Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics Announces Enrollment of First Three Patients in Proof-of-Concept Clinical Trial of RLF-TD011 for the Treatment of Epidermolysis Bullosa

GENEVA, FEB. 14, 2023 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF, RLFTY) ("Relief Therapeutics" or the "Company"), a biopharmaceutical company developing and commercializing novel, patent-protected products in select specialty and rare diseases, announced today the first three patients have been enrolled in a proof-of-concept, investigator-initiated study to evaluate RLF-TD011 as a treatment for epidermolysis bullosa (EB).

The primary aim of this study will be to assess changes in the skin microbiome (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, commensal organisms) before, during and after treatment with RLF-TD011, a self-administered, sprayable solution enabling targeted application while avoiding skin contact and cross-contamination. Patients with dystrophic or junctional EB whose wounds are colonized by *S. aureus* and / or *P. aeruginosa* will be treated with RLF-TD011 for eight weeks followed by discontinuation of treatment for four weeks with assessment of their wound microbiome at each stage. All study participants will have the option to continue treatment in a six-month open-label study extension.

“EB is a rare, inherited skin disease characterized by widely distributed, painful, chronic wounds that easily become infected, resulting in an elevated risk of sepsis and death. As there is no cure for EB, a crucial element of patient management involves rigorous and timely wound care,” said professor Amy Paller, M.D., chair, department of dermatology, Feinberg School of Medicine, Northwestern University and principal investigator of the study. “We are eager to assess the effect of RLF-TD011 on the microbiome in colonized dystrophic and junctional epidermolysis bullosa wounds and determine tolerability, symptom improvement, reduction of lesion size and wound closure.”

The study is currently enrolling up to 17 patients diagnosed with junctional epidermolysis bullosa (JEB) or dystrophic epidermolysis bullosa (DEB) with *S. aureus* or *P. aeruginosa* culture-positive wounds at Ann & Robert H. Lurie Children's Hospital of Chicago.

“The results of this study will be most valuable for the swift, effective and efficient execution of our clinical development plan for RLF-TD011,” said Nermeen Varawalla, M.D., Ph.D., chief medical officer, Relief Therapeutics. “These data will facilitate the design and conduct of follow-on, multi-center, pivotal registration clinical trials to determine the impact of RLF-TD011 on infection control, avoidance of chronic antibiotic use, accelerated wound healing and quality of life for patients living with EB.”

Additional information about this investigator-initiated study is available at ClinicalTrials.gov (NCT05533866).

ABOUT EPIDERMOLYSIS BULLOSA (EB)
Epidermolysis bullosa (EB), also known as “Butterfly Skin,” is a group of rare, genetic, life-threatening connective tissue disorders characterized by skin fragility and blistering, which may appear in response to minor injury, even from heat, rubbing or scratching. In severe cases, the blisters may develop into chronic wounds or occur inside the body, such as the lining of the mouth or stomach. There are four main types of EB, which are classified based on the depth, or level, of blister formation: EB simplex (EBS), junctional

EB (JEB), dystrophic EB (DEB) and Kindler syndrome.[1] Patients with JEB and DEB are at increased risk for serious complications, including aggressive squamous cell carcinoma.[2] Currently there is no cure or approved treatments for EB in the U.S.

The National Epidermolysis Bullosa Registry (NEBR) reports, based on 16 years of data, that the incidence of EB in the U.S. is 19.57 per 1 million live births and the prevalence is 11.07 per 1 million population.[3] Worldwide, EB impacts 500,000 lives.[4] The Company estimates the global market opportunity for EB to exceed $1.0 billion.

ABOUT RLF-TD011 (formerly known as APR-TD011)

RLF-TD011 (formerly known as APR-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] In a preliminary clinical trial, EB patients who administered RLF-TD011 demonstrated improvement in skin blistering and tissue repair within just two weeks of treatment, and the product candidate was shown to be well tolerated with a favorable safety profile.

RLF-TD011 has been granted orphan drug designation by the U.S. Food and Drug Administration (FDA) for the treatment of EB, which qualifies the sponsor of the treatment for certain development incentives, including seven-year marketing exclusivity after FDA marketing approval is received. Relief Therapeutics intends to seek qualified infectious disease product (QIDP) designation status for RLF-TD011, which may confer up to an additional five years of market exclusivity regardless of patent protection status. If approved by the FDA in this indication, RLF-TD011 would be the first topical treatment specifically indicated to improve the microbiome in EB 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 a class III medical device and in the U.S. as a 510(k) cleared unclassified device.

ABOUT RELIEF THERAPEUTICS

Relief Therapeutics is a Swiss, commercial-stage, biopharmaceutical company focused on development and commercialization developing and commercializing novel, patent-protected products in select specialty and rare diseases, including metabolic disorders, pulmonary diseases and connective tissue disorders. Relief Therapeutics' 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 continues to develop RLF-100 (aviptadil) for several pulmonary indications. Further, Relief Therapeutics is undertaking the clinical development of RLF-TD011 for the treatment of epidermolysis bullosa, an indication for which the FDA has granted orphan drug designation. Relief Therapeutics is also exploring the clinical development of

RLF-TD011 for the treatment of cutaneous t-cell lymphomas. 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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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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