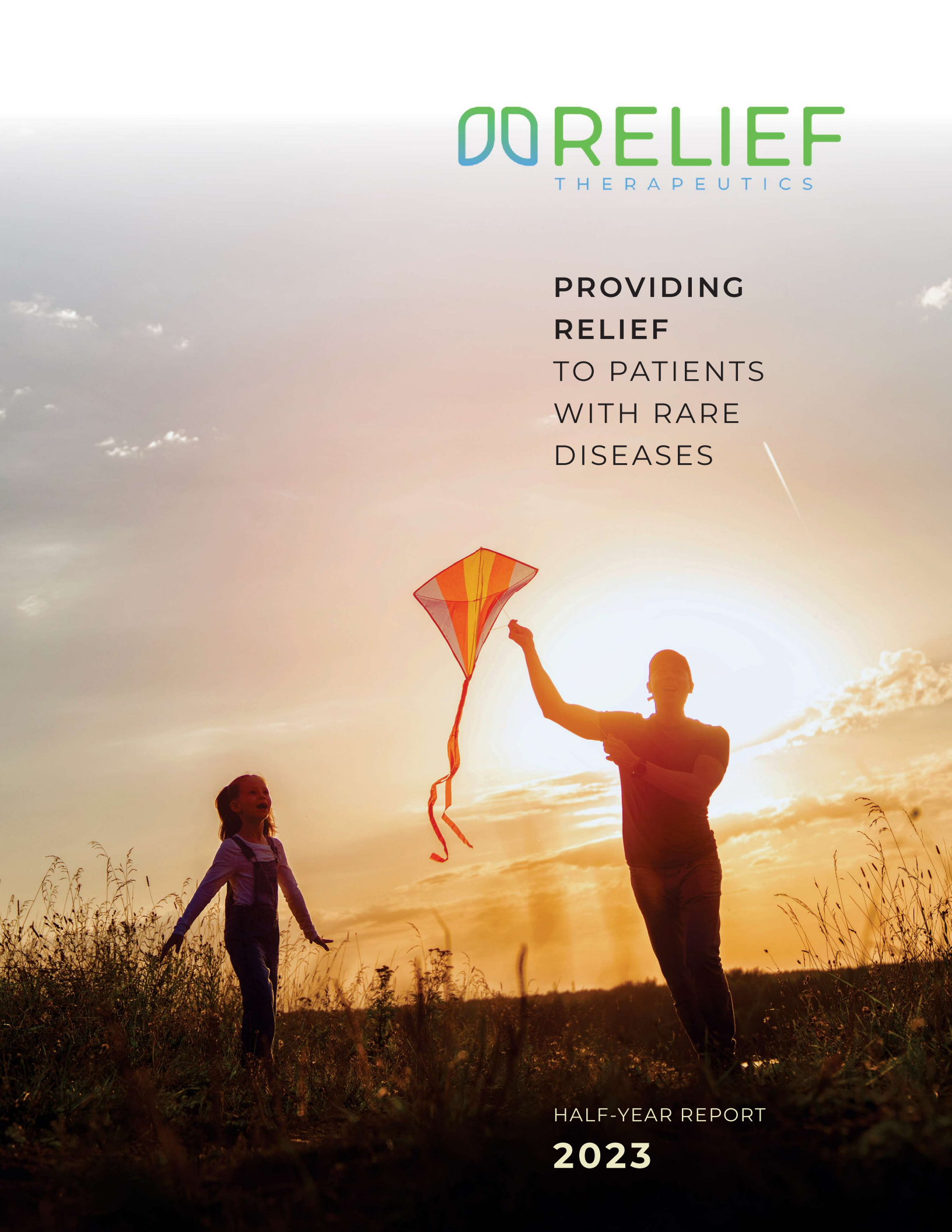
RELIEF
THERAPEUTICS

PROVIDING RELIEF TO PATIENTS WITH RARE DISEASES



HALF-YEAR REPORT

2023

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2023 TO DATE HIGHLIGHTS

JANUARY

Relief Therapeutics announced institutional review board (IRB) approval for the protocol of an IIT to evaluate **RLF-TD011**, a patent-protected hypochlorous acid topical spray, as an adjunctive treatment for patients diagnosed with cutaneous t-cell lymphoma (CTCL).

FEBRUARY

Relief Therapeutics provided an update on its financing strategy, including the Company's decision to voluntarily withdraw its Registration Statement on Form F-1 initially filed with the SEC on August 23, 2022, in order to explore alternative options for financing.

Relief Therapeutics announced the first three patients were enrolled in a proof-of-concept IIT to evaluate **RLF-TD011**, a self-administered, sprayable solution enabling targeted application while avoiding skin contact and cross-contamination, as a potential treatment for epidermolysis bullosa (EB).

Relief Therapeutics recognized Rare Disease Day 2023 and announced the U.S. availability of new **PKU GOLIKE BARS®**, a medical food for the dietary management of PKU.

MARCH

Acer provided an update on the commercial launch activities for **OLPRUVA™** (sodium phenylbutyrate; ACER-001) for oral suspension, noting progress with the build out of its commercial and medical affairs teams to support the U.S. commercial launch in Q2 2023, and drug availability anticipated by early July 2023.

Relief Therapeutics announced the availability of new **PKU GOLIKE BAR®** flavors in Europe.

Relief Therapeutics announced the results of pre-clinical research evaluating the metabolic impact of **PKU GOLIKE®** on nitrogen balance, muscle strength and glucose will be presented in a poster session at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting.

Acer announced results from a survey of UCD healthcare providers identifying preferred UCD treatment attributes that were presented at SIMD. The data showed taste and odor are the most important attributes when considering treatment options and adherence.

APRIL

World-renowned gene therapy pioneer Guangping Gao, Ph.D. was appointed as the chair of Relief Therapeutics' newly formed scientific advisory board (SAB).

Relief Therapeutics announced an executive leadership team change with the departure of Nermeen Varawalla, M.D., Ph.D., chief medical officer.

Relief Therapeutics announced full-year 2022 financial results and provided a corporate update.

Relief Therapeutics announced positive 12-month stability data for inhaled and intravenous preparations of **RLF-100®**.

Relief Therapeutics announced results of its extraordinary meeting of shareholders.

MAY

Acer Therapeutics announced that the **OLPRUVA™** commercial launch was progressing ahead of schedule.

Relief Therapeutics announced the implementation timeline for a reverse split of its ordinary shares.

Relief Therapeutics announced Swissmedic approval and operation of a new, good manufacturing practice-compliant laboratory.

JUNE

Relief Therapeutics announced results of the annual general meeting of shareholders.

Relief Therapeutics announced closing of a CHF 5 million private placement.

Relief Therapeutics and World Orphan Drug Alliance announced an exclusive, long-term distribution agreement to introduce **PKU GOLIKE®** in the Middle East.

JULY

Relief Therapeutics announced extension of distribution agreement for **PKU GOLIKE®** in the U.S. with Pentec Health. Subsequently, Pentec Health announced its acquisition of ZOIA Pharma.

AUGUST

Relief Therapeutics and Acer Therapeutics announced a new exclusive definitive licensing agreement for the development and commercialization of **OLPRUVA™** for the treatment of certain UCDs and other potential indications, superseding the March 2021 collaboration and license agreement between the companies. Subsequently, Acer announced that it was being acquired by Zevra Therapeutics, Inc.

SEPTEMBER

Relief Therapeutics announced in this report that it has discontinued the position of Head of Genetic Medicine, suspended its development activities in this domain, and dissolved the recently formed scientific advisory board. This decision falls within the Company's strategy to prioritize the use of its resources over the near term, as further discussed throughout this report, including in the Corporate Strategy Update in the Management's discussion and analysis of financial condition and results of operations.

LETTER TO OUR SHAREHOLDERS

DEAR SHAREHOLDERS,

The first half of 2023 has been challenging for Relief, as it has also been for others of our peers in the biopharmaceutical and biotechnology space. New financing, including equity, debt, non-dilutive or other forms, has been much more difficult to obtain than in recent years. Nevertheless, I want to reflect on several notable accomplishments for the Company in the first half of this year including our recent successful efforts to raise financing on favorable terms, as well as provide you with insights on where I see the future of Relief and why I am so enthusiastic about our business.

We continue to be a fully integrated, international biopharmaceutical enterprise with both an unlevered, clean balance sheet and a disciplined, cost-effective, capital-efficient approach to drug development. Our primary focus remains on rare diseases, specifically those in the metabolic, dermatological, and respiratory areas with unmet medical needs. This targeted approach enables us to maintain a lean organization, led by a seasoned executive team. We have also taken steps to streamline the Company and continue to focus on optimizing the cost-effectiveness of our operations in the context of the current financing environment. Considering available financial and operational resources, I am confident we are well positioned to effectively implement and realize our strategic initiatives and objectives over the coming periods.

KEY ADVANCEMENTS IN THE FIRST HALF OF 2023

In June 2023, we concluded a CHF 5 million PIPE financing with a well-known healthcare-focused institutional investor on favorable terms. In August 2023, we re-structured our collaboration with Acer Therapeutics, Inc. (Acer). Under the terms of the revised agreement, Acer will retain development and commercialization rights for OLPRUVA™ for the treatment of urea cycle disorders (UCDs) and any potential additional indications in the U.S. and other countries worldwide, excluding geographical Europe. Acer has provided Relief with a non-contingent USD 10 million upfront cash payment and shall provide an additional non-contingent USD 1.5 million cash payment in August 2024. Relief will also receive a 10 percent continuing royalty calculated on the net sales of OLPRUVA™ in the Acer territory up to a cumulative amount of USD 45 million. At the same time, Relief will retain development and commercialization rights for OLPRUVA™ in geographical Europe. We expect that the transition from a profit-based to a revenue-based royalty stream model will deliver earlier returns and provide enhanced predictability to Relief. In addition, Acer continues to make crucial progress in securing market access and reimbursement for OLPRUVA™ with U.S. payers. Subsequent to the restructuring

of our agreement with Acer on OLPRUVA™, Acer announced that it was being acquired by Zevra Therapeutics, Inc. (Zevra). We believe that this acquisition is likely to foster the launch of OLPRUVA™ in the U.S. and the continued development of the drug across new indications, considering Zevra's expertise and track record.

We further strengthened our intellectual property for the PKU GOLIKE® line of products. Our PKU GOLIKE products are the first prolonged-release, amino acid food for special medical purposes (FSMPs), developed using our Physiomimic Technology™ drug delivery platform, for the dietary management of phenylketonuria (PKU). PKU GOLIKE has been available in Europe since 2018. Then in late October 2022, with Pentec Health Inc., a leading national distributor in place, our newly assembled commercial team initiated the U.S. launch. Recently, Pentec acquired another distributor, ZOIA Pharma, which will broaden our reach into commercial payors and greatly improve reimbursement capabilities for GOLIKE patients and their families.

Our PKU GOLIKE BAR® product, which became available this year in two flavors in the U.S. and Europe, has been well received as an exciting new addition to the limited existing options for PKU patients. In the U.S., we continue to make significant progress, meeting with new dietitians, sending out more samples and converting sample users to sustained therapy users due in no small part to our successes in obtaining reimbursement with an increasing number of state-based reimbursement agencies and private payers. I have accompanied members of our U.S. sales team to meet with patients, their parents and registered dietitians. I am very pleased to see their reaction when sampling our products as they learn and discover the variety that PKU GOLIKE® brings to their dietary options. We are excited to continue our work with the PKU community and add more flavors and other forms of PKU GOLIKE®, including savory products such as crackers and biscuits that are currently in late-stage development. In June 2023, we announced an exclusive, long-term, distribution agreement with the World Orphan Disease Alliance (WODA) to introduce PKU GOLIKE® in the Middle East region.

Our development of a novel dosage form of an already FDA-approved prescription drug for the treatment of PKU is ongoing. This improved product, codenamed RLF-OD032, is expected to increase patient acceptance and compliance as well as enable easier, self or caregiver administered metered dosing and dispensing. We are expecting to start a pilot clinical study in Q1 2024 and anticipate filing for FDA approval in Q1 – Q2 2025 via a 505(b)(2) NDA for an anticipated commercial launch in Q4 2025 – Q1 2026. In December 2022, we and our collaboration partner Acer announced the U.S. Food and Drug Administration (FDA) approval of OLPRUVA™ for oral suspension for the long-term management of patients with certain UCDs. In Q3 2023, OLPRUVA™ became available to patients in the U.S. with a strategy to price the treatment competitively against currently available products.

We also made several advancements in our rare pulmonary disease program in the first half of 2023. In April 2023, we announced twelve-month stability data for our new formulation of RLF 100® which is shelf-stable at temperatures suitable for shipping and long-term storage, thus, potentially having significant clinical and commercial value. We have filed a new provisional patent application based on those results. Our objective is to establish our proprietary and patent-protected formulation of aviptadil acetate, RLF-100®, as the standard of care for the prevention and treatment of respiratory failure and its complications in both the acute intensive care and chronic ambulatory settings. We continue exploring the development of RLF-100® for the treatment of non-COVID-19-related ARDS, checkpoint inhibitor-induced pneumonitis (CIP), chronic berylliosis and pulmonary sarcoidosis, an indication for which we received an orphan drug designation (ODD) in August of 2020.

Finally, we continue the development of RLF-TD011, a patent-protected hypochlorous acid topical spray developed with our TEHCLO Nanotechnology™ platform in rare dermatological conditions, with an emphasis on connective tissue disorders. Our efforts are primarily focused on epidermolysis bullosa (EB), a devastating rare, inherited skin disease characterized by widely distributed, painful, chronic wounds that easily become infected, resulting in an elevated risk of sepsis and death. There are no cures or currently available therapies for EB. RLF-TD011 was granted ODD by the FDA for the treatment of EB. We are progressing with our proof-of-concept, investigator-initiated trial (IIT) at Northwestern University to evaluate RLF-TD011 as a treatment for EB. Results of this study are expected sometime between Q4 2023 and Q1 2024 depending on the enrollment and treatment pace.

Our existing cash reserves of approximately USD 20.5 million as of August 31, 2023, and projected revenue are expected to provide Relief with a cash runway well into 2025. Our focus is directed on the following:

- Advancing our pipeline: we are excited about the Q3 2023 U.S. launch of OLPRUVA™ for the treatment of UCDs and the anticipated development of OLPRUVA™ for the treatment of maple syrup urine disease (MSUD). We are evaluating filing a marketing authorization application for OLPRUVA™ for the treatment of UCDs in Europe. In addition, we are moving forward with the development of RLF-OD032 for the treatment of PKU. We also intend to advance our RLF-100® and RLF-TD011 programs, which we believe have significant potential in their respective indication fields.

- Maximizing value: we continue the commercial roll out of PKU GOLIKE in the U.S. and expand the PKU GOLIKE line of product offerings. We are actively working on maintaining and developing economic benefits from our legacy products to support our operations. We are also exploring new opportunities to leverage our drug delivery platform technologies.

- Expanding our portfolio: we continue to pursue a strategy to diversify our pipeline and bring assets to patients as quickly as possible through the ongoing evaluation of potential in-licensing opportunities that fit our profile and seeking partnerships with, or acquisitions of, companies with late-stage clinical molecules with a strong human safety profile, allowing for relatively short, capital-efficient clinical trials with clear endpoints.

I thank our employees and the many other people who make our work possible including our partners and collaborators, researchers, physicians, geneticists, dieticians, nutritionists and, especially, patients and their families. I also welcome our newest institutional and individual shareholders to the Relief family, and extend my thanks to our long-term shareholders for their continued support and trust in our vision. We are confident that our continued progress will enable us to deliver significant value to our shareholders in the long term. We remain united in our commitment to provide much needed relief to those suffering from rare and debilitating disorders. Thank you.

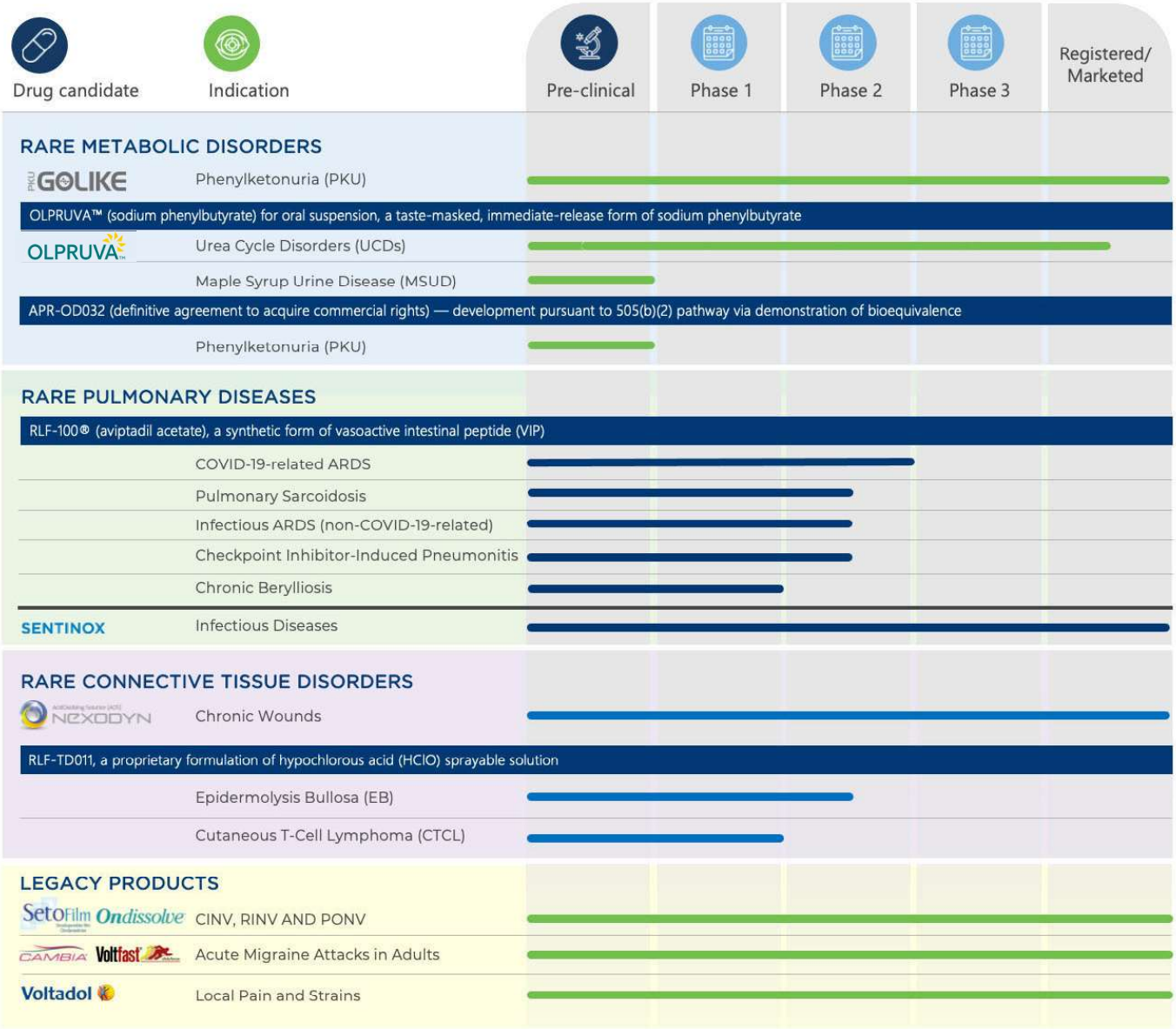
Sincerely,

Jack Weinstein
Chief Executive Officer
Relief Therapeutics

PORTFOLIO & PIPELINE

PORTFOLIO & PIPELINE

Relief's clinical development program currently focuses on pulmonary diseases and rare genetic, metabolic, and connective tissue disorders, with particular emphasis on conditions with dermatological manifestations. The diversified pipeline consists of differentiated assets that have the potential to effectively address significant unmet medical needs. In addition, the Company is commercializing several legacy products via licensing and distribution partners.



DRUG DELIVERY PLATFORM TECHNOLOGIES

Our drug delivery platform technologies enable us to optimize the therapeutic potential of established products with proven efficacy, known safety profiles or where proof-of-concept exists. These platforms have utility for development in other specialty or rare disease therapeutic areas, partnerships and out-licensing.

TEHCLO NANOTECHNOLOGY™

Our TEHCLO Nanotechnology™ platform consists of our proprietary, globally patent-protected electrode with nanocoating, the method for preparing and making highly stable aqueous solutions and our device for the electrolytic treatment of a fluid. The TEHCLO technology was used to develop RLF-TD011, Nexodyn and some of our legacy products.

Our TEHCLO intellectual property portfolio consists of four patent families. The first three families include 103 granted patents worldwide directed to systems and methods for generating APR's hypochlorous acid solution, compositions comprising APR's hypochlorous acid solution and methods for treating ocular disorders. These patents expire between October 2026 and June 2030, exclusive of any patent term adjustments or extensions, or any form of potential exclusivity. The fourth patent family will cover certain medical uses and, if granted, will expire no earlier than July 2040.

PHYSIOMIMIC TECHNOLOGY™

Our Physiomimic Technology™, used in the PKU GOLIKE® product line, is our globally patented, proprietary method to engineer amino acids to modify their release and absorption to mimic the physiological absorption of natural dietary proteins. This technology provides extended-release and taste and odor masking of the amino acids.

Our PKU GOLIKE® intellectual property portfolio consists of two patent families including 32 pending applications and 51 granted patents worldwide. Patents resulting from these families, if granted, will expire no earlier than 2036 and 2038, respectively, exclusive of any patent term adjustments or extensions, or any form of potential exclusivity.

RARE METABOLIC DISORDERS

PKU GOLIKE® FOR PHENYLKETONURIA

The PKU GOLIKE® line of products comprises phenylalanine-free foods for special medical purposes (FSMPs) for the dietary management of phenylketonuria (PKU) in both children and adults. Engineered with the Physiomimic Technology™, the Company's proprietary, patent-protected, drug delivery platform. PKU GOLIKE is the first prolonged-release amino acid mix product that mirrors the absorption profile of natural dietary proteins while offering effective taste and odor masking.

PKU is a rare, inherited disorder affecting more than 450'000 patients worldwide.[1] 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.[2]

Living with PKU requires a very strict, life-long, low protein diet and precise careful management. People living with PKU do not have the ability to metabolize Phe, which is found in most foods, and they require daily and high quantity supplementation of amino acid based FSMPs to prevent protein deficiency and optimize metabolic control. Currently available FSMPs may 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.[3]

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 is 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 are uniquely differentiated, offering improved metabolic management and the opportunity for better compliance for PKU patients of all age groups.

PKU GOLIKE is currently sold by a direct sales and marketing organization in the U.S., Germany, Italy, Switzerland, and Austria, and is marketed in the UK, Spain, Portugal, Israel and certain Middle Eastern countries by local distributors. PKU GOLIKE is available by prescription only and is considered a life-saving option for PKU patients.

PKU GOLIKE products have been commercially available in Europe since 2018. Relief launched the PKU GOLIKE family of products in the U.S. in late October 2022, with its recently assembled commercial infrastructure and team. In early 2023, the Company announced the U.S. and EU availability of the new PKU GOLIKE BARs in red fruit and tropical fruit flavors. These bars contain only natural fruits and have no added artificial flavors or colorants. More flavors of the bars and other forms of PKU GOLIKE, including savory options such as crackers and biscuits, are currently in late-stage development.

On August 23, 2022, APR was issued U.S. patent number 11,419,837, which covers certain formulations of PKU GOLIKE and supplements the PKU GOLIKE intellectual property portfolio, which includes U.S. patent number 10,500,180, which was issued on December 10, 2019. The patents will expire no earlier than September 27, 2036.

In March 2023, the Company presented the findings from pre-clinical research evaluating the metabolic impact of PKU GOLIKE on nitrogen balance, muscle strength and glucose in a poster session at the Society for Inherited Metabolic Disorders (SIMD) 44th Annual Meeting. The poster summarized 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 the amino acids, 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. 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. Detailed results from this study are available on the Relief website.

Relief plans to expand the PKU GOLIKE commercial infrastructure beyond the current countries to increase and accelerate future growth. This will be supported by newer formulations of PKU GOLIKE.

OLPRUVA™ (SODIUM PHENYLBUTYRATE, ACER-001) FOR ORAL SUSPENSION

In March 2021, Relief signed a collaboration and license agreement with Acer Therapeutics Inc. (Acer) 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). In August 2023, Relief and Acer announced a new exclusive definitive licensing agreement for the development and commercialization of OLPRUVA™ for the treatment of certain UCDs and other potential indications. This agreement supersedes the March 2021 collaboration and license agreement between the companies.

ACER-001 is a proprietary, coated powder formulation of sodium phenylbutyrate (NaPB) designed to be both taste-masked and immediate release. ACER-001 was developed using a multiple coating process, and the microparticles consist of an inert core center, a coated layer of active drug and a final taste-masking coating that quickly dissolves in the stomach to avoid a bitter taste while still allowing for rapid systemic absorption. ACER-001's taste-masked formulation is designed to improve the palatability of NaPB and could make it a compelling alternative to existing NaPB-based treatments, as the unpleasant taste associated with NaPB is cited as a major impediment to patient compliance with those treatments. Additionally, bioequivalence trials have shown ACER-001 to have similar relative bioavailability to BUPHENYL® under both fasted and fed conditions, along with significantly lower projected pricing compared to RAVICTI®.[4]

On December 22, 2022, the U.S. Food and Drug Administration (FDA) approved ACER-001 under the brand name OLPRUVA™ (sodium phenylbutyrate for oral suspension) as a prescription medicine for use with certain therapy, including changes in diet, for the long-term management of adults and children weighing 44 pounds (20 kg) or greater and with a body surface area (BSA) of 1.2 m^2 or greater, with UCDs, involving deficiencies of carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC), or argininosuccinic acid synthetase (AS). OLPRUVA™ is not used to treat rapid increase of ammonia in the blood (acute hyperammonemia), which can be life-threatening and requires emergency medical treatment.[5] Please see Important Safety Information and full Prescribing Information, including Patient Information.

On August 14, 2023, Acer announced that OLPRUVA™ kits were commercially available in all dosage strengths. Acer also announced its intention to add commercial and medical affairs resources, and the introduction of its patient support service called OLPRUVA™ Navigator.

OLPRUVA™ received FDA approval under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (FDCA), a regulatory pathway that allows applicants to rely, at least in part, on third-party data for approval. In Acer's new drug application (NDA), the Company cited pre-clinical and clinical safety and efficacy data from the reference listed drug (RLD), BUPHENYL® powder, which is approved as adjunctive therapy in the chronic management of patients with UCDs involving deficiencies of CPS, OTC or AS. In Acer's NDA, the Company also provided additional data including studies that evaluated the bioavailability and bioequivalence of OLPRUVA™ compared to BUPHENYL® powder. The data from these studies, presented at the Society for Inherited Metabolic Disorders (SIMD) Annual Meeting in April 2022 and the Genetic Metabolic Dieticians International (GMDI) Conference in May 2022, showed that OLPRUVA™ was bioequivalent to BUPHENYL® powder.[6,7]

Acer maintains its own intellectual property portfolio. Acer's patent portfolio for ACER-001 consists of three patent families. The first family includes 41 granted patents worldwide directed towards novel sodium phenylbutyrate particle formulations and methods of use. These patents have an expiration date of October 2036, exclusive of any patent term adjustments or extensions, or any form of potential exclusivity. If granted, additional patents would expire no earlier than October 2036. Acer's patent portfolio further includes PCT/US2021/040760 and PCT/US2022/040082. Patents granted from applications claiming priority to PCT/US2021/040760 will expire in July 2041, excluding any patent term adjustments or extensions, or any form of potential exclusivity. Patents granted from applications claiming priority to PCT/US2022/040082 will expire in April 2042, excluding any patent term adjustments or extensions or any form of potential exclusivity.

OLPRUVA IN UREA CYCLE DISORDERS (UCDS)

Urea cycle disorders (UCDs) are a group of rare, genetic disorders that can cause harmful ammonia to build up in the blood, potentially resulting in brain damage and neurocognitive impairments, if ammonia levels are not controlled. Any increase in ammonia over time is serious.[8] Therefore, it is important to adhere to any dietary protein restrictions and have alternative medication options to help control ammonia levels.

UCDs are a group of disorders caused by genetic mutations that result in a deficiency in any one of the six enzymes that catalyze the urea cycle, which can lead to an excess accumulation of ammonia in the bloodstream, a condition known as hyperammonemia. Acute hyperammonemia can cause lethargy, somnolence, coma and multi-organ failure. Chronic hyperammonemia can lead to headaches, confusion, lethargy, failure to thrive, behavioral changes and learning and cognitive deficits. Common symptoms of both acute and chronic hyperammonemia also include seizures and psychiatric symptoms.

The current treatment of UCDs consists of dietary management to limit ammonia production in conjunction with medications that provide alternative pathways for removing ammonia from the bloodstream. Some patients may also require individual branched-chain amino acid supplementation. Current medical treatments for UCDs include nitrogen scavengers, RAVICTI® and BUPHENYL®, in which the active pharmaceutical ingredients are glycerol phenylbutyrate (GPB) and NaPB, respectively. Their role is to provide an alternative way to excrete excessive nitrogen. According to a 2016 study by Shchelochkov et al., published in *Molecular Genetics and Metabolism Reports*, while nitrogen scavenging medications have been shown to be effective in helping to manage ammonia levels in some patients with UCDs, non-compliance with treatment is common. Reasons referenced for non-compliance associated with some available medications include unpleasant taste, the frequency with which medication must be taken, the number of pills and the high cost of the medication.

OLPRUVA™ for oral suspension is a proprietary and novel formulation that leverages the well-established efficacy of sodium phenylbutyrate in a novel, innovative dual-coating formulation designed for improved convenience and palatability[9] and will be available in single-dose envelopes, which may help people living with UCD to manage their condition.

In March 2023, Acer presented survey results at the 44th Annual Meeting of the Society for Inherited Metabolic Disorders. Data from a survey of UCD healthcare providers showed that optimizing nitrogen-binding medications for UCD treatment to facilitate and encourage increased patient adherence through masking taste/odor and/or enhancing other aspects of the patient experience may support improved outcomes in UCDs.

In accordance with Relief's exclusive license agreement with Acer, we intend to submit a marketing authorization application for approval of OLPRUVA for the treatment of UCDs in the UK and EU, subject to the performance of certain bridging studies necessary to extend the approval received in the United States into other countries of Europe where the access and reimbursement landscape is more favorable.

OLPRUVA IN MAPLE SYRUP URINE DISEASE (MSUD)

Maple syrup urine disease (MSUD) is a rare inherited disorder caused by defects in the mitochondrial branched-chain ketoacid dehydrogenase complex, which results in elevated blood levels of the branched-chain amino acids (BCAA), leucine, valine and isoleucine, as well as the associated branched-chain ketoacids (BCKA) in a patient's blood. Left untreated, this can result in neurological damage, mental disability, coma or death. There are currently no approved pharmacologic therapies in the U.S. or Europe for MSUD. Treatment of MSUD consists primarily of a severely restricted diet to limit the intake of BCAA, with aggressive medical interventions when blood levels of BCAA or BCKA become elevated.[10]

NaPB is approved for people with UCDs to control their ammonia levels in conjunction with a restricted diet. People with UCDs who are treated with NaPB have been found to have a BCAA deficiency, despite adequate dietary protein intake. Based on this clinical observation, NaPB is being explored as a treatment to lower BCAA and their corresponding BCKA in patients with MSUD.[11]

The FDA and EMA have granted orphan drug designation (ODD) to ACER-001 (OLPRUVA) for the MSUD indication.

Acer has been issued several patents protecting the usage of and composition of ACER-001. The recent approval of U.S. patent 11,202,767 covers methods of use claims related to ACER-001's multi-particulate dosage formulation for oral administration for the potential treatment of UCDs and MSUD and supplements previous issuance of U.S. patent 11,154,521 which covers pharmaceutical composition claims of ACER-001. Both patents have an expiration date in 2036. In addition, the China National Intellectual Property Administration (CNIPA) has issued Electronic Patent Certificate ZL202122004991.9 for the Utility Model patent directed to ACER-001. Specifically, the patent covers dosage form claims related to ACER-001's polymer coated formulation for oral administration as a potential treatment for UCDs and MSUD. This patent has an expiration date of August 24, 2031, and provides protection for ACER-001 in the context of potential commercialization in China. Acer has submitted an investigational new drug (IND) application to the FDA to evaluate the safety and efficacy of OLPRUVA for the potential treatment of MSUD. Acer expects to start clinical studies in MSUD, subject to available capital. It is anticipated that the data from these studies will be suitable for product registration in the U.S. and Europe and Relief expects to use such data to start the registration process in Europe.

RLF-OD032 IN PKU

In July 2022, Relief entered into a definitive agreement with the UK-based company Meta Healthcare Ltd. (Meta). Pursuant to the agreement, the Company has acquired the worldwide rights, title and interest, except in the UK, for a novel dosage form of a prescription drug already approved by the FDA and intended for the treatment of patients with phenylketonuria (PKU). This improved product is expected to increase patient acceptance and compliance as well as enable easier, self or caregiver administered metered dosing and dispensing.

According to the terms of the agreement, Meta transferred to Relief all data, know-how, as well as any intellectual property as developed or generated so far by Meta. Relief shall only be responsible for funding the remaining development work as well as for filing and prosecuting an NDA in all countries worldwide except for the UK where Relief shall grant a license back to Meta, enabling Meta to directly promote and commercialize the product in such country. Other than the initial acquisition payment and low double-digit royalty payments on net profit of the product in the various countries, Relief shall be under no obligation to fund or pay any other amount to Meta.

Relief expects to start the pilot clinical study in Q1 2024 and anticipate filing for FDA approval in Q1 – Q2 2025 via a 505(b)(2) NDA for an anticipated commercial launch in Q4 2025 – Q1 2026.

REFERENCES

[1] 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.

[2] 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.

[3] 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.

[4] RAVICTI® and BUPHENYL® are registered trademarks owned by or licensed to Horizon Therapeutics plc.

[5] OLPRUVA™ (sodium phenylbutyrate) for oral suspension. Prescribing information. Newton, MA: Acer Therapeutics Inc.

[6] Steiner R, et al. The Pharmacokinetics of Taste-Masked Sodium Phenylbutyrate (ACER-001) for the Treatment of Urea Cycle Disorders Under Fasting and Fed Conditions in Healthy Volunteers. SIMD April 2022.

[7] Cederbaum S, et al. Taste-Masked Coating of Sodium Phenylbutyrate (ACER-001) Improves the Palatability of Sodium Phenylbutyrate for Treatment of Urea Cycle Disorders. GMDI May 2022.

[8] Ah Mew N, et al. Urea cycle disorders overview [updated June 22, 2017]. In: Adam MP, Ardinger HH, Pagon RA, et al, eds. GeneReviews® [Internet]. University of Washington; 1993-2022. Accessed March 20, 2022.

[9] Cederbaum S, et al. Taste-Masked Coating of Sodium Phenylbutyrate (ACER-001) Improves the Palatability of Sodium Phenylbutyrate for Treatment of Urea Cycle Disorders. GMDI May 2022.

[10] Blackburn PR, Gass JM, Vairo FPE, et al. Maple syrup urine disease: mechanisms and management. *Appl Clin Genet.* 2017; 10:57-66. Published 2017 Sep 6. doi:10.2147/TACG.S125962.

[11] Brunetti-Pierri N, Lanpher B, Erez A, et al. Phenylbutyrate therapy for maple syrup urine disease. *Hum Mol Genet.* 2011; 20(4):631-640. doi:10.1093/hmg/ddq507

RLF-100® (AVIPTADIL ACETATE)

Aviptadil is a synthetic form of vasoactive intestinal peptide (VIP) consisting of 28 amino acids, which was first discovered in 1970. Although initially identified in the intestinal tract, human VIP is now known to be produced throughout the body and to be primarily concentrated in the lungs. VIP has shown a multimodal mechanism of action: decrease of inflammatory cytokines release leading to prevention of cytokine storm syndrome and viral replication, immunomodulating effect, vasodilating and bronchodilating effects and prevention of surfactant depletion. 70 percent of VIP in the body is bound to a less common type of cell in the lung, the alveolar epithelial type II (AT2) cell, which is critical to the absorption of oxygen into the body.

Aviptadil has a 20-year history of safe use in humans. For example, a combination of aviptadil with phentolamine is approved for the treatment of erectile dysfunction by intra-cavernous injections in countries outside the U.S.

It is our objective to establish our proprietary and patent-protected formulation of aviptadil, RLF-100® as the standard of care for the prevention and treatment of respiratory failure and its complications in both the acute intensive care and chronic ambulatory settings.

Since RLF-100's mechanism of action is not restricted to the protection of AT2 cells, we believe that its beneficial effects could extend to other types of acute lung injury (ALI) as supported by pre-clinical and preliminary clinical data in sepsis-induced ALI.

In April 2023, we announced twelve-month stability data for our new formulation of RLF-100 which is shelf-stable at all temperatures tested that are suitable for shipping and long-term storage, thus, potentially having significant clinical and commercial value. We have filed a new provisional patent application based on those results.

We continue exploring the development of RLF-100 for the treatment of COVID-19 and non-COVID-19-related ARDS, checkpoint inhibitor-induced pneumonitis (CIP), chronic berylliosis and pulmonary sarcoidosis, an indication for which we received ODD in August of 2020.

AVIPTADIL ACETATE IN COVID-19-RELATED ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

In March 2020, at the beginning of the first wave of the pandemic in the U.S., our former collaboration partner, NeuroRx Inc. (NeuroRx), submitted an IND application to the FDA for a Phase 2b/3 trial of intravenous (IV) aviptadil for the treatment of patients with critical COVID-19 respiratory failure. Within 24 hours, the FDA issued a "Study May Proceed" letter and the first patients were treated in April 2020 at Thomas Jefferson University Hospital in Philadelphia.

In late 2020, a Phase 2b/3 clinical study with aviptadil IV in patients with COVID-19-induced acute respiratory distress syndrome (ARDS) was completed in the U.S. by NeuroRx. In its press release reporting those results, NeuroRx announced that across all patients and sites, the aviptadil IV treated cohort met the primary endpoint for successful recovery from respiratory failure at days 28 (p=0.14) and 60 (p=0.13) and had a meaningful survival benefit after controlling for ventilation status and clinical site. However, they also reported that the trial did not demonstrate a statistically significant difference on the study's primary endpoint without statistical adjustment for these pre-specified covariates. Based on these findings, NeuroRx announced on June 1, 2021, the company applied to the FDA for Emergency Use Authorization (EUA) for aviptadil IV for the treatment of acute respiratory failure due to critical COVID-19 and that it planned to submit an NDA with the FDA. On November 5, 2021, NeuroRx announced the FDA declined its application for EUA of aviptadil IV for the treatment of acute respiratory failure due to critical COVID-19. Subsequent applications filed by NeuroRx with the FDA seeking EUA for more limited use of the product for the treatment of COVID-19 and for breakthrough therapy designation for the product were also denied in the first half of 2022.

In March 2021, NeuroRx announced that aviptadil IV was included in a National Institute of Health (NIH)-sponsored Phase 3 ACTIV-3b/TESICO clinical trial in severely ill patients with COVID-19. In May 2022, Relief learned trial was discontinued by its Data Safety Monitoring Board (DSMB) based on futility.

In December 2022, NeuroRx transferred to Relief all of the assets it used in the NRx aviptadil development program, including the regulatory filings, patent applications, clinical data, and the formulation of the aviptadil product it was previously developing. Relief now has the exclusive right and control going forward and the obligation to use commercially reasonable efforts to develop and commercialize an aviptadil product. NeuroRx has agreed not to compete in the development of an aviptadil product in the future.

While regulatory approval for aviptadil IV to treat COVID-19-induced ARDS has not been granted in the U.S., an unrelated pharmaceutical company received approval for this indication in India in early 2022 for their formulation of aviptadil, thereby substantiating Relief's original hypothesis.

Inhaled RLF-100® is being evaluated in an investigator-initiated trial at a site in Switzerland for the treatment of ARDS associated with COVID-19 (Leuppi/NCT04536350). While the study is in an advanced stage of recruitment, changing disease patterns have hindered the completion of patient recruitment. The lead investigator has reported that top-line data is now expected in the first quarter of 2024, subject to successful completion of patient enrolment, which remains challenging.

RLF-100® ADDITIONAL OPPORTUNITIES

RLF-100® is under development in both inhaled and IV formulations for other acute and chronic lung diseases, including as a potential treatment of pulmonary sarcoidosis, non-COVID-19-related acute respiratory distress syndrome (ARDS), checkpoint inhibitor-induced pneumonitis (CIP) and chronic berylliosis.

PULMONARY SARCOIDOSIS

Sarcoidosis is an inflammatory disease characterized by the formation of granulomas—tiny clumps of inflammatory cells that can develop in any part of the body. When the disease occurs in the lungs, it is called pulmonary sarcoidosis and is a form of interstitial lung disease (ILD) which are a group of immune-mediated disorders that cause progressive fibrosis of the lung interstitium (the extravascular and extracellular space between cells in tissue). The granulomas disrupt the intake of oxygen and can cause scarring on the lungs, preventing the lungs stretching fully, and therefore limiting their capacity. The prognosis for patients with pulmonary sarcoidosis ranges from benign and self-limiting to chronic, debilitating disease and death. Despite increasing advances in research, pulmonary sarcoidosis remains difficult to diagnose with limited treatment options to manage symptoms and no known cure. According to the Foundation for Sarcoidosis Research, approximately 200'000 Americans live with pulmonary sarcoidosis. Relief was granted ODD by the FDA for inhaled RLF-100 for the treatment of pulmonary sarcoidosis in August 2021.

CHECKPOINT INHIBITOR-INDUCED PNEUMONITIS (CIP)

Checkpoint inhibitor-induced pneumonitis (CIP) is a rare, potentially fatal form of lung inflammation following treatment with immune checkpoint inhibitors (ICIs). ICIs are a type of immune therapy used to treat cancer. CIP can result in cough, dyspnea, fever, chest pain, and in severe cases, lack of oxygen in the lungs (hypoxia) and respiratory distress. The use of inhaled RLF-100 for this indication will be further evaluated to explore whether such use could enhance compliance with chemotherapy and improve outcomes for cancer patients. Relief received a Swiss method-of-use patent protection related to the inhaled formulation of RLF-100 for the potential treatment of CIP extending into at least 2039.

BERYLLIOSIS / CHRONIC BERYLLIUM DISEASE (CBD)

Chronic beryllium disease (CBD) is an orphan lung disease caused by the inhalation of beryllium particles, dust or fumes in the workplace, resulting in severe inflammation of the lungs, coughing and increasing breathlessness (dyspnea). CBD is a clinical phenocopy of sarcoidosis. Currently there are no treatments approved for berylliosis. The *ex-vivo* effect of RLF-100 on mononuclear cells in the setting of CBD is currently being evaluated. Together with the results from the Phase 2b sarcoidosis trial, these results would justify the therapeutic use of inhaled RLF-100 in CBD, providing a rationale for the clinical trial design in this indication.

NON-COVID-19-RELATED, INFECTIOUS ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

Infectious acute respiratory distress syndrome (ARDS) is a potentially life-threatening condition in which the lungs become severely inflamed, leading to buildup of fluid in the lungs, preventing oxygen from getting to the bloodstream and the rest of the body. Infectious ARDS results from an injury or an infection (such as pneumonia, severe flu, sepsis, etc.) of the air sacs in the lung. Plans for clinical trials of RLF-100 for the treatment of infectious ARDS are in development.

SENTINOX

Sentinox, is a novel, acid-oxidizing solution containing hypochlorous acid in a nasal spray formulation that was developed by APR. Sentinox was certified in Europe on February 16, 2021, as a Class III medical device (certificate number EPT 0477.MDD21/4200.1). Sentinox is intended for irrigation, cleansing and moistening of the nasal cavities and is indicated to reduce the risk of infections caused by bacteria and viruses, including SARS-CoV-2, by lowering the nasal microbial load; symptomatic nasal care; and nasal care in cases of minor lesions/ alterations of the nasal mucosa.

Sentinox was evaluated in a randomized, controlled clinical trial to establish the efficacy and safety of the product in reducing viral load in the upper respiratory airways in recently COVID-19 infected individuals. The results were reported in March 2022. Considering the small sample size and the high variability in the baseline viral load observed within study groups, the primary endpoint was not reached; however, the results suggest the potential efficacy of Sentinox in the reduction of the nasal viral load, negativization and infectivity and confirmed its safety and tolerability. As a result, we initiated a confirmatory, controlled clinical trial in the prevention of viral and bacterial airborne infections in the fourth quarter of 2022. However, due to funding constraints and currently limited market potential given the evolution of the COVID-19 pandemic, we halted research and development activities related to Sentinox in the first half of 2023. Resumption may be implemented upon securing additional funding or collaborative partnerships.

RARE CONNECTIVE TISSUE DISORDERS

NEXODYN®

Nexodyn® acid-oxidizing solution (AOS) is proven to restart healing in chronic wounds by creating an ideal microenvironment to sustain the physiological healing process. A wealth of evidence and real-world experience has consistently shown accelerated wound closure with reduced infection rates and less wound-associated pain.

Nexodyn was developed using APR's proprietary TEHCLO Nanotechnology® and is a highly pure and stabilized hypochlorous acid (HClO >95% of free chlorine species), with acidic pH (2.5 - 3.0) and high reduction-oxidation potential (ORP 1.000 – 1.200 mV). The product is a self-administered sprayable solution with ancillary antimicrobial properties intended for use in the debridement, irrigation, cleansing and moistening of acute and chronic wounds (e.g., diabetic foot ulcers, pressure ulcers and vascular ulcers), post-surgical wounds, burns and other lesions. The product is certified in Europe as a Class III medical device and is certified as a 510(k) medical device in the U.S.

The anti-microbial and anti-inflammatory properties of Nexodyn AOS, along with its tolerability, absence of systemic exposure and convenient contactless delivery for topical applications could make this an attractive treatment candidate for the management of wounds in epidermolysis bullosa (EB), with the potential to be the only product approved for the control of wound infection in this disease, thereby reducing long-term antibiotic use, while assisting wound healing and decreasing wound-related pain, all of which would significantly benefit quality of life in patients with this genetic disorder.

RLF-TD011 IN EPIDERMOLYSIS BULLOSA

RLF-TD011 is a differentiated acid oxidizing solution of hypochlorous acid (HCIO) that combines strong antimicrobial action with anti-inflammatory properties, thereby allowing for infection control, reduction of wound colonization, alleviation of pain and itching and improved wound healing.

Developed with APR's proprietary, patent-protected TEHCLO Nanotechnology®, RLF-TD011 employs an exclusive combination of three physio-chemical properties – high-purity HCIO, hypotonic low pH and high oxidation-reduction potential (ORP), which is believed to support a faster physiological healing of wounds by creating a favorable wound microenvironment. HCIO is well known as a broad-spectrum, fast acting antimicrobial agent, which reinforced by low pH and high ORP contributes to the prevention and treatment of skin infections.

RLF-TD011 is an investigational drug candidate that has the potential for the treatment of wounds in epidermolysis bullosa (EB) as it is a self-administered, sprayable solution enabling targeted application while avoiding skin contact and cross-contamination. EB, also known as "Butterfly Skin," is a group of rare, genetic, life-threatening connective tissue disorders characterized by skin fragility and blistering, which may appear in response to minor injury, even from heat, rubbing or scratching. These widely distributed, painful, chronic wounds can easily become infected, resulting in an elevated risk of sepsis and death. A crucial element of patient management involves rigorous and timely wound care.

Subject to clinical demonstration of efficacy and safety in clinical trials, RLF-TD011 could play an important role in the reduction of inflammation by inhibiting the NF-kB pro-inflammatory pathway and, at the same time, may offer a faster wound healing in EB patients and by reducing the itching and pain linked to infections and inflammation. RLF-TD011 has consistently been shown to accelerate wound closure with reduced infection rates in clinical trials.[1,2,3] In a preliminary clinical trial, EB patients who administered RLF-TD011 demonstrated improvement in skin blistering and tissue repair within just two weeks of treatment, and the product candidate was shown to be well tolerated with a favorable safety profile.

In February 2023, Relief Therapeutics announced the first three patients were enrolled in a proof-of-concept, investigator-initiated study to evaluate RLF-TD011 as a treatment for EB (NCT05533866). Results of this study are expected sometime between Q4 2023 and Q1 2024 depending on the enrollment and treatment pace. The primary aim of this study will be to assess changes in the skin microbiome *(Staphylococcus aureus, Pseudomonas aeruginosa,* commensal organisms*)* before, during and after treatment with RLF-TD011.

RLF-TD011 was granted ODD by the FDA for the treatment of EB, which qualifies the sponsor of the treatment for certain development incentives, including seven-year marketing exclusivity after FDA marketing approval is received. Relief Therapeutics intends to seek qualified infectious disease product (QIDP) designation status for RLF-TD011, which may confer up to an additional five years of market exclusivity regardless of patent protection status. Good Manufacturing Practice (GMP) grade product is being prepared for clinical development under an FDA-authorized IND.

There are four main types of EB, which are classified based on the depth, or level, of blister formation: EB simplex (EBS), junctional EB (JEB), dystrophic EB (DEB) and Kindler syndrome.[4] In severe cases, the blisters may develop into chronic wounds or occur inside the body, such as the lining of the mouth or stomach. Patients with JEB and DEB are at increased risk for serious complications, including aggressive squamous cell carcinoma.[5] The National Epidermolysis Bullosa Registry (NEBR) reports, based on 16 years of data, that the incidence of EB in the U.S. is 19.57 per 1 million live births and the prevalence is 11.07 per 1 million population.[6] Worldwide, EB impacts 500'000 lives.[7] Currently there is no cure or approved

treatments for EB in the U.S. and RLF-TD011 could represent the first product specifically indicated for EB patients that provides a comprehensive solution to prevent or reduce wound colonization and infection. This, along with its anti-inflammatory action, could provide symptom relief and wound healing. The Company estimates the global market opportunity for EB to exceed USD 1.0 billion.

RLF-TD011 IN ONCOLOGY SUPPORTIVE CARE

RLF-TD011 is currently approved in Europe as a Class III medical device for the treatment of skin lesions and toxicities induced by cancer treatments, including anti-epidermal growth factor receptors (anti-EGFR) monoclonal antibodies, such as Cetuximab. The use of anti-EGFR inhibitors causes papulopustular manifestations due to their interference of epidermal growth factor receptor (EGFR) signaling in the skin with a high risk of secondary infections. Following commercial assessment, the company is planning to conduct a follow-on clinical study to renew product approval in Europe as a Class III medical device beyond 2024, when the new EU device regulations will apply. This clinical study will be a multi-center, post-market, double-blinded, placebo-controlled trial to evaluate the efficacy, safety and tolerability of RLF-TD011 in the management of skin lesions and reactions resulting from anti-EGFR monoclonal antibodies and/or radiotherapy treatments in oncology patients.

In January 2023, Relief Therapeutics announced that an independent institutional review board (IRB) approved the protocol of an investigator-initiated trial to evaluate RLF-TD011 as an adjunctive treatment for patients diagnosed with cutaneous T-cell lymphoma (CTCL) (NCT05728879). The study is designed to evaluate the effect of RLF-TD011, on the microbiome of CTCL skin lesions and determine tolerability, symptom improvement, and potential for reducing lesion size and skin disease activity. Relief plans to seek external funding or collaborative partnerships to conduct further evaluation of RLF-TD011 in this arena.

CTCL is a rare, heterogeneous group of non-Hodgkin's lymphomas characterized by abnormal accumulation of malignant t-cells in the skin that can result in the development of rashes, plaques and tumors. Because CTCL is rare and often looks like eczema or another common skin disease, it can be difficult to diagnose.[8] Advanced CTCL lesions harbor *Staphylococcus aureus*, which release toxins that stimulate malignant cells and drive disease progression. This often leads to recurrent skin infections with a high risk for sepsis and death. Treatment of advanced CTCL remains a challenge, with five-year disease-specific survival rates ranging from 70 percent for early stage to 24 percent for advanced disease, with the greatest mortality stemming from bacterial infections.

While there are many types of CTCLs, the most common diagnoses are mycosis fungoides, primary CTCL and primary cutaneous anaplastic large cell lymphoma.[9] The overall incidence rate of CTCL was 8.55 per 1 million with MF being the subtype with the highest incidence, at 5.42 per 1 million.[10] The overall incidence of CTCL in the U.S. and Europe has increased, a reflection of better diagnostic tools and increased awareness among physicians and patients, which has led to improved disease detection.[11]

According to Fortune Business Insights, the North American CTCL therapeutics market size is projected to reach an annual valuation of USD 587.4 million by 2028, registering a 13.6 percent compound annual growth rate (CAGR) in the 2021-2028 period.[12] The market value was estimated to be worth USD 225.9 million in 2020 and reached USD 240.9 million in 2021. The increasing burden of CTCL in the region is slated to increase the demand for novel CTCL therapeutics solutions. Cleveland Clinic reports that more than 3'000 new CTCL patients are diagnosed in the U.S. each year and about 16'000-20'000 individuals suffer from mycosis fungoides, the most common form of CTCL that is linked to skin-localized immune cell stimulation.

REFERENCES

[1] Iacopi E. et al. The Use of a Novel Super-Oxidized Solution on Top of Standard Treatment in the Home Care Management of Postsurgical Lesions of the Diabetic Foot Reduces Reinfections and Shortens Healing Time. *Int J Low Extrem Wounds.* 2018 Dec; 17(4):268-274.

[2] Strohal R, et al. The management of critically colonized and locally infected leg ulcers with an Acid-Oxidizing Solution: A pilot study. *Adv Skin Wound Care* 31(4):163-171, 2018.

[3] Ricci E, et al. The management of chronic ulcers with an AcidOxidizing Solution. *J Wound Care* 25(8):443-50, 2016.

[4] National Institute of Arthritis and Musculoskelatal and Skin Diseases: Epidermolysis Bullosa. Accessed Feb. 10, 2023. https://www.niams.nih.gov/health-topics/epidermolysis-bullosa.

[5] Condorelli AG, Dellambra E, Logli E, Zambruno G, Castiglia D. Epidermolysis Bullosa-Associated Squamous Cell Carcinoma: From Pathogenesis to Therapeutic Perspectives. Int J Mol Sci. 2019 Nov 14;20(22):5707. doi: 10.3390/ijms20225707. PMID: 31739489; PMCID: PMC6888002.

[6] Fine J-D. Epidemiology of Inherited Epidermolysis Bullosa Based on Incidence and Prevalence Estimates From the National Epidermolysis Bullosa Registry. *JAMA Dermatology.* 2016;152(11):1231-1238. doi:10.1001/jamadermatol.2016.2473.

[7] EB Research Network: Understanding EB and its Classification. Accessed Feb. 10, 2023. https://www.eb-researchnetwork.org/research/what-is-eb/.

[8] American Academy of Dermatology Association. Skin Cancer Types: Cutaneous T-Cell Lymphoma Signs & Symptoms. Accessed Feb. 10, 2023. https://www.aad.org/public/diseases/skin-cancer/types/common/ctcl/symptoms.

[9] IBID.

[10] Cai ZR, Chen ML, Weinstock MA, Kim YH, Novoa RA, Linos E. Incidence Trends of Primary Cutaneous T-Cell Lymphoma in the U.S. From 2000 to 2018: A SEER Population Data Analysis. *JAMA Oncol.* 2022;8(11):1690–1692. doi:10.1001/jamaoncol.2022.3236

[11] IBID.

[12] Fortune Business Insights. Accessed Jan. 14, 2023. https://www.globenewswire.com/en/news-release/2022/02/16/2385997/0/en/North-America-Cutaneous-T-Cell-Lymphoma-CTCL-Therapeutics-Market-Size-2022-2028-to-Reach-USD-587-4-Million-at-a-CAGR-13-6.html.

OTHER COLLABORATIONS

INVENIAI

On November 23, 2021, we entered into a collaboration agreement with InveniAI LLC (InveniAI), a U.S.-based company that has pioneered the application of artificial intelligence (AI) and machine learning across the biopharmaceutical and other industries, in order to identify promising drug candidates to treat rare and specialty diseases (the Collaboration Agreement).

Under the terms of the Collaboration Agreement, InveniAI will use its proprietary platform for the identification of potential pharmaceutical product opportunities and the related development pathway in select therapeutic areas by using its Pharma Big Innovation Data Lab, consisting of (i) its proprietary AlphaMeld platform, a cloud-based AI platform that uses its proprietary machine learning and deep learning based neural networks to identify product opportunities in therapeutic areas, (ii) its cross-functional teams at its Integrated Center of Excellence, and (iii) domain expertise, to generate novel pharmaceutical opportunities and the related development pathway for the development of such concepts.

In the collaboration it is expected that InveniAI will use its platform to navigate the volume of data for all regulatory agency approved drugs and their associated active ingredients to identify potential rare and specialty disease indications for development and commercialization by Relief Therapeutics (product concepts). InveniAI will seek to prioritize top product concepts, associated diseases, scientific packages and evidence to support the potential drug development opportunities for Relief Therapeutics. We anticipate the InveniAI platform will complement our existing capabilities in research and development and in drug reformulation. Based on product leads developed by InveniAI, we hope to develop proprietary versions of existing drugs, and to protect those drugs with long-lived intellectual property and defensible product claims.

Under the terms of the Collaboration Agreement, Relief Therapeutics paid InveniAI an initial up-front fee of USD 500’000. We will be required to pay success milestones for any products brought to us in connection with the InveniAI Collaboration Agreement ranging from USD 200’000 per product candidate for which we exercise our option to acquire intellectual property (IP) rights to USD 50 million for any required product reaching USD 1 billion per year in net sales. We will also be required to pay royalties on any such commercialized product in certain countries, a royalty of approximately 3 percent. We are not currently developing any product brought to us by InveniAI, and there can be no assurance that our collaboration with InveniAI will result in the development of new product candidates or product concepts.

LEGACY PRODUCTS

Our legacy products are revenue-generating, approved products marketed in various countries and regions of the world including the U.S. and Europe, originally developed and patented by APR and subsequently licensed to third parties for commercialization in the different territories. The rights on the legacy products were acquired by Relief Therapeutics as part of the 2021 acquisition of APR.

SETOFILM/ONDISSOLVE

SETOFILM is the first prescription-only medicine approved in Europe and Canada, developed as an orodispersible film (ODF) formulation. The product is available in 4 mg and 8 mg doses. Once placed on the tongue, it dissolves in a few seconds and is swallowed with saliva without the need for water. The innovative ODF form may reduce the patient pill burden and enable patients to take their medication virtually anywhere.

The product is indicated for radiotherapy induced nausea and vomiting (RINV), chemotherapy induced nausea and vomiting (CINV) as well as postoperative induced nausea and vomiting (PONV) in both adults and children of 6 months of age or older. The product has been formulated and developed using the RapidFilm drug delivery technology platform and is the form of a soluble film to be placed on the tongue where it dissolves in few seconds thus greatly improving patient compliance and avoiding possible risks of suffocation in kids.

The product is approved in Europe and Canada as prescription a drug, and it is marketed by Norgine B.V. and Takeda Pharmaceuticals respectively under license from APR.

CAMBIA™

Diclofenac potassium is an off-patent, potent non-steroidal anti-inflammatory drug (NSAID) widely used for treating inflammatory conditions and pain management. By applying its patented Dynamic Buffering Technology (DBT), APR developed the first and only NSAID approved by the FDA for the treatment of acute migraine attacks with or without aura in adults. The product is currently marketed as CAMBIA™ by Assertio Therapeutics Inc. (Nasdaq: ASRT) in the U.S. and Miravo Healthcare (formerly Nuvo Pharmaceuticals Inc.) in Canada, under an exclusive, royalty-bearing license agreement with APR.

In January 2022, APR received a notice of allowance from the U.S. Patent and Trademark Office (USPTO) for patent application number 16/713,052 entitled, “Ready to Use Diclofenac Packs” with an expiration date in 2039.

On February 28, 2022, Unimedica Laboratories Pvt. Ltd., India, sent APR a Notice of Certification under the Federal Food, Drug, and Cosmetic Act (FFDCA) related to the filing of an abbreviated new drug application (ANDA) for CAMBIA. While there can be no assurance, it is unlikely that Unimedica will get accelerated approval, and we reserve the right to seek to enforce our patents.

DBT and CAMBIA are currently protected by a family of four patents listed in the FDA Orange Book, all expiring in 2026. In 2023, based on litigation settlements between Assertio and specific generic filers, generic versions of CAMBIA became available in the U.S., significantly reducing our royalty income from CAMBIA. CAMBIA is currently available in the form of a dry powder packed into a single dose envelope to be poured and dissolved in water before administration.

VOLTADOL

Voltadol is a topical, locally applied and locally acting patch delivering diclofenac sodium, an off-patent, potent non-steroidal anti-inflammatory drug (NSAID) for the local treatment of painful, acute conditions such as muscle and joint strains. Unlike heat plaster, the patch contains an anti-inflammatory. It penetrates deep to the source of pain to provide powerful pain relief. The medicated patch provides up to two times more powerful deep pain relief, compared to a non-medicated, non-heated placebo patch. The patch also provides 12 hours continuous release of the active ingredient (diclofenac) to the site of pain. This means the patch only needs to be applied once in the morning and once in the evening to provide effective pain relief. The product is marketed in various countries as an over-the-counter medicine by GlaxoSmithKline (GSK) which recently spun-off the rights to Haleon.

Forward-looking statements: This report contains forward-looking statements, all of which involve certain assumptions, risks and uncertainties that are beyond the control of Relief Therapeutics and could cause our actual results to differ materially from the statements described. Forward-looking statements involve significant risks and uncertainties and actual results may vary materially. Please refer to our Cautionary Statement at the end of the management's discussion and analysis contained within this report.