Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics to Present Pre-Clinical Evidence for Improved Amino Acid Utilization with PKU GOLIKE® at the Society for Inherited Metabolic Disorders 44th Annual Meeting

The results of the preclinical study demonstrate improved muscle anabolism and function with a prolonged-release amino acid supplement using Physiomimic Technology™

GENEVA, March 17, 2023 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF, RLFTY) ("Relief Therapeutics"), a biopharmaceutical company committed to advancing treatment paradigms and delivering improvements in efficacy, safety and convenience to benefit the lives of patients living with rare diseases, today announced the Company will present the results of pre-clinical research evaluating the metabolic impact of PKU GOLIKE® on nitrogen balance, muscle strength and glucose. The data will be presented in a poster session at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting in Salt Lake City, March 18-21, 2023. The Company will also have an exhibit in booth #109 at the meeting.

People living with PKU do not have the ability to metabolize the amino acid phenylalanine (Phe) found in many foods and they require supplementation of amino acid-based foods for special medical purposes (FSMPs) to prevent protein deficiency and optimize metabolic control. These protein substitutes are typically characterized by altered kinetic profiles compared to that of a slowly absorbed and digested intact protein. The rate of amino acid absorption affects the post-prandial utilization of dietary nitrogen, and the prolonged release of amino acids could support anabolic requirements. Developed with Relief Therapeutics' proprietary, patent-protected Physiomimic Technology™ platform, PKU GOLIKE is the first prolonged-release, amino acid FSMP, characterized by a special coating that enables physiological absorption of the amino acids mirroring that of natural proteins.

"The results from this pre-clinical research demonstrate the important body composition benefits of the physiological absorption of our prolonged-release amino acid supplement PKU GOLIKE[1]," said Nermeen Varawalla, M.D., Ph.D., chief medical officer at Relief Therapeutics. "The findings provide direction for our forthcoming clinical research to confirm the metabolic benefits of PKU GOLIKE, assessing body composition and oxidative stress in active PKU patients, thereby substantiating our completed pre-clinical work."

Society for Inherited Metabolic Disorders 44th Annual Meeting
Poster #: 32
Abstract Title: *More Physiological Absorption of a Prolonged Release Amino Acid Supplement: Preclinical Evidence of Improved Amino Acid Utilization*
Date: Sunday, March 19, 2023
Time: 7 – 10 p.m. MDT
Location: Hyatt Regency in Salt Lake City
Presenter: Katie Draper MS, RDN, LD, medical science liaison, U.S. medical affairs at Relief Therapeutics

This poster summarizes the acute and long-term metabolic effects of PKU GOLIKE supplementation on the utilization of amino acids and glucose metabolism in a pre-clinical rat model using biomarkers for muscle metabolism, functional muscle performance and a glucose tolerance test. Due to the prolonged-

release of amino acids engineered with Physiomimic Technology, beneficial effects were observed on amino acid oxidation, muscle metabolism, grip strength and glucose tolerance in healthy rats. BUN (Blood urine nitrogen test) was significantly lower in the acute treatment with PKU GOLIKE indicating the potential to improve amino acid utilization in PKU patients resulting in a reduction of catabolic episodes.

Detailed results from this study will be available on Relief Therapeutics' website on the Events page following the poster presentation on Sunday, March 19.

ABOUT PHENYLKETONURIA (PKU)

Phenylketonuria (PKU) is a rare inherited disorder affecting more than 450,000 patients worldwide.[2] PKU is caused by a defect of the enzyme needed to break down phenylalanine (Phe), leading to a toxic buildup of Phe from the consumption of foods containing protein or aspartame. Untreated PKU can result in global developmental delay or severe irreversible intellectual disability, as well as growth failure, hypopigmentation, motor deficits, ataxia and seizures.[3] Treatment of PKU is lifelong to avoid these serious consequences and people living with PKU must follow a strict diet that limits intake of Phe from infancy onward. People living with PKU require supplementation of amino acids formulated as foods for special medical purposes (FSMP) to prevent protein deficiency.

Living with PKU requires a limited diet and very careful management. If left unmanaged, PKU can lead to devastating consequences, such as brain damage. People living with PKU do not have the ability to metabolize Phe, which is found in many foods and they require supplementation of amino acid-based foods for special medical purposes (FSMPs) to prevent protein deficiency and optimize metabolic control. Currently available FSMPs lead to poor or suboptimal clinical outcomes and compliance because they are rapidly absorbed and are characterized by an unpleasant odor and aftertaste. Such factors contribute to barriers to social interaction for PKU patients, further limiting FSMP compliance and exposing patients to the risks of poor disease control.[4]

ABOUT PKU GOLIKE®

PKU GOLIKE® products are phenylalanine-free foods for special medical purposes (FSMPs) for both children and adults. The special coating also masks the unpleasant taste, odor and aftertaste of the amino acids. PKU GOLIKE granules are flavorless and can be mixed with many foods**.** PKU GOLIKE products contain all 19 amino acids that people with PKU need to maintain neurological and muscular health and is fortified with 27 essential vitamins and minerals, including ones normally found in protein-rich foods like iron, calcium and vitamin B12. The PKU GOLIKE line of products are available in convenient packets (PKU GOLIKE *Plus*® 3-16 and 16+), medical food bars (PKU GOLIKE BAR®) and tablets to be chewed (PKU GOLIKE KRUNCH®). PKU GOLIKE products have been commercially available in Europe since 2018 and in the U.S. since October 2022. For more information in the U.S., please visit https://www.pkugolike.com/. Please note this site is intended for U.S. audiences only. For more information in Europe, please visit: https://www.apr.ch/apr-pharma-products/medical-prescription/pku-golike-family/.

ABOUT RELIEF THERAPEUTICS

Relief Therapeutics is a commercial-stage biopharmaceutical company committed to advancing treatment paradigms and delivering improvements in efficacy, safety and convenience to benefit the lives of patients living with rare diseases. Since founding in 2013, Relief Therapeutics continues to build a diversified pipeline of risk-mitigated assets to address metabolic, dermatology/connective tissue disorders as well as pulmonary and genetic diseases. Our portfolio also includes a balanced mix of marketed, revenue-generating products and the proprietary, globally patented Physiomimic™ and Tehclo® platform technologies which were obtained through the acquisition of APR Applied Pharma Research S.A. in June

2021. Our mission is being advanced by an international team of well-established, experienced biopharma industry leaders with extensive research, development and rare disease expertise. Relief Therapeutics' headquarters are located in Geneva, with additional offices in Balerna, Switzerland, Rome, Italy and Offenbach am Main, Germany. The Company 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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REFERENCES

[1] Giarratana N, Draper K, et al. More Physiological Absorption of a Prolonged Release Amino Acid Supplement: Preclinical Evidence of Improved Amino Acid Utilization. Molecular Genetics and Metabolism. Vol. 138, Issue 4, In progress (April 2023).

[2] Hillert A, Anikster Y, Belanger-Quintana A, et al. The Genetic Landscape and Epidemiology of Phenylketonuria. *Am J Hum Genet*. 2020;107(2):234-250. doi:10.1016/j.ajhg.2020.06.006

[3] Blau N, van Spronsen FJ, Levy HL. Phenylketonuria. *Lancet.* 2010 Oct 23;376(9750):1417-27. doi: 10.1016/S0140-6736(10)60961-0. PMID: 20971365.

[4] Ford, Suzanne et al. "Living with Phenylketonuria: Lessons from the PKU community." *Molecular genetics and metabolism reports.* Vol. 17 57-63. 18 Oct. 2018, doi:10.1016/j.ymgmr.2018.10.002.