Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics Reports the Successful Conclusion of the Patent Examination Procedure for the Patent Application Entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis"

Geneva, Switzerland, December 28, 2021 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF, RLFTY) ("**Relief**"), a biopharmaceutical company seeking to provide patients therapeutic relief from serious diseases with high unmet need, reported today that the Swiss Patent Office IPI has announced that it expects to conclude the patent application procedure by January 24, 2022 and to issue the patent entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis," as applied for by Relief's subsidiary, AdVita Lifescience GmbH, in 2020. The patent will be formally issued, at the earliest, one month after the conclusion of the patent examination procedure.

"The pending grant of this Swiss patent for the inhaled version of RLF-100™ (aviptadil) represents another important milestone for the Company and further solidifies our growing intellectual property portfolio," stated Raghuram (Ram) Selvaraju, Chairman of Relief. "The potential benefits of this inhaled formulation of RLF-100™ are intriguing and a number of studies to assess its advantages remain ongoing, including a clinical program in Europe as well as the National Institutes of Health ("NIH")-sponsored ACTIVE-3b/TESICO study and the I-SPY trial sponsored by Quantum Leap."

Immune checkpoint inhibitor therapy has become a new therapeutic option for several types of cancer, but immune related negative adverse events can limit their use. Outside of clinical studies, pneumonitis develops in as many as 10% to 20% of patients who are treated with immune checkpoint inhibitors, a complication that leads to discontinuation of treatment and to immunosuppressive therapy. Moreover, these patients suffer from recurrent pneumonitis even after immune checkpoint inhibitor treatment discontinuation and receipt of glucocorticoid treatment, according to current guidelines. Respiratory symptoms are demonstrated on computed tomography showing widespread consolidations and are denoted on Quality of Life Questionnaires. Patients experience severe lymphocytosis with a decreased number of regulatory T cells. As a result, there is an urgent need for an effective, safe treatment of checkpoint inhibitor–induced pneumonitis.

The unexpected finding that the synthetic form of Vasoactive Intestinal Peptide (aviptadil) administered via inhalation was well tolerated and led to dampening of alveolar inflammation, radiological and clinical improvement of pneumonitis resulting from a checkpoint inhibitor therapy for melanoma, was the basis for this issued Patent.

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Inhalation is the preferred route of aviptadil administration in that it, (1) acts quickly, minimizing potentially undesired negative side effects (2) avoids the hepatic first-pass metabolism, and (3) acts locally in the lungs. As the size variability among adult lungs is smaller than overall body size variability, the dosing reliability is also improved via inhalation.

This finding appeared in a Case Report Publication in the highly prestigious New England Journal of Medicine (Frye et al., 2020).

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 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 to Relief 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 symbols RLFTF and RLFTY. For more information, visit www.relieftherapeutics.com. Follow us on **LinkedIn**.

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