VALUATIONLAB
FINANCIAL ANALYSIS

RELIEF THERAPEUTICS

FOCUS AREA: TREATMENTS FOR SERIOUS RESPIRATORY DISORDERS SUCH AS (COVID-19) ARDS AND RARE DISEASES WITH HIGH UNMET MEDICAL NEED

KEY DATA			SIX: RLF
MARKET CAPITALIZATION (CHF MN)	299	**SHARE PRICE ON 18 FEBRUARY 200**	0.068
ENTERPRISE VALUE (CHF MN)	254	**RISK-ADJUSTED NPV PER SHARE** (CHF)	0.405
CASH (11 NOVEMBER 2021) (CHF MN)	45	**UPSIDE/DOWNSIDE** (%)	495%
MONTHLY OPERATING EXPENSE (CHF MN)	3.5	**RISK PROFILE**	SPECULATIVE
CASH LIFE	INTO LATE 2023	**SUCCESS PROBABILITY LEAD PROJECT**	65%
BREAK-EVEN (YEAR)	2023	**EMPLOYEES**	~50
FOUNDED (YEAR)	2016	**LISTED** (YEAR)	2009
KEY PRODUCTS:	**STATUS**	**MAJOR SHAREHOLDERS:**	**(%)**
- RLF-100 IV (COVID-19-INDUCED ARDS*)	US EUA**	- GEM GLOBAL YIELD FUND LLC	~22
- RLF-100 IV (NON-COVID-19 RELATED ARDS*)	PHASE II	- FOUNDERS & EXECUTIVE MANAGEMENT	3
- RLF-100 INHALED (PREVENTION COVID-19 RELATED ARDS*)	PHASE IIB/III	**- FREE FLOAT**	97
- RLF-100 INHALED (PULMONARY SARCOIDOSIS)	PHASE II	- DAILY VOLUME 3 MONTHS (SHARES)	17'070'000
- ACER-001 (UREA CYCLE DISORDERS)	FILED (US)		
- ACER-001 (MAPLE SYRUP URINE DISEASE)	PHASE II		
- GOLIKE (PHENYLKETONURIA)	MARKETED (EU)		
- APR-TD011 (EPIDERMOLYSIS BULLOSA)	PHASE II (2022)		
UPCOMING CATALYSTS:	**DATE**	**ANALYST(S):**	BOB POOLER
- "AVICOVID2" 1ST COHORT DATA RLF-100 INHALED PREVENTION COVID-19 ARDS*	H1 2022		BP@VALUATIONLAB.COM
- ACER-001 PDUFA DATE UREA CYCLE DISORDERS	5 JUNE 2022		+41 79 652 67 68
- START PHASE II TRIAL RLF-100 INHALED IN PULMONARY SARCOIDOSIS	H2 2022		

* ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME; ** EUA = EMERGENCY USE AUTHORIZATION; *** CMA = CONDITIONAL MARKETING AUTHORIZATION

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB ESTIMATES

What a Relief!

The legal battle intensifies – mediation on its way

Relief Therapeutics is a Swiss biopharmaceutical company focused on the development and commercialization of treatments for serious respiratory disorders and rare diseases. Key driver is aviptadil (branded RLF-100™ and ZYESAMI™ in the US), a first-in-class vasoactive intestinal peptide (VIP) with predominant biological activity in the lungs, targeting: 1) COVID-19 induced acute respiratory distress syndrome (ARDS); 2) prevention COVID-19 related ARDS 3) non-COVID-19 related ARDS; 4) pulmonary sarcoidosis, with blockbuster peak sales potential, and 5) checkpoint inhibitor pneumonitis (CIP). In March 2021, Relief added ACER-001, which is aimed at rare diseases such as urea cycle disorders (UCDs), with a 5 June 2022 PDUFA date, and maple syrup urine disease (MSUD). The acquisition of privately held Applied Pharma Research (APR) transformed Relief into a fully integrated biopharmaceutical company from a development-stage company, further diversifying the product offering with in-market products and pipeline projects including Golike for phenylketonuria (PKU) and APR-TD011 in development for epidermolysis bullosa (EB). CHF 45 mn cash provides funding into late 2023. We derive a sum-of-parts rNPV of CHF 0.405 per share and qualify the risk profile as Speculative with no substantial revenues, yet.

Key catalysts:

1) **PDUFA date ACER-001 in urea cycle disorders (5 June 2022):** Our rNPV for RLF-100 IV increases by CHF 0.005/share with a 90% success rate (average assuming US approved (100%) and EU filed (80%))
2) **"AVICOVID-2" results RLF-100 INHALED in prevention COVID-19 related ARDS (H2 2022):** Additional COVID-19 indication for RLF-100. Our rNPV increases by CHF 0.005/share with a 72.5% (average US 80% filing and EU 65% phase III) success rate on positive topline results.
3) **Start phase IIb trial RLF-100 INHALED in pulmonary sarcoidosis (H2 2022):** important non-COVID-19 indication with few treatments. Our success rate increases to 50% (phase II dose ranging) from 35% increasing the rNPV by CHF 0.021/share.

Recent Developments

Since our last Relief Therapeutics Valuation Report in November 2021 the legal battle between Relief and its US partner NRx Pharmaceuticals (formerly NeuroRx) has intensified with NRx filing a counterclaim against Relief seeking termination of the Collaboration Agreement for aviptadil (branded ZYESAMI™ in the US and RLF-100™ outside the US) and damages of at least USD 185 mn for breach of contract and defamation.

Relief continues to believe the legally binding Collaboration Agreement is still in full force and effect and that NRx is in breach of the agreement. NRx has engaged in a systematic campaign of misinformation and has failed to live up to multiple commitments it made to Relief in the context of the Collaboration Agreement. Relief has a forensic accounting firm's report on all the invoices that have been submitted to Relief and they do not add up to even an amount greater than what Relief and Relief's major shareholder GEM have contributed to in aggregate. Accordingly, NRx does not appear to have a supportable argument that Relief owes it more money and has not lived up to its contractual obligations. The statements that NRx has made in its public filings (e.g., that Relief owes over USD 25 mn) are not supportable based on the evidence submitted to date by NRx to Relief. Nor can NRx claim credit for the funds being spent by the NIH and Quantum Leap on the phase III "ACTIVE-3b/TESICO" and "I-SPY" trials, respectively. NRx has so far failed to obtain Emergency Use Authorization (EUA) for aviptadil. Relief believes it has been reasonable and pragmatic in attempting to remonstrate with NRx and its CEO Dr. Jonathan Javitt, but the company also intends to defend its rights and remains confident in the merits of its case. Relief and NRx have agreed to hold a mediation to amicably resolve the ongoing litigation between both parties on 22 February 2022.

RLF-100 news flow: Since our last update RLF-100 has made significant progress. The NIH-sponsored "ACTIV-3b/TESICO" phase III trial evaluating RLF-100 IV and Gilead's Veklury (remdesivir) in critical COVID-19 was cleared for full enrollment of the targeted 640 patients with no safety concerns. Trial completion is expected in October 2022 (according to clinicaltrials.gov). NRx filed again for US Emergency Use Authorization (EUA) as well as for Breakthrough Therapy Designation (BTD) in critical COVID-19 patients, albeit in a more targeted patient group. Note the last denial to grant an EUA by the FDA in November 2021 that led to a large share price drop in NRx, triggered two class action trials in the US against NRx and its CEO and CFO claiming they made false and/or misleading statements and/or failed to disclose that the RLF-100 IV EUA contained "insufficient data" regarding the potential benefits and risks of RLF-100 IV during the class action period.
NRx reported the first safety and survival report from the Right to Try use of RLF-100 IV in critical COVID-19 patients in the US with 84% of patients alive after the initial treatment period. NRx also expanded its US Expanded Access and Right to Try programs for RLF-100 IV in critical COVID-19 patients who have exhausted approved treatments and cannot participate in clinical trials. NRx agreed with Hungarian health authorities on a regulatory path for Emergency Use of RLF-100 IV in the Central European region starting with a compassionate care program to begin by the end of 2021.
NRx filed a provisional composition of matter patent application with the US Patent and Trademark Office that describes compositions of vasoactive intestinal peptide, the synthetic form of which is aviptadil that are both shelf stable and biologically active when used to treat COVID-19 and other diseases. Note that the formulation of aviptadil being used by NRx,

and any intellectual property is covered by the parties' Collaboration Agreement with respect to the development and commercialization of aviptadil. NRx is obligated to cross-license such formulation and all related IP to Relief.
Relief filed a US trademark for RLF-100™ (aviptadil) for pharmaceutical use in various indications. A certificate of registration is expected to be issued to Relief soon.
The Swiss Patent Office IPI announced its plans to issue a patent for RLF-100 INHALED for the use in drug-induced pneumonitis, including checkpoint inhibitor-induced pneumonitis (CIP) as applied for by Relief's subsidiary AdVita Lifescience in 2020. There is an urgent need for an effective, safe treatment of CIP. CIP develops in as many as 10% to 20% of patients who are treated with immune checkpoint inhibitors, a complication that leads to discontinuation of treatment and to immunosuppressive therapy.

ACER-001 news flow: A new patent was issued by the US Patent and Trademark Office for ACER-001 covering methods of use for treating urea cycle disorders (UCDs) and maple syrup urine disease (MSUD) further strengthening its IP position up to 2039. Four ACER-001 posters showing the compound as a potential alternative to sodium and glycerol phenylbutyrate for the treatment of UCDs are to be presented at the upcoming SIMD (Society for Inherited Metabolic Disorders) and GMDI (Genetic Metabolic Dieticians International) conferences in April and May, respectively.

APR news flow: A newly filed US formulation patent potentially extends APR's CAMBIA patent protection by approximately 13 years. CAMBIA is the first, and still the only, NSAID ever approved by the FDA for the treatment of acute migraine attacks in adults. CAMBIA is currently available in the form of a dry powder packed into a single dose sachet to be poured and dissolved in water before administration. APR has developed a liquid version of the same product packed into a portable, ready to use, stick pack to offer improved convenience and compliance to migraine patients and provide a potential life cycle management option to its current commercialization partners. The patent will have an expiration date in 2039.

Corporate news flow: All board proposals were approved at the Extraordinary General Meeting, while Michelle Lock was appointed a new Board member extending Relief's board to five members. Her deep strategic, operational and commercialization experience, at both big Pharma and emerging biotechnology companies, globally, will be an important addition to Relief's Board, especially as the company enters its next stage of growth. Relief filed additional forms at the SEC to transition its ADR program into a NASDAQ Stock Market listing planned for H1 2022.

Cash of CHF 45 mn, which together with exercising flexible financing tools, provides a cash runway into late 2023. Relief may need a maximum of CHF 25-30 mn in additional funding to reach positive operating cash flow status before the end of 2024, which is dependent upon timely approval of ACER-001 in the US.

We have conservatively lowered our forecasts for RLF-100 in COVID-19 related indications based on 1) the expectation of most experts that the COVID-19 pandemic is moving into the endemic phase and, 2) the emergence of very effective and convenient oral antiviral treatments. In the endemic phase, experts expect occasional flare-ups of COVID-19 infections like influenza, which may lead to hospitalization of high-risk and unvaccinated patients. Vaccines will remain an important first defense for high-risk patients, while treatments such as Pfizer's oral antiviral Paxlovid provides high-risk patients who become infected with COVID-19 an effective and convenient treatment option. Paxlovid cuts the risk

of hospitalization or death for high-risk COVID-19 patients by roughly 90% when taken early as first symptoms appear. Nevertheless, the continual emergence of new coronavirus variants that may be immune or more resistant to current vaccines pose a continued risk. Therefore, the need for new safe and effective treatments for COVID-19 patients is expected to persist, albeit in a smaller patient population. Consequently, our sum-of-parts rNPV for Relief declines by 22% to CHF 0.405/share from previously CHF 0.520/share.

SUMMARY RECENT PRESS RELEASES:

February 16 – "ACTIV-3b/TESICO" trial with RLF-100 IV cleared to full enrollment
The independent DSMB (Data Safety Monitoring Board) identified no new safety concerns after reviewing more than 448 (>70%) enrolled patients in the NIH-sponsored "ACTIV-3b/TESICO" phase III trial with the trial cleared to continue full enrollment to the targeted 640 patients. RLF-100 IV is the sole remaining investigational drug in the trial with recent closures of other treatment arms. Patient enrollment in Brazil, the EU and UK, and Scandinavia is expected to start in the coming months. The "ACTIV-3b/TESICO" trial is evaluating RLF-100 IV and Gilead's approved Veklury (remdesivir) in critical COVID-19 patients as monotherapy and in combination against placebo. Topline results are expected in H2 2022.

February 8 – US trademark filed for RLF-100™ (aviptadil) for pharmaceutical use
Relief has filed for a trademark for RLF-100™ (aviptadil) with the US Patent and Trademark Office (USPTO) that covers use for pharmaceutical preparations and substances for the treatment of viral, metabolic, endocrine, musculoskeletal, cardiovascular, cardiopulmonary, genitourinary, sexual dysfunction, oncological, hepatological, ophthalmic, respiratory, neurological, gastrointestinal, hormonal, dermatological, psychiatric and immune system related diseases and disorders; pharmaceutical preparations for the treatment of viral diseases and; pharmaceutical preparations for the treatment of viral infections, when the certificate of registration is received. The trademark application (U.S. Serial Number 90141290) filed on August 27, 2020 was published for opposition on January 4, 2022. No party has filed an opposition or extension request with the USPTO within the required 30 days after the publication date. A certificate of registration is expected to be issued to Relief within 11 weeks from the publication date.

February 1 – New US ACER-001 patent covering methods of use for UCDs and MSUD
The US Patent and Trade Office (USPTO) issued a new US patent 11,202,767 that covers methods of use claims related to ACER-001's multi-particulate dosage formulation for oral administration for the treatment of urea cycle disorders (UCDs) and maple syrup urine disease (MSUD). These claims are in addition to the US patent 11,154,521 issued by the USPTO in October 2021, which covers pharmaceutical composition claims of ACER-001. Both newly issued patents have an expiration date in 2036.

January 31 – All proposals approved at EGM - Michelle Lock new Board member
At Relief's EGM (Extraordinary General Meeting), Michelle Lock, who until recently was SVP and Head of Europe and International at Acceleron Pharma, was elected as new member of Relief's Board of Directors, for a term of office extending until completion of the 2022 AGM (Annual General Meeting). The appointment brings Relief's Board to five members. Ms. Lock has built a wealth of strategic and operational expertise from prior positions at Sage Therapeutics and over 20 years at Bristol-Myers Squibb. Her deep strategic, operational and commercialization experience, at both big Pharma and emerging biotechnology

companies, globally, will be an important addition to Relief's Board, especially as the company enters its next stage of growth, including RLF-100 for acute and chronic lung diseases, the expected launch of ACER-001 in urea cycle disorders (UCDs) and the US launch of the Golike product line for patients with phenylketonuria later this year.
Two other Board proposals were approved by shareholders, including:

1. Approval of the compensation of the members of the Board of Directors for the period from the 2021 Annual General Meeting until the 2022 Annual General Meeting
2. Approval of a general revision of the Articles of Association

January 27 – First safety and survival report from Right to Try use of RLF-100 IV
NRx received a first safety and survival report from a Southwestern hospital where RLF-100 IV was given to patients with COVID-19 respiratory failure under the US Federal Right to Try law that provides access to unapproved investigational treatments for patients who have been diagnosed with life-threatening diseases or conditions, who have tried all approved treatment options and who are unable to participated in a clinical trial to access certain unapproved treatments. The first 19 patients treated by 31 December 2021 during the omicron surge, three patients had died while 16 (84%) were reported to be alive by 22 January 2022. No serious events were reported.

January 27 – 4 ACER-001 posters to be presented at SIMD and GMDI conferences
Four ACER-001 abstracts for poster presentations were accepted at the upcoming SIMD (Society for Inherited Metabolic Disorders annual meeting in Orlando, Florida on 10-13 April, and the GMDI (Genetic Metabolic Dieticians International) conference in Las Vegas, Nevada on 4-7 May. The posters to be presented suggest ACER-001 could present a potential alternative to sodium and glycerol phenylbutyrate for the treatment of UCDs. ACER-001 has been filed for approval of treating UCDs in the US with a 5 June 2022 PDUFA date, when the FDA is expected to conclude its review. The four abstracts include:

1. The Pharmacokinetics of Taste-Masked Sodium Phenylbutyrate (ACER-001) for the Treatment of Urea Cycle Disorders Under Fasting and Fed Conditions in Healthy Volunteers
2. Taste-Masked Coating of Sodium Phenylbutyrate (ACER-001) Improves the Palatability of Sodium Phenylbutyrate for Treatment of Urea Cycle Disorders
3. ACER-001: a Potential Alternative to Sodium and Glycerol Phenylbutyrate for Treatment of Urea Cycle Disorders
4. Taste-masked Coating of Sodium Phenylbutyrate (ACER-001) Improves the Palatability of Sodium Phenylbutyrate for Treatment of Urea Cycle Disorders

January 24 – US patent allowance extends APR's CAMBIA protection until 2039
Relief's wholly owned subsidiary APR received a Notice of Allowance from the USPTO (US Patent and Trademark Office) for a key US patent application (number 16/713,052) covering ready to use diclofenac packs, branded CAMBIA to treat acute migraine attacks in adults. Diclofenac potassium is a generic, potent NSAID (non-steroidal anti-inflammatory drug) widely used therapeutically for inflammatory conditions and pain management. APR developed the first, and still the only, NSAID ever approved by the FDA for the treatment of acute migraine attacks in adults by applying its patented dynamic buffering technology (DBT). CAMBIA is currently marketed in the US by Assertio Therapeutics and in Canada by Miravo Healthcare (formerly Nuvo Pharmaceuticals) under an exclusive, royalty bearing license agreement with APR. DBT and CAMBIA are currently protected by a family of four patents listed in the FDA Orange Book, all expiring in 2026. CAMBIA is currently available in the form of a dry powder packed into a single dose sachet to be poured and dissolved in

water before administration. APR has developed a liquid version of the same product packed into a portable, ready to use, stick pack to offer improved convenience and compliance to migraine patients and provide a potential life cycle management option to its current commercialization partners. This new liquid dosage form is the subject matter of the new patent application allowed by the USPTO. Once issued, the patent will have an expiration date in 2039 potentially extending patent expiry by approximately 13 years.

January 19 – Expansion US Expanded Access and Right to Try programs RLF-100 IV
NRx has expanded its US Expanded Access and Right to Try programs for RLF-100 IV for patients with COVID-19 respiratory failure who have exhausted all approved therapies. These programs enable patients with respiratory failure from COVID-19, who have tried all approved medicines, including Gilead's Veklury (remdesivir), and who are not able to participate in a clinical study, to receive RLF-100 IV upon a physician's prescription. NRx will continue to provide RLF-100 IV to hospitals enrolled in the company's Expanded Access Protocol under US FDA guidelines as well as for patients treated und the Federal Right to Try Act.

January 14 – Collaboration Agreement remains in full force – Relief not in breach
Relief provided additional comments on NRx's (formerly NeuroRx) press release following the recent counterclaim against Relief, including:

- Notwithstanding the position taken by NRx in the NRx press release that the Collaboration Agreement between the parties has been cancelled, Relief continues to believe that the Collaboration Agreement between the parties with respect to aviptadil (branded ZYESAMI™ in the US and RLF100™ outside the US) remains in full force and effect, and that NRx, and not Relief, is in breach of that agreement.
- The press release includes numerous statements that Relief believes to be false and materially inaccurate. Among others, these include statements regarding the formulation of aviptadil that is the subject of the Collaboration Agreement, and statements made that suggest that Relief has not satisfied its financial obligations under the Collaboration Agreement (in a situation where Relief has advanced significant sums to NRx up to the maximum amounts required to be paid under the Collaboration Agreement and that amounts that NRx asserts are unpaid have not been paid as a direct result of NRx failing to provide the required supporting documentation). Moreover, NRx's egregious breaches of the Collaboration Agreement, as set forth in Relief's pleadings, excused any obligations that Relief might have had to fund additional amounts to NRx under the circumstances. Finally, Relief asserts that the statements in the NRx press release to the effect that Relief is misleading the public and its shareholders in its public statements and regulatory filings are false and likely defamatory.
- The NRx press release discusses a damages calculation that Relief believes to be completely Illogical and unsupported. The press release also makes statements, which Relief believes are inaccurate and misleading, to the effect that Relief's conduct was so egregious as to warrant the imposition of punitive damages. If anything, NRx's conduct, and not Relief's conduct, warrants the imposition of punitive damages.
- Relief asserts that the statements made in the press release regarding the Chairman of Relief, Ram Selvaraju, are false and likely defamatory. Relief expressly asserts that no members of Relief's board or management are criminals or have been incarcerated, and Relief believes that NRx's statements in the press release, and Jonathan Javitt's statements in his multiple posts on investor message boards regarding this topic, are false and likely defamatory as to Relief and its board and management.

Relief reports that the allegations in NRx's complaint will be responded to in an appropriate filing with the court after NRx's complaint is served on Relief. Further, in light of NRx's claims in its recently filed lawsuit, and the statements made in the NRx press release, Relief is considering whether to file additional claims against NRx and CEO Jonathan Javitt. While there can be no assurance, Relief remains confident in the validity of its claims against NRx and CEO Jonathan Javitt.

Finally, Relief wishes to clarify the record regarding statements made in the NRx press release about the date of the mediation, so that the market has clarity as to what occurred. Following the filing of Relief's complaint on 6 October 2021, the parties agreed to engage in an effort to attempt to amicably resolve the litigation, which included an agreement by NeuroRx to produce certain financial records to Relief prior to the mediation. The original date set for the mediation was 5 January 2022. However, when NeuroRx failed to meet its own deadline for producing the agreed-upon financial documents, the parties agreed to reschedule the mediation date to 22 February 2022. Therefore, the statement made in the NRx press release that Relief has unilaterally delayed the mediation is misleading and does not reflect the fact that had NeuroRx provided the financial records it agreed to provide prior to the mediation on the timeline that it committed to meet; the mediation would likely have taken place in early January.

January 12 – NRx files counterclaim against Relief – Initial comments by Relief
Relief's collaboration partner for aviptadil, NRx (formerly NeuroRx), has filed a lawsuit against Relief in the Supreme Court of the State of New York, County of New York on 12 January 2022. NRx's complaint alleges claims against Relief for breach of the Collaboration Agreement between the parties and damages of no less than USD 185 mn, for a declaration that the Collaboration Agreement has been cancelled, and for defamation. Relief believes that the Collaboration Agreement between the parties with respect to aviptadil remains in full force and effect, and that it is NRx, and not Relief, that is in breach of that agreement.

Relief notes that NRx's complaint includes numerous factual statements that Relief believes to be materially inaccurate. Relief also believes that the damages calculation alleged in NRx's complaint is completely Illogical and unsupported. Relief reports that the allegations in NRx's complaint will be responded to in an appropriate filing with the court after NRx's complaint is served on Relief. While there can be no assurance, Relief remains confident in the validity of its claims against NRx and CEO Dr. Jonathan Javitt.

Finally, Relief reports that its previously announced mediation with NRx, seeking to amicably resolve the litigation between the parties, remains scheduled for 22 February 2022 and that, notwithstanding the filing of the new complaint, Relief intends to participate in the upcoming mediation.

January 6 – NRx' third attempt to seek US EUA for RLF-100 IV in critical COVID-19
NRx filed an application to the FDA seeking EUA (Emergency Use Authorization) for RLF-100 IV to treat patients with critical COVID-19 who are at immediate risk of death from respiratory failure despite treatment with approved therapy including Gilead's Veklury (remdesivir) and who are ineligible for enrollment into the NIH-sponsored "ACTIV-3b/TESICO" phase III trial. This is NRx' third attempt to seek US EUA for RLF-100 IV in critical COVID-19 after the FDA declined the second EUA application in November 2021 citing "it was unable to issue the EUA due to insufficient data regarding the known and potential benefits of the medicine and the known and potential risks of RLF-100 IV in patients

suffering from Critical COVID-19 with respiratory failure". In its letter, the FDA noted that so far, it has reviewed safety in only 131 randomized patients treated with RLF-100 IV from the phase IIb/III "COVID-AIV" trial.

This triggered two class action trials in the US against NRx, its CEO Dr. Jonathan Javitt and CFO William Fricker claiming they made false and/or misleading statements and/or failed to disclose that the RLF-100 IV EUA contained "insufficient data" regarding the potential benefits and risks of RLF-100 IV; accordingly, the FDA was unlikely to approve the RLF-100 IV EUA in its present form; and as a result, the company's public statements were materially false and misleading at all relevant times throughout the class period (1 June to 4 November 2021), resulting in a stock tumble after the FDA turned down the EUA.

We do not fully understand how NRx will successfully attempt a new EUA review by the FDA of RLF-100 IV patients enrolled in the ACTIV-3b/TESICO trial as the trial is still actively recruiting patients and blinded, which would compromise the final results expected in October 2022 (according to clinicaltrials.gov). Therefore, we believe a successful EUA filing can only occur after positive topline results of the ACTIV-3b/TESICO trial in Q4 2022.

January 4 – Provisional RLF-100 COM patent filed at USPTO – IP to be shared
NRx filed a provisional composition of matter (COM) patent application with the USPTO (US Patent and Trademark Office) entitled, "Stable, Buffer-free Compositions of Vasoactive Intestinal Peptide (VIP)". The provisional application describes compositions of vasoactive intestinal peptide, the synthetic form of which is aviptadil (branded ZYESAMI in the US, RLF-100™ outside the US), that are both shelf stable and biologically active when used to treat COVID-19 and other diseases. Relief notes that the formulation of aviptadil being used by NRx, and any intellectual property (IP) that NRx may obtain with respect to such formulation, is covered by the parties' Collaboration Agreement with respect to the development and commercialization of aviptadil, and that under such agreement, NRx is obligated to cross-license such formulation and all related IP to Relief. The failure of NRx to cross-license its formulation of aviptadil to Relief is one of the alleged breaches of the Collaboration Agreement that is raised in Relief's previously filed breach of contract lawsuit against NRx, and its CEO Jonathan Javitt.

December 30 – NRx files for Breakthrough Therapy for RLF-100 IV in COVID-19
NRx has filed for a new BTD (Breakthrough Therapy Designation) request with the FDA for RLF-100 IV focused on patients with critical COVID-19 and respiratory failure who are at immediate risk of death despite treatment with Gilead's Veklury (remdesivir) and other approved therapies. The BTD request is based on an FDA request for clinical data on the effectiveness of RLF-100 IV compared to Veklury and other approved therapies. In November 2021, the FDA denied BTD for RLF-100 IV in critical COVID-19. The FDA noted that NRx did not distinguish the effects of RLF-100 IV from the reported effects of Veklury in critically ill COVID-19 patients. Based on the FDA's input, NRx has narrowed its BTD request to treatment of COVID-19 respiratory failure in patients who progress despite treatment with Veklury and other approved therapies. Patients treated with RLF-100 IV compared to placebo demonstrated a statistically significant (p=.03) 2.8-fold increased odds of being alive and free of respiratory failure at day 28 and day 60 and a highly significant (p=.006) four-fold increased odds of survival is seen in these patients.

December 28 – Swiss patent office to issue new "CIP" patent for RLF-100 INHALED
The Swiss Patent Office IPI announced its plans to issue the patent entitled, "Vasoactive Intestinal Peptide (VIP) for the Use in the Treatment of Drug-induced Pneumonitis," as applied for by Relief's subsidiary AdVita Lifescience in 2020. The patent will be formally issued, at the earliest, one month after the conclusion of the patent examination procedure. There is an urgent need for an effective, safe treatment of checkpoint inhibitor–induced pneumonitis (CIP). Immune checkpoint inhibitor therapy such as Merck & Co's Keytruda (pembrolizumab) has become a new therapeutic option for several types of cancer, but immune related negative adverse events can limit their use. CIP develops in as many as 10% to 20% of patients who are treated with immune checkpoint inhibitors, a complication that leads to discontinuation of treatment and to immunosuppressive therapy. Moreover, these patients suffer from recurrent pneumonitis even after immune checkpoint inhibitor treatment discontinuation and receipt of glucocorticoid treatment, according to current guidelines. The unexpected finding that the synthetic form of VIP (aviptadil, branded RLF-100™) administered via inhalation was well tolerated and led to dampening of alveolar inflammation, radiological and clinical improvement of pneumonitis resulting from a checkpoint inhibitor therapy for melanoma, was the basis for this patent.

December 16 – SEC filing to ultimately list Relief's ADRs on NASDAQ
Relief filed a Registration Statement on Form 20-F with the US SEC (Securities and Exchange Commission) to register Relief as a reporting company under the Securities Exchange Act of 1934. The registration statement is being filed to begin the process of up listing Relief's Level 1 ADR (American Depositary Receipt) program to a Level 2 ADR program and is part of the company's ongoing efforts to list its ADRs on the NASDAQ Stock Market during H1 2022. Relief's ADR program complements its existing primary listing of its ordinary shares on the SIX Swiss Exchange (symbol "RLF") and are quoted in the US on the OTCQB market (symbol "RLFTF"). Relief's ADRs, which represent 150 of Relief's ordinary shares, presently trade in the US OTC market (symbol "RLFTY").

December 15 – "ACTIV-3b/TESICO" trial to continue after no safety concerns
A fourth positive safety review was reported for the ongoing "ACTIV-3b/TESICO" (Therapeutics for Severely Ill Inpatients with COVID-19) critical care phase III trial sponsored by the US National Institutes of Health. The trial is designed to evaluate RLF-100 IV and Gilead's Veklury (remdesivir) in critical COVID-19 patients, as a monotherapy and in combination with placebo. The trial's independent Data Safety Monitoring Board (DSMB) found no new safety concerns after reviewing 348 (54%) patients and recommended continued enrollment to the targeted 640 patients.

December 10 – Regulatory pathway for Emergency Use RLF-100 IV in Hungary
NRx agreed with Hungarian health authorities on a regulatory path for Emergency Use of RLF-100 IV in the Central European region starting with a compassionate care program to begin by the end of 2021. The program is modeled on the FDA's approved Expanded Access Protocol (EAP) already implemented in the US. Confirmatory demonstration of clinical effect under this program will be submitted with safety and efficacy data in support of Emergency Use Authorization in Hungary.

Strategy & Cash Position

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". 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 with a special focus on respiratory and rare disease.

To strengthen and expand its pipeline, Relief signed a collaboration and license agreement with Acer Therapeutics (symbol: ACER), based in Newton, Massachusetts, USA, in March 2021, for the worldwide development and commercialization of ACER-001 for the treatment of 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 in a fully integrated commercial-stage biopharmaceutical company from a development-stage company. Relief's headquarters is based in Geneva, Switzerland and currently has ~50 employees following the APR acquisition. Relief will strategically grow the management team as the company evolves (for Management and Board biographies see page 67).

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). In November 2021, Relief's Level 1 ADR program was launched in the US under trading symbol "RLFTY" to facilitate US investors. Relief intends to transition its ADR program into a NASDAQ Stock Market listing in H1 2022.

Strategy to reposition RLF-100™ in respiratory disease, expand its product offering through APR acquisition and develop & commercialize ACER-001 in rare diseases
Relief's focus is the clinical development and commercialization of its key pipeline project aviptadil (designated RLF-100™ and branded under the trade name ZYESAMI™ in the US) in new treatment solutions for respiratory disease. The APR acquisition brings to Relief a pipeline 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. With APR's emerging commercial platform, Relief obtains a springboard for rolling out marketed products and a base for future product launches in Europe, providing a strong and evolving foundation extending beyond the company's current lead programs, RLF-100 and ACER-001, a late-stage compound for the rare diseases urea cycle disorders (UCDs) with a potential launch in 2022 and maple syrup urine disease (MSUD) in 2023, both with a high margin potential. Relief will continue to search for additional strategic acquisitions to further strengthen its pipeline.

RLF-100 has a promising profile to repurpose for respiratory disease

RLF-100 is a direct analog of vasoactive intestinal polypeptide (VIP), which was acquired from mondoBIOTECH. This legacy compound was 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 to repurpose RLF-100 for respiratory disease.

RLF-100 obtained Investigational New Drug (IND) clearance from the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for phase II clinical trials in acute respiratory distress syndrome (ARDS), a type of respiratory failure characterized by rapid onset of widespread inflammation in the lungs often caused by sepsis, infection, pancreatitis, trauma, pneumonia and aspiration, with a lack of effective treatments and a poor outcome with a mortality rate ranging between 35% and 50%. RLF-100 has been granted orphan drug designation (ODD) by both agencies for acute lung injury (ALI) including ARDS, and sarcoidosis, a rare disease caused by inflammation, particularly in the lungs with limited treatment options. Orphan drug designation (ODD) provides 7 years (US) and 10 years (EU) of market exclusivity from the approval date.

Change in priority after rapid arrival COVID-19 pandemic and early proof of efficacy

Relief's initial plans were to develop RLF-100 for pulmonary sarcoidosis. However, with the rapid arrival of the COVID-19 pandemic in early 2020, the company decided to repurpose the use of the RLF-100 to protect the lung from injury caused by COVID-19 infection. RLF-100 is believed to be the first COVID-19 therapeutic to demonstrate the ability to block replication of the COVID-19 virus in human lung cells and monocytes, while also preventing synthesis of cytokines in the lung and protecting the vulnerable type II alveolar cells. Early results from an ongoing US open label Expanded Access Program (EAP) dubbed "SANICARE" in 2020 demonstrated a 72% survival rate for patients given RLF-100 on top of best standard of care in critically ill COVID-19 patients with respiratory failure who were admitted to the intensive care unit (ICU).

Consequently, the company's priority changed to rapidly develop RLF-100 as treatment of COVID-19 induced acute respiratory distress syndrome (ARDS), a major complication of COVID-19 infection with a lack of effective treatments resulting in a high mortality rate, and for the prevention of COVID-19 related ARDS in hospitalized patients with moderate to severe COVID-19. Thanks to the global rollout of effective coronavirus vaccines, the SARS-CoV-2 pandemic is expected to become endemic soon with occasional flare-ups. In particular, the continual emergence of new coronavirus variants that may be immune or more resistant to current vaccines pose a continued risk. Therefore, the need for new safe and effective treatments for COVID-19 patients is expected to persist, albeit in a smaller patient population than during the pandemic.

RLF-100 is available in two different formulations with clinical development plans for four respiratory indications:

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 indications include:

- **COVID-19 induced ARDS** (peak sales CHF 50 mn – 3rd EUA filed): ongoing US open label Expanded Access Program (EAP) "SAMICARE" trial showed a 72% survival rate for RLF-100 in patients with COVID-19 induced ARDS; FDA Fast Track Designation granted June 2020; US double-blind phase IIb/III "COVID-AIV" trial in 196 COVID-19 induced ARDS patients started June 2020 reported positive 60-day topline results in March 2021; US Emergency Use Authorization (EUA) declined on 4 November 2021, third EUA filed on 4 January 2022, a grant would be transformational for Relief marking first commercial sales of RLF 100; EUA grant could trigger potential EU Conditional Marketing Authorization (CMA) in H1 2023; RLF-100 IV included into the "I-SPY COVID-19" platform trial assessing multiple experimental drugs in COVID-19 patients as well as NIH-sponsored phase III "ACTIV-3b/TESICO" trial
- **Non-COVID-19 ARDS** (peak sales CHF 450+ mn - phase IIb/III trial is under consideration, but with no clear guidance by the company at this time): clinical development in patients with acute respiratory distress syndrome (ARDS) not caused by COVID-19 but other causes such as sepsis, pancreatitis, trauma or pneumonia; phase IIb/III trial results potentially could come as soon as 2022; sNDA (supplemental New Drug Application) in 2023; US launch 2023, EU launch 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 in the home setting to address chronic respiratory diseases. RLF-100 INHALED key indications, include:
    - **Prevention COVID-19 related ARDS** (peak sales CHF 200+ mn - phase IIb/III): US phase IIb/III "AVICOVID-2" trial for prevention COVID-19 related ARDS started in February 2021; topline results due H2 2022; US approval and launch expected late 2022.
    - **Pulmonary sarcoidosis** (peak sales CHF 500+ mn – phase IIb start 2022): initial target indication for RLF-100 before onset of COVID-19 pandemic early 2020; promising POC results published in 2010; phase IIb dose ranging trial to start in 2022; approval and launch expected in 2025; orphan drug designation (ODD) granted in the US in 2007; eligible for 7 years US market exclusivity from date of approval.

ACER-001, a novel powder formulation of sodium phenylbutyrate (NaPB) designed to be both taste-masked and immediate release (IR) is targeted for development and commercialization in two rare diseases:

1) **Urea Cycle Disorders (UCDs):** (peak sales CHF 130+ mn – 505(b)(2) pathway): bioequivalence to Buphenyl obtained under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act; completing additional non-clinical work and 12-month long-term stability data; 5 June 2022 PDUFA date with first launches expected in 2022; potential 3 years Hatch-Waxman market exclusivity; taste-masked formulation US patent issued that protects the compound into 2036; potential to obtain Orphan Drug Designation in the EU providing 10 years market exclusivity; targeted to replace Horizon's UCDs drugs Buphenyl and Ravicti and attract new and non-compliant sufferers of UCDs

2) **Maple Syrup Urine Disease (MSUD):** (peak sales CHF 80+ mn – POC established): based on the encouraging POC results a phase IIb/III trial is planned for 2022; potential US launch in 2023 and EU launch in 2024; obtained Orphan Drug Designation in the US, which provides 7 years market exclusivity; there are currently no drugs approved to treat MSUD

APR acquisition adds marketed, niche and near-market products as well as high margin pipeline projects next to an emerging specialist sales platform

- **Marketed products:** (royalty revenues CHF ~14 mn): main royalty generating products consisting of multiple reformulations of existing drugs, including Cambia and Voltfast for acute migraine, Eminocs for acute pain and Voltadol for local pain and strains; commercialized by partners in return for royalties; several products to phase out in next few years
- **Niche disorders:** (peak sales TBD): including Nexodyn AOS, a sprayable HCIO solution for acute and chronic wounds; Setofilm/Zuplenz/Ondissolve, an oral dispersible film containing ondansetron for treating chemotherapy-, radiotherapy- and postoperative nausea and vomiting; Sentinox a ready to market class III medical device sprayable HCIO solution to block transmission of SARS-Cov-2 virus, approved in EU in February 2021; APR-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
- **Golike (phenylketonuria – PKU):** (peak sales CHF 50+ mn): first food for medical purposes (FSMP) engineered with delivery technology with an improved metabolic management and better compliance with minimized taste, odor, and aftertaste; complete line of products covering main age groups and individual habits; launched in EU in 2018; US launch likely in September 2022; US approval as prescription-only treatment could boost peak sales to CHF 200+ mn
- **APR TD-011 (epidermolysis bullosa - EB): (**peak sales CHF 900+ mn): novel HCIO sprayable solution with strong antimicrobial and anti-inflammatory properties; US Orphan Drug Designation (ODD) granted Q4 2019 on promising early-stage programs providing 7-years market exclusivity from approval date; potential for EU ODD with 10-years market exclusivity; discussions with regulators ongoing to finalize clinical development path, phase IIb trial to start mid 2022, potential launch in 2025

All set to develop and commercialize RLF-100 in COVID-19 disease and beyond, to develop and commercialize ACER-001 in several rare diseases and to expand product offering through APR acquisition

After a flurry of deals in since early 2020, Relief is now preparing to successfully develop, manufacture, distribute and commercialize RLF-100 in COVID-19-induced ARDS, prevention of COVID-19 related ARDS as well as non-COVID-19 ARDS and pulmonary sarcoidosis, develop and commercialize ACER-001 in UCDs and MSUD, and expand its product offering through the APR acquisition with sufficient funding for operations secured into late 2023.

- **Development & Commercialization agreements:**
  - **NRx Pharmaceuticals:** Relief entered into a Collaboration Agreement with NRx Pharmaceuticals (formerly known as NeuroRx Pharmaceuticals) in September

2020. NRx will conduct the clinical trials of RLF-100 in COVID-19 related respiratory disease (e.g., positive US phase IIb/III "COVID-AIV" trial in COVID-19 induced ARDS; US phase IIb/III "AVICOVID-2" trial in prevention COVID-19 related ARDS. NRx will lead commercialization in the US, Canada and Israel, while Relief will be responsible for Europe and ROW. Profits will be split 50/50 in the US, Canada and Israel, while they will be split 85/15 in Europe and 80/20 in ROW, in favor of Relief. Relief is in an ongoing dispute with NeuroRx and its CEO Dr. Javitt, alleging breaches in the Collaboration Agreement for the development and commercialization of Relief's RLF-100, leading to significant delays. In October 2021, Relief filed a US lawsuit against NeuroRx and its CEO Dr. Javitt. NRx filed a counterclaim against Relief in January 2022. Relief and NRx have agreed to hold a mediation to amicably resolve the ongoing litigation between both parties on 22 February 2022.

- **Quantum Leap:** NRx signed an agreement to include RLF-100 in the US "I-SPY COVID-19" trial, a platform trial assessing multiple experimental drugs in COVID-19 patients and sponsored by Quantum Leap, a 501c(3) charitable organization. RLF-100 will be included as one of the first drugs targeting respiratory failure in critically ill COVID-19 patients.
- **Syneos Health:** a global clinical research organization (CRO), is expected to run the European phase IIb/III clinical trial of RLF-100 in COVID-19 induced ARDS (if such a study is deemed necessary for approval by European regulators).
- **AdVita Lifescience:** In January 2021, Relief and AdVita signed a binding term sheet for Relief to acquire all shares of AdVita, a privately held German pharmaceutical company, in exchange for EUR 25 mn Relief common shares plus future contingent milestones up to EUR 20 mn, which was successfully closed in July 2021. Relief will gain pending IP rights that may cover RLF-100 INHALED formulation specifications and potential applications of RLF-100 INHALED in ARDS and checkpoint inhibitor-induced pneumonitis (CIP).
- **Acer Therapeutics:** In March 2021, a definitive agreement was signed between Relief and Acer Therapeutics for an exclusive collaboration and license agreement for the worldwide development and commercialization of ACER-001 in urea cycle disorders (UCDs) and maple syrup urine disease (MSUD), both rare diseases with a high margin potential. ACER-001 in UCDs is in late stage of development with launch expected in 2022 and potential peak sales of CHF 130+ mn. 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 ROW sales and a total of USD 6 mn milestones based on the first EU marketing approvals of 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.
- **TFF Pharmaceuticals:** In March 2021, US partner NRx signed a collaboration agreement with TFF Pharmaceuticals to determine the feasibility of formulating RLF-100 as a dry powder using TFF Pharmaceuticals' thin-film freezing (TFF) technology.
- **"ACTIV-3b/TESICO" trial:** in April 2021, RLF-100 IV was selected for inclusion in the NIH-sponsored global "ACTIV-3b/TESICO" phase III trial as one of two

drugs including Gilead's Veklury (remdesivir) in severely ill patients with COVID-19.
    - **APR acquisition:** closed in June 2021, adds marketed, niche and near products as well as attractive high margin pipeline projects next to an emerging European sales platform to launch current and future products.
- **Supply chain agreements:**
    - **Bachem Americas:** a long-time and cost-effective active pharmaceutical ingredient (API) manufacturer with almost a decade of experience of producing aviptadil, will provide commercial supplies of RLF-100 API with the ability to scale up rapidly.
    - **Nephron Pharmaceuticals:** will provide the "fill/finish" sterile injectable drug product.
    - **Polypeptide:** In October 2020, NeuroRx signed an agreement with Polypeptide for the supply of GMP grade Active Pharmaceutical Ingredient (API) of RLF-100 IV providing a second source of procuring API. The Company has agreed to purchase a total of USD 1,010,000 worth of product and services over the contract.
    - **Cardinal Health:** In August 2021, NRx signed an agreement with Cardinal Health to provide third party logistics and distribution of RLF-100 IV upon EUA approval in the US
    - **MannKind:** In August 2021, NRx signed an agreement to develop a dry powder inhaler formulation of RLF-100 based on MannKind's Technosphere platform to extend use to many pulmonary conditions beyond COVID-19
    - **AMRI:** a global contract and development and manufacturing organization (CDMO) will provide aseptic fill/finish manufacturing of RLF-100 for clinical trial medication at their Glasgow, UK, facility.

- **Funding agreements:**
    - **GEM Global Yield Fund:** Funding has been provided by Global Emerging Markets (GEM), Relief's largest shareholder with currently a ~22% equity stake. Recent financings are sufficient to fund operations and key clinical development projects into late 2023. In January 2021, Relief established a new CHF 50 mn SSF with GEM, with the potential to extend the cash reach substantially beyond this period.
    - **Private placements with US institutional investors:** In March 2021, gross proceeds of approximately CHF 10 mn was raised in a private placement with a single healthcare-dedicated US institutional investor followed by CHF 15 mn with two US institutional investors in end July 2021.

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

- Gain US Emergency Use Authorization (EUA) for RLF-100 IV in COVID-19 induced ARDS around year-end 2022 (initial EUA declined by FDA in December 2020, second EUA declined in November 2021), marking first commercial sales of RLF-100
- Resolve ongoing dispute with US partner NRx (formerly NeuroRx) and CEO Dr. Javitt either amicably, through a settlement, or the recently filed lawsuit in the Supreme Court of the State of New York. Mediation to resolve litigation amicably is set for 22 February 2022
- File for EU Conditional Marketing Authorization (CMA) for RLF-100 IV in COVID-19 induced ARDS shortly after a potential US authorization for emergency use (H1 2023)

- Alternatively, consider starting EU phase IIb/III trial of RLF-100 IV in COVID-19 induced ARDS if positive "COVID-AIV" trial not sufficient for EU CMA
- Complete US single pivotal phase IIb/III "AVICOVID-2" trial of RLF-100 INHALED in prevention COVID-19 related ARDS with results due H2 2022
- Integrate APR and Relief organizations and determine and execute key projects and priorities to accelerate growth.
- US approval of ACER-001 in UCDs with a 5 June 2022 PDUFA date and start POC trials in MSUD
- After successfully closing of the AdVita acquisition in July 2021 to expand the scope of development of RLF-100 INHALED in indications such as pulmonary sarcoidosis and checkpoint inhibitor pneumonitis (CIP)
- Consider starting potentially pivotal phase IIb/III trial of RLF-100 IV in non-COVID-19 ARDS with a potential supplemental New Drug Application (sNDA) pathway applied.
- Start phase IIb dose ranging trial of RLF-100 INHALED in pulmonary sarcoidosis in 2022 with results due 2023
- Accelerate clinical development plan for APR TD-011 in epidermolysis bullosa (EB).
- Strategically grow management team as the clinical pipeline evolves
- Explore partnerships and distribution agreements for RLF-100 in regions where Relief does not intend to establish its own commercial infrastructure (e.g., emerging markets)
- Continue to expand the clinical pipeline through selective product in-licensing and/or M&A

Almost CHF 120 mn raised since 2016

In 2020, Relief has been very successful in fund raising, 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**

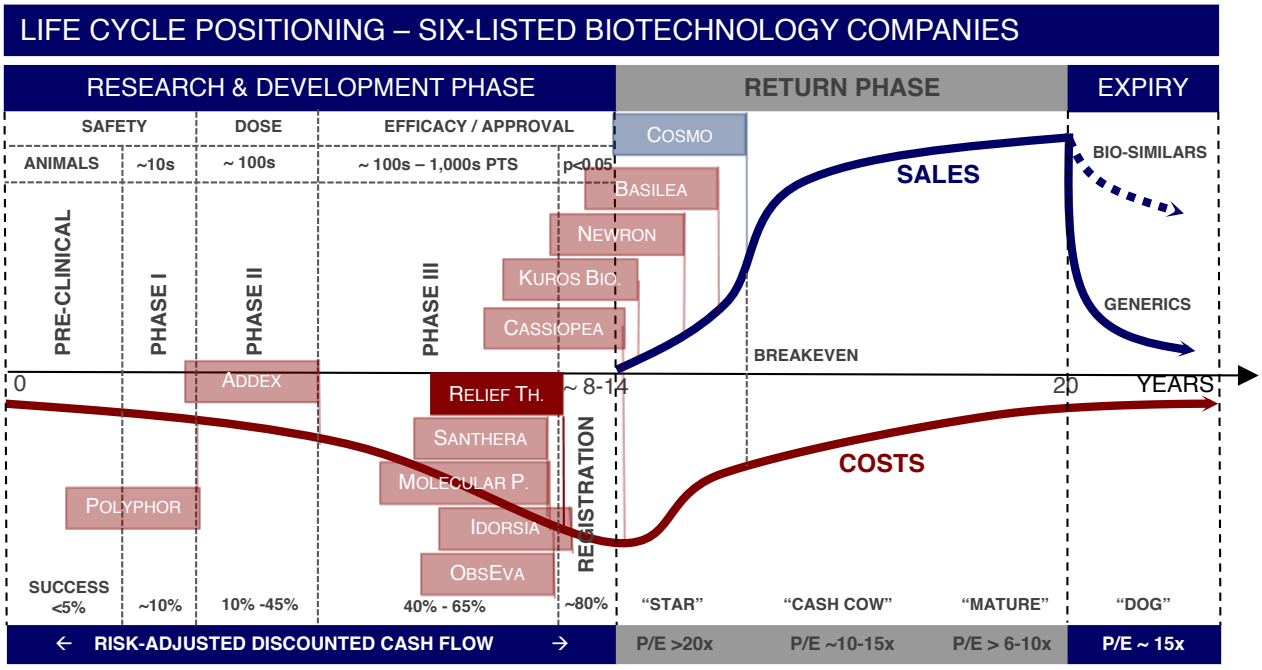
SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB

Recent 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 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 has the right to periodically, during a timeframe of up to three years, issue and sell shares to GEM. Relief will control the timing and maximum amount of any draw down, and retains the right, not the obligation, to draw down on the full commitment amount. GEM undertakes to subscribe to or acquire ordinary registered Relief common shares. Future subscription prices under the SSF will correspond to 90% of the average of the closing bid prices on the SIX Swiss Exchange during the reference period, which corresponds to 15 trading days following Relief's draw down notice. 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.

Life Cycle Positioning – Speculative

We qualify Relief's risk profile as Speculative with currently no substantial product revenues with a current cash runway into late 2023. The CHF 50 mn SSF with GEM has the potential to increase Relief's cash reach substantially beyond this period, albeit at the cost of share dilution. 2023 should be a transformational year for Relief, upon a potential grant of an US EUA for RLF-100 IV in COVID-19 induced ARDS expected around year-end 2022, marking first commercial sales for RLF-100. Other countries and regions outside the US such as the EU may also approve RLF-100 IV for COVID-19 induced ARDS due to the current lack of effective and safe treatments. This 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

Valuation Overview

Risk-adjusted sum-of-parts NPV points to a fair value of CHF 0.405 per share
We derive a sum-of-parts risk-adjusted (r)NPV of CHF 0.405 per share for Relief, with estimated cash and cash equivalents of CHF 0.010 per share (11 November 2021) and overhead expenses of CHF 0.033 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)	PERCENTAGE OF TOTAL
RLF-100 IV	COVID-19 INDUCED ARDS*	49	2023	0.006	65%	**0.004**	1%
RLF-100 INHALED	PREVENTION COVID-19 RELATED ARDS*	223	2022 (US) / 2023 (EU)	0.067	65%	**0.044**	10%
RLF-100 IV	NON-COVID-19 RELATED ARDS*	473	2023 (US) / 2024 (EU)	0.214	35%	**0.075**	17%
RLF-100 INHALED	PULMONARY SARCOIDOSIS	556	2025	0.141	35%	**0.049**	11%
ACER-001	UREA CYCLE DISORDERS (UCD)	142	2022 (US) / 2023 (EU)	0.054	80%	**0.043**	10%
ACER-001	MAPLE SYRUP URINE DISEASE (MSUD)	85	2024	0.042	35%	**0.015**	3%
GOLIKE	PHENYLKETONURIA (PKU)	56	2018 (EU) / 2021 (US)	0.028	100%	**0.028**	6%
APR-TD001	EPIDERMOLYSIS BULLOSA (EB)	955	2026	0.486	35%	**0.170**	39%
CASH POSITION (11 NOVEMBER 2021)		45		0.010		**0.010**	2%
TOTAL ASSETS				0.617		**0.438**	**100%**
OVERHEAD EXPENSES				-0.033		**-0.033**	
NPV/SHARE (CHF)				0.584		**0.405**	
SHARE PRICE ON 18 FEBRUARY 2022						0.068	
PERCENTAGE UPSIDE / (DOWNSIDE)						495%	

* ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME
ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

Relief's key drivers, include:

RLF-100 IV in COVID-19 induced ARDS - rNPV of CHF 0.004/share
In November 2021, the FDA declined to grant US Emergency Use Authorization (EUA) for RLF-100 IV based on the positive 60-Day topline trial results of the phase IIb/III "COVID-AIV" trial of RLF-100 IV in 196 patients with COVID-19 induced ARDS citing insufficient data to establish a positive benefit/risk. We believe this pushes back a potential new EUA filing by roughly a year upon positive ACTIC-3b/TESICO trial results expected in Q4 2022, despite NRx applying for a third EUA in January 2022. A US EUA could trigger a potential Conditional Marketing Authorization (CMA) in the EU in 2023. We now forecast peak sales of CHF 50 mn to be reached in 2023 and thereafter sales to gradually decrease due to the expected decline in COVID-19 cases with the pandemic moving into the endemic phase with occasional flare-ups. We calculate a rNPV of CHF 0.004/share for RLF-100 in COVID-19 induced ARDS, considering the profit split agreement with NRx in the US (50/50 profit split), Europe (85/15 profit split in favor of Relief) and ROW (80/20 profit split in favor of Relief) with a 65% (phase III) success rate and a WACC of 7%.

RLF-100 INHALED in prevention COVID-19 related ARDS – rNPV of CHF 0.044/share
The prevention of respiratory failure in patients with COVID-19 moderate and severe disease represents a larger market opportunity than for COVID-19 induced ARDS as far more patients are affected (~4x more patients than COVID-19 induced ARDS patients) with a longer treatment duration (4 weeks treatment compared to ~1 week) resulting in a higher price per treatment course per patient. We forecast peak sales of CHF 200+ mn for RLF-100 INHALED in prevention COVID-19 related ARDS. Our forecasts are based on the same decline in global COVID-19 cases as we expect for COVID-19 induced ARDS. The US phase IIb/III "AVICOVID-2" trial started in February 2021 with topline results due in H2 2022 with a US launch around year-end 2022 followed by the EU in 2023. We calculate a rNPV of CHF 0.044 per share for RLF-100 INHALED in prevention COVID-19 related ARDS considering the global NRx profit split agreement with a 65% (phase II/III) success rate.

RLF-100 IV in non-COVID-19 related ARDS – rNPV of CHF 0.075/share

We forecast peak sales for RLF-100 in ARDS not caused by COVID-19 but from other causes such as sepsis, pancreatitis, trauma or pneumonia, to amount to CHF ~500 mn. Phase IIb/III trials are expected to start in 2022 with results due early 2023. Assuming a supplemental New Drug Application (sNDA) approval, US launch could occur in 2023. EU launch is expected in 2024. For RLF-100 IV in ARDS (non-COVID-19), we calculate a rNPV of CHF 0.075 per share assuming a 35% (POC established) success rate and considering the global NRx profit split agreement.

RLF-100 INHALED in pulmonary sarcoidosis – rNPV of CHF 0.049/share

We forecast peak sales of RLF-100 INHALED in pulmonary sarcoidosis to amount to CHF 500+ mn with first launches expected in 2025. A phase IIb dose ranging trial is expected to start in H2 2022. 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 a rNPV of CHF 0.049 per share for RLF-100 INHALED in pulmonary sarcoidosis assuming a 35% (POC established) success rate and considering the global NRx profit split agreement.

ACER-001 in urea cycle disorders (UCDs) – rNPV of CHF 0.043/share

We forecast peak sales of ACER-001 in urea cycle disorders (UCDs) to amount to CHF 130+ mn. ACER-001, in-licensed from Acer Therapeutics, is a novel powder and immediate release (IR) formulation of sodium phenylbutyrate, is targeted to provide a compelling alternative to Horizon Therapeutics' Buphenyl (glycerol phenylbutyrate) with a novel taste-masking formulation that potentially can be taken without food at a competitive pricing. The FDA set a 5 June 2022 PDUFA data when it expects to conclude its review of ACER-001 in UCDs with a first launch in the US to occur in 2022. Relief is entitled to 60% of net profits in the Acer territories (US, Canada, Brazil, Turkey and Japan), while Acer will receive a 15% net royalty on ROW sales by Relief, next to regulatory milestones upon approval in the EU. We calculate a rNPV of CHF 0.043 per share for ACER-001 in UCD assuming an 80% (Section 505(b)(2)) success rate.

ACER-001 in Maple Syrup Urine Disease (MSUD) – rNPV of CHF 0.015/share

We forecast peak sales of ACER-001 in Maple Syrup Urine Disease (MUSD) to amount to CHF 80+ mn. Based on encouraging POC trial results, Acer and Relief plan to start phase IIb/III development of ACER-001 in MSUD in 2022 with a potential launch in the US in 2023 and in the EU in 2024. We calculate a rNPV of CHF 0.015 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.

Golike in phenylketonuria (PKU) – rNPV of CHF 0.028/share

We forecast peak sales of CHF 50+ mn for the 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. Golike is a family of products covering main age groups and individual habits including sachets, shake & drinks and bars being rolled out in the EU by distribution partners. Relief expects to launch Golike in the US by September 2022. US approval as a prescription-only treatment could boost peak sales to CHF 200+ mn. Our NPV for Golike amounts to CHF 0.028 per share.

APR-TD011 in epidermolysis bullosa (EB) – rNPV of CHF 0.170 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. APR-TD011 is 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 APR-TD011 in 2019 providing 7-years marketing exclusivity from approval in the US Discussions with regulatory authorities are ongoing to finalize clinical development path with a potential launch in 2026. We forecast peak sales for APR-TD011 to amount to CHF 900+ mn in EB and calculate a rNPV of CHF 0.170 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" on what the value could amount to, if all our assumptions were reached.

RLF-100 INHALED in CIP – phase I, launch 2025

The increasing use of immune checkpoint inhibitor (ICI) therapy in cancer has brought new hope of survival 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 a variety of adverse effects. In the lung, these attacks can induce checkpoint inhibitor pneumonitis (CIP) and is one of the complications associated with ICI therapy. CIP is defined as the occurrence of dyspnea and/or other respiratory symptoms, together with new inflammatory lesions on chest computed tomography (CT) after ICI treatment, following exclusion of pulmonary infection, tumor progression, and other reasons. The incidence of CIP reported in clinical trials was between 3% to 5%. The risk factors for CIP are unknown. Corticosteroids are currently the basic treatment for CIP, however, have side effects, which have to be closely monitored, while a number of patients are insensitive to corticosteroid treatment. There are no optimal recommendations for treatment of refractory CIP to date. 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 followed a phase IIb/III trial in CIP. First launches could occur in 2025 with peak sales conservatively amounting to CHF 150+ mn. Due to the lack of sufficient POC, we exclude forecasts for RLF-100 INHALED in CIP, yet

APR niche disorders and early-stage pipeline projects

Relief is currently assessing which APR products offer the optimal strategic fit combined with differentiation that can offer strong growth potential. Niche disorders include, Nexodyn AOS, a sprayable HCIO solution for acute and chronic wounds; Setofilm/Zuplenz/Ondissolve, an oral dispersible film containing ondansetron for treating chemotherapy-, radiotherapy- and postoperative nausea and vomiting; Sentinox a ready to market sprayable HCIO solution to block transmission of SARS-Cov-2 virus and APR-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 45 mn, Relief has a cash runway into late 2023 without factoring in potential revenues from RLF-100 sales, which could start as early as 2022, or exploiting the CHF 50 mn SSF with GEM. The company is fully financed to successfully complete its development plans for RLF-100, ACER-011 and APR-TD011.

Litigation risk: The pending dispute and US lawsuit with NRx and CEO Dr. Javitt could potentially delay clinical development timelines. In a counterclaim NRx is seeking at least USD 185 mn in damages for breach of contract and defamation.

Development risk: RLF-100 targeted indications are in different phases of clinical development. Most advanced are COVID-19 induced ARDS and prevention COVID-19 related ARDS, both in pivotal development with a 65% (phase II/III) success rate, followed by non-COVID-19 related ARDS and pulmonary sarcoidosis with a 35% (POC established) success rate. All indications for RLF-100 are targeted for respiratory disease, which could present a cluster risk. ACER-001 in UCDs is developed under Section 505(b)(2) providing an alternative pathway for filing an NDA with an 80% success rate and a 35% (POC) success rate in MSUD. For APR we only include APR-TD011 in EB with a 35% (POC) success rate.

Commercialization risk: Both RLF-100 and ACER-001 are specialty drugs, which do not require large sales forces. The sales uptake of RLF-100 in the two COVID-19 indications is largely dependent on the number of COVID-19 infections, hospitalizations, and stockpiling, which may be affected by the pandemic entering the endemic phase. New market entrants for treating COVID-19 patients may also impact sales uptake. The emerging APR European specialist sales force can be leveraged and expanded for upcoming product launches.

Pricing and reimbursement risk: Pricing and reimbursement for both RLF-100's COVID-19 indications should not provide a large hurdle given the lack of effective treatments and the ongoing global pandemic. We believe our pricing assumptions may prove conservative with the "COVID-AIV" topline results showing a significant survival benefit. ACER-001 is expected to be competitively priced vs. existing drugs for UCDs. Treatment costs for APR-TD011 in EB represents pricing for an orphan drug indication with no effective treatments.

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 5-year Hatch Waxman patent extension reaching to 2034 and 5 years NCE exclusivity. The EU patent of RLF-100 expires in July 2026. Market exclusivity in the EU beyond 2026 depends on whether RLF-100 is successful in receiving orphan drug exclusivity for COVID-19 induced ARDS. Assuming an earlier approval of RLF-100 INHALED in prevention COVID-19 related ARDS, cheaper generic versions of RLF-100 INHALED could appear after 2026 in the EU hampering sales uptake of RLF-100 INHALED in pulmonary sarcoidosis even when it enjoys orphan drug exclusivity for sarcoidosis. We conservatively assume cheaper generic competition in the EU after 2026. ACER-001 is likely to enjoy 7 years (US) and 10 years (EU) orphan drug exclusivity in both UCDs and MSUD as well as APR-TD011 in EB. A recently issued US formulation patent extends ACER-001 protection into 2036.

Catalysts

CATALYST TIMELINES

TIME LINE	PRODUCT	INDICATION	MILESTONE / EVENT	COMMENT	PER SHARE IMPACT ON RNPV
2022					
4 JAN	RLF-100	TREATMENT/PREVENTION RESPIRATORY DISORDERS	PATENT FILING	NRX FILED A PROVISIONAL PATENT FOR STABLE COMPOSITIONS OF AVIPTADIL (BRANDED RLF-100/ZYESAMI) SUITABLE FOR HUMAN USE	
6 JAN	RLF-100 IV	COVID-19 INDUCED ARDS*	3RD EMERGENCY USE AUTHORIZATION (EUA) FILED	NRX FILED AN APPLICATION TO THE FDA SEEKING EUA FOR RLF-100 IV TO TREAT CRITICAL COVID-19 PATIENTS AT IMMEDIATE RISK OF DEATH FROM RESPIRATORY FAILURE DESPITE OTHER APPROVED TREATMENTS INCLUDING GILEAD'S VEKLURY (REMDESIVIR); NOTE: THIS IS THE THIRD EUA FILING BASED LARGELY ON THE DATASET THE FDA DEEMED "INSUFFICIENT" TO GRANT EUA IN THE US	
12 JAN			NRX FILES COUNTERCLAIM AGAINST RELIEF	NRX FILES A COUNTERCLAIM AGAINST RELIEF SEEKING: DAMAGES NO LESS THAN USD 185 MN FOR BREACH OF CONTRACT, PREJUDGMENT INTEREST AT THE LEGAL RATE, A DECLARATION NEURORX DID NOTHING TO JUSTIFY RELIEF'S TERMINATION OF THE COLLABORATION AGREEMENT, A DECLARATION NEURORX IS FREE OF ANY OTHER OBLIGATION UNDER THE COLLABORATION AGREEMENT BECAUSE OF RELIEF'S PRIOR MATERIAL BREACH AND REPUDIATION, PUNITIVE DAMAGES, PAYMENT OF COSTS AND ATTORNEYS' FEES	
12/14 JAN			RELIEF COMMENTS ON NEURORX LAWSUIT	RELIEF CLAIMS THAT NEURORX'S COMPLAINT INCLUDES NUMEROUS STATEMENTS THAT ARE MATERIALLY INACCURATE, THE DAMAGES CALCULATION IS COMPLETELY ILLOGICAL AND UNSUPPORTED; RELIEF BELIEVES THE COLLABORATION AGREEMENT REMAINS IN FULL FORCE, STATEMENTS MADE AGAINTS RAM SELVARAJU ARE FALSE AND LIKELY DEFAMATORY, NO MEMBERS OF RELIEF'S BOARD OR MANAGEMENT ARE CRIMINALS OR HAVE BEEN INCARCERATED AND ARE FALSE AND LIKELY DEFAMATORY; THE ALLEGATIONS WILL BE RESPONDED TO IN AN APPROPRIATE COURT FILING; RELIEF LIKES TO AMICABLY RESOLVE THE LITIGATION AT THE UPCOMING MEDIATION ON 22 FEBRUARY	
19 JAN	RLF-100 IV	COVID-19 INDUCED ARDS*	EXPANSION US EXPANDED ACCESS AND RIGHT TO TRY PROGRAMS	EXPANSION OF US EXPANDED ACCESS AND RIGHT TO TRY PROGRAMS FOR RLF-100 IV FOR COVID-19 PATIENTS WHO HAVE PROGRESSED DESPITE TREATMENT WITH GILEAD'S VEKLURY (REMDESIVIR) AND OTHER APPROVED TREATMENTS AND ARE NOT ABLE TO PARTICIPATE IN THE ONGOING NIH-SPONSORED PHASE III "ACTIV-3B/TESICO" TRIAL	
24 JAN	CAMBIA	ACUTE MIGRAINE	US PATENT ISSUED	ALLOWANCE OF US PATENT 16/713,052 FOR APR'S FORMULATION OF THE NSAID DICLOFENAC FOR THE TREATMENT OF ACUTE MIGRAINE IN ADULTS APPLYING THE PATENTED DYNAMIC BUFFERING TECHNOLOGY (B+DBT)	
27 JAN	RLF-100 IV	COVID-19 INDUCED ARDS*	INITIAL RIGHT TO TRY PATIENT DATA	FIRST 19 PATIENTS TREATED BY 31 DECEMBER 2021, 3 (16%) DIED AND 16 (84%) REPORTED ALIVE BY 22 JANUARY 2022; NO SERIOUS EVENTS REPORTED; PATIENTS WERE TREATED AT FIRST ONSET OF RESPIRATORY FAILURE AFTER EXHAUSTING REMDESIVIR AND OTHER APPROVED THERAPIES; DATA PROVIDED TO FDA TO SUPPORT THIRD EUA APPLICATION	
27 JAN	ACER-001	UREA CYCLE DISORDERS (UCDS)	4 POSTERS PRESENTED AT SIMD AND GMDI CONFERENCES	4 ACER-001 ABSTRACTS WERE ACCEPTED FOR POSTER PRESENTATIONS AT THE UPCOMING SIMD (SOCIETY OF INHERITED METABOLIC DISORDERS) AND GMDI (GENETIC METABOLIC DIETICIANS INTERNATIONAL) CONFERENCES DEMONSTRATING THE USE OF ACER-001 AS A POTENTIAL ALTERNATIVE TO SODIUM AND GLYCEROL PHENYLBUTYRATE FOR TREATMENT OF UCDS	
28 JAN			EGM	EXTRAORDINARY GENERAL MEETING (EGM); MICHELLE LOCK ELECTED AS NEW BOARD MEMBER; SHAREHOLDERS APPROVED PROPOSED COMPENSATION OF BOARD MEMBERS AND GENERAL REVISION OF THE ARTICLES OF ASSOCIATION	
1 FEB	ACER-001	UREA CYCLE DISORDERS (UCDS) MAPLE SYRUP URINE DISEASE (MSUD)	US PATENT ISSUED	US PATENT 11,202,767 ISSUED COVERING ACER-100 METHODS OF USE FOR THE TREATMENT O UREA CYCLE DISORDERS (UCDS) AND MAPLY SYRUP URINE DISEASE (MSUD) EXTENDING PATENT EXPIRY TO 2036	
2 FEB			BOARD EXPANSION	MICHELLE LOCK WITH DEEP STRATEGIC, OPERATIONAL AND COMMERCIALIZATION EXPERIENDE APPOINTED AS NEW BOARD MEMBER EXPANDING RELIEF'S BOARD TO 5 MEMBERS	
8 FEB	RLF-100		US TRADEMARK FOR RLF-100™ FILED	RELIEF FILED A US TRADEMARK APPLICATION FOR RLF-100™ WITH THE USPTO COVERING PHARMACEUTICAL PREPARATIONS AND SUBSTANCES FOR VARIOUS DISEASES	
15 FEB	RLF-100 IV	COVID-19 INDUCED ARDS*	"ACTIV-3B/TESICO" TRIAL SAFETY REVIEW	NIH-SPONSORED PHASE III "ACTIV3B-TESICO" IN CRITICAL COVID-19 PATIENTS AFTER REVIEW OF MORE THAN 448 ENROLLED PATIENTS CLEARED TO CONTINUE ENROLLMENT TO 640 PATIENTS	
22 FEB			MEDIATION NRX DISPUTE	RELIEF AND NRX AGREED TO HOLD A MEDIATION TO AMICABLY RESOLVE THE ONGOING LITIGATION	
H1	RLF-100 INHALED	PREVENTION COVID-19 RELATED ARDS*	"AVICOVID-2" TRIAL - RESULTS 1ST PATIENT COHORT	TOPLINE DATA 1ST COHORT (144 IN-PATIENTS) OF US PHASE IIB/III "AVICOVID-2" TRIAL OF RLF-100 INHALED IN 288 PATIENTS WITH COVID-19 ASSOCIATED NON-ACUTE LUNG INJURY CONSISTING OF TWO PATIENT COHORTS: 1) 144 IN-PATIENTS AND 2) 144 OUT-PATIENTS	
H1	ACER-001	UREA CYCLE DISORDERS (UCDS)	EU MAA FILING	POTENTIAL FILING MARKETING AUTHORIZATION APPLICATION (MAA) FOR EU APPROVAL IN UCD'S	
H1			US NASDAQ LISTING	LISTING OF ADRS ON US NASDAQ STOCK MARKET TO FACILITATE US INVESTORS	
5 JUN	ACER-001	UREA CYCLE DISORDERS (UCDS)	US PDUFA DATE	US PDUFA DATE BY WHEN THE FDA IS EXPECTED TO CLOSE ITS REVIEW FOR US APPROVAL OF ACER-001 IN UCDS	+ CHF 0.005
MID	APR-TD011	EPIDERMOLYSIS BULLOSA	START PHASE IIB	START PHASE IIB TRIAL IN PATIENTS WITH EPIDERMOLYSIS BULLOSA (EB)	+ CHF 0.073
SEP	GOLIKE	PHENYLKETONURIA (PKU)	US LAUNCH	US LAUNCH OF GOLIKE PRODUCT LINE FOR PATIENTS WITH PHENYLKETONURIA BY RELIEF'S OWN US SPECIALIST SALES FORCE SPEARHEADED BY ANTHONY KIM	
H2	RLF-100 INHALED	PULMONARY SARCOIDOSIS	START PHASE IIB DOSE RANGING TRIAL	START PHASE IIB DOSE RANGING TRIAL OF RLF-100 INHALED IN PATIENTS WITH PULMONARY SARCOIDOSIS IN GERMANY	+ CHF 0.021
H2	ACER-001	MAPLE SYRUP URINE DISEASE (MSUD)	START CLINICAL DEVELOPMENT	START CLINICAL DEVELOPMENT OF ACER-001 IN MSUD	
H2	SENTINOX (APR-AOS2020)	PREVENTION COVID-19	POST MARKETING TRIAL RESULTS	POST MARKETING TRIAL RESULTS OF SENTINOX IN PREVENTING COVID-19 INFECTION AS A CLASS III MEDICAL DEVICE	
H2	RLF-100 IV	COVID-19 INDUCED ARDS*	"ACTIV-3B/TESICO" TRIAL RESULTS	TOPLINE DATA NIH-SPONSORED PHASE III "ACTIV-3B/TESICO" TRIAL IN CRITICAL COVID-19 PATIENTS	
H2	RLF-100 IV	NON-COVID-19 INDUCED ARDS*	START PHASE IIB/III TRIAL	START PHASE IIB/III TRIAL IN NON-COVID-19 INDUCED ARDS (ACUTE RESPIRATORY DISTRESS SYNDROME)	
H2	RLF-100 INHALED	PREVENTION COVID-19 RELATED ARDS*	"AVICOVID-2" TRIAL - RESULTS 2ND PATIENT COHORT	TOPLINE DATA 2ND COHORT (144 OUT-PATIENTS) OF US PHASE IIB/III "AVICOVID-2" TRIAL OF RLF-100 INHALED IN 288 PATIENTS WITH COVID-19 ASSOCIATED NON-ACUTE LUNG INJURY CONSITING OF TWO PATIENT COHORTS: 1) 144 IN-PATIENTS AND 2) 144 OUT-PATIENTS	+ CHF 0.005
H2	RLF-100 IV	COVID-19 INDUCED ARDS*	"I-SPY COVID-19 TRIAL" RESULTS	TOPLINE DATA "I-SPY-COVID" TRIAL	

* ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB

Technology & Pipeline

TECHNOLOGY PLATFORM - No proprietary technology platform but a S&D approach
Relief does not have a proprietary technology platform. The company 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" with a special focus on respiratory disease and orphan drug indications. Relief plans to expand its clinical pipeline through selective product in-licensing and/or M&A deals.

PIPELINE - Targeting multiple respiratory disorders and rare diseases

PRODUCT PIPELINE

PRODUCT	DRUG CLASS	INDICATION	STATUS	LAUNCH YEAR	PARTNER	PEAK SALES
RLF-100 IV*	INTRAVENOUS (IV) SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	COVID-19-INDUCED ARDS**	PHASE III	2023	NRX (US, CANADA, ISRAEL)	CHF 50 MN
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	PREVENTION COVID-19 RELATED ARDS**	PHASE IIB/III	2022 (US) 2023 (EU)	NRX (US, CANADA, ISRAEL)	CHF 200+ MN
RLF-100 IV*	INTRAVENOUS (IV) SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	NON-COVID-19 RELATED ARDS	PHASE II	2023 (US) 2024 (EU)	NRX (US, CANADA, ISRAEL)	CHF 450+ MN
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	PULMONARY SARCOIDOSIS	PHASE II	2025	NRX (US, CANADA, ISRAEL)	CHF 500+ MN
RLF-100 INHALED	INHALED SYNTHETIC HUMAN VASOACTIVE INTESTINAL PEPTIDE (VIP)	CHECKPOINT INHIBITOR-INDUCED PNEUMONITIS (CIP)	PHASE I	2025	NRX (US, CANADA, ISRAEL)	CHF 150+ MN
ACER-001	TASTE-MASKED, IMMEDIATE-RELEASE FORM OF SODIUM PHENYLBUTYRATE	UREA CYCLE DISORDERS (UCD)	PHASE III	2022 (US) 2023 (EU)	ACER (US, CANADA, BRAZIL, TURKEY, JAPAN)	CHF 130+ MN
ACER-001	TASTE-MASKED, IMMEDIATE-RELEASE FORM OF SODIUM PHENYLBUTYRATE	MAPLE SYRUP URINE DISEASE (MSUD)	PHASE I	2024	ACER (US, CANADA, BRAZIL, TURKEY, JAPAN)	CHF 80+ MN
GOLIKE	CONTROLLED-RELEASE AMINO ACID MIX PRODUCT WITH TASTE AND ODOR MASKING	PHENYLKETONURIA (PKU)	LAUNCHED (EU)	2018 (EU) 2021 (US)	APR APPLIED PHARMA RESEARCH (ACQUIRED IN 2021)	CHF 50+ MN
APR-TD011	SPRAYABLE HYPOTONIC ACID-OXIDIZING SOLUTION CONTAINING HYPOCHLOROUS ACID	EPIDERMOLYSIS BULLOSA (EB)	PHASE II (2022)	2025	APR APPLIED PHARMA RESEARCH	CHF 900+ MN
SENTINOX	CLASS III MEDICAL DEVICE	COVID-19 PREVENTION	APPROVED (EU)	2021	APPLIED PHARMA RESEARCH	TBD
NEXODYN AOS	CLASS III MEDICAL DEVICE	CHRONIC WOUNDS	APPROVED (EU)	2021	APPLIED PHARMA RESEARCH	TBD
APR-TM011	CLASS III MEDICAL DEVICE	SKIN TOXICITIES IN CANCER THERAPIES	APPROVED (EU)	2021	APPLIED PHARMA RESEARCH	TBD
APR-OM032	FOOD FOR SPECIAL MEDICAL PURPOSES (FSMP)	TYROSINEMIA (TYR)	CLINICAL	2023/202	APPLIED PHARMA RESEARCH	TBD
APR-OM033	FOOD FOR SPECIAL MEDICAL PURPOSES (FSMP)	MAPLE SYRUP URINE DISEASE (MSUD)	CLINICAL	2023/202	APPLIED PHARMA RESEARCH	TBD
APR-OM034	FOOD FOR SPECIAL MEDICAL PURPOSES (FSMP)	HOMOSITINURIA (HCU)	CLINICAL	2023/202	APPLIED PHARMA RESEARCH	TBD
APR-OD031	FOOD FOR SPECIAL MEDICAL PURPOSES (FSMP)	PHENYLKETONURIA (PKU)	PRECLINICAL	TBD	APPLIED PHARMA RESEARCH	TBD
APR-TD012	CLASS III MEDICAL DEVICE	HALEY HALEY DISEASE (HHD)	PRECLINICAL	TBD	APPLIED PHARMA RESEARCH	TBD
APR-TD013	CLASS III MEDICAL DEVICE	BURULI ULCER (BU)	PRECLINICAL	TBD	APPLIED PHARMA RESEARCH	TBD

* IV = INTRAVENOUS (IV) INFUSION; **ARDS = ACUTE RESPIRATORY DISTRESS SYNDROME; *** EUA = EMERGENCY USE AUTHORIZATION
ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: RELIEF THERAPEUTICS, VALUATIONLAB ESTIMATES

After divesting atexakin alfa, a low-dosage formulation of interleukin-6 (IL-6) in development for treating neuropathy, to Sonnet BioTherapeutics (NASDAQ symbol: SONN) in August 2019, Relief's key pipeline project is aviptadil (designated RLF-100™ and branded under the trade name ZYESAMI™ in the US). To strengthen and expand its pipeline, Relief signed a collaboration and license agreement with Acer Therapeutics (symbol: ACER), based in Newton, Massachusetts, USA, in March 2021, for the worldwide development and commercialization of ACER-001 a novel powder formulation of sodium phenylbutyrate (NaPB) designed to be taste-masked and immediate release (IR). ACER-001 adds a second late-stage pipeline project to Relief with a relatively high 80% (Section 505(b)(2)) success rate in urea cycle disorders (UCDs) and 35% (POC) success rate in maple syrup urine disease (MSUD), targeting lucrative, high priced, high margin, rare disease market opportunities.

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 in a fully integrated commercial-stage biopharmaceutical company from a development-stage company. The APR acquisition brings to Relief a pipeline 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 pipeline projects, include:

I) RLF-100 rapidly repurposed for COVID-19 respiratory complications
RLF-100 is a patented formulation of vasoactive intestinal polypeptide (VIP). VIP in combination with phentolamine mesylate, branded Invicorp by Senetek Pharmaceuticals, was originally developed as an intracavernosal injection for the treatment of erectile dysfunction and was approved in 1998 and is marketed in Europe. RLF-100 became part of Relief's pipeline through Relief's reverse merger with the corporate successor of mondoBIOTECH, originator of the drug, with the plan to reposition the compound in respiratory disease starting with pulmonary sarcoidosis. The rapid onset of the SARS-CoV-2 virus (COVID-19) pandemic in early 2020 resulted in a rapid repositioning of RLF-100 in treating and preventing critical COVID-19 patients with respiratory failure with the highest priority. Although most COVID-19 cases are mild, older patients and those with co-morbidities are at increased risk of developing a cytokine storm, characterized by a systemic inflammatory response leading to acute respiratory distress syndrome (ARDS) and organ failure. Acute respiratory failure is the primary cause of death in critically ill COVID-19-infected patients, with up to 80% of these patients dying despite intensive care and mechanical ventilation.

VIP involved in the control of airway tone, mucus secretion and vascular relaxation
RLF-100 is a recombinant form of vasoactive intestinal polypeptide (VIP), an abundant biologically active endogenous human peptide that was discovered in 1970 and possesses antiproliferative, anti-inflammatory, anti-cytokine, and immune-regulatory activities in animal models of respiratory distress, acute lung injury, and inflammation as has been shown in more than 100 peer-reviewed studies. Although first identified in the intestinal tract, VIP is now known to be produced throughout the body and to be primarily concentrated in the lungs where its predominant biological activity is observed. VIP is a member of the secretin family of peptides. It is one of the most important non-adrenergic, non-cholinergic inhibitory transmitters in the lung, where it is involved in the control of airway tone, vascular relaxation and airway mucus secretion.

In the respiratory system of humans, VIP-containing nerve fibers have been described in tracheo-bronchial smooth muscle, around submucosal glands and in the walls of pulmonary and bronchial vessels. The biological functions of VIP are mediated through two receptors, the vasoactive intestinal peptide receptor type 1 (VPAC1 receptor) and type 2 (VPAC2 receptor) and belong to the G protein-coupled receptor family. Both VPAC1 and VPAC2 receptors are expressed in human airways: VPAC1 receptor by bronchial epithelial cells, bronchial and vascular smooth muscle, and VPAC2 receptor by bronchial epithelial cells and bronchial glands.

RLF-100 has been tested alone in several pilot and phase II trials for respiratory indications, including:

- **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
- **Pulmonary sarcoidosis:** 20 patients were given 50 microgram (μg) RLF-100 INHALED by nebulizer 4 times daily for 4 weeks
- **Pulmonary hypertension:** 48 patients were given escalating doses from 50 – 200 μg RLF-100 INHALED by nebulizer 4 times daily for 12 weeks
- **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 all trials, RLF-100 was well tolerated with very few side effects. 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.

RLF-100 prevents deadly cytokine storm and viral replication of COVID-19

ARDS is the primary cause of death in COVID-19. RLF-100's active ingredient, vasoactive intestinal polypeptide (VIP), has demonstrated an immediate clinical response in patients with COVID-19 induced ARDS. The cause of death in COVID-19 is broadly attributed to cytokine storm – i.e., a massive release of inflammatory cytokines as viral particles infect and then cause rupture of pulmonary epithelium cells – that is not readily manageable using commercially available anti-cytokine drugs. Cytokine inhibition alone has been shown to be insufficient because the lethal damage caused by the coronavirus stems from viral replication in the Alveolar Type II (ATII) cell, with resulting cytopathic effects and cell rupture.

COVID-19 induced ARDS is caused by selective infection of the ATII cell by the SARS-CoV-2 coronavirus. The ATII cells are particularly vulnerable because of their high surface density of Angiotensin Converting Enzyme type 2 (ACE2) cell surface receptors, which serve as the route of entry for the virus. These specialized cells manufacture surfactant that coats the lung and is essential for oxygen exchange. Loss of surfactant causes collapse of the air sacs (alveolae) in the lung and results in respiratory failure.

The SARS-CoV-2 virus enters the ATII cell through binding of its spike protein to ACE2 surface receptors. ACE2 is not present on Alveolar Type I (ATI) cells, which comprise 95% of the pulmonary epithelium and those cells are not infected by the corona virus. Most importantly, approximately 70% of the VIP binds uniquely to VPAC1 receptors on ATII cells in the lung that is critical to transmission of oxygen to the body, the same cells that bind the SARS-CoV-2 virus via their ACE2 receptors. VIP protects those cells and the surrounding pulmonary epithelium by inhibiting replication of the SARS-CoV-2 virus, blocking cytokine synthesis, preventing apoptosis, and upregulating the production of surfactant, which is critical to pulmonary oxygenation.

While VIP clearly prevents cytokine storm, its primary effect is to block viral replication in the first place and to upregulate the production of surfactant that is critical to blood oxygenation. **Hence, VIP represents the first COVID-19 therapeutic to directly combat the replication of the SARS-CoV-2 virus at the site of injury.** Other than RLF-100, no currently proposed treatments for COVID-19 specifically target these vulnerable Type II cells. The US FDA has granted Investigational New Drug (IND) licenses for multiple pivotal clinical trials of RLF-100 in COVID-19 respiratory failure.

RLF-100 has potential in treating and preventing respiratory failure, including:

- **COVID-19 induced ARDS:** treating critically ill COVID-19 patients hospitalized on mechanical ventilation with a poor prognosis (positive 60-day topline results US phase IIb/III "COVID-AIV" trial reported in March 2021, US EUA declined on 4 November 2021, next pivotal "ACTIV-3b/TESICO" trial to report topline results in Q4 2022)
- **Prevention COVID-19 related ARDS:** preventing COVID-19 patients at risk of developing critical respiratory failure or life-threatening ARDS (US phase IIb/III "AVICOVID-2" trial started in February 2021 with results due in H2 2022)

- **Non-COVID-19 related ARDS:** treating patients with ARDS from other causes than COVID-19 with a high unmet medical need due to the lack of effective treatments. Relief considers starting a pivotal phase IIb/III trial with a potential supplemental New Drug Application (sNDA) pathway applied.
- **Pulmonary sarcoidosis:** A small POC trial showed promise in pulmonary sarcoidosis. Relief plans to start a phase IIb dose ranging trial of RLF-100 INHALED in patients with pulmonary sarcoidosis in 2022. The company expects first launches in 2025.
- **Checkpoint inhibitor pneumonitis (CIP):** is a potentially fatal complication if not treated correctly in 3-5% of patients receiving checkpoint inhibitors. Relief and AdVita are considering development of RLF-100 INHALED in CIP.

II) ACER-001 a novel taste-masked IR formulation of NaPB for various inborn errors of metabolism

ACER-001 is a taste-masked, immediate-release (IR) proprietary formulation of sodium phenylbutyrate (NaPB) developed by Acer using a microencapsulation process. 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. ACER-001 is being developed for the treatment of various inborn errors of metabolism, including UCDs and MSUD. Acer has been granted Orphan Drug Designation (ODD) by the FDA for the MSUD indication.

- **Urea cycle disorders – UCDs**: ACER-001 is targeted to provide a compelling alternative to Horizon Therapeutics' Buphenyl (glycerol phenylbutyrate) with a novel taste-masking formulation that potentially can be taken without food at a competitive pricing. The FDA set a 5 June 2022 PDUFA date with the US launch to occur first in 2022.
- **Maple syrup urine disorder – MSUD:** Based on encouraging POC trial results, Acer and Relief plan to start phase IIb/III development of ACER-001 in MSUD in H2 2022 with a potential launch in the US and EU in 2024.

III) Selected APR pipeline projects – Golike and APR-TD011 in rare diseases

The acquisition of APR expands 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 that 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.

- **Golike (phenylketonuria – PKU):** Golike is the first line of food for special medical purposes (FSMP) engineered with APR's drug delivery Physiomimic™ Technology offering an improved metabolic management for patients with PKU and a better compliance thanks to minimized taste, odor and aftertaste. Golike is approved in the EU and rolled out by distribution partners. US launch is expected by September 2022.
- **APR-TD011 (epidermolysis bullosa – EB):** is a sprayable hypochlorous (HClO) sprayable solution stemming from APR's Tehclo™ that combines strong antimicrobial activity with anti-inflammatory properties with the potential to become one of the first products ever approved for EB. A preliminary proof of concept trial showed promising results with improvement of skin blistering and tissue repair in just two weeks treatment. Relief expects to start phase II development in mid 2022 once the clinical development program has been finalized with regulators and expects first launches in 2026.

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

Forecasts & Sensitivity Analysis

RLF-100 (COVID-19 induced ARDS & prevention COVID-19 related ARDS; non-COVID-19 related ARDS)

Product Analysis

I) RLF-100 IV in COVID-19 induced ARDS:
Peak sales CHF 50 mn; rNPV CHF 0.004/share
We forecast global peak sales of around CHF 50 mn for RLF-100 IV in patients with COVID-19 induced ARDS. US Emergency Use Authorization (EUA) based on the pivotal "COVID-AIV" trial was declined in November 2021. NRx filed a third EUA in January 2022. We believe a successful EUA grant will only occur upon positive phase IIII "ACTIV-3b/TESICO" trial results expected in Q4 2022. A US EUA grant around year-end 2022, could potentially trigger EU conditional marketing authorization (CMA), marking first commercial launches for RLF-100. We assume patent protection until 2034 (US) and 2026 (EU). We calculate a rNPV of CHF 18 mn or CHF 0.004/share with a 65% (phase III) success rate (see page 43).

II) RLF-100 INHALED in prevention COVID-19 related ARDS:
Peak sales CHF 200+ mn; rNPV CHF 0.044/share
For RLF-100 INHALED in prevention COVID-19 related ARDS, we forecast global peak sales to reach CHF 200+ mn assuming US and EU launch in 2023. The sales potential for prevention COVID-19 related ARDS is higher than COVID-19 induced ARDS due to more COVID-19 patients affected and a longer treatment duration. We calculate a rNPV of CHF 192 mn or CHF 0.044/share assuming a 65% (phase II/III) success rate (see page 47).

III) RLF-100 IV in non-COVID-19 related ARDS:
Peak sales CHF 450+ mn; rNPV CHF 0.075/share
Global peak sales for RLF-100 IV in ARDS not caused by COVID-19 are expected to amount to roughly CHF 450+ mn assuming US launch in 2023 and EU launch in 2024. We calculate a rNPV of CHF 330 mn or CHF 0.075/share assuming a 35% (POC established) success factor (see page 50).

Significant market opportunity in COVID-19 disease and beyond

Early proof-of-concept (POC) data generated with aviptadil (designated RLF-100™ and branded under the trade name ZYESAMI™ in the US) in acute respiratory distress (ARDS) triggered the decision to assess the potential of RLF-100 in treating and preventing rapid respiratory decline in critically ill COVID-19 patients, which leads to life-threatening ARDS. Up to 80% of these patients die when critically ill, despite intensive care and mechanical ventilation. 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. In 2020, in a remarkable flurry of agreements, Relief secured a strategic development and commercialization partnership for RLF-100 with the US-based firm NRx, sufficient funding for the clinical development of RLF-100 in its key respiratory indications

through major shareholder GEM Global Yield Fund, and established supply chain agreements with Bachem Americas and Nephron Pharmaceuticals and ordered sufficient drug substance to treat large number of COVID-19 patients with RLF-100.

RLF-100 has potential in treating and preventing respiratory failure, including:

I) **COVID-19 induced ARDS:** treating critically ill COVID-19 patients hospitalized on mechanical ventilation with a poor prognosis (positive 60-day topline results US phase IIb/III "COVID-AIV" trial reported in March 2021, Third EUA filed in January 2022, "ACTIV-3b/TESICO" phase III topline results due Q4 2022)

II) **Prevention COVID-19 related ARDS:** preventing COVID-19 patients at risk of developing critical respiratory failure or life-threatening ARDS (US phase IIb/III "AVICOVID-2" trial started in February 2021 with results due in H2 2022)

III) **Non-COVID-19 related ARDS:** treating patients with ARDS from other causes than COVID-19 with a high unmet medical need due to the lack of effective treatments (phase IIb/III trial may start 2022 with results due in 2023)

The two COVID-19 indications gained highest priority due to the pandemic

The first two indications for RLF-100 have the highest priority given the high number of critically ill COVID-19 patients who develop life-threatening ARDS, overwhelming hospitals and intensive care units (ICUs) in many countries, globally. As a result, many countries have implemented strict lockdown measures at a high economic and social cost. The focal point of these lockdown measures is to prevent hospitals and ICUs to be overwhelmed with critically ill COVID-19 patients and being forced to ration lifesaving equipment and interventions to these patients as well as other critically ill patients. It is believed the SARS-CoV-2 pandemic is likely become an endemic virus. In the endemic phase, the number of infections becomes relatively constant across years, allowing for occasional flare-ups. To reach this steady state could take a few years or decades, depending on how quickly populations develop immunity. Experts believe the pandemic is currently moving into the endemic phase. However, the continual emergence of new coronavirus variants that may be immune or more resistant to current vaccines pose a risk. Subsequently, the need for new safe and effective treatments for COVID-19 patients is expected to persist.

Positive topline results US "COVID-AIV" trial with NRx applying for US EUA

In June 2020, Relief's US partner NRx started the single potentially pivotal US phase IIb/III "COVID-AIV" trial of RLF-100 IV in 196 patients with Covid-19 induced ARDS based on the promising early results seen in the US open label EAP "SAMICARE". In March 2021, NRx reported positive topline results after 60 days treatment. Across all patients and sites, RLF-100 IV met the primary endpoint for successful recovery from respiratory failure at days 28 ($p=0.014$) and 60 ($p=0.013$) and also demonstrated a meaningful benefit in survival ($p<0.001$) after controlling for ventilation status and treatment site. Based on these positive results NRx applied to the FDA for Emergency Use Authorization (EUA) on 31 May 2021, which was declined in November 2021 citing insufficient data to establish a positive benefit/risk. Despite NRx filing a third EUA for a smaller target population in January 2022, we believe an EUA grant will only be successful on positive phase III "ACTIV-3b/TESICO" topline results expected in Q4 2022. If authorized for emergency use, first commercial sales could follow shortly after approval. Upon a US EUA grant, Relief expects to apply for EU Conditional Marketing Authorization (CMA) for RLF-100 IV in COVID-19 induced ARDS adding to the commercial potential. Relief may not have to conduct a similar phase IIb/III trial in the EU if European regulators agree to accept the US pivotal trial results as indicative

of RLF-100 IV's safety and efficacy. We forecast peak sales in COVID-19 induced ARDS could amount to CHF 50 mn.

In February 2021, NRx started the US phase IIb/III "AVICOVID-2" trial in the prevention of COVID-19 related ARDS to assess the impact of RLF-100 INHALED on preventing respiratory failure in moderate to severe COVID-19 patients with respiratory symptoms. Results are due in H2 2022. We forecast higher peak sales of CHF 200+ mn for this indication than for COVID-19 induced ARDS due to the higher number of patients with a longer treatment duration.

In total, RLF-100 could achieve more than CHF 250 mn peak sales in COVID-19 associated respiratory disease, alone. Additionally, Relief expects to develop RLF-100 IV in non-COVID-19 related ARDS, caused by for instance by sepsis, trauma, or other serious lung infections. This would add another CHF 500 mn peak sales to our forecasts.

I) RLF-100 IV in COVID-19 induced ARDS - Peak sales CHF 50 mn; rNPV CHF 0.004/share

Strategic collaboration with NRx to develop and commercialize RLF-100
In March 2020, Relief entered a clinical development collaboration with the US privately held biopharmaceutical company NeuroRx (now NASDAQ-listed NRx Pharmaceuticals with symbol "NRXP"). NRx is led by former senior executives of Johnson & Johnson, Eli Lilly, Pfizer and AstraZeneca, including CEO Dr. Jonathan Javitt, who is leading the clinical trials of RLF-100 in COVID-19 related respiratory disease, including the completed US phase IIb/III "COVID-AIV" trial of RLF-100 IV in COVID-19 induced ARDS, which reported positive topline results in March 2021, and the ongoing US phase IIb/III "AVICOVID-2" trial of RLF-100 INHALED in prevention of COVID-19 related ARDS that started in February 2021 with results expected in H2 2022.

Collaboration Agreement signed to formalize and accelerate RLF-100 development
In September 2020, the relationship with NRx was formalized with an exclusive global collaboration agreement on RLF-100 to accelerate development and commercialization in key markets. Both companies agreed to share all profits from sales of RLF-100 for all indications related to COVID-19 and potentially other respiratory indications on a global basis. NRx will lead commercialization (and book sales) in the US, Canada, and Israel, while Relief will lead commercialization (and book sales) in Europe and the rest of the world (ROW). In the US, Canada and Israel, profits will be split on a 50/50 basis. Profits will be split in Europe 85/15 and in ROW 80/20, all in favor of Relief. Both companies will use a value-based pricing model, which will consider the efficacy profile and pharmacoeconomic benefits of RLF-100, in particular the potential impact on mortality.

Ongoing lawsuits may delay development and lead to considerable damages
Unfortunately, in April 2021 a pending dispute was announced between Relief and its partner NRx under the Collaboration Agreement, 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, stability issues with the formulation of RLF-100. In October 2021, Relief filed a lawsuit in the Supreme Court of the State of New York against NeuroRx and CEO Dr. Javitt alleging breaches in the Collaboration Agreement for the development and commercialization of Relief's RLF-100. NRx has still not provided all data of the US pivotal "COVID-AIV" phase IIb/III trial necessary for European filings, which has led to delays. In

January 2022, the legal battle intensified with NRx filing a counterclaim against Relief seeking termination of the Collaboration Agreement and damages of at least USD 185 mn for breach of contract and defamation. Relief and NRx have agreed to hold a mediation to amicably resolve the ongoing litigation between both parties on 22 February 2022.

RLF-100 included in US "I-SPY COVID-19" a platform trial assessing multiple drugs

In January 2021, NRx and Quantum Leap Healthcare Collaborative (Quantum Leap) signed a clinical trial participation agreement to include RLF-100 INHALED in the "I-SPY COVID-19" clinical trial. The "I-SPY COVID-19 trial is a platform trial assessing multiple drugs for the treatment of patients with critical COVID-19 who are hospitalized or in intensive care units (ICUs). The trial uses a similar protocol as a traditional clinical trial, but compares multiple investigational drugs combined with a "backbone" of the standard of care to rapidly identify those drugs that have a large impact on reducing disease severity, including reduced mortality, reducing or avoiding time on ventilation and other long-term comorbidities. RLF-100 will be included as one of the first drugs targeting respiratory failure in critically ill COVID-19 patients. Quantum Leap is the sponsor of the trial.

RLF-100 IV included in NIH-sponsored phase III "ACTIV-3b/TESICO" COVID-19 trial

RLF-100 IV has also been identified by the National Institutes of Health (NIH) as one of two drugs selected for inclusion in the multicenter phase III trial "ACTIV-3b/TESICO" (Therapeutics for Severely Ill In patients with COVID-19) that will include the US and multiple foreign countries. 640 patients will be randomly allocated to RLF-100 IV and Gilead's Veklury (remdesivir), the combination of both drugs, and placebo. The primary endpoint of the trial will be patient recovery from respiratory failure over 90 days. All safety updates by the independent DSMB showed no safety concerns with the trial to continue to fully enroll the targeted 640 patients. The trial is funded by the US Government COVID-19 Therapeutics Response and sponsored by the National Institute of Allergy and Infectious Diseases (NIAID). Topline results are expected in Q4 2022.

Supply chain agreements to provide RLF-100 on a timely basis in the US and Europe

In September 2020, Relief and NRx established supply chain agreements and ordered sufficient drug substance to prepare to treat to treat large number of COVID-19 patients with RLF-100. Bachem Americas and Nephron Pharmaceuticals have been contracted to manufacture commercial supplies of RLF-100 to ensure that adequate drug inventory will be immediately available upon approval. Bachem Americas is a long-time and cost-effective manufacturer of aviptadil API with the ability to scale up rapidly. Nephron Pharmaceuticals will provide the final form "fill/finish" sterile injectable drug product.

In November 2020, Relief appointed Syneos Health (NASDAQ symbol: SYNH), a global clinical research organization (CRO), to run the European phase IIb/III clinical trial, if required, of RLF-100 in COVID-19 induced ARDS, as well as future trials in other indications to be conducted in Europe. Relief also selected AMRI, a global contract and development and manufacturing organization (CDMO), who will provide aseptic final form "fill/finish" sterile injectable formulation RLF-100 at their Glasgow, UK, facility.

In March 2021, NRx announced a collaboration with TFF Pharmaceuticals to determine the feasibility of formulating RLF-100 as a dry powder using TFF Pharmaceuticals' Thin-Film Freezing (TFF) technology. This could expand the use of RLF-100 beyond an inhaled nebulized formulation to use in a more convenient dry powder inhaler (DPI).

In July 2021, NRx announced it has validated a commercial formulation for RLF-100 IV (aviptadil intravenous formulation) allowing for high volume manufacture with an anticipated one year or greater stability under appropriate storage conditions. Simultaneously, NRx achieved a 30-to-50-fold increase in its manufactured lot size of RLF-100 IV with the potential to deliver millions of doses worldwide and enabling stockpiling. The new formulation will be used in the ongoing clinical trials and programs, including the NIH-sponsored phase III "TESICO" trial and the phase II "I-SPY-COVID" adaptive platform trial as well as the Expanded Access Program and Right to Try program.

In August 2021, NRx signed an agreement with Cardinal Health to provide third party logistics and distribution of RLF-100 IV upon the potential EUA approval in the US. The partnership creates an efficient and highly flexible logistics and distribution model for NRx. Cardinal Health's expertise will enable RLF-100 IV to quickly reach patients in the intensive care units where limiting time to treatment is critical. Cardinal Health supplies more than 90% of hospitals in the US and has more than 20 years of experience of supporting rapid delivery of life-saving drugs.

In October 2021, NRx announced they have submitted a revised IND (Investigational New Drug) module on the manufacturing of RLF-100 IV to the FDA containing documentation that Nephron Pharmaceuticals is prepared to supply RLF-100 IV on a commercial scale. NRx also received notification that a European Qualified Person Auditor completed an inspection at a separate manufacturing facility with no adverse findings.

In November 2021, NRx reported the completion of an FDA Manufacturing Information review, without the imposition of any clinical hold, which enables NRx to distribute RLF-100, produced at commercial scale under GMP (Good Manufacturing Practices) for clinical trials and other future purposes. The FDA has now reviewed a GMP manufacturing process at a batch size of 10,000 – 100,000 doses with a current shelf life of 150 days. This new process, helped by Nephron Pharmaceuticals, replaces the handmade, 300 dose batches with a limited shelf life of 62 days. NRx will work together with the FDA to complete CMC (chemistry, manufacturing and controls) review that will be needed for any potential drug approval.

Largest shareholder GEM helps to provide sufficient funding into late 2023

Sufficient funding has been largely provided by GEM Global Yield Fund, LLC, Relief's largest shareholder with a ~22% equity stake. Recent financings have brought in approximately CHF 68 mn, largely from the Share Subscription Facility (SSF) agreement with GEM, which concluded in September 2020, and approximately CHF 25 mn from two private placements with US institutional investors in March and July 2021. 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 additional commercial supply of RLF-100 to meet demand as needed, as well as pursue further business development opportunities such as with ACER-001 and the APR acquisition.

EAP - Early clinical data supports use in critically ill COVID-19 patients

RLF-100 IV has showed the ability to induce rapid recovery from respiratory failure in the most critically ill COVID-19 patients. The first report of rapid clinical recovery under emergency use IND was posted by doctors from Houston Methodist Hospital in Texas. The report describes a 54-year-old man who developed COVID-19 while being treated for rejection of a double lung transplant and who came off a ventilator within four days. Similar

results were subsequently seen in more patients treated under emergency use IND and an FDA Expanded Access Program, which is open to patients who are too ill to be enrolled to the US phase IIb/III “COVID-AIV” trial. Patients with critical COVID-19 were seen to have a rapid clearing of classic pneumonitis findings on X-ray, accompanied by an improvement in blood oxygen and a 50% or greater average decrease in laboratory markers associated with COVID-19 inflammation.

In October 2020, topline results from 45 patients assessed in an open-label prospective study where 21 patients admitted to an intensive care unit (ICU) with critical COVID-19 and respiratory failure were treated with RLF-100 IV and compared to 24 control patients treated in the same setting. All patients had severe comorbidities that rendered them ineligible for the ongoing randomized, controlled phase IIb/III “COVID-AIV” trial being conducted to assess safety and efficacy of RLF-100 IV, and all patients were deteriorating despite treatment with approved therapies for COVID-19. At the 28-day time point, 90% of RLF-100 IV-treated patients had survived vs. 27% of control patients. At the 60-day time point, 81% of RLF-100 IV-treated patients survived, compared to only 17% of control patients. Those patients treated with RLF-100 IV demonstrated a 9-fold increased probability of survival and recovery from respiratory failure, with a high degree of statistical significance ($p<0.0001$). These positive results were published in the peer-reviewed “Journal of Infectious Diseases and Treatment” in October 2021.

In late November 2020, Relief and NRx reported additional data from the Expanded Access Protocol (EAP) patient population treated with RLF-100. The companies indicated that over 175 patients with critical COVID-19 and respiratory failure who also have severe comorbidities had been entered into the EAP program – it is now estimated that well over 200 patients have received RLF-100 IV via this program. All patients had severe comorbidities (such as organ transplant, recent heart attack, and cancer) that rendered them ineligible for the ongoing randomized, controlled phase IIb/III “COVID-AIV” trial being conducted to ascertain RLF-100 IV safety and efficacy; all patients were deteriorating despite treatment with approved therapies for COVID-19. Of the 90 patients who had reached 28 days of follow-up as of November 2020, 72% had survived to day 28. The availability of a substantially larger cohort of patients from the EAP program may be considered to partially address concerns pertaining to the lack of a control group or a randomized study design. It should be noted that, as indicated previously, these patients were critically ill and generally had exhausted all pharmacotherapy options. They could not have been enrolled into the phase IIb/III RLF-100 IV clinical trial.

In June 2021, NRx released additional positive results from the RLF-100 IV US Expanded Access Program (EAP). The EAP included 240 intensive care unit (ICU) patients suffering from critical COVID-19 with respiratory failure who had exhausted all approved therapies. The results of the EAP are similar to the results of the pivotal phase II/III “COVID-AIV” trial, which forms the base of the US Emergency Use Application submission in early June. At day 28, 65% of patients receiving RLF-100 IV and maximal intensive care were alive, while survival was higher in patients treated with high flow rate oxygen by nasal cannula (76%) than patients requiring either invasive or non-invasive mechanical ventilation (54%). The EAP data are being submitted by NRx to the FDA as “real world” evidence in support of the findings of the “COVID-AIV” trial.
The clinical findings may be based on evidence that VIP inhibits the replication of the SARS-CoV-2 virus in human lung cells and immune cells (monocytes), as discussed in the pipeline

section (see page 24). To date, no other antiviral agent has demonstrated rapid recovery from viral infection and demonstrated laboratory inhibition of viral replication.

Pivotal US phase IIb/III – "COVID-AIV" trial of RLF-100 IV started in June 2020

Based on these promising early results, Relief's strategic development and commercialization partner NRx started the single potentially pivotal US phase IIb/III "COVID-AIV" trial of RLF-100 IV in patients with COVID-19 induced ARDS in June 2020. Respiratory failure or ARDS is the hallmark of acute COVID-19 infection and is the most critical complication with a high mortality rate due to the lack of effective treatments. Up to 80% of these patients die despite intensive care and mechanical ventilation. Moreover, the number of COVID-19 induced ARDS patients has resulted in an acute shortage of hospital and ICU capacity in many countries, leading to drastic lockdown measures at high economic and social cost.

"COVID-AIV" is a multicentered, randomized, quadruple blind, placebo controlled phase IIb/III trial conducted at 10 hospitals in the US, which enrolled 196 patients with COVID-19 induced ARDS (critical COVID-19 with respiratory failure). Patients currently treated with high flow nasal oxygen, non-invasive ventilation or mechanical ventilation were treated with RLF-100 IV administered intravenously receiving escalating doses from 50 - 150 pmol/kg/hr over 12 hours plus maximal intensive care vs. placebo plus maximal intensive care. Resolution of respiratory failure (without relapse) and survival through the observation period was the prespecified primary endpoint specified by the FDA, originally intended to be assessed at 28 days (as required for ARDS trials) and then extended to 60 days (new requirement for COVID-19 induced ARDS) based on newly published FDA guidance for developing drugs and biological products for treatment and prevention of COVID-19 in February 2021. The 60-day observation framework implemented by the FDA for critically ill patients with COVID-19 is more consistent with the clinical course of this lethal disease than the 28-day time frame originally adapted from other conditions that cause respiratory distress.

Trial enrollment was completed in December 2020, while the trial received two consecutive positive reviews from the Data Monitoring Committee to continue the trial with no drug-related serious events or safety concerns.

Positive 60-day topline results pivotal "COVID-AIV" trial reported end March 2021

At the end of March 2021, NRx reported the 60-day topline results of the pivotal single phase IIb/III "COVID-AIV" trial of RLF-100 IV in critically ill patients with COVID-19. Across all patients and sites, RLF-100 IV met the primary endpoint for successful recovery from respiratory failure at days 28 ($p=0.014$) and 60 ($p=0.013$) and also demonstrated a meaningful benefit in survival ($p<0.001$) after controlling for ventilation status and treatment site. The analysis includes all 196 participants who were randomized and treated in the placebo-controlled, double-blind clinical trial conducted at 10 US hospitals. Treatment with RLF-100 IV or placebo was in addition to standard of care treatment that included steroids, convalescent plasma, antiviral therapy, anticoagulants, and various anti-cytokine drugs.

In addition to the robust overall significance across all 196 treated patients at all 10 clinical sites, the prespecified analysis of recovery from respiratory failure is clinically and statistically significant in the 127 patients treated by High Flow Nasal Cannula (HFNC) ($p=0.02$), compared to those treated with mechanical or non-invasive ventilation at tertiary care hospitals. In this group, RLF-100 IV patients had a 71% chance of successful recovery

by day 28 vs. 48% in the placebo group (p=0.017) and a 75% rate of successful recovery by day 60 vs. 55% in the placebo group (p=0.036). 84% of HFNC patients treated at tertiary medical centers with RLF-100 IV survived to day 60 compared with 60% of those treated with placebo (p=0.007).

The association of baseline oxygenation status (high flow nasal oxygen vs. ventilation) is not surprising in that patients who require mechanical or noninvasive ventilation in order to maintain blood oxygen are likely to have substantially more damage to the lining of their lungs compared to patients whose blood oxygen level can be maintained with high-flow oxygen delivered to the nose. The finding that patients fared substantially better in tertiary care centers as compared to regional hospitals may be influenced by the intensity of the public health crisis at the regional hospitals that participated in the study, all of which were operating at 200% or higher overcapacity in their intensive care units with implementation of temporary ICU beds and shortages of critical care staff.

Data shows RLF-100 IV prevents the dreaded "cytokine storm" in COVID-19

In July 2021, NRx presented data that identified a statistically significant effect of RLF-100 IV in preventing the sharp rise in cytokines also known as the "cytokine storm" commonly associated with mortality in patients with COVID-19 in the pivotal phase IIb/III "COVID-AIV" trial of RLF-100 IV in critically ill COVID-19 patients with respiratory failure. The data were collected as part of the trial. Patients treated with placebo experienced a statistically significant elevation in interleukin 6 (IL-6) cytokine levels, whereas those treated with RLF-100 IV had a minimal increase in IL-6. Change in cytokine level was a prespecified endpoint of the trial. The effect was noted across a diverse set of patients, suffering different levels of COVID-19 severity and treated in both tertiary care and community hospitals. NRx has submitted these findings to the FDA as a supplement to its pending application for EUA and is submitting a biomarker letter of intent to the FDA as part of its biomarker program, authorized under the 21st Century Cures Act. NRx continues to respond to FDA information requests for additional data in support of the currently pending EUA application for RLF-100 IV in treating critically ill patients with COVID-19.

US EUA declined by FDA pushing back potential US approval by roughly a year

RLF-100 IV is likely the first COVID-19 therapeutic to demonstrate advantages in both survival and recovery from critical COVID-19 in a randomized, double-blind multicenter trial. On the basis of these findings, NRx applied to the FDA for Emergency Use Authorization (EUA) on 31 May 2021, and to subsequently submit a New Drug Application (NDA). On 4 November 2021, the FDA declined to issue Emergency Use Authorization (EUA) for RLF-100 IV for the treatment of acute respiratory failure due to critical COVID-19. The FDA stated that it was unable to issue the EUA at this time due to insufficient data regarding the known and potential benefits of the medicine and the known and potential risks of RLF-100 IV in patients suffering from critical COVID-19 with respiratory failure. In its letter, the FDA noted that so far, it has reviewed safety in only 131 randomized patients treated with RLF-100 IV.

Third EUA filed for RLF-100 IV in critical COVID-19 patients

In January 2022, NRx filed an application to the FDA seeking EUA (Emergency Use Authorization) for RLF-100 IV to treat patients with critical COVID-19 who are at immediate risk of death from respiratory failure despite treatment with approved therapy including Gilead's Veklury (remdesivir) and who are ineligible for enrollment into the NIH-sponsored "ACTIV-3b/TESICO" phase III trial. This is NRx' third attempt to seek US EUA for RLF-100 IV in critical COVID-19. We do not fully understand how NRx will attempt a review by the

FDA as the trial is still actively recruiting and blinded, which would compromise the final results. Therefore, we believe the filing of a new US EUA can only occur after the topline results of the ACTIV-3b/TESICO have been announced in Q4 2022, leading to roughly a year's delay for a potential US approval for RLF-100 IV in treating COVID-19 related ARDS. Assuming the FDA grants an EUA, first commercial sales in the US could be expected in around year-end 2022, which would be transformational for Relief.

Potential EU approval also pushed back by roughly a year into H1 2023
Following US EUA, it is likely that the EMA would also grant Conditional Marketing Authorization (CMA) for RLF-100 IV to treat these critically ill COVID-19 patients. Relief plans to file for EU CMA following a potential US EUA grant in around year-end 2022. This could result in first EU commercial sales to start in H1 2023. Relief has secured API supply of up to 1 mn doses of RLF-100 IV with Bachem Americas. Relief expects that a small sales organization should be sufficient to successfully commercialize RLF-100 IV in the US and EU. The drug is targeted to be used by a relatively small number of respiratory medicine and critical care/ICU specialists and administered intravenously in a healthcare setting where critically ill patients are being treated.

Commercial potential of RLF-100 dependent on the success of COVID-19 vaccines
The commercial potential of RLF-100 in COVID-19 respiratory complications will be highly dependent on 1) the efficacy of RLF-100 IV on reducing mortality, morbidity and treatment duration freeing up scarce hospital and ICU capacity; 2) the trajectory of the ongoing COVID-19 pandemic; 3) emerging new treatments for critically ill COVID-19 patients; 4) the timing of approval, pricing and reimbursement and commercial rollout, among others. We will discuss in more detail below.

Efficacy of RLF-100 in reducing mortality
RLF-100 IV is likely the first COVID-19 therapeutic to demonstrate advantages in both survival and recovery from critical COVID-19 in a randomized, double-blind multicenter trial. This should justify rapid approval, premium pricing, and a sharp commercial uptake.

Trajectory of the COVID-19 pandemic – Global vaccination programs having impact
Broadscale and effective vaccination of the population combined with social distancing and lockdown measures will be key to contain the COVID-19 pandemic. Early in 2021 vaccination rates were severely lagging initial projections due to a short supply of vaccines and the complicated logistics involved in setting up and executing large scale vaccination programs prioritizing high-risk patients (elderly, additional comorbidities) and care givers. Vaccination rates in the high-income countries have increased significantly over the last few months with most high-risk patients fully vaccinated, resulting in significantly lower COVID-19 hospitalizations and critically ill patients treated in the ICU. Moreover, the recent omicron variant has led to a high number of infections globally, however, with significantly less critically ill patients that need to be treated in the hospital or ICU. Many experts believe the pandemic is currently moving into the endemic phase. In the endemic phase, the number of infections becomes relatively constant across years, allowing for occasional flare-ups. To reach this steady state could take a few years or decades, depending on how quickly populations develop group immunity. Several factors are expected to impact the trajectory of global COVID-19 infections, including:

1) **COVID-19 virus mutations:** It is not unusual for a virus to mutate and evolve as it spreads, and scientists have long cautioned that worrisome variants could emerge

with new outbreaks. In two years, COVID-19 has mutated into five "variants of concern," according to the WHO, based on the severity of disease, the effectiveness of medical countermeasures and the strain's ability to spread from person to person. The alpha, beta and gamma variants were all downgraded to "variants being monitored", with delta and omicron still considered variants of concern. The omicron variant has now become the dominant strain globally. Preliminary studies indicate illness caused by omicron is likely less severe than delta, which doubled the hospitalization rate of the original alpha strain but is also far more contagious. The longer the pandemic lasts, and the longer large groups remain unvaccinated, the more time the virus will have to spread and mutate.

Vaccine efficacy: The vaccines in use in high income countries appear to offer good protection against the omicron variant, and most scientists agree that fully vaccinated individuals likely face little risk. In the unlikely scenario that mutations significantly lower a vaccine's efficacy, it would take four to six weeks to develop a modified vaccine. Whereas the pandemic's trajectory in 2020 was fairly predictable, the evolution of the virus makes containment harder and the trajectory of the pandemic more unpredictable. It is also possible that the more contagious strains of the SARS-CoV-2 coronavirus spread so rapidly that they outstrip the pace at which vaccines can be deployed. Some of the newer strains may also prove capable of evading the immune protection elicited by vaccination, resulting in a game of cat and mouse with modified vaccines.

Vaccine duration of protection: One big unknown regarding all the COVID-19 vaccines is the duration of protection against the coronavirus. In the case of currently approved COVID-19 vaccines, measures of neutralizing antibody levels have been strong weeks after immunization. But it is too early to tell whether these antibody levels will remain strong for at least a year. If immunity to SARS-CoV-2 by vaccination is not long-lasting or permanent, the virus will likely enter into regular circulation, much like pandemic influenza. Regular global vaccination programs will be necessary requiring booster shots in portions of the population, especially in the older, more vulnerable population such as immunocompromised patients and adults with severe pre-existing medical conditions. Little information is available on whether the available COVID-19 vaccines will provide sufficient protection against new rapidly emerging mutations. If immunity to SARS-CoV-2 is permanent, the virus could disappear for 5 or more years after causing a major outbreak. A sufficiently high vaccination rate of 70-80% in the general population must be attained, too.

Anti-vaccine sentiment: Increased populism and distrust in science combined with the spread across social media platforms have led to increased anti-vaccine sentiment in the US and the EU. In the past, there was already an increasing mistrust in vaccination programs. For instance, in early 2000 there were false claims that vaccines for measles, mumps and rubella had the ability to cause autism, which were only debunked in a Lancet article in 2010. Around 2014/2015, the political far right in the US started an agenda pushing for "health/medical freedom" distrusting government agencies such as the National Institutes of Health (NIH), the CDC or the FDA. Increasing anti-vaccine sentiment may lead to a sizeable portion of the population not being vaccinated, forming a new pool of infection or mutations that could spread through the general population.

COVID-19 pandemic will not end overnight and is expected to persist for some time
Vaccines will be instrumental in the control of the COVID-19 pandemic, but their global distribution remains challenging, and their effect will not be immediate. As cases and deaths continue to rise across the world, non-pharmaceutical interventions such as lockdowns or social distancing measures to constrain the spread of COVID-19 will need to remain in place. In a recent "Nature" poll, 89% of scientists felt that the SARS-CoV-2 pandemic was either very likely or likely to become an endemic virus. In the endemic phase, the number of infections becomes relatively constant across years, allowing for occasional flare-ups. To reach this steady state could take a few years or decades, depending on how quickly populations develop immunity. In particular, the continual emergence of new coronavirus variants that may be immune or more resistant to current vaccines pose a risk. Consequently, the need for new safe and effective treatments for COVID-19 patients is expected to persist for many years to come.

Ultimately, COVID-19 is believed to become endemic and stay around for quite some time with still tens of thousands of critically ill patients hospitalized or in ICUs each year, similar to the influenza virus. As a reference, the annual disease burden of influenza in the US, according to the CDC, amounts to 9.3-45.0 mn influenza cases; 140,000-810,000 hospitalizations; 12,000-61,000 deaths (the top range of these burden estimates are from the 2017-2018 flu season). Patients with COVID-19 have almost 19 times the risk for ARDS than patients with influenza. The percentage of COVID-19 patients who died while hospitalized (21.0%) was more than five times that of influenza patients (3.8%), while the duration of hospitalization was almost three times longer for COVID-19 patients.

Effective COVID-19 treatments still needed even in the case of effective vaccines.
Despite the global rollout of effective COVID-19 vaccines, these vaccines will not cure patients suffering from COVID-19 symptoms as we discussed earlier. Once the virus has invaded the respiratory system of a patient, a vaccination is of little help. Therefore, new COVID-19 treatments are needed in addition to effective vaccines, and they are needed now to treat critically ill COVID-19 patients and save lives as well as early-intervention treatments to reduce disease progression, treatment times and costs. As the development of novel drugs can take more than 10 years from research to market, the pharmaceutical industry tried to repurpose existing drugs. Some current approaches to treat COVID-19 patients, include:

Antivirals among the first products to be approved – Paxlovid takes the lead
Antiviral drugs are prescription medicines (pills, liquid, an inhaled powder, or an intravenous solution) that fight against viruses in the body. In May 2020, Gilead's intravenous infusion Veklury (remdesivir) was the first product approved to treat COVID-19 but clinical evidence that has emerged since shows the antiviral leaves much room for improvement. Oral antivirals such as Pfizer's Paxlovid (PF-07321332) or Merck & Co's Lagevrio (molnupiravir) are amongst the most promising treatments in the fight against the global pandemic. Pivotal trials of both drugs were stopped early due to strong positive topline results seen during the planned interim analyses. Pfizer's Paxlovid appears to have become the most promising new oral antiviral treatment in the fight against the global pandemic cutting the risk of hospitalization or death by almost 90% in hospitalized high-risk adults with COVID-19 infection compared to around 50% for Merck & Co's Lagevrio. Both treatments have been granted US EUA or conditional approval in many countries globally and are being

rolled out worldwide. The US government has already secured millions of doses of both drugs.

Pfizer's Paxlovid reduces the risk of hospitalization or death by almost 90%

Pfizer's oral antiviral PF-07321332 (branded Paxlovid) is a specifically designed SARS-CoV-2-3CL protease inhibitor given in combination with a low dose of the older HIV antiviral ritonavir (branded Norvir by AbbVie) consists of three pills given twice daily. Paxlovid, significantly reduced hospitalization and death, based on an interim analysis of the phase II/III "EPIC-HR" trial of non-hospitalized adult patients with COVID-19, who are at high risk of progressing to severe illness. The scheduled interim analysis showed an 89% reduction in risk of COVID-19-related hospitalization or death from any cause compared to placebo in patients treated within three days of symptom onset (primary endpoint); 0.8% of patients who received Paxlovid were hospitalized through Day 28 following randomization (3/389 hospitalized with no deaths), compared to 7.0% of patients who received placebo and were hospitalized or died (27/385 hospitalized with 7 subsequent deaths). The statistical significance of these results was high ($p<0.0001$). Similar reductions in COVID-19-related hospitalization or death were observed in patients treated within five days of symptom onset; 1.0% of patients who received Paxlovid were hospitalized through Day 28 following randomization (6/607 hospitalized, with no deaths), compared to 6.7% of patients who received a placebo (41/612 hospitalized with 10 subsequent deaths), with high statistical significance ($p<0.0001$). In the overall study population through Day 28, no deaths were reported in patients who received Paxlovid as compared to 10 (1.6%) deaths in patients who received placebo.

The primary analysis of the interim data set evaluated data from 1,219 adults who were enrolled by September 29, 2021. At the time of the decision to stop recruiting patients by the independent Data Monitoring Committee, enrollment was at 70% of the 3,000 planned patients from clinical trial sites across North and South America, Europe, Africa, and Asia, with 45% of patients located in the United States. The review of safety data included a larger cohort of 1,881 patients in EPIC-HR, whose data were available at the time of the analysis. Treatment-emergent adverse events were comparable between Paxlovid (19%) and placebo (21%), most of which were mild in intensity. Among the patients evaluable for treatment-emergent adverse events, fewer serious adverse events (1.7% vs. 6.6%) and discontinuation of trial drug due to adverse events (2.1% vs. 4.1%) were observed in patients dosed with Paxlovid compared to placebo, respectively. In December 2021, Paxlovid was granted EUA for use in both high-risk COVID-19 adults and high-risk pediatric patients 12 years of age and older weighing at least 40 kg.

Merck's Lagevrio granted EUA in mild-to-moderate COVID-19

Merck & Co's oral antiviral molnupiravir (branded Lagevrio) was licensed from the privately held Ridgeback Therapeutics. In December 2021, Merck & Co and Ridgeback were granted Emergency Use Authorization (EUA) for Lagevrio for the treatment of mild-to-moderate COVID-19 in adults who are at risk for progressing to severe COVID-19 and/or hospitalization. The EUA was based on positive results from a planned interim analysis from the phase III "MOVe-OUT" clinical trial, which evaluated Lagevrio in non-hospitalized adult patients with mild-to-moderate COVID-19 who were at risk for progressing to severe COVID-19 and/or hospitalization. At the planned interim analysis, Lagevrio reduced the risk of hospitalization or death by

approximately 50%; 7.3% of patients who received Lagevrio were either hospitalized or died through Day 29 following randomization (28/385), compared with 14.1% of placebo-treated patients (53/377); p=0.0012. Through Day 29, no deaths were reported in patients who received Lagevrio, as compared to 8 deaths in patients who received placebo. The incidence of any adverse event was comparable in the Lagevrio and placebo groups (35% and 40%, respectively). The incidence of drug-related adverse events was also comparable (12% and 11%, respectively), and fewer subjects in the Lagevrio group discontinued therapy due to an adverse event compared to the placebo group (1.3% and 3.4%, respectively).

Note that Paxlovid and Lagevrio are not for use in late-stage or hospitalized patients and most likely must be administered within five days (or less) of infection to have a meaningful benefit. The lack of long-term safety data concerning Lagevrio and the likelihood of mutagenicity, potentially causing birth defects or cancer could likely result in a black box warning, which would hamper widespread use in its target population.

Atea and Roche's AT-527 fails "MOONSONG" phase II COVID-19 trial

In October 2021, Atea Pharmaceuticals and Roche's oral direct-acting antiviral AT-527 failed to achieve its primary endpoint of reduction from baseline in the amount of SARS-CoV2 virus in patients with mild to moderate COVID-19 compared to placebo in the phase II "MOONSONG" trial. Approximately two thirds of the overall trial population were low-risk patients with mild symptoms. However, in high-risk patients with underlying health conditions, a sufficient viral load reduction was observed in AT-527 treated patients compared to placebo. In November, Roche ended the partnership with Atea to jointly develop AT-527 in COVID-19.

Authorized antibodies underutilized due to complex administration issues

SARS-COV-2-targeting monoclonal antibodies (MAbs) are laboratory-produced antibodies that can help the immune system's attack on COVID-19. These MAbs block entry into human cells, thus neutralizing the virus. The following MAbs are authorized for use through an FDA EUA for the treatment of mild to moderate COVID-19 in adults and pediatric patients who are at high risk for progressing to severe COVID-19 and/or hospitalization:

- **REGEN-COV2 (casirivimab & imdevimab combo):** EUA cleared November 2021 from Regeneron/Roche; IV infusion
- **Sotrovimab:** EUA cleared May 2021 from GlaxoSmithKline/Vir; IV infusion
- **bamlanivimab & etesevimab combo:** EUA cleared February 2021 from Eli Lilly; IV infusion

With three MAbs now available under Emergency Use Authorizations in the US, it seems clear that monoclonal antibodies (MAbs) have a role to play in treating COVID-19. The extent to which they will be helpful is not yet known. However, these products have failed to show a benefit in severely ill patients. While clinical trials are still ongoing, the data so far indicate they are particularly beneficial for certain patients with mild or moderate symptoms whose own immune systems are not mounting a strong defense. Clinical evidence supporting each drug is not yet conclusive. On 25 June 2021, a pause on the distribution of bamlanivimab & etesevimab in the US was issued. Results from in vitro assays that are used to assess the susceptibility of viral

variants to particular MAbs suggest that the bamlanivimab & etesevimab combo is not active against either the P.1 (Gamma variant first identified in Brazil) or B.1.351 (Beta variant first identified in South Africa) SARS-Cov-2 variants.

These MAbs have not been widely used since the FDA cleared these products. The limitations of these MAbs have become clear as they have been rolled out. They must be infused in a healthcare setting, raising the risk that infected patients could endanger others at a hospital or a clinic. They are only authorized for patients at high risk of becoming hospitalized, a group the FDA has defined by age and certain underlying health conditions. Furthermore, the MAbs have to be given early in the disease course requiring fast testing and administration to get the right patients treated at the right time. A more convenient subcutaneous injection (sc) of REGEN-COV2 is being developed, which could be on the market soon to improve access and patient compliance. In April 2021, a phase III trial with REGEN-COV2 sc reduced the risk of symptomatic COVID-19 infections by 81% and the overall risk of progressing to symptomatic COVID-19 by 31%.

In January 2021, the US government agreed to pay as much as USD 2.6 bn for up to 1.25 mn additional doses of Regeneron's REGN-COV2. This comes on top of a previous agreement to buy 300,000 doses for USD 450 mn in July 2020. It values each dose at USD 2,080, up from USD 1,500 a dose in the earlier round.

FDA rejects Humanigen's lenzilumab and CytoDyn's leronlimab for EUA

Two investigational MAbs were recently rejected by the FDA for EUA in COVID-19. In May 2021, CytoDyn's leronlimab was rejected by the FDA citing that the data currently available do not support the clinical benefit of leronlimab for the treatment of COVID-19. In September 2021, Humanigen's lenzilumab was also rejected. The FDA noted that it was not able to conclude the known and possible benefits of lenzilumab outweigh the known and potential risks of its use as a COVID-19 therapy. The FDA invited the companies to present further data when it becomes available.

With complex administration schedules and what will presumably be big price tags, it is hard to see these MAb therapies playing a major role outside of wealthier regions.

Authorized immune modulators

Immune modulators are a category of drugs that help activate, boost, or suppress the immune function. In the case of COVID-19 infection, the immune system can become hyperactive which may result in worsening of disease. Immune modulators can help suppress this hyperinflammation. The following immune modulators are authorized for use through an FDA EUA for the treatment of certain patients with COVID-19:

- **Olumiant (baricitinib):** EUA cleared November 2020 from Eli Lilly; an oral immune modulator in combination with Gilead's Veklury (remdesivir) for treatment of hospitalized adults and pediatric patients (2 years or older) and requiring supplemental oxygen, invasive mechanical ventilaton (IVM) or extracorporeal membrame oxygen (ECMO)
- **Actemra (tocilizumab):** EUA cleared June 2021 from Roche/Genentech; is a MAb available as an IV infusion or subcutaneous injection that reduces inflammation by blocking the interleukin (IL)-6 receptor for the treatment of hospitalized adults and pediatric patients (2 years or older) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or IVM

or ECMO. Actemra is FDA-approved for the treatment of multiple inflammatory diseases, including rheumatoid arthritis.

CHF 50 mn global peak sales in COVID-19 induced ARDS with first launches in 2023
We have based our detailed bottom-up forecasts for RLF-100 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 COVID-NET, NCBI, NIH, CDC, WHO, AAAS, ERS, ATS, The Lancet, clinicaltrials.gov and Evaluate Pharma, among others. To account for regional differences, we provide detailed forecasts for the US, Europe and ROW (stockpiling orders only). We forecast until US formulation patent expiry of RLF-100 IV (including 5-year Hatch Waxman patent extension) in 2034. In the US, RLF-100 IV will also enjoy 5 years of New Chemical Entity (NCE) exclusivity following formal NDA approval (during which no generic introduction shall be possible) and potentially 7 years of Orphan Drug exclusivity for acute lung injury (ALI) including ARDS. We conservatively exclude Orphan Drug exclusivity for ALI as the number of COVID-19 induced ARDS patients is likely too high to qualify as an orphan disease. In Europe, we anticipate generic versions of RLF-100 IV to enter the market after EU formulation patent expiry in 2026. Note: in this report, we only provide 10-year forecasts for each indication of RLF-100 due to space considerations.

Detailed bottom-up forecasts point to CHF 30 mn US peak sales in COVID-19 ARDS
In 2023, we assume an average of 80% of the population fully vaccinated or infected and recovered with a 33% drop in the number of COVID-19 cases compared to 2022, of which approximately 1.9% will be hospitalized due to the omicron variant being less severe than delta, which doubled the hospitalization rate of the original alpha strain. The following years we expect the number of COVID-19 cases to continue to gradually decline but still expect tens of thousands to be affected by COVID-19, similar to the seasonal influenza.

Assuming an EUA for RLF-100 in the US around year-end 2022, we expect rapid and substantial uptake of RLF-100 IV in the target population. Peak sales for COVID-19 induced ARDS in 2023 are expected to amount to CHF 30 mn, assuming a USD 9,000 cost of treatment course per patient and a 45% penetration rate. US sales will be booked by partner NRx. M&S costs are expected to be relatively low at approximately USD 10 mn with only a few large buyers. Relief is entitled to 50% of the profits from sales of RLF-100 IV in the US

European sales to peak at approximately CHF 15 mn in 2023
For Europe, we apply the same approach as for the US and assume a similar decline of COVID-19 cases and hospitalization rates. EU conditional approval could follow shortly after a potential US EUA grant with launch to occur in H1 2023. We expect RLF-100 IV to reach peak sales of CHF 15 mn in COVID-19 induced ARDS in 2023, with a 40% peak penetration rate and a cost of treatment course per patient of EUR 4,000. Beyond 2023, we assume a similar decline in the number of COVID-19 cases and a similar penetration rate as in the US In Europe, Relief books sales, and accounts for COGS and M&S costs, with NRx entitled to 15% of the profits.

In the ROW territories, we only account for pandemic stockpiling in 2023 and 2024. We conservatively assume 10,000 treatment courses for each year at a cost of USD 500 per treatment course resulting in CHF 5 mn for each year (for details see the following page).

Forecasts & Sensitivity Analysis

RLF-100 IV - FINANCIAL FORECASTS FOR COVID-19 INDUCED ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

INDICATION	REDUCTION OF MORBIDITY AND MORTALITY IN PATIENTS WITH COVID-19 INDUCED ACUTE RESPIRATORY DISTRESS SYNDROME
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: US: USD 9,000; EU: EUR 4,000; PANDEMIC STOCKPILING COST TREATMENT COURSE: US: USD 1,000; EU: EUR 650
STANDARD OF CARE	PERSONALIZED LUNG-PROTECTIVE MECHANICAL VENTILATION COMBINED WITH GILEAD'S VEKLURY (REMDESIVIR) OR STEROIDS SUCH AS DEXAMETHASONE
UNIQUE SELLING POINT	POTENTIALLY FIRST TREATMENT TO REDUCE HIGH MORTALITY AND MORBIDITY IN PATIENTS WITH COVID-19 INDUCED ACUTE RESPIRATORY DISTRESS SYNDROME

7Ps ANALYSIS

PATENT	US: PATENT EXPIRY 2029, 5-YEAR HATCH-WAXMAN EXTENSION, 5 YEARS NCE EXCLUSIVITY; EU: PATENT EXPIRY 2026; ODD ARDS (COVID-19 ARDS LIKELY NOT ORPHAN)
PHASE	US PHASE IIB/III "COVID-AIV" POSITIVE 60-DAYS TRIAL RESULTS MAR 2021; US EUA Q4 2022; EU FILING CMA Q1 2023, EU CMA APPROVAL Q2 2023
PATHWAY	POSITIVE "COVID-AIV" RESULTS LIKELY TO TRIGGER EMERGENCY USE AUTHORIZATION; EU CONDITIONAL APPROVAL LIKELY ON POSITIVE US "COVID-AIV" TRIAL RESULTS
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	NEURORX COMMERCIALIZES IN US, CANADA & ISRAEL; RELIEF IN EUROPE & ROW; PROFIT SPLIT RELIEF/NEURORX: US, CANADA & ISRAEL = 50/50; EUROPE = 85/15; ROW = 80/20

REVENUE MODEL

UNITED STATES - NRX TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
POPULATION (MN)	332	333	335	337	339	341	343	345	347	350	352
GROWTH (%)	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%	0.6%
AVERAGE FULLY VACCINATED / INFECTED & RECOVERED (%)	0%	25%	70%	80%	85%	90%	93%	94%	95%	96%	97%
AVERAGE UNVACCINATED / UNPROTECTED POPULATION (MN)	332	250	101	67	51	34	24	21	17	14	11
COVID-19 INFECTION RATE (%)	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%	6.1%
COVID-19 CASES (MN)	20.2	15.2	6.1	4.1	3.1	2.1	1.5	1.3	1.1	0.9	0.6
GROWTH (%)		-25%	-60%	-33%	-25%	-33%	-30%	-14%	-16%	-20%	-25%
COVID-19 PATIENTS HOSPITALIZED (%)	3.9%	3.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%
COVID-19 PATIENTS WITH HOSPITALIZED	782'862	590'611	118'819	79'680	60'113	40'312	28'385	24'473	20'515	16'509	12'454
COVID-19 PATIENTS WITH ARDS (%)	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%
COVID-19 ARDS PATIENTS	258'345	194'902	39'210	26'294	19'837	13'303	9'367	8'076	6'770	5'448	4'110
PATIENTS TRANSFERRED TO ICU (%)	90%	90%	45%	45%	45%	45%	45%	45%	45%	45%	45%
COVID-19 ARDS PATIENTS IN ICU	232'510	175'411	17'645	11'832	8'927	5'986	4'215	3'634	3'046	2'452	1'849
PATIENTS RECEIVING HIGH FLOW NASAL CANNULA (HFNC) (%)	75%	75%	75%	75%	75%	75%	75%	75%	75%	75%	75%
PATIENTS RECEIVING HIGH FLOW NASAL CANNULA (HFNC)	174'383	131'559	13'233	8'874	6'695	4'490	3'161	2'726	2'285	1'839	1'387
ELIGIBLE PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE PATIENTS ON IVM	156'944	118'403	11'910	7'987	6'026	4'041	2'845	2'453	2'056	1'655	1'248
PENETRATION (%)	0%	0%	0%	45%	40%	35%	35%	35%	35%	35%	35%
NUMBER OF PATIENTS	0	0	0	3'594	2'410	1'414	996	859	720	579	437
COST TREATMENT COURSE PER PATIENT (CHF)	8'249	8'203	8'312	8'312	8'312	8'312	8'312	8'312	8'312	8'312	8'312
SALES (CHF MN) - NRX BOOKS SALES	**0**	**0**	**0**	**30**	**20**	**12**	**8**	**7**	**6**	**5**	**4**
CHANGE (%)					-33%	-41%	-30%	-14%	-16%	-20%	-25%
M&S (CHF MN) - PAID BY NRX	0	0	-1	-5	-4	-2	-1	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**-1**	**25**	**16**	**10**	**7**	**7**	**6**	**5**	**3**
PROFIT SPLIT (50/50)	0%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
RELIEF PBT (CHF MN) - PAID TO RELIEF	**0**	**0**	**0**	**13**	**8**	**5**	**4**	**3**	**3**	**2**	**2**
TAXES (CHF MN)	0	0	0	-1	-1	-1	0	0	0	0	0
PROFIT (CHF MN)	**0**	**0**	**0**	**11**	**7**	**4**	**3**	**3**	**3**	**2**	**2**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
COVID-19 CASES (MN)	17.3	13.9	6.1	4.4	3.5	2.6	1.7	1.2	1.0	0.9	0.7
GROWTH (%)		-20%	-56%	-29%	-20%	-25%	-33%	-30%	-14%	-17%	-20%
PATIENTS HOSPITALIZED (%)	3.9%	3.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%
COVID-19 PATIENTS HOSPITALIZED (~4%)	673'664	539'470	118'127	84'461	67'636	50'778	33'886	23'744	20'372	16'994	13'609
PATIENTS WITH ARDS (%)	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%	33%
COVID-19 ARDS PATIENTS (~33%)	222'309	178'025	38'982	27'872	22'320	16'757	11'182	7'835	6'723	5'608	4'491
PATIENTS TRANSFERRED TO ICU (%)	90%	90%	45%	45%	45%	45%	45%	45%	45%	45%	45%
COVID-19 ARDS PATIENTS IN ICU (~90%)	200'078	160'223	17'542	12'542	10'044	7'541	5'032	3'526	3'025	2'524	2'021
PATIENTS RECEIVING HIGH FLOW NASAL CANNULA (HFNC) (%)	75%	75%	75%	75%	75%	75%	75%	75%	75%	75%	75%
PATIENTS RECEIVING HIGH FLOW NASAL CANNULA (HFNC)	150'059	120'167	13'156	9'407	7'533	5'655	3'774	2'644	2'269	1'893	1'516
ELIGIBLE PATIENTS ON IVM (~90%)	135'053	108'150	11'841	8'466	6'780	5'090	3'397	2'380	2'042	1'703	1'364
PENETRATION (%)	0%	0%	0%	40%	40%	35%	18%	9%	4%	2%	1%
NUMBER OF PATIENTS	0	0	0	3'386	2'712	1'781	594	208	89	37	15
COST TREATMENT COURSE PER PATIENT (CHF)	4'308	4'333	4'330	4'330	4'330	4'330	4'330	4'330	4'330	4'330	4'330
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**15**	**12**	**8**	**3**	**1**	**0**	**0**	**0**
CHANGE (%)					-20%	-34%	-67%	-65%	-57%	-58%	-60%
COGS (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
R&D COSTS (CHF MN)	-11	-5	-9	0	0	0	0	0	0	0	0
M&S (CHF)	0	-1	-5	-10	-10	-1	0	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	**-11**	**-6**	**-14**	**5**	**2**	**7**	**2**	**1**	**0**	**0**	**0**
PROFIT SPLIT (85/15)	100%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**-11**	**-5**	**-12**	**4**	**1**	**6**	**2**	**1**	**0**	**0**	**0**
TAXES (CHF MN)	0	0	1	0	0	-1	0	0	0	0	0
PROFIT (CHF MN)	**-11**	**-5**	**-11**	**3**	**1**	**5**	**2**	**1**	**0**	**0**	**0**

ROW - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
PANDEMIC STOCKPILING (TREATMENT COURSES)		0	0	10'000	10'000						
COST TREATMENT COURSE PER PATIENT (CHF)	458	456	462	462	462	462	462	462	462	462	462
SALES (CHF MN) - RELIEF BOOKS SALES		**0**	**0**	**5**	**5**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE (%)					0%	-100%					
COGS (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT BEFORE TAX (CHF MN)	0	0	0	4	4	0	0	0	0	0	0
PROFIT SPLIT (80/20)	100%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	0	0	0	4	4	0	0	0	0	0	0
TAXES (CHF MN)	0	0	0	0	0	0	0	0	0	0	0
PROFIT (CHF MN)	**0**	**0**	**0**	**3**	**3**	**0**	**0**	**0**	**0**	**0**	**0**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**49**	**36**	**19**	**11**	**8**	**6**	**5**	**4**
CHANGE (%)					-26%	-47%	-44%	-26%	-21%	-22%	-26%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**53**	**39**	**21**	**12**	**9**	**7**	**5**	**4**
CHANGE (%)					-26%	-47%	-44%	-26%	-21%	-22%	-26%
GLOBAL PROFIT (CHF MN)	**-11**	**-5**	**-11**	**18**	**12**	**9**	**5**	**4**	**3**	**2**	**2**
CHANGE (%)		-50%	103%	-260%	-35%	-19%	-47%	-28%	-23%	-23%	-26%
WACC (%)	7%										
NPV TOTAL PROFIT (CHF MN)	**27**										
NUMBER OF SHARES (MN)	4'400										
NPV PER SHARE (CHF)	**0.006**										
SUCCESS PROBABILITY	65%	= PHASE III									
RISK ADJUSTED NPV PER SHARE (CHF)	**0.004**										

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	0.007	0.007	0.006	0.006	0.006	0.006	0.006
	95%	0.006	0.006	0.006	0.006	0.006	0.006	0.005
	90%	0.006	0.006	0.006	0.006	0.005	0.005	0.005
	85%	0.006	0.006	0.005	0.005	0.005	0.005	0.005
SUCCESS PROBABILITY	80%	0.005	0.005	0.005	0.005	0.005	0.005	0.005
	75%	0.005	0.005	0.005	0.005	0.005	0.004	0.004
	70%	0.005	0.005	0.004	0.004	0.004	0.004	0.004
	65%	0.004	0.004	0.004	**0.004**	0.004	0.004	0.004

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

II) RLF-100 INHALED in prevention COVID-19 related ARDS - Peak sales CHF 200+ mn; rNPV CHF 0.044/share

Prevention COVID-19 related ARDS second major COVID-19 indication for RLF-100
Prevention of COVID-19 related ARDS is another major complication of COVID-19 infection. These are COVID-19 patients with moderate to severe respiratory complications who are at risk to progress to critical respiratoy failure. Relief is first developing RLF-100 IV in treating critically ill COVID-19 patients with respiratory failure, followed by preventing worsening of patients at risk of developing critial COVID-19 respiratory failure with RLF-100 INHALED. This is a clinical development strategy we often see with cancer drugs. Clinical development is initially started in cancer patients with advanced disease and, if this is successful, earlier stages of disease with higher patient numbers are targeted to maximize the target population where the drug is potentially effective. Moreover, treatment duration is significantly longer in patients with moderate to severe disease than patients with critical or advanced disease.

Prevention of critical respiratory failure frees up scarce hospital and ICU capacity
Preventing COVID-19 patients with moderate to severe respiratory symptoms from progressing to critical respiratory failure with RLF-100 INHALED has major advantages. Prevention significantly reduces the number of patients being hospitalized, hence, the number of patients developing critical ARDS, which often results in death or costly long-term complications and negatively affects quality of life. Drugs that can successfully prevent the onset of critical respiratory failure have the potential to significantly reduce overall treatment costs and most importantly free up scarce hospital and ICU capacity with the potential to scale down dreaded lockdown measures with a high economic and social cost.

Authorized MAbs not ideal for treating patients with mild to moderate symptoms
The three authorized monoclonal antibodies (MAbs) from Regeneron (REGN-COV2), Eli Lilly (bamlanivimab) and GlaxoSmithKline/Vir (sotrovimab) have not been widely used since cleared by the FDA. They have failed to show a benefit in severely ill patients. While clinical trials are still ongoing, the data so far indicate they are particularly beneficial for certain patients with mild or moderate symptoms whose own immune systems are not mounting a strong defense. The limitations of both drugs have become clear as they have been rolled out. They must be infused in a healthcare setting, raising the risk that infected patients could endanger others at a hospital or a clinic. They are only authorized for patients at high risk of becoming hospitalized, a group the FDA has defined by age and certain underlying health conditions. Also, the MAbs have to be given early in the disease course requiring fast testing and administration to get the right patients treated at the right time.

RLF-100 INHALED has several advantages compared to MAbs
We believe the major advantage that RLF-100 INHALED has compared to current authorized MAbs is its less cumbersome route of administration. RLF-100 INHALED can be given in a outpatient (home) setting being an inhaled formulation of RLF-100, which can be inhaled via mesh nebulizer three times a day. MAbs have to be administered intravenously in a inpatient (hospital/clinic) setting by trained professionals. This also raises the risk that infected patients could endanger others at a hospital or a clinic. RLF-100 has been demonstrated to be safe and well tolerated with significantly lower COGS vs. MAbs, thus providing substantially more pricing flexibility. Finally, NRx, in collaboration with TFF Pharmaceuticals, is exploring the feasibility of formulating RLF-100 as a dry powder using its Thin-Film Freezing (TFF) technology, which would expand use in convenient dry powder inhalers (DPIs). In August 2021, NRx signed an agreement with MannKind Corporation to

develop a dry powder inhaler formulation of RLF-100 based on its Technosphere platform, that is the basis of its FDA approved inhaled insulin compound branded Afrezza. This potentially allows to extend the use of RLF-100 to many pulmonary conditions beyond COVID-19.

US phase IIb/III "AVICOVID-2" data in prevention COVID-19 related ARDS due H2 2022
In February 2021, Relief's partner NRx started the single potentially pivotal US phase IIb/III "AVICOVID-2" trial in COVID-19 patients with early signs of respiratory distress who will be given RLF-100 INHALED in the hope of preventing progression to ARDS and the need for mechanical ventilation. The multicenter, randomized, quadruple blind, placebo controlled phase IIb/III trial is expected to enroll 288 subjects, 144 hospitalized and 144 treated in an at home-setting with diagnosed COVID-19 infection but no evidence of ARDS. RLF-100 will be inhaled by mesh nebulizer 3 times daily at 100 μg per dose for the time of hospitalization. The primary endpoint is progression to ARDS at 28 days. Progression to ARDS is defined as the need for mechanical ventilation. Results of the US "AVICOVID-2" trial are due in H2 2022. On positve results, RLF-100 INHALED is expected to be approved and launched in the US in 2022.

Phase II trial RLF-100 INHALED in prevention COVID-19 related ARDS started in April
In April 2021, Relief, and partner AdVita announced the start of a phase II trial of RLF-100 INHALED for the prevention of COVID-19 related ARDS. The phase II trial is a randomized, double blind, placebo-controlled trial conducted at several clinical sites in Switzerland. 80 patients are expected to be enrolled who will receive either RLF-100 INHALED plus standard of care treatment or placebo plus standard of care treatment. The primary endpoint is the time (in days) from hospitalization to clinical improvement, up to day 28. Clinical improvement is defined as either alive hospital discharge or a decrease of two or more points on the WHO-recommended nine-point ordinal scale of clinical status (WHO, 2020). AdVita is providing all relevant documentation, financial support with the aid of Relief, and study drug for the trial. The trial is estimated to take approximately 6-12 months to complete, depending on the progression of the ongoing COVID-19 pandemic.

CHF 200+ mn global peak sales in prevention of COVID-19 related ARDS
Like RLF-100 IV in COVID-19 induced ARDS, we have based our bottom-up forecasts for RLF-100 INHALED in prevention of COVID-19 related ARDS largely on detailed data available in the US and extrapolated the data where possible to the EU, where detailed data is often lacking or not publicly available. We have based our estimates on the same sources. To account for regional differences, we provide detailed forecasts for the US and Europe. In the US, we forecast sales until formulation patent expiry (including 5 years of Hatch Waxman patent extension) until 2034. In Europe, we conservatively forecast generic versions of RLF-100 INHALED to enter the market after the formulation patent expires in 2026. We assume the same decline in the number of COVID-19 cases in the US and EU as we do for RLF-100 IV in COVID-19 ARDS.

US peak sales to reach more than CHF 130 mn in 2023
Roughly 50% of people infected with COVID-19 infection experience symptoms. Of these symptomatic patients almost 80% have respiratory complications. An estimated 55% have mild respiratory symptoms, approximately 30% have moderate symptoms ~10% severe symptoms, and ~5% are critical. Of the 30% patients with moderate respiratory symptoms, almost 38% of patients are in a recovery phase with lung impairment and are at risk of developing life-threatening ARDS. Most of these patients can be treated at home. We now

assume, RLF-100 INHALED will reach up to only a 5% peak penetration in these patients. Pfizer's Paxlovid with its convenient oral dosing and high efficacy should grab the largest market share, in our view. Approximately 90% of patients with severe respiratory complications are in a recovery phase with lung impairment, with many still hospitalized. We assume that RLF-100 INHALED could reach higher peak penetration rates in this population up to around 30%. Assuming a treatment cost of USD 10,000 per patient, patient compliance of 90% and US launch at end 2022, peak sales in the US are forecast to reach around CHF 130 mn in 2023 and gradually decline as the COVID-19 pandemic becomes endemic due to the ongoing vaccination programs. Relief has identified distribution channels for RLF-100 INHALED with more to be added in the future.

CHF 90+ mn peak sales in Europe with patent protection only until 2026

For Europe we apply the same approach as for the US. We assume first launches in 2023. Peak sales in Europe are expected to amount around CHF 90+ mn in 2024 and gradually decline due to the decline in the number of COVID-19 cases. Peak sales in Europe are lower than the US due to the lower number of COVID-19 cases to start with and a lower estimated treatment cost of EUR 5,600 per patient (for details see the following page).

Forecasts & Sensitivity Analysis

RLF-100 INHALED - FINANCIAL FORECASTS FOR PREVENTION COVID-19 RELATED ARDS

INDICATION	PREVENTION OF RESPIRATORY FAILURE IN PATIENTS WITH MODERATE TO SEVERE COVID-19
DOSAGE	3X DAILY 100 MICROGRAM RLF-100 INHALED BY MESH NEBULIZER
PRICE	TREATMENT COURSE PER PATIENT: US: 4X WEEKLY AT USD 2,500/WEEK = USD 10,000; EU: 4X WEEKLY AT EUR 1,400/WEEK = EUR 5,600
STANDARD OF CARE	NEW ORAL ANTIVIRAL TREATMENTS SUCH AS PFIZER'S PAXLOVID OR MERCK & CO'S LAGEVRIO (MOLNUPIRAVIR)
UNIQUE SELLING POINT	POTENTIALLY FIRST TREATMENT TO PREVENT RESPIRATORY FAILURE IN PATIENTS WITH MODERATE TO SEVERE COVID-19 DISEASE

7Ps ANALYSIS

PATENT	US: PATENT EXPIRY 2029, 5 YEARS NCE EXCLUSIVITY, HATCH-WAXMAN 5 YEARS PATENTS EXTENSION; EU: FORMULATION PATENT EXPIRES 2026
PHASE	US: PHASE IIB/III "AVICOVID-2" TRIAL RESULTS H2 2022, EUA FILING & LAUNCH EXPECTED IN H2 2022; EU: LAUNCH BASED ON "AVICOVID-2" TRIAL EXPECTED IN 2023
PATHWAY	ACCELERATED APPROVAL IN THE US AND EU BASED ON A SINGLE PIVOTAL PHASE IIB/III TRIAL LIKELY; CONFIRMATORY 2ND PHASE III TRIAL NEEDED FOR FULL APPROVAL
PATIENT	LOWER LIKELIHOOD OF PROLONGED RESPIRATORY COMPLICATIONS OR EVEN RESPIRATORY FAILURE AFTER COVID-19 INFECTION
PHYSICIAN	FIRST EFFECTIVE TREATMENT TO REDUCE THE RISK OF RESPIRATORY FAILURE IN AT RISK COVID-19 RECOVERING FROM COVID-19 INFECTION
PAYER	SIGNIFICANTLY REDUCES OVERALL TREATMENT COSTS SUCH AS HOSPITALIZATION OR LONG-TERM RECOVERY COSTS OF AT RISK COVID-19 PATIENTS
PARTNER	NEURORX COMMERCIALIZES IN US, CANADA & ISRAEL; RELIEF IN EUROPE & ROW; PROFIT SPLIT RELIEF/NEURORX: US, CANADA & ISRAEL = 50/50; EUROPE = 85/15; ROW = 80/20

REVENUE MODEL

UNITED STATES - NRX TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
COVID-19 CASES (MN)	20.2	15.2	6.1	4.1	3.1	2.1	1.5	1.3	1.1	0.9	0.6
GROWTH (%)		-25%	-60%	-33%	-25%	-33%	-30%	-14%	-16%	-20%	-25%
SYMPTOMATIC COVID-19 PATIENTS (%)	50%	50%	25%	25%	25%	25%	25%	25%	25%	25%	25%
SYMPTOMATIC COVID-19 PATIENTS	10'080'253	7'604'795	1'529'933	1'025'973	774'020	519'058	365'484	315'120	264'150	212'566	160'365
COVID-19 PATIENTS WITH RESPIRATORY COMPLICATIONS (%)	77%	77%	77%	77%	77%	77%	77%	77%	77%	77%	77%
COVID-19 PATIENTS WITH RESPIRATORY COMPLICATIONS	7'741'634	5'840'482	1'174'988	787'947	594'447	398'636	280'692	242'012	202'867	163'251	123'161
COVID-19 PATIENTS WITH MODERATE DISEASE (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
COVID-19 PATIENTS WITH MODERATE DISEASE	2'322'490	1'752'145	352'496	236'384	178'334	119'591	84'208	72'604	60'860	48'975	36'948
PATIENTS WITH LUNG IMPAIRMENT IN RECOVERY PHASE (%)	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%	38%
MODERATE COVID-19 PATIENTS WITH LUNG IMPAIRMENT	870'934	657'054	132'186	88'644	66'875	44'847	31'578	27'226	22'823	18'366	13'856
ELIGIBLE MODERATE COVID-19 PATIENTS WITH NALI (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE MODERATE COVID-19 PATIENTS WITH NALI	783'840	591'349	118'968	79'780	60'188	40'362	28'420	24'504	20'540	16'529	12'470
PENETRATION (%)	0%	0%	1%	3%	4%	4%	5%	5%	5%	5%	5%
NUMBER OF MODERATE PATIENTS TREATED	**0**	**0**	**595**	**1'994**	**2'107**	**1'614**	**1'279**	**1'103**	**924**	**744**	**561**
COVID-19 PATIENTS WITH SEVERE DISEASE (%)	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
COVID-19 PATIENTS WITH SEVERE DISEASE	774'163	584'048	117'499	78'795	59'445	39'864	28'069	24'201	20'287	16'325	12'316
PATIENTS WITH LUNG IMPAIRMENT IN RECOVERY PHASE (%)	94%	94%	94%	94%	94%	94%	94%	94%	94%	94%	94%
SEVERE COVID-19 PATIENTS WITH LUNG IMPAIRMENT	728'488	549'589	110'566	74'146	55'937	37'512	26'413	22'773	19'090	15'362	11'589
ELIGIBLE SEVERE COVID-19 PATIENTS WITH NALI (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE SEVERE COVID-19 PATIENTS WITH NALI	655'639	494'630	99'510	66'731	50'344	33'760	23'772	20'496	17'181	13'826	10'430
PENETRATION (%)	0%	0%	4%	19%	27%	31%	33%	33%	33%	33%	33%
NUMBER OF SEVERE PATIENTS TREATED	**0**	**0**	**3'980**	**12'679**	**13'593**	**10'466**	**7'845**	**6'764**	**5'670**	**4'562**	**3'442**
TOTAL NUMBER OF PATIENTS TREATED	**0**	**0**	**4'575**	**14'673**	**15'699**	**12'080**	**9'124**	**7'866**	**6'594**	**5'306**	**4'003**
TREATMENT COST PER WEEK(CHF)	2'291	2'279	2'309	2'309	2'309	2'309	2'309	2'309	2'309	2'309	2'309
TREATMENT WEEKS	4	4	4	4	4	4	4	4	4	4	4
COST OF THERAPY PER PATIENT (CHF)	9'166	9'115	9'235	9'235	9'235	9'235	9'235	9'235	9'235	9'235	9'235
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - NRX BOOKS SALES	**0**	**0**	**38**	**122**	**130**	**100**	**76**	**65**	**55**	**44**	**33**
CHANGE (%)				221%	7%	-23%	-24%	-14%	-16%	-20%	-25%
M&S (CHF MN) - PAID BY NRX	0	0	-32	-11	-12	-7	-5	-3	-3	-2	-2
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**6**	**111**	**119**	**93**	**71**	**62**	**52**	**42**	**32**
PROFIT SPLIT (50/50)	0%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**0**	**3**	**55**	**59**	**47**	**36**	**31**	**26**	**21**	**16**
TAXES (CHF MN)	0	0	0	-6	-7	-5	-4	-3	-3	-2	-2
PROFIT (CHF MN)	**0**	**0**	**3**	**49**	**53**	**42**	**32**	**28**	**23**	**19**	**14**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
COVID-19 CASES (MN)	17.3	13.0	6.1	4.4	3.5	2.6	1.7	1.2	1.0	0.9	0.7
GROWTH (%)		-25%	-53%	-29%	-20%	-25%	-33%	-30%	-14%	-17%	-20%
SYMPTOMATIC COVID-19 PATIENTS (%)	50%	50%	25%	25%	25%	25%	25%	25%	25%	25%	25%
SYMPTOMATIC COVID-19 PATIENTS	8'674'195	6'505'646	1'521'022	1'087'530	870'894	653'824	436'318	305'728	262'315	218'814	175'227
COVID-19 PATIENTS WITH RESPIRATORY COMPLICATIONS (77%)	6'661'781	4'996'336	1'168'145	835'223	668'847	502'137	335'093	234'799	201'458	168'049	134'574
COVID-19 PATIENTS WITH MODERATE DISEASE (30%)	1'998'534	1'498'901	350'443	250'567	200'654	150'641	100'528	70'440	60'437	50'415	40'372
MODERATE COVID-19 PATIENTS WITH LUNG IMPAIRMENT (38%)	749'450	562'088	131'416	93'963	75'245	56'490	37'698	26'415	22'664	18'906	15'140
ELIGIBLE MODERATE COVID-19 PATIENTS WITH NALI (90%)	674'505	505'879	118'275	84'566	67'721	50'841	33'928	23'773	20'398	17'015	13'626
PENETRATION (%)	0%	0%	0%	2%	4%	5%	5%	4%	2%	2%	1%
NUMBER OF MODERATE PATIENTS TREATED	0	0	0	1'691	2'709	2'542	1'696	832	500	292	164
COVID-19 PATIENTS WITH SEVERE DISEASE (10%)	666'178	499'634	116'814	83'522	66'885	50'214	33'509	23'480	20'146	16'805	13'457
SEVERE COVID-19 PATIENTS WITH LUNG IMPAIRMENT (94%)	626'874	470'155	109'922	78'595	62'938	47'251	31'532	22'095	18'957	15'813	12'663
ELIGIBLE SEVERE COVID-19 PATIENTS WITH NALI (90%)	564'186	423'140	98'930	70'735	56'645	42'526	28'379	19'885	17'061	14'232	11'397
PENETRATION (%)	0%	0%	0%	10%	25%	30%	30%	21%	15%	10%	7%
NUMBER OF SEVERE PATIENTS TREATED	**0**	**0**	**0**	**7'074**	**14'161**	**12'758**	**8'514**	**4'176**	**2'508**	**1'464**	**821**
TOTAL NUMBER OF PATIENTS TREATED	**0**	**0**	**0**	**8'765**	**16'870**	**15'300**	**10'210**	**5'008**	**3'008**	**1'756**	**985**
TREATMENT COST PER WEEK (CHF)	1'508	1'516	1'515	1'515	1'515	1'515	1'515	1'515	1'515	1'515	1'515
TREATMENT WEEKS	4	4	4	4	4	4	4	4	4	4	4
COST OF THERAPY PER PATIENT (CHF)	6'032	6'066	6'061	6'061	6'061	6'061	6'061	6'061	6'061	6'061	6'061
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**48**	**92**	**83**	**56**	**27**	**16**	**10**	**5**
CHANGE (%)					92%	-9%	-33%	-51%	-40%	-42%	-44%
COGS (CHF MN)	0	0	-1	-4	-6	-5	-3	-2	-2	-1	-1
R&D COSTS (CHF MN)	-1	-10	-8	0	0	0	0	0	0	0	0
M&S (CHF)	0	0	-5	-35	-35	-30	-25	-2	-1	-1	0
PROFIT BEFORE TAX (CHF MN)	**-1**	**-10**	**-14**	**9**	**51**	**49**	**27**	**23**	**13**	**8**	**4**
PROFIT SPLIT (85/15)	100%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%
RELIEF PROFIT BEFORE TAX (CHF MN)	**-1**	**-9**	**-12**	**7**	**44**	**41**	**23**	**19**	**11**	**6**	**3**
TAXES (CHF MN)	0	0	1	-1	-5	-5	-3	-2	-1	-1	0
PROFIT (CHF MN)	**-1**	**-9**	**-10**	**7**	**39**	**37**	**21**	**17**	**10**	**6**	**3**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**38**	**170**	**223**	**184**	**132**	**93**	**71**	**54**	**39**
CHANGE (%)				346%	31%	-17%	-28%	-30%	-23%	-25%	-28%
GLOBAL SALES (USD MN)	**0**	**0**	**41**	**184**	**241**	**199**	**142**	**100**	**77**	**58**	**42**
CHANGE (%)				346%	31%	-17%	-28%	-30%	-23%	-25%	-28%
GLOBAL PROFIT (CHF MN)	**-1**	**-9**	**-8**	**56**	**92**	**78**	**52**	**45**	**33**	**24**	**17**
CHANGE (%)		520%	-9%	-819%	64%	-15%	-33%	-14%	-26%	-27%	-30%
WACC (%)	7%										
NPV TOTAL PROFIT (CHF MN)	**295**										
NUMBER OF SHARES (MN)	4'400										
NPV PER SHARE (CHF)	**0.067**										
SUCCESS PROBABILITY	65%	= PHASE II/III									
RISK ADJUSTED NPV PER SHARE (CHF)	**0.044**										

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	0.072	0.070	0.069	0.067	0.065	0.064	0.063
	95%	0.068	0.067	0.065	0.064	0.062	0.061	0.059
	90%	0.065	0.063	0.062	0.060	0.059	0.058	0.056
	85%	0.061	0.060	0.058	0.057	0.056	0.054	0.053
SUCCESS PROBABILITY	80%	0.058	0.056	0.055	0.054	0.052	0.051	0.050
	75%	0.054	0.053	0.051	0.050	0.049	0.048	0.047
	70%	0.050	0.049	0.048	0.047	0.046	0.045	0.044
	65%	0.047	0.046	0.045	**0.044**	0.043	0.042	0.041
	60%	0.043	0.042	0.041	0.040	0.039	0.038	0.038

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

III) RLF-100 IV in non-COVID-19 related ARDS - Peak sales CHF 450+ mn; rNPV CHF 0.075/share

ALI and ARDS, a high unmet medical need with no approved treatments
Acute lung injury (ALI), including the most severe form known as acute respiratory distress syndrome (ARDS) or non-COVID-19 related 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. Non-COVID-19 related 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 non-COVID-19 related ARDS.

Small phase I trial established POC in non-COVID-19 related ARDS triggers development in COVID-19
In a small phase I trial conducted in 2005, 8 patients with severe non-COVID-19 related ARDS on mechanical ventilation were treated with ascending doses of aviptadil (RLF-100 IV). 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, non-COVID-19 related ARDS, and acute lung injury. These promising early results in non-COVID-19 related 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 prevention of COVID-19 related ARDS, with the highest priority.

Phase IIb/III ARDS trial expected to start in 2022
Following the start of the RLF-100 INHALED prevention COVID-19 related ARDS clinical trials, Relief plans to start a phase IIb/III trial of RLF-100 IV in non-COVID-19 related ARDS likely in 2022. Trial size and design have yet to be determined. Assuming RLF-100 IV is approved for COVID-19 induced ARDS, Relief plans to submit a supplemental New Drug Application (sNDA) in the US. An sNDA is an application to allow a company to make changes to the label of a product that is already the basis of an approved NDA. The FDA's Center for Drug Evaluation and Research (CDER) must approve all important NDA changes (in packaging or ingredients, for instance) to ensure the conditions originally set for the product are still met. This would expedite US approval for RLF-100 IV in non-COVID-19 related ARDS, which could happen as early as late 2022 with launch to occur in 2023. In the EU, we expect RLF-100 IV to receive accelerated approval in 2023, given the high unmet medical need and lack of approved drugs for ARDS followed by a launch in 2024.

Orphan drug exclusivity in Europe not expected to stop generics from 2026
ALI and non-COVID-19 related ARDS are considered orphan drug indications in the EU US. Based on the positive phase I trial in non-COVID-19 related ARDS, RLF-100 IV was granted ODD in the US (2001) and EU (2007), which could provide market exclusivity of 7 years (US) or 10 years (EU) from day of first approval. Assuming approval of RLF-100 IV in COVID-19 induced ARDS in end 2022, orphan drug market exclusivity in the US would reach until end 2029 and until Q2 2032 in the EU, theoretically. However, we do not expect RLF-100 IV in COVID-19 induced ARDS to qualify as an orphan drug as the number of patients is too high. In the US, the formulation patent and expected 5 years of Hatch Waxman extension prevents the launch of generic versions of RLF-100 IV until 2034. In the

EU, the formulation patent provides protection only until 2026. Without orphan drug exclusivity for COVID-19 induced ARDS, generic versions of RLF-100 IV to treat COVID-19 induced ARDS are likely to enter the market after the formulation patent expires in 2026. Officially, they may not be promoted for use in non-COVID-19 related ARDS, but large scale generic substitution should be expected due to the price difference. Consequently, in the EU we conservatively expect protection from generics only until the formulation patent expires in 2026.

Global peak sales of CHF 450+ mn to be reached in 2026

In the US, the number of non-COVID-19 related 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. We assume US launch in early 2023 based on a successful sNDA filing. With no treatment available for non-COVID-19 related ARDS, we expect a steep uptake with the peak penetration reaching up to 50%. Assuming a treatment cost of USD 9,000 per patient, US peak sales are forecasted to amount to more than CHF 400 mn in 2033, a year before the 5 years of Hatch Waxman patent extension expires in 2034.

In the EU, we expect first launches to occur in 2024 based on successful accelerated approval. We expect a steep uptake with market penetration peaking at 30% in 2025, a year before the EU formulaton patent expires. Assuming a treatment cost of EUR 4,000 per patient, EU peak sales of RLF-100 IV in non-COVID-19 related ARDS are expected to amount to approximately CHF 160 mn in 2026 (for details see the following page).

Forecasts & Sensitivity Analysis

RLF-100 IV - FINANCIAL FORECASTS FOR NON-COVID-19 RELATED ARDS

INDICATION	REDUCTION OF MORBIDITY AND MORTALITY IN PATIENTS WITH NON-COVID-19 RELATED 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: US: 9,000; EU: EUR 4,000 SIMILAR TO COVID-19 INDUCED ARDS TREATMENT COST
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 NON COVID-19 RELATED ARDS

7Ps ANALYSIS

PATENT	US: PATENT EXPIRY 2029, 5-YEAR HATCH-WAXMAN EXTENSION, 5 YEARS NCE EXCLUSIVITY; EU: PATENT EXPIRY 2026; ODD ARDS (COVID-19 ARDS NOT ORPHAN)
PHASE	PROOF OF CONCEPT ESTABLISHED; PHASE IIB/III TO START IN 2022; RESULTS 2022; SNDA END 2022; LAUNCH 2023; EU LAUNCH GUIDED FOR 2024
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	NEURORX COMMERCIALIZES IN US, CANADA & ISRAEL; RELIEF IN EUROPE & ROW; PROFIT SPLIT RELIEF/NEURORX: US, CANADA & ISRAEL = 50/50; EUROPE = 85/15; ROW = 80/20

REVENUE MODEL

UNITED STATES - NRX TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF ARDS PATIENTS	260'100	265'302	270'608	276'020	281'541	287'171	292'915	298'773	304'749	310'844	317'060
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	104'040	106'121	108'243	110'408	112'616	114'869	117'166	119'509	121'899	124'337	126'824
ELIGIBLE ARDS PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE ARDS PATIENTS	83'232	84'897	86'595	88'326	90'093	91'895	93'733	95'607	97'520	99'470	101'459
PENETRATION (%)	0%	0%	0%	4%	15%	30%	40%	45%	47%	49%	50%
NUMBER OF PATIENTS	0	0	0	3'533	13'514	27'568	37'493	43'023	45'834	48'740	50'730
COST TREATMENT COURSE PER PATIENT (CHF)	8'249	8'203	8'312	8'312	8'312	8'312	8'312	8'312	8'312	8'312	8'312
SALES (CHF MN) - NRX BOOKS SALES	**0**	**0**	**0**	**29**	**112**	**229**	**312**	**358**	**381**	**405**	**422**
CHANGE (%)					283%	104%	36%	15%	7%	6%	4%
COGS (CHF MN) - PAID BY RELIEF	0	0	0	0	0	0	-1	-1	-1	-1	-1
M&S (CHF MN) - PAID BY NRX	0	0	0	-15	-34	-57	-62	-54	-57	-61	-63
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**15**	**79**	**172**	**249**	**304**	**324**	**344**	**358**
PROFIT SPLIT (50/50)	0%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**0**	**0**	**7**	**39**	**86**	**125**	**152**	**162**	**172**	**179**
TAXES (CHF MN)	0	0	0	-1	-4	-9	-14	-17	-18	-19	-20
PROFIT (CHF MN)	**0**	**0**	**0**	**7**	**35**	**76**	**111**	**135**	**144**	**153**	**159**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF ARDS PATIENTS	344'570	351'462	358'491	365'661	372'974	380'434	388'042	395'803	403'719	411'793	420'029
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	137'828	140'585	143'396	146'264	149'190	152'173	155'217	158'321	161'488	164'717	168'012
ELIGIBLE ARDS PATIENTS (%)	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
ELIGIBLE ARDS PATIENTS	110'263	112'468	114'717	117'011	119'352	121'739	124'173	126'657	129'190	131'774	134'409
PENETRATION (%)	0%	0%	0%	0%	5%	20%	30%	15%	8%	4%	2%
NUMBER OF PATIENTS	0	0	0	0	5'968	24'348	37'252	18'999	9'689	4'942	2'520
COST TREATMENT COURSE PER PATIENT (CHF)	4'308	4'333	4'330	4'330	4'330	4'330	4'330	4'330	4'330	4'330	4'330
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**26**	**105**	**161**	**82**	**42**	**21**	**11**
CHANGE (%)						308%	53%	-49%	-49%	-49%	-49%
COGS (CHF MN)	0	0	0	0	0	-1	-1	-1	-1	-1	-1
R&D COSTS (CHF MN)	0	-2	-7	-7	0	0	0	0	0	0	0
M&S (CHF)	0	0	0	0	-16	-32	-39	-2	0	0	0
PROFIT BEFORE TAX (CHF MN)	**0**	**-2**	**-7**	**-7**	**10**	**73**	**121**	**79**	**41**	**21**	**10**
PROFIT SPLIT (85/15)	100%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**-2**	**-6**	**-6**	**9**	**62**	**103**	**67**	**35**	**17**	**9**
TAXES (CHF MN)	0	0	1	1	-1	-7	-11	-7	-4	-2	-1
PROFIT (CHF MN)	**0**	**-2**	**-6**	**-6**	**8**	**55**	**92**	**60**	**31**	**16**	**8**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**29**	**138**	**335**	**473**	**440**	**423**	**427**	**433**
CHANGE (%)					370%	142%	41%	-7%	-4%	1%	1%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**32**	**150**	**362**	**512**	**476**	**458**	**462**	**468**
CHANGE (%)					370%	142%	41%	-7%	-4%	1%	1%
GLOBAL PROFIT (CHF MN)	**0**	**-2**	**-6**	**1**	**43**	**132**	**203**	**195**	**175**	**169**	**167**
CHANGE (%)			261%	-116%	4622%	209%	54%	-4%	-10%	-4%	-1%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**943**	
NUMBER OF SHARES (MN)	4'400	
NPV PER SHARE (CHF)	**0.214**	
SUCCESS PROBABILITY	35%	= POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.075**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.165	0.159	0.153	0.150	0.142	0.137	0.132
	65%	0.153	0.147	0.142	0.139	0.132	0.127	0.123
	60%	0.141	0.136	0.131	0.129	0.122	0.117	0.113
	55%	0.129	0.125	0.120	0.118	0.112	0.108	0.104
SUCCESS PROBABILITY	50%	0.118	0.113	0.109	0.107	0.101	0.098	0.094
	45%	0.106	0.102	0.098	0.096	0.091	0.088	0.085
	40%	0.094	0.091	0.087	0.086	0.081	0.078	0.076
	35%	0.082	0.079	0.076	**0.075**	0.071	0.069	0.066
	30%	0.071	0.068	0.065	0.064	0.061	0.059	0.057

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

RLF-100 INHALED (Pulmonary Sarcoidosis)

RLF-100 INHALED pulmonary sarcoidosis - Peak sales CHF 550+ mn; rNPV CHF 0.049/share

We forecast peak sales of CHF 550+ mn for RLF-100 INHALED in pulmonary sarcoidosis in the US and EU. Relief is expected to start a phase IIb dose ranging trial in 2022 and believes first launches could occur in the US and EU in 2025 assuming fast track review, sNDA in the US and accelerated approval in the EU. We assume patent protection until 2034 in the US and patent protection in the EU until 2026 (we conservatively do not assume 10 years orphan drug exclusivity for sarcoidosis as generic versions of inhaled RLF-100 are likely to be approved for prevention COVID-19 related ARDS after formulation patent expiry in 2026) We assume an annual treatment cost per patient of USD 60,000 (US) and EUR 30,000 (EU) and peak penetration rates rising to ~8% (US) and ~3% (EU). Accounting for R&D costs (CHF ~17 mn), COGS, M&S costs (CHF ~20 mn) and the NRx profit split agreement, our rNPV amounts to CHF 217 mn or CHF 0.049 per share with a 35% (POC established) success rate and a WACC of 7% (for details see page 53).

Last but not least – Pulmonary sarcoidosis

Development of RLF-100 INHALED in pulmonary sarcoidosis was Relief's main priority until the rapid onset of the COVID-19 pandemic in early 2020 and critical COVID-19 associated respiratory indications with high unmet need became first priority. 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 years market exclusivity from the date of approval. We believe pulmonary sarcoidosis is a large 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. We forecast peak sales of roughly CHF 550+ mn for RLF-100 INHALED in pulmonary sarcoidosis.

RLF-100 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. Saroidosis 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 benefit over current treatments including corticosteroids such as oral or inhaled prednisone or immunsuppressants 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 VIP, and to increase the dose to therapeutically meaningful levels for pulmonary sarcoidosis, RLF-100 INHALED was specifcally 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 varibility, 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 2022
Initially, Relief wanted to start a randomized, multicenter, double blind, placebo controlled, phase III trial named "AVISARCO II" in 200 sarcoidosis patients with a treatment duration of 24 weeks, followed by a long-term follow up of an additional 24 weeks. However, with RLF-100 INHALED likely to be approved earlier in prevention of COVID-19 related ARDS, the company has changed its clinical development plans anticipating the potential for a sNDA (supplemental New Drug Application) in the US and accelerated approval in the EU. Relief now expects to start a phase IIb dose ranging trial of RLF-100 INHALED in patients with pulmonary sarcoidosis in 2022. The company expects first launches in 2025.

Global peak sales of CHF 550+ 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.

Approximately CHF 550 mn peak sales in the US with first launches in 2025
In the US, there are an estimated 25,000 newly diagnosed cases of sarcoidosis in the US each year. Each year, approximately 185,000 patients with sarcoidosis seek medical care. 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 60,000 per patient, a peak penetration rate of ~8%, and patient compliance of 60% to be expected for a chronic treatment. Assuming launch in 2025 and patent protection until 2034, we forecast US peak sales of CHF 550 mn in 2033.

Roughly CHF 30 mn peak sales in the EU with first launches in 2025
Our EU forecasts are based on the same patient breakdown as in the US, albeit with a higher patient population. We assume a lower annual treatment cost of EUR 30,000 per patient and first launches to occur in 2025 with patent expiry in 2026. We conservatively do not assume 10 years EU orphan drug exclusivity for sarcoidosis as generic versions of inhaled RLF-100 are likely to be approved for prevention COVID-19 related ARDS after formulation patent expiry in 2026. Consequently, our peak EU peak sales amount to a modest CHF 33 mn (for details see 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: US: USD 60,000; EU: EUR 30,000
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 EXPIRES IN 2029 WITH 5-YEAR HATCH-WAXMAN EXTENSION UP TO 2034; EU: PATENT EXPIRES 2026, ODD PROVIDES 10 YEARS EXCLUSIVITY? (NALI NOT ORPHAN)
PHASE	PHASE IIB DOSE RANGING TRIAL START TBD; RESULTS PHASE IIB TBD; PHASE III TBD, APPROVAL & LAUNCH GUIDED FOR 2025
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	NEURORX COMMERCIALIZES IN US, CANADA & ISRAEL; RELIEF IN EUROPE & ROW; PROFIT SPLIT RELIEF/NEURORX: US, CANADA & ISRAEL = 50/50; EUROPE = 85/15; ROW = 80/20

REVENUE MODEL

UNITED STATES - NRX TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
ANNUAL NEW CASES OF SARCOIDOSIS DIAGNOSED	25'500	26'010	26'530	27'061	27'602	28'154	28'717	29'291	29'877	30'475	31'084
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
SARCOIDOSIS PATIENTS SEEKING TREATMENT/YEAR	188'700	192'474	196'323	200'250	204'255	208'340	212'507	216'757	221'092	225'514	230'024
PULMONARY SARCOIDOSIS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
PULMONARY SARCOIDOSIS PATIENTS TREATED	169'830	173'227	176'691	180'225	183'829	187'506	191'256	195'081	198'983	202'963	207'022
CHRONIC/ADVANCED PATIENTS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CHRONIC/ADVANCED PULMONARY SARCOIDOSIS PATIENTS	50'949	51'968	53'007	54'067	55'149	56'252	57'377	58'524	59'695	60'889	62'107
PENETRATION (%)	0%	0%	0%	0%	0%	1%	3%	5%	6%	7%	7%
NUMBER OF PATIENTS	0	0	0	0	0	938	4'781	8'779	10'944	13'193	14'492
TREATMENT COST PER DAY (CHF)	151	150	152	152	152	152	152	152	152	152	152
TREATMENT DAYS	365	365	365	365	365	365	365	365	365	365	365
COST OF THERAPY PER PATIENT (CHF)	54'995	54'689	55'410	55'410	55'410	55'410	55'410	55'410	55'410	55'410	55'410
PATIENT COMPLIANCE (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
SALES (CHF MN) - NRX BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**31**	**159**	**292**	**364**	**439**	**482**
CHANGE (%)							410%	84%	25%	21%	10%
M&S (CHF MN) - PAID BY NRX	0	0	0	0	0	-25	-64	-73	-73	-66	-72
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**0**	**0**	**0**	**6**	**95**	**219**	**291**	**373**	**410**
PROFIT SPLIT (50/50)	0%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**0**	**0**	**0**	**0**	**3**	**48**	**109**	**146**	**186**	**205**
TAXES (CHF MN)	0	0	0	0	0	0	-5	-12	-16	-21	-23
PROFIT (CHF MN)	**0**	**0**	**0**	**0**	**0**	**3**	**42**	**97**	**130**	**166**	**182**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
ANNUAL NEW CASES OF SARCOIDOSIS DIAGNOSED	34'457	35'146	35'849	36'566	37'297	38'043	38'804	39'580	40'372	41'179	42'003
GROWTH (%)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
SARCOIDOSIS PATIENTS SEEKING TREATMENT/YEAR	254'982	260'082	265'283	270'589	276'001	281'521	287'151	292'894	298'752	304'727	310'822
PULMONARY SARCOIDOSIS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
PULMONARY SARCOIDOSIS PATIENTS TREATED	229'484	234'074	238'755	243'530	248'401	253'369	258'436	263'605	268'877	274'254	279'740
CHRONIC/ADVANCED PATIENTS (%)	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
CHRONIC/ADVANCED PULMONARY SARCOIDOSIS PATIENTS	68'845	70'222	71'627	73'059	74'520	76'011	77'531	79'081	80'663	82'276	83'922
PENETRATION (%)	0%	0%	0%	0%	0%	0%	2%	2%	1%	1%	1%
NUMBER OF PATIENTS	0	0	0	0	0	152	1'706	1'392	1'136	927	756
TREATMENT COST PER DAY (CHF)	89	89	89	89	89	89	89	89	89	89	89
TREATMENT DAYS	365	365	365	365	365	365	365	365	365	365	365
COST OF THERAPY PER YEAR (CHF)	32'313	32'495	32'472	32'472	32'472	32'472	32'472	32'472	32'472	32'472	32'472
PATIENT COMPLIANCE (%)	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**3**	**33**	**27**	**22**	**18**	**15**
CHANGE (%)							1022%	-18%	-18%	-18%	-18%
COGS (CHF MN)	0	0	0	0	0	-2	-13	-21	-24	-29	-31
R&D COSTS (CHF MN)	0	-1	-4	-5	-7	-2	0	0	0	0	0
M&S (CHF)	0	0	0	0	0	-2	-10	-7	-4	-3	-2
PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-4**	**-5**	**-7**	**-3**	**10**	**0**	**-7**	**-13**	**-18**
PROFIT SPLIT (85/15)	100%	85%	85%	85%	85%	85%	85%	85%	85%	85%	85%
RELIEF PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-3**	**-4**	**-6**	**-2**	**9**	**0**	**-6**	**-11**	**-16**
TAX RATE (%)	0%	0%	0%	0%	0%	11%	11%	11%	11%	11%	11%
TAXES (CHF MN)	0	0	0	0	0	0	-1	0	1	1	2
PROFIT (CHF MN)	**0**	**-1**	**-3**	**-4**	**-6**	**-2**	**8**	**0**	**-5**	**-10**	**-14**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**34**	**192**	**319**	**386**	**457**	**497**
CHANGE (%)							463%	66%	21%	18%	9%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**0**	**37**	**208**	**345**	**418**	**494**	**538**
CHANGE (%)							463%	66%	21%	18%	9%
GLOBAL PROFIT (CHF MN)	**0**	**-1**	**-3**	**-4**	**-6**	**1**	**50**	**97**	**124**	**156**	**168**
CHANGE (%)			305%	25%	60%	-110%	8169%	94%	28%	25%	8%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**620**	
NUMBER OF SHARES (MN)	4'400	
NPV PER SHARE (CHF)	**0.141**	
SUCCESS PROBABILITY	35%	= POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.049**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.112	0.108	0.103	0.099	0.095	0.091	0.087
	65%	0.104	0.100	0.096	0.092	0.088	0.084	0.081
	60%	0.096	0.092	0.088	0.085	0.081	0.078	0.074
	55%	0.088	0.085	0.081	0.078	0.074	0.071	0.068
SUCCESS PROBABILITY	50%	0.080	0.077	0.074	0.070	0.068	0.065	0.062
	45%	0.072	0.069	0.066	0.063	0.061	0.058	0.056
	40%	0.064	0.061	0.059	0.056	0.054	0.052	0.050
	35%	0.056	0.054	0.052	**0.049**	0.047	0.045	0.043
	30%	0.048	0.046	0.044	0.042	0.041	0.039	0.037

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

ACER-001 (Urea Cycle Disorders & Maple Syrup Urine Disease)

I) ACER-001 UCDs - Peak sales CHF 130+ mn; rNPV CHF 0.043/share

We forecast peak sales in the US and EU of approximately CHF 130+ mn for ACER-001 in urea cycle disorders (UCDs) assuming first launches in 2022 by Acer (US, Canada, Brazil, Turkey and Japan and Relief (EU, ROW). We calculate a rNPV of CHF 190 mn or CHF 0.043 per share assuming an 80% (Section 505(b)(2)) success rate and 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 up to USD 6 mn and up to USD 20 mn in US development and commercial launch costs (for details see page 59)

II) ACER-001 MSUD - Peak sales CHF 80+ mn; rNPV CHF 0.015/share

For ACER-001 in maple syrup urine disease (MSUD), we forecast peak sales in the US and EU to reach CHF 80+ mn assuming US launch in 2023 followed by EU launch in 2024. We calculate a rNPV of CHF 64 mn or CHF 0.015/share assuming a 35% (POC established) success rate and accounting for the same terms as for UCDs stated above (for details see page 61).

ACER-001 - new pipeline drug targeting lucrative rare diseases

In late January 2021, Relief and Acer Therapeutics signed and option agreement for exclusivity to negotiate a collaboration and license agreement for the worldwide development and commercialization of ACER-001 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 with ACER-001 to Relief's pipeline. 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 ACER-001 to amount to more than CHF 200 mn based on conservative pricing assumptions with first launches in UCDs to occur in 2022. These are ultra-niche markets and accordingly will not require substantial sales forces to penetrate. Prescribers and patients alike are very concentrated with detailed registries. Therefore, these sales ought to be highly accretive for Relief. Importantly, ACER-001 in UCDs is developed under Section 505(b)(2) providing an alternative pathway for filing an NDA with a high 80% success rate and entitled to 3-years Hatch-Waxman market exclusivity from the approval date. A 5 June 2022 PDUFA date was set by the FDA when it expects to complete its review of ACER-001 in UCDs. Additionally, the FDA granted Orphan Drug Designation for ACER-001 in MSUD providing 7 years market exclusivity from the approval date. Given the low number of patients with UCDs and MSUP in the EU, we believe Relief can successfully apply for ODD in the EU resulting in 10 years market exclusivity from the approval date. The recently granted US formulation patent with taste-masking claims for ACER-001 and a method of use patent for UCDs and MSUP extends protection up to 2036.

Attractive terms which can be financed through current cash or GEM SSR

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 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. Relief can fund the ACER-001 agreement out of its current cash position, from potential first commercial sales of RLF IV in COVID-19 induced ARDS or ultimately through the recently announced CHF 50 mn Share Subscription Facility (SSF) with largest shareholder GEM.

I) ACER-001 UCDs - Peak sales CHF 130+ mn; rNPV CHF 0.043/share

ACER-001 has an attractive profile in UCDs providing 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 the removal of ammonia from the bloodstream. Some patients may also require individual branched-chain amino acid supplementation.

Taste-masking a 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. ACER-001 is a taste-masked, immediate-release proprietary powder formulation of sodium phenylbutyrate (NaPB) developed by Acer using a microencapsulation process. 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. If ACER-001 is approved in UCDs, its 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 Pharma acquired Hyperion Therapeutics for approximately USD 1.1 bn in cash to expand and diversify its orphan drug product portfolio with Buphenyl and Ravicti.

Compelling data showing bioequivalence to Buphenyl…

In July 2020, Acer announced data from a food effect study in healthy volunteers showing that administration of ACER-001 in a fasted state increased systemic exposure of phenylbutyrate (PBA), phenylacetate (PAA) and phenylacetylglutamine (PAGN) levels compared to 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 ACER-001 bioequivalence (BE) trial in healthy volunteers (n=36), announced in February 2020, showed that ACER-001 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 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 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 ACER-001 to be given without food, another USP

Currently approved therapies for UCDs, including Buphenyl and Ravicti are required to be administered with food. Buphenyl is required to 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 Buphenyl food effect is unknown. Ravicti PK and pharmacodynamic (PD) properties were determined to be indistinguishable in fed or fasted states. 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 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 ACER-001 in UCDs patients. Results from this in silico model suggest that administration of 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 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 ACER-001 food effect study, published literature and in silico modeling suggest that 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.

ACER-001 developed under Section 505(b)(2) provides 3 years market exclusivity

Acer is developing 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. Moreover, after the successful BE trials, ACER-001 is highly likely to be approved by the FDA, which justifies an 80% success rate, in our view.

Several gene approaches stumble, are years away with prohibitive pricing
We do not expect gene therapy approaches - even if they prove highly effective clinically - to prevent achievement of market traction with 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' 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.

Successful US NDA filing with a 5 June 2022 PDUFA data set by the FDA
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 is 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 with a 5 June 2022 Prescription Drug User Fee Act (PDUFA) date when the FDA is expected to complete its review.

CHF 130+ mn peak sales in UCDs with first launches in 2022
We have based our detailed bottom-up forecasts for 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. We conservatively forecast until 7 years orphan drug exclusivity expiry in the US in 2029 and 2032 in the EU (assuming ODD due to the low number of patients in EU). The recently issued US formulation patent covering the taste-masking claims and method of use patent for UCDs and MSUP now extend protection up to 2036. The Hatch-Waxman Amendments under Section 505(b)(2) provide ACER-001 with potential market exclusivity for three years from FDA approval.

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 ACER-001 treatment. In the US, we conservatively assume an annual treatment cost of USD 120,000 per patient with a 90% patient compliance due to the improved formulation with taste-masking and the potential to take ACER-001 without food. Assuming launch in 2022 and peak market penetration conservatively reaching to ~12%, we forecast US peak sales of CHF 107 mn in 2028.

Applying a similar approach to the EU with an annual treatment cost of USD 60,000, launch in 2022 and a conservative peak market penetration of ~8%, we forecast CHF 47 mn peak sales for the EU in 2030 (for details see page 59).

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 would be addressable once and FDA approval has been secured. Prescribers and patients alike 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 ACER-001 has been well-known for an extended period and is relatively inexpensive to manufacture.

Forecasts & Sensitivity Analysis

ACER-001 - FINANCIAL FORECASTS FOR UREA CYCLE DISORDERS (UCDS)

INDICATION	TREATMENT OF HYPERAMMONEMIA (ACCUMULATION OF AMMONIA) IN PATIENTS WITH UREA CYCLE DISORDERS (UCD)
DOSAGE	TBD
PRICE	ANNUAL TREATMENT COST PER PATIENT; US WE ASSUME USD 120,000; EU/ROW: WE ASSUME USD 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	UNDER SECTION 505(B)(2) ACER-001 HAS PROVEN BIOEQUIVALENCE TO BUPHENYL WITH A HIGH LIKELIHOOD TO BE APPROVED JUSTIFYING A 80% SUCCESS RATE
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

REVENUE MODEL

UNITED STATES - ACER THERAPEUTICS TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF UREA CYCLE DISORDER (UCD) PATIENTS	9'600	9'696	9'793	9'891	9'990	10'090	10'191	10'293	10'396	10'500	10'605
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	7'680	7'757	7'834	7'913	7'992	8'072	8'153	8'234	8'316	8'400	8'484
ELIGIBLE UCD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE UCD PATIENTS	6'912	6'981	7'051	7'122	7'193	7'265	7'337	7'411	7'485	7'560	7'635
PENETRATION (%)	0%	0%	1%	3%	5%	8%	10%	11%	12%	9%	4%
NUMBER OF PATIENTS	0	0	71	214	360	581	734	815	898	680	305
ANNUAL TREATMENT COST PER PATIENT (CHF)	109'990	109'378	110'821	114'146	117'570	121'097	124'730	128'472	132'326	136'296	140'385
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - ACER THERAPEUTICS BOOKS SALES	**0**	**0**	**7**	**22**	**38**	**63**	**82**	**94**	**107**	**83**	**39**
CHANGE (%)				212%	73%	66%	30%	14%	13%	-22%	-54%
ROYALTIES (CHF MN) - PAID TO BAYLOR	0	0	0	0	-1	-1	-2	-2	-2	-2	-1
UPFRONT & MILESTONES (CHF MN) - PAID BY RELIEF	0	-9	0	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	-1	-1	-2	-3	-3	-4	-3	-1
R&D COSTS (CHF MN) - PAID BY RELIEF	0	-5	-4	0	0	0	0	0	0	0	0
M&S (CHF MN)	0	0	-4	-4	-4	-4	-4	-4	-4	-5	-5
PROFIT BEFORE TAX (CHF MN)	**0**	**-14**	**-1**	**17**	**32**	**56**	**74**	**85**	**97**	**75**	**32**
PROFIT SPLIT 60/40 IN FAVOR OF RELIEF			60%	60%	60%	60%	60%	60%	60%	60%	60%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**-14**	**0**	**10**	**19**	**34**	**44**	**51**	**58**	**45**	**19**
TAXES (CHF MN)	0	0	0	-1	-2	-4	-5	-6	-6	-5	-2
PROFIT (CHF MN)	**0**	**-14**	**0**	**9**	**17**	**30**	**40**	**45**	**52**	**40**	**17**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF UREA CYCLE DISORDER (UCD) PATIENTS	12'718	12'845	12'974	13'103	13'234	13'367	13'500	13'635	13'772	13'909	14'048
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	10'174	10'276	10'379	10'483	10'587	10'693	10'800	10'908	11'017	11'128	11'239
ELIGIBLE UCD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE UCD PATIENTS	9'157	9'248	9'341	9'434	9'529	9'624	9'720	9'817	9'916	10'015	10'115
PENETRATION (%)	0%	0%	0%	1%	2%	3%	4%	5%	6%	7%	8%
NUMBER OF PATIENTS	0	0	0	94	191	289	389	491	595	701	809
ANNUAL TREATMENT COST PER PATIENT (CHF)	64'626	64'989	64'944	64'944	64'944	64'944	64'944	64'944	64'944	64'944	64'944
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**6**	**11**	**17**	**23**	**29**	**35**	**41**	**47**
CHANGE (%)					102%	52%	35%	26%	21%	18%	15%
15% ROYALTIES (CHF MN) - PAID TO ACER	0	0	0	-1	-2	-3	-3	-4	-5	-6	-7
UPFRONT & MILESTONES (CHF MN) - PAID TO ACER	0	0	-4	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	0	-1	-1	-1	-2	-2	-2	-3
R&D COSTS (CHF MN)	0	-1	-1	0	0	0	0	0	0	0	0
M&S (CHF)	0	-1	-4	-5	-5	-5	-5	-6	-6	-6	-6
PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-9**	**-1**	**4**	**8**	**13**	**17**	**22**	**27**	**31**
TAXES (CHF MN)	0	0	1	0	0	-1	-1	-2	-2	-3	-3
PROFIT (CHF MN)	**0**	**-1**	**-8**	**-1**	**3**	**7**	**11**	**15**	**19**	**24**	**28**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**7**	**27**	**49**	**80**	**105**	**123**	**142**	**124**	**86**
CHANGE (%)				291%	79%	63%	31%	17%	15%	-12%	-31%
GLOBAL SALES (USD MN)	**0**	**0**	**8**	**30**	**53**	**87**	**114**	**133**	**153**	**135**	**93**
CHANGE (%)				291%	79%	63%	31%	17%	15%	-12%	-31%
GLOBAL PROFIT (CHF MN)	**0**	**-15**	**-8**	**9**	**20**	**37**	**51**	**61**	**71**	**63**	**45**
CHANGE (%)			-47%	-206%	140%	81%	37%	20%	17%	-11%	-29%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**237**	
NUMBER OF SHARES (MN)	4'400	
NPV PER SHARE (CHF)	**0.054**	
SUCCESS PROBABILITY	80%	SECTION 505(B)(2)
RISK ADJUSTED NPV PER SHARE (CHF)	**0.043**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	100%	0.060	0.058	0.056	0.054	0.052	0.050	0.049
	95%	0.057	0.055	0.053	0.051	0.050	0.048	0.046
	90%	0.054	0.052	0.050	0.049	0.047	0.045	0.044
	85%	0.051	0.049	0.047	0.046	0.044	0.043	0.041
SUCCESS PROBABILITY	80%	0.048	0.046	0.045	**0.043**	0.042	0.040	0.039
	75%	0.045	0.043	0.042	0.040	0.039	0.038	0.037
	70%	0.042	0.040	0.039	0.038	0.037	0.035	0.034
	65%	0.039	0.038	0.036	0.035	0.034	0.033	0.032
	60%	0.036	0.035	0.033	0.032	0.031	0.030	0.029

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

II) ACER-001 MSUD - Peak sales CHF 80+ mn; rNPV CHF 0.015/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 are unable to 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. Other than a highly restricted diet of branched-chain amino acid (BCCA) free synthetic foods and formula, there are no currently approved treatments for MSUD.

POC of treatment with NaPB (active ingredient 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 both 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 the variable response which 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 inhibition of the BCKDC kinase to activate 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 could start in 2022 with a potential US and EU launch in 2024
Based on these encouraging POC trial results Acer and Relief plan to start phase IIb/III development of ACER-001 in MSUD in 2022 with a potential launch in the US and EU in 2024.

CHF 80+ mn peak sales in MSUD with first launches in 2024
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 ACER-001 treatment. Applying the same conservative pricing as for UCDs and market penetration ranging between 25% (US) and ~30% (EU) we forecast peak sales for ACER-001 in MSUD to amount to CHF 85 mn (for details see following page).

Forecasts & Sensitivity Analysis

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 120,000; 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; UPON COMPLETION OF THE DEFINITIVE ACER AGREEMENT PHASE II DEVELOPMENT WILL BE STARTED
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	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF MAPLE SYRUP URINE DISEASE (MSUD) PATIENTS	2'499	2'524	2'549	2'575	2'601	2'627	2'653	2'680	2'706	2'733	2'761
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	1'999	2'019	2'040	2'060	2'081	2'101	2'122	2'144	2'165	2'187	2'209
ELIGIBLE MSUD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE MSUD PATIENTS	1'799	1'817	1'836	1'854	1'873	1'891	1'910	1'929	1'949	1'968	1'988
PENETRATION (%)	0%	0%	0%	0%	12%	18%	21%	25%	23%	15%	10%
NUMBER OF PATIENTS	0	0	0	0	225	340	401	482	448	295	199
ANNUAL TREATMENT COST PER PATIENT (CHF)	109'990	109'378	110'821	114'146	117'570	121'097	124'730	128'472	132'326	136'296	140'385
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - ACER THERAPEUTICS BOOKS SALES	**0**	**0**	**0**	**0**	**24**	**37**	**45**	**56**	**53**	**36**	**25**
CHANGE (%)						56%	21%	24%	-4%	-32%	-31%
ROYALTIES (CHF MN) - PAID TO BAYLOR	0	0	0	0	0	-1	-1	-1	-1	-1	-1
UPFRONT & MILESTONES (CHF MN) - PAID BY RELIEF	0	0	0	0	0	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	0	-1	-1	-2	-2	-2	-1	-1
R&D COSTS (CHF MN) - PAID BY RELIEF	0	-2	-6	0	0	0	0	0	0	0	0
M&S (CHF MN)	0	0	0	-4	-4	-4	-4	-4	-4	-4	0
PROFIT BEFORE TAX (CHF MN)	**0**	**-2**	**-6**	**-4**	**19**	**31**	**39**	**49**	**47**	**30**	**23**
PROFIT SPLIT 60/40 IN FAVOR OF RELIEF			60%	60%	60%	60%	60%	60%	60%	60%	60%
RELIEF PROFIT BEFORE TAX (CHF MN) - BOOKED BY RELIEF	**0**	**-2**	**-3**	**-2**	**11**	**19**	**23**	**29**	**28**	**18**	**14**
TAXES (CHF MN)	0	0	0	0	-1	-2	-3	-3	-3	-2	-2
PROFIT (CHF MN)	**0**	**-2**	**-3**	**-2**	**10**	**17**	**21**	**26**	**25**	**16**	**12**

EUROPE - RELIEF TERRITORY	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF MAPLE SYRUP URINE DISEASE (MSUD) PATIENTS	3'311	3'344	3'377	3'411	3'445	3'480	3'515	3'550	3'585	3'621	3'657
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	2'649	2'675	2'702	2'729	2'756	2'784	2'812	2'840	2'868	2'897	2'926
ELIGIBLE MSUD PATIENTS (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
ELIGIBLE MSUD PATIENTS	2'384	2'408	2'432	2'456	2'481	2'505	2'531	2'556	2'581	2'607	2'633
PENETRATION (%)	0%	0%	0%	0%	5%	11%	15%	18%	21%	23%	25%
NUMBER OF PATIENTS	0	0	0	0	124	276	380	460	542	600	658
ANNUAL TREATMENT COST PER PATIENT (CHF)	64'626	64'989	64'944	64'944	64'944	64'944	64'944	64'944	64'944	64'944	64'944
PATIENT COMPLIANCE (%)	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%	90%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**7**	**16**	**22**	**27**	**32**	**35**	**38**
CHANGE (%)						122%	38%	21%	18%	11%	10%
15% ROYALTIES (CHF MN) - PAID TO ACER	0	0	0	0	-1	-2	-3	-4	-5	-5	-6
UPFRONT & MILESTONES (CHF MN) - PAID TO ACER	0	0	0	0	-2	0	0	0	0	0	0
COGS (CHF MN)	0	0	0	0	0	-1	-1	-2	-2	-2	-2
R&D COSTS (CHF MN)	0	-1	-1	0	0	0	0	0	0	0	0
M&S (CHF)	0	0	0	0	-5	-5	-5	-5	-6	-6	-6
PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-1**	**0**	**-1**	**8**	**12**	**16**	**20**	**22**	**25**
TAXES (CHF MN)	0	0	0	0	0	-1	-1	-2	-2	-2	-3
PROFIT (CHF MN)	**0**	**-1**	**-1**	**0**	**-1**	**7**	**11**	**14**	**17**	**20**	**22**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**31**	**53**	**67**	**83**	**85**	**71**	**64**
CHANGE (%)						72%	26%	23%	3%	-16%	-11%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**34**	**58**	**73**	**90**	**92**	**77**	**69**
CHANGE (%)						72%	26%	23%	3%	-16%	-11%
GLOBAL PROFIT (CHF MN)	**0**	**-3**	**-4**	**-2**	**9**	**24**	**32**	**40**	**42**	**36**	**34**
CHANGE (%)			38%	-48%	-561%	159%	34%	27%	5%	-16%	-4%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**184**	
NUMBER OF SHARES (MN)	4'400	
NPV PER SHARE (CHF)	**0.042**	
SUCCESS PROBABILITY	35%	POC ESTABLISHED
RISK ADJUSTED NPV PER SHARE (CHF)	**0.015**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.032	0.031	0.030	0.029	0.027	0.026	0.025
	65%	0.030	0.029	0.028	0.027	0.026	0.025	0.024
	60%	0.028	0.026	0.025	0.025	0.024	0.023	0.022
	55%	0.025	0.024	0.023	0.023	0.022	0.021	0.020
SUCCESS PROBABILITY	50%	0.023	0.022	0.021	0.021	0.020	0.019	0.018
	45%	0.021	0.020	0.019	0.019	0.018	0.017	0.016
	40%	0.018	0.018	0.017	0.017	0.016	0.015	0.015
	35%	0.016	0.015	0.015	**0.015**	0.014	0.013	0.013
	30%	0.014	0.013	0.013	0.013	0.012	0.011	0.011

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

Golike (Phenylketonuria - PKU)

I) Golike in PKU - Peak sales CHF 50+ mn; rNPV CHF 0.028/share

Global peak sales for the Golike family of food for special medical purposes (FSM) products for phenylketonuria (PKU) are guided to reach CHF 50+ mn. Golike has already been launched in Europe with the US to follow by September 2022. Development as a prescription-only treatment in the US could boost peak sales substantially to more than CHF 200 mn. A strong growth path has been established by APR with a clear life cycle management strategy through 2024 with the rollout of additional complementary Golike products. Golike is marketed by an own direct sales team in selected European countries as well as established distribution partners. Assuming average COGS of 25%, R&D costs of 5% and M&S of 15% during the product life cycle, we calculate an NPV of CHF 123 mn or CHF 0.028 per share (for details see page 63)

Golike – A complete family of FSMP engineered products for phenylketonuria (PKU)

The recent acquisition of APR expands Relief's pipeline further with compounds targeting rare inherited metabolic recessive disorders such as Golike for patients with phenylketonuria (PKU). Golike is the first line of food for special medical purposes (FSMP) products engineered with APR's drug delivery Physiomimic™ Technology offering an improved metabolic management for patients with PKU and a better compliance thanks to minimized taste, odor and aftertaste. The proprietary and patented Physiomimic™ Technology is the first and only technology able to control and prolong release of multiple active ingredients (up to 19 amino acid mixes) simultaneously in the most prevalent, rare, inherited metabolic diseases. Beyond 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 treatment of this disease and possesses effective taste-masking properties. Golike was approved in the EU in 2018. A direct sales and marketing team is in place in selected European countries to support Golike, as well as established distribution partnerships for other countries in Europe and beyond. US commercial launch is planned to start no later than by September 2022.

PKU patients must maintain a lifelong strict diet to have a normal life span

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 low birth weight. PKU affects on average about 1 in 10,000 newborns in develop countries. Males and females are affected equally. Approximately 350,000 patients suffer from PKU in the world's key markets.

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 to be continued for life. Patients who are diagnosed early and maintain a strict diet can have normal health and a normal life

span. 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 to the prescribed diet. As seen on evidence, compliance becomes increasingly difficult with age due to diverse factors. Bad taste, odor and aftertaste of amino acid-based protein substitutes are still a big issue that generate an important number of adults out of diet. Moreover, scientific evidence indicates that significant sub-optimal health outcomes still exist 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.

Golike's minimized taste, odor and aftertaste offers better patient compliance

Golike is the first controlled-release amino acid mix product with effective taste and odor masking. With these characteristics, Golike is a uniquely differentiated product, offering improved metabolic management and better compliance for PKU patients of all age groups. The Golike line of products include sachets, shake and drink to be merged in a unique Ready to Drink formulation, while Golike krunch and bars will be launched soon and extended with different flavors over time.

Relief to expand APR's European sales infrastructure and seek US approval

Following APR's launch of Golike in Europe in 2018, Relief is planning to expand the commercial infrastructure beyond the current countries and to refine the marketing activities to increase and accelerate future growth. In other countries, Golike is available as a prescription only, fully reimbursed product for PKU. In the US, Golike has been granted Orphan Drug Designation, and Relief intends to assess options to pursue approval of Golike as a prescription product. US commercial launch is expected by September 2022. A strong growth path has been established by APR with a clear life cycle management strategy through 2024 with the rollout of additional complementary Golike products. Global peak sales for the Golike family of FSMP products for PKU are guided to reach CHF 50+ mn. Development as a prescription-only treatment with significantly in the US could boost peak sales substantially to more than CHF 200 mn.

GOLIKE - FINANCIAL FORECASTS FOR PHENYLKETONURIA (PKU)

REVENUE MODEL

EUROPE / US - RELIEF SALES FORCE	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
GOLIKE B2C PRODUCT SALES (CHF MN)	0.711										
GOLIKE B2B PRODUCT SALES (CHF MN)	1.112										
SALES (CHF MN) - RELIEF BOOKS SALES	**2**	**2**	**4**	**9**	**12**	**17**	**23**	**30**	**37**	**45**	**51**
CHANGE (%)	-32%	-1%	138%	99%	42%	41%	35%	30%	25%	20%	15%
COGS (%)		25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
COGS (CHF MN)		0	-1	-2	-3	-4	-6	-7	-9	-11	-13
R&D (%)		5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
R&D COSTS (CHF MN)		0	0	0	-1	-1	-1	-1	-2	-2	-3
M&S (%)		15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
M&S (CHF)		0	-1	-1	-2	-3	-3	-4	-6	-7	-8
PROFIT BEFORE TAX (CHF MN)		**1**	**2**	**5**	**7**	**9**	**13**	**16**	**21**	**25**	**28**
TAXES (CHF MN)		0	0	0	-1	-1	-1	-2	-2	-3	-3
PROFIT (CHF MN)	**0**	**1**	**2**	**5**	**6**	**8**	**11**	**15**	**18**	**22**	**25**

	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
GLOBAL SALES (CHF MN)	**2**	**2**	**4**	**9**	**12**	**17**	**23**	**30**	**37**	**45**	**51**
CHANGE (%)	-32%	-1%	138%	99%	42%	41%	35%	30%	25%	20%	15%
GLOBAL SALES (USD MN)	**2**	**2**	**5**	**9**	**13**	**18**	**25**	**32**	**40**	**48**	**56**
CHANGE (%)	-29%	-1%	135%	99%	42%	41%	35%	30%	25%	20%	15%
GLOBAL PROFIT (CHF MN)	**0**	**1**	**2**	**5**	**6**	**8**	**11**	**15**	**18**	**22**	**25**
CHANGE (%)			138%	99%	26%	41%	35%	30%	25%	20%	15%
WACC (%)	7%										
NPV TOTAL PROFIT (CHF MN)	**123**										
NUMBER OF SHARES (MN)	4'400										
NPV PER SHARE (CHF)	**0.028**										

ESTIMATES AS OF 21 FEBRUARY 2022

SOURCE: VALUATIONLAB ESTIMATES

APR-TD011 (Epidermolysis bullosa - EB)

I) APR-TD011 in EB - Peak sales CHF 900+ mn; rNPV CHF 0.170/share

We forecast global peak sales of more than CHF 900 mn for APR-TD011 in epidermolysis bullosa (EB) with first launches to occur in 2026. In the US, APR-TD011 will enjoy at least 7-years orphan drug market exclusivity based on granted ODD. In the EU, Relief will seek ODD, which would provide 10-years 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 a rNPV of CHF 748 mn or CHF 0.170 per share assuming an 35% (POC) success rate and accounting for COGS of 5%, R&D costs of roughly CHF 20 mn and M&S costs of ranging between CHF 15-25 mn for each region. (for details see page 66)

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

APR-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 a 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 with 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 commonly in males and females.

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

APR-TD011 was granted Orphan Drug Designation (ODD) in late 2019 by the US FDA. In a preliminary clinical trial, EB patients administered with APR-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. APR-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 APR-TD011, the sprayable hypochlorous acid (HCIO) solution, is approved as a Class III medical device under the Nexodyn brand for treating acute and chronic wounds.

Potentially pivotal phase IIb trial to start in 2022 after discussions with regulators

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. In particular, when taking into account 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 June 2021, The FDA granted Priority Review (6 months instead of 10) for Oleogel-S10 with a 30 November 2021 Prescription Drug User Fee Act (PDUFA) date by when the FDA has to complete its review. Relief plans to discuss next development steps with regulatory authorities later this year, with the goal of initiating a phase II phase IIb dose ranging trial in mid-2022. First launches of ADR-TD011 in EB could occur in 2026. In the US, the compound will enjoy at least 7-years orphan drug exclusivity from day of approval. Relief plans to apply for ODD in the EU, which will provide at least 10-years market exclusivity from approval if granted by the EMA.

Peak sales potential of CHF 900+ mn with first launches expected in 2026

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 APR-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 2026, 7-years 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 APR-TD011 in EB could easily amount to more than CHF 900+ mn in the US and the EU (for details see following page).

Forecasts & Sensitivity Analysis

APR-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; PHASE II CLINICAL TRIAL EXPECTED TO START IN MID-2022; FIRST LAUNCHES GUIDED FOR 2026
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	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF EPIDERMOLYSIS BULLOSA (EB) PATIENTS	25'250	25'503	25'758	26'015	26'275	26'538	26'803	27'071	27'342	27'616	27'892
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	12'625	12'751	12'879	13'008	13'138	13'269	13'402	13'536	13'671	13'808	13'946
PENETRATION (%)	0%	0%	0%	0%	0%	0%	10%	25%	35%	43%	48%
NUMBER OF PATIENTS	0	0	0	0	0	0	1'340	3'384	4'785	5'937	6'694
ANNUAL TREATMENT COST PER PATIENT (CHF)	64'161	63'804	64'645	66'585	68'582	70'640	72'759	74'942	77'190	79'506	81'891
PATIENT COMPLIANCE (%)	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**0**	**93**	**241**	**351**	**448**	**521**
CHANGE (%)								160%	46%	28%	16%
COGS (%)	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
COGS (CHF MN)	0	0	0	0	0	0	-5	-12	-18	-22	-26
R&D COSTS (CHF MN)	0	0	-4	-5	-6	-2	0	0	0	0	0
M&S (CHF MN)	0	0	0	0	0	-9	-23	-21	-18	-18	-18
PROFIT BEFORE TAX (CHF MN)	**0**	**0**	**-4**	**-2**	**-2**	**-11**	**65**	**208**	**315**	**408**	**476**
TAXES (CHF MN)	0	0	0	0	0	1	-7	-23	-35	-45	-52
PROFIT (CHF MN)	**0**	**0**	**-4**	**-2**	**-2**	**-10**	**58**	**185**	**280**	**363**	**424**

EUROPE - RELIEF SALES FORCE	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NUMBER OF EPIDERMOLYSIS BULLOSA (EB) PATIENTS	34'072	34'413	34'757	35'105	35'456	35'810	36'168	36'530	36'895	37'264	37'637
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	17'036	17'207	17'379	17'552	17'728	17'905	18'084	18'265	18'448	18'632	18'819
PENETRATION (%)	0%	0%	0%	0%	0%	0%	8%	23%	33%	41%	46%
NUMBER OF PATIENTS	0	0	0	0	0	0	1'447	4'201	6'088	7'639	8'657
ANNUAL TREATMENT COST PER PATIENT (CHF)	43'084	43'326	43'296	43'296	43'296	43'296	43'296	43'296	43'296	43'296	43'296
PATIENT COMPLIANCE (%)	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%	95%
SALES (CHF MN) - RELIEF BOOKS SALES	**0**	**0**	**0**	**0**	**0**	**0**	**60**	**173**	**250**	**314**	**356**
CHANGE (%)								190%	45%	25%	13%
COGS (%)	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%	8%
COGS (CHF MN)	0	0	0	0	0	0	-4	-13	-19	-24	-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	-8	-18	-14	-12	-12	-12
PROFIT BEFORE TAX (CHF MN)	**0**	**-1**	**-2**	**-2**	**-2**	**-10**	**37**	**146**	**220**	**279**	**317**
TAXES (CHF MN)	0	0	0	0	0	1	-4	-16	-24	-31	-35
PROFIT (CHF MN)	**0**	**-1**	**-2**	**-2**	**-2**	**-9**	**33**	**130**	**195**	**248**	**282**

	2020E	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
GLOBAL SALES (CHF MN)	**0**	**0**	**0**	**0**	**0**	**0**	**152**	**414**	**601**	**763**	**877**
CHANGE (%)								172%	45%	27%	15%
GLOBAL SALES (USD MN)	**0**	**0**	**0**	**0**	**0**	**0**	**165**	**448**	**651**	**826**	**949**
CHANGE (%)								172%	45%	27%	15%
GLOBAL PROFIT (CHF MN)	**0**	**-1**	**-6**	**-4**	**-3**	**-19**	**91**	**315**	**476**	**611**	**706**
CHANGE (%)			469%	-32%	-11%	448%	-584%	247%	51%	28%	16%

WACC (%)	7%	
NPV TOTAL PROFIT (CHF MN)	**2'138**	
NUMBER OF SHARES (MN)	4'400	
NPV PER SHARE (CHF)	**0.486**	
SUCCESS PROBABILITY	35%	POC ESTABLISHED IN WOUND HEALING
RISK ADJUSTED NPV PER SHARE (CHF)	**0.170**	

SENSITIVITY ANALYSIS

		WACC (%)						
	CHF/SHARE	5.5	6.0	6.5	7.0	7.5	8.0	8.5
	70%	0.387	0.371	0.355	0.340	0.326	0.312	0.300
	65%	0.359	0.344	0.330	0.316	0.303	0.290	0.278
	60%	0.332	0.318	0.304	0.291	0.279	0.268	0.257
	55%	0.304	0.291	0.279	0.267	0.256	0.246	0.235
SUCCESS PROBABILITY	50%	0.276	0.265	0.254	0.243	0.233	0.223	0.214
	45%	0.249	0.238	0.228	0.219	0.210	0.201	0.193
	40%	0.221	0.212	0.203	0.194	0.186	0.179	0.171
	35%	0.193	0.185	0.177	**0.170**	0.163	0.156	0.150
	30%	0.166	0.159	0.152	0.146	0.140	0.134	0.128

ESTIMATES AS OF 21 FEBRUARY 2022 SOURCE: VALUATIONLAB ESTIMATES

Management Team

Lean management team to rapidly expand as company evolves
Relief's management team strategy is to maintain a lean internal structure and a series of collaborations with relevant worldwide experts. The management team works collectively to execute all duties traditionally assigned to a CEO. Relief is firstly focused on building the right team to see RLF-100 through clinical development and to expand the management team as the company evolves. In parallel, the company is setting up a team of experts to handle all commercial aspects associated with a potential approval of RLF-100 to ensure reaching patients timely.

Management biographies

Jack Weinstein (Chief Financial Officer and Treasurer)
Jack Weinstein joined Relief in October 2020 as its US based Chief Financial Officer and Treasurer. 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.

Taneli Jouhikainen (Chief Operating Officer)
Dr. Taneli Jouhikainen has over 25 years of life sciences expertise. He joins Relief from Savara, a Nasdaq-listed clinical stage biopharmaceutical company focused on rare respiratory diseases, where he was Co-Founder and President & COO. Prior to this, he served at Akela Pharma Inc., a public clinical stage specialty pharmaceutical company focused on orphan drugs and inhalation products, first as Head of Corporate Development and subsequently as CEO until the company's merger with Nventa Biopharmaceuticals. He served in senior executive roles at various other life sciences companies, including LAB International, Inc. and Focus Inhalation Oy, and was Head of Clinical Development at Leiras, a subsidiary of Schering AG. Dr. Jouhikainen holds an M.D. and a Ph.D. in hematology and immunology from the University of Helsinki and an MBA from the Helsinki School of Economics.

Anthony M. Kim (Head US Commercial Operations)
Prior to joining Relief, for the past three years, Mr. Kim was Vice President, Global Commercial Development at Novocure, where he led a 21-person team in the planning and

U.S. marketing execution for that company's Optune® and Optune Lua™, FDA-approved, therapeutic devices that deliver alternating electrical fields to treat patients with Glioblastoma Multiforme and Mesothelioma. From 2017 to 2018, he was Executive Director of Marketing at Ignyta (subsequently acquired by Roche), during which time he led the development of the commercial launch plan for entrectinib, an oral, oncologic agent in pan-tumor clinical trials for patients with neurotrophic tyrosine receptor kinase (NTRK) and ROS1 fusion-positive disease. From 2012 to 2017, Mr. Kim held positions of increasing responsibility at Alexion Pharmaceuticals, Inc., most recently serving as Director, Head of U.S. Marketing, Hypophosphatasia, where he managed the U.S. marketing efforts for the launch of Strensiq, a novel, first-in-class enzyme replacement therapy for the treatment of hypophosphatasia, a rare inherited metabolic bone disorder. Earlier, from 2004 to 2012, Mr. Kim held various positions at Genentech, including Product Manager, Herceptin Marketing and Divisional Sales Manager, Rituxan Hematology. Mr. Kim received his Bachelor of Arts Degree from Harvard University and a Master of Business Administration from The Wharton School.

Paolo Galfetti (President of Relief Europe)
Paolo Galfetti is the CEO of APR Applied Pharma Research S.A. He 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.

Gilles della Corte, M.D. (Chief Medical Officer)
Gilles Della Corte, M.D., joined Relief in September 2020 as Chief Medical Officer. At Relief, Gilles is responsible for the clinical development of RLF-100 in Europe and coordinating closely with NRx, which is responsible for clinical trials in the US, as well as interactions with and submissions to regulatory authorities. He brings over 40 years of professional experience, including 30 years in the biopharmaceutical industry. Gilles held several senior clinical research positions at Merck Serono (previously Serono), where he was responsible for the development from proof of concept to life cycle management of projects in several disease areas, including cardiology, rheumatology, oncology and endocrinology. Earlier in his career, he also held positions of increasing responsibility at several clinical research organizations (CROs), pharmaceutical and start-up companies, including Rhone-Poulenc-Rorer, Servier, Solvay Pharma, as well as Phoenix Life Sciences, Larime, Omnicare Clinical Research, Therapharm, and Anergis. In 2016, Dr. Della Corte founded Dellmed Consulting, providing strategic advice and hands-on support for clinical development in various therapeutic areas, such as dermatology, oncology, allergy, and for CRO selection for companies ranging from biotech start-ups to well established pharmaceutical companies. Gilles holds an M.D. from Paris-Sud University (Paris XI) and is a Board-certified cardiologist with ten years of hospital practice.

Jeremy Meinen (VP Finance and Administration)
Jeremy Meinen joined Relief as ad-interim Chief Financial Officer in April 2020 and now serves as principal finance and accounting officer. 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.

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 has 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 post graduate 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 15 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 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. in biological sciences and technical writing from Carnegie Mellon University.

Tom Plitz (Member 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 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 counselling 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 (President of Relief Europe)
See biography above.

Income Statement

RELIEF THERAPEUTICS									SHARE PRICE (CHF)	0.068	
IFRS											
INCOME STATEMENT (CHF MN)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
PRODUCT SALES (INCL. PARTNER SALES)	**0**	**43**	**146**	**340**	**526**	**771**	**1'254**	**1'642**	**1'915**	**2'128**	**2'245**
CHANGE (%)			241%	132%	55%	46%	63%	31%	17%	11%	5%
PRODUCT SALES (RELIEF THERAPEUTICS)	**0**	**4**	**9**	**90**	**178**	**270**	**503**	**667**	**819**	**971**	**1'090**
CHANGE (%)			145%	870%	99%	51%	86%	33%	23%	18%	12%
ROYALTIES	**0**	**6**	**14**	**6**	**4**	**2**	**-1**	**-4**	**-7**	**-9**	**-11**
CHANGE (%)			144%	-56%	-30%	-52%	-134%	455%	73%	35%	24%
UPFRONT AND MILESTONE PAYMENTS	**0**	**-9**	**-4**	**0**	**-2**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE (%)			-59%	-100%		-100%					
OTHER REVENUES	**0.3**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE (%)	76%	226%	-100%								
REVENUES (EXCL. PARTNER SALES)	**0.3**	**1**	**20**	**96**	**181**	**272**	**502**	**664**	**813**	**962**	**1'079**
CHANGE (%)	76%	364%	1444%	391%	88%	51%	85%	32%	22%	18%	12%
COGS	**0**	**-3**	**-7**	**-10**	**-13**	**-18**	**-39**	**-64**	**-81**	**-97**	**-107**
CHANGE (%)			168%	34%	36%	31%	124%	62%	27%	20%	11%
GROSS PROFIT	**0.3**	**-1**	**12**	**86**	**167**	**254**	**463**	**600**	**732**	**865**	**971**
CHANGE (%)	76%	-640%	-927%	606%	94%	52%	82%	30%	22%	18%	12%
MARGIN (%)		-117%	62%	90%	93%	94%	92%	90%	90%	90%	90%
RESEARCH & DEVELOPMENT	**-13.7**	**-29**	**-52**	**-25**	**-22**	**-9**	**-1**	**-1**	**-2**	**-2**	**-3**
CHANGE (%)	20006%	113%	78%	-51%	-13%	-59%	-87%	30%	25%	20%	15%
MARKETING & SALES	**0**	**-2**	**-15**	**-52**	**-73**	**-96**	**-132**	**-62**	**-53**	**-52**	**-53**
CHANGE (%)			557%	237%	41%	32%	37%	-53%	-14%	-2%	1%
GENERAL & ADMINISTRATIVE	**-6**	**-8**	**-10**	**-12**	**-14**	**-16**	**-19**	**-22**	**-26**	**-31**	**-37**
CHANGE (%)	541%	35%	33%	16%	17%	17%	17%	18%	18%	18%	19%
OTHER GAINS/LOSSES	**-1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
OPERATING COSTS	**-21**	**-42**	**-85**	**-99**	**-122**	**-138**	**-191**	**-149**	**-162**	**-182**	**-200**
CHANGE (%)	1923%	103%	103%	16%	23%	14%	38%	-22%	9%	12%	10%
OPERATING COSTS (PER MONTH)	1.7	3.5	7.1	8.2	10.1	11.5	15.9	12.4	13.5	15.2	16.7
EBITDA	**-20**	**-41**	**-65**	**-3**	**59**	**134**	**311**	**514**	**650**	**780**	**879**
CHANGE (%)	2256%	100%	61%	-96%	-2289%	126%	133%	65%	27%	20%	13%
IMPAIRMENT (LOSS)/REVERSAL	**11**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
D&A	**0**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**
OPERATING RESULT	**-9**	**-40**	**-64**	**-2**	**60**	**135**	**312**	**515**	**652**	**781**	**880**
CHANGE (%)	-25%	337%	62%	-97%	-3677%	124%	132%	65%	26%	20%	13%
MARGIN (%)		-3136%	-329%	-2%	33%	50%	62%	78%	80%	81%	82%
GAIN FROM DISPOSAL OF A SUBSIDIARY	3										
NET FINANCIAL INCOME/(EXPENSES)	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**	**-1**
PROFIT/LOSS BEFORE TAXES BEFORE PROFIT SPLIT	**-6**	**-40**	**-65**	**-2**	**60**	**134**	**312**	**515**	**651**	**780**	**879**
CHANGE (%)	-49%	543%	61%	-97%	-2761%	125%	132%	65%	26%	20%	13%
MARGIN (%)		-3180%	-331%	-2%	33%	49%	62%	78%	80%	81%	82%
PROFIT SPLIT AGREEMENT WITH NRX & ACER											
- PROFITS RECEIVED FROM NRX/ACER		0	-1	83	137	202	306	421	480	511	507
- PROFITS PAID TO NRX		0	0	0	-7	-16	-21	-14	-6	-2	1
PROFIT/LOSS BEFORE TAXES - AFTER PROFIT SPLIT	**-6**	**-40**	**-66**	**81**	**190**	**320**	**597**	**922**	**1'125**	**1'290**	**1'387**
CHANGE (%)	-49%	537%	66%	-222%	135%	69%	87%	54%	22%	15%	8%
MARGIN (%)		-3153%	-338%	84%	105%	118%	119%	139%	138%	134%	129%
TAXES	**-2**	**0**	**7**	**-9**	**-21**	**-35**	**-66**	**-101**	**-124**	**-142**	**-153**
TAX RATE (%)	-25%	0%	11%	11%	11%	11%	11%	11%	11%	11%	11%
NET PROFIT/LOSS	**-8**	**-40**	**-59**	**72**	**169**	**285**	**531**	**821**	**1'001**	**1'148**	**1'235**
CHANGE (%)	5%	410%	48%	-222%	135%	69%	87%	54%	22%	15%	8%
MARGIN (%)		-3153%	-301%	75%	93%	105%	106%	124%	123%	119%	114%
EPS (CHF)	**-0.003**	**-0.009**	**-0.013**	**0.016**	**0.038**	**0.065**	**0.121**	**0.186**	**0.228**	**0.261**	**0.281**
CHANGE (%)	-9%	180%	48%	-222%	135%	69%	87%	54%	22%	15%	8%

ESTIMATES AS OF 21 FEBRUARY 2022 SOURCE: VALUATIONLAB ESTIMATES

Ratios I Balance Sheet I Cash Flow Statement

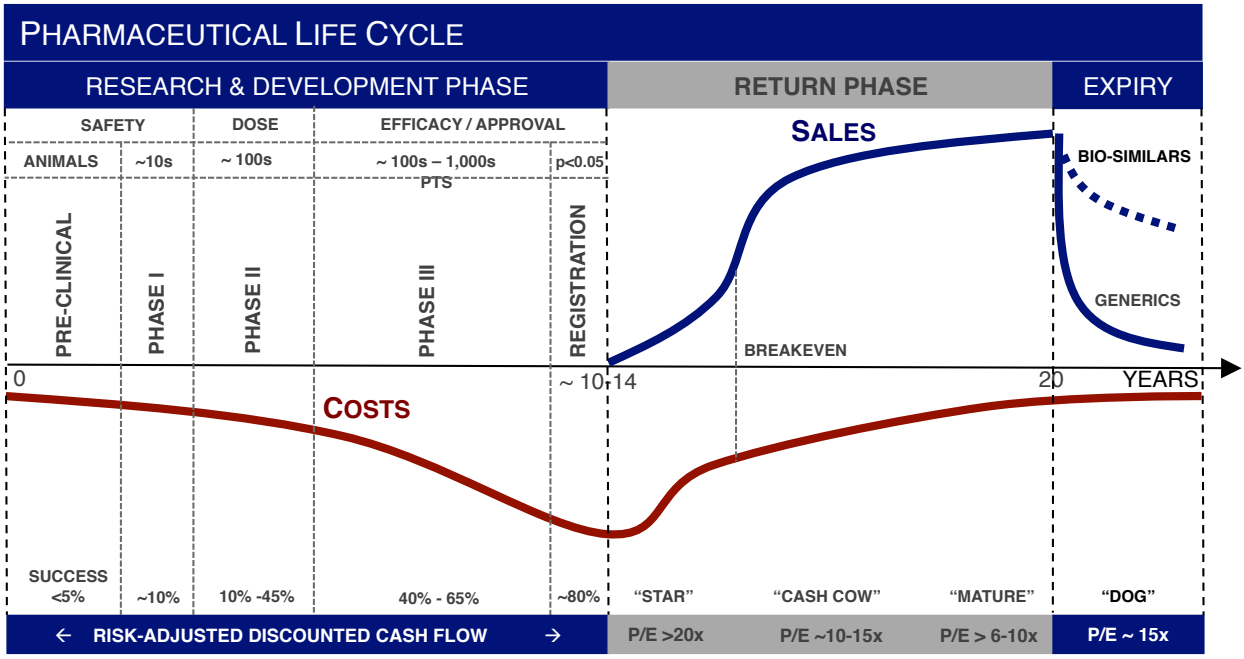
RELIEF THERAPEUTICS									SHARE PRICE (CHF)	0.068
IFRS										
RATIOS	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
P/E		-7.5x	-5.1x	4.2x	1.8x	1.1x	0.6x	0.4x	0.3x	0.3x	0.2x
P/S		236.5x	15.3x	3.1x	1.7x	1.1x	0.6x	0.5x	0.4x	0.3x	0.3x
P/NAV		4.6x	8.6x	2.8x	1.1x	0.5x	0.3x	0.2x	0.1x	0.1x	0.1x
EV/EBITDA		-6.4x	-4.0x	-151.1x	4.2x	1.9x	0.8x	0.5x	0.4x	0.3x	0.3x
PER SHARE DATA (CHF)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
EARNINGS	**-0.003**	**-0.009**	**-0.013**	**0.016**	**0.038**	**0.065**	**0.121**	**0.186**	**0.228**	**0.261**	**0.281**
CHANGE (%)	-9%	180%	48%	-222%	135%	69%	87%	54%	22%	15%	8%
CASH	**0.018**	**0.009**	**0.002**	**0.019**	**0.057**	**0.121**	**0.242**	**0.428**	**0.655**	**0.916**	**1.196**
CHANGE (%)	29064%	-48%	-73%	653%	205%	114%	99%	77%	53%	40%	31%
DIVIDENDS	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
PAYOUT RATIO (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
NET ASSET VALUE	**0.028**	**0.015**	**0.008**	**0.024**	**0.062**	**0.127**	**0.247**	**0.433**	**0.661**	**0.921**	**1.202**
CHANGE (%)	309%	-47%	-46%	204%	159%	104%	95%	75%	52%	39%	30%
BALANCE SHEET (CHF MN)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NET LIQUID FUNDS	**43.2**	**41**	**11**	**82**	**250**	**533**	**1'063**	**1'883**	**2'883**	**4'030**	**5'263**
TOTAL ASSETS	**78.0**	**76**	**46**	**117**	**284**	**568**	**1'098**	**1'918**	**2'918**	**4'065**	**5'298**
TOTAL SHAREHOLDERS' EQUITY	**67.0**	**65**	**35**	**106**	**273**	**557**	**1'087**	**1'907**	**2'907**	**4'054**	**5'287**
CHANGE (%)	369%	-4%	-46%	204%	159%	104%	95%	75%	52%	39%	30%
RETURN ON EQUITY (%)	-12%	-62%	-169%	68%	62%	51%	49%	43%	34%	28%	23%
TOTAL EQUITY	**67.0**	**65**	**35**	**106**	**273**	**557**	**1'087**	**1'907**	**2'907**	**4'054**	**5'287**
FINANCIAL DEBT	**0.0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
EMPLOYEES	5	49	59	68	78	86	94	104	109	114	120
CHANGE (%)	0%	880%	20%	15%	15%	10%	10%	10%	5%	5%	5%
CASH FLOW STATEMENT (CHF MN)	**2020**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**
NET PROFIT / (LOSS)	-7.8	-40	-59	72	169	285	531	821	1'001	1'148	1'235
DEPRECIATION & AMORTIZATION	0.0	-1	-1	-1	-1	-1	-1	-1	-1	-1	-1
OTHER NON-CASH ITEMS	-10.4	0	0	0	0	0	0	0	0	0	0
NET CASH USED IN OPERATING ACTIVITIES	**-18.3**	**-41**	**-60**	**71**	**168**	**284**	**530**	**819**	**1'000**	**1'147**	**1'233**
FREE CASH FLOW	**-15.2**	**-72**	**-60**	**71**	**168**	**284**	**530**	**819**	**1'000**	**1'147**	**1'233**
CASH FLOW FROM FINANCING ACTIVITIES	**58.2**	**70**	**30**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
CHANGE IN LIQUID FUNDS	**43.0**	**-2**	**-30**	**71**	**168**	**284**	**530**	**819**	**1'000**	**1'147**	**1'233**
ESTIMATES AS OF 21 FEBRUARY 2022									SOURCE: VALUATIONLAB ESTIMATES	

NOTE: With cash and cash equivalents of CHF 45 mn, Relief expects to fund operations into late 2023 without factoring in potential revenues from RLF-100 sales, which could commence in 2022 and the CHF 50 mn share subscription facility with GEM. The company is fully financed to successfully complete the US "AVICOVID-2" trial of RLF-100 INHALED in prevention COVID-19 related ARDS (started in February 2021) as well as the planned EU RLF-100 trials expected to start in 2022. Relief may need a maximum of CHF 25-30 mn in additional funding to reach positive operating cash flow status before the end of 2024, which is dependent upon timely approval of ACER-001 in the US.

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

Important Research Disclosures

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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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