

## **EARNINGS REPORT JANUARY – DECEMBER 2000**

- A clinical development candidate has been selected in the BMS collaboration and the collaboration was prolonged for one year to develop a second-generation compound.
- Extension of the Merck collaboration for two more years in October 2000.
- Initiated a strategic collaboration with Abbott Laboratories on type 2 diabetes in January 2000.
- Novalon Pharmaceuticals was acquired in May 2000 to become Karo Bio USA.
- New collaborations related to the Karo Bio USA's BioKey® Technology signed with Aventis Pharma, GPC Biotech AG, NovImmune S.A., and Boehringer Ingelheim Pharmaceuticals, Inc.
- Phase II clinical trials in the skin projects started.
- Group net sales increased to SEK 109.2 million (73.0), while loss after financial items increased to SEK -205.1 million (-35.1) due to goodwill depreciation following the acquisition of Karo Bio USA and due to progress and increased investments in the research programs.
- Group cash flow from operations amounts to SEK -48.0 million (-21.3) and the new share issue completed in May 2000 generated SEK 196.9 million in cash flow. As a consequence, cash and cash equivalents and short-term investments amounted to SEK 329.0 million (187.8) at year-end.

## **COLLABORATIVE PROJECTS**

### ***Abbott Laboratories – Type 2 Diabetes***

This collaboration started in January 2000. The aim of Karo Bio's collaboration with Abbott Laboratories is the discovery and development of therapeutic compounds based on a novel concept for the treatment of type 2 diabetes. In individuals with type 2 diabetes there is more blood sugar, glucose, produced than the body needs and the normal mechanisms for clearing the excess glucose do not work properly. The concept developed at Karo Bio to treat type 2 diabetes is to safely decrease the amount of glucose produced and shift a patient's glucose to a lower, healthier level. Within this collaboration with Abbott Laboratories, we focus upon selectively blocking the activity of the glucocorticoid receptor within the liver, the organ responsible for most glucose production. The organ selectivity of these therapeutic compounds is important since the glucocorticoid receptor has critical functions in other systems such as the immune system.

To date, we have proven that we can discover potent, liver selective glucocorticoid antagonists and demonstrated that some of these antagonists are active in animal models of diabetes. During the year selectivity and potency of several compound classes have been significantly improved. We intend to continue to optimize these compounds and do more extensive pharmacological characterizations within the year 2001 and to select clinical development candidates.

Abbott will pay Karo Bio royalties on future sales of products in addition to a total of 54 million USD in R & D funding and milestone payments for two products reaching the market.

### ***Bristol-Myers Squibb – Metabolic Disorders***

The collaboration with BMS started in the fall of 1997 with a focus on metabolic disorders using the thyroid hormone receptor as a target. The primary therapeutic indication is obesity. During the past two years a clinical development candidate has been selected. This compound demonstrated proof of principle in relevant animal models and the pre-IND testing is ongoing for this compound. Currently, BMS is complementing its previous IND studies with additional studies. During 2000 this successful collaboration was prolonged for an additional year with the aim to discover a second generation of compounds and to explore additional therapeutic indications.

BMS will pay Karo Bio royalties on future sales of products in addition to a total of 40 million USD in R & D funding and milestone payments for two products reaching the market.

### ***Merck & Co – Estrogen Receptor (ER)***

The Merck collaboration started in the autumn of 1997 and is directed toward the development of novel therapies for the treatment of diseases targeting the human estrogen receptors alpha and beta. Karo Bio was previously awarded US and European patents for the new estrogen receptor beta as a drug target and was recently awarded a Japanese patent on that receptor. The discovery of the new estrogen receptor beta has opened up the possibility of treating many female disorders in a new way. Classical diseases such as osteoporosis, postmenopausal symptoms and breast cancer as well as other diseases may be treated with new receptor-selective

compounds. The collaboration has been successful with the design and synthesis of selective compounds that in pre-clinical studies have led to prioritization of clinical indications for further development. Based on the accomplishments so far, during the year the collaboration was extended for an additional two-year period. Merck will carry out the clinical development of the therapeutic products and has global marketing rights. Karo Bio's upfront payment, research funding and milestone payments can amount to USD 80 million if two products for distinct therapies are developed as a result of the collaboration. Thereafter, royalties shall be paid upon sales of the products.

### ***BioKey® Collaborations***

Karo Bio has several genomics based drug discovery collaborations with companies such as Aventis, Serono, Bayer AG, GPC Biotech and Millennium Pharmaceutical Corporation. In these collaborations, Karo Bio uses its proprietary BioKey® probes technology to establish high throughput screens for the discovery of novel chemical compounds. These compounds act through drug targets discovered from our partner's genomics programs. In addition to receiving research support and milestone payments, Karo Bio is eligible to receive royalty payments upon sales of therapeutic products resulting from these collaborations.

## **INTERNAL PROJECTS**

### ***Skin Disorders - Thyroid Hormone Receptor (THR)***

Skin atrophy (thinning of the skin) is a problematic side effect in for example patients treated for psoriasis with steroids and often leads to bruises and impaired wound healing. Karo Bio has in animal studies previously shown that thyroid hormone effectively can block skin atrophy induced by steroids. Karo Bio has developed a product for skin atrophy and Phase II clinical trials are ongoing. In parallel a phase I mechanistic study regarding effects on human skin composition is under way.

### ***Cardiac Arrhythmia -THR***

Karo Bio's lead compound for cardiac arrhythmia, KB130015, has in previous pre-clinical studies shown promising properties as a potential new and safe anti-arrhythmia agent. Karo Bio is now in discussions with several companies for out-licensing of the compound. In addition a number of new potent and selective antagonists for the thyroid hormone receptor alpha has been generated. Since the alpha-receptor appears to play an important role for cardiac rhythm these compounds will now be evaluated for their potential to become new anti-arrhythmia pharmaceuticals.

### ***Glaucoma -THR***

Recently a new study has been completed where a thyroid hormone analog has been given as eye drops to normal rabbits. In this study local irritation, penetration and uptake were monitored. The conclusions are that the compounds caused no irritations, were well taken up and caused no significant lowering of pressure. Karo Bio will now seek a partner for the project.

### ***Exploratory Research Program***

Karo Bio has within the exploratory research program started several new activities during year 2000. This process has been significantly enhanced by access to the Karo Bio USA's BioKey® Technology. Classical nuclear receptors like the androgen receptor (AR), mineralocorticoid receptor (MR) and the glucocorticoid receptor (GR) are included. For AR Karo Bio acquired an exclusive European license in August 2000 and important indications are prostate cancer and male hormone replacement therapy. MR is an important target for treatment of hypertension and heart failure and GR for treatment of inflammation. In these projects screening for compounds has been initiated. Karo Bio has also initiated work on the orphan receptor LXR. Karo Bio has a strong proprietary position regarding this receptor which has become a new and exciting target for atherosclerosis.

### ***Antibacterial Program***

Antiinfective drugs constitute a worldwide market of over 26 billion USD with the majority being anti-bacterials. Resistance to existing drugs is developing at an alarming rate with resistance to vancomycin, the current drug-of-last-resort, by *Enterococcus* species now common. Emerging resistance to vancomycin by *Staphylococcus aureus* is of great concern. Thus, a diverse arsenal of new antibacterial agents is urgently needed to combat the diminishing efficacy of existing antibiotics.

Technologies for screening these targets now limit drug discovery efforts because most screening technologies rely on a biochemical assay. The cornerstone of the antibacterial program is the proprietary BioKey® technology that enables high throughput screening. BioKey® probes act as surrogate ligands and bind at essential sites that inhibit the function of the target protein. More than 10 molecular targets have been screened and several small-molecule lead compounds have been identified.

## **RESULTS AND FINANCING**

### ***Change in Accounting Policy***

Karo Bio has decided to early adopt the revised accounting standard for consolidations, RR 1:00, issued by the Swedish Financial Accounting Standards Council in August 2000. It is Karo Bio's opinion that early adoption of RR 1:00 in the first annual report including the Karo Bio USA acquisition leads to a better view of the financial position and result of Karo Bio. A delayed adoption would result in restatement of financial statements already issued.

The standard sets new guidelines for establishing the value of shares issued as consideration in an acquisition by a public company. RR 1:00 requires that the consideration is valued using the share price at the transaction date. Under the old standard, RR 1:96, the value was based on the average share price ten days before the acquisition was announced. The effect for Karo Bio of the revised accounting standard is the valuation of shares issued in conjunction with the acquisition of Karo Bio USA. For this acquisition, the transaction date is deemed to be the day when the transaction was completed and shares exchanged, May 10, 2000. On that day, the closing share price was SEK 305, compared to the average share price preliminarily used based on the old accounting standard, SEK 415.

This adjustment to the transaction value leads to the following adjustments in the financial statements of the Parent Company and the Group.

SEK million	Original preliminary recording	Adjusted value under RR 1:00
Investment in group companies	971.5	718.0
Increase in share premium reserve	942.2	688.7
Goodwill	963.4	709.9
Goodwill depreciation 2000	214.1	157.8
Goodwill depreciation full year	321.1	236.6

There are no other material effects on the financial statements from adopting RR 1:00. As the acquisition of Karo Bio USA was made during 2000, there are no effects from the change in accounting principle on periods prior to January 1, 2000.

The new accounting standard is effective for financial years beginning on 1 January 2002 or later, but early adoption is encouraged. If early adopted, it is required by RR 1:00 to early adopt three other new accounting standards regarding accounting for intangible assets, provisions and contingencies, and impairments. However, this adoption has no effect on the financial statements as of December 31, 2000.

### ***The Karo Bio Group***

Net sales for the year for the group increased to SEK 109.2 million (73.0), made up primarily of research funding from the group's partners. Group expenses increased according to plan to SEK 324.6 million (115.5), which is primarily due to increased goodwill depreciation by SEK 157.8 million following the acquisition of Karo Bio USA. The acquisition made increased activities in the R&D organization possible, leading to higher expenses for personnel and IT. Pension refund from SPP, included in operating loss, amounted to SEK 3.5 million, of which SEK 1.4 million affected cash flows during 2000.

Operating loss for the group increased to SEK -215.5 million (-42.5). Of the loss increase SEK 173.0 million, SEK 157.8 million is attributable to increased goodwill depreciation. Financial income increased to SEK 10.4 million (7.4).

Group cash flow from operations amounts to SEK -48.0 million (-21.3) primarily due to cash acquisition costs and repayment of loans in Karo Bio USA. Capital investments in equipment amounted to SEK 9.0 million (6.5) excluding the Karo Bio USA acquisition. Capital investments were mainly for X-ray crystallography equipment and software purchased for chemistry operations. As a consequence, cash and cash equivalents and short-term investments amounted to SEK 329.0 million (187.8) at year-end, including SEK 196.9 million from the directed new share issue.

### ***Acquisition of Karo Bio USA***

The acquisition of Karo Bio USA, Inc. was carried out as a non-cash issue. The recorded purchase price, including transaction costs, is SEK 718.0 million, (see further Change in Accounting Policy above). The acquisition brought goodwill of SEK 709.9 million that will be depreciated over a three-year period beginning at May 1, 2000, from which date the company is consolidated. Cash and cash equivalents in Karo Bio USA at the time of acquisition amounted to SEK 38.1 million.

### ***Parent Company***

The parent company is reporting a loss for the year of SEK -22.2 million (-29.8).

### ***Shareholders' Equity***

Shareholder's equity increased by SEK 699.8 million from the acquisition of Karo Bio USA, paid by issuance of 2,206,198 new shares and 88,064 warrants in accordance with the resolution of the annual general meeting April 26, 2000. Warrants were subsequently exercised, leading to 15,731 new shares.

The directed placement performed in May of 600,000 new shares generated an increase of SEK 196.9 million in equity.

Consequently, the company's share capital of SEK 59,995,505 is now divided among 11,999,101 shares at par value of SEK 5. In addition, there are warrants outstanding representing 157,333 shares.

## **ORGANIZATION**

There were 115 employees by the end of the year, compared to 80 in 1999. Of these, 33 are based in the United States and 98 are engaged in research.

In conjunction with the Annual General Meeting of 26 April, 2000, Torben Jørgensen was installed as President of Karo Bio. He succeeded Per-Olof Mårtensson who was appointed Chairman of the Board.

## **ANNUAL GENERAL MEETING AND FINANCIAL REPORTS**

The Board of Directors intends to convene the Annual General Meeting on Thursday 26 April 2001 at 4 p.m. In accordance with the Board's Policy for Dividend, the Board will propose that no dividend is paid for the financial year 2000.

Karo Bio intends to distribute financial reports as follows:

- Annual Report, 2 April.
- Quarterly Reports, 26 April, 12 July, 17 October.
- Earnings Report, 8 February 2002.

## CONDENSED CONSOLIDATED INCOME STATEMENT (KSEK)

	<u>2000</u>	<u>1999</u>
Net sales	109 158	72 979
<b><i>Operating expenses</i></b>		
Marketing expenses	-12 359	-6 614
Administrative expenses	-23 598	-11 721
Research and development expenses	-289 814	-95 694
Pension refund from SPP	3 473	-
Other operating expenses	<u>-2 351</u>	<u>-1 485</u>
	-324 649	-115 514
<b>Operating loss</b>	<b>-215 491</b>	<b>-42 535</b>
Income from financial investments	<u>10 399</u>	<u>7 405</u>
<b>Loss after financial income and expenses</b>	<b>-205 092</b>	<b>-35 130</b>
Tax	-	-
<b>LOSS FOR THE YEAR</b>	<b>-205 092</b>	<b>-35 130</b>
 <i>Depreciation of goodwill included in R&amp;D expenses</i>	 -162 916	 -5 156
<i>Other depreciation included in operating expenses</i>	<u>-8 689</u>	<u>-7 037</u>
	-171 605	-12 193

## CONDENSED CONSOLIDATED BALANCE SHEET (KSEK)

	<u>31 Dec 2000</u>	<u>31 Dec 1999</u>
<b>Assets</b>		
Intangible assets	578 453	31 558
Equipment	24 667	17 155
Other current assets	13 613	8 966
Short-term investments, cash and cash equivalents	328 967	187 846
<b>TOTAL ASSETS</b>	<b>945 700</b>	<b>245 525</b>
 <b>Shareholders' equity and liabilities</b>		
Shareholders' equity	901 079	209 175
Current liabilities	44 621	36 350
<b>TOTAL SHAREHOLDERS' EQUITY AND LIABILITIES</b>	<b>945 700</b>	<b>245 525</b>

## CONDENSED CONSOLIDATED CASH FLOW STATEMENT

	<u>2000</u>	<u>1999</u>
<i><b>Operating activities</b></i>		
Operating loss before financial items	-215 491	-42 535
Depreciation	171 605	12 193
Other items not affecting liquid assets	<u>38 293</u>	<u>-10</u>
	-5 593	-30 352
Financial income received and expenses paid	12 775	10 812
<b>Cash flow from operating activities before changes in working capital</b>	<b>-7 182</b>	<b>-19 540</b>
Changes in working capital	-28 029	4 204
<b>Cash flow from operating activities</b>	<b>-20 850</b>	<b>-15 336</b>
<i><b>Investing activities</b></i>		
Investment in group companies	-18 230	-
Investment in equipment	-9 009	-6 464
Sale of equipment	50	516
<b>Cash flow from investing activities</b>	<b>-27 189</b>	<b>-5 948</b>
<b>Cash flow from operations</b>	<b>-48 036</b>	<b>-21 284</b>
<i><b>Financing activities</b></i>		
Proceeds from new share issues	196 946	-
Repayment of loans	-7 789	-
<b>Cash flow from financing activities</b>	<b>189 157</b>	<b>-</b>
<b>Cash flow for the year</b>	<b>141 121</b>	<b>-21 284</b>
<b>Liquid assets at the end of the year</b>	<b>328 967</b>	<b>187 846</b>
<b>KEY RATIOS</b>		
Equity ratio	95%	85%
Equity per share, end of period, SEK	75:10	22:79
Loss per share, weighted average number of shares, SEK	-18:76	-3:83
Loss per share, fully diluted weighted average number of shares, SEK	-18:58	-3:83
Weighted average number of shares, 000	10 932	9 177
Fully diluted weighted average number of shares, 000	11 036	9 177
Number of shares, end of period, 000	11 999	9 177

Huddinge, February 8, 2001

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