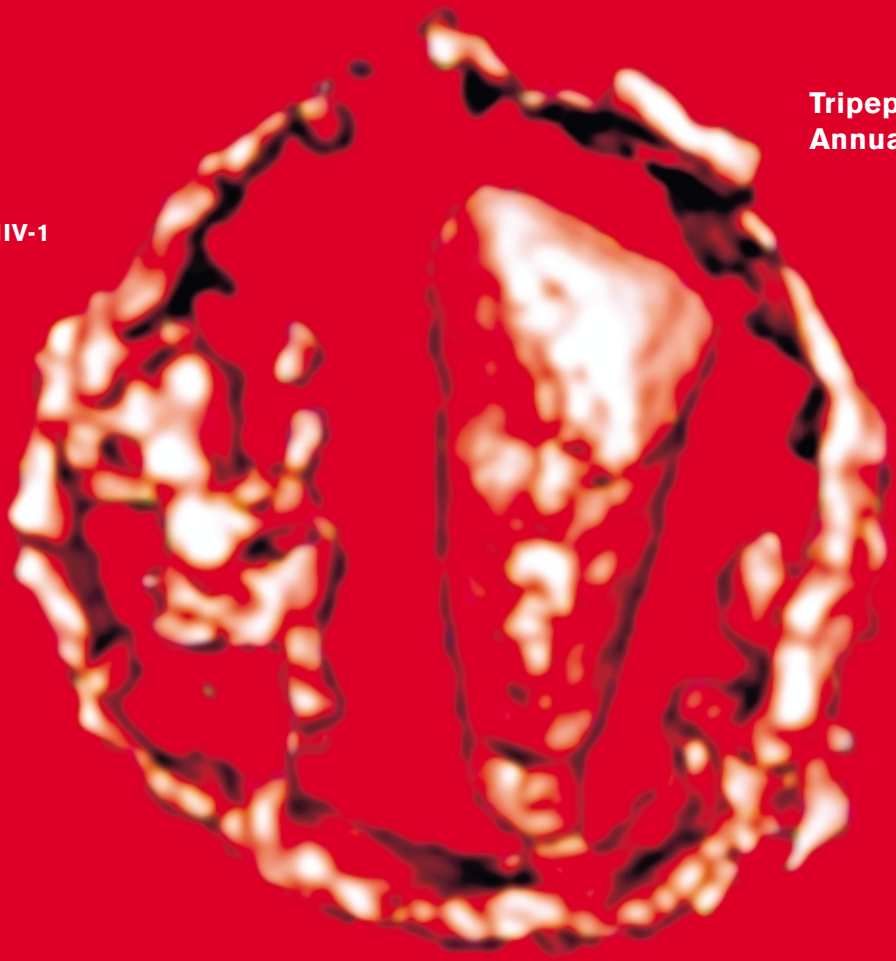
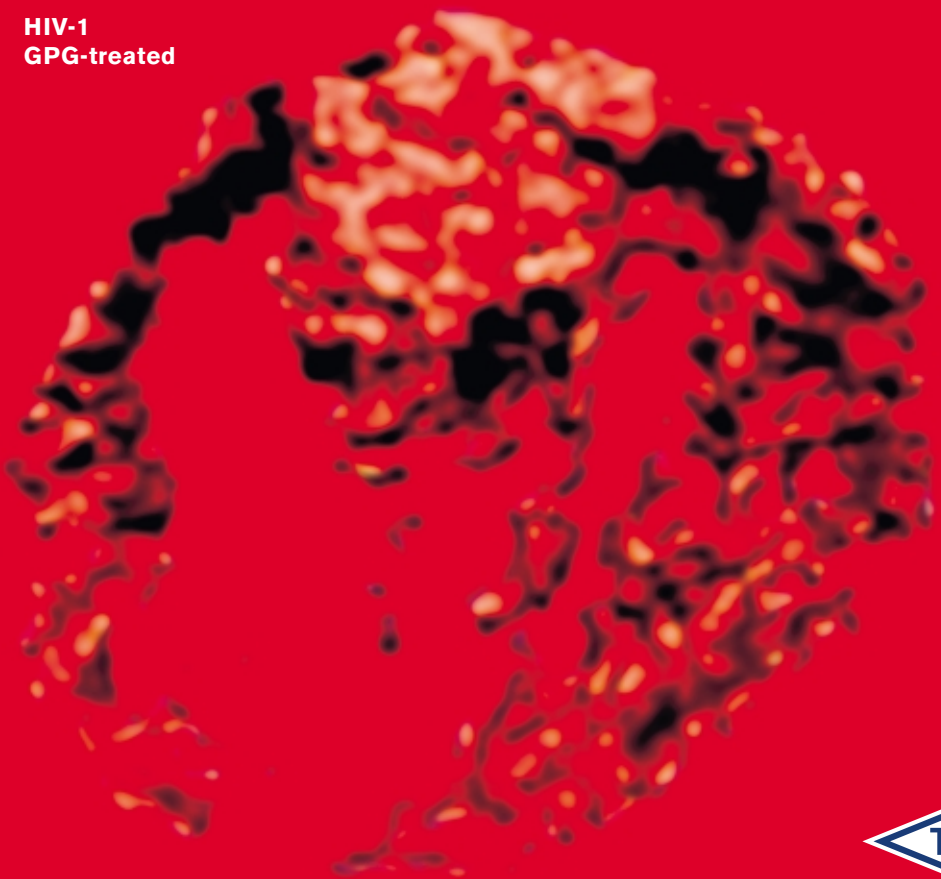
Tripep.
Annual Report. 2000.

HIV-1



HIV-1
GPG-treated



TRIPEP

The pictures on the front cover
were taken by Assoc Professor Stefan Höglund of Uppsala University, one of the researchers with whom Tripep has close cooperation.

The back cover
is taken from the February 2001 advertising campaign by Tripep.

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This annual report
has been prepared in Swedish. In the event of any discrepancies between the Swedish annual report and the translation, the former will prevail.

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CONTENTS

Invitation to the Annual General Meeting of Shareholders

Tripep's Annual General Meeting of shareholders will be held on 2nd April 2001 at 9.30 am in the lecture theatre of the Swedish Society of Medicine (Svenska Läkaresällskapet), Klara Östra Kyrkogata 10, Stockholm.

Breakfast will be served from 9.00 am.

A shareholder has the right to participate in the annual shareholders' meeting, provided he is entered in the shareholders' register maintained by VPC (the Swedish Securities Register Centre) by 23rd March 2001 and has notified his intention to participate no later than 15.00 pm on 28th March 2001.

A shareholder who has registered his shares as a nominee shareholder must temporarily register them in his own name at VPC. Any shareholder who desires such a re-registration must inform the nominee administrator in good time before 23rd March 2001.

Notification of an intention to attend Tripep's annual shareholders' meeting 2001 must have reached Anna Welin at Hill and Knowlton Sweden AB no later than 15.00 pm on 28th March 2001.

- Address. Box 154 11, 104 65 Stockholm
- Telephone. 08-402 89 06
- Fax. 08-402 89 99
- E-mail. awelin@hillandknowlton.se

In the notification, the shareholder shall state his name, Personal identification number or Registered Organisation number, address and telephone number, and the number of assistants (maximum 2) that the shareholder wishes to bring with him to the shareholders' meeting.

Future meetings

The dates of future meetings in the year 2001 will be decided at the first Board meeting following the annual shareholders' meeting on 2nd April.

Tripep in brief

Tripep is a research company that was formed in 1997 with the aim of developing and commercialising GPG, a drug targeting HIV. GPG was discovered in 1993 and during 1998, Tripep was able to establish that GPG works against HIV via a completely new mechanism. This mechanism provides the basis for a new platform technology; *Protein-Polymerisation-Inhibitors* (PPI). Using PPI-technology, Tripep can search for new pharmaceutical agents with the potential to treat other chronic diseases. Tripep is initially focusing on combating Hepatitis C virus and inhibiting the inflammatory protein TNF-α which is involved in chronic intestinal inflammation and rheumatoid arthritis.

Tripep's second platform is called *Re-directing Antibody Specificity* (RAS). RAS means that an antibody that already exists in the body is guided towards a new target. RAS-peptides redirect the antibody to attack a new specific target; for example, surface structures on substances involved in infectious diseases, toxin-induced illnesses, cancer and autoimmune diseases. In cooperation with researchers at the Karolinska Institute, the first RAS molecule is being developed as a potential drug against certain nosocomial infections.

Tripep also has a licence for *Parvo-Virus-Capsid-technology* (PVK). PVK is of potential use when it is necessary to inhibit the growth of blood cells or blood vessels. Tripep has identified three possible therapeutic uses of PVK: treating Polycytemia vera (PCV, an overproduction of red blood cells), as treatment prior to bone marrow transplantation and inhibiting angiogenesis for the treatment of solid tumours. The first application which is being developed, in cooperation with Swedish Orphan AB, is the treatment for PCV.

Tripep is also developing therapeutic and prophylactic vaccines against HIV and the Hepatitis C virus. These projects are being carried out in cooperation with the Vaccine Research Institute of San Diego and are based on original inventions for which Tripep has patents or has applied for patents.

Tripep has approximately 40 collaborators of whom Tripep employs 14 while the others work via research institutes and other centres. Seven of our collaborators are Professors and an additional 14 are Ph.D.s.

The year in brief

- A phase II-study of GPG was started in October.
- Six research projects, besides GPG, have been started during the year.
- Tripep was quoted on the OM Stockholm Exchange O-list on 14th July 2000.
- The company has established the organisational structure required to develop pharmaceuticals from the preliminary stage through to a finished product. This includes our own research laboratories, research collaborations, preclinical, clinical and production operations.
- The company has ensured its financing for the next two years as follows:
  - A private investment of SEK 51 million in February,
  - An industrial fund loan of SEK 35 million in May,
  - A new emission of SEK 202.5 million in connection with the quotation on the OM Stockholm Exchange.

Key data.

	2000	1999
Yield on capital employed, %	neg	neg
Yield on equity, %	neg	neg
Solidity, %	89.0	49.0
Debt/equity ratio, times	0.05	-0.07
Proportion of risk-bearing capital, %	89.0	49.0
Cash flow, SEK million	-54.0	-12.6
Net investment in fixed assets, SEK million	5.1	1.2
Total research and development, SEK million	20.7	6.1
Salaries, fees and social costs, SEK million	11.3	1.6
Average number of employees	12	3
Earnings per share, SEK	-3.75	-6.88
Equity per share, SEK	15.06	1.27

Business idea, vision, aim and strategy

Business idea

- Tripep's business idea is to develop and commercialise pharmaceuticals, particularly those based on the company's patented technologies.

Vision

- To create an innovative pharmaceutical company based on both its own and licenced research.

Aim

- To develop, apply for approval of and register GPG during the first quarter of 2003.
- To licence the rights to the marketing of GPG to a larger pharmaceutical company no later than 2002. Under certain circumstances, Tripep may also market and sell GPG under its own management.
- To identify by the year 2003, a number of new candidate drugs based on the company's patented technologies, either from our own research or in cooperation with others.
- To create and maintain strong international patent position. This is best achieved if the patent application is initially drafted by a US based patent agent. For this purpose, Tripep employs one of the world's foremost patent agents, the American company Knobbe Martens Olson & Bear.

Strategy

- To draw up a separate plan for each compound that has the potential of becoming a drug. This plan will describe how the development process shall be carried out – either under our own management, as with GPG, or in cooperation with others as is the case with PCV. Tripep has the potential, internally and through its network of cooperative partners and subcontractors, to take a substance all the way from the initial idea to large-scale production as a registered pharmaceutical agent. Our internal expertise, together with a flexible strategy makes it possible to optimize the development and value of each project in accordance with Tripep's operational and financial circumstances.
- To use part of the cash flow generated by GPG to add further value to our platform technologies through the development of novel pharmaceutical agents for use in the areas of medicine of interest.

A SUBSTAN

The history of Tripep

1986: Professor Anders Vahlne together with Associate Professor Bo Svennerholm, Associate Professor Peter Horal and others form the company Syntello AB.

1987: Syntello AB sells a diagnostic HIV-1/HIV-2-test based on synthetic peptides to Pharmacia Diagnostics.

1989: Professor Vahlne forms Syntello Vaccine Development AB/KB together with Hans Möller and others, with the aim of developing a peptide-based HIV-vaccine. During the next three years, the company develops a prototype vaccine. While this vaccine is being developed, GPG is identified, a substance which strongly inhibits HIV. It is decided that GPG could be developed into an effective anti-HIV drug.

1993: Syntello Vaccine Development moves to the USA through a reverse acquisition of the company General Biometrics Inc. The company name is changed to Syntello Inc. In parallel with the development of the prototype HIV vaccine, a licence is acquired for an anti-cancer drug. Syntello Inc decides to prioritize the development of this cancer treatment and changes its name to Maxim Pharmaceuticals Inc. Maxim Pharmaceuticals Inc is today quoted on Nasdaq and on the OM Stockholm Exchange.

1996: Professor Vahlne and Hans Möller leave Maxim Pharmaceuticals Inc and get, amongst other things, all the HIV-related technology they helped to develop.

1997: Tripep is formed with the intention of commercializing GPG. The company acquires the RAS technology from Matti Sällberg and a licence for the PVK-project from Kristina Broliden, both researchers at the Karolinska Institute.

At the time of its formation, Tripep receives a total of SEK 18 million through a directed new emission. Hans Möller becomes Chairman of the Board.

1998: Anders Vahlne's research team shows that GPG works via a novel mechanism, completely different from all previously known anti-HIV drugs. The mechanism of GPG action forms the basis of the platform technology PPI, which has potential applications in the treatment of other diseases. With the aim of exploiting the demonstrated potential of GPG, Hans Möller is appointed Managing Director of Tripep in November 1998.

2000: A new directed investment of SEK 51 million occurs and Tripep receives an Industrial Fund loan of SEK 35 million. In July, a new emission is carried out in connection with the quotation on the OM Stockholm Exchange which yields SEK 202.5 million. Hans Möller resigns as Board Chairman and is replaced by Harry Faulkner. A number of research projects are started and GPG enters phase II-studies. Cooperation with the company Swedish Orphan is initiated.


“But perhaps most important of all was that the work to develop GPG lived up to our own very high expectations.”
Hans Möller Managing Director, Tripep

The Managing Director speaks

The moment I opened my eyes on New Year's Day I knew it; this year will be decisive. I had a gut feeling that something big was going to happen. The feeling was well-founded; we have made great advances, especially during the past year. The year 2000 was an exceptional year for Tripep!

We have developed from a one-project company with many other ideas into a company with seven well-functioning research projects. We have progressed from minimal research and manufacturing resources to having more than 40 collaborators alongside both a preclinical and a clinical organisation. We went from having no money in the cash-box to gaining a quotation on the Stock Exchange and generating money which will completely fund the company for another two years. But perhaps most important of all was that the work to develop our first pharmaceutical agent – GPG, an HIV inhibitor – lived up to even our own very high expectations.

Tripep is a biotechnological research company that builds on an ability to think in a new and different way within several different fields of medicine. In the company, there are several extremely talented researchers. Around them we are building, step by step, the organisation required if the work of these researchers is to bear fruit.

Our seven research projects aim to develop the following: an HIV-vaccine, two Hepatitis C vaccines (one prophylactic and one therapeutic), a treatment for the blood disease Polycytemia vera (PCV), a TNF-α-inhibitor (effective against for example, rheumatoid arthritis), an anti-Hepatitis C medicine, an anti-Staphylococcus drug, and the jewel in the crown – GPG, our anti-HIV drug.

GPG is to all appearances unique among HIV-medicines. It seems to be active against all HIV-strains, it appears unable to provoke HIV resistance and has so far given no side-effects. What we have learnt during the development of GPG was presented at a major conference on clinical HIV-research in Glasgow in October. Our results were well received and attracted the attention of many.

If the results of the GPG phase II-study, which are expected to be produced during the summer, confirm what previous studies have shown, we shall have taken a great step towards producing a finished pharmaceutical agent. An anti-HIV drug could generate billions in profit. If the answers from the GPG phase II-study are not as positive as we expect, we at Tripep are still convinced that it has the potential to become a successful anti-HIV drug, with some modifications of its development plan.

To summarise; last year was very successful for Tripep. This year will be decisive.

Hans Möller
MANAGING DIRECTOR, TRIPEP

Activities

Tripep is a research company that has the potential to develop pharmaceutical agents from the initial idea all the way to a finished product. The company develops parts of its product portfolio together with industrial partners who contribute both expertise and resources.

The company has a small core organisation and a number of cooperative partners and subcontractors. Tripep has found that such a dispersed, virtual organisation is flexible and cost-effective and provides access to the best talent. Having this structure also means that the company can work quickly and avoid the financial risks which a large operation can accumulate.

The company is based in the Novum research park at Huddinge University Hospital, on the Southern campus of the Karolinska Institute. Experimental research into our biotechnologies is carried out in the University's laboratories, while more industrially-directed research is carried out in Tripep's own laboratories.

Of our 40 collaborators, 14 are employed by the company while the others work in research institutes. All individuals have signed confidentiality and non-competitive agreements.

Patents

Tripep's patents are handled by the US based company Knobbe Martens Olson & Bear, which has been ranked as the leading patent agent in Western USA for five consecutive years.

Tripep has taken out a patent insurance *(Intellectual Property Litigation Insurance)* against breach of contract, one's own or another's encroachment and legal action against encroachment.

The company holds ten patents and has a further 19 patent applications. The patents granted cover GPG, an HIV-vaccine and RAS as platform technology. The patent applications involve other Tripep technologies.

Research partners

We believe that close cooperation with researchers and clinics is vital for Tripep's success. The company cooperates with groups working within Sweden's leading reasearch institutions: the Karolinska Institute, Sahlgrenska University Hospital and Uppsala University. Researchers at the Karolinska Institute are working on all of Tripep's biotechnologies, whereas those at Uppsala University and the Sahlgrenska University Hospital are focusing on GPG and other PPI-projects.

During 2000, Tripep started three completely new research collaborations. Together with researchers from the University College of Dublin, Tripep is working on an antiviral drug against Hepatitis C based on the PPI-technology. We are also collaborating with researchers at the Vaccine Research Institute of San Diego to develop further potential HIV and Hepatitis C vaccines.

Development partners

In December 2000, a long-term joint venture between Tripep and Swedish Orphan was started in order to develop a new drug for the treatment of *Polycytemia vera* (PCV). Tripep supplies the knowledge of drug development and Swedish Orphan contributes knowledge about so-called *orphan drugs*. Orphan drugs are medicines against diseases which affect only a small number of people and the development of which is supported by favourable regulations in order to make their development profitable.

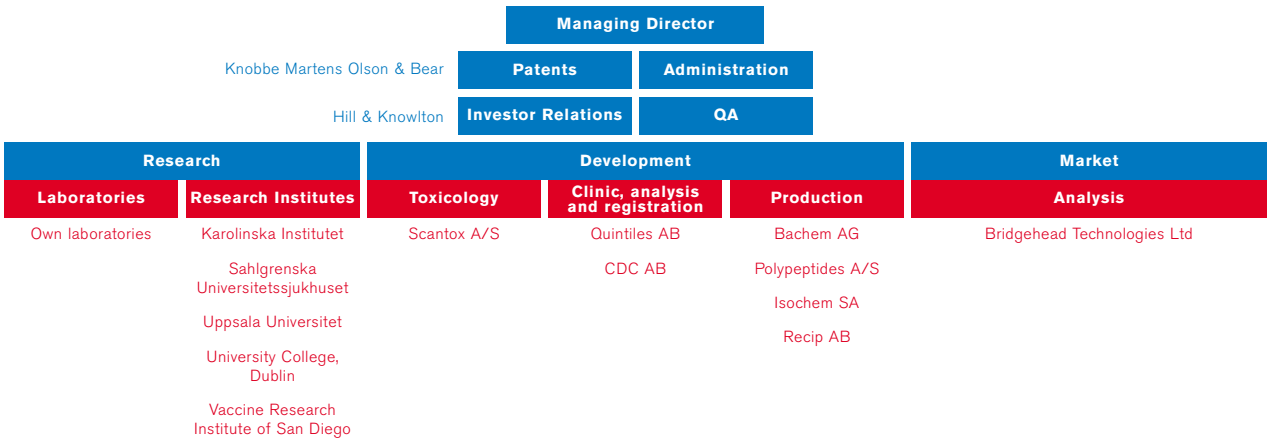
CLINICAL TRIALS, ANALYSIS AND REGISTRATION

Tripep has contracted Quintiles AB and Clinical Data Care to carry out clinical trials, analysis and registration.

The company also cooperates with the American company Covance to develop assays for GPG and with Professor Baltzarini at the Rega Institute in Belgium to perform, amongst other things, GPG resistance studies.

TOXICOLOGY

The safety studies, which Tripep is obliged to carry out, are performed by the Danish company Scantox A/S, one of the leading companies in Europe in this field.



PRODUCTION

Tripep is cooperating with four companies with respect to production:

- Bachem AG,
  a Swiss company quoted on the Swiss stock exchange which focuses on peptides and has strength in medium-scale production.
- Polypeptides A/S,
  a Danish company which focuses on medium-scale production.
- Isochem SA,
  a French national company engaged in the large-scale production of for example, peptides.
- Recip AB,
  a privately owned Swedish pharmaceutical company with its own production and development departments which also carries out extensive contract production of pharmaceutical formulations and packaging.

All of Tripep's producers can manufacture according to GMP *(Good Manufacturing Practice)* and have been audited by the American *Food and Drug Administration* (FDA).

Market partners

Tripep commissions the British company Bridgehead Technologies to make market investigations and advise on strategic decisions. Bridgehead Technologies has highly qualified staff with extensive experience, particularly of the pharmaceutical industry.

Investor Relations and Public Relations

Hill & Knowlton, an international PR-group with offices in 34 countries, is Tripep's IR- and PR-consultant.

Research portfolio

Tripep today has a broad research portfolio with a number of potentially very profitable products. GPG, a possible anti-HIV drug with a completely new mechanism of action, is based on our PPI platform technology. PPI can be used to develop more drugs and Tripep is engaged in the search for further potential pharmaceutical agents for the treatment of chronic infections. At present, research is focused on the Hepatitis C virus and on the search for a means to inhibit the inflammatory protein TNF-α that occurs in for example, chronic intestinal inflammation and rheumatoid arthritis.

In connection with the formation of Tripep, the RAS technology *(Redirecting Antibody Specificity)* that was developed by Professor Matti Sällberg at the Karolinska Institute was also acquired. Briefly, this technology means that a RAS-peptide given to a patient binds antibodies which already exist in the body of the patient for example, antibodies against polio. The RAS-peptide then redirects the polio antibody to attack a new, specific target. The first application that is being developed using RAS-technology is against multi-resistant Staphylococci, which among other diseases is an important cause of *nosocomial infections*.

Another Tripep technology is the licenced PVK *(Parvo-Virus-Capsid-technology)* developed by Associate Professor Kristina Broliden at the Karolinska Institute. PVK exploits the fact that parvovirus B19-capsids inhibit cell growth when they adhere to a structure on the surface of certain cells. Possible applications of this technology are those where the growth of blood cells or blood vessels needs to be inhibited and Tripep has identified three such situations needing therapy: Polycytemia vera, bone marrow transplantations and solid tumours.

Tripep is also engaged in a number of vaccine development projects involving both Hepatitis C and HIV. Professor Matti Sällberg is directing a project which aims to develop a therapeutic vaccine against Hepatitis C infections. The project started in 2000 and is based on a new genetic vaccine for which Tripep has applied for a patent.

Together with the Vaccine Research Institute of San Diego, Tripep is developing prophylactic vaccines against HIV and Hepatitis C. (Read more about Tripep's research on pages 18–19.)

Viruses

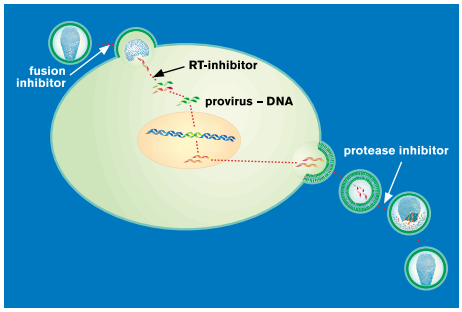


Figure 1. HIV attaches to the cell surface and its envelope fuses with the cell's plasma membrane. This can be prevented by a fusion inhibitor (T20). The genetic material (RNA) of the virus is transformed to provirus-DNA by an enzyme (reverse transcriptase, RT). This event can be blocked with RT inhibitors (NRTI and NNRTI). HIV maturation can be blocked by preventing the HIV protease from cleaving the precursor protein into the smaller capsid proteins, that is the building blocks of the capsids (the inner shell of the virus).

Viruses are very small infectious particles that lack cellular organisation. Thus, they have no life of their own, unlike, for example, bacteria. The only way for a virus to propagate is as a parasite in living cells that it transforms into virus-making factories.

A virus particle consists of a small core of genetic material (RNA or DNA), which is protected by one or several shells. The innermost shell is called the capsid and for many viruses it looks like a lantern made of snowballs. In other viruses, the capsid is spiral-shaped. The subunits which make up the capsid are called capsomers – "the snowballs" in the lantern. Only if this shell is intact is the virus able to propagate (that is infect a new cell).

Drugs against HIV

The figure above shows schematically how the HIV-virus uses a cell – a white blood cell called a *T-helper lymphocyte* – to propagate its genetic code. Since the process takes place in several steps, there are a number of positions where the virus is open to interference.

In order to infect the cell, the HIV-virus must first attach to the surface of the cell. In order for this to take place, a protein in the envelope (outer shell) of the virus (gp120) binds to a protein (CD4) on the surface of the cell. The envelope of the virus then fuses with the plasma membrane of the cell. The genetic material of the virus (in this case RNA) will be read and converted to DNA with the help of an enzyme which the virus carries with it as an essential tool since it is not present in the cell. This enzyme is called *reverse transcriptase* (RT) and is specific to the virus. The conversion of RNA to DNA by RT is necessary so that the genetic code of the virus, in the form of so-called 'provirus-DNA', can be inserted, in a random manner, into one of the cell chromosomes. When this has taken place, the cell is infected and has been transformed to a 'host' for reproduction of the virus. There are two groups of drugs, NRTI (Nucleoside-analogue-RT-Inhibitors) and NNRTI (Non-Nucleoside-analogue-RT-Inhibitors), which inhibit RT. (The different members of these two groups are shown in the table on the next page.)

Other HIV-inhibiting drugs are directed towards a later stage in the life cycle of the virus. The group of medicines called *protease inhibitors* (PI) prevent the protease of the virus from creating the p24-molecules that assemble into the capsid (inner shell) of new virus particles. Protease inhibitors ensure that immature virus particles are formed, which are unable to spread the viral infection throughout the body.

Drugs under development

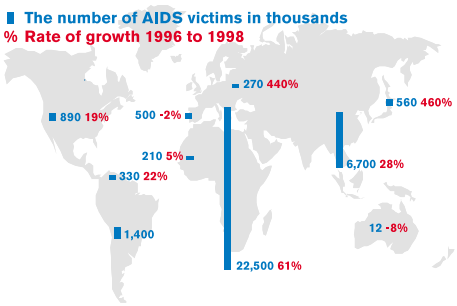
HIV is one of the world's most research intensive areas. Compounds with new modes of action under development include drugs *(integrase-inhibitors)* which prevent the virus' genetic material from being integrated into the genetic material of the cell. As far we know, there is, as yet, no such drug under clinical testing.

The American company Trimeris has developed a 36 amino acid synthetic peptide which prevents the virus' envelope from fusing with the outer membrane of the cell and thus stops the virus from entering the cell. The peptide (T20), a fusion inhibitor, is given as an injection and is being clinically evaluated in phase III-studies. HIV developing resistance to T20 has already been demonstrated.

A new class of anti-HIV pharmaceutical agents includes the so-called 'nucleotide inhibitors of reverse transcriptase' for example, tenofovir. These drugs function in the same way as NRTI.

Tripep's substance GPG uses a completely new anti-HIV mechanism (see pages 12–13) and is unique since resistance has not yet developed in spite of three years of provocation in test-tube experiments. GPG's method of attacking HIV is expected to be the fourth means of defense against the virus, hopefully with significant advantages compared to current treatments including T20.

HIV in the world



Aids in the world.

Since the early 1980s, more than 57 million[1] people are estimated to have been infected by HIV-1 and of these, 21 million[1] have died of AIDS. More than two thirds of all those who are today carriers of the HIV-virus live in Africa, south of the Sahara, which is also the region where the infection has had the longest time to establish itself. Today, the most rapid rate of increase of the infection is in South-East Asia.

Within the EU and the USA, the patient population amounts to about 1.42 million[1] of whom, half are undergoing some kind of treatment. Approximately 300,000 of these patients are carriers of a multi-resistant HIV-virus.

Treatment

The treatment of HIV-1 aims to prevent the propagation of the virus and this is currently achieved using drugs that inhibit two types of virus-specific enzymes: *protease* and *reverse transcriptase* (RT). Protease inhibitors (PI) and agents that inhibit reverse transcriptase (NRTI and NNRTI) constitute the main groups of currently approved HIV-inhibiting drugs.

In the western world today, there are many HIV-positive people who are symptom-free thanks to the HIV-inhibiting drugs that have been developed during recent years. A combination therapy with three to five drugs, so-called *HAART-treatment* (Highly Active Anti-Retroviral Therapy), has, during the last three to four years, greatly reduced the mortality rate in the west.

This HIV-treatment is often complicated by severe side-effects, the development of resistance and the varying ability of the patients to complete the desired treatment. Treatment with HIV-inhibiting drugs is a life-long commitment that requires punctuality and motivation. In spite of HAART, most patients develop resistance sooner or later. So far, 50 per cent of all the patients who are on HAART have developed some kind of treatment-resistance and this figure is rising – only two years ago, the proportion was 30 per cent.

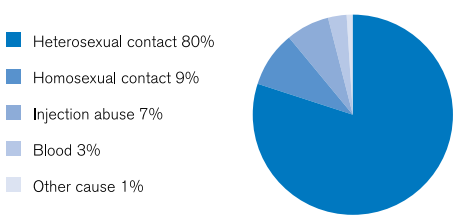
Approved anti-HIV-1-drugs[2].

Substance	Trademark	Company	Cost of treatment per patient per year (USD)
NRTI			
Lamivudine+Zidovudin	Combivir	GlaxoWellcome	6,228
AZT, Zidovudine	Retrovir	GlaxoWellcome	3,360
ddC, Zalcitabine	Hivid®	Roche	2,520
ddI, Didanosine	Videx®	Bristol-Myers Squibb	2,424
d4T, Stavudine	Zerit®	Bristol-Myers Squibb	3,108
3TC, Lamivudine	Epivir®	Glaxo Wellcome	2,868
Abacavir	Ziagen®	Glaxo Wellcome	3,540
NNRTI			
Nevirapine	Viramune®	Boehringer Ingelheim	3,060
Efavirenz	Stocrin®	MSD/Dupont Pharm	4,668
Delavirdine	Rescriptor®	Pharmacia & Upjohn	2,676
PI			
Indinavir	Crixivan®	MSD	6,000
Saquinavir	Fortovase®/Invirase®	Roche	5,220/6,840
Ritonavir	Norvir®	Abbott	7,344
Nelfinavir	Viracept®	Roche/Agouron	6,756
Amprenavir	Agenerase®[3]	Glaxo Wellcome	6,400

The spread of HIV

HIV is spread through sexual contact, infected needles in the case of intra venous drug abuse, blood transfusions and from mothers to children primarily during birth. Today, 10–15 per cent of those who have recently been infected in the Western world have an already completely or partially resistant HIV-virus.

The spread of HIV.



[1] SOURCE: Unaids.org
[2] SOURCE: 1999 HIV Drug Guide Jan/Feb 1999
[3] Approved in USA, not in Europe

GPG – a completely new anti-HIV mechanism

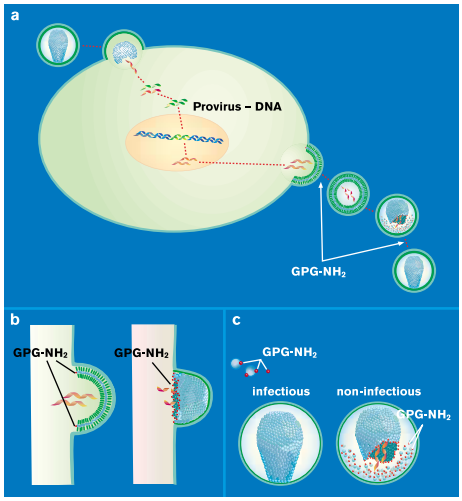


Figure 2. GPG is a tripeptide consisting of the amino-acids Glycine–Proline–Glycine. GPG binds to the uncleaved HIV capsid protein already inside the cell, thereby slowing down or arresting the budding off of the virus particles leading to a premature activation of the virus protease in turn resulting in incomplete virus capsid structures trapped in the cell's plasma membrane (b). In those particles that do bud off GPG will be bound to the cleaved capsid protein, that is the building blocks of the inner "snow lantern" structure, thereby preventing them from binding to one another. Thus the assembly of a mature virus capsid (inner shell) is affected.

The drug in Tripep's research portfolio which is closest to being launched is GPG, a potential HIV-inhibiting drug which attacks the virus in a completely new way (see figure 2). GPG is based on the PPI technology and acts by binding to the p24-molecules of the virus capsid, thereby inhibiting the budding off of viruses and preventing the crystallization process which gives the virus its protective capsid structure (see figures 2, 3 and 4 on this spread).

GPG is based on PPI technology platform. GPG is a tripeptide-amide, which means that it consists of three amino acids with a chemically-modified carboxyl terminal. GPG consists of the amino acids, Glycine–Proline–Glycine, and corresponds to a conserved amino acid sequence in the capsid protein of the HIV-virus. Binding to the capsid protein, thereby preventing the development of a protective virus shell structure is a completely new method of attacking HIV.

GPG is a unique anti-viral substance and it has a large number of advantages over other active HIV-drugs which often have serious disadvantages. The most important advantage of GPG is that the substance has so far been shown to have an effect on all HIV-strains tested and seems to be totally devoid of side-effects. It has also, during three years of continuous test-tube experiments, not yet been possible to provoke HIV to develop any resistance to GPG, which has been relatively easy to do with all approved HIV-pharmaceutical agents.

New ways of attacking the HIV-virus are necessary since the struggle against HIV and AIDS is a war against a moving enemy. HIV, which gives rise to the immunodeficiency disease AIDS, has a remarkable ability to mutate and circumvent the inhibiting drugs which it encounter. This has so far occured with all known HIV-drugs, and already more than 300,000 people in Tripep's primary markets – North America and Europe – are now infected with multi-resistant viruses.

Income from licence agreements.

Research and development cooperation within the pharmaceutical industry is paid for differently depending on the clinical phase at which the cooperation is started, the type of drug concerned, the size of the current market and the strategy which the pharmaceutical company in question has.

Pharmaceutical companies prefer to acquire licences for products in phase III which are directed against diseases which lack a satisfactory treatment. The products which satisfy these requirements normally receive higher royalties and other payments. In number, most licence agreements are entered into in the preclinical phase, while most of the agreements entered into during the clinical phase create a higher value.

Commonly occurring payment intervals have been compiled by Tripep's market consultant, Bridgehead Technologies, and are shown in the table below;

Clinical phase when agreement is reached	Single payment at the beginning of the agreement (USDm)[1]	Total milestone-payments (USDm)[2]	Royalty (%)
Preclinical phase	3–7	10–25	3–7
Phase I	5–10	12–25	5–9
Phase II	7–12	15–30	10–15
Phase III	10–15	15–50	15–35

[1] Single payments from pharmaceutical companies to biotech companies tend, in early phases, to consist of more than 50 per cent of directed new emissions to licence-purchasers with the remainder in cash. In later phases, the greater part is in cash.

[2] The milestone-payments indicated do not include payments to employees or business costs.

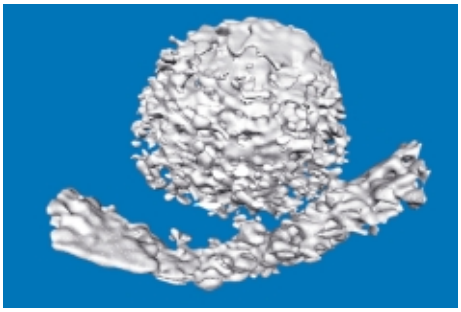


Figure 3. Three-dimensional electronmicrograph of an incomplete HIV capsid which has been trapped in to the cell's plasma membrane.

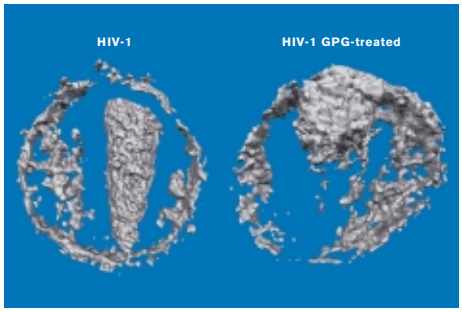


Figure 4. Three-dimensional electronmicrograph of HIV particles. To the left: an intact capsid with a normal conformation. To the right, an HIV particle produced in the presence of GPG, having an incomplete capsid structure (inner shell).

The market

Unmet pharmaceutical needs in the treatment of HIV create a number of marketing advantages for GPG:

- Rapid penetration of the market.
  Since effective treatment against HIV is lacking, the demand is great and a completely new anti-HIV drug would have a great impact among the 300,000 people in the western world infected with multi-resistent virus. Current therapeutic standard also means that the physicians involved are used to new compounds. This means that the market for anti-HIV drugs is easier to penetrate than other pharmaceutical areas.
- Short development time thanks to special regulatory rules.
  The development time to a finished product is shortened considerably thanks to the fact that the degree of national and global urgency quickens the authorities' registration process.
- Economic potential.
  New HIV-inhibiting drugs often sell for USD 200–600 million during the first twelve months after being launched.

Studies

Tripep was formed in 1997 to develop and commercialise GPG. Our aim is to be able to apply for approval and registration of GPG during the first quarter of 2003 and to licence the marketing rights to a larger pharmaceutical company.

In 1998, Tripep established that the compound has a completely new mechanism of action against HIV (see figure 2). This explained what we discovered by accident in the early 1990s – that GPG is strongly active against HIV-viruses in a test-tube.

The phase I/II-study, CTN 001, Tripep's initial safety and efficacy study on HIV-infected persons, was completed during February with good results. In the study, GPG showed a very good tolerance and the median decrease in the number of virus copies was approximately 50 per cent. In the full dosage group (nine patients) the decrease in the number of virus copies was approximately 65 per cent. This positive result was very satisfactory given the short treatment time (two weeks), the fact that no other HIV-drugs were administered (monotherapy) as a parallel treatment and knowing that the maximum antiviral effect is not usually reached until after one to three months of treatment. The reduction of virus in the patient's blood came later than expected, but the effect remained during the whole follow-up period of 14 days. These unexpected results have, in test-tube studies, been shown to depend on the fact that it takes a long time for GPG to be absorbed by white blood cells. After a week, a plateau concentration has still not been reached in the target cell. However, once inside the blood cell, the half-life of GPG is long. The study aroused great interest when it was presented in October at the Fifth International Congress on Drug Therapy in HIV Infection in Glasgow.

The phase I-study on healthy volunteers, which was presented during the fourth quarter of 2000 showed that the pharmacodynamic effect, that is the viral reduction effect in the body, remained for longer than had been expected. The effect was still evident twelve hours after the patient had received the dosage. This, in combination with GPG's long half-life inside the infected cell, may mean that one dose per day is sufficient. The phase-I study also confirmed that GPG has a very positive toxicity profile and no pharmaceutical-related side-effects could be established.

In the summer of 2001, GPG may take a decisive step towards becoming a finished product, as the results from the phase II-study begun in October 2000 will become available. The phase-II study will show more clearly both the clinical effect on multi-resistant HIV-patients of GPG and the optimum dose. At least 45 HIV-infected persons who have not responded sufficiently to existing treatments are included in phase II study. This is also the first test of GPG in its correct context, that is, as one of several pharmaceuticals in a combination therapy, so-called *HAART* (High Active Anti-Retroviral Therapy).

ASSEVERA

The study is being carried out in ten different centres in Europe.

The results will constitute the basis of Tripep's application for clinical tests (IND, Investigational New Drug approval), in the USA. The most important questions, which the study shall provide answers to, are the following:

- How active is GPG when it is taken together with other drugs in the HAART?
  In test-tube experiments, GPG has shown addative effects with other drugs.
- Is the effect better than in the phase I/II-study?
  Here we expect a positive answer since the previous study (phase I/II) was too short. When the study was designed, we did not know about the slow uptake of GPG by the target cells (white blood cells). Test-tube experiments have shown that this uptake from the bloodstream into the target cell (where GPG has its effect) takes more than eight days. The phase I/II-study comprised 14 days of treatment and a two-week follow-up whereas, the ongoing phase II-study comprises six weeks of treatment and a four-week follow-up.
- What is the optimum dose of GPG?
- Does the unique side-effect profile from previous trials in human beings and animals remain?

If the results in the phase II-study are favourable, the path lies open for the third and last trial stage: large-scale clinical testing on 600–1,000 patients, which is estimated to begin during the third quarter of 2001. If the phase II-tests are found to be slightly less favourable, it is still probable that GPG will become a successful drug, but the process will take longer time. For example, it may then be necessary to adjust the dosage of GPG to give the optimum effect.

Advantages of GPG

The pre-clinical tests and the test-tube experiments have, in combination with the first studies on humans, shown that GPG has several important advantages compared with known HIV-drugs:

- GPG is effective against all HIV-strains.
  Thanks to its unique mechanism of action, GPG is effective even against HIV-viruses which have developed a resistance towards the available drugs. With GPG treatment, fewer virus particles are produced by the infected cell and those which are produced cannot infect new cells.
- There is, as yet, no resistance against GPG.
  For the existing drugs against HIV it has been shown, in in vitro experiments, that it is possible to provoke the development of a resistance in the HIV-virus. The more rapidly resistance appears in a test-tube, the more rapidly it also appears in treated patients. In spite of extensive continuous test-tube experiments over a period of three years, Tripep has not succeeded in provoking resistance towards GPG.
- GPG seems to have a unique side-effect profile.
  The animal tests have shown a very low toxicity for GPG. Doses as high as 300 milligrams/kilo body weight have given no symptoms or changes in experimental animals following daily intravenous treatment for a month. Only slight symptoms appeared in some animals which were given a dose which was more than three times as high (one gram/kilo body weight). No GPG-related side-effects have been established on human beings, either in a phase I-study on eight healthy volunteers who were treated with one dose, or in a phase I/II-study on HIV-patients who were treated with several doses.
- The GPG-treatment is simple.
  Another positive feature of GPG is that the treatment is simple. The GPG-molecule is small and the preparation can be given orally. GPG has a slow onset and needs 10–14 days to attain sufficient concentration in target cells. However, once inside the target cell the half-life of GPG is long. Enrichment of GPG in the target cell may mean that the dose can be reduced after a time with undiminished effect, possibly down to one dose per day.

GPG production

GPG consists of only three amino acids and can therefore be produced in a soluble phase. GPG is also a very stable substance.

Proteins and peptides

GPG is a synthetically-modified peptide. Only a few peptides have previously become approved as drugs, because there are a number of problems with the absorption and stability of peptides in the body. However, Tripep has succeeded in showing such favourable properties of a modified tripeptide that GPG and the PPI-technology itself could stimulate a paradigm shift within the field of peptide-based pharmaceutical agents.

Many of the most common problems in using peptides as drugs do not apply to GPG becasue of the unique properties of the molecule. GPG can be given in tablet form since:

- it is stable in acidic and gastric juices,
- the limited decomposition which takes place in the small intestine is well compensated for by the rapid absorption from intestine to blood,
- it remains effective in the blood plasma for about 12 hours after oral intake.

Therapeutic peptides.

Problem	Other peptides	GPG
Degradation in stomach	High degradation, acid-sensitive	No degradation, acid-stable
Degradation in small intestine	High degradation of proteases	Little, slow degradation of proteases
Intestinal absorption	No or very poor oral absorption	Very good absorption with an active transport mechanism
Half-time	Short, 2–5 minutes	Long, circa 50 minutes in test animals, probably several hours in humans
Production	Usually difficult and expensive	Simple and easy to scale-up

From idea to finished product

It normally takes 8–13 years to produce a pharmaceutical product, from an idea in the laboratory to an approved drug. Of this time, clinical studies and treatment by the authorities take 6–8 years. During recent years, however, the latter stage has been shortened to about 5–6 years through increased efficiency in both industry and authorities. In order to quicken the process further, in particular with respect to epidemic diseases such as HIV, the drug agencies in the USA (FDA) and Europe (EMEA) have created special priority regulations for certain diseases.

Treatment-resistant HIV-infection is given such priority, Tripep has therefore made the strategic choice to direct clinical studies towards this condition in order to obtain as rapid a registration as possible. The basic demands for showing effect and good safety are of course unchanged, but the internal handling by the authorities is more efficient in these programs and the company can receive help in the planning of studies and in the presentation of the registration application.

A pharmaceutical agent is created

Pharmaceutical development takes place in a multi-stage process where only a few of the substances tested reach the market. Certain parts of the process are controlled by authorities which evaluate effect and safety aspects. The development is usually divided into three main stages:

- Research stage or discovery stage.
  Develop candidate drugs (CD). The risk of failure is high, about 90 per cent.
- Preclinical stage.
  CD is tested on animals and in cell cultures to investigate the toxicity of the substance, its effect, dosage, pharmacokinetics etcetera.
- Clinical phase.
  This is usually divided into three study phases, I–III. With the help of these studies, data are compiled which are submitted to the drug-approving authorities. Since no drugs are completely non-toxic, the authorities also make a risk/utility assessment where the drug must have predominantly positive properties to be approved.

To ensure a high royalty, in the 15–35 per cent interval, Tripep chooses to develop drugs under its own management prior to approval and registration.

Program for rapid treatment by medical authorities.

Authority	Program	Condition
FDA	Fast track program	Serious or grave illness and a non-satisfied medical demand for new therapy.
	Accelerated approval	Serious or grave illness and a meaningful therapeutic addition compared with existing treatment.
	Priority review policy	Permits the use of "surrogate end points" (in this case a reduction in the number of HIV-copies in the blood). Significant improvement compared with existing products.
EMEA	Accelerated approval	The degree of seriousness of the illness, lack of suitable therapy and the assumption of a great therapeutic value.
	Registration under exceptional circumstances	Unusual illnesses, the present scientific knowledge is incorrect and it is unethical to refrain from treatment.
	Accelerated evaluation	The degree of seriousness of the illness, lack of suitable therapy and great therapeutic value is assumed.

Interview with Professor Sven Britton

Sven Britton, head physician at the Karolinska Institute and Professor of infectious diseases, was one of the first physicians in Sweden to be called upon as expert on HIV when the virus became known in the middle of the 1980s. He has also become known for his support for the distribution of nursing resourses to the most HIV-exposed regions of the world. With respect to the HIV-situation in Sweden and in the world, Sven Britton believes in providing information combined with HIV-inhibiting medicines. He considers Tripep's results to date from the GPG-studies to be sensational.

"That no resistance has been developed in test-tubes in three years is highly exceptional. But I have not seen the results as a whole yet, so it is perhaps best to wait with the ovations for a while yet," he says.

Sven Britton emphasizes that it is necessary that new drugs and new mechanisms of attack against HIV are developed now that there are viruses which are resistant to all the inhibiting drugs on the market.

"I believe that there are few people who realise the gravity of this development. It is known today that it is necessary to use several inhibitory medicines in parallel to reduce the virus production in the body. During the first years, drugs were not used in combination but we ought to have realised that resistance would arise considering the enormous amount of mutation possibilities in a virus which multiplies once a second."

"It is thus important to keep down the virus production in the body not only for the patient, but also for the possibility of combating the virus globally. This has not been given proper attention until recent years."

Sven Britton says that it is not completely clear whether the HIV-viruses which are resistant have mutated or whether they have occurred naturally in a small proportion all the time, but with a low survival rate. In the latter case, there is hope that the resistant strains may be less virulent, since there is a reason why this gene combination gets its chance first when the most potent varieties have been suppressed. It can, for example, be so that the resistant virus multiplies much more slowly than the original virus.

Although there is an enormous amount of research into HIV, the breakthroughs are few. Sven Britton is happy that a new inhibitory drug and a new mechanism of attack have been discovered in Sweden.

"60–70 times more money is invested in HIV than in malaria, which actually claims more victims. So it is not more resources that are needed, but more really good ideas," says Sven Britton.

"That no resistance has been developed in test-tubes in three years is highly exceptional."

Other research projects

At the end of the year 2000, Tripep had finished building up its research department and the system of collaboration required for the company to be able to handle other projects besides GPG. Ten more researchers in the fields of biomedicine and biochemistry have been employed to develop new pharmaceutical agents based on the company's two platforms, PPI and RAS. With its new research facilities, Tripep is also working on producing new GPG-like molecules in order to be able to identify and patent new anti-HIV drugs. A new and important method of finding these molecules uses advanced computers and graphical software to identify binding pockets for GPG. The other research projects on which Tripep is focusing during 2001 are:

- Inhibitory drug against Hepatitis C.
  In cooperation with researchers at University College, Dublin, Tripep is working, using PPI-technology, to develop a modified tripeptide which can function as an inhibitor of Hepatitis C (see figure 5), analogous to the action of GPG against HIV.
- TNF-α-inhibitor.
  In rheumatoid arthritis and the chronic intestinal illness Crohn's disease, the inflammatory protein TNF-α is produced and causes damage in the body. Antibody therapy which inhibits TNF-α has been shown to give dramatic relief from the symptoms of these diseases. Tripep is carrying out a project based on PPI-technology, under its own management to develop a tripeptide which inhibits the formation of functional TNF-α (see figure 6). The project is at the research stage and screening of the synthesized peptides for activity has begun.
- Drugs against Staphylococci infections.
  Multi-resistant Staphylococci which among other diseases is seen in nosocomial infections are a great problem in the western world, since few antibiotics have any effect on these bacteria any longer. In a collaborative project with Professor Jan-Ingmar Flock of the Karolinska Institute, Tripep has developed a unique way of attacking resistant Staphylococci. The project is based on Tripep's patented RAS-technology and means that existing antibodies are redirected to attack the Staphylococci (see figure 7). As a consequence of the

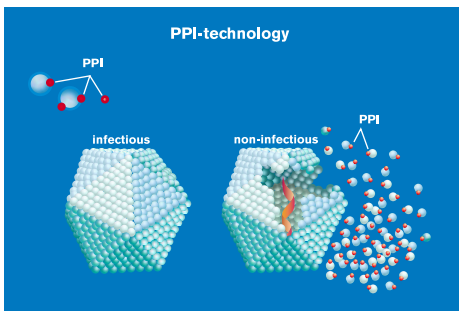


Figure 5. The Hepatitis C virus capsid ("snow lantern") must be intact if the virus is to be able to infect new cells and spread in the body. The basis of the PPI-technology is to find small molecules (modified tripeptides) which prevents the capsid's building blocks ("snowballs") from binding together.

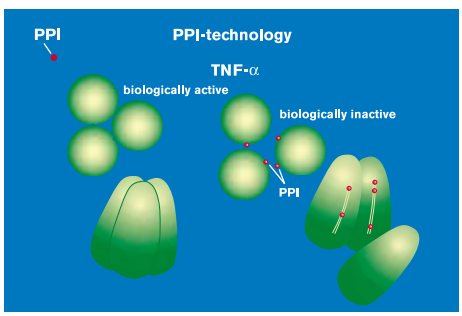


Figure 6. The biologically active form of the inflammatory protein TNF-α consists of three identical proteins joined together. PPI-technology can be used to prevent these proteins from binding to each other and TNF-α is thus rendered inactive.

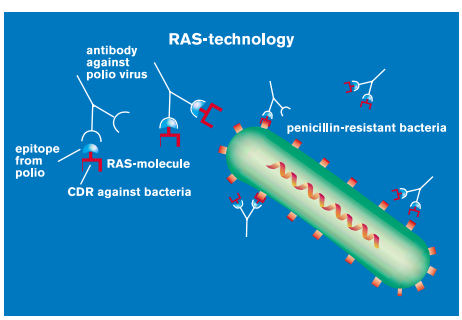


Figure 7. By directing the antibodies which we already have in our bodies, for example after a vaccination, it is possible to attack bacteria which are resistant to antibiotics. The RAS (Redirecting Antibody Specificity)-molecule consists of one part which binds to antibodies which we already possess and another part which recognises and binds to the bacterium.

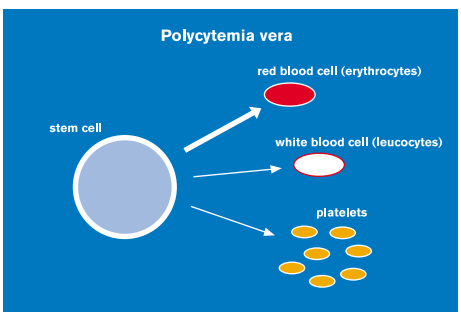


Figure 8. The illness Polycytemia vera is associated primarily with an overproduction of red blood cells. The PVK-technology utilises a protein from parvovirus B19, which binds to a receptor called P-antigen on the stem cells that develop into red blood cells and the endothelium of blood vessels. As a result of the PVK peptide binding to the P-antigen, the growth of red blood cells and other cells of the blood as well as the generation of new blood vessels is inhibited.

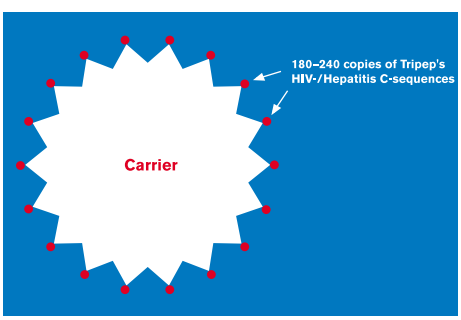


Figure 9. HIV and Hepatitis C genetic sequences are introduced into the capsid of a hepadna virus. This virus carrier can then induce very strong immune responses against HIV and hepatitis C.

promising results that the project has so far produced Tripep has accordingly broadened its patent protection.

➔ Drugs against PCV.

The blood disease Polycytemia vera (PCV), which is primarily characterised by an uncontrolled growth of red blood cells (see figure 8), is an illness without a cure. PCV makes the blood viscous which increases the risk of cardiac or cerebral thrombosis. Patients today are treated with cytotoxins and blood-letting. In cooperation with Swedish Orphan AB, Tripep is developing a potential new drug against PCV. Any drug against this relatively rare disease is covered in the USA, EU, Japan and Australia by a so-called orphan-drug legislation which means, amongst other things, more rapid treatment by the authorities. Swedish Orphan has extensive knowledge of the development and marketing of orphan drugs.

➔ Therapeutic vaccine against jaundice (Hepatitis C).

There is no registered vaccine against Hepatitis C virus. However, Tripep has identified and applied for a patent for a new vaccine gene with unique properties which could lead to a good therapeutic vaccine. By inducing an immune defence which kills virus-infected cells, the vaccine may be included as a component in a combination therapy against chronic Hepatitis C infections. There is a great need for therapy against this illness; 200–300 million people in the western world are infected by Hepatitis C, and in its most common form, 80 per cent of the patients do not respond to the current treatment.

➔ Prophylactic/therapeutic vaccine against HIV and prophylactic vaccine against Hepatitis C.

Tripep is carrying out research, in cooperation with world-leading researchers at the Vaccine Research Institute of San Diego (VRISD), to develop a protective vaccine against HIV-1. Tripep has patents on genetically stable parts of the capsid protein in HIV-1 which can activate antibodies that neutralize the virus. These patents were obtained in 1994 and derive from the work which Tripep's founders carried out before they formed Tripep. The preparation is intended both as a component in a preventive HIV-vaccine and as a therapeutic vaccine together with inhibiting drugs. Tripep and VRISD are also cooperating in seeking a preventive vaccine against Hepatitis C. The basis for this cooperation is Tripep's knowledge in developing the active components of the vaccine, while VRISD's strength lies in creating a strong antibody defence. See figure 9.

Human capital

The collected knowledge of our collaborators is Tripep's greatest asset. We have therefore worked out an warrant program which means that all collaborators, both employees and contracted personnel, are part-owners of Tripep.

Since it is Tripep's ambition to employ the best researchers, it is also our policy to pay competitive salaries. Our employees can also receive individual bonuses for especially praiseworthy contributions.

Tripep handpicks its collaborators on the basis of their high competence. The average level of education in the company is high and seven full Professors are included in the organisation. In our recruiting, we place a great emphasis on having an entrepreneurial spirit, possessing a driving force to participate in and develop the company and successfully fitting into the small and highly specialised team that constitutes Tripep. At the end of the year, the number of full-time collaborators was about 40 (13 the previous year) of whom 14 were employees (five the previous year). During the year, new cooperation was initiated with both domestic and international researchers. A fact that clearly demonstrates that Tripep is an interesting employer is that nobody has ever resigned from the company.

Tripep is a creative place of work, largely thanks to the many researchers included in the organisation.

Work procedure

The virtual form of work makes it possible for the company to have a small efficient core organisation and at the same time carry out research at a number of important institutions. Many functions – for example, Investor Relations and PR, testing and production – are handled by cooperation partners and subcontractors, to ensure that Tripep has as flexible an organisation as possible and can focus on – the research work. The decentralized organisation is held together with the help of modern information technology and gives the company flexibility and access to the best forces within each field.

It is also important to emphasise that Tripep has the necessary resources for handling contacts with the authorities for example, during the approval of clinical tests.

Tripep's agreements with all contract researchers guarantees the company the ownership of research results and patents. The agreements also contain confidentiality obligations.

Tripep's human capital also includes a Scientific Advisory Board with a number of world-leading researchers in the medical field.

Assoc Professor Kristina Broliden (the PVK-project).

Professor Matti Sällberg (the RAS- and vaccine-projects).

Round-table discussion

On 13th February 2001, a number of people gathered together for a round-table discussion. The starting-point was Tripep's and RFHP's joint advertising campaign on the theme of HIV and AIDS. The discussion dealt with HIV and money, the western world and the third world, responsibility and credibility.

MA There was a time when condoms were distributed to everybody, and now people no longer speak of the HIV-danger. Now we see that sexually-transmitted diseases are increasing again and the number of HIV-infected people is also rising. Can Tripep inform people about safe sex equally as well as the Government?

TA It's easier for a company in this line of business. We are screened by the Medical Products Agency and it has an institutional legitimacy regardless of whether we are a private company. There are close links between science and research and pharmaceutical companies. Compare this with the oil business – a government representative who says something about an oil company following an oil spillage ... there is an enormous credibility gap there.

POP But there are investigations which show that the credibility of a medical message decreases as soon as a pharmaceutical logo is included.

TA But the Public Health Institute also lacks credibility. One works in a field which is legitimized by research and science, but one is not responsible for it oneself. You cannot just place government against private inductry, the scientific status is also very important.

POP The message has much greater credibility if the sender stands with both feet on the ground. You (turning to **AL**) are credible because you are HIV-infected. It doesn't matter what your background is; if you are a doctor, if you work at RFSU or if you work at the Public Health Institute. I am credible because I know a lot about HIV.

HM It's a question of both credibility and responsibility. This advertising campaign is running in Dagens Industri, Svenska Dagbladet and Dagens Nyheter because it is in these papers that I can justify our existance to my shareholders. But information must also be spread to those who do not read the newspapers. It's here that the responsibility of the government comes in.

TA Is it the purpose of this campaign to create better investor relations? Is it more money that you want?

HM Fortunately, we have money to complete this project. Therefore, our aim is not to raise money, it is not the intention.

CL With respect to credibility, an American investigation shows that the pharmaceutical industry lies and swims with the cosmetics industry and the politicians, at the bottom level. A little higher up, we find banking and finance, while research and universities are very high up. People are beginning to talk about *stakeholders value*, not only shareholders value; about contributing to different housing projects or taking care of HIV-infected black men in the big cities. This has not been seen in Sweden at all yet, and there it can be said that you at Tripep are setting an example ...

Participants

- Maria Arnholm **(MA)** MODERATOR, CONSULTANT NETWORK
- Tom Andersson **(TA)** PRINCIPAL, BERGHS SCHOOL OF COMMUNICATIONS
- Andreas Berglöf **(AB)** RFHP (THE NATIONAL ASSOCIATION FOR HIV-INFECTED PERSONS)
- Anders Licke **(AL)** HIV-POSITIVE
- Carina Lundberg **(CL)** MARKETING MANAGER, FOLKSAM CAPITAL ADMINISTRATION, FORMERLY MD OF KPA FONDER
- Hans Möller **(HM)** MD, TRIPEP
- PehrOlov Pehrson **(POP)** MANAGER AND HEAD PHYSICIAN, THE HIV-RECEPTION AT HUDDINGE HOSPITAL
- Ylva Strömberg **(YS)** DOCTORS WITHOUT BORDERS

IF WE WANT

YS The drugs which exist today are intended for those who live in the northern part of the globe. In the southern part, the people don't have access to these drugs. When I see an advertising campaign such as this, I immediately think: What is Tripep getting out of this? The really tough problem is that 95 per cent of the world's HIV-positive people live in poor countries and do not have access to these medicines, that problem is so heavy and burning and costs such a hell of a lot of money ... No one wants to touch it, and certainly not the pharmaceutical industry.

TA Would you in 'Doctors without Borders' be able to do the same thing as RFHP has done? To merge with someone in order to bring forward the third world?

YS We wouldn't merge with a pharmaceutical company. They are one of the parties which we lobby against, so that would be very strange.

TA But if a pharmaceutical company wanted to do so in light of the fact that it is socially and politically correct to combat HIV, would you then be prepared to join an alliance to promote such a debate?

YS 'Doctors without Borders' is today participating in round-table discussions with the EU, the WTO, the WHO – and the pharmaceutical industry is also there. But before we see the result of these discussions, I wouldn't join a campaign together with the pharmaceutical industry. In precisely the same way as I wouldn't hug Leif Pagrotsky in Dagens Nyheter either. For he has not shown which issues Sweden will support in the WTO. And if Astra comes ... will he change his opinion then?

HM We have approximately one and a half million HIV-infected people in the western world and the problem with the disease is that there are no drugs which are efficient and easy to administer. The medicines make enormous demands on the competence of the doctors. It's not a question of a simple pill which you can place in cans in the middle of the capitals on the African continent, which people can then go and take and the problem will be solved.

YS Why shouldn't HIV-positive people in Africa be able to cope with the treatment which HIV-positive people in Sweden cope with?

POP I don't believe that people in Africa should take the same medicine as HIV-positive people in Sweden. In Sweden, we can afford an individualistic perspective, which does not exist in Africa or South-East Asia. There one must have a social perspective which aims primarily to limit the spread of the infection.

MA Isn't that a very tragic message? If what is researched in the western world can't be used in Africa?

POP It's possible that Tripep's product, which has very small side-effects, can become such a drug ... But we must not have dreams about saving the world yet. The best vaccine which exists, the measles vaccine, is 35 years old. In spite of this, many millions of children in the world have died from measles since then. The solution is not natural, but something else.

YS I feel that it is very important not to use the fact that it is complicated as an excuse. If we say that we must find something simpler, the problem is postponed for ten years ... and in ten years, we have no one left to treat. Or else we have so many that the situation is totally chaotic. Something must be done now – even if it is difficult.

CL Schopenhauer has said that a truly good deed is a deed which a person does only to help another. There must be no element of helping oneself. So with respect to commercial companies, we can disregard good deeds. I believe that it is important to remember this. This is the difference between Doctors without Borders and the pharmaceutical companies.

TO BE CYNI

AB But we at RFHP are making use of Tripep in this way. We publish our message and hopefully receive the funds needed to carry out our activity. We work for the HIV-positive and we need all the money we can get, so it may be worth testing without having complete results. We shall see where this leads.

AL In Sweden, our culture says that it is the government which shall pay for everything. Previously, when I've suggested that we seek sponsoring, it has been said that we can't do that for then we would lose all our grants.

MA Ylva, do you at Doctors without Borders feel that it is right that the pharmaceutical companies earn money for what they do?

YS It is self-evident that the pharmaceutical companies must make money from their products. On the other hand, I believe that agreements must be reached between governments and pharmaceutical companies and between global organisations and pharmaceutical companies, so that it will still be profitable to research and develop pharmaceuticals for diseases which affect the poor parts of the world. If we want to be cynical, we can thank homosexual white men in the western world – for if this group hadn't been struck by AIDS, there would never have been any research into HIV and AIDS. There was no new research into TB until the multi-resistant tuberculosis bacteria appeared in New York, although it had existed for a long time in poor countries.

MA I should like to raise the question of the increase in sexually-transmitted diseases a little more. Does it depend only on the fact that there is too little information?

POP Yes, to a great extent. In Sweden, we say that to avoid sexually-transmitted diseases, you should use a condom and everything will be alright. This is an oversimplification. In the USA, people talk of harm reduction and risk reduction. There is a great difference between having vaginal or oral sex with an HIV-infected person and having anal intercourse. It is a question of a 100 times greater risk.

CL Why are we so afraid, why don't we speak plainly about this?

POP Because then we point to certain groups. If you, as a woman, have intercourse with a black man whom you pick up on the street, the risk of contracting HIV is 100 times greater than if you pick up a white man. But this takes us to the border of racism and discrimination. It's the same for me as a man – if I have unprotected sex with a man, the risk is 100 or 1,000 times greater than if it's with a woman.

MA My homosexual friends in Stockholm say that they believe that one of the reasons why HIV continues to spread is that there, because of HIV-inhibiting medicines, nobody dies from HIV infection any longer.

AL I wouldn't argue in that way, that just because there are inhibiting medicines I can have unprotected sex. Information is very important. The new group of HIV-positive persons are heterosexual white women, because they do not absorb the information available. In the 60s, there was free sex and we had approximately 30,000 cases of gonorrhoea each year at that time, and today it hardly exists at all. We have got that far through information and infection protection follow-up, plus the fact that there are medicines.

CL In my youth, there was an advertising campaign ... tonight 1,000 Swedes will catch gonorrhoea. This made an impression on me as a teenager. You see very little such information targeted to sexually extrovert young people or women on a holiday trip. I believe that it is possible to find sponsorship partners amongst insurance companies and others. There need not be any contradiction between informing in Sweden and having a strong involvement in combating the epidemic in the third world. One should not exclude the other.

Risks

A few of the factors which may be important for Tripep's future development, in addition to the risks inherent in the research project, are indicated below. These factors are not presented in any order of priority and the analysis does not claim to be exhaustive.

Investing in a research company such as Tripep is always associated with high risks. Since Tripep is based on several technologies, the total risk is smaller than if the company had only been based on GPG.

Before any of Tripep's products under development can begin to be sold, Tripep or its cooperative partners must prove that the potential pharmaceutical agents are safe and effective for humans. This is done through preclinical and clinical tests. The preclinical results do not, however, always do justice to the results attained in tests on humans.

Future capital requirement

Tripep estimates that the company's financial position after the latest new emission, is sufficient to carry out the planned activity until at least the first quarter of 2003. A further capital addition may however be needed within a few years, even though this is not judged to be the case today.

Cooperation partners

Tripep will, in the foreseeable future, be dependent on contracts with other companies with respect to research, preclinical and clinical tests, production and sales of potential products.

Patents and rights

Tripep's future success is partly dependent on the company's ability to obtain patent protection of potential products and to keep its own and its cooperation partners' research secret.

The company management has learned that a good patent protection is best attained if the patent application is initially drafted by a North American patent agent. Tripep cooperates with one of the foremost patent agents in the world in order to achieve as good a patent protection as possible.

Tripep has five patents and four patent applications covering GPG and the PPI-technology and two patents and nine patent applications regarding RAS technology and the PVK-project. The company also has three patents and four patent applications regarding an HIV-vaccine and two other patent applications.

During 2000, Tripep took out a patent insurance, *(Intellectual Property Litigation Insurance)*, against breach of contract, one's own or another's encroachment and legal action against encroachment.

Public supervision and examination

The continuous development of potential pharmaceuticals and the production and marketing of finished products is subject to supervision from the authorities. Even if a drug has been approved in one country, supervision authorities in another country can make further demands before granting approval.

Before marketing, all pharmaceuticals which are developed by Tripep or on a licence from Tripep must undergo an extensive process of approval by the authorities. This process, which includes preclinical and clinical testing of each individual drug, can take many years and requires considerable resources. Data from preclinical and clinical testings can be interpreted in different ways, and this may delay, limit or prevent approval by the authorities. Delays or rejections may also occur during the product development period as a consequence of changes in the policies of the authorities with respect to the approval of pharmaceuticals.

It cannot be guaranteed that approval from the authorities can be obtained for drugs which are developed or marketed on a licence from Tripep. The American supervisory authority FDA (Food and Drug Administration) has for example, declared that the administration will not approve a drug unless it is at least as effective as already approved pharmaceuticals.

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Even after approval has been granted, the company and the marketed pharmaceutical will be under supervision from the authorities. If hitherto unknown problems are discovered, this may lead to restrictions in their use or to the withdrawal of the product from the market.

Product responsibility and insurance

The company's activity involves a risk of product responsibility, which is an unavoidable risk in research and development, preclinical and clinical tests and the production, marketing and sales of pharmaceuticals. Tripep is today a member of the Drug Insurance Association, which provides insurance protection for damage regarding clinical tests. For clinical tests in another country, the company takes out insurance in the country concerned.

Competition

The pharmaceutical and biotechnology industry is developing rapidly and will probably continue to do so in the future. Many companies are active within the research and development of therapeutic products, and they may compete with products from Tripep. Some of these companies have far greater resources than Tripep for example, regarding research, development, contacts with authorities, marketing and financial resources. All these factors may constitute considerable competitive factors.

Dependence on key persons

The company is to a great extent dependent on a number of key persons. The loss of one or several of these could have a negative influence on the possibility of reaching the planned development goals. It is also decisive for the success of the Company to be able to attract and keep qualified scientific employees. In the employment contract of the collaborators and in the agreements relating to contracted researchers there are competition clauses which are time-limited. These prevent the employees from working on competitive activites during a certain period after giving their notice.

Price development

Potential investers should pay attention to the fact that historically, fluctuations in the price of shares in biotechnology companies have been large. Factors such as the results of preclinical and clinical tests, information about new substances from Tripep, its cooperation partners or competitors, results of patent disputes, statements from the permission-granting authorities and the general market situation for biotechnology shares can have a considerable influence on the future price development of Tripep shares.

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Administrative report

Activity

Tripep is a biotechnological research company which develops and commercialises pharmaceuticals based on patented technologies. Tripep was formed in 1997 with the aim of developing GPG, a potential HIV-inhibiting drug. GPG is the substance in the company's currrent research portfolio which is closest to being launched.

At the end of the year 2000, Tripep built up its research department and the new links which are required in order to handle research projects other than GPG in a satisfactory manner. A certain adjustment of priorities has taken place within the research portfolio during the year, partly as an adaptation to existing resources but primarily because of some very interesting scientific discoveries.

Research and future prospects

GPG

The phase I/II-study, CTN 001, Tripep's initial safety and efficacy study on HIV-infected persons, was completed during February with good results. In the study, GPG showed a very good tolerance and the median decrease in the number of virus copies was approximately 50 per cent. In the full dosage group (nine patients) the decrease in the number of virus copies was approximately 65 per cent. This positive result was very satisfactory given the short treatment time (two weeks), the fact that no other HIV-drugs were administered as a parallel treatment and knowing that the maximum antiviral effect is not usually reached until after one to three months of treatment.

The phase I-study, CTN 003, on healthy volunteers, was completed during the fourth quarter of 2000 and showed that the pharmacodynamic effect of GPG lasts for longer than expected. The study also confirmed GPG's favourable side-effect profile.

The phase-II study of GPG, CTN 002, was started in October 2000 and the results will be presented during the summer of the year 2001.

OTHER RESEARCH

- Therapeutic vaccine against Hepatitis C.

  During 2000, Tripep started the development of a vaccine against Hepatitis C infections. The project is led by Professor Matti Sällberg and builds on a new vaccine gene for which Tripep has applied for a patent.

- Prophylactic/therapeutic vaccine against HIV and prophylactic vaccine against Hepatitis C.

  Tripep has a patent on genetically stable parts of the HIV-1 envelope protein which can activate antibodies that kill HIV-1. Together with the Vaccine Research Institute of San Diego, Tripep started a project during 2000 which aims to develop a protective vaccine against HIV. In a parallel project, a prophylactic vaccine against Hepatitis C is also being developed.

- PVK/PCV.

  Together with Swedish Orphan AB, Tripep is developing a potentially new drug for treatment of the blood disease Polycytemia vera (PCV). This collaboration began in November and builds on Tripep's knowledge within the field of pharmaceutical development and Swedish Orphan's knowledge of the development and marketing of so-called orphan drugs.

- TNF-α-inhibitor.

  TNF-α is an inflammatory protein which causes damage in for example, rheumatoid arthritis and the chronic intestinal illness known as Crohn's disease. Using its PPI-technology, Tripep is developing a small molecule which inhibits the production of TNF-α. This project is being run under Tripep's own management and is at present in the research stage. Screening of the synthesized peptides for activity has started.

- Pharmaceutical for the treatment of Staphylococcus Aureus.

  Tripep has started a cooperative project with Professor Jan-Ingmar Flock at the Karolinska Institute. This collaboration aims to develop a unique method of attacking and destroying resistant Staphylococci. The technology builds on Tripep's patent-protected RAS-technology and aims to redirect existing antibodies so that they attack the Staphylococci. Multiresistant Staphylococci lead to so-called no-

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socomial infections which is a big problem in hospitals in the western world. The results from this project are promising.

Environmental influence

Tripep has carried out a first environmental audit of its activity, in accordance with the *Green index model*. We can report that there is nothing in our activity which leads to any load on the environment. An inspection will take place annually. It is Tripep's ambition to economise with natural resources and raw materials. This is done by regularly evaluating and improving our work routines from an environmental point of view. The necessary activity permit exists.

Investments

During the year Tripep has invested SEK 2.2 million in patent rights. In connection with the establishment of Tripep in the Novum research park, the company invested in its own laboratories with an area of 300 square metres. The costs of rebuilding amounted to SEK 1.2 million and the net cost of inventory purchases was approximately SEK 2.1 million. Besides this, inventory acquisitions – primarily computer equipment – have cost about SEK 0.4 million.

Cooperation contract

During 2000, Tripep signed a cooperation agreement with Swedish Orphan AB regarding the PVK/PCV-project. The cooperation takes place in the form of a joint venture where both parties own equal shares. Polycytemia vera (PCV) is a blood disease which is covered by the orphan drug legislation. Swedish Orphan AB is focused on the development and marketing of drugs within this group of pharmaceuticals. The cooperation with Swedish Orphan is in line with Tripep's strategy of developing parts of its project portfolio together with partners who can provide both competence and resources.

Stock exchange quotation

Tripep was quoted on 14 July 2000 on the OM Stockholm Exchange's O-list. The new emission was fully sold and the company's share capital increased to SEK 2.75 million, distributed in 13,750,000 shares. This means that SEK 202.5 million in funds was added to the company excluding emission costs.

Patent insurance

Tripep has taken out a patent insurance, (Intellectual Property Litigation Insurance), covering breach of contract, one's own or another's encroachment and legal action against encroachment.

Options

During the year, Tripep has sold options to key persons at the market price as follows:

- Series A: 1,120 options
- Series B: 24, 000 options
- Series C: 536,600 options

Sales have yielded SEK 2.7 million, which has been entered directly against own capital. All those in Tripep who intend to work for the company in the long term now own options.

After these sales, Tripep owns subscription options in Tripep as follows:

- Series A: 53 880
  (Duration 2004-08-14, subscription rate SEK 20)
- Series B: 526 000
  (Duration 2004-08-14, subscription rate SEK 160)
- Series C: 13 400
  (Duration 2004-08-14, subscription rate SEK 60)

All or parts of these options can, after a decision by the Board, be sold to employees/cooperation partners at the market price in order to create incentives.

The Industrial Fund owns a further 175,000 subscription options (duration 2003-12-30, subscription rate SEK 0.20). These options were issued in May when the company received a conditional loan for the GPG-project of SEK 35 million to be repaid no later than 2004-12-30. The loan is granted in two instalments of which, the first sum of SEK 20 million has been withdrawn and the second can be withdrawn when the company makes a decision with regard to the phase-III trial of GPG. If the company does not wish to withdraw the second instalment, 75,000 options will become invalid.

For further information about options, see note 8.

Result for the year

The business costs amounted to SEK 56.7 million (13.8) distributed between external research and development costs (R&D-costs) of SEK 17.0 million (3.4), internal R&D-costs of SEK 10.4 million (2.7) – of which, SEK 2.5 million (0) are included in staff costs and SEK 0.8 million (0) are included in the depreciation of material fixed assets – administration and loan costs of SEK 15.6 million (7.6) and capital purchasing costs of SEK 13.7 million (0.1).

The cost increase was due to a strong increase in research activity and to the fact that during the year, the company carried out a number of preclinical studies, two clinical studies and started a third clinical study. The capital purchasing costs correspond to 5.5 per cent of the acquired capital. The company has as yet no income.

Financial position

As a result of the new emission in February of SEK 51 million, an Industrial Fund loan in May of SEK 35 million (of which SEK 20 million has been withdrawn) and a new emission of SEK 202.5 million in July, the financing of the company has been guaranteed for a further two years.

To the Industrial Fund loan are connected detachable options which give the right to take out 175,000 options of SEK 0.20 each (see above).

The company's liquid assets amounted to SEK 222.4 million (2.2) on 31 December. The own capital amounted to SEK 207.1 million (2.5). The company's share capital of SEK 2.75 million (2) was distributed on 13,750,000 shares (2,000,000) at a nominal value of SEK 0.20 (1.00). In addition, subscription options (including the Industrial Fund) have been issued corresponding to 2,175,000 shares of which, 593,280 are owned by the company. During the year, the company has transformed 1,000,000 preference shares into ordinary shares and has carried out a 5:1 split.

The company has no interest-bearing debts other than the Industrial Fund loan.

For more detailed information about the development of the share capital, please see note 8.

Financial risks

The liquid capital of the company amounted to SEK 222.4 million (2.2) on 31 December 2000. Of these, 212.5 (0) were placed in interest funds and return funds through an administration which is handled by Handelsbanken.

During the year 2000, interest from the liquid placements was between 3.25 and 7.2 per cent. The company has received net interest amounting to SEK 4.9 million.

Currency risk

Tripep has a currency exposure in that essential costs are in foreign currency. Examples of such costs are the costs of substances, preclinical and clinical studies and certain research collaborations. These currency exposures are not risk-covered.

Proposal for treatment of losses

The following funds are at the disposal of the shareholders' meeting:

Balanced result	0
This year's result	-51,622,425
Total, SEK	-51,622,425

The Board and the Managing Director propose that the loss shall be covered by a reduction of the premium fund in the sum of SEK 51,622,425.

Dividend

The Board proposes no dividend for the year 2000.

The work of the Board

The Board of Tripep consists of six persons with great competence within the fields of pharmaceutical development, marketing and economic and strategical questions. The rapporteur at Board meetings has been the Managing Director and the company's research manager and development manager. The Board has had eleven meetings during 2000.

The company's Scientific Advisory Board (SAB) has had one ordinary meeting and a large number of in formal contacts during the year. The company has contract collaboration with three of the members of the SAB, in addition to their work within the SAB.

Results sheet

SEK	Note	2000	1999
Net turnover		0	0
Other business income		252,906	0
Total income		252,906	0
Business costs			
Research and development costs		-5,276,669	-2,731,451
External research and development costs		-15,366,678	-3,373,654
Other external costs	2	-9,768,264	-3,572,015
Staff costs	3	-11,745,376	-1,440,342
Depreciation of tangible plant assets	7	-878,820	-19,391
Depreciation of intangible plant assets		0	-2,658,157
Items affecting comparability	4	-13,679,881	-66,845
Other business costs		-12,638	0
Total business costs		-56,728,326	-13,861,855
BUSINESS RESULT		-56,475,420	-13,861,855
Result of financial investments			
Depreciation of short-term placements		-6,301,654	0
Interest income and similar items	5	11,666,894	122,525
Interest costs		-512,245	-26,460
Total result of financial investments		4,852,995	96,065
RESULT AFTER FINANCIAL ITEMS		-51,622,425	-13,765,790
Tax on the year's result		0	0
THE YEAR'S RESULT		**-51,622,425**	**-13,765,790**

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Balance sheet

SEK	Note	00-01-01--00-12-31	99-01-01--99-12-31
ASSETS			
FIXED ASSETS			
Intangible fixed assets			
Patents	6	3,892,747	1,604,242
Advance patents		270,454	369,195
Total intangible fixed assets		4,163,201	1,973,437
Tangible fixed assets			
Equipment	7	2,080,067	28,465
TOTAL FIXED ASSETS		6,243,268	2,001,902
CURRENT ASSETS			
Short-term claims			
Other short-term claims		1,440,194	907,116
Prepaid costs and accrued income		2,716,481	93,946
Total short-term claims		4,156,675	1,001,062
Short-term placements		212,486,970	0
Cash and bank		9,935,772	2,189,095
TOTAL CURRENT ASSETS		226,579,417	3,190,157
TOTAL ASSETS		**232,822,685**	**5,192,059**

SEK	Note	00-01-01--00-12-31	99-01-01--99-12-31
EQUITY AND LIABILITIES			
EQUITY	8		
Restricted equity			
Share capital (13,750,000 shares of SEK 0.20 each)		2,750,000	2,000,000
Premium fund		255,998,075	14,309,265
Total restricted equity		258,748,075	16,309,265
Free equity			
Balanced result		0	0
The year's result		-51,622,425	-13,765,790
Total free equity		-51,622,425	-13,765,790
TOTAL EQUITY		207,125,650	2,543,475
LIABILITIES			
Long-term liabilities	9		
Conditional loan		20,035,000	2,000,000
Total long-term liabilities		20,035,000	2,000,000
Short-term liabilities			
Supplier liabilities		1,283,003	126,805
Other liabilities		834,665	2,700
Accrued costs and prepaid income	10	3,544,367	519,079
Total short-term liabilities		5,662,035	648,584
TOTAL EQUITY AND LIABILITIES		**232,822,685**	**5,192,059**
MEMORANDUM ITEMS			
Pledged securities		None	None
Contingent liabilities		None	None
Bank guarantee, rental agreement		200,000	None

Cash flow analysis

SEK	2000	1999
CASH FLOW FROM THE CURRENT ACTIVITY		
Result after finance net	-51,622,425	-13,765,790
Depreciation	878,820	2,677,549
Capital gain	12,638	29,418
Cash flow from the current activity before changes in working capital	-50,730,967	-11,058,823
Cash flow from changes in working capital		
Increase in claims	-3,155,613	-452,066
Increase in short-term liabilities	5,013,451	147,314
Cash flow from the current activity	-48,873,129	-11,363,575
THE INVESTMENT ACTIVITY		
Acquisition of fixed tangible assets	-2,943,060	-8,700
Acquisition of fixed intangible assets	-2,189,764	-1,193,504
Cash flow from the investment activity	-5,132,824	-1,202,204
CASH FLOW FROM THE FINANCING ACTIVITY		
New emissions	253,500,000	7,056,000
Options	2,704,600	338,000
Loans raised	20,035,000	2,000,000
Amortization of liability	-2,000,000	-200
Cash flow from the financing activity	274,239,600	9,393,800
THE YEAR'S CASH FLOW	**+220,233,647**	**-3,171,979**
Liquid assets at the beginning of the year	2,189,095	5,361,074
Liquid assets at the end of the year	222,422,742	2,189,095

Notes

Note 1 Accounting and evaluation principles

The regulations in the Accounting Act relating to the layout of result and balance sheets and evaluation have been followed. The accounting and evaluation principles are unchanged in comparison with the previous year. The company's accounting and evaluation principles are in accordance with the recommendations of the Swedish Financial Accounting Standards Council.

CLAIMS
Claims are recorded in the sum which is estimated to be paid considered individually.

FIXED ASSETS
Equipment is depreciated according to the 30%-rule. Intangible fixed assets with respect to patents shall be written off over the estimated economical lifespan. Depreciation will be started when the product is fully developed. Since 1999, costs for research and development are charged directly.

CLAIMS AND LIABILITIES IN FOREIGN CURRENCY
Claims and liabilities in foreign currency are evaluated at the exchange rate on the balance day. Profits and losses on claims and liabilities of a business nature are reported net among other business incomes or other business costs.

Note 2 Auditing fee

	2000	1999
To the company's auditor and auditing company, payment has been paid:		
– For auditing and other examination according to the Swedish Companies Act etcetera and for consultation and other assistance resulting from observations made during the audit	45,000	20,000
– For separate consultation, assistance etcetera given by Ernst & Young AB and related companies	110,000	46,982
	155,000	66,982

Note 3 Staff

	2000	1999
Average number of employees	12	3
– thereof men	71%	91%
SALARIES AND OTHER COMPENSATIONS		
Board	227,290	241,000
Managing Director[1]	2,137,331	0
Other employees	5,559,173	983,578
Total salaries and other compensations	7,923,794	1 224,578
Social costs	3,346,149	417,615
– thereof pension costs	528,837	12,000

[1] An agreement about severance pay exists, which means that 18 months' salary will be paid in the case of notice on the company's part.

Note 4 Items affecting comparability

	2000	1999
Costs in connection with emission	3,486 304	66,845
Costs in connection with Stock Exchange introduction	10,193 577	0
Total items affecting comparability	13,679 881	66,845

Note 5 Interest income and similar result items

	2000	1999
Interest income and similar result items	3,020,473	122,525
Currency exchange profit	2,104	0
Dividends	8,644,317	0
Total interest incomes and similar results items	11,666,894	122,525

Note 6 Patents

	00-01-01--00-12-31	99-01-01--99-12-31
Ingoing purchase value	1,604,242	410,738
The year's activated expenses	2,228,505	1,193,504
Outgoing purchase value	3,892,747	1,604,242

Note 7 Equipment

	00-01-01--00-12-31	99-01-01--99-12-31
PURCHASE VALUE		
Ingoing purchase value	64,637	55,937
The year's purchases	2,943,060	8,700
Sales/disposals	-30,822	0
Outgoing purchase value	2 976,875	64,637
ACCUMULATED DEPRECIATION		
Ingoing accumulated depreciation	-36,172	-16,781
Sales/disposals	18,184	0
The year's depreciation	-878,820	-19,391
Outgoing accumulated depreciation	-896,808	-36,172
Outgoing book value	2,080,067	28,465

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Operational leasing	Premises
The company has entered into a rental agreement of operational nature as follows:	
Fees which expire	
year 2001	588,000
year 2002–2005	588,000
year 2006 or later	0
During the year, SEK 594,247 has been paid in rent.	

Note 8 Changes in capital

	Share capital	Premium fund	Balanced result	The year's result	Total
Total at the beginning of the year	2,000,000	14,309,265	0	-13,765,790	2,543,475
Allocation of the previous year's result		-13,765,790	0	13,765,790	0
New emission, directed	300,000	50,700,000			51,000,000
New emission, Stock Exchange introduction	450,000	202,050,000			202,500,000
Subscribed options series A		100,800			100,800
Subscribed options series B		424,600			424,600
Subscribed options series C		2,179,200			2,179,200
The year's result				-51,622,425	-51,622,425
Total at the end of the year	2,750,000	255,998,075	0	-51,622,425	207,125,650

A directed new emission has been carried out during the year. Thereafter, the nominal value of the shares has changed through a 5:1 split from SEK 1 to 20 öre each. The share capital has thereby increased to SEK 2,300,000 and the number of shares has increased to 11,500,000. A new emission has thereafter been carried out, as a result of which the share capital has increased to SEK 2,750,000 and the number of shares to 13,750,000. 561,720 options have been sold during the year, and this has added SEK 2,704,600 to the premium fund.

Subscription options	Number	Thereof owned by the company	Subscription rate, SEK	Duration
A	900,000	53,880	20	2004-08-14
B	550,000	526,000	160	2006-08-14
C	550,000	13,400	60	2006-08-14
The industrial fund	175,000	0	0.20	2003-12-30
Sum	2,175,000	593,280		

If all subscription options are purchased in full, SEK 139,035,000 is added to the company capital, whereof SEK 435,000 is added to the share capital. The total number of shares should thereafter amount to 15,925,000. If all subscription options are taken up, this thus corresponds to an owner proportion of 13.7 per cent.

Note 9 Long-term liabilities

	Liability	Payment due		
	00-12-31	within 1 year	between 1 and 5 years	later than 5 years
Loan with subscription options	35,000	0	35,000	0
Conditional loan	20,000,000	0	20,000,000	0
Total	20,035,000	0	20,035,000	0

Note 10 Accrued costs and prepaid income

	00-01-01--00-12-31	99-01-01--99-12-31
Holiday salary liability	285,719	36,800
Social security costs	994,873	62,918
Accrued salaries	900,000	118,118
Special salary tax	122,069	0
Other items	1,241,706	301,243
Total accrued costs and prepaid income	3,554,367	519,079

Audit report

TO THE GENERAL MEETING OF THE SHAREHOLDERS OF TRIPEP AB
CORPORATE IDENTITY NUMBER 556541-1898

We have audited the annual accounts, the accounting records and the administration of the Board of Directors and the Managing Director of Tripep AB for the year 2000. These accounts and the administration of the company are the responsibility of the Board of Directors and the Managing Director. Our responsibility is to express an opinion on the annual 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 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 Managing Director, as well as evaluating the overall presentation of information in the annual 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 Managing Director. We also examined whether any Board member or the Managing Director 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 the opinion set out below.

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

We recommend to the general meeting of the shareholders that the income statement and the balance sheet be adopted, that the loss be dealt with in accordance with the proposal in the administration report and that the members of the Board of Directors and the Managing Director be discharged from liability for the financial year.

Huddinge February 2001
ERNST & YOUNG AB

Anders Wiger
AUTHORIZED PUBLIC ACCOUNTANT

Shares and owners

Tripep's shares were quoted on the OM Stockholm Exchange O-list on 14 July 2000. The introduction rate was SEK 90.
The number of shares in Tripep amounts to 13,750,000. The share capital amounts to SEK 2,750,000. Each share signifies an equal right to a share in Tripep's assets and profits and entitles the owner to one vote.

Since the Stock Exchange introduction in July 2000, Tripep's share value has decreased from SEK 90 to SEK 80 on 29 December 2000 – a decrease of 11 per cent. Affärsvärlden's general index decreased during the same period by about 23 per cent while Affärsvärlden's pharmaceutical index increased by about 17 per cent. At the end of 2000, Tripep's Stock Exchange value amounted to SEK 1.1 billion.

The highest price of SEK 145 paid for Tripep shares during year 2000 was reached on 6 and 11 September. The lowest price paid was SEK 55 on 21 December. The number of Tripep shares sold on the OM Stockholm Exchange during 2000 amounted to 2.4 million. The average number of shares sold per day was about 20,000.

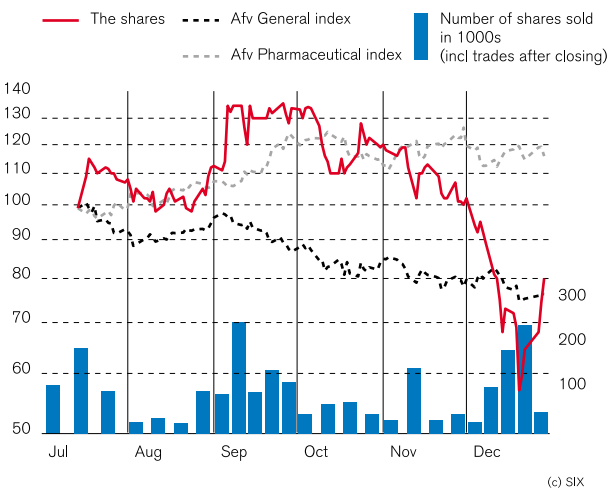
Shareholders

The number of shareholders in Tripep on 29 December 2000 was 2,208, of which 84 were foreign owners. The ten largest shareholders were associated with 78.9 per cent of the votes and capital at the end of 2000.

Dividend policy

No dividend will be paid to the shareholders until the company can predict a long-term profitability thanks to the launching of products on the market. During the next few years, it is improbable that any dividend will be paid.

The shares.



The eleven largest shareholders.

Shareholders	Number of shares	Share of capital and votes, %
HealthCap KB	3,093,225	22.5
Anders Vahlne	1,400,000	10.2
Johan Malmsten and via companies	1,361,800	9.9
Servisen Private Equity Fund Ltd	1,029,590	7.5
Foreign owners and administrators	842,685	6.1
Banco funds	773,900	5.6
Peter Horal	700,000	5.1
Hans Möller	700,000	5.1
Bo Svennerholm	700,000	5.1
Anders and Christina Sönnerborg	250,000	1.8
Matti Sällberg	250,000	1.8
Total number of shares the eleven largest shareholders	11,101,200	80.7
TOTAL NUMBER OF SHARES	13,750,000	

Data per share.

	2000	1999
Earnings, SEK	-3.75	-6.88
Dividend, SEK	-	-
Equity, SEK	15.06	1.3
Outstanding shares, millions	13.75	2,0

Board and management

Harry Faulkner

Born 1931. Chairman of the Board. Board member since 2000. Chairman of the Boards of Arcona AB, B&N Nordsjöfrakt AB and SEB Fondförvaltning AB. Board member of EQT Denmark B V, Ratos AB, Scandinavian Equity Partners, Stockholms Auktionsverk AB and Tetra Laval AG (Switzerland). Harry Faulkner has previously been Managing Director, Chief Executive and Board member of Alfa Laval and has been a Board member of Astra AB and Genentech Inc.

SHAREHOLDING IN TRIPEP: 30,000.
OPTION HOLDING: 80,000 of series C.
DIRECTOR'S FEE: SEK 100,000.

Lars Lindegren

Born 1937. Board member since 2000. Chairman of the Board of Metcon Medicin AB and Board member of Karlshamns AB, Supratek Pharma Inc and PhotoCure ASA.

SHAREHOLDING IN TRIPEP: 30,000.
OPTION HOLDING: 40,000 av series C.
DIRECTOR'S FEE: SEK 65,000.

Johan Malmsten, M D, Ph D

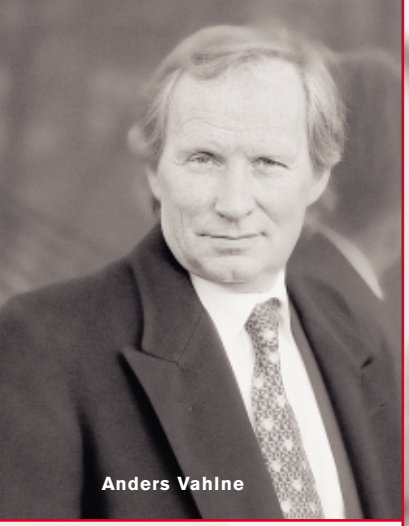
Born 1948. Board member since 1997. Owner and Managing Director of Malmsten Invest AB. Chairman of the Richard C Malmsten memorial fund and Board member of Stille AB, Safelogic AB and Supratek Pharma Inc.

SHAREHOLDING IN TRIPEP: 680,900 and 680,900 via companies.
OPTION HOLDING: 40,000.
DIRECTOR'S FEE: SEK 25,000.

Magnus Persson, M D, Ph D

Born 1960. Board member since 1997. Board member and part owner of HealthCap AB, Chairman of the Board of Bio Stratum AB, Board member of CDC AB, Clinitrac AB, Prolifix Ltd, Arpida AG, Lica Pharmaceuticals A/S and Wilnor AB.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 0.
DIRECTOR'S FEE: SEK 25,000.



Anders Vahlne

Jack Spira

Hans Möller

Anders Vahlne, M D, Ph D
Born 1946. Employed since 1997. Professor of clinical virology at the Karolinska Institute. Deputy Managing Director of Tripep with responsibility for research. Board member since 1997. Board member of Resistentia Pharmaceuticals AB, member of scientific advisory Board of Supratek Pharma Inc and Accuro Immunology AB.

SHAREHOLDING IN TRIPEP: 1,400,000.
OPTION HOLDING: 210,000 of series A.

Jack Spira, M D, Ph D
Born 1953. Deputy Managing Director with responsibility for development. Employed since 1999. Previously worked in pharmaceutical development at Kabi, Kabi-Pharmacia, Pharmacia during ten years and was thereafter Nordic medical Director for Ares Serono. Has also been European medical Director with responsibility for haematology and oncology at Genetics Institute, a division within American Home Products.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 85,000 of series A and 65,000 of series C.

Hans Möller
Born 1955. Employed since 1999. Managing Director of Tripep since 1998. Board member since 1997. Has previously worked with financial issues within the pharmaceuticals industry, that is through the formation of the risk capital company Linc of which he was Managing Director for several years. Has also been Managing Director for the SBI-quoted company Nordic Trucker Line AB (later Ecta Resurs AB). Chairman of the Board of Resistentia Pharmaceuticals AB and Board member of Sir/Tiger AB.

SHAREHOLDING IN TRIPEP: 700,000.
OPTION HOLDING: 210,000 of series A and via company. 250,000 of series C.

Scientific Advisory Board

Prof Jan Balzarini, M D, Ph D
Born 1953. World-leading researcher within the anti-viral field (HIV). Professor in the medical faculty, Rega Institute for Medical Research, Leuven, Belgium. Internationally recognised developer of antiviral agents.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 20,000 of series C.

Prof William W Hall, M D, Ph D
Born 1949. Professor of medical microbiology at Dublin University College. Dr Hall is a world-leading expert on retroviruses. Member of the editorial staffs of the Journal of Neurovirology, AIDS Research and Human Retroviruses, AIDS Journal and Neuropathology. President Elect of the International Retrovirology Association.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 20,000 of series A and 20,000 of series C.

Prof Hilary Koprowski, M D, Ph D
Dr Koprowski is a world authority within the field of virus research. He has previously participated in the development of polio vaccine and rabies vaccine and was also active in the founding of Centocor Inc.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 20,000 of series A and 20,000 of series C.

Prof Ragnar Norrby, M D, Ph D
Born 1943. Director-general of the Swedish Institute for Infectious Disease Control since 15 January 2001. Professor of infectious diseases at Lund University. Professor Norrby is an internationally leading infections physician and antibiotics researcher.

SHAREHOLDING IN TRIPEP: 0.
OPTION HOLDING: 20,000 of series C.

Prof Anders Sönnerborg, M D, Ph D
Born 1955. Adjunct professor at the Karolinska Institute. Senior Vice-President of Regulatory Affairs, Chairman of the Swedish Physicians against AIDS Research Fund, member of the international committee Noah's Ark-Red Cross Foundation, chairman of the Swedish reference group for antiviral therapy, member of the European panel for evaluation of tests for HIV-resistance and of the committee for Standardization and quality assurance.

SHAREHOLDING IN TRIPEP: 250,000 (together with Christina Sönnerborg).
OPTION HOLDING: 40,000 of series A.

Definitions

Return on capital employed
Result before tax plus financial costs in relation to average capital employed. Capital employed refers to the balance sheet total with deduction for non-interest-bearing liabilities.

Return on equity
The year's result in relation to the average equity.

Solidity
Equity at the end of the year in relation to the balance sheet total at the end of the year.

Net degree of liability reduction
Interest-bearing liabilities at the expiration of the year minus liquid funds in relation to own capital.

Proportion of risk-bearing capital
Sum of own capital and latent tax in relation to the balance sheet total.

Cash flow
The year's cash flow from the currrent activity and the investment activity.

Equity per share
Equity divided by the number of shares at the end of the year.

Earnings per share
The year's result divided by the number of shares at the end of the year. Splits and emissions have been taken into account.

TRIPEP

Fewer and fewer Swedes seem to practice safe sex, because the number of persons infected by gonorrhoea, syphilis and chlamydia is increasing again. It is extremely alarming that the number of HIV-infected persons is also increasing. HIV, which leads to AIDS, is one of the world's most aggressive and dangerous viruses. There are two ways of stopping the spread of the disease. Both cost money. One way is to produce a vaccine against the virus and to develop better medicines. Tripep, which is a Swedish research company within the biotechnology field which is quoted on the stock exchange, is working on this. The other way is to increase people's knowledge about how the HIV-virus is spread and how they can protect themselves against it. Here, we also wish to make a contribution. With this advertisement, we support the continuing struggle of the National Association for HIV-Infected Persons (RFHP) against the spread and the effects of HIV and AIDS. You can make your contribution to RFHP's postgiro account 90 08 38-4. Thank you.

RFHP

More information about Tripep can be found on www. tripep.se and about RFHP on www.rfhp.a.se.