# BIOINVENT ANNUAL REPORT

2002





# BioInvent in brief

Antibodies today are a strong growth segment within the pharmaceuticals market and are expected to account for a major portion of drug sales in the future.

BioInvent will be a leading player in this market by developing antibody-based drug candidates against diseases where there is a great need for treatments.

Partnerships are a prerequisite for success. BioInvent works with partners that provide access to interesting target structures for antibody-based drugs and that contribute to resource-intensive clinical development, marketing and distribution.

BioInvent's operation is based on the entire chain, from the n-CoDeR antibody library for fast and efficient selection of human antibodies, to production in a facility that is approved for manufacturing biological drugs.

This platform is the starting point for the development of the Company's own drug candidates as well as development partnerships with international pharmaceutical and biotech companies. The year in brief

2002

- • BioInvent is developing drugs against arteriosclerosis and HIV. Rights acquired from prominent research groups in Sweden and the US.
- • New customers. Three-year agreement with Oxford GlycoSciences (OGS) for joint development of antibody-based drugs. Other new customers in 2002 include CellControl Laboratories AG and Pharmacia Diagnostics AB.
- • New agreements for increased cooperation with existing customers. Important expansion of partnerships with GlaxoSmithKline Biologicals, ImmunoGen and Igeneon.
- • Net revenue for January December **2002** increased to SEK 87.1 million (58.3).
- • Cash flow from current operations and investment activity for January December 2002 amounted to SEK -47.1 million (-74.8). Liquid funds at year end: SEK 343.6 million (338.7).
- • Loss after net financial items for January December 2002: SEK -46.2 million (-43.5).

# **Contents**



# Stronger focus on products

BIOINVENT ANNUAL REPORT 2002

In 2002 we made important progress in implementing our strategy as a drug development company. Two new agreements have laid the foundation for BioInvent's internal development of antibody-based drugs against arteriosclerosis and HIV – two disease areas that are in great need of improved treatments.

BioInvent has also been successful as a partner in other types of projects through increased cooperation with new and existing partners.

**Internal drug projects** BioInvent has been focusing strongly during the year on gaining access to unique target structures and developing antibody-based drugs against these. The overall strategy is to find target structures from academic or other external innovative environments. BioInvent is concentrating on disease areas where the need for treatments is great.

The Company is looking to find a development and commercialisation partner, in the early clinical phase, who will have primary responsibility for continued clinical development, 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. This enables BioInvent to build a portfolio of drug candidates with a favourable risk profile without being too dependent on an individual project's success.

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 in a further phase in the process being carried out by BioInvent. If it is deemed favourable, projects may even be outlicensed before they have reached the clinical phases.

The Company's processing and production capacity make it possible for the projects to generate greater value, because the products, apart from pre-clinical and clinical documentation, will include manufactured materials and the necessary processing and manufacturing documentation. Our partners will thus have access to a product concept where several important technical requirements are met so that they can focus on efficient clinical development and commercialisation.

## New type of drug against HIV

In 2002 BioInvent acquired the rights to develop and commercialise antibody-based drugs against HIV. The Company is focusing on special target structures on the so-called Tat protein.

The Tat protein is vital for the HIVs ability to replicate itself. Antibody-based drugs against these target structures are expected to be able to block Tat activity so that the number of HIV particles in the blood of the patient is reduced significantly.

A number of potential product candidates have been selected from the Company's antibody library. In a first pre-clinical phase, the ability to reduce Tat activity *in vitro* is being tested.

# New type of drug against arteriosclerosis

BioInvent has also acquired the rights to develop antibody-based drugs against target structures associated with arteriosclerosis. Cardiovascular diseases are a major medical problem and cause over 50 per cent of all deaths in the Western world. Modern research in this field is focusing to a great extent on understanding inflammatory processes and the role of the immune system in the development of arteriosclerosis.

BioInvent's project is in line with this approach. The research group behind the target structures has shown that there are strong links between these target structures and the inflammatory processes that lead to plaque formation in the vessel walls.

The expectation is that antibodies aimed at the relevant target structures will be able to stabilise the plaque formation and possibly also reduce it. Preliminary tests on animals support this hypothesis. A number of product candidates will be tested in further *in vivo* tests in a first pre-clinical phase.

**External development projects** Partnerships are a prerequisite for success. BioInvent has acted as a partner in the development of antibody-based drugs for a considerable length of time. This activity has also enabled BioInvent to develop proprietary drugs. As a partner and supplier to others, we have been able to create the technical platform – including library technology and processing and production expertise – which we are now using to generate value in our own projects. The development of a proprietary drug is a way of ensuring that we optimise the benefits of the knowledge and technology we have established and in which we have invested consistently.







Collaboration with others, however, is and will remain crucial to our success. We are therefore maintaining our flexible approach and continuing to play an important role in external development projects. For BioInvent this is also a way of managing the financial risks associated with our own development processes.

In 2002 several new partnership agreements were reached and existing ones were expanded. BioInvent currently works with the following important partners:

## Oxford GlycoSciences

In 2002 a development partnership with Oxford GlycoSciences (OGS) was initiated in the form of a three-year agreement for the joint development and commercialisation of antibody-based drugs. Under the agreement, OGS will deliver at least five antigens per year and BioInvent will produce antibodies against these. BioInvent can select one product candidate per year for joint development. OGS will be responsible for the clinical development and commercialisation of the remaining product candidates. The partnership is focusing on the cancer field.

# GlaxoSmithKline Biologicals (GSK)

BioInvent and GSK extended their development services agreement considerably in February 2002. Under the new agreement, which will last for three years, BioInvent will deliver antibodies from n-CoDeR for GSK's research and development work.

» The development of proprietary drugs is a way of ensuring that we optimise the benefits of our knowledge and technology«

## ImmunoGen

BioInvent's collaboration with the US-based ImmunoGen was extended in December 2002 to include a new agreement for cGMP manufacturing of an antibody. During the year, BioInvent successfully manufactured another antibody for ImmunoGen. Both of the antibodies are included in product candidates in the cancer field

## Igeneon

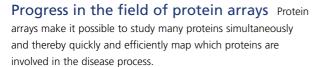
In December 2002 BioInvent extended its collaboration with the Austrian company Igeneon. The agreement is for cGMP manufacturing of antibody-based drug candidates in the cancer field. BioInvent is currently working with two of Igeneon's product candidates.

### **Antisoma**

Another collaboration that developed well in 2002 was an agreement with the UK company Antisoma. Antisoma entered into an agreement in the autumn with the pharmaceutical giant Roche which attracted much attention. This agreement includes licensing of a number of product candidates produced by BioInvent.

New customers in 2002 include CellControl Laboratories AG and Pharmacia Diagnostics AB.





Protein arrays can be used in research and development, for example, to identify new target structures or in diagnostics where several parameters need to be studied simultaneously.

BioInvent has an important competitive advantage in the form of its antibody library, n-CoDeR. The antibodies from BioInvent's library are constructed in such a way that they have very good potential to tolerate the strains of being used on a protein array.

In 2002 BioInvent focused on developing important technology components in cooperation with the Company's academic network. Progress has been made that strengthens the project's commercial potential. In 2003 BioInvent will continue to look into what form commercialisation should take.

# Markets and the external environment

Sales of antibody-based drugs increased to an estimated USD 4 billion in 2002, compared to USD 3 billion in 2001 and new products were launched onto the market. Furthermore, numerous product candidates – around 270 – are under clinical development. This makes antibodies the largest category of protein-based drugs.

In the fourth quarter of 2002 Humira, the first antibody-based drug that was developed with the help of library technology, was launched. This supports the idea of the antibody field as an area that will contribute to the development of many drugs of the future.

The negative economic trend has hampered business activity in this sector. We believe, however, that the pharmaceutical industry will continue to require new product candidates to meet growth goals, which increases BioInvent's prospects of implementing its business model.

**Stronger finances** In 2002 the Company became stronger financially, despite considerable investments and the fact that many targets were reached.

BioInvent currently has adequate financing. We hold a strong position and have guaranteed our access to several interesting target structures. These factors enable us to be confident about our progress in 2003.

**Thank you** Finally, I would like to thank everyone who has contributed to BioInvent's development during another exciting year – both our employees and our partners.

Svein Mathisen, President and CEO BioInvent International AB (publ.)



# BioInvent's business concept and strategy

# **Business concept**

BioInvent is developing antibody-based drugs based on a leading technology platform.

BioInvent will be the best partner both for parties with unique ideas as well as for major pharmaceutical companies.

BioInvent is active in a field where the ultimate purpose is to prevent, alleviate and cure illnesses. BioInvent's vision is, by the end of this decade, to be a leading and successful antibody-based drug development company, have several product candidates under development and, in cooperation with strategic partners, have one or more products ready for launch and/or registration.

Three types of projects To achieve its goals, BioInvent works with three different types of development projects – all of them aiming to bring new, innovative antibody-based drugs to the market. The types of projects differ in terms of the way that BioInvent participates in the value chain and the extent of its participation.

The simplest project type involves providing development services where the Company delivers crucial technology as part of a partnership programme. This may involve the production of materials for all clinical phases or basic research tools for the validation of new target structures.

In the case of development partnerships, BioInvent and its partners have a broader collaboration in the development of anti-body-based drugs. BioInvent's task is to select and optimise product candidates aimed at the target structures that the partner delivers and to produce the clinical material, while the partner is responsible for pre-clinical and clinical development.

In both of these types of projects, the partner owns the product and is responsible for commercialisation.

In order to generate as much value as possible, BioInvent also develops proprietary drug candidates against diseases where there is a great need for treatment. The Company's overall strategy is to find target structures in academic or other innovative external environments. BioInvent gains control of the target structures in question through licensing agreements.

In early clinical phases the product candidates are then normally outlicensed to a development partner who has overall responsibility for continued clinical development and for marketing and distribution.

**Partnerships as strategic choices** Partnerships are a prerequisite for success. BioInvent's business model is dependent upon collaboration with partners in several areas:

- For access to target structures resulting from a strategic decision not to create the Company's own development programme for the discovery of new target structures.
- In clinical phases to guarantee that each project receives the technical and financial resources that are required, without tying up excessive amounts of BioInvent's resources in individual projects.
- By acting as a partner and supplier to customers that require the knowledge and capacity that BioInvent possesses.







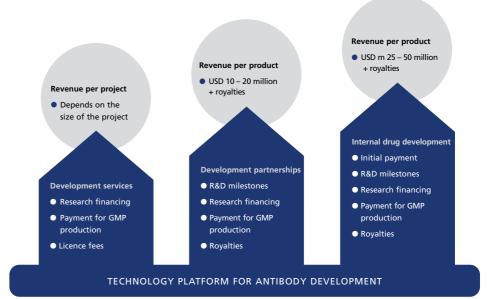
The business model has many benefits. The objective of the business model is to achieve a balance between the risks the Company takes today and the growth potential that the project portfolio represents. This balance will be achieved through:

- Multiple revenue sources due to the fact that the project portfolio contains projects that are customer-financed and are highly profitable for Biolnvent, as well as Biolnvent's own projects that provide prospects for greater value growth in the longer term.
- Less dependence on the success of an individual product candidate due to its ability to participate in many product development projects.
- Long-term value growth can be guaranteed as soon as success is achieved in a few of the projects in which the Company is participating.

**Revenue model** The three types of projects involve different forms of payment. The aim is for the current strategy over time to generate a balanced cash flow through revenues and partnership financing. The Company's long-term profitability is guaranteed through royalties and milestone payments from projects that successfully reach the market.

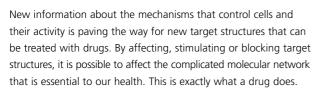
Three types of revenue:

- Research financing in the form of payment for a number of researchers who work with customers' projects.
- Payment for the production of antibodies.
- *R&D milestones* consisting of payment from customers when goals are reached.
- Licence fees and initial payments in the form of fees for access to the Company's technology.
- Royalties involving payment of a percentage of the sales of the end product. Royalties will vary, depending largely on the type of project and when the product candidate is outlicensed.



The figure shows BioInvent's revenue model for the various types of projects. The amounts are estimates and relate to development projects that go as far as the registration phase.

# Antibodies make ideal drugs



The networks are very complicated. If you affect one function, there is a palpable risk that you will affect another. This is commonly known as side effects.

**Part of the immune system** Antibodies are part of the immune system and are among the human body's most important defence mechanisms against diseases.

Each antibody seeks out and binds to "its own" corresponding antigen – a characteristic that makes antibodies ideal for the treatment of a number of diseases. Antibodies are already being used to treat cancer and infectious diseases.

Antibodies are the most sophisticated molecules created by nature in terms of their ability to bind to various substances. Human antibodies are particularly suitable as drugs since they are perceived as coming from the human body and already have a biological function in the body.

## **ANTIBODIES**

Antibodies form part of the body's immune system, protecting us from attack by the foreign microorganisms that we are constantly subjected to.

Antibodies have played an important role in medicine for some time. They were used for the first time back in 1888. One of the earliest applications was a serum against pneumonia.

Antibodies seek out, recognise and bind with high precision and specificity to the very structure they were once produced to fight. The structures that stimulate the body to produce antibodies are substances that are foreign to the human body called antigens. Antigens can be virus proteins, bacterial proteins or other components of contagions such as toxins. Cancer cells often have surface structures that are not present on normal cells and may therefore be perceived as foreign to the body.

When an individual is exposed to an antigen, the immune system, which has, among other things, antibody producing B cells, is activated. The B cells then begin to produce specific antibodies against the antigen.

The immune system also develops a memory for the antigen. This is shown through an increase in the production of antibodies with raised specificity when the individual is exposed to the antigen again. Vaccination is an example of how we can use this memory function in the immune system.

Antibodies, or immunoglobilins as they are also called, are large proteins, larger and more complex molecules than traditional pharmaceutical substances. The part of the antibody that recognises an antigen is only a tiny part of this molecule and is called its Complementarity Determining Region (CDR).

To reduce the complexity and facilitate development, researchers working with antibody development often work with fragments of whole antibodies – usually in the so-called single chain and Fab format. Both of these contain the vital CDRs.

The natural role of antibodies is to bind to the contagion, the cell or substance that carries the antigen and render it harmless. This happens when the antibody communicates the binding of the contagion to cleaning cells such as macrophages, when it binds so-called natural killer cells to the antigen-expressing cell or when it activates a cascade of enzyme activity on the cell's surface, leading to the death of the cell.

Antibodies with a therapeutic purpose are produced when a single antibody-producing cell is multiplied on a large scale. In this way exact copies, or monoclonal antibodies, can be produced on a large scale. This principle was discovered in 1975 and resulted in a Nobel Prize in 1984.

Monoclonal antibodies can be used for a therapeutic purpose in many ways, for example by seeking out and binding to their specific antigen and using natural mechanisms to remove or kill the intruder or the cell that carries the antigen, such as a cancer cell. In order to kill cancer cells, a strategy is also used whereby the antibody's target-seeking characteristics are used to transfer substances such as radioactive isotopes to a tumour in order to kill it.

The target-seeking and specific binding abilities of antibodies are being used to an increasing extent. These can be used to block undesired protein interactions that cause diseases, such as inflammatory and autoimmune diseases, to develop.





Proteomics is the study of proteins and how they work together. Significant advances have been made in proteomics since the human genome was mapped, but this is only the beginning.

There are hundreds of different types of cells with over 10,000 proteins in each. Altogether, there are believed to be 300,000 – 500,000 different proteins in the human body, many of which could be potential target structures. Today's drugs, however, are aimed at no more than 420 target structures.

Advances in proteomics will provide the pharmaceutical industry with access to an estimated 1,000 – 10,000 potential target structures which are suitable for treatment with antibodies. However, this will take time. Even though the road from potential to validated target structures is long, there is no doubt that this progress has opened a new door for drug development.

**Strong growth market** Annual sales in the total prescription drugs market are at around USD 300 billion. The growth rate is around 10 per cent per year.

Up to now, antibody-based drugs have accounted for only a

fraction of sales, even though their growth rate is several times higher. To date, there are twelve FDA approved antibody-based drugs. Sales of these in 2002 amounted to just over USD 4 billion, compared to just under USD 3 billion in 2001.

The market develops very well. The main areas are still cancer and autoimmune/inflammation, and the flow of new drug candidates in clinical phases is strong.

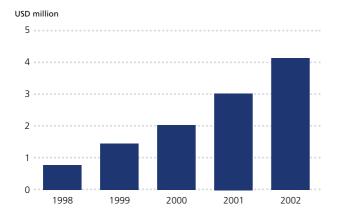
In 2002 Humira, the first antibody-based drug developed with the help of antibody library technology, was launched. The previously approved therapeutic antibodies, Rituxan and Remicade, have now passed the blockbuster level with over USD 1 billion in annual sales.

# A change in the competitive environment

Historically, BioInvent has mainly competed with two types of companies: contract producers and companies that focus on delivering antibody technology.

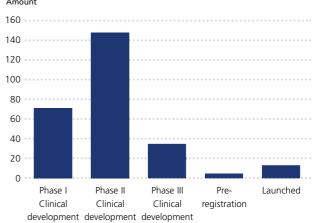
With a stronger focus on product development, the competitive picture is changing and BioInvent's current competitors are all companies developing drugs against the same diseases/target structures, regardless of whether these are antibody-based or not.

# SALES OF APPROVED ANTIBODY-BASED DRUGS



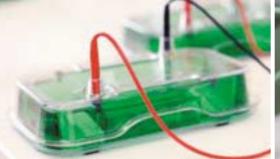
Source: The Company's analysis.

# ANTIBODY-BASED DRUGS IN CLINICAL DEVELOPMENT PHASES



Source: PharmaProjects and the Company's analysis.







# Development of antibody-based drugs –

**various phases** The development of antibody-based drugs is based on target structures. The therapeutic relevance of the target structure in the course of a disease may be validated in varying degrees. A target structure that is not documented, in terms of its role in the course of a disease, must be subjected to an evaluation and validation process where an analysis is conducted of how suitable the structure is for treatment with drugs. The amount of time this takes varies greatly from case to case.

When suitable target structures have been identified and validated, antibody candidates against these are selected from n-CoDeR. In the process the ability of individual antibodies to bind to, and carry out the desired function against, the target structure is studied.

When the candidates have been identified, the actual process of product development begins with pre-clinical studies of the candidates' effects and side effects in various models. The subsequent clinical tests on humans are usually carried out in three phases starting with Phase I studies of how the drug is absorbed and distributed in the body and how it is broken down and secreted in healthy research volunteers. This is followed by Phase II studies of the clinical effect on smaller groups of patients which are then followed by Phase III studies that are larger in scope and carried out on large groups of

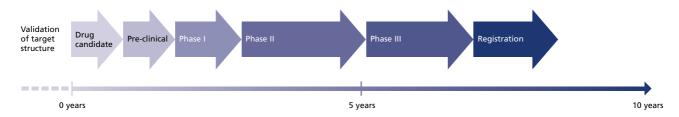
patients. In this phase, the effects and side effects are also compared with those of the main drugs currently used. After successful clinical studies, applications are submitted to the relevant authorities to have the drug approved and registered for marketing and sale.

Parallel to the clinical development process, studies are carried out on the properties of the drug candidates in relation to the prospects of cost-efficient production of raw materials and finding a suitable means of distributing the drug. Antibody-based drugs are produced in a living host cell. The cell line and the associated production process must be developed, optimised and documented so that the drug can be registered.

# Platform that meets major requirements

BioInvent's technology platform meets important requirements of players in this market. The ability to quickly select an appropriate product candidate against a given target structure and to produce it in a flexible facility, combined with BioInvent's many years of experience in participating in its customers' development projects, provides a major competitive advantage in the process of moving from idea to antibody-based drug as efficiently as possible.

# ESTIMATED TIME REQUIRED FOR DEVELOPING AN ANTIBODY-BASED DRUG FOR A SELECTED TARGET STRUCTURE



The times given for the various phases are based on experiences from PharmaProjects and the Company's analysis.



# Development with great potential

BioInvent has extensive expertise and experience in participating in antibody-based drug development processes. Combined with the Company's technology platform, this is the starting point for both internal drug development projects and various types of collaboration with partners.

# BioInvent's internal drug development

BioInvent is developing proprietary drug candidates in order to generate maximum value for the Company. Initially this is being done through target structures that are suitable for treatment with antibodies.

BioInvent is focusing on indication areas where there is a great need for treatments, such and cardiovascular diseases, cancer and infectious diseases.

BioInvent has built up a reputation in the industry which means that researchers and companies with interesting target structures contact the Company themselves. BioInvent also systematically looks for target structures among leading research groups in academic environments and within the rest of the biotech community.

Careful analysis The analysis of conceivable target structures begins with an assessment of their potential for treatment with antibodies. The target structures are evaluated taking into account the biological, therapeutic and legal aspects, among others. The analysis is concluded with an assessment of the market, potential, competition and patent situation. To date, two projects have been approved and have passed through the eye of the needle, i.e. contract negotiations with the source. These are projects that will develop new types of drugs against HIV and arteriosclerosis. Analysis and negotiations are, of course, constantly underway for a number of projects.

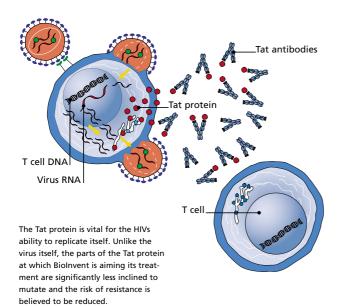


New type of drug against HIV HIV is one of the most widespread epidemics to affect mankind up to now. Although there are treatments that provide relatively good results today, there is no cure. The development of resistance to the treatments and unpleasant side effects are a great source of concern for both the healthcare sector and the affected individuals.

The resistance is the result of the HIVs great variability and adaptability. When treatment is started, the virus changes quickly to adapt to the new conditions, thus rendering the treatment ineffective.

The virus has the ability to force its way into certain cells in the immune system and take control over the gene pool. Instead of producing important proteins for the immune system, virus particles are produced. In order for the virus to replicate itself, the cell must be activated. The virus carries its own protein (Tat = transactivator of transcription), which can activate the cell and also convert its production of proteins from cell proteins to virus-specific proteins. In this way the virus can take control of the protein synthesis in the cell and convert it into virus production. The Tat protein also leaves the infected cell and activates immune cells around it. This makes the activated cells receptive to virus infection and they become programmed for virus replication. The Tat protein is thus vital for the HIVs ability to replicate itself.

# FIGHTING HIV VIA THE TAT PROTEIN



Studies show that a disease will develop more slowly in people who spontaneously develop antibodies against Tat. BioInvent's antibodies aimed at Tat are expected to be able to inhibit Tat activity and thereby prevent the spread of HIV to new cells thereby reducing the extent of the virus to arrest the development of the disease.

Antibodies aimed at proteins associated with HIV have been tested before in clinical trials but have not provided the desired protection. The reason for this is believed to be that HIV mutates and changes very quickly and therefore releases itself from the intended grasp of the antibody. Another common factor in these early approaches is that the antibodies were aimed at the virus components on the surface of the virus particle. When the antibodies can no longer bind to the mutated virus particle, it could no longer be affected by the antibodies and therefore it escaped from the protection that they were supposed to provide.

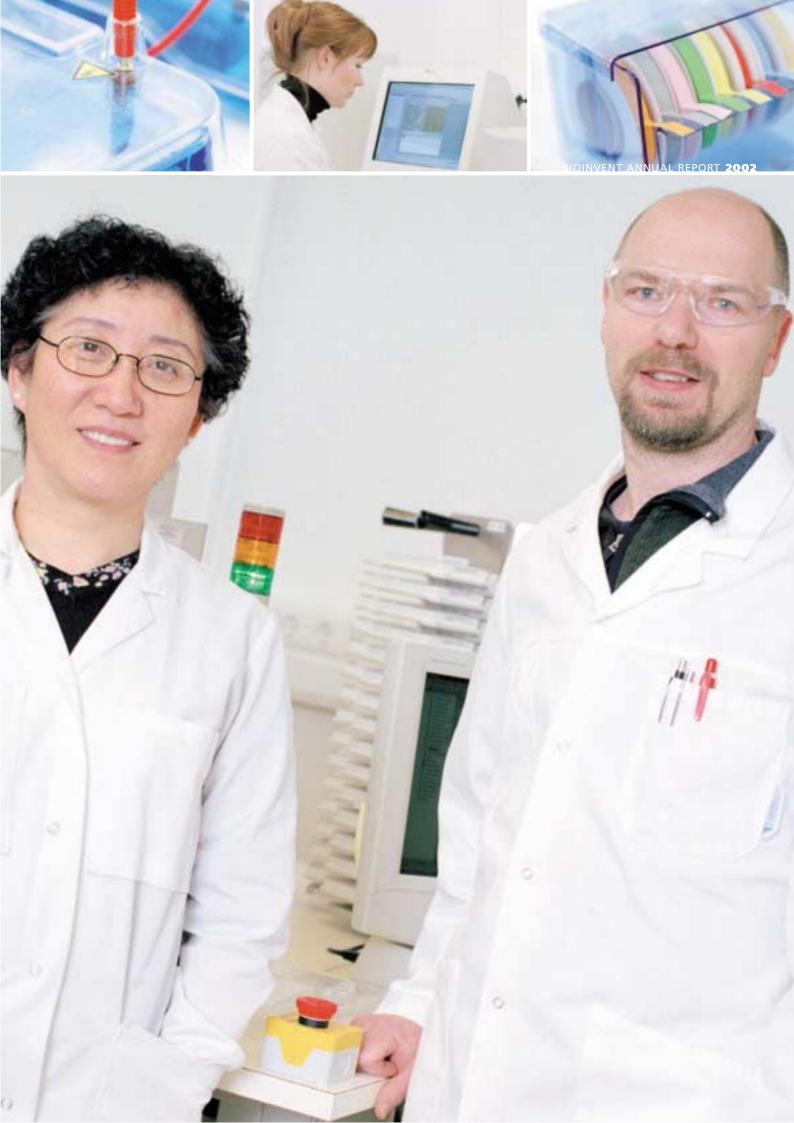
Biolnvent's approach differs in several important ways from earlier ones. The antibodies developed by the Company are aimed at the Tat protein. By binding to the Tat protein they are expected to neutralise the Tat protein's transactivating capacity and thereby strongly reduce the ability of all of the virus particles to replicate themselves – regardless of whether they are mutated or not. This approach is thus not sensitive to the virus's ability to mutate and change, which is where other approaches have failed.

If the Tat protein itself mutated, variations would of course arise that specific antibodies would not be able to inhibit. The Tat protein has also been shown to vary to some extent among different strains of HIV, although some parts of the protein are constant in over 95 per cent of all strains.

Another unique characteristic of BioInvent's treatment method is that it is aimed at these constant parts of the Tat molecule, and consequently the antibodies against Tat with which BioInvent is working will probably have a lasting effect. Although the cells that are already infected will not be affected, the risk of new cells being infected with the virus will be reduced. In addition, the number of virus particles in the blood can probably be reduced to such a low level that the development of the disease will be arrested and the patient will become symptom free.

A number of product candidates have already been selected from the Company's antibody library. In a first pre-clinical phase the ability of these to reduce Tat activity *in vitro* is being tested.

BioInvent has acquired the rights from Thymon LLC in New Jersey, USA. This company was formed in 1996 by Dr. Gideon Goldstein who was involved in the development of the first therapeutic monoclonal antibody, Orthoclone OKT3TM, during his tenure at Ortho Pharmaceutical Corporation.



# New type of drug against arteriosclerosis

BioInvent has acquired the rights to develop antibody-based drugs against oxidised forms of certain lipoproteins, which are target structures associated with arteriosclerosis. Cardiovascular diseases are a major problem and cause over 50 per cent of all deaths in the Western world. Modern research in this field is focusing to a great extent on understanding inflammatory processes and the role of the immune system in the development of arteriosclerosis.

BioInvent's project is very much in line with this approach. The research group behind the target structures has shown that there are strong links between these target structures and inflammatory processes that lead to plaque formation in the vessel walls and future complications, such as infarction and stroke. There are signs that indicate that the spontaneously formed antibodies against these oxidized lipoproteins in humans can protect against diseases in the future.

Plaque is formed when fat particles stored in the vessel walls

cause inflammation, cell death and scar tissue. There is a risk that this plaque will be broken down by the blood flow and may lead to the formation of blood clots and infarction.

BioInvent feels confident that antibodies will be able to stabilise the plaque formation and possibly also reduce it. Preliminary *in vivo* tests support this hypothesis. BioInvent plans to develop therapeutically active human antibodies against the target structures associated with disease. The administration of these antibodies to patients is expected to be able to protect against the formation of blood clots and infarction.

Biolnvent has acquired the rights to these unique target structures from Forskarpatent and they are the result of research conducted by Professor Jan Nilsson and his team at the MAS University Hospital in Malmö, Sweden. The team has been studying the relationship between arteriosclerosis and the immune system for many years. They have found evidence that antibodies have a protective role in the development of arteriosclerosis.









**External development projects** In external development projects, BioInvent develops drugs with a partner. The aim is to play an important role in a large number of development projects. This is also an effective way of further increasing the Company's expertise and experience.

**Development partnerships** In development partnerships, Biolnvent participates in the development of drugs with a partner. The partner is responsible for target structures and the pre-clinical and clinical programme as well as commercialisation. Biolnvent is responsible for selection of product candidates and production of materials for the clinical programme and the associated regulatory documentation.

In development partnerships, BioInvent's partners carry the financial risk. BioInvent is paid for selecting a drug candidate from the n-CoDeR antibody library and for production of antibodies for development. Development partnerships provide BioInvent with additional revenue potential in the form of the resulting milestone payments and royalties if a drug is successfully developed.

The OGS example BioInvent started to work with Oxford GlycoSciences (OGS) back in 2001. The agreement reached was for basic research tools for evaluating the target structures from OGS's research with the help of antibodies from BioInvent. In March 2002 the partnership was expanded significantly and a three-year agreement was signed for the joint development and commercialisation of antibody-based drugs.

Under the agreement OGS will deliver at least five antigens per year and BioInvent will produce antibodies against these with the help of the n-CoDeR antibody library. The antibodies will then be manufactured at BioInvent's facility.

The agreement also involves the following:

- the opportunity for joint development of at least one new drug candidate per year, with an equal share of development costs and revenues as a result.
- milestone payments and royalties paid to Biolnvent for the other drug candidates that are developed by OGS.



**Development services** BioInvent has many years of experience of delivering vital technology for its customers' drug development programmes. This includes everything from production of materials for clinical phases to research tools based on n-CoDeR library technology.

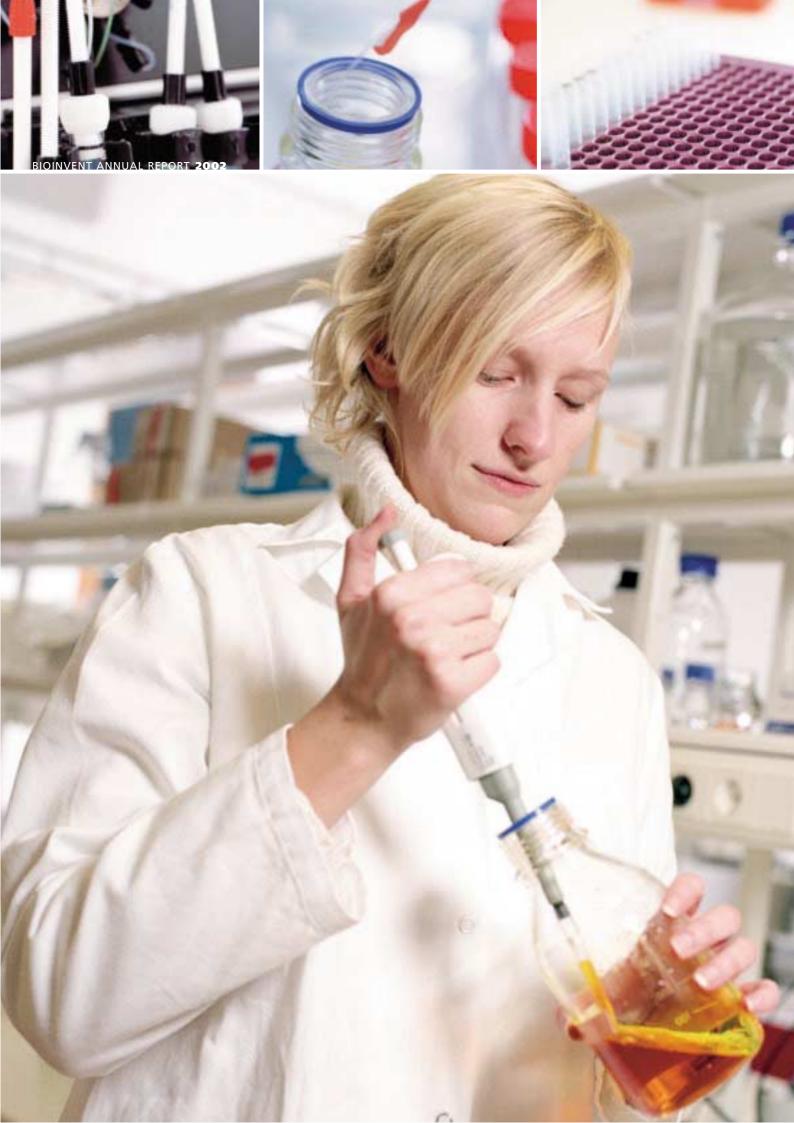
Contract manufacturing is the part of BioInvent's operation with the longest tradition in the Company. BioInvent has manufactured antibodies for customers in the pharmaceutical industry since the 1980s. Antibody manufacturing will, in all probability, be a bottleneck in the global market for many years to come.

Customers are closely tied to antibody manufacturers, because process development, production and product characterisation are time-consuming and complex procedures.

BioInvent's manufacturing collaboration with the US-based ImmunoGen was expanded in 2002. This was also the case with the Austrian company Igeneon AG. New customers in 2002 include CellControl Laboratories AG and Pharmacia Diagnostics AB.

Development services also include the selection of antibodies from n-CoDeR, whereby Biolnvent selects antibodies for customers' internal research needs.

An example of this kind of collaboration is an agreement with GlaxoSmithKline Biologicals (GSK). BioInvent significantly expanded its partnership with this company in February 2002. Under the new agreement, which will last for three years, BioInvent will deliver antibodies from n-CoDeR for GSK's research and development work.



# Advanced platform for development

BioInvent's technology platform is a solid foundation for development of antibody-based drugs – both for BioInvent and its partners. The n-CoDeR antibody library enables human antibodies with unique characteristics to be produced. Manufacture takes place in a facility that is approved for the production of biological drugs.

# n-CoDeR: antibody library with unique advantages The beginning of the 1990s saw the arrival of technology that made it possible to create entirely human antibodies. With more than 15 billion antibodies, n-CoDeR is an important tool in the development of new drugs.

n-CoDeR is a large collection of different antibody genes that are stored in bacteria in test tubes. The bacteria act as production units for the antibodies, which can then be screened to identify which antibodies bind to a specific target structure.

The library was created based on naturally occurring antibody genes. CDR loops are then isolated and copied many times (see diagram). The different CDR loops are then joined in new combinations in a single master antibody framework. This so-called CDR shuffling is the basic idea behind BioInvent's antibody library.

Every component comes from nature, but the combinations are to a large extent new. The rich variation and unique combinations make it possible to build an antibody repertoire that is greater than nature itself is able to create. BioInvent calls this "evolution beyond nature."

With its antibody library, BioInvent has successfully selected antibodies with high affinity to most types of antigens. The potential therefore exists to produce human antibodies that are well suited for therapy against most of the human target structures of interest.

**Automated process** In order to be able to generate an antibody in the library, a screening process must be carried out. If you allow the bacteria with antibody fragments to produce all of the conceivable antibodies, the volume would be so large – hundreds of litres – that it would not be possible to conduct effective, industrial screening.

Instead a technology called phage display is used. Phages are bacterial viruses that are entirely harmless to humans and that can display antibodies for antigens in the screening process.

With phage display, the entire antibody library is formatted to the phage format and the phages are then passed over a surface to which antigens/target structures have been attached. Phages with the "correct" antibodies bind to the antigen and all other antibodies are washed away. The desired antibody gene can

# The genetic code (DNA) for antibodies is isolated from the human immune system. DNA is divided into smaller parts. The parts are copied. The copied DNA is combined randomly and new antibody gene combinations are obtained in a single The new genes are collected master framework. in bacteria and a collection of more than ten billion different antibody genes makes up the antibody library.

n-CoDeR's STRUCTURE

then be isolated directly from the phage and used to multiply and produce the desired antibody in large quantities. This saves time and streamlines the screening process.

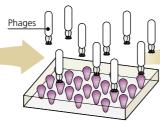
The use of n-CoDeR is well suited to automation and allows the process of antibody generation to be entirely industrialized.

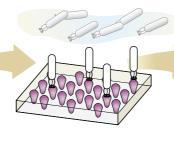
BioInvent has a robot that enables the screening of up to 20,000 antibody fragments per 24-hour period. It selects clones, carries out automatic analysis, sorts through a multitude of antibodies at a

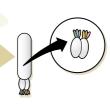
## **PHAGE DISPLAY**

- The antibody library is stored in small test tubes. Many copies of the library exist.
- The library is formatted to phage format and the phages are then passed over a surface onto which the antigen has been attached.
- Phages with antibodies that do not bind to the antigen are washed away.
- 4 Phages with antibodies that bind to the antigen can be isolated.









much higher speed, increases parallelity and reduces the likelihood of errors

# Different formats for different purposes

The n-CoDeR antibody library is constantly being developed and refined. In 2002 BioInvent presented n-CoDeR-Fab, a new antibody library built according to BioInvent's unique principles.

The new Fab format is even better suited for the development of therapeutic antibodies, because the stage from antibody fragment in the library to a complete antibody is shorter in the Fab format than in the alternative single chain format. Single chain, on the other hand, is better suited for antibodies that are to be used as basic research tools and for protein arrays.

Production resource with a key role BioInvent acts as a partner in its customer's development projects and

offers vital expertise and capacity in antibody manufacturing. The company offers, among other things, cell line development, development of manufacturing processes and manufacture in a facility that is approved for the production of biological drugs.

The production facility is a pilot plant and its greatest strengths are its flexibility and parallelity. These are important factors for companies that are involved in the development of drugs, which is a process where speed and time are often critical considerations. The facility can support around twelve Phase III programmes per year and it is currently used, among other things, for Phase III studies in the US.

The manufacturing process starts with the isolation of antibody DNA from the n-CoDeR antibody library. This is then inserted into the genome of an antibody-producing cell. The cell multiplies and a cellbank is produced and stored frozen for use in future production. When cell lines are cultivated, antibodies are produced

**n-CODER'S COMPETITIVE ADVANTAGE** There are many competing antibody technologies, but several factors make n-CoDeR highly competitive. It...

- consists only of natural components. The principle enables n-CoDeR to provide a great amount of variation;
- contains only entirely human antibodies;
- produces antibodies **entirely in the laboratory**. This increases control and productivity, since production is not affected by the natural variations that occur in animals;
- has **high affinity**, i.e. produces antibodies that bind firmly to the target;
- has **high specificity** i.e. produces antibodies with a high capacity to recognize a molecule with certain characteristics, but ignore a similar one even when they are side by side.







that are then purified in several stages. Finally, the antibodies are characterised and tested before they are released as drugs.

**Valuable experience** Through many years of experience in contract manufacturing and partnership projects, BioInvent has gained a good understanding of the regulations that apply in several different countries.

BioInvent's regulatory expertise is value-added that may prove crucial for the Company in the future. There is also a wealth of knowledge within the organisation about how to optimise documentation and how to handle factors that can have a practical impact on a project, both from an industrial and economic perspective.

If production processes or production facilities are changed, documentation is required to show that the product is the same after the change. Production for clinical development therefore requires both flexibility and great trust between the parties involved.

Effective tool to analyse proteins Analysing the proteins in the human body is a difficult task and there is a great need for a more effective tool in both the pharmaceutical industry as well as in healthcare. BioInvent is working on development of a protein array – a tool that makes it possible to study many proteins simultaneously.

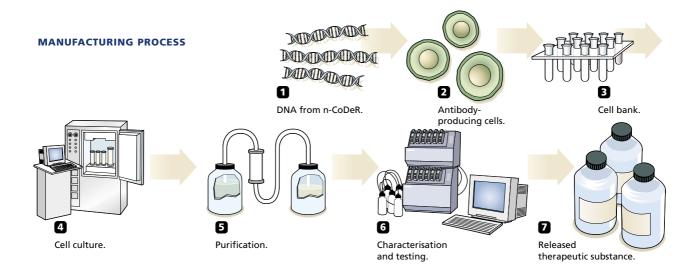
A protein array is made up of drops of antibodies on a chip the size of a thumbnail. Extract from test tissue is then added and if this contains an antigen to any of the antibodies on the array, binding will occur. The binding process can be analysed automatically. The goal is to develop an automated system to study the differences in protein content in a cell or tissue. This would make it possible to make a diagnosis and to select possible target structures for drug development.

Analysis at high speed Protein arrays can be used by pharmaceutical companies in their research and development, e.g. in the field of toxicology or in the process of identifying new target structures for drugs. Protein arrays can also be used in diagnostics when it is necessary to study several parameters simultaneously, e.g. to measure the effect of a drug on different components in the blood, or to monitor a patient undergoing treatment to be able to quickly assess results.

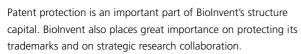
The array offers the parallelity that is necessary for high speed processes, and makes it possible to study many proteins simultaneously and thereby quickly and efficiently map protein networks or identify which proteins are involved in the disease process.

Important competitive advantage BioInvent is not the only player to develop protein arrays. However, the Company has an important competitive advantage in its n-CoDeR antibody library. Antibodies are sensitive substances, but the antibodies produced by BioInvent are constructed in such a way that they are able to withstand being used on protein arrays. Tests have shown that they can tolerate being placed on the chip and that they can be dehydrated and can survive there.

In 2002 the Company focused on developing important technology components in cooperation with the Company's academic network. Progress was made that improves the project's commercial potential.



# Structure capital ensures that value stays within the Company



The biotech industry is complicated from a patent perspective, and an active patent strategy can be crucial. BioInvent is constantly seeking to increase the number of patents to provide an effective protection for its products and technologies. New patent applications are first submitted in the UK and the US to take advantage of the differences in the US and European patent laws. Patents are then submitted in other geographical areas that are considered to be of interest.

BioInvent currently has thirteen patent families and patent applications within the field of technology for the development of human antibodies and methods for manufacturing protein arrays (see table).

Important trademark protection In addition to its patents, BioInvent has also protected several trademarks. The name "BioInvent" is protected in Sweden as the registered company name. "BioInvent" and "n-CoDeR" are protected trademarks in all countries in the EU. The Company also has trademark applications pending for these in the US and Canada.

**Strategic research collaborations** An important part of Biolnvent's strategy is to develop a research base with strong links to academic research. This has led to close collaboration with various research teams in the academic world. The goal is to expand and strengthen the network of contacts within academic research to gain access to technologies that reinforce the Company's prioritised areas.

BioInvent's collaboration with the Department of Immunotechnology at the Wallenberg Laboratory at Lund University, Sweden is particularly extensive.

# **BIOINVENT'S PATENT PORTFOLIO**

# Technology for human antibody libraries

- CDR shuffling a method for in vitro molecular evolution of the function of proteins. Approved in Australia. The patent application claims priority from 1997.
- A method for in vitro molecular evolution of the function of antibodies. The patent application claims priority from 2001.

## Identifying target structures

 Combined ligand and receptor display. Approved in the US and Australia. The patent application claims priority from 1995.

## Methods for selection from libraries

- Methods for selecting specific bacteriophages. Approved in the US, Australia and Europe. The patent claims priority from 1002
- Improved method for selection of specific phages.
   Approved in the US, Australia and Europe. The patent application claims priority from 1995.

## **Protein arrays**

 Methods for creating micro-arrays based on biological materials. The patent application claims priority from 2000.

## Other patents

- Method for producing human monoclonal antibodies.
   Approved in the US, Canada, Europe and Japan. The patent claims priority from 1986.
- In addition to the above-mentioned patents, five priority patent applications were submitted in 2002 and one so far in 2003. These applications relate to target structures for drugs for B-cell lymphoma, techniques and methods for the selection and identification of binding proteins against antigen structures in complex mixtures, techniques and methods for new library and display structures, and techniques and methods for protein arrays.

# Licensed rights

- Licensed technology from Dyax for the use of phage display technology.
- Licensed technology from Biosite for display technology linked to the Fab library.
- Licensed right to develop antibody-based drugs against a group of target structures associated with HIV.
- Licensed right to develop antibody-based drugs against target structures associated with oxidised forms of certain lipoproteins.





# Profitable staff development

BioInvent's rapid growth increases the need for management development as well as orientation and skills development for the employees. In order for BioInvent to continue to succeed, the Company needs a corporate culture with a strong focus on the strategy and business concept.

In 2002 BioInvent invested in skills development, both in general and more specifically at the individual level. The management development programme covers team building, leadership, meeting techniques and communication, as well as preventive personnel care, for example, in the form of stress management. About 30 employees participated in the 2002 project skills course and others will take the course in 2003.

During the year, a joint review of the Company's values and core values was initiated. BioInvent is a locally-based company with a local history and roots, but one that operates in a global market. The goal is to attract and keep expertise and employees who, despite differing experiences and backgrounds, share the same vision of BioInvent as a successful company.

Burnout and high incidences of absence due to illness are topical issues in Sweden today. During the second quarter, a special study was therefore conducted of the amount of overtime worked. The amount was 1.18 per cent, which is just over half of the average among private sector employees. The amount of overtime was reduced during the year.

Absence due to illness during the second quarter was at 2.3 per cent, i.e. clearly below the average for private sector employees.

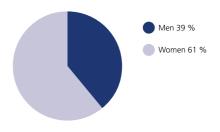
In 2002 BioInvent continued to grow, albeit at a slower pace than in the past. After two years of intensive recruitment activity, 2003 will be a year of consolidation and development of the existing employees.

The staff turnover is relatively low. Four employees left the Company in 2002.

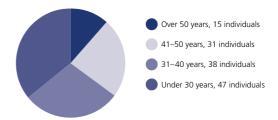
**Ethics and morals** BioInvent will act as a good member of society at all levels, i.e. with respect to the environment, the law and the economy etc. The way in which the employees and management treat each other within BioInvent is of particular importance. BioInvent has many employees with roots in different countries. BioInvent also works literally in an international environment and the blend of backgrounds of the employees is therefore both a strength and a prerequisite for success.

Naturally, neither gender, religion nor ethnicity affect the recruitment process, pay structure or any other treatment of Biolnvent's employees.

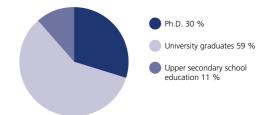
# PERCENTAGE OF MEN/WOMEN



# AGE DISTRIBUTION



## **EDUCATION**



# Financial summary

## **BIOINVENT ANNUAL REPORT 2002**

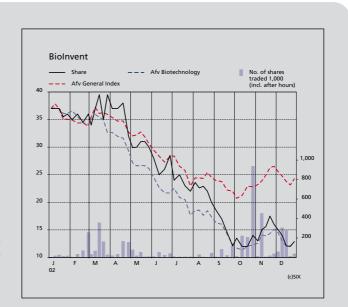
All figures are as of 31 December 2002, unless otherwise indicated.

# Share data

BioInvent International AB (publ) has been listed on the O-list of the Stockholm Exchange (Stockholmsbörsen) since 12 June 2001. In 2002 the Company received SEK 52.0 million in new issue funds in connection with a new partnership agreement with Oxford GlycoSciences. As of 31 December 2002, the Group's liquid funds amounted to SEK 343.6 million (338.7).

Number of shares29,475,556Share price (closing price)SEK 12.50Market capitalisationSEK 368.4 millionTechnology valueSEK 24.8 million

The technology value is measured as the difference between the market capitalisation and the Company's liquid assets.

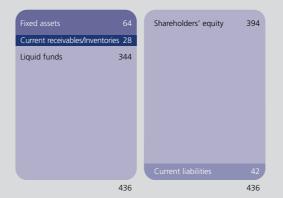


# Financial data

# 2002, SEK million

Net revenue	87
Operating loss	-62
Loss after net financial items	-46
Cash flow from current operations	-11
Cash flow from investment activity	-37
Cash flow from financing activity	52
Cash flow for the year	5
Equity/assets ratio, %	90
Number of employees at year-end	130

# Capital structure



# Ownership data

As of 31 December 2002 the number of shareholders was 1,372. On the same date, institutional investors owned 72 per cent of the shares in BioInvent International. Foreign owners held 18 per cent.

68 per cent of the shares were publicly owned. Public ownership refers to individuals that directly or indirectly own less than 10 per cent of the share capital or votes.



Shareholders	No. of shares	Percentage of capital and votes
BioInvent's management	5,509,668	18.7
Stiftelsen Industrifonden	3,953,295	13.4
Pronova a.s.	1,942,787	6.6
Alecta	1,374,450	4.7
Oxford GlycoSciences	1,331,251	4.5
Sjätte AP-fonden	1,201,237	4.1
Fjärde AP-fonden	1,188,750	4.0
Nordea Bank S A	1,089,550	3.7
Nordea Fonder	925,300	3.1
Förenade Liv	877,116	3.0
Industritjänstemannaförbundet	710,250	2.4
Other shareholders	9,371,902	31.8
Total	29,475,556	100.0

# Financial information

BioInvent endeavours to provide its shareholders with up-to-date and accurate financial information on an ongoing basis. This includes distributing printed reports and the annual report to all shareholders.

In addition to this service, current and past reports are available on the Company's website:

www.bioinvent.com. Visitors to the website can also follow the Company's development by reading current press releases etc.

## Calender 2003

Annual report 2002	27 March 2003
Interim report, January – March	10 April 2003
Annual General Meeting	10 April 2003
Interim report, January – June	17 July 2003
Interim report, January – September	16 October 2003
Financial statement 2003	12 February 2004

# Investor relations

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Jonas Källmén, CFO +46 (0)46 286 38 12 jonas.kallmen@bioinvent.com

# Five-year review

# BIOINVENT ANNUAL REPORT 2002

Income statement, SEK million	2002	2001	2000	1999	1998
Net revenue	87.1	58.3	24.1	11.0	14.2
Cost of goods and services sold	-50.2	-39.9	-24.6	-14.6	-11.7
Sales and administrative costs	-38.0	-27.5	-16.5	-8.2	-5.4
Research and development costs	-61.5	-45.3	-23.2	-13.6	-10.5
Other operating revenue and costs	0.2	0.1	1.1	0.0	0.8
Operating profit/loss	-62.4	-54.3	-39.1	-25.4	-12.7
Net financial items	16.3	10.8	4.6	0.3	0.4
Loss after net financial items	-46.2	-43.5	-34.5	-25.0	-12.3
Tax on profit for the year	-	-	-	-	-
Profit/loss for the year	-46.2	-43.5	-34.5	-25.0	-12.3
Balance sheet, SEK million	2002	2001	2000	1999	1998
Intangible fixed assets	19.7	-	_	_	-
Tangible fixed assets	43.8	40.5	22.7	11.9	4.2
Inventories etc.	2.8	1.6	1.2	7.5	4.8
Current receivables	25.6	29.8	18.9	3.7	3.5
Short-term investments	-	-	10,2	-	-
Liquid funds	343.6	338.7	141.2	20.2	25.6
Total assets	435.5	410.5	194.3	43.3	38.1
Shareholders' equity	394.3	388.4	159.6	23.7	30.1
Non-interest-bearing liabilities	41.3	22.1	34.6	14.6	8.0
Interest-bearing liabilities	-	-	-	5,0	-
Total shareholders' equity and liabilities	435.5	410.5	194.3	43.3	38.1
Cash flow and investments, SEK million	2002	2001	2000	1999	1998
Operating profit/loss	-62.4	-54.3	-39.1	-25.4	-12.7
Adjustments for depreciation and interest	29.7	18.7	7.7	1.8	1.4
Change in working capital	22.1	-13.6	1.0	3.7	-0.5
Cash flow from current operations	-10.6	-49.2	-30.4	-19.9	-11.8
Cash flow from investment activity	-36.5	-25.6	-13.9	-9.2	-2.2
Cash flow from financing activity	52.0	272.2	165.4	23.6	22.6
Increase/decrease in liquid funds	4.9	197.4	121.1	-5.5	8.6

Key financial ratios	2002	2001	2000	1999	1998
Net revenue growth, %	49.4	141.9	119.3	-22.6	11.5
Capital structure					
Net working capital, SEK million	-12.9	9.3	-4.3	-3.4	0.3
Net working capital/net revenue, %	-14.8	15.9	-18.0	-30.8	2.1
Operating capital, SEK million	50.7	49.8	18.4	8.6	4.5
Operating capital/net revenue, %	58.2	85.4	76.4	77.9	31.4
Capital employed, SEK million	394.3	388.4	159.6	28.7	30.1
Capital employed/net revenue, %	452.9	666.6	662.6	261.5	212.1
Shareholders' equity, SEK million	394.3	388.4	159.6	23.7	30.1
Capital turnover, times	0.2	0.2	0.3	0.4	0.6
Equity/assets ratio, %	90.5	94.6	82.2	54.8	79.0
Investments					
Intangible fixed assets, SEK million	22.5	-	-	-	-
Tangible fixed assets, SEK million	14.0	25.6	13.9	9.2	2.2
Employees					
Number of employees, average	124	96	55	36	31
Net revenue per employee, SEK million	0.7	0.6	0.4	0.3	0.5
Data per share	2002	2001	2000	1999	1998
Earnings per share, SEK*	•••••	• • • • • • • • • • • • • • • • • • • •	•••••	•••••	• • • • • • • • • • • • • • • • • • • •
Before dilution	-1.60	-1.69	-1.62	-1.45	-0.85
Average number of shares					
Before dilution (1,000)	28,939	25,697	21,336	17,278	14,479
After full dilution (1,000)	28,940	25,753	22,077	17,544	14,661
Shareholders' equity per share, SEK					
Before dilution	13.38	13.80	7.03	1.26	1.75
After full dilution	13.38	13.77	6.80	1.24	1.73
Number of shares at end of period					
Before dilution (1,000)	29,476	28,144	22,722	18,807	17,179
After full dilution (1,000)	29,476	28,200	23,463	19,072	17,361
Dividend	-	-	-	-	-

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

The figures in the tables are rounded to one decimal, while the calculations are made using a greater number of decimals. As a result it may appear that certain tables do not add up.

# **Definitions**

## Net working capital

Non-interest-bearing current assets less non-interest-bearing short-term liabilities.

# Operating capital

The balance sheet total less non-interest-bearing liabilities and other non-interest-bearing provisions and liquid

**Capital employed**The balance sheet total less non-interest-bearing liabilities and non-interest-bearing provisions.

# Shareholders' equity

The sum of non-restricted and restricted equity.

# Capital turnover

Net revenue divided by the average capital employed.

# Equity/assets ratio

Shareholders' equity as a percentage of the balance sheet total.

**Number of employees, average**Weighted average number of employees during the year.

## Earnings per share

Profit/loss for the year divided by the average number of shares.

**Shareholders' equity per share** Shareholders' equity divided by the number of shares at the end of the period.

# The BioInvent share

## **BIOINVENT ANNUAL REPORT 2002**

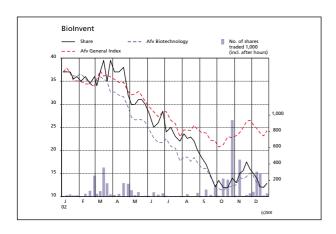
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**Share capital** BioInvent's share capital as of 31 December 2002 was SEK 14.7 million distributed between 29,475.556 shares with a nominal value of SEK 0.50 per share. On 31 December 2002 outstanding warrants equivalent to 1,259,500 shares had been issued, of which warrants for 652,650 shares were held by BioInvent for sale to employees at market terms. All of the warrants held by the Company were returned to the parent company in February 2003 and BioInvent intends to cancel them before the end of March 2003. When the shares held by the Company are cancelled and all of the remaining warrants that have been issued are exercised, the number of shares in the Company will be 30,082,406. Each share entitles the holder to one vote at shareholders' meetings and all shares carry equal rights to the Company's assets and profit.

# **Turnover and price trend** In 2002, 4.7 million Biolnvent shares were traded. Calculated as a percentage of the total number of shares at year-end, this is equivalent to a turnover in volume of 16 per cent. The average turnover per trading day was around 18,840 shares.

The quoted price for BioInvent shares fell during the year from SEK 37 to SEK 12.50, which is a fall of 66.2 per cent. This can be compared to Affärsvärlden's General Index and Affärsvärlden's index for biotech companies which fell by 37.3 and 66.7 per cent respectively during the same period. At the end of 2002 BioInvent's market capitalisation amounted to SEK 368.4 million.

A trading unit consists of 500 BioInvent shares.



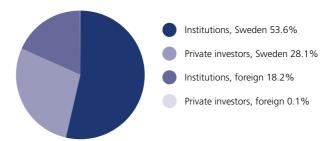
# Analysts who monitor BioInvent

Alfred Berg Fondkommission, Mattias Häggblom D. Carnegie, Angelica Fatourous Handelsbanken, Susanna Urdmark JP Nordiska, Conny Granelli

# Ownership structure

As of 31 December 2002, the number of shareholders was 1,372. Institutional investors owned 72 per cent of the share capital and votes. Foreign owners held 18 per cent of the share capital and votes. Around 64 per cent of the shareholders own fewer than 500 shares each.

# Distribution of shareholders as of 31 December 2002



# List of shareholders as of 31 December 2002

Percentage of

	No. of	capital and
Shareholder	shares	votes, %
Stiftelsen Industrifonden	3,953,295	13.4
Pronova a.s.	1,942,787	6.6
Alecta	1,374,450	4.7
Oxford GlycoSciences	1,331,251	4.5
Carl Borrebaeck	1,291,704	4.4
Sjätte AP-fonden	1,201,237	4.1
Fjärde AF-fonden	1,188,750	4.0
Nordea Bank S A	1,089,550	3.7
Per-Olof Mårtensson	1,043,301	3.5
Svein Mathisen	1,043,301	3.5
Cristina Glad	1,043,301	3.5
Roland Carlsson	1,043,301	3.5
Nordea fonder	925,300	3.1
Förenade liv	877,116	3.0
Industritjänstemannaförbundet	710,250	2.4
Other shareholders	9,416,662	31.9
Total	29,475,556	100.0

# **Share statistics**

Size of holding	No. of shares	No. of shares in %	No. of share- holders	No. of share- holders in %
1–500	160,117	0.5	882	64.3
501-1,000	151,789	0.5	170	12.4
1,001–2,000	166,273	0.6	98	7.1
2,001–5,000	210,750	0.7	85	6.2
5,001–10,000	327,825	1.1	41	3.0
10,001–20,000	391,019	1.3	25	1.8
20,001–50,000	980,459	3.3	32	2.3
50,001–100,000	309,150	1.1	4	0.3
100,001–500,000	4,119,011	14.0	16	1.2
500,001–1,000,000	5,112,935	17.4	7	0.5
1,000,001–5,000,000	17,546,228	59.5	12	0.9
Total	29,475,556	100.0	1,372	100.0

# Changes in the share capital

Year Transaction	Increase in share capital, SEK	Increase in no. of shares	Share capital, SEK	No. of shares	Nominal value of shares, SEK
······································	capital, 3EK	Silaies	JER	311a1E3	Silales, JEK
1996 BioInvent International AB was fo	unded¹)		100,000	10,000	10.00
1997 New share issue	7,140	714	107,140	10,714	10.00
1997 Bonus issue	857,120	85,712	964,260	96,426	10.00
1998 Share split 1:10		867,834	964,260	964,260	1.00
1998 New share issue <sup>2)</sup>	181,000	181,000	1,145,260	1,145,260	1.00
1999 New share issue <sup>3)</sup>	108,527	108,527	1,253,787	1,253,787	1.00
2000 New share issue <sup>4)</sup>	250,000	250,000	1,503,787	1,503,787	1.00
2000 Warrants exercised	11,013	11,013	1,514,800	1,514,800	1.00
2001 Bonus issue	9,846,200		11,361,000	1,514,800	7.50
2001 Share split 1:15		21,207,200	11,361,000	22,722,000	0.50
2001 Warrants exercised	461,152.5	922,305	11,822,152.5	23,644,305	0.50
2001 New shares issue <sup>5)</sup>	2,250,000	4,500,000	14,072,152.5	28,144,305	0.50
2002 New share issue <sup>6</sup>	665,625.5	1,331,251	14,737,778	29,475,556	0.50

- 1) BioInvent International AB was established by its managers, Stiftelsen Industrifonden, Pronova a.s. and Aragon Fondkommission.
  2) In November 1998 the Company carried out a directed issue of 181,000 new shares aimed at institutional investors. The issue price was SEK 125 and approximately
- SEK 22.6 million was raised for Bioinvent International AB after deduction for issue costs.

  3) In November 1999 the Company carried out a directed issue of 108,527 new shares aimed at institutional investors. The issue price was SEK 175 and SEK 18.7 million
- was raised for BioInvent International AB after deductions for issue costs.
- 4) In March 2000 the Company carried out a directed issue of 250,000 shares aimed at institutional investors. The issue price was SEK 720 and SEK 169.0 million was raised for
- BioInvent International AB after deductions for issue costs.
  5) New share issue in connection with the listing. The issue price was SEK 62 and SEK 261.6 million was raised for BioInvent International AB after deductions for issue costs.
- 6) In March 2002 the Company carried out a directed issue of 1,331,251 new shares for Oxford GlycoSciences. The issue price was SEK 39 and this raised SEK 52.0 million for BioInvent International AB after deductions for issue costs.

# Overview of outstanding warrant programmes

Programme	Subscription period	Subscription price	Increase in no. of shares	Increase in share capital, SEK	Increase in share- holders' equity, SEK
IV	2/1 2002–30/6 2003	86.67	409,500	204,750	35,491,365
V	15/1 2002–16/3 2004	77.00	850,000	425,000	65,450,000
Total			1,259,500*	629,750	100,941,365

By the end of 2002, BioInvent International AB had launched five warrant programmes aimed mainly at the Company's employees. Warrant programmes I – III were fully exercised in connection with the stock exchange listing. As of 31 December 2002, warrants for 1,259,500 shares had been issued, of which warrants for 652,650 shares were held by the Company for sale to the employees at market terms.

\* All warrants being held by the Company were returned to the parent company in February 2003 and BioInvent intends to cancel them before the end of March 2003. After the warrants held by the Company are cancelled and after all of the remaining issued warrants are exercised, the number of shares will be 30,082,406.

# Dividend and dividend policy

BioInvent International AB has paid no dividends since the Company was established in 1996. The Company will continue to focus on research and development of new products. The financial resources will be used to finance these projects. The Board does not therefore intend to propose the payment of any dividends over the next few years.

# Directors' report

## **BIOINVENT ANNUAL REPORT 2002**

**Operations** BioInvent develops and manufactures antibody-based drugs and research tools. BioInvent's operation covers the entire development chain, from library technology for fast and efficient selection of human antibodies to production in a facility that is approved for manufacturing biological drugs.

This platform is the starting point for development partnerships with international pharmaceutical and biotech companies. Agreements are in place with, among others, Antisoma, GlaxoSmithKline, Igeneon, ImmunoGen, Pharmacia and Oxford GlycoSciences.

Three types of projects Biolnvent works with three different types of development projects: internal drug projects, projects with external partners in the form of development partnerships and development services. The aim is to secure short-term revenue while creating prospects for long-term profitability through proprietary drug candidates.

**Internal drug projects** BioInvent has been focusing strongly during the year on gaining access to unique target structures and developing antibody-based drugs against these. The main strategy is to find target structures from academic and other innovative external environments. BioInvent is concentrating on indication areas where there is a great need for medical treatments. The Company intends to find development and commercialisation partners in an early clinical phase.

BioInvent constantly evaluates target structures in a variety of indication areas. Among the most important events during the year are two agreements linked to projects in the HIV and arteriosclerosis fields.

New type of drug against HIV In 2002 BioInvent acquired the rights to develop and commercialise antibody-based drugs against HIV. The Company is focusing on special target structures on the so-called Tat protein.

The Tat protein is vital for the HIVs ability to replicate itself. Antibody-based drugs against these target structures are expected to be able to block Tat activity so that the number of HIV particles in the blood of the patient can be substantially reduced.

A number of potential product candidates have been selected from the Company's antibody library. In a first pre-clinical phase, the ability to reduce Tat activity *in vitro* is being tested.

New type of drug against arteriosclerosis Biolnvent has also acquired the rights to develop antibody-based drugs against target structures associated with arteriosclerosis. Cardiovascular diseases are a major medical problem and cause more than 50 per cent of all deaths in the Western world. Modern research in this field is focusing to a great extent on understanding inflammatory processes and the role of the immune system in the development of arteriosclerosis

BioInvent's current project is in line with this approach. The research group behind the target structures has shown that there are strong links between these target structures and inflammatory processes that lead to plaque formation in the vessel walls.

Antibodies aimed at the relevant target structures are believed to be able to stabilise the plaque formation and possibly also reduce it. Preliminary tests on animals support this hypothesis. A number of product candidates will be tested in further *in vivo* tests in a first pre-clinical phase.

**External development projects** During the year several new partnerships were established and at the same time the Company extended existing collaboration. BioInvent currently collaborates with the following important partners:

Oxford GlycoSciences (OGS) In 2002 a development partnership with OGS was initiated in the form of a three-year agreement for the joint development and commercialisation of antibody-based drugs. Under the agreement, OGS will deliver at least five antigens per year and BioInvent will produce antibodies against these. BioInvent is entitled to select one product candidate per year for joint development. OGS will be responsible for the clinical development and commercialisation of the remaining product candidates. The partnership is focusing on the cancer field.

GlaxoSmithKline Biologicals (GSK) BioInvent and GSK extended their development services agreement considerably in February 2002. Under the new agreement, which will last for three years, BioInvent will deliver antibodies from n-CoDeR for GSK's research and development work.

ImmunoGen BioInvent's collaboration with the US-based ImmunoGen was extended in December 2002 to include a new agreement for cGMP manufacturing of an antibody. During the year, BioInvent successfully manufactured another antibody for ImmunoGen. Both of the antibodies are included in product candidates in the cancer field.

**Igeneon** In December 2002 BioInvent extended its collaboration with the Austrian company Igeneon. The agreement concerns cGMP manufacturing of antibody-based drug candidates in the cancer field. BioInvent is currently working with two of Igeneon's product candidates.

Antisoma Another collaboration that developed well in 2002 was the agreement with the UK company Antisoma. In the autumn 2002 Antisoma entered into an agreement with the pharmaceutical company Roche which attracted much attention. This agreement includes licensing of a number of product candidates produced by Biolnvent.

New customers in 2002 include CellControl Laboratories AG and Pharmacia Diagnostics AB.

**Progress in the field of protein arrays** Protein arrays make it possible to study many proteins simultaneously and thereby quickly and efficiently map which proteins are involved in the disease process.

Protein arrays can be used within research and development, for example, to identify new target structures or in diagnostics where several parameters need to be studied simultaneously.

In 2002 BioInvent focused on developing important technology components in cooperation with the Company's academic network. Important progress has been made that strengthens the project's commercial potential and discussions regarding collaboration have been opened with commercial partners.

**Other information** The dispute with Resistentia that arose in 2001 was resolved in mediation at the end of 2002.

No important events have taken place since the end of the financial year.

**Sales and result** The net revenue for January – December increased to SEK 87.1 million (58.3). Revenue is generated from payment for development services and development partnerships.

The loss after net financial items for the January – December period was SEK -46.2 million (-43.5). The result was affected by an increase in the Company's research and development capacity as well as intensified marketing activity. The Group's research and development costs for January – December amounted to SEK 61.5 million (45.3). Depreciation according to plan of SEK 13.5 million (7.9) was deducted from the operating result for the period.

**Financial position and cash flow** The cash flow in 2002, including new issue funds, was positive despite considerable investments to gain access to interesting target structures and in other parts of the operation. The goal over time is to achieve a balanced cash flow in the form of revenue and financing from partners. The cash flow must, however, be allowed to vary certain years depending on the composition of the project portfolio.

The cash flow for January – December from current operations and investment activity amounted to SEK -47.1 million (-74.8). The improvement, despite increased investments, is mainly the result of non-recurring payments received from customers. The accumulated cash flow for January – December was SEK 4.9 million (197.4) after payment was received in 2002 from Oxford GlycoSciences for new shares in the amount of SEK 52.0 million and after new issue funds in the amount of SEK 261.6 million were raised in connection with the listing in 2001. As of 31 December 2002 the Group's liquid funds amounted to SEK 343.6 million (338.7).

The shareholders' equity at the end of the period was SEK 394.2 million and the Company's share capital was SEK 14.7 million. The equity/assets ratio at the end of the period was 90.5 (94.6) per cent. The Group has no interest-bearing liabilities.

As of 31 December, BioInvent had issued warrants for 1,259,500 shares, of which warrants for 652,650 shares are held by the Company for sale to employees at market terms. All of the warrants held by the Company were returned to the parent company in February 2003 and BioInvent intends to cancel them before the end of March 2003.

The Group's accumulated, unutilised loss carried forward as of 31 December 2002 amounted to SEK 208 million. BioInvent has not yet reported a taxable profit nor does it expect to do so in the near future. No tax claim at any value relating to the loss carried forward has been entered into the accounts.

**Investments** The Group's investments in tangible fixed assets amounted to SEK 14.0 million (25.6) and are mainly related to equipment for research and development activity. Investments in intangible fixed assets amounted to SEK 22.5 million (-) and are related to acquisitions of target structures and new technology.

Merger The subsidiaries BioInvent Production AB and BioInvent Therapeutic AB merged with the parent company effective 31 October 2002. The merger was reported in accordance with BFNAR 1999:1 – Merger of wholly-owned subsidiaries. The consolidated value method was applied, whereby the parent

company recorded the merged subsidiaries' assets and liabilities at the values they had in the consolidated accounts. The merger resulted in a loss of SEK -120.0 million, which is the difference between the consolidated value of assets and liabilities in the subsidiaries and the parent company's book value of shares in the subsidiaries.

The merger is the result of an organisational change to create a unit that focus on projects where all of the Company's expertise and technologies in the antibody drug field can be integrated.

Parent company Following the merger described above, the BioInvent Group consists of the parent company BioInvent International AB and the subsidiary BioInvent Finans AB which administers the warrants issued by BioInvent International AB. The merger affects the accounts from 1 January 2002 and the parent company's revenue and final position after that date are essentially the same as the Group's. The net revenue for the January – December period amounted to SEK 87.1 million (-). The loss after net financial items for January – December amounted to SEK -46.2 million (-0.2).

**Currency exposure** The currencies that apply in agreements with customers and suppliers are, wherever possible, to be SEK, USD, GBP or EUR. Currency exposure is primarily eliminated by matching of flows in the same currency. When matching is not possible, the currency exposure is mainly eliminated by hedging through forward contracts.

**Organisation** The number of employees has increased from 110 in 2001 to 130 at the end of 2002.

**Environmental impact** The Group's operations require certain permits according to the Environmental Code. Accordingly, Biolnvent has obtained permits for the manufacture of pharmaceutical substances using biosynthetic processes. The external environment is affected by limited emissions into water.

#### Account of the Board's work in 2002

The Board of Directors consists of seven members. The Board held sixteen meetings in 2002, of which three were per capsulam meetings. In addition to reviewing the business with respect to budget and strategic planning, the Board spent a considerable amount of time addressing other issues relating to the Company's strategic focus, the external environment, the financial situation,

research and development issues, interim reports and the yearend financial statements as well as the provision of external information.

The Board's remuneration committee addresses and reaches decisions on issues relating to remuneration and benefits to all senior executives with the exception of the CEO, whose salary and benefits are set by the Board of Directors. The committee also deals with other remuneration issues of great importance, such as incentive schemes. These are subject to final approval by the Board of Directors. The remuneration committee consists of the Chairman of the Board, Per-Olof Mårtensson, and two other Board members, Björn Ogenstam and Kenth Petersson.

BioInvent has no specific nominating committee working with Board member nominations, but instead works according to the Swedish Companies Act's principle of allowing every shareholder to propose candidates for membership of the Board. Shareholders wishing to nominate a candidate are requested to submit their proposal to the Chairman of the Board, Per-Olof Mårtensson, in a letter addressed to BioInvent's office in Lund, Sweden.

The Company's auditors report their observations personally to the Board after auditing the financial statements and on their findings with respect to the Company's internal control.

For information about the Board members, please refer to page 50.

**Proposed appropriation of losses** At the disposal of the Annual General Meeting is an accumulated loss (SEK):

	, , , , , , , , , , , , , , , , , , ,
Brought forward	0
Result of merger	-120,006,701
Loss for the year	-46,167,015
	-166 173 716

The Board of Directors and the CEO propose that the share premium reserve be reduced by SEK -166,173,716 to cover the accumulated loss.

**The Group** According to the consolidated balance sheet, the accumulated loss amounts to SEK -166.2 million, SEK 1 thousand is allocated to the restricted equity.

For more information about the Group's and the Company's results and financial position, please refer to the income statements, balance sheets and cash-flow statements that follow, and to the notes that accompany these. All figures shown are in SEK thousands unless otherwise indicated.

# **Income statements**

		Gr	oup	Parent company		
	Note	2002	2001	2002	2001	
Net revenue	•••••	87,053	58,270	87,053	-	
Net revenue		37,033	30,270	37,033		
Operating costs						
Cost of goods and services sold		-50,195	-39,863	-50,195	_	
Sales and administrative costs		-37,983	-27,472	-37,983	-13,862	
Research and development costs		-61,487	-45,255	-61,487	-1,127	
Other operating revenue		772	521	772	3,251	
Other operating costs		-576	-458	-576	-45	
				•••••		
Operating profit/loss	2, 3, 4, 5, 6	-62,416	-54,257	-62,416	-11,783	
Result from financial investments						
Interest income and similar items		16,319	10,976	16,319	11,712	
Interest costs and similar items		-69	-189	-70	-139	
Profit/loss for the year	• • • • • • • • • • • • • • • • • • • •	-46,166	-43,470	-46,167	-210	
Earnings per share, average number of sl	hares, SEK*					
Before dilution		-1.60	-1.69			
Average number of shares						
Before dilution (thousand)		28,939	25,697			
After full dilution (thousand)		28,940	25,753			

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

# Balance sheets

### BIOINVENT ANNUAL REPORT 2002

		Group		Parent company		
	Note	2002	2001	2002	2001	
Assets	•		•		•••••	
Fixed assets						
Intangible fixed assets	7					
Acquired intangible assets		19,726	-	19,726	-	
Tangible fixed assets	8					
Equipment		36,522	32,029	36,522	613	
Investments in rented premises		7,294	8,479	7,294	-	
·			•			
Financial fixed assets						
Shares in subsidiaries	9	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-	100	142,200	
•••••	• • • • • • • • • • • • • • • • • • • •		• • • • • • • • • • • • • • • • • • • •			
Current assets		63,542	40,508	63,642	142,813	
Inventories etc.						
Work in progress	10	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	_	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-	
Raw materials and consumables		2,827	1,564	2,827	-	
			•			
Current receivables						
Receivables from subsidiaries			_		6,235	
Accounts receivable		8,777	18,163	8,777	40	
Other receivables		6,343	4,222	6,343	2,023	
Prepaid expenses and accrued income	11	10,464	7,432	10,464	2,682	
•••••	• • • • • • • • • • • • • • • • • • • •			• • • • • • • • • • • • • • • • • • • •		
		25,584	29,817	25,584	10,980	
Liquid funds	12	343,584	338,662	343,351	359,540	
Total assets		435,537	410,551	435,404	513,333	

		Group		Group Parent			company
	Note	2002	2001	2002	2001		
Shareholders' equity and liabilities	•••••		•••••		•••••		
Shareholders' equity	13						
Restricted shareholders' equity							
Share capital		14,738	14,072	14,738	14,072		
Share premium reserve		545,685	445,170	545,685	494,561		
Other restricted reserves		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	100	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-		
•••••	• • • • • • • • • • • • • • • • • • • •	560,423	459,342	560,423	508,633		
Accumulated loss			,		•		
Profit/loss brought forward		-120,007	-27,456	-120,007	0		
Profit/loss for the year		-46,166	-43,470	-46,167	-210		
		-166,173	-70,926	-166,174	-210		
Total shareholders' equity	• • • • • • • • • • • • • • • • • • • •	394,250	388,416	394,249	508,423		
Current liabilities							
Work in progress, net debt	10	16,244	2,932	16,244	-		
Accounts payable		12,861	6,933	12,861	1,130		
Liabilities to subsidiaries			-	105	105		
Other liabilities		2,374	3,583	2,137	1,002		
Accrued costs and deferred income	14	9,808	8,687	9,808	2,673		
		41,287	22,135	41,155	4,910		
Total shareholders' equity and liabilities	• • • • • • • • • • • • • • • • • • • •	435,537	410,551	435,404	513,333		
ional suarchonals equity and nationals		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	,		5.5,555		
Memorandum items							
Pledged assets			-		-		
Contingent liabilities			-		-		

# Cash flow statements

#### BIOINVENT ANNUAL REPORT 2002

		Group		Parent company	
	Note	2002	2001	2002	2001
Current operations	• • • • • • • • • • • • • • • • • • • •		•••••		• • • • • • • • • • • • • • • • • • • •
Operating profit/loss		-62,416	-54,257	-62,416	-11,783
Adjustments for non-cash items					
Depreciation		13,475	7,854	13,475	132
•••••	• • • • • • • • • • • • • • • • • • • •	-48,941	-46,403	-48,941	-11,651
			10,102		,05.
Interest received		16,319	10,976	16,319	11,712
Interest paid		-69	-189	-70	-139
Cash flow from current operations	• • • • • • • • • • • • • • • • • • • •	•••••	•••••	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •
before changes in working capital		-32,691	-35,616	-32,692	-78
before changes in tronking capital		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	33,010	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	,,
Change in working capital					
Change in inventories etc.		-1,263	-384	-1,263	-
Change in current receivables		4,233	-10,933	4,233	1,476
Change in current liabilities		19,152	-12,490	19,020	-11,228
Change in short-term investments			10,231		10,231
Cash flow from current operations	•	-10,569	-49,192	-10,702	401
Investment activity					
New share issue, subsidiaries		0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-100
Conditional shareholders' contributions to subsidia	ries	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	-60,000
Acquisition of intangible fixed assets		-22,501	-	-22,501	-
Acquisition of tangible fixed assets		-14,008	-25,619	-14,008	-584
Merger of subsidiaries	15		-	-20,978	-
Cash flow from investment activity		-36,509	-25,619	-57,487	-60,684
Cash flow after investment activity		-47,078	-74,811	-68,189	-60,283
Financing activity					
New share issues	• • • • • • • • • • • • • • • • • • • •	52,000	272,252	52,000	272,252
Cash flow from financing activity		52,000	272,252	52,000	272,252
Increase/decrease in liquid funds		4,922	197,441	-16,189	211,969
Opening liquid funds		338,662	141,221	359,540	147,571
Liquid funds at year-end	• • • • • • • • • • • • • • • • • • • •	343,584	338,662	343,351	359,540

### **NOTE 1** Accounting and valuation principles

The annual report has been prepared in accordance with the Annual Accounts Act and the recommendations and statements from the Swedish Financial Accounting Standards Council. The accounting principles are the same as those applied the previous year. The Financial Accounting Standards Council's recommendation RR 15 regarding the reporting of intangible assets, which went into force on 1 January 2002, has been applied since 1 January 2000. The Company also applies other new recommendations from the Council that went into force on 1 January 2002. These new recommendations have, however, not had any impact on the parent company's or the Group's accounting.

**Merger** The subsidiaries BioInvent Production AB (Co. reg. no. 556230-7537) and BioInvent Therapeutic AB (Co. reg. no. 556540-4323) merged with the parent company effective 31 October 2002. The merger was reported in accordance with BFNAR 1999:1 – Merger of wholly-owned subsidiaries. The consolidated value method was applied, whereby the parent company recorded the merged subsidiaries' assets and liabilities at the values they had in the consolidated accounts. The merger resulted in a loss of SEK -120.0 million, which is the difference between the consolidated value of assets and liabilities in the subsidiary and the parent company's book value of shares in the subsidiary. On the date of the merger, 31 October 2002, the merged subsidiaries' net revenue amounted to SEK 71.4 million and their operating loss to SEK -50.7 million.

The merger is the result of an organisational change to create a unit that focus on projects where all of the Company's expertise and technologies in the antibody drug field can be integrated.

**Consolidated financial statements** Following the merger described above, the BioInvent Group consists of the parent company BioInvent International AB and the subsidiary BioInvent Finans AB which administers the warrants issued by BioInvent International AB.

The consolidated financial statements have been prepared using the acquisition method in accordance with the Swedish Financial Accounting Standards Council's recommendation RR 1:00 on consolidated accounts. According to this method, the shareholders' equity in the subsidiaries upon acquisition is entirely eliminated. Only the portion of the subsidiaries' equity that is accrued after the acquisition is entered in the Group's equity.

**Revenue recognition** The Swedish Financial Accounting Standards Council's recommendation RR 11 is applied for the recognition of revenue. The Group's revenue is generated by various types of development services and partnerships. Revenue from these projects is recognized according to the percentage of completion method. According to this method, revenue, costs and thereby also profit/loss are reported during the accounting period as the work/service is being carried out.

**Research and development costs** The Swedish Financial Accounting Standards Council's recommendation RR 15 is applied for reporting intangible assets. Research costs are expensed as they occur. Development costs are capitalized provided that the criteria stipulated in RR 15 are met.

In 2002 two target structures that were acquired by BioInvent under licence for use in projects to develop proprietary drug candidates in the HIV and arteriosclerosis fields were capitalized. Acquisitions of non-exclusive licences for the display of antibody fragments from BioInvent's antibody library were also capitalized.

**Depreciation of fixed assets** Tangible fixed assets and acquired intangible assets such as technology licences and licensed target structures are depreciated and amortized in a systematic manner over the estimated usage period. However, the Company is conservative in its estimate of the usage period of acquired intangible assets taking into account the rapid development within the biotech industry. Ongoing assessments are made of the possible need for write-down of fixed assets, i.e. if the recovery value is less than the reported value.

Equipment	5 years
Investments in rented premises	5–10 years
Acquired intangible assets	3–5 years

**Leasing** The Swedish Financial Accounting Standards Council's recommendation RR 6 is applied for reporting of leasing agreements. The Group's leasing agreements have been categorised as operational leases, and accordingly, leasing charges are expensed during the period.

**Taxes** The Swedish Financial Accounting Standards Council's recommendation RR 9 on income taxes is applied. The Group's accumulated, unutilised tax carried forward as of 31 December 2002 amounted to SEK 208 million. BioInvent has not yet reported a taxable profit and does not expect to do so in the near future. No tax claim at any value relating to the loss carried forward has been entered in the accounts. There are no tax claims pertaining to temporary differences.

**Receivables and liabilities** Receivables are assessed individually and entered at the amounts that are expected to be received. Liabilities have been entered as nominal amounts. Receivables and liabilities in foreign currencies are valued at closing day exchange rates. The difference between the acquisition value and the closing day value is taken up as income or costs. In cases where receivables and liabilities have been hedged through forward contracts, the forward rate is used to value the underlying receivable or liability.

**Inventories** Inventories are valued at the lowest of the acquisition value and the actual value on the closing day. The first-in/first-out principle applies.

#### NOTE 2 Average number of employees

	2002			2001	
	No. of employees	Of which women	No. of employees	Of which women	
Parent company	124	61 %	8	50 %	
Subsidiaries	-	-	88	55 %	
Group total	124	61 %	96	54 %	

#### NOTE 3 Salaries, other remuneration and social security costs

	2002			2001	
		Social security		Social security	
	Salaries and other	costs (of which	Salaries and other	costs (of which	
	remuneration	pensions)	remuneration	pensions)	
Parent company	42,827	21,173	4,112	2,767	
		(5,386)		(960)	
Subsidiaries	-	-	28,662	13,400	
		(-)		(3,120)	
Group total	42,827	21,173	32,774	16,167	
•		(5,386)		(4,080)	

#### Pension costs distributed among the Board members, the CEO and other employees.

		2002		2001
	Board	Other	Board	Other
	and CEO	employees	and CEO	employees
Parent company	379	5,007	745	215
Subsidiaries	-	-	170	2,950
Group total	379	5,007	915	3,165

745 of the parent company's pension costs in 2001 related to the CEO, of which the main part was for retroactive adjustment in line with the ITP pension plan.

#### Salaries and other remuneration distributed between the Board of Directors, the CEO and other employees.

	2002			2001	
	Board	Other	Board	Other	
	and CEO	employees	and CEO	employees	
Parent company	1,784	41,043	1,752	2,360	
Subsidiaries	-	-	761	27,901	
Group total	1,784	41,043	2,513	30,261	

#### Benefits for senior executives

**Principles** The Board's fees are determined at the Annual General Meeting after proposals have been submitted by the Board represented by the Chairman of the Board. The fees are shared among the Board in accordance with a decision by the Board.

Salary levels for senior executives shall be competitive and set according to market terms. The CEO's fixed salary is determined by the Board on an annual basis. Fixed salaries for other senior executives are determined annually by the Board's remuneration committee. In addition to a fixed salary, variable remuneration may be paid according to the incentive scheme described below.

BioInvent's incentive scheme for the CEO and other senior executives consists of a bonus model that was introduced at the beginning of 2003. No variable remuneration was paid out in 2002 or in previous periods. Bonuses of 0–30 per cent of fixed cash annual salaries may be paid out to

the senior executives and are currently based on financial targets and milestones being reached. The bonus amounts are set annually by the Board. Bonuses payments, which are settled annually at the end of the year, are pensionable.

**Benefits for top management** In 2002 the Board's fees were set at a total of 690. Of this amount, the Chairman was paid a fee of 250 and four external Board members each received a fee of 110.

The President and CEO, Svein Mathisen, received a fixed, gross cash salary of 1,094 in 2002 and 49 in other benefits (primarily car benefits). No variable remuneration was paid in 2002. Svein Mathisen has a pension provision within the framework of the ITP plan. The retirement age is 65. The total cost of Svein Mathisen's pension benefits amounted in 2002 to 379, of which 138 was financed through so-called salary exchange (reduction in salary in exchange for pension benefits). Svein Mathisen's employment contract can be terminated by the Company with a 6-month period of notice.

If notice is given by the Company, Svein Mathisen is entitled to a redundancy payment equivalent to 18 monthly salaries.

No warrants or other financial instruments in BioInvent were acquired by top management in 2002. In previous years warrants for 195,000 shares in BioInvent (Programme IV) were acquired with the following distribution: Karl Olof Borg, 45,000, Björn Nilsson, 75,000 and Kenth Petersson, 75,000.

**Benefits to other senior executives** The other senior executives are individuals who, in addition to the CEO, are part of the Group management team. The retirement age for these individuals is 65, after which time a pension will be paid according to the ITP pension plan. The Company is

entitled to terminate employment contracts with six-month's notice. No redundancy payment entitlement exists over and above the payment of salaries during the period of notice.

Other senior executives received total salaries and other remuneration (primarily car benefits) amounting to 3,926. No variable remuneration was paid out in 2002. The total pension costs relating to other senior executives amounted to 973 in 2002.

No warrants or other financial instruments in BioInvent were acquired by other senior executives in 2002. In previous years warrants for 40,000 shares in BioInvent (Programme V) were acquired.

#### **NOTE 4** Auditor's fees

	Group		Parent company	
	2002	2001	2002	2001
Ernst & Young				•
Audit assignments	119	93	119	40
Other assignments	258	251	258	241
Total	377	344	377	281

### NOTE 5 Depreciation according to plan

	Group		Parent	company
	2002	2001	2002	2001
Cost of goods and services sold	4,097	3,379	4,097	-
Sales and administrative costs	435	269	435	132
Research and development costs	8,943	4,206	8,943	-
Total	13,475	7,854	13,475	132

Depreciation of fixed assets is included in the items in the income statement as indicated above.

## NOTE 6 Operational leasing

The Group and the parent company have signed rental agreements with the following undertakings.

	Group	Parent company
Payments due:		
Year 2003	11,157	11,157
Year 2004–2007	29,461	29,461
Year 2008 or later	5,212	5,212
Total	45,830	45.830

# NOTE 7 Intangible fixed assets

	Group		Parent company	
	2002	2001	2002	2001
Acquired intangible fixed assets	•••••	• • • • • • • • • • • • • • • • • • • •	•	• • • • • • • • • • • • • • • • • • • •
Opening acquisition value	-	-	-	-
Acquisition	22,501	-	22,501	-
Closing accumulated acquisition value	22,501	-	22,501	<del>-</del>
Opening depreciation	-	-	-	-
Depreciation for the year	-2,775	-	-2,775	-
Closing accumulated depreciation	-2,775	-	-2,775	-
Closing residual value according to plan	19,726	-	19,726	=

# NOTE 8 Tangible fixed assets

	Group		Parent	ompany
	2002	2001	2002	2001
Equipment	•••••	• • • • • • • • • • • • • • • • • • • •	•••••	•••••
Opening acquisition value	52,533	34,760	797	213
Transfer as a result of merger	-	-	51,736	-
Purchases	13,919	22,825	13,919	584
Disposals	-6,300	-5,052	-6,300	-
Closing accumulated acquisition value	60,152	52,533	60,152	797
Opening depreciation	-20,504	-18,852	-184	-52
Transfer as a result of merger	-	-	-20,320	-
Disposals	6,300	5,052	6,300	-
Depreciation for the year	-9,426	-6,704	-9,426	-132
Closing accumulated depreciation	-23,630	-20,504	-23,630	-184
Closing residual value according to plan	36,522	32,029	36,522	613

	Group Parent company			
	2002	2001	2002	2001
Investments in rented premises	•••••	• • • • • • • • • • • • • • • • • • • •	•	••••••
Opening acquisition value	10,551	7,757	-	-
Transfer as a result of merger	-	-	10,551	-
Purchase	88	2,794	88	-
Closing accumulated acquisition value	10,639	10,551	10,639	-
Opening depreciation	-2,072	-922	-	-
Transfer as a result of merger	-	-	-2,072	-
Depreciation for the year	-1,273	-1,150	-1,273	-
Closing accumulated depreciation	-3,345	-2,072	-3,345	-
Closing residual value according to plan	7,294	8,479	7,294	-

### NOTE 9 Shares in subsidiaries

		Share of	Share of	Par	Book
	Co. reg. no.	equity	votes	value	value
•••••	• • • • • • • • • • • • • • • • • • • •		• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •
BioInvent Finans AB	556605-9571	100 %	100 %	100	100

BioInvent Finans AB's head office is in Lund, Sweden.

## NOTE 10 Work in progress, net debt

		Group		Parent company
	2002	2001	2002	2001
Invoiced amounts	107,128	58,886	107,128	-
Value of work completed	-90,884	-55,954	-90,884	-
Total	16,244	2,932	16,244	-

# NOTE 11 Prepaid expenses and accrued income

	Group		Parent company	
	2002	2001	2002	2001
Prepaid rent	2,868	2,074	2,868	133
Accrued interest income	6,054	1,419	6,054	1,419
Other items	1,542	3,939	1,542	1,130
Total	10,464	7,432	10,464	2,682

## NOTE 12 Liquid funds

Liquid funds consist of bank balances and investments in commercial papers in SEK with a K1 rating.

## NOTE 13 Shareholders' equity

#### Group

	Share	Share premium	Other restricted	Accumulated	
	capital	reserve	reserves	loss	Total
Amount at beginning of year	14,072	445,170	100	-70,926	388,416
Directed issue	666	51,334			52,000
Transfer between restricted and unrestricted reserves		49,181	-100	-49,081	0
Profit/loss for the year				-46,166	-46,166
Total	14,738	545,685	0	-166,173	394,250

#### Parent company

	Share	Share premium	Restricted	Profit/loss	Profit/loss	
	capital	reserve	equity	brought forward	for the year	Total
Amount at beginning of year	14,072	494,561	0	0	-210	508,423
Directed issue	666	51,334				52,000
Appropriation of previous year's result		-210			210	0
Merger-related loss				-120,007		-120,007
Profit/loss for the year					-46,167	-46,167
Total	14,738	545,685	0	-120,007	-46,167	394,249

The share capital as of 31 December 2002 after completion of the directed new share issue consists of 29,475,556 shares with a nominal value of SEK 0.50 per share. The financial implications of the merger are described in Note 1 Accounting and valuation principles.

## NOTE 14 Accrued expenses and deferred income

	Group		P	arent company
	2002	2001	2002	2001
Payroll liability	4,813	4,448	4,813	999
Social security fees	3,230	2,689	3,230	689
Other items	1,765	1,550	1,765	985
Total	9,808	8.687	9.808	2.673

## NOTE 15 Merger of subsidiaries, effects on the cash-flow statement

The table below specifies the effects on the parent company's cash-flow statement in 2002 in connection with the merger of the subsidiaries.

	Paren	nt company
	2002	2001
Inventories	-1,564	-
Current receivables	-18,837	-
Current liabilities	17,225	-
Shares in subsidiaries	142,100	-
Tangible fixed assets	-39,895	-
Shareholders' equity, merger-related loss	-120,007	-
Merged net assets	-20,978	-

The merged net assets of -20,978 correspond to a reduction of the parent company's liquid funds.

Lund, Sweden 4 March 2003

Per-Olof Mårtensson Karl Olof Borg Carl Borrebaeck
Chairman of the Board

Björn O Nilsson Björn Ogenstam Kenth Petersson

Svein Mathisen
President and CEO

Our Audit report was submitted on 5 March 2003 ERNST & YOUNG AB

> Åke Stenmo Authorised Public Accountant

# Audit report

#### To the general meeting of shareholders in BioInvent International AB (publ)

Corporate identity number 556537-7263

We have audited the annual accounts, the consolidated accounts, the accounting records and the administration of the board of directors and CEO of BioInvent International AB (publ) for the 2002 financial year. These accounts and the administration of the company are the responsibility of the board of directors and the CEO. Our responsibility is to express an opinion on the annual accounts, the consolidated accounts and the administration based on our audit.

We conducted our audit in accordance with generally accepted auditing standards in Sweden. Those standards require that we plan and perform the audit to obtain reasonable assurance that the annual accounts and the consolidated accounts are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the accounts. An audit also includes assessing the accounting principles used and their application by the board of directors and the CEO, as well as evaluating the overall presentation of information in the annual accounts and the consolidated accounts. As a basis for our opinion concerning discharge from liability, we examined significant decisions, actions taken and circumstances of the company in order to be able to determine the liability, if any, to the company of any board member or the CEO. We also examined whether any board member or the CEO has, in any other way, acted in contravention of the Companies Act, the Annual Accounts Act or the Articles of Association. We believe that our audit provides a reasonable basis for our opinion set out below.

The annual accounts and the consolidated accounts have been prepared in accordance with the Annual Accounts Act and thereby give a true and fair view of the company's and the group's financial position and results of operations in accordance with generally accepted accounting principles in Sweden.

We recommend to the general meeting of shareholders that the income statements and balance sheets of the parent company and the group be adopted, that the parent company's loss be dealt with in accordance with the proposal in the Directors' Report, and that the members of the board of directors and the CEO be discharged from liability for the financial year.

Lund, Sweden 5 March 2003

**ERNST & YOUNG AB** 

Åke Stenmo Authorised Public Accountant



# The Board of Directors



Facts: Certified pharmacist. Born 1937. Lives in Nyhamnsläge, Sweden. President and CEO of Karo Bio AB 1991 - 2000.

Chairman of the Board of BioInvent International AB since 1997. Other board appointments: Chairman of the Board of Karo Bio AB and

Member of the boards of Maxim Pharmaceuticals Inc., Photocure AS and others. Shareholding: 1,043,301 shares in BioInvent International AB. No warrants.

#### **Carl Borrebaeck**

President 1990 – 1994.

Facts: Doctor of Science. Born 1948. Lives in Hjärup, Sweden. Chief Scientific Officer of BioInvent International AB. One of the founders of BioInvent Production AB where he held the position as

Professor at the Department of Immunotechnology at Lund University, Sweden. Member of the Board of BioInvent International AB since 1997. Other board appointments: Chairman of the Board of Forskarpatent i Syd AB Member of the Boards of Teknikbrostiftelsen i Lund AB, Teknoseed AB, Alligator Bioscience AB and others

Shareholding: 1,291,704 shares in BioInvent International AB. No warrants.









#### **Svein Mathisen**

Facts: Master of Science, Engineering Physics. Born 1956. Lives in Malmö, Sweden.

President and CEO of BioInvent International AB. Employed by BioInvent International AB since 1997. President and CEO of BioInvent Production AB 1995 – 1996. Member of the Board of BioInvent International AB since 2001. Shareholding: 1.043.301 shares in BioInvent International AB. No warrants.

#### Björn Ogenstam

Facts: MBA. Born 1959. Lives on the island of Ingarö, Sweden. Vice President Industrifonden.

Member of the Board of BioInvent International AB since 2002. Other board appointments: Member of the board of Powerbox International AB. Shareholding: No shares or warrants in BioInvent International AB.

#### **Kenth Petersson**

Facts: Bachelor of Arts. Born 1956. Lives in Stockholm, Sweden. Partner Science Pacific.

Member of the Board of BioInvent International AB since 1997. Other Board appointments: Member of the boards of Alligator Bioscience AB, Coding Technologies and others.

Shareholding: 44,760 shares in BioInvent International AB. Warrants for 75,000 shares.



#### **Karl Olof Borg**

Facts: Doctor of Pharmacy. Born 1941. Lives in Malmö, Sweden. Vice President of Research at Active Biotech AB 1998 – 2000. Associate professor in analytical biochemistry at Uppsala University, Sweden. Member of the Board of BioInvent International AB since 2001. Other board appointments: Chairman of the Board of Cartela AB. Member of the boards of Actar AB, M/E Biotech A/S, Medicarb AB, 7 TM Pharma A/S and others.

Shareholding: No shares in BioInvent International AB. Warrants for 45,000 shares.



Facts: Doctor of Science. Born 1956. Lives in Sollentuna, Sweden. President and CEO of Karo Bio AB since 2001.

Vice President of Research and Global Vice President of Amersham Biotech AB 1998 - 2001.

Associate professor at the Royal Institute of Technology (KTH) in Stockholm,

Member of the Board of BioInvent International AB since 1999. Shareholding: No shares in BioInvent International AB. Warrants for 75,000 shares.



# Senior executives



#### Svein Mathisen President & CEO

Facts: Master of Science, Engineering Physics. Born 1956. Lives in Malmö, Sweden.

Employed by BioInvent International AB since 1997.

President and CEO of BioInvent Production AB 1995 – 1996.

Member of the Board of BioInvent International AB since 2001.

Shareholding: 1,043,301 shares in BioInvent International AB.

No warrants.

#### Carl Borrebaeck Chief Scientific Officer

Facts: Doctor of Science. Born 1948. Lives in Hjärup, Sweden.

One of the founders of BioInvent Production AB where he held the position as President 1990 – 1994.

Professor at the Department of Immunotechnology at Lund University, Sweden. Member of the Board of BioInvent International AB since 1997.

Other board appointments: Chairman of the Board of Forskarpatent i Syd AB.

Member of the boards of Teknikbrostiftelsen i Lund AB, Teknoseed AB, Alligator Bioscience AB and others.

Shareholding: 1,291,704 shares in BioInvent International AB. No warrants.

#### Roland Carlsson Vice President Lead Candidates

Facts: Ph.D. Born 1949. Lives in Lund, Sweden.
Vice President Research at Bioinvent since 1987.
Associate professor at the Department of Immunotechnology at Lund University, Sweden.

Shareholding: 1,043,301 shares in BioInvent International AB. No warrants







#### Martin Wiles Vice President Business Development

FaCts: Ph.D. Chemistry. MBA. Born 1963. Lives in Copenhagen, Denmark. Employed in 2003.

 $1999-2003\ \text{Head}$  of Business Development at KS Biomedix Holdings Plc. (listed on the London Stock Exchange).

Shareholding: No shares or warrants in BioInvent International AB.

#### Cristina Glad Executive Vice President

Facts: Doctor of Science, Biochemistry. MBA, born 1952. Lives in Malmö, Sweden.

President and CEO of BioInvent Production AB since 1997 – 2002. Director of Manufacturing and Business Development for the Company

Employed since 1987.

Shareholding: 1,043,301 shares in BioInvent International AB. No warrants.

#### Jonas Källmén Chief Financial Officer

Facts: Master of Science, International Economics and BA. Born 1965. Lives in Malmō, Sweden. Employed by Biolinvent since 2001. CFO for Precise Biometrics AB 1999 – 2001. General Manager of Tetra Pak Nordic Treasury AB 1996 – 1999.

Shareholding: No shares in BioInvent International AB.
Warrants for 40,000 shares.





# Glossary

#### BIOINVENT ANNUAL REPORT **2002**

**Affinity** Binding strength of an antibody; its ability to bind firmly to an antigen.

**Antibody** Reaction product evoked by antigens. Antibodies are proteins from the group collectively called immunoglobulins and can now be produced in laboratories.

**Antigen** A substance that is foreign to the body and that can elicit a response in the body. The antigen can stimulate the immune system by reacting with an antibody or T cells (an important group of white blood cells that have a key role in the immune system).

The word antigen comes from the Greek "anti" meaning "against" and "genes" meaning "generating." It has nothing to do with the word "gene" in the context of "hereditary disposition."

Arteriosclerosis Hardening of the arteries.

**Autoimmunity** Immune reaction against an organism's own cells.

**B** cell A type of white blood cell that produces antibodies.

**Biological drugs** Drugs, e.g. antibodies that are produced by living cells.

**Blockbuster** Drug that has sales of over USD 1 billion per year.

**CDR** Complementarity Determining Region. The parts of the antibody that recognises and binds to the antigen.

**Cell culture** Cells kept alive outside the body in special containers.

**Cell line** Cultured cells with the same genetic information.

**Clinical trials** Studies carried out on humans to test the effect of future drugs.

**DNA** Deoxyribonucleic acid. The chemical material in a cell that contains the genetic code – genetic information.

**Drug candidate/product candidate** A substance with the potential to be developed into a drug.

**Genome** The complete set of genes in an individual.

**Genomics** The study of the genome.

**GMP** Good Manufacturing Practice. A set of instructions for manufacturing pharmaceuticals ensuring their quality and safety.

**Human antibodies** Antibodies originating from humans.

**Immunoglobulins** A class of proteins that includes all types of antibodies. Also called gammaglobulins.

**In vitro** Within a test tube or another artificial environment. (Opposite to in vivo).

**In vivo** "Within the living body." In biomedicine, something that is done to a living organism. In everyday speech, synonymous with experiments on animals.

**Library technology** Technology that creates variations in molecules, e.g. antibodies.

**Milestone payment** Payment when milestones are reached in a drug development project; often linked to the successful implementation of phases in clinical development.

Phage Virus that can infect bacteria.

**Phage display** Technology for expressing molecules, e.g. antibodies, on the phage surface.

**Plaque** Deposits of foreign materials, for example on vessel walls.

**Pre-clinical development** Testing and documentation of a drug candidate's properties in a model system.

**Protein** The proteins are important building blocks in the human body. There are many thousands of different proteins.

**Proteome** The entire set of proteins in an individual.

**Proteomics** The study of the proteome.

**Royalty** Payment linked to the sale of a drug; often a percentage of sales.

**Screening** Searching and final identification of antibody fragments that bind to a given antigen.

**Selection** Selection of a number of possible antibody fragments that bind to a given antigen.

**Specificity** The ability of antibodies to recognise the "right" antigen and ignore all others.

**Target structure** The proteins in the body upon which a drug can have an effect. An antigen can be a target structure upon which antibodies can have a therapeutic effect.

**T cells** A group of white blood cells that have a key role in the immune system.

**Therapy** Treatment; here generally with a drug.

**Toxin, toxic** Toxic substance, with toxic effect.

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