Relief Therapeutics Holding AG

Switzerland | Biotechnology

Initiation of Coverage

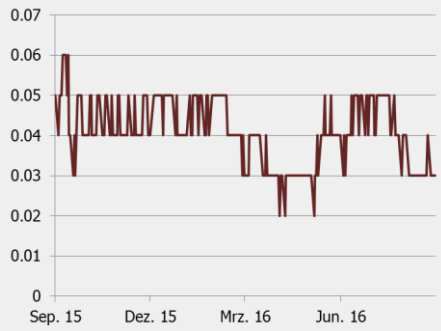
26 September 2016

Company Data

Price:	CHF 0.03
Market Cap:	CHF58m
Free Float (%):	12.8%
Nr. Of shares:	1'946'627'375
Avg. traded vol. (1 year):	445'727
Bloomberg:	RLF SW
Reuters:	RLFB.S
ISIN:	CH0100191136

Source: SIX Swiss Exchange and Bloomberg

Share Price Development



Source: Bloomberg

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Addressing diabetes and respiratory disease

Relief Therapeutics Holding AG ('Relief Therapeutics' or 'Relief' or 'the company') is a Switzerland-based biotechnology company developing a rich pipeline of candidates, primarily aimed at diabetic complications and respiratory diseases. The company is currently developing two drug candidates; Aviptadil, set to enter a pivotal Phase III trial in sarcoidosis, and Atexakin alfa, aimed at peripheral neuropathies, which is slated to enter Phase II testing in patients with diabetic neuropathy. Both studies could start in the first half of 2017. Atexakin alfa is the subject of a worldwide exclusive license from Merck KGaA and was originally developed by Serono S.A.

- **Attractive potential in underserved markets**

  The company is developing drug candidates to address markets in which there currently are no approved effective therapies. While Aviptadil targets orphan disease indications, including sarcoidosis and acute lung injury (ALI), Atexakin alfa (recombinant human interleukin-6, or rhIL-6) targets larger markets, including peripheral diabetic neuropathy (PDN) and chemotherapy-induced peripheral neuropathy (CIPN). Given the benign safety profile of Aviptadil and the lack of existing treatments for sarcoidosis, we anticipate higher penetration rates and pricing power in future for Aviptadil targeted for sarcoidosis. Atexakin alfa, on the other hand, could constitute the basis for a new class of neuropathy-targeting anti-nociceptive (pain-suppressing) drugs that may treat both the pain-related and non-pain related symptoms due to diabetes-induced neuropathic complications. We believe this market is yet to be established and expanded, and could help the company to establish a substantial commercial franchise.

- **Commercial exclusivity through proprietary patents and orphan drug designations**

  Relief has 23 patent families and 10 orphan drug designations in the EU and the US for its candidates across a range of indications. For Aviptadil, the oldest patent expires in 2026, while for Atexakin alfa, the first patent (for DN) expires in 2022/2023, with potential for five years of term extension in the US under Hatch-Waxman rules. We also note that Atexakin alfa is a biologic agent, which would be entitled to a minimum of 10 years of market exclusivity in Europe and 12 years in the US. In our view, the company is well-positioned with lengthy commercial windows for both of its lead product candidates.

- **Strengthening the pipeline through acquisitions**

  Relief recently executed a term sheet to acquire FirstString Research Inc., a US-based biotechnology company, in an all-stock transaction. The proposed acquisition could reinforce Relief's pipeline by bringing in Granexin gel, a Phase III-ready drug candidate, indicated for the treatment of Diabetic Foot Ulcers (DFUs) and Venous Leg Ulcers (VLUs). We think that the company may seek to consummate similar acquisitions/ partnerships in future to consolidate its market position.

- **Valuation**

  We have valued Relief using a risk-adjusted Net Present Value (rNPV) approach. Using a discount rate of 22.9%, we have calculated an rNPV of CHF99.6mn for Aviptadil in sarcoidosis, based on favourable Ph II safety and efficacy data. We estimate peak sales for Aviptadil for sarcoidosis to be CHF290.0mn. Atexakin alfa for DN has been assigned an rNPV of CHF194.6mn using a 22.9% discount rate. Aviptadil for ALI has been assigned an rNPV of CHF96.8mn using the same discount rate. In summary, we derive a total firm value of CHF356.4mn or a share value of CHF0.19, based on 1,937 million shares as of September 2016. Under the condition that Relief Therapeutics will be able to raise sufficient funding for its current programs, we believe the stock offers attractive upside potential from current levels.

Important disclosures are on the last page of this report. Relief Therapeutics Holding AG is a research client of Research Dynamics. The equity research reports are prepared for informational purposes only.

TABLE OF CONTENTS

INVESTMENT HIGHLIGHTS

Attractive drug pipeline addressing major unmet medical needs

- **Focus on orphan disease indications with Aviptadil**

  We consider Relief to have significant upside given its targeting of orphan disease indications (sarcoidosis and ALI), which are substantial unmet medical needs. For sarcoidosis, there are no drugs approved specifically to treat this disorder. Systemic corticosteroids like prednisone are currently used to treat sarcoidosis patients. These, however, are associated with many side effects, including excessive weight gain, acne, diabetes, high blood pressure, glaucoma, cataracts and osteoporosis, among others. In ALI too, apart from putting patients on mechanical ventilators, there is currently no approved therapy available. Phase II clinical data with Aviptadil has demonstrated a benign safety profile and efficacy on lung function parameters that bode well, in our view, for sarcoidosis and ALI sufferers.

  In our view, therefore, the company has the potential to penetrate the market as an early market entrant in providing a novel solution for the treatment of these two indications. This could also allow the company to charge a premium price for Aviptadil in the US, in keeping with other orphan drug examples.

  Beyond its potential in orphan disease areas like sarcoidosis and ALI, Aviptadil may have applicability in far larger markets as well. These include chronic obstructive pulmonary disease (COPD) and pulmonary arterial hypertension (PAH), potentially billion-dollar market opportunities for the company.

- **Disease modifying anti neuropathic drugs (DeMANDs) for the treatment of peripheral neuropathies**

  The company is also developing Atexakin alfa (a low-dosage formulation of human interleukin-6 (IL-6), which could represent a new class of drugs to address both painful and non-painful symptoms of peripheral neuropathy.

  Current treatments, such as Lyrica (pregabalin), address only the pain-related facets of DN. These drugs completely neglect the non-pain related symptoms such as loss of balance, lack of sensation and autonomic dysfunctions (heart, bladder, sexual and digestive function) that negatively impact quality of life. Thus far, no disease-modifying drugs have been approved to treat peripheral neuropathies. This, coupled with the fact that the World Health Organization (WHO) projects the number of worldwide DN patients to exceed 300 million in 2050, may present an attractive commercial opportunity in our view.

- **Potentially best-in-class treatment for chronic wounds**

  Relief has executed a term sheet to acquire FirstString Research, Inc., a privately-held US biotechnology firm based in Charleston, South Carolina. FirstString's lead drug candidate, Granexin gel, is entering Phase III development. Granexin targets chronic wounds and has generated positive Phase II data in a series of randomized, double-blinded, controlled clinical trials. The drug is administered topically on a once-weekly basis, providing a high degree of convenience that should allow long-term compliance. Diabetic foot ulcers (DFUs), which represent a particularly difficult-to-treat chronic wound type, represent a common comorbidity of diabetes and typically present in the same diabetic patients who suffer from peripheral neuropathy. Thus, we believe there are strong synergies between Atexakin alfa and Granexin, and that these two agents could potentially target overlapping patient populations. FirstString has also built a promising pipeline around the same technology platform that gave rise to Granexin, with applicability in areas such as ophthalmology, acute wound care and counterterrorism.

Financing backed by a global investor

The company, currently, has a CHF25.0mn Share Subscription Facility (SSF) in place with GEM Global Yield Fund LLC S.C.S. and GEM Investments America, LLC (collectively 'GEM'). Under this facility, the company can issue shares up to CHF25.0mn to GEM (valid until December 2018), subject to the company's trading liquidity on the SIX Swiss Exchange. In addition, GEM has provided the company with a one-year letter of financial support (valid until the 2017 shareholder meeting), confirming GEM's intention to provide the company with the liquidity it needs to meet the obligations as they come due.

We have, however, observed, based on the total estimated R&D cost, that Relief will need additional financing to fund all necessary clinical trials for Aviptadil and Atexakin alfa. We believe that the company may look for various alternative sources of funding including, but not limited to, federal grants, similar to FirstString Research, Inc. ('FirstString') - the company which Relief is currently in the process of acquiring. FirstString has thus far funded 40% of its total R&D cost through grants provided by the federal government in the US. Other sources of funding for Relief also remain a possibility. Given these multiple potential sources of capital, we remain confident that Relief will be able to advance its pipeline in a timely and efficient manner.

Substantial barriers to competitive entry through market protection via both issued patents and orphan drug designations

The company currently holds 23 patent families covering a range of indications. Relief also holds Orphan Medicinal Product Designations (OMPD)/Orphan Drug Designations (ODD) in both the EU and the US markets, and expects to apply for more of these in the future. The company currently holds 10 orphan drug designations for its drugs in various indications. This should help the company to build and maintain its exclusive market position for the relevant pipeline candidate granted the OMPD/ODD once the marketing approval has been received. All of the company's drug candidates are protected by patents (for Aviptadil, none of the patents expire before 2026) and/or have obtained orphan drug designations.

Additionally, for molecules that have never been marketed before, such as Atexakin alfa, the company can also apply for Patent Term Extension (PTE) in the US and Supplementary Protection Certificate (SPC) in the EU. Both represent an extension for 5 years of each respective patent term. As a biologic drug, Atexakin alfa should also qualify for 10 years of market exclusivity in the EU and 12 years in the US. From our perspective, this makes a strong case for investing in the stock.

Expanding pipeline via strategic acquisitions and partnerships

In our view, Relief is likely to opportunistically seek to acquire products and/or enter into in-licensing agreements to strengthen its current pipeline and complement its existing portfolio. In this context, the company recently signed a term sheet through which it proposed to acquire FirstString in an all-stock transaction. This acquisition will bring in a Phase III-ready candidate in the form of Granexin gel for chronic wounds, along with some early-stage clinical assets. The proposed acquisition will broaden the company's current pipeline, which would then have two Phase III-ready assets (the second being Aviptadil). The company also holds worldwide development and commercial rights to Atexakin alfa, licensed-in from Merck KGaA, which is slated to enter Phase II testing in peripheral neuropathies in 2017. We believe that the company could enter into similar agreements in the future in order to strengthen its product pipeline.

Expected upcoming milestones

Event	Timing
Completion of acquisition of FirstString Research, Inc.	4Q 2016
Initiation of Phase III testing of Granexin gel in chronic wounds	H1 2017
Beginning of the Phase III clinical trial - Avisarco III - for Aviptadil in sarcoidosis involving 200 patients	H1 2017
Initiation of Phase IIa study for Atexakin alfa in DN patients, involving less than 50 patients	H1 2017
Interim data release from Phase III Granexin program	1Q 2018
Top-line data from Phase III Granexin program	Mid-2018
Submission of Granexin gel for regulatory approval	Late 2018
Final report on Avisarco III trial	Q3 2019
Approval and launch of Granexin gel in US (possibly also EU)	Late 2019
Market authorization for Aviptadil (sarcoidosis)	Q1 2020
Source: Company Data	

COMPANY OVERVIEW

Relief Therapeutics is a clinical-stage biotechnology company with a portfolio of drug candidates based on endogenously-occurring molecules (naturally found in the human body). The company's leading product candidates are Aviptadil for the treatment of sarcoidosis (currently poised to enter a pivotal Phase III trial, AVISARCO III) and low-dose interleukin-6 (Atexakin alfa) for peripheral neuropathy (slated to enter Phase II, AtexaDiaNe). Aviptadil for sarcoidosis focuses on an orphan disease market, in which positive data from a single pivotal Phase III trial could be sufficient to secure approval.

The company's other lead candidate - Atexakin alfa - is the subject of an exclusive worldwide development and commercialization agreement with Merck-Serono, a division of Merck KGaA. This drug has already undergone multiple clinical trials with a total capital investment of over €100.0mn. Based on its mechanism of action, along with the fact that the US Food and Drug Adminstration (FDA) has not yet approved any disease-modifying drugs, Atexakin alfa holds the potential to become the first disease-modifying therapeutic for peripheral neuropathy with the ability to regenerate peripheral nerves. According to Datamonitor, the peripheral diabetic neuropathy market is estimated to reach $4.1bn in 2019.

Following the completion of the merger terms between Relief Therapeutics SA and THERAMetrics holding AG in July 2016, the merged entity (Relief Therapeutics Holding AG) has decided to focus its resources primarily on the development of select pipeline candidates drugs - '**Main Development Programs I**'. These comprise two drug candidates, i.e. Aviptadil for sarcoidosis – slated to enter pivotal Phase III testing - and a second program, Atexakin alfa for DN – slated to enter Phase II testing. The pending acquisition of FirstString Research would add Granexin gel for chronic wounds, another Phase III asset, to the primary programs Relief is seeking to advance. On a secondary level, Relief intends to pursue further tangible opportunities by developing Aviptadil for ALI as well as Atexakin alfa for CIPN. Together these constitute '**Main Development Programs II**'. The company also possesses an extensive early-stage pipeline consisting of at least 10 projects across various therapeutic indications in oncology, ophthalmology, pulmonology and infectious diseases.

Aviptadil for sarcoidosis as well as ALI has the potential to treat patients affected by orphan diseases. For Aviptadil in sarcoidosis, the company has adopted an Orphan Medicinal Product Designation (OMPD) from the European Medicines Agency (EMA) for Europe, and for Aviptadil in ALI, the company has received an OMPD/ODD from the EMA and from the FDA for the US market. Atexakin alfa, for DN and CIPN, targets relatively larger markets with high unmet medical needs requiring new, more efficacious treatments with reduced side-effects.

The company signed a term sheet in July 2016 for a proposed acquisition of FirstString Research, Inc., a US-based privately-held clinical-stage biotechnology company. The proposed acquisition will take place as an all-stock transaction, which would bring in a Phase III-ready asset, Granexin gel for the treatment of chronic wounds, particularly diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs), along with other preclinical and early-stage clinical assets, to Relief's existing drug pipeline. FirstString's product candidates are based on characterization of the functions of connexin protein signaling. The proposed Granexin Phase III program has been reviewed and authorized by the FDA. Both Aviptadil for sarcoidosis and Granexin are expected to yield top-line data in 2018.

The proposed transaction would involve the issuance of new shares of Relief Therapeutics Holding AG common stock to the existing equity holders of FirstString. The transaction has been approved by the boards of both companies, and we anticipate that it could be formally consummated before the end of 2016.

Relief Therapeutics Holding AG is listed on the SIX Swiss Exchange (under the symbol RLF) and is headquartered in Zurich, Switzerland, with offices in Geneva, Switzerland.

Product Pipeline

The pipeline contains several Medicinal Product Candidate (MPCs) as shown below. While the Main Development Programs – Aviptadil and Atexakin alfa – will be advanced internally, Relief may co-develop or out-license certain other programs.

Exhibit 1: MPCs and Main Development Programs

Main development programs	Pre-clinical	Phase I	Phase II	Phase III	Filed	Market
Granexin – Chronic Wounds	Preparation of Ph III – H1 2017			Expected time to market: ~2.5-3 years		
Aviptadil – Sarcoidosis	Preparation of Ph III – H1 2017			Expected time to market: ~3-4 years		
Atexakin alfa – Diabetic neuropathy	Preparation of Ph II – H1 2017		Expected time to market: ~5 years			
Aviptadil – Acute lung injury	Preparation of Ph II – H1 2017		Expected time to market: ~6 years			
Atexakin alfa – Chemotherapy-induced peripheral neuropathy	Preparation of Ph II – H1 2017		Expected time to market: ~5 years			

Programs in consideration	Pre-clinical	Phase I	Phase II	Phase III	Filed	Market
Interferon gamma – Idiopathic pulmonary fibrosis			Ph II drug for Europe and US; Ph III with 300 patients required			
Octreotide – Drug-resistant tuberculosis		About 300 patients required				
Thymopentin – Sarcoidosis		About 200 patients required				
Alpha Melanotropin – Chronic beryllium disease		About 150 patients required				

Source: Company Data

Exhibit 2: MPCs – Patents and Commercialization rights

Product Candidate	Indication / Use	Patents	Commercialization rights
Aviptadil	Sarcoidosis	Issued patents for the indication, and adopted orphan drug designation in EU	THERAmetrics, centurion
Atexakin alfa	Peripheral neuropathy	Issued patents in the US and Europe	Relief, MERCK
Aviptadil	ALI	Issued patents for the indication, and adopted orphan drug designations in EU and US	THERAmetrics
Atexakin alfa	Neuropathy induced by chemotherapy	Issued patents in the US, pending in Europe	Relief, MERCK
Atexakin alfa	Microvascular disorders	Issued patents in the US, pending in Europe	Relief, MERCK
Interferon gamma	Inhaled drug for idiopathic pulmonary fibrosis	Orphan drug designation adopted in the US and EU	THERAmetrics
Octreotide	Multi- and extensively drug-resistant tuberculosis	Issued and validated patents in the UK, France, Switzerland and the US	THERAmetrics
Thymopentin	Sarcoidosis	Orphan drug designation adopted in the US	THERAmetrics
Alpha melanotropin	Chronic beryllium disease	Issued and validated patents in the UK, France, Switzerland, orphan drug designation adopted in the US	THERAmetrics

Source: Company Data

Drug Repurposing and Repositioning 2.0 (DRR2.0) Bio-mathematical technology platform

DRR2.0 tool is a bio-mathematical technology platform that has been developed by the company as a methodology in order to identify promising drug candidates for a potential repositioning and repurposing, targeting underserved medical indications. The company holds exclusive rights to the software. In building a network of biomedical entities from scientific literature, the system has been used to generate various components of Relief's IP and OMPD/ODD pipeline.

DRR2.0 is a hypothesis-generating tool based on syntactic parsing and semantic analysis of biomedical literature and on mathematical analysis of the resulting knowledge representation.

The functions of DRR2.0 include the ability to suggest the possible action mechanism of a drug in relation to a disease, ranking drugs according to their ability to provide best treatment options for a given disease, and ranking which diseases are best addressed by a given drug. The tool offers a user-friendly graphic interface to browse its network representation of biomedical knowledge and to quickly examine the underlying literature.

DRR2.0 is based on the 25+ million publications available on PubMed and manages information on 4,900 drugs, 9,400 diseases, 13,000 genes and 2,000 relevant biomedical entities. The system can be customized according to the clients' need to integrate their unpublished proprietary data.

The company currently has a consultancy agreement with Grünenthal GmbH valid for 2016 for the use of the DRR2.0 system. In addition, it has business relations with two other undisclosed clients for commercial use of the DRR2.0 system. This platform could offer additional opportunities for the company in the future. We expect Relief to pursue further options to monetize this platform going forward.

Company History

2007: In March 2007, mondoBIOTECH Holding AG (mondoBIOTECH) was founded. mondoBIOTECH was a Switzerland-based company focused on the discovery of MPCs by repositioning known drugs for the treatment of rare pulmonary diseases.

2013: In June 2013, mondoBIOTECH changed its name to THERAMetrics holding AG (THERAMetrics) and, in September 2013, as a result of a business combination with the Clinical Research Organization (CRO) company Pierrel Research International AG and its international CRO subsidiaries, THERAMetrics became the parent company of a global tech-based Contract Research and Development Organization (TCRDO).

In May 2013, Relief Therapeutics SA was incorporated by Gaël Hédou, Michel Dreano and Yves Sagot, former Merck Serono employees, with the aim to develop treatments to address unmet medical needs.

2015: In September 2015, Relief Therapeutics SA signed an in-licensing agreement with Merck Serono, a division of Merck KGaA, giving the former worldwide exclusive rights to develop and commercialize Atexakin alfa. Under the terms of the agreement, Relief Therapeutics SA will develop Atexakin alfa for the treatment of neuropathies.

2016: In May 2016, THERAMetrics exited the CRO business by selling its major CRO subsidiaries in Italy, Germany and Romania to Accelovance Inc.

In July 2016, THERAMetrics and Relief Therapeutics SA merged, with the shareholders of Relief Therapeutics SA becoming the majority owners of the combined company. The acquisition was carried out by way of an exchange of 5'750 THERAMetrics shares for each outstanding share of Relief Therapeutics SA common stock. As a result, the company issued 1'196'937'250 new shares against contribution in kind of 208,163 shares of Relief Therapeutics SA. The combined entity changed its name from THERAMetrics holding AG to Relief Therapeutics Holding AG.

BUSINESS MODEL

The company's focus is on developing medicinal product candidates (MPCs) for the treatment of patients suffering from diseases for which no adequate drugs / treatments are available in the market. For this purpose, Relief works on compounds which are already known and considered safe – in particular, peptides (e.g., vasoactive intestinal peptide or VIP, the basis for Relief's Aviptadil candidate) and other biological immuno-modulating substances (e.g., cytokines, such as interleukin-6, the basis for Relief's Atexakin alfa candidate).

Relief's primary goal is to build a cash-generating, profitable and sustainable business with the aim of either self-commercializing or licensing out the MPCs to third parties (such as pharmaceutical and biotechnology companies) at various stages of clinical development and market approval.

Revenue Model

Reducing costs by outsourcing clinical trials and focusing on rapid development programs

The company aims to remain a lean business organization by relying on its internal expertise to select suitable programs and design the quickest-to-market route of development. Relief specifically targets programs that can be advanced efficiently through low-cost, rapid clinical trials involving short evaluation periods.

In order to achieve its strategic objectives, Relief plans to outsource clinical trials by engaging suitable external providers, ensuring cost-effective drug development.

Massive investments coupled with low productivity in R&D are driving companies in the pharmaceutical and biotechnology industry to aggressively reduce development and manufacturing costs by outsourcing their research and manufacturing activities to Clinical Research Organizations (CROs) and Contract Manufacturing Organizations (CMOs), respectively. In order to keep the costs low and operations sustainable in an increasingly competitive drug manufacturing market, we believe that this is a step taken in the right direction by the company.

Generating income by outsourcing commercialization of MPCs

Just as the trials will be outsourced, commercialization will likely be entrusted on a country-by-country basis to specialized partners. We expect the company to generate sufficient sales-based royalties through these out-licensing agreements to support its current and future development programs.

This model provides the company with flexibility in managing overhead costs, while retaining control over the design, planning and management of projects that will be supervised and coordinated by a specialized team of in-house experts who will interact with the partners through every stage of the process.

Criteria for project selection

The company plans to focus primarily on developing its selected MPCs toward market authorization. The targeted markets range from niche orphan disease indications like sarcoidosis and ALI, to significantly larger markets covering diabetic complications such as peripheral neuropathies and diabetic foot ulcers, which present huge market potential for the company. The criteria for the projects in the development pipeline are:

- Selected MPCs must already be clinical-stage compounds
- Selected MPCs should have a documented regulatory history of safe administration in human beings
- Selected MPCs are primarily molecules of natural human origin, which regulate cell interaction, communication and behavior within the human body, and their mechanisms of action are well researched
- Clinical programs have a favorable risk/reward ratio and expected – compared to other programs – short time to market, with trials involving short evaluation periods and objective outcome measures to evaluate efficacy

Important agreements and rights

The company currently has a strong pipeline of development programs. The proposed acquisition of FirstString, which has a Phase III-ready asset in the form of Granexin gel in its pipeline, should further reinforce Relief's portfolio of drug candidates. We note that the combined intellectual property portfolio of Relief and

FirstString is slated to span a very broad array of candidate programs. Relief currently holds the below-mentioned licenses, patent rights and designations:

- Out-licensing agreement for development and commercialization of Aviptadil for the treatment of sarcoidosis to Centurion Pharma. Markets covered under the agreement include Turkey, Bahrain, Egypt, Iran, Iraq, Israel, Jordan, Kuwait, Lebanon, Yemen, United Arab Emirates, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Syria, Tunisia, Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine, Uzbekistan, Serbia, Macedonia, Bosnia & Herzegovina and Albania
- In-licensing agreement for the worldwide exclusive rights for R&D and commercialization of Atexakin alfa for treatment of peripheral neuropathies and microvascular diseases from Ares Trading SA (Merck Serono), a subsidiary of Merck KGaA. The agreement does not include any upfront payments, development milestones or right of first refusal. Relief is obligated to pay certain royalties to Merck Serono, which would account for single-digit percentages of net sales if Relief commercializes the drug independently; higher percentage rates would apply to the share of proceeds from sub-licensing of Atexakin alfa if Relief elects to out-license the candidate
- 23 different issued and validated patent families for Aviptadil, Atexakin alfa, alpha melanotropin, interferon gamma, octreotide, urocortin, Peptide YY, somatostatin, neuropeptide EI, acetalin-2, gonadorelin, proadrenomedullin, valorphin, astressin, stresscopin-related peptide, exorphin C, defensin HNP2, galanin, and a proprietary renin inhibitor, for a variety of lung diseases, diabetic neuropathy, infectious diseases and hyper-proliferative diseases
- 10 orphan medicinal product designations adopted with the European Union (EU) and/or the FDA for Aviptadil in sarcoidosis, ALI/acute respiratory distress syndrome, pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension; alpha melanotropin in chronic beryllium disease; Interferon gamma in idiopathic pulmonary fibrosis; Peptide YY in hepatocellular carcinoma; thymopentin in cutaneous sarcoidosis

Intellectual Property

Exhibit 3: Atexakin Alfa-related Patents

Title	Patent	Owner	Status	Expiration
Use of gp130 activators in diabetic neuropathy	EP 1 434 597B	Ares Trading	Granted	Oct. 2022
	US 7465441	Ares Trading	Granted	Aug. 2023
	US 2010-0189684	Ares Trading	Granted	Oct. 2022
IL-6 for therapy or prevention of Chemotherapy-induced neuropathy	EP 1740200 A	Ares Trading	Pending	(Apr. 2025)
	US 7951359	Ares Trading	Granted	Sep. 2026
Use of IL-6 in vascular complications	EP 1786457 A	Ares Trading	Pending	(Aug. 2025)
	US 8,003,090	Ares Trading	Granted	Aug. 2025

Source: Company Data

As shown in the above exhibit, Atexakin alfa (for diabetic neuropathy) is patented until 2022/2023 with potential for 5 years' term extension, leading to 10-12 years of data exclusivity protection. Other indications are patented until 2025/2026.

Exhibit 4: Aviptadil-related Patents

Title	Patent	Owner	Status	Expiration
Formulation of aviptadil	EP 1 855 661	The Company	Granted	March 2026
	US 8,178,489		Granted	July 2029
	CN 101247794		Granted	March 2026
	IN1363/MUMNP/ 2007 246915		Granted	March 2026
	MX/a/2007/010930		Granted	March 2026
Aviptadil in pulmonary hypertension	US 8,153,599	The Company	Granted	Dec 2027

Source: Company Data

As shown in Exhibit 4, none of the patents for Aviptadil are slated to expire prior to 2026, with the last patent expiring in 2029. This gives sufficient time for Relief to penetrate the market based on Aviptadil's expected launch in 2020.

Exhibit 5: Other Patents

Title	Patent	Owner	Status	Expiration
Alpha melanotropin for chronic beryllium disease	EP 2 187 954	The Company	Granted	Sept 2028
Interferon gamma for pulmonary fibrosis	EP 1 455 813	The Company	Granted	Dec 2022
Octreotide for tuberculosis	EP 2 188 016 US 8,541,364 JP 5385280	The Company	Granted Granted Granted	Sept 2028 Sept 2028 Sept 2028
Peptide YY for HBV infections	US 8,193,149 JP 5385278	The Company	Granted Granted	Sept 2028 Sept 2028
Somatostatin for HBV infections	EP 2 190 535 US 8,211,856 JP 5384502	The Company	Granted Granted Granted	Sept 2028 Sept 2028 Sept 2028
Defensin HNP2 for excessive angiogenesis	JP 5491396	The Company	Granted	Sept 2028
Galanin for excessive angiogenesis	JP 5395794	The Company	Granted	Sept 2028
Stresscopin-related peptide for angiogenesis	EP 2 190 447 JP 5480140	The Company	Granted Granted	Sept 2028 Sept 2028
Astressin for excessive angiogenesis	JP 5395792	The Company	Granted	Sept 2028
Urocortin for HBV infections	EP 2 187 940 JP 5385283	The Company	Granted Granted	Sept 2028 Sept 2028
Exorphin C for excessive angiogenesis	JP 5385284	The Company	Granted	Sept 2028
Renin inhibitor for excessive angiogenesis	EP 2 187 915 JP 5384501	The Company	Granted Granted	Sept 2028 Sept 2028
Neuropeptide EI for excessive angiogenesis	EP 2 187 901 JP 5385276	The Company	Granted Granted	Sept 2028 Sept 2028
Acetalin-2 for tuberculosis and HBV infections	EP 2 187 913 US 8,338,380 JP 5385281	The Company	Granted Granted Granted	Sept 2028 Sept 2028 Sept 2028
Valorphin for tuberculosis	EP 2 197 477	The Company	Granted	Sept 2028
Proadrenomedullin for tuberculosis	JP 5385277	The Company	Granted	Sept 2028
Gonadorelin for tuberculosis	US 8,349,805 JP 5385279	The Company	Granted Granted	Sept 2028 Sept 2028
Pro-Ser-Hyp-Gly-Asp-Trp for excessive angiogenesis	JP 5385282	The Company	Granted	Sept 2028

Source: Company Data

Beyond the patents for the main product candidates (Aviptadil and Atexakin alfa), the company holds a rich list of patients for various other indications including tuberculosis, HBV infections and pulmonary fibrosis, among others. We would also note that FirstString Research, which is in the process of being acquired by Relief, holds a broad array of issued patents covering its lead product candidate, Granexin gel, as well as its proprietary technology platform focusing on regulation of cell-cell communication processes underlying tissue responses to injury. These patent claims cover composition-of-matter (COM), formulation and method-of-use for Granexin gel and other drug candidates in the FirstString pipeline, and expire in the 2026 – 2033 timeframe, without factoring in potential Hatch-Waxman patent term extensions in the US or supplementary protections in the EU.

PRINCIPAL DEVELOPMENT PROGRAMS

Relief Therapeutics is a drug development company focusing on clinical stage projects, primarily developing drugs of natural human origin (peptides and proteins) with a history of clinical testing and use in human patients.

The company currently concentrates its initial efforts on diabetic complications and respiratory diseases. A focus on additional MPCs and indications will be considered as opportunities develop.

Aviptadil for the treatment of sarcoidosis

In March 2015, the company signed a licensing agreement with Centurion Pharma on Aviptadil indicated for sarcoidosis. Under the terms of the agreement, the two firms will cooperate in the development and registration of Aviptadil for the treatment of sarcoidosis in Turkey and in other neighboring countries.

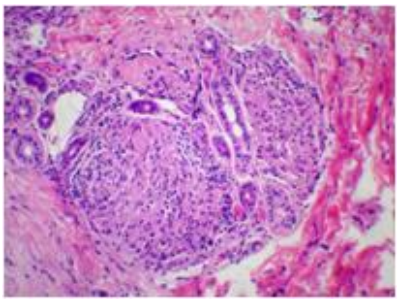
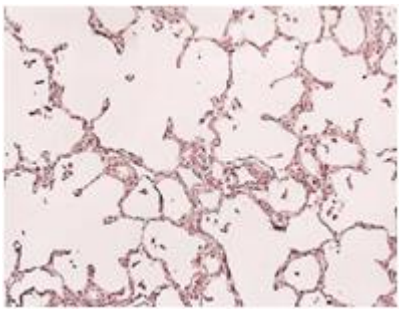
Indication: Sarcoidosis

Sarcoidosis, also known as Besnier-Boeck-Schaumann disease, is an autoaggressive systemic granulomatous disease that primarily affects the lungs but can affect almost all organs of the body. Sarcoidosis commonly develops in younger and middle-aged adults, most probably following exposures to poorly degradable antigens of infectious or environmental origin which trigger an exaggerated immune reaction. It is a globally occurring disease with potential severe manifestations in the skin (16-35% of the patients), in the eyes (12%), in the lymph glands (5-15%), in the liver (12%), heart, kidney, bones or the central nervous system of the patients in addition to the lungs, affected in more than 90% of the patients.

In most cases, sarcoidosis leads to constitutional clinical manifestations like dry unproductive cough, severe chronic fatigue and dyspnea on exertion, and may also lead to terminal stages of lung fibrosis. Sarcoidosis can be identified from the formation of noncaseating granuloma characterized by the accumulation, proliferation and exaggerated spontaneous activity of macrophages and T-lymphocytes at sites of inflammation.

Treatment of sarcoidosis involves suppressing the initiation of granuloma formation by inhibiting antigen processing and presentation, limiting inflammatory lesions that are interfering with organ function, preventing fibrosing processes, and inhibiting constitutional manifestations like cough, severe chronic fatigue and exertional dyspnea.

Exhibit 6: Sarcoid Lung vs. Healthy Lung

Sarcoid Lung	Healthy Lung
	

Source: Company Data

Rationale and Development

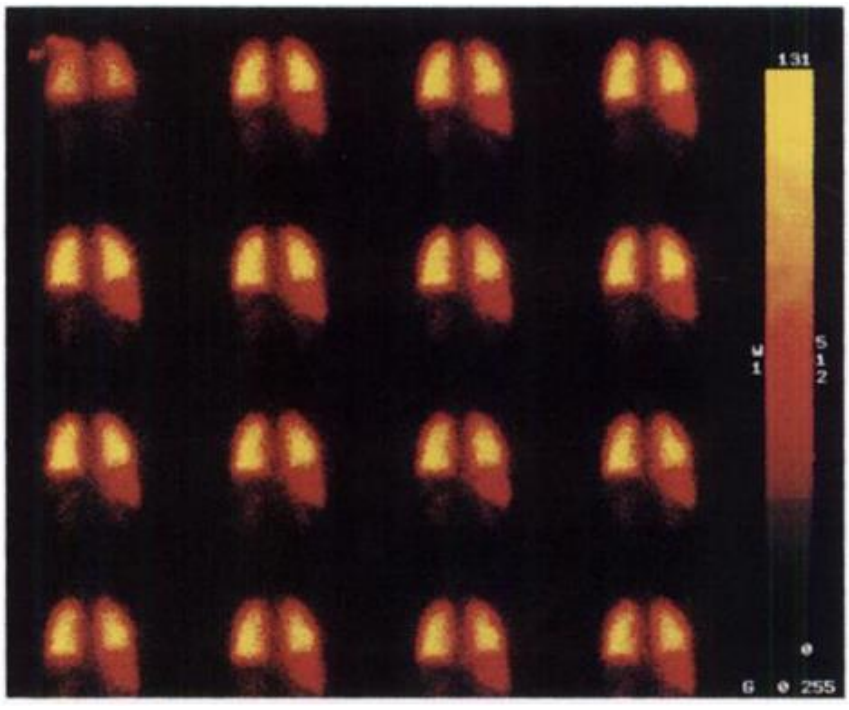
Aviptadil (Vasoactive Intestinal Peptide, or VIP) is a biologically active endogenous human peptide, acting as a ligand on specific G-protein coupled transmembrane receptors. It is one of the signal molecules of the neuroendocrine-immune network comprising antiproliferative, anti-inflammatory, and immune-regulatory features. Its predominant biological activity is performed in the lungs, and a vast body of experimental, pharmacological and clinical evidence suggests Aviptadil to be an attractive candidate for the treatment of sarcoidosis. Reduced VIP expression is considered a pathological hallmark of pulmonary disease. Treatment using Aviptadil, therefore, could restore lung homeostasis. A number of clinical Phase I/II trials using systemic administration of Aviptadil have been performed in humans since the 1970s. The population tested using this mode of administration experienced mild gastrointestinal side-effects. Aviptadil is currently approved as a combination therapy with phentolamine as injectable treatment for erectile dysfunction in UK, Denmark, Sweden, Norway, Finland and New Zealand.

In order to avoid systemic side effects, and so as to increase the dose to therapeutically meaningful values for respiratory diseases, the company has decided to use inhalation as the route of administration for Aviptadil in sarcoidosis patients. Relief is specifically working on a nebulizer, which the patients would need to use up to 4 times per day for effective results. Administered in this way, the drug would act locally on the lung tissue, without affecting the other parts of the human body, and would avoid hepatic first-pass metabolism while achieving rapid onset of action. According to the company, the drug is not expected to cause any asthmatic side-effects. As the size variability among adult lungs is smaller than the overall body size variability, dosing reliability is also improved when inhaling.

In a Phase II study done at the University of Freiburg in Germany (A. Prasse et al., 2010), nebulized Aviptadil was administered to patients with sarcoidosis. The study showed that Aviptadil can induce regulatory T-cells and downregulate patients' inflammatory status, whereas there were no obvious side-effects or systemic immunosuppression. This study supports the rationale for Aviptadil as an attractive future therapy to dampen exaggerated immune responses in lung disorders.

All regulatory preclinical acute and chronic pharmacological and toxicological tests have been performed in various animals (mice, rats, rabbits, dogs, and monkeys) with an excellent safety profile, allowing initiation of clinical trials in sarcoidosis.

Exhibit 7: Aviptadil receptors in healthy human lungs



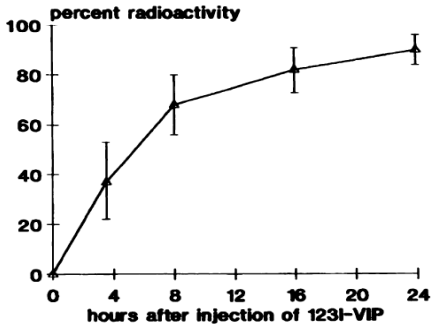
Images were acquired during the first 8 mins after injection (1frame/30sec). Peak lung activity represented 40% ±7% of the injected dose at 0.7 hr and declined to 21% ±7% at 3.5, to 14% ±3% at 7 and to 8% ±4% at 22 hr post injection.

Source: Virgolini et al., 1995

As shown in the exhibit on the previous page, Intravenous (IV) injection of 150 MBq ^{123}I-VIP (300 pmole) shows rapid binding in the lung which is the primary site of uptake of the labelled peptide.

Exhibit 8: Aviptadil distribution and excretion as a function of time after IV injection of Iodine-123-VIP in healthy humans

Organ	Time postinjection of ^{123}I-VIP (hr)			
	0.7 ± 0.2 (0.5–1)	3.5 ± 0.5 (2–4)	7.2 ± 1.4 (6–8)	22.5 ± 2.3 (18–26)
Lung	40.3 ± 6.6 (26–52)	21.5 ± 7.0 (13–34)	13.9 ± 3.2 (10–24)	8.2 ± 4.0 (6–14)
Liver	6.5 ± 1.2 (4–8)	3.5 ± 1.5 (2–6)	2.3 ± 1.3 (1–4)	1.5 ± 1.2 (0.5–3)
Kidneys	4.2 ± 2.4 (2–7)	3.2 ± 1.9 (2–6)	2.2 ± 0.9 (1.5–4)	1.1 ± 0.4 (0.5–2)
Bladder	4.5 ± 2.5 (2–8)	7.4 ± 4.8 (2–9)	6.4 ± 2.7 (2.5–9)	4.3 ± 2.9 (2.5–7.5)
Thyroid	0.5 ± 0.2 (0.1–0.9)	0.4 ± 0.2 (0.1–0.8)	0.7 ± 0.2 (0.9 ± 0.3)	0.8 ± 0.3 (0.4–1.2)



Radioactivity was excreted through the urinary tract. Cumulative radioactivity measured in the urine is shown.

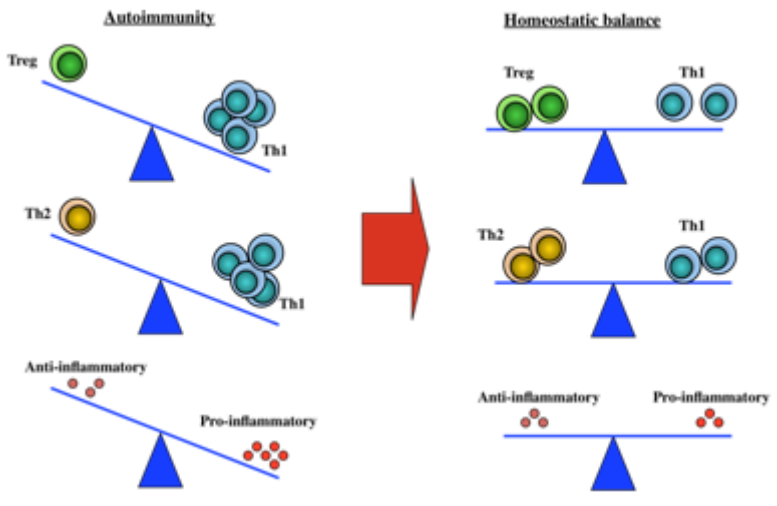
Source: Virgolini et al., 1995

Mechanism of Action

VIP is an inhibitory neurotransmitter of the nonadrenergic, noncholinergic autonomic nervous system and also a Th-2 cytokine. Its action is mediated through VIP receptor type-1 (VPAC1) and VIP receptor type-2 (VPAC2), which are also activated by Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP) that also belongs to the glucagon-secretin superfamily.

Among its functions as a neurotransmitter, VIP exerts potent bronchodilatory effects, which are independent of the adrenergic and cholinergic receptors and cyclooxygenase, quantitatively 100-fold more potent compared to the adrenergic bronchodilation induced by isoproterenol. Furthermore, it causes a 50-fold more potent vasodilation than prostacyclin to both pulmonary and systemic arteries. Its vasodilatory action is independent of the endothelium. Finally, VIP is implicated in the regulatory mechanism of mucous secretion by increasing the total Cystic Fibrosis Transmembrane Receptor (CFTR) levels, with a resulting three-fold increase in Cl- efflux in bronchial epithelial cells.

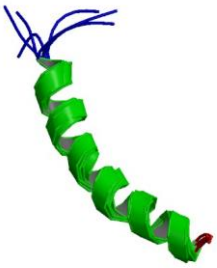
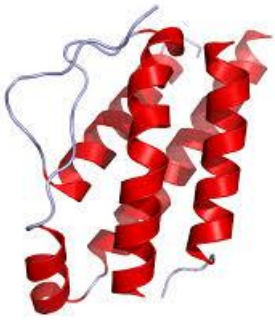
Exhibit 9: Mode of Action



Source: Gonzalez-Rey et al., 2007

VIP also exerts elaborate immunomodulatory effects, mostly anti-inflammatory. It is secreted by Polymorphonuclear cells (PMN) and T-lymphocytes. VIP acts on T-lymphocytes and inhibits their proliferation. As shown in the above exhibit, it also acts as a differentiation factor of the T-lymphocytes and promotes T-helper 2 lymphocytes (Th2) differentiation against T-helper lympocytes (Th1). It also promotes regulatory T-cells (Tregs) induction. There are contradictory data regarding its impact on mast cell degranulation and chemokine production for which more studies are necessary. Moreover, VIP inhibits humoral immunity and also neutrophil chemotaxis. Studies have shown that VIP acts directly on type 2 lung cells, which express VIP receptors, inhibiting their apoptosis. Moreover, recent data show that VIP, through its anti-inflammatory action inhibits pulmonary vascular remodeling in patients with pulmonary arterial hypertension. Finally, there are certain data indicating that VIP suppresses Toll-Like Receptor 4 (TLR-4). It also inhibits excessive TNF-α, IL-6, IL-12, IL-17, CD40, CD80, CD83, CD86, HLA class II, TLR2, and TLR4 expression in sarcoidosis patients.

Exhibit 10: 3D structures of VIP and Interleukin-6

VIP	Interleukin-6
	

Source: Company Data

Positioning and Competition

Current treatments for sarcoidosis include corticosteroids (e.g., prednisone). These agents are sometimes used in association with additional immunosuppressant agents, like methotrexate. However, none of these drugs are specifically approved for the treatment of sarcoidosis, and long-lasting treatments with corticosteroids and/or immunosuppressive therapy is not recommended due to severe negative side-effects. Also, the use of several anti-tumor necrosis factor alpha (anti-TNF-α) therapeutics to decrease inflammation has been rather inconclusive until now.

At present, Aviptadil is the only known experimental drug for sarcoidosis that could potentially suppress clinical symptoms of sarcoidosis with no significant negative side-effects. Aviptadil could, if successful, be positioned as a first-in-class drug for chronic sarcoidosis prescribed by specialists. Therefore, we anticipate that there would be a favorable outlook for reimbursement by healthcare organizations.

Aviptadil has a global patent coverage with issued and validated patents in the US, the UK, France, Germany, Italy, Turkey, China, Mexico, India, Switzerland, Spain, the Netherlands, Sweden, Belgium, Denmark, Ireland and Austria. As mentioned before, none of these patents is expiring prior to 2026.

With its expected launch date in 2021, the drug has a peak sales potential of CHF290.0mn in the market for sarcoidosis.

Clinical Trial Design and Timeline

Following a Phase II trial in 20 sarcoidosis patients demonstrating a suppression of inflammatory mechanisms of the lung, in combination with amelioration of dry cough and of exertional dypnea, the company intends to conduct a Phase III clinical trial campaign named Avisarco III. In accordance with the guidelines of the EMA, who adopted the OMPD for Aviptadil in sarcoidosis, a potential positive outcome in the Phase III program might lead to EU-wide market authorization.

The clinical trial design is based on the previous data obtained during the phase II study, where Aviptadil inhalation demonstrated a very good efficacy on dry cough and dyspnea with a very good safety outcome. Furthermore, it was found mechanistically that Aviptadil significantly restores immune tolerance by promoting regulatory T-lymphocytes and dampens inflammatory mechanisms in the lungs.

The phase III study Avisarco III will be a multicentric, placebo controlled, double blind, and randomized study involving 200 sarcoidosis patients indicated for active treatment. The treatment duration will be for 24 weeks for each patient, followed by a long-term follow up of an additional 24 weeks.

The beginning of the clinical trial (first patient enrolled) is forecasted in H1 2017 and final report on the trial is expected in Q3 2019 and market authorization projected in Q1 2020. The company has 13 clinical centers in Germany ready to initiate the study. The Principal Investigator (PI) for the same has already been recruited. The predicted R&D cost till the time to market is CHF7.0mn.

Clinical Phase II trials

In an open-label clinical Phase II study, conducted by the Department of Pneumology of the University of Freiburg, 20 patients (13 males, 7 females; mean age, 49.6 +/- 13.1 yr) with histologically proved sarcoidosis and active disease were treated with 50 mg synthetic nebulized VIP for 4-weeks. The objective was to test whether Aviptadil has an immunoregulatory role. Sarcoid alveolitis was used as a prototype of immune-mediated chronic lung inflammation. The main results of the study showed that Aviptadil inhalation was safe, well-tolerated, and significantly reduced the production of TNF-α by cells isolated from bronchoalveolar lavage fluids of these patients. Aviptadil treatment significantly increased the numbers of bronchoalveolar lavage $CD4^+CD127^-CD25^+$ T cells, which showed regulatory activities on conventional effector T cells. *In vitro* experiments demonstrated the ability of Aviptadil to convert naive $CD4^+CD25^-$ T cells into $CD4^+CD25^+FoxP3^+$ regulatory T cells, suggesting the generation of peripheral regulatory T cells by Aviptadil treatment.

The results of the study did not show any severe adverse event during the period of treatment with Aviptadil. In particular, no instances of a significant drop in blood pressure were observed, nor were there any occurrences of tachycardia (increased heart rate). In all, 19 adverse events were recorded in 12 patients. Although a large proportion of the adverse events could be directly related to the invasive diagnostic procedures (i.e., dry throat, hoarseness, syncope, cough, and hemoptysis), none of them could unequivocally be attributed to the study medication. Concerning severity, they were all rated as "mild" with the exception of a case of syncope and a case of common cold, both rated as "moderate" and directly after bronchoscopy. Most of the adverse events disappeared spontaneously. In two cases flatulence and diarrhea were reported. Laboratory chemistry revealed no influence of the study medication on blood differential cell counts or liver enzymes. The increase in creatinine was statistically significant ($P < 0.048$), although clinically "non-significant".

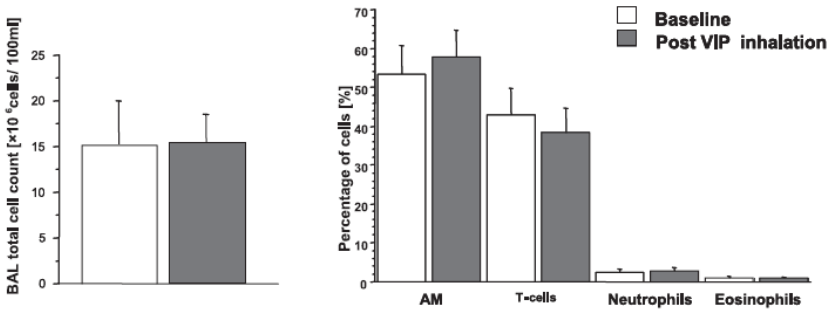
Exhibit 11: Characteristics of patients with sarcoidosis included in the study at baseline (day 0) and at the end of the treatment period (day 28)

	Mean (SD) Day 0	Mean (SD) Day 28	n	*P* Value
Pulmonary function test				
Residual volume, L	1.93 (0.54)	1.95 (0.53)	20	n.s.
Vital capacity, L	3.71 (1.03)	3.69 (1.01)	20	n.s.
Total lung capacity, L	5.64 (1.14)	5.64 (1.17)	20	n.s.
FEV_1, L	2.71 (0.81)	2.73 (0.83)	20	n.s.
FEV_1/VC MAX	72.93 (8.56)	73.75 (9.43)	20	n.s.
PO_2, mm Hg	76.4 (8.35)	77.2 (7.58)	20	n.s.
Pco_2, mm Hg	38.75 (3.14)	38.95 (3.57)	20	n.s.
D_{LCO}	7.65 (2.42)	7.27 (2.21)	19	n.s.
BAL differential cell count				
Cell count, 10^6/100 ml	13.9 (11.4)	14.3 (8.3)	20	n.s.
BAL AM, %	53 (21)	56 (19)	20	n.s.
BAL L, %	44 (20)	39 (18)	20	n.s.
BAL N, %	2 (2)	3 (3)	20	n.s.
BAL E, %	1 (1)	1 (2)	20	n.s.
BAL-cell cytokine production				
TNF-α, pg/ml	2,869 (6,506)	559 (831)	18	0.04
TGF-β1, pg/ml	979 (312)	1,040 (139)	18	n.s.
IL-13, pg/ml	14 (19)	11 (20)	16	n.s.
IP-10, pg/ml	144 (241)	120 (160)	18	n.s.
MIP-1α, pg/ml	2,081 (2,703)	952 (747)	18	0.04
IFN-γ, pg/ml	522 (937)	146 (249)	18	0.063
IL-17, pg/ml	448 (415)	259 (257)	18	0.079
Laboratory chemistry				
CRP, mg/L	7.2 (7.3)	8.7 (9)	18	n.s.
sIL-2R, U/ml	1,700 (1,582)	1,780 (1,724)	20	n.s.
Neopterin, nmol/L	15.5 (9.4)	16.5 (11)	20	n.s.
ACE, U/L	62.2 (33.5)	71.5 (40.3)	20	n.s.
Safety data				
Creatinine, mg/dl	0.96 (0.13)	1.02 (0.15)	19	0.048
AST, U/L	31.5 (9)	30.5 (7.4)	19	n.s.
ALT, U/L	28.2 (18.4)	27.5 (19.6)	19	n.s.
LDH, U/L	218 (31)	216 (26)	18	n.s.
CK, U/L	94 (47)	93 (75)	19	n.s.
Leukocytes, $10^3/\mu l$	6.04 (1.56)	6.01 (1.89)	20	n.s.
Platelets, $10^3/\mu l$	246 (37)	256 (43)	20	0.08
Systolic BP, mm Hg	122 (15)	122 (14)	20	n.s.
Diastolic BP, mm Hg	83 (11)	80 (10)	20	n.s.
Heart rate, bpm	74 (9)	74 (11)	20	n.s.

Source: Prasse et al., 2010

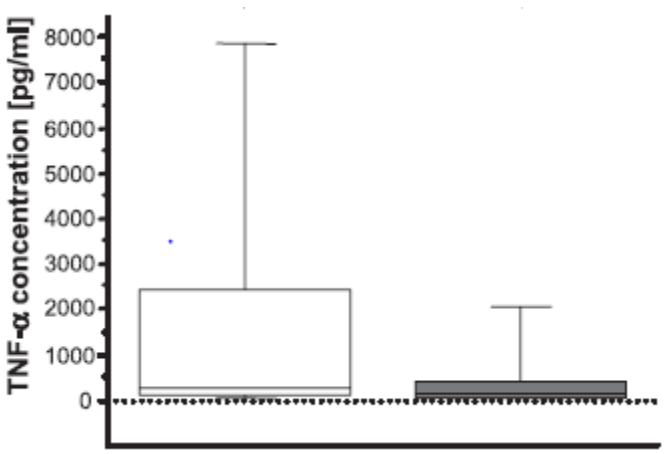
As can be observed in the above exhibit, there was no statistical difference between pulmonary function data comparing Day 0 with Day 28. Neither total nor differential BAL cell counts were significantly altered after the VIP treatment period. However, the 28-day treatment period was in all likelihood too short to demonstrate a therapeutic impact on lung function parameters.

Exhibit 12: BAL total cell count



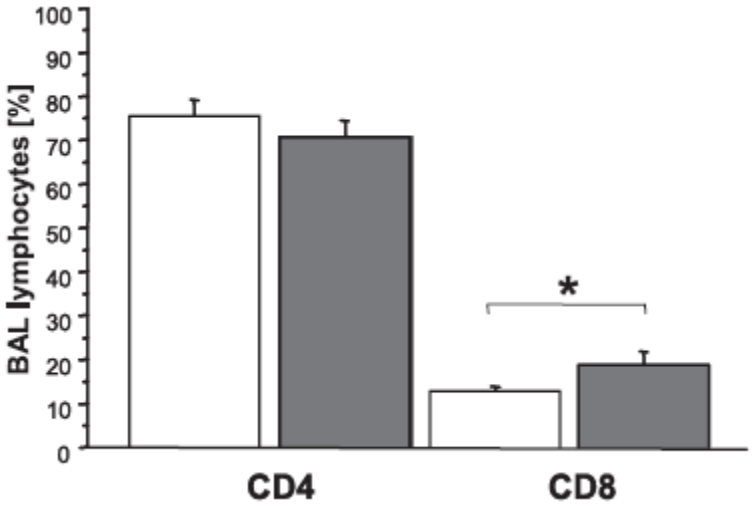
Source: Prasse et al., 2010

Exhibit 13: TNF-α concentration



Source: Prasse et al., 2010

Exhibit 14: BAL lymphocytes (%)



Source: Prasse et al., 2010

As shown in the figures above and on the previous page, VIP inhalation increased the percentage of Bronchoalveolar Lavage (BAL) $CD8^+$ T cells and decreased spontaneous TNF-α production by BAL cells. Patients with active sarcoidosis were treated with Aviptadil for 28 days. BAL cells were isolated before (baseline, open bars) and at the end of Aviptadil treatment (shaded bars), and the cell counts and spontaneous cytokine production were determined.

Clinical Phase I trials

In all, 116 healthy volunteers were treated systemically via injection with various dosages to assess pharmaco-kinetics, metabolic and circulatory effects.

Patient trials

Aviptadil has also been used in roughly 1,000 patients (860 in erectile dysfunction) who were treated systemically via injection with various dosages in asthma, ALI, pulmonary hypertension, venous ulcers.

About 200 patients were treated via inhalation in asthma, chronic inflammatory response syndrome, pulmonary arterial hypertension, COPD, and sarcoidosis.

Atexakin alfa for the treatment of Diabetic Neuropathy

Relief Therapeutics SA signed a worldwide, exclusive license agreement in August 2015, with Ares Trading SA, a subsidiary of Merck KGaA, Germany, for the research, development and commercialization of Atexakin alfa for the treatment of peripheral neuropathies. The transfer of rights from Merck KGaA was part of the organizational restructuring which began in 2012 by closing down of the Geneva headquarters of its biotech unit Merck Serono and eventually scaling back the Swiss operations. The agreement does not include any conditions related to upfront payments, development milestones or the right of first refusal. However, there are some exit provisions and royalties involved (royalties account for 7% of net sales). In addition, Merck KGaA would be entitled to higher percentage shares of sub-licensing revenues in the event that Relief were to out-license the candidate to a third-party for final commercialization.

Indication: Diabetic Neuropathy

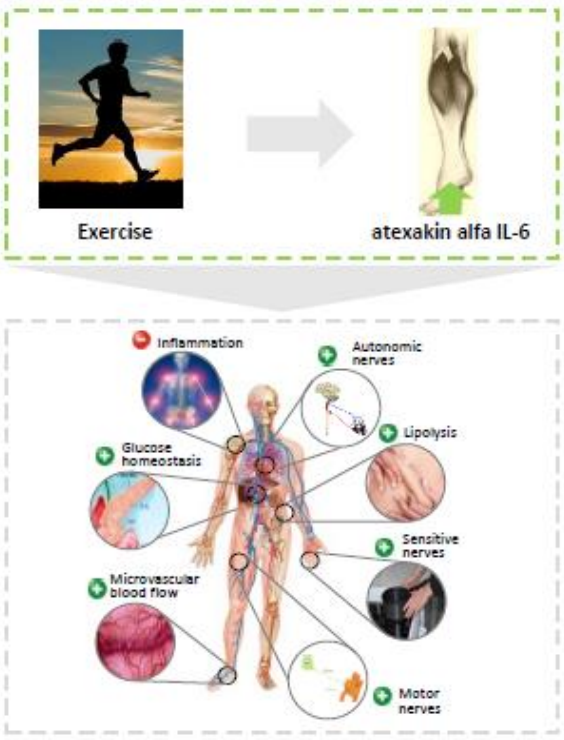
Neuropathy is diagnosed in 20-40% of diabetic patients that, according to the World Health Organization projections, are predicted to exceed 300 million patients worldwide in 2050. Diabetic neuropathy is progressive and develops as diabetes persists. It is characterized by the degeneration of peripheral nerves starting at the arms' and legs' extremities, and then progressing to internal organs. This condition remains extremely serious as patients experience pain, as well as non-pain-related signs such as loss of balance, lack of sensation and autonomic dysfunctions (heart, bladder, sexual and digestive function). These deficits contribute to the degradation of the patients' quality of life and reduce their life expectancy.

The current available treatments address only the pain component of the disease, neglecting disease progression and non-pain-related disturbances. Furthermore, in current clinical practice, drugs prescribed to reduce pain are only partially efficacious in a subpopulation of patients and are associated with major side-effects, thereby postponing their introduction as potential medication. Yet, pain medication represents a market of several billion US dollars per year and the global diabetic neuropathy market is expected to grow at a Compound Annual Growth Rate (CAGR) of 8.4% over 2014-2018.

Besides, once initiated, nerve degeneration and deficient microvascularization, an intertwined pathology, only worsen and lead to additional disabilities (foot ulcer, amputations etc.).

Atexakin alfa is patented until 2022/2023 for Diabetic Neuropathy with five years extension for the first time on the market, leading to 10-12 years data exclusivity protection.

Exhibit 15: Clinical observations - Exercise improves Type 2 Diabetes and DN symptoms



Source: Company Data

Pulsatile IL-6 at physiological doses mimics the benefits of exercise by stimulating microvascular blood flow, decreasing inflammation and increasing lipolysis.

Rationale and Development

Atexakin alfa is a low-dosage formulation of Interleukin-6 (IL-6), a cytokine of 185 amino acids with pleiotropic functions in different tissues and organs. In the nervous system, IL-6 behaves in a neurotrophic-like fashion (nerve growth stimulator), inducing anti-apoptotic genes expression (reduction of programmed cell death), promoting nerve regeneration and remyelination (nerve insulation), protecting neurons from toxic injuries. These biological activities of IL-6 are mediated by a specific membrane receptor system comprising two different proteins. Activation of the receptors of IL-6 leads to a cascade of signaling events leading to cellular protection and differentiation. In particular in the nervous system, IL-6 stimulates the restoration of nerves' integrity and function.

These beneficial effects of Atexakin alfa were confirmed in several animal models of peripheral neuropathies, including diabetic neuropathy, as well as in other traumatic models such as spinal cord or optic nerve injury and permanent focal cerebral ischemia in rats. Furthermore, in diabetic neuropathy models, Atexakin alfa administration restored the vascular dysfunction associated with established diabetes, thereby completing the pleiotropic therapeutic activities of the molecule.

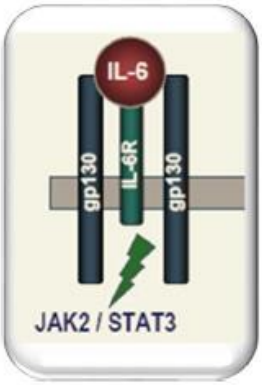
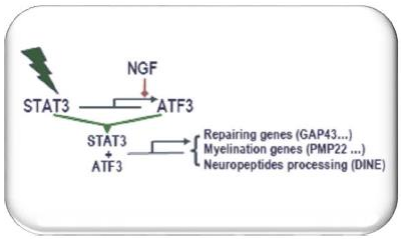
In the last years, converging data demonstrate that in type 2 diabetic patients the combination of diet and supervised physical exercise has a beneficial impact including on nerves' integrity. A transient secretion of IL-6 from muscle has been shown to accompany exercise. Certain of the exercises' benefits could be mimicked by injection of recombinant IL-6 in humans. This lends support to the benefits seen with Atexakin alfa in the animal models of diabetic neuropathy.

Disabilities often prevent type 2 diabetic patients with diabetic neuropathy from exercising to an adequate level. Furthermore in their case, endogenous IL-6 production upon exercise is lower than in healthy volunteers, suggesting that the underlying disease disturbs endogenous IL-6 induction.

All these observations suggest that providing additional IL-6, at doses mimicking physiological pulsatile elevation of circulating IL-6 levels that normally occurs during strenuous exercise, will support neuronal repair leading to the reinstatement of normal sensations and slowing down of the disease progression.

Mechanism of Action

Exhibit 16: IL-6 is neuro-regenerative through specific gene expression

IL-6 responsive cells	Neuro-restorative pathway
	

Source: Company Data

Physiological IL-6 acts as a paracrine hormone stimulating regeneration. Among the functions it performs are inducing neurite outgrowth related genes, modulating myelin proteins expression, protecting neurons from various injuries, maintaining mitochondria integrity and regulating processing of pain-inducing neuro-peptides.

Positioning and Competition

A disease modifier treatment, which acts by slowing or stopping the course of the disease, re-establishing adequate sensations and stimulating vascular function, has the potential to prevent the occurrence of painful and non-painful symptoms, and potentially diabetic consequences such as foot sores and ulcers. Such a treatment can potentially create a new market segment beyond the current pain killer treatments.

The company's specific targeted market comprises Disease Modifying Anti Neuropathic Drugs (DeMAND) to address both painful and non-painful symptoms. The market presents an attractive opportunity for the company as the FDA has not formally approved any disease modifying drugs yet.

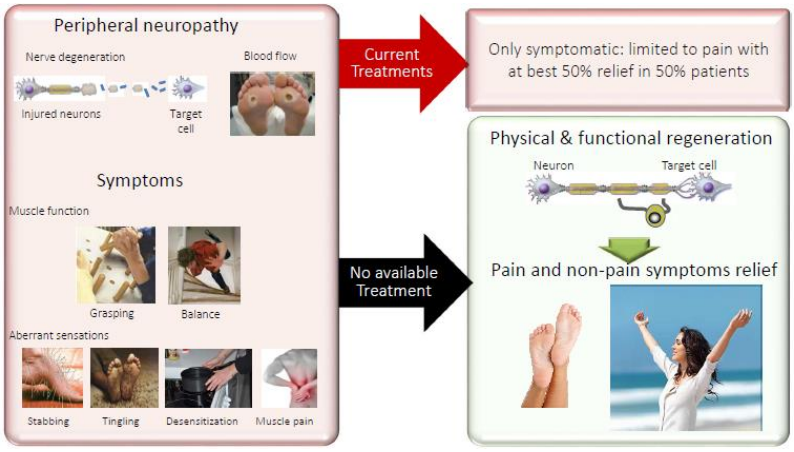
Aldose reductase inhibitors (ARI), α-lipoic acid and vitamins B are the few drugs that have demonstrated modest benefits in reducing the disease course. The market of ARI has never expanded beyond Japan and α-lipoic acid is only prescribed in Germany. Relief's most advanced competitor, VM202, a plasmid expressing the hepatocyte growth factor, has successfully completed Phase II and is slated to enter Phase III clinical testing. Ersatta (C-protein, CBX129801, Cebix Inc.) for the treatment of type 1 diabetes recently failed to demonstrate efficacy in a Phase II clinical trial, even though it was granted a fast track status by the FDA. Additional competition may also come from Actovegin (ultrafiltrated blood calf serum, Nycomed/Takeda), which has completed a phase III clinical trial for diabetic peripheral polyneuropathy. However, little information on the current development of this drug is available. Finally, ARA 290, a peptide derived from erythropoietin, is in a Phase II clinical trial by Araim Pharmaceuticals.

Although a few other compounds are under clinical development, given the limited number of new mechanisms of action and limited efficacy for neuroprotection, the competitive space is favorable for the development of new active and safe molecules to address the non-painful symptoms and disease progression in DN.

Successful clinical development of Atexakin alfa as a potentially disease-modifying drug could either result in DeMANDs becoming first-line treatments replacing the symptomatic treatments available, or DeMANDs being administered broadly to patients as complementary adjuncts to existing symptomatic treatments. In both cases the potential market represents multiple billions of US dollars globally. The drug has a peak sales potential of CHF2.8bn with its expected launch in 2022.

Atexakin alfa will be positioned as a first-in-class drug prescribed by specialists. Therefore, favorable reimbursement by health care providers is expected.

Exhibit 17: Peripheral neuropathy – Current Scenario



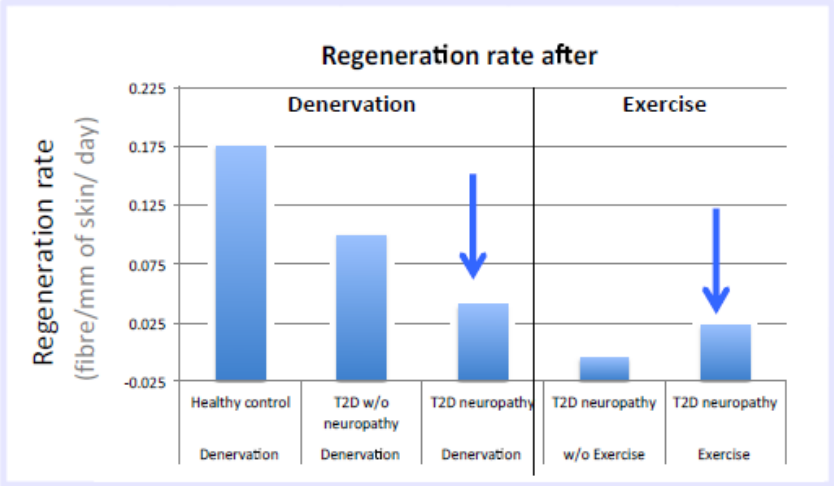
Source: Company Data

Clinical Trial Design and Timeline

For Atexakin alfa, the company intends to engage into a Phase II clinical trial campaign with the aim to rapidly generate relevant data to drive decision on late stage development. The Phase II program will start with a focused, cost-contained trial assessing objective and quantifiable end points following limited treatment duration. The trial is entitled "A randomized, single-centre, double-blind, placebo-controlled Phase II study to assess efficacy and safety of subcutaneously administered low doses rh-IL-6 in improving sensory nerves density and quality of life of type 2 diabetes-induced distal symmetrical polyneuropathy (DSPN) patients" (AtexaDiaNe). This trial will involve type 2 diabetic patients with mild-to-moderate DSPN with a placebo-controlled, randomized design testing safety and efficacy at both the physiological and clinical aspects of one dose of Atexakin alfa. The company's planned Phase IIa clinical trial will require fewer than 40 diabetic patients with mild neuropathies. The trial duration is expected to be short (four months). Phase IIb testing would involve a larger population of diabetes patients and is expected to be conducted for a longer duration (likely six months).

Previous Clinical Trials

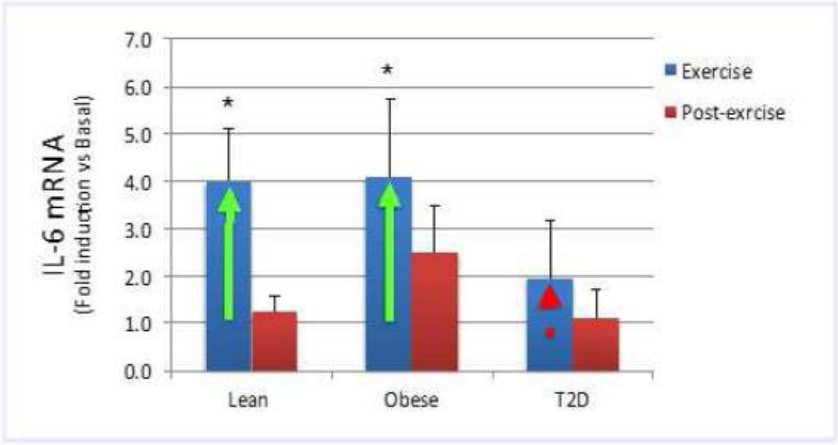
Exhibit 18: Clinical observations - Partial benefit of exercise in Type 2 Diabetes patients



Adapted from:
Kluding et al., 2012, J Diab Complicat. 26, 424-29
Polydefkis et al., 2004, Brain 127, 1602-15

The above exhibit shows that type 2 diabetes patients experience a lower rate of regeneration after exercise than after experimental denervation.

Exhibit 19: Clinical observations - Partial benefit of exercise in Type 2 Diabetes patients



Adapted from:
Tantiwong et al., Am J Physiol Endocrinol Metab 299:E794-E801

The above exhibit shows the effects of insufficient IL-6 induction by physical exercise in type 2 diabetes patients. The results shown above indicate that abnormal exercise-induced IL-6 in type 2 diabetes patients correlates with lower regenerative capabilities.

Based on previous clinical investigations of recombinant human IL-6 as a thrombopoietic factor in different clinical settings, and treating more than 700 patients, the maximum tolerated dose (MTD) is already well-established. The selected dosage range for the envisaged diabetic peripheral neuropathy (DPN) clinical trials are considered safe as these doses are up to 50 times lower than the MTD level. Moreover, the clinical-grade batch of Atexakin alfa that has been approved by the Medicines & Healthcare products Regulatory Agency (MHRA) of the UK in 2004 for use in clinical trials is readily usable for the upcoming Phase IIa DPN trial. No new clinical-grade material would need to be manufactured until after this trial is complete.

The beginning of the clinical trial (first patient enrolled) is forecasted during H1 2017, while the final report on the trial is expected in H1 2018. The manufacturing process (including the engineering and optimization of the Chinese Hamster Ovary or CHO cell line for use in recombinant manufacturing, production scale up, purification) has already been developed. One of the main advantages of having obtained the Atexakin alfa product candidate through a licensing agreement with an established company like Merck KGaA is the assurance that all preclinical development work has been conducted in a thorough and comprehensive manner and all production processes have been developed in an optimized way. There is extensive documentation supporting all aspects of the project.

Business partners are ready to operate and the Phase IIa (proof-of-concept or PoC) program has already been designed and validated by key opinion leaders (KOLs); data from this program could be obtained within less than two years. The total overall R&D cost for this program up to market entry is estimated to be CHF50-55mn. Phase III trials could enroll 300 – 500 subjects each and regulators are likely to require two such pivotal studies for approval in DPN.

Following the conclusion of this Phase II study and depending on the outcome of the trial, the company could decide to continue clinical development on its own or search for co-development partners for completion of Phase III studies and marketing. Atexakin alfa is expected to be launched in the 2021/2022 timeframe.

ADDITIONAL DEVELOPMENT PROGRAMS

Aviptadil for the treatment of ALI

ALI and its most severe form, acute respiratory distress syndrome (ARDS), are both clinical conditions with high mortality rates. According to the American-European Consensus Conference (AECC), ALI/ARDS is defined as a syndrome of reduced pulmonary gas exchange caused by diffuse inflammatory processes with increased vascular permeability.

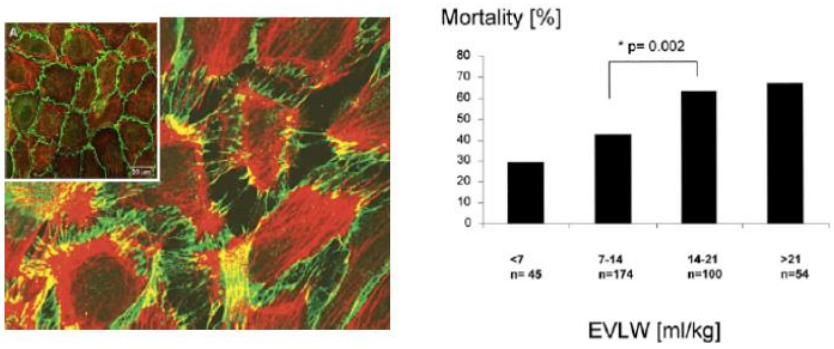
ALI results from catastrophic damage to the lungs, which causes fluid to leak into the alveoli preventing blood oxygenation. Possible causes of ALI are inhalation of high amounts of smoke or toxic gases, severe burns, near-drowning, drug overdose, blood or lung infections, inflammation of the pancreas, lung contusion, and trauma to another part of the body. Patients with ALI have difficulty breathing, tachycardia (rapid heartbeat), and they may progress into fatal multi organ failure. ARDS differs from ALI only by the degree of hypoxemia.

Irrespective of the initiating clinical condition inducing ALI/ARDS, lung respiratory function is compromised by alveolar filling with high protein pulmonary oedema, surfactant dysfunction resulting in the flooding of the lungs' microscopic air sacs responsible for the exchange of gases such as oxygen and carbon dioxide.

ALI affects about 190,000 patients in the US, and about 172,000 people in the EU, with no gender, race or geographical difference. ALI is an intensive care unit indication, which may be considered attractive as it is uniquely hospital-based.

ALI is a life-threatening disease because it causes severe breathing problems. These can be fatal in up to 50% of the patients, causing death via asphyxiation.

Exhibit 20: ALI – Key characteristics



Source: Sakka et al., 2002

As shown in the above exhibit, the loss of barrier function and an increase in vascular permeability results in edema formation and an increase in Extravascular Lung Water (EVLW) correlates with mortality.

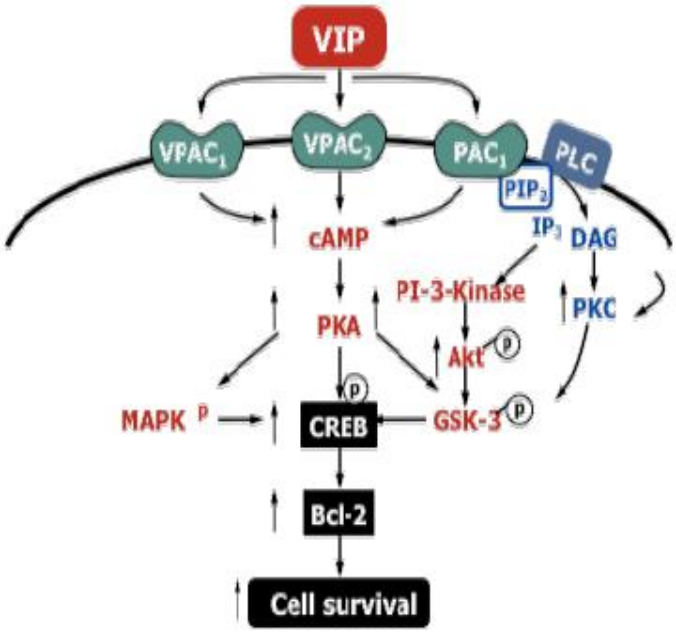
There is currently no pharmacological therapy approved for ALI/ARDS and the only intervention consists in mechanical ventilation. The introduction of sophisticated mechanical ventilation, often including high oxygen concentration, reduced acute mortality in multicenter ALI/ARDS trials from about 40% to 31%. However, mechanical ventilation could itself generate a mechanical stress leading to barotrauma and worsen the ALI/ARDS outcome.

Based on its proven biological properties of lung preservation and homeostasis, Aviptadil appears to be an attractive candidate for the ALI indication. This rationale is supported by the demonstration of pharmacological effects in numerous animal model systems of ALI, in which Aviptadil was highly protective, restored barrier function at the endothelial / alveolar interface and thereby protected the lung and other organs from failure.

Besides its potential in the treatment of sarcoidosis and ALI, we believe Aviptadil may have massive potential for the treatment of other lung-related disorders including chronic obstructive pulmonary disease (COPD) and pulmonary arterial hypertension (PAH). The market for these indications is relatively large and presents attractive monetizing opportunities for the company. Relief could achieve peak sales level of $12bn and $1bn for COPD and PAH respectively.

Mechanism of Action

Exhibit 21: Aviptadil for ALI



Source: Said & Dickman, 2000

Aviptadil increases cyclic Adenosine Monophosphate (cAMP) levels, thereby inhibiting overly elevated NFκB activation, followed by regulation of TNF-α, IL-6, IL-12, IL-17, CD40, CD80, CD83, CD86, HLA class II, TLR2, and TLR4 expression. It also helps in prevention of apoptosis by inhibiting exaggerated Fas ligand (FasL), perforin, granzyme B and caspase expression and inducing expression of bcl-2, an anti-apoptotic protein. Aviptadil also plays a critical role in the enhancement of synthesis of pulmonary surfactant, inhibition of exaggerated chemokine-dependent leukocyte recruitment and exaggerated iNOS production.

Clinical Trial

The initial Phase II clinical trial of Aviptadil in ARDS was conducted as an open-label safety and preliminary efficacy study in eight patients with ARDS complicating sepsis. The eight ARDS patients received Aviptadil (i.v. 50 pmol/kg/h) as a starting dose with the possibility to escalate to a higher dose (100 pmol/kg/h). One patient discontinued treatment due to bronchial obstruction and died due to severe respiratory failure (non-drug related event). The remaining seven patients concluded treatment periods of either 6h (n=3) or 12h (n=4). Three patients escalated to the higher dose. After 30 days of monitoring, six patients had survived and one subject had died from a cerebral artery infarct which was not considered to be a drug-related event. Positive End Expiratory Pressure (PEEP) reduction was achieved in three patients (including two, who received the higher dose). In two patients receiving 12h infusions, there was a moderate decrease in systolic blood pressure which was reversed after slowing the infusion and administration of a saline bolus. No other side-effects were observed.

Aviptadil was well tolerated and clinical observations provided a basis for further development as a treatment option for ALI/ARDS patients, and probably also for pediatric / neonatal respiratory distress syndrome.

In summation, therefore, Aviptadil should be considered capable of providing a unique product profile as the first pharmacological support in ALI/ARDS, an acute life-threatening disease with very high medical need. Aviptadil in ALI/ARDS is expected to be positioned as a first-in-class drug prescribed by intensive care specialists. Therefore, favorable reimbursement by health care organizations is expected. The drug could also be launched with a small, hospital-based sales force, which makes this indication a candidate for an opportunity that Relief could target independently if necessary.

Atexakin alfa for the treatment of Chemotherapy-Induced Peripheral Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a common treatment-related adverse effect associated with several widely-used chemotherapeutic drugs that are often employed in cancer patients. CIPN not only imposes the risk of necessary dose reductions of chemotherapy and also early discontinuation, thereby compromising the treatment of cancer, but also has a substantial impact on the long-term quality of life in cancer survivors. The overall incidence of CIPN is estimated to be approximately 40% in patients. With an estimated cumulative total of 30 million cancer survivors in the US and EU territories alone, CIPN represents a major market opportunity. Unfortunately, this condition currently has no efficient treatments and practitioners tend to under-diagnose or ignore CIPN.

A series of pre-clinical experiments has demonstrated that Atexakin alfa could block, in both preventive and curative modes, CIPN induced by platinum-containing drugs (e.g., carboplatin, cisplatin or oxaliplatin), taxanes (e.g., paclitaxel, docetaxel) or vinca alkaloids (e.g., vincristine and vinblastine). As observed in models of DPN, the effects of Atexakin alfa on pain and motor symptoms in CIPN were accompanied by preservation/restoration of nerve fibers integrity, confirming disease-modifying activity and not solely a painkiller effect.

Pre-clinical experiments also demonstrated that Atexakin alfa treatment did not interfere with chemotherapeutic agents' efficacy. This corroborated the data collected during previous clinical trials assessing Atexakin alfa's effects on platelets preservation in cancer patients under chemotherapy. Clinical trials using Atexakin alfa proved the reversibility of side-effects and determined a safety margin of 50 times for the selected doses for the CIPN clinical trials.

Accordingly, given this body of evidence, Relief considers Atexakin alfa capable of providing a unique solution as the first pharmacological supportive care drug specifically aimed at treating CIPN, either in the form of co-medication with chemotherapeutic agents or after cancer has been cured. Considering the substantial unmet medical need and the elevated cost of care associated with cancer patients who suffer from CIPN and who may interrupt or cease chemotherapy because of CIPN, favorable reimbursement by health care organizations should be anticipated.

Currently, the company has issued and validated patients in the US and pending patients in the EU. Phase II proof-of-concept testing could be achieved in a clinical protocol aimed at enrolling approximately 100 subjects, which would permit the testing of up to four doses of Atexakin alfa against placebo. While the design of this study and pivotal trials in the CIPN indication would likely involve 3 – 6 months' duration of evaluation, such trials are unlikely to be difficult to enroll or execute and accordingly this opportunity appears to be an attractive line extension possibility for Atexakin alfa. Relief does not, however, plan to undertake clinical development in CIPN until after the initial Phase IIa trial in DPN has been completed and only if this study validates the hypothesis that Atexakin alfa can exert beneficial effects on peripheral neuropathy in the human clinical setting.

Further Opportunities

The company owns certain Intellectual Property (IP) rights (issued and validated patents and/or OMPD/ODD from the EU and the US) that are currently outside of the company's strategic focus. These IP rights might potentially generate further revenue streams through upfront payments, milestone and eventually royalty payments subject to out-licensing agreements with interested parties.

Although this activity will not be pursued at the early stage of the company in order to focus on the development of its most advanced and promising MPCs, only limited time would need to be devoted to promote these opportunities externally.

Among all of the issued and validated patent families of the company's MPCs, the following opportunities have been in particular considered to be potentially out-licensed:

Interferon gamma

Repositioned from chronic granulomatous disease, malignant osteopetrosis into inhaled treatment of Idiopathic Pulmonary Fibrosis (IPF), at development stage clinical phase II. IPF is a chronic, progressive illness of the lung, with a median survival time of only a few years after the onset of symptoms. IPF is a form of Interstitial Lung Diseases (ILD) where healthy tissue is progressively replaced by components of the connective and supporting tissue.

Interferon gamma is a natural human cytokine that exerts a wide range of biological effects, especially within the immune system. The anti-fibrotic (anti-scarring) properties of the drug are well documented.

Alpha melanotropin

Repositioned from multiple sclerosis into injectable treatment of Chronic Beryllium Disease (CBD), ready to start development for clinical phase II. CBD is an occupational hypersensitivity disorder caused by continued beryllium exposure. The main symptoms include dry coughing, fatigue, weight loss, chest pain and increasing shortness of breath.

Alpha melanotropin is an endogenous human peptide initially described in the year 1957. To date, over 5,100 scientific publications and over 530 review articles describe the immunomodulatory, anti-inflammatory and antipyretic effects of Alpha melanotropin.

Octreotide

Repositioned from acromegaly, acute variceal haemorrhage, chylothorax, gastroenteropancreatic diseases into inhaled treatment of drug-resistant tuberculosis, at development stage preclinical phase. Tuberculosis (TB) is a life threatening and highly contagious airborne disease caused by infection with mycobacterium tuberculosis. TB typically affects the lungs but it may also affect any other organ of the body. It is usually treated with a regimen of drugs taken for six months to two years depending on the type of infection. Drug-resistant TB is one that is resistant to single or combined anti-tuberculosis treatments and is a major global threat, justifying the development of novel therapeutics.

Octreotide is a synthetic analogue of somatostatin. It exerts a potent inhibitory effect on the release of anterior pituitary growth hormone, thyroid-stimulating hormone and peptides of the gastroenteropancreatic endocrine system.

BUSINESS STRATEGY

Focus on safe bioactive MPCs of human origin, in particular peptides and small proteins

Relief primarily focuses on bioactive products of human origin. The firm believes that products of human origin, and in particular peptides and small proteins, offer better efficacy and safety profiles vs. organic small molecule drugs. This is even more pertinent when assessing the opportunities presented by Aviptadil and Atexakin alfa, because these agents are being positioned in diseases that are known to involve dysregulation or under-expression of the endogenous forms of these molecules (namely, VIP and IL-6), and thus Relief is actually pursuing complement/substitution/replacement therapy with its lead programs. In our view, the concept of better safety and efficacy for peptides and small proteins vs. small molecule drugs is justified, because protein-based pharmaceuticals are not only larger in molecular weight vs. small molecules, but also contain more complex compositions and higher order structures. Given this characteristic, peptides and proteins possess highly specific and effective functions due to their complex molecular structure. At the same time, they are highly potent therapeutics, which present reduced likelihood of interference with biological processes.

As a consequence, the company expects the risk of failure of development associated with toxicity and other adverse effects to be significantly lower for the programs it pursues, including its current primary development programs Aviptadil and Atexakin alfa for various indications, as compared to compounds that are not naturally-occurring (i.e., non-human origin, as is the case with organic small molecules). Also, both Aviptadil and Atexakin alfa have already been tested in clinical trials for other indications and favorable safety data is available for both. This should allow Relief to explore further potential for the targeted indications.

Focus on diseases with attractive market potential

Based on the company's core strategy, the current focus of its principal development programs is on attractive, underserved markets by developing drugs for unmet medical needs. For example, one of the lead clinical indications for Atexakin alfa is DPN, which is diagnosed in 20% – 40% of diabetic patients and which is predicted to afflict in excess of 300 million patients by the year 2050. Crucially, this disease remains largely undertreated. In particular, no disease-modifying drugs exist on the market that can stop the evolution of the disease and reconstruct the degenerated nerves, which is the company's goal with its MPC Atexakin alfa. Moreover, the other principal MPC of the company's principal development programs – Aviptadil for sarcoidosis – targets a market which lacks efficacious treatments that could significantly improve patients' quality of life and survival rate. There are no drugs currently available that are specifically approved to treat sarcoidosis. This situation thus provides an attractive opportunity for the company to advance a specific drug to address this orphan indication.

Moreover, Relief possesses an entire pipeline of line extension opportunities focusing on additional indications for its lead compounds, including Aviptadil in ALI and Atexakin alfa for CIPN. ALI and its most severe form, ARDS, are life-threatening diseases with fatality rates of 30% – 50%. ALI has a high incidence rate (200,000 per year in the US). In the absence of any existing treatments, Aviptadil could become the first-line treatment in ICUs to reduce mortality. CIPN is a treatment-related adverse effect associated with broadly-used "workhorse" chemotherapy drugs applied in the treatment of cancer. The occurrence of CIPN in cancer patients is estimated to be roughly 40%. There are estimated to be a cumulative 30 million cancer survivors in the US and Europe. The lack of effective treatments for CIPN makes this an attractive future opportunity for Relief to target using Atexakin alfa.

Market protection through issued patents and OMPD / ODD

The company's strategy is to seek patent protection for its MPCs and also seek to apply for the OMPD/ODD status (in both the EU and the US) to help to build and defend the exclusive market position of the relevant MPC granted by an OMPD/ODD once marketing approval has been received. This strategy substantially reduces the risks that potential competitors might develop the same molecules for the same indications. Based on this strategy, all of the drug candidates in the product pipeline, including the Main Development Programs consisting of the MPCs Aviptadil and Atexakin alfa, are protected by proprietary patents, are under exclusive license agreement, and/or have obtained orphan medicinal product designations.

Mentioned below is the list of OMPDs/ODDs which the company has adopted with US FDA and EU:

US FDA

- Aviptadil in pulmonary arterial hypertension
- Aviptadil in acute lung injury
- Alpha melanotropin in chronic beryllium disease
- Interferon gamma in idiopathic pulmonary fibrosis
- Peptide YY in hepatocellular carcinoma
- Thymopentin in cutaneous sarcoidosis

EU

- Aviptadil in sarcoidosis
- Aviptadil in ALI
- Aviptadil in pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
- Interferon gamma in idiopathic pulmonary fibrosis

Lifecycle management strategy supported by patent extension and data exclusivity rights

For molecules that have never been marketed before, such as Atexakin alfa, Patent Term Extension (PTE) can be applied for in the US and Supplementary Protection Certificate (SPC) in the EU. Both represent an extension for five years of each respective patent term. In addition, biologics like Atexakin alfa would benefit from 10 and 12 years of data exclusivity in the EU and the US, respectively, under current legislation governing biologic drugs. During the entire data exclusivity period, the use of company-generated data by potential competitors to support their marketing approval applications for generic versions of the branded products is thus prevented.

Outsourcing and strict project management

With the aim to stay a lean organization, Relief works with leading clinicians and regulatory experts on the set-up of clinical protocols as well as with third party manufacturers for the synthesis of drug product and with clinical development service providers to implement clinical trials. Outsourcing or collaborating with other parties is a cost-effective and operationally efficient way to achieve its business goals. Rising costs and falling productivity, among other trends, are driving companies in the biotechnology and pharmaceutical companies to outsource an increasing range of functions to CROs to achieve cost savings. Besides providing substantial global capacity to drug developers, CROs have become a critical contributor to clinical trial programs. According to a recent report by ResearchandMarkets, clinical trials conducted by CROs are completed up to 30% more quickly than those conducted in-house by pharma companies. This translates into a considerable cost savings and a faster market launch.

Furthermore, this model provides the company with flexibility in managing overhead costs while maintaining its ability to keep control of the design, planning and management of the projects that will be taken care of by a specialized team of in-house experts able to competently interact with its partners throughout every stage of the process.

INDUSTRY OVERVIEW AND COMPETITIVE LANDSCAPE

Relief Therapeutics is focused on developing drugs for the treatment of diabetic complications and respiratory diseases, with a primary focus currently on sarcoidosis and DPN. While the market for sarcoidosis is a niche market and presents attractive market potential for the prospective entrants, the market for DN is relatively large, with a report from Datamonitor predicting that the peripheral diabetic neuropathy market is estimated to reach $4.1bn in 2019. The company's target market for DN, however, comprises disease-modifying anti-neuropathic drugs to address both painful and non-painful symptoms.

Sarcoidosis

Sarcoidosis is an inflammatory disease that affects organs throughout the body. The condition is characterized by the formation of granulomas, which are nodules containing collections of inflammatory cells. The disease can significantly impact an individual's quality of life and can be fatal if not managed properly. Sarcoidosis has a variable clinical presentation and progression. About 60-70% of the time, sarcoidosis cures itself within a year or two but approximately 30% of all patients with sarcoidosis develop chronic disease. Mortality occurs in 1-5% of patients. Pulmonary fibrosis is the most common cause of death. Approximately 36,000 new cases of sarcoidosis occur each year in the US.

Exhibit 22: Organs and symptoms commonly involved in sarcoidosis

Site of Involvement	Frequency (%)	Signs and Symptoms
Lungs	90	Dry cough, dyspnea, bilateral hilar lymphadenopathy
Liver/Spleen	50-80	Hepatosplenomegaly, abnormal liver function
Eyes	50	Uveitis, iritis, photophobia, dry eyes
Bone and bone marrow	40	Osteolytic lesions, osteopenia, osteoporosis
Skin	25	Indurated purple plaques, erythema nodosum
Heart/central nervous system	5-10	Cardiac arrhythmias, congestive heart failure, facial nerve palsy
Parotid gland	4-6	Parotitis, uveoparotitis, facial palsy

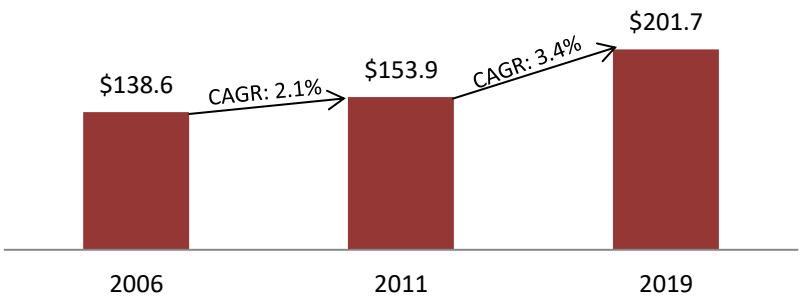
Source: Suresh L, Radfar L. Oral sarcoidosis: a review of literature. Oral Dis. 2005

The reasons for the occurrence of the disease are not yet known and the diagnosis of sarcoidosis is also challenging as signs and symptoms of the condition are very broad, sometimes mimicking symptoms of other diseases. There is no single diagnostic test to detect the disease. Usually, it is detected by a chest radiograph (x-ray) or chest computed tomography (CT) scan, which most commonly shows enlarged lymph nodes.

Currently, there is no drug approved expressly to treat or cure sarcoidosis. Due to the unavailability of approved therapies, the current line of treatment is dominated by off-label therapies, such as corticosteroids (cortisone, prednisone and prednisolone), immunosuppressant drugs (methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil and leflunomide), tumor necrosis factor alpha (TNF-α) blockers (infliximab, etanercept and adalimumab), anti-malarial drugs (chloroquine and hydroxychloroquine), and other anti-inflammatory drugs.

Key therapy for the treatment of the disease involves corticosteroids (e.g., prednisone), a class of steroid hormones, which non-specifically suppress chronic inflammation. Drugs like prednisone are sometimes used in association with additional immunosuppressant agents like methotrexate. Long-lasting treatment with corticosteroids and/or immunosuppressive therapy is not recommended due to the high likelihood of severe negative side-effects, including permanent damage to the immune system and the incidence of opportunistic infections.

Exhibit 23: Global sarcoidosis therapeutics market



Source: ASDReports

An analysis by the research firm ASDReports done in March 2012 (shown in the above exhibit) shows that the global sarcoidosis therapeutics market stood at $138.6mn in 2006, and grew at a Compound Annual Growth Rate (CAGR) of 2.1% to reach $153.9mn in 2011. According to the firm's estimates, the market is expected to reach $201.7m by 2019, growing at a CAGR of 3.4%.

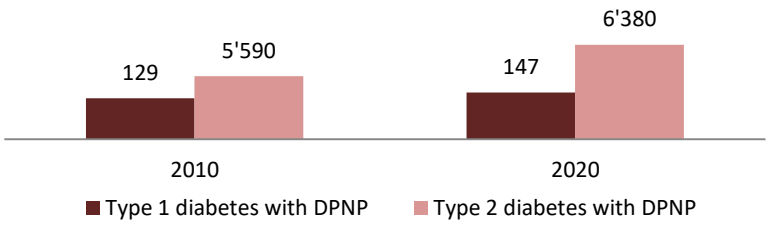
Diabetic Peripheral Neuropathy (DPN)

DPN is a progressive disease and develops as diabetes persists. It is characterized by the degeneration of peripheral nerves starting at the arms' and legs' extremities, and then progressing to internal organs. This condition remains extremely serious, as sufferers experience both severe pain as well as non-pain-related symptoms such as loss of balance, lack of sensation and autonomic dysfunctions (heart, bladder, sexual and digestive function). These deficits contribute to the degradation of the patients' quality of life and reduce their life expectancy.

Neuropathy is diagnosed in 20 to 40% of diabetic patients. According to World Health Organization projections, the total worldwide population afflicted with this debilitating co-morbidity of diabetes is predicted to exceed 300 million patients by the year 2050.

According to research conducted by Datamonitor in 2011, the number of prevalent cases of types 1 and 2 diabetes mellitus are on the rise in the seven major markets (the US, Japan, France, Germany, Italy, Spain, and the UK). The aging population of the seven major markets plays a significant role in these increases over time because the prevalence of diabetes sharply increases with increasing age.

Exhibit 24: Types 1 and 2 diabetes cases with Diabetic Peripheral Neuropathic Pain (DPNP) in seven major markets ('000s)



Source: Datamonitor

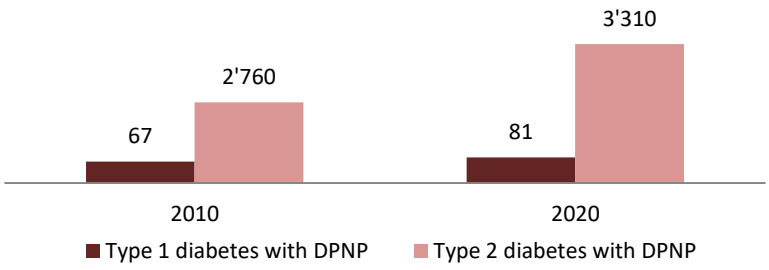
As shown in the above exhibit, during 2010 and among the diagnosed diabetic population, there were 128,500 and 5.59 million prevalent types 1 and 2 diabetes cases with DPNP in the 7 major markets mentioned above. Both the categories are expected to show an increase of 14% till 2020, resulting in 147,000 (type 1) and 6.38 million (type 2) DPNP cases by that time.

Each of the 7 major markets is expected to experience an increase in DPNP cases (ranging between 3% and 20%) of each diabetes type between 2010 and 2020.

The risk of diabetic peripheral neuropathy (DPN) and DPNP among diabetics is substantially influenced by the duration of disease. Similarly, various studies support that older age is independently associated with an increased risk of neuropathy, DPN, or DPNP among diabetics. Both of these factors will likely drive the number of DPNP cases higher in the years to come as the populations of the seven major markets age.

US researchers estimate that 60–70% of people with diabetes have some form of neuropathy. Across all covered markets, estimates for the prevalence of DPN among diabetics range from 13% to 54%, with the lower estimates typically pertaining to type 1 diabetics and symptomatic individuals. Pain is a condition commonly associated with diabetic neuropathy and DPN. The prevalence of DPNP is believed to range from 10% to 20% among all diabetics and from 40% to 50% among diabetics with neuropathies.

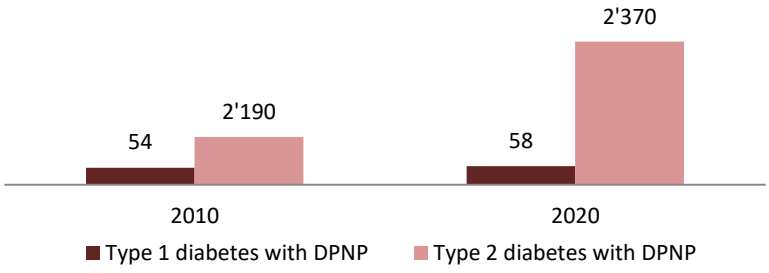
Exhibit 25: Types 1 and 2 diabetes cases with DPNP in the US (`000s)



Source: Datamonitor

As shown in the above exhibit, the US had the largest number of prevalent DPNP cases among all 7 major markets with 67,300 type 1 cases and 2.76 million type 2 cases, in 2010. This formed approximately 50% of all cases in the 7 major markets. By 2020, the number of cases in the US will increase to 80,800 (type 1) and 3.31 million (type 2), constituting slightly more than half of all cases in the 7 major markets.

Exhibit 26: Types 1 and 2 diabetes cases with DPNP in the 5 major EU markets (`000s)



Source: Datamonitor

As can be seen in the above exhibit, in the 5 major EU markets, there were 53,500 diabetes type 1 and 2.19 million diabetes type 2 prevalent DPNP cases in 2010. This constitutes 42% (type 1) and 39% (type 2) of all cases estimated for the 7 major markets for 2010. Between 2010 and 2020, the number of diabetes types 1 and 2 DPNP cases will each increase by 8.0% to 57,800 and 2.37 million cases, respectively.

The available treatments available in the market currently address only the pain component of the disease and they do not target the disease progression and non-pain-related disturbances. Also, the drugs currently prescribed to reduce pain are associated with major side-effects. In contrast, Relief Therapeutics is focused on developing a truly disease-modifying anti-neuropathic drug which addresses both the pain-related and non-pain related symptoms.

No disease-modifying drugs have as yet been approved to treat DPN. The exhibit below mentions key players currently developing drugs for the treatment of DPN.

Exhibit 27: Competitive space

Drug Candidate	Company	Status
VM202	VM BioPharma	Ph II complete; to enter Ph III
Ersatta	Cebix Inc.	Failed to show efficacy in Ph II
Actovegin	Nycomed/Takeda	Completed Ph III; latest update on the same is not available
ARA 290	Araim Pharmaceuticals	Currently in Ph II trials

Source: Company Data

Although a few other compounds are under clinical development, given the limited number of new mechanisms of action and limited efficacy for neuroprotection, the competitive space is favorable for the development of new active and safe molecules to address the non-painful symptoms and disease progression in DN.

GROWTH OPPORTUNITIES & KEY DRIVERS

Sarcoidosis – A niche market with attractive potential

Sarcoidosis is a globally occurring disease with potential severe manifestations, especially in the lungs (affecting over 90% of the patients). Currently, systemic corticosteroids like prednisone are used for the treatment of sarcoidosis. Sometimes, prednisone is also used in association with additional immunosuppressant agents like methotrexate. However, none of these drugs are specifically approved for the treatment of sarcoidosis and using corticosteroids-based drugs and/or immunosuppressive therapy for a long time is not recommended due to their severe negative side-effects.

The company is currently testing Aviptadil – a proprietary inhaled formulation of vasoactive intestinal peptide (VIP) – which is an endogenous human peptide acting as a ligand on specific G-protein coupled transmembrane receptors. Its predominant biological activity is performed in the lungs, and evidence suggests Aviptadil to be an attractive candidate for the potential treatment of sarcoidosis.

The company has decided to use inhalation of the drug as the route of administration for sarcoidosis patients. This is to avoid the side-effects observed with systemic delivery and also to be able to increase the dose to therapeutically meaningful values for respiratory diseases.

Moreover, inhaled drugs have been observed to act quickly, minimize undesired negative side-effects, avoid the hepatic first-pass metabolism, and act locally in the affected organ. As the size variability among adult lungs is smaller than the overall body size variability, dosing reliability is also improved when inhaling. All these points make a positive case for Aviptadil to succeed in the market as potentially the only drug for sarcoidosis that could suppress its clinical symptoms with any significant negative side-effects.

Growing market for Diabetic Peripheral Neuropathy (DPN)

DPN is classified as a neurological disorder, which is associated with diabetes mellitus. This disorder affects all peripheral nerves such as the autonomic nervous system, motor neurons, and pain fibers. According to the World Health Organization (WHO), around 350 million people across the globe currently suffer from diabetes and around 80% of them live in middle- and low-income countries. Furthermore, DPN affects around 50% of the worldwide diabetic population.

The company is currently developing Atexakin alfa, which is a low-dosage formulation of recombinant human interleukin-6 (rhIL-6), a cytokine of 185 amino acids with pleiotropic functions in different tissues and organs. IL-6 stimulates the restoration of nerves' integrity and function. Data from the past studies has shown that a combination of diet and supervised physical exercise has a beneficial impact on nerves' integrity in type 2 diabetic patients. IL-6 has been shown to mimic certain benefits of exercise in humans.

The company's focus is on the development of a disease-modifying anti-neuropathic drug (DeMAND) to address both painful and non-painful symptoms. Currently, there are no formally approved disease-modifying drugs available to treat DPN. Therefore, the current scenario presents a significant market opportunity to develop molecules aimed at addressing both the non-painful symptoms and disease progression in DPN, which cannot be treated with existing marketed drugs.

With the introduction of new drugs and treatments by leading players, the global DN market is expected to be highly competitive in the years to come. Going forward, partnerships and acquisitions are expected to benefit leading players to maintain their dominance in the global DN market.

Future drug pipeline

The company currently owns IP rights for various product candidates that are currently out of its focus area but these might potentially generate future revenues for the company through upfront payments, milestone and royalty payments subject to certain out-licensing agreements. Some of the MPCs which the company might consider out-licensing in the future include interferon gamma indicated for the treatment of idiopathic pulmonary fibrosis (IPF), alpha melanotropin, indicated for the treatment of chronic beryllium disease and octreotide, indicated for the treatment of tuberculosis (TB).

IP rights and OMPDs/ODDs for company's MPCs

The company has an extensive list of issued and validated patents for its MPCs. Beyond applying for patents, the company also applies for OMPD/ODD in both the EU and the US markets. It currently holds 23 different patent families along with 10 OMPDs for its MPCs. Being an emerging drug development company, this strategy becomes all the more important for the company as it gives an exclusivity over the developed drug for the specific indication and also safeguards its interest to some extent from the established players already operating in the market.

In-licensing Opportunities

The company holds worldwide exclusive rights for the R&D and commercialization of Atexakin alfa, for the treatment of peripheral neuropathies and microvascular diseases, from Ares Trading SA - a subsidiary of Merck KGaA. Relief Therapeutics was conferred these rights in 2015. There were no upfront payments, development milestones or any condition for the right of first refusal included in the terms of the agreement with Merck. Royalties to Merck will account for 7% of net sales if Relief self-commercializes the drug.

Similarly, the company has plans to look for additional in-licensing opportunities to further expand its current drug portfolio apart from reinforcing its position in the market for the primary disease indications.

Strategic acquisitions

The company signed a term sheet to acquire FirstString, a US-based clinical-stage biotechnology company, in an all-stock transaction in July 2016. This acquisition transaction will bring in a Phase III-ready asset, Granexin gel for the treatment of diabetic foot ulcers and venous leg ulcers, together with a pipeline of preclinical and early-stage clinical assets. The prospective acquisition will expand company's pipeline of drug candidates and would enable it to advance both Granexin gel and Aviptadil into Phase III testing in the coming months.

Apart from bringing in an advanced drug candidate to Relief Therapeutics' pipeline, FirstString would also bring in the capability for the former to procure non-dilutive funding for its further drug development programs. FirstString has raised approximately 40% of the total amount that it has spent thus far on R&D through government grants, especially in the form of Small Business Innovation Research (SBIR)/Small Business Technology Transfer (STTR) grants from the federal government.

The company plans to seek to conduct similar strategic acquisitions in the future, in line with its focused business strategy. However, we anticipate that in the coming years Relief shall be primarily aligned towards conducting drug development in the diabetes and respiratory disease arenas, with a particular focus on orphan drug markets, rapid clinical development pathways, and specialty drug niches that can permit retention of maximum strategic flexibility (i.e., preservation of a choice as to whether to commercialize independently or with the aid of regional or global partners).

KEY RISKS

The company is currently not profitable but expects to become profitable, however not in the foreseeable future

The company has never been profitable. Historical losses were due primarily to the unprofitable CRO business, which has been divested. Now that the company has repositioned itself as a drug-developing biotechnology company, its activities will focus on developing MPCs. Hence, it is not expected to become profitable in the foreseeable future. The company has not commercialized any product or generated any revenues from the sale or out-licensing of products and it is not expected to generate any product revenues in the near future.

Liquidity constraints

The group is currently facing liquidity constraints and needs to both cover its ongoing costs and fund its drug development and research activities. The group has a CHF25.0mn Share Subscription Facility (SSF) granted by its largest shareholder to manage its liquidity needs. However, the SSF is subject to certain restrictions based on company's trading liquidity on the SIX Swiss Exchange. Furthermore, the company will need some additional financing to be able to conduct the clinical trials in the next few years. Although the SSF with GEM would support the clinical development of the company's principal programs, it would not be sufficent to fund all the future programs. There is a risk that the company might not be able to raise additional funding in the future.

Dependence on third party development and manufacturing providers

The company relies on third party service providers and manufacturers to successfully carry out its drug development programs. These service providers may not be able to successfully complete the clinical development and obtain marketing approval for the respective MPCs within the time frame and cost estimated by management, or at all. Further, if partners terminate agreements prematurely or if there are delays in development and commercialization of the relevant MPCs, the group will not be able to meet its targets.

MPCs may not be able to achieve the estimated revenue level

The company's ability to reach the forecaseted level of revenue depends on the acceptance of its MPCs by physicians, patients and other market participants. The availability of third party reimbursement for its MPCs is uncertain, and it may be difficult to obtain and/or maintain targeted price levels.

Competition from other drug development companies and institutions

The company's competitors, including both pharmaceutical and biotechnology companies as well as other market participants like universities and teaching hospitals targeting the same indications/MPCs, will be in a position to take advantage if they are able to achieve patent protection, obtain regulatory approvals or accomplish the market launch of their products before Relief Therapeutics is able to do so. This might adversely affect the group's business.

Expanding current portfolio

The group plans to expand its current pipeline of drug candidates through either acquisition or in-licensing of patents from other parties. It may face competition from other players in acquiring promising MPCs. This may reduce group's business prospects to expand its portfolio of marketable MPCs and hence, may negatively impact its business.

Loss or failure to renew intellectual property rights which belong to third parties

The group's one of the leading MPCs - Atexakin alfa - is developed based on patents owned by Ares Trading SA. Relief Therapeutics has an exclusive license for R&D and commercialization of these patents which is subject to certain conditions. In a scenario, if these conditions are not met, the group could potentially lose the exclusive license and the right to exploit the related patents.

VALUATION

We have conservatively valued Relief Therapeutics based on a risk-adjusted Net Present Value (rNPV) approach and, under the condition that the company can obtain sufficient funding to drive its current programs forward, arrive at a summary valuation based on the company's two most promising drug candidates in the three indications of CHF356.4mn or CHF0.19 per share (based on 1,937 million shares as of September 2016).

We have primarily assigned values to Aviptadil for sarcoidosis and ALI, and Atexakin Alfa for DN. Besides these, the company also has other programs in its pipeline targeting various other indications including CIPN, IPF, drug-resistant TB and CBD. We believe that, although, these programs strengthen the company's drug pipeline, they do not materially impact its valuation. Also, the potential impact of the FirstString acquisition or the potential future sales contribution of Granexin gel in diabetic foot ulcers has not been factored into the valuation. Lastly, with respect to Aviptadil for sarcoidosis & ALI and Atexakin Alfa for DN, we have only factored in the revenues from the US and the EU markets. However, these product candidates could potentially also be marketed in other territories including Japan, China and India, generating additional revenues in the future.

We also think that the company's drug repurposing and repositioning (DRR2.0) software tool does not affect company's valuation to a large extent, although it might present potential revenue opportunities in the future. We have not currently included the same in the valuation.

We have applied a discount rate of 22.9% to company's lead product candidate Aviptadil, indicated for the treatment of sarcoidosis to arrive at an rNPV of CHF99.6mn. We have used a 63.0% probability of success given the fact that the drug has already cleared Phase II and the favourable safety and efficacy data for the same is available. We estimate that the drug would achieve peak sales of CHF290.0mn in 2027.

Company's other product candidate Atexakin Alfa for the treatment of DN has also successfully cleared the Phase I clinical trials and is currently preparing to enter Phase II. We have applied a 31.5% probability of success and a discount rate of 22.9% to arrive at an rNPV of CHF194.6mn. We estimate that the drug would achieve peak sales of CHF2.8bn in 2029.

We have also ascribed value to Aviptadil for ALI, which has also cleared Phase I clinical trials. We believe that the drug holds great potential given the lack of available treatments and high fatality rate (50%) among the patients suffering from the ALI. We have used a discount rate of 22.9% along with 31.5% probability of success to arrive at an rNPV of CHF96.8mn. We estimate that the drug would achieve peak sales of CHF432.1mn in 2029.

The following tables detail our key assumptions used to develop the valuation model for the two most promising drug candidates in three different indications.

Exhibit 28: Risk-Adjusted NPV-Based Valuation Methodology – Aviptadil for sarcoidosis

Aviptadil - Sarcoidosis	Base Case
Total Patients with Sarcoidosis[1]	173,942
Patients seeking treatment	86,971
Peak market share	22%
Treatment revenue/year/patient[2]	15,157
Peak sales (mn)[3]	290
Launch	2021
Peak sales year	2027
Patent expiration[4]	2026
Discount rate	23%
Probability of success[5]	63%
Risk-adjusted NPV (mn)	100
NPV per share	0.05
Estimated Net Cash Position (Q3 2017)	10
Total enterprise value	89
Shares Outstanding (mn) (Q3 2017)	1,937

Notes on assumptions:
[1] Sarcoidosis patients - The US and European Union (in peak sales year)
[2] Revenue/year/patient - premium pricing justified as no other effective treatment, without negative side effects, currently available
[3] Peak sales - treatment revenue/year/patient x total patients x peak market share
[4] Earliest patent expiry year
[5] Scheduled to enter Phase 3 clinical trials in H1 2017 and is covered under the orphan drug designation

Source: Research Dynamics; values in CHF

Exhibit 29: Risk-Adjusted NPV-Based Valuation Methodology – Atexakin alfa for diabetic neuropathy

Atexakin Alfa - DN	Base Case
Total Patients with Painful Diabetic neuropathy[1]	14,837,485
Total Patients with Postherpatic neuralgia[1]	184,444
Patients seeking treatment[2]	7,604,421
Peak market share	10%
Treatment revenue/year/patient[3]	3,662
Peak sales (mn)[5]	2,785
Launch	2022
Peak sales year	2029
Patent expiration	2026
Discount rate	23%
Probability of success[5]	32%
Risk-adjusted NPV (mn)	195
NPV per share	0.10
Estimated Net Cash Position (Q3 2017)	10
Total enterprise value	184
Shares Outstanding (mn) (Q3 2017)	1,937

Notes on assumptions:
[1] Painful Diabetic neuropathy and postherpatic neuralgia patients - The US and European Union (in peak sales year)
2 Patients with painful diabetic neuropathy and postherpatic neuralgia seeking treatment
[3] Revenue/year/patient - estimated to start at CHF2,500 for US and CHF2,000 for EU
[4] Peak sales - treatment revenue/year/patient x total patients x peak market share
[5] Probability of success - Atexakin Alfa is scheduled to enter phase 2 trials in H12017
[5] Scheduled to enter Phase 3 clinical trials and is covered under the orphan drug designation

Source: Research Dynamics; values in CHF

Exhibit 31: Risk-Adjusted NPV-Based Valuation Methodology – Aviptadil for acute lung injury

Aviptadil - ALI	Base Case
Total Patients with ALI[1]	544,902
Peak market share[2]	18%
Treatment revenue/year/patient[3]	4,406
Peak sales (mn)[4]	432
Launch	2022
Peak sales year	2029
Patent expiration	2026
Discount rate	23%
Probability of success[5]	32%
Risk-adjusted NPV (mn)	97
NPV per share	0.05
Estimated Net Cash Position (Q3 2017)	10
Total enterprise value	87
Shares Outstanding (mn) (Q3 2017)	1,937

Notes on assumptions:
[1] ALI patients - The US and European Union (in peak sales year)
[2] Higher penetration justified as no pharmacological treatment currently available
[3] Revenue/year/patient - based on currently available treatments cost per year
[4] Peak sales - treatment revenue/year/patient x total patients x peak market share
[5] Probability of success - Aviptadil for treatment of ALI is scheduled to enter phase 2 trials in H12017

Source: Research Dynamics; values in CHF

ADDITIONAL DETAILS

The company has an experienced management team with industry professionals who possess substantial expertise, diverse backgrounds and complementary skill sets in innovation, science, development, marketing and finance.

Management Team

Raffaele Petrone
Vice-Chairman of the Board and Chief Executive Officer

Mr. Petrone has been the Vice-Chairman of the Board of Directors since May 2016. He has also been serving as the company's Chief Executive Officer since October 2013. He started his career in the family business, the Petrone Group, before founding Fin Posillipo S.p.A., a pharmaceutical holding company which operates in the area of strategic investments, finance and business development. Mr. Petrone currently serves as Chairman of the Petrone Group, as Chief Executive Officer of Pierrel S.p.A. and also on the boards of directors of several other companies including Pierrel Research International AG, BCN Farma and Cerma Sarl.

Timothy Snyder
Chief Financial Officer

Mr. Snyder has been Chief Financial Officer of the firm since May 2014. He spent the first nine years of his career with Deloitte and then served as Finance Director and Chief Financial Officer at several companies in the US and Europe – primarily in the private equity sector. He has held various leadership roles in the areas of turn-arounds and restructurings. Mr. Snyder also has experience with post-merger integrations and the assimilation & streamlining of financial processes.

Gael Hedou, Ph.D.
Chief Operating Officer

Dr. Hedou started his industrial career at GlaxoSmithKline, where he led a laboratory supporting both preclinical and clinical projects in psychiatric diseases. In 2008, he joined Merck KGaA to participate in the implementation of the drug discovery and development strategy in Parkinson's disease. He has expertise in the field of drug discovery and project management. Dr. Hedou is one of the co-founders of Relief Therapeutics SA, where he supported the strategic positioning and fundraising campaign of the firm as a managing partner and administrator.

Yves Sagot, Ph.D.
Chief Scientific Officer

Dr. Sagot is one of the co-founders of Relief Therapeutics SA and currently serves as the Chief Scientific Officer of Relief Therapeutics Holding AG. In 1999, he joined Serono International SA, where he worked on neurodegenerative and neuroinflammatory diseases as the group leader and the technological platform leader. Following Merck KGaA's takeover of Serono in 2007, Dr. Sagot worked on therapeutic target validation for Alzheimer and Parkinson's diseases through internal and external partnerships with both public and private institutions.

Michel Dreano, Ph.D.
Member of the Board and Chief Business Officer

Dr. Dreano is one of the co-founders of Relief Therapeutics SA, where he served as managing partner and Chairman/President. In 1983, he joined Battelle Memorial Institute in Geneva, where he headed a group focused on production of recombinant proteins. In 1989, he moved to Serono International SA, where he worked first as a drug developer and then as a project / alliance manager. In 2007, following the acquisition of Serono International SA by Merck KGaA, Dr. Dreano managed international research projects and integrated the business development department. In 2012, he created an independent consulting firm specialized in the management of multidiplinary and cross-national R&D projects. Dr. Dreano serves as the founder and executive member of the Board at ReMedys, a not-for-profit foundation. He holds a Ph.D. in cell biology from the University of Burgundy and a Ph.D. in microbiology from the Institut Pasteur in France.

Dorian Bevec, Ph.D.
Chief Development Officer

Dr. Bevec is a co-founder of the former mondoBIOTECH. Earlier, he worked as the head of Molecular Biology and project team leader at the Sandoz Research Institute in Vienna for ten years and at Axxima AG in Martinsried for two years.

Board of Directors

Raghuram Selvaraju, Ph.D., M.B.A.
Chairman of the Board

Dr. Selvaraju was elected Chairman of the Board of Relief Therapeutics in May 2016. He currently serves as Managing Director and Senior Healthcare Analyst at Rodman & Renshaw, a unit of H.C. Wainwright & Co., LLC, a full-service investment bank headquartered in New York, US. Prior to rejoining Rodman & Renshaw, he was the Managing Director and Senior Healthcare Analyst at MLV & Co LLC's Research Division till August 2015. Earlier, Dr. Selvaraju served as Managing Director, Head of Healthcare Equity Research and Director of Equity Research at Aegis Capital Corporation, Research Division from March 2012 through October 2014. He also served as Senior Vice President in Equity Research and Senior Biotechnology Analyst at Morgan Joseph TriArtisan LLC, Research Division since May 2011. From 2010 to March 2011, Dr. Selvaraju served as a Senior Equity Research Analyst covering the biotechnology and pharmaceuticals sectors at Noble Financial Group, Inc., Research Division. From 2009 to 2010, he served as Senior Vice President and Head of Healthcare Equity Research at Hapoalim Securities USA, Inc., the wholly-owned broker-dealer subsidiary of Bank Hapoalim B.M., one of Israel's largest financial services firms, covering biotechnology, specialty pharmaceuticals, molecular analytics, and diagnostics. Prior to starting his career in equity research, he worked at the Serono Pharmaceutical Research Institute from 2000 to 2004 as a pharmaceutical researcher. Dr. Selvaraju has a total of over 15 years of experience in the biotechnology and pharmaceutical sectors. He holds a Ph.D. in molecular neuroscience and cellular immunology and a Master's degree in molecular biology from the University of Geneva in Switzerland, as well as an M.B.A. degree from Cornell University in Ithaca, New York and a bachelor's degree in cell, molecular and developmental biology and technical writing from Carnegie-Mellon University in Pittsburgh, Pennsylvania.

Raffaele Petrone
Vice Chairman of the Board and Chief Executive Officer

Michel Dreano, Ph.D.
Member and Chief Business Officer

Peter de Svastich
Member

Mr. Svastich currently serves as the Managing General Partner of Global Emerging Markets (GEM) Limited. From April 2013 to March 2015, he worked as the Principal Executive Officer, President, Principal Financial Officer, Treasurer and Secretary at Global Group Enterprises Corp. and is currently the President of WH Management Inc. Since September 2012, Mr. Svastich has been a Managing Director of GEM Group, head of Latin America/Southern Europe/Administration. He has also worked as the Chief Financial Officer, Chief Operating Officer and Chief Compliance Officer for a number of hedge funds and funds of funds. Apart from this, Mr. Svastich has worked with various companies in the investment management and finanicals sevices industry serving in various positions of increasing responsibility.

Antonio Amato, M.D.
Member

Dr. Amato has been a member of the Board of Directors since May 2016. Currently, he is the Director of the Clinical Trial Center at the Agostino Gemelli University Hospital of the School of Medicine at Università Cattolica del Sacro Cuore, Rome, and was originally elected as a member of the Scientific Advisory Board of the company on 28 July 2014. Dr. Amato has spent more than 20 years in pharmaceutical R&D and was a part of the Sigma Tau SpA team for the clinical development and product registration of the combination drug Eurartesim (dihydroartemisinin/piperaquine) against malaria, the first-ever centralized approval by the European Medicines Agency in this indication.

DETAILED FINANCIAL STATEMENTS

Table 1: Relief Therapeutics Holding AG (RLF) – Historical Income Statements, Financial Projections

FY end December 31
CHF in thousands

	H1 2016 A	H2 2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Revenue												
Aviptadil-Sarcoidosis	-	-	-	-	-	-	54,013	111,686	138,563	179,062	222,110	255,085
Atexakin Alfa-DN	-	-	-	-	-	-	-	184,841	382,855	594,694	615,774	850,053
Aviptadil-ALI	-	-	-	-	-	-	-	57,132	98,443	162,824	210,391	260,963
Total Revenues	**335**	**-**	**-**	**-**	**-**	**-**	**54,013**	**353,659**	**619,861**	**936,581**	**1,048,274**	**1,366,101**
Operating expenses excluding D&A												
Service expense	971											
Personnel expense	206											
COGS		-	-	-	-	-	3,781	24,756	43,390	65,561	73,379	95,627
Sales & Marketing		-	-	-	-	-	2,701	17,683	30,993	46,829	52,414	68,305
G&A	28	500	3,000	3,000	3,000	3,000	2,161	14,146	24,794	37,463	41,931	50,000
R&D		-	10,000	15,000	20,000	25,000	22,000	15,000	20,000	25,000	30,000	50,000
Royalty to Merck	-	-	-	-	-	-	-	12,939	26,800	41,629	43,104	59,504
EBITDA	**(870)**	**(500)**	**(13,000)**	**(18,000)**	**(23,000)**	**(28,000)**	**23,371**	**269,134**	**473,884**	**720,099**	**807,446**	**1,042,665**
% margin		na	na	na	na	na	43%	76%	76%	77%	77%	76%
Amortization and depreciation expense	180	183	365	365	365	364	364	364	364	364	364	363
EBIT	**(1,050)**	**(683)**	**(13,365)**	**(18,365)**	**(23,365)**	**(28,364)**	**23,007**	**268,770**	**473,520**	**719,735**	**807,083**	**1,042,302**
Interest income	1	1	13	41	77	65	61	354	1,082	2,257	3,791	5,671
Interest expense	143	-	-	-	-	-	-	-	-	-	-	-
Profit / (Loss) before taxes	**(1,192)**	**(682)**	**(13,352)**	**(18,324)**	**(23,287)**	**(28,299)**	**23,068**	**269,124**	**474,602**	**721,992**	**810,874**	**1,047,972**

Source: Company reports and Research Dynamics estimates.

Table 2: Relief Therapeutics Holding AG (RLF) – Historical Balance Sheets, Financial Projections

FY end December 31
CHF in thousands

	H1 2016 A	H2 2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Property, plant and equipment	12	11	9	7	6	4	4	3	2	2	1	1
Goodwill	18,797	18,797	18,797	18,797	18,797	18,797	18,797	18,797	18,797	18,797	18,797	18,797
Intangible assets	3,632	3,450	3,087	2,724	2,361	1,998	1,634	1,271	908	545	182	(182)
Loans and other non-current assets	4	4	4	4	4	4	4	4	4	4	4	4
Non-current assets	**22,445**	**22,262**	**21,897**	**21,532**	**21,167**	**20,803**	**20,439**	**20,075**	**19,711**	**19,348**	**18,984**	**18,621**
Trade receivables	161	-	-	-	-	-	4,439	29,068	50,947	76,979	86,160	112,282
Tax receivables	48	-	-	-	-	-	-	-	-	-	-	-
Other current assets and other receivables	92	-	-	-	-	-	-	-	-	-	-	-
Cash and cash equivalents	131	301	10,314	22,355	39,432	12,961	35,894	246,985	618,808	1,186,642	1,846,540	2,689,967
Current assets	**432**	**301**	**10,314**	**22,355**	**39,432**	**12,961**	**40,334**	**276,053**	**669,755**	**1,263,621**	**1,932,700**	**2,802,250**
TOTAL ASSETS	**22,877**	**22,563**	**32,211**	**43,887**	**60,599**	**33,764**	**60,773**	**296,128**	**689,466**	**1,282,969**	**1,951,684**	**2,820,870**
Share Capital	6,548	11,917	34,917	64,917	104,917	105,917	105,917	105,917	105,917	105,917	105,917	105,917
Reserves	35,336	35,336	35,336	35,336	35,336	35,336	35,336	35,336	35,336	35,336	35,336	35,336
Retained Earnings	(25,368)	(26,050)	(39,402)	(57,726)	(81,014)	(109,313)	(86,245)	145,610	534,783	1,126,817	1,791,734	2,651,071
Total Equity	**16,516**	**21,202**	**30,850**	**42,526**	**59,239**	**31,940**	**55,008**	**286,862**	**676,036**	**1,268,069**	**1,932,986**	**2,792,323**
Non-current borrowings	-	-	-	-	-	-	-	-	-	-	-	-
Defined benefit obligation	436	436	436	436	436	436	436	436	436	436	436	436
Deferred tax liabilities	678	678	678	678	678	678	678	678	678	678	678	678
Non-current liabilities	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**	**1,114**
Trade payables	1,456	247	247	247	247	710	4,651	8,152	12,317	13,786	17,583	27,433
Current borrowings	3,397	-	-	-	-	-	-	-	-	-	-	-
Tax payables	1	-	-	-	-	-	-	-	-	-	-	-
Other current payables and liabilities	393	-	-	-	-	-	-	-	-	-	-	-
Current liabilities	**5,247**	**247**	**247**	**247**	**247**	**710**	**4,651**	**8,152**	**12,317**	**13,786**	**17,583**	**27,433**
TOTAL EQUITY AND LIABILITIES	**22,877**	**22,563**	**32,211**	**43,887**	**60,599**	**33,764**	**60,773**	**296,128**	**689,466**	**1,282,969**	**1,951,684**	**2,820,870**

Source: Company reports and Research Dynamics estimates.

Table 3: Relief Therapeutics Holding AG (RLF) – Historical Cash Flow Statement, Financial Projections

FY end December 31
CHF in thousands

	H1 2016 A	H2 2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Cash Flow from Operations												
Net Income		(682)	(13,352)	(18,324)	(23,287)	(28,299)	23,068	231,854	389,174	592,034	664,917	859,337
Adjustments												
Add: Depreciation & Write offs		183	365	365	365	364	364	364	364	364	364	363
Less: Change in Receivables		(301)	-	-	-	-	4,439	24,628	21,880	26,032	9,180	26,123
Add: Change in Current Liabilities		(1,603)	-	-	-	464	3,941	3,501	4,165	1,469	3,798	9,849
Cash from operations	**(2,376)**	**(1,802)**	**(12,987)**	**(17,959)**	**(22,923)**	**(27,471)**	**22,933**	**211,090**	**371,823**	**567,834**	**659,898**	**843,427**
Cash Flow from Investing												
Purchase (sale) of equipment		-	-	-	-	-	-	-	-	-	-	-
Cash from Investing Activities	**(346)**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Cash Flow from Financing												
Proceeds from equity, net		1,972	23,000	30,000	40,000	1,000	-	-	-	-	-	-
Cash from Financing Activities	**1,674**	**1,972**	**23,000**	**30,000**	**40,000**	**1,000**	**-**	**-**	**-**	**-**	**-**	**-**
Beginning cash balance		131	301	10,314	22,355	39,432	12,961	35,894	246,985	618,808	1,186,642	1,846,540
Increase (decrease) in cash		170	10,013	12,041	17,077	(26,471)	22,933	211,090	371,823	567,834	659,898	843,427
Ending cash balance	**131**	**301**	**10,314**	**22,355**	**39,432**	**12,961**	**35,894**	**246,985**	**618,808**	**1,186,642**	**1,846,540**	**2,689,967**

Source: Company reports and Research Dynamics estimates.

Table 4: Relief Therapeutics Holding AG (RLF) – Aviptadil Estimated Sales – sarcoidosis

FY end December 31
CHF in thousands, except the patients and population data

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
US Population	321,368,864	323,995,528	326,625,791	329,256,465	331,883,986	334,503,458	337,108,968	339,698,079	342,267,302	344,814,299	347,334,912	349,825,585
Patients with Sarcoidosis	64,274	64,799	65,325	65,851	66,377	66,901	67,422	67,940	68,453	68,963	69,467	69,965
% of total population	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%
EU Population	509,164,624	510,048,018	510,899,856	511,705,332	512,474,771	513,200,555	513,891,835	514,546,003	515,162,090	515,754,662	516,328,506	516,885,778
Patients with Sarcoidosis	101,833	102,010	102,180	102,341	102,495	102,640	102,778	102,909	103,032	103,151	103,266	103,377
% of total population	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%	0.02%
Total Patients	166,107	166,809	167,505	168,192	168,872	169,541	170,200	170,849	171,485	172,114	172,733	173,342
Patients seeking treatment	83,054	83,405	83,753	84,096	84,436	84,771	85,100	85,425	85,743	86,057	86,367	86,671
Aviptadil penetration rate	0%	0%	0%	0%	0%	0%	5%	10%	12%	15%	18%	20%
Patients receiving Aviptadil	-	-	-	-	-	-	4,255	8,542	10,289	12,909	15,546	17,334
Average annual revenue per patient	-	-	-	-	-	-	12,694	13,075	13,467	13,871	14,287	14,716
Total yearly revenue	**-**	**-**	**-**	**-**	**-**	**-**	**54,013**	**111,686**	**138,563**	**179,062**	**222,110**	**255,085**

Source: Research Dynamics estimates.

Table 5: Relief Therapeutics Holding AG (RLF) – Atexakin alfa Estimated Sales – Diabetic neuropathy and Postherpetic neuralgia

FY end December 31
CHF in thousands, except the patients and population data

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
US Population	321,368,864	323,995,528	326,625,791	329,256,465	331,883,986	334,503,458	337,108,968	339,698,079	342,267,302	344,814,299	347,334,912	349,825,585
Patients with diabetes	39,700,000	40,024,482	40,349,410	40,674,387	40,998,976	41,322,570	41,644,439	41,964,282	42,281,669	42,596,310	42,907,691	43,215,374
% of total population	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%	12.35%
Patients with painful diabetic neuropathy	4,367,000	4,402,693	4,438,435	4,474,183	4,509,887	4,545,483	4,580,888	4,616,071	4,650,984	4,685,594	4,719,846	4,753,691
% of diabetics with diabetic neuropathy	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%
Patients with diabetic neuropathy seeking treatment	2,183,500	2,201,347	2,219,218	2,237,092	2,254,944	2,272,742	2,290,444	2,308,036	2,325,492	2,342,797	2,359,923	2,376,846
Patients with Herpes Zoster	1,028,380	1,036,786	1,045,203	1,053,621	1,062,029	1,070,411	1,078,749	1,087,034	1,095,255	1,103,406	1,111,472	1,119,442
% of total population	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Patients with Postherpatic neuralgia	102,838	103,679	104,520	105,362	106,203	107,041	107,875	108,703	109,526	110,341	111,147	111,944
% of Herpes Zoster patients	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
Total addressable population	2,286,338	2,305,026	2,323,738	2,342,454	2,361,147	2,379,783	2,398,319	2,416,739	2,435,018	2,453,138	2,471,070	2,488,790
Atexakin Alfa penetration rate	0%	0%	0%	0%	0%	0%	0%	1%	2%	3%	3%	4%
Patients receiving Atexakin Alfa	-	-	-	-	-	-	-	23,080	46,510	70,284	70,798	95,074
Average annual revenue per patient	-	-	-	-	-	-	-	2,985	3,075	3,167	3,262	3,360
US revenue	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**68,898**	**143,003**	**222,584**	**230,937**	**319,428**
EU Population	509,164,624	510,048,018	510,899,856	511,705,332	512,474,771	513,200,555	513,891,835	514,546,003	515,162,090	515,754,662	516,328,506	516,885,778
Patients with diabetes	45,824,816	45,904,322	45,980,987	46,053,480	46,122,729	46,188,050	46,250,265	46,309,140	46,364,588	46,417,920	46,469,566	46,519,720
% of total population	9%	9%	9%	9%	9%	9%	9%	9%	9%	9%	9%	9%
Patients with diabetic neuropathy	9,407,730	9,452,168	9,496,344	9,540,065	9,583,388	9,626,168	9,668,417	9,710,076	9,751,088	9,791,565	9,831,498	9,870,860
% of diabetics with diabetic neuropathy	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%	11%
Patients with diabetic neuropathy seeking treatment	4,703,865	4,726,084	4,748,172	4,770,033	4,791,694	4,813,084	4,834,209	4,855,038	4,875,544	4,895,783	4,915,749	4,935,430
Patients with Herpes Zoster	642,738	647,991	653,252	658,513	663,768	669,007	674,218	679,396	684,535	689,629	694,670	699,651
% of total population	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Patients with Postherpatic neuralgia	64,274	64,799	65,325	65,851	66,377	66,901	67,422	67,940	68,454	68,963	69,467	69,965
% of Herpes Zoster patients	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
Total addressable population	4,768,139	4,790,883	4,813,497	4,835,884	4,858,071	4,879,985	4,901,631	4,922,978	4,943,998	4,964,746	4,985,216	5,005,395
Atexakin Alfa penetration rate	0%	0%	0%	0%	0%	0%	0%	1%	2%	3%	3%	4%
Patients receiving Atexakin Alfa	-	-	-	-	-	-	-	48,550	97,511	146,873	147,472	197,417
Average annual revenue per patient	-	-	-	-	-	-	-	2,388	2,460	2,534	2,610	2,688
EU revenue	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**115,943**	**239,852**	**372,110**	**384,836**	**530,624**
Total yearly revenue	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**184,841**	**382,855**	**594,694**	**615,774**	**850,053**

Source: Research Dynamics estimates.

Table 6: Relief Therapeutics Holding AG (RLF) – Aviptadil Estimated Sales – Acute lung injury

FY end December 31
CHF in thousands, except the patients and population data

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
US Population	321,368,864	323,995,528	326,625,791	329,256,465	331,883,986	334,503,458	337,108,968	339,698,079	342,267,302	344,814,299	347,334,912	349,825,585
Patients with ALI	200,000	201,635	203,272	204,909	206,544	208,174	209,796	211,407	213,006	214,591	216,160	217,710
% of total population	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%
EU Population	509,164,624	510,048,018	510,899,856	511,705,332	512,474,771	513,200,555	513,891,835	514,546,003	515,162,090	515,754,662	516,328,506	516,885,778
Patients with ALI	316,872	317,422	317,952	318,454	318,932	319,384	319,814	320,221	320,605	320,974	321,331	321,678
% of total population	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%	0.06%
Total patients	516,872	519,057	521,224	523,363	525,476	527,558	529,610	531,628	533,611	535,565	537,491	539,388
Aviptadil penetration rate	0%	0%	0%	0%	0%	0%	0%	3%	5%	8%	10%	12%
Patients receiving Aviptadil	-	-	-	-	-	-	-	15,949	26,681	42,845	53,749	64,727
Average annual revenue per patient	-	-	-	-	-	-	-	3,582	3,690	3,800	3,914	4,032
Total yearly revenue ($m)	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**57,132**	**98,443**	**162,824**	**210,391**	**260,963**

Source: Research Dynamics estimates.

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