# PRESS RELEASE

(for OH-pictures from the President & CEO's speech, see www.activebiotech.com)

## ACTIVE BIOTECH SHAREHOLDERS' MEETING 12 APRIL 2000

- **The ETEC project continues with full force**
- **Vaccine sales during the first quarter of the year: turnover increased by 48 % compared to the previous year**
- **The sales of Dukoral and SBL Cholera Vaccine increased by 255%**
- **Preliminary results after financial posting: +20 million SEK.**
- **MGA Holding: a new big shareholder in Active Biotech AB**

### Sven Andréasson's (President & CEO) speech at the shareholders' meeting

### The ETEC project

Two weeks ago we announced new information regarding our vaccine project, ETEC, against tourist diarrhoea. In this information we explained that the first effect study that had been carried out in Mexico and Guatemala had not given the expected result according to the applicable definition of clinical effect. We further announced that, as a consequence of this, we could not hand in a registration application for the product in Europe during this year as earlier planned. This information was given after our preliminary analyses and discussions with our co-operation partner, SmithKline Beecham Biologicals.

The reaction from the market was very strong. A great deal of attention was given to the matter in the media and many shareholders have contacted us. The same day that we announced this information, we also had a telephone conference with a number of pharmaceutical analysts. Most of them considered that the fall in the share price was an 'over reaction'.

Allow me therefore to begin by elucidating and making the situation clear regarding the ETEC project. Before I begin, I ask Karl Olof Borg, Vice President, to provide a short presentation on the methods and regulations involved in clinical trials as well as a short description of the ETEC study in question.

**Karl Olof Borg:**

The clinical study of new pharmaceuticals and vaccines is an activity that is strongly regulated and controlled by different authorities in different countries. This is easy to understand because the results from clinical studies constitute the most important knowledge and documentation available when authorities decide to pass a product for clinical use and marketing.

## Regulations and Routines for Clinical Studies

The ”International Conference of Harmonization” (ICH) draws up proposals for regulations, lays down the general outlines and demands for the documentation of new pharmaceutical products. In this work, people from the registration authorities in Europe, the USA and Japan as well as experts from the pharmaceutical industry and the research society co-operate.

The registration authorities in different countries decide which regulations should apply during the testing phase and the evaluation phase of clinical trials. This is depicted in what is called guidelines for ”Good Clinical Practice”.

In our work, we strictly follow the international demands that apply and prepare internal routines that every co-worker has to follow.

## Basis valuation in Clinical Trials

Studies that form a basis for the registration of a new product should be prospective. This means that one should, in advance, account for the purpose of the study and how it will be conducted in a trial plan. This plan must be approved by the country’s pharmaceuticals authority; in Sweden it is the Swedish Medical Products agency, in the USA, the Food and Drug Administration (FDA). The ethical committee of the hospital where the trial will be conducted must also approve the study. An important part of the trial plan is that there must be a determined statistical plan of how the analysis of the data will occur.

## Design of the ETEC studies: Guatemala-Mexico

The clinical study of the ETEC-vaccine that I will now talk about had the following programme. American students who intended to attend a language course in Guatemala or Mexico were asked whether they would like to take part in a study of a vaccine against so-called tourist diarrhoea. Half of the students were given the drinkable ETEC vaccine, the other half were given a water solution that could not be identified as not being the vaccine in appearance, but which did not contain any active component. The product that was used was, at the time of manufacture, marked with a number. Information about what each given bottle contained, the ETEC vaccine or Placebo, existed on the so-called random list. This list was kept filed in such a way that only an authorised person had access to it after such a time as the entire study had been carried out and all the information had been collected.

This entire procedure using the so-called double blind technique is to ensure that nobody in the treatment chain knows whether an effective or ineffective product is being used in his/her particular case and thus allowing this to influence their response. If any test candidate should suffer a serious side effect or mishap, and be in need of receiving efficient attention, there is a routine available to be able to break the code for that person.

## Blind and Controlled Clinical Testing

This picture shows the final phase of a clinical study. All information from the study is collected in a database in a systematic way and the accuracy of the data is then verified. The amount of data from only one study is extensive. For example, in our ETEC study, 12 400 microbiological tests have been carried out.

When all the information is in the database, it is locked, which means that it is no longer possible to make any changes. The decision to lock the database is taken by the person within the company who is medically responsible for the study. In parallel to the final control of the information in the database, one can make a compilation of the entire study material without knowing whether a particular person has received the ETEC vaccine or Placebo. These combinations are checked only after the database has been locked.

The next phase is that the code existing on the random list can be broken by a previously appointed authorised person who must follow a given routine, for example, in order to obtain access to the safe in the archives. Once the code has been broken, there is, for the first time, the possibility of analysing the outcome of the clinical trial.

The database was locked on the 15th of March. The code for the study was broken on the 16th of March at 17.45 p.m., this having been precisely recorded. The following day, the code from the random list was fed into the computer and thereafter we were able to start work according to our statistical plan of analysis. On the evening of the 16$^{th}$, it was possible to manually retrieve the first results from the study. On the afternoon of the 17$^{th}$, I informed Active Biotech's President & CEO that we were not entirely satisfied with the results that we saw.

## Results from the first study

The primary clinical effect objective for the study was to show a protective effect of the vaccine on all tourist diarrhoeas caused by an infection with the ETEC bacterium, regardless of the degree of difficulty. In this respect we did not attain the aim of the study. Subsequent analyses have however shown that we have, with the vaccine, most likely reduced the number of the more severe diarrhoeas, those that substantially affect the everyday lives of those travellers that took part in the study.

Further analyses of this study will give us very valuable information, which we will be able to use of in the new study that has been initiated. Eventual changes in the new study that we want to conduct will be submitted to the registration authority in the USA, the FDA, for approval.

**ETEC: Active Biotech pioneer**

Active Biotech is a pioneer in the area that we, in simplified terms, call tourist diarrhoea. All of those who have been out and travelled in the world surely know from their own experiences what we are talking about. A holiday trip or a business negotiation can be dramatically affected if one has contracted it.

The market potential is significant for a vaccine that protects against, or alleviates severe diarrhoea. In this area, Active Biotech, or historically SBL, lies in the absolute front line regarding the development of vaccines as well as their clinical evaluation. This competence has been built up over many years, partly through the collaboration with research groups in, amongst others, Gothenburg and Baltimore, and partly through the huge cholera project that was carried out in Bangladesh during the 80's when SBL was still Statens Bakteriologiska Laboratorium (the State Bacteriological Laboratory).

What one must bear in mind is that diarrhoea caused by ETEC is a "third world infection". Trials of the vaccine's effectiveness can be made, in part, on an "industrialised country's population" or travellers, and in part, on a "developing country's population". Due to various reasons, it is usually easier to determine the effect in a "developing country's population" where the infection is considerably more common and strikes harder. The trials that are being conducted in Mexico and Guatemala today are formulated, to the greatest possible extent, to mimic an ordinary "tourist situation", i.e. vaccination occurs before a trip to a risk area and the traveller stays away for approx. 2 weeks. Not only are a large number of people required in these studies, the design of study protocol must be also be such that analyses of different types of, and degrees of diarrhoea are possible.

After having analysed the preliminary data from the first study in Mexico and Guatemala, we were forced to verify that the clinical objective had not been attained, and that the study could not be used as part of the registration application for the ETEC vaccine. The great surprise which everyone, including our external research partners, expressed, has now been exchanged for intensive work partly on analysing the reference samples of the vaccine that were given in the trial in order to establish whether the vaccine fulfilled the required technical specification and partly on analysing the material in the so-called "sub groups" in order to establish what degree of effect we can show in the different patient groups. This work is being conducted in co-operation with SmithKline Beecham and is expected to take approx. 6-8 weeks.

It is clear that the clinical aim was too widely defined in this study which means that we have not yet been able to prove the ETEC vaccine's effect in the way that is required by a registration authority.

**Fewer cases**

We observed substantially fewer cases of severe diarrhoea among those who were vaccinated compared to those who were given placebos and interpret this as the vaccine having a protective effect against the more severe forms of diarrhoea. We even see a clear tendency where diarrhoeas that would have become severe have been alleviated; i.e. the vaccine also has a relieving effect. We will use this information for the further development of the vaccine.

It should also be mentioned that we do not have any side-effect problems, which is also very positive.

**How great will the delay be**?

It is too early to say. We will have a number of meetings with those responsible for the trial, our research contacts and co-operation partners in order to list what else needs to be done in order to guarantee that the ETEC vaccine comes onto the market with the least possible delay. It is also possible that we will increase our trial program with further studies in ”a developing country’s” population in order to add additional substance to the clinical documentation.

**Broad experience**

Once we are able to produce the product – can we still conquer the market?

We have obtained broad experience in the marketing of travel vaccines through our work with Dukoral in Sweden. Dukoral, as is well known, is a drinkable travel vaccine against, among other things tourist diarrhoea, which we sell in Sweden and in Norway. Outside of these countries, the product is sold with great success as a pure cholera vaccine under the name SBL Cholera Vaccine. Our sales figures, which I will get back to, show a strong increase and we have only reached approx. 15% of its estimated potential. We are preparing and planning a strategy for an application for Dukoral to be sold without prescription in order to be able to communicate directly to an increased degree with the consumer.

As we have earlier informed, work is also in progress with the documentation of the SBL Cholera Vaccine in order to be able to apply for registration in the US, and on the basis of this documentation, a central application for the EU can also be submitted.

**Is there a market outside industrialised countries?**

The ETEC vaccine could also fill a very important medical need in the third world. According to studies, approx. 800 000 – 1 million children die every year because of ETEC infections. This is, as seen from a global perspective, the real target group. Money is, to an increasing extent, being placed at the disposal of vaccination programmes for the third world, for example through the so-called DOMI programme with the Bill Gates Foundation as sponsor. We perceive this market as being very important for the continued development of ETEC, even if it, in purely commercial terms, represents a lesser value than the industrialised market.

## Clinical Programme

**What is to be expected in further clinical results where our newfound knowledge can be of use?**

We have the following clinical programmes in progress:
The effect study in Guatemala and in Mexico, the one that we recently finalised.

The other study that commenced in November 99 – here we can now draw knowledge from the first study. This is scheduled for completion this autumn, whether we will increase the number of travellers is too early to say, but it is something that must be taken into consideration. This study is being run under the management of SmithKline Beecham. Furthermore, there is also an effect study in Kenya (the so-called Swegyvac) on 770 travellers. The results will be available during this year.

We also have effect studies in co-operation with the US Army and the Israeli army directed partly towards 1600 soldiers in Israel, partly towards 400 children in Egypt. Furthermore, we have also had several new requests from Swedish and foreign research groups to start new studies.

Concerning ETEC, I would finally like to say that we have carried its development forward substantially and we have also learned a great deal. Naturally, we now wish that we had had all this knowledge several years ago when the first study was proposed.

This is the price for being the first in an area, leading the development and setting new standards. We will carefully plan any further clinical development in order to secure that the vaccine reaches the market with the least possible delay and with the maintenance of the greatest possible sales potential.

I am personally convinced that we have an effective product with considerable potential. If this is correct, I also believe that we will be able to demonstrate this in a way that the registration authorities can accept.

Moreover, other competing companies as well as ourselves have assessed that the market for such a vaccine amounts to approx. USD 400 million – it is this market that we are aiming for.

## Co-workers

For natural reasons I have dedicated a great deal of time to ETEC today..……

Active Biotech is however not a one-product company but a company with a balanced portfolio both when it comes to breadth and when it comes to development stages. During 1999, extensive work has been done to create an efficient organisation as well as a focused project portfolio. Furthermore, we have worked intensively, supported by external consultant assistance, with our strategy and business planning throughout the spring.

Allow me to give you a short survey of what Active Biotech is today:

## Organisation

I will begin with our co-workers. Since December last year, we have had a new organisation and executive group for the company. The different legal units, so far, still remain on paper but the purpose is to reduce and simplify even this in the long run. We have chosen the simplest possible organisation form with functional responsibility, completed with a project organisation that runs horizontally through the company.

Allow me to give a short introduction to the Executive group:

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| Karl-Olof Borg | Karl-Olof is Vice President and has spent 30 years in the industry, the major part being in ASTRA and Pharmacia. He is a member nominee for the new board of directors and will leave his operative post on the 30th June this year. |
| Tomas Leanderson | Tomas has been responsible for Research and Development since 1999. He comes from Lund University where he is Professor of Immunology. |
| Anders Kärnell | Anders who is Head of Medical Affairs is unfortunately not able to take part today as he is in Israel working with ETEC studies there. (We will just have to excuse him!) Anders also started working with us during 1999. He was previously Head of the bacteriological laboratory at Huddinge hospital. |
| Börje Haag | Börje is the newest in the company and took up office in February being responsible for production. He was previously in charge of Pharmacia's bio plant in Strängnäs, Sweden. |
| Håkan Fröderberg | Håkan is responsible for the home market and was previously working within ASTRA in various parts of the marketing organisation. |
| Hans Enander | Hans also started working with us last year and is responsible for our international activities, in the main with our cholera vaccine. He has previously worked for both ASTRA and Pharmacia. |
| Mats Lidgard | Mats is responsible for Law, patents etc. as well as personnel. Mats was previously principal lawyer at Pharmacia and has been with us since the middle of last year. |
| Mats Blom | Mats B has a background as a consultant from Gemini, and is today responsible for Business development and Finance(acting). A new Head of Finance is under recruitment. |

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|---|---|
| Björn Sjöstrand | Björn has an administrative background from the Karolinska Institute and Danderyd's hospital. He is responsible for what we call "operations" which corresponds to among other matters, properties, IT, administration and SBL distribution. |
| Lennart Molvin | Lennart has a great deal of experience within ACTIVE and is responsible for information and "Investor Relations". He previously worked with IKEA. |

It is my belief that this group has a collected pharmaceutical experience, which in time surpasses 150 years. I am happy to have assimilated such a managerial team. However a couple of key positions still remain to be recruited.

## Our co-workers

A brief introduction of our co-workers. Active Biotech is a company funded on intellectual capital with many gifted people. As is evident from this picture, more than half work in Research and Development, the remaining are distributed in Production, Marketing and Service. More than 80% of all our co-workers have a higher education and the proportion of PhD's and PhD candidates is 20%.

Half of our co-workers are below 40 years of age with the age group 20-29 amounting to slightly more than 15% of the workforce. The proportion of women is slightly greater than 60%.

Our ability to attract and retain skilled co-workers is decisive to the success of the company.

To increase our attractiveness as a company and to secure that we are placed at the right market level in our wage structure, we now have a need for a new programme for subscription options for the personnel.

The proposed programme is being handled under a particular point later on the agenda.

## We have clustered

I now move on to Active Biotech's product and project portfolio. I want to show how we, in the management, have made our activities clear in our planning work.

In the work with our business plan we divided our products and projects into three categories, namely

1 Base business **– our base business**

Included here:
The vaccines: Polio, Cholera, and Dukoral for ETEC in the Nordic countries
Our licensed products: Children vaccines from SB for the Nordic countries and
SBL Distribution: Our distribution unit for vaccines in Sweden

*2 Blockbuster candidates –* ***our 3 great potentials***

The ETEC Vaccine
SAIK our product candidate for multiple sclerosis,
TTS our cancer products for non-small cell lung cancer and kidney cancer, which we are taking over from Pharmacia.

*3 Other projects*

These are projects in an early phase within the area of immune modulation. These projects strengthen our skills and position in order to enable already existing late projects and develop new pharmaceuticals. Among the projects, the development of a vaccine against tonsillitis and drugs within autoimmunity and cancer can be mentioned.

**Risk/reward**

In this diagram we want to illustrate these three categories with regard to their calculated project value and relative risk. Our base business, in blue down by the right side of the diagram, indicates a cash flow with a low risk as the main part of the businesses already existing on the market.
The three large red circles indicate possible values and also the probability and risk for our three main projects.

The fact that other projects in green indicate lower values in combination with very high risk is normal for projects that are at such an early stage of the development.

Whilst awaiting our revised plan for the clinic on ETEC, we have not yet adjusted this picture. What I want to make clear is that we have a well-balanced portfolio and that we are not a one-product company despite the fact that we, for natural reasons, have focused a great deal of attention on ETEC which lies closest to the market.

**The project portfolio in balance**

The relative value of our projects, adjusted for risk, are according to our own assessments:

| | |
|---|---|
| ETEC | approx. 30% |
| SAIK | approx. 35% |
| TTS | approx. 20% |
| Other | approx. 15% |

I think that we have succeeded well with obtaining a balance even concerning the value on our projects. The portfolio of products and projects is relatively well balanced even with respect to time. The size of the circles represent the relative size for the sales potential and the projects are here inlaid in the order of the development stage they are presently in.

## Available liquidity

Finally, to our finances. From the company's foundation it has been fundamental to our strategy to be financially strong.

Active Biotech today has more in the bank than two years ago. With a combination of good capital administration and successful property sales, the company's strong position has been fortified. However, this good financial position must not lull us into a false sense of security, a firm cost control and valuation of all our projects must take place continuously.

## Vaccine sales

The sales for the first three months have begun well. In total, the turnover of vaccines increased by 48% compared to the same period last year. The strongest increase is in own manufactured vaccines, mainly Dukoral against ETEC and cholera. Here the increase is 158%.

Our agency activity, first and foremost children vaccines from SmithKline Beecham, has shown an increase of 6%.

The turnover also increased for SBL Distribution; here the growth is 19%.

The Dukoral picture speaks for itself. The green bars represent the sales for the year 1999 and the blue this year's sales so far. The sales of Dukoral and SBL Cholera Vaccine (the same product with different uses as you know) have increased by 255% compared to the same period last year.

The export share has increased from 20% to 54%. This is partly the result of successful work by our sales organisation in the Swedish and Norwegian markets. It is also partly due to a strong increase in the international sales of the SBL Cholera Vaccine after the WHO recommendation last year. As it is known, our vaccine is the only vaccine in the world that is recommended for vaccination against cholera. Furthermore, discussions are currently ongoing with the WHO and Médecins Sans Frontières regarding the establishment of a larger stockpile of one million doses of the vaccine for rapid use in cases of emergency and threatening epidemics.

## Preliminary results for quarter 1

The results for the first three months are still preliminary. The vaccine sales, with a 48% increase, have already been commented on.

In connection with the closure of the contract research programme for Pharmacia, and in order to continue running the TTS programme under our own management, the contract research turnover will drop. Totally, the turnover will increase by 14%.

The estimated operative result is negative. Thanks to very successful capital administration we can however, probably show a positive result of approx. 20 million SEK after financial posting for the first quarter of the year.

The definitive report for the first quarter will be submitted on the 25th of May.

The prognosis for the whole year still remains, the operative result will be improved but we assess that the deficit will come to approx. 150 million SEK. This may be adjusted after the closure of current negotiations concerning, among other things, the sale of the polio vaccine.

Finally I would like to say, against the background of what Bo Håkansson has informed us about, that we, in the management and I personally, are proud to work in the company that you created Bo – from a small project in Lund via the buying of SBL and Lund Research Center, you have created a platform for a new pharmaceutical company in Sweden. Even if the entrepreneur now leaves, your spirit will remain here. We will never have a calm day!! Thank you and good luck with your new projects!

Thank you for your attention – we are now at your disposal for questions.

Sven Andréasson, President & CEO

**New board of directors**

Elected new members were Else-Maj Rosenlöf, Håkan Åström and Karl Olof Borg.

Svend Holst-Nielsen, Mats Pettersson, Sven Andréasson, Anders Williamsson and Hugo Thelin were re-elected. At the statutory board meeting after the meeting, Hugo Thelin and Håkan Åström were elected as the chairman of the board and vice chairman respectively.

Lund 12th April 2000

Active Biotech AB

Sven Andréasson
President & CEO

**Active Biotech AB is a Swedish biotechnology company focused on the research and development of pharmaceuticals and vaccines; our core competence being our knowledge of the human immune system. We have a high quality project portfolio and considerable financial resources. Important products include our Dukoral, SBLCholera vaccine, a vaccine against tourist diarrhoea (ETEC), innovative drugs against MS (SAIK) and cancer (TTS). The turnover of Active Biotech was SEK 267 million in 1999.**

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