Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics Reports Two Publications of Positive Data on Nexodyn® AOS for Hard-to-Heal Ulcers

A Prospective Series on Wound Bed Preparation with Nexodyn® AOS and Standard of Care and a 32-Week Follow-Up Study Published in the Peer Reviewed Journal of Wound Care

Geneva, Switzerland, October 20, 2021 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF) ("**Relief**"), a biopharmaceutical company seeking to provide patients therapeutic relief from serious diseases with high unmet need, today announced that its wholly owned subsidiary, APR Applied Pharma Research SA ("**APR**"), reported two papers published in the peer reviewed *Journal of Wound Care*, concluding that the company's Nexodyn® acid-oxidizing solution (AOS), developed with APR's proprietary Tehclo® technology, may represent a valuable therapeutic addition to standard of care (SOC) for the management of hard-to-heal ulcers requiring long periods of treatment. The data also confirmed the safety of Nexodyn® AOS.

Conducted by Elia Ricci, M.D., Director of the Difficult Wound Healing Unit, St. Luca Clinic, Department of Surgery A, Pecetto Torinese (TO), Piedmont, Italy, the prospective case series evaluated the clinical impact of Nexodyn® AOS in addition to SOC. Between February 2015 and February 2017, a total of 60 patients with hard-to-heal ulcers of various etiologies took part in the study. Patients were treated for 70 days with Nexodyn® AOS and the usual SOC wound dressings. The follow-up study, also conducted by Dr. Ricci, included a subset of 31 patients (51.7%) whose wounds had not fully healed by day 70, who opted to continue with treatment for another 22 weeks (for a total treatment time of 32 weeks).

By day 70, 68.3% of wounds had healed or improved, and a significant mean wound size reduction of 21% from baseline was observed ($p<0.001$), despite a mean baseline wound duration of 20.6 months. 90% of patients were able to control signs of infection with a significant reduction versus baseline. Additionally, Bates–Jensen and wound bed preparation (WBP) scores improved with a significant increase of patients with 100% granulation tissue, and pain scores fell significantly over time. Overall, use of Nexodyn® AOS plus SOC allow a decreased number of dressing changes. In the follow-up study, by week 32, 35.5% (n=11) of wounds healed completely and 83.9% showed improvement. Additionally, all wounds were free of infection and colonization, the WBP score improved (100% A1–A2 at T196), and pain scores fell. This follow-up evaluation, coupled with the primary study, suggests that Nexodyn® AOS may represent a valuable and safe therapeutic option in addition to SOC for the management of hard-to-heal ulcers for long periods of treatment.

"The publication of additional data provides further evidence of the effectiveness of Nexodyn® AOS, developed with our proprietary, globally patented Tehclo® nanotechnology platform, in addition to SOC – in particular, its ability to reactivate the healing process in hard-to-heal lesions," stated Paolo Galfetti, Chief Executive Officer of APR and President of Relief Europe. "Also of note, the study showed that Nexodyn® AOS, with its antimicrobial properties, can create an optimal microenvironment, reducing the bioburden, modulating inflammation by inactivating matrix metalloproteinases and increasing oxygenation. Additionally, clinical benefit was observed even in wounds with less favorable initial conditions, such as a large area and/or depth or long duration, adding further evidence that Nexodyn® AOS is an important treatment for hard-to-treat wounds."

Raghuram (Ram) Selvaraju, Chairman of the Board of Relief added, "These results reinforce the importance of Nexodyn® AOS as a critical wound healing treatment and provide additional real-world evidence to support our belief that an adaptation of Nexodyn® AOS may also become an effective therapeutic option for wound healing in patients suffering from epidermolysis bullosa (EB)."

About Nexodyn® Acid-Oxidizing Solution (AOS)

Nexodyn® Acid-Oxidizing Solution (AOS) is a Tehclo®-based product proven to restart wound healing in stalled wounds by creating the ideal microenvironment to sustain the physiological healing process. A wealth of evidence and real-world experience consistently show accelerated closure with reduced infection rates and less wound-associated pain.

Nexodyn® AOS is a solution with three main features: highly pure and stabilized hypochlorous acid (HClO >95% of free chlorine species), acidic pH (2.5 – 3.0) and high Reduction-Oxidation Potential (ORP 1.000 – 1.200 mV). The product is a sprayable solution with ancillary antimicrobial properties intended for use in the debridement, irrigation, cleansing and moistening of acute and chronic wounds (e.g., diabetic foot ulcers, pressure ulcers, and vascular ulcers), post-surgical wounds, burns and other lesions. The product is certified in the European Union as a Class III medical device.

ABOUT RELIEF

Relief focuses primarily on clinical-stage programs based on molecules with a history of clinical testing and use in human patients or a strong scientific rationale. Relief's lead drug candidate, RLF-100™ (aviptadil), a synthetic form of Vasoactive Intestinal Peptide (VIP), is in late-stage clinical testing in the U.S. for the treatment of respiratory deficiency due to COVID-19. As part of its pipeline diversification strategy, in March 2021, Relief entered into a Collaboration and License Agreement with Acer Therapeutics for the worldwide development and commercialization of ACER-001. ACER-001 is a taste-masked and immediate release proprietary powder formulation of sodium phenylbutyrate (NaPB) for the treatment of Urea Cycle Disorders and Maple Syrup Urine Disease. In addition, Relief's recently completed acquisitions of APR

Applied Pharma Research SA and AdVita Lifescience GmbH bring a diverse pipeline of marketed and development-stage programs.

RELIEF THERAPEUTICS Holding SA is listed on the SIX Swiss Exchange under the symbol RLF and quoted in the U.S. on OTCQB under the symbol RLFTF. For more information, visit www.relieftherapeutics.com. Follow us on **LinkedIn**.

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