

## 2010 Annual Report

### 1. About Biotec Pharmacon ASA

The company's activity is divided into two business segments:

- Beta-glucans for use in medical devices and pharmaceutical products
- Marine enzymes for use in genetic research and molecular diagnostics

The business segment marine enzymes is handled by the subsidiary ArcticZymes AS (formerly Biotec Marine Biochemicals AS), whereas the business segment beta-glucans was separated into a wholly owned subsidiary under the name Biotec BetaGlucans AS from the start of 2011. This leaves Biotec Pharmacon ASA as a holding company with group management and common support functions, while the operational activities are carried out in the two subsidiaries.

All the Group's operations have been located in Tromsø from the beginning of 2010. The premises in Oslo are sublet for the remaining lease period. In early 2011, the business moved to new offices in the new Barents BioCenter at the Research Park at the University of Tromsø. This is expected to further enhance the close cooperation with the University, in new and more efficient premises. The company's production facility at Nordøya Industrianlegg remains as before.

The Company completed a successful share issue in late 2010, which together with a subsequent repair offering secures the required financial flexibility.

For the glucan operations, the company's goal for 2010 was to understand and document the reasons why the phase III studies within diabetic wounds failed to meet expectations, and on the basis of this decide on a realistic strategy for the continuation of this business.

For the enzyme operations the targets were mainly to secure continued revenue growth while strengthening the pipeline of new products.

The Board is very pleased with the results the administration has achieved in these areas.

### 2. Beta-glucans

The glucan operation, which is organized in the company Biotec BetaGlucans AS, develops products based on its unique patent-protected soluble beta-1,3/1,6-glucan (SBG). This bioactive substance is produced at the company's GMP-approved (Good Manufacturing Practice) manufacturing facility in Tromsø. The immunomodulatory properties of this group of substances have been shown to be promising in the treatment of several immune-related diseases, and the company is now initially focusing on developing products for topical (on skin) wound care. The company also has projects in early stages within immune therapy of cancer, oral lesions from radiation therapy (oral mucositis), and inflammatory bowel disease (IBD).

The current wound care project has reached a stage where the company is actively

seeking partners for further product development, commercialization and distribution. The product showed promising results for use on diabetic ulcers in phase II but failed in phase III.

During 2010, the company has documented that the main part of the phase III trial was conducted with a product lacking the necessary biological activity and wound adhering properties, as the product was not stable in the polyethylene containers used in the study.

The part of phase III trials that was conducted with an active product showed performance in line with the phase II study. However, this part had too few treated patients to show a statistically significant treatment effect from SBG.

There is still a large need for new products for the treatment of diabetic ulcers, and the company sees a substantial market potential for SBG-based wound healing products. The hydrogel based products currently used to treat diabetic ulcers are with few exceptions classified as medical devices. The company has therefore considered launching the first products under this category instead of returning to the pharmaceutical development program.

The Irish Medicines Agency has reviewed what classification such a glucan based product could be granted in the EU. The conclusion was that it may be classified as a Class 2B device, which is a less demanding class of such products. This assessment is not a final approval, but suggests that such a product may be approved as a medical device within the EU.

There is a clear link, however, between the different classification types and the prices that can be achieved for the product. In short, the development costs will be lower for a class 2B product, but the product will also have a lower retail price, and established clinical documentation may only to a very limited degree be used in the marketing of such a product. Given the urgent need for new products for advanced wound care, it is, however, grounds to expect that even such a product will have a substantial market potential.

Biotec Pharmacon is now in discussions with potential partners for the development of a wound care product with particular focus on diabetic ulcer. If such a product is approved as a medical device, it may also be used in other areas of wound care.

In parallel with the efforts to develop a product for topical wound care, the company has developed technologies to produce various other beta-glucans. In animal models these appear to have more direct pharmacological effects on wounds. This means that future product releases may fall into the more demanding regulatory categories, and make it possible to launch a pharmaceutical product at a later date. These newly developed product candidates will also be evaluated with respect to improved efficacy within the other therapeutic areas the company is working on.

Due to the reduced organizational capacity, the projects for treatment of oral mucositis, immune therapy of cancer and treatment of inflammatory bowel disease were given lower priority in 2010. However, substantial investments have earlier been made in these areas over several years, and the company has secured the

technology platforms together and patent rights that may be utilized at a later stage. Oral mucositis is an inflammation with subsequent ulceration of the mucous membranes of the mouth and pharynx, and a common and very painful complication when using radiation therapy and chemotherapy against cancer. Biotec Pharmacon has conducted two clinical studies to test the effect of SBG against oral mucositis. Unfortunately, the product that was used in the Phase III study had the same stability problems as the product used for diabetic ulcer. The company has obtained an orphan drug designation for the use of SBG for this indication, and will consider how to best move this project forward.

The company has a partnership with Memorial Sloan-Kettering Cancer Center (MSKCC) in New York on the use of SBG in combination with antibody-based cancer treatments. Early stage clinical trials have been conducted to establish a safety profile and assess the treatment efficacy. The company is in dialogue with MSKCC to discuss how to continue the cooperation.

In collaboration with the Immunology group at the Laboratory for Immunohistochemistry and Immunopathology at the National Hospital in Oslo, the company has for several years had a research program to determine whether SBG may affect the development of inflammatory bowel disease (IBD). As for diabetic ulcer there are a very limited number of drugs available for effective treatment of IBD, and a need for new products to help this large patient group. Studies in an experimental animal model showed that beta-glucan had significant effects in preventing the development of ulcerative colitis. The collaboration has also led to new insights into the behavior of beta-glucan when administered to mucous membrane surfaces, and resulted in new patents on the use of soluble beta-glucan in the treatment of inflammatory bowel disease. A continuation of this project will require collaboration with an external partner.

### **3. Marine enzymes:**

The enzyme operation is organized in the subsidiary ArcticZymes AS (previously Biotec Marine Biochemicals AS), and is selling a portfolio of cold adapted enzymes. Such enzymes are used in molecular biology both in research and in routine diagnostics. Application of high-quality enzymes with special temperature properties improves the results of PCR based DNA and RNA analyses.

The company's enzymes are included in products (kits) from leading companies, both in approved *in vitro* diagnostics (IVD) kits, in products for the research market, and in already established test procedures.

The company's enzymes are unique in their origin from organisms living in the cold Arctic Sea. These enzymes are active at low temperatures, while their thermal sensitivity makes it easy to inactivate the enzymes by heating the reaction. Other enzymes require more time consuming and costly extraction protocols and often also lead to large losses of sample material. Many of the procedures that include the company's enzymes are included use very limited amounts of DNA or RNA, in which case the elimination of the extraction loss is a particular advantage for the customer.

The company has generally good patent protection for its products. The company is

currently marketing five unique enzymes from Arctic organisms. Given the phasing-out of (native) SAP, all the enzymes are now recombinant (artificially manufactured in micro-organisms), and thus independent of the supply of biological materials.

- Shrimp Alkaline Phosphatase (SAP) - Alkaline phosphatase from shrimp
- Double-Strand Specific DNase (ds-DNase) from Shrimp
- Heat-labile Double-Strand Specific DNase (HL-dsDNase) - mutant of dsDNase
- Cod Uracil-DNA glycosylase (Cod UNG) - UNG from Cod
- Salt active nuclease (SAN) - General nuclease from a marine bacterium in Svalbard

Distribution of SAP is taking place through an exclusive agreement with the American company U.S. Biochemicals, a subsidiary of Affymetrix, whereas the other products are being sold on a non-exclusive basis through various channels. The majority of sales have traditionally been to customers using the products in their own proprietary kits, but an increasing portion of the sales now goes through the company's own sales channels under our own brand name. These sales increased by more than 380% compared to 2009. The company also sees a greater geographical spread, as total sales in Europe increased by 234% last year. A large part of this sale was under ArcticZymes' own brand.

The company has generally experienced a significant increase in the activity level during 2010, and also strengthened its workforce with several new employees. Some key people were transferred to the enzyme activities in connection with the reorganization of Biotec Pharmacon at the end of 2009, which immediately led to higher activity. Overall, the staff increased by three people in late 2009 and 1 in 2010, to a total of 9 employees at the end of 2010. This does not include administration, IP, finance and quality functions, which all are being handled by the parent company.

The increase in the number of employees provides a basis for a continued strong growth in revenues but first and foremost in the number of customer-controlled trials. During 2009, ArcticZymes started eight such trials, whereas the corresponding figure for 2010 was 98 trials. Such trials are often a necessary requirement for sales to new customers, and the strong increase creates expectations for further sales growth.

The main product is still SAP (Shrimp Alkaline Phosphatase), which is mainly being marketed towards the international research and diagnostics market. Our distributor U.S. Biochemicals launched our new recombinant SAP in May 2010, and the production of SAP based on natural ingredients is now terminated. This shift has been very successful and the customers in particular see major advantages in terms of stability and reproducibility with the new product version. The new recombinant product has minimal batch variations compared with the previous version, and the production can easily be scaled up.

Sales of Cod UNG (Cod Uracil-DNA Glycosylase) show continued strong growth, adjusted for a large one-time sale in 2009. Cod UNG is ArcticZymes' second largest product, and even though the sales figures are still lower than for SAP, the potential may be larger. This enzyme is strongly linked to the diagnostic market, where it has clear competitive advantages compared to existing glycosylase enzymes.

Siemens Healthcare Diagnostics in late 2008 launched kits where the Cod UNG enzyme was included in their new qPCR platform for bacterial and viral diagnosis. These products have so far only been approved in the European Union (CE-IVD), where they have been well received. However, the largest potential for this product is assumed to be the United States. However, a significant sales increase can only be expected once the customer has obtained FDA approval. The Cod UNG enzyme is moreover being tested for implementation in end-used products (kits) at a significant number of other international research and diagnostics companies.

ArcticZymes has also launched a double-strand-specific nuclease (dsDNase) from shrimps. This enzyme is now in the process of being introduced in end-user products at a number of the major players in the molecular biology market, which is expected to increase sales substantially. Sales of dsDNase increased almost fivefold in 2010, albeit from a very low starting point.

Two new products were launched in March 2010 - an enhanced version of dsDNase known as HL-dsDNase, and a salt active nuclease (SAN) - both of which complement the company's other products. The heat lability and the RNA purification abilities of the HL-dsDNase enzyme have been further improved in our laboratories, while the properties of the SAN enzyme enable it for use in protein purification. Both new products were well received in the market, and are already in trials at a large number of customers. The launch of the HL-dsDNase has generated leads at a large number of new customers, and this enzyme is thus essential for the company's sales increase for products under own brand.

The company expects continued strong growth ahead. More staff means more resources for research, closer customer collaboration on application development, and not the least increased marketing activities.

The company has for several years had a close cooperation with the University of Tromsø, and actively participated in most of the University's research projects of relevance to marine enzymes. The company's active participation in the MabCent program has led to several unique product candidates that will be evaluated for possible commercialization.

The cooperation with the University of Tromsø was further strengthened through the acquisition of Marimol AS, which held the rights to the commercialization of enzymes from the MARZymes project. This is a large 5-year project that has received significant governmental funding for enzyme bio-prospecting in the Arctic region. ArcticZymes is working closely with research groups in the MARZymes project to ensure that the project activities are commercially relevant.

In addition to the enzyme activities, the company is also involved in activities at Svalbard, through a collaborative project searching for interesting enzymes in eukaryotic microorganisms (microalgae). ArcticZymes is generally well positioned to launch new unique cold active enzymes to the molecular biology market in the coming years.

#### **4. Parent Company Activities**

At the end of the year the Group had 29 employees, of which 22 in the operational activities (13 in beta-glucans and 9 in enzymes), and 7 in administration, patenting, finance and quality assurance in the parent company. Group Managing Director Svein Lien also has the operating responsibility for the beta-glucan business area, whereas Jan Buch Andersen has the corresponding responsibilities for the enzyme activities.

During 2010, the company worked to sublease the Oslo premises for the remaining lease period to May 2013. This is now completed, and the Oslo office has been closed.

The work to obtain ISO accreditation under the ISO 13485 standard started in 2010, and the most important aspects are expected to be completed by the end of 2011. This will be a great advantage in the work to develop the first beta-glucan based product as a medical device, and will also be important for the enzyme business in their work towards large and demanding international companies.

The IPR function is handled through the parent company. Several patent applications were filed during 2010 within the beta-glucan area, which will significantly strengthen the protection. These last applications were based on work carried out after the phase III studies, where a number of new findings were made relating to the development of a wound healing product. The company also acquired new patentable knowledge about the use of and production of beta-glucans. A number of patent applications were approved in important markets, including a patent for the use of SBG in combination with antibody-based cancer treatment that was approved in the United States in May 2010.

## **5. Income statement and Balance Sheet**

### Income Statement

The income statement of Biotec Pharmacon is prepared according to International Financial Reporting Standards (IFRS). The Biotec Pharmacon Group had sales of NOK 25.9 million in 2010, compared with NOK 24.1 million in 2009, for the continuing operations after the disposal of Immunocorp Consumer Health AS. The company's revenue primarily comes from sales of products within the business area marine enzymes, whereas the beta-glucans business currently sells products exclusively to the former subsidiary Immunocorp Consumer Health AS. Sales of marine enzymes increased 23% from the previous year, whereas sales of beta-glucans to consumer health fell by 34% from 2009.

This loss for the Group was NOK -28.5 million compared to a loss of NOK -99.4 million in 2009. Group net cost (EBIT) in the beta-glucan area was NOK 31.9 million in 2010, compared with NOK 73.8 million in 2009. Operating profit for marine enzymes was NOK 10.3 million in 2010, an improvement of NOK 2.0 million from the previous year. Corporate costs were NOK 7.6 million in 2010. In 2009 these costs were NOK 19.6 million, including costs to prepare for litigation of patents in the United States and for the subsequent settlement.

### Cash Flow

The Group's cash flow from operations was NOK -25.0 million in 2010, compared with NOK -89.0 million in 2009. Cash flow from investing activities was NOK -1.4 million, against NOK 14.1 million in 2009. The positive cash flow from investing activities in 2009 was mainly due to the disposal of Immunocorp Consumer Health AS, which took place at the end of the year. The Group has in 2010 invested net NOK 1.8 million in fixed assets. Net cash flow from financing activities was NOK 20.1 million in 2010, including a capital increase at the end of 2010, compared with NOK 0.1 million in 2009. Net cash flow in 2010 was this NOK -6.3 million, compared with NOK -75.0 million in 2009.

### Balance

The equity of the Biotec Pharmacon Group was NOK 36.4 million at the end of 2010, compared to NOK 61.2 million at the beginning of the year. The equity ratio was 53% (before registration of share issue, see shareholder information). Liquid assets amounted to NOK 43.3 million as of 31.12.2010, compared to NOK 49.6 million at the end of the previous year. The company has no interest-bearing debt. The company has an undrawn credit facility with a bank of NOK 10 million.

### Parent Company

Sales revenues in the parent company Biotec Pharmacon ASA was NOK 6.9 million and the full year result NOK -36.7 million. Comparable numbers for 2009 were NOK 36.8 million in sales revenues and a net result of NOK -97.1 million. The development of the beta-glucan area has been organized in the parent company Biotec Pharmacon ASA. The parent company's results were in 2009 negatively affected by a net loss before tax of NOK -19.0 million from the divestment of Immunocorp Consumer Health AS per 30 December 2009, and further negatively affected by NOK 30.7 million because a previously activated deferred tax asset was expensed in its entirety per 31.12.2009 based on the assumption that future taxable profits will be delayed compared with assessments made in 2008. This will be reevaluated during 2011.

The Board proposes that the loss of NOK -36.7 million in the parent company Biotec Pharmacon ASA is covered through transfers from other equity. The parent company has no distributable equity as of 31.12.2010, but the board will propose to the company's Annual General Meeting that the share premium account is reduced by conversion to other equity, in order to ensure financial flexibility.

The results for 2010 reflect the priorities that the Board has communicated to the stock market after the reorganization in early 2010. As expected, the research and development costs in the glucan area were significantly reduced compared to the previous year. All material events subsequent to the Balance date are mentioned in the report from the Board of Directors.

The Board of Directors is not aware of any issues of material significance for the company's financial position beyond issues described in this report and in the accounts.

The financial statements are prepared on the basis of continued operation. This assumption is based on the company's plans, the actual funding situation, and on the company's the long-term forecasts.

Biotec Pharmacon will actively seek to enter into one or more partner agreements for its beta-glucan product portfolio during 2011. The Board and management will seek to further strengthen the company's financial strength and flexibility.

## **6. Shareholder Information**

The company's share price increased 55% during the year, from NOK 4.94 to NOK 7.64. In December 2010, the company completed a successful private placement of 3.5 million shares at NOK 6.30 per share, directed towards a limited numbers of shareholders. The registration of this capital increase was not carried out until 7 January 2011, and proceeds from the issue were thus temporarily recorded as current liabilities. The company had 1,313 shareholders at the end of the year, whereof the 10 largest controlled 35.2% of the share capital.

After the registration of the issue on 7 January, 2011, the number of shares increased to 27,137,910, and the company's share capital to NOK 27,137,910.

Subsequent to the private placement, the company in the first quarter of 2011 carried out a repair issue of 1,200,000 shares at NOK. 6.30 per shares, to those existing shareholders who were not invited to participate in the December issue.

The Board wishes to stimulate employees to become shareholders in the company both through an option program for all employees and through offering employees the opportunity to buy shares with the discounts applicable within current tax regulations. During the year, the employees received an offer to buy a given number of shares at a 20% discount, limited to NOK 1,500 per employee. 63% of the employees made use of the offer.

In May 2010, the Board received authorization from the General Meeting to issue up to 1,000,000 shares as part of an incentive program for the employees in the company. Based on this authority the Board introduced an option program for all employees except the CEO, who has a separate agreement. This program was made effective for one year, reflecting the uncertain situation for the company at the time. A total of 250,000 options were issued, and 214,906 options were exercised by the deadline at the end of March 2011. The remaining options were cancelled.

As per today the company has registered 28,510,181 shares, with a share capital of NOK 28,510,181. The last 42,635 options that were exercised at the end of March, will be recorded as share capital at the payment due date in early April 2011.

## **9. Feil! Hyperkoblingsreferansen er ugyldig.Risks**

The Group is exposed to various types of financial and operational risks.

Currency risk results from the fact that approximately 80% of sales revenue is in foreign currency, particularly USD, whereas the company's cost base primarily is in NOK and Euro. A higher USD exchange rate against the NOK will affect the results in a positive direction, whereas a lower USD will have the opposite effect. Euro fluctuations will have a fairly neutral effect. As a general rule, the Group only carries out forward hedging of major individual items affecting cash flows. The Group's exposure may in the longer run be changed by new product launches.

The group has no interest bearing debt. Interest bearing investments are made only in the form of bank deposits, commercial papers, or in bond funds with short maturities. The Group thus has very limited exposure to interest rate risk. It takes no risk in the stock market. The Group has no significant concentrations of credit risk, and there was no recorded loss on accounts receivable during the year.

The company's funding risk was significantly reduced through the share issue that was completed in December 2010, and further strengthened with the subsequent repair issue in the first quarter of 2011.

There are substantial costs associated with conducting clinical trials of products, and there will always be a risk that trials for any particular indication may go wrong. In addition, there is significant risk associated with the technical development of the substance and the regulatory efforts to ensure recognition and thus the opportunity to sell the finished product in the market.

The group seeks to protect its intellectual property rights through patent protection. Risk nevertheless remains that other companies may dispute such rights. Similarly, the Group may have to take on the costs to defend its rights against infringement from other companies.

The enzyme business is dependent on a number of distributors and partners for the majority of sales. Within the glucan activities, the company has announced that it is in dialogue with several potential partners for its first product for topical wound management. Although these dialogues are developing positively, there is no guarantee that this work will lead to good commercial arrangements that ensure a successful launch and sales development.

Many key employees are central to the success of the company's businesses. These key individuals are involved in the development of products, technologies, production processes and quality control, purchasing and marketing, and other activities in the company. The company also depends on recruiting new qualified personnel. There is no guarantee that the company will be able to retain key personnel or be able to recruit key people in the future.

The company is dependent on certain key suppliers to manufacture products. The raw material for production of beta-1,3/1,6-glucan is delivered from one central supplier. The company may, if necessary, change providers over time, but cannot exclude that such changes could have a temporary negative impact on its operations.

## **8. Working environment and staff**

At the end of 2010 there were 29 full- and part-time employees in the group, of which 20 employees of the parent company Biotec Pharmacon and 9 of ArcticZymes AS. After the separation and the glucan operation into the wholly owned subsidiary Biotec BetaGlucans AS in January 2011, there are seven employees left in the parent company. The Company in 2010 completed a staff reduction of 14 positions as a consequence of the failed phase III in 2009, although ArcticZymes had an increase of 1 person during the year.

Sick leave totaled 195 days for the Group in 2010, which corresponds to 2.9% compared with 4.1% for 2009. The low level is particularly encouraging given that the company went through a turbulent year with a reorganization process and significant downsizing. There were no serious accidents or accidents resulting in injury or material damage during the year. The working environment is generally considered to be good. Legal requirements and other procedures are being implemented as the company changes. In February 2011, the company moved to new premises in the Research Park at the University of Tromsø.

The company is committed to facilitating the recruitment and development of employees of both genders. Gender equality is practiced in that women and men are valued equally with regards to career opportunities and remuneration. At year end there were 11 women and 18 men employed in the Group. In senior positions, there were 3 women and 9 men. The board consists of 5 persons, whereof 2 of the 4 shareholder-elected directors were women and 2 men. The employee representative is male.

## **9. Environment**

The company's activities have limited impact on the environment. Chemicals that can not be recycled in the production process are collected and returned to an approved manufacturer for environmentally sound recycling. The energy usage in production is modest.

## **10. Corporate governance**

The Board has established principles of corporate governance in line with the Norwegian Code of Practice.. A detailed overview is given on the homepage.

## **11. Outlook**

The company will continue to develop its business activities within the current two business areas in the future. Within the glucan business area, the main focus will be the development of a topical wound management product. The short-term goals for this work are to determine the composition and design for the first product and to secure partnership agreement(s).

Furthermore, the company will clarify which target it may realistically set for the other application areas for beta-glucans.

Within the enzyme business, the growth in product sales under own brand makes it

attractive to strengthen the resources on sales and marketing through the establishment of local representation in main international markets. The company has a clear expectation of further increased demand for the enzyme products.

The company expects continued high research and development activity in both segments. It is expected that the company will be close to obtaining an ISO 13485 accreditation for the entire group during 2011.

Overall, the Board believes that the work and results achieved in 2010 represent a strong foundation for future growth. The Board would like to thank all staff for their efforts in 2010.

Tromsø, 28 March 2011

Svein Mathisen  
Chairman

Ingrid Wiik  
Vice Chairman

Ingrid Alfheim  
Board member

Gunnar Rørstad  
Board member

Morten Elde  
Board member  
elected by employees

Svein W.F. Lien  
CEO