Bio Tie THERAPIES

Annual Report 2003

Contents

Information for Shareholders

ANNUAL GENERAL MEETING

The Annual General meeting of Biotie Therapies Corp. will be held on Thursday March 25, 2004 commencing at 10 o'clock, at the auditorium of Restaurant Alabama in Turku (Lemminkäisenkatu 14-18, B).

Shareholders are entitled to participate in the Annual General Meeting if they are registered in the Company's register of shareholders maintained by the Finnish Central Securities Depository Ltd no later than March 15, 2004.

Shareholders wishing to participate in the Annual General Meeting must notify the Company thereof no later than March 22, 2004 at 16.00 (4.00 p.m.) either in writing to Biotie Therapies Corp., Ms Virve Nurmi, Tykistökatu 6, FIN-20520 Turku, Finland, or by telephone at +358 2 274 8911 during office hours 9.00–16.00 from Monday to Friday. The letter of participation must arrive at the Company before the expiry of the above mentioned period for notification. Any letters of authorization must be submitted in connection with the notification of participation.

FINANCIAL PUBLICATIONS

This annual report and the Company's financial reports are published in Finnish and English. The interim reports will be published as follows:

- January – March,
  on Friday, April 23, 2004
- January – June,
  on Thursday, August 5, 2004
- January – September,
  on Friday, October 22, 2004

To order these publications, please send your request to Biotie Therapies Corp., Ms Virve Nurmi, Tykistökatu 6, FIN-20520 Turku, Finland or call her at +358 2 274 8911. The publications can also be ordered via info@biotie.com

INVESTOR RELATIONS

BioTie's investor relations are the responsibility of
Jari Saarinen, President and CEO
Tel. +358 2 274 8954
jari.saarinen@biotie.com

BioTie in Brief

Biotie Therapies is a biotechnology company specializing in dependence disorders, inflammatory diseases and glycomics applications. The company's products focus on widespread diseases from which tens of millions of patients suffer and for which there is no effective treatment. The company develops drugs for significant indications such as alcohol dependency, rheumatoid arthritis, inflammatory bowel disease, psoriasis, thrombosis and cancer. Drugs may also be developed for other indication areas.

BioTie's History

Biotie Therapies is in its present form a result of the merger of three Finnish biotechnology companies; Contral Pharma Corporation, Biotie Therapies Corp. and Carbion Inc. in October 2002. The new combined company was named Biotie Therapies Corp.

The research and development operations of Contral Pharma had focused on drug therapy for dependence disorders. Contral Pharma was founded in 1998 for the development and commercialization of nalmefene, an opioid antagonist intended for the treatment of alcoholism and alcohol abuse.

BioTie's research activities were focused on inflammatory diseases, thrombosis and cancer. Professors Markku Jalkanen and Sirpa Jalkanen founded BioTie in June 1992 based on their research work at the University of Turku and the National Public Health Institute. BioTie commenced operations in its first research premises in BioCity, Turku in 1996. In fall 1998, BioTie introduced pilot production facilities that met GMP requirements. In summer 1999, BioTie submitted its first clinical trial application to conduct clinical research with its own drug to the National Agency for Medicines. BioTie's shares were listed on the NM list of the Helsinki Exchanges in June 2000.

Focusing on the development of glycomics-based drugs for the treatment of cancer, viral and bacterial infections, Carbion's research activities were based on academic research at the carbohydrate and protein chemistry laboratories of the Institute of Biotechnology of the University of Helsinki. Contral Pharma owned 50.1 per cent of Carbion.

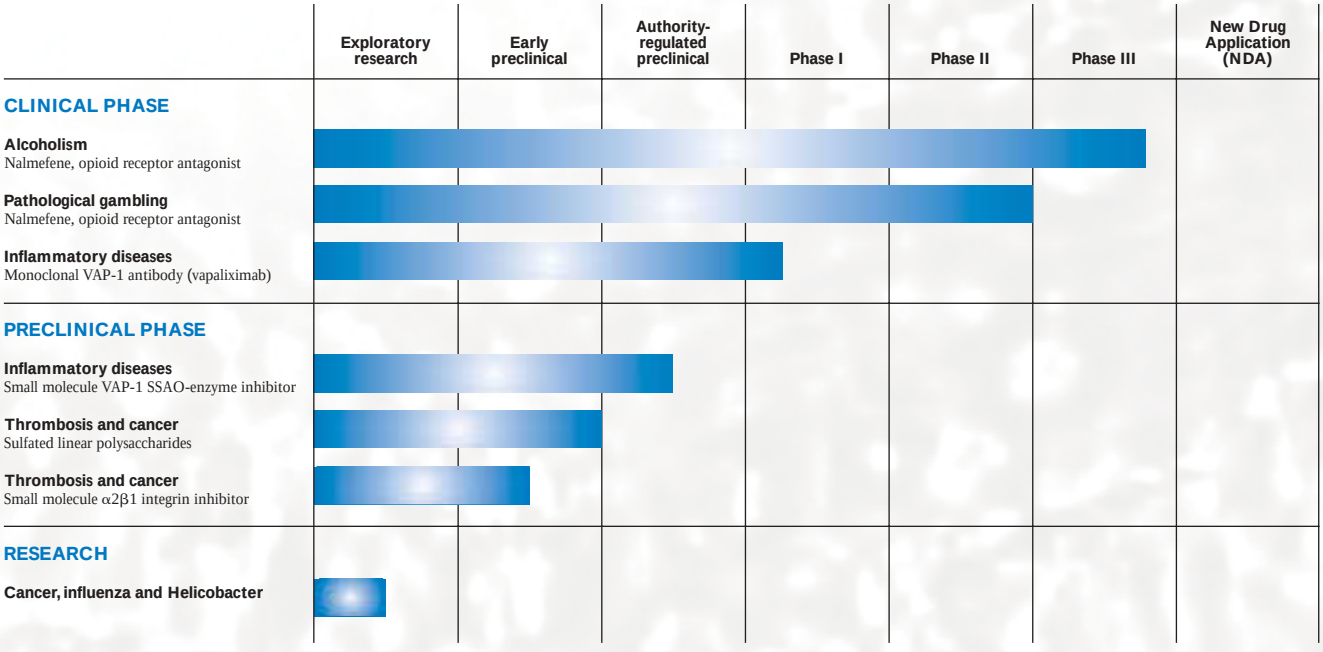
Key Figures

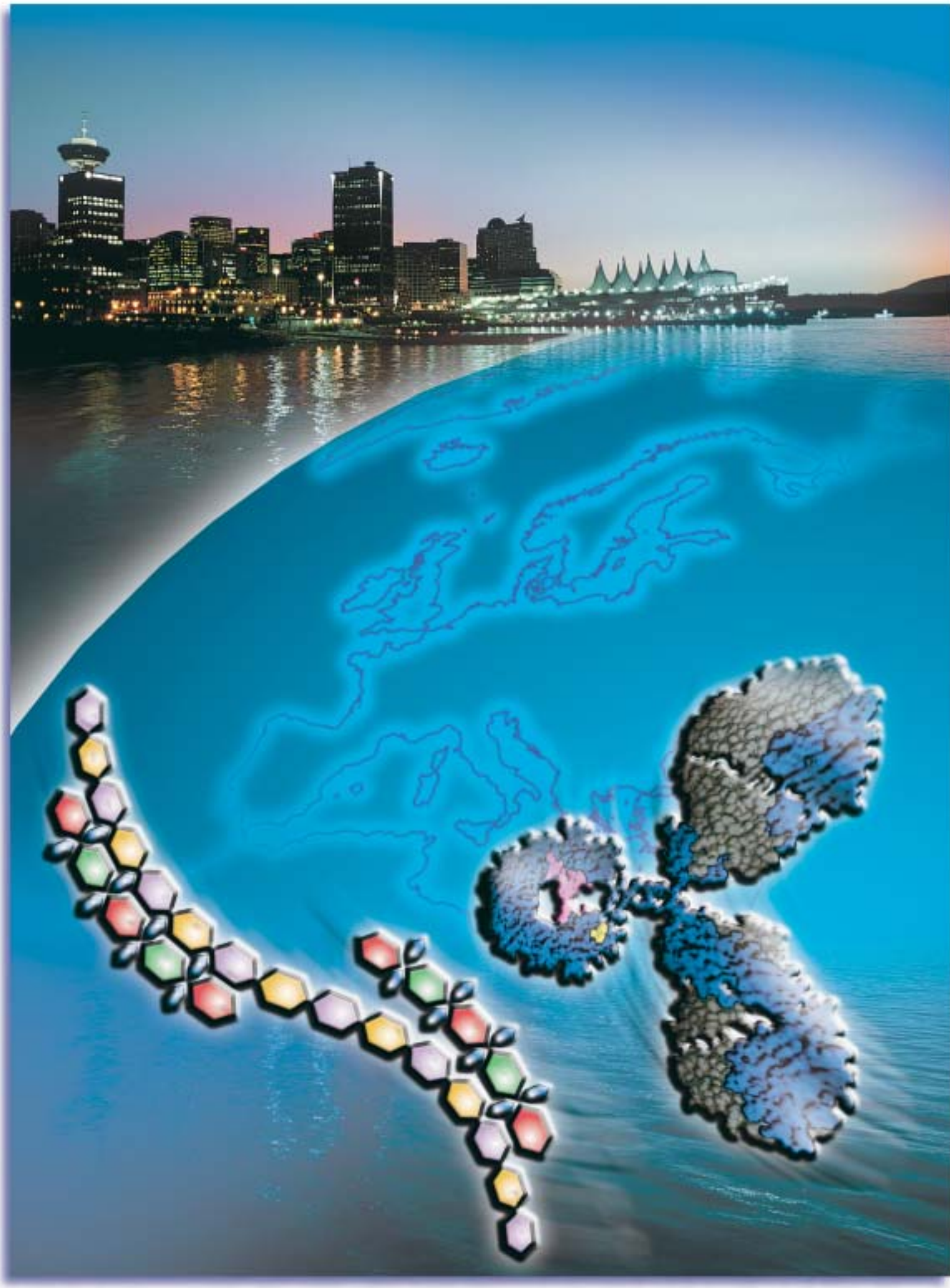
1000 EUR	1.1.–31.12.2003 12 months	1.1.–31.12.2002 12 months
Research and development expenses	11 888	21 541
Operating profit (loss)	-12 395	-26 256
Cash flow before financing activities	-12 057	-25 712
Cash and cash equivalents	10 422	8 691
Personnel at the end of the period	55	112

The Year 2003 in Brief

- The company entered into a licensing agreement on its VAP-1 antibody program with the Japanese company Seikagaku Corporation. The agreement is valued at USD 16.7 million, including a signing fee and milestone payments.
- During the spring, BioTie completed two phase III clinical studies with nalmefene in heavy alcohol drinkers and one phase II clinical study in patients suffering from pathological gambling.
- In May 2003, the company completed the first phase I clinical study with the VAP-1 antibody vapaliximab. Based on the results, a decision was made to modify its molecular structure and simultaneously commence the development of a humanized (non-chimeric) and a fully human VAP-1 antibody.
- The company acquired the rights to independent utilization of the immaterial property rights in the bioheparin project.
- The company implemented an efficiency improvement program in order to focus the project portfolio and to lower costs. As a result, the costs were lowered by EUR 10 million (40%) in 2003 compared with the previous year.
- During the second quarter, BioTie raised EUR 10.5 million of new capital through a new issue pursuant to the shareholders' pre-emptive subscription right.
- In April 2003, the National Technology Agency (Tekes) granted additional funding of EUR 5.9 million for the company's research and development programs.
- The operating profit (loss) was EUR -12.4 million (in 2002 EUR -26.3 million). Cash flow before financial activities was EUR -12.1 million (in 2002 EUR -25.7 million)
- The company's liquid assets amounted to EUR 10.4 million (in 2002, EUR 8.7 million) as at December 31, 2003.

BioTie's Product Pipeline





President's Review

The year 2003 was characterized by continuing economic recession and difficult capital market situation which affected the biotechnology sector significantly. Towards the end of the year, however, the international financial markets seemed to recover, there was an upward trend in stock prices and a few biotechnology IPOs were seen in Nasdaq. Nevertheless, the recovery of the biotechnology sector seems to take significantly longer in Europe compared to North America.

The consolidation in the biotechnology sector continued as the companies aimed at synergy benefits from larger research portfolios. Announced in the summer, the merger of Biogen and IDEC Pharmaceuticals in the United States was the most significant biotechnology merger during the past year. Due to the difficult financing situation, consolidation continued in Finland, too.

Biotechnology is clearly changing from a future promise into reality. According to Biotechnology Industry Organization, a total of approximately 370 biotechnological drugs targeted at the treatment of about 200 different diseases have already progressed to clinical studies. More than 325 million people worldwide have been helped by the more than 150 biotechnology drugs and vaccines approved by the U.S. Food and Drug Administration (FDA). Of the biotech medicines on the market, 70 percent were approved in the last six years. Biosciences are introducing concrete methods of curing diseases for which no efficient therapies were available previously.

BioTie's drug development projects proceeded significantly during the year 2003. In the spring we completed phase III clinical studies of the nalmefene product intended for the treatment of alcoholism and alcohol abuse and phase II clinical studies for the treatment of impulse control disorders. The research results are encouraging and show that heavy drinking days and pathological gambling can be reduced by drug therapy. In accordance with our strategy, we aim at commercializing the nalmefene project at its present stage of development and launching it to the market in cooperation with licensing partners.

We also completed the first phase I clinical study of the chimeric monoclonal antibody (vapaliximab) in the VAP-1 antibody program using healthy volunteers. On the basis of the study, the decision was made to modify the molecular structure of VAP-1 antibody to develop it further. The company commenced the development of humanized (non-chimeric) and fully human-derived VAP-1 antibody. It is estimated that the selection of the antibody offering the best benefits will be made in the second quarter of 2004.

In the spring we entered into a significant licensing agreement on VAP-1 antibody program with the Japanese pharmaceutical company Seikagaku. The agreement is valued at USD 16.7 million.

In January 2004 we completed the efficiency improvement program for the company's operations, aiming at focusing the resources on the key drug development projects and lowering costs. The program was implemented as planned. The company's resources were focused on selected therapy areas for the treatment of inflammatory diseases and dependence disorders as well as glycomics. Operating costs decreased by EUR 10 million, i.e. 40 per cent compared with the previous year.

In spite of the difficult financing situation of the field, BioTie succeeded in raising EUR 10.5 million of new capital in the share issue in June. Furthermore, the National Technology Agency (Tekes) granted EUR 5.9 million for the company's research and development programs. The additional funding secured the financing of our operations at least until end of 2004. As a result of the improved financing situation, BioTie's share was transferred from the Pre-list of the Helsinki Exchanges to the NM list in October 2003. This contributed to considerable increase in trading with BioTie's share towards the end of the year.

During the past year, we took steps that are significant in the history of the company. My special thanks go to BioTie's personnel for their excellent work and commitment to our company during difficult times. I also wish to thank our shareholders for their trust and our partners for smooth collaboration. We have built a strong basis for the future, and I believe that BioTie is now well positioned for development and commercialization of the drug development projects.

Jari Saarinen
President and CEO

Business Model

The revenues of biotechnology and drug development companies comprise of

- upfront payments
- milestone payments
- royalties from the sales of products agreed on in cooperation agreements.

The amount of payments for drug development projects depends on the development stage and market potential of the project, as well as the type of agreement and the scope of the licensed rights.

UPFRONT PAYMENTS

Upfront payments are usually paid upon entering a collaboration agreements. The amount of the upfront payment depends on the project's market potential, development phase, scope of collaboration and the number of potential indications. The payments for an early-stage (preclinical or clinical phase I studies) candidate drug amount to a few million dollars, while the average payments for a candidate drug at a later phase (clinical phase III studies and marketing authorization) amount to tens of millions of dollars. The largest upfront payments have been as high as hundreds of millions of dollars.

MILESTONE PAYMENTS

Milestone payments are made when the compound passes important steps in the development process. Typical milestones include showing the efficacy of the candidate drug in animal tests (so-called Proof of Principle) and completion of phase I and II clinical studies (so-called Proof of Concept) or phase III clinical studies as well as applying for and obtaining marketing authorization.

Milestone payments vary from tens of millions to hundreds of millions of dollars depending on the product's development stage.

ROYALTIES

The flow of sales-related revenues of drug development and biotechnology companies commences after the drug has been launched to the market and the company licensing the drug has started to pay sales royalties to the licensor. Royalties are calculated as percentage of the sales of the product. In many cases, the contracting parties do not publish the royalty percentage.

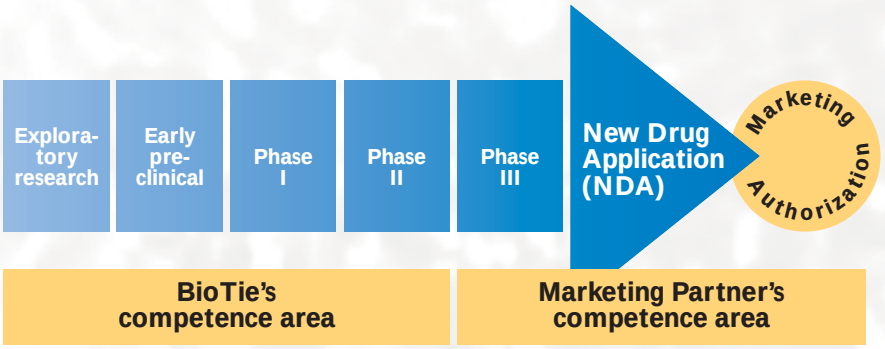
The amount of royalty varies greatly depending on the development phase of the product. The royalties of early-stage products (discovery phase or phase I clinical studies) vary from a few per cent to ten per cent. The royalties for later-stage products (phase II-III clinical studies and sales authorization) can be as high as tens of per cent.

The Vision

BioTie's objective is to become a leading biotechnology company in selected therapy areas.

Strategy

- BioTie focuses on the treatment of inflammatory diseases, dependence disorders and applications of glycomics.
- The research and development activities of BioTie are focused on preclinical and early-stage clinical research.
- BioTie's broad scientific network acts as a source of new product ideas. The company has an extensive local and international network of research collaborators. Through these it has access to high-quality research projects and the opportunity to license the results for itself for further development.
- BioTie has a well integrated internal and external drug development operations. The company seeks to master key areas of preclinical and early-stage clinical research and production process development. The company focuses its own resources to areas where it has developed, or can develop, a competitive advantage, where most added value is created or where there are strategic reasons to keep the knowledge in the company.
- BioTie licenses candidate drugs to pharmaceutical companies. According to its strategy, products will be licensed at an optimal stage of project's development, taking into account the development stage of the product and the financial resources available to the company; primarily when the efficacy of the candidate drug has been demonstrated. BioTie aims at entering into comprehensive (covering North America and Europe) development and marketing agreements with international pharmaceutical companies.



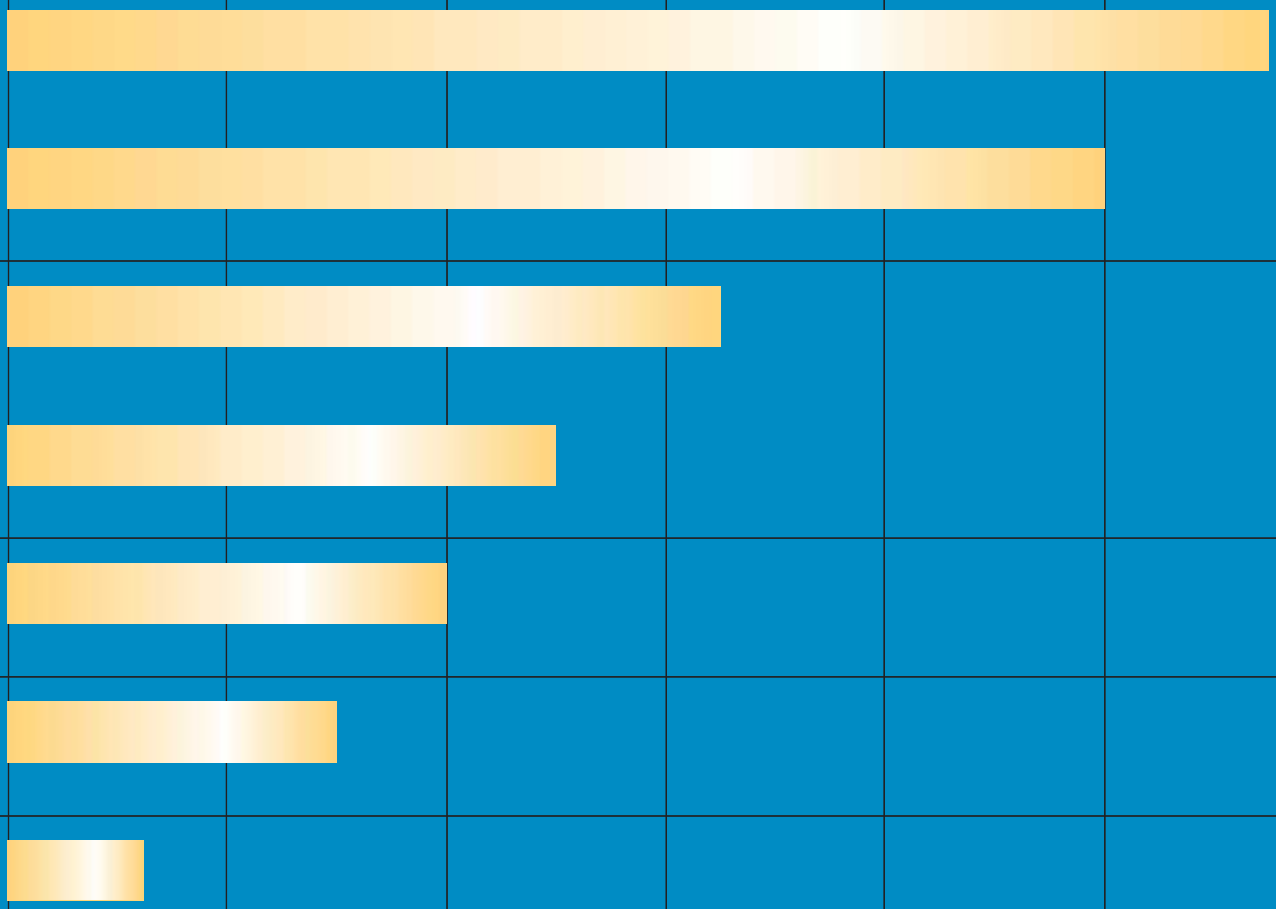
Research and Product Development

	PRODUCT	POTENTIAL INDICATIONS
OPIOID RECEPTOR	**Nalmefene**	Alcoholism and alcohol abuse
	Nalmefene	Pathological gambling
VAP-1	**Monoclonal VAP-1 antibody (vapaliximab)**	Treatment of moderate to severe inflammatory diseases.* Treatment of severe, life-threatening inflammatory conditions.**
	Small molecule VAP-1 SSAO-enzyme inhibitor	Treatment of mild and moderate inflammatory diseases.*
COAGULATION FACTORS	**Biosynthetic low-molecular weight heparin (bioheparin) made from non-animal-derived material**	Prevention and treatment of thrombosis in patients with deep vein thrombosis, pulmonary thrombosis, myocardial infarction or unstable angina pectoris. Treatment of hemodialysis patients.
α2β1-INTEGRIN	**Small molecule α2β1 integrin inhibitor**	Treatment of myocardial and cerebral infarction and prevention of vascular thrombosis. Treatment of malignant tumors such as melanoma, ovarian cancer, gastric cancer and prostatic cancer.
RESEARCH		Cancer, influenza and Helicobacter

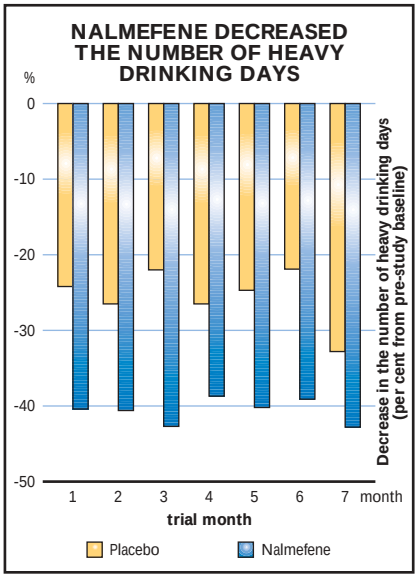
* Rheumatoid arthritis, asthma, hepatitis and inflammatory bowel diseases (Crohn's disease, ulcerative colitis), psoriasis and other inflammatory skin diseases.

** Ischemic reperfusion injury caused by myocardial or cerebral infarction, organ transplant rejection and ARDS (adult respiratory distress syndrome).

EXPLORATORY RESEARCH	EARLY PRECLINICAL	AUTHORITY-REGULATED PRECLINICAL	PHASE I	PHASE II	PHASE III
The discovery phase of a product candidate.	Evaluation of lead or preferred compounds for safety, pharmacology and proof of efficacy in non-human models.	Evaluation of a Candidate Drug for safety, pharmacology and proof of efficacy in non-human models.	A clinical trial for safety, pharmacology and dose-determining drug regimen.	A clinical trial to determine first potential therapeutic doses followed by a larger trial to determine efficacy of chosen therapeutic doses (Proof of Concept).	Pivotal clinical trial to determine efficacy and safety as primary support for regulatory approval.

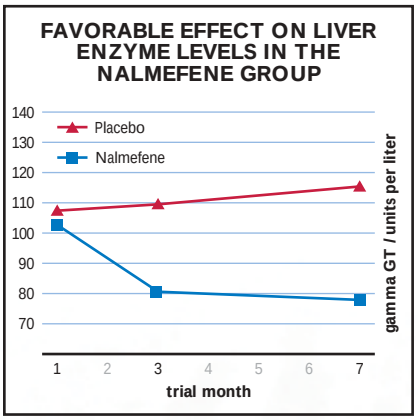


Dependence Disorders



In the Finnish multi-center study with 400 patients, the number of heavy drinking days in the nalmefene group decreased almost by half during the seven months' treatment period. Prior to the study, the average number of heavy drinking days was 16 per month. In the placebo group, the number of heavy drinking days decreased by about one third.

A heavy drinking day: Consumption of at least five (four for women) portions of alcohol.



In the Finnish alcohol study, the blood levels of gamma GT (a hepatic enzyme) decreased significantly in nalmefene users during the seven months' treatment. No corresponding improvement was observed in the placebo group.

NEUROBIOLOGICAL DISTURBANCES IN THE BACKGROUND

Dependence disorders are complex behavioral syndromes, but they have distinct neurobiological underpinnings that can be targeted with pharmacological interventions. A neural pathway in the brain, called the mesocorticolimbic "reward" pathway, is one of the most important mediators of alcohol and drug reinforcement, and disturbances in the function of this pathway are thought to have a central role in the development of substance dependence. The activity of this pathway is modulated in multiple ways, of which opioidergic mechanisms are among the most important.

The consumption of alcohol induces beta-endorphin release in the brain. Beta-endorphin is an endogenous compound that activates opioid receptors. Endorphins are responsible for many of the pleasurable effects of alcohol; they also activate opioid receptors in the mesocorticolimbic system, which leads to reward (reward can be thought of as a pleasurable feeling providing positive reinforcement, such that the behavior is likely to be repeated). Over an extended period of time, the process of reinforcement may lead to the development of dependence, which is characterized by loss of voluntary control over alcohol intake and alcohol craving. An opioid antagonist, such as BioTie's nalmefene, prevents beta-endorphin from binding to and activating opioid receptors.

Recent research results have suggested that reinforcement may also be an important feature in the pathophysiology of impulse control disorders such as pathological gambling, and that the neurobiological basis of impulse control disorders may have substantial similarity to that of addictions. In essence, they may be forms of "behavioral addiction", in which the behavior gradually becomes compulsive and the patient develops a strong craving for gambling.

HEAVY DRINKING CAN BE REDUCED BY DRUG THERAPY

In spring 2003 the company completed the first clinical phase III trials with nalmefene tablet being developed for the treatment of alcoholism. The study focused on the safety and efficacy of nalmefene in the treatment of alcoholism and alcohol abuse without supporting psycho-social therapy in patients who felt that they were unable to control their drinking. The participating patients were instructed to use the drug whenever they were about to start drinking alcohol.

In a 400-patient multi-center study carried out in Finland, the number of heavy drinking days was reduced almost by half among the patients in the nalmefene group during the seven months of treatment. The patients in the placebo group reduced their drinking by about a third, and the difference between the groups receiving nalmefene and placebo was statistically significant. There was considerable improvement in hepatic enzyme levels of the patients in the nalmefene group during the study, whereas these levels in the placebo group remained unchanged or were slightly impaired.

A multi-center study of 150 patients in Great Britain also showed an almost 50% decrease in the number of heavy drinking days, and the difference between the nalmefene group and placebo group was in the same range as in the Finnish study. However, the difference did not reach statistical significance, because the number of

patients discontinuing the study prematurely was higher than expected.

In both studies, the patients receiving nalmefene felt that the treatment was beneficial more often than the patients receiving placebo. No serious adverse effects related to the use of nalmefene were observed.

ENCOURAGING RESULTS IN PATIENTS SUFFERING FROM PATHOLOGICAL GAMBLING

In late spring, the company completed a clinical phase II study with the nalmefene product to be developed for the treatment of impulse control disorders. This multi-center, placebo-controlled study of 200 patients in the United States focused on the safety and efficacy of nalmefene in patients suffering from pathological gambling.

A psychometric scale developed by Drs. Hollander and DeCaria (Mount Sinai Hospital, New York) measuring gambling-related thoughts, urges and behavior was used for primary evaluation of efficacy. On the basis of the study results nalmefene was effective in patients suffering from pathological gambling: after four months' treatment, mean scores on this scale were almost twice as high in patients who were on placebo when compared to the patients receiving nalmefene. The difference between the study groups was statistically significant. No serious adverse effects related to the use of nalmefene were observed during the study.

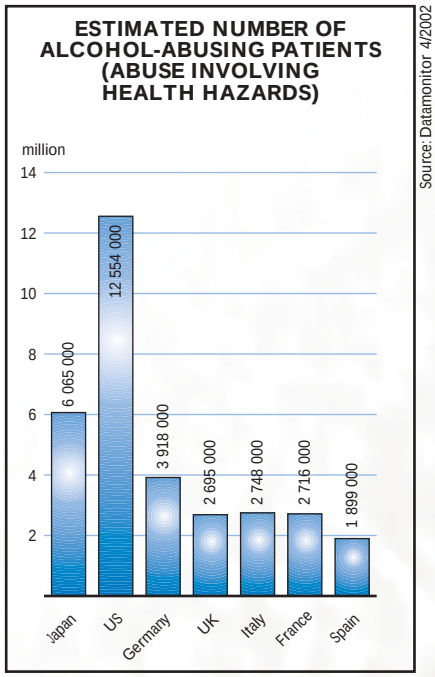
A NEW GROWING MARKET

It is estimated that there are 30-60 million alcoholics and alcohol abusers in the western world. In the United States alone, it is estimated that alcoholism and alcohol-induced diseases and accidents, decrease in productivity and premature deaths are causing approximately 200 billion dollars costs to society every year.

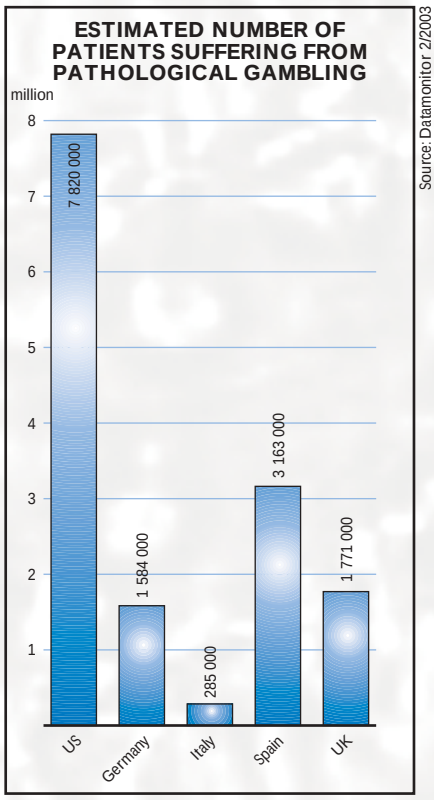
All drugs presently used for the treatment of drinking problems are therapies supporting other treatments, usually a psycho-social treatment program. The purpose of use of the currently available drugs supporting the treatment of alcoholism is to maintain abstinence. The efficacy of these therapies has been limited, and consequently, they have not been in frequent use. BioTie is the first company to study the efficacy of a drug intended for the treatment of drinking problems, primarily focusing on decreasing the level of alcohol consumption, without further psycho-social treatment or a sole goal of abstinence.

It is estimated that 1-3 per cent of the adult population in the United States and Europe suffer from pathological gambling. Psycho-social therapy is currently the main treatment modality for patients suffering from pathological gambling. To the company's knowledge, the recently completed study is the first large-scale clinical study aiming at developing a drug therapy for this indication. As there is no drug specifically for impulse control disorders, the drug developed for this indication has significant market potential.

In accordance with its strategy, BioTie aims to commercialize the project at its present stage of development. The company is looking for licensing partners that would be responsible for further research of nalmefene and launching the drug to the market.



Source: Datamonitor 4/2002



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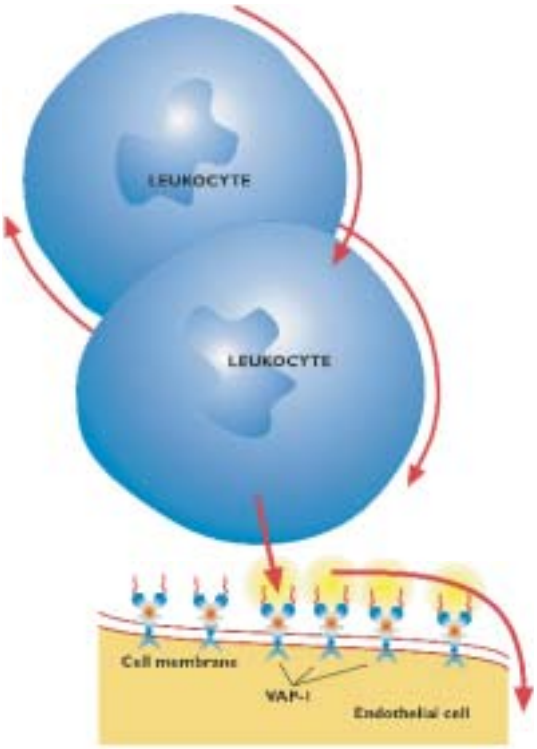
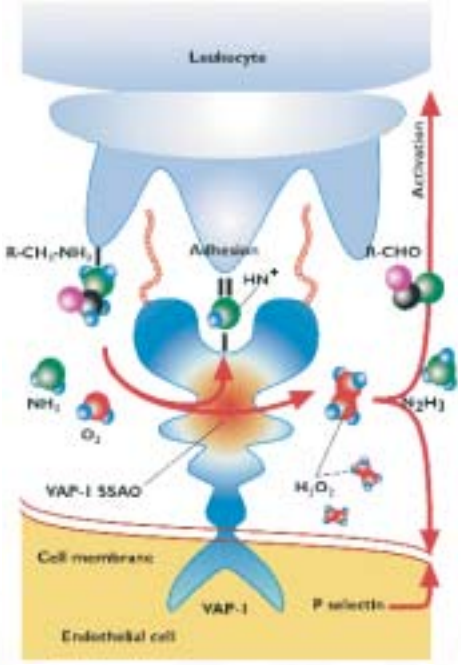
VAP-1 as Target Molecule for Drug Development



VAP-1 receptors appear in the blood vessel at the site of inflammation. With the aid of these receptors, leukocytes bind to the blood vessel at the inflammation site and find their way into the inflamed tissue.



VAP-1 also promotes the inflammatory reaction enzymatically. VAP-1 SSAO enzyme promotes the transfer of leukocytes to inflamed tissue and generates hydrogen peroxide locally, which promotes inflammatory reactions.

In normal immune defense reactions, white blood cells (leukocytes) migrate from the blood circulation to sites of antigenic insult in the tissue to identify and destroy invading pathogens, such as viruses and bacteria.

In autoimmune disorders such as rheumatoid arthritis, multiple sclerosis, inflammatory bowel diseases (Crohn's disease, ulcerative colitis) and psoriasis there is a "false alarm" in the affected tissue that triggers an inflammatory response and an attack on the patient's own tissue. In rheumatoid arthritis, for example, leukocytes infiltrate the joint and destroy the synovial membrane causing arthritis which leads to bone erosion and disability. This process of leukocyte infiltration also occurs in the acute inflammatory response to ischemic reperfusion damage caused by myocardial infarction and rejection reactions in organ transplants, resulting in further damage to the tissue. All these disorders caused by different factors have one pathogenic mechanism in common, namely, the pathological accumulation of leukocytes in the affected tissue.

VAP-1 (vascular adhesion protein-1) is an adhesion receptor expressed on endothelial cells lining the blood vessels which mediates the interactions of leukocytes with the vessel wall and assists their migration from the blood to sites of inflammation in tissue. Expression of VAP-1 is induced on the endothelial surface of vessels at inflammatory sites, and studies have shown that inflammation can be relieved by inhibiting the function of VAP-1.

VAP-1 also has an enzyme activity that can enhance inflammatory reactions. The products of the VAP-1 semicarbazide-sensitive amine oxidase (SSAO) enzyme include hydrogen peroxide, which is a known inflammatory mediator that further stimulates the inflammatory response. Studies have shown that blocking the function of the VAP-1 SSAO enzyme reduces the adhesion of leukocytes to endothelial cells and alleviates the inflammation.

The VAP-1 drug development programs of BioTie are targeted at the treatment of chronic inflammatory diseases such a rheumatoid arthritis. The drugs being developed block the function of VAP-1, thus preventing harmful accumulation of white blood cells at the site of inflammation.

MONOCLONAL ANTIBODIES

Antibodies are part of the natural immune defense system of the human body. Binding to their targets very accurately, antibodies can neutralize harmful target cells and proteins. Monoclonal antibodies are derived from clones i.e. identical copies of a single cell, and they can be easily isolated and produced in a laboratory. They have great utility in the diagnosis and treatment of disease. At present over 100 monoclonal antibodies are being clinically developed, representing approximately 20 per cent of all biotechnology drugs in clinical development and there are 11 therapeutic antibody drugs on the market.

VAP-1 ANTIBODY PROJECT

In 2003, BioTie completed the clinical phase I study of the chimeric monoclonal antibody (vapaliximab) in the VAP-1 antibody program. The study focused on the tolerability, safety and pharmacokinetics of vapaliximab. The drug was safely administered to 30 healthy subjects, and no serious adverse effects were observed.

On the basis of the first clinical study, however, the pharmacokinetic properties of vapaliximab did not meet the criteria required for the treatment of chronic diseases.

In order to further develop the properties of vapaliximab, it was decided to modify its molecular structure. In a joint decision made with Seikagaku Corporation, the licensing partner, the company has simultaneously commenced the

development of a humanized (non-chimeric) and a fully human VAP-1 antibody. The development work focuses on studying the strategic advantages of these different antibody technologies and the antibody offering the best advantages will be selected for further development. The selection for further development is expected in the second quarter of 2004.

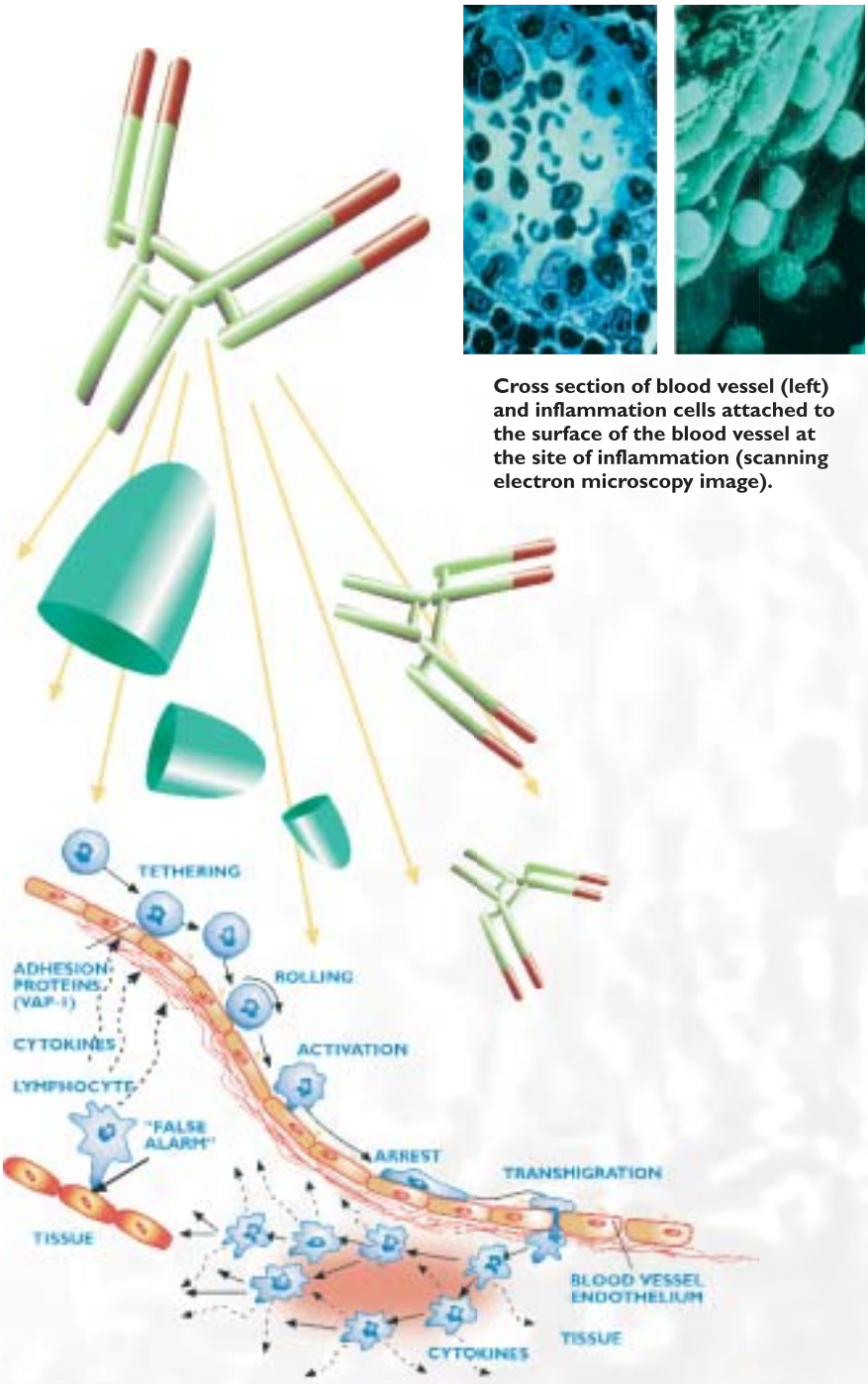
The most important collaboration partners in the antibody program in 2003 were Seikagaku Corporation, University of Turku, University of Cambridge and Boehringer Ingelheim.

VAP-1 SSAO ENZYME INHIBITOR

The enzymatic activity of VAP-1 affects the adhesion of leukocytes to the endothelial cells lining the blood vessels. Blocking the enzymatic function of VAP-1 significantly decreases the accumulation of leukocytes in the inflammatory site.

In collaboration with Åbo Akademi University, the company succeeded in crystallizing VAP-1 during 2003. Crystallization provides a basis for defining the three-dimensional structure of VAP-1, which can be utilized in the further development of small molecule inhibitors.

The small molecule inhibitors developed by BioTie have proved effective in rheumatoid arthritis models generally used by the pharmaceutical industry. VAP-1 SSAO small molecule inhibitors reduce the clinical symptoms of experimental rheumatoid arthritis in rats in a statistically significant manner compared with a control group receiving placebo. The results support the view that the VAP-1 SSAO enzyme plays a crucial role in inflammatory diseases, and therapy based on VAP-1 blocking may thus be clinically valuable. The VAP-1 SSAO small molecule inhibitor is developed for oral administration in the treatment of chronic inflammatory diseases such as rheumatoid arthritis.

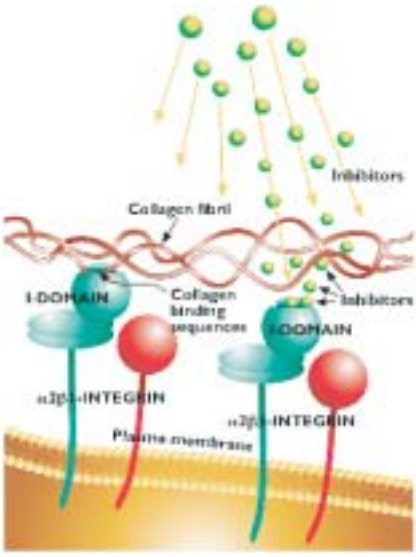


Cross section of blood vessel (left) and inflammation cells attached to the surface of the blood vessel at the site of inflammation (scanning electron microscopy image).

THE FIRST LICENSING AGREEMENT ON ANTIBODY TECHNOLOGY

In 2003, BioTie entered into its first significant licensing agreement. The regional licensing agreement on antibody technology with the Japanese company Seikagaku Corporation entered into force in summer 2003. The value of the licensing agreement totals USD 16.7 million, comprising of a signing fee of USD 2.5 million and milestone payments of USD 14.2 million. The agreement covers three indications: rheumatoid arthritis, psoriasis and ulcerative colitis. The geographical area included in the agreement represents approximately 10 per cent of the global pharmaceutical markets. Furthermore, Seikagaku has a separate option right worth a total of USD 16.7 million to BioTie's VAP-1 SSAO small molecular inhibitor.

Other Research Projects



POSSIBLE APPLICATIONS OF COLLAGEN RECEPTOR α2β1 INTEGRIN INHIBITORS

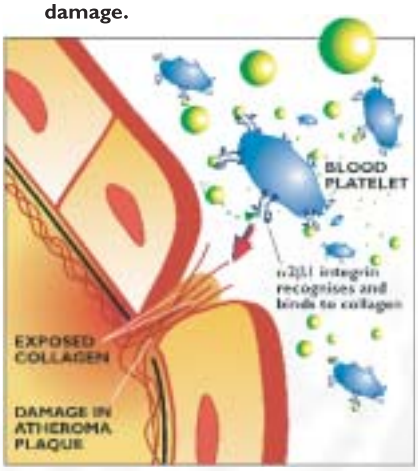
Cardiovascular diseases

- **Myocardial infarction**
- **Stroke**
- **Diabetes related rethinopathy**

Cancer diseases

- **Melanoma**
- **Ovarian cancer**
- **Gastric cancer**
- **Bone metastases prostate cancer**
- **Inhibition of tumor angiogenesis of cancer growth**

Thrombus formation requires activation and aggregation of blood platelets. Antithrombotic therapy using α2β1 integrin inhibitors is targeted to inhibit thrombosis by blocking the binding of platelets to collagen fibrils exposed upon endothelial damage.



BioTie's other drug development projects include integrin inhibitors and applications of glycobiology such as sulfated linear polysaccharides and a technology platform for glycomics. These drug development projects are currently at the discovery research or preclinical study phase.

INTEGRIN INHIBITORS

Interactions between cells and collagen are necessary for many physiological functions. The same interactions may, however, also promote mechanisms associated with diseases, such as thrombosis and cancer spread. In this drug discovery project, BioTie has been concentrating on the collagen receptor known as α2β1 integrin and the company is developing compounds inhibiting this receptor for the prevention of thrombus formation and cancer.

TREATMENT AND PREVENTION OF THROMBOSIS BY USING α2β1 INTEGRIN INHIBITOR

Adhesion of blood platelets to collagen is mediated by α2β1 integrin. The endothelial cell layer of the healthy arterial wall prevents interaction of circulating blood platelets with collagen. At the site of endothelial damage, collagen is exposed and the platelets adhere to the damaged endothelial surface initiating a cascade of events leading to thrombus formation. Preventing blood platelets from adhering to collagen and subsequent activation of the blood platelets will prevent thrombus formation.

Due to genomic polymorphism, some people have a larger quantity of α2β1 integrin on the surface of their platelets, and consequently, an increased risk of thrombosis. Epidemiological studies have shown that high levels of α2β1 integrin can be considered a significant risk factor for coronary and cerebral thrombosis in people of working age. Blocking α2β1 integrin function in patients with high levels of α2β1 integrin would be useful in prevention of thrombosis.

TREATMENT OF CANCER WITH α2β1 INTEGRIN INHIBITOR

Cancer cells also use integrins when moving through tissues and when forming metastases. Melanoma, prostate cancer, gastric cancer and ovarian cancer are diseases in which the α2β1 integrin seems to contribute to the spread of the cancerous cells. In patients with prostate cancer, bone metastases are a significant clinical problem. α2β1 integrin is a mediator in the formation of prostate cancer metastases into bone.

α2β1 INTEGRIN AS A TARGET FOR DRUG DEVELOPMENT

The drug discovery program is based on the detailed three-dimensional structure of the part of the integrin receptor responsible for binding to collagen, the so-called I-domain. Computer-aided modeling of integrin and an I-domain binding peptide sequence originally isolated from snake venom have been utilized in the design of small molecule inhibitors against α2β1 function. The company submitted a patent application for the first inhibitors isolated in 2003. Inhibitors have been shown to prevent interaction of human blood platelets after contact with collagen as well as adhesion of cancer cells to collagen and their penetration through collagen matrices in laboratory conditions. The research program has been conducted in collaboration with the University of Turku, Åbo Akademi University and the University of Jyväskylä.

GLYCOMICS OPENING NEW OPPORTUNITIES

Glycomics focuses on studying the role of carbohydrates in the body. Following genomics and proteomics, glycomics is expected to form the next major breakthrough in development of novel drug therapies. Clinically the most widely used carbohydrate drug at the moment is animal-derived heparin that is used for the treatment of thrombosis. Other applications of glycomics include drug therapy for cancer, infectious diseases, inflammatory diseases, rejection reactions or prevention of the diseases by vaccines as well as their diagnosis. BioTie is investigating the possibilities of using carbohydrate based drugs for the treatment of thrombosis, prevention and treatment of infection, treatment of inflammatory diseases, focused treatment of cancer and as cancer vaccines.

SULFATED LINEAR POLY-SACCHARIDES – BIOHEPARIN

Animal-derived heparin has been used in the treatment of patients since the 1940's. BioTie's bioheparin represents a new, non-animal-derived, carbohydrate drug molecule with a sugar structure and it is produced using technology patented by the company. Bioheparin is primarily intended for the treatment of thromboembolic diseases, such as deep vein thrombosis, pulmonary embolism and persistent chest pain caused by coronary artery disease.

During the review period, BioTie and Inalco S.p.A. agreed that both parties have the right to act independently and utilize the immaterial rights of the bioheparin project commercially. This so-called Freedom to Operate status grants BioTie royalty-free, global, non-exclusive rights to utilize and commercialize three patents of Inalco, while Inalco can act similarly as regards the patents jointly owned by the companies. BioTie continues the research and commercialization operations together with its partners.

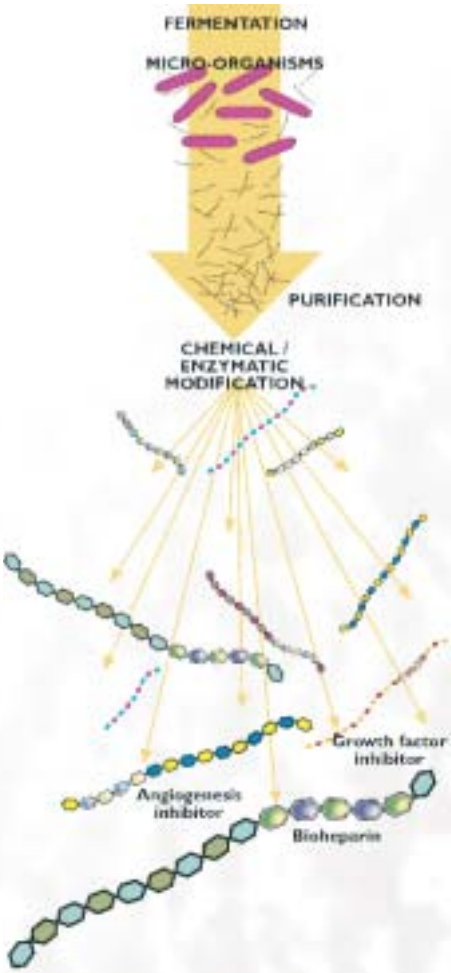
The development of bioheparin intended for the hemodialysis markets in collaboration with Shimizu Pharmaceuticals continued in accordance with the collaboration and research agreement.

SULFATED LINEAR POLYSACCHARIDES IN THE TREATMENT OF CANCER

By utilizing the production technology of bioheparin, growth factor inhibitors of cancer cells can be produced chemically and enzymatically by modifying polysaccharide molecules. The efficacy of such inhibitors has already been shown by studies inhibiting the formation of cancer metastases in mice.

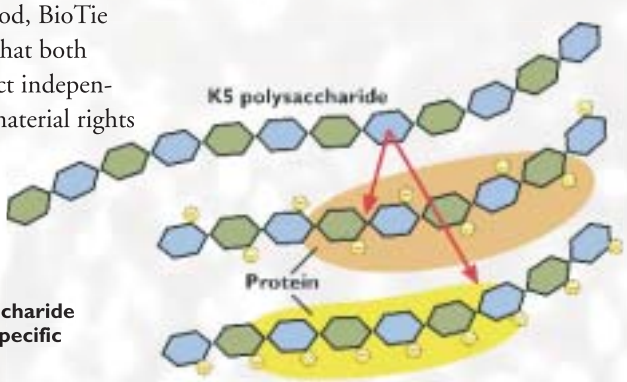
TECHNOLOGICAL PLATFORM OF GLYCOMICS

BioTie uses glycomics technology for the accurate mapping of cancerous cells and their carbohydrate structures. This has made it possible to find new structures that can be used in the diagnostics and treatment of cancer.



POSSIBLE INDICATION AREAS OF K5 POLYSACCHARIDES

- **Thrombosis**
- **Cancer**
- **Angiogenesis**
- **Inflammation**
- **Infectious diseases**
- **Arthritis**
- **Degenerative arthritis**
- **Asthma**



The sulfation of K5 polysaccharide determines its binding to specific target proteins.

Network of Scientific Collaboration

BioTie has created close collaborations for key areas of its drug development operations, namely, basic research, drug development and production technologies and drug production.

EXTENSIVE NETWORK OF TOP RESEARCHERS TO SUPPORT DRUG DEVELOPMENT

BioTie has an extensive collaborative network of Finnish and international researchers, through which the company has access to a large pool of international high-quality research projects.

The most important academic collaborative partners of the company include:

- Professor David Adams, University of Birmingham. During the last few years, Professor Adams's research group has been studying leukocyte adhesion mechanisms and diseases of the liver.

- Mike Clark, PhD, University of Cambridge. Dr. Clark is one of the pioneers in the development of monoclonal antibody drugs.

- Professor Jyrki Heino, University of Turku. Professor Heino's research group focuses on the structure-function analysis of integrin and the cell signaling related to collagen receptors. Professor Heino's research group was the first to describe the binding of the $\alpha 2\beta 1$ integrin receptor and its peptide ligand at the molecular level.

- Professor Sirpa Jalkanen, University of Turku and National Public Health Institute. Professor of the Academy of Finland and Director of the Center of Excellence. She has been involved in the analysis of leukocyte migration mechanisms in connection with physiological and pathological conditions for more than fifteen years.

- Professor Mark Johnson, Åbo Akademi University. Head of information and structure unit. At present his research group is studying the three-dimensional stucture of proteins and drug discovery work using structure based drug design.

- Dr. Karl-Anders Karlsson and the glycobiological research group at the University of Gothenburg. Dr. Karlsson's research group is a leader in the research of the infection mechanisms of pathogens. By using its glycolipid libraries separated from human and animal tissue, the group has characterized several carbohydrate receptors.

- Professor Ulf Lindahl, University of Uppsala. His research work has focused on the structure, biosynthesis and function of carbohydrates such as heparin. The development project of a technology suitable for the production of bioheparin and other similar sugar-structure molecules arose from projects financed by the EU Commission.

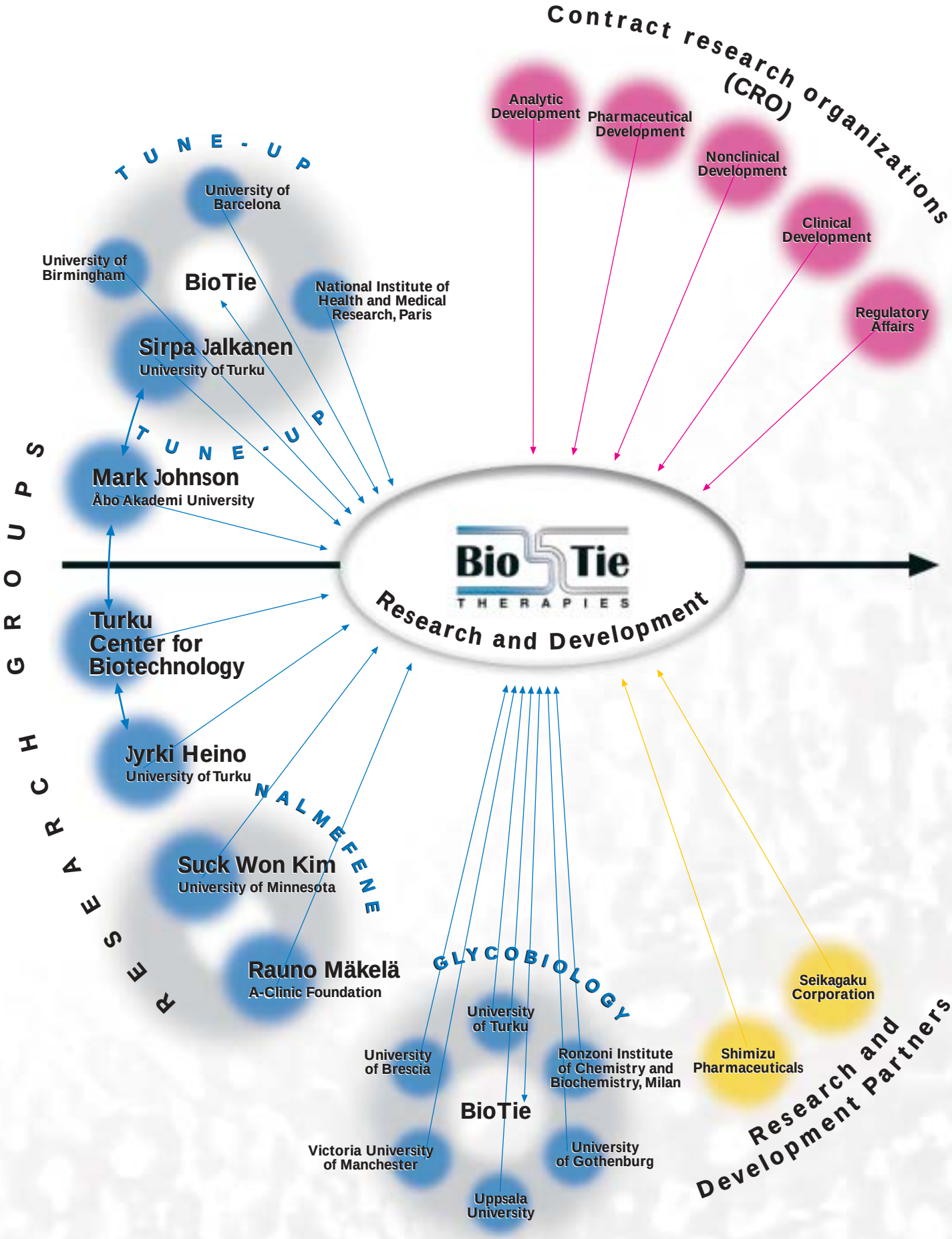
- Professor Benito Casu and Dr. Giangiacomo Torri, Istituto Scientifico di Chimica e Biochimica "G. Ronzoni", Italy. Experts in carbohydrates similar to heparin.

- The company participates in the following research programs financed by the European Union: Therapeutic Utilization of Novel Enzymes with Unique Adhesion Properties (TUNEUP) and Heparanase Inhibitors in Antiangiogenic and Antimetastatic Cancer Therapy (HEPARANASE). The researchers participating in the programs represent the highest expertise in the target areas in the whole of Europe. The company has the right of first refusal concerning the utilization of new discoveries and technologies. Coordinated by Professor Sirpa Jalkanen (MediCity Turku), the TUNEUP 2000-2003 program focuses on the enzymatic properties of VAP-1.

The HEPARANASE 2002-2005 program studies the ability of K5-based polysaccharides to prevent the neovascularization necessary for cancer growth and the formation of metastases. The HEPARANASE program is coordinated by Professor Benito Casu (Ronzoni Istitute, Italy).

- Professor Suck Won Kim, University of Minnesota, Psychiatry Department. Dr. Kim is one of the world's leading experts in drug therapies for impulse control disorders.

- Chief Physician Rauno Mäkelä, A-Clinic Foundation, the largest substance abuse treatment and prevention organization in Finland.


Contract research organizations (CRO)
Analytic Development
Pharmaceutical Development
Nonclinical Development
Clinical Development
Regulatory Affairs
TUNE-UP
University of Barcelona
University of Birmingham
BioTie
National Institute of Health and Medical Research, Paris
Sirpa Jalkanen
University of Turku
TUNE-UP
Mark Johnson
Åbo Akademi University
RESEARCH GROUPS
Bio Tie THERAPIES
Research and Development
Turku Center for Biotechnology
Jyrki Heino
University of Turku
NALMEFENE
Suck Won Kim
University of Minnesota
Rauno Mäkelä
A-Clinic Foundation
GLYCOBIOLOGY
University of Turku
University of Brescia
Ronzoni Institute of Chemistry and Biochemistry, Milan
BioTie
Victoria University of Manchester
University of Gothenburg
Uppsala University
Seikagaku Corporation
Shimizu Pharmaceuticals
Research and Development Partners

Board of Directors

Hannu Hanhijärvi, *Chairman of the Board of Directors of BioTie*
D.D.S., Ph.D., born 1947. Member of the Board of Directors since 1998. He has served as the Director of the Venture Capital Life Sciences Unit of the Finnish National Fund for Research and Development (Sitra) since 1998. Before joining Sitra, he served in several management positions within the Finnish pharmaceutical and health care industry, i.a. as Deputy Managing Director of Leaf Group and as Research and Development Manager of Leiras Oy. Mr Hanhijärvi has also acted as professor of pharmacology and toxicology at the University of Kuopio. He is a member and chairman of the Board of Directors in many companies in Finland and abroad.

Juha Jouhki
M.Sc. (Eng.), born 1966. Member of the Board of Directors of BioTie since 2002. Mr. Jouhki is one of the co-founders of ContrAl Clinics and Contral Pharma. In 1996-1999, he served as Managing Director of ContrAl Clinics and in 1998-2002 as Chairman of the Board of Directors of Contral Pharma. He is currently Managing Director of Thominvest Oy. Mr. Jouhki has been and is a member of the Board of Directors in many companies.

Kalevi Kurkijärvi
Ph.D. (Biochemistry), born 1952. Member of the Board of Directors of BioTie since 1995, Chairman of the Board of Directors in 1995-2000. Dr. Kurkijärvi is a founding partner and Chairman of the Board of Directors of Bio Fund Management Ltd. He also acts as the Chairman and CEO of his family company Biketex Ltd. Dr. Kurkijärvi has worked as the Director of Venture Capital Life Sciences Unit at the Finnish National Fund for Research and Development (Sitra) and as the Executive Vice President of Wallac Ltd and as the President of Pharmacia Diagnostics Production Ltd. He has been and is a member of the Board of Directors in many companies in Finland, Sweden, UK and USA.

Management Team

Jari Saarinen, *President and CEO*
M.Sc. (Econ.), born 1959. Employed by BioTie since 2000, as Chief Financial Officer from 2000-2002. Prior to BioTie, he was Deputy General Manager, Global Services Division of MacGREGOR Group in 1999-2000 and Senior Vice President, Finance of MacGREGOR Group in 1992-1998. In 1983-1992 he held various Controller positions in the Kone Corporation in Finland, the United States and Canada.

Kai Lähdesmäki, *Vice President, Business Development*
M.Sc. (Pol. Sc.), born 1945. Employed by BioTie since 1999. Prior to BioTie, he was President and Member of the Board of Directors of MediNet International Ltd in 1990-1999. In the years 1973-1990, he was employed by Farmos Group as Area Sales Manager, Export Director, and for the last six years as Director of the international operations of the Group and member of the internal Board of the company.

Timo Veromaa, *Vice President, Research and Drug Development*
M.D., Ph.D., Special Competence in Pharmaceutical Medicine, born 1960. Employed by BioTie since 1998. Previously Medical Director of Schering Oy 1996-1998 and Research and Project Manager of Collagen Corporation (California, USA) in 1994-1996. Postdoctoral Fellow at Stanford University (California, USA) in 1990-1993, Researcher at the University of Turku in 1988-1990.

Personnel

At the end of 2003, BioTie had a staff of 55, more than 2/3 of which worked in Turku and less than 1/3 at the Viikki unit. At the beginning of the year, the number of employees was 103. The decrease resulted from restructuring of operations and concentrating on the focus areas.

37 of the employees are women and 18 men. The mean age of the employees is 37. Most of the employees (65%) have a university degree (22% are doctors), 8% are engineers, 13% laboratory technicians/analysts and 14% have some other educational background. One of the strengths of Biotie Therapies lies in the balanced expertise and experience of the personnel both in the academic world and in business life.

One of the most important goals of the company is to retain its crucial resource, i.e. the professional personnel with high motivation. Due to the adaptation measures, the past year was extremely challenging for the company and its personnel. Nevertheless, the company succeeded in the task and managed to retain its key resources. During the year, the focus was on strengthening the basic professional skills, providing leadership training and supporting the process of changes. Towards the end of the year, a development program for BioTie's organization and operations was commenced.

One particular strength of the personnel is a wide variety of contacts with science communities and drug development organizations. Members of BioTie's personnel act as experts in a number of working groups, e.g. in Tekes projects. BioTie's experts actively contribute to scientific publications and lecture at scientific congresses and other training events.

The broad ranging and challenging restructuring of its business has brought out the best in BioTie's personnel. Staff has exhibited stamina, flexibility and a sense of co-responsibility. That is vital to the success of any small organization. Employees of the company have demonstrated a readiness to embrace change in good spirit. Accordingly BioTie is confident that it has a high-quality work force with the desire and experience to innovate. Such commitment and good team spirit will serve company well in future.

Report from the Board of Directors

REVIEW OF 2003 OPERATIONS

BioTie Therapies Corp. is a drug development company focusing on dependence disorders, inflammatory diseases and glycobiology. Candidate drugs are primarily developed until phase II clinical studies (Proof of Concept). Research and product development is carried out in cooperation with academic research groups and with contract research organizations and contract manufacturing organizations.

EFFICIENCY IMPROVEMENT PROGRAM

The company implemented an efficiency improvement program in order to focus the project portfolio and to lower costs. The operating costs in 2003 were reduced by EUR 10 million or 40% compared to the previous year.

BioTie transferred ContrAl Clinics – business, specialized in the treatment of excessive drinking and alcoholism, to a new company owned by the key personnel of the Clinics- business. In the arrangement the four employees working with the BioTie's Contral Clinic -business, the assets as well as the agreements and liabilities relating to the business were transferred to the new company as of 1 January 2003 against nominal consideration. The transferred business had been unprofitable and its turnover in 2002 was EUR 0.2 million. BioTie is not a shareholder in the new company but by virtue of BioTie's capital loan granted to the new entity it may subscribe a maximum 25% of the shares of the new company.

BioTie sold, in accordance with an agreement signed on 30 January, 2003 its process development and production unit to a new company, Biovian Ltd which is owned by the company's management, key personnel and BioTie. In the transaction 14 employees, the assets as well as the agreements and liabilities relating to the unit were transferred to Biovian Ltd as of 1 February 2003. BioTie remains as a significant customer and a shareholder with 9.9 % of the shares of Biovian Ltd.

In order to adapt the company's cost structure the co-determination procedure at BioTie was initiated in May and involved all personnel groups. As a result of the co-determination procedure, the employment of nine employees at administration, business development, research and development departments was terminated.

As the final phase of the company's efficiency improvement program, BioTie decided in January 2004 to focus its operations to Turku. BioTie had studied alternatives for optimizing the costs of the Viikki research unit, including ownership rearrangements as of spring 2003.

The unit at Viikki, Helsinki, was closed down. A total of 16 people have been employed in discovery phase research and support functions at the Viikki unit. The employment agreement of 14 employees was terminated in January 2004 after the conclusion of the co-determination procedure.

DRUG DEVELOPMENT PROJECTS AT THE CLINICAL PHASE

Nalmefene for the treatment of alcoholism

During the second quarter BioTie completed the first phase III clinical studies of the nalmefene tablet intended for the treatment of alcoholism. The studies were performed in Finland and the United Kingdom and focused on the safety and efficacy of nalmefene in the treatment of alcoholism and alcohol abuse without supporting psycho-social therapy in patients who considered themselves to be incapable of controlling their drinking.

Both studies were multi-center and placebo-controlled. In Finland, 400 patients and in the UK, 150 patients participated in the study. The duration of drug therapy in both studies was 28 weeks. Patients were instructed to take the study drug before drinking alcohol.

In the Finnish study, the number of heavy drinking days decreased almost by half in nalmefene users. In the placebo group, the number of heavy drinking days decreased by about one third and the difference between the nalmefene and placebo groups was statistically significant. In the British study, the number of heavy drinking days was also reduced by half in the nalmefene group, and the difference between the groups was in the same range as in the Finnish study. However, the difference was not statistically significant in the British study, because a higher than expected proportion of patients dropped out from the study. In both studies, the patients receiving nalmefene felt that the treatment was beneficial more often than the patients receiving placebo. No serious adverse effects related to the use of nalmefene were observed during the studies.

All drugs presently used for the treatment of drinking problems are therapies supporting other treatments, usually a psycho-social treatment program. The purpose of use of the currently available drugs supporting the treatment of alcoholism is to maintain abstinence. BioTie is the first company to study the efficacy of a drug intended for the treatment of drinking problems, primarily focusing on decreasing the level of alcohol consumption, without the goal of abstinence.

The results demonstrate that heavy drinking can be reduced by drug therapy alone.

Nalmefene for the treatment of impulse control disorders

During the second quarter BioTie completed a phase II clinical study of nalmefene tablet intended for the treatment of impulse control disorders. The multi-center, placebo-controlled study of 200 patients in the U.S. focused on the safety and efficacy of daily oral administration of nalmefene in patients suffering from pathological gambling.

A psychometric scale (PG-YBOCS, developed by Drs. Hollander and DeCaria at Mount Sinai Hospital, New York) measuring gambling-related thoughts, urges and behavior was used for primary evaluation of efficacy. Based on the study results nalmefene was effective in patients suffering from pathological gambling: after four months´ treatment, mean scores on the PG-YBOCS scale were almost twice as high in patients who were on placebo when compared to the patients receiving nalmefene. The difference between the study groups was statistically significant. No serious adverse effects resulting from to the use of nalmefene were observed during the study.

During the financial year, the company continued the analysis of the results of clinical research of nalmefene. The final reports of all three nalmefene studies are estimated to be completed during the first half of 2004. The results will be also reported at international scientific conferences.

COMMERCIALIZATION OF THE NALMEFENE PROJECT

According to its strategy BioTie seeks to out-license the project at its current development phase.

DRUG DEVELOPMENT PROJECT FOR VAP-1 MONOCLONAL ANTIBODIES

Vapaliximab is a chimeric IgG2 antibody. It has been developed in collaboration with Cambridge University, the University of Turku and Boehringer Ingelheim. Vapaliximab is primarily intended for the treatment of chronic inflammatory diseases such as rheumatoid arthritis.

Clinical studies with the chimeric antibody (vapaliximab, BTT-1002) commenced during the second half of 2002,

and the company announced results of the trial during the second quarter of 2003. No serious adverse events were reported in the 30 subjects dosed with the study drug. The results from the first phase I clinical study with vapaliximab suggest, however, that the pharmacokinetic profile of the antibody is not consistent with the needs of a product for chronic conditions.

In order to further develop the properties of vapaliximab, a decision was made to modify its molecular structure. By a joint decision made together with the licensing partner, the company additionally commenced the development of a humanized (non-chimeric) and a fully human VAP-1 antibody. This development project will focus on studying the strategic advantages of these antibody technologies in VAP-1 blockade and choosing the antibody offering the best advantages for further development. It is estimated that the decision on the antibody offering the best advantages for further development will be made during the second quarter of 2004.

COMMERCIALIZATION OF THE VAP-1 ANTIBODY PROJECT

In April, BioTie entered into a regional licensing agreement on the company's VAP-1 antibody program with the Japanese company Seikagaku Corporation. The licensing agreement entered into force as of 30 June, 2003. According to the terms of the licensing agreement, Seikagaku will have the exclusive right to the VAP-1 monoclonal antibody developed by BioTie, as well as the right to commercial exploitation of the patents in Japan, Taiwan, Singapore, New Zealand and Australia. The regional licensing agreement covers all indications but is now targeted at the following three indications: rheumatoid arthritis, psoriasis and ulcerative colitis.

The value of the licensing agreement totaling USD 16.7 million, comprising of a signing fee of USD 2.5 million and USD 14.2 million as milestone payments payable in accordance with the jointly agreed clinical development milestones. Once the antibody has been launched on the market in the licensed region, BioTie will also receive significant royalty income during the lifetime of the company's patents.

In accordance with the terms of the licensing agreement, Seikagaku Corporation will also have an option to an exclusive license on BioTie's small-molecule VAP-1 SSAO enzyme inhibitor. The licensing option covers the same indications and territory as the present agreement. The value of the option agreement totals USD 16.7 million.

RESEARCH

The screening program and preclinical research of VAP-1 SSAO small-molecule inhibitors progressed as planned. During 2003, the company succeeded in crystallizing the VAP-1 receptor in cooperation with Åbo Akademi University. The crystallization is the basis for defining the three-dimensional structure of the VAP-1 receptor, which can be significantly utilized in the development of small-molecule inhibitors. The company submitted a patent application concerning the crystal structure of VAP-1. VAP-1 SSAO small-molecule inhibitor will be initially developed for the treatment of chronic inflammatory diseases, such as rheumatoid arthritis.

The screening and preclinical development of new $\alpha 2\beta 1$ integrin inhibitors continued in cooperation with the University of Turku, Åbo Akademi University and the University of Jyväskylä. $\alpha 2\beta 1$ integrin inhibitors provide new methods for preventing thromboses caused by vascular damage as well as preventing cancer metastasis.

The development of bioheparin intended for the hemodialysis market continued in accordance with the research and collaboration agreement with Shimizu Pharmaceuticals. The term of the agreement ended on December 31, 2003, however the collaboration is still ongoing. Bioheparin represents a new type of drug molecule with sugar structure that has been produced by using the technology patented by the company in cooperation with the Italian company Inalco SpA.

BioTie and Inalco S.p.A concluded the negotiations on the continuation of the bioheparin project on July 23, 2003. According to the mutual understanding reached between the two parties, the parties will remain free to operate independently and exploit commercially the intellectual property rights related to the project. Due to this so-called Freedom to Operate, BioTie will have royalty-free, global and non-exclusive right to exploit and commercialize the three Inalco patents. Inalco will be entitled to operate correspondingly as regards the patents jointly owned by the parties. BioTie continues research and commercialization activities together with its partners.

By using glycomics technology, the company has identified new sugar structures specific to cancer cells, as well as continuing the application of polyvalent technology in the research and development of drugs with sugar structure.

As for VAP-1 receptor research and polysaccharides technology, BioTie continued participating in two research consortiums financed by the European Union that study new applications for VAP-1 SSAO enzyme inhibitors and modified polysaccharide compounds. BioTie has the primary rights in the consortium to commercial utilization of the research results.

REVENUES

Revenues for the financial year stood at EUR 2.2 million and consisted mainly of the signing fee of the collaboration agreement with Seikagaku Corporation (EUR 2.2 million). Seikagaku withheld 10% withholding tax from the signing fee paid in July. According to the tax treaty between Japan and Finland, BioTie may deduct withholding tax from income tax payable in Finland during the year the payment was made or the following year. The withholding tax is reported under income tax but it is not booked in receivables as it is uncertain whether it can be utilized.

Revenues in the previous year were EUR 0.2 million and consisted of the operations of the clinics business.

FINANCIAL RESULTS

The operating profit (loss) for the financial year was EUR –12.4 million. The corresponding figure for the previous year was EUR –26.3 million. Research and development costs for the period amounted to EUR 11.9 million (in 2002 EUR 21.5 million). A cost provision of EUR 0.4 million was booked for closure of the operations in Viikki. The costs of the share issue amounted to EUR 0.7 million. The patent protection of company's projects has been strengthened further. Patent costs have been booked as expenses.

FINANCING

In April, the National Technology Agency (Tekes) granted additional funding of EUR 5.9 million for BioTie's drug development projects. The R&D subsidies and capital loans granted in April cover certain drug development costs of the company from October 2002 to mid-2004. The funding granted for different development projects by Tekes varies from one project to another and covers 50–60 per cent of the costs of the projects. The share of capital loan funding of the amount granted during 2003 is EUR 4.7 million.

During the second quarter, Biotie Therapies raised EUR 10.5 million of new capital through a new issue pursuant to the shareholders' pre-emptive subscription right.

BioTie's equity ratio was –32.3 % on December 31, 2003 (–19.1 % in 2002). Cash and cash equivalents totaled EUR 10.4 million on December 31, 2003 (EUR 8.7 million in 2002). Cash and cash equivalents together with already granted R&D financing are sufficient to finance the operations of the company until the end of 2004 without income from commercialization of products. The company does not expect milestone payments from the agreement with Seikagaku Corporation during 2004.

At the end of the financial year the company's capital loans amounted to EUR 11.0 million and loans EUR 5.7 million.

INVESTMENTS AND CASH FLOW

The company's investments in the financial year amounted to EUR 57 thousand (EUR 1 090 thousand in 2002). The investments mainly comprised of equipment for research and development operations. Cash flow before financing was EUR –12.1 million (EUR –25.7 million in 2002).

SHAREHOLDERS' MEETINGS HELD DURING THE REPORTING PERIOD

The Annual General Meeting of Biotie Therapies Corp. was held on April 29, 2003. The Meeting addressed and resolved the matters listed in Section 12 of the Articles of Association of the company as well as the proposals of the Board of Directors to authorize the Board of Directors to resolve on a share issue and to convey the company's own shares. The Annual General Meeting adopted the income statement as well as the balance sheet and discharged the members of the Board of Directors and the Managing Director from liability. Same members of the Board of Directors and same accountants were appointed to continue.

The Annual General Meeting authorized the Board of Directors, in accordance with the proposal of the Board of Directors, to resolve on increase of share capital by issuing new shares, granting option rights or taking convertible loans. On the basis of the authorization the company's share capital can be increased in one or more issues so that the company's share capital may increase by a maximum of EUR 50 000 and the number of shares by a maximum of 2 500 000 shares. The authorization will be valid until the next Annual General Meeting; however, not longer than one year from the close of the Annual General Meeting.

The Annual General Meeting also authorized the Board of Directors to decide on conveyance of own shares in the company's possession. The authorization covers the 819 000 shares in the company's possession, which account for less than 4.7 per cent of the company's share capital and votes before the share issue executed in June. The authorization will be valid until the next Annual General Meeting; however, not longer than one year from the close of the Annual General Meeting.

An Extraordinary General Meeting of Biotie Therapies Corp. was held on May 26, 2003. The Extraordinary General Meeting of Biotie Therapies Corp. resolved, in accordance with the proposal of the Board of Directors, that the share capital of the company was to be increased pursuant to the pre-emptive subscription right of the shareholders. It was resolved that the share capital of the company was to be increased by new issue by a minimum of EUR 0.02 and a maximum of EUR 524 236.76 by issuing at least one (1) and at most 26 211 838 new shares, each with a counter book value of EUR 0.02. The subscription price of the shares was EUR 0.4 per share.

The second Extraordinary General Meeting of Biotie Therapies Corp. held on June 19, 2003 addressed the demand of certain shareholders, Jukka Keski-Pukkila, Markku Jalkanen, Kauko Kurkela, Juhani Saarinen and Erkki Tenhunen, to arrange a special inspection in the company in accordance with Chapter 10, Section 14 of the Companies Act concerning the following matters: (i) The communications of the company relating to stock exchange, financing, press and other communications and matters that are the basis for the communications, and (ii) the company's communications and other matters relating to the stock exchange release of the company on May 7, 2003 and the new issue pursuant to the shareholders pre-emptive subscription right, its preparation, extent and pricing. In the Extraordinary General Meeting, shareholders representing more than 1/10 of the company's shares supported the demand to arrange a special inspection, in accordance with Chapter 10, Section 14 of the Companies Act. The application concerning the inspection and BioTie's response to the application have been submitted to the State Provincial Office of Western Finland. The company regards the application groundless. The resolution is expected within the first half of 2004.

The Shareholders' Meeting of merged Biotie Therapies Corp. (business identity code 0889985-8) held on April 29, 2003 approved the final accounts presented by the Company's Board of Directors and President, which comprised of the financial statements for the period January 1, 2002 – October 30, 2002 as well as an account of the distribution of merger consideration. At the same time the Meeting discharged the members of the Board and the President from liability for the financial period that ended with the dissolving of the Company.

INCREASE OF THE COMPANY'S SHARE CAPITAL AND NEW SUBSCRIPTION

The situation in the capital market continued to be difficult. Since other relevant alternatives to finance the company turned out to be unsuccessful, the Board of Directors of the company resolved to propose to the Extraordinary General Meeting organizing of a share issue pursuant to the shareholders' pre-emptive subscription right the purpose of which was to guarantee the financing of the company until the end of the year 2004.

After Mandatum & Co, the organizer of the share issue, had consulted the major shareholders of the company, the Board of Directors of the company resolved to propose that the share capital of the company would be increased by new issue at maximum by EUR 524 236.76 by issuing a maximum of 26 211 838 new shares. The Extraordinary General Meeting resolved that the subscription price shall be EUR 0.40 per share and that a shareholder shall, according to the terms and conditions of the share issue, be entitled to subscribe for three (3) new shares per two (2) old shares owned.

On June 23, 2003 The Board of Directors of Biotie Therapies Corp. approved all subscriptions based on the primary and secondary pre-emptive subscription rights, which were made in accordance with the terms and conditions of the share issue during the period of June 4, 2003 – June 18, 2003 in the share issue pursuant to the pre-emptive subscription right of the shareholders. 12 500 508 shares were subscribed for through the exercise of the primary pre-emptive subscription rights. In addition, 891 601 shares were subscribed for through the exercise of the secondary pre-emptive subscription right. 1 808 subscriptions were made in the primary subscription and 557 subscriptions were made pursuant to the secondary pre-emptive subscription right.

The Board of Directors decided to offer for subscription, in accordance with the terms and conditions of the share issue, a total of 12 819 729 shares, which were not subscribed for pursuant to the primary and secondary subscription to Aboa Venture Ky, Bio Fund Ventures III Ky, Suomi Insurance Company Ltd, Suomi Mutual Life Insurance Company, Pohjola Non-Life Insurance Company Ltd and the Finnish Industry Investment Ltd. On June 25, 2003, The Board of Directors of Biotie Therapies Corp. approved the subscriptions for the shares made by the parties determined by the Board of Directors and the share issue was subscribed in full.

Following the share issue, Biotie Therapies Corp.'s registered share capital was increased by EUR 524 236.76 and amounted to EUR 873 727.94. The number of shares was increased by 26 211 838 shares to 43 686 397 shares.

CONVERTIBLE BONDS

On December 31, 2003, the company had a Convertible Capital Loan of approximately EUR 1 850 067.19 (original capital FIM 11 000 000) that entitles to subscribe a total number of 990 000 shares of the company, and a convertible bond of approximately EUR 672 752.71 (original capital FIM 4 000 000) that entitles to subscribe a total of 288 000 shares of the company. Based on the loans the share capital of the company can increase by a maximum of 1 278 000 shares and the share capital by at most EUR 25 560. The subscription period of the first bond ended on November 30, 2003 and of the second on December 31, 2003.

AUTHORIZATION OF THE BOARD OF DIRECTORS TO INCREASE THE SHARE CAPITAL AND TO ASSIGN THE COMPANY'S OWN SHARES.

The Board of Directors has authorization to increase the share capital until March 24, 2004. Based on the authorization, the share capital may be increased by at most EUR 50 000 corresponding to 2 500 000 shares. After the end of the financial year 2 000 000 shares have been used for the option program launched in January 2004.
The Board of Directors has authorization to assign company's own shares. The authorization covers the 819 000 shares that are in the company's possession.

OPTION PROGRAMS

Biotie Therapies Corp. has issued option rights by December 31, 2003 in terms of a total of six different option programs. As a result of these option rights the share capital of BioTie can increase by a maximum of 926 527 shares i.e. EUR 18 530.54.

BOARD OF DIRECTORS AND MANAGEMENT

During the financial year Biotie Therapies Corp.'s Board Members were Hannu Hanhijärvi (chairman), Juha Jouhki and Kalevi Kurkijärvi.

Jari Saarinen acted as President and CEO of Biotie Therapies Corp.

AUDITORS

The general meeting of shareholders held on April 29, 2003, elected the following auditors for the company: Johan Kronberg, Authorized Public Accountant and PricewaterhouseCoopers Oy, with Tomi Moisio, Authorized Public Accountant as the main responsible auditor.

GROUP STRUCTURE

The parent company of the group is Biotie Therapies Corp. The group has a subsidiary named Biotie Therapies International Ltd, which was not operational during the financial year.

PERSONNEL AND ORGANIZATION

During the reporting period, the company's personnel was on average 66 (115 in 2002) and at the end of the financial year 55 (112 on December 31, 2002).

EVENTS AFTER THE FINANCIAL YEAR

As the final phase of the company's efficiency improvement program, BioTie decided to close down the unit at Viikki and focus its operations to Turku. A total of 16 people were employed in discovery phase research and support functions at the Viikki unit. The employment agreement of 14 employees was terminated in January 2004 after the conclusion of the co-determination procedure.

Based on the authorization of the Annual General Meeting the Board of Directors of Biotie Therapies Corp. resolved in its meeting of January 14, 2004 to issue option rights, which shall be offered for subscription, in deviation from the shareholders' pre-emptive subscription right, to certain key persons and to a wholly owned subsidiary nominated by the Board of Directors. The program covers the entire personnel of the company but not the Board of Directors. In accordance with the decision made by the Board of Directors, a prerequisite for the subscription of the option scheme is that the holder of a subscription right surrenders, in connection with the subscription, the possible option rights the company has issued previously.

The option rights shall entitle the holder to subscribe for a maximum of 2 000 000 new shares of Biotie Therapies Corp. in the aggregate. Due to the subscriptions the share capital of the company may increase by a maximum of EUR 40 000. In the event the shares subscribed on the basis of the issued option rights are subscribed in full, the proportion of the subscribed shares shall be approximately 4.4 percent of the share capital of the company after the registration of the increase in the share capital, without taking into account the new shares to be possibly subscribed pursuant to the convertible loans and other option schemes issued by the company.

MOST SIGNIFICANT CHANGES IN ACCOUNTING POLICIES

BioTie will apply IFRS 1 "First-time Adoption of International Financial Reporting Standards" business combination exemption, which allows first time adopter not to apply IFRS rules retrospectively to business combinations taken place prior to the transition date 1.1.2004.

The most significant change in conversion to IFRS is the inclusion of capital loans as part of the liabilities. In addition the interest on capital loans shall be recognized as an expense to the income statement and as a liability in the balance sheet. Currently capital loans are included in the shareholders' equity and the interest effect is not recognized as a liability, but disclosed in the notes.

In addition i.e. the recognition of options as an expense, treatment of development costs and recognizing revenue from license fees causes changes to the current practice. The option schemes granted after November 7, 2002 and for which the vesting period is not expired by the January 1, 2005 are recognised as an expense. The older option schemes are not affected by this change. The development costs should be capitalized according to IFRS when the IAS 38 criteria are met. For now BioTie's drug development projects are at the research phase and have not yet fulfilled the IFRS capitalization criteria. The signing fee of the licensing agreements should be recognized as revenue over the length of the contract instead of the current treatment where the signing fee is recognized as revenue when the contract has been signed.

DESCRIPTION OF THE IFRS ADOPTION PLAN

The company will present the first IFRS financial statement with comparatives for the year 2005. The first IFRS interim report is probably presented at March 31, 2005.

OUTLOOK FOR THE YEAR 2004

In the short term, BioTie focuses its research and development operations on the following projects:

- Nalmefene for the treatment of alcoholism and dependence disorders
- VAP-1 antibody for the treatment of inflammatory diseases
- Small molecule VAP-1 SSAO inhibitor for the treatment of inflammatory diseases
- $\alpha 2\beta 1$ integrin inhibitor for the treatment of thrombosis, cancer and inflammatory diseases
- Glycomics.

BioTie is looking for collaboration partners for its VAP-1 and bioheparin projects.

It is estimated that the decision in the VAP-1 antibody program on the antibody offering the best advantages for further development will be made during the second quarter of 2004.

The company´s target is to commercialize the nalmefene project at its current development phase during 2004.

Cash flow before financing is expected to remain approximately at the same level as in 2003 assuming no income from lisencing agreements in 2004.

THE BOARD OF DIRECTORS' PROPOSAL FOR HANDLING OF THE LOSS

Furthermore, the Board of Directors proposes that the accumulated losses will be covered from the share premium fund by EUR –12 432 779.10, and that the rest will remain in retained earnings.

Income Statement

1 000 €	1.1.-31.12.2003 Group	1.1.-31.12.2002 Group	1.1.-31.12.2003 Parent company	1.1.-31.12.2002 Parent company
Revenues	**2 243**	**153**	**2 243**	**91**
Cost of sales	0	0	0	0
Gross profit	2 243	153	2 243	91
Research and development expenses	-11 888	-21 541	-11 888	-9 892
Sales and marketing expenses	0	-178	0	-178
General and administrative expenses	-3 082	-3 197	-3 082	-1 517
Merger goodwill depreciation	0	0	-477	-2 828
Consolidation goodwill depreciation	-477	-189	0	0
Other operating income	1 542	824	1 542	86
Other operating expenses	-734	-2 128	-734	-428
Operating profit (loss)	**-12 395**	**-26 256**	**-12 395**	**-14 667**
Financial income and expenses	180	340	180	118
Profit (loss) before extraordinary items	**-12 215**	**-25 916**	**-12 215**	**-14 549**
Extraordinary items +/-	0	-321	0	-321
Profit (loss) before appropriations and taxes	**-12 215**	**-26 236**	**-12 215**	**-14 870**
Minority interest	0	103	0	0
Taxes	-218	0	-218	0
Net income (loss)	**-12 433**	**-26 133**	**-12 433**	**-14 870**

Balance Sheet

1 000 €	31.12.2003 Group	31.12.2002 Group	31.12.2003 Parent company	31.12.2002 Parent company
ASSETS				
Fixed assets and other long-term investments				
Intangible assets	1 633	2 053	1 633	2 053
Merger goodwill	0	0	626	1 103
Consolidation goodwill	626	1 103	0	0
Tangible assets	249	386	249	386
Investments	10	0	19	9
	2 518	**3 542**	**2 527**	**3 551**
Current assets				
Current receivables	1 090	1 287	1 090	1 287
Securities	8 985	6 343	8 985	6 343
Cash in hand and at banks	1 437	2 347	1 429	2 339
	11 512	**9 978**	**11 504**	**9 969**
Total	**14 030**	**13 520**	**14 030**	**13 520**
EQUITY AND LIABILITIES				
Shareholders´ equity				
Share capital	874	349	874	349
Share premium fund	21 899	23 661	21 899	11 938
Retained earnings	-14 870	-460	-14 870	0
Net income for the period	-12 433	-26 133	-12 433	-14 870
Capital loans	10 958	8 288	10 958	8 288
	6 428	**5 706**	**6 428**	**5 706**
Mandatory provisions	**450**	**27**	**450**	**27**
Liabilities				
Long-term debt	5 885	5 251	5 885	5 251
Current liabilities	1 267	2 536	1 267	2 536
	7 152	**7 787**	**7 152**	**7 787**
Total	**14 030**	**13 520**	**14 030**	**13 520**

Cash Flow

1 000 €	1.1.-31.12.2003 Group	1.1.-31.12.2002 Group	1.1.-31.12.2003 Parent company	1.1.-31.12.2002 Parent company
Cash flow from operating activities				
Operating profit	-12 395	-26 256	-12 395	-14 667
Depreciation	1 081	1 645	1 081	3 147
Taxes	-218	0	-218	0
Extraordinary items +/-	0	-321	0	-321
Change in mandatory provisions	423	-111	423	27
Change in working capital	-1 071	80	-1 071	1 827
Financial income and expenses	180	340	180	118
Net cash from operating activities	**-12 000**	**-24 622**	**-12 000**	**-9 868**
Cash flow from investing activities				
Capital expenditure	-57	-1 090	-57	-5 447
Net cash used in investing activities	**-57**	**-1 090**	**-57**	**-5 447**
Cash flow before financing activities	**-12 057**	**-25 712**	**-12 057**	**-15 315**
Cash flow from financing activities				
Change in long-term debt	3 304	3 219	3 304	8 293
Carbion merger compensation	0	0	0	1 014
Share issue	10 485	15 426	10 485	15 426
Net cash from financing activities	**13 788**	**18 645**	**13 788**	**24 734**
Net increase (+) or decrease (-) in cash and cash equivalents	**1 731**	**-7 067**	**1 731**	**9 419**
Cash and cash equivalents at the beginning of the period	**8 691**	**6 276**	**8 682**	**5 626**
Impact of changes in group structure	**0**	**9 481**	**0**	**-6 363**
Cash and cash equivalents at the end of the period	**10 422**	**8 691**	**10 414**	**8 682**

ACCOUNTING PRINCIPLES

Biotie Therapies Corporation's financial statements have been prepared in accordance with Finnish legislation, which in all material respects is based on the provisions of EU Directives 4 and 7.

The scope of consolidated financial statements

The financial statements of the year 2002 cover the operations of the companies merged on October 30, 2002: the old Biotie Therapies Corp, Carbion Inc and Contral Pharma Ltd, throughout the calendar year 2002. The old BioTie's Income Statement has been consolidated to group accounts with direct consolidating method. The acquisition cost of the shares has been first eliminated from the restricted equity of the subsidiary and after that from the share premium fund resulting from the targeted issue and from the other share premium fund. Consequently, no group assets were formed. Furthermore, the financial statement of the year 2002 includes the old BioTie's subsidiary Biotie Therapies International Ltd, which has been consolidated by using the acquisition cost method. The intra-group transactions have been eliminated.

The financial statements of the year 2003 include the subsidiary Biotie Therapies International Ltd, which has been consolidated by using the acquisition cost method.

Research and development costs

Research and development costs are charged as expenses during the year in which they occur.

Fixed assets

Fixed assets have been recorded in the balance sheet at their direct acquisition cost, allowing for depreciation according to plan. Depreciation is based on estimated useful life of various assets as follows:

	Useful life (years)	**Depreciation method**
Machinery and equipment	4	Straight-line depreciation
Computer programs	4	Straight-line depreciation
Patents	10	Straight-line depreciation
Consolidation goodwill	3	Straight-line depreciation

Computer programs and equipment used in R&D are fully depreciated during the year they are acquired in accordance with the Act on Taxation of Business income.

Leasing

Leasing payments are charged to rental expense. The company has no significant lease contracts. Leasing commitments are disclosed in the notes to the financial statements.

Mandatory provisions

Mandatory provisions in the balance sheet are defined as commitments related to the current or prior financial years which on the balance sheet are certain or likely to materialize, but there is uncertainty as to the amount or the timing of the obligation. The estimated provisions are based on information available on the balance sheet date.

Pension liabilities

The pension plan has been arranged with external insurance companies. Pension costs are included in personnel costs.

Subsidies

R&D subsidies are presented in other operating income or in the balance sheet.

Foreign currency

Receivables and liabilities in foreign currencies have been valued at the closing rate of the balance sheet date.

1 000 €	1.1. - 31.12.2003 Group	1.1. - 31.12.2002 Group	1.1. - 31.12.2003 Parent company	1.1. - 31.12.2002 Parent company
1. Revenues				
Seikagaku-collaboration agreement	2 178	0	2 178	0
Contral Clinics-business	0	91	0	91
Shimizu Pharmaceutical-collaboration agreement	0	57	0	0
Service business	65	0	65	0
Other revenue	0	5	0	0
Total	2 243	153	2 243	91
2. Personnel costs				
Wages and salaries	3 604	4 953	3 604	2 146
Pension expenses	519	822	519	335
Other personnel expenses	225	379	225	88
Total	4 348	6 153	4 348	2 570
Salaries to president and remuneration of board members	246	363	246	190
The average number of personnel	66	115	66	78
Personnel at the end of period	55	112	55	112
3. Depreciation				
Intangible rights	420	541	420	277
Merger goodwill	0	0	477	2 828
Consolidation goodwill	477	189	0	0
Intangible rights, R&D	7	716	7	0
Machinery and equipment	173	196	173	42
Machinery and equipment, R&D	3	3	3	0
Total*)	1 081	1 645	1 081	3 147
*) of which related to R&D computer programs and equipment	10	719	10	0
4. Other operating income				
Research and development subsidies of The National Technology Agency (Tekes)	1 285	387	1 285	45
Research and development subsidies of EU	60	116	60	-14
Ministry of Trade and Industry	0	19	0	19
Rents	175	210	175	23
Other	22	92	22	12
Total	1 542	824	1 542	86
5. Other operating expenses				
Costs from the share issue	734	0	734	0
Costs from the merger	0	2 128	0	428
Total	734	2 128	734	428
6. Financial income and expenses				
Interest income	237	43	237	16
Other financial income	1	342	1	120
Interest expenses	-55	-40	-55	-13
Other financial expenses	-2	-5	-2	-4
Total	180	340	180	118
7.Extraordinary items				
Interest of Contral Pharma's convertible bonds	0	321	0	321

8. Fixed assets and other long-term investments

Group = Parent company	Other long-term investments	Intangible assets	Intangible assets R&D	Machinery and equipment
Historical cost on 1.1.2003	1 098	3 058	825	862
Capital expenditure 1.1.-31.12.	0	0	7	36
Historical cost on 31.12.2003	1 098	3 058	832	898
Accumulated depreciation	-996	-1 106	-825	-477
Total before depreciation	101	1 952	7	422
Depreciation	-101	-319	-7	-173
Net book value on 31.12.2003	0	1 633	0	249

1 000 €	1.1. - 31.12.2003 Group	1.1. - 31.12.2002 Group	1.1. - 31.12.2003 Parent company	1.1. - 31.12.2002 Parent company
Group = Parent company	Machinery and equipment R&D	Consolidation/ Merger goodwill	Total	
Historical cost on 1.1.2003	1 279	1 431	8 553	
Capital expenditure 1.1.-31.12.	3	0	47	
Historical cost on 31.12.2003	1 282	1 431	8 600	
Accumulated depreciation	-1 279	-328	-5 011	
Total before depreciation	3	1 103	3 588	
Depreciation	-3	-477	-1 081	
Net book value on 31.12.2003	0	626	2 508	

9. Group companies

			2003	2002
Biotie Therapies International Ltd, Turku		Book value 9	100%	100%
Ownership in partner companies				
Contral America Inc., USA			25%	25%

10. Current receivables

Trade receivables	0	32	0	45
Loan receivables	0	1	0	0
VAT-receivables	90	743	90	743
Other receivables	53	114	53	102
Prepaid expenses and accrued income*)	947	396	947	396
Total	1 090	1 287	1 090	1 287
*) of which R&D subsidy	768	242	768	242

11. Short-term investments

Market value	9 171	6 567	9 171	6 567
Book value	8 985	6 343	8 985	6 343
Difference	186	224	186	224

1 000 €	1.1. - 31.12.2003 Group	1.1. - 31.12.2002 Group	1.1. - 31.12.2003 Parent company	1.1. - 31.12.2002 Parent company
12. Shareholders' equity				
Share capital at the beginning of the period	349	128	349	128
Transfer from share issue 10.1.2002		7		7
Bonus issue		9		9
Share subscription with option rights		9		9
Merger compensation of BioTie		133		133
Merger compensation of Carbion		9		9
Conversion of interest debt		1		1
Institutional Offering		54		54
Share issue	524		524	
Share capital at the end of the period	874	349	874	349
Share premium fund at the beginning of the period	23 661	8 241	11 938	8 241
Transfer from share issue 10.1.2002		3 993		3 993
Bonus issue		-9		-9
Convertion of interest debt		309		309
Institutional Offering		15 054		15 054
Merger compensation of Carbion		1 006		1 006
Consolidation of old BioTie		5 232		-6 491
Transfer from retained earnings	-11 723	-10 165		-10 165
Share issue	9 960		9 960	
Share premium fund at the end of the period	21 899	23 661	21 899	11 938
Share issue at the beginning of the period		4 000		4 000
Transfer from share issue 10.1.2002		-4 000		-4 000
Share issue at the end of the period	0	0	0	0
Retained earnings at the beginning of the period	-26 593	-10 624	-14 870	-10 165
Consolidation of subsidiaries		-1		0
Transfer from share premium fund	11 723	10 165		10 165
Retained earning at the end of the period	-14 870	-460	-14 870	0
Net income (loss) for period	-12 433	-26 133	-12 433	-14 870
Capital loans at the beginning of the period	8 288	5 206	8 288	5 004
Change during period	2 670	50	2 670	
Consolidation of BioTie		3 032		3 032
Consolidation of Carbion				252
Capital loans at the end of the period	10 958	8 288	10 958	8 288
Shareholders' equity, total	**6 428**	**5 705**	**6 428**	**5 706**
Distributable funds at the end of the period	-27 303	-26 593	-27 303	-14 870

Change in numbers of shares and share capital

Measure	Par value/ Accounting equivalent value (EUR)	Subscription price (EUR)	Number of shares before	Number of shares after	Change in share capital (EUR)	New share capital (EUR)	Registered
Foundation	1,68	1,68	0	20 000	33 638	33 638	11.5.1998
New issue	1,68	67,28	20 000	25 500	9 250	42 888	6.5.1999
New issue	1,68	84,10	25 500	27 100	2 691	45 579	8.10.1999
Split 1:10	0,17	–	27 100	271 000	–	45 579	12.6.2000
Share subscription with option rights	0,17	0,17	271 000	320 600	8 342	53 921	15.8.2000
Merger compensation	0,17	0,17	320 600	686 755	61 583	115 504	21.2.2001
New issue	0,17	100,00	686 755	761 755	12 614	128 118	29.5.2001
Share subscription with option rights	0,17	0,17	761 755	762 375	104	128 222	29.5.2001
New issue	0,17	101,00	762 375	801 978	6 661	134 883	10.1.2002
Bonus issue	0,18	–	801 978	801 978	9 473	144 356	3.6.2002
Split 1:9	0,02	–	801 978	7 217 802	–	144 356	3.6.2002
Share subscription with option rights	0,02	0,02	7 217 802	7 648 722	8 618	152 974	3.6.2002
Conversion of interest debt	0,02	5,60	7 648 722	7 704 072	1 107	154 082	8.10.2002
New issue, Institutional Offering	0,02	5,60	7 704 072	10 401 922	53 957	208 038	8.10.2002
Consolidation of BioTie	0,02	2,38	10 401 922	17 033 722	132 636	340 675	31.10.2002
Consolidation of Carbion	0,02	2,38	17 033 722	17 459 559	8 517	349 191	31.10.2002
Share subscription with option rights	0,02	0,02	17 459 559	17 474 559	300	349 491	30.4.2003
New issue	0,02	0,40	17 474 559	43 686 397	524 237	873 728	26.6.2003

[1] Date refers to date of registration in the Trade Register maintained by the National Board of Patents and Registration.

Non-convertible capital loans

The National Technology Agency (Tekes) has granted capital loans of EUR 11 486 333.41. EUR 8 439 312.41 have been paid to the company by the end of the financial year. EUR 8 435 616.41 have been recorded as capital loans and EUR 3 696.00 as long-term liabilities. The amount recorded as long term liabilities will be booked as capital loans as soon as the approved expenses are accrued and settlement concerning expenses has been approved.

The loan period is 8 years. The interest rate is the base rate set by the Ministry of Finance minus 1%, however, at least 3%. The loans are instalment-free for 4 or 5 years, after that loans will be paid in equal shares. Accumulated interests on capital loans are recorded as expenses in the financial statement and as increase of long-term liabilities in the balance sheet until the end of the year 2001.

Convertible bonds

The company had a convertible bond of EUR 2 522 818.90. The subscription period of EUR 1 850 067.19, that entitles to subscribe a total of 990 000 shares of the company, began on June 1, 2000, and ended on November 30, 2003. Par value of the shares is total EUR 19 800. The interest rate is 10% pa. The subscription period is June 1, 2000-December 31, 2003 of EUR 672 751.71 that entitles to subscribe a total of 288 000 shares, par value EUR 5 760. The interest rate is 10% pa. Accumulated interest of convertible bonds, EUR 1 017 598.79, is not recorded to financial statement.

	31.12.2003 Group	31.12.2002 Group	31.12.2003 Parent company	31.12.2002 Parent company
Accumulated interest on capital loans	1 708	1 262	1 708	1 262
Recorded as expenses	176	176	176	176
Total	1 884	1 438	1 884	1 438

13. Options (status 31.12.2003)

1. Options 1998

Number of option rights, total	12 000
Subscribed	12 000
Shares subscribed	9 977
Option rights remaining	2 023
Entitling to subscribe a total of 182 100 shares	
Subscription period	1.1.2000-31.12.2004
Subscription terms	90 shares for one option right 1 share for EUR 0.02

2. Options 2000 I

Number of option rights, total	560
Subscribed	560
Shares subscribed	0
Option rights remaining	560
Entitling to subscribe a total of 50 400 shares	
Subscription period	31.8.2003-31.12.2004
Subscription terms	90 shares for one option right 1 share for EUR 6.33

3. Options 2000 II

Number of option rights, total	1 100
Subscribed	1 100
Shares subscribed	0
Option rights remaining	1 100
Entitling to subscribe a total of 99 000 shares	
Subscription period	A-series (550): 31.8.2002-31.12.2004 B-series (550): 1.9.2003-31.12.2004
Subscription terms	90 shares for one option right 1 share for EUR 6.33

4. Options 2002 I

Number of option rights, total	12 000
Subscribed	12 000, of which 3 000 cancelled
Shares subscribed	0
Option rights remaining	9 000
Entitling to subscribe a total of 81 000 shares	
Subscription period	C-series (4500): 1.5.2004-1.5.2005 D-series (4500): 1.10.2005-1.10.2006
Subscription terms	9 shares for one option right 1 share for EUR 6.78

5. Options 2002 II

Number of option rights, total	38 736
Subscribed	38 736
Shares subscribed	0
Option rights remaining	38 736
Entitling to subscribe a total of 38 736 shares	
Subscription period	1.1.2003-31.3.2006
Subscription terms	1 shares for one option right 1 share for EUR 0.35

6. Options 2002 III

Number of option rights, total	475 291
Subscribed	475 291
Shares subscribed	0
Option rights remaining	475 291
Entitling to subscribe a total of 475 291 shares	
Subscription period	A-series (178 721): 31.10.2002-31.12.2005 B-series (170 087): 1.1.2003-31.12.2005 C-series (63 241): 1.1.2003-31.12.2005 D-series (63 242): 1.1.2004-31.12.2005
Subscription terms	1 share for one option right A ja B series: 1 share for EUR 4.32 C ja D series: 1 share for EUR 10.74

14. Mandatory provisions	**1.1. - 31.12.2003 Group**	**1.1. - 31.12.2002 Group**	**1.1. - 31.12.2003 Parent comany**	**1.1. - 31.12.2002 Parent company**
Rents for unutilized premises	27	27	27	27
Costs for closure of the operations in Viikki	423	0	423	0
Total	450	27	450	27

15. Long-term liabilities	**1.1. - 31.12.2003 Group**	**1.1. - 31.12.2002 Group**	**1.1. - 31.12.2003 Parent company**	**1.1. - 31.12.2002 Parent company**
Loans from The National Technology Agency (Tekes)	5 708	5 075	5 708	5 075
Interest of Capital loans	176	176	176	176
	5 885	5 251	5 885	5 251

16. Instalments of Capital loans and long-term liabilities

	Capital loans	Long-term liabilities	Total
Due next year	3 975	0	
Due next 2-5 years	4 598	1 024	
Due after 5 years	2 386	4 684	
Total	10 958	5 708	16 667

17.Current liabilities	**1.1. - 31.12.2003 Group**	**1.1. - 31.12.2002 Group**	**1.1. - 31.12.2003 Parent company**	**1.1. - 31.12.2002 Parent company**
Advances received	43	0	43	0
Accounts payable	502	988	502	988
Other debts	72	453	72	453
Accrued expenses and prepaid income*)	651	1 095	651	1 095
Total	1 267	2 536	1 267	2 536
*) of which accrued vacation pay	386	629	386	629

18. Contingent liabilities

Due next year	280	377	280	377
Due later on	172	291	172	291
Total	451	667	451	667

19. Deferred tax receivables

Deferred tax assets arising from previous years' losses are not recorded in the balance sheet.

20. Own shares

The parent company of the group possesses 819 000 own shares at EUR 0.80 per share, the market value of the shares was EUR 655 200 at the end of the financial period. The company has received the shares in the merger with Contral Clinics. Shares are not recorded in the balance sheet.

PROPOSAL TO THE ANNUAL GENERAL MEETING

The Board of Directors proposes to transfer the loss EUR –12 432 779,10 of the period to retained earnings.

Helsinki, January 27, 2004

Hannu Hanhijärvi
Chairman of the Board

Jari Saarinen
President and CEO

Juha Jouhki

Kalevi Kurkijärvi

AUDITOR'S REPORT

To the shareholders of Biotie Therapies Corp.

We have audited the accounting, the financial statements and the corporate governance of Biotie Therapies Corp. for the period 1.1. – 31.12.2003. The financial statements, which include the report of the Board of Directors, consolidated and parent company income statements, balance sheets and notes to the financial statements, have been prepared by the Board of Directors and the President and CEO. Based on our audit we express an opinion on these financial statements and on corporate governance of the parent company.

We have conducted the audit in accordance with Finnish Standards on Auditing. Those standards require that we perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining on a test basis evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by the management as well as evaluating the overall financial statement presentation. The purpose of our audit of corporate governance is to examine that the members of the Board of Directors and the President and CEO of the parent company have legally complied with the rules of the Companies Act.

In our opinion the financial statements have been prepared in accordance with the Accounting Act and other rules and regulations governing the preparation of financial statements. The financial statements give a true and fair view, as defined in the Accounting Act, of both the consolidated and parent company's result of operations as well as of the financial position. The financial statements with the consolidated financial statements can be adopted and the members of the Board of Directors and the President and CEO of the parent company can be discharged from liability for the period audited by us. The proposal by the Board of Directors regarding the distributable assets is in compliance with the Companies Act.

Turku, February 6, 2004

PricewaterhouseCoopers Oy
Authorized Public Accountants

Johan Kronberg
APA

Tomi Moisio
APA

Key Figures

1 000 €	1.1.2003 –31.12.2003 12 months	1.1.2002 –31.12.2002 12 months	1.1.2001 –31.12.2001 12 months	1.1.2000 –31.12.2000 12 months	1.1.1999 –31.12.1999 12 months
Business development					
Revenues	2 243	153	173	0	0
Personnel on average	66	115	32	9	6
Personnel at end of the period	55	112	44	10	7
Research and development expenses	11 888	21 541	6 333	3 478	1 532
Capital expenditure	57	1 090	729	10	206
Profitability					
Operating profit (loss)	-12 395	-26 256	-6 684	-3 059	-1 612
as percentage of revenues, %	-552.6	-17 177.5	-3 863.6	-	-
Profit (loss) before extraordinary items	-12 215	-25 916	-6 497	-3 088	-1 595
as percentage of revenues, %	-544.5	-16 954.8	-3 755.5	-	-
Profit (loss) before taxes	-12 215	-26 236	-6 497	-3 088	-1 595
as percentage of revenues, %	-544.5	-17 164.7	-3 755.5	-	-
Balance sheet					
Cash and cash equivalents	10 422	8 691	6 276	2 013	1 336
Shareholders' equity	6 428	5 706	6 951	299	2 169
Balance sheet total	14 030	13 520	7 934	2 684	2 324
Financial ratios					
Return on equity, %	-	-	-	-	-
Return on capital employed, %	-103.9	-288.5	-174.1	-245.8	-73.9
Equity ratio, %	-32.3	-19.1	22.0	-163.1	-55.9
Gearing, %	-138.0	-181.0	-57.4	-60.8	-164.1
Per share data					
Earnings per share (EPS), €	-0.40	-2.49	-0.85	-0.99	-0.60
Shareholders' equity per share, €	-0.10	-0.13	0.22	-1.24	-0.48
Dividend per share, €	-	-	-	-	-
Pay-out ratio, %	-	-	-	-	-
Effecting dividend yield, %	-	-	-	-	-
P/E ratio	-	-	-	-	-
Share price					
– Lowest share price, €	0.40	0.67			
– Highest share price, €	1.61	2.66			
– Average share price, €	0.71	1.13			
– 31.12. share price, €	0.80	0.67			
Market capitalization, mill. €	34.9	11.7			
Trade of shares					
– Number of shares traded	12 189 112	446 478			
– As percentage of all shares, %	27.9	2.6			
Adjusted weighted average number of shares during the period	31 116 906	10 376 551	7 268 435	3 061 227	2 643 424
Adjusted number of shares at the end of the period	43 686 397	19 399 508	8 019 779	3 458 889	2 710 000
Adjusted weighted average number of shares during the period, fully diluted	33 336 433	9 574 876			
Adjusted number of shares at the end of the period, fully diluted	45 905 924	17 559 570			

Formulas for the Calculation of the Financial Ratios

In the following formulas capital loans are included interest-bearing liabilities and not in shareholders´ equity.

Return on equity %

$$\frac{\text{Profit (loss) before extraordinary items - taxes}}{\text{Shareholders' equity – capital loans}} \times 100$$

Return on capital employed %

$$\frac{\text{Profit (loss) before taxes + interest expenses and other financial expenses}}{\text{Balance sheet total – advances received}} \times 100$$

Equity ratio %

$$\frac{\text{Shareholders' equity}}{\text{Balance sheet total – advances received}}$$

Gearing %

$$\frac{\text{Interes-bearing liabilities – cash and cash equivalents}}{\text{Shareholders' equity}}$$

Earnings per share (EPS)

$$\frac{\text{Profit before extraordinary items, appropriations and taxes – minority interest – taxes}}{\text{Adjusted average number of shares during the period}}$$

Shareholders' equity per share

$$\frac{\text{Shareholders' equity}}{\text{Adjusted average number of shares during the period}}$$

Dividend per share

$$\frac{\text{Dividends paid for the financial year}}{\text{Adjusted number of shares at the end of the period}}$$

Pay-out ratio

$$\frac{\text{Dividends paid for the financial year}}{\text{Profit before taxation – income taxes – minority interests}} \times 100$$

Effective dividend yield

$$\frac{\text{Dividend per share}}{\text{Average share price at the end of the period}} \times 100$$

P/E Ratio

$$\frac{\text{Average share price at the end of the period}}{\text{Earnings per share (EPS)}}$$

Shares and Shareholders

SHARE CAPITAL AND SHARES

The shares of Biotie Therapies Corp. are traded in the NM list of the Helsinki Exchanges (HEX). All the shares are of the same type and carry identical rights. All the shares can be transferred freely and each share produces one vote. The counter book value of each share is EUR 0.02.

The share capital of BioTie increased by EUR 300 through subscriptions made on the basis of option rights. The increase was entered into the Trade Register on April 30, 2003. As a result of the share issue in June 2003, the registered share capital of Biotie Therapies Corp. increased by EUR 524 236.76 to EUR 873 727.94, and the number of shares by 26 211 838 to 43 686 397 shares. The increase in share capital was entered into the Trade Register on June 26, 2003.

In accordance with the Articles of Association, the minimum number of shares is 10 000 000 and the maximum 400 000 000 shares.

LISTING AND TICKER CODE

The share of the company was transferred from the Pre list to the NM list of the Helsinki Exchanges on October 8, 2003. The share's ticker code is BTH1V and the lot size in HEX is 100 shares.

BIOTIE'S SHARE PRICE DEVELOPMENT

At the end of the financial year, BioTie's share price was EUR 0.80, the highest price was EUR 1.61 and the lowest EUR 0.40. The average rate was EUR 0.71. BioTie's market capitalization at the beginning of the financial year was EUR 12 million and at the end of the financial year EUR 35 million.

The average monthly trading during the financial year was 1 015 759 shares and during the last quarter 2 125 853 shares. The value of shares traded during the financial year totaled EUR 8.6 million.

The Finnish taxation value of BioTie's shares in 2003 was EUR 0.55 per share.

THE BOARD'S AUTHORITY TO INCREASE SHARE CAPITAL AND TRANSFER THE COMPANY'S OWN SHARES

The Board of Directors' authorization to issue shares is valid until March 24, 2004. The share capital can be increased on authorization by a maximum of EUR 50 000 i.e. 2 500 000 shares. A total of 2 000 000 shares out of the authorization were used for the option program issued by the company in January 2004. The Board of Directors has the authorization to assign the company's own shares up to March 24, 2004. The authorization covers the 819 000 shares possessed by the company.

SHAREHOLDERS

At the end of the financial year, BioTie's shareholders numbered 3 740. The ten largest shareholders owned 69.16% of the shares. The number of nominee-registered and foreign-registered shares totaled 88 101 shares i.e. 0.2 % of the shares.

BOARD OF DIRECTORS' AND PRESIDENT'S HOLDINGS

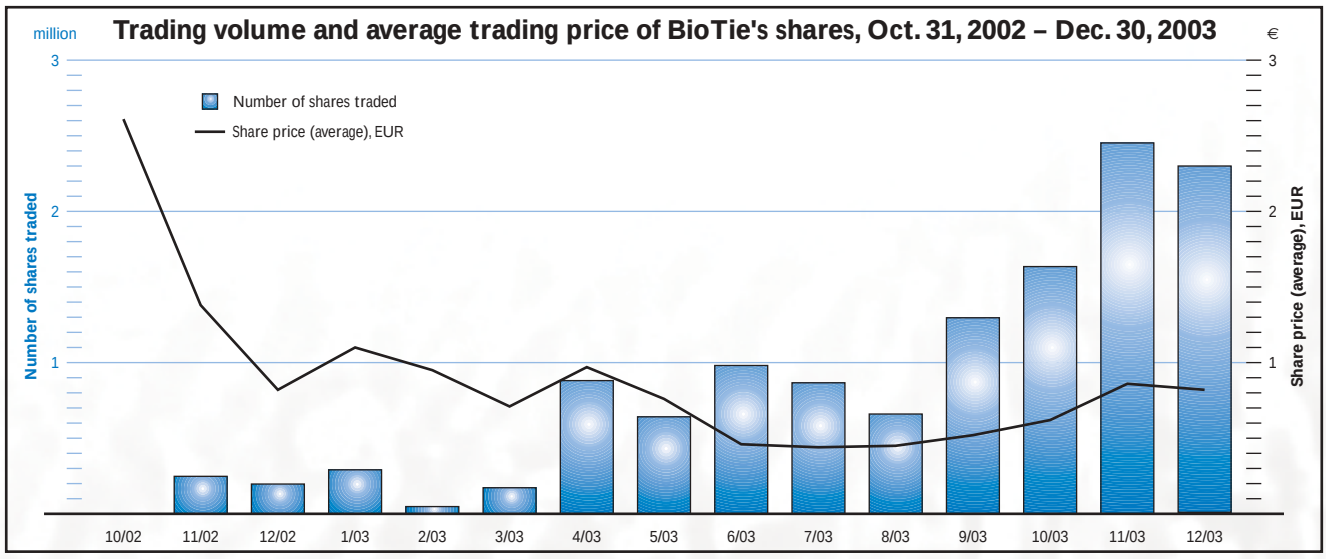
The Members of the Board of Directors and the President own altogether 917 970 shares of BioTie, i.e. 2.14 % of the total number of shares. Furthermore, based on option rights, they may subscribe for a maximum of 85 728 shares which would represent 0.20 % of the shares. The Members of the Board of Directors and the President would jointly hold 2.29 % of the shares if their option rights were exercised.

OPTION SCHEMES

Biotie Therapies Corp. has issued option rights by 31.12.2003 pursuant to a total of six different option programs. As a result of these option rights, the share capital of BioTie may be increased by a maximum of EUR 18 530.54, corresponding 926 527 shares.

INSIDERS

The company follows the insider directives of the Helsinki Exchanges that entered into force on March 1, 2000.



THE TEN LARGEST SHAREHOLDERS OF BIOTIE ON 16 JANUARY, 2004

	Shareholder	Number of shares	% of shares
1	FINNISH INDUSTRY INVESTMENT LTD	10 604 102	24.74
2	FINNISH FUND FOR RESEARCH AND DEVELOPMENT (SITRA)	9 924 566	23.15
3	Funds administered by BioFund Management Oy		
	BIO FUND VENTURES III KY	1 785 715	4.17
	BIO FUND VENTURES I KY	1 440 983	3.36
4	Funds administered by Aboa Venture Management Oy		
	ABOA VENTURE KY 1	639 942	1.49
	ABOA VENTURE KY II	336 747	0.79
	GANAL VENTURE KY	7 906	0.02
	KARHU PÄÄOMARAHASTO KY	7 871	0.02
	VAKKA-SUOMEN PÄÄOMARAHASTO KY	7 978	0.02
5	DREADNOUGHT FINANCE OY	992 316	2.31
6	JOUHKI JUHA	917 970	2.14
7	THE LOCAL GOVERNMENT PENSIONS INSTITUTION	878 181	2.05
8	MUTUAL LIFE INSURANCE COMPANY SUOMI	845 206	1.97
9	MUTUAL PENSION INSURANCE COMPANY TAPIOLA	675 914	1.58
10	NON-LIFE INSURANCE COMPANY LTD POHJOLA	579 944	1.35
TEN LARGEST SHAREHOLDERS, TOTAL		**29 645 341**	**69.16**
	Other shareholders	13 222 056	30.84
	Total shares issued	42 867 397	100

The number of the company's own shares held by Biotie Therapies Corp. is 819 000.

DISTRIBUTION OF SHAREHOLDERS DECEMBER 31, 2003

Number of shares	Shareholders	% of shares
1-500	2 164	0.98
501-1000	491	0.91
1001-10000	935	7.54
10001-100000	115	7.86
100001-500000	22	13.12
500001-	13	69.46
Total	**3 740**	**99.87**
In joint account		0.13

TYPE OF SHAREHOLDERS DECEMBER 31, 2003

	% of shares
Corporations	44.05
Financial and insurance institutions	5.00
Public entities	3.60
Non-profit organizations	24.96
Households	22.16
Foreign	0.10
Nominee registered	0.20

Patents

KEY PATENTS AND PATENT APPLICATIONS OF BIOTIE'S IPR PORTFOLIO

Nalmefene patent families	**Granted**
US 4882335	21.11.1989
US 5096715	17.11.1992
US 5086058	4.2.1992
EP 0346830	10.5.1995
EP 0531415	20.11.1996
EP 0429039	08.03.1995
JP 3059213	21.4.2000
US 5780479 (exclusive license/Minnesota University)	14.7.1998
International patent application WO 03/015783	pending
VAP-1 monoclonal antibody patent families	
US 5580780	3.12.1996
US 6066321	23.5.2000
US 5512442	30.4.1996
EP 0656906	8.9.1999
JP 3431922	23.5.2003
JP 3500384	5.12.2003
European patent application EP979271 and corresponding patent applications in the United States and Japan	pending
International patent application WO 03/093319	pending
International patent application WO 99/58572 (non-exclusive license/Cambridge University)	pending
VAP-1 SSAO inhibitor patent families	
US 6624202	23.9.2003
European patent applications EP 1301495 and EP 1313718 both corresponding patent applications in the United States and Japan	pending
International patent application WO 03/00603	pending
Other research projects	
Integrin inhibitors	
US 6096707	1.8.2000
EP 0994898	26.3.2003
Japan patent application	pending
Sulphated linear polysaccharides	
Several patent applications based on international patent applications WO 98/48006, WO 02/46379 (co-owned/Inalco)	pending
Several patent applications based on international patent apaplications WO 96/14425, WO 98/42754, WO 01/72848, WO 01/02597 (semi-exclusive license/Inalco)	pending
Glycobiology	
Several patent applications based on international patent applications WO 01/723398, WO 01/97819, WO 02/056793, WO 03/059924, WO 03/002127, WO 03/002128, WO03/016464, WO 03/016915, WO 01/43751	pending

Main Stock Exchange Releases in 2003 in Brief

January 2, 2003
BIOTIE THERAPIES CORP. HAS TRANSFERRED CONTRAL CLINICS -BUSINESS TO A NEW COMPANY
Biotie Therapies Corp. has in accordance with an agreement transferred ContrAl Clinics -business, specialized in the treatment of excessive drinking and alcoholism, to a new company owned by the key personnel of the Clinics-business. With the arrangement BioTie will focus, in accordance with its strategy, on drug development.

January 31, 2003
BIOTIE THERAPIES CORP. SELLS ITS PROCESS DEVELOPMENT AND PRODUCTION UNIT
Biotie Therapies Corp. will in accordance with an agreement signed on 30 January, 2003 sell its process development and production unit to a new company, Biovian Ltd which is owned by the company's management, key personnel and BioTie. In the transaction 14 employees, the assets as well as the agreements and liabilities relating to the unit will be transferred to Biovian Ltd as of 1 February, 2003.

April 24, 2003
BIOTIE REPORTS RESULTS OF TWO PHASE III CLINICAL STUDIES IN ALCOHOLISM AND ALCOHOL ABUSE
The Finnish trial demonstrated that the nalmefene tablet intended for the treatment of alcoholism reduced the number of heavy drinking days almost by half without psycho-social therapy. In the placebo group, the number of heavy drinking days was reduced by about 1/3 and the difference between the groups was statistically significant. The UK trial had a similar trend but the difference between nalmefene and placebo groups was not statistically significant due to a higher than expected patient drop-out rate.

April 28, 2003
BIOTIE THERAPIES CORP. ENTERS INTO A LICENSING AGREEMENT COVERING THE VAP-1 ANTIBODY TECHNOLOGY WITH JAPANESE SEIKAGAKU CORPORATION
BioTie Therapies has entered into a licensing agreement on the company's VAP-1 antibody program with the Japanese company Seikagaku Corporation. According to the terms of the licensing agreement, Seikagaku will have the exclusive right to the VAP-1 monoclonal antibody developed by BioTie Therapies, as well as the right to commercial exploitation of the patents in Japan, Taiwan, Singapore, New Zealand and Australia. The regional licensing agreement covers all indications but is now targeted at the following three indications: rheumatoid arthritis, psoriasis and ulcerative colitis.

The value of the licensing agreement totals USD 16.7 million (EUR 15.2 million), comprising of a signing fee of USD 2.5 million, which will be paid once the agreement has entered into force, and USD 14.2 million as milestone payments payable in accordance with the jointly agreed clinical development milestones.

April 28, 2003
THE NATIONAL TECHNOLOGY AGENCY (TEKES) HAS GRANTED ADDITIONAL FUNDING OF EUR 5.9 MILLION FOR BIOTIE'S DRUG DEVELOPMENT PROJECTS
The National Technology Agency (TEKES) has granted additional funding of EUR 5.9 million for BioTie's drug development projects. The R&D subsidies and loans with favorable conditions granted in April cover certain drug development costs of the company from October 2002 to mid 2004.

The funding granted for the development projects by Tekes varies from one project to another and covers 50–60 per cent of the costs of the projects. The share of capital loan funding of the amount now granted is EUR 4.7 million.

May 23, 2003
BIOTIE ANNOUNCES RESULTS OF PHASE I TRIAL WITH VAPALIXIMAB IN HEALTHY VOLUNTEERS
Results from the company's first phase I trial in healthy volunteers demonstrate that vapaliximab can be safely dosed in humans. No serious adverse events were reported in the 30 subjects dosed with the study drug. Further analysis of the drug's profile is ongoing to determine if structural modifications to the existing antibody would be beneficial. In parallel, BioTie will evaluate the merits of developing a humanized (non-chimeric) or a fully human VAP-1 monoclonal antibody.

May 30, 2003
RESULTS FROM A PHASE II CLINICAL STUDY SUGGEST NALMEFENE EFFECTIVE IN THE TREATMENT OF PATHOLOGICAL GAMBLING
A phase II study in patients suffering from pathological gambling demonstrated that nalmefene reduced gambling-related urges and behavior statistically significantly compared to placebo.

A psychometric scale (PG-YBOCS, developed by Drs. Hollander and DeCaria at Mount Sinai Hospital, New York) measuring gambling-related thoughts, urges and behavior was used for primary evaluation of efficacy. Based on the study results nalmefene was effective in patients suffering from pathological gambling: after four months´ treatment, mean scores on the PG-YBOCS scale were almost twice as high in patients who were on placebo when compared to the patients receiving nalmefene. The difference between the study groups was statistically significant. No serious adverse effects related to the use of nalmefene were observed during the study.

June 2, 2003
THE CO-DETERMINATION PROCEDURE AT BIOTIE THERAPIES COMPLETED
In order to adapt the company's cost structure the co-determination procedure at Biotie Therapies Corp. has been completed. The procedure commenced in May and involved all personnel groups. As a result of the co-determination procedure, the employment of nine employees at the administration, business development, research and development departments will be terminated.

In addition to the completed co-determination procedure the company is studying possibilities of reducing the development risk and costs related to the company's glycomics technology platform. The company is examining alternatives of entering into research collaboration agreements in glycomics and other arrangements including change of ownership during 2003.

June 25, 2003
FINAL SUBSCRIPTIONS OF BIOTIE THERAPIES CORP. SHARE ISSUE
The company raised new capital in the amount of EUR 10.5 million.

Following the share issue, Biotie Therapies Corp.'s registered share capital will amount to EUR 873 727.94, consisting of 43 686 397 shares.

July 4, 2003
LICENSING AGREEMENT WITH SEIKAGAKU CORPORATION ENTERED INTO FORCE
BioTie has on 4 July, 2003 received confirmation from Seikagaku Corporation that the licensing agreement concerning VAP-1 antibody program has entered into force as of 30 June, 2003.

July 23, 2003
BIOTIE AND INALCO HAVE AGREED ON THE CONTINUATION OF THE BIOHEPARINE-PROJECT
Last week the Italian Inalco S.p.A terminated the Co-Development and License Agreement with BioTie, and it is now announced that BioTie and Inalco S.p.A have concluded the negotiations on the continuation of the bioheparin project on 23 July, 2003. According to the mutual understanding reached between the two parties, the parties will remain free to operate independently and commercially exploit the intellectual property rights related to the project. Due to this so-called Freedom to Operate, BioTie will have royalty-free, global and non-exclusive right to exploit and commercialize the three Inalco patents. Inalco will be entitled to operate correspondingly as regards the patents owned jointly by the parties.

October 8, 2003
BIOTIE THERAPIES CORP.´S QUOTATION TO THE HELSINKI EXCHANGES NM LIST
The Biotie Therapies Corp. share will be quoted on the Helsinki Exchanges NM List as of October 8, 2003.

Glossary

Adhesion
Adhering, clinging together.

Angiogenesis
Formation of new blood vessels (e.g. in cancerous tumors).

Antibody
A protein which is produced by the immune system of humans and higher animals and which binds to a specific antigen (e.g. a microbe).

Antigen
A foreign substance that stimulates an immune response.

Autoimmune disease
A disease where an individual's immune system attacks its own tissues. Tissues under such an attack are damaged in the process. E.g. rheumatoid arthritis.

Bioheparin
Biotechnologically produced heparin.

Biotechnology
The application of biological research techniques for the development of products which improve human health, animal health and agriculture.

Collagen
The most important structural protein of the body. Gives the tissues their structural strength.

Crohn's disease
An inflammatory bowel disease where the inflammation goes through the entire bowel wall in a certain region of the intestine (regional ileitis).

Endothelium
The thin layer of specialized epithelial cells that lines the cavities of the heart and of the blood and lymph vessels.

Enzyme
A protein that facilitates a biochemical reaction in a cell. In general, these biochemical reactions cannot occur unless the enzyme is present.

Glycomics
Research of molecules with carbohydrate structure.

Glycomics platform (technology platform)
Analyzing methods for studying sugar structures (carbohydrates) on the cell surface and their role in different diseases, for example, for the development of drug therapies.

Glycosaminoglycan
A sugar compound present in the body.

GMP
Good Manufacturing Practice.
A quality assurance system required by authorities and for use in the manufacture of drugs.

Growth factors
Proteins regulating cell proliferation, function and differentiation.

Helicobacter
A bacterium (Helicobacter pylori) causing an infection that may in the long-term result in gastric ulcer.

Hemodialysis
A treatment technique which removes wastes and excess water from the body. Hemodialysis is needed when the kidneys do not function properly (renal insufficiency).

Heparin
A drug that prevents the blood from clotting. Structurally, heparin is a linear polysaccharide.

Inflammation
A reaction focused on a physical, chemical or biological damage, characterized by increased blood flow and increased permeability of blood vessel walls. Clinical symptoms include redness, swelling and pain.

Inflammatory Bowel Disease (IBD)
Inflammatory Bowel Disease, for example, ulcerative colitis and Crohn's disease.

IgG2, IgM
A protein present in the body as an antibody. Calculated by its structure (IgG, IgM etc.) Ig refers to immunoglobulin.

Immune defense
A defense system of the body that eliminates intruders with the purpose to protect the body from pathogens (see autoimmune disease).

Impulse control disorders (ICD)
These disorders include e.g. pathological gambling, kleptomania and pyromania.

Indication
The purpose of use of a drug or the disease for which the drug is used.

Infarction
Acute obstruction of circulation caused by e.g. thrombosis and leading to necrosis in a tissue.

Infection
Invasion of the body by pathogens such as bacteria or viruses resulting in an infectious disease. For example, influenza, viral infection of the respiratory tract marked by fever.

Inhibitor
Blocker; a factor that inhibits or slows down e.g. an enzymatic reaction or physiological functions.

Integrin
Intercellular receptor.

Ischemia
Lack of oxygen in a tissue.

Monoclonal antibody
An antibody produced by identical, cloned cells.

Nalmefene
Studied and used for the treatment of alcoholism, nalmefene acts by blocking opioid receptors in the central nervous system.

Opioid receptor
A receptor in the central nervous system, into which e.g. beta-endorphin binds. Changes in opioid receptor -mediated neurotransmission are important in the development of dependence disorders.

Peptide
Amino acids chained together by peptide bonds.

Polysaccharide
Chain formed by sugar rings.

Protein
A biological molecule consisting of many amino acids chained together by peptide bonds. The sequence of amino acids in a protein is determined by the sequence of nucleotides in a DNA molecule.

Proof of Concept
That stage of drug development confirming that the findings of animal tests are also applicable in humans.

Psoriasis
A chronic skin disease marked by faster than normal growth of keratinocytes. The symptoms include reddish, distinctive lesions covered with scales.

Receptor
A protein usually found on the surface of a cell. It transmits messages into the cell from, e.g. hormones, growth factors or neurotransmitters.

Rheumatoid arthritis
A chronic, autoimmune disease of the joints marked by destruction of tissues particularly in the synovial membranes. Often leads to disability.

Small molecule drugs
Drug substances that have a low molecular weight. Small molecules penetrate cell membranes and the blood brain barrier more easily than larger molecular weight compounds such as proteins, peptides and carbohydrates. They can usually be administered orally.

Small molecule heparin
A heparin derivative with smaller molecular weight than that of so-called non-fractionated heparin.

SSAO
Semicarbazide-sensitive amine oxidase. The SSAO enzyme of the VAP-1 molecule produces substances that amplify the inflammatory reaction, e.g. hydrogen peroxide.

Synthesis
Manufacture of compounds, e.g. drug substances.

Thrombosis
Blood clot.

VAP-1
Vascular Adhesion Protein-1. An adhesion molecule that mediates white blood cell adhesion and migration from the blood into tissues. VAP-1 also produces substances that amplify the inflammatory reaction through its SSAO enzyme activity. Target for the company's anti-inflammatory drugs.

VAP technology
Focusing on the research of VAP-1 (see VAP-1) protein and factors affecting it. The goal is to develop drug therapies blocking VAP-1 function.

White blood cell
Leukocyte; the common name for granulocytes, lymphocytes and monocytes in the blood and connective tissue.

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