Corporate Registration Number 556309-3359

# KARO #BIO SEMI-ANNUAL REPORT

1 JANUARY – 30 SEPTEMBER, 2000

- The preclinical studies in the BMS project have successfully been completed and an IND (application to start clinical trials) is in preparation.
- Karo Bio has obtained an exclusive European license for the androgen receptor (receptor for male sex hormone) as a drug discovery target.
- Net sales for the period increased to 73.3 (46.0) MSEK
- Cash flow from operating activities for the period was –41.1 (-24.8) MSEK. However, net results after financial items for the period declined to SEK –172.3 (-32.2), due to depreciation of goodwill in the amount of SEK 133.8 (3.8) million.

#### **OPERATIONS**

Nuclear receptors are validated drug targets and a number of important pharmaceuticals act via these receptors. There is however a strong need for improvements regarding side effects, efficacy and in the possibility to treat diseases where there today is an unmet clinical need. The possibility to develop new and superior pharmaceuticals with improved properties regarding efficacy and side effects is based on access to advanced technologies. In this field Karo Bio has been an international leader with access to receptor structures, in house x-ray crystallography, medicinal chemistry and biochemical and cellular selection systems.

Karo Bio is determined to maintain and strengthen its competitive position and to expand its operations within the field of nuclear receptors. This is the background for the acquisition of Novalon Pharmaceuticals and the establishment of Karo Bio USA. The integrated company is now strengthened in areas such as screening, compound selection for development and in pharmacological evaluation of genomics targets. This has led to a strengthening of the ongoing projects but also to the start of several new projects focused on new indications and new nuclear receptors. The number of employees has increased to 120 compared to 80 at year-end 1999 and 81 October 1999.

Karo Bio is presently engaged in six research programs:

#### • Estrogen receptors (ER):

Women's health problems including menopausal symptoms, osteoporosis, cardiovascular disease and cancer.

#### • Thyroid hormone receptors (THR):

Cardiac arrhythmia, metabolic disorders, glaucoma and skin diseases.

#### • Glucocorticoid receptor (GR):

Type 2 diabetes.

#### • Exploratory research:

Evaluation of new indications regarding classical nuclear receptors and discovery and characterization of new receptors.

#### • Infectious diseases program:

Development of new antibiotics.

#### • Genomics:

Identification and development of pharmaceutical compounds that act via new target proteins.

#### COLLABORATIVE PROJECTS

#### <u>Abbott Laboratories – type 2 diabetes (GR)</u>

The collaboration with Abbott has progressed well since the start of the program on the first of January this year. The program aims at development of liver selective antagonists for the glucocorticoid receptor. Karo Bio has previously demonstrated that liver selective glucocorticoid antagonists lower glucose levels in diabetic animals. Recently, new scientific data from different research groups support the rationale for targeting the liver. For example studies in knock-out mice have provided new insights for deciphering the mysteries of type 2 diabetes. With such animals it has been shown that the liver plays a key role in the development of type 2 diabetes.

#### Merck & Co. – estrogen receptors (ER)

The project continues to make progress. Recent preclinical studies at Merck indicate that estrogen receptor subtypes could be important targets for drug development. In the scientific community the field of female endocrinology is presently focused on the role of the classical estrogen receptor and the new and proprietary ER beta receptor. This research has enhanced our understanding of the role of the receptors in health and disease conditions.

#### <u>Bristol-Myers Squibb – thyroid receptor (THR)</u>

This collaboration targets obesity and metabolic disorders by development of novel and agonists of thyroid hormone receptor activity. Compounds have been selected for clinical trials, and preparations for the IND filing have been initiated. The initial target indication is obesity, for which there is a large unmet medical need. Apart from the success in pre-clinical product development and demonstration of proof of principle,

the project has also provided important scientific information that may lead to new marketing opportunities resulting from additional indications. The objective in the recently announced collaboration extension is the discovery of new compounds for additional therapeutic indications. This work will go on in parallel with the clinical development of first generation compounds.

#### Other collaborations

The BioKey<sup>™</sup> technology of Karo Bio USA is a novel assay technology utilized in several collaborations for genomics-based drug discovery. Currently KB USA collaborates with the following companies: Bayer AG, Millennium Pharmaceuticals Inc., Novartis Research Foundation, Ares Serono, GPC Biotech AG and Nov Immune.

**INTERNAL PROJECTS** 

#### Skin Disorders - THR

The phase II clinical study for treatment of skin atrophy is proceeding according to plan. The remaining patients shall be treated and evaluated during this fall. This is also the case for the mechanistic phase I study, which goes on in parallel. The focus in this study is to evaluate how the product affects the structural proteins in the skin. Those proteins are important for building up and maintaining a healthy skin composition.

#### Cardiac arrhythmia - THR

The lead compound KB 130015 is a promising compound for treatment of cardiac arrhythmia and currently Karo Bio is seeking a partner for the clinical development. Apart from this compound Karo Bio is engaged in development of new compounds targeting THR subtypes.

#### Glaucoma – THR

The animal study in rabbits with different formulations for eye drops has been finalized. A report shall be available before year-end.

#### The infectious disease program

The program aims at the development of new broad-spectrum antibiotics. There is a great need for such products due to development of resistance to most of the antibiotics in use today. A number of new bacterial targets have been identified and validated in the program. A massive screening effort has also led to identification of novel lead structures.

#### **Exploratory research**

In close collaboration with its academic network Karo Bio continues to explore new receptors and projects. A new important contribution is the acquisition of an exclusive European license for the receptor for the male sex hormone (AR). This makes it possible for Karo Bio to target areas like for example prostate cancer, hormone replacement therapy and acne. Other projects are inflammation targeting GR, heart failure/hypertension targeting MR and the orphan receptor LXR for metabolic disorders. These areas have become considerably strengthened through access to the Karo Bio USA technology.

During the period Karo Bio has also solved a number of new receptor structures with various compounds, which has significantly enhanced our possibilities for design of new and selective compounds. This work has been conducted internally with equipment installed earlier this year.

#### Karo Bio USA Inc.

The Molecular Braille drug discovery technology is focused on nuclear receptors. This important technology will be utilized at both company research locations.

In addition the team in the US continues to perfect the industrial scale process for high through-put drug screening (HTS) using the company's proprietary BioKey assays. At this time, the screening group has completed 11 HTS assays for genomic drug targets for the discovery of broad-spectrum antibiotics and has developed an equal number of assays for corporate partners.

#### INCOME AND PROFIT/LOSS

The acquisition of Novalon Pharmaceutical Corporation (Karo Bio USA Inc.) was carried out as a non-cash issue. The recorded purchase price, including transaction expenses, was SEK 971 million. The acquisition brought goodwill of SEK 963 million that will be depreciated over a three years period beginning at May 1, 2000, the day the company was consolidated. Net sales for the Group during the period amounted to SEK 73.3 (46.0) million, with net sales for the Parent Company of SEK 70.4 (46.0) million. Income included a down payment from Abbott in January. Costs for the Group, including goodwill, rose to SEK 253.1 (84.2) million. The largest items are attributable to the depreciation of goodwill relating to the acquisition of Karo Bio USA, the Company's costs from May 1 - the date the Company was consolidated -, payroll costs due to increases in the work force since 1999, software for the chemistry activities and various success fees. The last item was reported under "other operating expenses." It should also be mentioned that the Company took possession of new premises at the beginning of the year and that heightened research activity has led to increased purchases of chemicals and consumable material.

The Group's cash flow from operating activities during the period was SEK –41.1 (-24.8) million. However, net results for the Group declined to SEK –172.3 (-32.2) million, as a result of depreciation of goodwill relating to the acquisition of Novalon in

the amount of SEK 133,8 million. The Parent Company is reporting net results of SEK –17.9 (-28.3) million. The difference between the Group and the Parent Company consists mainly of the depreciation of goodwill totaling SEK 137.7 (3.9) million.

Earnings per share for the period were SEK -16:30 (-3:51), computed on the average number of shares. As a result of the negative result and the consolidated losses carried forward for the Group of SEK 496 million, income for the period was not taxable.

#### LIQUIDITY AND SHAREHOLDERS' EQUITY

Liquid funds in the Group, including short-term investments, amounted to SEK 331,4 million as of 30 September 2000 (187.8 as of 31 December 1999). Shareholders' equity was SEK 1.186,9 million as of 30 September (SEK 209.2 million as of 31 December 1999).

The Company's share capital of SEK 59,931.405 was distributed among 11,986,281 shares with par value of SEK 5 each. In addition, there are warrants outstanding corresponding to 170,153 shares.

#### **INVESTMENTS**

Investments in equipment by the Group and the Parent Company during the period amounted to SEK 5.2 million (2.1) and SEK 4.4 million (2.1), respectively. Investments were mainly for X-ray crystallography equipment and software purchased for chemistry operations. The X-ray crystallography equipment is now in full operation and will give Karo Bio the opportunity to rapidly determine receptor structures inhouse

SCHEDULED RELEASES OF FINANCIAL INFORMATION

Earnings report for 2000

8 February, 2001

The Company's independent auditor has not reviewed this report.

### CONSOLIDATED INCOME STATEMENT (SEK k)

	JANUARY - SEPTEMBER		WHOLE YEAR
	2000	1999	1999
Net sales	73 358	46 038	72 979
Operating expenses			
Marketing expenses	-7 568	-4 800	-6 614
Administration expenses	-14 658	-8 860	-11 721
Research and development expenses	-229 130	-70 568	-95 694
Other costs	<u>-1 781</u>	Ξ	<u>-1 485</u>
	-253 137	-84 228	-115 514
Operating result	-179 779	-38 190	-42 535
Financial items	7 472	5 944	7 405
Operating result after financial items	-172 307	-32 246	-35 130
Tax	-	-	-
NET LOSS  Depreciation according to plan included	-172 307	-32 246	-35 130
in operating expenses (of which	143 818	9 357	12 193
depreciation on goodwill	137 658		5156)

### CONSOLIDATED BALANCE SHEET (SEK k)

Assets	30 Sept	30 Sept 2000	31 Dec 1999
Intangible fixed assets	<b>2000</b> 857 115	32 873	31 558
Equipment	23 387	14 761	17 155
Operating receivables	15 726	11 321	8 966
Liquid funds and short-term investments	<u>331 355</u>	<u>182 297</u>	<u>187 846</u>
TOTAL ASSETS	1 227 583	241 252	245 525
Shareholders' equity and liabilities			
Shareholders' equity	1 186 872	212 039	209 175
Loans and leasing dept	4 374	-	-
Operating liabilities	<u>36 337</u>	<u>29 213</u>	<u>36 350</u>
TOTAL EQUITY AND LIABILITIES	1 227 583	241 252	245 525

## CONSOLIDATED CASH-FLOW STATEMENT (SEK k)

	JANUARY - SEPTEMBER		WHOLE YEAR
	2000	1999	1999
Operating result before financial item	-179 779	-38 190	-42 535
Depreciation	143 818	9 357	12 193
Other items not affecting liquid assets	Ξ	<u>=</u>	<u>-10</u>
	-35 961	-28 833	-30 352
Financial income received	5 605	4 873	11 300
Financial expenses paid	<u>-312</u>	<u>-131</u>	<u>-488</u>
	5 293	4 742	10 812
Change in operating capital	-10 477	-701	4 204
CASH FLOW FROM			
OPERATING ACTIVITIES	-41 145	-24 792	-15 336
Investments in tangible fixed assets	-5 242	-2 041	-5 948
Investments in subsidiaries	<u>-6 972</u>		<u>-</u>
CASH FLOW FROM		_	_
INVESTING ACTIVITIES	-12 214	-2 041	-5 948
New share issue <b>CASH FLOW FOR THE PERIOD</b>	196 868 <b>143 509</b>	<u>-26 833</u>	<u>-21 284</u>
LIQUID FUNDS AT END OF PERIOD	331 355	182 297	187 846
KEY RATIOS			
Equity ratio, %	96	88	85
Equity per share, SEK Earnings (-loss per share), average number of	99:02	23:10	22:79
shares, SEK Earnings (-loss per share), after exercise of	-16:30	-3:51	-3:83
all warrants, SEK	-16:18	-3:51	-3:83
Average number of shares *	10 572	9 177	9 177
Number of shares, end of period *	11 986	9 177	9 177
Number of shares, average number after			
exercise of all warrants *	10 652	9 177	9 177
Number of shares, end of period after exercise of all warrants *	12 156	9 177	9 177

<sup>\* 000</sup> 

### Huddinge October 10, 2000

Torben Jørgensen President

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