Ad hoc announcement pursuant to Art. 53 LR

Relief Reports Full-Year 2021 Results and Provides Corporate Update

Geneva, Switzerland, March 31, 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 reported its results for the full-year ended December 31, 2021 and provided a corporate update.

"2021 was a transformative year for Relief, marking a period during which we became a fully integrated, highly nimble, capital-efficient, commercial-stage biopharmaceutical company with operations in both Europe and the U.S. Importantly, we also launched a Level 1 ADR program in the U.S. and, in December, filed a Registration Statement to begin the process of moving to a Level 2 ADR program as part of our ongoing effort to up list to the Nasdaq Stock Market during the first half of 2022," stated Raghuram Selvaraju, Ph.D., Chairman of the Board of Directors of Relief. "Operationally, our acquisition of APR Applied Pharma Research SA ("APR"), in June, immediately added a number of commercialized products, including PKU GOLIKE®, for the treatment of phenylketonuria ("PKU") and provided a European based commercial infrastructure that we will leverage for future product launches. We also plan to develop proprietary products, and third-party products on a fee for service basis under the APR umbrella and are confident that this strategy can generate meaningful additional revenue, going forward."

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 has submitted a New Drug Application ("NDA") to the U.S. Food and Drug Administration ("FDA") under the 505(b)(2) pathway for ACER-001 in UCDs, which was recently accepted for filing and with a Prescription Drug User Fee Act ("PDUFA") target action date of June 5, 2022. If approved, we anticipate U.S. commercialization in the second half of 2022. We also plan to submit a Marketing Authorization Application for approval of ACER-001 for the treatment of UCDs in the EU. Should we be granted approval, the drug will be marketed through APR's commercial infrastructure. We also intend to assess ACER-001 in a clinical program for Maple Syrup Urine Disease ("MSUD") during 2022.

"Our 2021 acquisition of AdVita Lifescience GmbH ("AdVita") provided key pending intellectual property that may cover an improved inhaled formulation of RLF-100® (aviptadil), in development for several lung diseases, including acute respiratory distress syndrome (ARDS) and checkpoint inhibitor-induced pneumonitis (CIP), and, during the year, AdVita was granted Orphan Drug Designation ("ODD") by the FDA for inhaled RLF-100 for the treatment of pulmonary sarcoidosis. At the same time, an intravenous formulation of aviptadil continues to be evaluated as a treatment for severely ill COVID-19 patients in the ACTIVE-3b/TESICO study sponsored by the U.S. National Institutes of Health ("NIH"), while the inhaled formulation is in clinical trials for patients with critical COVID-19 and moderate and severe COVID-19 patients.

"The sheer growth of our pipeline and marketed products has necessitated the expansion of our management team and we were pleased to appoint Nermeen Varawalla, MD, PhD, to the position of Chief

Medical Officer; Anthony M. Kim, as Senior Vice President and Head of U.S. Commercial Operations; and Christopher Wick, as Senior Director, Head of U.S. Sales. We ended the year on a strong financial footing with a cash position of CHF 44.8 million (U.S. $48.1 million) and a forecasted cash runway well into 2023. We expect that, with a successful launch of ACER-001 and the potential expansion of our PKU GOLIKE franchise into the U.S., Relief could achieve positive operating cash flow status during 2024. 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 evaluate in-licensing and acquisition opportunities to further expand and diversify our pipeline."

Key Clinical Development Highlights:

RLF-100® (aviptadil), IV

- In March 2021, the parent company, NRx Pharmaceuticals, Inc. (Nasdaq: NRXP) ("NRx"), of Relief's collaboration partner for RLF-100, NeuroRx, Inc. ("NeuroRx"), announced top-line 60-day results for the phase 2b/3 trial of RLF-100 (aviptadil) for the treatment of patients with critical COVID-19 respiratory failure. These findings formed the basis for NeuroRx's Emergency Use Authorization ("EUA") application to the FDA, submitted in June 2021.
- In April 2021, NRx announced that RLF-100 had been selected for inclusion in ACTIV-3b/TESICO (Therapeutics for Severely Ill Inpatients with COVID-19), an international, phase 3, multicenter clinical trial being sponsored by the NIH.
- In June 2021, NRx announced additional positive results from the RLF-100 U.S. Expanded Access Protocol ("EAP"). These EAP data were then submitted to the FDA and were characterized by NRx as "real world" evidence in support of the findings from the phase 2b/3 trial.
- In July 2021, NRx reported that it identified a statistically significant effect of RLF-100 in preventing the sharp rise in cytokines, commonly associated with mortality in patients with COVID-19. According to NRx, the data was collected as part of the ongoing U.S. phase 2b/3 trial and the findings were submitted to the FDA as a supplement to the pending EUA application.
- In July 2021, NRx announced the successful validation of the commercial formulation of RLF-100 for IV use, allowing for high volume manufacture, with an anticipated one year or greater stability, under appropriate storage conditions.
- In July 2021, NRx announced that the Nation of Georgia's Prime Minister and Minister of Health had issued an EUA for aviptadil.
- In August 2021, NRx provided a safety update on RLF-100 from the NIH sponsored ACTIV-3b/TESICO study, noting that the study's Data Safety Monitoring Board ("DSMB") found no new safety concerns in the trial and recommended continued enrollment.
- In September 2021, Relief received scientific advice from the Medicines and Healthcare Products Regulatory Agency ("MHRA") in the United Kingdom relating to RLF-100, for the treatment of respiratory deficiency due to severe COVID-19. Relief also held discussions with the European

Medicines Agency ("EMA") pertaining to the regulatory path forward for RLF-100 in the EU. Relief informed EMA that it would proceed with further dialogue with the MHRA once it has compiled critical information related to the study conduct, clinical data and the drug product.

- In September 2021, NRx announced top line data demonstrating improved outcomes at one year in highly comorbid patients with COVID-19, who were treated with RLF-100, providing a threefold, statistically significant increase in the likelihood of survival at one year. According to NRx, this was consistent with the increased odds of 60-day survival seen in the previously reported results from the phase 2b/3 randomized controlled trial of RLF-100.
- In October 2021, NRx announced that they had submitted a revised Investigational New Drug ("IND") module on the manufacturing of aviptadil to the FDA, containing documentation that confirmed Nephron Pharmaceuticals, Inc. is prepared to supply aviptadil on a commercial scale.
- In November 2021, NRx reported that it was declined its EUA by the FDA for the use of IV aviptadil for the treatment of acute respiratory failure due to critical COVID-19.
- In November 2021, NRx announced receipt of the FDA's response to NRx's October 8, 2021 submission of updated manufacturing information for aviptadil. According to NRx, the FDA review allowed for high volume production of aviptadil and also reported that the shelf life of aviptadil had been extended from 62 days to 150 days. In November 2021, NRx reported that the FDA had denied Breakthrough Therapy Designation for aviptadil.
- In November 2021, NRx reported that it had completed an analysis to identify clinical evidence that indicates a substantial improvement after treatment with aviptadil in patients with Critical COVID-19 and Respiratory Failure over existing therapies, such as remdesivir. Conducted by Prof. David Schoenfeld, who, according to NRx, is one of the world's most widely published statisticians with unique expertise in life-threatening diseases of the lung, the analysis examined the subgroup of patients in the COVID-AIV trial (NCT 04311697) that remained in respiratory failure, despite treatment with remdesivir. According to NRx, the analysis identified a statistically significant (P=.03) 2.5-fold increased odds of being alive and free of respiratory failure at the 60 days primary endpoint and a statistically significant (P=.006) four-fold higher odds of being alive at day 60 among patients treated with aviptadil compared to those treated with placebo.
- In December 2021, NRx announced it had agreed with Hungarian Health Officials on a regulatory path for emergency use of aviptadil in the Central European region, beginning with a compassionate care program.
- In January 2022, NRx announced that it had submitted another application to the FDA seeking EUA for the use of aviptadil to treat patients with critical COVID-19 who are at immediate risk of death from respiratory failure despite treatment with approved therapy, including remdesivir, and who are ineligible for enrollment into the ACTIV-3b/TESICO NIH-sponsored trial.
- In January 2022, NRx announced enhancements to its Expanded Access and Right to Try programs. NRx stated that these programs enable patients with respiratory failure from COVID-19, who have tried all approved medicines, including remdesivir, and who are not able to participate in a clinical study, to receive aviptadil upon a physician's prescription. NRx has also reported that it is making

aviptadil available as an investigational medicine under the Federal Right to Try Act.

- In February 2022, NRx announced results of a review conducted by the DSMB of the National Institute of Allergy and Infectious Diseases of the NIH on February 14, 2022. According NRx, the DSMB reviewed data on 448 ICU patients with Critical COVID-19 Respiratory Failure who were enrolled in the ACTIV-3b/TESICO trial. NRx reported that no new safety concerns were identified and the study was cleared to continue enrollment to 640 patients. NRx also stated that the TESICO protocol was submitted by NIH and cleared by the FDA as a phase 3 trial that, if positive, may be used in the submission of a NDA for aviptadil.
- In March 2022, Relief received a certificate of registration (Reg. No. 6,674,978) for a trademark for RLF-100 from the United States Patent and Trademark Office ("USPTO"), covering RLF-100 for a broad range of diseases.
- In March 2022, NRx reported that, in light of their strategic focus and the ongoing hostilities in Eastern Europe, it is no longer pursuing opportunities in the Nation of Georgia or elsewhere in the Caucuses region or Europe. They further reported that they have not sold any doses under their previously reported EUA in Georgia.

RLF-100® (aviptadil), Inhaled

- In January 2021, a clinical trial participation agreement for the inclusion of an inhaled formulation of RLF-100 into the I-SPY COVID-19 clinical trial was signed between NeuroRx and Quantum Leap Healthcare Collaborative™ of San Francisco, for a phase 2 adaptive platform trial (NCT04488081) aimed at improving treatment for severely and critically ill COVID-19 patients, which began treating patients in July 2021
- In January 2021, Relief and the former shareholders of AdVita signed a binding term sheet for Relief to acquire all shares of AdVita, giving Relief access to all of AdVita's assets including further pending IP rights that may cover RLF-100 inhaled formulation specifications for its potential application in the treatment of lung diseases such as ARDS, pulmonary sarcoidosis and CIP. The acquisition closed in July 2021.
- In April 2021, Relief and AdVita announced the initiation of an investigator-sponsored, randomized, double-blind, placebo-controlled phase 2 trial (NCT 04536350) evaluating the inhaled formulation of RLF-100 for the prevention of COVID-19-related ARDS.
- In August 2021, Relief received ODD from the FDA for inhaled RLF-100, for the treatment of sarcoidosis, adding to existing ODD designations for APR-OD031 for PKU and APR-TD011 for epidermolysis bullosa.
- In September 2021, AdVita received regulatory clearance to commence a phase 2 clinical trial in Germany to evaluate inhaled aviptadil for the treatment of sarcoidosis.
- In December 2021, Relief reported that the Swiss Patent Office IPI had announced that it expected to conclude the patent application procedure by January 24, 2022 and to issue the patent entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis,"

as applied for by AdVita in 2020. In general, such patents are formally issued, at the earliest, one month after the conclusion of the patent examination procedure.

ACER-001

- In March 2021, Relief signed a Collaboration and License Agreement with Acer for the worldwide development and commercialization of ACER-001 for the treatment of UCDs and MSUD.
- In October 2021, the FDA accepted Acer's NDA for ACER-001, submitted in August 2021 under the Section 505(b)(2) regulatory pathway, and assigned a Prescription Drug User Fee Act (PDUFA) target action date of June 5, 2022. Relief believes that, if approved, ACER-001 could be available commercially in the U.S. during 2022.
- In October 2021, Acer was issued patent No. 17/196,416 by the USPTO, for certain claims related to ACER-001, covering ACER-001's taste-masked, multi-particulate dosage formulation for oral administration, providing intellectual property protection into 2036.

APR Applied Pharma Research SA

- In May 2021, Relief and the former shareholders of APR signed a binding term sheet for Relief to acquire all of the outstanding shares of APR, a privately held Swiss pharmaceutical company with over 25 years' experience in identifying, developing and commercializing known molecules engineered with drug delivery systems in niche and rase diseases on a global basis. The transaction closed in June 2021.
- In September 2021, APR expanded its PKU GOLIKE product line with the launch, in Germany and Italy, of PKU GOLIKE KRUNCH®, a convenient chewable tablet for the dietary management of PKU.
- In October 2021, APR reported positive interim results from its clinical trial of Sentinox in SARS-CoV-2 infected patients, initiated in May 2021, suggesting that Sentinox could be effective in reducing the SARS-CoV-2 viral load in the upper respiratory tract. Final data was reported in March 2022, and, although the primary endpoint was not reached due to limited sample size, the results suggest the potential efficacy of Sentinox, with a better response in subjects dosed 3 times/day, versus the control group, in the reduction of the nasal viral load, negativization and infectivity and confirmed its safety and tolerability.
- 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 widely used therapeutically for inflammatory conditions and pain management.
- In March 2022, APR announced the acquisition of the worldwide commercial rights (ex UK and Ireland) from the UK based company, Meta Healthcare Ltd., to a novel, differentiated dosage form of a prescription drug already approved by the FDA and intended for the treatment of patients with PKU.

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Management and Board Additions

- As part of the acquisition of APR, Paolo Galfetti, Chief Executive Officer of APR, also assumed the position of President, Relief Europe, with overall responsibility for Relief's activities in the EU and UK.
- Relief expanded the Board of Directors with highly experienced life science industry executives Patrice Jean, Ph.D., Tom Plitz, Ph.D., Paolo Galfetti and Michelle Lock.
- To match its fast pace of development, Relief has appointed Nermeen Varawalla, MD, as Chief Medical Officer; Anthony M. Kim, to the newly created position of Senior Vice President and Head of U.S. Commercial Operations; and Christopher Wick, to the newly created position of Senior Director, Head of U.S. Sales.
- Additionally, Jeremy Meinen, who serves as Relief's Vice President of Finance and Administration, assumed the role of Chief Accounting Officer and Marco Marotta, who became part of Relief upon the acquisition of APR, was promoted to Chief Business Officer, responsible for business development activities across the entire company.

Business Update

- In November 2021, Relief filed a registration statement on Form F-6 with the U.S. Securities and Exchange Commission ("SEC"), taking the first step to establish a Level 1 American Depositary Receipt ("ADR") program in the U.S.
- In November 2021, the registration statement became effective, and Relief's ADRs began trading on the over-the-counter ("OTC") market on November 18, 2021; each ADR represents 150 of Relief's ordinary shares.
- In November 2021, Relief signed a collaboration agreement with InveniAI LLC, a U.S. based pioneer in the application of artificial intelligence and machine learning across biopharma and other industries, in order to identify promising drug candidates to treat rare and specialty diseases.
- In December 2021, Relief filed a Registration Statement on Form 20-F with the SEC to register Relief as a reporting company under the Securities Exchange Act of 1934.
- In March 2022, Relief filed Amendment No. 1 to its Registration Statement on Form 20-F with the SEC. The registration statement and Amendment were filed to begin the process of up-listing Relief's Level 1 ADR program in the U.S. to a Level 2 ADR program and is part of Relief's ongoing efforts to list its ADRs on the Nasdaq Stock Market during the first half of 2022. The Nasdaq listing will only occur after the registration statement has become effective, which is subject to an SEC review, and the filing by Relief of a listing application with the Nasdaq, which has not yet occurred.

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Financial Highlights for the 12 Months Ended December 31, 2021

Results of Operation

- The Group's portfolio of marketed products generated CHF 3.3 million in revenue during the 6-month period from July to December 2021, following the acquisition of APR on June 28, 2021. Costs of sales incurred from third parties in the same period amounted to CHF 1.2 million. Prior to the acquisition of APR, the Group had no operating revenue.
- In 2021, the Group recognized other gains of CHF 1.2 million (2020: CHF 0.3 million), mainly in relation with the write-off of financial liabilities.
- Outsourced research and development expenses increased from CHF 13.7 million to CHF 19.0 million and were driven by development funding of ACER-001 in the U.S. and development activities for RLF-100. Furthermore, the Group invested in the development of APR's technology platforms.
- Personnel expenses increased from CHF 2.6 million to CHF 9.1 million. The business combinations with APR and AdVita increased the number of full-time equivalents and consultants from a dozen to six dozen, before organizational adjustments realized in the fourth quarter of 2021. As of December 31, 2021, the Group employed 55 full time equivalents and consultants.
- The addition of APR and AdVita, as well as increased needs of professional services for operations and financing activities, resulted in an increase of administrative expenses from CHF 3 million to CHF 6.8 million.
- In 2021, amortization and depreciation expenses amounted to CHF 2.0 million (2020: nil), mainly driven by the amortization of certain intangible assets acquired with APR.
- Net financial expenses were CHF 1.2 million (2020: CHF 0.5 million), mainly constituted by the Share Subscription Facility fee, by the effect of the passage of time in the fair value measurement of contingent liabilities, and by negative interests charged on the Group's Swiss francs deposits.
- Income tax gain of CHF 0.8 million resulted from variations of deferred tax assets and liabilities (2020: CHF 1.6 million loss). The Group did not have to pay or accrue income tax in jurisdictions where it is present.
- The Group incurred a net loss of CHF 34.7 million in 2021, compared to a net loss of CHF 7.8 million in 2020.

Balance sheet and cash flows

- In 2021, Relief acquired the two companies, APR and AdVita, and the ACER-001 license. On the asset side, the consolidation of the two subsidiaries and the capitalization of the acquisition cost of the license essentially resulted in an increase of intangible assets from CHF 30.8 million to CHF 192.3 million. On the liability side, the transactions essentially resulted in the recognition of provisions for contingent liabilities of CHF 30.8 million and deferred tax liabilities of CHF 21.5 million. Mainly as a result of the two acquisitions, the balance sheet of the Group increased by CHF 173.6 million to CHF 251.6 million.

- Other current assets increased from CHF 3.5 million to CHF 8.5 million and are primarily constituted by CHF 5.3 million unused advance payments made to Acer under the collaboration agreement.
- In 2021, the Group raised cash gross proceeds of CHF 75.9 million through private placements and sales of treasury shares. In addition, the issuances of shares for partial payments of the APR and AdVita acquisitions increased equity reserves by CHF 74.4 million. Overall, total shareholders' equity increased from CHF 67 million to CHF 215.8 million prior to the allocation of the 2021 comprehensive loss of CHF 34.3 million.
- Cash used by the Group in 2021 was primarily related to its operating activities and the acquisition of APR and ACER-001 license. The Group ended the year with a solid cash position of CHF 44.8 million (2020: CHF 43.2 million) and forecasted a cash runway well into 2023.

Further details are available in Relief's 2021 Annual Report, which is available for download in the financial reports section of Relief's website.

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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. Follow us 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

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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 NeuroRx will provide RELIEF THERAPEUTICS Holding SA with the data from its phase 2b/3 trial needed to seek approval of RLF-100 in the EU and UK, (ii) whether the phase 2 trial evaluating inhaled aviptadil for the treatment of sarcoidosis will be successful, (iii) whether RLF-100 will be granted EUA in the United States, (iv) whether the pending disputes between Relief and its U.S. collaboration partner, NeuroRx can be resolved, (v) whether inhaled aviptadil will ever be approved by the EU and/or the U.S. for the treatment of sarcoidosis or for any other indications, (vi) whether ACER-001 will be approved for commercialization by the FDA, and (vii) those risks discussed in RELIEF THERAPEUTICS Holding SA'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.