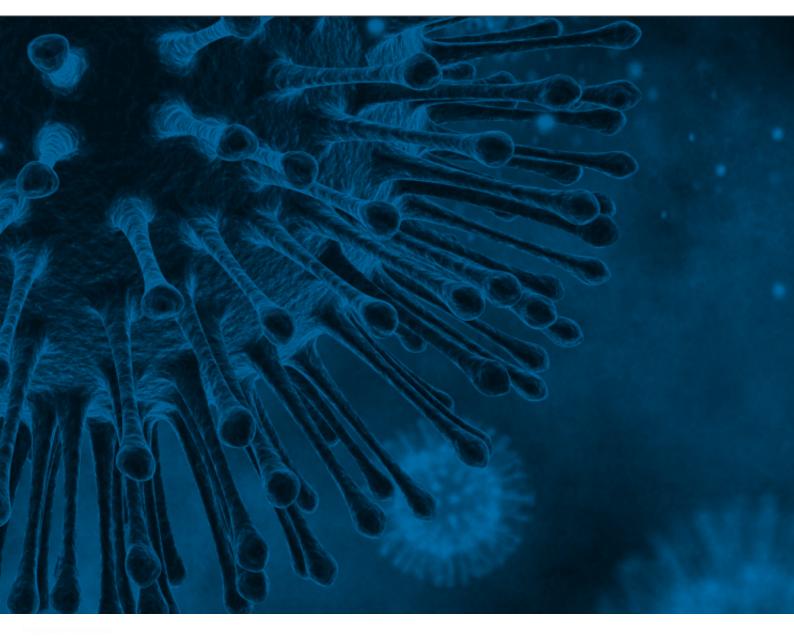
# ENZYMATICA AB (PUBL)

SUBSCRIPTION PERIOD NOVEMBER 14 - 28, 2018



Please note that this document is only a translated summary of the Swedish prospectus. Any decision to invest in Enzymatica AB (publ) ("Enzymatica" or the "Company") shall be based on the prospectus as a whole. The Board of Directors of Enzymatica has prepared a prospectus in connection with the rights issue. The prospectus has been approved and registered by the Financial Supervisory Authority (Sw. Finansinspektionen) in accordance with Chapter 2, Sections 25 and 26 of the Swedish Financial Instruments Trading Act (1991:1980) (Sw. Lagen (1991:1980) om handel med finansiella instrument). The prospectus is available on Enzymatica's website, www.penser.se, and can be ordered free of charge from Erik Penser Bank (e-mail: emission@penser.se). The prospectus is in Swedish and includes a presentation of Enzymatica, the rights issue and the risks associated with an investment in the Company and the participation in the rights issue. This summary is not intended to replace the prospectus as a basis for the decision to subscribe for shares in the Company and does not constitute a recommendation to subscribe for shares in the Company. Investors who want to invest or are considering investing in Enzymatica are recommended to read the prospectus. Please note that this is an English translation. In case of translational discrepancies to the Swedish version, the latter shall apply.



# **RISK FACTORS**

An investment in securities is associated with risk. Prior to any investment decision, it is important to carefully analyze the risk factors considered relevant to the future development of the Company and its share. The risk factors that are considered to be material for Enzymatica are described below in no particular order. This refers to risks concerning circumstances attributable to Enzymatica and/or the industry, as well as risks that are more general in nature and risks associated with the share and the Rights Issue. Some risks are beyond the Company's control. The presentation below does not claim to be complete and naturally all risk factors cannot be predicted or described in detail, so a comprehensive evaluation must include the other information in this Prospectus, as well as a general business environment analysis.

The risks and uncertainties described below could have a material adverse effect on Enzymatica's business, financial condition and/or results of operations. They could also cause the shares in Enzymatica to decline in value, which could result in the Company's shareholders losing all or part of their invested capital. Additional risks that are not currently known to Enzymatica could also have a corresponding adverse effect.

# RISKS RELATED TO ENZYMATICA'S OPERATIONS AND INDUSTRY

# Funding needs and capital

Enzymatica mainly engages in sales, research and development of products against infectious diseases. The Company is currently in an expansion phase that entails significant costs for the Company. Enzymatica is therefore dependent on the acquisition of capital in the future to finance its operations and planned activities. Any delays relating to clinical studies, product development, or expansion, or prematurely discontinued collaborations with the Company's partners, could have a negative impact on cash flow. There is also a risk that the Company may be unable to raise capital, which could result in temporary suspension of development or Enzymatica may be forced to conduct business at a slower pace than desired, which could have a negative impact on the Company's business. In the event that Enzymatica is unable to raise additional capital, or find other external financing, there is a risk that the Company will be unable to develop its operations as planned. Should the Company be unable to gain access to additional funding under satisfactory terms and conditions, it may adversely affect the Company's business, financial condition, results of operations and growth opportunities.

# Distribution of products

Enzymatica conducts business through direct contact with pharmacies and health stores in the Scandinavian market. In the UK the Company collaborates with a sales and marketing company. The strategy for markets outside Scandinavia is to use distributors. Consequently, Enzymatica's future expansion depends on successful collaborations with various partners. Enzymatica has extensive contractual relationships with these partners but such collaborations can be terminated. A terminated partnership with a major partner would have a negative impact on Enzymatica's growth, sales and earnings.

# Suppliers

The Company's strategy is to enter into strategic partnerships, in which partners handle aspects of the products' manufacturing process. Enzymatica's future supply of products depends on subcontractors that can manufacture the Company's products. The Company has strategic agreements with its most important subcontractors. Nevertheless, agreements can be terminated. Interruptions in deliveries due to terminated agreements or loss of production should a subcontractor encounter unforeseeable events could have a negative impact on Enzymatica's sales and earnings.

# Key individuals and employees

Enzymatica's key individuals and employees are highly skilled and have extensive experience within the Company's operations. The Company's ability to retain and recruit qualified employees for all positions within the Company is of great significance for the Company's future success and growth potential. If the Company should lose one or more key personnel or if the Company is unable to continue to hire qualified employees moving forward, this could result in delays or disruptions in the Company's business as well as losses of important knowledge related to production and handling of enzymes, which could have a negative impact on the Company's financial condition, results of operations and growth potential.

# **Product development**

Continued development of existing and new products and solutions are of great importance for Enzymatica. If the Company should lose its ability to develop products, or if products cannot be launched on schedule, or if the market reception is worse than expected, such factors could have a negative impact on Enzymatica's sales and earnings trend.

# Intellectual property rights

Enzymatica's continued development depends on continued successful research and, to some extent, on the ability to protect future revenue flows by protecting the intellectual property rights of the Company's product. There is a risk that current and future patent, brands and other intellectual property rights held by Enzymatica will not provide adequate protection against infringement and competition, e.g. competitors may develop new products that could meant that Enzymatica's existing and future intellectual property rights could be circumvented and replaced. Moreover, patents are inherently limited in time. Some of Enzymatica's patents will expire in 2020, including a user patent for the enzyme that is an important component in Enzymatica's products, and it is therefore important for Enzymatica to maintain and renew other patents that are relevant for its products. There is a risk that Enzymatica's products will be subject to increased competition, which could have a negative impact on the Company's business, financial condition, sales and results of operations.

Enzymatica strives to protect its own innovations in conjunction with its own development initiatives to ensure a return on the investments the Company makes in product development, but it is uncertain whether the Company's innovations can be subject to patent protection or that the innovations will not infringe on the intellectual property rights of others. Infringement and plagiarism are risks to which the Company can be exposed. Moreover, there is a risk that Enzymatica, for unknown reasons, may be drawn into legal proceedings due to alleged infringement of the rights of others. Businesses can also be subject to unfounded lawsuits relating to patent infringement. As in any dispute, disputes due to plagiarism and infringement can be expensive and time consuming and therefore have a negative impact on Enzymatica's business, financial condition and results of operations.

# Competition

There is also a risk that new competitors with a larger resource base regarding expertise and capital could enter Enzymatica's market and offer better methods and more effective products than Enzymatica, which could have a significant negative impact on Enzymatica's business, financial condition and results of operations.

# **Product liability**

Tests, marketing and sales of medical devices and solutions are associated with a risk for liability claims and there is no guarantee that Enzymatica will not be subject to claims for compensation related to product liability. The Company has a customary insurance coverage for such claims.

# Regulatory permits and authorization

Obtaining regulatory permits and authorization can be time consuming and may delay, raise the cost of, or prevent further development or commercialization of a product. In many cases, in order to initiate and conduct clinical trials and to be able to market and sell ColdZyme®, permits or authorization must be obtained regarding the use of health claims from the affected authority in the respective jurisdiction. Obtaining permits and authorization can be time consuming and may delay, raise the cost of, or prevent further commercialization of ColdZyme; for example, interpretations of what clinical studies are required for authorization may vary, or production or the product may not be considered to meet applicable requirements. The authorities may also make assessments that differ from Enzymatica's regarding, for example, interpretation of data from studies or the quality of data. Changes in the practices and procedures of authorities, as well as new and amended rules and reclassifications of existing products, may require further work or ultimately result in failure to obtain the necessary permits, or having them rescinded. Regulatory requirements and the practices of authorities differ between jurisdictions. Just because Enzymatica has received the necessary permits in one jurisdiction is no guarantee that it will be able to obtain similar permits in another jurisdiction. If the necessary permits or authorizations are not obtained, or are associated with unpredictable terms and conditions, there is a risk that the product could not be launched, that the launch of the product could be postponed and thereby result in increased costs, or declining sales of the product because a health claim cannot be used. This would in turn entail a material negative impact on Enzymatica's potential for revenue and therefore on Enzymatica's business, financial condition and results of operations.

# Marketing

There are special rules regarding the health claims that may be used when marketing medical devices. Such rules may affect the Company's opportunities for marketing ColdZyme on its own or via distributors on the markets on which Enzymatica is or may become active. For example, marketing of ColdZyme may be affected because certain health claims may not be used.

An example of this type of risk concerns the ruling by the Chamber for Commercial Disputes at the Regional Court of Frankfurt regarding restrictions on the marketing of ViruProtect® cold spray in Germany. ViruProtect, which is the name under which ColdZyme® is marketed in Germany, Belgium and Austria, is currently sold and marketed through Enzymatica's distributor STADA Arzneimittel AG ("STADA"). The ruling is based on the requirements under German legislation for conducting clinical studies for medical devices, which the Chamber for Commercial Disputes at the Regional Court of Frankfurt holds that ViruProtect does not meet. STADA has appealed the court ruling and the case is still in progress. If the court ruling stands after STADA's appeal and the restrictions on marketing the product are not lifted or if the marketing terms and conditions cannot be met, or if similar decisions are taken in other countries where Enzymatica sells the product this could have a material negative impact on Enzymatica's business, financial condition and results of operations.

# Legislation and regulations

Manufacturing, marketing and distribution of medical devices and equipment takes place in a regulated market with strict rules for marketing, clinical evaluation, approval and quality testing. In addition, new laws or regulations could be adopted that would require Enzymatica to adapt its product or marketing. Such regulations could mean that the Company's sales opportunities would be limited, or that the Company's product could become obsolete or unusable. If restrictions should be imposed on Enzymatica's product by authorities, or if the Company should not receive the necessary competent authority approval in the future, it could have a negative impact on Enzymatica's business, financial condition and results of operations.

The EU's new regulatory framework for medical devices, Regulation (EU) 2017/745 on medical devices ("MDR") came into force in May 2017. The MDR applies in parallel with the previous legislation on medical devices (Directive 93/42/EEC) for a period of three years, i.e. until May 2020, when the MDR must begin to be applied. The new regulation imposes increased demands on Enzymatica, including transparency and traceability of medical devices throughout the supply chain. Moreover, higher demands are made on the measures Enzymatica must take before launching a medical device and even more stringent requirements for oversight after the product has been launched. There is a risk that Enzymatica's product, like other competing products on the market, will be reclassified as a result of the MDR, which will impose more stringent demands on the Company such as requirements for third party certification, aftermarket monitoring and to conduct clinical studies. The Company has actively worked for a number of years to ensure that ColdZyme would meet the requirements set by the new regulation at the time of its entry into force. If ColdZyme does not meet the requirements under the new regulation and therefore does not receive the necessary competent authority approval in the future, it could have a material negative impact on Enzymatica's business, financial condition and results of operations.

The Company's product, ColdZyme, is currently classified as a medical device class 1 in Europe. Even if the product's current classification continues to be accepted, it may be questioned by competent authorities. These considerations may in turn have the consequence that relevant authorities in the markets in which ColdZyme is sold decide that the product is subject to authorization on a different legal basis than is currently the case, or that the product must be reclassified. Such decisions could entail additional work or ultimately the withdrawal of required permits, which could entail a risk that Enzymatica would incur increased costs, or that sales of the product would decline because a health claim cannot be used. Other than MDR, there are no such ongoing cases at the time of the Prospectus.

In addition, the business is also exposed to financial risk factors such as market risk (including currency risk, interest rate risk and price risk), credit risk and liquidity risk, as well as capital structure.

# **BACKGROUND AND USE OF PROCEEDS**

Enzymatica AB is a Swedish life science company that develops and sells medical devices for infection-related diseases. The products are based on a barrier technology that includes marine enzymes. The company's first product is ColdZyme® Mouth Spray, which can prevent colds and reduce the duration of disease. The product has been launched in about ten markets. The strategy is to continue to grow by strengthening the Company's position in existing markets and expanding into new geographic markets through established partners.

The Company is raising capital according to this Prospectus to strengthen the Company's financial position and to enable continued growth initiatives. In addition, the proceeds from the rights issue will be used to repay the bridge loan of SEK 31.4 million, including interest, that the Company borrowed in June 2018.

According to the Board of Directors, the available working capital is not sufficient for Enzymatica's current needs for the upcoming twelve-month period. In light of the above, the Company's Board of Directors decided on the Rights Issue totaling approximately SEK 98.7 million before issue costs. The Extraordinary General Meeting approved the Board of Directors' decision on November 5, 2018. As of September 30, 2018, the Company's cash and cash equivalents totaled SEK 9.5 million. At the time of this Prospectus, the existing working capital is deemed to be sufficient to run the business according to plan through December 20, 2018, at which time the bridge loan of SEK 31.4 million, including interest, is due in full.

According to the Company, the working capital deficit for the upcoming twelve-month period is estimated at about SEK 60 million. If fully subscribed, the Rights Issue, less issue expenses of SEK 7.2 million, will raise SEK 91.5 million for the Company, which the Company considers to be sufficient to meet its working capital requirement for the upcoming twelve-month period. In connection with the Rights Issue Enzymatica has obtained subscription commitments from a number of major shareholders. The subscription commitments total about SEK 28.2 million, or 28.6 percent of the Rights Issue.

In addition, the Company has signed an agreement for underwriting commitments of SEK 70.5 million, or about 71.4 percent of the Offering. The Rights Issue is therefore covered by a total of subscription and underwriting commitments of a total of about SEK 98.7 million, corresponding to 100.0 percent of the total proceeds. However, these commitments are not secured by bank guarantee, restricted cash, mortgage or similar arrangement.

The net proceeds of SEK 91.5 million are intended to be allocated to the following purposes in order of priority:

- Repayment of bridge loan including interest SEK 31.4 million
- Investments in continued clinical studies about SEK 25 million
- Financing of expanded market initiatives about SEK 5 million
- Investment in production equipment about SEK 5 million
- Strengthening of the Company's working capital about SEK 25 million

The Board of Directors of Enzymatica is responsible for the content of this Prospectus. The Board of Directors hereby provides an assurance that Enzymatica has taken all reasonable care to ensure that the information contained in this Prospectus is, as far as the Board of Directors knows, true and that nothing has been omitted that could affect its meaning.

Lund November 12, 2018 Enzymatica AB (publ) Board of Directors

# **COMMENTS FROM THE CEO**

# STRONG INTERNATIONAL EXPANSION PROVIDES GREAT POTENTIAL FOR ENZYMATICA

Enzymatica is a life science company with a platform technology based on enzymes from deep-sea cod with the aim of restoring the body's natural skin and mucous membrane barriers in order to prevent, relieve and reduce the duration of infection-related illnesses. Our first product, ColdZyme® Mouth Spray, which can prevent and reduce the duration of colds, has been shown to have highly convincing efficacy in several small and large patient studies.

# **Extensive international market**

The market potential of ColdZyme is large. Colds are among the most common illnesses in the world. Adults in the developed world suffer from 2-3 colds each year and there is a clear global trend toward increased self-treatment. Every year pharmacies, health stores and grocery stores sell over-the-counter cold remedies for about USD 56 billion¹ to consumers. ColdZyme has become established in a short period of time as one of the best-selling over-the-counter cold products in the Swedish market with over a 5 percent market share (rolling 12-month data) and we recently overtook Nezeril in market share². Enzymatica's vision is that ColdZyme has the potential to contribute to a world with fewer and milder colds.

# **Growth strategy**

ColdZyme is currently sold in about ten markets. The strategy is to continue to grow by strengthening the Company's position in existing markets and expanding into new geographic markets through established partners. In 2017 we signed a contract with the German distributor STADA for sales of ColdZyme in Germany, Austria and Belgium. In the middle of October we signed a contract with one of the largest Japanese pharmaceutical companies regarding registration, marketing, distribution and sales of ColdZyme in Japan. The contract is a milestone in Enzymatica's development and provides us with access to one of the world's largest pharmaceutical markets with a population of about 127 million, as well as a cold remedy market with annual sales of almost SEK 10 billion<sup>3</sup>. Through this contract ColdZyme can potentially be sold to between 22,000 and 27,000 pharmacies and grocery stores in Japan. This is the second large partner, in addition to STADA, with which we have signed a contract and we have thus once again received confirmation of our barrier technology. With the addition of this most recent contract and the contract with ABEX Pharmaceuticals from last summer for the South African market, we now have access to four of six continents.

# Strengthened documentation

At the same time that we have entered into international distributor contracts we are working intensively to strengthen the documentation for ColdZyme. On October 1 we presented the preliminary results of a prospective, randomized controlled multicenter study in Germany. In this explorative study we investigated the ability of four different cold scales to detect the positive effects of ColdZyme among patients with colds compared with a control group of patients with colds who were not treated with our product. All four symptom scales were able to show a significant better effect when using ColdZyme. In addition, the use of medicines for symptomatic relief of colds was significantly lower among those who used ColdZyme. The consistently positive results strongly indicate that ColdZyme reduces both the intensity of symptoms and the duration of colds. With these results we also have a much better understanding of how to design future studies to measure the efficacy of ColdZyme with the aim of strengthening and broadening our product claims.

We have conducted many other studies that show the beneficial effects of ColdZyme. An in-vitro study published in 2017 shows that ColdZyme deactivates five of our most common virus families that cause colds. In summary, ColdZyme has been shown to be effective against more than 90% of our most common cold viruses. The results from the COLDPREV clinical study showed that illness duration was 54% shorter among healthy adults who were experimentally inoculated with Rhinovirus and treated with ColdZyme. A number of observational studies have also shown shorter duration of colds when the studied group used ColdZyme.

# The issue will allow for further investments

In summary, we believe there is substantial potential for ColdZyme and that the Company is well-positioned for continued growth that will result in rising profitability. The impending rights issue will strengthen the Company's financial position while enabling continued growth initiatives and implementation of the company's clinical program. In addition, the proceeds from the rights issue will be used to repay the bridge loan of SEK 31.4 million, including interest, that the Company borrowed in June 2018.

Lund November 12, 2018 Fredrik Lindberg, CEO Enzymatica AB (publ)

<sup>&</sup>lt;sup>1</sup> Euromonitor, Global Market Report, MAT 2017

<sup>&</sup>lt;sup>2</sup> Nielsen Answers v.41, 2018

<sup>&</sup>lt;sup>3</sup> IMS Pharmatrend, Japan week 52



# **BUSINESS DESCRIPTION**

# INTRODUCTION

Enzymatica is a Swedish life science company that develops and sells medical devices for infection-related diseases. The products are based on a barrier technology that includes marine enzymes. The company's first product is ColdZyme® Mouth Spray, which can prevent colds and reduce the duration of disease. The product has been launched in about ten markets. The strategy is to continue to grow by strengthening the Company's position in existing markets and expanding into new geographic markets through established partners.

# **BUSINESS CONCEPT**

"We use cold-adapted marine enzymes from the North Atlantic to create a clinically proven barrier solution that captures and deactivates cold viruses, thereby helping consumers all over the world to protect themselves from colds.

# **GOAL**

Enzymatica's goal is to establish ColdZyme as one of the leading brands in the colds category.

# **BUSINESS MODEL**

For the cold product ColdZyme the Company is working with two principal business models, adapted based on opportunity and risk. In both cases the product is sold to consumers via the pharmacy and health chains under its own brand or a combined brand, known as co-branding.

In Sweden, Denmark and Norway Enzymatica ColdZyme has its own industry-experienced sales force. This model provides Enzymatica with high margins and control, but also with higher risk since the Company is responsible for the fixed costs for both the sales organization and for market investments. In markets outside Sweden, Denmark and Norway, Enzymatica sells via distributors who are responsible for the market investment. The model provides lower gross margins, but also entails lower costs and risks. In the UK a combination of the two models is currently applied under an arrangement in which Enzymatica provides the market investment and sales is handled by the distributors

# **ENZYME TECHNOLOGY**

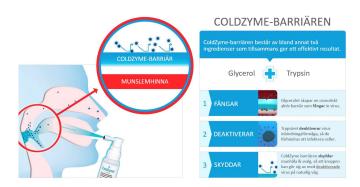
Enzymatica uses a marine enzyme, a cold-adapted trypsin that forms in the pancreas of cod. The enzyme is extracted as a byproduct of fish processing (from fish waste) and therefore leaves no negative ecological footprint. The unique properties of the enzyme make it super-active at body temperature, about 37 °C (98.6 °F), and its enzymatic activity is more than 40 times higher than the corresponding enzyme in mammals.1 These properties make the enzyme highly effective in protecting against disease-related microorganisms such as viruses

# COLDZYME MOUTH SPRAY TREATS THE CAUSE -**INSTEAD OF THE SYMPTOMS**

According to the Company, ColdZyme® Mouth Spray is unique in the market since it treats the cause of the cold, the actual cold viruses. Other cold products on the market treat the symptoms by alleviating the effects of the cold. ColdZyme is easy to use and works immediately by forming a protective barrier in the mouth and throat.

# BARRIER TO BLOCK VIRUS IN THE THROAT

The barrier works through osmosis - it captures the cold virus and deactivates the ability of the virus to infect cells, which protects the mouth and throat and allows the body to rid itself of the virus naturally. ColdZyme Mouth Spray may reduce the risk of colds and reduce the course of disease if it is used at an early phase of infection2.



# **COLDZYME HAS DOUBLE EFFECT**

## Prevention

ColdZyme can be used to prevent colds. People are constantly exposed to cold viruses and the risk higher in environments with more potential virus carriers, such as on planes, public transportation, in large crowds, or when colleagues at work or family members have colds. Many amateur and elite athletes use ColdZyme preventively, especially to prevent lost training and racing days, since athletes who catch colds suffer twice - from the cold itself, and from getting out of shape.

# **Treatment**

Once a cold occurs, ColdZyme can be used to reduce its duration. Treating a cold with ColdZyme at an early stage reduces the viral load, which thereby shortens the duration of the cold.

# **WELL-DOCUMENTED PRODUCT**

ColdZyme is well-documented in the general population, as well as in special groups where ColdZyme can help them avoid colds or reduce the duration if they should catch a cold. In 2017 Enzymatica published the results from several studies on the use of ColdZyme, including clinical studies, observation studies and one in vitro study3.

One study that was carried out in the autumn of 2017 shows that ColdZyme® deactivates the majority of viruses that cause colds4. The published study was carried out by Microbac, an independent accredited and certified laboratory in the US.

The in vitro study is based on standardized and validated methods for investigating viral cell damaging effects when inoculated on host cells. ColdZvme was able to deactivate the majority of known viral types that cause colds. ColdZyme deactivated the effects of rhinovirus type 1A by 91.7%, rhinovirus type 42 by 92.8%, human influenza A virus H3N2 by 96.9%, RSV virus by 99.9%, adenovirus type 2 by 64.5% and human corona virus by 99.9 %. ColdZyme had no harmful effect on the cells that were studied.5

A Gudmundsdóttir and H. M. Palsdottir. "Atlantic cod trypsins: from basic research to practical applications." Marine Biotechnology, vol. 7, no. 2, pp. 77–88, 2005

<sup>&</sup>lt;sup>2</sup> Clarsund et al, OJRD, 2017, 7, 125-135, A Randomized, Double-Blind, Placebo-Controlled Pilot Clinical Study on ColdZyme® Mouth Spray against Rhinovirus-Induced Common Cold

<sup>3</sup> http://www.enzymatica.se/forskning-utveckling/kliniska-studier

Stefansson et al, A medical device forming a protective barrier that deactivates four major common cold viruses. Virology Research Reviews, Issue 5, 2017

<sup>5</sup> Stefanson et al, ColdZyme forms a protective barrier in the throat that deactivates five major common cold viruses, Swedish Otolaryngology Congress 2018



# THE COMMON COLD – ONE OF THE MOST COMMON INFECTIOUS DISEASES

he common cold is an infection of the upper respiratory tract and one of the most common infectious diseases. Colds are highly contagious, especially during the first few days. Most people catch colds at some time during the year, with the most frequent occurrence in winter.

Colds are caused by viruses that enter the mucosal cells, primarily in the mouth, nose and throat. When someone with a cold coughs or sneezes, the virus can spread up to 16 feet. In addition to direct contact and airborne transmission, the cold virus can also be transmitted by touching door handles, bus seats and other surfaces. A virus particle can survive outside the body for up to seven hours. Virus particles can be found in the body for a period of time before cold symptoms emerge. When the immune system weakens for some reason, the cold can develop.

More than two hundred viruses are associated with colds, the most common of which is the rhinovirus. After a cold, the body has some immunity to new infections of the same virus type. However, sensitivity is unchanged to other types of cold viruses.

Adults suffer from colds caused by viruses an average of two to four times per year, and sometimes more. Children in day care and school comprise the group that have the most colds, but the frequency decreases with increased age as immunity builds up against more strains and as direct contact with other children declines.

Disease-causing viruses are tiny biological particles that cannot be seen with the naked eye. Unlike bacteria, viruses can only reproduce in living tissue, but they can survive longer even on inhospitable surfaces. Viruses consist of genetic material and a protective protein coat with anchoring proteins that allow the virus to attach to body cells and penetrate them. Once inside, their genetic material uses the body cells to produce new viruses.

Viruses cause many diseases, such as the common cold and the flu. Viruses have the ability to replace the proteins on the protein coat that the body's immune system learns to recognize so it can destroy the virus. Once these proteins are modified, the body's immune system has difficulty protecting the body against a new infection.

# INFECTION WITH THE COMMON COLD, STEP BY STEP

- The cold virus is deposited on, for example, the front portion of the nasal passages either via contaminated fingers or airborne droplets from someone who has coughed or sneezed. Even small amounts of virus are sufficient to cause infection.
- Next the virus is transported to the throat where it binds to the mucosal cells, marked with a red circle in the figure below.
   After binding to surface proteins on the cells of the mucous
- 3. After binding to surface proteins on the cells of the mucous membrane, the virus enters the host cell\* and the infection begins. Once inside, new virus particles are produced and ultimately the host cell dies and releases newly made viruses that can infect new host cells. This process, from initial infection until the first release of newly produced viruses, takes about ten hours, and is called the incubation period.
- 4. After approximately ten more hours the infected person begins to experience cold symptoms such as sore throat, fatigue and sneezing. As a countermeasure the mucous membranes of the nose and throat swell and produce fluid, causing a runny nose and mucous discharge. The cold usually reaches its maximum intensity 36-72 hours after initial infection.
- \* Host cell: Cell that harbors a virus or foreign microorganism.





During the 2018 cold season an exploratory study was conducted in Germany with the aim of evaluating different cold symptom scales. The study included 400 participants who were randomly requested either to start treatment with ColdZyme at the first sign of cold symptoms, or not to start any treatment. In all 269 individuals with confirmed colds were included and assessed in the study. Preliminary analysis of the study shows consistently positive results with ColdZyme and strongly indicate that ColdZyme reduces both the intensity of symptoms and the duration of colds. The study results create a strong foundation on which to continue to build the brand and to broaden the product claims within the scope of Enzymatica's clinical program.1

# **SOCIOECONOMIC BENEFITS**

Colds are the single biggest cause of sickness absence, corresponding to just over 30 percent of all sick leave according to occupational health company Previa. According to a survey carried out by Nordeg and commissioned by Enzymatica, major socioeconomic benefits can be achieved by reducing the number of sick days due to colds2. The report shows that a reduction of a single sick day would result in an annual savings of SEK 1.4 billion for the Swedish society, based on 10 percent of all 4.7 million full-time employed individuals.

# **COMMERCIALIZATION OF COLDZYME**

According to Enzymatica, ColdZyme holds a unique position in the cold segment because the product attacks the cause of the cold, the cold virus, instead of the symptoms after the individual is already sick. The cold segment consists mainly of drugs for symptomatic treatment and herbal remedies. ColdZyme is intended for self-care and has been available at Swedish pharmacies and in health stores since 2013. In Europe, Enzymatica has direct sales in the Swedish, Danish and Norwegian markets, and sells through partners in Spain, Finland, Greece and on Iceland. In the UK ColdZyme is sold through a sales agent. In Germany, the largest OTC market in Europe, ColdZyme is sold through the pharmaceutical company STADA, which successfully launched the product in the fall of 2017. The contract also includes Belgium and Austria.

## Sweden

In 2018 ColdZyme has continued to strengthen its position as a brand in Swedish pharmacies. ColdZyme has increased it's market share in Sweden from 4,9 % up to 5,3 % over the last twelve months. Throughout the period from January - September 2018 sales of Cold-Zyme increased by 10.4 % in volume, compared to market growth by 2.2 % for the same period.3 The larger package size, ColdZyme 20 ml, is used mainly for prevention and frequent use, and the smaller package, ColdZyme OneCold 7 ml, serves as an entry level product, and for use with a single cold, or on an occasion when the user wants to prevent a cold, such as an airplane trip.

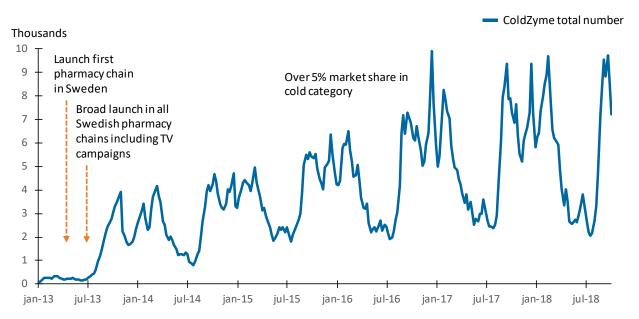
# With partners in other geographic markets

Enzymatica is continuing its international expansion and intends to reach out with ColdZyme on several markets. The product is registered so it can be sold in countries within the EEA. In markets outside the home market, Enzymatica sells ColdZyme through national, regional and global distributors who often sell ColdZyme under other brand names.

In Spain ColdZyme is distributed under the Cortagrip® brand by the pharmaceutical company Esteve. It is one of the ten largest pharmaceutical companies in Spain. During 2018 Esteve has continued to market the product at pharmacies, along with a television campaign for both pharmacies and consumers prior to cold season. In Spain the cold season is short but intensive. It begins in November/December and ends in February.

In Finland ColdZyme is sold by the pharmaceutical company Tamro. Tamro markets the product through campaigns in digital and social media, as well as through advertising in publications. The Company also works with trade fairs, education and pharmacy visits in Finland. Tamro has succeeded in maintaining the penetration level and is undergoing robust growth in a competitive market. The competition in Finland mainly comes from zinc products.

# ColdZyme sales in Swedish pharmacies 2013 – October 15<sup>th</sup> 2018



<sup>&</sup>lt;sup>1</sup> Enzymatica data on file. https://newsclient.omxgroup.com/cdsPublic/viewDisclosure.action?disclosureId=857122&lang=sv
<sup>2</sup> Larsson B, Nordeg, Studie av den samhällsekonomiska effekten för den svenska befolkningen vid användning av ColdZyme Munspray

<sup>&</sup>lt;sup>3</sup> Nielsen Answers v.41, 2018

# Germany, Belgium and Austria

In Germany, Belgium and Austria STADA launched ColdZyme under the ViruProtect® brand (co-branding with ColdZyme) in the fall of 2017. ViruProtect is positioned within the segment Immunostimulants in the cold category. The segment includes products that pharmacists recommend and that consumers take for early cold symptoms to avoid colds or to experience milder symptoms. As of late 2017 and early 2018, ViruProtect had captured about a 7% market share within immunostimulants in Germany, corresponding to about 1% of the total cold segment¹. The trend was similar in Belgium and Austria, which correlate with ColdZyme's trend during the launch year in Sweden

Restrictions have been imposed on marketing ViruProtect in the German market, which means that Enzymatica's distributor cannot place more orders for ViruProtect during the remainder of 2018. Enzymatica expects the net effect of the sales lost in Germany, and the continued increase in sales in other markets, to result in a decline of about 15-20 percent of annual sales compared with sales of SEK 59 million for 2017. Enzymatica's German distributor has appealed the court ruling and the court is expected to answer the appeal in 2019.

## United Kingdom

In the UK ColdZyme is sold through the two largest pharmacy chains, Boots and Lloyds. Distribution is managed by a contract sales force, but the intention is to find a strong partner who will be responsible for both sales and marketing.

# Australia and New Zealand

Enzymatica has a cooperation agreement with Symbion, a leading wholesaler in Australia and New Zealand. Under this agreement, Endeavour Consumer Health within Symbion has exclusive rights to sell, market and distribute ColdZyme on these two markets. The agreement is Enzymatica's first outside the EU.

The regulatory conditions for medical devices in Australia differ from the European and ColdZyme will therefore be registered in a higher class. Work with registration is ongoing.

# South Africa

Enzymatica has entered into a distribution agreement with ABEX Pharmaceuticals for marketing and sales of ColdZyme® cold spray on the South African market. ABEX sells to all major pharmacy chains, as well as to grocery stores in South Africa. ABEX plans to launch ColdZyme in early 2019, with a focus on the South African winter season which extends from March to July. An extensive marketing campaign will be conducted including advertising in traditional media and in-store advertising, as well as radio commercials and marketing in social media.

The South African cold market is estimated at ZAR 2.1 billion, corresponding to about SEK 1.4 billion.<sup>2</sup> Most cold preparations provide symptomatic relief and only a few cold sprays focus on the cold virus. Consequently, ABEX sees great opportunities to position ColdZyme as an extremely interesting treatment option within the segment.

# Japan

Enzymatica has signed a contract with a major Japanese pharmaceutical company for registration, marketing, distribution and sales of ColdZyme, which will probably be sold with co-branding, using a local brand together with the ColdZyme brand. Access to the Japanese market is subject to approval by the registration authority, with expected launch in 2020. Through the contract with the Japanese pharmaceutical group Enzymatica will have access to between 5,000 and 10,000 pharmacies, and as many as 17,000 supermarkets to sell ColdZyme in the Japanese market.

The Japanese cough and cold market is estimated at USD 1.1 billion, which is the equivalent of about SEK 10 billion, and the market for over-the-counter (OTC) products is estimated at USD 3.9 billion, or about SEK 35 billion.<sup>3</sup> ColdZyme has no direct competitor on the market at this time, though there are various types of mouth spray that are similar products with a barrier function.

# **ENZYMATICA GROWTH STRATEGY**

The Company's growth strategy is based on three cornerstones.

# Increase market share on existing markets

In Scandinavia, where the company has its own sales organization, the Company will strengthen its market position, while maintaining its margin.

ColdZyme is now an established product on the Swedish market and is among the top-selling cold products in Swedish pharmacies. Denmark follows the Swedish development curve.

# Geographic expansion

The Company currently has distribution agreements with established partners on the following markets:

Spain

2

- United Kingdom
- Finland
- Germany, Belgium and Austria
- Australia and New Zealand
- South Africa
- Japan

Enzymatica intends to reach out with ColdZyme on more markets and continue its international expansion. The product is registered so it can be sold in countries within the EEA and the Company considers itself to be well prepared regarding the new EU legislation for medical devices, which has to be applied in May 2020.

# More unique products

The Company's enzyme-based product portfolio will grow as a result of our own research and development. The strategy is to identify medical needs, primarily related to upper respiratory tract infections, for which there is no treatment or treatment is not fully effective.

The strategy moving forward includes strengthening the Company's technology platform with more products and continuing to pursue research in barrier technology.

<sup>&</sup>lt;sup>1</sup> IMS Pharmatrend, Germany week 52

<sup>&</sup>lt;sup>2</sup> IMS Pharmatrend, South Africa week 52

<sup>&</sup>lt;sup>3</sup> IMS Pharmatrend, Japan week 52

# PRODUCT DEVELOPMENT

Enzymatica is focusing on product development based on the tested and patented barrier technology on which the cold product ColdZyme® is based. Over the next few years the Company aims to expand the range of enzyme-based products for colds. In the long term the focus will be on developing products for other indications.

# **Barrier technology**

The barrier in ColdZyme consists of a transparent hypertonic solution that includes glycerol and enzymes. A hypertonic solution is one where the concentration is higher outside the cell than inside it, and therefore water is emitted from the cell. The main mechanism of action of the barrier is based on its ability to generate a viscous osmotic barrier on the mucous membrane in the mouth/throat that draws fluid out of the mucous membrane. This fluid contains viruses. When applied to the mouth/throat, as in the case of ColdZyme, the presence of virus declines, thereby facilitating a faster natural recovery from the common cold.

# Enzyme from deep-sea fish

A key sub-component of the effective barrier is the enzyme extracted from deep-sea cod. The enzyme from deep-sea cod is a cold-adapted trypsin that has evolved to be active at a temperature of around four degrees C. As a result of this adaptation to the cold, this type of enzyme has become extremely effective at higher temperatures and the catalytic activity is many times higher than in equivalent enzymes in humans.

# Regulatory framework for medical devices

Enzymatica is in an internationalization phase with launches in Europe and a number of selected additional markets, with extensive registration and documentation requirements. Enzymatica is continually working on regulatory matters and is compiling the documentation required to register a product in selected markets. In 2017 a new regulatory framework for medical devices for Europe was published, the Medical Device Regulation, which has to be applied in May 2020. Efforts to meet the requirements of the new regulatory framework are ongoing and have been assigned high priority.

Enzymatica's quality and regulatory work focuses on the following:

- The ongoing initiative to continually strengthen the documentation for the main product, ColdZyme Mouth Spray. This documentation includes data regarding the quality, safety, function and clinical advantages of the products.
- Continually work to establish a quality assurance system that meets the increased external requirements and facilitates a long-term, efficient and structured initiative. This work includes establishment of registration strategies early in development projects for new products. This approach will ensure that the right documentation is available when the project results in a commercially viable product.

# PRODUCT DEVELOPMENT STRATEGY

# Enzymatica's product development strategy has the following priorities:

- Optimize ColdZyme (production, technical documentation, regulatory status outside the EU, clinical studies, new patents, etc.).
- Strengthen and expand existing claims through additional studies.
- Formulate new ColdZyme versions ("line extensions") to expand the product offering and to increase shelf exposure in the pharmacies.
- Explore new indications with the same formulation and function, which requires minimal lead time for product development (existing storage studies, toxicity tests, etc., can be used).
- Develop new product formulations for use within the file of ear, nose and throat (ENT).
- 6. Develop new products for completely new indications.

# **STRATEGIC DIRECTION FOR COLDZYME 2018 – 2023**

Below is an illustration of Enzymatica's strategy moving forward. The Company will continue to focus on international expansion and to strengthen existing claims and documentation for the main product, ColdZyme Mouth Spray.



# International expansion

ColdZyme is currently sold in about ten markets. The strategy is to continue to grow by strengthening the Company's position in existing markets and expanding into new geographic markets through established partners. In 2018 the Company signed distributor contracts with partners for a number of strategic markets, which further confirms the Company's business model and barrier technology.

# Additional studies

Enzymatica is in an internationalization phase with launches in Europe and a number of selected additional markets, with extensive registration and documentation requirements. Enzymatica is continually working on regulatory matters and is compiling the documentation required to register a product in selected markets. Efforts to meet the requirements of the new regulatory framework, which will come into force commencing in May 2020, are ongoing and have been assigned high priority.

# Expand the product offering

To meet the needs of specific customer preferences, or to focus on specific customer categories, Enzymatica intends to develop new ColdZyme versions ("line extensions"). Line extensions will be developed based on the results from studies and market surveys. By broadening the product offering and increasing shelf exposure in pharmacies, the potential customer base of ColdZyme users can be broadened to include a larger number of customers.

# COLDZYME - THE MOST RECOM-MENDED COLD PRODUCT AT PHARMACIES\* Enzymatica conducted a new market sur-

vey showing that ColdZyme® Mouth Spray is the cold product that pharmacy staff in Sweden recommend most. The majority of consumers who asked for help and recommendations at the pharmacy regarding colds were advised to use ColdZyme.

Market research company GfK was commissioned by Enzymatica to conduct a market survey at 93 pharmacies in the Stockholm, Gothenburg and Skåne met-ropolitan areas. "Mystery shoppers" who pretended to be consumers with symptoms that included feeling sick and a sore throat. They asked pharmacy staff to recommend something that could help with a cold.

ColdZyme was the product recommended more often than other cold products cold. ColdZyme was recommended by 67 percent of pharmacy staff, while only 26 percent recommended the product that received the second highest number of vo-tes. The results are statistically significant.

# COLDZYME COLD SPRAY REDU-CES PRESCHOOL STAFF SICK-

NESS ABSENCE\*\*

Enzymatica conducted an evaluation of ColdZyme® Mouth Spray for colds among preschool staff during cold season. The results show that the use of ColdZyme redu-ced sickness absence by more than three days, from 7.4 to 4.1 days. In cases where the staff in the study did catch a cold, the symptoms of infection were less severe.

Enzymatica conducted an observation study with 15 people who used ColdZyme to prevent colds during "cold season" (Octo-ber-March). The 15 people, who work at a preschool, all completed the study. Participants were instructed to use ColdZyme as soon as they were exposed to cold viruses, and also to use ColdZyme at the first sign of cold symptoms and continue until the symptoms disappeared. Sickness absence records for the control period during

The purpose of the study was to evaluate whether ColdZyme can be used to prevent colds or to reduce the duration and severity of colds among preschool staff, thereby reducing socioeconomic costs. "Conditions at preschools are conducive to the spread of infections. An infected child can easily infect the staff, resulting in reduced work capacity and sickness absence.

The study results show that when taken preventively and at the first signs of cold symptoms, ColdZyme reduced short-term sick leave among personnel from 7.4 to 4.1 days during a six-month period compared with the control period," says Fredrik Lindberg, CEO of Enzymatica.

As a result, average sickness absence decreased by 3.3 days compared with the previous year. In addition, study participants reported that they had not noticed any side effects when using ColdZyme.

# STUDY OF ELITE ATHLETES -FEWER SICK DAYS AND IMPROVED

QUALITY OF LIFE\*\*\*

Enzymatica conducted a study in which

Swedish elite athletes used ColdZyme® Mouth Spray to protect against and reduce the symptoms of colds. The results of the study show that ColdZyme reduced the number of sick days by more than 50 percent in the two groups of hockey players and biathlon skiers compared with previous control periods. The study also down with colds and who used ColdZyme experienced milder symptoms and improved quality of life compared with untreated common colds.

Enzymatica conducted a study of elite athletes who used ColdZyme for 3-12 months during the winter seasons 2012–2014 in Sweden. In all, 11 biathlon skiers and 29 hockey players participated and submitted information on number of days absent from training and competition. In addition, those who came down with colds responded to questions about their symptoms and quality of life.

-"The study results show that the average number of sick days per athlete and month when using ColdZyme significantly declined, by 51 percent for the biathlon skiers and 67 percent for the hockey players, compared with the control periods when ColdZyme was not used," says Ulf Blom, Executive Vice President of Marketing and Sales at Enzymatica.

The athletes in the study who became infected reported milder symptoms and sig-nificant improvement in quality of life (for example, improved sleep and performance) compared with common cold sufferers not treated with ColdZyme. Nine of 11 bi-athlon skiers reported that they felt better or much better when using ColdZyme and that they had milder or much milder cold symptoms.

-"Using ColdZyme has been very important for my training as a biathlon skier. Before I began using ColdZyme I could have 30 to 40 days of sick leave per season, compared with 3-5 days when using ColdZyme," s Torstein Stenersen, who belongs to the Swedish biathlon team.



<sup>\*\*</sup> Clarsund, M. (2017) Evaluation of ColdZyme Mouth Spray against Common Cold in

Preschool Staff. Open Journal of Respiratory Diseases, 7, 136-140
\*\*\* Clarsund, M. (2017) Evaluation of ColdZyme Mouth Spray for the Protection against Common Cold in Elite Athletes to Reduce Unwanted Absence from Training and Competition. Open Journal of Respiratory Diseases, 7, 103-109

# SUCCESSFUL INTEGRATION STRENGTHENS ENZY-MATICA'S VALUE CHAIN

In 2016 Enzymatica acquired the Icelandic company Zymetech. In 2017 the two organizations were successfully integrated through joint teams for production, research, product development, patents and business. The purpose of the organization is to coordinate resources and increase cooperation to leverage the aggregate knowledge within the company. As a result of the acquisition and the integration process, Enzymatica has full control of the value chain.

The acquisition of Zymetech was strategically important for Enzymatica and provided the opportunity to achieve international expansion. The Company gained international exclusive rights to a patent-protected enzyme, a key component of ColdZyme® Mouth Spray, as well as control over production of the enzyme, access to international research and development expertise and Zymetech's research portfolio. As a result of the acquisition, Enzymatica has been able to sign exclusive agreements with leading international distributors to obtain broad market coverage. One example of this is the agreement signed in 2017 with the German pharmaceutical company STADA for marketing and sales of ColdZyme in the German, Belgian and Austrian markets. In 2018 the Company signed distributor contracts with partners for a number of strategic markets, which further confirms the Company's business model and barrier technology.

# PATENT PROTECTION AND PRODUCTION

Enzymatica has patent protection for its products in, for example, the EU, China, Australia, Russia and Canada. Since Enzymatica is the sole producer of the deepwater enzyme in question, the Company has global control of enzyme production, which could significantly delay competition in key countries where there is not full patent protection. Enzymatica thus has exclusive rights in countries with patenwt protection until 2020 and a technological lead of several years over the rest of the world. Enzymatica has an active patent strategy and continually files patents for new applications. For more information about Enzymaticas granted patents and patent applications, see table below.

# **DESIGN & DEVELOPMENT**

Enzymatica has refined its research portfolio in recent years. The focus has been on documentation and research related to ColdZyme. Enzymatica is working in close collaboration with clinical researchers to develop medical devices in the therapeutic area upper respiratory tract infections.

Enzymatica has extensive knowledge in enzyme technology, applied enzyme research, and processing and formulation of the relevant enzyme, which also allows for a broadening of the areas of use for ColdZyme and facilitates development of new products based on the two companies' common technology platform. Access to international research expertise and clinical data provide the opportunity for a broader product portfolio in the long term.

# **CONTROL OVER THE ENTIRE VALUE CHAIN**

After the merger with Zymetech, the Company's operations cover the entire value chain from production of enzymes to the sale of medical devices. The Company combines expertise in enzyme research and development of medical devices with its experience of global market penetration and sales. Enzymatica has the opportunity to offer exclusive rights to the active enzyme that is part of the Company's product development and thus has full control of enzyme production, product development and registration. Products are manufactured through contract manufacturing in accordance with Enzymatica's specifications and quality requirements. Marketing and sales are both in-house and through partners, depending on the market.

# **RESEARCH AND DEVELOPMENT**

Strengthening the clinical documentation for the ColdZyme Mouth Spray is a key part of Enzymatica's R&D activities. The Company's total research and development expenses amounted to SEK 14.5 (12.3) million in 2017, of which SEK 0 (7.6) million was capitalized on the balance sheet. The Company's total research and development expenses amounted to SEK 15,7 million for the period January – September 2018, of which SEK 0.0 million was capitalized on the balance sheet.



Product	Countries/markets	Granted, year	Status	Regarding	Expiration, year	Number of patents/ patent applications
ColdZyme	Europe, Australia, Canada, China, India, Iceland, South Korea, Mexiko, Norway, New Zeeland, Poland, Russia, USA	2000	Granted	Enzyme from cod for medicinal and cosmetic use	2020	1
Unspecified	International applications	-	Applications	-	-	7

# **CORPORATE RESPONSIBILITY AND SUSTAINABILITY**

Enzymatica wants to be a good stakeholder in the community and take responsibility for sustainable social development. As a medical device company, Enzymatica focuses on human health and well-being, and wants to use resources, regardless of whether they are raw materials, energy or human, as wisely and sustainably as possible, and in a way that does not limit the ability of future generations to make their own choices. Regarding basic research, production and sales of products, the Company cooperates to a large extent with partners, many of whom actively work with sustainability issues.

# **Quality and safety**

Enzymatica develops medical devices in an environment that is regulated by directives and standards. The Company's procedures and documentation are formulated in accordance with the respective regulatory requirements. Documentation requirements are applicable for the entire life cycle of the product to guarantee that the product lives up to its performance claims. In summary, we take responsibility for ensuring that our products are safe, maintain a high standard of quality and live up to their claimed performance.

During the first half of 2018 Enzymatica completed an initiative aimed at ensuring that the Company lives up to the requirements of the EU's data protection regulation (GDPR). This effort involved taking inventory, analyzing and implementing measures to comply with the new rules.

In 2018 Enzymatica's quality management system was certified to EN ISO 13485:2016 and the Company's enzyme production facility on Iceland adopted the Good Manufacturing Practice standard.

# **Environment**

Enzymatica does not engage in any activities that are subject to reporting obligations under the Environmental Code but the import of the enzyme, which is a key component in ColdZyme, is reported to the chemical inspection product registry. The enzyme used in the products is extracted as a byproduct during fish processing and does not contribute to depletion of cod stocks. The wrapping and other packaging materials used for the products are recyclable. The contract manufacturer in Spain and most of the Company's sales channels (pharmacies and health stores) are certified to environmental standard ISO 14001.

## Code of conduct

Corporate responsibility involves more than risk management to ensure that Enzymatica remains a reliable partner for its stakeholders Enzymatica attaches great importance to behaving correctly in business-related situations. Enzymatica's Code of Conduct clarifies how the Company should behave as a business partner, employer and stakeholder in the community. The Code of Conduct supports the UN Global Compact, which includes ten principles about human rights, environmental protection and anti-corruption measures. Laws, regulations and norms set the minimum levels for the Company's actions.

The Code of Conduct applies to all Enzymatica employees and board members, as well as others who represent the Company, such as consultants.

# A safe workplace that encourages personal growth

Enzymatica's corporate culture is an important factor underlying the development of the Company. Participation, strong commitment and employees with the right skills are important tools for the Company to continue to pursue positive growth and development.

Working at Enzymatica should be safe, sound and promote personal development. The Company's working methods and organization should be such that all employees have the opportunity to influence their personal development and the development of the Company. The employees should have the resources and opportunities for development necessary to maintain a high level of expertise within their field. The work environment should be characterized by respect and trust for each individual employee. Harassment and all forms of discrimination are unacceptable and employees are expected to treat each other in the same way that they themselves would like to be treated. Matters regarding the work environment, health and safety are regulated by the Company's Code of Conduct and handled within the framework of Swedish legislation.

In 2017 Enzymatica also filled several key positions including our Chief Commercial Officer, Chief Operating Officer and Chief Financial Officer. The significant international experience that they contribute is valuable and crucial for both the Company's continued expansion and in negotiations with international partners.

