Ad hoc announcement pursuant to Art. 53 LR

Relief Reports Half-Year 2022 Results and Provides Corporate Update

Geneva, Switzerland, September 15, 2022 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF, RLFTY) ("Relief"), a Swiss, commercial-stage biopharmaceutical company seeking to provide patients therapeutic benefit from selected specialty, rare and ultra-rare diseases with high unmet need, today reported its results for the half-year ended June 30, 2022 and provided a corporate update.

"We achieved significant progress during the first half of 2022, continuing to execute on our goal of becoming a fully integrated, capital-efficient, commercial-stage biopharmaceutical company targeting rare and specialty disease indications. In particular, we have focused on preparations for the impending U.S. launch of PKU GOLIKE®, a differentiated medical food product engineered with the patent protected, proprietary Physiomimic drug delivery technology, for the dietary management of phenylketonuria ("PKU"), which is currently marketed in Europe, and we look forward to the U.S launch in the fourth quarter of this year, " stated Raghuram Selvaraju, Ph.D., Chairman of the Board of Directors of Relief. "The planned commercial introduction into the U.S. necessitated an expansion of our sales organization and commercial capabilities, and we were pleased to have appointed a number of highly seasoned biotech executives to lead this effort. These included Christopher Wick as Executive Director, Head of U.S. Sales; Drew Cronin-Fine, as Executive Director, Head of U.S. Marketing; and David McCullough, as Senior Director and Head of U.S. Market Access, all reporting to Anthony Kim, Senior Vice President, and Head of U.S. Commercial Operations. We also acquired from Meta Healthcare Ltd. the worldwide commercialization rights (except in the UK) for a novel dosage form of an already FDA-approved prescription drug, intended for the treatment of patients with PKU, adding to our offerings and solidifying our position in this market. We anticipate filing for registration approval through a 505(b)(2) NDA during 2023, further evidencing our cost-effective approach to drug development."

Dr. Selvaraju added, "Meanwhile, we continue to work closely with our partner, Acer Therapeutics Inc. ("Acer"), for a potential U.S. launch of ACER-001, a taste-masked, immediate-release, proprietary powder formulation of sodium phenylbutyrate (NaPB) to treat urea cycle disorders ("UCDs"). Acer resubmitted a New Drug Application ("NDA") to the FDA under the 505(b)(2) pathway for ACER-001 in UCDs in July 2022. The FDA accepted the NDA and assigned a Prescription Drug User Fee Act ("PDUFA") target action date of January 15, 2023. Assuming approval, we anticipate U.S. commercialization in the first half of 2023, marking an important milestone for the collaboration and representing our second commercialized product in the U.S. We also plan to submit a Marketing Authorization Application for approval of ACER-001 for the treatment of UCD in the U.K. and EU. Additionally, Acer submitted an Investigational New Drug ("IND") application to the FDA to evaluate the safety and efficacy of ACER-001 for the potential treatment of Maple Syrup Urine Disease ("MSUD"). We anticipate clinical studies to begin in the fourth quarter of 2022 and expect that data from these studies would be suitable for product registration in the U.S. and Europe. During the year, we also significantly strengthened the intellectual property portfolio of ACER-

001 with receipt of patents covering methods-of-use claims for the potential treatment of UCDs and MSUD.

“We also made progress in our program targeting pulmonary diseases. Importantly, we announced promising three-month initial stability data on a new formulation of RLF-100®, which appears to be shelf-stable at temperatures suitable for shipping and long-term storage, thus, potentially having significant clinical and commercial value. We intend to continue to develop RLF-100® for a range of lung diseases. The inhaled formulation of RLF-100® is presently being evaluated in a European study for COVID-19-infected patients (the “Leuppi Study”), for which we expect to report top-line data sometime before year end 2022, subject to completion of patient enrollment. Additional indications include, pulmonary sarcoidosis, for which we have Orphan Drug Designation (“ODD”), and for which, during 2023 we plan to initiate a phase 2b dose-ranging study in 72 patients. We expect to schedule a pre-IND meeting with the FDA to confirm the efficacy and safety endpoints as well as the proposed dosing regimen and, based on a positive outcome, expect to begin this phase 2b study during 2023. We plan to also explore RLF-100® for checkpoint inhibitor-induced pneumonitis, for the treatment of non-COVID-19-related acute respiratory distress syndrome (“ARDS”) and to conduct a European proof-of-concept of RLF-100® in the treatment of chronic berylliosis.

“In parallel to these activities, we continue to develop APR-TD011 for the treatment of epidermolysis bullosa (“EB”), for which we have received FDA ODD. Based on strong clinical results, GMP-grade pharmaceutical product is being prepared for clinical development under an FDA-authorized IND, with a clinical trial slated to start in the second quarter of 2023. Additionally, we will leverage our collaboration agreement with InveniAI LLC, a pioneer in the application of artificial intelligence which, we believe, will meaningfully complement our existing drug development expertise and generate numerous promising additions to our pipeline. We have also instituted an effort to pursue the inception and advancement of next-generation, disruptive genetic medicines, taking advantage of innovations in genetic technologies including gene therapy and genome editing to facilitate the development of potentially curative therapies for areas of high unmet medical need.

“Last year, we launched a Level 1 ADR program in the U.S. and are aggressively moving to a Level 3 ADR and an associated Nasdaq Stock Market listing, which we expect to occur in the fourth quarter of this year. To that end, on August 23, 2022, we filed an F-1 Registration Statement with the U.S. Securities and Exchange Commission to register our ADSs for sale in the United States. We ended June of 2022 with a solid cash position of CHF 29.9 million, providing a forecasted cash runway into the third quarter of 2023. We also expect that, with the launch of the PKU GOLIKE® franchise in the U.S. and a successful launch of ACER-001 in early 2023, Relief could achieve cash flow breakeven in late 2024 and positive operating cash flow in early 2025.

Today, we are a more mature, forward integrated, commercial-stage specialty drug company with a deep pipeline and multiple opportunities for growth and we will continue to actively pursue a strategy to diversify our pipeline and are continuously evaluating in-licensing and acquisition opportunities.”

Key Clinical Development Highlights:

PKU GOLIKE®

- In March 2022, APR Applied Pharma Research SA ("APR") announced that the International Journal of Molecular Sciences had published in vivo data on metabolic responses to formulations of amino acid mixtures for the treatment of PKU. The peer reviewed journal's paper indicated that prolonged release of amino acids, such as those present in formulations like PKU GOLIKE®, may have beneficial effects on the dietary treatment of PKU.
- In April 2022, APR received a Notice of Allowance from the USPTO for Patent Application No. 15/303,121, entitled, "Modified Release Orally Administered Amino Acid Formulations." The allowance covers certain formulations of PKU GOLIKE® in APR's product line and supplements APR's PKU GOLIKE® intellectual property portfolio, which includes U.S. Patent No. 10,500,180.

ACER-001

- In February 2022, Relief announced that Acer was issued U.S. patent 11,202,767 from the USPTO covering methods of use claims related to ACER-001's multi-particulate dosage formulation for oral administration for the potential treatment of UCD and MSUD. The patent builds upon previous issuance of U.S. patent 11,154,521, covering pharmaceutical composition claims of ACER-001.
- In June 2022, Acer and Relief announced that the FDA had issued a Complete Response Letter ("CRL") regarding the New Drug Application ("NDA") for ACER-001 for UCD. The CRL stated that the FDA could not approve the NDA for ACER-001 for UCD in its current form due to an incomplete inspection of Acer's third-party contract packaging manufacturer. The FDA did not cite any other approvability issues in the CRL related to the NDA. Acer noted that it was actively working with its third-party contract packaging manufacturer and cooperating with the FDA to address the CRL and stated its intent to resubmit an updated NDA for ACER-001 for UCD in early-to-mid Q3 2022.
- Subsequently, in July 2022, Relief announced that Acer had resubmitted its NDA for ACER-001 for the treatment of UCD to the FDA. Acer has advised Relief that the resubmission addressed, in full, the items raised by the FDA in the CRL. Later that same month, Relief and Acer announced the resubmitted NDA was accepted for review by the FDA, which designated the NDA as a Class 2 resubmission and set a PDUFA target action date of January 15, 2023.
- In July 2022, Acer and Relief announced the submission of an IND application to the FDA to evaluate the efficacy and safety of ACER-001 for the potential treatment of MSUD.
- In August 2022, Relief and Acer announced that the European Commission had granted orphan medicinal product designation in the EU to ACER-001 for the potential treatment of patients with MSUD.

APR-OD32

- In March 2022, APR announced the acquisition of the worldwide commercial rights (excluding UK) from the UK-based company Meta Healthcare Ltd. ("Meta") for a novel, differentiated dosage form of a prescription drug already approved by the U.S. FDA and intended for the treatment of patients with PKU. This improved product is expected to enhance patient acceptance and compliance as well as enable easier, self or caregiver administered dosing and dispensing.
- In July 2022, the final agreement was executed. Pursuant to the final agreement, Meta shall transfer to Relief all data, know-how, as well as any intellectual property related to "APR-OD32" as developed or generated by Meta. Relief shall only be responsible for funding the remaining development activities as well as for filing and obtaining a new drug application in all countries worldwide except for the UK where Relief shall grant a license back to Meta, enabling Meta to market the product in that country.

RLF-100® (aviptadil)

- In April 2022, Relief reported that the Swiss Patent Office IPI issued a patent WO2020/225246 entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis," to Relief's subsidiary, AdVita Lifescience GmbH ("AdVita"). The patent provides intellectual property protection to Relief's inhaled formulation of RLF-100® into at least 2039.
- In May 2022, Relief provided a corporate update noting that it intends to continue clinical assessment of both inhaled and IV formulations of RLF-100® for pulmonary indications, including (1) the continuation of the European study of inhaled RLF-100® for COVID-19-infected patients (2) the initiation of a clinical trial of RLF-100® in early 2023 in patients with sarcoidosis (3) the exploration of RLF-100® for checkpoint inhibitor-induced pneumonitis (4) testing of RLF-100® in the treatment of non-COVID-19-related ARDS and (5) conducting a European proof-of-concept of RLF-100® in the treatment of chronic berylliosis.

Sentinox

- In March 2022, APR Applied Pharma Research SA ("APR") reported final data from its clinical trial of Sentinox in SARS-CoV-2 infected patients. Although the primary endpoint was not achieved, the results suggest the potential efficacy of Sentinox, with a better response in subjects dosed 3 times per day versus the control group, in the reduction of the nasal viral load, negativization and infectivity and confirmed its safety and tolerability.

CAMBIA

- In January 2022, APR received a Notice of Allowance from the USPTO for Patent Application No. 16/713,052 entitled, "Ready to Use Diclofenac Packs." Diclofenac potassium is an off-patent, potent non-steroidal anti-inflammatory drug ("NSAID") widely used therapeutically for inflammatory conditions and pain management.

Management and Board Additions

- Relief expanded the Board of Directors with highly experienced life science industry executive Michelle Lock.
- To match its fast pace of development, Relief has appointed seasoned executives to newly created roles including, Christopher Wick, as Executive Director, Head of U.S. Sales; Drew Cronin-Fine as Executive Director, Head of U.S. Marketing, and David McCullough as Senior Director and Head of U.S. Market Access.
- Additionally, Relief appointed Serene Forte, Ph.D., MPH, to the newly created role of Senior Vice President, Head of Genetic Medicine, to spearhead Relief's new genetic medicine initiatives.

Business Update

- On July 20, 2022, Relief's Registration Statement on Form 20-F under the Securities Exchange Act of 1934 became effective, and Relief is now a publicly reporting company in the United States.
- In August 2022, Relief filed a Registration Statement on Form F-1 under the Securities Act of 1933 for a proposed offering of its ordinary shares in the form of American Depositary Shares ("ADSs"). The number of ADSs to be offered and the price range for the proposed offering have not yet been determined. As part of the registration process, Relief plans to apply to list its ADSs on the Nasdaq stock market, and such listing is expected to become effective on effectiveness of its registration statement. There can be no assurance that Relief's Form F-1 registration statement will become effective, that Relief will successfully complete an offering of its ADSs, or that Relief will be successful in its efforts to up-list its ADSs to the Nasdaq Stock Market. Any offering, if made, will only be made by an effective prospectus.
- On August 22, 2022, Relief announced that it has agreed to a tentative settlement of its pending litigation with NRx Pharmaceuticals and its subsidiary, NeuroRx, Inc. relating to Relief's September 2020 collaboration agreement with NeuroRx. The parties have agreed to work collaboratively to finalize the settlement within the next 30 days. Further, the parties have agreed to stay the litigation for an additional 60 days to allow for the negotiation and execution of the definitive settlement agreement and related terms. Terms of the settlement will be reported following execution of the definitive settlement terms. There can be no assurance that the settlement will be completed.

Financial Highlights for the Six Months Ended June 30, 2022

Results of Operations

- In the first six months of 2022, Relief generated CHF 3.24 million of revenue from product sales, licensing fees, and royalties. Prior to the business combination with APR at the end of June 2021, Relief did not generate any revenue.

- Other gains were CHF 1.3 million for the six months ended June 2022, compared to CHF 0.9 million for the six months ended June 2021. In the current period, other gains consisted mainly of a change in the fair value of provisions for contingent liabilities and an impairment reversal following the repayment of a loan issued to NeuroRx in 2020 and for which Relief had recorded a complete impairment allowance. In the comparative period, other gains related to write-offs of liabilities.
- External research and development expenses increased to CHF 10.6 million for the six-month period ended June 30, 2022, from CHF 8.3 million for the six months ended June 30, 2021, an increase of CHF 2.3 million primarily due to higher expenses incurred by Acer under the license and collaboration agreement and secondarily due to the addition of in-process programs through the acquisition of APR in June 2021. The increase in expenditures associated with ACER-001 and other in-process programs was partially offset by a reduction of CHF 5.7 million in development expenses associated with RLF-100.
- Personnel expenses increased to CHF 5.8 million in the six-month period ended June 30, 2022, compared to CHF 3.4 million for the six-month period ended June 30, 2021, an increase of CHF 2.4 million mainly due to an increase in employee headcount resulting from the acquisitions of APR and AdVita and the establishment of our U.S. sales force. As of June 30, 2022, Relief had 57 full-time equivalents on its payroll.
- Other administrative expenses increased to CHF 4 million in the six-month period ended June 30, 2022, compared to CHF 3.2 million for the six-month period ended June 30, 2021, an increase of CHF 0.8 million primarily attributable to expanded activities with the addition of APR and AdVita. Consulting expenses associated with the preparation of the market launch of PKU GOLIKE® in the U.S. further contributed to the increase. Legal fees remain flat as costs related to Relief's effort to become a publicly reporting company in the United States and to list its ADSs on Nasdaq were offset by a reduction in costs incurred for other legal and regulatory matters.
- Relief conducted an impairment test of intangible assets as of June 30, 2022, and concluded that the carrying amount of certain assets, mainly intangible assets associated with PKU GOLIKE® and Sentinox™, exceeded their recoverable amount. As a result, the company recognized a non-cash impairment charge on intangible assets of CHF 8.2 million in the current period. The impairment charge reflects a reduction of estimated future net cash flows from PKU GOLIKE® following changes in market assumptions, and, for Sentinox™, a one-year delay in the estimated launch date.
- Amortization and depreciation expenses were CHF 2 million for the six-month ended June 2022 and were nil for the six months ended June 2021. Prior to the acquisition of APR in June 2021, Relief did not have amortizable intangible assets nor material property, plant, and equipment assets on its balance sheet.
- Financial expenses increased to CHF 1.1 million in the six-month period ended June 30, 2022, compared to CHF 0.3 million for the six-month period ended June 30, 2021, an increase of CHF 0.8 million primarily due to the recognition of an interest expense of CHF 0.7 million in relation

with contingent liabilities that may become due upon achievement of milestones contractually agreed with the former shareholders of APR and AdVita.

- Income taxes were a gain of CHF 1.6 million in the six months ended June 2022, compared to income tax expenses of CHF 0.01 million for the six-month period ended June 30, 2021. The income tax gain resulted mainly from the amortization of intangible assets and a corresponding reduction in the temporary difference between the carrying amount of these assets and their tax base.
- Net loss for the period was CHF 26.5 million, compared to a net loss of CHF 14.7 million for the same period last year.

Relief's Half-Year 2022 Report, including the interim consolidated financial statements, is available for download here.

###

ABOUT RELIEF

Relief 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'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 has a Collaboration and License Agreement with Acer Therapeutics for the worldwide development and commercialization of ACER-001 (sodium phenylbutyrate) for the treatment of various inborn errors of metabolism, including Urea Cycle Disorders ("UCDs") and Maple Syrup Urine Disease ("MSUD"). Relief also continues to develop aviptadil for several rare pulmonary indications. Further, Relief is in clinical development for APR-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; APR-TD011 has been granted Orphan Drug Designation by the FDA. Finally, Relief 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, visit www.relieftherapeutics.com. Follow Relief on LinkedIn.

CONTACT:

RELIEF THERAPEUTICS Holding SA
Jack Weinstein
Chief Financial Officer and Treasurer
contact@relieftherapeutics.com

FOR MEDIA/INVESTOR INQUIRIES:

Rx Communications Group, LLC
Michael Miller
+1-917-633-6086
mmiller@rxir.com

Disclaimer: This press release contains forward-looking statements. Forward-looking statements involve known and unknown risks and uncertainties, which may cause actual results in future periods to differ materially from forecasted results. A number of factors, including (i) whether the commercialization of PKU GOLIKE® in the United States will be successful, (ii) whether ACER-001 for the treatment of UCDs will be approved for commercialization in the United States and successfully commercialized, (iii) whether Relief's current and future clinical trials and studies will be successful, (iv) whether the tentative settlement of pending litigation with NRx and NeuroRx will be successfully concluded, (v) whether Relief's registration statement on Form F-1 will become effective and Relief will be able to successfully conclude an offering of its ADSs in the United States, (vi) whether Relief's efforts to list its ADSs on the Nasdaq Stock Exchange will be successful, (vii) whether Relief will achieve breakeven cash flow and positive cash flow, and if so, whether such breakeven or positive cash flow will be achieved on the timetable described in this press release , and (viii) those factors described in Relief's reports to the SIX Swiss Exchange and the Securities and Exchange Commission could adversely affect Relief, 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. Copies of Relief's filings with the SEC are available on the SEC EDGAR database at www.sec.gov.

This press release is not intended to and does not constitute an offer to sell or the solicitation of an offer to buy any securities in the United States or any other jurisdiction, nor shall there be any offer or sale of securities in the United States or any other jurisdiction in which such offer, solicitation, or sale would be unlawful unless registered and/or qualified under applicable securities laws. This press release does not constitute a prospectus according to art. 35 of the Swiss Financial Services Act dated 15 June 2018, as amended ("FinSA"), or art. 27 et seqq. of the SIX Swiss Exchange Listing Rules. There is no intention or permission to publicly offer, solicit, sell or advertise, directly or indirectly, any securities of Relief in or into Switzerland within the meaning of FinSA. Further, the ADSs have not been registered under the Securities Act of 1933, as amended (the "Act"), and no public offering of securities shall be made in the United States except by means of a prospectus meeting made available by Relief that contains detailed information about Relief and its management, as well as financial statements meeting the requirements of the Act.