PRESS RELEASE

Relief and AdVita Announce Initiation of Phase 2 Trial with Inhaled RLF-100 for the Prevention of COVID-19-related Acute Respiratory Distress Syndrome

Investigator-sponsored trial being conducted at major medical centers in Switzerland

Relief provides update on RLF-100 clinical development in Europe

Geneva, Switzerland, and Gundelfingen, Germany, April 22, 2021 – RELIEF THERAPEUTICS Holding AG (SIX: RLF, OTCQB: RLFTF) ("**Relief**"), a biopharmaceutical company with its lead compound RLF-100™ (aviptadil) in advanced clinical development to treat COVID-19-induced lung injury, and AdVita Lifescience GmbH ("**AdVita**"), a Germany-based, privately held pharmaceutical company developing effective products and strategies to improve the treatment and diagnosis of rare lung diseases, today announced that the first patient is expected to be enrolled next week in a phase 2 trial evaluating the inhaled formulation of RLF-100 for the prevention of COVID-19-related acute respiratory distress syndrome ("ARDS").

The study, "Inhaled Aviptadil for the Prevention of COVID-19 Related ARDS" (NCT 04536350), is a randomized, double-blind, placebo-controlled phase 2 trial being conducted at several clinical sites in Switzerland. The trial is expected to enroll 80 patients, who will receive either RLF-100 together with standard of care or placebo plus standard of care. The primary endpoint is the time (in days) from hospitalization to clinical improvement, up to day 28. Clinical improvement shall be defined as either alive hospital discharge or a decrease of two or more points on the WHO-recommended nine-point ordinal scale of clinical status (WHO, 2020). The Principal Investigator of the trial is Prof. Dr. Joerg D. Leuppi, M.D., Ph.D., Professor for Internal Medicine, University of Basel, Head of the University Clinic of Medicine Cantonal Hospital Baselland, Liestal, Switzerland. AdVita is providing all relevant documentation, financial support with the aid of Relief, and study drug for the trial. It is estimated that the study will take approximately 6-12 months to complete, depending on the progression of the ongoing COVID-19 pandemic.

Prof. Dr. Joerg D. Leuppi, M.D., Ph.D., lead investigator of the study, commented: "There remains a significant unmet medical need for effective, safe treatments for COVID-19 patients, despite the increase in vaccination rates and the better understanding we now have on how to treat this potentially deadly infection. RLF-100 is a synthetic form of human Vasoactive Intestinal Polypeptide ("VIP"), which is highly concentrated in the lungs and has been shown in clinical studies to reduce inflammation. We believe that RLF-100 has the potential to prevent COVID-19 patients from developing serious lung disease which end in the ICU needing mechanical ventilation and look forward to seeing the results from this phase 2 trial."

Dorian Bevec, Ph.D., CDO of AdVita, commented: "We are delighted that Professor Leuppi and his team are conducting this trial. We are also excited to be working with the Relief team jointly moving forward the development of inhaled RLF-100 in the treatment of moderate to severe COVID-19-induced respiratory deficiency and other potential indications, such as pulmonary sarcoidosis, and look forward to contributing our expertise with this important drug candidate to the development plan."

Gilles Della Corte, M.D., Chief Medical Officer of Relief, said: "This study will be helpful in building the clinical database for inhaled RLF-100 in preventing COVID-19 patients from developing acute respiratory distress syndrome. The results will provide important insight as we advance the development of this product candidate in Europe."

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Relief also today provided an update on development plans for RLF-100 in Europe.

Intravenous (IV) formulation: Relief is currently preparing a European phase 2b/3 study with IV RLF-100 in COVID-19 patients. Once an Emergency Use Authorization ("EUA") application is submitted by partner, NeuroRx, Inc., to the U.S. Food and Drug Administration ("FDA") and a decision is made, Relief will determine the best path forward for the development of IV RLF-100 in Europe and other territories. Relief continues to see the potential value of RLF-100 to help patients with COVID-19-induced lung injury and hopes that, should the FDA grant EUA for RLF-100, this could expedite the clinical assessment of RLF-100 in Europe.

Clinical development of IV RLF-100 in non-COVID-19-induced ARDS is also under consideration.

Inhaled formulation: Relief will decide on additional clinical development pathways for inhaled RLF-100 in patients with moderate to severe COVID-19-induced lung injury, leveraging the learnings from the study by Prof. Leuppi.

Relief also plans to initiate a phase 2 dose-finding study with inhaled RLF-100 in pulmonary sarcoidosis in Europe in the second half of 2021.

Additional indications such as Beryllium Disease and checkpoint inhibitor-induced Pneumonitis are under consideration.

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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. In January 2021, AdVita and Relief announced the signing of a binding term sheet for Relief to acquire all shares of AdVita to expand the scope of development of inhaled aviptadil. The transaction is expected to close in the second quarter of 2021. 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.

RELIEF THERAPEUTICS Holding AG is listed on the SIX Swiss Exchange under the symbol RLF and quoted in the U.S. on OTCQB under the symbol RLFTF.

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ABOUT ADVITA LIFESCIENCE GMBH

AdVita Lifescience GmbH was founded in 2019 with the purpose of developing effective products and strategies to improve the therapy and diagnosis of rare lung diseases.

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