Ad hoc announcement pursuant to Art. 53 LR

Relief Therapeutics' Wholly Owned Subsidiary, APR Applied Pharma Research, Reports In Vivo Data Published in the Peer Reviewed, *International Journal of Molecular Sciences,* Indicating Prolonged Release of Amino Acids Using Its Physiomimic™ Technology May Have Benefits for the Treatment of PKU

Data In Animal Models Suggest That APR's Controlled Release Amino Acid (AA) Mix, Formulated With the Physiomimic™ Technology, May Have Beneficial Effects on Both AA Oxidation and Catabolism With a Direct Impact on Muscle Mass, Strength And Glyceamia

Geneva, Switzerland, March 28, 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 data published in the peer reviewed *International Journal of Molecular Sciences*, indicating that prolonged release of amino acids ("**AA**") formulated with APR's Physiomimic™ Technology may have benefits for the dietary management of phenylketonuria ("**PKU**"). The full article can be accessed here.

The paper, entitled, "In Vivo Metabolic Responses to Different Formulations of Amino Acid Mixtures for the Treatment of Phenylketonuria (PKU)," evaluated the impact of a prolonged release of AA formulation on nitrogen balance, both in acute and long-term experimental studies to evaluate the impact on selected metabolic and functional parameters relative to the natural slow-release reference protein casein or free AA controls. Authors of the paper, including Prof. Dr. Júlio César Rocha, Assistant Professor at NOVA Medical School, Faculty of Medical Sciences, NOVA University of Lisbon Reference Centre for Inherited Metabolic Diseases – Centro Hospitalar Universitário de Lisboa Central, and CINTESIS Portugal, concluded that the prolonged release of an amino acid mix, found in PKU GOLIKE®, may have beneficial effects on both AA oxidation and catabolism, with a direct impact on muscle mass and muscle strength as well as on other metabolic pathways such as glycaemia, in normal rats. The results of this study also supported further studies in human subjects aimed at demonstrating the beneficial effects of the Physiomimic™ Technology AA formulation for the dietary treatment of PKU.

"The paper's conclusions confirm the advantages of prolonged AA absorption using our patented Physiomimic™ Technology, which has already been demonstrated in humans," stated Paolo Galfetti, Chief Executive Officer of APR and President of Relief Europe. "The prolonged release of AAs made possible through our Physiomimic™ Technology and used in the currently commercialized PKU GOLIKE® family of products in Europe, we believe, leads to absorption of AAs more closely resembling the natural

protein in healthy humans, providing a distinct advantage for the treatment of patients with PKU. We are relentlessly working to bring PKU GOLIKE® as a treatment to PKU patients in the U.S. within 2022 while we are in the process of generating further clinical evidence that will support PKU GOLIKE as a prescription product."

About PKU GOLIKE®

The PKU GOLIKE® family of products are food for special medical purposes (FSMP) or medical formulas in the US consisting of a phenylalanine-free amino acid mix in granules. Engineered with the Company's patented Physiomimic™ Technology platform, PKU GOLIKE® is the first prolonged-release amino acid product, characterized by a special coating that ensures a more physiological absorption of the amino acids, while also masking their unpleasant taste, odor and aftertaste.

About Phenylketonuria or PKU

PKU is a rare inherited disorder caused by a defect of the enzyme needed to break down phenylalanine, leading to a toxic buildup of phenylalanine when eating foods that contain protein or aspartame. Excessive levels of phenylalanine in the blood cause accumulation in the brain, which hampers proper brain development and results in neurophysiological dysfunction. Treatment of PKU is lifelong, requiring patients to follow a strict diet that severely limits phenylalanine (and, thus, protein) content. This necessitates supplementation of phenylalanine free-amino acid-mix) to prevent protein deficiency and optimize metabolic control.

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

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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 PKU GOLIKE® provides the benefits described in the paper published in Nutrients, (ii) whether PKU GOLIKE® will be approved as a prescription product in the United States, and (iii) those risks discussed in Relief's press releases and filings with the SIX, 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 do not undertake to update any forward-looking statements contained herein as a result of new information, future events or otherwise.