Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics' Wholly Owned Subsidiary, APR Applied Pharma Research, Reports Final Data from Its Clinical Trial of Novel Nasal Spray, Sentinox, in SARS-CoV-2 Infected Patients

Despite Primary Endpoint not Being Met, Due to Small Sample Size, Results Show a Very Positive Trend in Efficacy Parameters with a Clean Safety and Tolerability Profile

Geneva, Switzerland, March 17, 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, today announced that its wholly owned subsidiary, APR Applied Pharma Research SA ("**APR**"), reported final data from its clinical trial of nasal spray, Sentinox, in SARS-CoV-2 infected patients.

The post-market, interventional, randomized, controlled clinical study (NCT04909996, clinicaltrials.gov) enrolled 57 patients who were randomized to receive Sentinox treatment 0.5 ml into each nostril, performed 3 times/day or 5 times/day for 5 days as add-on to the standard therapy, vs. no Sentinox treatment group. The study was designed to assess the efficacy and safety of Sentinox spray in terms of viral load reduction, negativization and infectivity in recently infected SARS-CoV-2 individuals. It was conducted by the Hygiene Unit of IRCCS Policlinico San Martino Hospital in Genoa, Italy, and coordinated by Prof. Giancarlo Icardi.

Considering the small sample size and the high variability in the baseline viral load observed within study groups, the primary endpoint was not reached; however, the results of the study suggest the potential efficacy of Sentinox, with a better response for 3 times/day, versus the control group, in the reduction of the nasal viral load, negativization and infectivity.

The final analysis on the intention-to-treat ("**ITT**") population of 54 patients who completed the study showed an about 90% (over 1.0 Log10) reduction of viral load after 5 days of treatment with Sentinox 3 times/day versus the control group.

Additional analyses have been conducted in patients stratified according to baseline value of RT-PCR cycles: in the subgroup with medium (Ct 20-30) viral load, the use of Sentinox significantly reduced the viral load of 1.9761 Log10 (p=0.0178) at day 5 compared to the control group, suggesting a positive trend in the treatment effect.

Further efficacy analyses on the ITT population showed that negativization in the Sentinox 3 times/day group started at day 4; at day 6 patients with negative swab were almost two-fold compared to the control

group (47% in Sentinox group versus 22% in no treatment group) (p=0.0005). Similar results were obtained in the analysis conducted in the 20-30 RT PCR cycles subpopulation.

Analysis on infectivity data was conducted in the ITT population: patients were considered "not infectious" (patient likely not be able to spread virus to others) when the cycle threshold value of >35 cycles was achieved *(Carrouel et al. 2021; Jang et al. 2021; Iwanami et al. 2021; Choudhuri et al. 2020).*

In the 3 times/day Sentinox group, 71% of patients were non-infectious versus 44% in the control group at day 6 (p<0.0001).

Overall safety data monitored through clinical examination showed a good safety profile for Sentinox. This has been confirmed also by VAS and LIKERT scale results.

Prof. Giancarlo Icardi, head of the Hygiene Unit of IRCCS Policlinico San Martino Hospital in Genoa (Italy) and lead investigator, commented, "Globally our data suggest that Sentinox represents a promising and safe option in reducing the time for obtaining a negative result due to a significant reduction in the nasal viral load. Our findings are particularly encouraging and indicate that, by reducing the nasal viral load, Sentinox could also have the potential to reduce the chances of spreading the virus to others and to interfere with the spreading of the virus to the lungs, preventing a clinical deterioration. Further larger scale studies are suggested."

Paolo Galfetti, Chief Executive Officer of APR and President of Relief Europe added, "We will continue to investigate the potential of Sentinox nasal spray to reduce nasal viral load and test the hypothesis that such reduction will interfere with the spreading of the virus to the lungs and, by doing so, prevent a clinical deterioration. We believe that further clinical studies can potentially confirm Sentinox as a preventive option, not only against SARS-CoV-2 infection, but as a treatment for a wide array of viruses and bacteria in the future."

About Sentinox

Sentinox is an acid-oxidizing solution (AOS) containing hypochlorous acid at 0.005%, certified in Europe on February 16, 2021 as Class III Medical Device (Certificate Nr. EPT 0477.MDD.21/4200.2). The device is intended for irrigation, cleansing and moistening of the nasal cavities and is indicated for (i) reducing the risk of infections caused by bacteria and viruses, including SARS-CoV-2, by lowering the nasal microbial load, (ii) symptomatic nasal care and (iii) nasal care in case of minor lesions/alterations of the nasal mucosa.

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 with a PDUFA decision date of June 5, 2022. Finally, Relief's acquisitions of APR Applied Pharma Research SA and AdVita Lifescience GmbH, last summer 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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