

# **BIOINVENT INTERIM REPORT** 1 JANUARY – 30 SEPTEMBER 2003

<b>Promising pre-clinical data for BioInvent's HIV-project.</b> The Company's antibodies against HIV prevent efficiently the spread of the virus between human cells.
<b>Progress within BioInvent's Atherosclerosis project.</b> Antibodies tested in pre-clinical animal models indicate a clear effect in the blood vessels.
New drug project initiated with a view to develop an antibody-based therapy for osteoarthritis. Rights to target structures acquired from Cartela AB.
Organisational changes implemented, increasing the Company's focus on proprietary drugs.
Net revenue for January – September 2003: SEK 50.7 million (65.3).
<b>Loss after net financial items for January – September 2003</b> : SEK -65.2 million (-29.8) and <b>loss per share after net financial items</b> : SEK -2.21 (-1.04).
Cash flow from current operations and investment activity for January – September 2003: SEK –39.4 million (-14.7). Liquid funds at the end of the period: SEK 304.6 million (376.0).

# **Operations**

BioInvent develops antibody-based drug candidates against diseases where there is a significant unmet medical need. The antibody field is a strongly growing segment in the pharmaceuticals market and is expected to account for a large portion of drug sales of the future.

BioInvent carries out proprietary drug projects for diseases such as AIDS, atherosclerosis, cancer and osteoarthritis. Within these projects, the Company is looking to find development and commercialisation partners in the early clinical phase who will have primary responsibility for continued clinical development as well as marketing and distribution. An active partnership strategy provides individual projects with the technical and financial resources that are needed without tying up excessive amounts of BioInvent's resources in individual projects.

The optimal timing for outlicensing of BioInvent's drug candidates will be determined from case to case based on cost, risk, skill requirements, and the value generated if BioInvent carries out a further phase in the process. If it is deemed favourable, projects may even be outlicensed before they have reached the clinical phases.

BioInvent's technology platform provides a solid foundation for the development of antibody-based drugs. The n-CoDeR antibody library makes it possible to quickly produce human antibodies with unique characteristics, and production takes place in the Company's facility which is approved for the manufacture of biological drugs. This technology platform is also used to develop drugs on behalf of the Company's partners. BioInvent's partners include Antisoma, Celltech, GlaxoSmithKline, Igeneon, ImmunoGen and Pharmacia Diagnostics.

# Proprietary drug projects

**HIV-infection** is one of the most serious epidemics in our time. HIV has a high degree of variability and adaptability. When a new treatment is introduced, the virus changes quickly and develops resistance to the treatment, making it ineffective. Most therapies used today develop such resistance.

The Tat protein is vital for HIV's ability to replicate itself and spread to new cells. Antibody-based drugs against the Tat protein are expected to be able to block its activity so that the number of HIV particles in the patient's blood can be reduced to such an extent that the development of the disease will be arrested. The antibodies that BioInvent develops are targeted at the parts of the Tat protein that are unchanged (conserved) between different virus strains. Moreover, the target structures circulate freely in the blood and are not directly connected to a virus particle. This prevents feedback from being sent to the virus telling it to change and adapt to avoid being affected by the antibodies.

Based on the characteristics of the unique target the Company expects that the antibodies against these conserved parts of Tat, will prevent the development of resistance and will therefore have a lasting effect.

The Company has produced product candidates aimed at these target structures. Pre-clinical tests carried out at Smittsskyddsinstitutet and the Karolinska Institute show that these can effectively prevent the spread of the virus between human cells *in vitro*. The absence of resistance is now being tested in expanded pre-clinical trials. Based on these results, the final product candidate will be selected for pre-clinical safety tests and clinical trials.

The project is based on patent rights licensed from Thymon LLC, USA,

**Atherosclerosis** can lead to blood clot formation and infarction. In the industrialised world infarction is the main cause of death. Atherosclerosis develops as a result of plaque formation in the blood vessels. This plaque may be pulled apart by the blood flow, which may lead to blood clot formation and infarction.

New research has shown strong links between oxidized forms of certain lipoproteins and the inflammatory processes that lead to plaque formation in the vessel walls. Antibodies aimed at these oxidized lipoproteins are expected to be able to stabilise plaque formation and possibly also reduce it.

The Company has identified a number of product candidates against the relevant target structures. These antibodies are being tested in pre-clinical animal models at the MAS University Hospital in

Malmö. The results show a reduction in the plaque formation in the blood vessels by approximately 50 per cent, despite the fact that the treatment has only been underway for a short period of time.

In the ensuing pre-clinical programme, the antibodies will be tested in so-called transgenic animal models that express the human target structure. The purpose of these trials is to confirm earlier results in a model that in a more secure way predicts the effects that may be expected in humans.

The patent rights is the result of research at the MAS University Hospital in Malmö and have been licensed in from Forskarpatent i Syd AB.

**Cancer** is a heterogeneous disease, which makes it more difficult to develop drugs aimed directly at tumour cells for the purpose of killing them. A new and interesting strategy is to attack the tumour's blood supply by blocking the growth of new blood vessels to the tumour – so-called angiogenesis. This starves the tumour and prevents it from growing.

BioInvent's angiogenesis project is based on the discovery of a new and central receptor called angiomotin. Angiomotin is only expressed on normal cells in new blood vessels that are developing and is believed to be crucial to the growth of new blood vessels. Aiming the antibodies at the relevant target structure prevents tumours from developing their own new blood vessels and thereby blocks their nutrient supply.

Antibodies from n-CoDeR will be tested in existing *in vitro* and *in vivo* models at the Karolinska Institute to study their ability to prevent the growth of new blood vessels in growing tumours and thereby arrest the tumour's growth.

The project is based on patent rights acquired from a research group at Karolinska Institutet.

**Osteoarthritis** is a disease of the joints caused by an imbalance in the formation of cartilage. The disease leads to stiffness, poor function and pain in joints in the fingers, knees and hips etc. The only treatment alternatives today for osteoarthritis are pain medication and surgery where the affected joints are replaced with new artificial ones.

Osteoarthritis is very widespread, and in the US alone, an estimated 40 million people suffer from osteoarthritis. For seven million of these the disease limits the activity level and causes costs for the society of over USD 60 billion.

New research has discovered that a specific protein (belonging to a class of receptors called integrins) is found in large quantities on the cells that are responsible for synthesis of new cartilage tissue. Data from this research provides strong indications that this target structure can be linked to regulation and control of the cartilage tissue in the joints. BioInvent intends to develop a therapeutic antibody that will bind the protein in question and cause an agonistic (=stimulating) effect. This kind of antibody is expected to be able to stimulate the synthesis of new cartilage tissue and thereby slow the progression of osteoarthritis.

After the end of the reporting period, BioInvent acquired the rights to develop antibody-based drugs against the specific integrin from Cartela AB. The agreement is a continuation of an earlier collaboration where BioInvent and Cartela showed that antibodies against the protein in question could be isolated in n-CoDeR. In the first phase of the project these as well as new antibodies from n-CoDeR will be evaluated in various *in vitro* and *in vivo* models to further validate the protein's relevance as a target structure for the treatment of osteoarthritis with antibodies.

#### **External development projects**

BioInvent is currently working on projects with the following important partners:

**Antisoma** Since 1996 Antisoma has been a regular consumer of BioInvent's production services. BioInvent produces several of Antisoma's antibody-based drug candidates for clinical trials, for example Pemtumomab (Theragyn) which is currently in advanced clinical phase III studies.

**Celltech** In 2002 a development partnership was initiated with Oxford GlycoSciences (OGS) through a three-year agreement for the development and commercialisation of antibody-based drugs. Celltech,

a British biotech company, subsequently acquired OGS. The scientific partnership is focusing on the cancer field.

**GlaxoSmithKline** (GSK) Under the agreement with GSK, BioInvent delivers antibodies from the n-CoDeR antibody library for GSK's research and development work in the vaccine field.

**ImmunoGen and Igeneon** Under the agreements with both the US company ImmunoGen and Austrian Igeneon, BioInvent produces antibody-based drug candidates for development programmes conducted by these customers.

## **Organisation**

In September BioInvent announced that it would be implementing a reorganization which would include staff cuts. The purpose of the reorganization is to further increase the focus on developing proprietary antibody-based drugs. This requires a changed personnel structure and a reduction in the number of staff within certain areas of expertise.

The staff reduction was concluded during the period and all costs relating to it have been deducted from the profits for the period. After the reorganization BioInvent has 104 employees compared to 125 the same time last year. 85 (104) of these are working with research and development.

#### **Protein arrays**

During the year the Company has looked at various ways of commercialising the protein array project. Limited access to venture capital and cuts in development budgets within the industry that delivers instruments for drug development, has in general curtailed opportunities for commercialisation of new projects in the field of proteomics.

Since BioInvent is concentrating its resources on developing proprietary antibody-based drugs, and taking into consideration the present climate in the market for new systems within proteomics, the Company will focus its protein array activities on one project. The purpose of the project is to develop a system for global analysis of the proteome, which may have great significance in the discovery of new target structures for drug development. The project is in an early research phase, but is expected to have sufficient market potential to be able to attract the attention of an industrial partner.

The level of activity in other projects is being reduced to certain research activity by existing academic partners where the rights to the research are controlled by BioInvent.

#### Sales and revenue

Net revenue from external development projects for January – September amounted to SEK 50.7 million (65.3). Net revenue for July – September amounted to SEK 16.9 million (25.0).

The capacity utilisation has been lower than during the same period last year. The organizational and staffing changes have resulted in a better balance between capacity and the projects the Company currently conducting.

The loss after net financial items for January – September was SEK -65.2 million (-29.8). Apart from a fall in net revenue, the result was also affected by increased research and development costs relating in particular to proprietary drug development projects. The Group's research and development costs for January – September amounted to SEK 96.6 million (80.5) after re-classification (see "Accounting Principles" below). The operating result for the period was reduced by restructuring costs in the amount of SEK 4.3 million. The concluded reorganization and staff reduction is expected to result in annual cost savings of some SEK 20 million starting from the first quarter of 2004.

Depreciation according to plan of SEK 13.4 million (9.5) was deducted from the operating result for the period.

# Financial position and cash flow

The cash flow for January – September from current operations and investment activity amounted to SEK -39.4 million (-14.7). A reduction in operating capital of SEK 14.3 million, mainly resulting from temporary variations, had a positive effect on the cash flow for this period. Apart from the weaker

result, the difference compared to the same period last year is mainly due to non-recurring payments received from customers last year. As of 30 September 2003, the Group's liquid funds amounted to SEK 304.6 million (376.0).

The shareholders' equity amounted to SEK 329.4 million at the end of the period. The Company's share capital was SEK 14.7 million and the equity/assets ratio at the end of the period was SEK 89.5 (89.6) per cent. The Group had no interest-bearing liabilities.

## Warrant programme

The Annual General Meeting on 10 April voted in favour of a warrant programme equivalent to a maximum of 300,000 shares aimed at senior executives and key individuals. So far 161,000 warrants have been acquired by the employees at market terms. The remaining warrants are reserved for future recruitments. The subscription period for the warrants is 1 January - 30 April 2007 and the subscription price is SEK 23.

At the time this report was published warrants equivalent to 516,850 shares had been issued, including those from earlier programmes, of which warrants equivalent to 144,000 shares were held by the Company for sale to the employees at market terms. The resulting maximum potential dilution is 1.8 per cent.

#### **Investments**

The Group's investments in tangible fixed assets amounted to SEK 1.5 million (7.6). Investments in intangible fixed assets amounted to SEK 0.4 (18.5).

## **The Parent Company**

The net revenue for January – September amounted to SEK 50.7 million. The parent company reported a loss after net financial items for January – September of SEK -65.2 million.

#### **Benefits for senior executives**

During the period the senior executives within the Company acquired warrants equivalent to 60,000 shares.

## **Nominating committee**

The Annual General Meeting on 10 April 2003 decided to appoint a nominating committee consisting of the Chairman of the Board as the convenor and a representative from each of the Company's three largest shareholders as of 30 September 2003. The nominating committee's assignment will be to present proposals before the next Annual General Meeting regarding the election of Board members and setting of Board fees, and, where applicable, the election of auditors and setting of auditor's fees.

The following representatives has been appointed to the nominating committee: Jörgen Lönngren (Stiftelsen Industrifonden), Ramsay Brufer (Alecta), Björn Franzon (Fjärde AP-fonden) and Per-Olof Mårtensson (Chairman of the Board). Pronova a.s. has decided to not appoint a representative.

## **Accounting principles**

This interim report has been prepared in accordance with the recommendation on interim reports (RR 20) issued by the Swedish Financial Accounting Standards Council. The accounting principles are the same as those used in the preparation of the most recent annual report. From 1 January 2003, however, a re-classification was made in the income statement whereby the item "Cost of goods and services sold" has been removed. This was done to achieve a better representation of the Group's operations. The change has not had any impact on the result.

## **Upcoming financial reports**

BioInvent will present the following financial reports:

Financial statement for 2003

12 February 2004

# Consolidated income statement in brief (SEK thousands)

	3 MONTHS 2003 July-Sept.	3 MONTHS 2002 July-Sept.	9 MONTHS 2003 JanSept.	9 MONTHS 2002 JanSept.	12 MONTHS 2002 JanDec.
Net revenue	16,861	25,004	50,712	65,293	87,053
Operating costs					
Research and development costs	-30,307	-27,731	-96,562	-80,535	-111,682
Sales and administrative costs	-9,779	-7,700	-28,518	-27,165	-37,983
Other operating revenue and costs	_9	42	<u> 197</u>	660	<u>196</u>
Operating profit/loss	-23,216	-10,385	-74,171	-41,747	-62,416
Profit/loss from financial investments	2,434	4,502	8,959	11,942	16,250
Profit/loss	-20,782	-5,883	-65,212	-29,805	-46,166
Earnings per share, average no. of shares, SEK*					
Before dilution	-0,71	-0,20	-2,21	-1,04	-1,60
Average no. of shares					
Before dilution (thousands)	29,476	29,476	29,476	28,761	28,939
After full dilution (thousands)	29,508	29,476	29,505	28,763	28,940

<sup>\*</sup> The outstanding warrants lead to no dilution of earnings per share as a redemption to shares would lead to an improvement of earnings per share.

# Consolidated balance sheet in brief (SEK thousands)

	2003 30 Sept.	2002 30 Sept.	2002 31 Dec.
Assets	<i>во вери</i>	о вери	or bee.
Fixed assets			
Intangible fixed assets	15,379	16,960	19,726
Tangible fixed assets	36,642	40,132	43,816
Current assets			
Inventories etc.	2,961	2,367	2,827
Short-term receivables	8,332	22,688	25,584
Liquid funds	304,596	376,006	343,584
Total assets	367,910	458,153	435,537
Shareholders' equity and liabilities			
Shareholders' equity	329,405	410,611	394,250
Short-term liabilities	38,505	47,542	41,287
Total shareholders' equity and liabilities	367,910	458,153	435,537

# Consolidated cash-flow statement in brief (SEK thousands)

	2003	2002	2003	2002	2002
	July-Sept.	July-Sept.	JanSept.	JanSept.	JanDec.
Current operations					
Operating profit/loss	-23,216	-10,385	-74,171	-41,747	-62,416
Depreciation	4,504	4,768	13,429	9,548	13,475
Interest received and paid	2,434	4,502	8,959	11,942	16,250
Cash flow from current operations before change in					
working capital	-16,278	-1,115	-51,783	-20,257	-32,691
Change in working capital	1,787	-5,644	14,336	31,733	22,122
Cash flow from current operations	-14,491	-6,759	-37,447	11,476	-10,569
Investment activity					
Acquisition of intangible fixed assets	-	-9,258	-425	-18,501	-22,501
Acquisitions of tangible fixed assets	-237	<u>-2,742</u>	<u>-1,483</u>	<u>-7,631</u>	<u>-14,008</u>
Cash flow from investment activity	-237	-12,000	-1,908	-26,132	-36,509
Cash flow from operations	-14,728	-18,759	-39,355	-14,656	-47,078
Financing activity					
Warrant premiums*	-	-	367	_	-
New share issues				52,000	52,000
Cash flow from financing activity	-	-	367	52,000	52,000
Change in liquid funds	-14,728	-18,759	-38,988	37,344	4,922
Liquid funds at end of period	304,596	376,006	304,596	376,006	343,584

<sup>\*</sup> Premiums, not exercised warrants

Change in shareholders' equity for the Group (SEK thousands)

	Share capital	Share premium reserve	Other restricted reserves	Accumulated loss	Total
Shareholders' equity on 31 December 2001	14,072	445,170	100	-70,926	388,416
Directed new share issue Transfer between restricted	666	51,334			52,000
and unrestricted reserves		49,181	-100	-49,081	0
Profit/loss for the period				-29,805	-29,805
Shareholders' equity on 30 September 2002	14,738	545,685	0	-149,812	410,611
Profit/loss for the period				-16,361	-16,361
Shareholders' equity on 31 December 2002	14,738	545,685	0	-166,173	394,250
Transfer between restricted					
and unrestricted reserves		-166,174	1	166,173	0
Warrant premiums		367			367
Profit/loss for the period	_			-65,212	-65,212
Shareholders' equity on 30 September 2003	14,738	379,878	1	-65,212	329,405

The share capital as of 30 September 2003 was 29,475,556 shares, each with a nominal value of SEK 0.50.

#### **Key financial ratios**

	2003 30 Sept.	2002 30 Sept.	2002 31 Dec.
Shareholders' equity per share at end of period, SEK			
Before dilution	11.18	13.93	13.38
After full dilution	11.16	13.93	13.38
Number of shares at end of period			
Before dilution (thousands)	29,476	29,476	29,476
After full dilution (thousands)	29,505	29,478	29,476
Equity/assets ratio, %	89.5%	89.6%	90.5%
Number of employees at end of period	104	125	130

#### *Lund, 16 October 2003*

#### Svein Mathisen, President and CEO

We have briefly examined this interim report for the period 1 January 2003 – 30 September 2003 in accordance with the recommendation issued by the Swedish Institute of Authorised Public Accountants (FAR). A brief examination is very limited compared to a full audit. We have found nothing to indicate that this interim report does not meet the requirements of the stock exchange and annual accounts laws.

Lund, 16 October 2003

#### ERNST & YOUNG AB

#### Åke Stenmo Authorised Public Accountant

#### **Contact:**

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