

## An Interview with President Shirow Enoki



President Shirow Enoki

What were the major factors contributing to the recovery of Seikagaku's performance after three years of decline?



Enoki: After three years of declines in both sales and profits, due to continuous reductions in the reimbursement price and the market entry of many generic products, I am very happy to report a solid recovery in our performance. The main factors contributing to this resurgence are the regaining of domestic market share of the Company's major products, ARTZ® and ARTZ Dispo®, a hyaluronic acid formulation for osteoarthritis in knee and shoulder joints, and the steady growth of its market.

In 1995, the sales of generic products was begun in Japan, and thereafter there was an erosion in net sales, with the market entry of 23 generics companies. Until the coming of the generics, our market share for ARTZ® and ARTZ Dispo® was 100%. But by 1997, with the

introduction of generics, our share had fallen to 62%.

The decline was also due to a reduction in the reimbursement price in Japan's medical insurance programs. From 1996 to 1998, the reimbursement price of ARTZ® and ARTZ Dispo® was reduced by an average of 13% each year, under the policy of the Ministry of Health and Welfare of Japan, in order to improve the long-term financial balance of the medical insurance system. In the past fiscal year, we were able to regain some percentage of market share, to 68%. This was the result of the vigorous sales activities of our partner, Kaken Pharmaceutical Co., Ltd. and the withdrawal of several generic companies from the market, which were competing only by way of very cheap pricing. However, the remaining generic brands are sold by large pharmaceutical companies which are firmly established in the market. That is one of the reasons why we are stating fairly conservative prospects for our performance in 1999.

Another major factor contributing to the recovery of our performance was that, since 1994, the total market in Japan for ARTZ® and ARTZ Dispo® has grown an average of 8% per year. The expansion of this market is due primarily to the aging of Japanese society and the growing number of senior citizens who have joint problems. Also, the participation of the additional sales force of many generic companies helped to expand this market, and even after their withdrawal, demand still remains strong meaning that the regained market share



ARTZ Dispo<sup>®</sup>  
 This product is a disposable syringe containing Sodium Hyaluronate. It facilitates the injection process and minimizes the risk of infection.



ARTZAL<sup>®</sup> and ARTZ<sup>®</sup>  
 In the European market, these products are sold in several countries by Astra and Sankyo Pharma.



Blood collection from horse - shoe crabs at ACC for endotoxin and beta-glucan detection kits.

turned out to be larger sales volume than what we once lost. Also contributing to our solid performance in 1998 were royalties received through sales contracts with representative companies.



Through your alliance with Smith & Nephew Inc., SUPARTZ<sup>®</sup> will be sold in the United States, but what are your growth strategies for world markets and what are the market share prospects?



Enoki: A look at the sales of hyaluronic acid products by region shows that the market is largest in Japan. We are the largest company in the world producing hyaluronic acid products and have made a worldwide marketing agreement for SUPARTZ<sup>®</sup> (brand name ARTZ<sup>®</sup> in Japan) with Smith & Nephew (S&N), and they are now making preparations to launch SUPARTZ<sup>®</sup>.

Prior to the conclusion of an exclusive contract with Smith & Nephew, we filed an application for the pre-marketing approval of SUPARTZ<sup>®</sup> with the FDA in the United States at the beginning of December last year. The U.S. FDA had already finished the GMP audit of our production facilities in the spring of 1999. Of course the most important market is the United States, so if we can secure the approval of the U.S. FDA, then S&N will start sales and marketing activities for us. We hope that SUPARTZ<sup>®</sup> can soon be launched in the U.S. market (in 2000) as the third product in that market.

The next step will be the efforts to be included

in the various reimbursement plans in the major insurance programs, after which the real growth of sales will start. So we have set our prospects for the next financial year at around 500 million, which is not much different from the current level. Although we are firmly committed to penetrating the U.S. and major European markets, along with those of Canada, Australia and South Africa in a few years, we are not expecting major growth next year or the year after. As S&N is a leading global company in the orthopedic field, with a worldwide sales network, we hope to promote overseas operations effectively with this strong partner over the long term.



After your acquisition of ACC, what are the prospects for endotoxin reagents, what about market volume and strategy and what kind of technical cooperation and R&D activities do you plan to carry out?



Enoki: ACC, The Associates of Cape Cod, is located in Falmouth, Massachusetts, on the so-called elbow of Cape Cod. The late Dr. Stanley W. Watson, a researcher at the Woods Hole Oceanographic Institution, established this company based on the research he had carried out on the American horseshoe crab (genus Limulus), which has been around for more than two hundred million years. It does not have an advanced immunity system like human beings or other mammals, but its blood system reacts to



Research at ACC focuses on novel approaches to endotoxin and beta-glucan detection.



EMDOGAIN®  
EMDOGAIN® promotes peri-  
odontal tissue regeneration.



OPEGAN® 0.6, OPEGAN® 1.1  
OPEGAN® is supplied in different dosages to meet requirements of ophthalmologic practitioners.

endotoxins of gram-negative bacteria quite sensitively. So using that capability, ACC succeeded in creating very sensitive reagents for endotoxins, which are now used widely in the manufacturing process of the pharmaceutical industry and are expected to undergo strong worldwide growth. On the other side of the Pacific, Seikagaku Corporation has been carrying out the same business, based on the Pacific horseshoe crab (genus *Tachypleus*), over the past 20 years.

We have been proceeding with the transfer of reagent production to ACC and the integration of research activities with Falmouth, and the first products will be introduced to the market during this term. ACC was a good acquisition which will allow us to integrate the technology and manufacturing know-how independently developed, and these cooperative efforts are expected to contribute significantly to Company earnings and efficiency.



What kind of contribution to sales has  
EMDOGAIN® made?



Enoki: EMDOGAIN® is the trade name of a medical device developed by BIORA AB of Sweden for their enamel matrix protein. If properly applied on the tooth surface during flap surgery, EMDOGAIN® can result in the substantial regeneration of lost periodontal attachment. Formerly, caries were the major reason for the loss of teeth in Japan, but now periodontitis is the predominant cause for loss of teeth in aged people. However, until the arrival of

EMDOGAIN®, there were practically no effective ways to regenerate lost periodontal attachment.

BIORA first launched EMDOGAIN® in Europe under CE-Marking in 1995. We started our cooperation with BIORA in 1997, before approval of EMDOGAIN® by the U.S. FDA, and obtained approval in Japan from the Ministry of Health and Welfare on January 23, 1998. Since then, this innovative and effective approach to periodontitis has attracted wide attention both from academic institutions as well as from periodontal practitioners, and EMDOGAIN® has already been adopted at 20 out of a total of 29 dental university-affiliated hospitals in Japan. There is also a campaign that has been proposed by the Ministry of Health and Welfare and dental organizations called 80—20. It is a movement to have people keep at least 20 teeth at the age of 80 to maintain the quality of life. At that age, less than 20% of the Japanese population has 20 teeth. We believe that EMDOGAIN® can very nicely fit into this campaign and contribute to a more pleasant life for senior citizens in Japan.

At this moment, there are practically no competitors for this innovative application, and we hope to establish a fairly solid business within two to three years. So far, more than 100,000 units of EMDOGAIN® have been sold worldwide, and we will soon reach a rate of use similar to that of the U.S.



## What is your mid-term perspective with respect to growth and strategies?



Enoki: We succeeded in recovering market share for ARTZ® and ARTZ Dispo® to a certain level, 68% of total market share, but 20% of the total 32% share now held by the generics represents major pharmaceutical companies with a very strong market presence. So we believe that it will be difficult to continue the pace of recovery we achieved in 1998. We will have a steady performance in 1999, with smaller growth and improvement in sales and operating profits. However, we have to admit that there exists a substantial uncertainty beyond the year 2000, as we cannot foresee the direction of the reorganization of the medical insurance systems of Japan.

While there will be a recovery for 1998 and 1999, the Japanese market for hyaluronic products has become fairly mature, so the major growth prospects for the Company are overseas. That is the reason why we have been trying to develop overseas markets for a number of years.

Overall, our domestic short-term strategies include ongoing expansion of the sales of EMDOGAIN®. We are also promoting an additional application for OPEGAN®, which we obtained approval in January 1999. We have also developed new versions, OPEGAN®0.6 and OPEGAN®1.1, and sales began in July 1999.

Our overseas short-term strategies are focused on the expansion of the sales of ARTZ® in overseas markets and an increase in the sales of reagents overseas in cooperation with ACC.

In the area of R&D activities, our lecithinized SOD product, used for the treatment for ulcerous inflammations of the colon (colitis ulcerosa), is undergoing clinical testing.

Other R&D activities include cooperation with IDEC Pharmaceuticals, Inc. of San Diego, U.S.A. to develop anti-CD-23 antibodies for the treatment of allergic diseases such as hay fever. We announced a tie-up this year with Taisho Pharmaceuticals Co., Ltd. to combine forces for the R&D, sales and distribution of this product in Asia and Europe. Taisho has a good sales organization and marketing strength, along with strong R&D capabilities, so we look forward to vigorous activities in the joint development and marketing of this product with Taisho.

We have been maintaining a stable expenditure on R&D, in spite of variations in total sales, focused upon the R&D of glycoconjugates. Seikagaku was established as a company aiming at the development of drugs based on glycoscience a long time ago, and it was the intention of our founder to stick to our field of expertise to thrive, grow and prosper as a specialty company in the field that we know best glycoconjugates.

