Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics Announces IRB Approval of Investigator-Initiated Trial Evaluating RLF-TD011 as an Adjunctive Treatment for Cutaneous T-Cell Lymphoma

GENEVA, JAN. 17, 2023 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF, RLFTY) (Relief), a biopharmaceutical company identifying, developing and commercializing novel, patent protected products in select specialty, rare and ultra-rare disease areas, announced independent institutional review board (IRB) approval for the protocol of an investigator-initiated trial to evaluate RLF-TD011 as an adjunctive treatment for patients diagnosed with cutaneous t-cell lymphoma (CTCL). The study will evaluate the effect of RLF-TD011, a patent-protected hypochlorous acid topical spray, on the microbiome of CTCL skin lesions and determine tolerability, symptom improvement, and potential for reducing lesion size and skin disease activity.

The study will enroll participants at Northwestern department of dermatology in Chicago. Microbiome assessments will be performed under the leadership of co-principal investigator Alan Zhou, M.D., MSc., fellow of the American Academy of Dermatology and assistant professor of dermatology at Northwestern University.

CTCL is a rare, heterogeneous group of non-Hodgkin's lymphomas in which malignant t-cells infiltrate the skin. Advanced CTCL lesions harbor *Staphylococcus aureus*, which release toxins that stimulate malignant cells and drive disease progression. This often leads to recurrent skin infections with a high risk for sepsis and death.

"Treatment of advanced CTCL remains a challenge, with five-year disease-specific survival rates ranging from 70 percent for early stage to 24 percent for advanced disease, with the greatest mortality stemming from bacterial infections," said Dr. Alan Zhou. "This proof-of-concept clinical study will look at the microbiome changes and clinical improvement in 30 patients over an eight-week study period. We will evaluate how the bactericidal activity of this unique hypochlorous acid skin spray, previously shown to kill methicillin-sensitive and methicillin-resistant *Staphylococcus aureus*, as well as *Pseudomonas aeruginosa*—could improve the CTCL microbiome to potentially decrease pruritus, erythema, scaling, lesion size and overall skin disease activity, with the goal of delaying disease progression and reducing death."

"This investigator-initiated trial represents an important step in the clinical development pathway of RLF-TD011," said Nermeen Varawalla, M.D., D.Phil., M.B.A., chief medical officer, Relief Therapeutics. "Data from this study will be utilized to facilitate the design and conduct of follow-on, multi-center, pivotal clinical trials, which will potentially serve as the clinical support for our eventual submissions to the U.S. Food and Drug Administration and European Medicines Agency for RLF-TD011 as an effective, convenient and well-tolerated treatment for CTCL, thereby addressing an important unmet medical need in an intractable, incurable disease."

ABOUT CUTANEOUS T-CELL LYMPHOMAS

Cutaneous t-cell lymphomas (CTCLs) are a rare group of disorders known as non-Hodgkin's lymphomas characterized by abnormal accumulation of malignant t-cells in the skin that can result in the development of rashes, plaques and tumors. Because CTCL is rare and often looks like eczema or another common skin disease, it can be difficult to diagnose. While there are many types of CTCLs, the most common diagnoses are mycosis fungoides, primary CTCL and primary cutaneous anaplastic large cell lymphoma.[1] The overall incidence rate of CTCL was 8.55 per 1 million with MF being the subtype with the highest incidence, at 5.42 per 1 million.[2] The overall incidence of CTCL in the U.S. and Europe has increased, a reflection of better diagnostic tools and increased awareness among physicians and patients, which has led to improved disease detection.[3]

According to Fortune Business Insights, the North American CTCL therapeutics market size is projected to hit an annual valuation of USD $587.4 million by 2028, registering a 13.6 percent compound annual growth rate (CAGR) in the 2021-2028 period.[4] The market value was estimated to be worth USD $225.9 million in 2020 and reached USD $240.9 million in 2021. The increasing burden of CTCL in the region is slated to increase the demand for novel CTCL therapeutics solutions. Cleveland Clinic reports that more than 3,000 new CTCL patients are diagnosed in the U.S. each year and about 16,000-20,000 individuals suffer from mycosis fungoides, the most common form of CTCL that is linked to skin-localized immune cell stimulation.

ABOUT RLF-TD011

RLF-TD011 was developed using the TEHCLO® proprietary technology and is a highly pure and stabilized hypochlorous acid (HClO >95% of free chlorine species), with pH between 2.5 - 3.0 and high reduction-oxidation potential (ORP 1.000 - 1.200 mV). It is a self-administered, sprayable solution enabling targeted application while avoiding skin contact and cross-contamination. RLF-TD011 has consistently been shown to accelerate wound closure with reduced infection rates in clinical trials.[5,6,7] If approved in this indication, it will be the first product specifically indicated to improve the microbiome in CTCL resulting in symptom control and halting disease progression.

RLF-TD011 is currently registered under the brand name Nexodyn® AcidOxidizing Solution (AOS) for use in the debridement, irrigation, cleansing and moistening of chronic wounds and acute wounds, post-surgical wounds, cuts, abrasions, burns and other lesions. Nexodyn AOS is certified in the EU as class III medical device and in the U.S., as a 510(k) cleared unclassified device.

ABOUT RELIEF THERAPEUTICS Holding SA

Relief Therapeutics is a Swiss, commercial-stage, biopharmaceutical company focused on identification, development and commercialization of novel, patent protected products intended for the treatment of rare and ultra-rare diseases including metabolic disorders, pulmonary diseases and connective tissue disorders. Relief Therapeutic's diversified pipeline consists of assets that have the potential to effectively address significant unmet medical needs, including PKU GOLIKE®, engineered with the proprietary Physiomimic™ technology, which is the first prolonged-release amino acid product commercialized for the dietary management of phenylketonuria (PKU). Relief Therapeutics has a collaboration and license agreement with Acer Therapeutics for the worldwide development and commercialization of Olpruva™ (sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including urea cycle disorders (UCDs) and maple syrup urine disease (MSUD). Relief Therapeutics also continues to develop aviptadil for several rare pulmonary indications. Further, Relief Therapeutics is undertaking the clinical development of RLF-TD011, a differentiated acid oxidizing solution of hypochlorous acid intended for the treatment of epidermolysis bullosa (EB), a group of rare, genetic, life-threatening connective tissue disorders; RLF-TD011 has been granted orphan drug designation by the U.S. FDA. Finally, Relief Therapeutics is commercializing several legacy products via licensing and distribution partners.

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, please visit www.relieftherapeutics.com or follow Relief Therapeutics on LinkedIn and Twitter.

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Disclaimer: This communication expressly or implicitly contains certain forward-looking statements concerning RELIEF THERAPEUTICS Holding SA. Such statements involve certain known and unknown risks, uncertainties and other factors, including (i) whether the study described above will be successful (ii) whether APR-TD011 (Nexodyn™ AOS) will ever be approved in the U.S., the U.K., or the E.U. for the treatment of EB or any other disease, and (iii) those risks discussed in RELIEF THERAPEUTICS Holding SA's press releases and filings with the SIX and with the U.S. Securities and Exchange Commission, which could cause the actual results, financial condition, performance or achievements of RELIEF THERAPEUTICS Holding SA to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. RELIEF THERAPEUTICS Holding SA is providing this communication as of this date and does not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.

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[1] https://www.aad.org/public/diseases/skin-cancer/types/common/ctcl/symptoms

[2] Cai ZR, Chen ML, Weinstock MA, Kim YH, Novoa RA, Linos E. Incidence Trends of Primary Cutaneous T-Cell Lymphoma in the US From 2000 to 2018: A SEER Population Data Analysis. *JAMA Oncol.* 2022;8(11):1690–1692. doi:10.1001/jamaoncol.2022.3236

[3] Cai ZR, Chen ML, Weinstock MA, Kim YH, Novoa RA, Linos E. Incidence Trends of Primary Cutaneous T-Cell Lymphoma in the US From 2000 to 2018: A SEER Population Data Analysis. *JAMA Oncol.* 2022;8(11):1690–1692. doi:10.1001/jamaoncol.2022.3236

[4] Fortune Business Insights (https://www.globenewswire.com/en/news-release/2022/02/16/2385997/0/en/North-America-Cutaneous-T-Cell-Lymphoma-CTCL-Therapeutics-Market-Size-2022-2028-to-Reach-USD-587-4-Million-at-a-CAGR-13-6.html)

[5] Iacopi E. et al. The Use of a Novel Super-Oxidized Solution on Top of Standard Treatment in the Home Care Management of Postsurgical Lesions of the Diabetic Foot Reduces Reinfections and Shortens Healing Time. Int J Low Extrem Wounds. 2018 Dec; 17(4):268-274

[6] Strohal R, et al. The management of critically colonized and locally infected leg ulcers with an Acid-Oxidizing Solution: A pilot study. Adv Skin Wound Care 31(4):163-171, 2018.

[7] Ricci E, et al. The management of chronic ulcers with an AcidOxidizing Solution. J Wound Care 25(8):443-50, 2016.