Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics Announces that its Subsidiary, AdVita Lifescience GmbH, was Issued a Swiss Patent Entitled "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis"

Geneva, Switzerland, April 1, 2022 – 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 issued a patent WO2020/225246 entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis," to Relief's subsidiary, AdVita Lifescience GmbH. The patent will provide intellectual property protection for the inhaled formulation of RLF-100® (aviptadil) into at least 2039.

The patent generally relates to vasoactive intestinal peptide (VIP) for use in the treatment of drug-induced pneumonitis. In particular, it relates to VIP for use in the treatment of checkpoint inhibitor-related pulmonary pneumonitis (CIP) and methotrexate-induced pneumonitis.

"The granting of this Swiss patent for the inhaled version of RLF-100 serves to further strengthen our growing intellectual property portfolio for this highly promising drug candidate," stated Raghuram (Ram) Selvaraju, Chairman of Relief. "Clinical studies to assess the potential advantages of RLF-100 remain ongoing, including a clinical program in Europe and the National Institutes of Health ("NIH")-sponsored ACTIVE-3b/TESICO study."

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), a copy of which can be found here.

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 through Relief's collaboration partner in the U.S., NeuroRx, Inc. Relief also has a Collaboration and License Agreement with Acer Therapeutics for the worldwide development and commercialization of ACER-001, 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. Acer's new drug application for ACER-001 for use as a treatment of urea cycle disorders was recently accepted by the FDA for filing with a PDUFA decision date of June 5, 2022. Finally, Relief's acquisitions last summer of APR Applied Pharma Research SA and AdVita Lifescience GmbH brought 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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