptors to the brain.
- Clexio's immunohistochemistry studies demonstrated that α2-adrenergic receptors are expressed in the skin
- Novel proprietary formulation designed to achieve high skin/plasma ratio and Depot effect

*CLE-400 is an investigational new drug that has not been approved for commercial distribution

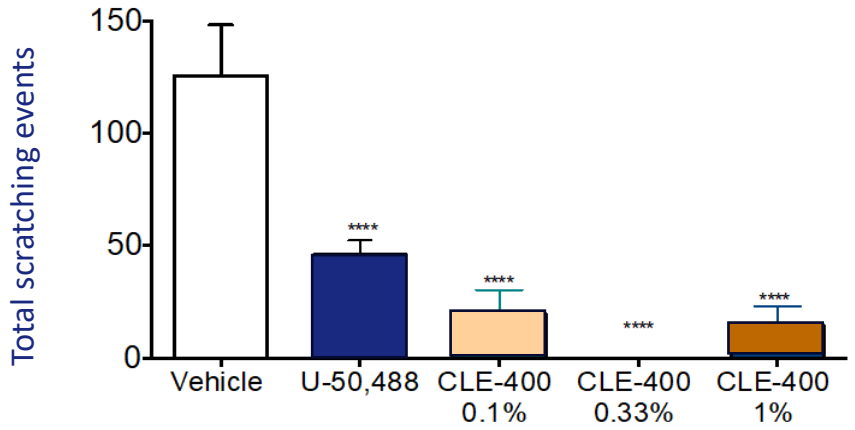
[1] approved for veterinary use for sedation and analgesia (IM, IV, sublingual)

Clexio

Robust effect demonstrated in multiple pharmacological models

Mice Pruritus Model (Chloroquine-induced Itch)

Total over 15 min, 0 min after chloroquine-induced itch MALES and FEMALES



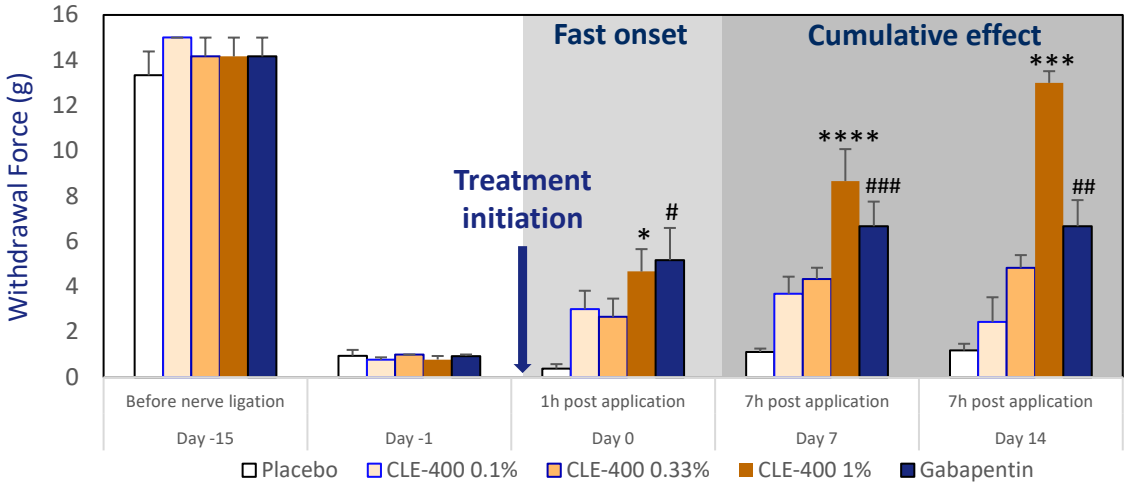
****P < 0.0001 compared to vehicle-treated group. N=7-8 per group.
One-way ANOVA with Fisher's LSD test

- 3 doses CLE-400 administered topically once daily for 5 days (last application 30 min prior to chloroquine challenge)
- Positive control: U-50,488 (kappa opioid receptor agonist) injected IP once 30 min prior to chloroquine challenge

CLE-400 significantly suppressed chloroquine-induced scratching behaviors at all dose levels

Pig Neuropathic Pain Model (Peripheral Neuritis Trauma)

A decreased withdrawal force indicates a higher pain.

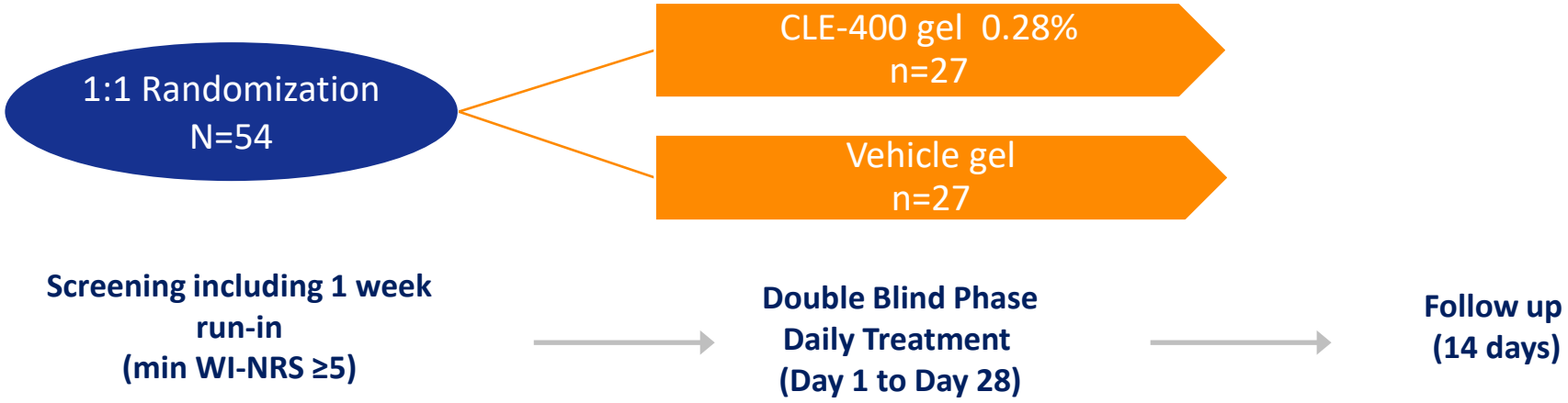


Mean (± SEM) group withdrawal response (g) following von Frey stimulation:
*P<0.05; **P<0.01; ***p<0.001; ****p<0.0001 CLE-400 1% vs. placebo
#P<0.05; ##P<0.01; ###p<0.001; ####p<0.0001 Gabapentin vs. placebo

CLE-400 exhibited a dose-dependent analgesic effect

Ongoing Phase 2 PoC Study in Notalgia Paresthetica

A 4-week randomized, double-blind, vehicle-controlled study to assess the efficacy, safety and tolerability of CLE-400 0.28% gel as treatment of Notalgia Paresthetica, conducted in the US



- Primary Efficacy Endpoint: Percent change from baseline in weekly mean WI-NRS score at Week 4
- First Patient was Dosed in Q1 2024, Top Line Results expected in Q1 2025
- If positive results: move to Phase 3 in NP; in parallel, expand to additional neuropathic itch or pain indications

Thank you

Orna.goren@clexio.com

https://www.Clexio.com