VALUATIONLAB
FINANCIAL ANALYSIS

RELIEF THERAPEUTICS

FOCUS AREA: TREATMENTS FOR SERIOUS RARE METABOLIC, PULMONARY AND CONNECTIVE TISSUE DISORDERS WITH HIGH UNMET MEDICAL NEED

KEY DATA			SIX: RLF
MARKET CAPITALIZATION (CHF MN)	87	**SHARE PRICE ON 6 APRIL 2023**	0.020
ENTERPRISE VALUE (CHF MN)	58	**RISK-ADJUSTED NPV PER SHARE** * (CHF)	0.303
CASH (30 JUNE 2022) (CHF MN)	30	**UPSIDE/DOWNSIDE** (%)	1432%
MONTHLY OPERATING EXPENSE (CHF MN)	2.6	**RISK PROFILE**	SPECULATIVE
CASH RUNWAY	THROUGH Q3 2023	**SUCCESS PROBABILITY LEAD PROJECT**	90%
BREAK-EVEN (YEAR)	LATE 2024	**EMPLOYEES**	67
FOUNDED (YEAR)	2016	**LISTED** (YEAR)	2009
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- PKU GOLIKE (PHENYLKETONURIA - PKU)	MARKETED	- GEM GLOBAL YIELD FUND LLC	26.2
- RLF-OD032 - (PHENYLKETONURIA - PKU)	IND (US)	- APR SELLER'S GROUP	4.7
- OLPRUVA/ACER-001 (UREA CYCLE DISORDERS - UCDS)	APPROVED (US)	- RELIEF THERAPEUTICS INTERNATIONAL S.A.	6.8
- OLPRUVA/ACER-001 (MAPLE SYRUP URINE DISEASE - MSUD)	PHASE II	**- FREE FLOAT**	89
- RLF-100 INHALED (PULMONARY SARCOIDOSIS)	PHASE II	- DAILY VOLUME 3 MONTHS (SHARES)	5,350,000
- RLF-100 INHALED (ACUTE RESPIRATORY DISTRESS SYNDROME - ARDS)	PHASE II		
- RLF-TD011 (EPIDERMOLYSIS BULLOSA - EB)	PHASE II (2023)		
- RLF-TM011 (CANCER TREATMENT INDUCED SKIN LESIONS)	CLASS III MD (EU)		
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- OLPRUVA (ACER-001) US LAUNCH IN UREA CYCLE DISORDERS	EARLY JULY		BP@VALUATIONLAB.COM
- RLF-100 INHALED START PHASE IIB SARCOIDOSIS TRIAL	Q2/Q3 2023		+41 79 652 67 68
- ACER-001 EU FILING IN UREA CYCLE DISORDERS	H2 2023		

* NOTE: 5,931 MN SHARES USED FOR CALCULATION OF RISK-ADJUSTED NPV/SHARE, ASSUMING ADDITIONAL CHF 30 MN NEEDED TO REACH PROFITABILITY

ESTIMATES AS OF 10 APRIL 2023

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB ESTIMATES

Play ACE!

Olpruva US launch early July – reverse stock split

Relief Therapeutics is a Swiss biopharmaceutical company focused on developing and commercializing treatments for rare and ultra-rare diseases, including metabolic disorders, pulmonary diseases, and connective tissue disorders, with a diversified product pipeline in various stages of development. Key drivers in metabolic disorders include PKU GOLIKE (launched in the EU and US) and RLF-OD032 (in-licensed from Meta Healthcare) for phenylketonuria (PKU), and ACER-001 (in-licensed from Acer Therapeutics and branded Olpruva™ in the US) for treating urea cycle disorders (approved in the US) and maple syrup urine disease (MSUD). The key driver in pulmonary diseases is aviptadil (branded RLF-100™ and ZYESAMI™ in the US) in development for pulmonary sarcoidosis, acute respiratory distress syndrome (ARDS), checkpoint inhibitor-induced pneumonia (CIP), and chronic berylliosis. RLF-TD011 in development for epidermolysis bullosa (EB) is the key driver for rare connective tissue disorders. The acquisition of privately held Applied Pharma Research (APR) in 2021 transformed Relief into a fully integrated biopharma company from a development-stage company. A cash position of CHF 29.9 mn (30 June 2022) provides a cash runway through Q3 2023. We estimate an additional CHF 30 mn funding is required to reach the targeted breakeven in late 2024. We derive a sum-of-parts rNPV of CHF 0.303 per share, based on 5,931 mn shares (34% share dilution) to account for the CHF 30 mn funding gap, and qualify the risk profile as Speculative with no substantial revenues, yet.

Key catalysts:

1) **US launch of Olpruva (ACER-001) in UCDs (early July 2023):** branded "Olpruva" by Acer in the US, adds another high-priced, high-margin, rare disease product to Relief's revenue stream, Acer is building out its commercial and medical affairs team and expects Olpruva availability in the US by early July 2023.
2) **RLF-100 INHALED start phase IIb sarcoidosis trial (Q2/Q3 2023):** our success factor increases to 50% (phase IIb) from 35% (POC completed), increasing our rNPV for RLF-100 INHALED in pulmonary sarcoidosis by CHF 0.029 per share.
3) **EU filing of ACER-001 in UCDs (H2 2023):** submission of the Marketing Authorization Application (MAA) for potential EU approval in UCDs in 2024.

Recent developments

Below is an overview of the latest developments since our last Relief Therapeutics Valuation Report was issued in late December 2022.

April 5 – CMO to leave in Q2 – Medical affairs team to report to COO
Chief Medical Officer Nermeen Varawalla, M.D., Ph.D., will leave Relief in Q2 2023 to pursue other opportunities. The medical affairs team will report to Chief Operating Officer Paolo Galfetti until a replacement is hired. Clinical development and regulatory responsibilities will continue to be supported by consultants already contracted with Relief.

April 4 – EGM to be held on 28 April 2023 to vote on a 400 to 1 reverse stock split
Relief has called for an Extraordinary General Meeting on 28 April 2023, at 10 am in Geneva, for shareholders to consider and vote on the consolidation (or reverse split) of its ordinary shares at the ratio of 400 current shares to 1 new share in preparation for a planned listing on the NASDAQ Stock Market in the US. This would enable Relief to meet the minimum share price needed to list on NASDAQ. The US listing should provide greater liquidity and broader access to capital needed to implement its clinical development, commercialization, and business development plans.

This action represents a technical adjustment and has no impact on the value or the market capitalization of Relief. For instance, Relief's closing share price of CHF 0.01981 would then amount to CHF 7.92 per share, while our rNPV of CHF 0.303 per share would amount to CHF 121.20 per share, providing the same equity upside of 1,432% from the current low share price. The current listing on the SIX Swiss Exchange will not be affected by the dual listing.

> **How it will be implemented.** In the reverse split, shares will be rounded down to the next lower whole number of new merged registered shares upon exchange by applying the ratio. The resulting fractions will be compensated in cash at a fixed price corresponding to the three-day volume-weighted average price (VWAP) of Relief's share prior to the reverse split. The percentage interest in the company's equity for the shareholder will remain unchanged (other than because of the payment of cash in lieu of fractional shares).
>
> **Examples of rounding down method and cash compensation of fractions:**
>
> - 399 current shares → 0 new shares + compensation for 399 current shares in cash
> - 400 current shares → 1 new share
> - 401 current shares → 1 new share + compensation for 1 current share in cash

Only the reverse stock split, including required consequential amendments with respect to share capital-related provisions, will be proposed for a shareholder vote at the EGM. No other items will be considered. Any other changes to Relief's Articles of Association that are required due to the change in Swiss corporate law that went into effect on 1 January 2023, and must be implemented by the end of 2024, will not be the subject of the EGM. The company expects to submit these changes to its shareholders at the next Annual General Meeting (date yet to be announced).

April 3 – Dr. Guangping Gao appointed as Chair of the new Scientific Advisory Board
The world-renowned gene therapy pioneer Dr. Guangping Gao has been appointed as the Chair of Relief's newly formed Scientific Advisory Board (SAB). He has made foundational contributions to the discovery and characterization of adeno-associated virus (AAV) serotypes which were instrumental in the resurgence of gene therapy. In his advisory role, Dr. Gao will serve as an integral resource, providing scientific review and high-level technical and strategic guidance related to gene therapy targets, research and preclinical development, and strategic research alliances as the company works to expand its portfolio. Relief launched its genetic medicines initiative with the objective of developing life-altering, potentially curative therapies for patients suffering from devastating rare diseases that currently lack treatment options. The company is leveraging its strength and experience to identify monogenic disorders in therapeutic areas that align with its areas of focus, such as rare metabolic diseases. The SAB will support the company's genetic medicines initiative, and additional appointments are forthcoming.

March 22 – Survey results of UCD healthcare providers presented at SIMD meeting
Relief's US partner Ace Therapeutics presented data from a survey of urea cycle disorders (UCDs) healthcare providers showing taste and odor are the most important tributes when considering nitrogen-binding medications (such as sodium phenylbutyrate and glycerol phenylbutyrate) and patient compliance in patients with UCDs at the Society of Inherited Metabolic Disorders (SIMD) annual meeting in Salt Lake City, USA. Nitrogen-binding medications can be efficacious in the treatment of UCDs if patients comply with their prescribed treatment. However, 25% of life-threatening hyperammonemic crises in patients with UCDs are thought to be caused by a lack of adherence to medications and/or diet, and certain attributes of existing nitrogen-binding medications may negatively impact adherence. Alternative treatment options are urgently needed."

Of the 51 healthcare providers that completed the survey, most reported dissatisfaction with current treatment options [mean rating (SD)=5.4 (1.7); Likert scale with 1 = not at all satisfied through 9 = extremely satisfied]. The results of the survey show that taste and odor are the most important attributes for both prescribing and patient adherence and compliance. The authors concluded that optimizing nitrogen-binding medications for UCD treatment to facilitate and encourage increased patient adherence through masking taste and odor and/or enhancing other aspects of the patient experience may support improved treatment outcomes.

Relief/Acer's recently approved ACER-001(branded Olpruva in the US) for treating UCDs in the US leverages the well-established efficacy of sodium phenylbutyrate in an innovative dual-coating formulation designed for tastiness. It will be available in single-dose envelopes, which may help UCD patients better manage their condition. In two previous phase I trials, Olpruva suspension had overall lower flavor intensity scores than Buphenyl (sodium phenylbutyrate) powder when administered within five minutes of preparation.

March 17 – PKU GOLIKE preclinical evidence for improved amino acid utilization presented at SIMD meeting
Preclinical research evaluating the metabolic impact of PKU GOLIKE on nitrogen balance, muscle strength and glucose was presented at the Society for Inherited Metabolic Disorders (SIMD) Annual Meeting in Salt Lake City, USA, on 18-21 March 2023. People living with phenylketonuria (PKU) do not have the ability to metabolize the amino acid phenylalanine (Phe) found in many foods, and they require supplementation of amino acid-based foods for

special medical purposes (FSMPs) to prevent protein deficiency and optimize metabolic control. These protein substitutes are typically characterized by altered kinetic profiles compared to that of a slowly absorbed and digested intact protein. The rate of amino acid absorption affects the post-prandial utilization of dietary nitrogen, and the prolonged release of amino acids could support anabolic requirements. PKU GOLIKE, developed with the company's proprietary Physiomimic Technology platform, is the first prolonged-release, amino acid FSMP, characterized by a special coating that enables physiological absorption of the amino acids mirroring that of natural proteins.

The data presented shows the acute and long-term metabolic effects of PKU GOLIKE supplementation on the utilization of amino acids and glucose metabolism in a preclinical rat model using biomarkers for muscle metabolism, functional muscle performance, and a glucose tolerance test. Due to the prolonged release of amino acids engineered with Physiomimic Technology, 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.

March 16 / February 28 – New PKU GOLIKE bars available in Europe and the US
New PKU GOLIKE bars, developed with Relief's proprietary Physiomimic Technology platform, were launched in Europe in mid-March and previously in the US at the end of February 2023. The new PKU GOLIKE BARs come in tropical and red fruit flavors and contain natural ingredients and real fruit. The new grab-and-go bars are ready to use and easy to carry. The 5 g protein equivalent have 20 bars in each box, and the 10 g protein equivalent have 10 bars in each box. Living with PKU requires a limited diet and very careful management. If left unmanaged, PKU can lead to devastating consequences, such as brain damage. People living with PKU do not have the ability to metabolize the amino acid phenylalanine (Phe) found in many foods, and they require supplementation of amino acid-based foods for special medical purposes (FSMPs) to prevent protein deficiency and optimize metabolic control. Currently available FSMPs 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. The PKU GOLIKE family of products are next-generation, prolonged-release amino acid medical foods for the dietary management of PKU.

Relief also disclosed that it had transferred most of the funds it held with Credit Suisse and has no funds with recently closed US banks.

March 15 – Update on Acer's preliminary launch activities for Olpruva in the US
Acer, the originator and US collaboration partner for ACER-001 (branded Olpruva in the US), provided an update on its commercial launch activities for Olpruva in urea cycle disorders (UCDs). In support of the Olpruva launch in Q2 2023, Acer is actively adding resources to establish its commercial and medical affairs presence in the US. As a part of its commercialization strategy, it has recently introduced its patient support service, Olpruva Navigator, designed to assist UCD patients with support, access, education, and patient adherence to treatment. Acer is actively engaged in negotiations regarding access for Olpruva with major commercial payers and state Medicaid organizations, with drug availability anticipated by early July 2023. A pricing strategy was established that reflects

the commitment to deliver innovative treatments that are responsibly priced and accessible to those in need. Acer intends to price Olpruva competitively, at a significant discount to Horizon's Ravicti (glycerol phenylbutyrate), while implementing predictable pricing that will not increase beyond the rate of inflation. A portion of Olpruva's revenue will be invested back into additional solutions aimed at improving outcomes for UCD patients.

February 14 – RLF-TD0011 POC trial in EB assessing changes in the skin microbiome
The first three patients have been enrolled in an investigator-initiated, proof-of-concept (POC) trial to evaluate RLF-TD011 as a treatment for epidermolysis bullosa (EB). EB is a rare, inherited skin disease characterized by widely distributed, painful, chronic wounds that easily become infected, resulting in an elevated risk of sepsis and death. As there is no cure for EB, a crucial element of patient management involves rigorous and timely wound care. The primary aim of the POC trial is to assess changes in the skin microbiome (*Staphylococcus (S.) aureus*, *Pseudomonas (P.) aeruginosa*, commensal organisms) before, during, and after treatment with RLF-TD011, a self-administered, sprayable solution enabling targeted application while avoiding skin contact and cross-contamination. Patients with dystrophic or junctional EB with wounds colonized by *S. aureus* and/or *P. aeruginosa* will be treated with RLF-TD011 for 8 weeks, followed by treatment discontinuation for 4 weeks with an assessment of their wound microbiome at each stage. All study participants will have the option to continue treatment in a 6-month open-label trial extension. The trial currently enrolls up to 17 patients diagnosed with junctional epidermolysis bullosa (JEB) or dystrophic epidermolysis bullosa (DEB) with *S. aureus* or *P. aeruginosa*-culture-positive wounds at Ann & Robert H. Lurie Children's Hospital of Chicago.

The POC trial data will facilitate the design and conduct of follow-on, multi-center, pivotal registration clinical trials to determine the impact of RLF-TD011 on infection control, avoidance of chronic antibiotic use, accelerated wound healing, and quality of life for patients living with EB.

February 8 – Relief plans to reverse split its shares and then apply for NASDAQ listing
Relief provided an update on its financing strategy. The company voluntarily withdrew its Registration Statement on Form F-1 initially filed with the US Securities and Exchange Commission (SEC) on 23 August 2022, in order to explore alternative options for financing, including non-dilutive sources of capital, with the goal of listing its ordinary shares on the NASDAQ Stock Market in the US.

In January 2023, changes to Swiss corporate law became effective, allowing Swiss companies to reverse split their ordinary shares. The current number of outstanding shares is partly the result of successive reverse mergers over the life of Relief's underlying listed vehicle. The reverse split will significantly reduce the number of outstanding shares, meeting the minimum share price requirement for a NASDAQ listing, and is expected to increase the shares' attractiveness for investors while boosting the company's public image. If the reverse split is completed successfully, Relief will file an application to list its ordinary shares on the Nasdaq Stock Market instead of its American depository shares (ADSs). Shareholders can vote on the proposed reverse share split of 400 current shares for 1 new share at the Extraordinary General Meeting on 28 April 2023 in Geneva (see above).

January 17 – Investigator-initiated POC trial of RLF-TD011 in CTL
An independent Institutional Review Board (IRB) approved the protocol of an investigator-initiated proof-of-concept (POC) trial of RLF-TD011 as an adjunctive treatment for patients

diagnosed with cutaneous t-cell lymphoma (CTCL) to determine the effect on the microbiome of CTCL skin lesions, tolerability, symptom improvement, and potential for reducing lesion size and skin disease activity. The trial will enroll 30 CTCL patients over an 8-week treatment period at the Northwestern Department of Dermatology in Chicago, Illinois, US. Upon positive POC trial data, this will be used to design and conduct international, multi-center, pivotal trials, which can serve as registrational trials for US and EU approval of RLF-TD011 in CTCL.

CTCL is a rare, heterogeneous group of non-Hodgkin's lymphomas (NHLs) in which malignant T-cells infiltrate the skin. The overall CTCL incidence rate was 8.55 per 1 mn, with mycosis fungoides being the subtype with the highest incidence, at 5.42 per 1 mn. Cleveland Clinic reports that more than 3,000 new CTCL patients are diagnosed in the US annually. About 16,000-20,000 individuals suffer from mycosis fungoides, the most common form of CTCL linked to skin-localized immune cell stimulation. The overall incidence of CTCL in the US and Europe increased thanks to better diagnostic tools and increased awareness among physicians and patients. The North American CTCL drug market was valued at USD 226 mn in 2021 and is expected to reach USD 587 mn in 2028, according to Fortune Business Insights.

Advanced CTCL lesions harbor *Staphylococcus aureus*, which releases toxins that stimulate malignant cells and drive disease progression. This often leads to recurrent skin infections with a high risk of sepsis (blood poisoning) and death. Five-year disease-specific survival rates range from 70% for early-stage disease to 24% for advanced disease, with the greatest mortality caused by bacterial infections. RLF-TD011 has been shown to kill methicillin-sensitive and methicillin-resistant *Staphylococcus aureus* (MSSA and MRSA, respectively) as well as *Pseudomonas aeruginosa*, with the potential to improve the CTCL microbiome and decrease pruritus (itching skin), erythema (red/pink skin spots), scaling, lesion size and overall skin disease activity, and the aim to delay disease progression and reduce death.

Investment case, strategy & cash

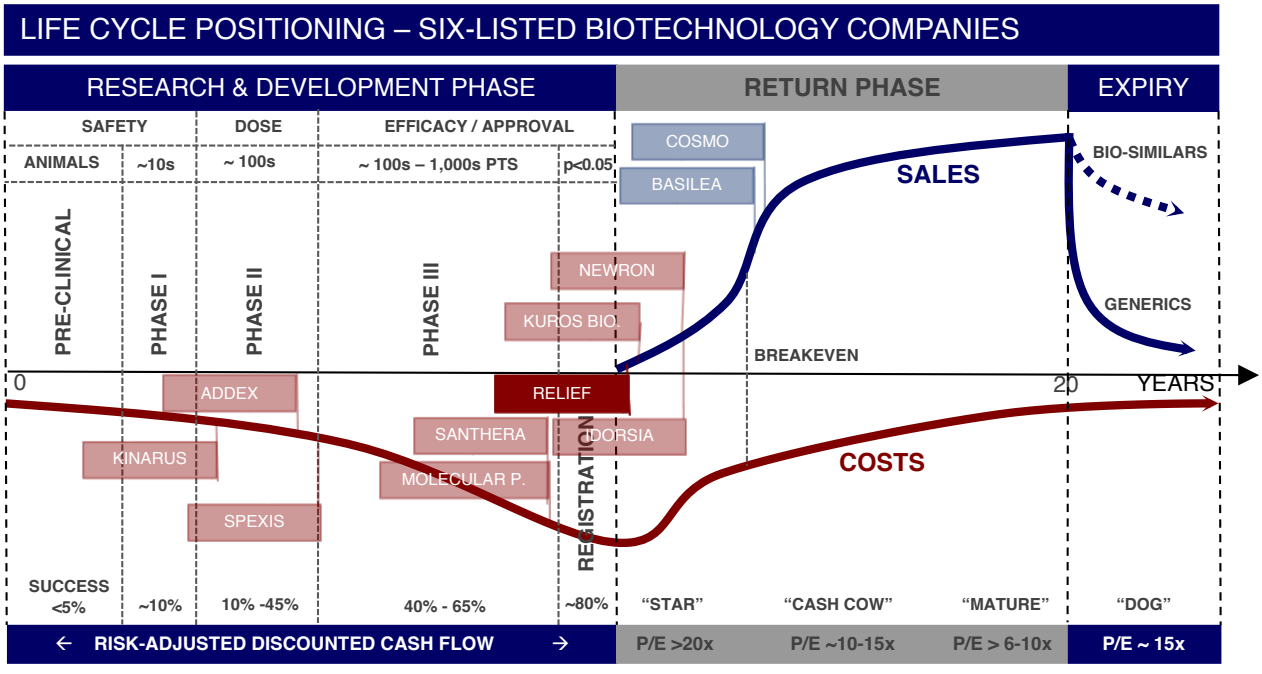
Investment case in a nutshell

In the past two years, Relief has rapidly transformed from a virtual company with a single product, RLF-100 (aviptadil), only in development for COVID-19 infection, into a full-fledged biopharmaceutical company with emerging revenues from a diversified product portfolio in rare metabolic, pulmonary, and connective tissue disorders, all with high margins. The recent US launch of PKU GOLIKE (phenylketonuria - PKU) and the upcoming US launch of ACER-001 (branded Olpruva™ in the US by Acer Therapeutics) in urea cycle disorders (UCDs) should provide a boost to short and medium-term revenues. The successful development of RLF-100 in rare pulmonary disorders such as pulmonary sarcoidosis and acute respiratory distress syndrome (ARDS), RLF-TD011 in epidermolysis bullosa (EB), and RLF-OD032 in PKU should boost medium and long-term revenues substantially. Relief has a cash runway through Q3 2023. We believe approximately CHF 30 mn is needed to fully execute Relief's development and commercialization plans and reach the breakeven target for late 2024.

Based on our detailed bottom-up forecasts for the Relief's key drivers, all with ample patent life and market exclusivity, we calculate a sum-of-the-parts risk-adjusted NPV of CHF 1,340 mn or CHF 0.303 per share (based on 5,931 mn shares to account for an estimated CHF 30 mn funding gap) providing equity upside of 1,432% from the current share low price.

Life Cycle Positioning – Speculative

We qualify Relief's risk profile as Speculative, with currently no substantial product revenues yet cash runway limited through Q3 2023. US sales of PKU GOLIKE, a successful US launch of Olpruva / ACER-001, and the successful development of its key pipeline projects should lead to a substantial increase in Relief's value as well as a marked improvement in the company's risk profile (see Important Disclosures for our Risk Qualification).



SOURCE: VALUATIONLAB

Providing patients therapeutic RELIEF from serious diseases with high unmet need

Relief Therapeutics Holding SA (Relief) was formed in 2016 following the reverse merger of Relief Therapeutics SA, which was founded in 2013 as a private company by three former Merck Serono executives, and THERAMetrics Holding AG (formerly mondoBIOTECH Holding AG, which was founded in 2007 and listed on the SIX Stock Exchange in 2009). Relief is a Swiss biopharmaceutical company focused "on providing patients with therapeutic RELIEF from serious diseases with high unmet medical need" with the aim to become a fully integrated, capital-efficient, commercial-stage biopharmaceutical company in rare and specialty disease indications. Development activities of the company focus primarily on clinical-stage projects based on molecules of natural origins (e.g., peptides and proteins) with a history of clinical testing (benign safety and tolerability) and use in human patients (proof-of-concept) or a strong scientific rationale. Relief's clinical development program is currently focused on three therapeutic areas: rare metabolic disorders, rare pulmonary diseases, and rare connective tissue disorders, with particular emphasis on conditions with dermatological manifestations. In the future, the company wants to develop new, potentially curative gene therapies for rare diseases.

In June 2021, Relief acquired the privately held Applied Pharma Research (APR), based in Balerna, Switzerland, with sales and marketing subsidiaries in Rome, Italy, and Offenbach, Germany, which transformed Relief into a fully integrated commercial-stage biopharmaceutical company. The company will continue to search for additional strategic acquisitions to strengthen its pipeline further. Relief's headquarters is based in Geneva, Switzerland, and currently has ~65 employees following the APR acquisition. Relief will strategically grow the management team as the company evolves (for Management and Board biographies, see page 44).

Relief's primary listing is on the SIX Swiss Stock Exchange (symbol: RLF), with an additional listing on the OTC Markets at OTCQB (symbol: RLFTF). Relief intends to reverse split its ordinary shares in the ratio of 400 current shares to 1 new share to meet the minimum price (USD 4 per share minimum bid price) needed for the NASDAQ and then apply for a potential NASDAQ Stock Market listing (symbol: RLFT). The American Depository Receipts (ADRs) will cease to trade over-the-counter, and the "RLFTY" ticker symbol will disappear.

Key products targeting rare metabolic, pulmonary, and connective tissue disorders

In the past two years, Relief transformed from a virtual company with a few employees and a single product, aviptadil (branded RLF-100™ and ZYESAMI™ in the US), targeted for the treatment of COVID-19 infections, to a full-fledged biopharmaceutical company with a diversified product pipeline in different development stages targeting high-margin rare diseases, which can be commercialized by an own small specialist sales force in the major countries and regions to maximize profitability.

Relief's key product drivers for its three therapeutic areas currently include:

- **Metabolic disorders** include PKU GOLIKE, a controlled-release amino acid mix product with taste and odor masking available in the EU and US for phenylketonuria (PKU), RLF-OD032 in development for PKU, and ACER-001 in development for urea cycle disorders (UCDs) and maple syrup urine disease (MSUD).
  - **PKU GOLIKE (PKU)** peak sales CHF 70 mn: launched in the lucrative US market in October 2022 with an exclusive US service provider; the higher-priced US market should boost sales growth substantially

- **RLF-OD032 (PKU)** peak sales CHF 80 mn: global rights (excluding the UK) acquired from Meta Healthcare (Meta) in July 2022; RLF-OD032 will be developed as a novel dosage form of an already FDA-approved prescription drug intended for PKU patients; US filing 505(b)(2) of the new drug application (NDA) planned for H1 2024; US approval and launch expected in H1 2025; Relief owes Meta Healthcare an undisclosed initial upfront payment and low double-digit royalty payments on the net profit
- **Olpruva/ACER-001 (UCDs)** peak sales CHF 350+ mn: global rights (excluding the US, Canada, Brazil, Turkey, and Japan) in-licensed from Acer Therapeutics (Acer) in 2021; approved in the US in late December 2022 (ahead of 15 January 2023 PDUFA date); US launch expected in Q2 2023; EU marketing authorization application (MAA) filing planned for H2 2023; EU approval and launch expected in 2024; net profits from Acer's territories will be split 60%/40% in favor of Relief, Acer will receive a 15% royalty on net sales in Relief territories
- **Olpruva/ACER-001 (MSUD)** peak sales CHF 150+ mn: start clinical development in H2 2023; approval and launch expected in 2025; same profit split with Acer as for UCDs

- **Pulmonary diseases** include RLF-100 (aviptadil), available in an intravenous (IV) and inhaled formulation for treating respiratory diseases. With the outbreak of the COVID-19 pandemic, RLF-100 IV was developed by Relief's US former development partner, NRx Pharmaceuticals (NRx), for the treatment of ARDS induced by COVID-19, a hallmark of severe SARS-Cov-2 infection in high-risk patients. The inhaled formulation, RLF-100 INHALED, was developed to prevent COVID-19-associated ARDS.

  Unfortunately, the US pivotal "COVID-AIV" trial for treating COVID-19-induced ARDS with RLF IV produced mixed results, missing its primary endpoint but showing efficacy in a subpopulation of patients with a favorable safety profile. RLF-100 IV was also discontinued for futility in the phase III "ACTIV-3B/TESICO" trial in critical COVID-19 patients. The FDA declined to grant Emergency Use Authorization (EUA) to NRx three times, including a EUA application for the subpopulation that showed an effect. Once Relief receives the RLF-100 data package from NRx, the company will assess the development pathway forward for COVID-19, where a high unmet medical need remains. We have conservatively excluded forecasts for RLF-100 IV in COVID-19-induced ARDS from our model due to the decline in the number of COVID-19 infections and hospitalizations with the pandemic's transition to endemic status and higher regulatory hurdles, which impact development timelines and costs, as well as potential peak sales.

  We consider RLF-100 INHALED in late-stage development for the prevention of COVID-19-associated ARDS a "wild card". In the phase III "I-SPY COVID-19" trial, no benefit was seen with nebulized RLF-100 INHALED for the prevention of COVID-19-associated ARDS in high-risk patients, and the drug was discontinued in the trial. In late 2023, topline data from the European investigator-sponsored "Leuppi Study" with RLF-100 INHALED for the prevention of COVID-19-associated ARDS is expected. Relief will decide on further development for this indication once it has the "Leuppi Study" data and assessed the NRX data package. We conservatively excluded RLF-100 INHALED for the prevention of COVID-19-associated ARDS for the same reasons as for RLF-100 IV for the treatment of COVID-19-induced ARDS, as well as emerging new treatment options for this indication, such as Pfizer's more convenient oral drug Paxlovid. We believe the "Leuppi Study" must produce strong positive results for further development

in this indication. In our view, the likelihood of this occurring is low in light of the discontinuation of the "I-SPY-COVID-19" trial. Hence, we consider RLF-100 INHALED in the prevention of COVID-19-associated ARDS a "wild card".

Importantly, Relief has filed a new provisional patent application for a new formulation of RLF-100 (aviptadil) based on promising six-month stability data at all temperatures tested, including in refrigerated and room temperature environments. Aviptadil is a notoriously unstable compound. The new stability patent would provide patent protection for RLF-100 up to 2042 if issued. We conservatively base our RLF-100 forecasts on granted market exclusivities, particularly Orphan Drug Designation (ODD) in pulmonary sarcoidosis and ARDS, which provide 7-year and 10-year market exclusivity in the EU and US, respectively, from the date of approval.

Relief's current development plans for RLF-100 include:

- **RLF – 100 IV (acute respiratory distress syndrome - ARDS)** peak sales CHF 650+ mn: the phase IIb/III trial to start in H2 2023; approval and launch in 2026
- **RLF-100 INHALED (pulmonary sarcoidosis)** peak sales CHF 500+ mn: phase IIb/III trial to start in Q2/Q3 2023; approval and launch in 2027
- **RLF-100 INHALED (checkpoint inhibitor-induced pneumonitis - CIP)** peak sales CHF 250+ mn: a proof-of-concept (POC) trial is planned for 2024 with results due in 2025; upon positive POC results, we will include CIP into our forecasts
- **RLF-100 IV (chronic berylliosis)** peak sales TBD: a proof-of-concept (POC) trial is planned for 2024 with results due in 2025; upon positive POC results, we will include chronic berylliosis into our forecasts

- **Rare connective tissue disorders** include RLF-TD011, a sprayable hypotonic acid-oxidizing solution containing hypochlorous acid in development for epidermolysis bullosa (EB).
  - **RLF-TD011 (epidermolysis bullosa – EB)** peak sales CHF 850+ mn: highest peak sales opportunity stemming from the APR product portfolio; start of POC trial in February 2023 with results in 2023, pivotal trial planned to start in 2024 with results due 2025; filing in 2026 and approval expected in 2027
  - **RLF-TD011 (cutaneous t-cell lymphoma - CTCL) NEW** peak sales TBD: an investigator-initiated POC trial will start in 2023 with results due in 2024; upon positive POC data, registrational trials for US and EU approval could start in 2024

Definitive settlement agreements resolve pending NRx litigation – Relief regained NRx's RLF-100 rights for no more than USD 30 mn in cumulative royalties & undisclosed milestones

On 16 November 2022, Relief and NRx Pharmaceuticals (NRx) announced they entered into definitive settlement agreements to resolve their pending litigation, which were closed on 20 December 2022. Since April 2021, a pending dispute was ongoing between Relief and NRx under the Collaboration Agreement for RLF-100, including the refusal to share clinical trial data of the pivotal "COVID-AIV" trial, unpaid clinical trial invoices, the funding of the "AVICOVID-2" trial, and stability issues with the formulation of RLF-100, among others.

NRx will transfer to Relief all of the assets that it previously used in its aviptadil (branded RLF-100™ and ZYESAMI™ in the US) development program, including its regulatory filings, patent applications, clinical data, and the formulation of the aviptadil product it was

previously developing. Relief will have the exclusive right and control going forward and the obligation to use commercially reasonable efforts to develop and commercialize an aviptadil product. Relief has agreed to use commercially reasonable efforts to continue the existing US "Right-to-Try" Program for aviptadil for at least 2 years. Relief will pay NRx milestone payments and royalties based on a percentage of future sales if it can successfully obtain commercial approval of an aviptadil product (whether for COVID-19 or any other indication) up to a maximum of USD 30 mn in aggregate. NRx has agreed not to compete in the development of an aviptadil product in the future.

EGM on 28 April for shareholders to vote for a reverse share split and NASDAQ listing
Relief has called for an Extraordinary General Meeting on 28 April 2023 in Geneva for shareholders to consider and vote on the consolidation (or reverse split) of its ordinary shares at the ratio of 400 current shares to 1 new share in preparation for a planned listing on the NASDAQ Stock Market in the US. This would enable Relief to meet the minimum share price (USD 4 minimum bid) needed to list on NASDAQ. The US listing should provide greater liquidity and broader access to capital needed to implement its clinical development, commercialization, and business development plans.

Cash runway through Q3 2023 – cash flow breakeven late 2024 – cash positive 2025
With a cash position of CHF 29.9 mn (30 June 2022), Relief projects a cash runway through Q3 2023. With the launch of the PKU GOLIKE franchise in the US in October 2022 and a successful US launch of Olpruva (ACER-001) in UCDs in Q2 2023, the company believes it could achieve cash flow breakeven in late 2024 and positive operating cash flow in early 2025. We calculate Relief will need approximately CHF 30 mn to reach the projected cash flow breakeven in late 2024. Note that potential (non-dilutive) funding could come from licensing agreements of its key products to partners in regions outside the US and Europe, for instance, in Japan, China, Asia, and Latin America, among others. To account for the estimated CHF 30 mn funding gap, we conservatively calculate our per share forecasts based on 5,931 mn shares, which includes 4,416 mn shares outstanding plus an estimated ~1.5 bn new shares, which amounts to a share dilution of 34% based on the current low share price.

Almost CHF 120 mn raised since 2016

In 2020 and 2021, Relief was very successful in fundraising, when more than 90% of funds since inception were raised on the back of encouraging early data of RLF-100 in treating critically ill COVID-19 patients with respiratory complications in the ongoing US open-label Expanded Access Program. Since the company went public via a reverse merger in 2016, the company has raised a total of CHF 116.3 mn, mainly from GEM Global Yield Fund, LLC, which has become Relief's largest shareholder with currently a ~22% equity stake in Relief.

MONEY RAISED	CHF MN
IPO (INITIAL PUBLIC OFFERING) - REVERSE MERGER WITH THERAMETRICS HOLDING AG	0
PRIVATE PLACEMENTS / SECONDARY OFFERINGS / OTHERS	116.3
TOTAL RAISED	**116.3**

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB

In March 2021, Relief raised gross proceeds of approximately CHF 10 mn in a private placement to a single healthcare-dedicated US institutional investor. An additional CHF 15 mn gross proceeds were raised in a private placement to two US institutional investors in July 2021. Since August 2021, Relief has raised approximately CHF 26 mn from treasury shares, which constitutes a meaningful recent source of equity funding.

Other financings have raised approximately CHF 57.9 mn, largely through the Share Subscription Facility (SSF) agreement with GEM, which was concluded in September 2020. In January 2021, Relief established a new CHF 50 mn SSF with GEM, which it intends to use, if necessary, to fund the purchase of an additional commercial supply of RLF-100 to meet demand as needed, to fund the potential definitive agreement with Acer on the development and commercialization of ACER-001 in UCDs and MSUD, as well as pursue further business development opportunities.

Relief's key priorities for the next 12-18 months include:

- Successfully complete the POC trial of RLF-TD011 in epidermolysis bullosa (EB) in 2023
- US launch of ACER-001 in UCDs in Q2 2023; file an MAA in the EU for UCDs in H2 2023; start POC trials in MSUD in H2 2023
- Start the phase IIb/III trial of RLF-100 INHALED in pulmonary sarcoidosis in Q2/Q3 2023
- Start the phase IIb/III trial of RLF-100 IV in acute respiratory distress syndrome (ARDS) in H2 2023
- Start a proof-of-concept (POC) trial of RLF-100 INHALED in checkpoint inhibitor-induced pneumonitis (CIP) in 2024
- Start a POC trial of RLF-100 IV in chronic berylliosis in 2024
- Strategically grow the management team as the clinical pipeline evolves
- Explore partnerships and distribution agreements for its products in regions where Relief does not intend to establish its own commercial infrastructure (e.g., Japan, China, Asia, Latin America, and emerging markets)
- Broaden its in-house pipeline through the collaboration with InveniAI and the nascent genetic medicines initiative established earlier this year
- Continue to expand the clinical pipeline through selective product in-licensing and/or M&A

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 0.303 per share
We derive a sum-of-parts risk-adjusted (r)NPV of CHF 0.303 per share for Relief, with cash and cash equivalents of CHF 0.005 per share (30 June 2022) and overhead expenses of CHF 0.013 per share, assuming a WACC of 7% (reflecting the low Swiss interest environment).

SUM OF PARTS

PRODUCT	INDICATION	PEAK SALES (CHF MN)	LAUNCH YEAR (EST)	UNADJUSTED NPV/SHARE * (CHF)	SUCCESS PROBABILITY	RNPV/SHARE * (CHF)
PKU GOLIKE	PHENYLKETONURIA (PKU)	71	2018 (EU) / 2022 (US)	0.038	100%	**0.038**
RLF-OD032	PHENYLKETONURIA (PKU)	72	2024	0.045	35%	**0.016**
OLPRUVA / ACER-001	UREA CYCLE DISORDERS (UCD)	347	2023 (US) / 2024 (EU)	0.193	90%	**0.174**
OLPRUVA / ACER-001	MAPLE SYRUP URINE DISEASE (MSUD)	163	2025	0.075	35%	**0.026**
RLF-100 INHALED	PULMONARY SARCOIDOSIS	500	2027	0.193	35%	**0.067**
RLF-100 IV	ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)	666	2026	0.353	35%	**0.124**
RLF-100 INHALED **	CHECKPOINT INHIBITOR-INDUCED PNEUMONITIS (CIP)	274	2028	0.096	0%	**0.000**
RLF-100 INHALED	PREVENTION COVID-19 RELATED ARDS** - **"WILD CARD"**	99	2024 (US) / 2025 (EU)	0.036	0%	**0.000**
RLF-TD011	EPIDERMOLYSIS BULLOSA (EB)	866	2027	0.343	35%	**0.120**
CASH POSITION (30 JUNE 2022)		30		0.005		**0.005**
TOTAL ASSETS				0.647		**0.316**
OVERHEAD EXPENSES				-0.013		**-0.013**
NPV/SHARE (CHF)				0.634		**0.303**
SHARE PRICE ON APRIL 07, 2023						0.020
PERCENTAGE UPSIDE / (DOWNSIDE)						1432%

* NOTE: 5,931 MN SHARES USED FOR CALCULATION OF RISK-ADJUSTED NPV/SHARE, ASSUMING ADDITIONAL CHF 30 MN NEEDED TO REACH PROFITABILITY
ESTIMATES AS OF 10 APRIL 2023 SOURCE: VALUATIONL

Relief's current key drivers include:

PKU GOLIKE in phenylketonuria (PKU) – rNPV of CHF 0.038/share
We forecast peak sales of around CHF 70 mn for PKU GOLIKE, the first food for special medical purposes (FMSP) engineered product for patients with phenylketonuria (PKU) with a drug delivery technology offering better metabolic management and better compliance due to minimized taste, odor, and aftertaste. PKU GOLIKE is a family of products covering the main age groups and individual habits, including sachets, shakes & drinks, and bars being rolled out in the EU by distribution partners. PKU GOLIKE was just launched in the US by Relief's own specialist sales force and the help of a leading US service provider in October 2022. US approval as a prescription-only treatment could boost our peak sales to CHF 200+ mn. Our NPV for PKU GOLIKE in PKU amounts to CHF 0.038 per share.

RLF-OD032 in phenylketonuria (PKU) – rNPV of CHF 0.016/share
In July 2022, the global rights (excluding the UK) for RLF-OD032 were acquired from Meta Healthcare for an undisclosed upfront payment and low double-digit royalty payments on the net profit. RLF-OD032 is a novel dosage form of an already FDA-approved prescription drug intended for phenylketonuria (PKU) patients. The US 505(b)(2) filing of the new drug application (NDA) is planned for H1 2024, with first approvals and launches expected to occur in 2025. Relief guides for global peak sales (excl. the UK) of around CHF 80 mn. RLF-OD032 adds to the company's product offering for PKU patients, which can be leveraged through the existing sales infrastructure in the EU and US. We calculate an rNPV of CHF 0.016 per share, assuming a conservative 35% success rate, despite the fact that RLF-OD032 is a novel dosage form of an already FDA-approved prescription drug, as the compound has not yet been disclosed due to competitive reasons.

Olpruva/ACER-001 in urea cycle disorders (UCDs) – rNPV of CHF 0.174/share
We forecast peak sales of ACER-001 in urea cycle disorders (UCDs) to amount to CHF

350+ mn. ACER-001, in-licensed from Acer Therapeutics, is a novel powder and immediate-release (IR) formulation of sodium phenylbutyrate. It is targeted to provide a compelling alternative to Horizon Therapeutics' Buphenyl (glycerol phenylbutyrate) with a novel taste-masking formulation that can possibly be taken without food at competitive pricing. On 27 December 2022 (ahead of its 15 January 2023 PDUFA date), ACER-001 received FDA approval for UCDs, with the US launch expected to follow in Q2 2023. Relief is entitled to 60% of net profits in the Acer territories (US, Canada, Brazil, Turkey, and Japan). Acer will receive a 15% net royalty on ROW sales by Relief next to regulatory milestones upon approval in the EU. We calculate an rNPV of CHF 0.174 per share for ACER-001 in UCDs, assuming a 90% success rate, the average of US (100%) approved, and EU (80%) filing.

Olpruva/ACER-001 in maple syrup urine disease (MSUD) – rNPV of CHF 0.026/share
We forecast peak sales of ACER-001 in maple syrup urine disease (MUSD) to amount to CHF 150+ mn. Based on encouraging POC trial results, Acer and Relief plan to start clinical development of ACER-001 in MSUD in H2 2023, with a potential launch in 2025. We calculate an rNPV of CHF 0.026 per share for ACER-001 in MSUD, assuming a 35% (POC) success rate and considering the regulatory milestones, profit split, and sales royalties according to the proposed global agreement with Acer.

RLF-100 INHALED in pulmonary sarcoidosis – rNPV of CHF 0.067/share
We forecast peak sales of RLF-100 INHALED in pulmonary sarcoidosis to amount to CHF 500+ mn, with first launches expected in 2027. A phase IIb dose-ranging trial is expected to start in Q2/Q3 2023. Pulmonary sarcoidosis is a rare disease caused by inflammation, particularly in the lungs, with limited treatment options. Pulmonary sarcoidosis was the initial indication Relief targeted for clinical development of RLF-100 before the COVID-19 pandemic emerged in early 2020 and COVID-19 indications were prioritized. We calculate an rNPV of CHF 0.067 per share for RLF-100 INHALED in pulmonary sarcoidosis, assuming a 35% (POC established) success rate.

RLF-100 IV in ARDS – rNPV of CHF 0.124/share
We forecast peak sales for RLF-100 IV in ARDS caused by, for instance, sepsis, pancreatitis, trauma, or pneumonia, to amount to CHF 650+ mn. Phase IIb/III trials are expected to start in H2 2023, with the first launches expected in 2026. For RLF-100 IV in ARDS, we calculate an rNPV of CHF 0.124 per share, assuming a 35% (POC established) success rate.

RLF-100 INHALED in the prevention of COVID-19-associated ARDS ("WILD CARD"– not included in our forecasts)
The results of the European investigator-sponsored "Leuppi Study", expected in late 2023, together with the assessment of the NRx data of RLF-100, will determine further development in the prevention of COVID-19-associated ARDS, in our view. We forecast peak sales of CHF 100 mn in this shrinking market due to the pandemic becoming endemic and emerging new treatment options such as Pfizer's convenient oral Paxlovid treatment. Due to the discontinuation of RLF-100 INHALED in the phase III "I-SPY-COVID-19" trial, where no benefit was seen, we have conservatively excluded RLF-100 INHALED forecasts in the prevention of COVID-19-associated ARDS.

RLF-TD011 in epidermolysis bullosa (EB) – rNPV of CHF 0.120 per share
Epidermolysis bullosa (EB) is a group of rare, genetic, life-threatening connective tissue disorders characterized by skin blistering throughout the body and risk of severe impact to

external organs affecting ~250,000 patients worldwide. RLF-TD011 is an HCIO sprayable solution that combines strong antimicrobial action and anti-inflammatory properties with the potential to become one of the first products ever to be approved for EB. A preliminary POC trial showed improvement in skin blistering and tissue repair in just two weeks. The US FDA granted Orphan Drug Dedication for RLF-TD011 in 2019, providing 7-year marketing exclusivity from approval in the US. Discussions with regulatory authorities are ongoing to finalize the clinical development path with a potential launch in 2027. We forecast peak sales for RLF-TD011 to amount to CHF 850+ mn in EB and calculate an rNPV of CHF 0.120 per share, assuming a 35% (POC established in wound healing) success rate.

Currently, no value attributed to early-stage pipeline projects
We have conservatively not accounted for Relief's early-stage pipeline projects due to the lack of sufficient proof-of-concept now. Relief's unadjusted NPV provides a "sneak preview" of what the value could be if all our assumptions were reached.

RLF-100 INHALED in CIP – phase I, launch 2028
The increasing use of immune checkpoint inhibitor (ICI) therapy in cancer has brought new hope to patients with advanced tumors. However, the immune system activated by ICI therapy, mainly activated T-cells, can attack normal tissues and organs in the body and lead to various adverse effects. In the lung, these attacks can induce checkpoint inhibitor pneumonitis (CIP), which is one of the complications associated with ICI therapy. The incidence of CIP reported in clinical trials was between 3% to 5%. There are no optimal recommendations for the treatment of refractory CIP to date except for corticosteroids with side effects that must be monitored. Based on a compelling case report where a patient with refractory CIP was given RLF-100 INHALED over a period of six months resulting in improved lung function and good clinical conditions, Relief plans to develop the compound in this indication and to start a POC trial in 2024 followed by a phase IIb/III trial in CIP. The first launches could occur in 2028, with peak sales conservatively amounting to CHF 250+ mn. Due to the lack of sufficient POC, we currently exclude forecasts for RLF-100 INHALED in CIP.

RLF-TD011 in CTCL (NEW) – POC, launch TBD
In January 2023, Relief announced a US investigator-initiated POC trial was started as an adjunctive therapy in 30 patients with cutaneous T-cell lymphoma (CTCL) with results due in 2023. CTCL is a rare, heterogeneous group of non-Hodgkin's lymphomas (NHLs) in which malignant t-cells infiltrate the skin, and a potential new indication for RLF-TD011. Upon positive results, Relief plans to start international, multi-center, registrational trials for US and EU approval of RLF-TD011 in CTCL. First launches could occur in 2025/2026. Due to the lack of POC, we currently exclude forecasts for RLF-TD011 in CTCL.

APR niche disorders and early-stage pipeline projects
Relief is assessing which APR products offer the optimal strategic fit combined with differentiation that can offer strong growth potential. Niche disorders include, **Setofilm/Zuplenz/Ondissolve**, an oral dispersible film containing ondansetron for treating chemotherapy-, radiotherapy- and postoperative nausea and vomiting; **Nexodyn AOS**, a sprayable HCIO solution for acute and chronic wounds; **Sentinox,** an EU-cleared Class III medical device and novel nasal sprayable HCIO solution intended to block transmission of airborne viruses and bacteria, including the SARS-Cov-2 virus (confirmatory trial required for this indication), and **RLF-TM011** approved as a Class III medical device in the EU for the prevention and treatment of skin rashes associated with cancer treatments.

Sensitivities that can influence our valuation

Funding risk: With a cash position of CHF 29.9 mn (30 June 2022), Relief has a cash runway through Q3 2023, with cash flow breakeven guided for late 2024 and positive cash flow in 2025. The company needs an estimated CHF 30 mn to fully fund its development and commercialization plans. The CHF 30 mn is expected to be largely raised through non-dilutive development and commercialization agreements with partners in regions outside the US and Europe, where Relief intends to commercialize its products by its own small specialist sales force to maximize profitability.

Development risk: Relief's products and indications are in different phases of development, with several already available such as PKU GOLIKE, which just launched in the US and is available in the EU since 2018. Olpruva/ACER-001 in UCDs received US approval, justifying a 90% success probability, the average US (100%) approval, and EU (80%) filing. POC in MSUD should start in H2 2023, with a 35% (POC) success rate. Development plans for RLF-100 include ARDS and pulmonary sarcoidosis with a 35% (POC established) success rate and CIP and chronic berylliosis, excluded from our forecasts due to the lack of sufficient POC. All indications for RLF-100 are targeted for respiratory disease, which could present a cluster risk. Recently acquired RLF-OD032 for PKU has a conservative 35% success rate, despite that it is already an FDA-approved drug in a different formulation, however, not disclosed yet due to competitive reasons. RLF-TD011 in EB has a 35% (POC) success rate.

Commercialization risk: All of Relief's products are high-margin rare disease specialty drugs, which do not require large sales forces to commercialize successfully. The former APR European specialist sales force and the recently built US sales force for PKU GOLIKE can be leveraged and expanded for upcoming product launches. Sales uptake and market penetration will be dependent on how successfully Relief's sales force can compete against established competitors, which may differ from our forecasts.

Pricing and reimbursement risk: PKU GOLIKE is priced according to its competitive profile compared to existing PKU treatments. Olpruva/ACER-001 is expected to be competitively priced vs. existing drugs for UCDs. Pricing for RLF-100 in its various orphan indications, as well as RLF-TD011 in EB, represents pricing for rare disease indications with no effective treatments currently available.

Manufacturing risk: Relief has secured sufficient RLF-100 treatment courses for its first approved indications with Bachem Americas, Nephron, and AMRI. Multiple future distribution partnerships are currently under discussion.

Intellectual property risk: RLF-100 could enjoy US patent protection until 2029 with a 5-year Hatch Waxman patent extension reaching 2034 and 5 years of NCE exclusivity. The EU patent of RLF-100 expires in 2026. The compound also enjoys orphan drug designation exclusivity for ARDS and pulmonary sarcoidosis in the US and EU, providing 7-year and 10-year market exclusivity, respectively, from the approval date. If a recently filed stability patent is issued, patent protection could be extended until 2042. Olpruva/ACER-001 is likely to enjoy 7 years (US) and 10 years (EU) of orphan drug exclusivity in UCDs and MSUD, as well as RLF-TD011 in EB. A recently issued US formulation patent extends Olpruva/ACER-001's patent protection into 2036.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE / EVENT	COMMENT	PER SHARE IMPACT ON RNPV
2023					
JAN 17	RLF-TD011	CUTANEOUS T-CELL LYMPHOMA (CTCL) **(NEW)**	START POC TRIAL	START OF INVESTIGATOR-INITIATED US POC TRIAL AS ADJUNCTIVE THERAPY IN 30 PATIENTS WITH CUTANEOUS T-CELL LYMPHOMA (CTCL); RESULTS DUE IN 2023; POTENTIAL NEW INDICATION FOR RLF-TD011	
FEB 8			UPDATE ON FINANCING STRATEGY	CHANGES IN SWISS CORPORATE LAW NOW ALLOW A REVERSE SPLIT OF RELIEF'S ORDINARY SHARES, WHICH WILL BE PROPOSED TO SHAREHOLDERS AT AN EGM ON 28 APRIL 2023; IF APPROVED RELIEF WILL FILE AN APPLICATION TO LIST ITS ORDINARY SHARES ON THE NASDAQ STOCK MARKET INSTEAD OF ITS AMERICAN DEPOSITARY SHARES (ADSS); CONSEQUENTLY RELIEF WITHDREW ITS REGISTRATION STATEMENT ON FORM F-1	
FEB 14	RLF-TD011	EPIDERMOLYSIS BULLOSA	START POC TRIAL	START OF INVESTIGATOR-INITIATED PROOF-OF-CONCEPT (POC) TRIAL IN UP TO 17 PATIENTS WITH EPIDERMOLYSIS BULLOSA (EB) WITH RESULTS DUE IN 2023; POC DATA WILL FACILITATE THE DESIGN AND CONDUCT OF PIVOTAL REGISTRATION TRIALS FOR RLF-TD001 IN EB	
FEB 28 / MAR 15	PKU GOLIKE	PHENYLKETONURIA (PKU)	NEW PKU GOLIKE BARS IN THE US	NEW TROPICAL AND RED FRUIT FLAVORED PKU GOLIKE BARS LAUNCHED IN THE US (28 FEBRUARY) AND IN EUROPE (15 MARCH); THE GRAB-AND-GO BARS ARE READY TO USE AND EASY TO CARRY; MORE FLAVORS AND OTHER PKU GOLIKE PRODUCTS ARE IN DEVELOPMENT	
MAR 15	OLPURUVA (ACER-001)	UREA CYCLE DISORDERS (UCDS)	US PRELIMINARY LAUNCH ACTIVITIES	US PARTNER ACER THERAPEUTICS REPORTED US PRELIMINARY LAUNCH ACTIVITIES ARE PROGRESSING AND THEY ARE BUILDING OUT THEIR COMMERCIAL AND MEDICAL AFFAIRS TEAMS TO SUPPORT US LAUNCH IN Q2 2023 WITH OLPRUVA AVAILABILITY BY EARLY JULY; A SURVEY DESIGNED TO QUANTIFY HEALTHCARE PROVIDERS' TREATMENT PREFERENCES FOR UCDS TO BE PRESENTED AT THE SIMD 2023	
MAR 17	PKU GOLIKE	PHENYLKETONURIA (PKU)	DATA PRESENTED AT SIMD CONFERENCE	PRECLINICAL EVIDENCE FOR IMPROVE AMINO ACID UTILIZATION WITH PKU GOLIKE PRESENTED AT THE SOCIETY FOR INHERITED METABOLIC DISORDERS (SIMD) ANNUAL MEETING IN SALT LAKE CITY, USA	
MAR 22	OLPURUVA (ACER-001)	UREA CYCLE DISORDERS (UCDS)	SURVEY DATA	ACER REPORTED DATA FROM A SURVEY OF UCD HEALTHCARE PROVIDERS SHOWING TASTE AND ODOR ARE THE MOST IMPORTANT ATTRIBUTES WHEN CONSIDERING TREATMENT AND PATIENT COMPLIANCE	
APR 3			NEW APPOINTMENT NEW SAB	WORLD-RENOWNED GENE THERAPY PIONEER DR. GUANGPING GAO APPOINTED AS CHAIR OF RELIEF'S NEWLY FORMED SCIENTIFIC ADVISORY BOARD (SAB)	
APR 5			MANAGEMENT TRANSITION	CHIEF MEDICAL OFFICER NERMEEN VARAWALLA, M.D., PH.D. WILL LEAVE COMPANY IN Q2 2023 TO PURSUE OTHER OPPORTUNITIES; MEDICAL AFFAIRS TEAM WILL REPORT TO CHIEF OPERATING OFFICER PAOLO GALFETTI UNTIL A REPLACEMENT IS HIRED	
APR 14			FY 2022 RESULTS	RELEASE OF THE FY 2022 RESULTS AND ANNUAL REPORT	
APR 28			EGM (REVERSE SHARE SPLIT)	EXTRAORDINARY GENERAL MEETING (EGM) HELD FOR SHAREHOLDERS TO DECIDE ON A PROPOSED REVERSE SHARE SPLIT WITH A 400 TO 1 RATIO TO MEET THE MINIMUM SHARE PRICE CRITERIA TO LIST ON THE US NASDAQ STOCK MARKET ENABLING GREATER LIQUIDITY AND BROADER ACCESS TO CAPITAL	
Q2			US NASDAQ LISTING	UPON A SUCCESSFUL EGM VOTE FOR REVERSE SHARE SPLIT, THE COMPANY PLANS A LISTING ON US NASDAQ STOCK MARKET WITH TICKER "RLFT"TO FACILITATE US INVESTORS; ADRS WILL CEASE TO TRADE OTC AND THE "RLFTY" TICKER WILL DISAPPEAR	
Q2	OLPURUVA (ACER-001)	UREA CYCLE DISORDERS (UCDS)	US LAUNCH	US LAUNCH WITH PARTNER ACER THERAPEUTICS OF OLPRUVA (ACER-001) IN UCDS FOLLOWING EARLIER THAN EXPECTED FDA APPROVAL AT THE END OF DECEMBER 2022	
Q2	SENTINOX	PREVENTION AIRBORNE INFECTIONS	START CONFIRMATORY TRIAL	START OF A CONFIRMATORY, CONTROLLED, CLINICAL TRIAL IN THE PREVENTION OF VIRAL AND BACTERIAL AIRBORNE INFECTIONS	
Q2/Q3	RLF-100 INHALED	PULMONARY SARCOIDOSIS	START PHASE IIB DOSE RANGING TRIAL	START PHASE IIB DOSE RANGING TRIAL OF RLF-100 INHALED IN 72 PATIENTS WITH PULMONARY SARCOIDOSIS OVER A 12-WEEK PERIOD WITH THE OPTION FOR PATIENTS TO PARTICIPATE IN AN EXTENSION TRIAL	+ CHF 0.029
H2	ACER-001	UREA CYCLE DISORDERS (UCDS)	EU MAA FILING	FILING MARKETING AUTHORIZATION APPLICATION (MAA) FOR EU APPROVAL IN UCD'S	
H2	OLPRUVA / ACER-001	MAPLE SYRUP URINE DISEASE (MSUD)	START CLINICAL DEVELOPMENT	START OF CLINICAL TRIALS TO EVALUATE THE SAFETY AND EFFICACY OF ACER-001 IN MSUD; DATA FROM THESE TRIALS EXPECTED TO BE SUITABLE FOR APPROVALS IN THE US AND EU	
H2	RLF-100 IV	ARDS*	START PHASE IIB/III TRIAL	START PHASE IIB/III TRIAL IN ARDS (ACUTE RESPIRATORY DISTRESS SYNDROME)	
LATE	RLF-100 INHALED	PREVENTION COVID-19 RELATED ARDS*	TOPLINE DATA "LEUPPI STUDY"	TOP LINE DATA EUROPEAN INVESTIGATOR-SPONSORED TRIAL FOR THE PREVENTION OF ARDS ASSOCIATED WITH COVID-19 (SUBJECT TO ENROLMENT OF ELIGIBLE PATIENTS, WHICH CURRENTLY IS PROCEEDING SLOWLY WITH A LACK OF COVID-19 PATIENTS)	

* ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME; ** CIP = CHECKPOINT INHIBITOR-INDUCED PNEUMONITIS

ESTIMATES AS OF 10 APRIL 2023

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB

Technology & Pipeline

TECHNOLOGY PLATFORM

Relief applies a “search and development” approach to build its pipeline with compounds to “provide patients with therapeutic RELIEF from serious diseases with high unmet medical need”, currently with a focus on rare genetic metabolic disorders, pulmonary diseases, and connective tissue disorders with particular emphasis on conditions with dermatological manifestations. These products typically target lucrative, high-priced, high-margin market opportunities that can be commercialized through a relatively small specialist sales force.

The company has a collaboration agreement with InveniAI LLC that applies artificial intelligence (AI) and machine learning across biopharma and other industries to help identify promising drug candidates to treat rare and specialty diseases for Relief’s product pipeline.

The acquisition of APR expanded Relief’s pipeline further with compounds targeting inherited metabolic recessive disorders and niche disorders. APR has developed these compounds with the help of its two core formulation technologies, including its Physiomimic™ Technology, which is able to modify the release of clinically relevant amino acids by prolonging their absorption profiles, and Tehclo™ a globally patented nano-technology platform applied to the production of a unique hypochlorous acid (HClO) solution that ensures the most consistent quality for best-in-class clinical outcomes.

Furthermore, Relief plans to expand its clinical pipeline through selective product in-licensing and/or M&A deals.

PIPELINE - Targeting multiple rare metabolic, pulmonary, and tissue disorders

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH YEAR	PARTNER	PEAK SALES
RARE METABOLIC DISORDERS:						
PKU GOLIKE	CONTROLLED-RELEASE AMINO ACID MIX PRODUCT WITH TASTE AND ODOR MASKING	PHENYLKETONURIA (PKU)	LAUNCHED (EU)	2018 (EU) 2022 (US)	APR APPLIED PHARMA RESEARCH	CHF 70 MN
RLF-OD32	UNDISCLOSED	PHENYLKETONURIA (PKU)	IND	2024	ACQUIRED GLOBAL RIGHTS (EXCL. UK) FROM META HEALTHCARE	CHF 80 MN
OLPRUVA/ACER-001	TASTE-MASKED, IMMEDIATE-RELEASE FORM OF SODIUM PHENYLBUTYRATE	UREA CYCLE DISORDERS (UCD)	APPROVED (US)	2023 (US) 2024 (EU)	ACER (US, CANADA, BRAZIL, TURKEY, JAPAN)	CHF 350 MN
OLPRUVA/ACER-001	TASTE-MASKED, IMMEDIATE-RELEASE FORM OF SODIUM PHENYLBUTYRATE	MAPLE SYRUP URINE DISEASE (MSUD)	PHASE I	2025 (US) 2026 (EU)	ACER (US, CANADA, BRAZIL, TURKEY, JAPAN)	CHF 150+ MN
RARE PULMONARY DISEASES:						
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	PULMONARY SARCOIDOSIS	PHASE II	2027		CHF 500+ MN
RLF-100 IV*	INTRAVENOUS (IV) SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)	PHASE II	2026		CHF 650+ MN
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	CHECKPOINT INHIBITOR-INDUCED PNEUMONITIS (CIP)	POC (2023)	>2025		CHF 250+ MN
RLF-100 IV*	INTRAVENOUS (IV) SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	BERYLLIOSIS	POC (2023)	>2025		TBD
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	PREVENTION COVID-19-RELATED ARDS** **"WILD CARD"**	PHASE IIB/III	2024 (US) 2025 (EU)		CHF 100 MN
SENTINOX	CLASS III MEDICAL DEVICE	COVID-19 PREVENTION	APPROVED (EU)	2021	APPLIED PHARMA RESEARCH	TBD
RARE CONNECTIVE TISSUE DISORDERS:						
RLF-TD011	SPRAYABLE HYPOTONIC ACID-OXIDIZING SOLUTION CONTAINING HYPOCHLOROUS ACID	EPIDERMOLYSIS BULLOSA (EB)	PHASE II (2022)	2027	APR APPLIED PHARMA RESEARCH	CHF 850+ MN
RLF-TD011	SPRAYABLE HYPOTONIC ACID-OXIDIZING SOLUTION CONTAINING HYPOCHLOROUS ACID	CUTANEOUS T-CELL LYMPHOMA (CTCL) **NEW**	PHASE II (2023)	TBD	INVESTIGATOR-INITIATED POC TRIAL	TBD
RLF-TM011	CLASS III MEDICAL DEVICE	SKIN TOXICITIES IN CANCER THERAPIES	APPROVED (EU)	2021	APR APPLIED PHARMA RESEARCH	TBD
NEXODYN AOS	ACID-OXIDIZING SOLUTION	CHRONIC WOUNDS	APPROVED (EU)	2021	APPLIED PHARMA RESEARCH	TBD
LEGACY PRODUCTS:						
SETOFILM/ONDISSOLVE	ORODISPERSABLE FILM FORMULATION OF ONDANSETRON (ANTI-EMETIC)	NAUSEA AND VOMITING			NORGINE (EUROPE), TAKEDA (CANADA)	TBD
CAMBIA/VOLTFAST	DYNAMIC BUFFERING TECHNOLOGY (BDT) FORMULATION OF DICLOFENAC (NSAID)	ACUTE MIGRAINE ATTACKS IN ADULTS			ASSERTIO THERAPEUTICS (US), MIRAVO (CANADA)	TBD
VOLTADOL	MATRIX PATCH TECHNOLOGY TOPICAL FORMULATION OF DICLOFENAC (NSAID)	LOCAL PAIN AND STRAIN (OVER-THE-COUNTER)			HALEON	TBD

* IV = INTRAVENOUS (IV) INFUSION; **ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME; *** EUA = EMERGENCY USE AUTHORIZATION

ESTIMATES AS OF 10 APRIL 2023

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB ESTIMATES

Diversified product portfolio at various development stages targeting rare diseases
Relief's diversified product portfolio currently consists of product candidates at various stages of development, including marketed products, near-to-market products, and a varied clinical development portfolio that offers exciting growth opportunities with multiple synergies across Relief's pipeline projects.

Relief's key product candidates in its three main therapeutic indications include:

1) RARE METABOLIC DISORDERS

- **PKU GOLIKE (phenylketonuria – PKU)** (peak sales CHF 70 mn): PKU GOLIKE is the first line of food for special medical purposes (FSMP) engineered with APR's drug delivery Physiomimic™ Technology offering improved metabolic management for patients with PKU and a better compliance thanks to minimized taste, odor, and aftertaste; a complete line of products covering main age groups and individual habits; available in the EU and rolled out by distribution partners; recently launched in the US in October 2022 and commercialized with help of a US service provider

- **RLF-OD032 (phenylketonuria – PKU)** (peak sales CHF 80 mn): worldwide rights (excluding the UK) in-licensed from Meta Healthcare in July 2022 for an undisclosed initial payment and low double-digit royalty payments on net profits; development of a novel dosage form of an already FDA-approved prescription drug; novel dosage form expected to increase patient acceptance and compliance; compound currently undisclosed due to competitive reasons; Relief guides for peak sales of approximately CHF 80 mn; filing of the 505(b)(2) NDA in H1 2024

- **Olpruva/ACER-001 (urea cycle disorders – UCDs / maple syrup urine disease - MSUD):** (peak sales CHF 500+ mn): in-licensed from Acer Therapeutics in 2021; novel powder formulation of sodium phenylbutyrate (NaPB) targeted to provide a compelling alternative to Horizon Therapeutics' Buphenyl (glycerol phenylbutyrate) with an innovative taste-masking and immediate-release (IR) formulation that potentially can be taken without food at competitive pricing; developed for the treatment of various inborn errors of metabolism, including UCDs and MSUD; Orphan Drug Designation (ODD) granted in the US and the EU for MSUD
    - **Urea Cycle Disorders (UCDs)** (peak sales CHF 350+ mn – approved in the US): bioequivalence to Buphenyl obtained under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act; approved in the US in late December 2022 with launches expected in Q2 2023; potential 3-year Hatch-Waxman market exclusivity; taste-masked formulation US patent issued that protects the compound into 2036; US patent Olpruva/ACER-001 kit expected to be issued in soon provides extension into 2038; EU MAA filing H2 2023; potential to obtain Orphan Drug Designation in the EU providing 10-year market exclusivity; targeted to replace Horizon's UCDs drugs Buphenyl and Ravicti and attract new and non-compliant sufferers of UCDs
    - **Maple Syrup Urine Disease (MSUD)** (peak sales CHF 150+ mn – POC established): IND filed in July 2022; based on the encouraging POC results, a phase IIb/III trial is planned to start in H2 2023; potential launches expected in 2025; obtained Orphan Drug Designation in the US and EU, which provides 7-year and 10-year market exclusivity, respectively; there are currently no drugs approved to treat MSUD

2) RARE PULMONARY DISEASES

- **RLF-100 (various rare lung diseases)** (peak sales CHF 1.4+ bn): aviptadil (branded RLF-100) is a direct analog of the vasoactive intestinal polypeptide (VIP). Originally developed in combination with phentolamine mesylate and has been marketed in Europe since 1998 for the treatment of erectile dysfunction. RLF-100 is a synthetic form of VIP, an abundant biologically active endogenous human peptide that possesses anti-proliferative, anti-inflammatory, and immune-regulatory activities. Its predominant biological activity is observed in the lung. Hence, Relief's plan is to repurpose RLF-100 for rare respiratory diseases. RLF-100 is available in two different formulations, an intravenous (IV) for a healthcare setting and an inhaled formulation for at home, with clinical development plans for:

  1) **IV formulation:** RLF-100 IV is an intravenous (IV) injection formulation of aviptadil developed for use in a healthcare setting to treat acute respiratory diseases. RLF-100 IV key indication includes:
     - **ARDS** (peak sales CHF 650+ mn - phase II): clinical development in patients with acute respiratory distress syndrome (ARDS) caused by for instance, sepsis, pancreatitis, trauma, or pneumonia; high unmet medical need due to the lack of effective treatments; a phase IIb/III trial is planned for H2 2023; first launches guided for 2026
     - **Chronic berylliosis** (peak sales TBD – POC trial planned for 2024):

  2) **Inhaled formulation:** RLF-100 INHALED is an inhaled formulation of aviptadil developed to be administered locally by a mesh nebulizer, which can be used at home to address chronic respiratory diseases. RLF-100 INHALED key indications include:
     - **Pulmonary sarcoidosis** (peak sales CHF 500+ mn – phase IIb/III start Q2/Q3 2023): initial target indication for RLF-100 before the onset of COVID-19 pandemic in early 2020; promising POC results published in 2010; phase IIb dose-ranging trial to start in Q2/Q3 2023; first launches expected in 2027; orphan drug designation (ODD) granted in the US in 2007; eligible for 7-year US market exclusivity from the date of approval
     - **Checkpoint inhibitor-induced pneumonitis (CIP)** (peak sales CHF 250+ mn – POC trial planned for 2024):
     - **Prevention of COVID-19 associated ARDS ("WILD CARD"** peak sales CHF ~100 mn - phase IIb/III): preventing COVID-19 patients at risk of developing critical respiratory failure or life-threatening ARDS; discontinued in the phase III "I-SPY-COVID-19" trial with no benefit seen; European investigator-sponsored "Leuppi Study" results expected in late 2023; only strong "Leuppi Study" data could support further development

- **SENTINOX (prevention of COVID-19 infection)** (peak sales TBD): a novel nasal sprayable HCIO solution to block transmission of airborne viruses and bacteria, including the SARS-Cov-2 virus; a confirmatory trial is planned to start in Q2 2023, approved in the EU as a Class III medical device in 2021

3) RARE CONNECTIVE TISSUE DISORDERS

- **RLF-TD-011 (epidermolysis bullosa - EB)** (peak sales CHF 850+ mn): a novel hypochlorous (HCIO) sprayable solution stemming from APR's Tehclo™ platform that combines strong antimicrobial activity with anti-inflammatory properties with the potential to become one of the first-ever products approved for EB. A preliminary proof of concept (POC) trial showed promising results with improvement of skin blistering and tissue repair in just two weeks of treatment; US Orphan Drug Designation (ODD) granted in 2019 on promising early-stage programs providing 7-year market exclusivity from approval date; potential for EU ODD with 10-year market exclusivity; discussions with regulators ongoing to finalize clinical development path, POC trial started in February 2023, first launch expected in 2027
- **RLF-TD011 (cutaneous t-cell lymphoma - CTCL) NEW** peak sales TBD: an investigator-initiated POC trial will start in 2023 with results due in 2024; upon positive POC data, registrational trials for US and EU approval could start in 2024 with approval expected in 2025/2026
- **RLF-TM011 (skin toxicities in cancer therapies)** (peak sales TBD): RLF-TM011 approved in the EU for the prevention and treatment of skin rashes associated with cancer treatments; Relief assessing which products offer the optimal strategic fit combined with differentiation that can offer strong growth potential
- **NEXODYN (chronic wounds)** (peak sales TBD): Nexodyn AOS, a sprayable HCIO solution for acute and chronic wounds

Legacy APR products (royalty revenues of CHF ~15 mn): main royalty-generating products consist of multiple reformulations of existing drugs, including Cambia and Voltfast for acute migraine attacks in adults, Eminocs for acute pain and Voltadol for local pain and strains; Setofilm/Zuplenz/Ondissolve, an oral dispersible film containing ondansetron for treating chemotherapy-, radiotherapy- and postoperative nausea and vomiting; commercialized by partners in return for royalties; several products to phase out in next few years

In the following section, we will provide an in-depth analysis and forecasts for Relief's key drivers:

Forecasts & Sensitivity Analysis

PKU GOLIKE / RLF-OD032 (phenylketonuria - PKU)

I) PKU GOLIKE in PKU - Peak sales CHF 70 mn; rNPV CHF 0.038/share

We expect global peak sales for the PKU GOLIKE family of food for special medical purposes (FSMP) products for phenylketonuria (PKU) to reach approximately CHF 70 mn. PKU GOLIKE has been available in Europe since 2018 and was launched in the US in October 2022. A strong growth path has been established with a clear life cycle management strategy through 2024 with the rollout of additional complementary PKU GOLIKE products. PKU GOLIKE is marketed by Relief's own direct sales team in selected European countries and the US and distributed by established service partners. Assuming average COGS of approximately 25-30% (including the cost of the service providers) and M&S of less than CHF 10 mn during the product life cycle, we calculate an NPV of CHF 228 mn or CHF 0.038 per share (see page 24). NOTE: Development as a prescription-only treatment in the US could boost peak sales substantially to above CHF 200 mn.

II) RLF-OD032 in PKU – Peak sales CHF 80 mn; rNPV CHF 0.016/share

Relief guides for global peak sales (excluding the UK) of RLF-OD032 amount to around CHF 80 mn. RLF-OD032 is an undisclosed novel dosage form of an already FDA-approved prescription drug intended for the treatment of PKU patients. Relief anticipates the filing of the 505(b)(2) NDA in 2024, with the first launches targeted for H1 2025. RLF-OD032 can be leveraged with Relief's existing sales infrastructure for PKU GOLIKE. We calculate an rNPV of CHF 95 mn or CHF 0.016 per share based on their peak sales guidance and a conservative 35% success rate, as the compound has not yet been disclosed due to competitive reasons.

PKU GOLIKE – A complete family of FSMP-engineered products for phenylketonuria

The 2021 acquisition of APR expanded Relief's pipeline further with compounds targeting rare inherited metabolic recessive disorders, such as PKU GOLIKE for patients with phenylketonuria (PKU). PKU GOLIKE is the first line of food for special medical purposes (FSMP) products engineered with APR's drug delivery Physiomimic™ Technology offering improved metabolic management for patients with PKU and better compliance thanks to minimized taste, odor, and aftertaste. FSMP products are specifically intended for patients with a limited, impaired, or disturbed capacity to take, digest, absorb, metabolize, or excrete ordinary foods, or certain nutrients or metabolites; or with other medically nutrient requirements whose dietary management cannot be achieved by modification of the normal diet alone. FSMPs should be used only under medical supervision and must carry labeling information about their intended use.

The proprietary and patented Physiomimic™ Technology is the first and only technology able to control and prolong the release of multiple active ingredients (up to 19 amino acid mixes) simultaneously in the most prevalent, rare, inherited metabolic diseases. Beyond PKU GOLIKE, APR is developing optimized amino acid mix-based products for other rare metabolic disorders, such as tyrosinemia, homocystinuria, and maple syrup urine disease (MSUD). For MSUD, such a product is expected to be highly complementary to Relief's ACER-001, which is also in development for treating this disease and possesses effective

taste-masking properties.

PKU GOLIKE was approved in the EU in 2018 and, most recently, launched in the US in October 2022. An own specialist sales infrastructure is in place in selected European countries and the US to support PKU GOLIKE, as well as established distribution partnerships for other countries in Europe and beyond.

PKU patients must maintain a lifelong strict diet to have a normal lifespan
PKU is a rare inherited disorder caused by a defect of the enzyme needed to break down phenylalanine, leading to a toxic buildup of the amino acid phenylalanine (Phe) when eating foods that contain protein or aspartame that can eventually lead to serious health problems. Untreated PKU can lead to intellectual disability, seizures, behavioral problems, and mental disorders. It may also result in a musty smell and lighter skin. A baby born to a mother who has poorly treated PKU may have heart problems, a small head, and a low birth weight. PKU affects, on average, about 1 in 10,000 newborns in developed countries. Males and females are affected equally. Approximately 350,000 patients suffer from PKU in the world's key markets.

The standard of care for PKU is mainly based on two essential pillars:

1. **A lifelong low-protein diet** (that limits Phe intake from foods)
2. **Protein substitute administration** (to support physiological protein synthesis)

The diet should begin as soon as possible after birth and continue for life. Patients who are diagnosed early and maintain a strict diet can have normal health and a normal lifespan. The main objective of the treatment is to maintain Phe levels in the recommended range, and the efficacy of the treatment is strongly influenced by compliance with the prescribed diet. Compliance becomes increasingly difficult with age due to diverse factors. Bad taste, odor, and aftertaste of amino acid-based protein substitutes are still major issues that prevent an important number of adults from following their diet. Moreover, scientific evidence indicates that significant sub-optimal health outcomes still exist even in compliant PKU patients. This is mainly due to the absorption profile of free amino acids (AA), which is very different from that of intact natural proteins. Free amino acids bypass the digestive phase giving place to plasma levels of amino acids that are higher, peak faster, and decrease more quickly. Thus, the diverse kinetic profile of free amino acids has an impact on body metabolism and consequently affects the health of people with PKU.

PKU GOLIKE's minimized taste, odor, and aftertaste offer better patient compliance
PKU GOLIKE is the first controlled-release amino acid mix product with effective taste and odor masking. With these characteristics, PKU GOLIKE is a uniquely differentiated product, offering improved metabolic management and better compliance for PKU patients of all age groups. The PKU GOLIKE line of products includes sachets and a unique Ready to Drink formulation, while PKU GOLIKE Krunch and bars will be launched soon and extended with different flavors over time.

Relief to expand APR's European and US sales infrastructure
Following APR's launch of PKU GOLIKE in Europe in 2018, Relief is planning to expand the commercial infrastructure beyond the current countries and refine the marketing activities to increase and accelerate future growth. In other countries, PKU GOLIKE is available as a prescription-only, fully reimbursed product for PKU. In October 2022, PKU GOLIKE was

launched in the US by Relief's commercial team and a leading US medical nutrition provider for patient access and support services. This triggered a cash payment of CHF 2.8 mn and a share payment of approximately 150 mn ordinary shares of Relief to the former shareholders of APR Applied Pharma Research SA, pursuant to the June 2021 acquisition agreement. In the US, PKU GOLIKE has been granted Orphan Drug Designation, and Relief intends to assess options to pursue approval of PKU GOLIKE as a prescription product. A strong growth path has been established by APR with a clear life cycle management strategy through 2024 with the rollout of additional complementary PKU GOLIKE products.

We forecast global peak sales for the PKU GOLIKE family of FSMP products for PKU to reach approximately CHF 70 mn. Development as a prescription-only treatment in the US could boost peak sales substantially to more than CHF 200 mn.

PKU GOLIKE - FINANCIAL FORECASTS FOR PHENYLKETONURIA (PKU)

REVENUE MODEL

UNITED STATES - EXCLUSIVE DISTRIBUTOR	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
SALES (CHF MN)	**1**	**5**	**11**	**16**	**21**	**25**	**28**	**31**	**33**	**35**	**36**
CHANGE (%)		478%	100%	50%	28%	17%	15%	10%	6%	6%	3%
COGS (%) (INCL. US SERVICE PROVIDER COSTS)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
COGS (CHF MN)	0	-2	-3	-5	-6	-7	-8	-9	-10	-10	-11
M&S (CHF MN)	0	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
PROFIT BEFORE TAX (CHF MN)	**0**	**2**	**6**	**10**	**13**	**16**	**18**	**20**	**22**	**23**	**23**
TAXES (CHF MN)	0	0	0	-1	-1	-2	-2	-2	-2	-3	-3
PROFIT (CHF MN)	**0**	**2**	**6**	**10**	**12**	**14**	**16**	**18**	**19**	**20**	**21**

EUROPE - RELIEF SALES FORCE	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
SALES (CHF MN)	**3**	**6**	**10**	**14**	**18**	**21**	**24**	**26**	**28**	**30**	**32**
CHANGE (%)	234%	120%	73%	42%	30%	17%	15%	9%	8%	7%	7%
COGS (%)	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
COGS (CHF MN)	-1	-1	-2	-3	-4	-5	-6	-6	-7	-7	-8
M&S (CHF)	-3	-3	-3	-3	-3	-3	-3	-3	-4	-4	-4
PROFIT BEFORE TAX (CHF MN)	**-1**	**1**	**4**	**7**	**10**	**12**	**14**	**16**	**17**	**19**	**20**
TAXES (CHF MN)	0	0	0	0	-1	-1	-2	-2	-2	-2	-2
PROFIT (CHF MN)	**-1**	**1**	**4**	**7**	**9**	**11**	**13**	**14**	**15**	**17**	**18**

	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E
GLOBAL SALES (CHF MN)	**3**	**11**	**20**	**30**	**38**	**45**	**52**	**56**	**60**	**64**	**67**
CHANGE (%)	360%	218%	86%	46%	29%	17%	15%	9%	7%	6%	5%
GLOBAL SALES (USD MN)	**4**	**12**	**22**	**33**	**42**	**49**	**57**	**62**	**66**	**70**	**74**
CHANGE (%)	343%	230%	86%	46%	29%	17%	15%	9%	7%	6%	5%
GLOBAL PROFIT (CHF MN)	**-1**	**4**	**10**	**16**	**21**	**25**	**29**	**32**	**34**	**37**	**39**
CHANGE (%)	-200%	-572%	192%	57%	27%	20%	17%	10%	7%	7%	5%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**228**
NUMBER OF SHARES (MN)	5,931
NPV PER SHARE (CHF)	**0.038**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	85	0.053	0.051	0.049	0.047	0.045	0.044	0.042
	80	0.050	0.048	0.046	0.044	0.043	0.041	0.040
	75	0.047	0.045	0.043	0.041	0.040	0.039	0.037
PEAK SALES (CHF MN)	70	0.043	0.042	0.040	**0.038**	0.037	0.036	0.035
	65	0.040	0.039	0.037	0.036	0.035	0.034	0.032
	60	0.037	0.036	0.035	0.033	0.032	0.031	0.030
	55	0.034	0.033	0.032	0.030	0.029	0.028	0.027

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

RLF-OD032 in phenylketonuria (PKU) – rNPV of CHF 0.016/share

In July 2022, the global rights (excluding the UK) for RLF-OD032 were acquired from Meta Healthcare for an undisclosed upfront payment and low double-digit royalty payments on the net profit. RLF-OD032 is a novel dosage form of an already FDA-approved prescription drug intended for phenylketonuria (PKU) patients. The US 505(b)(2) filing of the new drug application (NDA) is planned for 2024, with the first launches expected to occur in H1 2025. Relief guides for global peak sales (excluding the UK) of approximately CHF 80 mn. RLF-OD032 adds to the company's product offering for PKU patients, which can be leveraged through the existing sales infrastructure. We calculate an rNPV of CHF 95 mn or CHF 0.016 per share, assuming a conservative 35% success rate as the compound has not yet been disclosed due to competitive reasons.

Olpruva/ACER-001 (urea cycle disorders – UCDs & maple syrup urine disease - MSUD)

I) Olpruva/ACER-001 UCDs - Peak sales CHF 350+ mn; rNPV CHF 0.174/share
We forecast global peak sales of around CHF 350 mn for Olpruva/ACER-001 in urea cycle disorders (UCDs), assuming a US launch in early July 2023 by Acer (US, Canada, Brazil, Turkey, and Japan rights) followed later by Relief (Europe, ROW rights). We calculate an rNPV of CHF 1,030 mn or CHF 0.174 per share assuming a 90% success rate, the average of US (100%) approved and EU (80%) filing while accounting for the 60% net profit split Relief is entitled to from Acer territories and 15% net royalties Acer is entitled to from Relief territories next to regulatory milestone payments of up to USD 6 mn and up to USD 20 mn in US development and commercial launch costs (see page 30)

II) Olpruva/ACER-001 MSUD - Peak sales CHF 150+ mn; rNPV CHF 0.026/share
For Olpruva/ACER-001 in maple syrup urine disease (MSUD), we forecast peak sales in the US and EU to reach CHF 166 mn assuming the first launches occur in 2025. We calculate an rNPV of CHF 156 mn or CHF 0.026/share, assuming a 35% (POC established) success rate and accounting for the same terms as for UCDs stated above (see page 32).

Olpruva/ACER-001 – high-margin drug targeting rare diseases

In January 2021, Relief and Acer Therapeutics signed an option agreement for exclusivity to negotiate a collaboration and license agreement for the worldwide development and commercialization of ACER-001 (branded Olpruva™ in the US by Acer) for the treatment of Urea Cycle Disorders (UCDs) and Maple Syrup Urine Disease (MSUD). The definitive agreement was reached in March 2021, effectively adding a new attractive, late-stage, low-risk, high-priced, high-margin rare disease compound to Relief's pipeline with Olpruva/ACER-001. Until recently, Relief's pipeline only consisted of RLF-100 in various lucrative respiratory indications, including COViD-19 complications. We conservatively forecast peak sales for both rare disease indications for Olpruva/ACER-001 to amount to more than CHF 500 mn based on conservative pricing assumptions, with the first launch in UCDs to occur in the US in Q2 2023. These are ultra-niche markets and, accordingly, will not require a substantial sales infrastructure to penetrate. Prescribers and patients are very concentrated with detailed registries. Therefore, these sales ought to be highly accretive for Relief. In late December 2022, ahead of its scheduled 15 January 2023 PDUFA date, Olpruva/ACER-001 was approved by the FDA for treating patients with UCDs in the US. The compound was developed under Section 505(b)(2), providing an alternative pathway for filing an NDA, and is entitled to 3-year Hatch-Waxman market exclusivity from the approval date. Following the US approval, Relief intends to submit a Marketing Authorization Application (MAA) for approval of Olpruva/ACER-001 in the EU and UK in H2 2023.

Long patent life and market exclusivities protect until at least up to 2036

The FDA and EMA have granted Orphan Drug Designation for Olpruva/ACER-001 in MSUD, providing 7-year and 10-year market exclusivity, respectively, from the date of approval. Acer has also been issued several patents protecting the usage of and composition of Olpruva/ACER-001. In February 2022, a method of use patent for Olpruva/ACER-001 was issued by the USPTO for treating UCDs and MSUD, extending its patent protection until September 2036. In addition, in China, a patent was issued providing Olpruva/ACER-001 patent protection in UCDs and MSUD until August 2031.

Attractive terms with a 60% profit split for the US in favor of Relief

Under the terms of the agreement, Acer received a USD 1 mn non-refundable payment for exclusivity until 30 June 2021 (for the initial option agreement signed in January 2021), and an additional USD 10 mn in cash and will retain development and commercialization rights in the US, Canada, Brazil, Turkey, and Japan, with a 60% profit split in favor of Relief. Acer will receive 15% net sales royalties from Relief for sales in its territories (Europe, ROW) and a total of up to USD 6 mn milestones based on the first EU marketing approvals of Olpruva/ACER-001 in UCDs and MSUD. Relief will pay up to USD 20 mn in US development and commercial launch costs for the UCDs and MSUD indications, of which USD 15 mn has been paid to date.

I) Olpruva/ACER-001 UCDs - Peak sales CHF 350+ mn; rNPV CHF 0.174/share

Olpruva/ACER-001's attractive profile in UCDs offers a lucrative switch opportunity

UCDs are a rare group of disorders caused by genetic mutations that result in a deficiency in 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, while 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. UCDs is an ultra-rare orphan disease with the incidence estimated to be at least 1:35,000 births. Partial defects of the urea cycle make the number much higher. UCDs are estimated to affect less than 10,000 patients in the US and a slightly higher number of patients in the EU based on the size of the EU population. 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.

Taste masking the first USP with the potential to improve patient compliance

Current drugs such as Horizon Therapeutics' Buphenyl (glycerol phenylbutyrate) and Ravicti (sodium phenylbutyrate) are effective treatments in managing ammonia levels. However, they are pricy, must be taken frequently with food, and include unpleasant taste, leading to patient non-compliance. Olpruva/ACER-001 is a taste-masked, immediate-release proprietary powder formulation of sodium phenylbutyrate (NaPB) developed by Acer using a microencapsulation process. Olpruva/ACER-001 microparticles consist of a core center, a layer of active drug, and a taste-masking coating which dissolves in the stomach, allowing taste to be neutralized while still allowing for rapid systemic release. Olpruva/ACER-001's taste-masked properties could make it a compelling alternative to existing NaPB-based treatments, such as Buphenyl and Ravicti as the unpleasant taste associated with NaPB is cited as a major impediment to patient compliance with those treatments. In 2019, sales of Buphenyl and Ravicti amounted to USD 239 mn, up 19% yoy. Note that in March 2015, Horizon Therapeutics acquired Hyperion Therapeutics for approximately USD 1.1 bn in cash to expand and diversify its orphan drug product portfolio with Buphenyl and Ravicti. In December 2022, Amgen announced it would acquire Horizon Therapeutics for approximately USD 27.8 bn in cash.

Compelling data showing bioequivalence to Buphenyl…

In July 2020, Acer announced data from a food effect study in healthy volunteers showing that administration of Olpruva/ACER-001 in a fasted state increased systemic exposure of

phenylbutyrate (PBA), phenylacetate (PAA), and phenylacetylglutamine (PAGN) levels compared to a fed state, and therefore based on modeling data may improve disease management in patients with UCDs when compared to currently approved treatments requiring administration with food.

Results from Part B of the Olpruva/ACER-001 bioequivalence (BE) trial in healthy volunteers (n=36), announced in February 2020, showed that the compound was bioequivalent to Buphenyl and were within the parameters recommended by the FDA's Guidance for Industry, "Statistical Approaches to Establishing Bioequivalence." The BE trial included a food effect study, which evaluated the pharmacokinetics (PK) of sodium phenylbutyrate (NaPBA), showing that administration of Olpruva/ACER-001 in a fasted state achieved more than two times the maximum concentration (Cmax) of PBA compared to administration of the same dose of Olpruva/ACER-001 in a fed state. These results are consistent with previously published data by Nakano, *et al.* that evaluated PK of NaPBA in patients with progressive familial intrahepatic cholestasis, also demonstrating that administration of NaPBA in a fasted state significantly increased PBA peak plasma concentration compared to administration of NaPBA in a fed state.

…and the potential of Olpruva/ACER-001 to be given without food, another USP

Currently approved therapies for UCDs, including Buphenyl and Ravicti, must be administered with food. Buphenyl must be administered in a fed state due to its aversive odor and taste, with side effects including nausea, vomiting, and headaches, which often lead to discontinuation of treatment. Additionally, prescribing information states that the Buphenyl food effect is unknown. Ravicti pharmacokinetic (PK) and pharmacodynamic (PD) properties were determined to be indistinguishable in fed or fasted states. Olpruva/ACER-001 is uniquely formulated with its multi-particulate, taste-masked coating to allow for administration in a fasted state while still allowing for rapid systemic release.

Based on the results from the food effect study within the Olpruva/ACER-001 BE trial, Acer commissioned Rosa & Co. LLC to create a PhysioPD PK model to evaluate the potential food effect on exposure, tolerability, and efficacy of Olpruva/ACER-001 in UCDs patients. Results from this in silico model suggest that administration of Olpruva/ACER-001 in a fasted state required approximately 30% less PBA to achieve comparable therapeutic benefit in a fed state. In addition, the model predicted that administration of Olpruva/ACER-001 in a fasted state compared to administration of Buphenyl or Ravicti (same amounts of PBA) in their required fed states is expected to result in higher peak blood PBA, PAA and PAGN concentrations, predicting a 43% increase in urinary PAGN levels (a negative correlation between blood ammonia area under the curve and 24-hour urinary PAGN amount has been demonstrated). The results of the Olpruva/ACER-001 food effect study, published literature, and *in silico* modeling suggest that Olpruva/ACER-001 administered in a fasted state, and likely just 10 minutes prior to meals, could offer UCD patients a safe and better disease management option compared to currently approved products that are required to be taken with food.

Olpruva/ACER-001 developed under Section 505(b)(2) provides 3-year exclusivity

Acer developed Olpruva/ACER-001 under Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, which provides a potentially streamlined path for companies that have developed improvements to drug products previously approved by the FDA. Section 505(b)(2) provides an alternative pathway for submission of an NDA, referred to as a 505(b)(2) application, when some or all of the safety and efficacy investigations relied on for

approval were not conducted by or for the applicant and for which the applicant has not obtained a right of reference but for which the relevant information is publicly available. The Hatch-Waxman Amendments also provide pharmaceutical products approved under Section 505(b)(2) with potential market exclusivity for three years from FDA approval date.

Several genetic approaches stumble and are years away with prohibitive pricing

We do not expect gene therapy approaches - even if they prove highly effective clinically - to prevent the achievement of market traction with Olpruva/ACER-001 since these will inevitably need to be priced at USD 500,000 to USD 1,000,000 or more per patient (since they are one-time treatments) and accordingly shall only address a small segment of the overall market. Ultragenyx's DTX301 is the most advanced gene therapy for curative approaches to ornithine transcarbamylase (OTC) deficiency, the most common urea cycle disorder with phase I/II ongoing. Translate Bio's MRT5201 is on clinical hold, while CureVac handed rights to ARCT-810 back to Arcturus Therapeutics in 2019.

US FDA approval of Olpruva/ACER-001 ahead of 15 January 2023 PDUFA date

In May 2021, Relief's partner Acer announced a positive outcome from a pre-NDA (New Drug Application) meeting with the FDA to discuss the content of Acer's planned NDA submission of ACER-001 for the treatment of patients with UCDs (urea cycle disorders). Based on FDA feedback, the proposed data package was deemed to be sufficient to support an NDA submission under Section 505(b)(2) regulatory pathway for this indication. In August 2021, Acer filed an NDA under Section 505(B)(2) regulatory pathway for US approval of ACER-001 in urea cycle disorders (UCDs) and shortly after received acceptance of filing triggering the FDA review initially with a 5 June 2022 Prescription Drug User Fee Act (PDUFA) date when the FDA was expected to complete its review. However, shortly after the initial PDUFA date, the FDA issued a Complete Response Letter (CRL), citing the need to inspect a third-party contract packaging manufacturer because the facility was not ready for inspection. In July 2022, Acer announced that the FDA had accepted for review the resubmitted NDA designated as a Class 2 resubmission and set a new PDUFA date of 15 January 2023. In late December 2022, the FDA approved Olpruva/ACER-001 in UCDs ahead of its scheduled PDUFA date. The US launch is expected in Q2 2023.

CHF 350+ mn peak sales in UCDs with US launch expected in Q2 2023

We have based our detailed bottom-up forecasts for Olpruva/ACER-001 largely on detailed data available in the US and extrapolated the data where possible to other regions, where detailed data is often lacking or not publicly available. We have based our estimates on sources such as NORD, GARD, NIH, HHS, and Acer Therapeutics, among others.

To account for regional differences, we provide detailed forecasts for the US and Europe. Sales in regions such as Canada, Brazil, Turkey, Japan, and Asia could provide substantial upside to our forecasts. The recently issued US formulation patent covering the taste-masking claims and method of use patent for UCDs and MSUP now extends protection up to 2036. The Hatch-Waxman Amendments under Section 505(b)(2) provide Olpruva/ACER-001 with potential market exclusivity for three years from FDA approval. Additionally, the compound enjoys ODD exclusivity for MSUD in the EU and US providing 10-year and 7-year market exclusivity, respectively.

Based on estimated incidence figures of individual UCDs (CPS1, OTC, ASS1, ASL, ARG1, ornithine translocase, and citrin deficiencies) from Ah New N *et al.* "Urea Cycle Disorders Overview", we estimate there are approximately 9,500 UCDs patients in the US. We assume

~80% of these patients have been diagnosed and that ~90% are eligible for Olpruva/ACER-001 treatment. In the US, we conservatively assume an annual treatment cost per patient of USD 300,000 per patient with 90% patient compliance due to the improved formulation with taste masking and the potential to take Olpruva/ACER-001 without food. Assuming a US launch in Q2 2023 and peak market penetration conservatively reaching up to 15%, we forecast US peak sales of CHF 306 mn.

Applying a similar approach to the EU with an annual treatment cost of USD 60,000, a launch in 2024, and a conservative peak market penetration of ~10%, we forecast CHF 55 mn peak sales for the EU (for details, see the following page).

Sales forecasts may prove conservative and will be highly accretive for Relief

Note that these peak sales forecasts are conservative and expected to be highly accretive for Relief. For instance, our pricing assumptions are decidedly conservative when compared to current Buphenyl (USD 200k-400k) and Ravicti (USD 200k-1.2 mn) pricing and the prices of other ultra-orphan small molecule drugs, potentially resulting in higher market penetration than forecast. We have not captured sales outside the US and EU, which could be meaningful. Some of these markets, such as Brazil, should be addressable now that FDA approval has been secured. Prescribers and patients are very concentrated with detailed registries and can be covered by a sales force of ~10 people in the US and 15-20 in the EU. Relief might use a contract commercial organization (CCO) with substantial experience in selling ultra-orphan drugs. The API of Olpruva/ACER-001 has been well-known for an extended period and is relatively inexpensive to manufacture.

Forecasts & Sensitivity Analysis

OLPRUVA/ACER-001 - FINANCIAL FORECASTS FOR UREA CYCLE DISORDERS (UCD)

INDICATION	TREATMENT OF PATIENTS WITH UREA CYCLE DISORDERS WITH DEFICIENCIES INVOLVING OF CPS*, OTC**, OR AS***
DOSAGE	ADJUNCTIVE TO STANDARD OF CARE THERAPY FOR UCDS
PRICE	ANNUAL TREATMENT COST PER PATIENT WE ASSUME; US: USD 300,000; EU/ROW: EUR 60,000
STANDARD OF CARE	HORIZON THERAPEUTICS' BUPHENYL AND RAVICTI
UNIQUE SELLING POINT	POTENTIALLY FIRST FORM OF SODIUM PHENYLBUTYRATE THAT CAN BE TAKEN WITHOUT FOOD WITH UNIQUE TASTE-MASKING FORMULATION AT A COMPETITIVE PRICE

7Ps ANALYSIS

PATENT	ISSUED US FORMULATION (TASTE-MASKING) PATENT EXPIRES 2036; ORPHAN DRUG DESIGNATION EXCLUSIVITY IN THE US (7 YEARS) AND EU (10 YEARS) FROM APPROVAL DATE
PHASE	APPROVED IN THE US (DEC 2022) UNDER SECTION 505(B)(2) ACER-001 HAS PROVEN BIOEQUIVALENCE TO BUPHENYL; EU MAA FILING Q2 2023
PATHWAY	DEVELOPED UNDER SECTION 505(B)(2) FOR IMPROVEMENTS TO PRODUCTS PREVIOUSLY APPROVED BY THE FDA
PATIENT	MORE CONVENIENT THERAPY THAT CAN BE GIVEN WITHOUT FOOD AND HAS UNIQUE TAST-MASKING FORMULATION MAKING IT EASIER TO TAKE
PHYSICIAN	HIGHER PATIENT COMPLIANCE DUE TO THE TASTE-MASKING FORMULATION AND FIRST FORM OF SODIUM PHENYLBUTYRATE THAT CAN BE GIVEN WITHOUT FOOD
PAYER	OVERALL LOWER TREATMENT COSTS DUE TO COMPETITIVE PRICING AND POTENTIALLY HIGHER PATIENT COMPLIANCE COMPARED TO IN-MARKET DRUGS
PARTNER	GLOBAL RIGHTS ACQUIRED FROM ACER; ACER RETAINS US, CANADA, BRAZIL, TURKEY & JAPAN RIGHTS; RELIEF ENTITLED TO 60% PROFITS ACER TERRITORIES

* CPS = CARBAMYLPHOSPHATE SYNTHASE; ** OTC = ORNITHINE TRANSCARBAMYLASE; *** AS = ARGININOSUCCINIC ACID SYNTHASE

REVENUE MODEL

UNITED STATES - ACER THERAPEUTICS TERRITORY	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF UREA CYCLE DISORDER (UCD) PATIENTS	9,793	9,891	9,990	10,090	10,191	10,293	10,396	10,500	10,605	10,711	10,818
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
UCD PATIENTS DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
UCD PATIENTS DIAGNOSED	7,834	7,913	7,992	8,072	8,153	8,234	8,316	8,400	8,484	8,568	8,654
ELIGIBLE UCD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE UCD PATIENTS	7,051	7,122	7,193	7,265	7,337	7,411	7,485	7,560	7,635	7,712	7,789
PENETRATION (%)	0%	3%	5%	9%	12%	13%	14%	15%	15%	15%	15%
NUMBER OF PATIENTS	0	178	360	654	880	963	1,048	1,134	1,145	1,157	1,168
ANNUAL TREATMENT COST PER PATIENT (CHF)	236,438	234,744	241,787	249,040	256,511	264,207	272,133	280,297	288,706	297,367	306,288
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - ACER THERAPEUTICS BOOKS SALES	**0**	**44**	**89**	**161**	**217**	**237**	**258**	**279**	**282**	**285**	**288**
CHANGE (%)			102%	82%	35%	9%	9%	8%	1%	1%	1%
ROYALTIES (CHF MN) - PAID TO BAYLOR	0	-1	-2	-3	-4	-5	-5	-6	-6	-6	-6
UPFRONT & MILESTONES (CHF MN) - PAID BY RELIEF	0	0	0	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	-1	-3	-5	-7	-8	-9	-9	-9	-9	-10
R&D COSTS (CHF MN) - PAID BY RELIEF	-6	-1	0	0	0	0	0	0	0	0	0
M&S (CHF MN)	0	-2	-3	-3	-3	-3	-3	-3	-3	-3	-3
PROFIT BEFORE TAX (CHF MN)	**-6**	**39**	**81**	**150**	**203**	**222**	**242**	**262**	**265**	**267**	**270**
PROFIT SPLIT 60/40 IN FAVOR OF RELIEF	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**-3**	**23**	**49**	**90**	**122**	**133**	**145**	**157**	**159**	**160**	**162**
TAXES (CHF MN)	0	0	0	-5	-13	-15	-16	-17	-17	-18	-18
PROFIT (CHF MN)	**-3**	**23**	**49**	**86**	**108**	**119**	**129**	**140**	**141**	**143**	**144**

EUROPE - RELIEF TERRITORY	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF UREA CYCLE DISORDER (UCD) PATIENTS	12,974	13,103	13,234	13,367	13,500	13,635	13,772	13,909	14,048	14,189	14,331
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
UCD PATIENTS DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
UCD PATIENTS DIAGNOSED	10,379	10,483	10,587	10,693	10,800	10,908	11,017	11,128	11,239	11,351	11,465
ELIGIBLE UCD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE UCD PATIENTS	9,341	9,434	9,529	9,624	9,720	9,817	9,916	10,015	10,115	10,216	10,318
PENETRATION (%)	0%	0%	2%	4%	7%	9%	10%	10%	10%	10%	10%
NUMBER OF PATIENTS	0	0	143	385	680	884	992	1,001	1,011	1,022	1,032
ANNUAL TREATMENT COST PER PATIENT (CHF)	60,071	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**8**	**21**	**37**	**48**	**53**	**54**	**54**	**55**	**56**
CHANGE (%)				169%	77%	30%	12%	1%	1%	1%	1%
15% ROYALTIES (CHF MN) - PAID TO ACER	0	0	-1	-3	-5	-7	-8	-8	-8	-8	-8
UPFRONT & MILESTONES (CHF MN) - PAID TO ACER	0	0	0	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	-1	-3	-6	-7	-8	-8	-8	-8	-8
R&D COSTS (CHF MN)	-1	0	0	0	0	0	0	0	0	0	0
M&S (CHF)	0	0	-2	-3	-3	-3	-3	-3	-3	-3	-3
PROFIT BEFORE TAX (CHF MN)	**-1**	**0**	**3**	**11**	**22**	**30**	**34**	**34**	**35**	**35**	**35**
TAXES (CHF MN)	0	0	0	-1	-2	-3	-4	-4	-4	-4	-4
PROFIT (CHF MN)	**-1**	**0**	**3**	**11**	**20**	**27**	**30**	**31**	**31**	**31**	**31**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (CHF MN)	**0**	**44**	**96**	**182**	**253**	**285**	**311**	**333**	**336**	**340**	**343**
CHANGE (%)			120%	89%	39%	12%	9%	7%	1%	1%	1%
GLOBAL SALES (USD MN)	**0**	**48**	**106**	**199**	**278**	**312**	**341**	**365**	**369**	**373**	**376**
CHANGE (%)			120%	89%	39%	12%	9%	7%	1%	1%	1%
GLOBAL PROFIT (CHF MN)	**-4**	**23**	**52**	**96**	**128**	**145**	**159**	**170**	**172**	**174**	**176**
CHANGE (%)	377%	-626%	126%	86%	33%	13%	10%	7%	1%	1%	1%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**1,145**	
NUMBER OF SHARES (MN)	5,931	
NPV PER SHARE (CHF)	**0.193**	
SUCCESS PROBABILITY	90%	AVERGAGE OF US (100%) APPROVED AND EU (80%) FILING
RISK ADJUSTED NPV PER SHARE (CHF)	**0.174**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	0.217	0.209	0.202	0.193	0.188	0.182	0.176
	95%	0.206	0.199	0.192	0.183	0.179	0.173	0.167
	90%	0.195	0.188	0.182	**0.174**	0.169	0.164	0.158
	85%	0.184	0.178	0.172	0.164	0.160	0.155	0.150
SUCCESS PROBABILITY	80%	0.173	0.167	0.161	0.154	0.151	0.146	0.141
	75%	0.163	0.157	0.151	0.145	0.141	0.136	0.132
	70%	0.152	0.146	0.141	0.135	0.132	0.127	0.123
	65%	0.141	0.136	0.131	0.125	0.122	0.118	0.114
	60%	0.130	0.125	0.121	0.116	0.113	0.109	0.106

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

II) Olpruva/ACER-001 MSUD - Peak sales CHF 150+ mn; rNPV CHF 0.026/share

MSUD – treating an ultra-rare disease with no available drug treatments
Maple syrup urine disease (MSUD) is a rare but serious inherited condition whereby the human body cannot process certain amino acids (the "building blocks" of protein), causing a harmful build-up of substances in the blood and urine. The human body breaks down protein foods such as meat and fish into amino acids. Any amino acids that are not needed are usually broken down and removed from the body. Infants with MSUD cannot break down the amino acids leucine, isoleucine, and valine. Very high levels of these amino acids are harmful. Without treatment, severe, life-threatening symptoms can develop, including seizures (fits) or falling into a coma. Some children with untreated MSUD are also at risk of brain damage and developmental delay. One of the characteristic symptoms of MSUD is sweet-smelling urine, which gives the condition its name. Besides a highly restricted diet of branched-chain amino acid (BCCA) free synthetic foods and formula, there are no currently approved treatments for MSUD.

POC treatment with NaPB (active ingredient Olpruva/ACER001) established in MSUD
Therapy with sodium phenylacetate/benzoate or sodium phenylbutyrate (NaPB) in UCDs patients has been associated with a selective reduction in branched-chain amino acids (BCAA) in spite of adequate dietary protein intake. Based on this clinical observation, the potential of phenylbutyrate treatment to lower BCAA and their corresponding a-keto acids (BCKA) in patients with classic and variant late-onset forms of maple syrup urine disease (MSUD) was investigated. In vitro and in vivo experiments to elucidate the mechanism for this effect were also performed. BCAA and BCKA are significantly reduced following phenylbutyrate therapy in control subjects and in patients with late-onset, intermediate MSUD. In vitro treatment with phenylbutyrate of control fibroblasts and lymphoblasts resulted in an increase in the residual enzyme activity, while treatment of MSUD cells resulted in a variable response that did not simply predict the biochemical response in the patients. In vivo phenylbutyrate increases the proportion of active hepatic enzyme and unphosphorylated form over the inactive phosphorylated form of the E1a subunit of the branched-chain a-keto acid dehydrogenase complex (BCKDC). Using recombinant enzymes, it was shown that phenylbutyrate prevents phosphorylation of E1a by inhibiting the BCKDC kinase from activating BCKDC overall activity, providing a molecular explanation for the effect of phenylbutyrate in a subset of MSUD patients. Therefore, phenylbutyrate treatment may be a valuable treatment for reducing the plasma levels of neurotoxic BCAA and their corresponding BCKA in a subset of MSUD patients.

Phase IIb/III trials to start in H2 2023 with a potential launch in 2025
Based on these encouraging POC trial results Acer and Relief plan to start phase IIb/III development of Olpruva/ACER-001 in MSUD in H2 2023, with a potential launch in the US and EU in 2025.

CHF 150+ mn peak sales in MSUD assuming the same pricing as for UCDs
The estimated number of patients affected with MSUD in the US is approximately 2,500, and ~3,300 in the EU. We assume 80% are not diagnosed, and 90% are eligible for Olpruva/ACER-001 treatment. Applying the same pricing as for UCDs and market penetration of approximately 25%, we forecast global peak sales for Olpruva/ACER-001 in MSUD to amount to CHF 166 mn (for details, see the following page).

Forecasts & Sensitivity Analysis

OLPRUVA/ACER-001 - FINANCIAL FORECASTS FOR MAPLE SYRUP URINE DISEASE (MSUD)

INDICATION	TREATMENT FOR PATIENTS WITH MAPLE SYRUP URINE DISEASE
DOSAGE	TBD
PRICE	ANNUAL TREATMENT COST PER PATIENT; US WE ASSUME USD 300,000; EU/ROW: WE ASSUME USD 60,000
STANDARD OF CARE	OTHER THAN HIGHLY RESTRICTED DIET OF BRANCHED-CHAIN AMINO ACID (BCCA) FREE SYNTHETIC FOODS AND FORMULA THERE ARE NO CURRENTLY APPROVED TREATMENTS
UNIQUE SELLING POINT	POTENTIALLY FIRST TREATMENT TO BE APPROVED FOR MSUD

7Ps ANALYSIS

PATENT	PENDING FORMULATION (TASTE-MASKING) PATENTS EXPIRE 2036; ORPHAN DRUG DESIGNATION EXCLUSIVITY IN THE US (7 YEARS) AND EU (10 YEARS) FROM APPROVAL DATE
PHASE	POC HAS BEEN ESTABLISHED; PIVOTAL TRIAL TO START h2 2023; US LAUNCH GUIDED FOR 2025; EU LAUNCH 2026
PATHWAY	US ORPHAN DRUG DESIGNATION GRANTED; FAST TRACK REVIEW, US ACCELERATED APPROVAL & EU CONDITIONAL APPROVAL EXPECTED DUE TO THE LACK OF TREATMENTS
PATIENT	FIRST TREATMENT APPROVED FOR MSUD WITH THE POTENTIAL FOR A LESS RESTRICTED DIET OF BCCA-FREE SYNTHETIC FOODS AND FORMULAS
PHYSICIAN	FIRST EFFECTIVE TREATMENT FOR MSUD THAT LIMITS VERY HIGH LEVELS OF LEUCINE, ISOLEUCINE AND VALINE, WHICH ARE HARMFUL AND BE LIFE-THREATENING.
PAYER	LOWER OVERALL TREATMENT COSTS DUE TO LESS HARMFUL, SERIOUS OR LIFE-THREATENING SYMPTOMS SUCH AS SEIZURES OF FALLING INTO A COMA
PARTNER	GLOBAL RIGHTS ACQUIRED FROM ACER; ACER RETAINS US, CANADA, BRAZIL, TURKEY & JAPAN RIGHTS; RELIEF ENTITLED TO 60% PROFITS ACER TERRITORIES

REVENUE MODEL

UNITED STATES - ACER THERAPEUTICS TERRITORY	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF MAPLE SYRUP URINE DISEASE (MSUD) PATIENTS	2,549	2,575	2,601	2,627	2,653	2,680	2,706	2,733	2,761	2,788	2,816
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MUSD PATIENTS DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MSUD PATIENTS DIAGNOSED	2,040	2,060	2,081	2,101	2,122	2,144	2,165	2,187	2,209	2,231	2,253
ELIGIBLE MSUD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE MSUD PATIENTS	1,836	1,854	1,873	1,891	1,910	1,929	1,949	1,968	1,988	2,008	2,028
PENETRATION (%)	0%	0%	0%	10%	18%	21%	25%	25%	25%	25%	25%
NUMBER OF PATIENTS	0	0	0	189	344	405	487	492	497	502	507
ANNUAL TREATMENT COST PER PATIENT (CHF)	283,725	273,489	273,489	273,489	273,489	273,489	273,489	273,489	273,489	273,489	273,489
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - ACER THERAPEUTICS BOOKS SALES	**0**	**0**	**0**	**47**	**85**	**100**	**120**	**121**	**122**	**124**	**125**
CHANGE (%)					82%	18%	20%	1%	1%	1%	1%
ROYALTIES (CHF MN) - PAID TO BAYLOR	0	0	0	-1	-2	-2	-2	-2	-2	-2	-2
UPFRONT & MILESTONES (CHF MN) - PAID BY RELIEF	0	0	0	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	-2	-3	-3	-4	-4	-4	-4	-4
R&D COSTS (CHF MN) - PAID BY RELIEF	-1	-1	0	0	0	0	0	0	0	0	0
M&S (CHF MN)	0	0	-2	-2	-2	-2	-2	-2	-2	-2	-2
PROFIT BEFORE TAX (CHF MN)	**-1**	**-1**	**-2**	**42**	**78**	**93**	**112**	**113**	**114**	**115**	**116**
PROFIT SPLIT 60/40 IN FAVOR OF RELIEF	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**-1**	**-1**	**-1**	**25**	**47**	**56**	**67**	**68**	**68**	**69**	**70**
TAXES (CHF MN)	0	0	0	-1	-5	-6	-7	-7	-8	-8	-8
PROFIT (CHF MN)	**-1**	**-1**	**-1**	**24**	**42**	**50**	**60**	**60**	**61**	**62**	**62**

EUROPE - RELIEF TERRITORY	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF MAPLE SYRUP URINE DISEASE (MSUD) PATIENTS	3,377	3,411	3,445	3,480	3,515	3,550	3,585	3,621	3,657	3,694	3,731
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
MUSD PATIENTS DIAGNOSED (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
MSUD PATIENTS DIAGNOSED	2,702	2,729	2,756	2,784	2,812	2,840	2,868	2,897	2,926	2,955	2,985
ELIGIBLE MSUD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE MSUD PATIENTS	2,432	2,456	2,481	2,505	2,531	2,556	2,581	2,607	2,633	2,660	2,686
PENETRATION (%)	0%	0%	0%	1%	5%	11%	16%	20%	23%	25%	25%
NUMBER OF PATIENTS	0	0	0	25	127	281	413	521	606	665	672
ANNUAL TREATMENT COST PER PATIENT (CHF)	60,071	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781	59,781
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**1**	**7**	**15**	**22**	**28**	**33**	**36**	**36**
CHANGE (%)					405%	122%	47%	26%	16%	10%	1%
15% ROYALTIES (CHF MN) - PAID TO ACER	0	0	0	0	-1	-2	-3	-4	-5	-5	-5
UPFRONT & MILESTONES (CHF MN) - PAID TO ACER	0	0	0	-2	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	0	-1	-2	-3	-4	-5	-5	-6
R&D COSTS (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
M&S (CHF)	0	0	-1	-3	-3	-3	-3	-3	-3	-3	-3
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**-1**	**-4**	**2**	**7**	**12**	**16**	**19**	**22**	**22**
TAXES (CHF MN)	0	0	0	0	0	-1	-1	-2	-2	-2	-2
PROFIT (CHF MN)	**0**	**0**	**-1**	**-4**	**2**	**7**	**11**	**15**	**17**	**19**	**19**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**48**	**91**	**115**	**142**	**149**	**155**	**159**	**161**
CHANGE (%)					91%	26%	24%	5%	4%	3%	1%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**53**	**100**	**126**	**156**	**164**	**170**	**175**	**177**
CHANGE (%)					91%	26%	24%	5%	4%	3%	1%
GLOBAL PROFIT (CHF MN)	**-1**	**-1**	**-3**	**20**	**43**	**56**	**71**	**75**	**78**	**81**	**81**
CHANGE (%)	-27%	51%	182%	-824%	112%	29%	26%	6%	4%	3%	1%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**444**	
NUMBER OF SHARES (MN)	5,931	
NPV PER SHARE (CHF)	**0.075**	
SUCCESS PROBABILITY	35%	POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.026**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.059	0.057	0.055	0.053	0.051	0.049	0.047
	65%	0.055	0.053	0.051	0.049	0.047	0.046	0.044
	60%	0.051	0.049	0.047	0.045	0.044	0.042	0.040
	55%	0.047	0.045	0.043	0.042	0.040	0.039	0.037
SUCCESS PROBABILITY	50%	0.042	0.041	0.039	0.038	0.036	0.035	0.034
	45%	0.038	0.037	0.035	0.034	0.033	0.032	0.030
	40%	0.034	0.033	0.031	0.030	0.029	0.028	0.027
	35%	0.030	0.029	0.027	**0.026**	0.025	0.025	0.024
	30%	0.025	0.025	0.024	0.023	0.022	0.021	0.020

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

RLF-100 (acute respiratory distress syndrome – ARDS & pulmonary sarcoidosis)

I) RLF-100 IV ARDS - Peak sales CHF 650+ mn; rNPV CHF 0.124/share

Global peak sales for RLF-100 IV in acute respiratory distress syndrome (ARDS) are expected to amount to CHF 650+ mn, conservatively assuming a treatment price per patient of USD 9,000 in the US and EUR 4,000 in the EU with penetration rates reaching 45% due to the lack of effective treatments. Relief plans to start a phase IIb/III trial in H2 2023, with the first launches expected in 2026, assuming priority review in the US and accelerated approval in the EU. We have conservatively based our forecasts on US patent protection until 2034 and 10-year orphan drug market exclusivity in the EU (the current EU patent expires in 2026). Accounting for R&D costs (CHF ~15 mn), COGS, and M&S costs (not more than CHF 20 mn), we calculate an rNPV of CHF 725 mn or CHF 0.124 per share, assuming a 35% (POC established) success factor (see page 37).

RLF-100 INHALED pulmonary sarcoidosis - Peak sales CHF 500 mn; rNPV CHF 0.067/share

We forecast global peak sales of CHF 500 mn for RLF-100 INHALED in pulmonary sarcoidosis. A phase IIb dose-ranging trial is expected to start in Q2/Q3 2023, with the first launches to occur in 2027, assuming similar review times, patent protection, market exclusivity, R&D, COGS, and M&S costs similar as for ARDS. We assume an annual treatment cost per patient of USD 50,000 (US) and EUR 20,000 (EU) with a conservative peak penetration rate of up to 7%. Our rNPV for RLF-100 INHALED in pulmonary sarcoidosis amounts to CHF 401 mn or CHF 0.067 per share with a 35% (POC established) success rate and a WACC of 7% (see page 40).

NOTE: Significant upside to our forecasts is likely if the recently filed stability patents are issued by the patent authorities, extending patent protection for RLF-100 up to 2042 without considering patent term adjustments or Hatch-Waxman extensions.

ARDS and pulmonary sarcoidosis back in focus post-pandemic

Development of RLF-100 in rare respiratory diseases such as acute respiratory distress syndrome (ARDS) and pulmonary sarcoidosis was Relief's main priority until the rapid onset of the COVID-19 pandemic in early 2020 shifted priorities. Critical COVID-19-associated respiratory indications with a high unmet medical need, such as treating and preventing COVID-19-induced ARDS in high-risk patients, became the first priority. Post-pandemic, Relief has shifted back its development priorities for RLF-100 to the original rare pulmonary indications, which are not related to COVID-19 infection. RLF-100 is available in an intravenous (IV) formulation for the healthcare setting and an inhaled formulation through a nebulizer, which can be used at home.

Relief's current development plans for RLF-100 include:

- **RLF – 100 IV (acute respiratory distress syndrome - ARDS)** peak sales CHF 650+ mn: the phase IIb/III trial planned to start in H2 2023; first launches in 2026
- **RLF-100 INHALED (pulmonary sarcoidosis)** peak sales CHF 500+ mn: pre-IND (investigation new drug) meeting with the FDA in December 2022; phase IIb/III trial planned to start in Q2/Q3 2023; first launches in 2027

- **RLF-100 INHALED (checkpoint inhibitor-induced pneumonitis - CIP)** peak sales CHF 250+ mn: a proof-of-concept (POC) trial is planned for 2024, with results due in 2025; upon positive POC results, we will include CIP in our forecasts
- **RLF-100 IV (chronic berylliosis)** peak sales TBD: a POC trial is planned for 2024, with results due in 2025; upon positive POC results, we will include chronic berylliosis in our forecasts

A small phase I trial established POC in ARDS triggered development in COVID-19
Prior to the development of RLF-100 in COVID-19 indications, RLF-100 was tested alone in several pilot and phase II trials for respiratory indications, including:

1) **Acute lung injury (ALI):** 8 patients were given a single infusion of 50 picomol/hour/kg of body weight of RLF-100 IV for 6 or 12 hours
2) **Pulmonary sarcoidosis:** 20 patients were given 50 micrograms (μg) RLF-100 INHALED by nebulizer 4 times daily for 4 weeks
3) **Pulmonary hypertension:** 48 patients were given escalating doses from 50 – 200 μg RLF-100 INHALED by nebulizer 4 times daily for 12 weeks
4) **Pulmonary fibrosis:** 15 patients were given 100 μg RLF-100 INHALED by nebulizer 3 times daily for 24 weeks

In the pulmonary sarcoidosis and acute lung injury trials, a significant reduction of inflammation was observed with a decrease in TNF-alpha levels in the pulmonary sarcoidosis and acute lung injury trials; in all trials, RLF-100 was well tolerated with very few side effects, with the most notable of these were diarrhea and transient 10 mmHg hypotension at high intravenous doses; there is no lethal dose of VIP with extensive safety documentation in four animal species, including primates.

In the small phase I trial conducted in 2005, 8 patients with severe ARDS on mechanical ventilation were treated with ascending doses of aviptadil (branded RLF-100). Seven of the 8 patients were successfully extubated and were alive at the five-day time point. Six left the hospital, and one died of an unrelated cardiac event. Aviptadil has been used on a compounded basis in certain ICUs for many years in the belief that it preserves life and restores function in pulmonary hypertension, ARDS, and acute lung injury. These promising early results in ARDS triggered Relief's decision in early 2020 to reposition RLF-100 IV to treat COVID-19 respiratory complications, including COVID-19-induced ARDS, and the prevention of COVID-19-associated ARDS, with the highest priority.

RLF-100 developed to treat & prevent COVID-19-induced ARDS during the pandemic
During the COVID-19 pandemic, RLF-100 IV was developed by Relief's former US development partner NRx Pharmaceuticals (NRx), for treating ARDS induced by COVID-19. ARDS is the hallmark complication in critically ill COVID-19 patients, with no effective and safe treatments available yet. Early promising results from the ongoing US open-label Expanded Access Program (EAP) dubbed "SAMICARE" showed a 72% survival rate for critically ill COVID-19 patients with ARDS and on mechanical ventilation treated with RLF-100 IV, triggering pivotal development. Unfortunately, the US pivotal "COVID-AIV" trial for treating COVID-19-induced ARDS with RLF IV produced mixed results missing its primary endpoint but showing efficacy in a subpopulation of patients with a favorable safety profile. RLF-100 IV was also discontinued for futility in the phase III "ACTIV-3B/TESICO" trial in critical COVID-19 patients. The FDA declined to grant Emergency Use Authorization (EUA) to NRx three times, including a EUA application for the subpopulation that showed an effect.

Conservatively excluding forecasts for RLF-100 in COVID-19

Once Relief receives the RLF-100 data package from NRx – pending litigation was resolved through definitive settlement agreements closed on 20 December 2022 - the company will assess the development pathway forward for COVID-19, where a high unmet medical need remains. We have conservatively excluded forecasts for RLF-100 IV in COVID-19-induced ARDS due to the decline in the number of COVID-19 infections and hospitalizations with the pandemic becoming endemic, and higher regulatory hurdles, which impact development timelines and costs, as well as potential peak sales.

RLF-100 INHALED for the prevention of COVID-19-associated ARDS a "wild card"

RLF-100 INHALED is in late-stage development for the prevention of COVID-19-associated ARDS, which we consider a "wild card" and is excluded from our forecasts. In the phase III "I-SPY COVID-19" trial, no benefit was seen with nebulized RLF-100 INHALED for the prevention of COVID-19-associated ARDS in high-risk patients, and the drug was discontinued in this trial. In late 2023, topline data of the European investigator-sponsored "Leuppi Study" with RLF-100 INHALED for the prevention of COVID-19-associated ARDS is expected. Relief will decide on further development in this indication once it has the "Leuppi Study" data and has assessed the NRx data package. We conservatively excluded RLF-100 INHALED for the prevention of COVID-19-associated ARDS for the same reasons as for RLF-100 IV in the treatment of COVID-19-induced ARDS, as well as the emergence of new treatment options for this indication, such as Pfizer's more convenient oral drug Paxlovid. We believe the "Leuppi Study" must produce strong positive results for further development in this indication. In our view, the likelihood of this occurring is low in light of the discontinuation of the "I-SPY-COVID-19" trial.

The recently filed stability patent could extend RLF-100 patent protection up to 2042

Importantly, Relief has filed a new provisional patent application for a new formulation of RLF-100 (aviptadil) based on promising six-month stability data at all temperatures tested, including in refrigerated and room temperature environments. Aviptadil is a notoriously unstable compound. The new stability patent would extend patent protection for RLF-100 up to at least 2042 if granted. We conservatively base our RLF-100 forecasts on granted market exclusivities, in particular Orphan Drug Designation (ODD) in pulmonary sarcoidosis and ARDS, which provide 7-year and 10-year market exclusivity in the EU and US, respectively, from the date of approval.

I) RLF IV ARDS - Peak sales CHF 650+ mn; rNPV CHF 0.124/share

ARDS – A significant opportunity remains

Acute lung injury (ALI), including the most severe form known as acute respiratory distress syndrome (ARDS), is a life-threatening condition in which the capacity of the lungs to oxygenate is greatly reduced, even if oxygen is administered in high concentrations, for instance, through mechanical ventilation. ARDS is typically caused by blood infections (most common cause), lung infections, trauma to other parts of the body, severe burns, or inhaling high concentrations of smoke and toxins. Up to 50% of these patients die despite intensive care and mechanical ventilation. There are no specific drugs approved for treating ARDS (including treating COVID-19-induced ARDS).

A phase IIb/III ARDS trial is expected to start in H2 2023

Based on the promising results of RLF-100 IV in the small, early ARDS trial, as well as the strong efficacy signals seen in a subpopulation in the pivotal COVID-19 trials, Relief plans to start a phase IIb/III trial of RLF-100 IV in ARDS in H2 2023. The trial size and design have yet to be determined and finalized. Relief guides for first approvals and launches of RLF-100 IV in ARDS in 2026. In the US, the compound will enjoy patent protection until 2034, while in the EU, the granted orphan drug designation (ODD) will provide 10-year market exclusivity from the approval date. In the case of EU approval in 2026, market exclusivity could last up to 2036. RLF-100 IV also enjoys ODD market exclusivity in the US, which amounts to 7 years of exclusivity from the approval date. Based on the ODD in ARDS, we expect RLF-IV to receive accelerated approval in the EU and priority review in the US, given the high unmet medical need and lack of approved drugs for ARDS.

Global peak sales of CHF 650+ mn for RLF-100 IV in ARDS

In the US, the number of ARDS patients is estimated at 250,000 each year, of which 40% are hospitalized, and an estimated 80% are eligible for treatment with RLF-100 IV. This number excludes high-risk COVID-19 patients who are hospitalized and develop ARDS. This could provide a potential upside to our forecasts. Relief guides for an EU and US launch in 2026. With no treatment available for ARDS, we expect a steep uptake, with the peak penetration reaching up to around 50%. Assuming a treatment cost of USD 9,000 per patient and patent protection until 2034, US peak sales are forecasted to amount to more than CHF 400 mn.

In the EU, we expect a similar steep uptake, with the market penetration also peaking at 45%. Assuming a treatment cost of EUR 4,000 per patient and ODD market exclusivity until 2036, EU peak sales of RLF-100 IV in ARDS are expected to amount to approximately CHF 250 mn (for details, see the following page).

Forecasts & Sensitivity Analysis

RLF-100 IV - FINANCIAL FORECASTS FOR ARDS (ACUTE RESPIRATORY DISTRESS SYNDROME)

INDICATION	REDUCTION OF MORBIDITY AND MORTALITY IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)
DOSAGE	ONE OR MORE ESCALATING DOSES FROM 50-150 PMOL/KG/HR INTRAVENOUS ADMINISTATION OVER 12 HOURS OVER A COURSE OF A WEEK
PRICE	COST TREATMENT COURSE PER PATIENT WE ASSUME: US: 9,000; EU: EUR 4,000
STANDARD OF CARE	PERSONALIZED LUNG-PROTECTIVE MECHANICAL VENTILATION COMBINED WITH STEROIDS SUCH AS DEXAMETHASONE
UNIQUE SELLING POINT	POTENTIALLY FIRST TREATMENT TO REDUCE HIGH MORBIDITY AND MORTALITY IN PATIENTS WITH ARDS

7Ps ANALYSIS

PATENT	US: PATENT + EXTENSION UP TO 2034, ODD 7-YEAR EXCLUSIVITY; EU: PATENT EXPIRES 2026, ODD 10-YEARS EXCLUSIVITY; NEW STABLE FORMULATION PATENT EXPIRY 2042
PHASE	PROOF OF CONCEPT ESTABLISHED; PHASE IIB/III TO START Q2/Q3 2023; RESULTS 2024; FILING 2025; LAUNCH 2026
PATHWAY	ACCELERATED APPROVAL IN THE US AND EU BASED ON A SINGLE PIVOTAL PHASE IIB/III TRIAL LIKELY; POTENTIAL FOR A CONFIRMATORY 2ND PHASE III TRIAL POSSIBLE
PATIENT	HIGHER LIKELIHOOD TO SURVIVE HOSPITALIZATION WITH LESS COMPLICATIONS AND HOSPITAL DAYS THAN CURRENT INEFFECTIVE TREATMENT OPTIONS
PHYSICIAN	FIRST SAFE AND EFFECTIVE TREATMENT TO SIGNIFICANTLY REDUCE MORTALITY AND MORBIDITY FOR PATIENTS WITH OTHERWISE POOR TREATMENT OUTCOME
PAYER	SIGNIFICANTLY REDUCES OVERALL TREATMENT COSTS WITH MORE CRITICAL PATIENTS SURVIVING WITH LESS DAYS SPENT IN ICU OR HOSPITAL WITH LESS COMPLICATIONS
PARTNER	RELIEF REGAINED NRX RIGHTS (US, CANADA & ISRAEL) WITH MILESTONE AND ROYALTY PAYMENTS CAPPED AT USD 30 MN - MARKET GLOBALLY BY OWN SALES FORCE

REVENUE MODEL

UNITED STATES - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF ARDS PATIENTS	270,608	276,020	281,541	287,171	292,915	298,773	304,749	310,844	317,060	323,402	329,870
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ARDS PATIENTS HOSPITALIZED (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
ARDS PATIENTS HOSPITALIZED	108,243	110,408	112,616	114,869	117,166	119,509	121,899	124,337	126,824	129,361	131,948
ELIGIBLE ARDS PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE ARDS PATIENTS	86,595	88,326	90,093	91,895	93,733	95,607	97,520	99,470	101,459	103,489	105,558
PENETRATION (%)	0%	0%	0%	0%	4%	15%	30%	40%	45%	45%	45%
NUMBER OF PATIENTS	0	0	0	0	3,749	14,341	29,256	39,788	45,657	46,570	47,501
COST TREATMENT COURSE PER PATIENT (CHF)	8,512	8,205	8,205	8,205	8,205	8,205	8,205	8,205	8,205	8,205	8,205
SALES (CHF MN)	**0**	**0**	**0**	**0**	**31**	**118**	**240**	**326**	**375**	**382**	**390**
CHANGE (%)						283%	104%	36%	15%	2%	2%
COGS (CHF MN)	0	0	0	0	0	0	0	-1	-1	-1	-1
M&S (CHF MN)	0	0	0	0	-5	-6	-6	-6	-6	-6	-6
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**25**	**112**	**234**	**320**	**368**	**375**	**383**
TAXES (CHF MN)	0	0	0	0	-3	-12	-26	-35	-40	-41	-42
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**22**	**100**	**208**	**285**	**327**	**334**	**341**

EUROPE - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF ARDS PATIENTS	358,491	365,661	372,974	380,434	388,042	395,803	403,719	411,793	420,029	428,430	436,999
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
ARDS PATIENTS HOSPITALIZED (%)	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%	40%
ARDS PATIENTS HOSPITALIZED	143,396	146,264	149,190	152,173	155,217	158,321	161,488	164,717	168,012	171,372	174,799
ELIGIBLE ARDS PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE ARDS PATIENTS	114,717	117,011	119,352	121,739	124,173	126,657	129,190	131,774	134,409	137,098	139,840
PENETRATION (%)	0%	0%	0%	0%	4%	15%	30%	40%	45%	45%	45%
NUMBER OF PATIENTS	0	0	0	0	4,967	18,999	38,757	52,710	60,484	61,694	62,928
COST TREATMENT COURSE PER PATIENT (CHF)	4,005	3,985	3,985	3,985	3,985	3,985	3,985	3,985	3,985	3,985	3,985
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**20**	**76**	**154**	**210**	**241**	**246**	**251**
CHANGE (%)						283%	104%	36%	15%	2%	2%
COGS (CHF MN)	0	0	0	0	0	0	-1	-1	-1	-1	-1
R&D COSTS (CHF MN)	0	-2	-4	-4	0	0	0	0	0	0	0
M&S (CHF)	0	0	0	0	-8	-8	-8	-8	-9	-9	-9
PROFIT BEFORE TAX (CHF MN)	**0**	**-2**	**-4**	**-4**	**12**	**67**	**145**	**201**	**231**	**236**	**241**
TAXES (CHF MN)	0	0	0	0	-1	-7	-16	-22	-25	-26	-26
PROFIT (CHF MN)	**0**	**-2**	**-4**	**-3**	**10**	**60**	**129**	**179**	**206**	**210**	**214**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**51**	**193**	**394**	**537**	**616**	**628**	**641**
CHANGE (%)						283%	104%	36%	15%	2%	2%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**55**	**212**	**433**	**589**	**675**	**689**	**703**
CHANGE (%)						283%	104%	36%	15%	2%	2%
GLOBAL PROFIT (CHF MN)	**0**	**-2**	**-4**	**-3**	**33**	**159**	**338**	**463**	**533**	**544**	**555**
CHANGE (%)			100%	-13%	-1049%	385%	112%	37%	15%	2%	2%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**2,095**	
NUMBER OF SHARES (MN)	5,931	
NPV PER SHARE (CHF)	**0.353**	
SUCCESS PROBABILITY	35%	= POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.124**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.282	0.271	0.260	0.247	0.240	0.231	0.222
	65%	0.262	0.251	0.241	0.230	0.223	0.214	0.206
	60%	0.242	0.232	0.223	0.212	0.206	0.198	0.190
	55%	0.221	0.213	0.204	0.194	0.189	0.181	0.174
SUCCESS PROBABILITY	50%	0.201	0.193	0.186	0.177	0.171	0.165	0.159
	45%	0.181	0.174	0.167	0.159	0.154	0.148	0.143
	40%	0.161	0.155	0.149	0.141	0.137	0.132	0.127
	35%	0.141	0.135	0.130	**0.124**	0.120	0.115	0.111
	30%	0.121	0.116	0.111	0.106	0.103	0.099	0.095

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

II) RLF-100 INHALED pulmonary sarcoidosis - Peak sales CHF 500+ mn; rNPV CHF 0.067/share

Pulmonary sarcoidosis is an untapped market with early efficacy signals for RLF-100
Pulmonary sarcoidosis is a rare inflammatory disease that primarily affects the lungs but can affect almost all organs. Glucocorticoids, such as oral or inhaled prednisone, are first-line treatments, while immunosuppressants, such as methotrexate, are given to severe patients or if glucocorticoids are ineffective or not tolerated. Chronic treatment with glucocorticoids and/or immunosuppressants is not recommended due to severe negative side effects and complications. In an early phase II trial, RLF-100 INHALED established proof-of-concept with a good effect on dry cough and shortness of breath (dyspnea) with a very good safety profile. Given the small number of patients, pulmonary sarcoidosis is qualified as an orphan disease in the US and EU. RLF-100 INHALED was granted Orphan Drug Designation in the EU (2007), providing up to 10-year market exclusivity from the approval date. We believe pulmonary sarcoidosis is a largely untapped market with a market potential amounting to approximately USD 1.7 bn for new effective, safe, and well-tolerated drugs, which can be given chronically.

RLF-100 is specifically designed to be inhaled to reduce systemic side effects
Sarcoidosis is a chronic disease of unknown cause that affects many organs and tissues, most commonly the lungs. Sarcoidosis is characterized by specific microscopic lesions called granulomas. In general, two-thirds of cases resolve spontaneously, and one-third of cases are long-term. In a minority of patients, the disease can be life-threatening. RLF-100 INHALED may provide significant benefits over current treatments, including corticosteroids such as oral or inhaled prednisone or immunosuppressants such as methotrexate. Targeting the underlying pathophysiology of sarcoidosis, which manifests in dry cough, dyspnea, and fatigue, would be a clinically meaningful achievement since it would avoid unnecessary glucocorticoid therapy with its detrimental side effects. RLF-100 INHALED's method of action in sarcoidosis is related to its ability to influence the immune system, which may decrease the inflammatory processes seen in sarcoidosis by acting on white blood cells (lymphocytes and monocytes) involved in the formation of the granulomas. To avoid the side effects observed with systemic delivery of the vasoactive intestinal protein (VIP) and to increase the dose to therapeutically meaningful levels for pulmonary sarcoidosis, RLF-100 INHALED was specifically designed to be administered through inhalation with a nebulizer. Inhaled drugs act quickly, minimize undesired negative side effects, avoid the hepatic first-pass metabolism and act locally in the affected organ. As the size variability among adult lungs is smaller than the overall body size variability, dosing reliability is also improved when inhaling.

RLF-100 INHALED targeted for chronic use in pulmonary sarcoidosis on positive POC
A small phase II POC trial dubbed "AVISARCO" conducted in Germany in 20 sarcoidosis patients with RLF-100 INHALED demonstrated a noticeable effect on sarcoid inflammation, dry cough, dyspnea, and quality of life. RLF-100 INHALED is currently the only known drug in development for pulmonary sarcoidosis that could potentially suppress clinical symptoms of sarcoidosis with no significant side effects. Based on these encouraging POC results, Relief plans to position RLF-100 INHALED as a first-in-class drug for chronic pulmonary sarcoidosis prescribed by specialists.

Phase IIb dose-ranging trial in pulmonary sarcoidosis expected to start in Q2/Q3 2023
Relief plans to start a randomized, multicenter, double-blind, placebo-controlled, phase III trial named "AVISARCO II" in approximately 200 sarcoidosis patients with a treatment duration of 24 weeks, followed by a long-term follow-up of an additional 24 weeks in Q2/Q3 2023. The company expects the first launches to occur in 2027.

Global peak sales of CHF 500+ mn in pulmonary sarcoidosis
We have based our detailed bottom-up forecasts for RLF-100 INHALED in pulmonary sarcoidosis largely on detailed data available in the US and extrapolated the data where possible to other regions, where detailed data is often lacking or not publicly available. We have based our estimates on sources such as the NIH, NCBI, CDC, EMA, WHO, ERS, ATS, clinicaltrials.gov and Evaluate Pharma, among others.

CHF 400+ mn peak sales in the US with first launches in 2027
In the US, each year, approximately 185,000 patients with sarcoidosis seek medical care, with an estimated 25,000 newly diagnosed cases of sarcoidosis. Most sarcoidosis patients, approximately 90%, suffer from pulmonary sarcoidosis, of which an estimated 30% have chronic or advanced disease. We assume an annual treatment cost of USD 50,000 per patient, a peak penetration rate of ~7%, and patient compliance of 60% in line with chronic treatment. Assuming a US launch in 2027 and patent protection until 2034, we forecast US peak sales of CHF 443 mn.

CHF 70 mn peak sales in the EU with first launches in 2027
Our EU forecasts are based on the same patient breakdown as in the US, albeit with a higher patient population. We assume a significantly lower annual treatment cost of EUR 20,000 per patient and the first launches in the EU member states to occur in 2027, and 10-year orphan drug designation market exclusivity until 2037. Consequently, our EU peak sales are expected to amount to CHF 70 mn (for details, see the following page).

Forecasts & Sensitivity Analysis

RLF-100 INHALED - FINANCIAL FORECASTS FOR PULMONARY SARCOIDOSIS

INDICATION	TREATMENT OF PULMONARY SARCOIDOSIS
DOSAGE	TBD
PRICE	ANNUAL TREATMENT COST PER PATIENT WE ASSUME: US: USD 50,000; EU: EUR 20,000
STANDARD OF CARE	GLUCOCORTICOIDS SUCH AS PREDNISONE OR ANTIMETABOLITES SUCH AS METHOTREXATE (STEROID-SPARING AGENT)
UNIQUE SELLING POINT	POTENTIALLY FIRST EFFECTIVE AND SAFE TREATMENT FOR PATIENTS WITH PULMONARY SARCOIDOSIS

7Ps ANALYSIS

PATENT	US: PATENT + EXTENSION UP TO 2034, ODD 7-YEAR EXCLUSIVITY; EU: PATENT EXPIRES 2026, ODD 10-YEARS EXCLUSIVITY; NEW STABLE FORMULATION PATENT EXPIRY 2042
PHASE	PHASE IIB DOSE RANGING TRIAL START Q2/Q3 2023; APPROVAL & LAUNCH EXPECTED 2027
PATHWAY	ACCELERATED APPROVAL IN THE US AND EU BASED ON A SINGLE PIVOTAL PHASE IIB/III TRIAL LIKELY; POTENTIAL FOR A CONFIRMATORY 2ND PHASE III TRIAL POSSIBLE
PATIENT	IMPROVED QUALITY OF LIFE AND LESS COMPLICATIONS AND HOSPITALIZATIONS THAN WITH CURRENT STANDARD OF CARE
PHYSICIAN	FIRST EFFECTIVE, SAFE AND WELL TOLERATED TREATMENT THAT REDUCES PULMONARY COMPLICATIONS AND HOSPITALIZATIONS
PAYER	SIGNIFICANTLY REDUCES OVERALL TREATMENT COSTS WITH LESS COMPLICATIONS AND LESS DAYS SPENT IN HOSPITAL
PARTNER	RELIEF REGAINED NRX RIGHTS (US, CANADA & ISRAEL) WITH MILESTONE AND ROYALTY PAYMENTS CAPPED AT USD 30 MN - MARKET GLOBALLY BY OWN SALES FORCE

REVENUE MODEL

UNITED STATES - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
ANNUAL NEW CASES OF SARCOIDOSIS DIAGNOSED	26,530	27,061	27,602	28,154	28,717	29,291	29,877	30,475	31,084	31,706	32,340
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
SARCOIDOSIS PATIENTS SEEKING TREATMENT/YEAR	196,323	200,250	204,255	208,340	212,507	216,757	221,092	225,514	230,024	234,625	239,317
PULMONARY SARCOIDOSIS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
PULMONARY SARCOIDOSIS PATIENTS TREATED	176,691	180,225	183,829	187,506	191,256	195,081	198,983	202,963	207,022	211,162	215,386
CHRONIC/ADVANCED PATIENTS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CHRONIC/ADVANCED PULMONARY SARCOIDOSIS PATIENTS	53,007	54,067	55,149	56,252	57,377	58,524	59,695	60,889	62,107	63,349	64,616
PENETRATION (%)	0%	0%	0%	0%	0%	1%	3%	5%	6%	7%	7%
NUMBER OF PATIENTS	0	0	0	0	0	975	4,975	9,133	11,386	13,726	15,077
TREATMENT COST PER DAY (CHF)	130	125	125	125	125	125	125	125	125	125	125
TREATMENT DAYS	365	365	365	365	365	365	365	365	365	365	365
COST OF THERAPY PER PATIENT (CHF)	47,288	45,581	45,581	45,581	45,581	45,581	45,581	45,581	45,581	45,581	45,581
PATIENT COMPLIANCE (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**27**	**136**	**250**	**311**	**375**	**412**
CHANGE (%)							410%	84%	25%	21%	10%
ROYALTY (%)	0%	0%	0%	0%	0%	3%	3%	3%	3%	1%	0%
ROYALTIES (CHF MN) - PAID TO NRX	0	0	0	0	0	-1	-4	-7	-9	-4	0
UPFRONT & MILESTONE PAYMENTS (CHF MN) - PAID TO NRX	0	0	0	0	0	-1	0	0	0	0	0
COGS (CHF MN)	0	0	0	0	0	-2	-10	-18	-23	-27	-30
M&S (CHF MN)	0	0	0	0	0	-5	-6	-6	-6	-6	-6
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**0**	**17**	**116**	**218**	**274**	**338**	**376**
TAXES (CHF MN)	0	0	0	0	0	-2	-13	-24	-30	-37	-41
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**0**	**15**	**104**	**194**	**243**	**301**	**335**

EUROPE - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
ANNUAL NEW CASES OF SARCOIDOSIS DIAGNOSED	35,849	36,566	37,297	38,043	38,804	39,580	40,372	41,179	42,003	42,843	43,700
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
SARCOIDOSIS PATIENTS SEEKING TREATMENT/YEAR	265,283	270,589	276,001	281,521	287,151	292,894	298,752	304,727	310,822	317,038	323,379
PULMONARY SARCOIDOSIS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
PULMONARY SARCOIDOSIS PATIENTS TREATED	238,755	243,530	248,401	253,369	258,436	263,605	268,877	274,254	279,740	285,334	291,041
CHRONIC/ADVANCED PATIENTS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CHRONIC/ADVANCED PULMONARY SARCOIDOSIS PATIENTS	71,627	73,059	74,520	76,011	77,531	79,081	80,663	82,276	83,922	85,600	87,312
PENETRATION (%)	0%	0%	0%	0%	0%	1%	2%	4%	5%	6%	6%
NUMBER OF PATIENTS	0	0	0	0	0	395	1,613	3,291	4,196	4,708	5,239
TREATMENT COST PER DAY (CHF)	55	55	55	55	55	55	55	55	55	55	55
TREATMENT DAYS	365	365	365	365	365	365	365	365	365	365	365
COST OF THERAPY PER YEAR (CHF)	20,024	19,927	19,927	19,927	19,927	19,927	19,927	19,927	19,927	19,927	19,927
PATIENT COMPLIANCE (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**5**	**19**	**39**	**50**	**56**	**63**
CHANGE (%)							308%	104%	28%	12%	11%
ROYALTY (%)	0%	0%	0%	0%	0%	2%	2%	2%	2%	2%	0%
ROYALTIES (CHF MN) - PAID TO NRX	0	0	0	0	0	0	0	-1	-1	-1	0
UPFRONT & MILESTONE PAYMENTS (CHF MN) - PAID TO NRX											
COGS (CHF MN)	0	0	0	0	0	-1	-4	-7	-9	-10	-12
R&D COSTS (CHF MN)	0	-2	-5	-5	-2	-1	0	0	0	0	0
M&S (CHF)	0	0	0	0	0	-4	-8	-8	-8	-8	-9
PROFIT BEFORE TAX (CHF MN)	**0**	**-2**	**-5**	**-5**	**-2**	**-1**	**7**	**23**	**32**	**36**	**42**
TAX RATE (%)	0%	0%	0%	5%	11%	11%	11%	11%	11%	11%	11%
TAXES (CHF MN)	0	0	0	0	0	0	-1	-3	-3	-4	-5
PROFIT (CHF MN)	**0**	**-2**	**-5**	**-4**	**-2**	**-1**	**7**	**21**	**28**	**32**	**38**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**31**	**155**	**289**	**362**	**432**	**475**
CHANGE (%)							395%	86%	25%	19%	10%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**0**	**34**	**170**	**317**	**397**	**474**	**521**
CHANGE (%)							395%	86%	25%	19%	10%
GLOBAL PROFIT (CHF MN)	**0**	**-2**	**-5**	**-4**	**-2**	**14**	**110**	**215**	**272**	**333**	**373**
CHANGE (%)			150%	-5%	-63%	-985%	667%	95%	26%	23%	12%

WACC (%)	7%
NPV TOTAL PROFIT (CHF MN)	**1,142**
NUMBER OF SHARES (MN)	5,931
NPV PER SHARE (CHF)	**0.193**
SUCCESS PROBABILITY	35% = POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.067**

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.155	0.149	0.142	0.135	0.130	0.125	0.120
	65%	0.144	0.138	0.132	0.125	0.121	0.116	0.111
	60%	0.133	0.127	0.122	0.116	0.112	0.107	0.103
	55%	0.122	0.117	0.112	0.106	0.102	0.098	0.094
SUCCESS PROBABILITY	50%	0.111	0.106	0.102	0.096	0.093	0.089	0.086
	45%	0.100	0.096	0.091	0.087	0.084	0.080	0.077
	40%	0.089	0.085	0.081	0.077	0.075	0.071	0.068
	35%	0.078	0.074	0.071	**0.067**	0.065	0.062	0.060
	30%	0.067	0.064	0.061	0.058	0.056	0.054	0.051

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

RLF-TD011 (epidermolysis bullosa - EB)

I) RLF-TD011 in EB - Peak sales CHF 850+ mn; rNPV CHF 0.120/share

We forecast global peak sales of more than CHF 850 mn for RLF-TD011 in epidermolysis bullosa (EB), with the first launches to occur in 2026. In the US, RLF-TD011 will enjoy at least 7 years of orphan drug market exclusivity based on granted ODD. In the EU, Relief will seek ODD, which would provide 10-year market exclusivity. We assume an annual treatment price per patient of USD 70,000 in the US and EUR 40,000 in the EU, with a conservative 50% peak penetration rate in eligible EB patients in both regions. We calculate an rNPV of CHF 698 mn or CHF 0.120 per share, assuming a 35% (POC) success rate and accounting for COGS of 5%, R&D costs of roughly CHF 20 mn, and M&S costs of around CHF 5 mn for each region. (see page 43)

NOTE: A US investigator-initiated POC trial of RLF-TD011 as an adjunctive therapy in cutaneous T-cell lymphoma (CTCL) started with results due. Upon positive POC results, CTCL could become a new indication with additional upside to our forecasts.

RLF-TD011 is potentially the first effective and convenient treatment for EB

RLF-TD011 is a sprayable hypochlorous acid (HClO) solution that combines strong antimicrobial activity with anti-inflammatory properties based on APR's Tehclo™ technology with the potential to become one of the first products ever approved for EB. Tehclo™ is a globally patented nano-technology platform applied to the production of a unique HClO solution that ensures the most consistent quality for best-in-class clinical outcomes. APR TD011 is designed to be a complete treatment for EB patients to prevent or reduce infections and inflammation through modulation of the wound microenvironment to support faster physiological wound healing.

EB is a rare disease characterized by life-ruining skin blistering, which can be fatal

Epidermolysis bullosa (EB) is a group of rare, genetic, life-threatening connective tissue disorders characterized by easy blistering of the skin and mucous membranes throughout the body with the risk of severely impacting internal organs. Blisters occur with minor trauma or friction and are painful. Its severity can range from mild to fatal. Those with mild cases may not develop symptoms until they start to crawl or walk. Complications may include esophageal narrowing, squamous cell skin cancer, and the need for amputations. EB is caused by a mutation in at least one of 16 different genes. Some types are autosomal dominant while others are autosomal recessive. The underlying mechanism is a defect in attachment between or within the layers of the skin.

The main types of EB include:

1. **Epidermolysis bullosa simplex (EBS):** is a form of EB that causes blisters at the site of rubbing. It typically affects the hands and feet and is typically inherited in an autosomal dominant manner, affecting the keratin genes KRT5 and KRT14. Therefore, there is a failure in keratinization, which affects the integrity and the ability of the skin to resist mechanical stresses. EBS accounts for roughly 92% of EB cases, and patients tend to die in infancy.
2. **Dystrophic epidermolysis bullosa (DEB):** is an inherited variant affecting the skin and other organs. DEB is caused by genetic defects (or mutations) within the human COL7A1 gene encoding the protein type VII collagen (collagen VII). DEB-causing mutations can be either autosomal dominant or autosomal recessive. Epidermis

bullosa pruriginosa and albopapuloid epidermolysis bullosa (Pasini's disease) are rare subtypes of this disease. DEB accounts for roughly 5% of EB cases and patients tend to die in early adulthood.

3. **Junctional epidermolysis bullosa (JEB):** is an inherited disease affecting laminin and collagen. This disease is characterized by blister formation within the lamina lucida of the basement membrane zone and is inherited in an autosomal recessive manner. It also presents blisters at the site of friction, especially on the hands and feet, and has variants that can occur in children and adults. JEB accounts for roughly 1% of EB cases, and patients tend to die in infancy.

The diagnosis is suspected based on symptoms and confirmed by skin biopsy or genetic testing. There is no cure for the condition. Management involves daily wound care, bandaging, pain control, controlling infections, nutritional support, and prevention and treatment of complications. There are an estimated 250,000 patients with EB worldwide, with an estimated 30,000 patients in the European Union (EU) and 20,000 patients in the US EB occurs equally common in males and females.

POC shows promising results with improvement of skin blistering in just 2 weeks

RLF-TD011 was granted Orphan Drug Designation (ODD) in late 2019 by the US FDA. In a preliminary clinical trial, EB patients administered with RLF-TD011 demonstrated improvement in skin blistering and tissue repair within just two weeks of treatment and was shown to be well tolerated with a favorable safety profile. RLF-TD011 has shown favorable safety and tolerability through exposure to more than 300 individuals with various types of skin wounds and lesions. Moreover, the same active ingredient in RLF-TD011, the sprayable hypochlorous acid (HClO) solution, is approved as a Class III medical device under the Nexodyn brand for treating acute and chronic wounds.

POC trial started in February 2023, potentially pivotal phase IIb trial planned for 2024

The next trial is slated to be a phase IIb dose-ranging trial with the potential (depending on its scope) to be regarded as registrational in nature. When considering the limited size of the phase III “EASE” trial that Amryt Pharma (symbol: AMYT) did with Oleogel-S10 (Filsuvez), a topical gel, in 223 adults and children with either junctional EB, dystrophic EB, or Kindler syndrome across 28 countries. Patients with EB simplex were excluded from the trial. In March 2022, the FDA issued a Complete Response Letter for Oleogel-S100, denying treatment of the cutaneous manifestations of dystrophic and junctional EB, requesting additional efficacy data. Relief started a proof-of-concept (POC) trial in February 2023 with data expected in 2023. The company intends to initiate a phase IIb dose-ranging trial in 2024, with topline data to be released in 2025. The first launches of RLF-TD011 in EB are guided to occur in 2027. In the US, the compound will enjoy at least 7-year orphan drug exclusivity from the day of approval. Relief plans to apply for ODD in the EU, which will provide at least 10 years of market exclusivity from approval if granted by the EMA.

Peak sales potential of CHF 850+ mn with first launches expected in 2027

In the US, there are an estimated 25,000 EB patients with approximately 35,000 in the EU. We conservatively assume roughly 50% of patients are eligible for RLF-TD011 treatment with an annual treatment cost per patient of USD 70,000 in the US and EUR 40,000 in the EU. Assuming first launches in 2027, 7-year US orphan drug market exclusivity, based on granted ODD in 2019, and 10 years in the EU (the EU has yet to grant ODD) from approval, global peak sales of RLF-TD011 in EB could easily amount to more than CHF 850 mn in the US and the EU (for details, see the following page).

Forecasts & Sensitivity Analysis

RLF-TD011 - FINANCIAL FORECASTS FOR EPIDERMOLYSIS BULLOSA (EB)

INDICATION	TO PREVENT OR REDUCE INFECTIONS AS WELL AS INFLAMMATION IN SKIN BLISTERING AND TO IMPROVE TISSUE REPAIR IN PATIENTS WITH EPIDERMOLYSIS BULLOSA
DOSAGE	TBD
PRICE	ANNUAL TREATMENT COST PER PATIENT; WE ASSUME USD 70,000 IN THE US AND EUR 40,000 IN THE EU/ROW
STANDARD OF CARE	NO APPROVED TREATMENT FOR EB; SUPPORTIVE TREATMENTS SUCH AS PAIN AND WOUND MANAGEMENT TO PREVENT INFECTIONS AND SUSTAIN WOUND HEALING
UNIQUE SELLING POINT	CONVENIENT AND WELL TOLERATED SPRAY WITH FAST REDUCTION OF SKIN BLISTERING AND IMPROVEMENT IN TISSUE REPAIR

7Ps ANALYSIS

PATENT	PRIMARY PROTECTION IS MARKET EXCLUSIVITIES SUCH AS ORPHAN DRUG DESIGNATION (ODD) GRANTED IN THE US IN Q4 2019; RELIEF WILL SEEK ODD IN THE EU
PHASE	PHASE I COMPLETED; POC STARTED FEBRUARY 2023, RESULTS IN 2023; FIRST LAUNCHES GUIDED FOR 2027
PATHWAY	IN THE US CONSIDERED A COMBINATION OF A MEDICAL DEVICE AND PHARMACEUTICAL REQUIRING CLINICAL TRIALS; EU REGULATORY PATHWAY TO BE DETERMINED
PATIENT	IMPROVED QUALITY OF LIFE THROUGH LESS SKIN BLISTERING AND PAIN CAUSED BY INFECTIONS AND INFLAMMATION
PHYSICIAN	FIRST CONVENIENT AND EFFECTIVE TREATMENT SPECIFICALLY FOR EPIDERMYLOSIS BULLOSA WITH FAST REDUCTION OF SKIN BLISTERING
PAYER	LOWER OVERALL TREATMENT COSTS DUE TO LESS SKIN BLISTERING AND IMPROVED TISSUE REPAIR
PARTNER	RELIEF EXPECTS TO SELL APR-TD011 THROUGH AN OWN SPECIALIST SALES FORCE IN THE KEY MARKETS INCLUDING THE US AND EU

REVENUE MODEL

UNITED STATES - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF EPIDERMOLYSIS BULLOSA (EB) PATIENTS	25,758	26,015	26,275	26,538	26,803	27,071	27,342	27,616	27,892	28,171	28,452
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
ELIGIBLE EB PATIENTS (%)	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
ELIGIBLE EB PATIENTS	12,879	13,008	13,138	13,269	13,402	13,536	13,671	13,808	13,946	14,085	14,226
PENETRATION (%)	0%	0%	0%	0%	0%	10%	25%	35%	43%	48%	10%
NUMBER OF PATIENTS	0	0	0	0	0	1,354	3,418	4,833	5,997	6,761	1,366
ANNUAL TREATMENT COST PER PATIENT (CHF)	66,202	65,728	67,700	69,731	71,823	73,978	76,197	78,483	80,837	83,263	85,760
PATIENT COMPLIANCE (%)	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**95**	**247**	**360**	**461**	**535**	**111**
CHANGE (%)							160%	46%	28%	16%	-79%
COGS (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
COGS (CHF MN)	0	0	0	0	0	-5	-12	-18	-23	-27	-6
M&S (CHF MN)	0	0	0	0	0	-4	-4	-4	-4	-4	-4
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**0**	**87**	**231**	**339**	**434**	**504**	**102**
TAXES (CHF MN)	0	0	0	0	0	-10	-25	-37	-48	-55	-11
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**0**	**77**	**206**	**301**	**386**	**449**	**90**

EUROPE - RELIEF SALES FORCE	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
NUMBER OF EPIDERMOLYSIS BULLOSA (EB) PATIENTS	34,757	35,105	35,456	35,810	36,168	36,530	36,895	37,264	37,637	38,013	38,394
GROWTH (%)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
ELIGIBLE EB PATIENTS (%)	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
ELIGIBLE EB PATIENTS	17,379	17,552	17,728	17,905	18,084	18,265	18,448	18,632	18,819	19,007	19,197
PENETRATION (%)	0%	0%	0%	0%	0%	8%	23%	33%	41%	46%	50%
NUMBER OF PATIENTS	0	0	0	0	0	1,461	4,243	6,149	7,716	8,743	9,598
ANNUAL TREATMENT COST PER PATIENT (CHF)	40,048	39,854	39,854	39,854	39,854	39,854	39,854	39,854	39,854	39,854	39,854
PATIENT COMPLIANCE (%)	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**55**	**161**	**233**	**292**	**331**	**363**
CHANGE (%)							190%	45%	25%	13%	10%
COGS (%)	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
COGS (CHF MN)	0	0	0	0	0	-4	-12	-17	-22	-25	-27
R&D COSTS (CHF MN)	0	-1	-2	-2	-2	-2	0	0	0	0	0
M&S (CHF)	0	0	0	0	0	-5	-5	-5	-5	-5	-6
PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-2**	**-2**	**-2**	**44**	**143**	**210**	**265**	**301**	**331**
TAXES (CHF MN)	0	0	0	0	0	-5	-16	-23	-29	-33	-36
PROFIT (CHF MN)	**0**	**-1**	**-2**	**-2**	**-2**	**39**	**128**	**187**	**236**	**268**	**294**

	2022E	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**150**	**408**	**593**	**753**	**866**	**475**
CHANGE (%)							171%	45%	27%	15%	-45%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**0**	**165**	**448**	**651**	**826**	**950**	**521**
CHANGE (%)							171%	45%	27%	15%	-45%
GLOBAL PROFIT (CHF MN)	**0**	**-1**	**-2**	**-2**	**-2**	**116**	**334**	**488**	**622**	**716**	**385**
CHANGE (%)	-100%		100%	-5%	-6%	-6645%	186%	46%	27%	15%	-46%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**2,036**	
NUMBER OF SHARES (MN)	5,931	
NPV PER SHARE (CHF)	**0.343**	
SUCCESS PROBABILITY	35%	POC
RISK ADJUSTED NPV PER SHARE (CHF)	**0.120**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
SUCCESS PROBABILITY	70%	0.274	0.263	0.253	0.240	0.233	0.224	0.215
	65%	0.255	0.244	0.235	0.223	0.217	0.208	0.200
	60%	0.235	0.226	0.217	0.206	0.200	0.192	0.185
	55%	0.215	0.207	0.199	0.189	0.183	0.176	0.169
	50%	0.196	0.188	0.180	0.172	0.167	0.160	0.154
	45%	0.176	0.169	0.162	0.154	0.150	0.144	0.138
	40%	0.157	0.150	0.144	0.137	0.133	0.128	0.123
	35%	0.137	0.132	0.126	**0.120**	0.117	0.112	0.108
	30%	0.117	0.113	0.108	0.103	0.100	0.096	0.092

ESTIMATES AS OF 10 APRIL 2023

SOURCE: VALUATIONLAB ESTIMATES

Management Team

Management biographies

Jack Weinstein (Chief Executive Officer)

Jack Weinstein joined Relief in October 2020 as its US-based Chief Financial Officer and Treasurer. In December 2022, he was appointed as the new CEO of Relief. He brings over 40 years of wide-ranging executive management expertise, including as a CFO, investment banker and consultant in the biopharmaceutical and life sciences industries. Jack has extensive experience in finance and healthcare investment banking, corporate and business development as well as FDA regulatory and intellectual property strategies. He has successfully completed a variety of corporate finance transactions, including public and private financings, as well as merger and acquisition transactions. Before joining Relief, Jack served as Managing Director and Head of Healthcare Investment Banking at Avalon NetWorth, an independent New York-based boutique investment bank. Prior to Avalon, he was CFO, Treasurer and Vice President of Business Development at Catalyst Pharmaceuticals, Inc. (NASDAQ symbol: CPRX), a biopharmaceutical company developing prescription pharmaceutical products to treat orphan diseases. Jack eventually took the company public through a full-blown IPO on the Nasdaq Global Market. He also was President and Founder of The Sterlington Group, Inc. a consulting firm providing strategic, business development, regulatory and “CFO” consulting services, including M&A advisory and raising equity and debt for middle-market companies. Adding to his credentials, Jack gained experience at several other investment banking and consulting firms. He holds an MBA from Harvard University.

Jeremy Meinen (Chief Financial Officer)

Jeremy Meinen joined Relief as ad-interim Chief Financial Officer in April 2020 and served as principal finance and accounting officer. In December 2022, Jeremy was appointed as CFO, succeeding Jack Weinstein who became CEO. Prior to joining Relief, Jeremy provided financial consulting and controlling services to companies in various industries. He began his career in an international audit firm, where he held positions of increasing responsibility and scope over more than six years. Jeremy holds a Master of Science in finance from Bocconi University and a Bachelor of Arts degree in Business Administration from the University of Geneva. He is a Swiss-certified public accountant.

Paolo Galfetti (Chief Operating Officer, President of Relief Europe, and CEO of APR)

Paolo has over twenty years of management experience in the pharmaceutical sector, including in the areas of business development and licensing, operational, strategic management, clinical research, and pharmaceutical discovery and development. He joined APR in 1995 as head of licensing and business development and was appointed CEO in 2002. Under his leadership, APR has brought its first product onto the market and developed a rich pipeline of product candidates. Paolo also was a founding partner, CEO and board member of the Institute for Pharmacokinetic and Analytical Studies AG (IPAS), a Swiss contract research organization, as well as CEO and board member of Farma Resa s.r.l., an Italian CRO. Paolo is a Chartered Financial Analyst (CFA) and has a bachelor’s degree in economics from the Commercial University Bocconi, Milan, Italy.

Marco Marotta (Chief Business Officer)
Marco Marotta is the Chief Business Officer of Relief, responsible for business development activities across the entire company, including strategic partnering, management of the InveniAI collaboration, and Relief's various in-licensing and out-licensing initiatives. He has deep expertise in operations, sales and business development within the pharmaceutical industry. He joined APR Applied Pharma Research SA (APR) in 2015 (acquired by Relief in June 2021), where he was initially focused on reshaping and optimizing the entire end-to-end supply chain process and was subsequently appointed Corporate Director, Business Development and Licensing. During his tenure with APR, Mr. Marotta was instrumental in successfully increasing the organization's presence in Asia and South America, as well as executing multiple key licensing and co-development deals. Mr. Marotta holds a Master of Science in Engineering from the University Federico II in Napoli and an Executive MBA from Bocconi University in Milan.

Giorgio Reiner (Corporate Director R&D APR Applied Pharma Research)
Giorgio Reiner is the Chief Scientific Officer (CSO) and Head of Research & Development Operations of APR Applied Pharma Research S.A. He has over 25 years of work experience in Research and Development in areas including organic drug synthesis, pharmaceutical process development and analytical control. Mr. Reiner joined APR in 2000 and currently serves as Chief Scientific Officer (CSO) and Head of Research & Development Operations. Mr. Reiner holds a graduate degree in pharmaceutical chemistry and technology from the University of Pharmacy in Milan, Italy. He has completed postgraduate courses in toxicology as well as in cosmetic technology. Mr. Reiner is author of scientific publications and inventor or co-inventor of several patents covering synthesis processes, drug delivery technologies and pharmaceutical compositions and formulations.

Board of Directors biographies

Raghuram (Ram) Selvaraju, PhD, MBA (Chairman of the Board)
Raghuram Selvaraju is a Managing Director of Equity Research at H.C. Wainwright & Co., a leading full-service investment bank headquartered in New York, USA, whose research focuses on the healthcare sector. He has over 17 years of experience on Wall Street and previously was a pharmaceutical researcher at Serono in Switzerland. In addition, Ram has appeared numerous times on Bloomberg, CNBC, Business News Network and BTV where he discussed drug development trends, healthcare reform policy, and pharma and biotech M&A. Prior to joining H.C. Wainwright, he held Senior Research positions at MLV & Co., Aegis Capital, Hapoalim Securities USA and Rodman & Renshaw LLC. Ram was Head of Healthcare Equity Research at both Aegis and Hapoalim Securities. He was ranked #1 by TipRanks across all analysts and all sectors in 2021 and was the top-ranked healthcare analyst in The Wall Street Journal Best On The Street survey in 2006. Ram has also been ranked by StarMine for earnings estimate accuracy in 2007 and 2010. He became the youngest-ever recipient of the Serono Pharmaceutical Research Institute's Inventorship Award for exceptional innovation and creativity in 2003. Ram earned his Ph.D. in cellular immunology and molecular neuroscience and an M.S. in molecular biology from the University of Geneva in Switzerland on the basis of his drug development research. Ram holds an M.B.A. from the Cornell University accelerated one-year program for scientists and engineers. He also has a B.S. degree in biological sciences and technical writing from Carnegie Mellon University.

Tom Plitz, Ph.D. (Vice Chairman of the Board)
Tom Plitz is Chief Executive Officer of Chord Therapeutics SA, a privately held biopharmaceutical firm based in Geneva, Switzerland. He has more than two decades of experience in pharmaceutical R&D, most recently as Chief Scientific Officer of the rare disease company Wilson Therapeutics. Wilson Therapeutics was acquired for USD 855 mn by Alexion Pharmaceuticals in April 2018. Tom's previous assignments include senior roles at Serono, Merck, and Shire, where he worked across multiple therapeutic areas, including neuroinflammatory, metabolic, and rare diseases. Tom holds a Ph.D. from the Technical University of Munich, Germany.

Patrice P. Jean (Member of the Board)
Dr. Patrice P. Jean is the Chair of the Life Sciences Practice at Hughes Hubbard & Reed, an international law firm based in New York City. She has over a decade of experience counseling leading and startup pharmaceutical, chemical, and biotechnology companies in all areas of patent law, including asserting and defending patent rights underlying core technologies and innovations. Dr. Jean graduated summa cum laude from Xavier University of Louisiana in 1993 with a degree in biochemistry, and she holds a Ph.D. in molecular biology from Princeton University. She graduated from Columbia University School of Law in 2002, where she was Editor-in-Chief of the Columbia Science & Technology Law Review. Dr. Jean currently serves as Vice-President of the New York Intellectual Property Law Education Foundation and is a Board member of the New York Intellectual Property Law Association.

Michelle Lock (Member of the Board)
Ms. Lock was recently appointed as Chief Operating Officer of Zug, Switzerland-based Covis Pharma Group, a global specialty pharmaceutical company that markets therapeutic solutions for patients with life-threatening conditions and chronic illnesses. Previously, Ms. Lock served as the Senior Vice President and Head of Europe and International at Acceleron Pharma Inc, a biopharmaceutical company dedicated to the discovery, development, and commercialization of therapeutics to treat serious and rare diseases. Before that, she was a consultant to biotechnology companies, providing leadership, guidance, and strategic support to managements seeking to establish or improve their international businesses based in Switzerland. Earlier, Ms. Lock was Senior Vice President & Head of Europe/International at Sage Therapeutics, a clinical-stage biopharmaceutical company committed to discovering, developing, and commercializing novel medicines to transform the lives of patients with life-altering central nervous system (CNS) disorders. During her career, Ms. Lock also spent 24 years with Bristol-Myers Squibb (BMS) in positions of increasing responsibility in sales, commercial, general management, regional leadership and business strategy. In her most recent role at BMS, she served as Vice President and General Manager for EU Country Clusters & Global Capabilities Hub leadership, Switzerland, driving the company's leadership efforts in immuno-oncology. Ms. Lock earned a degree in Science/Nursing at Royal Melbourne University, Australia and studied General Management and Internal General Management at CEDEP, France. She has served as Honorary Ambassador between Switzerland and the U.S. since 2018, as well is a past member of the Board of Directors of the Swiss American Chamber of Commerce and the Interpharma Switzerland Pharmaceutical Industry.

Paolo Galfetti (Chief Operating Officer, President of Relief Europe, and CEO of APR)
See biography above.

Income Statement

RELIEF THERAPEUTICS									SHARE PRICE (CHF)	0.021		
IFRS												
INCOME STATEMENT (CHF MN)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PRODUCT SALES (INCL. PARTNER SALES)	**40**	**91**	**105**	**154**	**293**	**479**	**876**	**1,577**	**2,156**	**2,538**	**2,793**	**2,479**
CHANGE (%)		126%	16%	47%	91%	63%	83%	80%	37%	18%	10%	-11%
PRODUCT SALES (RELIEF THERAPEUTICS)	**1**	**3**	**15**	**36**	**73**	**167**	**530**	**1,192**	**1,750**	**2,130**	**2,382**	**2,067**
CHANGE (%)		164%	334%	144%	101%	128%	217%	125%	47%	22%	12%	-13%
ROYALTIES	**1**	**7**	**7**	**6**	**3**	**-2**	**-7**	**-13**	**-19**	**-22**	**-17**	**-14**
UPFRONT AND MILESTONE PAYMENTS	**0**	**0**	**0**	**0**	**-2**	**0**	**-1**	**0**	**0**	**0**	**0**	**0**
OTHER REVENUES	**2**	**1**	**1**	**1**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
CHANGE (%)	497%	-20%	0%	8%	7%	7%	6%	6%	6%	5%	5%	0%
REVENUES (EXCL. PARTNER SALES)	**4**	**12**	**23**	**44**	**76**	**167**	**524**	**1,180**	**1,733**	**2,110**	**2,366**	**2,055**
CHANGE (%)	1545%	160%	99%	88%	74%	120%	214%	125%	47%	22%	12%	-13%
COGS	**-1**	**-2**	**-5**	**-9**	**-14**	**-20**	**-37**	**-69**	**-96**	**-115**	**-130**	**-116**
CHANGE (%)		82%	128%	86%	62%	44%	85%	84%	39%	20%	13%	-10%
GROSS PROFIT	**3**	**10**	**19**	**35**	**62**	**147**	**486**	**1,112**	**1,637**	**1,995**	**2,237**	**1,939**
CHANGE (%)	1137%	186%	93%	88%	76%	137%	232%	128%	47%	22%	12%	-13%
MARGIN (%)	75%	83%	80%	80%	82%	88%	93%	94%	94%	95%	95%	94%
RESEARCH & DEVELOPMENT	**-19**	**-9**	**-10**	**-15**	**-18**	**-10**	**-10**	**-13**	**-18**	**-18**	**-19**	**-19**
CHANGE (%)	39%	-55%	12%	52%	25%	-44%	3%	21%	41%	2%	2%	2%
MARKETING & SALES	**0**	**-3**	**-4**	**-8**	**-12**	**-30**	**-49**	**-53**	**-54**	**-55**	**-57**	**-58**
CHANGE (%)			35%	91%	48%	139%	63%	10%	2%	2%	2%	2%
GENERAL & ADMINISTRATIVE	**-16**	**-17**	**-13**	**-13**	**-14**	**-14**	**-14**	**-15**	**-15**	**-15**	**-15**	**-16**
CHANGE (%)	182%	7%	-22%	2%	2%	2%	2%	2%	2%	2%	2%	2%
OTHER GAINS/LOSSES	**-1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
OPERATING COSTS	**-37**	**-31**	**-32**	**-45**	**-58**	**-74**	**-111**	**-149**	**-183**	**-204**	**-220**	**-209**
CHANGE (%)	79%	-16%	3%	42%	29%	27%	49%	35%	22%	11%	8%	-5%
OPERATING COSTS (PER MONTH)	3.1	2.6	2.6	3.8	4.9	6.2	9.2	12.5	15.2	17.0	18.4	17.4
EBITDA	**-32**	**-19**	**-9**	**-1**	**18**	**93**	**413**	**1,031**	**1,550**	**1,906**	**2,146**	**1,846**
CHANGE (%)	59%	-41%	-56%	-84%	-1375%	429%	346%	149%	50%	23%	13%	-14%
D&A	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**
OPERATING RESULT	**-34**	**-21**	**-11**	**-3**	**15**	**91**	**411**	**1,029**	**1,548**	**1,904**	**2,144**	**1,844**
CHANGE (%)	277%	-38%	-50%	-67%	-540%	489%	354%	150%	50%	23%	13%	-14%
MARGIN (%)	-763%	-181%	-45%	-8%	20%	54%	78%	87%	89%	90%	91%	90%
NET FINANCIAL INCOME/(EXPENSES)	**-1**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**
PROFIT/(LOSS) BEFORE TAXES	**-35**	**-23**	**-12**	**-5**	**14**	**89**	**409**	**1,027**	**1,546**	**1,902**	**2,142**	**1,842**
CHANGE (%)	467%	-35%	-46%	-57%	-357%	553%	361%	151%	51%	23%	13%	-14%
MARGIN (%)	-790%	-196%	-53%	-12%	18%	53%	78%	87%	89%	90%	91%	90%
TAXES	**1**	**0**	**0**	**0**	**-7**	**-25**	**-47**	**-96**	**-139**	**-169**	**-193**	**-161**
NET PROFIT/(LOSS)	**-35**	**-23**	**-12**	**-5**	**6**	**63**	**362**	**931**	**1,406**	**1,733**	**1,949**	**1,681**
CHANGE (%)		-34%	-46%	-57%	-222%	882%	471%	157%	51%	23%	12%	-14%
MARGIN (%)	-772%	-196%	-53%	-12%	9%	38%	69%	79%	81%	82%	82%	82%
EPS (CHF)	**-0.010**	**-0.005**	**-0.003**	**-0.001**	**0.001**	**0.014**	**0.082**	**0.211**	**0.318**	**0.392**	**0.441**	**0.381**
CHANGE (%)		-46%	-46%	-57%	-222%	882%	471%	157%	51%	23%	12%	-14%

ESTIMATES AS OF 4 APRIL 2023 SOURCE: VALUATIONLAB ESTIMATES

Ratios I Balance Sheet I Cash Flow Statement

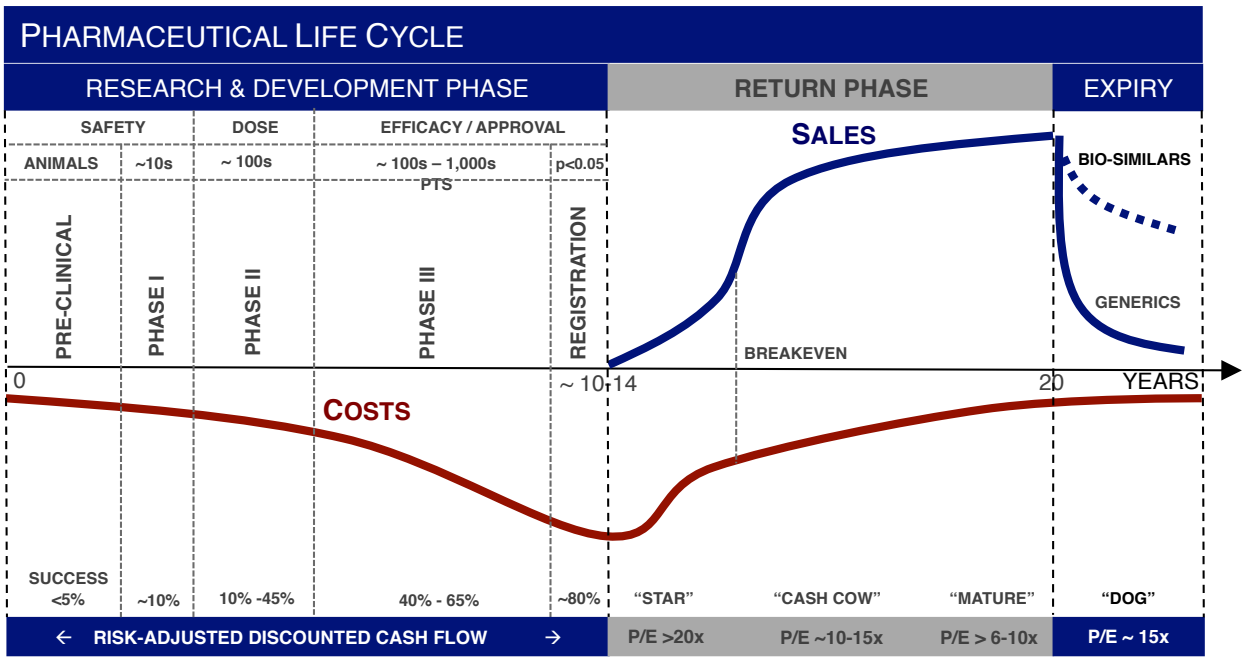
RELIEF THERAPEUTICS										SHARE PRICE (CHF)	0.020	
IFRS												
INCOME STATEMENT (CHF MN)	**2021**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**	**2032E**
PRODUCT SALES (INCL. PARTNER SALES)	**40**	**91**	**105**	**152**	**293**	**479**	**876**	**1,577**	**2,156**	**2,538**	**2,793**	**2,479**
CHANGE (%)		126%	16%	45%	93%	63%	83%	80%	37%	18%	10%	-11%
PRODUCT SALES (RELIEF THERAPEUTICS)	**1**	**3**	**15**	**35**	**73**	**167**	**530**	**1,192**	**1,750**	**2,130**	**2,382**	**2,067**
CHANGE (%)		164%	334%	131%	112%	128%	217%	125%	47%	22%	12%	-13%
ROYALTIES	**1**	**7**	**7**	**6**	**3**	**-2**	**-7**	**-13**	**-19**	**-22**	**-17**	**-14**
UPFRONT AND MILESTONE PAYMENTS	**0**	**0**	**0**	**0**	**-2**	**0**	**-1**	**0**	**0**	**0**	**0**	**0**
OTHER REVENUES	**2**	**1**	**1**	**1**	**2**	**2**	**2**	**2**	**2**	**2**	**2**	**2**
CHANGE (%)	497%	-20%	0%	8%	7%	7%	6%	6%	6%	5%	5%	0%
REVENUES (EXCL. PARTNER SALES)	**4**	**12**	**23**	**42**	**76**	**167**	**524**	**1,180**	**1,733**	**2,110**	**2,366**	**2,055**
CHANGE (%)	1545%	160%	99%	80%	81%	120%	214%	125%	47%	22%	12%	-13%
COGS	**-1**	**-2**	**-5**	**-9**	**-14**	**-20**	**-37**	**-69**	**-96**	**-115**	**-130**	**-116**
CHANGE (%)		82%	128%	84%	64%	44%	85%	84%	39%	20%	13%	-10%
GROSS PROFIT	**3**	**10**	**19**	**33**	**62**	**147**	**486**	**1,112**	**1,637**	**1,995**	**2,237**	**1,939**
CHANGE (%)	1137%	186%	93%	79%	86%	137%	232%	128%	47%	22%	12%	-13%
MARGIN (%)	75%	83%	80%	80%	82%	88%	93%	94%	94%	95%	95%	94%
RESEARCH & DEVELOPMENT	**-19**	**-9**	**-10**	**-15**	**-18**	**-10**	**-10**	**-13**	**-18**	**-18**	**-19**	**-19**
CHANGE (%)	39%	-55%	12%	52%	25%	-44%	3%	21%	41%	2%	2%	2%
MARKETING & SALES	**0**	**-3**	**-4**	**-8**	**-12**	**-30**	**-49**	**-53**	**-54**	**-55**	**-57**	**-58**
CHANGE (%)			35%	91%	48%	139%	63%	10%	2%	2%	2%	2%
GENERAL & ADMINISTRATIVE	**-16**	**-17**	**-13**	**-13**	**-14**	**-14**	**-14**	**-15**	**-15**	**-15**	**-15**	**-16**
CHANGE (%)	182%	7%	-22%	2%	2%	2%	2%	2%	2%	2%	2%	2%
OTHER GAINS/LOSSES	**-1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
OPERATING COSTS	**-37**	**-31**	**-32**	**-45**	**-58**	**-74**	**-111**	**-149**	**-183**	**-204**	**-220**	**-209**
CHANGE (%)	79%	-16%	3%	41%	30%	27%	49%	35%	22%	11%	8%	-5%
OPERATING COSTS (PER MONTH)	3.1	2.6	2.6	3.7	4.9	6.2	9.2	12.5	15.2	17.0	18.4	17.4
EBITDA	**-32**	**-19**	**-9**	**-3**	**18**	**93**	**413**	**1,031**	**1,550**	**1,906**	**2,146**	**1,846**
CHANGE (%)	59%	-41%	-56%	-63%	-661%	429%	346%	149%	50%	23%	13%	-14%
D&A	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**
OPERATING RESULT	**-34**	**-21**	**-11**	**-5**	**15**	**91**	**411**	**1,029**	**1,548**	**1,904**	**2,144**	**1,844**
CHANGE (%)	277%	-38%	-50%	-50%	-393%	489%	354%	150%	50%	23%	13%	-14%
MARGIN (%)	-763%	-181%	-45%	-13%	20%	54%	78%	87%	89%	90%	91%	90%
NET FINANCIAL INCOME/(EXPENSES)	**-1**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**	**-2**
PROFIT/(LOSS) BEFORE TAXES	**-35**	**-23**	**-12**	**-7**	**14**	**89**	**409**	**1,027**	**1,546**	**1,902**	**2,142**	**1,842**
CHANGE (%)	467%	-35%	-46%	-43%	-293%	553%	361%	151%	51%	23%	13%	-14%
MARGIN (%)	-790%	-196%	-53%	-17%	18%	53%	78%	87%	89%	90%	91%	90%
TAXES	**1**	**0**	**0**	**0**	**-7**	**-25**	**-47**	**-96**	**-139**	**-169**	**-193**	**-161**
NET PROFIT/(LOSS)	**-35**	**-23**	**-12**	**-7**	**6**	**63**	**362**	**931**	**1,406**	**1,733**	**1,949**	**1,681**
CHANGE (%)		-34%	-46%	-43%	-192%	882%	471%	157%	51%	23%	12%	-14%
MARGIN (%)	-772%	-196%	-53%	-17%	9%	38%	69%	79%	81%	82%	82%	82%
EPS (CHF)	**-0.010**	**-0.005**	**-0.003**	**-0.002**	**0.001**	**0.014**	**0.082**	**0.211**	**0.318**	**0.392**	**0.441**	**0.381**
CHANGE (%)		-46%	-46%	-43%	-192%	882%	471%	157%	51%	23%	12%	-14%
ESTIMATES AS OF 10 APRIL 2023											SOURCE: VALUATIONLAB ESTIMATES	

NOTE: With a cash position of CHF 29.9 mn (30 June 2022), Relief projects a cash runway through Q3 2023. With the launch of the PKU GOLIKE franchise in the US in October 2022 and a successful launch of ACER-001 in UCDs in Q2 2023, the company believes it could achieve cash flow breakeven in late 2024 and positive operating cash flow in early 2025. We calculate Relief will need approximately CHF 30 mn to reach the projected cash flow breakeven in late 2024. Note that potential (non-dilutive) funding could come from licensing agreements of its key products to partners in regions outside the US and Europe, for instance, in Japan, China, Asia, and Latin America, among others.

Appendix

Pharmaceutical life cycle

To determine the value of a prescription (bio)pharmaceutical compound, it is critical to understand its life cycle. Fortunately, all compounds follow the same life cycle. The clock starts ticking after the compound is patented, providing 20 years of protection from generic competition. Market exclusivities can extend this protection period. Additional protection is provided by orphan drug status (10 years in EU, 7 years in US). The average Research & Development Phase takes 8-14 years, leading to an effective Return Phase of 6-12 years. The Development Phase has 3 distinct Phases, focused on safety (Phase I), dose (Phase II) and efficacy/clinical benefit (Phase III). The compound is filed for registration/approval at the FDA (US) or EMA (EU). The Return Phase is characterized by a star, cash cow, and mature phase. After patent expiry (or loss of market exclusivity) generic manufacturers may copycat the branded prescription drug, at significantly lower costs, leading to a sales and earnings implosion of the branded drug.



SOURCE: VALUATIONLAB

Success Probabilities & Royalties

In our risk-adjusted NPV calculations, we use standardized success probabilities based on historical clinical success rates. The success rate increases as the project progresses through development. Sales and earnings forecasts are based on the clinical and competitive profile of the compound. The more advanced the compound is, the more accurate the forecasts become as the target market can be defined. We conservatively exclude projects that lack Phase IIa proof-of-concept data in our valuations.

SUCCESS PROBABILITIES & ROYALTIES

DEVELOPMENT STAGE	AIM	WHAT / WHO	SUCCESS PROBABILITY (%)	COSTS (USD MN)	ROYALTIES (%)
PRE-CLINICAL	SAFETY & PHARMACOLOGY DATA	LAB TESTS / ANIMALS - NO HUMANS!	< 5	3	
PHASE I	SCREENING FOR SAFETY	HEALTHY VOLUNTEERS (10'S)	5-15	3	< 5
PHASE IIA	PROOF-OF-CONCEPT	PATIENTS WITH DISEASE (10'S)	10-25		
PHASE II	ESTABLISH THE TESTING PROTOCOL	PATIENTS WITH DISEASE (100'S)	15-35	5	5-15
PHASE IIB	OPTIMAL DOSAGE	PATIENTS WITH DISEASE (100'S)	20-45	5-10	
PHASE III	EVALUATE OVERALL BENEFIT/RISK	PATIENTS WITH DISEASE (1,000'S)	40-65	> 20-1,000	10-25
REGULATORY FILING	DETERMINE PHYSICIAN LABELING	CLINICAL BENEFIT ASSESSMENT	80-90		
APPROVAL	MARKETING AUTHORIZATION	PHYSICIANS FREE TO PRESCRIBE	100		15-30

SOURCE: VALUATIONLAB, TUFTS, FDA, EMA, CLINICALTRIALS.GOV

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Our financial analyses are based on the "Directives on the Independence of Financial Research" issued by the Swiss Bankers Association in January 2008.

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Risk Qualification

Speculative	less than 1 year cash and breakeven beyond 1 year
High Risk	profitable within 2 years and 1 approved product/key indication (patent expiry > 5 years)
Medium Risk	profitable and/or sales from at least 2 marketed products/key indications (patent expiry > 5 years)
Low Risk	profitable and sales from >2 marketed products/key indications (patent expiry > 5 years)

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