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Novaremed Announces Completion of Enrollment in NIH-sponsored Phase 2b Study with Non-opioid NRD.E1 for the Treatment of Chronic Pain Associated with Diabetic Peripheral Neuropathy

- *Last patient first visit (LPFV) marks completion of enrollment of 127 adult and elderly patients in the randomized, placebo-controlled trial -- topline data is expected in Q4 2025*
- *This study builds on Phase 2a proof-of-concept results, which showed a clinically meaningful placebo-corrected reduction in pain and favorable tolerability of NRD.E1 in patients with painful diabetic peripheral neuropathy (PDPN) [1]*

Basel, Switzerland, 6 May 2025 – Novaremed AG, a privately held clinical-stage biopharmaceutical company, announces that recruitment is completed in the National Institutes of Health (NIH) -sponsored Phase 2b EN21-01 trial (ClinicalTrials.gov identifier NCT05480228). The study evaluates Novaremed's non-opioid investigational drug NRD.E1 for the treatment of chronic pain associated with diabetic peripheral neuropathy, and is funded by the NIH Helping to End Addiction Long-term Initiative, or NIH HEAL Initiative. Topline Phase 2b data readout is expected in Q4 2025.

The Phase 2b study is a 12-week, multicenter, randomized, double-blind, placebo-controlled clinical trial with the primary objective to demonstrate that a once daily dose of NRD.E1 80 mg is superior to placebo in relieving chronic pain among patients with painful diabetic peripheral neuropathy. The study will further assess safety, tolerability, pharmacokinetics, and the compound's impact on sleep and quality of life. Study completion, with the last patient's last visit (LPLV), is anticipated in Q3 2025 and the topline results are expected in Q4 2025.

Jessica Robinson-Papp, MD, MS, FAAN, Lead Primary Investigator and Professor at the Icahn School of Medicine at Mount Sinai (New York, USA), commented: "Completing the study enrollment is a major milestone for us. Achieving it was a deeply collaborative effort including multiple academic medical centers, the NIH, and the Novaremed team. It wasn't always easy, but the goal of developing desperately needed new non-opioid pain therapies was an ongoing source of inspiration. We're especially grateful to all the people with painful diabetic peripheral neuropathy who made this study possible with their participation."

"We are proud and grateful to mark this important milestone alongside the study team within the HEAL Early Phase Pain Investigation Clinical Network and the NIH," said **Camilla Mittelholzer, PhD, CSO and Head of R&D at Novaremed**. "Currently, approved medications for painful diabetic peripheral neuropathy provide inadequate pain relief and are associated with many intolerable side effects. Completing enrollment in this study brings us closer to Phase 2b study results, which hopefully will support the continued development of NRD.E1 as a novel, non-opioid treatment option for patients experiencing chronic pain."

About NRD.E1

NRD.E1 (or NRD135S.E1), an orally active small molecule with a novel mechanism of action, is being developed to treat chronic pain associated with diabetic peripheral neuropathy. The mechanism of action of NRD.E1 is different from that of approved pain therapies as it does not bind to opioid receptors or other receptors associated with opioid mode of action.

Completed clinical studies with NRD.E1 include Phase 1 studies and one Phase 2a proof-of-concept study [1, 2]. NRD.E1 was well tolerated as single dose up to 1200 mg and repeated doses of 300 mg/day for five consecutive days. The studies revealed dose-dependent absorption, small increased exposure to NRD.E1 at peak when administered with food and no relevant accumulation after oral administration. The Phase 2a study was a randomized, double-blind, placebo-controlled, dose-finding, proof-of-concept study in 88 patients with moderate to severe PDPN. The study investigated NRD.E1 at 10, 40, or 150 mg/day or placebo over a 3-week treatment period and showed clinically relevant placebo-corrected pain reductions at 40 and 150 mg/day. NRD.E1 was selected by the NIH as the only oral agent to be included in the EPPIC-Net master protocol to assess treatments for PDPN. The US FDA granted Fast Track Designation to NRD.E1 for the treatment of PDPN.

References:

[1] Tiecke E., Rainisio M., Eisenberg E., Wainstein J., Kaplan E., Silverberg M., Hochman L., Mangialaio S. (2022) NRD.E1, an innovative non-opioid therapy for painful diabetic peripheral neuropathy – a randomized proof of concept study. *European Journal of Pain* (https://onlinelibrary.wiley.com/doi/10.1002/ejp.1989).

[2] Tiecke E., Rainisio M., Guentert T., Müller S., Hochman L., Kaplan E., Mangialaio S. (2022). First-in-human single-ascending-dose, multiple-dose and food interaction studies of NRD.E1, an innovative non-opioid therapy for painful diabetic peripheral neuropathy. *Clinical Pharmacology in Drug Development (CPDD)* (https://accp1.onlinelibrary.wiley.com/doi/10.1002/cpdd.1103).

About the NIH HEAL Initiative

The *NIH HEAL Initiative* is an NIH-wide effort to speed scientific solutions to the overdose epidemic, including opioid and stimulant use disorders, and the crisis of chronic pain. HEAL programs include those focused on identifying, developing, and testing new non-addictive pain therapies. The *EPPIC-Net (Early Phase Pain Investigation Clinical Network)* is part of the NIH HEAL Initiative and seeks to enhance the treatment of acute and chronic pain and reduce reliance on opioids by accelerating early-phase clinical trials of non-addictive treatments for pain.

For more information: https://heal.nih.gov and https://heal.nih.gov/research/clinical-research/eppic-net

About painful diabetic peripheral neuropathy

Peripheral nerve injury from various etiologies may ultimately result in chronic and severe intractable neuropathic pain. PDPN is a frequent complication of diabetes and represents the most common form of neuropathic pain with a high unmet medical need. Worldwide, two-thirds or an estimated 8.1 million diabetes patients with PDPN requiring treatment do not obtain sufficient pain relief with current therapies. Many of the currently available products for the treatment of chronic neuropathic pain have limited efficacy and are often not well tolerated. The increasing prevalence of diabetes as well as the limitations of the available therapies make the prevention and treatment of PDPN a condition of high unmet medical need.

About Novaremed

Novaremed AG, a privately held clinical-stage biopharmaceutical company, is developing a pipeline of innovative medications for chronic pain management to address the high unmet medical need for better pain relief and as an alternative to opioids. Its lead product is NRD.E1, an orally active non-opioid small molecule with a novel mechanism of action, has FDA Fast Track Designation and is being studied in an NIH-sponsored Phase 2b clinical trial for the treatment of PDPN as part of the NIH HEAL Initiative. Novaremed aims to address high unmet patient and societal needs for better relief from pain and peripheral neuropathy associated with diabetes by providing novel, non-opioid chronic pain therapies and countering overreliance on addictive treatments. For more information: www.novaremed.com.

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