

Annual Report

2003

BioInvent in brief

BioInvent develops antibody-based drug candidates against diseases where there is a significant unmet medical need.

The antibody field is a segment with strong growth in the pharmaceuticals market and is expected to account for a large portion of drug sales in the future.

BioInvent conducts proprietary drug projects in disease areas such as AIDS, atherosclerosis, cancer and diseases of the joints. The scope and strength of BioInvent's technology platform is also used by partners in the development of new drugs. BioInvent's partners include Antisoma, Celltech, GlaxoSmithKline, ImmunoGen, Igeneon and XOMA.

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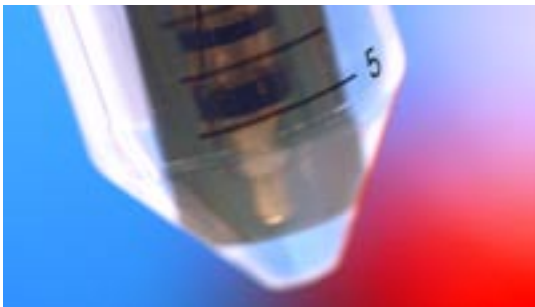
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Comments by the CEO – A growing and innovative project portfolio

“Over the past few years BioInvent has developed into an exciting, antibody-based pharmaceutical company with a growing and innovative project portfolio and a technology platform that is a solid basis from which to initiate new projects – all protected by strong patents. This foundation gives us every reason to look ahead at 2004 with confidence.”

These are the words of BioInvent’s President and CEO, Svein Mathisen, who also states that the Company is continuing to move its positions forward in the value chain by developing proprietary antibody-based drugs.

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Our business and strategy – Focus on antibody-based drugs

BioInvent focuses on developing antibody-based drugs. Value is first and foremost generated through investment in innovative medical concepts for the treatment of diseases where there is a significant unmet medical need. This value will be realized within the framework of strategic partnerships with established pharmaceutical companies. If the Company’s development work continues to progress successfully, BioInvent will sign partnership agreements in the late pre-clinical phase or the early clinical phase. Current revenue from partnerships where BioInvent carries out work on behalf of customers strengthen and complement the Company’s own development.

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The development process – From target protein to antibody-based drug

BioInvent develops human antibodies that are similar to naturally occurring antibodies and have a natural function in the body. This can save both time and money at the same time as there is a lower risk of side effects than when chemical drug molecules are developed. Although the statistical documentation is still limited, experiences up to now indicate that antibodies and other biological drugs have a greater chance of reaching the market than chemical molecules. The drawback with a complex manufacturing process is counterbalanced by the fact that the Company has its own manufacturing resources.

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The project portfolio – Developing the portfolio

So far BioInvent has initiated projects within disease areas such as AIDS, atherosclerosis, cancer and osteoarthritis. By expanding the portfolio – which is a high priority – the risk and opportunities are spread over a number of projects. Part of the risk associated with proprietary development is counterbalanced by partnerships providing a regular source of revenue.

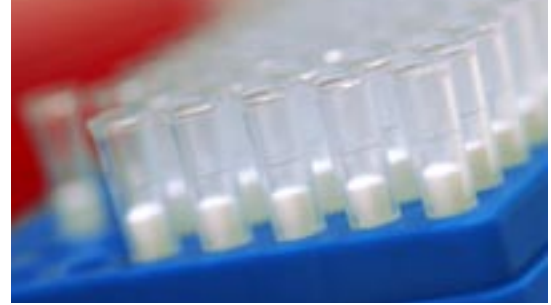
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HIV – New treatment principle with potential to avoid resistance

The Tat protein is crucial for HIV's ability to replicate itself and spread to new cells. BioInvent's antibodies against the Tat protein are expected to be able to neutralize such activity so that the number of HIV particles in the patient's blood is reduced to such an extent that the progress of the disease is arrested. Because the target protein has unique characteristics, BioInvent expects the antibodies against them to prevent the development of resistance and therefore have a lasting effect.

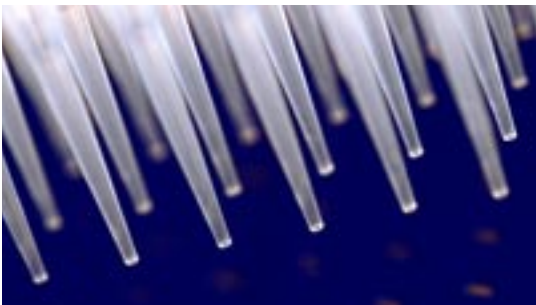
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Cancer – Antibody-based drugs are expected to block the nutrient supply to tumours

Tumours over a certain size are dependent on the formation of blood vessels for their growth and survival. BioInvent develops antibodies that are expected to be able to prevent the tumour from developing its own new blood vessels and thereby block its nutrient supply. Antibodies are targeted at a new and central receptor, called angiomin. Angiomin can act as a natural means of retarding the formation of new blood vessels around the tumour and is therefore an attractive target protein for drugs that aim to block the nutrient supply.

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Atherosclerosis – Antibody-based drug is expected to reduce the risk of infarction

Atherosclerosis occurs when cholesterol is deposited on the inside of the vessel walls causing plaque formation. New research shows strong links between oxidized forms of a lipoprotein that is part of the LDL particle, which is also known as "the bad cholesterol", and damaging inflammation in the vessel wall. Inflammations of this kind can lead to plaque breaking away, which in turn can cause infarction. BioInvent's antibodies that target these oxidized lipoproteins are expected to be able to reduce the inflammation and thereby stabilise the plaque formation and possibly even reduce it.

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Osteoarthritis – Antibody-based drugs are expected to regulate the synthesis of cartilage

Articular cartilage is necessary in order for joints to retain their flexibility. If there is an imbalance in the body's ability to maintain this cartilage, osteoarthritis occurs. This is a disease of the joints that causes stiffness, pain and poor function of the joints in the fingers, knees and hips etc. BioInvent is developing antibodies that target the integrins $\alpha 10\beta 1$ and $\alpha 11\beta 1$, which can be linked to the formation and regulation of cartilage tissue in the joints.

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Annual General Meeting

The Annual General Meeting will be held on Thursday, 22 April 2004 at 4 p.m. Notice to attend will be announced in the usual way. The annual report will be distributed to the shareholders no later than two weeks before the AGM. Shareholders wishing to attend in the AGM must be registered in the shareholders' register kept by the Swedish Securities Register Centre (VPC) no later than Thursday, 8 April 2004 and should inform BioInvent of their intention to attend no later than 4 p.m. on Friday, 16 April 2004 at the address: Sölvegatan 41, 223 70 Lund, attn: Marie Serve, or by fax +46 (0)46 211 08 06 or by phone +46 (0)46 286 85 50.

In order to participate in the proceeding at the AGM, shareholders with nominee-registered shares should request their bank or broker to have the shares temporarily owner-registered with VPC. Such registration must be made on Thursday April 8, 2004 at the latest, and the banker or broker should therefore be notified in due time before said date.

Upcoming financial information

BioInvent intends to present the following financial reports in 2004:

Interim reports: 21 April, 15 July, 14 October 2004.

Financial statement 2004: 17 February 2005



Patent protection – A prerequisite for every project

Strong patent protection is essential for all projects run by BioInvent. Our product candidates are protected partly through licensing agreements regarding target proteins, and partly by the fact that the product candidates are developed using the Company's proprietary, patented technologies. During the course of the projects, we strengthen our patent protection on a regular basis by patenting the specific product candidates as soon as they are identified and by patenting new results.

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Human resources – Attract the highest level of expertise

BioInvent is in every respect a knowledge-intensive company, and its most important resource by far is the employees. Just over 90 per cent of the Company's 104 employees are university graduates and 34 per cent have Ph.D. status. A total of 84 individuals work in research and development.

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Quality, ethics and environment

BioInvent will act as a good member of society, assuming its responsibilities with respect to its partners, the employees and their work environment, as well as the global environment.

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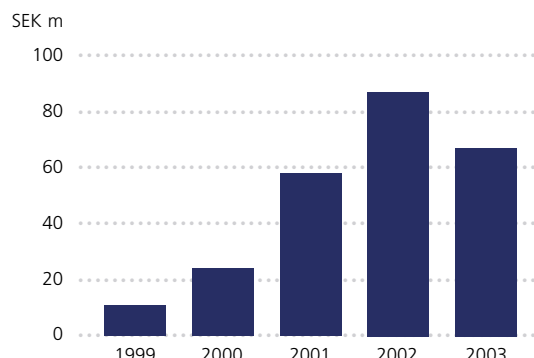
Risk analysis – Risk and risk management

Developing a new drug is a costly and risky process. In order to reduce the level of risk, BioInvent works with partners during several stages in the value chain. By building a broad project portfolio, the risk is spread over a number of projects. Up to now, however, the portfolio has been relatively limited with only a few projects in the early clinical phase, which means that a setback in an individual project can have a noticeably negative impact on the Company.

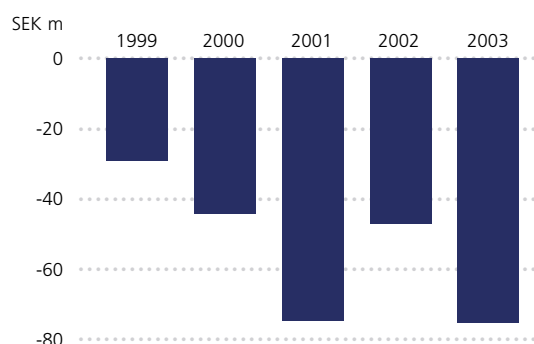
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The Board and auditors, senior executives and financial sections

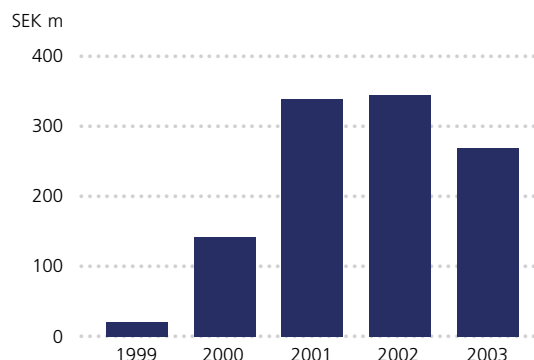
Net revenue



Cash flow from current operations and investment activity



Liquid funds at year-end



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Investor Relations

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Financial reports are also available at www.bioinvent.com

Legal disclaimer

This report contains statements about the future, consisting of subjective assumptions and forecasts for future scenarios. Predictions for the future only apply as of the date they are made and are, by their very nature, in the same way as research and development work in the biotech segment, associated with risk and uncertainty. With this in mind, the actual outcome may deviate significantly from the scenarios described in this report.

A growing and innovative project portfolio

As I look back for a moment at 2003, I am happy to report that we are developing a very interesting project portfolio. Within several indication areas, each with a significant unmet clinical need, we have succeeded in moving innovative projects further forward in the value chain. We have taken some important steps in our projects for the treatment of HIV and atherosclerosis and new projects have been launched focusing on treatments for widespread diseases such as cancer and osteoarthritis.

Increased emphasis on proprietary drug projects This clearly illustrates the strategy that was decided upon almost three years ago – to move our positions forward in the value chain by developing proprietary antibody-based drugs. To further emphasize this strategy, the Company implemented a re-organisation last autumn to transfer more resources to the development of proprietary drug candidates.

As a result of these changes, the finances and structure of the Company are now well suited to our goal of moving the projects forward in the value chain and initiating new projects.

Progress with the project portfolio We have shown that we can deliver new product candidates in a short space of time. In the two projects that are most advanced, we have, in just over a year, developed and optimised product candidates with biological effects in relevant clinical models. This demonstrates the strength of our technology platform.

Within the HIV project, the pre-clinical tests carried out at Smittskyddsinstitutet and the Karolinska Institute in Stockholm show that the product candidates the Company has developed effectively prevent the spread of the virus between human cells *in vitro*. The next milestone is gathering data to support the assumption that the product candidates prevent the virus from developing resistance to the therapy.

Most of the current therapies result in the development of resistance and it is this development that limits the arsenal that physicians have at their disposal for treatment. If we can succeed in documenting the absence of the development of resistance, the Company's product candidates will generate great interest, both within the pharmaceutical industry and among treating physicians.

The product candidates that we have developed for the treatment of atherosclerosis have shown promising effects in pre-clinical animal models. The unwanted plaque formation in the vessel walls has been

reduced by half, despite the fact that the treatment has only been under way for a short period. So far, clinical studies focusing on existing therapies have only shown marginal effects on established plaque formation, which, if it is destabilised can lead to infarction, the largest cause of death in the industrialised world today. Success in the future pre-clinical and clinical programme should therefore represent significant financial potential.

Provided that we achieve the anticipated success in the pre-clinical studies in progress within the areas of HIV and atherosclerosis, we expect to be able to select product candidates for pre-clinical safety tests as early as this year.

We are continuing to develop our customer portfolio by licensing technology and carrying out development assignments on behalf of customers. This is an important aspect of our strategy, partly because the revenue that such projects generate counterbalances part of the risk that our own projects involve, and partly because they contribute to creating a broader commercial interface that helps us to develop our technical and commercial skills.

The portfolio will be expanded further In addition to moving existing projects forward in the value chain, we will be prioritising the work of expanding our portfolio in 2004. This will enable us to reduce our dependence on the success of individual projects and have a more balanced level of risk. In our decisions regarding initiating new projects, the criteria will still be whether they meet our high expectations for medical relevance, the unmet clinical need and patent protection.

Because it takes a relatively short space of time to deliver new product candidates, we are able to quickly build a broad project portfolio. The key is access to good target proteins. It is therefore important for the Company to establish itself as a natural partner for parties that have a good idea – regardless of whether they are from academia or the industrial sector.

All of the projects in the portfolio are examples of BioInvent's ability to ally itself with strong external research groups in order to gain access to innovative target proteins as a basis for new drug projects. We believe that a strategy that combines the Company's expertise and resources within antibody development with high quality and specialised external biological research, is the best way to strengthen and expand the product portfolio.



Financial flexibility through new contracts

In 2004 we will prioritise our efforts to form partnerships for individual projects; partly in order to ensure our financial flexibility, and partly to ensure that the project can progress in an efficient and optimal way with the technical and financial resources needed, thus avoiding an excessive portion of our assets being tied up in individual projects.

As a supplier of technology, we have already proved our ability to reach commercially viable agreements. This is valuable experience that we will take with us when we finalise agreements regarding our own drug projects. I believe that the pharmaceutical industry will continue to need to license projects in order to reach its growth objectives. The projects that we conduct address areas where there is great market potential – indication areas that are being monitored by the large pharmaceutical companies in their search for new drug candidates. Provided that our development programmes are successful, this fact increases our chances of entering into profitable agreements – even in the early development phase. It is important to have flexibility regarding the timing of outlicensing, so that we can ensure that our financial commitments are always well adjusted to the amounts permitted by the balance sheet.

Over the past few years, BioInvent has developed into an exciting, antibody-based pharmaceutical company with a growing and innovative project portfolio and a technology platform that is a solid basis from which to initiate new projects – all protected by strong patents. This foundation gives us every reason to look ahead at 2004 with confidence.

Finally, I would like to thank everyone who has contributed to BioInvent's progress during an exciting year in 2003, both our employees and our partners.

Svein Mathisen, President and CEO BioInvent International AB.



2003 in brief

- **Promising pre-clinical data for BioInvent's HIV projects:** The Company's antibodies against HIV effectively prevent the spread of the virus between human cells.
- **Progress within BioInvent's projects for treating atherosclerosis:** Antibodies tested in pre-clinical animal models show a clear reduction of plaque in the blood vessels.
- **Strengthening the project portfolio:** Drug projects launched for the treatment of major widespread diseases such as cancer and diseases of the joints (osteoarthritis) based on new therapeutic principles.
- **Cross-licensing agreement signed with the US pharmaceutical company XOMA regarding antibody technologies.**
- **Strengthening of the patent portfolio:** European patent granted for the n-CoDeR® antibody library.
- **Net revenues:** SEK 66.7 million (87.1).
- **Cash flow from current operations and investment activity:** SEK -75.5 million (-47.1). **Liquid funds at the end of the year:** SEK 268.5 million (343.6).
- **Loss after net financial items** amounted to SEK -89.7 million (-46.2) and **loss after net financial items per share** amounted to SEK -3.04 (-1.60).

Focus areas in 2004

- Moving the existing projects further forward in the value chain with the aim of selecting product candidates within individual projects.
- Expanding the project portfolio to include additional projects.
- Prioritising the efforts to form partnerships for individual projects.

Focus on antibody-based drugs

BioInvent is established within the field of antibody-based drug development and continues to focus on this area. The Company is currently conducting innovative projects within various disease areas such as AIDS, atherosclerosis, cancer and osteoarthritis. All are areas where there is a great need for new treatment options.

The basis of our operations is a strong technology platform that makes it possible to quickly and effectively isolate human antibodies, optimise the complex proteins, and finally, produce the quantities that are needed for clinical development programmes – and possibly also for commercial products.

The platform provides good opportunities for further expanding the project portfolio. The Company will initiate new projects within indication areas where there is a significant need for new treatment options. Important criteria when choosing such projects are:

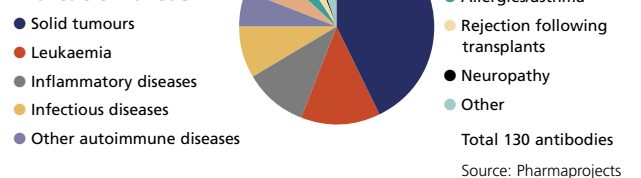
- Significant market potential
- Strong patent protection
- High level of innovation
- The target protein and its biology are suitable for treatment with antibodies

By diversifying and expanding the portfolio, BioInvent avoids becoming all too dependent on the success of individual projects. BioInvent's vision is, by the end of this decade, to be a leading and prosperous company within the development of antibody-based drugs, with several product candidates in development and – in cooperation with strategic partners – one or more products in the registration and/or launch phase.

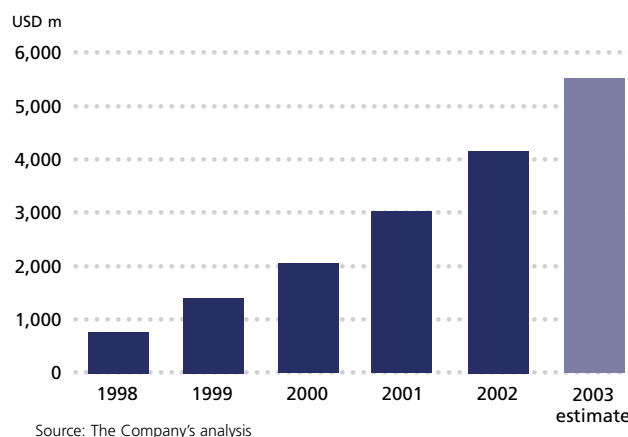
A pharmaceutical segment experiencing strong growth Antibodies are the single largest class of drugs, apart from vaccines, in development today. Altogether, there are 130 different products in clinical phases within a number of medical areas. The main one is cancer, but autoimmune and inflammatory diseases are also important areas.

So far 17 antibody products have been registered and approved. Combined, they accounted for sales of USD 5.6 billion in 2003, compared to just over USD 4 billion in 2002.

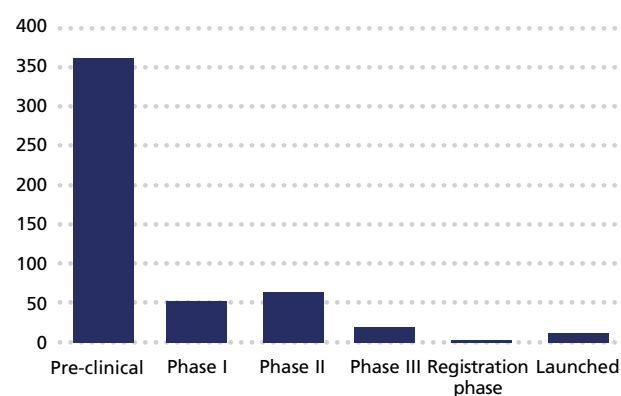
Antibodies in clinical trials within different indication areas



Sale of approved antibody-based drugs



Number of antibodies in different clinical phases



Product candidates that are tested on several indications are only counted once.
Source: Pharmaprojects



BioInvent's role in the value chain BioInvent focuses on developing antibody-based drugs and documenting their effects in pre-clinical and early clinical trials. The starting point for the projects is a target protein to which the actual antibody binds specifically. The target protein should be closely connected to the development of a disease.

BioInvent is not normally involved in the discovery phase for such target proteins. Instead the Company seeks alliances with external research groups, either in academic settings or in the industrial sector, that have discovered target proteins linked to diseases where there are large groups of patients and limited treatment options.

These research groups provide not only target proteins, but also significant biological and medical expertise within their indication areas. They also contribute, to a great extent, relevant *in vitro* and *in vivo* models used in testing the selected product candidates. Control over the relevant target proteins is achieved mainly through a licensing agreement.

So far, BioInvent has signed several licensing agreements that give the Company access to innovative and unique target proteins for the development of antibody-based drugs. The strategy of finding target proteins externally eliminates a large portion of the risk associated with the discovery phase in a drug project, and makes it possible for BioInvent to build a portfolio of projects that spans several medical areas.

The Company will seek partnerships with established pharmaceutical companies that will assume the primary responsibility for clinical development, marketing and distribution. Agreements will be signed in the final phase of pre-clinical development or in the early clinical phase. The timing is determined by such factors as cost, risk, skills requirements and the value in a further phase in the process being carried out by BioInvent. Such partnerships ensure that the projects, at an early stage, are supplied with knowledge and resources from large pharmaceutical companies, and also that BioInvent avoids tying up large amounts of its resources in individual projects.

BioInvent's partners will have sole responsibility for the main portion of clinical studies, marketing and distribution. BioInvent will, however, retain the production rights for the clinical programme and for the manufacture of the commercial product in cases where the Company's production capacity is sufficient. This is believed to be of strategic importance, since active participation in the project ensures that the Company's interests can be optimised.

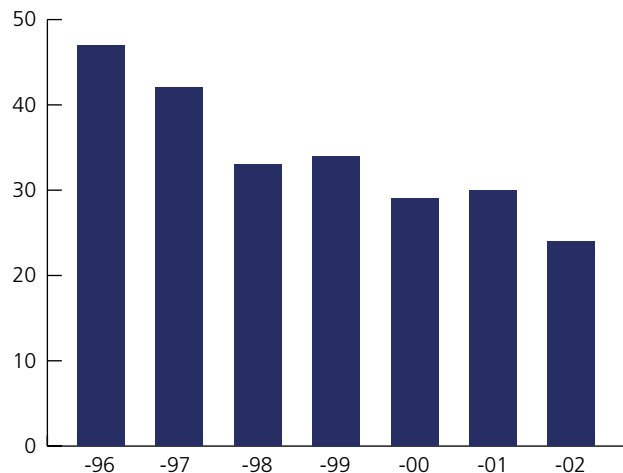
The strategic role that BioInvent assumes in the value chain means that the Company is the sole responsible for development for a period of two to five years. Thereafter, an established pharmaceutical company takes over the primary responsibility. The duration of the period is determined primarily by to what degree the target protein is validated in relation to the development of the disease in question and by BioInvent's commercial assessment.

As a partner and supplier, BioInvent has been able to build the technology platform that the Company is now using to generate value in proprietary projects. The Company's portfolio of proprietary projects will continue to be supplemented by research and production assignments on behalf of partners. Such assignments generate revenue that counterbalances a portion of the risk associated with BioInvent's development of proprietary drugs.



The pharmaceutical industry's need for new projects BioInvent's strategy of entering into alliances with pharmaceutical companies to get projects through clinical development to full commercialisation is based on the industry's need for new innovative projects. The number of product launches has fallen significantly in

Number of new, approved drugs in the US



Source: Nature Reviews Drug Discovery

recent years – a trend that is very troubling for the industry's growth plans. The problem is exacerbated by the fact that patents for more and more products are expiring, which results in competition from cheap imitations.

Antibodies already form a large portion of both product candidates in clinical phases and new products on the market, and are on the way to being developed into a strong and established treatment format. This provides great opportunities for companies that focus on this type of drug.

Revenue model BioInvent's business model means that the Company receives revenue in the following ways:

- From a development partner who buys into the Company's proprietary projects. These revenue flows are expected to comprise:

- Access fee when agreements are signed.

- R&D milestones payments when projects pass pre-determined milestones. The number of milestones increases the earlier in the development process the agreement is signed. The earlier the agreement is signed, the larger the portions of the payment are due later in the course of the project.

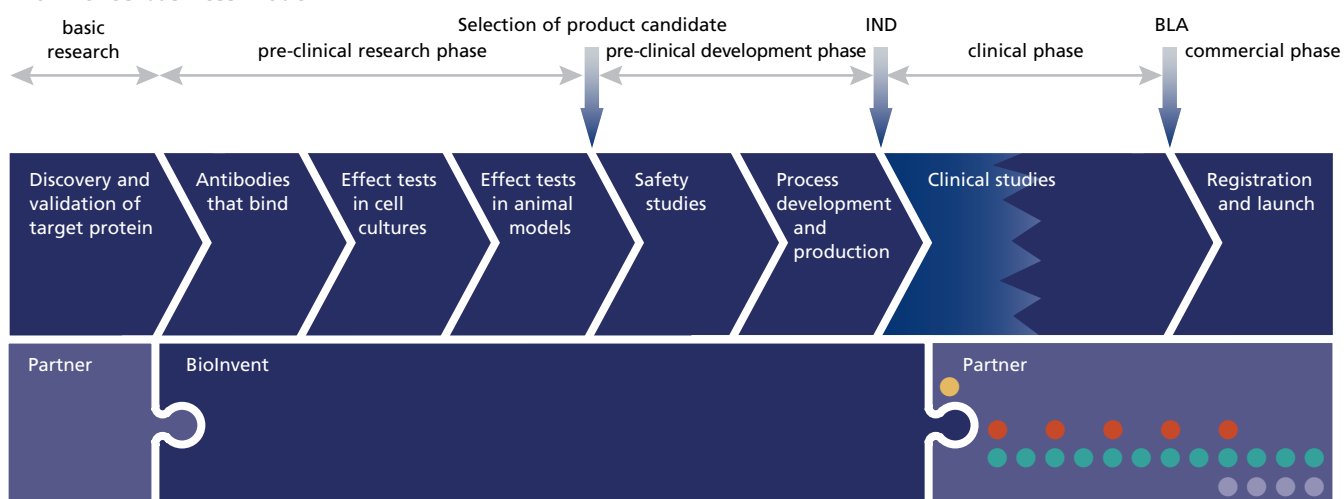
- Payment for manufacturing of the product, for the clinical programme and possibly also for the commercial product.

- Royalty, involving a percentage of sales of the end product.

The initial access fee and R&D milestone payments that can be paid out depend on in which development phase the agreement is signed, the level of innovation and the market potential within the indication areas the product addresses. The accumulated amount for such payments, provided that the product reaches the market, is around SEK 300 – 600 million in connection with outlicensing in the late pre-clinical phase, rising to SEK 600 – 1,000 million after the first clinical effect data is obtained. Access fee at the time an agreement is signed is normally around 10 – 15 per cent of the amount. The royalty rate will normally be in the range of 10 – 20 per cent, and the level depends on whether the agreement is signed in the late pre-clinical phase or after the first clinical effect data is obtained.

Accumulated compensation for production of materials for the clinical programme may vary from SEK 100 million to SEK 150 million, depending on the material requirement in the development process and on condition that the product passes all of the clinical phases with the Company as the sole manufacturer.

BioInvent's business model



BioInvent has sole responsibility for the project for a period of two to five years before a commercial partner takes over primary responsibility. The timeframe varies depending on to what degree the target protein is validated and on BioInvent's commercial assessment.

- Access fee
- R&D milestones
- Compensation for production
- Royalties

- From customers for whom BioInvent carries out manufacturing and research assignments. Revenue is based on:
 - Assignments where BioInvent (or the customer, based on a licence) isolates and optimises an antibody-based drug candidate, against a target protein defined by the customer. Payment for these assignments is in the form of research financing (or licensing fees), R&D milestone payments and royalty on sales of the end product.
 - Assignments where BioInvent manufactures antibodies that are owned by customers. Payment for these assignments is in the form of a fixed, agreed sum.
 - Assignments where BioInvent delivers antibodies that are used as research tools for a customer's research programme. Payment for these assignments is in the form of a fixed fee for the number of researchers that participate in the programme.

Up to now, BioInvent's revenue has been generated by manufacturing and research assignments. With the partnership strategy and the role in the development chain that BioInvent is aiming for, revenue from

proprietary projects is expected to increase and subsequently be the dominant source. The fact that a larger portion of the Company's capacity is used for proprietary projects, and the contribution of R&D milestones, will make the revenue flows more volatile in the immediate future.

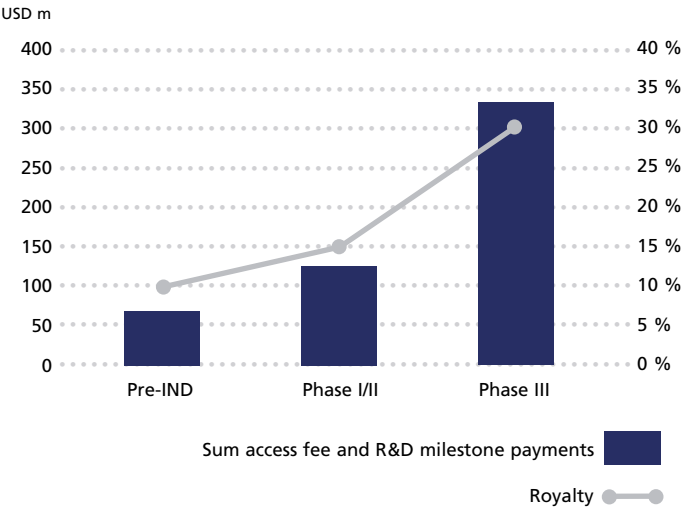
Research and development costs BioInvent's technology platform is an important tool in each antibody programme. Because it is validated and does not require any significant amount of new investment, the Company can isolate, optimise and manufacture product candidates in the required quantities very cost-effectively and with the necessary parallelity to enable effective development of the portfolio.

The pre-clinical and clinical development will, however, add new costs as the project portfolio is expanded and individual projects are moved forward in the development chain. BioInvent's value-generating role in this chain means, however, that the Company ties up relatively limited amounts of resources in individual projects before the first payment from a partner is received – provided that the project progresses successfully.

The Company's business model involves future payment commitments within the projects to the groups or researchers that have discovered the target proteins in question. This applies to R&D milestones and royalties, payments that have been agreed upon under the respective licensing agreements and linked to the progress of the projects. Success-related payments of this nature are matched according to the business model with corresponding success-related revenue from BioInvent's development partners.

Under the licensing agreements that the Company has entered into so far, the R&D milestones and royalties for the owners of the target proteins are at a level that reflects the fact that the Company is licensing a medical concept in the form of a target protein and not a product candidate. Consequently, these amounts are significantly lower than the amounts that are expected from a development partner.

Examples of value when pharmaceutical companies license new drug candidates



The study is based on a number of agreements entered into in various development phases. The values are the average of amounts with a wide spread.
Source: Mercer Management Consulting

Cash flow and profitability The goal is for access fees and manufacturing for clinical programmes within the Company's proprietary drug projects, together with revenue flows from manufacturing and development assignments, over time to provide a balanced cash flow. The long-term profitability is ensured through royalties and milestone payments and compensation for possible commercial production within projects that successfully reach the market.



From target protein to antibody-based drug

All drug development is based on a target protein, i.e. the protein that the drug is to affect. The discovery and identification of new target proteins is an uncertain and drawn out process that involves many scientific disciplines. The research may be based on in-depth biological knowledge where there is strong proof that a protein is linked to a certain disease, while other common strategies are to study differences between genetic expression and protein levels between normal and diseased cells. Thus potential target proteins with possible links to different diseases can be identified. Comprehensive studies of the function at the protein level, as well as the network that effects the protein interferes with are necessary.



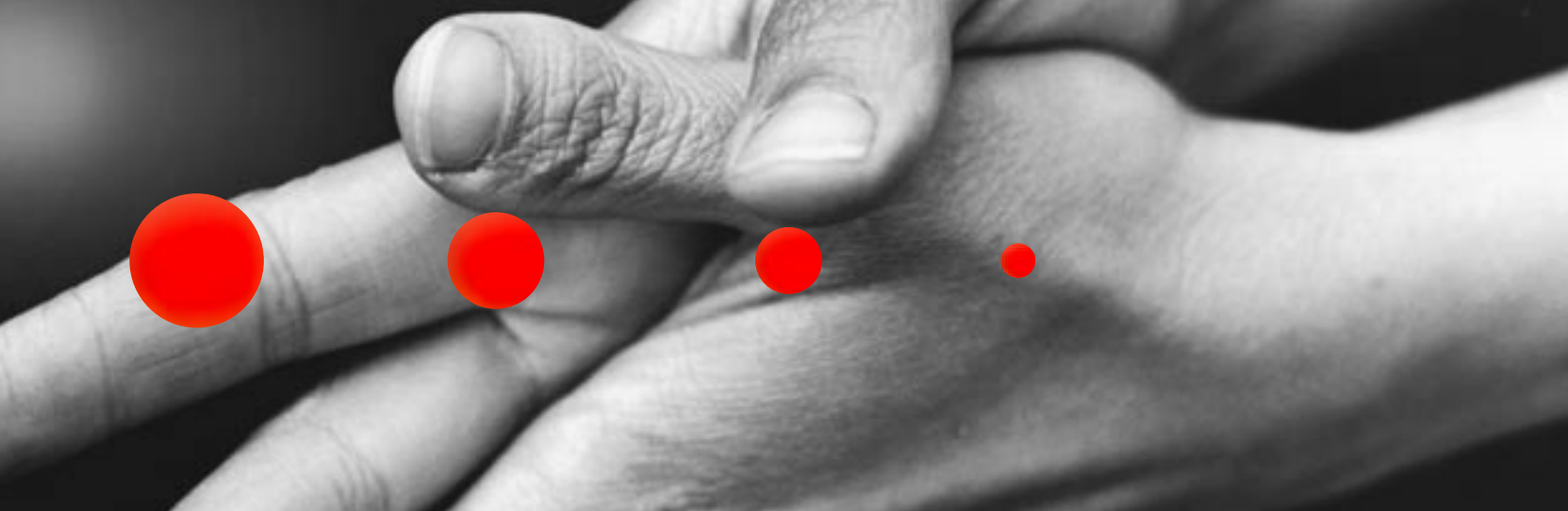
Validation of the target protein The next stage in the process is to validate the target protein by studying the effect on it in different disease models. The validation process is iterative and is often conducted parallel to the production of the therapeutic substance.

Antibodies are important tools in the validation process. By finding an antibody that binds to the target protein and that either blocks or stimulates its function, researchers can study the impact of such actions. Unlike other validation tools, an antibody of this kind may itself be a possible product candidate and thus a lot of time can be saved in the development process.

Antibodies that bind In order to create substances that bind to the target protein, BioInvent uses its patented antibody library, n-CoDeR®. This is a collection of more than 15 billion human antibodies, clearly more than can be created by the human immune system on any given occasion. The diversity of the library is sufficient for it to offer binders to all target proteins that may be suitable for treatment with antibody-based drugs. Within traditional pharmaceutical chemistry and substance screening, where the libraries are 10,000 – 100,000 times smaller, it is necessary to use several, customised libraries in order to cover a whole spectrum of target proteins.

The n-CoDeR antibody library is screened with the help of automated processes and the first antibodies can normally be tested for their binding properties after just a few weeks. Since antibodies have a natural ability to bind specifically to target proteins in a living organism, the screening of the antibody library provides – in one and the same process – both a possible drug candidate and validation of its ability to bind to the target protein. In traditional pharmaceutical chemistry, comprehensive optimisation of the first model substance is usually necessary, often in a process of trial and error, in order to achieve the optimal binding properties.

Effect tests in cell cultures When candidates with the right binding abilities have been found, their functional characteristics are tested in different cell biological systems. Screening of n-CoDeR usually results in several hits that bind well to the target protein in



question. This provides a number of alternatives that can be studied further and increases the likelihood of finding one or more candidates with good characteristics that can be tested in relevant animal models.

Effect tests in animal models The supply of animal models that correlate with diseases in humans varies from indication area to indication area. Using suitable animal models is expected to be able to reduce the risks in the clinical development programme.

Biolnvent has no resources of its own for conducting tests on animals. Any tests on animals for the purpose of studying the effect of antibodies, is instead done in cooperation with partners and authorised contract research institutes that comply with strict rules governing this type of activity.

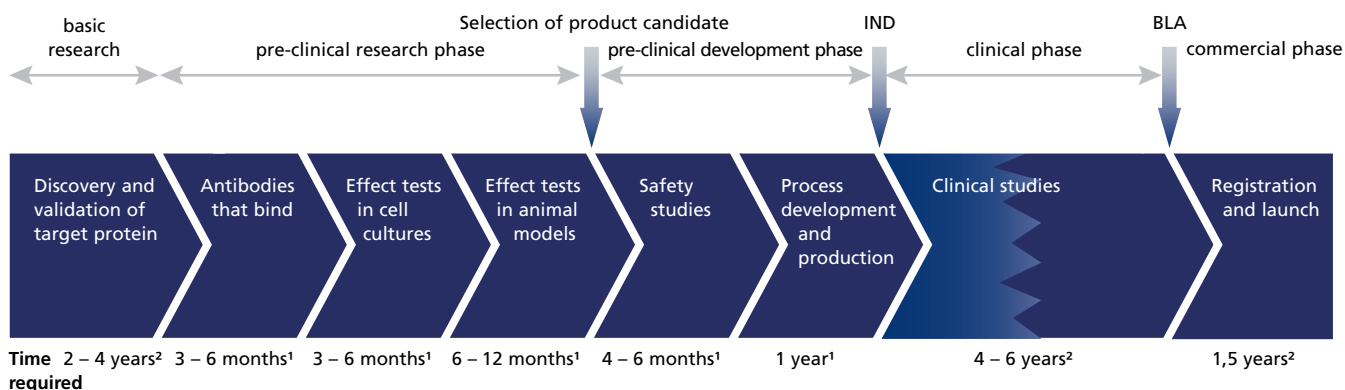
Safety studies When satisfactory pre-clinical effects have been documented, a product candidate is selected for safety studies and later clinical studies in humans. The safety tests normally involve the study of side effects in animal models and analysis of absorption, distribution, metabolism and secretion of the drug candidate. Biolnvent develops human antibodies not recognised as foreign and

that have a natural function in the body, which should reduce the risk of side effects. Biolnvent believes that the tests therefore will be less demanding than those for traditional drug candidates, resulting in considerable savings in both time and costs.

When the safety studies have been completed and satisfactory results have been achieved, the documentation is compiled and sent to the authorities in the form of an application to start clinical studies, a so-called IND (Investigational New Drug) application.

Manufacturing by Biolnvent The manufacturing of antibody-based drugs differs from the manufacturing of traditional drugs insofar as living host cells – usually animal cells – are used for manufacturing. The genetic code for antibodies is integrated in the host cell's own DNA, and a cell line is developed enabling stable and high-level production of the antibody. The actual production process is done through cultivation in a so-called fermentor, where the cells multiply while synthesising and secreting new antibody molecules into the nutrient solution they are cultivated in. This is then purified in several stages to separate the antibodies from the unwanted components.

Development of antibody-based drugs



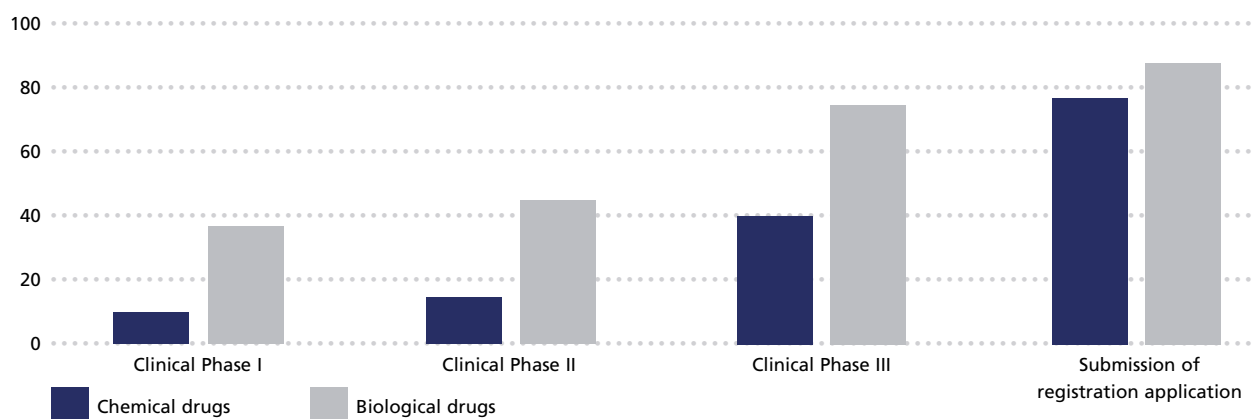
¹) The Company's estimates

²) Based on data from PAREXEL's R&D Statistical Sourcebook 2003/2004

The figure shows the development process as a sequential process. The process will often be iterative and several parts of the process can be carried out simultaneously. One example is manufacturing, which Biolnvent carries out parallel to the late pre-clinical studies.

Cumulative level of success for biological drugs compared to chemical drugs

Level of success at beginning of respective phase



The figure shows the past level of success in reaching the market after different clinical phases are initiated.

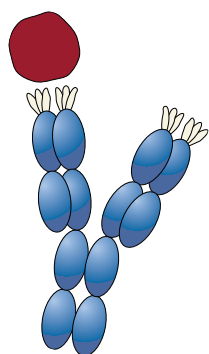
Source: CMR International, March 2003

The complexity of the manufacturing processes is the reason for BioInvent's strategic decision to build up its own production resources. This gives the Company maximum control and flexibility for the individual projects. Since BioInvent has access to its own manufacturing resources, the Company usually carries out the first stages of the manufacturing processes before selecting the final product candidates. The final phases in manufacturing the product for the first clinical studies are then carried out parallel to the safety tests. This saves a lot of time and makes it possible to quickly reach the clinical phase.

Clinical development Clinical studies on humans are normally carried out in three phases, starting with Phase I studies, where the emphasis is on analysis of the safety aspect and issues relating to the drug's mechanism of action. The Phase I studies are normally

carried out on healthy human subjects. These are followed by Phase II studies with analysis of the drug's effect on small groups of patients, followed by Phase III studies on broader groups of patients. In Phase III studies, the effects and side effects are compared with those of current drugs on the market. After successful clinical studies, applications are made to the relevant authorities to get the drug approved and registered for commercialisation and sale (BLA application).

Since antibodies have a natural biological function in the body, the mechanism of action should in many contexts be easier to predict than in the case of traditional drugs, which are often synthetically combined organic molecules. Even if the statistical documentation is still somewhat limited, studies indicate that antibodies and other biological drugs have a far greater chance than chemical molecules of reaching the market (see graph above).



An antibody can be illustrated by using a "Y" where the ability to bind to the target protein is in the two arms.

Antibodies – Proteins well suited as drugs

Antibodies are a vital part of the immune system and constitute one of the human body's most important defence mechanisms against disease. When a pathogenic contagion is discovered, the immune system reacts by producing millions of antibodies. These bind specifically to the substance thereby activating other mechanisms in the immune system which then eliminate the contagion.

The specific binding abilities of the antibodies make it possible to treat many diseases accurately and effectively. One way is to use the natural mechanisms of action that are described above. Another is to use the target-seeking and specific binding abilities of the antibodies and:

- link them up with, for example, radioactive isotopes, which kill cells and tissue locally where the antibody binds;
- allow them to block undesired protein interactions that cause disease, for example, inflammatory and autoimmune diseases;
- use them to initiate signals by binding to specific proteins, which stimulate or inhibit the activity of the given cells.

n-CoDeR – An effective source of new product candidates

n-CoDeR is a collection of more than 15 billion human antibody genes that are stored in bacteria in test tubes. The bacteria act as production units for the antibodies, which are then screened in order to identify which antibodies bind to a specific target protein.

Antibodies are large proteins. The part of the antibody that recognises a target protein is only a very small part of this molecule and is called its Complementarity Determining Region (CDR), which consists of six elements or loops. n-CoDeR dramatically increases the genetic variability in the CDRs. CDR loops are isolated from natural antibodies and copied many times. These elements are then allowed to switch places at the same time as they are joined randomly in new combinations in a single master antibody framework. This leads to very high genetic variability, which increases the likelihood of finding an antibody with the desired properties

The library is built from naturally occurring antibody genes. 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”.

In order to be able to generate an antibody from the library, a screening process is carried out. If bacteria with antibody fragments were allowed to produce all of the conceivable antibodies, the volume would be so large – hundreds of litres – as to make it impossible to conduct effective, industrial screening. Instead, a technology called phage display is used whereby bacterial viruses are used to display antibodies for target proteins in the screening process. The bacterial viruses are called phages and are entirely harmless to humans.

With phage display, the entire antibody library is formatted to the phage format and the phages are then passed over a surface to which target proteins have been attached. Phages with the “correct” antibodies bind to the target protein and all other antibodies are washed away. The desired antibody gene can then be isolated from the phage and used to multiply and produce the desired antibody in large quantities.

n-CoDeR is well suited for automation and allows the process of antibody generation to be entirely industrialised. Among other things, BioInvent has a robot that enables screening of up to 20,000 antibody fragments per 24-hour period. It selects clones, carries out automatic analysis, screens through a multitude of antibodies at a much faster pace, increases parallelity and reduces the likelihood of errors.

Through its structure, n-CoDeR contains genes that code for fragments of whole antibody molecules. These antibody fragments are selected from the library and then re-formatted with the help of an optimised process where the genes that code for the fragment are joined with the genes that code for the rest of the antibody. Thereafter, the entire antibody can be produced.

Using the n-CoDeR antibody library, BioInvent has successfully selected antibodies with high affinity for most types of antigens. The potential therefore exists for the Company to be able to generate human antibodies that are well suited for therapy against most target proteins of interest.



Developing the portfolio

BioInvent’s strategy is to develop antibody-based drugs. This is done partly through BioInvent’s proprietary drug projects and partly through development and production assignments where BioInvent carries out parts of development programmes on behalf of different partners.

Up to now, BioInvent has initiated projects within disease areas such as HIV, atherosclerosis, cancer and osteoarthritis. The basis of these projects is the technology platform the Company has developed and cooperation with external research groups with innovative medical concepts. The platform and BioInvent’s business model make it possible for the Company to build a broad portfolio of drug candidates. The Company is constantly seeking target proteins to use as a basis for new drug projects. By expanding the portfolio to include new projects while sticking to the business model, BioInvent spreads risk and opportunities over a number of projects.

Project evaluation Important success factors in the Company’s efforts to expand the project portfolio is the ability to identify and focus on the right projects and ensure the right decisions are taken at important toll gates. To do this, BioInvent has formed a special project evaluation committee, which has an important role in

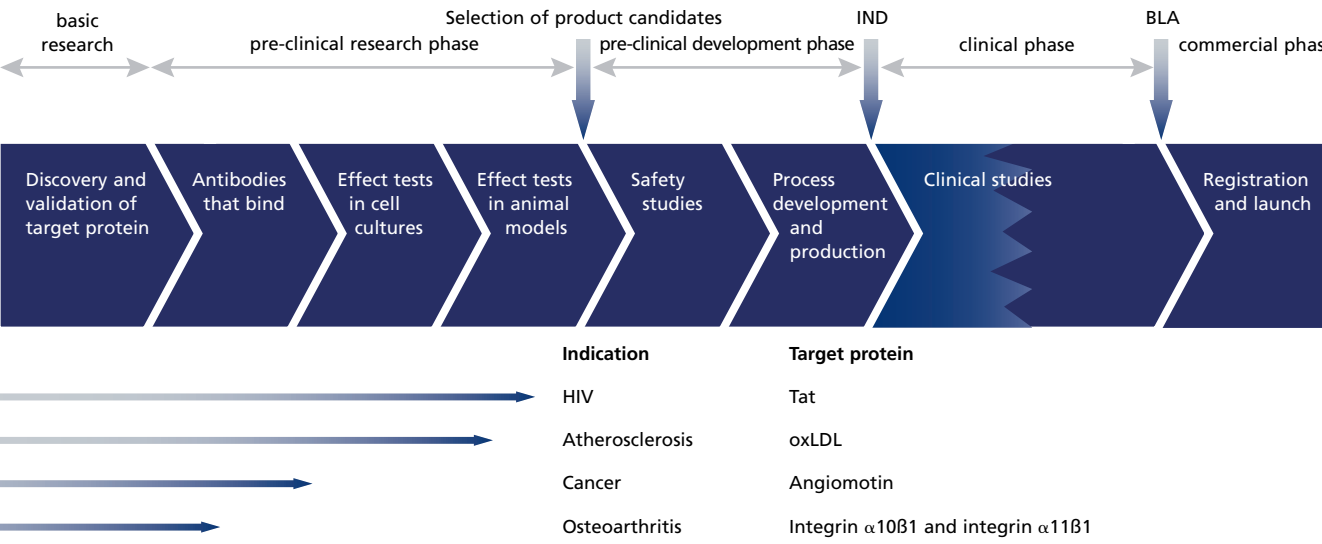
advising BioInvent’s management. Matters concerning the initiation of new projects and which direction to take at important toll gates are handled by the committee before management takes decisions and before possible final sanction is provided by the Board. The committee is headed by professor Carl Borrebaeck, the Company’s Senior Scientific Advisor. The committee consists of individuals with extensive expertise within the medical areas that the various projects address.

Development and manufacturing projects

BioInvent has always maintained a strong customer focus and an important part of the business model is to balance part of the risk associated with proprietary projects with business that generates a regular source of revenue. The following partnerships have generated revenue in 2003:

Antisoma This company has been a recurring customer since 1996. In this partnership BioInvent produces several of Antisoma’s antibody-based drug candidates for clinical studies, for example, Pentumomab (Theragyn), which is currently in advanced clinical Phase III studies.

BioInvent’s portfolio of proprietary drug projects





Celltech In 2002 BiInvent initiated a development partnership with Oxford GlycoSciences (OGS) for the development and commercialisation of antibody-based drugs. The UK biotech company Celltech has since acquired OGS. This scientific partnership is focusing on the cancer field.

GlaxoSmithKline (GSK) BiInvent has developed antibodies for use in GSK's research and development work within the vaccine field. BiInvent has been working with GSK since 2001. The agreement in its current form will expire at the end of April 2004. The partnership is believed to have been a valuable one for both parties and may lead to new joint projects.

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

In November BiInvent entered into an agreement with the US pharmaceutical company XOMA which gives XOMA the right to use the n-CoDeR[®] antibody library for its research programmes and certain rights to develop and commercialize therapeutic and diagnostic antibodies for use as drugs. If future product development is successful, this might provide BiInvent with revenues in the form of milestone payments and royalties on product sales.

In February, after the end of the reporting period, BiInvent entered into a production agreement with a returning customer, the Danish company ALK-Abelló for the commercial delivery of antibodies for a new allergy test that is being marketed by Bayer Diagnostics. This agreement is in line with BiInvent's strategy to secure long-term supply agreements within the field of antibody production.

Exploratory research In order to exploit the Company's technology platform commercially to the greatest extent possible, BiInvent is conducting exploratory research, primarily within the following areas:

Protein arrays In an early stage project, a system is developed for global analysis of the proteome, which may have great significance in the discovery of new target proteins for drug development. The aim is for the system to enable detection of differences in protein expression between different samples, e.g. from diseased and healthy tissue. The system is based on antibodies isolated from the n-CoDeR antibody library.

Leukaemia In an early stage project conducted in cooperation with a research group at Lund University, tumour-specific genes in certain B-cell tumours are studied as well as the proteins that these code for. The aim is to validate these proteins as targets for antibody-based therapy.



New treatment principle with potential to avoid resistance

Clinical need Human Immuno Deficiency Virus (HIV) causes an infection that affects and weakens a patient's immune system by attacking the T helper cell CD4⁺. T helper cells play an important role in the immune system by controlling the body's defences against infectious agents to which we are constantly exposed. When the level of CD4 positive T cells falls, the patient becomes susceptible to infectious agents that the immune system can normally handle. At this point the infection has reached the stage known as Acquired Immuno Deficiency Syndrome (AIDS), a deadly disease.

Current treatments for HIV aim to improve the patient's quality of life and prolong life by preventing the virus from multiplying and thereby preserving the function of the immune system. Specific drugs have been developed that reduce the amount of the virus in the blood and thereby enable the T-helper cells to multiply again. Up to now, however, this changeable virus has relatively quickly developed resistance to these drugs. This resistance is possible because of HIV's great variability and adaptability. When treatment is started, the virus changes quickly to adapt to the new conditions, thus rendering the therapy ineffective.

By using a cocktail of drugs in combination, a better effect is achieved and the virus is more effectively inhibited over a longer period than with the individual drugs. Combination therapy of this kind is the standard treatment today and strengthens the immune system and delays the onset of AIDS.



Elisabet Lindh Elliot, who is responsible for regulatory issues and Leonard Larsson, who is responsible for clinical trials, prepare studies regulated by the authorities within the HIV project.

The treatment requires a precise intake of the drugs at specific times in order to prevent HIV from responding by building up resistant strains. However, sooner or later resistance is developed and many patients experience unpleasant side effects.

The development of resistant HIV strains increases the mortality rate and is a very difficult problem for the medical profession. An article in Nature Reviews Drug Discovery (2003) states that of 335,000 HIV patients treated in the US, 240,000 were troubled by side effects and 270,000 developed resistance to more than one type of drug. Around 52,000 developed resistance to all three of the usual classes of drugs.

Consequently, new, effective HIV drugs are needed that can control the development of the virus in the patient without contributing to the development of resistant HIV strains.

Market and competition The number of people infected with HIV/AIDS in the western world is estimated at around 1.8 million.

In 2001 the market for HIV drugs, which is very dynamic, was worth more than USD 5 billion. The most successful treatment at this time is the cocktails in which several active substances are combined.

At present, 43 drug candidates with HIV as the primary indication are undergoing clinical studies.

Biolnvent's therapeutic principle Biolnvent's strategy for the treatment of HIV is to block and neutralise the Tat protein – a target protein that is vital for HIV's ability to multiply and spread to new cells.

When HIV attacks and forces its way into the immune system's T helper cells, it takes control of their genetic make-up. Instead of producing important proteins for the immune system, they start to produce virus proteins. Tat (**T**rans-**a**ctivator of **t**ranscription) is produced in this way and then leaves the infected cell to activate immune cells around it. These activated cells become receptive to virus infection. Tat affects the process in another way, i.e. by changing the cell's production of proteins from cell proteins to virus-specific proteins, thus programming the cell for virus replication.

Antibody-based drugs against the Tat protein are expected to neutralise its activity and thereby prevent the spread of the virus to new and healthy cells. This will reduce the number of HIV particles in the blood of the patient to such an extent that the progress of the disease will be delayed. This assumption is supported by studies that show that, in the case of people with antibodies developed spontaneously against Tat, the disease progresses more slowly.

An important and unique characteristic of Biolnvent's approach is that the antibodies target parts of the Tat protein that are unchanged (preserved) between different virus strains. Another important factor

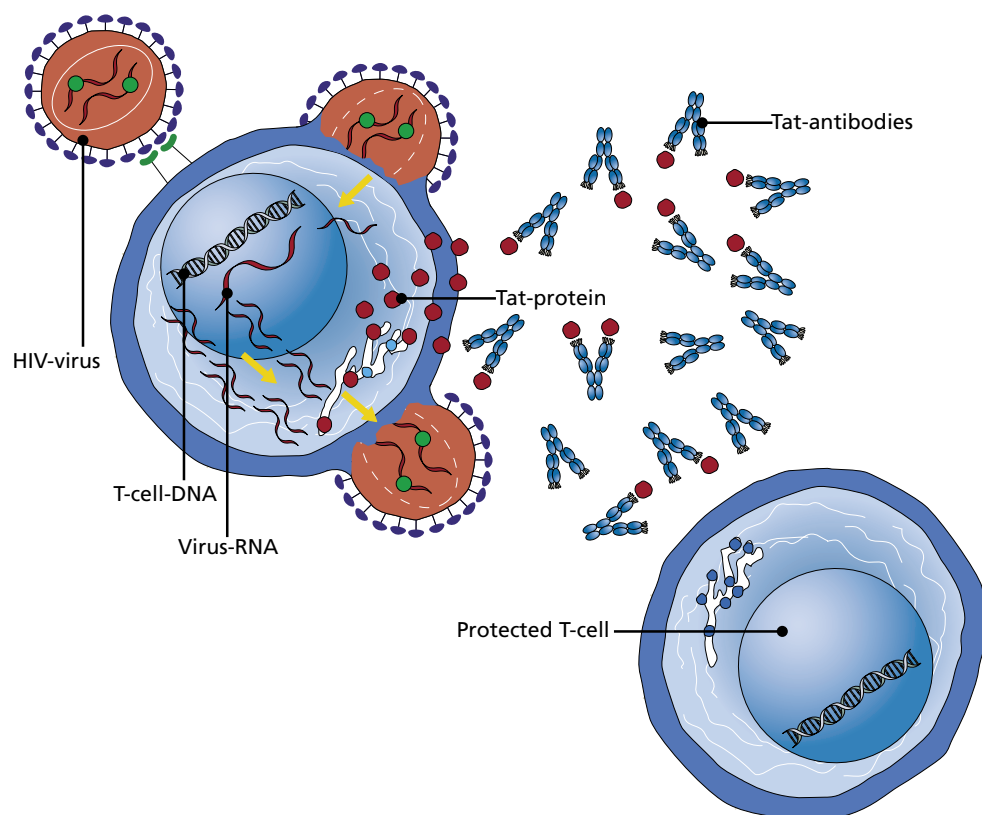
Sales of drugs for the treatment of HIV in USD m

| Type | Drug | Company | 2003 (Estimate) | 2004 (Estimate) |
|--------------------|---|----------------------|-----------------|-----------------|
| NRTI | Tenofovir disoproxil | Gilead | 500 | 690 |
| | Lamivudine | GlaxoSmithKline | 465 | 430 |
| | Stavudine | Bristol-Myers Squibb | 400 | 350 |
| | Abacavir/Lamivudine/Zidovudine ¹ | GlaxoSmithKline | 680 | 800 |
| | Lamivudine/Zidovudine ¹ | GlaxoSmithKline | 880 | 840 |
| | Emtricitabine | Gilead | 11 | 90 |
| NNRTI | Efavirenz | Bristol-Myers Squibb | 550 | 650 |
| Protease inhibitor | Lopinavir/Norvir ¹ | Abbott | 760 | 885 |
| | Nelfinavir | Pfizer | 230 | 150 |
| | Amprenavir | GlaxoSmithKline | 57 | 15 |
| | Fosamprenavir calcium | GlaxoSmithKline | 0 | 85 |
| Fusions inhibitor | Enfuvirtide | Trimeris/Roche | 90 | 354 |

¹ Cocktail therapy with several active substances in one tablet.

Source: Nature Reviews Drug Discovery (2003)

Fighting HIV using the Tat protein



Blocking and neutralising the Tat protein prevents the spread of the virus to healthy cells. The Tat protein is not linked to a virus particle and BioInvent's human antibody is aimed at preserved regions of the protein. These two characteristics are expected to minimise the risk of the development of resistance.

is that the Tat protein circulates freely in the blood and is not directly linked to a virus particle. This obstructs the virus's ability to change and adapt to the antibody's effect. Due to these two characteristics, the Company expects that antibodies against the preserved parts of Tat will prevent the development of resistance – and will therefore have a lasting effect.

Project status Pre-clinical tests show that the product candidates the Company has produced are able to prevent the spread of the virus between human cells *in vitro*. The tests were carried out at Smittskyddsinstitutet and the Karolinska Institute in Stockholm. The absence of resistance is also currently being tested in extended pre-clinical trials.

Alongside the pre-clinical work, process development is under way for cell lines to be used for large-scale production of the drug candidate. This work has progressed to an advanced stage.

Provided that the pre-clinical studies continue to be successful, the Company expects to select a product candidate for pre-clinical safety tests this year.

Patent protection Patents are pending for the parts of the Tat protein that are preserved between different virus strains, the use of these in drug development and products that targets at these target proteins. The patents were applied for by Gideon Goldstein through Thymon LLC, USA. Several patents have been granted in the

US and Australia. Patent applications have also been submitted in major markets such as Europe, Canada, Japan and China etc.

The rights to use these patents for the development of drugs (excluding vaccines) were licensed exclusively from Thymon LLC in July 2002.



Goldstein studied internal medicine in Australia and earned his PhD working under Nobel prizewinner Frank Macfarlane Burnett in the early 1960s. Burnett's Darwinistic approach to infectious disease stimulated Goldstein to go into research. A decade later he became involved with product development at Johnson & Johnson, one of the results of which was the first therapeutic monoclonal antibody in the market, for treating acute rejection of organ transplants.



Interview with Gideon Goldstein

"HIV has a life cycle in which virus infection persists in the patient. The virus has developed its own function for avoiding attacks by the immune system. My original idea was to find out how this works, and then develop a treatment that blocks it."

I followed several different paths, but it was when the Tat (transactivator of transcription) protein first appeared in the literature that I got a break: Tat protein has an inhibitory effect on the immune system and is essential to maintaining persistence of the virus; hence it presented a possible target for fighting HIV.

Before I came to Bioinvent we had successfully identified two parts of the Tat protein's protein sequence, two epitopes that it is not only possible to influence with antibodies, but that are also constant. There is no theoretical basis to suspect that treating with blocking antibodies could create resistance.

In order to make any progress, we needed a partner and once we began talking to Bioinvent it all came together quickly, because of their superior method of creating antibodies with high affinity from their antibody library n-CoDeR. It was helpful to meet a group on the scientific level that you find at BioInvent.

And it wasn't long before we found several promising antibodies! It's thanks to Bioinvent's enormous library and the phage display method, that it was possible to produce them.

My idea is to treat the individual with a monthly maintenance dose, which minimizes replication of the virus, both to prevent the patient's condition from progressing to AIDS, and to prevent the person from infecting others", says Gideon Goldstein, who hopes to be involved in the development well into the clinical phase.



atherosclerosis

Antibody-based drug is expected to reduce the risk of infarction

Clinical need Atherosclerosis is characterised by stenosis of the blood vessels and occurs when cholesterol is deposited on the inside of the vessel walls causing plaque formation. The plaque narrows the blood vessels and impedes the blood flow. This condition can lead to angina pectoris. If the plaque pulls apart, a thrombosis or blood clot will form which can block the blood vessel entirely or break away and be carried away by the blood flow. Such a blood clot may lodge in the heart causing infarction and if it reaches any of the blood vessels in the brain, it will cause a stroke.

Development of atherosclerosis may begin early in a person's teens, although the symptoms often do not appear until 30 or 40 years later. According to a report from Datamonitor (2002), the estimated prevalence of atherosclerosis in the US and the five largest markets in Western Europe is almost 33 million. The figure grows as people get older, but it is hard to accurately calculate how many people are actually affected, since atherosclerosis may be present without any visible symptoms until the onset of the acute stage. These cardiovascular diseases are responsible for about half of all deaths in the western world today.

An important risk factor for the development of atherosclerosis is high cholesterol levels in the blood and the current treatment strategy is therefore to lower cholesterol levels. Statins are the most common group of drugs used for this purpose. Statins reduce the level of lipids



Elisabeth Sonesson is head of BioInvent's atherosclerosis project.



in the blood by blocking an enzyme needed for cholesterol formation. Treatment with statins has significantly reduced the number of people developing cardiovascular diseases associated with atherosclerosis.

A large number of the patients treated with statins still suffer from heart attacks or stroke. There is therefore a significant medical need for a new treatment for atherosclerosis, where the aim is to stabilise plaque that may break free and hopefully also reduce its size. Since a drug of this kind would have great commercial potential, considerable research initiatives are under way in this field. Major clinical studies are analysing, among other things, the effect of statins on the size of the plaque.

Market and competition Lipid-lowering drugs are the second largest group of drugs in the world, with sales in 2000 of USD 17.2 billion. According to Nature Reviews Drug Discovery, the market is expected to increase to USD 24 billion by 2007.

In terms of value, statins account for the largest portion of the drugs used to treat atherosclerosis. Over a dozen companies are now competing for this market. The big seller in this class of drugs is atorvastatin, which is the drug with the highest sales of all of the categories.

Biolnvent's treatment principle Biolnvent's strategy for the treatment of atherosclerosis is to eliminate the undesired effect of oxidized forms of a lipoprotein that is part of the LDL particle. LDL is known as "the bad cholesterol." New research has shown strong links between these oxidized particles and harmful inflammatory processes in the vessel walls. These inflammations can result in the plaque pulling apart, which causes blood clots.

The oxidized LDL particles can be used as target proteins for antibody-based drugs. These are believed to be able to reduce inflammation and thereby stabilise the plaque formation and possibly also reduce it.

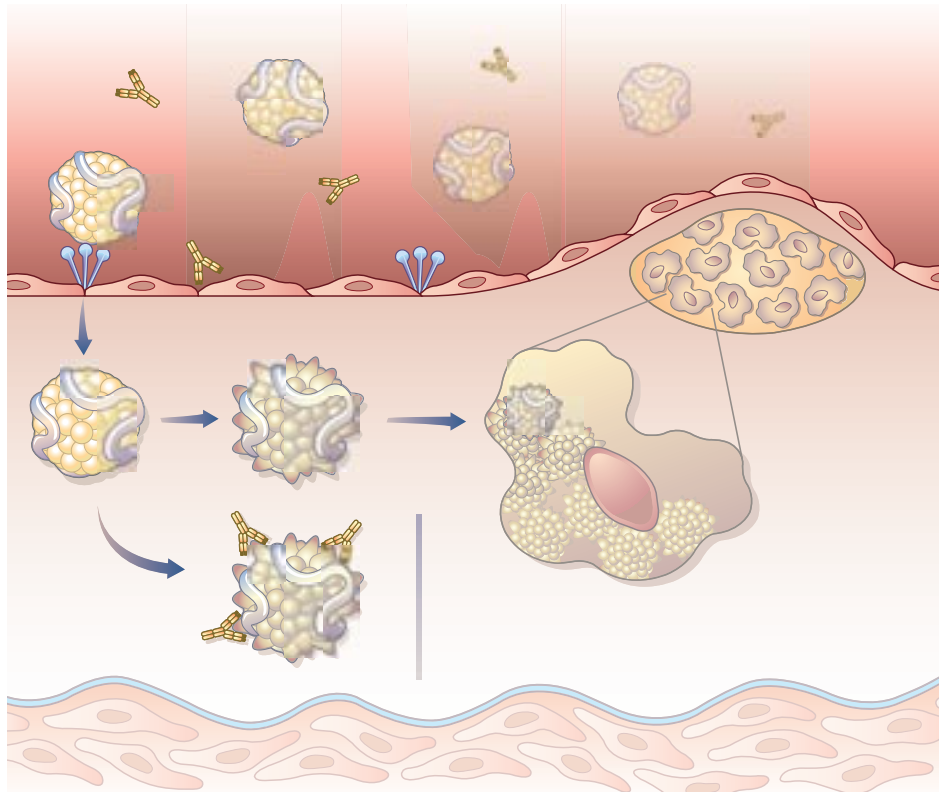
The concept of protecting the vessels against atherosclerosis with the help of antibodies against the target proteins is supported by earlier research. This protection was shown to be linked to an increased level of naturally occurring antibodies against the target proteins. The study shows that development of plaque is reduced when the amount of antibodies increases. There is therefore good reason to believe that antibodies aimed at the target protein will protect against atherosclerosis.

Sales of lipid-reducing drugs, USD m

| Drug | Company | 2002 | 2007 (Estimate) |
|----------------------------|-------------------------|---------------|-----------------|
| Atorvastatin | Pfizer | 7,100 | 9,500 |
| Simvastatin | Merck | 5,300 | 5,000 |
| Rosuvastatin | AstraZeneca | | 1,700 |
| Other statins | Several companies | 3,600 | 2,700 |
| Total statins | | 16,000 | 18,900 |
| Ezetimib/simvastatin | Merck / Schering-Plough | | 3,100 |
| HDL-metabolism inhibitor | Pfizer | | 1,200 |
| Other lipid-reducing drugs | Several companies | 1,200 | 1,200 |
| Total | | 17,200 | 24,200 |

Source: Nature Reviews Drug Discovery (2003)

Antibodies are expected to reduce undesired inflammations in the vessel walls



BioInvent's antibody-based drugs are aimed at oxidized LDL and are expected to reduce inflammatory processes and stabilise plaque formation in atherosclerosis. This reduces the risk of fatal complications such as acute myocardial infarction and stroke.

Project status The product candidates identified by the Company have been shown to very significantly reduce plaque formation in pre-clinical animal models. The experiments conducted at the MAS University Hospital in Malmö show that plaque formation in the vessel walls has been reduced by half, despite the fact that the treatment has only been under way for a short period.

At this time, the antibodies are being tested in animal models that express the human target protein. The purpose of these studies is to confirm earlier results in a model that can more reliably predict the effects that may be expected in humans. Additional studies to fully document the mechanism of action and which therefore allow the selection of the most suitable antibody, will continue during the year.

Provided that the pre-clinical studies continue to be successful, the Company expects to select a product candidate for pre-clinical safety tests this year.

Patent protection Patents are pending in around 40 countries including major markets such as the US, Europe, Canada, Japan, Australia, China and India for the oxidized forms of the LDL particle that cause the harmful inflammations in the vessel walls, the use of these in drug development and products that are aimed at these target proteins.

The patent applications are based on research at the MAS University Hospital in Malmö and Cedars-Sinai in Los Angeles. The rights to use future patents for the development of drugs (excluding vaccines) were licensed exclusively by BioInvent in December 2002.

Jan Nilsson is a cardiologist from the Karolinska Institute, where he worked with cardiovascular research until the end of the 1990s. He then moved to Malmö to become a professor of experimental cardiovascular research at the MAS University Hospital's Wallenberg Laboratory. He is also a guest professor at UCLA (University of California, Los Angeles) since six years and dean of the faculty of medicine at Lund University.



Interview with Jan Nilsson

"For some time now we have been studying what happens to blood fats (LDL) which are stored in so-called plaque in the vessel walls, and we have noticed, among other things, the strong inflammatory reactions that these give rise to when they are oxidized. Other researchers have shown that the body forms antibodies against these oxidized LDL particles. Our research has shown that the antibodies seem to be able to 'cool down' the inflammatory reaction in the vessel walls and make it easier for the immune system to take care of the plaque.

As a cardiologist I know that heart attacks and stroke are caused when the plaque becomes so inflamed that it breaks up and forms clots. We are already skilled at taking care of patients who have suffered an infarction of the heart, but we are not as good at preventing them. Consequently, there is a great need for better treatments for people in the risk zone.

In the beginning, experts focused mainly on a treatment that would stimulate the body's own production of antibodies and we are still actively pursuing this line of research. One disadvantage, however, is that it takes several weeks before the full effect is achieved. In our work, we are therefore aiming to produce and inject pre-fabricated antibodies in the blood that can quickly affect the plaque formation. Oxidized LDL is, however, a fairly complex structure and from the beginning we did not know which part of it that activated the generation of antibodies.

Once we had established the target protein, we needed help to artificially produce human antibodies against it. There are only a handful of companies working in this field in the world, and BioInvent was a strong contender in many ways, i.e. geographically, and not least because of its unique antibody library. We have already been able to establish that we made the right choice. The project has so far generated a number of specific antibodies that have been tested in relevant systems – with encouraging results. They are now undergoing further tests to find the one that is the most suitable to be developed into a drug."



cancer



Lena Nielsen is responsible for developing the cell lines that will produce the final product. Her team constitutes a common resource for all development projects.

Antibody-based drugs are expected to block the nutrient supply to tumours

Clinical need Cancer is a heterogeneous disease, which makes it more difficult to develop drugs aimed directly at tumour cells with the aim of killing them. A new and interesting strategy is to attack the blood supply to tumours by blocking the growth of new blood vessels.

The growth of new blood vessels is a process called angiogenesis. These vessels supply growing tissue with nutrients and transport waste away from the tissue. Tumours over a certain size are dependent on the formation of new blood vessels to grow and survive. A substance that inhibits the growth of new blood vessels would therefore be able to reduce the tumour and increase the patient's chances of survival.

Such treatment can be used for a number of different forms of cancer, for example in pancreatic, colorectal, breast and ovarian cancer, as well as lung cancer and lymphoma. Within each of these diseases there is a sales potential from a few hundred million dollars to a few billion dollars.

Market and competition The interest in angiogenesis inhibitors in cancer treatment has increased strongly over the past few years. One of the main reasons for this is that the antibody called bevacizumab (Avastin) has shown very positive results in a clinical study, showing that it can prolong the life of patients. This is an important confirmation of the fact that angiogenesis inhibitors are effective and can be used to supplement current standard therapies.

Bevacizumab acts by binding to an angiogenesis-promoting factor, VEGF, which some tumours secrete. The product was recently approved by the US Food and Drug Administration (FDA) in a combination treatment of colon cancer.

Angiostatin is another angiogenesis inhibitor that is in clinical trials. Angiostatin is one of the first natural angiogenesis inhibitors to be discovered. The drug showed a good effect in animal studies and was well tolerated in tests on humans. One clinical problem, however, was the fact that very large amounts of the drug were needed, since angiostatin only lasts for a short while in humans and only binds weakly to its receptor.

BioInvent's treatment principle BioInvent's strategy for inhibiting angiogenesis is to focus on the receptor to which angiostatin binds and works through, namely the angiotin. The strategy is to develop an antibody that binds to angiotin and passes on the effect of the natural ligand (angiostatin).

A human antibody has a long half-life period – three weeks compared to three hours for angiostatins, which means that it survives much longer in humans. BioInvent's technology for developing

antibodies also means that the strength of the bond between the antibody and the angiomin is customized to avoid the problems that are linked to the natural ligand. Based on this, it is expected that antibody-based drugs will be able to share the benefits of the angiostatin – but without its disadvantages.

Angiomin is believed to be crucial for the formation of new vessels. By targeting antibodies at this target protein, it is possible to slow down the formation of new blood vessels in a tumour's proximity, regardless of which growth signal the tumour sends out. VEGF is one such signal. Not all tumours send out VEGF, some rely instead on other signals, such as IL8 or bFGF. VEGF inhibitors are therefore not effective against all tumours, and there is also the risk of the development of resistance when the tumour begins to secrete other angiogenesis-promoting factors. This drawback is not thought to be linked to the antibody aimed at angiomin.

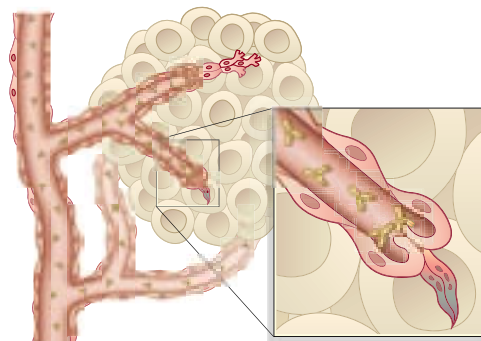
An antibody-based drug aimed at angiomin is therefore expected to have the potential to effectively block the tumour's supply of new blood vessels and thereby prevent its growth by starving it.

Project status A number of antibodies with specificity for the relevant target protein have been identified in Biolnvent's n-CoDeR® antibody library. These antibodies are currently being tested in existing *in vitro* and *in vivo* models at the Karolinska Institute to assess their

ability to prevent the growth of new blood vessels in growing tumours and thereby arrest the tumour's growth.

Patent protection Patents are pending in around 30 countries, including major markets such as the US, Europe, Canada, Japan, Australia and China for the target protein angiomin, the use of this in drug development and products that target it.

The patent applications, which were acquired by Biolnvent in April 2003, are based on research at the Karolinska Institute.



Angiomin is present on the surface of the cells of blood vessels that grow in a tumour's proximity. Biolnvent's antibodies that are currently being developed bind to angiomin and therefore prevent the vessels from growing further. This starves the tumour and its growth is arrested.

Lars Holmgren earned his doctorate at Karolinska Institute and worked on his Post doc in Boston in the middle of the 1990s with Judah Folkman, a pioneer in angiogenesis research. After three years, Holmgren returned to Stockholm and the Karolinska Institute, where he started his own research activities with a team of eight individuals at Cancercentrum Karolinska. Their main project is focusing on angiomin.



Interview with Lars Holmgren

"I was involved in identifying angiostatin when I was working on my Post-doc in Boston in 1994. But angiostatin has a short half-life period. Treatment involves high concentrations and frequent injections – two a day – a regimen that may be difficult for some people. We therefore started to think along different lines. One was to look for a new molecule that binds to the angiostatin. This was how we found angiomin, a receptor for angiostatin and a possibility for us to produce a substance with better properties than the angiostatin itself: limited side effects, long half-life period and high affinity.

Antibodies were the most obvious means of finding such a substance. If antibodies are used it should, for example, be sufficient to have one injection a month and a much lower dose.

We were looking for a partner and quickly decided on Biolnvent, which has its own technology in the form of the n-CoDeR antibody library. In addition, Biolnvent has established its own interest in this project, which is important so that a constant focus is maintained and there is no risk of the project losing its high priority.

In the case of cancer treatment, I believe above all in treating patients diagnosed with cancer who have had a solid tumour removed, but where there is still a high risk of a relapse. Antibody therapy against angiomin should be able to keep their metastases in check."

osteoarthritis



Bo Jansson is responsible for BioInvent's pre-clinical activities within the osteoarthritis project.

Antibody-based drugs are expected to regulate the synthesis of cartilage

Clinical need Osteoarthritis is a disease of the joints caused by an imbalance in the body's own maintenance of articular cartilage. The symptoms are stiffness, pain and reduced function in the joints of the fingers, knees and hips etc.

The disease affects mainly the elderly, and the number of cases is rising as the average life expectancy increases. Many people under the age of thirty also have signs of osteoarthritis. In the US alone, an estimated 40 million people suffer from the disease. The activity level of seven million of these people is limited by the disease, which causes costs for society of over USD 60 billion.

There is currently no treatment that slows the development of osteoarthritis. The only option available is pain medication, until it becomes necessary to have surgery to replace damaged joints with artificial ones.

Market and competition Drug development has in recent years focused on pain relief by developing so-called COX-2 inhibitors. According to Decision Resources, substances for symptomatic relief were sold for a value of USD 3.6 billion in 2001, of which COX-2 inhibitors accounted for 59 per cent.

There are, however, no drugs that directly affect the disease and its development. New drugs for osteoarthritis might revolutionise the treatment and create a very large market.

BioInvent's treatment principle BioInvent intends to treat arthritis by targeting antibodies at the integrins $\alpha 10B1$ or $\alpha 11B1$. These target proteins have in research conducted by BioInvent's partner Cartela AB been shown to have a positive effect on both new formation and breakdown of cartilage tissue. Increasing the volume of articular cartilage is expected to provide pain relief and restore flexibility.

Articular cartilage is necessary for the flexibility of the joints. It consists of connective tissue and cartilage forming cells. By forming new cartilage tissue, the cells responsible for cartilage formation maintain the function of the articular cartilage. Antibody therapy targeting at the proteins $\alpha 10B1$ or $\alpha 11B1$, is believed to affect the balance between formation and destruction of cartilage and thereby affect the course of the disease. This is different from current osteoarthritis drugs, which only provide pain and symptomatic relief.

Project status A large number of antibodies with specificity for the relevant target proteins have been identified. These will be tested in a series of *in vitro* and *in vivo* models to assess their effect on cartilage formation.

Patent protection Patents are pending in around 20 countries including the major markets such as the US, Europe, Canada, Japan and Australia for the target proteins $\alpha 10B1$ and $\alpha 11B1$, their use in drug development and products that target them.

The rights to develop antibody-based drugs against specific integrins were licensed exclusively from Cartela AB in October 2003.

Evvy Lundgren-Åkerlund earned her doctorate in medical chemistry at Uppsala University in 1987 and has been an associate professor at Lund University since 1993. She came to Lund University in 1990, where she formed her own research group to work with research on integrins. At the end of 2000, she founded Cartela AB and is the company's Managing Director. Cartela is a biotech company which, based on expertise in the field of integrins, is developing diagnostics and therapy for the treatment of diseases of the joints.



Interview with Evvy Lundgren-Åkerlund

"My research group at Lund University and Donald Gullberg's research group at Uppsala University discovered these integrins at the end of the 1990s. We were also the first ones to realize what they could be used for, something that made it possible to stake our claim on the field by applying for patents – and consequently also to commercialise our ideas.

Integrins are 'signalling' cell surface proteins and they can be used to regulate the function of cells using different substances, such as antibodies. The discovery of the integrins $\alpha 10B1$ and $\alpha 11B1$, which are expressed on cells in cartilage (so-called chondrocytes), have provided us with new opportunities to affect the development of diseases of the joint such as osteoarthritis.

Chondrocytes are crucial to the function of the cartilage. When they no longer can maintain a normal balance in replacement of the cartilage's connective tissue molecules, the cartilage is broken down. We want to redress the balance, and in cooperation with BioInvent, we hope to also be able to influence the functions of the chondrocytes using antibodies that target integrins.

We want to work with BioInvent to evaluate these antibodies in pre-clinical models, first in vitro and later on in animal models. When we have jointly identified antibodies with a positive effect on the development of the disease in animal models for osteoarthritis and/or rheumatoid arthritis, BioInvent will continue the development process.

The goal is obviously an antibody-based drug for the treatment of diseases of the joints. We believe that BioInvent is a good choice as a partner in this development work. The Company's expertise within the field of human antibodies has enabled us to increase the pace of our work and brings us closer to finding a drug to treat osteoarthritis."

Patent protection – A prerequisite for every project

Working to achieve effective patent protection is an important aspect of all projects run by BioInvent. The Company protects its product candidates partly through agreements that are signed when licensing target proteins, and partly through the development of product candidates using the Company's proprietary, patented technologies. Patent protection is reinforced during the course of the projects by patenting specific product candidates as they are identified and also by patenting other important results.

Patents provide time-limited sole rights Patents provide time-limited sole rights to commercialise an invention, for example through sales and manufacturing. It is the actual idea's formulation and use that is protected, which means that not only the products, but also the methods and usage can be patented.

In order for an invention to be able to be patented, it must fulfil certain criteria: it must be able to be industrialized, which means, among other things, that the innovation must be able to be reproduced, i.e. the results should be the same every time the invention is used; it must be new, which means that it may not be known anywhere in the world; and it must involve an inventive step, which means that the invention must not be obvious in relation to what is previously known.

Protection in several countries By its nature, a patent is a national right, only valid in the country where it is registered. This does not, however, prevent the same invention from being protected by parallel patents in several countries. In most countries patent applications are examined by the national patent office, which, following a review, either denies or grants the patent.

Through the worldwide convention the Patent Cooperation Treaty (PCT), the initial examination of patent applications has been concentrated to a few patent offices, including the Swedish and US ones. According to the convention, applicants need only submit one application, an international application (PCT application). The application is first searched and examined by the selected patent office and then the applicant can fulfil the application process in the countries that are indicated in the PCT application (the national phase). This initial search and examination is consultative to the countries carrying out their own examinations.

The European Patent Convention (EPC), covering most of the European countries, makes it possible to evaluate patent applications at a supranational level through the European Patent Office in Munich. This examination replaces the national process in all member states that the applicant indicates on the application. If a patent is granted, it is valid in all the countries indicated as soon as it has been translated into the respective languages.

BioInvent's intellectual property In order to take advantage of the differences between the US and European patent laws, BioInvent usually first files patent applications in both the UK and the US. After initial search and examination, the patent applications go through the PCT system, with the European Patent Office acting as the examining authority. After the PCT stage, the patent is examined at the national level at most of the major patent offices, e.g. in the US and Japan. In Japan, BioInvent uses the option for deferred examination (previously seven years, now three), which means that most of the Company's Japanese applications are still pending. BioInvent's own patent professional uses the help of reputable US and UK patent lawyers to achieve optimal patent protection.

The patent protection for the n-CoDeR[®] antibody library, which is the source of the Company's product candidates, was strengthened through the European patent that was granted in November. The new patent covers methods for the creation of both the antibody library and the individual antibody components within it. BioInvent has already been granted equivalent patents in Australia and patent applications are pending in the US among other countries.

The rights to develop antibody-based drugs aimed at the target proteins that are the basis of the company's drug projects have been acquired through exclusive licences or the acquisition of patents (see also the project descriptions on pages 14 – 25). For these rights BioInvent will pay licensing fees in the form of milestone payments and royalties following successful product development (see also the section on research and development costs on page 7).

Through exclusive licences or patents and patent applications under its own name, BioInvent has over 150 individual patents or patent applications. One of these can provide patent protection in several countries, e.g. in Europe. They cover the Company's core technology for the development of antibody-based drug candidates, as well as

various aspects of this, such as various antibody products under development and their use as drugs. The most important ones are shown in the table at the end of this section.

Biolnvent has also licensed technology that complements the Company's own technology platform where this is deemed to provide a competitive advantage. Non-exclusive licences relating to phage display have therefore been acquired from Dyax and Biosite. In November Biolnvent entered into an agreement with the US pharmaceutical company XOMA concerning non-exclusive rights to use

XOMA's expression technology for the purpose of developing antibody-based drugs. Biolnvent will pay licence fees for some of these in the form of (royalties) following successful product development. It is the Company's opinion that these have been set on market terms.

In addition to its patents, Biolnvent has also protected individual trademarks. The company name "Biolnvent" is protected in Sweden as a registered company name. 'Biolnvent' and 'n-CoDeR' are protected trademarks in all countries in the EU and in the US. The Company has also applied for trademark protection for these in Canada.

Biolnvent's most important patents, patent applications and exclusive licences

| | | Status in the largest markets | | |
|---|----------|-------------------------------|---------|----------|
| | | Europe | USA | Expires* |
| Products | | | | |
| HIV | | | | |
| Two patent families relating to epitopes on the Tat molecule | Licence | Pending | Granted | 2021 |
| Atherosclerosis | | | | |
| Two patent families relating to oxidized forms of LDL | Licence | Pending | Pending | 2023 |
| Antiangiogenesis | | | | |
| Two patent families relating to angiostatin binding proteins** | Acquired | Pending | Pending | 2024 |
| Osteoarthritis | | | | |
| A number of patent families relating to the integrins $\alpha 10\beta 1$ and $\alpha 11\beta 1$ | Licence | Pending | Pending | 2020 |
| Leukaemia | | | | |
| Target proteins for drugs for B-cell lymphoma | Own | Pending | Pending | 2024 |
| Technology | | | | |
| Technology for the human antibody library | | | | |
| CDR shuffling – a method for <i>in vitro</i> molecular evolution of the function of proteins (n-CoDeR®) | Own | Granted | Pending | 2018 |
| A method for <i>in vitro</i> molecular evolution of the function of antibodies | Own | Pending | Pending | 2021 |
| Techniques and methods for new library and display structures | Own | Pending | Pending | 2023 |
| Methods for selection from the library | | | | |
| Methods for selecting specific bacteriophages | Own | Granted | Granted | 2015 |
| Improved method for selection of specific phages | Own | Granted | Granted | 2017 |
| Techniques and methods for selection and identification of binding proteins against antigen structures in complex compounds | Own | Pending | Pending | 2023 |
| Protein arrays | | | | |
| Methods for producing microarrays based on biological material | Own | Pending | Pending | 2021 |
| Identification of target proteins | | | | |
| Techniques and methods for proteome analysis | Own | Pending | Pending | 2024 |
| Combined ligand and receptor display | Own | Pending | Granted | 2016 |

Technology rights licensed on a non-exclusive basis

| | Status on the largest markets | | |
|---|-------------------------------|---------|----------|
| | Europe | USA | Expires* |
| Technology from Dyax relating to the use of Phage display technology | Pending | Granted | 2015 |
| Technology from Biosite relating to display technology linked to the Fab format | Granted | Granted | 2012 |
| Technology from XOMA relating to the expression of antibody fragments | Granted | Granted | 2014 |

* The patent period expires in the year indicated on condition that the patent is granted. In the case of several patent families, the last year is indicated.

** The patent was acquired and registered in Biolnvent's name.

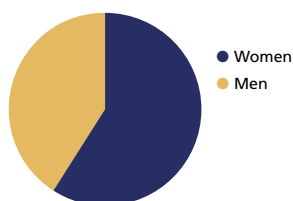
Attract the highest level of expertise

BioInvent is in every respect a knowledge-intensive company. One of the Company's strategic objectives is therefore to create and maintain a working environment that is attractive, allows for development and enables the Company to retain skilled individuals.

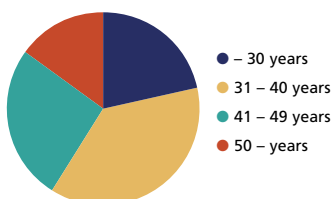
Development, wage and the ability to influence one's sphere of activity are crucial factors affecting an employee's well-being, involvement and motivation level. BioInvent has therefore developed a system that involves a clearly defined role and career structure, annual appraisals as a basis for professional and personal development, and annual wage reviews to establish individual wages.

BioInvent continued during 2003 to focus on competence development – both in general and at the individual level. In addition to external training within a broad spectrum of the relevant disciplines, BioInvent also offered a number of internal courses. One example is the management development programme tailored to the Company's needs, which was launched in 2002. Training in project management and quality control are examples of internal competence development that were offered during the year.

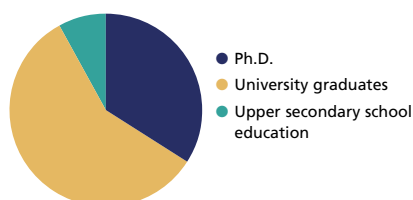
Percentage of women/men



Age distribution



Education



Organisation Just over 90 per cent of the Company's 104 employees are university graduates and 34 per cent have Ph.D. status. A total of 84 individuals work within research and development.

All research and development work is run in project form with a project matrix comprising the following main areas:

- *Pre-clinical* involving 33 employees with wide-ranging expertise in fields such as immunology, molecular biology, cell biology, protein chemistry, screening and automation. They are mainly responsible for the early development of new antibody-based drug candidates.
- *Protein chemistry and pharmacy* involving 41 employees with wide-ranging expertise in fields such as molecular and cell biology, analytical chemistry, protein chemistry, chemical technology and large-scale cultivation and purification of recombinant proteins. They are responsible for developing the cell lines that will produce the product and process development in general for all production, characterisation and quality control of the product according to the directions from authority regulations.
- *Product development* currently involving three employees. The functions are being established and the responsibilities involve pre-clinical safety testing and preparations for clinical trials where the company will use external contract research organisations.
- *Quality assurance* involving seven employees who are responsible for quality assurance and regulatory issues regarding requirements from the authorities with respect to the development and production of drugs.

The management and support functions comprise 20 individuals. The support functions cover business development, patents, human resources, finance and IT.

Working environment BioInvent places great emphasis on offering a pleasant and safe working environment. The Company uses regulated working methods to minimise the risk of accidents and work-related illnesses.

In spring 2003 a comprehensive, proactive programme was implemented focusing on stress and stress-prevention for management and employees.



Quality, ethics and environment

Biolnvent will act as a good member of society. The Company has a responsibility to its partners, the employees and their work environment, and to the global environment.

Quality The pharmaceutical industry is heavily regulated. The authorities monitor how products are developed, tested, manufactured, documented and marketed. Biolnvent has many years' experience of quality work and has the ambition to constantly improve the quality of its work and to ensure a thorough quality mentality .

The Company's organisation and facilities have been approved by the Swedish Medical Products Agency for the production of biological drugs and also has GMP approval according to the applicable EU regulations.

Environmental impact Biolnvent works actively with environmental issues and consistently endeavours to reduce the use of substances that may be harmful to the environment and ensure that environmental impact is kept to a minimum. The goal is also to use chemical substances and other resources effectively so that the Company's impact

on the environment is minimized in this respect as well. The Group's operations require permits according to the Swedish Environmental Code, and reports are required to be submitted to the Lund Municipality.

The external environment is affected by limited emissions into water and air. Waste is sorted at source and special routines are in place for the management of environmental waste.

Genetically modified organisms Biolnvent uses genetically modified micro-organisms in its research and development work and has permits for the so-called contained use of such organisms according to the Swedish Work Environment Authority's directions.

Testing on animals In the development of a drug it is unfortunately impossible to entirely avoid testing on animals, although Biolnvent has so far only conducted such testing to a very limited extent. Non-animal based models are used to the greatest possible extent. In cases where tests are carried out on animals, these are conducted by professional laboratories that strictly adhere to the applicable regulations.



Risks and risk management

BioInvent's business is affected by several factors that can impact the Company's earnings and financial position. The risks can be categorised into operational risk and financial risk. Below is a description of the operational risk factors that are believed to have the greatest significance for BioInvent's development and how the Company handles them in order to minimise the risk level.

Business-related risk

Risk in drug development Developing a new drug up to its launch costs just under USD 900 million (Source: Tufts Center for the Study of Drug Development, May 2003). At the same time, statistically, only one in ten drug candidates in clinical Phase I reach the market. The likelihood of reaching the market increases as the project is moved forward in the development chain. However, the costs also increase, rising sharply in the later clinical phases. Altogether, the risk associated with developing a new drug is very high.

The strategic role that BioInvent plays in the value chain is adjusted according to the resource requirement and risk situation in drug development. By recruiting target proteins externally, one eliminates part of the risk associated with the discovery phase in every drug project. Of course, there is still the risk of investing in the wrong project – a risk that the Company tries to reduce through careful project evaluation before every decision.

BioInvent's strategy of allying itself with development partners for clinical development, marketing and distribution, means that the projects get the benefit of expertise and experience and that BioInvent's own investment requirement in individual projects is reduced. This reduces BioInvent's risk level because the Company is able to invest in several projects.

The technology platform that BioInvent uses to develop and produce product candidates is validated through a number of partnerships with customers. This reduces the risk associated with the technology that is used. Of course, the high level of risk associated with the target proteins that are selected for drug development still remains.

Building up a large project portfolio will, in the long term, make the Company less dependent on the success of individual projects. At this point, however, the portfolio is relatively limited with a few projects in early phases – which means that a setback in an individual project may have a significantly negative impact on the Company.

Competition and fast technology development The market for all of the Company's future products is characterised by significant competition and fast technological development. BioInvent's competitors consist, among others, of major international pharmaceutical and biotech companies. Many of the competitors have far greater resources than BioInvent. There is always a risk that the Company's product concept will be subject to competition from a similar product or that entirely new product concepts will prove superior.

By allying itself with external research groups in the forefront of medical development, the Company hopes to gain access to target proteins that can be developed for long-term competitive medical treatment options. In order to further strengthen the Company's own position, great emphasis is placed on strong patent protection.

The selection of future partners will also be a crucial factor affecting BioInvent's competitiveness. The Company will therefore look for partnerships with companies that have an established and strong infrastructure, a strategic commitment to future product development and can provide the necessary resources.

Biotechnology and patent risk For obvious reasons, patenting inventions or innovations within the biotech field is a relatively new phenomenon. Scientific and technical progress within this field is generally characterised by a high level of complexity and is not always easy to fit an innovation into the framework of the traditional basis for patent examination. This situation has made it difficult for patent authorities to accurately assess the innovations in relation to earlier known technology and to identify such known technology. Because of these problems, the validity of many granted biotech patents is uncertain and they risk being declared invalid if they are subject to the scrutiny of a court.

Thus, there is no guarantee that products and processes which are actually covered by granted patents, will not be attacked or contested by competitors or that granted patents will not infringe upon competitors' patents.

BioInvent monitors and evaluates the activities, patents and patents applications of competitors on an ongoing basis for the purpose of identifying activities that are covered by the Company's intellectual property and patents that could cover parts of the Company's sphere of activity. It may be necessary to initiate legal proceedings to defend



the Company's current and future patents, or to determine the extent and validity of patents that belong to a third party. The Company is not currently involved in any legal disputes.

Financial risk The Company's financial policy, which has been approved by the Board of Directors and is subject to constant review, contains guidelines and rules for handling financial risk. The day-to-day risk management is ultimately the responsibility of the CEO, but certain areas are delegated to the director of Business Control.

Obtaining additional financial funds The focus on producing drug candidates is expected to involve significant costs and only generate annual revenue from products on the market in the longer term. With this in mind, the business is expected to continue to report a negative cash flow. The capital requirement is financed through (i) the sale of rights to individual projects, (ii) partnerships that ensure project financing, and (iii) shareholders' equity.

If BioInvent fails to secure such financing, this may negatively affect the Company's business, financial position and operation income. In order to create maximum financial flexibility, the Company's financial policy contains guidelines stipulating that the net funds may not for a long duration fall below 24 months' cash flow, as long as the Company's cash flow is negative.

Currency risk Commercial flows involving incoming and outgoing payments in various currencies give rise to a transaction risk. Around 15 per cent of the 2003 revenues were invoiced in foreign currencies, USD and EUR. Around 10 per cent of the costs in 2003 were invoiced in foreign currencies, mainly in USD, GBP, EUR and DKK. Currency exposure is primarily eliminated by matching flows in the same currency. When matching is not possible, the currency exposure is eliminated through hedging. Forward contracts are only entered into when a binding commitment exists. Realised forward contracts for flows in 2003 had a positive effect of the operating earnings in the amount of SEK 0.6 million.

Interest risk Interest risk is when the value of financial instruments can vary because of changes in interest rates. BioInvent's exposure to market risk for changes in interest levels is mainly related to bank

balances and holdings in commercial papers. To reduce the fluctuation in market interest rates, the excess liquidity is invested so that the investments mature on a regular basis over the subsequent twelve-month period.

The average interest rate in 2003 was 3.5 per cent. A change in the interest rate of one per cent in 2003 would have affected the net interest income in the amount of around SEK 3 million.

Liquidity and credit risk Liquidity risk is minimised by liquidity planning and investment in financial instruments that can be redeemed at short notice. Only investments in interest-bearing securities with low credit risk and high liquidity are permitted. There are also limitations in the amount that can be invested with an individual counterparty to avoid concentration of credit risks.

The excess liquidity in 2003 was deposited in banks and invested in commercial papers with a rating of K1. Commercial papers carry fixed interest and may have terms of up to one year.

BioInvent works with established and credit-worthy counterparties. A credit assessment is carried out for all partners who will receive some form of credit. In addition, BioInvent monitors receivables on a constant basis. The Company's exposure to doubtful receivables is therefore low.



The Board and auditors



Per-Olof Mårtensson



Karl Olof Borg



Carl Borrebaeck



Svein Mathisen



Björn Nilsson



Björn Ogenstam



Kenth Petersson

Per-Olof Mårtensson

Facts: Certified pharmacist. Born 1937. Lives in Nyhamnsläge, Sweden. President and CEO of Karo Bio AB 1991–2000. Chairman of the Board of Biolnvent International AB since 1997. Other board appointments: Chairman of the Board of Karo Bio AB and Alligator Bioscience AB. Member of the boards of Maxim Pharmaceuticals Inc., Photocure ASA, Forskarpatent i Syd AB, Lunds universitets Utvecklingsbolag AB, PCI Biotech A/S. Shareholding: 1,043,301 shares in Biolnvent International AB.

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. Member of the Board of Biolnvent International AB since 2001. Other board appointments: Chairman of the Board of Pharmexa A/S. Member of the boards of Cartela AB, Actar AB, 7 TM Pharma A/S, T-Cellic A/S, Medicon A/S, Galenica AB. Shareholding: -

Carl Borrebaeck

Facts: Doctor of Science. Born 1948. Lives in Hjärrup, Sweden. Professor at the Department of Immunotechnology at Lund University. Senior Scientific Advisor to the Company. Member of the Board of Biolnvent 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, Alligator BioScience AB, Eurocine AB. Shareholding: 1,291,704 shares in Biolnvent International AB.

Svein Mathisen

Facts: Master of Science, Engineering Physics. Born 1956. Lives in Malmö, Sweden. President and CEO of Biolnvent International AB since 1997. Member of the Board of Biolnvent International AB since 2001. Shareholding: 1,043,301 shares in Biolnvent International AB.

Björn Nilsson

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. Chairman of the organisation Sweden Bio. Member of the Board of Biolnvent International AB since 1999. Shareholding: -

Björn Ogenstam

Facts: MBA. Born 1959. Lives on the island of Ingarö, Sweden. Vice President Industrifonden. Member of the Board of Biolnvent International AB since 2002. Other board appointments: Chairman of the Board of Degerfors Formnings AB. Member of the boards of Powerbox International AB, Svenskt Rekonstruktionskapital AB. Shareholding: -

Kenth Petersson

Facts: Bachelor of Arts. Born 1956. Lives in Stockholm, Sweden. Partner Science Pacific. Member of the Board of Biolnvent International AB since 1997. Other board appointments: Member of the boards of Alligator Bioscience AB, Coding Technology AB. Shareholding: 44,760 shares in Biolnvent International AB.

Auditor

Ernst & Young AB
Auditor in charge: Åke Stenmo, Authorised Public Accountant. Born 1945. Lives in Lund, Sweden. Auditor for Biolnvent International AB since 2000.

Senior executives



Svein Mathisen



Roland Carlsson



Cristina Glad



Per-Anders Johansson



Martin Wiles



Elisabet Lindh Elliot



Stefan Ericsson



Eva Kullenstein

Svein Mathisen President and CEO

Facts: Master of Science, Engineering Physics. Born 1956. Lives in Malmö, Sweden.
President and CEO of Biolnvent International AB since 1997
Member of the Board of Biolnvent International AB since 2001.
Shareholding: 1,043,301 shares in Biolnvent International AB.

Roland Carlsson Vice President Pre-clinical Research

Facts: Ph.D. Born 1949. Lives in Lund, Sweden.
Employed since 1987.
Associate professor at the Department of Immunotechnology at Lund University.
Shareholding: 1,043,301 shares in Biolnvent International AB.

Cristina Glad Executive Vice President

Facts: Doctor of Science, Biochemistry. MBA. Born 1952. Lives in Malmö, Sweden.
Employed since 1987.
Shareholding: 1,043,301 shares in Biolnvent International AB.

Per-Anders Johansson Director Antibody Manufacturing and Procurement

Facts: Master of Science, Chemistry. Born 1955. Lives in Lund, Sweden.
Employed since 1984.
Shareholding: 249,576 shares in Biolnvent International AB.

Martin Wiles Vice President Business Development

Facts: Ph.D. Chemistry. MBA. Born 1963. Lives in Copenhagen, Denmark.
Employed since 2003.
1999–2003 Head of Business Development at KS Biomedix Holdings Plc. (listed on the London Stock Exchange).
Shareholding: No shares in Biolnvent International AB.
Warrants equivalent to 50,000 shares.

Elisabet Lindh Elliot Director Quality Assurance & Regulatory Affairs

Facts: Ph.D. Born 1949. Lives in Malmö, Sweden.
Employed since 2002. 1999–2002 responsible for QA & Regulatory Affairs at Active Biotech AB.
Shareholding: No shares in Biolnvent International AB.
Warrants equivalent to 5,000 shares.

Stefan Ericsson Director Business Control

Facts: MBA. Born 1963. Lives in Lund, Sweden.
Employed since 1998.
Shareholding: 23,250 shares in Biolnvent International AB.
Warrants equivalent to 5,000 shares.

Eva Kullenstein Director Human Resources

Facts: Master of Behavioural Science. Born 1965. Lives in Malmö, Sweden.
Employed since 2002.
Shareholding: 400 shares in Biolnvent International AB.
Warrants equivalent to 7,500 shares.

The Group management team consists of:
Svein Mathisen, Roland Carlsson, Cristina Glad, Per-Anders Johansson and Martin Wiles.

The BioInvent share

Share data

| | 2003 | 2002 |
|------------------------------------|-------|-------|
| Share price (last paid price), SEK | 10.30 | 12.50 |
| Market capitalisation, SEK million | 303.6 | 368.4 |

BioInvent International AB (publ) has been listed on the O-list of the Stockholm Exchange (Stockholmsbörsen) since 12 June 2001. A trading unit consists of 500 shares.

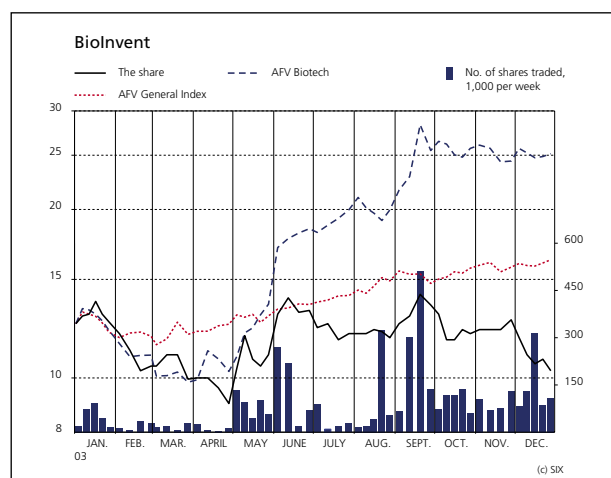
Share capital The share capital in BioInvent amounted to SEK 14.7 million as of 31 December 2003, distributed between 29,475,556 shares with a nominal value of SEK 0.50 per share.

After all of the issued warrants are exercised, the number of shares would be 29,775,556. 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 2003, 4.7 (4.7 in 2002) million BioInvent shares were traded for a value of SEK 56.4 (99.7) million. Calculated as a percentage of the total number of shares at year-end, this is equivalent to a turnover volume of 16 per cent (16). The average turnover per trading day was around 18,701 (18,840) shares.

The quoted price for BioInvent shares fell during the year from SEK 12.50 to SEK 10.30, which is a fall of 17.6 per cent. This can be compared to Affärsvärlden's General Index and Affärsvärlden's index for biotech companies, which rose by 29.7 and 97.3 per cent respectively during the same period. The highest price paid in 2003 was SEK 14.50 and the lowest listing was SEK 8.50.

Beta value BioInvent's beta value as of 31 December 2003 was 1.30. The beta value is calculated on a 24-month historical share price and indicates the extent to which BioInvent's share price fluctuates in comparison to Affärsvärlden's General Index. A share that has the same price fluctuation as the index has a beta value of 1.0. Shares with greater price fluctuations than the index have a beta value greater than 1.0, and vice versa.

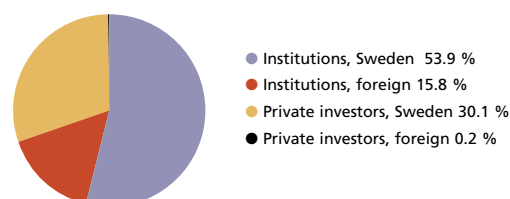


Analysts who monitor BioInvent

| | |
|----------------------------|--------------------|
| Alfred Berg Fondkommission | Mattias Häggblom |
| D. Carnegie | Angelica Fatourous |
| Handelsbanken | Susanna Urdmark |
| Kaupthing Bank | Conny Granelli |
| Swedbank | Maarten de Chateau |

Ownership structure The number of shareholders increased during the year by 240 to 1,612 shareholders. Institutional investors owned 70 (72) per cent of the share capital and votes. Foreign owners held 16 per cent (18) of the share capital and votes. The ten largest shareholders own 54 per cent (52) of the shares. Around 56 per cent (64) of the shareholders own fewer than 500 shares each.

Distribution of shareholders as of 31 December 2003



List of shareholders as of 31 December 2003

| Shareholder | No. of shares | Percentage of capital and votes % |
|-------------------------------|-------------------|-----------------------------------|
| Stiftelsen Industrifonden | 3,953,295 | 13.4 |
| Pronova a. s. | 1,942,787 | 6.6 |
| Nordea fonder | 1,382,600 | 4.7 |
| Alecta | 1,374,450 | 4.7 |
| Fjärde AP-fonden | 1,370,550 | 4.6 |
| Celltech Group Plc | 1,331,251 | 4.5 |
| Carl Borrebaeck* | 1,291,704 | 4.4 |
| Sjätte AP-fonden | 1,201,237 | 4.1 |
| Per-Olof Mårtensson m. bolag* | 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 Bank S A | 934,050 | 3.2 |
| IndustriTjänstemannaförbundet | 710,250 | 2.4 |
| Skandia | 685,900 | 2.3 |
| Other shareholders | 9,124,278 | 31.0 |
| Total | 29,475,556 | 100.0 |

*Board member or part of the Group management team.

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 available 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.

Share statistics

| Size of holding | No. of shareholders | No. of shareholders in % | No. of shares in % |
|-----------------------|---------------------|--------------------------|--------------------|
| 1 – 500 | 903 | 56.0 | 0.6 |
| 501 – 1,000 | 260 | 16.1 | 0.8 |
| 1,001 – 2,000 | 158 | 9.8 | 1.0 |
| 2,001 – 5,000 | 127 | 7.9 | 1.3 |
| 5,001 – 10,000 | 61 | 3.8 | 1.7 |
| 10,001 – 20,000 | 31 | 1.9 | 1.7 |
| 20,001 – 50,000 | 32 | 2.0 | 3.4 |
| 50,001 – 100,000 | 6 | 0.4 | 1.6 |
| 100,001 – 500,000 | 17 | 1.1 | 15.1 |
| 500,001 – 1,000,000 | 5 | 0.3 | 11.7 |
| 1,000,001 – 5,000,000 | 12 | 0.7 | 61.1 |
| Total | 1,612 | 100.0 | 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 |
|------|--|--------------------------------|---------------------------|--------------------|---------------|------------------------------|
| 1996 | BioInvent International AB was founded ¹⁾ | | | 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 ²⁾ | 181,000 | 181,000 | 1,145,260 | 1,145,260 | 1.00 |
| 1999 | New share issue ³⁾ | 108,527 | 108,527 | 1,253,787 | 1,253,787 | 1.00 |
| 2000 | New share issue ⁴⁾ | 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 share issue ⁵⁾ | 2,250,000 | 4,500,000 | 14,072,152.5 | 28,144,305 | 0.50 |
| 2002 | New share issue ⁶⁾ | 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.

Overview of outstanding warrant programmes as of 31 December 2003

| Programme | Subscription period | Subscription price | Increase in no. of shares | Increase in share capital, SEK | Increase in share-holders' equity, SEK |
|--------------|-----------------------|--------------------|---------------------------|--------------------------------|--|
| V | 15/1 2002 – 16/2 2004 | 77.00 | 216,850 | 108,425 | 16,697,450 |
| VI | 1/1 2007 – 30/4 2007 | 23.00 | 300,000 | 150,000 | 6,900,000 |
| Total | | | 516,850 | 258,425 | 23,597,450 |

By the end of 2003, BioInvent International AB had launched six warrant programmes aimed mainly at the Company's employees. Warrant programmes I-III were fully exercised in connection with the stock exchange listing. Warrant programme IV was not exercised. The subscription period for warrant programme V expired on 16 February 2004 and no shares were subscribed for.

On 10 April, the Annual General Meeting voted in favour of a warrant programme, VI, equivalent to 300,000 shares aimed at senior executives and key individuals. Parts of the Group manage-

ment team (see page 33) with large shareholdings are excluded from this warrant programme. So far, 161,000 warrants have been acquired by employees at market terms. The remaining 139,000 are reserved for future new recruitments. The warrant programme could provide a maximum potential dilution of 1.0 per cent.

At the end of the year, warrants equivalent to 516,850 shares had been issued. The subscription period for warrants, equivalent to 216,850 shares – programme V, expired on 16 February 2004 and no shares were subscribed for.

Five-year review

| Income statement, SEK million | 2003 | 2002 | 2001 | 2000 | 1999 |
|---|---------------|--------------|--------------|--------------|--------------|
| Net revenues | 66.7 | 87.1 | 58.3 | 24.1 | 11.0 |
| Research and development costs | -131.0 | -111.7 | -85.2 | -47.8 | -28.2 |
| Sales and administrative costs | -36.7 | -38.0 | -27.5 | -16.5 | -8.2 |
| Other operating revenues and costs | 0.3 | 0.2 | 0.1 | 1.1 | 0.0 |
| Operating profit/loss | -100.7 | -62.4 | -54.3 | -39.1 | -25.4 |
| Net financial items | 11.1 | 16.3 | 10.8 | 4.6 | 0.3 |
| Profit/loss after financial items | -89.7 | -46.2 | -43.5 | -34.5 | -25.0 |
| Tax on profit for the year | - | - | - | - | - |
| Profit/loss for the year | -89.7 | -46.2 | -43.5 | -34.5 | -25.0 |
| Balance sheet, SEK million | 2003 | 2002 | 2001 | 2000 | 1999 |
| Intangible fixed assets | 19.4 | 19.7 | - | - | - |
| Tangible fixed assets | 34.5 | 43.8 | 40.5 | 22.7 | 11.9 |
| Inventories etc. | 9.9 | 13.7 | 9.9 | 3.0 | 3.2 |
| Current receivables | 10.9 | 25.6 | 29.8 | 29.1 | 3.7 |
| Liquid funds | 268.5 | 343.6 | 338.7 | 141.2 | 20.2 |
| Total assets | 343.2 | 446.4 | 418.8 | 196.1 | 39.0 |
| Shareholders' equity | 305.0 | 394.3 | 388.4 | 159.6 | 23.7 |
| Non-interest-bearing liabilities | 38.2 | 52.2 | 30.4 | 36.4 | 10.3 |
| Interest-bearing liabilities | - | - | - | - | 5.0 |
| Total shareholders' equity and liabilities | 343.2 | 446.4 | 418.8 | 196.1 | 39.0 |
| Cash flow, SEK million | 2003 | 2002 | 2001 | 2000 | 1999 |
| Operating profit/loss | -100.7 | -62.4 | -54.3 | -39.1 | -25.4 |
| Adjustments for depreciation and interest | 30.0 | 29.7 | 18.7 | 7.7 | 1.8 |
| Changes in working capital | 4.5 | 22.1 | -13.6 | 1.0 | 3.7 |
| Cash flow from current operations | -66.2 | -10.6 | -49.2 | -30.4 | -19.9 |
| Cash flow from investment activities | -9.2 | -36.5 | -25.6 | -13.9 | -9.2 |
| Cash flow from financing activities | 0.4 | 52.0 | 272.2 | 165.4 | 23.6 |
| Change in liquid funds | -75.1 | 4.9 | 197.4 | 121.1 | -5.5 |

| Key financial ratios | 2003 | 2002 | 2001 | 2000 | 1999 |
|---------------------------------------|-------|-------|-------|-------|-------|
| Net revenue growth, % | -23.4 | 49.4 | 141.9 | 119.3 | -22.6 |
| Net working capital, SEK million | -17.4 | -12.9 | 9.3 | -4.3 | -3.4 |
| Net working capital/net revenue, % | -26.1 | -14.8 | 15.9 | -18.0 | -30.8 |
| Operating capital, SEK million | 36.5 | 50.7 | 49.8 | 18.4 | 8.6 |
| Operating capital/net revenue, % | 54.7 | 58.2 | 85.4 | 76.4 | 77.9 |
| Capital employed, SEK million | 305.0 | 394.3 | 388.4 | 159.6 | 28.7 |
| Capital employed/net revenue, % | 457.1 | 452.9 | 666.6 | 662.6 | 261.5 |
| Shareholders' equity, SEK million | 305.0 | 394.3 | 388.4 | 159.6 | 23.7 |
| Return on shareholders' equity, % | -25.6 | -11.8 | -15.9 | -37.6 | -93.0 |
| Return on capital employed, % | -25.6 | -11.8 | -15.9 | -36.6 | -85.1 |
| Capital turnover, times | 0.2 | 0.2 | 0.2 | 0.3 | 0.4 |
| Equity/assets ratio, % | 88.9 | 88.3 | 92.7 | 81.4 | 60.9 |
| Intangible fixed assets, SEK million | 6.2 | 22.5 | - | - | - |
| Tangible fixed assets, SEK million | 3.0 | 14.0 | 25.6 | 13.9 | 9.2 |
| Number of employees, average | 119 | 124 | 96 | 55 | 36 |
| Net revenue per employee, SEK million | 0.6 | 0.7 | 0.6 | 0.4 | 0.3 |

| Data per share | 2003 | 2002 | 2001 | 2000 | 1999 |
|-------------------------------------|--------|--------|--------|--------|--------|
| Earnings per share, SEK* | | | | | |
| Before dilution | -3.04 | -1.60 | -1.69 | -1.62 | -1.45 |
| Shareholders' equity per share, SEK | | | | | |
| Before dilution | 10.35 | 13.38 | 13.80 | 7.03 | 1.26 |
| After full dilution | 10.34 | 13.38 | 13.77 | 6.80 | 1.24 |
| Cash flow per share | -2.56 | -1.63 | -2.91 | -2.08 | -1.69 |
| Average number of shares | | | | | |
| Before dilution (1,000) | 29,476 | 28,939 | 25,697 | 21,336 | 17,278 |
| After full dilution (1,000) | 29,502 | 28,940 | 25,753 | 22,077 | 17,544 |
| Number of shares at end of period | | | | | |
| Before dilution (1,000) | 29,476 | 29,476 | 28,144 | 22,722 | 18,807 |
| After full dilution (1,000) | 29,502 | 29,476 | 28,200 | 23,463 | 19,072 |
| Share price, 31 December | 10.30 | 12.50 | 37.00 | - | - |
| Dividend | - | - | - | - | - |

* The outstanding warrants lead to no dilution of earnings per share, as a redemption to shares would lead to an improvement of earnings per share.

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 funds.

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.

Return on shareholders' equity

Profit/loss after financial items as a percentage of the average shareholders' equity.

Return on capital employed

Profit/loss after financial items plus financial costs as a percentage of average capital employed.

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 after financial items 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.

Cash flow per share

Cash flow from current operations and investment activities divided by the average number of shares.

Directors' report

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

BioInvent conducts proprietary drug projects in disease areas such as AIDS, atherosclerosis, cancer and osteoarthritis. The scope and strength of BioInvent's technology platform is also used by partners in the development of new drugs. BioInvent's partners include Antisoma, Celltech, GlaxoSmithKline, Igeneon, ImmunoGen and XOMA.

Proprietary drug projects

HIV infection *Background:* HIV infection is one of the most serious epidemics of our time. HIV has a high degree of variability and adaptability. When a new treatment is introduced, the virus usually changes quickly and develops resistance to the treatment, making it ineffective.

The Tat protein is vital for HIV's ability to replicate itself and spread to new cells. Antibody-based drugs against the Tat protein are expected to be able to neutralise its activity so that the level of HIV particles in the patient's blood is reduced to such an extent that the development of the disease will be arrested. The antibodies that BioInvent develops are targeted to parts of the Tat protein that are unchanged (conserved) between different virus strains. The target protein circulates freely in the blood and is not directly connected to a virus particle. Thus, the virus's capacity to change and adapt to avoid the effect of the antibodies is blocked. Based on the characteristics of the unique target protein, the Company expects that the antibodies against these conserved parts of the Tat protein will prevent the development of resistance and will therefore have a lasting effect.

The project is based on patent rights licensed in July 2002 from Thymon LLC, USA.

Project status: Pre-clinical tests carried out at Smittskyddsinstitutet and the Karolinska Institute show that the product candidates the Company has produced are able to prevent the spread of the virus between human cells *in vitro*. Currently the absence of resistance is also being tested in extended pre-clinical trials.

Alongside the pre-clinical work, process development is underway for cell lines that will be used for large-scale production of the drug candidate. This work has progressed to an advanced stage.

Atherosclerosis *Background:* Atherosclerosis can lead to blood clot formation and infarction. In the industrialised world infarction is the main cause of death. Atherosclerosis develops as a result of plaque formation in the blood vessels. There is a risk that these plaques will be pulled apart by the blood flow, which may lead to infarction.

New research has shown strong links between oxidized forms of certain lipoproteins and the inflammatory processes that lead to plaque formation in the vessel walls. Antibodies aimed at

these oxidized lipoproteins are expected to be able to stabilise plaque formation and possibly also reduce it.

The patent rights for the project are the result of research at the MAS University Hospital in Malmö and Cedars-Sinai in Los Angeles. The rights were licensed in December 2002.

Project status: The product candidates identified by the Company have been shown to very significantly reduce plaque formation in pre-clinical animal models. The experiments conducted at the MAS University Hospital in Malmö show that plaque formation in the vessel walls has been reduced by half, even though the treatment has only been under way for a short period. At this time, the antibodies are being tested in animal models that express the human target protein. Additional studies are also in progress to fully document the mechanisms of action.

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

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

The project is based on patent rights acquired in April 2003 from a research group at the Karolinska Institute.

Project status: A number of antibodies with specificity for the relevant target protein have been selected in BioInvent's n-CoDeR® antibody library. These antibodies will now be tested in existing *in vitro* and *in vivo* models at the Karolinska Institute to assess their ability to prevent the growth of new blood vessels in growing tumours and thereby arrest the tumour's growth.

Osteoarthritis *Background:* Osteoarthritis is a disease of the joints caused by an imbalance in the formation of cartilage. The disease leads to stiffness, poor function and pain in joints in the fingers, knees and hips etc. The only treatment alternatives today for osteoarthritis are pain medication and surgery in which the affected joints are treated by artificial replacement. Osteoarthritis is very widespread, and in the US alone, an estimated 40 million people suffer from the disease. The activity level of seven million of these people is limited by the disease, which causes costs for society of over USD 60 billion.

New research has discovered that a specific protein (belonging to a class of receptors called integrins) is found in large quantities on the cells that are responsible for synthesis of new cartilage tissue. Data from this research provides strong indications that this target protein can be linked to regulation and control of the cartilage

tissue in the joints. BioInvent intends to develop a therapeutic antibody that will bind to the protein in question. This kind of antibody is expected to be able to stimulate the synthesis of new cartilage tissue and thereby slowing down the progression of osteoarthritis.

The rights to develop antibody-based drugs against the specific integrin were licensed in October 2003 from Cartela AB.

Project status: Antibodies with specificity for the relevant target proteins have been identified. These will be tested in a series of *in vitro* and *in vivo* models to assess their effect on cartilage formation.

Partners BioInvent has always had a strong customer focus, and an important aspect of the Company's business model is to balance part of the risk of proprietary projects with business that generates steady revenue. The following partnerships generated revenue in 2003:

- **Antisoma** Since 1996 this company has been a partner. BioInvent produces several of Antisoma's antibody-based drug candidates for clinical trials, for example Pentumomab (Theragyn), which is currently in advanced clinical phase III studies.

- **Celltech** In 2002 a development partnership was initiated with Oxford GlycoSciences (OGS) for the development and commercialisation of antibody-based drugs. Celltech, a British biotech company, subsequently acquired OGS. Scientifically this collaboration is focusing on the cancer field.

- **GlaxoSmithKline (GSK)** BioInvent has been developing antibodies to be used in GSK's research and development work in the vaccine field. BioInvent has been working with GSK since 2001. The agreement will expire in its current form at the end of April. The partnership is believed to have been a valuable one for both parties and may lead to new joint projects.

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

In November BioInvent entered into a cross-licensing agreement with the US pharmaceutical company XOMA. Under the agreement, BioInvent has the right to use XOMA's expression technology for the purpose of developing antibody-based drugs. The agreement also provides BioInvent with a new customer for its n-CoDeR antibody library, in that XOMA has acquired a license to use the library in its research programme with certain rights to develop and commercialize antibodies for use as drugs and diagnostics.

In February, after the end of the reporting period, the Company entered into a production agreement with a returning customer, the Danish company ALK-Abelló, for the commercial delivery of

antibodies for a new allergy test that is being marketed by Bayer Diagnostics. This agreement is in line with BioInvent's strategy to secure long-term supplier agreements within the field of antibody production.

Patents In November the European Patent Office granted a patent for the n-CoDeR antibody library. The patent covers methods to create both the n-CoDeR antibody library itself, as well as individual antibody components in the library. BioInvent has already been awarded a similar patent in Australia, and patent applications have been filed in the US and other countries.

Organisation As of 31 December, BioInvent had 104 employees, compared to 130 at the same time the previous year. 84 (108) of these work in research and development. The reduction in staff is the result of reorganisation, the purpose of which was to focus further on developing proprietary antibody-based drugs. This resulted in a change in the personnel structure and a reduction in the number of staff within certain areas of expertise.

Starting in April 2004, Carl Borrebaeck, a member of BioInvent's Board, will be associated with the Company as Senior Scientific Advisor. Previously Carl Borrebaeck was BioInvent's Chief Scientific Officer.

Sales and revenue Net revenue amounted to SEK 66.7 million (87.1). The revenue comes from payments for development and production assignments. The capacity utilisation for such assignments was lower than the previous year. The level of utilisation is affected partly by the actual demand and partly by the amount of capacity that needs to be used for BioInvent's proprietary drug projects.

The loss after net financial items amounted to SEK -89.7 million (-46.2). Apart from a fall in net revenue, the result was also affected by increased research and development costs relating, in particular, to proprietary drug development projects. The Group's research and development costs amounted to SEK 131.0 million (111.7) after re-classification (see "Accounting Principles" on page 46).

Depreciation according to plan of SEK 18.9 million (13.5) was deducted from the operating result. The increase in depreciation is mainly due to investments in intangible fixed assets. The net financial income was SEK 11.1 million (16.2).

Financial position and cash flow The cash flow from current operations and investment activity amounted to SEK -75.5 million (-47.1). Apart from a weaker result, the difference between this and the cash flow for the same period the previous year is the result of substantial non-recurring payments from customers in 2002. These effects were neutralised to a certain extent by the lower level of investment. As of 31 December 2003, the Group's liquid funds amounted to SEK 268.5 million (343.6).

The shareholders' equity amounted to SEK 305.0 million at the end of the year. The Company's share capital was SEK 14.7 million, and the equity/assets ratio at the end of the period was 88.9 (88.3) per cent. The Group had no interest-bearing liabilities. BioInvent's warrant programme is described in the section under the heading "The BioInvent share" on page 35.

Investments The Group's investments in tangible fixed assets amounted to SEK 3.0 million (14.0) and relate mainly to equipment for research and development activity. The level of investment the previous year was affected by the purchase of automation equipment. Investments in intangible fixed assets amounted to SEK 6.2 million (22.5) and relate mainly to cash payment for purchased target proteins used for proprietary drug projects, as well as licenses for the future use of expression technology.

The parent company BioInvent consists of the parent company, BioInvent International AB, and the subsidiary BioInvent Finans AB which administers the warrants issued by BioInvent International AB. The parent company coincides essentially with the Group. Net revenue amounted to SEK 66.7 million (87.1). The parent company reported a loss after net financial items of SEK -89.7 million (-46.2).

Adjustment to IFRS The Company's accounting principles have been gradually adjusted to coincide with the current recommendations of the Swedish Financial Accounting Standards Council's recommendations, and the only significant differences between these and the coming IFRS principles are in the area of financial instruments. At this time, it is not possible to gain a precise understanding of what difference the new standards will make, since IAS 39 has not been finally established. Note 14, however, presents the situation on the closing day. The effects described there shall, according to the IFRS principles, be taken up in the balance sheet. The adjustment to RR29 Remuneration to employees, which will be made in 2004, will not affect the Company's accounting of pensions, since all pension payments within the Company are premium-related.

The Company has reviewed the situation and found that the above effects are the only ones to have an impact on the Company's accounting during the transition to the IFRS principles established today.

The work of the Board The Board's composition is presented in a separate section on page 32. One of the members, Björn Ogenstam, is employed by the Company's largest shareholder Stiftelsen Industrifonden. The President and CEO, Svein Mathisen, sits on the Board. The Board fees were set by the Annual General Meeting at the same amount as the previous year and total SEK 690,000 to be distributed between the Board members at their discretion.

The Board works according to rules of procedure which are revised and adopted by the Board at least once a year. The rules of procedure mainly consist of instructions for the Board's work and instructions for the distribution of responsibility between the Board and the CEO, as well as instructions for financial reporting.

The Board held eight ordinary meetings in 2003 and three extraordinary meetings. Lawyer Peter Idsäter acted as the Board's secretary in 2003.

A remuneration committee has been appointed consisting of Chairman of the Board Per-Olof Mårtensson, and two other Board members, Björn Ogenstam and Kenth Petersson. The Board's remuneration committee works with and takes decisions regarding the remuneration and benefits for all of the senior executives with the exception of the CEO, whose remuneration is determined by the Board. The committee also addresses other remuneration issues of great importance, e.g. bonus schemes.

The Board has looked at the issue of whether a special audit committee should be formed, but has so far found that issues to be handled by this committee are so significant in nature that it is more appropriate for them to be handled by the Board in its entirety. The Company's auditors report therefore personally to the Board their observations after reviewing the financial statements and provide their assessment of the Company's internal control.

Pursuant to a decision by the Annual General Meeting, a nominating committee has been appointed, consisting of Jörgen Lönngren (Stiftelsen Industrifonden), Ramsay Brufer (Alecta), Björn Franzon (Fjärde AP-fonden) and Per-Olof Mårtensson (Chairman of the Board). The nominating committee prepares proposals to present to the Annual General Meeting concerning Board members, auditors and fees.

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

| | |
|-------------------|-------------|
| Brought forward | - |
| Loss for the year | -89,659,734 |
| | -89,659,734 |

The Board of Directors and the CEO propose that the share premium reserve be reduced by SEK 89,659,734 to cover the accumulated loss.

The Group According to the consolidated balance sheet, the accumulated loss amounts to SEK -89.7 million. No allocation to the restricted equity is required. 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 and table of changes in shareholders' equity that follow, and to the notes that accompany these. All amounts are shown in SEK thousands unless otherwise indicated.

Income statements

| | Note | Group 2003 | Group 2002 | Parent company 2003 | Parent company 2002 |
|---|------|-----------------|----------------|------------------------|------------------------|
| Net revenues | | 66,716 | 87,053 | 66,716 | 87,053 |
| <i>Operating costs</i> | | | | | |
| Research and development costs | | -131,049 | -111,682 | -131,049 | -111,682 |
| Sales and administrative costs | | -36,673 | -37,983 | -36,673 | -37,983 |
| Other operating revenues | | 557 | 772 | 557 | 772 |
| Other operating costs | | -297 | -576 | -297 | -576 |
| Operating profit/loss | 1–6 | -100,746 | -62,416 | -100,746 | -62,416 |
| <i>Result from financial investments</i> | | | | | |
| Interest income and similar items | | 11,143 | 16,319 | 11,143 | 16,319 |
| Interest costs and similar items | | -57 | -69 | -57 | -70 |
| Profit/loss after financial items | | -89,660 | -46,166 | -89,660 | -46,167 |
| Tax on profit for the year | 7 | - | - | - | - |
| Profit/loss for the year | | -89,660 | -46,166 | -89,660 | -46,167 |
| Earnings per share, average no. of shares, SEK* | | | | | |
| Before dilution | | -3.04 | -1.60 | | |
| Average no. of shares | | | | | |
| Before dilution (thousands) | | 29,476 | 28,939 | | |
| After full dilution (thousands) | | 29,502 | 28,940 | | |
| Proposed dividend per share | | | | - | |

* The outstanding warrants lead to no dilution of earnings per share, as a redemption to shares would lead to an improvement of earnings per share.

Balance sheets

| | Note | Group 2003 | 2002 | Parent company 2003 | 2002 |
|-------------------------------------|------|----------------|----------------|------------------------|----------------|
| Assets | | | | | |
| Fixed assets | | | | | |
| Intangible fixed assets | | | | | |
| Acquired intangible fixed assets | 8 | 19,357 | 19,726 | 19,357 | 19,726 |
| Tangible fixed assets | | | | | |
| | 9 | | | | |
| Equipments | | 28,228 | 36,522 | 28,228 | 36,522 |
| Investments in rented premises | | 6,320 | 7,294 | 6,320 | 7,294 |
| Financial fixed assets | | | | | |
| Shares in subsidiaries | 10 | - | - | 100 | 100 |
| | | 53,905 | 63,542 | 54,005 | 63,642 |
| Current assets | | | | | |
| Inventories etc. | | | | | |
| Work on contract | 11 | 6,718 | 10,870 | 6,718 | 10,870 |
| Raw materials and consumables | | 3,180 | 2,827 | 3,180 | 2,827 |
| | | 9,898 | 13,697 | 9,898 | 13,697 |
| Current receivables | | | | | |
| Accounts receivables | 14 | 3,972 | 8,777 | 3,972 | 8,777 |
| Other receivables | | 1,971 | 6,343 | 1,971 | 6,343 |
| Prepaid expenses and accrued income | 12 | 4,963 | 10,464 | 4,963 | 10,464 |
| | | 10,906 | 25,584 | 10,906 | 25,584 |
| Liquid funds | | | | | |
| | 14 | 268,476 | 343,584 | 268,475 | 343,351 |
| Total assets | | 343,185 | 446,407 | 343,284 | 446,274 |

| | Note | 2003 | Group 2002 | 2003 | Parent company 2002 |
|---|------|----------------|----------------|----------------|------------------------|
| Shareholders' equity and liabilities | | | | | |
| Shareholders' equity | | | | | |
| <i>Restricted shareholders' equity</i> | | | | | |
| Share capital | | 14,738 | 14,738 | 14,738 | 14,738 |
| Share premium reserve | | 379,878 | 545,685 | 379,878 | 545,685 |
| Other restricted reserves | | 1 | - | - | - |
| | | 394,617 | 560,423 | 394,616 | 560,423 |
| <i>Accumulated loss</i> | | | | | |
| Profit/loss brought forward | | - | -120,007 | - | -120,007 |
| Profit/loss for the year | | -89,660 | -46,166 | -89,660 | -46,167 |
| | | -89,660 | -166,173 | -89,660 | -166,174 |
| Total shareholders' equity | | 304,957 | 394,250 | 304,956 | 394,249 |
| Current liabilities | | | | | |
| Work on contract | 11 | 16,107 | 27,114 | 16,107 | 27,114 |
| Accounts payable | 14 | 6,057 | 12,861 | 6,057 | 12,861 |
| Liabilities to subsidiaries | | - | - | 435 | 105 |
| Other liabilities | | 3,582 | 2,374 | 3,247 | 2,137 |
| Accrued expenses and deferred income | 13 | 12,482 | 9,808 | 12,482 | 9,808 |
| | | 38,228 | 52,157 | 38,328 | 52,025 |
| Total shareholders' equity and liabilities | | 343,185 | 446,407 | 343,284 | 446,274 |
| Memorandum items | | | | | |
| Pledged assets | | - | - | - | - |
| Contingent liabilities | | - | - | - | - |

Cash flow statements

| | Group | | Parent company | |
|--|----------------|----------------|----------------|----------------|
| | 2003 | 2002 | 2003 | 2002 |
| Current operations | | | | |
| Operating profit/loss | -100,746 | -62,416 | -100,746 | -62,416 |
| Adjustments for non-cash items | | | | |
| Depreciation | 18,867 | 13,475 | 18,867 | 13,475 |
| | -81,879 | -48,941 | -81,879 | -48,941 |
| Interest received | 11,143 | 16,319 | 11,143 | 16,319 |
| Interest paid | -57 | -69 | -57 | -70 |
| Cash flow from current operations before changes in working capital | -70,793 | -32,691 | -70,793 | -32,692 |
| Changes in working capital | | | | |
| Changes in inventories, etc. | 3,799 | -3,846 | 3,799 | -3,846 |
| Changes in current receivables | 14,678 | 4,233 | 14,678 | 4,233 |
| Changes in short-term liabilities | -13,929 | 21,735 | -13,697 | 21,603 |
| Cash flow from current operations | -66,245 | -10,569 | -66,013 | -10,702 |
| Investment activities | | | | |
| Acquisition of intangible fixed assets | -6,244 | -22,501 | -6,244 | -22,501 |
| Acquisition of tangible fixed assets | -2,986 | -14,008 | -2,986 | -14,008 |
| Merger of subsidiaries | - | - | - | -20,978 |
| Cash flow from investment activities | -9,230 | -36,509 | -9,230 | -57,487 |
| Cash flow after investment activities | -75,475 | -47,078 | -75,243 | -68,189 |
| Financing activities | | | | |
| Warrant premiums | 367 | - | 367 | - |
| Directed new share issues | - | 52,000 | - | 52,000 |
| Cash flow from financing activities | 367 | 52,000 | 367 | 52,000 |
| Change in liquid funds | -75,108 | 4,922 | -74,876 | -16,189 |
| Opening liquid funds | 343,584 | 338,662 | 343,351 | 359,540 |
| Liquid funds at year-end | 268,476 | 343,584 | 268,475 | 343,351 |

Change in shareholders' equity

Group

| | Share capital | Share premium reserve | Other restricted reserves | Accumulated loss | Total |
|---|---------------|-----------------------|---------------------------|------------------|----------------|
| Shareholders' equity 31 December 2001 | 14,072 | 445,170 | 100 | -70,926 | 388,416 |
| Directed new share 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 |
| Shareholders' equity 31 December 2002 | 14,738 | 545,685 | 0 | -166,173 | 394,250 |
| Transfer between restricted and unrestricted reserves | | -166,174 | 1 | 166,173 | 0 |
| Warrent premiums | | 367 | | | 367 |
| Profit/loss for the year | | | | -89,660 | -89,660 |
| Shareholders' equity 31 December 2003 | 14,738 | 379,878 | 1 | -89,660 | 304,957 |

Parent company

| | Share capital | Share premium reserve | Profit/loss brought forward | Profit/loss for the year | Total |
|--|---------------|-----------------------|-----------------------------|--------------------------|----------------|
| Shareholders' equity 31 December 2001 | 14,072 | 494,561 | 0 | -210 | 508,423 |
| Directed new share issue | 666 | 51,334 | | | 52,000 |
| Appropriation of profit/loss | | -210 | | 210 | 0 |
| Merger-related loss | | | -120,007 | | -120,007 |
| Profit/loss for the year | | | | -46,167 | -46,167 |
| Shareholders' equity 31 December 2002 | 14,738 | 545,685 | -120,007 | -46,167 | 394,249 |
| Appropriation of profit/loss | | -166,174 | 120,007 | 46,167 | 0 |
| Warrant premiums | | 367 | | | 367 |
| Profit/loss for the year | | | | -89,660 | -89,660 |
| Shareholders' equity 31 December 2003 | 14,738 | 379,878 | 0 | -89,660 | 304,956 |

The share capital as 31 December 2003 consists of 29,475,556 shares with a nominal value of SEK 0.50 per share.

Accounting principles and information notes

Accounting principles The annual report has been prepared in accordance with the Annual Accounts Act and the recommendations and statements from the Swedish Accounting Standards Council. The accounting principles are the same as those applied the previous year. In addition, the Company applies the Swedish Accounting Standards Council's new recommendations that went into effect on 1 January 2003. These have had no impact on earnings, whereas RR27 Financial Instruments: Information and classification, has had an impact on the presentation of the annual accounts. From 1 January 2003, there has been a reclassification in the income statements, whereby the term "Cost of goods and services sold" has been removed. The purpose is to achieve a better representation of the Group's operations. The change has not had any impact on the Company's financial result. BioInvent develops proprietary drug candidates and drug candidates in partnership with customers. The cost of development and production assignments relating to antibodies has historically been reported as "Cost of goods and services sold." However, this resource currently is an increasingly important, integrated part of the development of proprietary drug candidates, and is therefore included in "Research and development costs" in the income statement.

In the section "Risk analysis" on page 30, an account is given of the financial risks and the principles for managing these risks.

Consolidated financial statements The BioInvent Group consists of the parent company, BioInvent International AB, and the wholly-owned subsidiary BioInvent Finans AB, which administers the warrants issued by BioInvent International AB. The consolidated financial statements are prepared using the acquisition method. Accordingly, the shareholders' equity in the subsidiaries upon acquisition is entirely eliminated. The Group's equity consists of the equity in the parent company and the equity in the subsidiaries accrued after the acquisition.

Revenue and work on contract Revenue is reported at the actual value of what has been received or will be received. Revenue is reported to the extent it is deemed likely that the Company will benefit financially and the revenue can be calculated in a reliable way.

The Group's revenue in 2003 was generated through various types of development and production assignments. Revenue from such projects, where the Company delivers a service, is recognised according to the percentage of completion method. According to this method, revenue, costs and profit/loss are reported during the accounting period when the work is carried out. The percentage of completion is established through an assessment of work completed in relation to the total work to be carried out in the respective project.

In the balance sheets, receivables from customers and liabilities to customers are reported as "Work on contract" on both the assets and liabilities side of the balance sheet.

Research and development costs Research costs are expensed as they occur. Costs for development of new products are not capitalized, unless the criteria in the Swedish Financial Accounting Standards Council's recommendation RR15 have been met. Since the Company's drug projects are quite a long time away from being registered as products that can be sold and thereby generate a financial gain for the Company, no costs for development of products are capitalized, i.e. no intangible assets developed by BioInvent have been capitalized.

In 2003 acquired intangible fixed assets relating to rights for target proteins, and licences for the future use of expression technology have been capitalized. BioInvent's proprietary drug projects are based on target proteins that are usually acquired from external research groups. Cash payment for the acquisitions is capitalized taking into account the fact that a market value exists since the price was arrived at through negotiation between two independent parties. Acquisitions of other intangible assets, such as rights to certain technologies that can be widely used by BioInvent are also capitalized based on the idea that the price was arrived at through negotiation between two independent parties. The principles for depreciation are outlined under "Fixed assets" below.

Leasing The Group's leasing agreements have been categorised as operational leases. Leasing charges are expensed over the period of the agreement.

Taxes Deferred tax is reported in accordance with the balance sheet method, which means that deferred tax is calculated for all identified temporary differences between, on the one hand, the fiscal value of assets and liabilities, and on the other hand, their reported value. See also Note 7: Tax on profit/loss for the year.

Fixed assets Fixed assets are valued at the acquisition value less the accumulated depreciation/amortization. Tangible fixed assets and acquired intangible fixed assets, such as technology licences and licensed target proteins, 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 fixed assets, taking into account the constant, 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.

Depreciation/amortization according to plan is as follows:

| | |
|----------------------------------|--------------|
| Equipments | 5 years |
| Investments in rented premises | 5 – 10 years |
| Acquired intangible fixed assets | 3 – 5 years |

Inventories Inventories are valued according to the lowest value principle and the first in, first out (FIFO) method. This means that the inventories are reported at the lowest of the acquisition value according to the FIFO method, and the actual value.

Receivables Receivables are reported at the lowest of the nominal value and the amounts that are expected to be received.

Transactions in foreign currencies Transactions in foreign currencies are translated when they are entered in the accounts into the reporting currency (SEK), according to the spot rate on the date of transaction. Receivables and liabilities in foreign currencies have been translated at closing day exchange rates. Exchange rate

gains and exchange rate losses on operating receivables and liabilities are charged to the operating profit/loss. Gains and losses on financial receivables and liabilities are reported as financial items. Receivables and liabilities, hedged through forward contracts, are translated at the current rate of exchange on the date the hedge was executed, and the arbitrage premium (the difference between the forward rate and the current rate when the hedging contract is entered into) is distributed over the contract's term.

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

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 Mergers of wholly-owned subsidiaries.

NOTE 1 Average number of employees

| | 2003 | | 2002 | |
|--------------------|------------------|----------------|------------------|----------------|
| | No. of employees | Of which women | No. of employees | Of which women |
| Parent company | 119 | 57 % | 124 | 61 % |
| Subsidiaries | - | - | - | - |
| Group total | 119 | 57 % | 124 | 61 % |

NOTE 2 Absence due to illness

| | 2003 | 2002 |
|-----------------------------|--------------|--------------|
| Short-term absence | 1.6 % | 1.6 % |
| Long-term absence > 60 days | 1.6 % | 1.2 % |
| Total absence | 3.2 % | 2.8 % |
| Women | 2.5 % | 2.3 % |
| Men | 0.7 % | 0.5 % |
| 29 years or younger | 0.4 % | 0.2 % |
| 30 – 49 years | 2.2 % | 2.0 % |
| Older than 50 years | 0.6 % | 0.6 % |

Absence is indicated as a percentage of total normal working time.

NOTE 3 Salaries, other remuneration and social security costs

| | 2003 | | 2002 | |
|--------------------|---------------------------------|---|---------------------------------|---|
| | Salaries and other remuneration | Social security costs (of which pensions) | Salaries and other remuneration | Social security costs (of which pensions) |
| Parent company | 51,483 | 26,878 (8,110) | 42,827 | 21,173 (5,386) |
| Subsidiary | - | - (-) | - | - (-) |
| Group total | 51,483 | 26,878 (8,110) | 42,827 | 21,173 (5,386) |

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

| | 2003 | | 2002 | |
|--------------------|---------------|-----------------|---------------|-----------------|
| | Board and CEO | Other employees | Board and CEO | Other employees |
| Parent company | 1,914 | 49,569 | 1,784 | 41,043 |
| Subsidiaries | - | - | - | - |
| Group total | 1,914 | 49,569 | 1,784 | 41,043 |

Pension costs distributed between Board members, the CEO and other employees

| | 2003 | | 2002 | |
|--------------------|---------------|-----------------|---------------|-----------------|
| | Board and CEO | Other employees | Board and CEO | Other employees |
| Parent company | 386 | 7,724 | 379 | 5,007 |
| Subsidiaries | - | - | - | - |
| Group total | 386 | 7,724 | 379 | 5,007 |

Benefits for senior executives

Principles The Board's fees are determined at the Annual General Meeting based on proposals from the nominating committee. The fees are shared among the Board members at the discretion of the Board. There is no separate fee for committee work.

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.

Biolnvent'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 2003. Variable performance-related remuneration of 0 – 30 per cent of fixed cash annual salaries may be paid out on an annual basis to senior executives.

Benefits for the Board and CEO The Board's fees were set by the 2003 Annual General Meeting at 690. Of this amount, the Chairman was paid a

fee of 250 and the four external Board members each received a fee of 110.

The President and CEO, Svein Mathisen, received a fixed gross cash salary in 2003 of 1,224 and 53 in other benefits (primarily car benefits). No variable remuneration was paid out in 2003. 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 2003 to 386. Svein Mathisen and the Company have a mutual period of notice of six months. If notice is given by the Company, Svein Mathisen receives redundancy pay equivalent to 18 monthly salaries. The redundancy pay is not deducted from other income. If Svein Mathisen resigns, no redundancy pay is payable. Neither the Board members nor the CEO acquired any warrants or other financial instruments in Biolnvent in 2003. In previous years, warrants for 195,000 shares in Biolnvent (Programme IV), were acquired on market terms with the following distribution: Karl Olof Borg, 45,000; Björn Nilsson, 75,000; and Kenth Petersson, 75,000. The subscription period for Programme IV expired on 30 June 2003 and no shares were subscribed for.

Benefits for 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 and the other top executives have a mutual period of notice of six-months.

If notice is given by one specific member of Group management, the executive is entitled, under special circumstances, to redundancy pay equivalent to six monthly salaries. Redundancy pay is not deducted from other income. If notice is given by the Company, no redundancy pay is payable. Other individuals are not entitled to redundancy pay over and above the payment of salaries during the period of notice. Other senior executives received total remuneration and other benefits (primarily housing and car benefits) amounting to 4,883. No variable remuneration was paid out in 2003. The total pension costs relating to other senior executives amounted to 1,498 in 2003.

Other senior executives acquired warrants in 2003 on market terms equivalent to 60,000 shares in BioInvent (Programme VI). In previous years,

warrants were acquired on market terms equivalent to 40,000 shares (Programme V). The subscription period for Programme V expired on 16 February 2004 and no shares had been subscribed for.

Academic partnerships An important aspect of BioInvent's strategy is to develop and maintain a research base with ties to a number of academic institutions. One such relationship, with the Department of Immunotechnology at Lund University, is particularly strong. BioInvent provides research funding to the institution and in return BioInvent obtains the results and patent rights that arise from the partnership. Carl Borrebaeck is Professor of the Department of Immunotechnology, where he has responsibility for these activities. In his capacity as a board member and Chief Scientific Officer of BioInvent, Carl Borrebaeck has not participated in preparations or decisions relating to the agreements that BioInvent has entered into with the Department of Immunotechnology. Starting in April 2004, Carl Borrebaeck will be associated with the Company as Senior Scientific Advisor. See also the Directors' Report under the heading "Organisation," on page 39.

Percentage of men/women

| | 2003 | | 2002 | |
|-------------------------|--------|----------------|--------|----------------|
| | Number | Of which women | Number | Of which women |
| The Board and CEO | 7 | - | 7 | - |
| Other senior executives | 5 | 20 % | 5 | 20 % |

NOTE 4 Information about auditors' fees

| | Group | | Parent company | |
|--------------------------|------------|------------|----------------|------------|
| | 2003 | 2002 | 2003 | 2002 |
| Ernst & Young | | | | |
| Audit assignments | 148 | 119 | 148 | 119 |
| Other assignments | 237 | 258 | 237 | 258 |
| Total | 385 | 377 | 385 | 377 |

NOTE 5 Depreciation according to plan

| | Group | | Parent company | |
|--------------------------------|---------------|---------------|----------------|---------------|
| | 2003 | 2002 | 2003 | 2002 |
| Research and development costs | 18,391 | 13,040 | 18,391 | 13,040 |
| Sales and administrative costs | 476 | 435 | 476 | 435 |
| Total | 18,867 | 13,475 | 18,867 | 13,475 |

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

NOTE 6 Operational leasing

| | Group | Parent company |
|--------------------|---------------|----------------|
| Payments due: | | |
| Year 2004 | 9,989 | 9,989 |
| Years 2005 – 2008 | 22,872 | 22,872 |
| Year 2009 or later | 1,381 | 1,381 |
| Total | 34,242 | 34,242 |

Rental agreements of an operational nature are included as above. Payments due in 2005 and later are mainly related to production premises.

NOTE 7 Tax on profit for the year

The Group's accumulated unutilised loss carry-forward amounted to SEK 298 million as of 31 December 2003. It is unclear when these loss carry-forwards will be utilized for deduction against taxable earnings. Deferred

income tax recoverable relating to loss carry-forward is therefore not reported at any value. There are no deferred taxes that relate to temporary differences.

NOTE 8 Intangible fixed assets

| | Group | | Parent company | |
|---|---------------|---------------|----------------|---------------|
| | 2003 | 2002 | 2003 | 2002 |
| Acquired intangible fixed assets | | | | |
| Opening acquisition value | 22,501 | - | 22,501 | - |
| Acquisitions | 6,244 | 22,501 | 6,244 | 22,501 |
| Closing accumulated acquisition value | 28,745 | 22,501 | 28,745 | 22,501 |
| Opening depreciation | -2,775 | - | -2,775 | - |
| Depreciation for the year | -6,613 | -2,775 | -6,613 | -2,775 |
| Closing accumulated depreciation | -9,388 | -2,775 | -9,388 | -2,775 |
| Closing residual value according to plan | 19,357 | 19,726 | 19,357 | 19,726 |

NOTE 9 Tangible fixed assets

| | Group | | Parent company | |
|---|----------------|----------------|----------------|----------------|
| | 2003 | 2002 | 2003 | 2002 |
| Equipments | | | | |
| Opening acquisition value | 60,152 | 52,533 | 60,152 | 797 |
| Transfer as a result of merger | - | - | - | 51,736 |
| Acquisitions | 2,658 | 13,919 | 2,658 | 13,919 |
| Disposals | -3,640 | -6,300 | -3,640 | -6,300 |
| Closing accumulated acquisition value | 59,170 | 60,152 | 59,170 | 60,152 |
| Opening depreciation | -23,630 | -20,504 | -23,630 | -184 |
| Transfer as a result of merger | - | - | - | -20,320 |
| Disposals | 3,640 | 6,300 | 3,640 | 6,300 |
| Depreciation for the year | -10,952 | -9,426 | -10,952 | -9,426 |
| Closing accumulated depreciation | -30,942 | -23,630 | -30,942 | -23,630 |
| Closing residual value according to plan | 28,228 | 36,522 | 28,288 | 36,522 |

NOTE 9 Tangible fixed assets, continues

| | Group | | Parent company | |
|---|---------------|---------------|----------------|---------------|
| | 2003 | 2002 | 2003 | 2002 |
| Investments in rented premises | | | | |
| Opening acquisition value | 10,639 | 10,551 | 10,639 | - |
| Transfer as a result of merger | - | - | - | 10,551 |
| Acquisitions | 328 | 88 | 328 | 88 |
| Closing accumulated acquisition value | 10,967 | 10,639 | 10,967 | 10,639 |
| Opening depreciation | -3,345 | -2,072 | -3,345 | - |
| Transfer as a result of merger | - | - | - | -2,072 |
| Depreciation for the year | -1,302 | -1,273 | -1,302 | -1,273 |
| Closing accumulated depreciation | -4,647 | -3,345 | -4,647 | -3,345 |
| Closing residual value according to plan | 6,320 | 7,294 | 6,320 | 7,294 |

Investments in rented premises mainly refers to investments in production premises.

NOTE 10 Shares in subsidiaries

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

BiolInvent Finans AB's registered office is Lund.

NOTE 11 Work on contract

| | Group | | Parent company | |
|-----------------------------------|----------------|----------------|----------------|----------------|
| | 2003 | 2002 | 2003 | 2002 |
| Value of work completed | 29,845 | 64,279 | 29,845 | 64,279 |
| Invoiced amounts | -23,127 | -53,409 | -23,127 | -53,409 |
| Receivables from customers | 6,718 | 10,870 | 6,718 | 10,870 |
| Value of work completed | 47,878 | 26,604 | 47,878 | 26,604 |
| Invoiced amounts | -63,985 | -53,718 | -63,985 | -53,718 |
| Liabilities to customers | -16,107 | -27,114 | -16,107 | -27,114 |

Receivables from customers and liabilities to customers are reported in the balance sheet as work on contract in the balance sheet's assets and liabilities sections respectively.

NOTE 12 Prepaid expenses and accrued income

| | Group | | Parent company | |
|-------------------------|--------------|---------------|----------------|---------------|
| | 2003 | 2002 | 2003 | 2002 |
| Prepaid rent | 1,358 | 2,868 | 1,358 | 2,868 |
| Accrued interest income | 1,300 | 6,054 | 1,300 | 6,054 |
| Other items | 2,305 | 1,542 | 2,305 | 1,542 |
| Total | 4,963 | 10,464 | 4,963 | 10,464 |

NOTE 13 Accrued expenses and deferred income

| | Group | | Parent company | |
|----------------------|---------------|--------------|----------------|--------------|
| | 2003 | 2002 | 2003 | 2002 |
| Payroll liabilities | 5,060 | 4,813 | 5,060 | 4,813 |
| Social security fees | 3,169 | 3,230 | 3,169 | 3,230 |
| Other items | 4,253 | 1,765 | 4,253 | 1,765 |
| Total | 12,482 | 9,808 | 12,482 | 9,808 |

NOTE 14 Financial instruments

The Group's financial instruments consist of derivatives, bank balances and holdings in commercial papers, as well as warrant programmes. The Group also has other financial instruments, such as accounts receivable and accounts payable that arise in day-to-day operations. Transactions with derivatives, primarily forward contracts, are executed for the purpose of managing the currency risk that the Group's operations entail.

The risk analysis section on page 30 describes the financial risks and how these are managed. BioInvent's warrant programme is described in the BioInvent share section on page 35.

Actual values Below is a comparison of the reported values and the actual values of the Group's financial instruments.

| | Book value | | Actual value | |
|------------------------------|----------------|----------------|----------------|----------------|
| | 2003 | 2002 | 2003 | 2002 |
| <i>Financial assets</i> | | | | |
| Accounts receivable | 3,972 | 8,777 | 3,972 | 8,777 |
| Liquid funds | | | | |
| -Bank balances | 3,218 | 12,875 | 3,218 | 12,875 |
| -Commercial papers | 265,254 | 330,701 | 266,661 | 337,245 |
| Total | 272,444 | 352,353 | 273,851 | 358,897 |
| <i>Financial liabilities</i> | | | | |
| Accounts payable | -6,057 | -12,861 | -6,057 | -12,861 |
| Total | -6,057 | -12,861 | -6,057 | -12,861 |

The actual value of commercial certificates includes accrued interest on the closing day and value adjustment related to the prevailing level of interest on the closing day.

Interest risk Below is the book value, on the due dates, on the Group's financial instruments that are exposed to interest risk.

Year 2003

| | < 1 year | 1 – 5 year | > 5 year | Total |
|-------------------------------|----------------|------------|----------|----------------|
| <i>Floating interest rate</i> | | | | |
| Liquid funds | | | | |
| -Bank balances | 3,218 | - | - | 3,218 |
| Total | 3,218 | - | - | 3,218 |
| <i>Fixed interest</i> | | | | |
| Liquid funds | | | | |
| -Commercial papers | 265,254 | - | - | 265,254 |
| Total | 265,254 | - | - | 265,254 |

NOTE 14 Financial instruments, continues

Year 2002

| | < 1 year | 1 – 5 year | > 5 year | Total |
|-------------------------------|----------------|------------|----------|----------------|
| <i>Floating interest rate</i> | | | | |
| Liquid funds | | | | |
| -Bank balances | 12,875 | - | - | 12,875 |
| Total | 12,875 | - | - | 12,875 |
| <i>Fixed interest</i> | | | | |
| Liquid funds | | | | |
| -Commercial papers | 330,701 | - | - | 330,701 |
| Total | 330,701 | - | - | 330,701 |

Hedge accounting – cash-flow hedging On 31 December 2003 a forward contract was in place for the purpose of hedging future invoicing of partners for which the Group has a firm delivery commitment. According to the contract, Biolnvent will sell EUR 0.3 million on 3 May 2004 for an effective rate of SEK 9.22/EUR 1. The terms of the forward contract coincide with the payment terms for delivery commitments.

In addition, Biolnvent has outstanding forward contracts as of 31 December 2003 for the purpose of hedging purchasing commitments in January 2004. The amounts in the contracts are small and therefore not reported.

Lund, Sweden 4 March 2004

Per-Olof Mårtensson
Chairman of the Board

Karl Olof Borg

Carl Borrebaeck

Björn Nilsson

Björn Ogenstam

Kenth Petersson

Svein Mathisen
President and CEO

Our Audit report was submitted on 5 March 2004
ERNST & YOUNG AB

Åke Stenmo
Authorised Public Account

Audit report

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

Co. reg. no. 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 2003 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, 5 March 2004

ERNST & YOUNG AB

Åke Stenmo
Authorised Public Accountant

Glossary

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

Angiogenesis Formation of new blood vessels.

Angiomotin Receptor for angiotatin and target protein for treatment targeting angiogenesis.

Angiostatin Natural substance that inhibits angiogenesis.

Animal model Animals used for testing in which a disease that is very similar to a human disease has been introduced.

Antigen A substance that is foreign to the body and that can stimulate the immune system.

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

Atherosclerosis Condition where deposits of fats and minerals form on the walls of large blood vessels.

Autoimmunity Immune reaction directed against the body's own tissue.

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

Biological drugs Drugs, identical or very similar to naturally occurring molecules.

BLA Biologics License Application, application to the FDA for permit to market biological drugs in the US.

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

Cell culture Maintenance of cells in the laboratory.

Cell line Cultured cells with the same genetic origin.

Chondrocytes Cartilage-forming cells.

Clinical trials Studies carried out on humans to test the efficacy and safety of future drugs.

DNA Deoxyribonucleic acid. The naturally occurring molecule that contains an organism's genetic material.

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

Endothelial cells Cells that line the inside of blood vessels.

Expression system Production in host cells of proteins.

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

HIV Human Immuno Deficiency Virus. A virus that causes infections that weaken a patient's immune system and can lead to AIDS.

Human antibodies Antibodies that are perceived by the immune system as human.

Immunology Study of the origins and consequences of immune responses (i.e. antibody and cell responses).

IND Investigational New Drug. Application to the US Food and Drug Administration for a permit to initiate clinical studies.

Inflammation Condition where there is irritation of tissue following damage to the tissue or infection.

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.

Iterative A process that is carried out several times.

LDL Carrier molecule of cholesterol. (See Lipoprotein). Commonly known as "the bad cholesterol".

Ligand The naturally occurring molecule that binds to a receptor.

Lipoprotein Compounds of proteins that transport lipids in the blood, for example HDL and LDL.

Lymphoma Disease involving a tumour in the lymphoid tissue.

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

Metabolism All of the biochemical reactions that take place in living organisms.

Metastasis Secondary tumour.

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

Osteoarthritis Degenerative disease of the joints, caused by an imbalance in the body's ability to maintain articular cartilage.

oxLDL Oxidized LDL. A substance that can contribute to blood clots or infarction; a target protein for the development of a treatment for atherosclerosis.

Phages Virus that can infect bacteria.

Phage display Technology for expressing molecules, e.g. antibodies, on the surface of phages.

Pharmacy The science of making and dispensing drugs.

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.

Prevalence The fraction of people suffering from a certain disease at a given time.

Protein The proteins are the most important building blocks in all organisms. There are many thousands of different proteins.

Resistance The ability of e.g. micro-organisms to avoid treatment that is originally effective. Resistance is developed when genes change and vary and the inhibitor therapy favours the variations that survive and multiply.

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

Screening Searching and final selection of the antibody fragments that bind the best 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.

Statins A group of drugs that reduce the level of cholesterol in the blood.

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

Therapeutic antibody Antibody that is used for treatment of a disease; antibody-based drug.

Therapy Treatment; here in general with drugs.

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

Toxin, toxic Toxic substance, with toxic effect.

Toxicology Scientific study of poisons and their effects.

Validation Assessment of a or target protein to discover if it has the desired effect or characteristics.



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