

24 JANUARY AT 9.00 A.M.

FINANCIAL STATEMENT BULLETIN OF BIOTIE THERAPIES CORP., JANUARY 1 -  
DECEMBER 31, 2001

## The year 2001 in brief

- BioTie signed a collaboration agreement with Shimizu Pharmaceutical, a member of Takeda Group, on the development of BioHeparin for the Japanese hemodialysis market.
- Regulatory authorities in an EU member country gave a positive opinion to start clinical studies with Bioheparin.
- The first phase I/II clinical trials in BioTie's VAP-1 antibody therapy program were completed.
- The development schedule of the second generation VAP-1 antibody drug Huvap has been accelerated by approximately six months.
- Small molecule VAP-1 SSAO inhibitor (Vapill) has been shown to be efficacious in animal models of rheumatoid arthritis.
- The National Technology Agency (Tekes) granted 3.4 million euros additional funding for BioTie's drug development projects.
- A court ruling in the patent dispute with Orion Corporation is expected during the first quarter of 2002. The Company believes that Orion's claims are without merit and is defending it's patent's vigorously.
- Operating profit (loss) amounted to EUR -10.2 million (EUR -6.9 million in 2000). Research and Development investments increased by 63 %.
- Cash and cash equivalents amounted to EUR 9.5 million on 31.12.2001

## Review of 2001 operations

BioTie is a drug development biotech company focusing on inflammation, thrombosis and cancer. Operations are conducted in collaboration with leading academic institutions, clinical research organizations and contract manufacturers.

## Drug Development Projects

## VAP-1 antibody therapy program

The first phase I/II clinical trials in BioTie's VAP-1 antibody therapy program were completed during the financial year.

The studies evaluated safety, tolerability, and pharmacology of a mouse monoclonal antibody (Vapantix) in patients with nickel allergy of the skin and in patients with ulcerative colitis. Altogether 18 patients received a single intravenous infusion of the monoclonal

antibody drug developed by BioTie (0.05 to 0.5 mg/kg). Vapantix was well tolerated and no serious adverse events were observed.

The primary goal of the studies was to evaluate safety of Vapantix. The effect on clinical disease activity in ulcerative colitis patients, however, was preliminarily assessed. Of the nine patients receiving Vapantix infusions four had clinically active disease immediately prior to drug infusion. After a one-month follow-up, the clinical condition of all these four patients had improved.

The development schedule of BioTie's second generation VAP-1 antibody drug Huvap has been accelerated by approximately six months. The company estimates that Huvap will enter into clinical development mid 2002 instead of by end 2002 as previously planned.

Huvap is a second generation molecule of Biotie's VAP-1 antibody therapy program. It is a humanised IgG2 monoclonal antibody against VAP-1. Biotie's first generation drug, Vapantix, is a mouse monoclonal IgM antibody against VAP-1.

Both Huvap and Vapantix block the function of the VAP-1 inflammation receptor. However, Huvap may be administered to patients repeatedly due to its humanization and due to its modified structure it is also expected to be safer than therapeutic monoclonal antibodies currently on the market. Huvap is primarily intended for the treatment of chronic inflammatory diseases. BioTie has developed its second generation VAP-1 antibody inhibitor in collaboration with Cambridge University, Turku University, and Boehringer Ingelheim Pharma.

Due to the acceleration of Huvap's drug development, BioTie will postpone the decision to start the planned phase II clinical study with Vapantix until mid 2002. At that time the company will have data available on Huvap's potential to be developed for the targeted VAP-1 antibody therapy indications, including Vapantix indications.

Small molecule VAP-1 SSAO inhibitor (Vapill)

BioTie's small molecule VAP-1 SSAO inhibitor (Vapill) has been shown to be efficacious in two animal models of rheumatoid arthritis. Vapill reduced clinical symptoms in experimental arthritis models in mice and in rats. The effect on disease severity was statistically significant when compared to control groups on placebo treatment. Vapill lead molecule was also efficacious in animal models of acute inflammation.

These results demonstrate the key role of VAP-1 SSAO enzyme in inflammatory diseases.

As reported earlier the small molecule VAP-1 SSAO inhibitor (Vapill) project has been delayed by six months as the development of

industrial scale drug substance production has taken longer than expected.

### BioHeparin

BioTie's BioHeparin has been demonstrated to be efficacious in preventing venous thrombosis in animals. The antithrombotic effect of BioHeparin and animal-derived heparin is based on the same mechanism, i.e., on the ability to inhibit the function of blood coagulation enzymes.

BioTie completed the authority regulated animal study phase, in which the safety of the drug will be assessed, during 2001 as previously planned. Regulatory authorities in an EU member country gave a positive opinion to start clinical studies with Bioheparin.

BioHeparin is intended for the treatment and prevention of thrombosis. BioHeparin is a novel biotechnology-derived polysaccharide drug based on BioTie's proprietary BALP (Biologically Active Linear Polysaccharides) technology.

### Alpha2-integrin blockers

BioTie's collaborative research program together with University of Turku, Åbo Akademi University and University of Jyväskylä on alpha2-betal integrin collagen receptor resulted in the generation of novel small molecule inhibitors. The new inhibitors offer novel ways to prevent trombosis caused by vascular injury. In addition, many cancer cells use alpha2-integrin for their spreading in the tissues and therefore, also certain cancers belong to the possible clinical indications of alpha2-integrin inhibitors.

The drug research program is based on three-dimensional modeling of the alpha2-integrin receptor structure and utilization of known receptor-binding structures to guide the design and synthesis of small molecule inhibitors. The new inhibitors were submitted for BioTie's preclinical study phase in January 2001.

### Discovery Research

BioTie's drug discovery program focuses on developing company's core competence and providing new scientific information on its main research areas. The company actively seeks to identify - within the frame of its core technology areas - novel targets for drug development. In the areas of VAP-1 antibody therapy program and BALP-technology, BioTie has continued collaboration in two European Union funded scientific research consortia, BANG and TUNE-UP. In the scientific research consortia, the aim is to discover new indication

areas for BALP-compounds and SSAO-inhibitors. In both consortia, BioTie holds the first right of commercial exploitation of the results.

The C5-epimerase enzyme, required in the manufacturing process of Bioheparin, has been expressed in yeast cells in order to develop an industrial-scale production system. During the reporting period BioTie strengthened patents covering C5-epimerase and SSAO inhibitors. At the end of 2001 the company signed a letter of intent to license a new protein, occurring in lymphatic and blood vessels, as a drug development target. Antibodies which block the function of this protein have been demonstrated to inhibit the binding of inflammatory and cancer cells to tissues.

#### Collaboration agreements

BioTie signed a collaboration agreement with Shimizu Pharmaceutical, a member of Takeda Group, in December, 2001. According to the collaboration agreement, BioTie will develop in cooperation with Shimizu a BioHeparin - using the proprietary BALP-technology (Biologically Active Linear Polysaccharides)- for the treatment of hemodialysis. As the drug molecule has been evaluated and developed, Shimizu will pay for BioTie significant milestone payments. Shimizu will pay the signing fee during the first quarter of 2002. From future product sales in Japan, BioTie will receive royalties.

BioTie and Rhodia Chirex (UK) signed a process development and pilot-scale manufacturing agreement for the production of Vapill drug substance in April, 2001. Rhodia Chirex is a leading European drug substance manufacturer the clients of which include leading global pharmaceutical companies.

After the signing of this agreement the manufacturing arrangements for industrial scale drug substance production have now been secured for all BioTie drug development projects entering the clinical studies.

- Vapantix is being produced in-house
- Huvap manufacturing is outsourced to Boehringer Ingelheim Pharma in Biberach, Germany, a world leading biopharmaceutical manufacturer
- Vapill drug substance manufacturing is outsourced to Rhodia Chirex (UK)
- BioHeparin is produced by Inalco S.p.A., Italy, a long-time partner of BioTie.

The company actively seeks to identify - within the frame of its core technology areas - novel targets for drug development.

## Financial Results

Operating profit (loss) for the financial year amounted to EUR -10.2 million. In 2000, the corresponding figure was EUR -6.9 million. BioTie has, according to its strategy, increased investments in its drug development projects, in discovery research and in building up its operational organization. Research and development costs were EUR 11.3 million (EUR 7.0 million in 2000) during 2001, which is an increase of 63 %.

## Financing

The Company's financial position remained good throughout the year.

The National Technology Agency (Tekes) granted 3.4 million euros additional funding in June for BioTie's drug development projects. The funding covered the period starting from second half of year 2000 to the end of 2001. Financing was in form of R&D subsidies and loans with favourable conditions and varied between 42-54 per cent, depending on the project. The funding granted by Tekes ended on December 31 2001. The company has sought further funding.

BioTie's equity ratio was 43.9 % on 31 December 2001 (80.0 % in 2000). Cash and cash equivalents amounted to EUR 9.5 million on 31 December 2001 (EUR 16.0 million in 2000).

At the end 2001, the company had capital loans of EUR 3.0 million and loans of EUR 1.8 million.

## Group structure

The group's parent company is Biotie Therapies Corp. A subsidiary, Biotie International Ltd was established in 2001. The subsidiary was not operational during the financial year.

## Investments

The Company's investments during the financial year amounted to EUR 0.2 million (EUR 1.1 million in 2000). Investments consisted mainly of equipment used in research and development operations.

## The Annual General Meeting

The Annual General Meeting of Biotie Therapies Corp. was held on 6 April 2001 in Turku. The meeting handled the matters pursuant to the Companies Act and the Company's Articles of Association.

The Annual General Meeting resolved in accordance with the proposal of the Board of Directors that section 11 of the Articles of

Association shall be amended so that invitation to the shareholders shall be delivered not earlier than two months before and at the latest 17 days before the General Meeting. Section 11 of the Articles of Association was also amended so that in order to have the right to participate to the General Meeting a shareholder must report to the company no later than on the date mentioned in the invitation, which date may be ten days before the General Meeting at the earliest.

Authorisation to the Board of Directors to resolve to increase the share capital

The Annual General Meeting passed a resolution in accordance with the proposal of the Board of Directors and the modification proposed at the Annual General Meeting to authorise the Board of Directors to resolve to increase the share capital by issuing new shares and/or to take a convertible loan in one or more issues of new shares or loans in a manner whereby the authorisation to be granted now, together with any outstanding, valid authorisations to increase the share capital or shares to be subscribed pursuant to the convertible loan, with respect to the total increase and the total number of voting rights relating to the issued shares, may correspond to a maximum of one fifth of the total share capital and all voting rights in the company, registered as of the date of the decision of the General Meeting and the date of the decision of the Board of Directors to increase the share capital. Thus the maximum increase of share capital is 37.149,86 euros, corresponding 3.714.986 shares of the company. The authorization includes a right for the Board of Directors to deviate from the shareholders' pre-emptive subscription right and a right to resolve subscription prices and other terms of subscription.

The authorisation is effective for a period of one year from the date of the resolution of the Annual General Meeting. The Board of Directors has no outstanding authorisation to acquire own shares. Group companies do not have any own shares.

Granting of option-rights

The Annual General Meeting of Biotie Therapies Corp. resolved in accordance with the proposal of the Board of Directors to grant a total of up to 50,000 option rights. The option rights entitle their holders to subscribe for a maximum of 500,000 new shares of Biotie Therapies Corp. The option rights shall be offered free of charge and in deviation from the shareholders' pre-emptive subscription right, in a manner determined by the Board of Directors, to be subscribed by key personnel of Biotie Therapies Corp., members of the Board of Directors, the Managing Director and/or a subsidiary designated by the Board of Directors. A total of up to 25,000 option rights may be offered to the members of the Board of Directors on

the basis of the option program. All option rights were subscribed during the financial year. The subscription price was EUR 5,6514 per share, the weighted average trading price of BioTie shares during March 19-30, 2001 on the Helsinki Stock Exchange.

The Annual General Meeting made also a resolution in accordance with the proposal of the Board of Directors to amend the terms of option rights granted on the basis of option programs resolved 14 February 2000, 24 February 2000 and 26 April 2000, 23 May 2000 as well as 26 June 2000. The terms shall be amended so that shares subscribed pursuant to the option rights entitle to dividends from the moment the subscription has been registered in the Trade Register.

By the end of financial year, on the basis of option rights and option certificates granted to the Board of Directors in 2000, 15,000 shares of Biotie Therapies Corp. have been subscribed. As a result of the above mentioned share subscriptions, the share capital of the Company was increased by 150 euros. The increase of share capital was entered into Trade Register 12 April 2001.

At the end of 2001 the company had issued and outstanding a total of 147,772 option rights all of which have been subscribed by 68 persons. Each option right entitles its holder to subscribe for ten new shares with accounting equivalent value of EUR 0.01. If all issued and outstanding option rights are exercised, the share capital of the Company may be increased by up to EUR 14,777.20, corresponding to 1,477,720 new shares. The subscription price in option rights programs 1-4 is EUR 2.271 and in program 5 is EUR 5.6514. Shares subscribed pursuant to the option rights will entitle their holder to any dividends declared and paid in respect of the financial period during which the shares are registered into the Trade Register. If all the option rights are exercised, this would represent 7.4 % of the total number of shares and option rights after subscription.

The Board of Directors

The Annual General Meeting appointed the following persons as members to the Board of Directors: Hannu Hanhijärvi, Risto Jalonen, Markku Jalkanen and Kalevi Kurkijärvi and Jeffrey Jonas and Björn Mattsson as new members. At the assembly meeting of the Board of Directors held on 6 April 2001, Björn Mattsson was appointed as the chairman of the Board of Directors.

## Auditors

Johan Kronberg, Authorised Public Accountant and SVH PricewaterhouseCoopers with Tomi Moisio Authorised Public Accountant, acting as the main responsible auditor, were elected as the Company's auditors.

## Organisation and Personnel

During the year, the Company's personnel grew to 71 (65 at the end of 2000). The average number of personnel during the year was 68 (55 in 2000).

## Share Price

The sale and subscription price of BioTie's shares in the IPO was EUR 6.80 per share on 29 June 2000 and the closing price on 29 December 2000 was EUR 6.50. At the end of the financial year the share price was EUR 4.05, 37.7 % percent lower than a year ago. During the same period the HEX portfolio index fell by 22.3 %, the Nasdaq Biotech index fell by 13.1 % and the NEMAX Biotech index fell by 51.4 %. The highest price for BioTie's share during the year was EUR 6.84 and the lowest was EUR 3.60. The average share price was EUR 5.17. BioTie's market capitalization at the end of 2001 was EUR 75 million.

The average monthly trading was 101 793 shares. The value of shares traded during 2001 was EUR 6.3 million. The lot size in HEX for BioTie's shares is 100.

The main shareholders own 13,699,230 shares, i.e., 73.7 % of shares.

## Litigation

On 4 January 2000, the Company was served a summons concerning legal action initiated by Orion Corporation relating to some of the Company's patents. In the action pending in Helsinki District Court, Orion claims that the right for the patents/patent applications relating to VAP-1, CD-44, Syn-1, Syn-Therapi, Syn-Ecto and Syn-Fire inventions should be transferred to Orion. Further, Orion claims that it has the exclusive right to use the inventions, described in the said patents/patent applications in its business. On 27 April 2000, the Company submitted its statement of defense to the District Court, contesting any and all of Orion's claims. Consequently no provision has been made for legal expenses. Orion has in its reply on 29 December, 2000 added one patent (VAP-1 Amine Oxidase) to its above mentioned initial claims. On 7 May 2001 the Company gave its rejoinder, in which the company contested Orion's claim for the last-mentioned patent also. The preparatory hearing in the Helsinki district court ended in December 2001 and the main hearing started 22

January 2002. The Helsinki district court is expected to give judgement in February-March 2002.

#### Outlook for 2002

The clinical studies of BioHeparin will start during the first quarter of 2002. The second generation molecule of Biotie's VAP-1 antibody therapy program, Huvap will enter into clinical development phase mid 2002. The evaluation of Vapill lead compound is continuing. If the evaluation is positive, the company expects IND filing in the first quarter of 2003. The company continues its ongoing licensing negotiations with international pharmaceutical companies.

In 2002, BioTie will invest significantly in the BALP-technology and evaluates new application areas to the technology. The production unit of the company will be upgraded to a multi-purpose facility to enable development of antibody drugs based on novel target molecules.

A court judgement in the patent dispute with Orion Corporation is expected during the first quarter of 2002.

The growth rate of R&D expenses will slow down compared to previous year. The company is evaluating strategic options to strengthen its financial position.

#### Proposal to the Annual General Meeting

The Board of Directors proposes that the Company shall not distribute dividend from the financial period, and that the loss -9,702,551.66 EUR of the period will be transferred to company's equity.

## INCOME STATEMENT

1000 EUR	1.1.- 31.12.2001 12 kk	1.1.- 31.12.2000 12 kk
Revenues	0	2
Cost of sales	0	0
Gross profit	0	2
Research and development expenses	-11,336	-6,961
General and administrative expenses	-268	-162
Other operating income	1,450	946
Other operating Expenses	0	-691
Operating profit (loss)	-10,154	-6,865
Financial income and Expenses	451	-464
Profit(loss)before extraordinary items	-9,703	-7,329
Extraordinary items +/-	0	0
Profit (loss) before appropriations and taxes	-9,703	-7,329
Taxes	0	0
Net income (loss)	-9,703	-7,329

## BALANCE SHEET

1000 EUR	31.12.2001	31.12.2000
Assets		
Fixed assets and other long term investments		
Intangible assets	1,652	1,944
Tangible assets	179	223
	1,831	2,167
Current assets		
Current receivables	899	736
Securities	6,776	4,681
Cash in hand and at banks	2,705	11,275
	10,380	16,693
Total	12,211	18,859
Equity and liabilities		
Shareholders equity		
Share capital	186	186
Share premium fund	22,211	22,177
Reserve fund	0	0
Retained earnings	-7,329	0
Net income for the period	-9,703	-7,329
Capital loans	3,032	2,397
	8,396	17,430
Mandatory provisions	138	235
Liabilities		
Long term debt	1,839	504
Current liabilities	1,838	689
	3,677	1,194
Total	12,211	18,859

## CASH FLOW

1000 EUR	1.1.- 31.12.2001	1.1.- 31.12.2000
	12 kk	12 kk
Cash flow from operating Activities		
Operating profit	-10,154	-6,865
Depreciation	516	596
Change in mandatory provisions	-97	235
Change in working capital	986	-100
Financial income and expenses	451	-464
Net cash from operating activities	-8,298	-6,598
Cash flow from investing activities		
Investments	-180	-1,065
Net cash used in Investing activities	-180	-1,065
Cash flow before investing activities	-8,478	-7,663
Cash flow from financing activities		
Change in long term debt	1,969	348
Share issue	34	18,416
Net cash from financing activities	2,003	18,764
Net increase (+) or decrease(-) in cash and cash equivalents	-6,475	11,102
Cash and cash equivalents in the beginning of the period	15,956	4,854
Cash and cash Equivalents at the end of the period	9,481	15,956

## KEY FIGURES

	1.1.- 31.12.2001 12 kk	1.1.- 31.12.2000 12 kk
1000 EUR		
Business Development		
Personnel on average	68	55
Personnel at the end of period	71	65
Research and development costs	11,336	6,961
Capital expenditure	180	1,065
Profitability		
Revenues	0	2
Operating profit (loss)	-10,154	-6,865
as percentage of revenues, %	n.a.	n.a.
Profit (loss) before extraordinary items	-9,703	-7,329
as percentage of revenues, %	n.a.	n.a.
profit (loss) before taxes	-9,703	-7,329
as percentage of revenues, %	n.a.	n.a.
Balance sheet		
Cash and cash equivalents	9,481	15,956
Shareholders equity	8,396	17,430
Balance sheet total	12,211	18,859
Financial ratios		
Return on equity, %	-95,1	-77,2
Return on capital employed, %	-68.0	-59,5
Equity ratio, %	43.9	80,0
Gearing, %	-85.8	-86,8
Per share data		
Earnings per share (EPS), EUR	-0.52	-0,43
Shareholders' equity per share, EUR	0.29	0,81
Dividend per share, EUR	-	-
Pay-out ratio, %	n.a.	n.a.
Effective dividend yield, %	n.a.	n.a.
P/E-ratio	n.a.	n.a.
Share price		
Lowest share price, EUR	3.60	5.50
Highest share price, EUR	6.84	8.00
Average share price, EUR	5.17	6.80
28.12. share price, EUR	4.05	6.50

14(14)

Market capitalization, MEUR	75	121
Trading of shares		
Number of shares trades	1,221,512	1,505,682
As percentage of all	6.6	8,1
Adjusted weighted average number of shares during the period	18,587,875	17,244,365
Adjusted number of shares at the end of the period	18,589,930	18,574,930
Adjusted weighted average number of shares during the period, fully diluted	19,112,520	17,613,183
Adjusted number of shares at the end of the period, fully diluted	18,832,810	19,220,809

#### CONTINGENT LIABILITIES

1000 EUR	31.12.2001	31.12.2000
Lease commitments	442	324
Accrued interest of capital loans	305	183

Biotie Therapies Corp.  
Board of Directors

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