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Novaremed Expands its Pipeline of Non-opioid Treatment Candidates for Chronic Pain Indications Through Acquisition of Metys Pharmaceuticals

- *Acquisition of Metys broadens Novaremed's pipeline focused on novel, non-opioid development candidates for chronic pain indications with the addition of two complementary development projects*
- *Expansion of pipeline allows Novaremed to target a wider segment of neuropathic pain indications, adding chemotherapy-induced peripheral neuropathy (CIPN) to its current focus on painful diabetic peripheral neuropathy (PDPN)*
- *Transaction significantly advances Novaremed's strategy to emerge as a leading Company in the non-opioid pain management space*
- *Election of Andrew J. Oakley to the Board of Directors of Novaremed strengthens leadership team*

Basel, Switzerland, September 7, 2021 – Novaremed AG, a privately held clinical-stage biopharmaceutical company, announces the acquisition of Metys Pharmaceuticals AG (Metys), including all of its development programs, in an all-share transaction. The acquisition broadens Novaremed's existing pipeline by adding both clinical and preclinical development projects based on an innovative approach for non-opioid chronic pain treatment, the Company's focus area. Moreover, it enables Novaremed to target a wider spectrum of neuropathic pain indications, potentially also addressing broader applications by including prevention in addition to the treatment of pain. On the corporate side, Novaremed is strengthening its leadership team with a new board member, Andrew J. Oakley.

"The acquisition of Metys perfectly fits our strategy of pioneering the development of non-opioid pain treatments, aiming to deliver effective and well tolerated medications to patients while simultaneously addressing the urgent need for non-addictive treatments. I am delighted that industry expert Andrew Oakley is joining Novaremed's Board of Directors and look forward to his support in the pursuit of our ambitious goals," said **Isaac Kobrin, Executive Chairman of the Board of Novaremed**. "Our key objectives for the coming months are threefold: we plan to initiate the Phase 2b study with our promising lead candidate NDR.E1 for the treatment of painful diabetic peripheral neuropathy (PDPN), advance our new pipeline candidates from the Metys acquisition and, in parallel, will approach private and institutional investors to raise additional capital to support our pipeline which bears potential to provide next generation pain therapies."

"I am pleased and excited about the acquisition of Metys by Novaremed as it represents a validation of our unique approach to the management of the progressive symptoms of peripheral sensory neuropathy. We have a clear pathway for our Phase 2 candidate MP-101 for the management of chemotherapy-induced painful symptoms of peripheral neuropathy, and our preclinical candidate MP-103 is being prepared for Phase 1," said **Michael Scherz, PhD, founder and Chief Executive Officer of Metys Pharmaceuticals**. "We share the commitment to provide novel therapies to prevent, reduce or alleviate the burden of chronic

pain and improve patient's quality of life, thereby addressing an urgent unmet medical need and ultimately also reducing overreliance on opioids. Integrating Metys' technologies and pipeline into Novaremed represents the best way forward towards accomplishing these goals."

Broader pipeline of non-opioid development candidates

Going forward, Novaremed's pipeline to address neuropathic pain will focus on three non-opioid development projects with entirely different modes of action:

NRD.E1, an orally active small molecule with a novel mechanism of action and patent protection until 2040, acts as a Lyn kinase modulator and is the Company's lead compound being developed to treat PDPN. Novaremed successfully completed a double-blind, placebo-controlled Phase 2a dose-finding proof-of-concept study in which NRD.E1 showed a clinically relevant reduction in patient-reported pain (measured as an improvement in mean neuropathic pain score) and was very well tolerated at all doses tested. Moreover, the results suggested similar or greater pain relief, and better tolerability than reported for standard approved therapies. On the basis of these positive results, Novaremed is ready to proceed with a 12-week, double-blind, placebo-controlled Phase 2b study in patients with moderate to severe PDPN in the US, where it has an open IND and Fast Track Designation from the FDA.

MP-101, a Phase 2 clinical candidate, is an orally available modulator of glutamate signaling. It works by preventing or reversing the ramped-up signaling that occurs in the spine and brain as a result of damaged peripheral nerves. MP-101 is a patented non-racemic mixture of the dimiracetam enantiomers with patent protection until 2039. In previous Phase 1 and Phase 2 clinical studies, in a total of 176 human subjects, a benign safety and tolerability profile comparable to placebo was noted for dimiracetam, and no signs or symptoms of sedation, dependence or withdrawal symptoms emerged. Based on pre-clinical proof of concept trials of chemotherapy-related neuropathy and pre-IND discussions with the FDA, MP-101 is being developed for the management of chemotherapy-induced neuropathy and neuropathic pain. The Phase 2 trial is expected to start in the first quarter of 2023.

MP-103, a glutamate signaling modulator orally active in diverse rodent models for prevention and treatment of peripheral nerve injury symptoms, is set to start of Phase 1 clinical development in the first half of 2023.

Enlarged pipeline addresses a high unmet medical need with a wider indication focus

With its three development candidates, Novaremed seeks to address a wider spectrum of neuropathic pain, including the most common forms of painful diabetic peripheral neuropathy (PDPN) and chemotherapy-induced peripheral neuropathy (CIPN). Sensory symptoms of peripheral neuropathy, including neuropathic pain are highly prevalent conditions, and their incidence is rising as both diabetes and cancer become more frequent. 1 in 5 diabetes patients develops PDPN and half of them require treatment due to the severity of symptoms. In cancer, 4 in 5 patients undergoing neurotoxic chemotherapy develop CIPN, highlighting the necessity for early intervention or prevention. Novel treatments for these often debilitating and intractable chronic pain conditions are urgently needed due to limited efficacy and poor tolerability of many standard of care therapies. Importantly, Novaremed's non-opioid pipeline also aims to address the high medical need for treatments without a risk of physical dependence and abuse, an inherent danger with commonly prescribed opioid-based therapies. Novaremed sees potential for its pipeline candidates beyond PDPN and CIPN and intends to evaluate opportunities in additional neuropathic pain indications, thereby further widening its initial indication focus.

Strengthening the leadership team

Andrew J. Oakley, Board member of Metys, will join the Board of Directors of Novaremed. He is an experienced pharmaceutical and biotech industry professional and currently serves as Chief Financial Officer of Autolus Therapeutics (NASDAQ: AUTL). Previously, he held CFO positions at listed pharmaceutical companies Sosei Group (TSE:4565), Vectura Group plc (LSE: VEC) and Actelion Ltd, where he led the finance function for over a decade. Before joining Actelion, Andrew held senior finance positions for Accenture as well as executive positions in major multinational building material companies. Andrew holds a Bachelor of Economics Degree from Macquarie University and an MBA from London Business School and has been a Member of the Australian Institute of Chartered Accountants since 1987.

About peripheral neuropathy and associated neuropathic pain

Peripheral nerve injury from various etiologies may ultimately result in chronic and severe intractable neuropathic pain. Painful diabetic peripheral neuropathy (PDPN) and chemotherapy-induced peripheral neuropathy (CIPN) are frequent complications of diabetes and cancer treatment and represent the most common forms of neuropathic pain with a high medical need. Worldwide, two-thirds or an estimated 8.1 million diabetes patients with PDPN requiring treatment do not obtain substantial pain relief with current therapies. Over 80% or about 3.1 million cancer patients receiving neurotoxic chemotherapy develop CIPN, a leading cause for therapy reduction and/or discontinuation. Many of the currently available drugs for the treatment of chronic neuropathic pain have limited efficacy, are often not well tolerated and bear a danger of addiction. The increasing prevalence of diabetes and cancer as well as the limitations of the available therapies make the prevention and treatment of chronic neuropathic pain a condition of high unmet medical need.

About NRD.E1

NRD.E1 (or NRD135S.E1), a Lyn kinase modulator, is a new orally available chemical entity being developed for the treatment of PDPN. The mechanism of action of NRD.E1 is different to that of approved pain therapies as it does not bind to or interact with receptors associated with pain nor does it bind to opioid receptors.

Completed clinical studies with NRD.E1 include three Phase 1 studies (single and multiple ascending dose studies and food-effect study). The Phase 2a proof-of-concept study (ClinicalTrials.gov identifier: NCT02345291) was a 3-week, dose-finding, placebo-controlled, randomized, multi-center study in 88 patients with moderate to severe PDPN and compared three doses (10, 40 and 150 mg/day) of NRD.E1 to placebo. Results showed a clinically relevant, dose-related pain reduction and a favorable tolerability profile of NRD.E1 at all tested doses.

Novaremed has an open IND for NRD.E1 to conduct a 12-week, placebo-controlled Phase 2b study to assess efficacy, safety and tolerability of NRD.E1 in 120 patients with moderate to severe PDPN in the US. The primary endpoint is the change from the baseline to Week 12 in the weekly mean of daily pain, as measured by an 11-point Numeric Rating Scale. The secondary objectives of the study are to evaluate the pharmacokinetics, safety and tolerability of NRD.E1, confirm the absence of withdrawal symptoms after abrupt drug interruption, and assess the effect of NRD.E1 on insomnia and quality-of-life indicators.

In December 2020, the U.S. Food and Drug Administration (FDA) granted Fast Track Designation to NRD.E1 for the treatment of PDPN.

About Novaremed

Novaremed AG, a privately held clinical-stage biopharmaceutical company, is innovating chronic pain management through the development of effective and safe treatment options 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 IND-approval to proceed with a Phase 2b clinical trial for the treatment of painful diabetic peripheral neuropathy (PDPN). The earlier stage pipeline addressing chronic pain includes the development candidates MP-101 (Phase 2 stage), targeting prevention and treatment of chemotherapy-induced peripheral neuropathy (CIPN), and MP-103 (preclinical stage). Novaremed's clinical development portfolio aims to satisfy high medical patient needs and societal demands by alleviating the burden of pain associated with diabetes and cancer for patients and countering overreliance on addictive treatments. Novaremed Ltd (Israel) and Metys Pharmaceuticals AG (Switzerland) are fully-owned subsidiaries of Novaremed AG, domiciled in Basel (Switzerland). For more information: www.novaremed.com.

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