Ad hoc announcement pursuant to Art. 53 LR

Relief Reports Half-Year 2021 Results and Provides Corporate Update

Geneva, Switzerland, September 24, 2021 – RELIEF THERAPEUTICS Holding SA (SIX: RLF, OTCQB: RLFTF) ("**Relief**"), a biopharmaceutical company seeking to provide patients therapeutic relief from serious diseases with high unmet need, today reported its results for the half-year ended June 30, 2021 and provided a corporate update.

"While we await the FDA's decision on the Emergency Use Authorization (EUA) for IV RLF-100 (aviptadil), filed by our collaboration partner NeuroRx, Inc. (NeuroRx), we have successfully transformed Relief into a fully-integrated, multi-product, revenue-generating biopharmaceutical company," stated Raghuram Selvaraju, Ph.D., Chairman of the Board of Directors of Relief. "A critical component of our success so far this year was the acquisition of APR Applied Pharma Research SA (APR), which expanded and diversified our specialty drug pipeline, added a number of key commercialized products, including the PKU GOLIKE® family of products for the treatment of phenylketonuria (PKU), provided a European based commercial infrastructure that we hope to leverage for future product launches, including ACER-001, and offers an internal R&D capability that we plan to use for the development our own products as well as for third-party products on a fee for service basis."

Dr. Selvaraju continued, "Through our collaboration with Acer Therapeutics, we recently filed a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) for ACER-001, a proprietary powder formulation of sodium phenylbutyrate (NaPB), designed to be both taste-masked and immediate release, for the treatment of urea cycle disorders (UCDs) and maple syrup urine disease (MSUD). We look forward to the potential acceptance of the filing for regulatory review, which we expect to receive next month."

"Also important was our recent acquisition of AdVita Lifescience GmbH (AdVita), from which we gained key pending intellectual property that may cover an improved inhaled formulation of RLF-100 (aviptadil), in development for a number of lung diseases, including acute respiratory distress syndrome (ARDS), and checkpoint inhibitor-induced pneumonitis (CIP). In parallel, IV RLF-100 continues to be evaluated as a treatment for severely ill COVID-19 patients, while the inhaled formulation is being tested in two clinical trials, one for patients with critical COVID-19 and another for moderate and severe COVID-19 patients. As we look ahead, and with a firm financial footing in place, we will maintain our commitment to pursuing additional strategic opportunities, both in-license and acquisition related, in order to aggressively expand and diversify our business."

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Clinical Development Highlights:

RLF-100 (aviptadil), IV

- In March 2021, Relief's collaboration partner, NeuroRx, Inc. (NeuroRx) announced top-line 60-day results for the phase 2b/3 trial of RLF-100™ 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 U.S. Food and Drug Administration (FDA).
- In April 2021, NeuroRx announced that RLF-100 had been selected for inclusion in TESICO (Therapeutics for Severely Ill Inpatients with COVID-19), an international, phase 3, multicenter clinical trial being sponsored by the U.S. National Institutes of Health (NIH).
- In June 2021, NRx Pharmaceuticals Inc. (NRx), the parent company of NeuroRx, announced that NeuroRx had submitted its EUA application to the FDA for the use of RLF-100 in the treatment of critically ill COVID-19 in patients with respiratory failure. NeuroRx also reported that it plans to submit a New Drug Application (NDA) to the FDA.
- 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. The data was collected as part of the ongoing U.S. phase 2b/3 trial and NeuroRx reported that it had submitted these findings 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 RLF-100.
- In August 2021, NRx provided a safety update on RLF-100 which is being tested in the ACTIV-3 Critical Care phase 3 study sponsored by the NIH, designed to evaluate RLF-100 and remdesivir in critical COVID-19 patients, as a monotherapy and in combination against placebo. They reported that the study's Data Safety Monitoring Board found no new safety concerns in the trial and recommended continued enrollment.
- In August 2021, NRx reported a new analysis showing that patients with acute respiratory failure due to Critical COVID-19 who were treated with aviptadil demonstrated improvement in blood oxygen, indicative of improved lung function, within a day of starting treatment. NRx noted that this analysis appears to support its plan to submit an application for Breakthrough Therapy Designation to the FDA and that, if granted, could confer Priority Review to the aviptadil NDA, when submitted.

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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™ (Quantum Leap) of San Francisco.
- 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.
- In April 2021, Relief and AdVita announced the initiation of an investigator-sponsored, randomized, double-blind, placebo-controlled phase 2 trial evaluating the inhaled formulation of RLF-100 for the prevention of COVID-19-related ARDS.
- In July 2021, NeuroRx and Quantum Leap began treating patients with inhaled RLF-100 in the I-SPY COVID-19 Trial (NCT04488081), a phase 2 adaptive platform trial aimed at improving treatment for severely and critically ill COVID-19 patients.
- In July 2021, Relief and the former shareholders of AdVita closed a definitive agreement for Relief to acquire all shares of AdVita, under which Relief paid the AdVita shareholders EUR 25 million in Relief common shares.
- In August 2021, Relief received Orphan Drug Designation (ODD) from the FDA for inhaled RLF-100, for the treatment of sarcoidosis, adding to existing ODD designations for APR-OD031 for phenylketonuria (PKU) and APR-TD011 for epidermolysis bullosa (EB).
- 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.

ACER-001

- In March 2021, Relief signed a Collaboration and License Agreement with Acer Therapeutics, Inc. (Acer) for the worldwide development and commercialization of ACER-001 for the treatment of Urea Cycle Disorders (UCDs) and Maple Syrup Urine Disease.
- In May 2021, Acer announced the outcome of its Type B pre-NDA meeting with the FDA for ACER-001, for the treatment of UCDs. Based on the FDA's feedback, both Relief and Acer noted that the proposed data package would likely be sufficient to support a Q3 2021 NDA submission under the Section 505(b)(2) regulatory pathway.
- Subsequently, in August 2021, Relief and Acer announced the submission of the NDA to the FDA for ACER-001 for UCDs. Relief anticipates submitting a Marketing Authorization Application for approval of ACER-001 for UCDs in the European Union before the end of 2021. Pending a positive decision by regulators, management believes that ACER-001 could be launched in both the U.S. and Europe during 2022.

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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 May 2021, APR initiated a pivotal clinical trial with its novel nasal spray, Sentinox, a Class III medical device, in patients with mild COVID-19.
- In September 2021, APR expanded its PKU GOLIKE® product line with the launch, in Germany and Italy, of PKU GOLIKE® KRUNCH, giving patients a convenient chewable tablet for on-the-go dietary management of phenylketonuria, a rare, recessive metabolic genetic disorder affecting approximately 350,000 people, globally. Management hopes to announce its plans to market PKU GOLIKE® in the U.S. before year end 2021.

Management and Board Additions

- As part of the acquisition of APR, Paolo Galfetti, Chief Executive Officer of APR, has also assumed the position of President, Relief Europe, with overall responsibility for Relief's activities in the EU and UK.
- The Board of Directors was expanded with the appointment of Patrice Jean, Ph.D., joining Raghuram (Ram) Selvaraju, MBA, Ph.D. (Relief's Chairman of the Board), Tom Plitz, Ph.D. and Paolo Galfetti to round out Relief's relevant life sciences Board level expertise.
- Taneli Jouhikainen, M.D. was appointed to the newly created position of Chief Operating Officer.

Financial Highlights for the Six Months Ended June 30, 2021

- The operating loss amounted to CHF 14.5 million with operating expenses of CHF 15.4 million and a one-time gain of CHF 0.9 million following a third-party debt write-off.
- The period is marked by a significant growth in operating and administrative expenses. Service expenses of CHF 8.3 million (HY2020: CHF 2.9 million) were mainly driven by development activities for RLF-100 and ACER-001. Personnel expenses increased to CHF 3.4 million (HY2020: CHF 0.2 million) as the conduct and oversight of development and administrative projects required additional skilled professionals. Legal and administrative services reached CHF 3.2 million (HY2020: CHF 0.4 million), reflecting the company's need of legal and professional services in relation to its business activities, including the acquisition of APR and AdVita.
- Cash used in operating activities has ramped up to CHF 17.7 million from CHF 3.2 million over the same period last year.

- Net loss for the period was CHF 14.7 million (HY2020: CHF 8.3 million profit)
- Relief acquired APR in exchange for CHF 21.5 million in cash and CHF 45 million in Relief shares. The sellers are also entitled to receive contingent milestone payments of up to CHF 35 million in a combination of cash and Relief shares upon completion of pre-agreed milestones. APR was consolidated in the balance sheet of the group on June 30, 2021, and will contribute to the group's income statement in the second semester 2021.

Jack Weinstein, Chief Financial Officer and Treasurer of Relief noted: "Relief remains well funded and, based on current programs, we believe we have sufficient reserves to support multiple clinical programs through key value inflection points. Since the beginning of the year to June 30, we bolstered our balance sheet with CHF 30 million in equity financings. We have also been able to take advantage of the flexibility provided by our additional share listing, giving the company, as of September 24, an available cash position of CHF 40 million."

Post Reporting Period

- On July 26, 2021, Relief announced that it had entered into a definitive agreement with two U.S. institutional investors to purchase in a private placement an aggregate of 71,428,572 shares of Relief common stock at a purchase price of CHF 0.21 per share, raising aggregate gross proceeds of CHF 15 million.
- On July 27, 2021, the company issued and listed an additional 1 billion common shares. Relief used a total of 413,956,419 shares comprising 135,741,063, 206,786,784 and 71,428,572 shares, respectively, to meet its obligations to the AdVita sellers, the APR sellers and the provision of shares for the CHF 15 million private placement. The remaining shares can be used to support Relief's current and future business development activities, and to provide additional working capital.
- On July 27, 2021, Relief acquired AdVita in exchange of EUR 25 million in Relief shares and possible future contingent payments of EUR 20 million payable in cash.

Further details are available in Relief's Half Year 2021 Report, which is available for download at https://relieftherapeutics.com/investor-relations

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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 lead 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. As part of its pipeline diversification strategy,

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in March 2021, Relief entered into a Collaboration and License Agreement with Acer Therapeutics for the worldwide development and commercialization of ACER-001. ACER-001 is 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. In addition, Relief's recently completed acquisition of APR Applied Pharma Research SA brings 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 symbol RLFTF. For more information, visit www.relieftherapeutics.com. Follow us on **LinkedIn**.

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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 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, or (vi) those risks discussed in RELIEF THERAPEUTICS Holding SA's 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.