Press Release
GRÜNENTHAL

Grünenthal and Averitas Pharma announce completion of recruitment for Phase III clinical trial with QUTENZA® in post-surgical neuropathic pain

- The Phase III trial AV001 aims to evaluate QUTENZA® in post-surgical neuropathic pain (PSNP), a debilitating complication of surgery occurring after approximately 10 percent of all surgical procedures[1], thus affecting more than 3 million people with surgical procedures per year in the U.S.[2]
- QUTENZA® is a topical system, non-systemic, non-opioid pain treatment that is currently approved in the US for the treatment of neuropathic pain associated with postherpetic neuralgia (PHN) and neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults.
- Topline results are expected in Q4 2025 and Averitas Pharma aims to submit a supplemental new drug application (sNDA) for a US label extension in 2026, subject to positive data.

Aachen, Germany, & Morristown, N.J., 7 November 2024 – Grünenthal announced today that its U.S. subsidiary, Averitas Pharma, Inc., has completed recruitment for the Phase III clinical trial AV001. The trial investigates the efficacy, safety and tolerability of QUTENZA® (capsaicin) 8% topical system in post-surgical neuropathic pain (PSNP) and if successful could support an extension of the U.S. label.

“Patients who undergo surgery and end up developing post-surgical neuropathic pain, may experience debilitating complications that often are not treated appropriately,” says Lizandra Marcondes, M.D., PhD, Senior VP Medical Affairs & Drug Safety US, Averitas Pharma. “We believe QUTENZA® may be a clinically meaningful treatment option that could address the unmet needs of many patients in the United States who suffer from Post-surgical neuropathic pain and may not be satisfied with available oral, systemically acting medicines. We look forward to completing the Clinical Trial with the goal to file a supplemental new drug application to the U.S. Food and Drug Administration (FDA) in 2026, assuming positive data.”

AV001 is a randomized, double-blind 42 week trial including 410 patients who have been suffering from moderate to severe PSNP for at least six months. The primary endpoint of the trial is a reduction in the average pain intensity after 12 weeks compared to baseline. In addition, the trial assesses other outcomes including reduction in the average pain intensity after 42 weeks, progressive response over time with repeated treatment, reduction of the treatment area over

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[1] Rosenberger DC, Pogatzki-Zahn EM. Chronic post-surgical pain - update on incidence, risk factors and preventive treatment options. BJA Educ. 2022 May;22(5):190-196. doi: 10.1016/j.bjae.2021.11.008. Epub 2022 Feb 24.

[2] https://www.cdc.gov/nchs/fastats/inpatient-surgery.htm (Accessed November 2024)

several applications, and quality of life outcomes such as sleep interference, physical activity, anxiety, and depression. When completed, AV001 will be the first blinded randomized controlled trial in post-surgical neuropathic pain that evaluates the long term treatment effects of a topical neuropathic pain treatment.

“The completion of enrollment is an exciting milestone. With our current indications, adults with painful diabetic peripheral neuropathy of the feet and postherpetic neuralgia, we have advanced the trajectory of QUTENZA® in the U.S. by expanding access to a much-needed non-opioid therapy option for a large, underserved patient population,” adds Marv Kelly, President Averitas Pharma. “By adding post-surgical neuropathic pain to the U.S. label if results are positive, we would have the potential to fill an unmet treatment need for additional patients in pain.”

When Grünenthal acquired the US-rights for Qutenza® in 2018, the US-label comprised the treatment of neuropathic pain associated with postherpetic neuralgia. Since then, Grünenthal re-launched the product and significantly increased patients’ access to Qutenza®. In 2020, the U.S. FDA approved the product for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults. With AV001, Grünenthal and Averitas hope to include another major indication in the field of peripheral neuropathic pain in the U.S. label. Topline results are anticipated in Q4 2025 and, assuming positive data, Averitas Pharma aims to submit a supplemental new drug application (sNDA) in 2026.

About QUTENZA

QUTENZA (capsaicin) 8% topical system is approved in the US for the treatment of neuropathic pain associated with postherpetic neuralgia, and for the treatment of neuropathic pain associated with diabetic peripheral neuropathy (DPN) of the feet in adults. Important U.S. safety information is available below and at www.qutenza.com.

In Europe, QUTENZA is indicated for the treatment of peripheral neuropathic pain in adults either alone or in combination with other medicinal products for the treatment of pain. For further information please visit www.grunenthalhealth.com.

About post-surgical neuropathic pain

Post-surgical neuropathic pain (PSNP) is defined as chronic pain that develops after a surgical procedure and persists beyond the healing process, i.e., at least three months after the surgery. The pain is either localized to the surgical field or area of injury, projected to the innervation territory of a nerve situated in this area, or referred to a dermatome (after surgery/injury to deep somatic or visceral tissues).[3] It is identified by symptoms of neuropathic nerve pain such as burning, stabbing or shooting pain, numbness, and changes to physical sensation or sensitivity to temperature or touch. PSNP occurs after approximately 10 percent of all surgical procedures[1], thus affecting more than 3 million people with surgical procedures per year in the U.S.[2]

About Averitas Pharma, Inc.

Averitas Pharma is a specialty pharmaceutical company dedicated to delivering innovative, effective, non-opioid pain management options to patients in the U.S. The company was formed in 2018 as a subsidiary

[3] ICD 11 - https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/985186256

of GRT U.S. Holding, Inc. and member of the Grünenthal Group. For more information, visit www.averitaspharma.com.

Follow us on LinkedIn: https://www.linkedin.com/company/averitaspharma/

About Grünenthal

Grünenthal is a global leader in pain management and related diseases. As a science-based, fully integrated pharmaceutical company, we have a long track record of bringing innovative treatments and state-of-the-art technologies to patients worldwide. Our purpose is to change lives for the better – and innovation is our passion. We are focusing all our activities and efforts on working towards our vision of a World Free of Pain.

Grünenthal is headquartered in Aachen, Germany, and has affiliates in 27 countries across Europe, Latin America, and the U.S. Our products are available in approx. 100 countries. In 2023, Grünenthal employed around 4,400 people and achieved revenues of €1.8 billion.

More information: www.grunenthal.com

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IMPORTANT US-SAFETY INFORMATION

Do not dispense QUTENZA to patients for self-administration or handling. Use only on dry, unbroken skin. Only physicians or healthcare professionals are to administer and handle QUTENZA, following the procedures in the label.

Warnings and Precautions

- **Severe Irritation:** Whether applied directly or transferred accidentally from other surfaces, capsaicin can cause severe irritation of eyes, mucous membranes, respiratory tract, and skin to the healthcare professional, patients, and others. Do not use near eyes or mucous membranes, including face and scalp. Take protective measures, including wearing nitrile gloves and not touching items or surfaces that the patient may also touch. Flush irritated mucous membranes or eyes with water

and provide supportive medical care for shortness of breath. Remove affected individuals from the vicinity of QUTENZA. Do not re-expose affected individuals to QUTENZA if respiratory irritation worsens or does not resolve. If skin not intended to be treated comes into contact with QUTENZA, apply Cleansing Gel and then wipe off with dry gauze. Thoroughly clean all areas and items exposed to QUTENZA and dispose of properly. Because aerosolization of capsaicin can occur with rapid removal, administer QUTENZA in a well-ventilated area, and remove gently and slowly, rolling the adhesive side inward.

- **Application-Associated Pain:** Patients may experience substantial procedural pain and burning upon application and following removal of QUTENZA. Prepare to treat acute pain during and following application with local cooling and/or appropriate analgesic medication.
- **Increase in Blood Pressure:** Transient increases in blood pressure may occur with QUTENZA treatment. Monitor blood pressure during and following treatment procedure and provide support for treatment-related pain. Patients with unstable or poorly controlled hypertension, or a recent history of cardiovascular or cerebrovascular events, may be at an increased risk of adverse cardiovascular effects. Consider these factors prior to initiating QUTENZA treatment.
- **Sensory Function:** Reductions in sensory function (generally minor and temporary) have been reported following administration of QUTENZA. Assess for signs of sensory deterioration or loss prior to each application of QUTENZA. If sensory loss occurs, treatment should be reconsidered.
- **Severe Application Site Burns:** Full-thickness (third-degree) and deep partial-thickness (second-degree) burns have been reported following administration of QUTENZA. Cases of full-thickness (third-degree) burns, requiring hospitalization and skin grafting have been reported in patients who received QUTENZA for an unapproved indication and/or frequency of dosing at an application site where there had been prior skin trauma. Ensure that dosage and administration recommendations are followed.

Adverse Reactions

The most common adverse reactions (≥5% and > control group) in all controlled clinical trials are application site erythema, application site pain, and application site pruritus.

To report SUSPECTED ADVERSE REACTIONS, contact Averitas Pharma, Inc. at 1-877-900-6479 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information.