

Operating and Financial Review and Prospects

The following discussions should be read in conjunction with our financial statements and the notes thereto included elsewhere in this Annual Report. We refer to 'Forward-looking statements' as well as to 'Risk factors' for certain factors that may affect our operating results. Unless otherwise mentioned all amounts in this section are in thousands of Euro, except share and option data.

General

We are a fully integrated biopharmaceutical Company, focused on developing, producing and marketing vaccines and antibodies against infectious diseases for private and public markets worldwide. We have a portfolio of well-known vaccines and a pipeline of potential new vaccines and antibodies. We combine proprietary technologies to discover, develop and produce a variety of vaccines and antibodies to combat infectious diseases.

Summary of the full year financial results

Total revenue and other operating income for the year ended December 31, 2008 were € 283,309, which represent a 32.9% increase over the € 213,116 in revenues and other operating income reported in 2007. The increase in total revenues and other operating income is mainly attributable to increased sales of paediatric vaccines, travel and endemic vaccines and higher license revenues.

Total operating expenses amounted to € 129,691 (2007: € 125,918). R&D expenses of € 70,229 (2007: € 63,995) reflect our continued focus on (pre-) clinical development.

We achieved profitability for the full year 2008, reporting a net profit of € 14,586, compared to a net loss of € 42,910 in 2007. This amounted to € 0.22 net profit per share in 2008, compared to a net loss per share of € 0.66 in 2007.

Cash and cash equivalents at December 31, 2008 amounted to € 170,969 (2007: € 163,248).

Our operating cash flow was € 254 negative in 2008, compared to a positive operating cash flow of € 22,194 in 2007. The reduction is mainly due to the build-up of Quinvaxem inventory for sales in 2009.

Segments

We operate in one reportable segment, which comprises the development, production and marketing of products that combat infectious diseases. The Group early adopted IFRS 8 'Operating Segments', which replaces IAS 14, 'Segment reporting', as of January 1, 2007. The Management Board is identified as the 'chief operating decision maker'. The Management Board reviews the consolidated operating results regularly to make decisions about resources and to assess overall performance.

In 2007, our segmentation was based on the two segments that were reported to our Management Board:

- Vaccines: developing, producing and marketing vaccines worldwide to combat infectious diseases; and
- Proteins: leverage our novel, proprietary technologies to develop monoclonal antibodies to combat infectious diseases.

In 2008, the Management Board decided to integrate both business units and reduce the complexity of our organization. In 2008, the separate segments were no longer reported to the Management Board.

Retrospective application of newly adopted accounting policies

We adopted IFRIC 14, 'IAS 19 – The limit on a defined benefit asset, minimum funding requirements and their interactions' in 2008. This interpretation provides guidance on assessing the limit of the surplus in a defined benefit pension plan that can be recognized as an asset. It also explains how a pension asset or liability may be affected by a statutory or contractual minimum funding requirement. Our pension fund in Switzerland has a minimum funding requirement and the application of the interpretation resulted in an increase in the assets recorded on the Group's balance sheet of € 7,853 (2007: € 4,918, 2006: € 746) and a corresponding increase in the Group's equity of € 6,165 (2007: € 3,861, 2006: € 586). As a result of the adoption of IFRIC 14, the result for the year increased by € 2,101 (2007: € 3,037, 2006: € 367). As required by IFRS, all comparative figures were adjusted as if the interpretation had always been applied.

Acquisitions and divestments

In 2006, we acquired a controlling interest in the Swiss biotech Company Berna Biotech AG (Berna Biotech), in a share exchange. In September 2006, we acquired the remaining 1.6% minority interest in Berna Biotech. In October 2006, we purchased the assets and liabilities of Florida-based Berna Products Corp. (BPC) from Acambis plc. In November 2006, we acquired Stockholm-based SBL Vaccin Holding AB (SBL) from the private equity firm 3i and the financial group SEB.

2007 is the first year that includes the consolidated results of the acquired companies for a full year. Our 2006 financial results included one month of SBL's financial results, three months of BPC's financial results and ten months of Berna Biotech's financial results.

Economic and industry-wide factors

Various economic and industry-wide factors are relevant to us and could affect our business, including the factors set forth below.

Our financial strength and ability to adapt to the current market and economic conditions are dependent, in part, on the success of our existing products, the cost of bringing novel products to market and the success of our licensees in developing commercial products using our technology. Our industry is subject to extensive government regulation, and we must make significant expenditures to comply with these regulations. Our business success is dependent in a significant part on our success in establishing intellectual property rights, either internally or through licenses of third-party intellectual property rights, and protecting our intellectual property rights.

Our sales are exposed to seasonal variations, and the majority of our sales is made in the second half of the year. This is specifically the case for our influenza vaccines as vaccination programs mainly take place in the second half of the year. Furthermore, our travel vaccines sales are subject to seasonal travel patterns. The 2008 flu season was comparable to 2007 in our major markets in Europe.

To be successful, we must retain qualified clinical, scientific, marketing, administrative and management personnel. We face significant competition for experienced personnel. In 2008, the number of employees of the Group remained stable at 1,126 employees (2007: 1,126).

The above economic and industry-wide factors are discussed in more detail in the section 'Risk factors'.

Result of operations

Revenues

The table below shows our revenues for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Product sales	226,055	177,569	103,918	27.3	70.9
License revenues	30,202	12,211	16,955	147.3	(28.0)
Service fees	10,900	14,006	10,694	(22.2)	31.0
Total revenues	267,157	203,786	131,567	31.1	54.9

In 2008, total revenues increased by € 63,371 or 31.1% from € 203,786 in 2007 to € 267,157 in 2008. The increase is attributable to an increase in product sales of € 48,486 or 27.3% and license revenues of € 17,991 or 147.3%. The increase is partly offset by a decrease in revenue from service fees of € 3,106 or (22.2%).

Total revenues grew by € 72,219 in 2007 or 54.9 % from € 131,567 in 2006 to € 203,786 in 2007. The increase is primarily attributable to increases in sales of paediatric vaccines by € 41.438 or 115.3 % and travel and endemic vaccines by € 24.210 or 104.9 % and higher revenues related to the acquisitions made in the second half of 2006.

Reference is made to '4.4 Geographical segments' in the financial statements for the breakdown of our revenues by geographic segment.

Product sales

Our product sales by type of product in 2008, 2007 and 2006, as well as the percentage change between the periods, are shown below:

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Paediatric vaccines	111,039	77,371	35,933	43.5	115.3
Respiratory vaccines	32,474	33,188	40,386	(2.2)	(17.8)
Travel and endemic vaccines	55,572	47,282	23,072	17.5	104.9
Other products	26,970	19,728	4,527	36.7	335.8
Total product sales	226,055	177,569	103,918	27.3	70.9

In 2008, product sales grew by € 48,486 or 27.3%. The increase is primarily attributable to increased sales of paediatric vaccines of € 33,668 or 43.5%, travel and endemic vaccines of € 8,290 or 17.5% and other products of € 7,242 or 36.7%.

In 2008, paediatric vaccines grew mainly due to increased Quinvaxem sales. Supranational organizations awarded us additional contracts for Quinvaxem and Hepavax Gene amounting to \$ 140 million for the period 2008-2009. Travel and endemic vaccines showed considerable growth on an overall basis. 'Other products' include sales of vaccine and proteins trade goods that we distribute for third parties and also sales of conjugates to Wyeth. The increase in other products mainly relates to increased sales under our distribution agreement with Talecris as 2008 includes a whole year of sales under this agreement for the first time.

Our core product portfolio consists of seven vaccines: Quinvaxem, Hepavax-Gene, MoRu-Viraten (paediatric vaccines), Inflexal V (respiratory), Dukoral, Epaxal and Vivotif (travel and endemic vaccines). The aggregated revenues for our core product portfolio amounted to € 191,631 in 2008 (2007: € 151,791, 2006: € 92,144) and represented 84.8% (2007: 85.5%, 2006: 88.7%) of our total product sales.

In 2008, sales to our two largest customers, which are in the paediatric vaccines area, amounted to € 85,142 or 37.6% and € 18,390 or 8.1 % of net product sales. In 2007, sales to these customers accounted for € 45,480 or 25.6% and € 23,457 or 13.2% of net product sales, respectively.

In 2007, product sales grew by € 73,651 or 70.9 %. The growth in revenue from product sales was mainly due to increased revenue from sales of paediatric vaccines of € 41,438 or 115.3%, travel and endemic vaccines of € 24,210 or 104.9 % and sales of other products of € 15,201 or 335.8 %. The increase in product sales was partly offset by a decrease in respiratory vaccines of € 7,198, mainly caused by lower influenza vaccine sales as a result of a mild flu-season in 2007.

The majority of our sales are export sales. Domestic product sales amount to € 3,743 or 1.7% (2007: € 717 or 0.4% and 2006: nil). Almost all of our license revenues and service fees are billed to foreign parties.

License revenues

In 2008, license revenues increased by € 17,991 or 147.3% to € 30,202 compared to 2007. This increase mainly results from milestone payments related to the rabies and influenza programs from sanofi pasteur and upfront fees received from Talecris for the exclusive production rights of two specific proteins.

In 2007, our license revenues decreased to € 12,211, a reduction of € 4,744 or 28.0% compared to 2006, which was mainly due to one-off issuance fees included in contracts with DSM and sanofi pasteur in 2006. The underlying agreements with DSM and sanofi pasteur are still in effect. The decrease was partly offset by recognized issuance fees on contracts signed in 2007 with MedImmune, ADImmune and Wyeth that totaled € 4.3 million and numerous other smaller contracts.

In December 2007, we signed an exclusive collaboration and commercialization agreement with sanofi pasteur related to our rabies monoclonal antibodies. We received a payment of € 10.0 million, which will be recognized as license revenues over the period that the development activities are performed. We will be eligible for additional potential milestone payments of up to € 66.5 million.

Service fees

In 2008, service fees amount to € 10,900, a decrease of € 3,106 or 22.2 % compared to 2007. In 2008, service fees on the sanofi pasteur influenza project were less compared to 2007. Service fees include revenues relating to various collaboration agreements. Typically we do not retain the residual interest on products developed under these agreements. We are more selective in the programs that we want to carry out and we tend to put more focus on the profitability of these types of programs.

In 2007, service fees amounted to € 14,006, an increase of € 3,312 or 31.0% compared to 2006. This increase was mainly attributable to consulting services provided to ADImmune and increased service fees in Sweden realized on miscellaneous projects.

Cost of goods sold

The following table shows our cost of goods sold for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Cost of product sales	138,790	124,557	83,518	11.4	49.1
Cost of service fees	6,965	10,327	6,971	(32.6)	48.1
Total cost of goods sold	145,755	134,884	90,489	8.1	49.1

Cost of product sales

Costs of product sales comprise direct labor, materials, and overhead costs incurred in performing work under various collaboration agreements directly related to product sales. The cost of product sales increased in 2008 mainly due to an increase in product sales of 27.3%. This increase was partly offset by the reduction in purchase price allocation charges in 2008. The 2008 cost of product sales includes additional expenses of € 3,473 (2007: € 10,191) relating to the purchase price allocations of the businesses acquired by the Group. The gross margin on product sales amounts to 38.6% (2007: 29.9%). The percentage increase in gross margin is mainly due to the strengthening of the US Dollar in the second half of 2008, product-mix changes, improvements in production performance and a reduction of the purchase price allocation charges in 2008.

Cost of service fees

Cost of service fees comprises direct labor, materials and overhead costs related to work under various collaboration agreements. We do not retain the residual interest on products developed under the agreements and will normally not have ownership of intellectual property rights on these products.

In 2008, the cost of service fees decreased by € 3,362 or 32.6 % compared to 2007. The decrease reflects the lower level of service fee revenues, which reduced our expenses. The gross margin on service fees was 36.1% in 2008 compared to 26.3% in 2007. In 2008, there has been a shift in strategy to focus more on programs that generate higher margins.

In 2007, the cost of service fees increased by € 3,356 or 48.1% compared to 2006, which is primarily attributable to the increase of the service fee revenues by 31.0%. The gross margin on service fees was 26.3 % in 2007 compared to 34.8% in 2006.

Other operating income

The following table shows our other operating income for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Government grants	5,380	7,086	6,901	(24.1)	2.7
Other operating income	10,772	2,244	2,455	380.0	(8.6)
Total other operating income	16,152	9,330	9,356	73.1	(0.3)

Government grants

In 2008, government grants decreased by € 1,706 or 24.1% compared to 2007. The grants decreased as several projects were completed in 2007. The most significant grants in 2008 were received from NIH and from SenterNovem, an agency of the Dutch Ministry of Economic Affairs, for numerous research projects.

In 2007, government grants were stable compared to 2006. The most significant grants in 2007 were received from NIAID for further research on HIV and from SenterNovem.

Other income

Other income mainly consists of the reimbursement of development costs and funding received from non-governmental agencies. Other income also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses. Other income increased by € 8,528 or 380.0% mainly due to reimbursement of development costs on the rabies program, for which the partnership with sanofi pasteur started in 2008, and increased funding from non-governmental agencies in 2008.

The amount of other income in 2007 was stable compared to 2006.

Other operating expenses

The following table shows our other operating expenses for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Research and development	70,229	63,995	67,606	9.7	(5.3)
Selling, administrative and general	64,350	61,752	46,732	4.2	32.1
Restructuring	—	—	3,120	—	—
(Reversal of impairment)/ impairment	(4,888)	171	30,416	(2,958.5)	(99.4)
Total other operating expenses	129,691	125,918	147,874	3.0	(14.8)

Research and development expenses

Research and development expenses consist of personnel expenses, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation of property, plant and equipment and amortization of intangible assets related to research and development, and lease expenses for lab space and equipment lease. Research and development expenses also include fees we pay to third parties who conduct research on our behalf.

Research and development expenses increased in 2008 by € 6,234 or 9.7% compared to 2007. This increase is mainly attributable to increased expenditures on the rabies program for which two phase II clinical trials were performed.

Research and development expenses comprised 54.2% of total other operating expenses in 2008 (2007: 50.8%). We expect that research and development expenses will continue to be a significant portion of our overall expenses in the future.

In 2007, research and development expenses decreased by € 3,611 or 5.3% compared to 2006, which was primarily attributable to the cost-saving effect of the restructuring program that took place in 2006 to centralize research and development activity in Leiden and phasing out work on both a vaccine candidate as well as on programs at the Center of Mammalian Cell Culture.

Selling, general and administrative expenses

Selling, general and administrative expenses consist of personnel expenses and other operating expenses in marketing and sales, finance, human resources, investor relations, legal and general management.

These expenses increased in 2008 by € 2,598 or 4.2% to € 64,350 in 2008 compared to € 61,752 in 2007. This increase is primarily due to the overall growth of the Group as a whole. Specific items are the increased distribution and sales expenses as a result of increased revenues, annual salary increases and the recognition of specific provisions. The increase in selling, general and administrative programs is partly offset by cost reductions realized through our Healthy Ambition program.

Selling, general and administrative expenses increased in 2007 by € 15,020 or 32.1% to € 61,752 in 2007, compared to € 46,732 in 2006. Selling costs increased as a result of the cost base of the companies acquired in 2006, which are for the first time included for a whole year in 2007. General and administrative expenses also included integration costs of the 2006 acquisitions and additional costs relating to compliance with internal control over financial reporting requirements under US law.

Restructuring

A restructuring program in our Italian subsidiary Berna Biotech Italia Srl. was executed in 2008. A total provision of € 684 was recognized, of which € 610 is recorded in restructuring provisions as per year-end

2008. The majority of this provision was paid in the first quarter of 2009. The costs for the restructuring are included in the applicable operating expenses as they have an operating nature.

There were no restructuring expenses in 2007.

The restructuring expense in 2006 is related to centralizing R&D functions in Leiden and phasing out R&D projects in Switzerland, including the candidate vaccine Aerugen, and the Center of Mammalian Cell Culture. The decision to concentrate R&D in Leiden was made to increase efficiency in R&D spending. The provision was recognized in 2006 as recognition criteria were met at that time. The actual reduction in the number of staff employed was effected in the first quarter of 2007.

Impairment

In the first quarter of 2008, we reversed € 5,219 of previously impaired property, plant and equipment. In 2008, we entered into an exclusive agreement with Wyeth Pharmaceuticals in which we will develop and manufacture certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that were impaired in 2006 as described below. We reassessed the recoverable amount of the asset and as the outcome exceeded the carrying value of nil, we partially reversed the previously recognized impairment loss on this building.

In the fourth quarter of 2008, we recognized an impairment charge of € 331 for the animal housing facility in Bern, Switzerland that was not in use anymore. As there was no alternative use for this building for any of the Group's other activities and the building cannot be sold directly to other parties as it is on our campus, the Group impaired the carrying value to zero.

In 2007, we recognized an impairment charge of € 171 for a warehouse in Korea that was demolished to make way for the construction of a light railway.

In 2006, we recognized a total impairment of € 30,416. The impairment related to two buildings in Switzerland including installed equipment, for an amount of € 19,568 and to acquired in-process research and development related to the Tetra vaccine for an amount of € 10,848.

Operating profit/ (loss)

The following table shows our operating profit/ (loss), for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Operating profit/ (loss)	7,863	(47,686)	(97,440)	(116.5)	(51.1)

The movements in operating loss are explained by the operating results discussed above.

Financial income and expense, net

The following table shows our financial income and expenses, net, for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Financial income and expenses	(2,662)	1,378	1,747	(293.2)	(21.1)
Results investments non-consolidated companies	(128)	(996)	(1,956)	(87.1)	(49.1)
Results on disposal non-consolidated companies	1,570	2,186	—	(28.2)	—
Disposal of subsidiaries	(367)	—	—	—	—
Total financial income/ (expense), net	(1,587)	2,568	(209)	(161.8)	(1,328.7)

Financial income and expenses

Financial income and expenses mainly consist of interest income and expenses, foreign exchange losses and other financial expenses.

In 2008, the negative result on net financial income and expenses totaled € 2,662 and consists of interest income of € 5,021, foreign exchange losses of € 3,926, interest expenses of € 2,719 and other financial expenses of € 1,038.

The net financial income and expenses decreased by € 4,040 or 293.2 % compared to 2007. The decrease is primarily attributable to foreign exchange losses of € 3,926. These losses mainly resulted from a weaker Euro in conjunction with Euro receivables in Switzerland, as the Swiss Franc is the functional currency of our subsidiary Berna Biotech AG. In addition, foreign exchange losses were realized on Euro liabilities and losses on US Dollar transactions in Korea.

See – ‘Financial risk management – 3.2 Foreign currency risk’ in the financial statements for more details on foreign currency risk management including the use of hedging instruments by the Group.

Other changes in the net financial income and expenses were:

- A reduction of interest income by € 690, mainly caused by a lower average cash balance in 2008 compared to 2007;
- Increased interest expenses of € 438 as a result of increased finance leases and short-term financial liabilities; and
- An increase other financial expenses of € 292 primarily due to factoring arrangements engaged in during 2008.

In 2007, net financial income and expenses decreased by € 369 or 21.1% compared to 2006. The decrease was primarily attributable to:

- Increased negative foreign exchange results of € 1,142 as the foreign currencies in which we traded lost value compared to the Euro;
- Increased interest expenses of € 544 as a result of additional charges relating to leasing and the full year effect of our 2006 acquisitions; and

- An increase in other financial expenses of € 402 primarily due to factoring arrangements engaged in during 2007. The decrease was partly offset by increased interest income of € 1,993 resulting primarily from higher interest rates in 2007.

Results investments non-consolidated companies

At December 31, 2008, we had one associate, ADImmune Corp and one joint venture, Percivia. In July 2008, we sold our investment in Kenta Biotech AG. The results of investments in non-consolidated companies include the results of Kenta Biotech AG up to the moment of the sale. The results of investments in non-consolidated companies are accounted for under the equity method and amount to a total loss in 2008 of € 128 (2007: € 996). The decrease of € 868 or 87.1% compared to 2007 year is mainly due to the reduced losses on Kenta Biotech AG.

In 2007, the losses from investments in non-consolidated companies were reduced by € 960 or 49.1%. The decrease was primarily attributable to the reduced losses in Pevion Biotech AG and Kenta Biotech AG.

Results on disposal non-consolidated companies

On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Inagro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain in 2008 of € 1,570 on the sale.

On November 5, 2007 the Group sold all of the 2.9 million shares it owned in Pevion Biotech AG for an amount of € 6,081 to other shareholders of Pevion Biotech AG. The Group realized an accounting gain in 2007 of € 2,186 on the sale.

Disposal of subsidiaries

In November 2008, we sold our fully-owned subsidiary Etna Biotech Srl to Zydus Cadila. The sale resulted in net proceeds of € 182 and an accounting loss on disposal of € 367.

Income tax

The table shows our income tax for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Income tax	8,310	2,208	10,451	276.4	(78.9)

In 2008, tax income increased by € 6,102 or 276.4%. The increase resulted from a change in deferred tax of € 11,503 (2007: € 3,024) that mainly consists of carry forward losses not previously recognized in our subsidiary Berna Biotech AG for € 8,585 and a reduced expected tax realization rate on our deferred tax liabilities of € 3,384 in Korea. The increase is partially offset by current tax charges of € 3,200 compared to € 811 in 2007 as a result of taxable income in Sweden, Korea, Spain and the US.

The Group has a negative effective tax rate of 132.4% in 2008 compared to positive effective tax rates of 4.9% in 2007 and 10.7% in 2006. Our effective tax rate was impacted by numerous items.

The effective tax reconciliation starts with our IFRS profit/ (loss) per subsidiary multiplied by the domestic rate of tax in the country in which our subsidiaries are domiciled. In 2008, our total profit under IFRS of € 6,276 had a negative correlation with our total taxes based on domestic rates of € 820. This effect was mainly caused by a loss under IFRS in our Dutch operation at a tax rate of 25.5% and a profit of our Korean subsidiary at a lower average tax rate of 21.0%.

In addition, the following transactions significantly affected our effective tax rate reconciliation:

- We reached an agreement with the Dutch tax authorities to retroactively change the valuation of our intellectual property, to avoid the evaporation of unrecognized tax carry forward losses. This agreement allows us to recognize € 72,000 of our intellectual property as assets for tax purposes. Under IFRS no deferred tax assets were recognized on these temporary differences, which on a combined basis with the utilization of previously unrecognized carry forward losses in our Dutch fiscal unity in 2008, causes a net negative tax effect of € 6,103;
- We reassessed the valuation of our carry forward losses and recognized previously unrecognized carry forward losses in our subsidiary Berna Biotech AG, which resulted in a taxation gain of € 8,585;
- As of the year 2012, we will benefit from a tax holiday to our investment in the Incheon, Free Economic Zone, Korea, which will significantly reduce the effective Korean income tax rate for a period of 5 years. The reduced expected realization rate for our deferred tax liabilities in Korea resulted in a taxation gain of € 3,384;
- In 2008, we benefited in Korea from a research and development tax credit for an amount of € 2,916; and
- Non-deductible stock-option expenses are recognized in the Netherlands for an amount of € 1,251 in 2008.

See – '1 General information – 1.4 Use of estimates and judgments' in the financial statements section for a description of estimates and management judgments in determining the tax position and '5.4 Income tax' in the financial statements for a numerical reconciliation of our effective tax rates.

Changes in the underlying timing differences in 2007 resulted in a taxation income of € 3,024 in 2007 compared to € 10,922 in 2006.

Liquidity

We have a strong cash position, which we believe makes it possible to continue financing important development programs. Our cash and cash equivalents amounted to € 170,969 and € 163,248 as of December 31, 2008 and 2007, respectively. We believe that our liquidity is sufficient for our present requirements.

In 2009, we entered into a mortgage loan facility in Korea for an amount of KRW 50 billion to partly finance the investments in the new Korean facility.

Cash flows

The following table shows our cash flow statement for each of the years in the three-year period ended December 31, 2008 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2008	2007	2006	08 vs. 07	07 vs. 06
Profit/ (loss) of the period	14,586	(42,910)	(87,198)	(134.0)	(50.8)
Adjustments for non-cash items	18,801	44,593	58,505	(57.8)	(23.8)
Changes in net working capital	(30,381)	24,208	(23,174)	(225.5)	(204.5)
Interest and taxes paid	(3,260)	(3,697)	(2,087)	(11.8)	77.1
Net cash flows from/ (used in) operating activities	(254)	22,194	(53,954)	(101.1)	(141.1)
Net cash flows from/ (used in) investing activities	(8,907)	(24,241)	23,159	(63.3)	(204.7)
Net cash flows from financing activities	16,626	11,244	78,731	47.9	(85.7)
Effect of exchange rates on cash and cash equivalents	256	(3,786)	(1,833)	(106.8)	106.5
Net increase/ (decrease) in cash and cash equivalents	7,721	5,411	46,103	42.7	(88.3)
Cash and cash equivalents at beginning of period	163,248	157,837	111,734	3.4	41.3
Cash and cash equivalents at end of period	170,969	163,248	157,837	4.7	3.4

Net cash flows from/ (used in) operating activities

In 2008, our net cash flow from operating activities decreased by € 22,448 or 101.1% compared to 2007. The decrease resulted from an increase of our working capital by € 54,589 and a reduction in the adjustments for non-cash items by € 25,792. The decrease is partly offset by € 57,496 due to improved results in 2008 compared to 2007.

In 2008, the decrease in changes in the net-working capital compared to 2007 amounted to € 54,589. The year 2008 had relatively stable cash flows on the monetary working capital items compared to positive cash flows in 2007. The decrease in 2008 compared to 2007 mainly resulted from inventories for € 30,993 due to build-up of Quinvaxem inventory for 2009 sales, and other current liabilities for € 22,327.

In 2008, adjustments for non-cash items were reduced by € 25,792. This reduction was mainly caused by:

- One-off cash receipts in 2007 in the amount of € 11,500 in 2007 relating to the non-current deferred revenue on the ADImmune technology license and the rabies program;
- Non-cash revenues realized in 2008 for an amount of € 4,728 that related to the above transactions; and
- Partial reversal of the impairment loss on one of our buildings in Switzerland in 2008 for an amount of € 5,219 as we now perform contract manufacturing at this location.

In 2007, our net cash flow from operating activities increased by € 76,148 or 141.1 % compared to 2006. The increase resulted from a reduction of our working capital by € 47,382 and a reduction of our net loss by € 44,288. The increase is partly offset by a decrease in the adjustments for non-cash items of € 13,912 and an increase in interest and taxes paid by € 1,610 in 2007.

Net cash flows from/ (used in) investing activities

Our cash flow used in investing activities amounted to € 8,907 in 2008, compared to € 24,241 in 2007.

In 2008, the most significant cash flows used in investing activities resulted from investments made in property, plant and equipment for an amount of € 15,787. These investments mainly related to our new Korean production facility, investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently acquired from third parties, as well as investments in our new filling line in Madrid, Spain.

In 2008, the most significant cash flows from investing activities were from the following transactions:

- Interest received of € 4,395 in 2008 (2007: € 5,274);
- The sale of all shares owned by the Group in Kenta Biotech AG for € 1,570 to Ingro Finanz AG; and
- Restricted deposits that were transferred to cash and cash equivalents for € 1,500.

In 2007, the most significant cash flows used in investing activities were from the following transactions:

- Investments were made in property, plant and equipment for an amount of € 27,156, which mainly related to our new GMP production facility in Leiden, the Netherlands and investments in our facilities in Bern, Switzerland to improve production processes and allow in-house production of materials currently acquired from third parties; and
- The Group acquired a 20% equity-stake in ADImmune Corp. in March 2007 for € 8,553.

In 2007, the most significant cash flows from investing activities were from the following transactions:

- The sale of all shares owned by the Group in Pevion Biotech AG, Switzerland for € 6,081 to other shareholders of Pevion Biotech; and
- Interest received of € 5,274 in 2007.

Net cash flows from/ (used in) financing activities

Our cash flow from financing activities amounted to € 16,626 in 2008, € 11,244 in 2007 and € 78,731 in 2006.

In 2008, the cash flow from financing activities increased by € 5,382 or 47.9% compared to 2007 and, mainly related to:

- Additional short-term financing facilities in Korea for an amount of € 22,222; and
- Finance leases with proceeds of € 12,368 relating to our GMP-facility in Leiden, the Netherlands and our Spanish filling-line.

The most significant cash flows used in financing activities mainly related to:

- Redemption of a Korean Won-denominated privately placed bond in Korea for € 11,869 and a partial redemption of a short-term Euro loan also in Korea for € 1,455;
- Settlement of financial liabilities relating to factored Italian trade accounts receivable by € 5,653 for which the Group did not substantially transfer all the risks and rewards in 2007; and
- Repayment of finance lease liabilities for an amount of € 1,922.

In 2007, the cash flow from financing activities decreased by € 67,487 or 85.7% compared to 2006 as we limited the use of additional financing and funded our operations and investments with our own resources. The cash flow from financing activities in 2007 mainly related to:

- Factoring of trade accounts receivable in Italy for an amount of € 5,653; and
- Finance leases with proceeds of € 4,247. These finance leases mainly related to equipment for the new production and development facility in Leiden.

Critical accounting policies and estimates

The methods, estimates and judgments we use in applying our most critical accounting policies have a significant impact on the results we report in our financial statements. Please see '1 General information – 1.4 Use of estimates and judgments' in the financial statements for further details on our most critical policies and the methods, estimates and judgments used.

In addition to the critical accounting policies and estimates, the Group chooses to disclose the impact of discounts, rebates and returns.

Discounts, rebates and returns

At the time sales revenue is recognized, we also record estimates for revenue deductions, including discounts, rebates and product returns. We report net sales after deducting all sales deductions from gross sales revenue. The following table identifies the items that reduced our gross product revenue as at the end of the periods ended December 31, 2008, 2007 and 2006.

In thousands of Euro

	2008	2007	2006
Product sales, gross	227,791	179,395	105,059
Discounts and rebates	945	626	291
Returns	791	1,200	850
Total discounts, rebates and returns	1,736	1,826	1,141
Product sales, net	226,055	177,569	103,918

Discounts and rebates

Discounts include prompt payment discounts and charge backs. In 2008, our discounts and rebates amounted to € 945.

We generally offer our US wholesalers a prompt-pay cash discount as an incentive to remit payment in full within one month after the date of an invoice. Prompt-pay discount calculations are based on the gross amount of each invoice. We account for these discounts by reducing product sales by the estimated discount amount when the product is sold.

Wholesaler charge backs, customary in our industry, are arrangements that relate to contractual agreements to sell products to Group Purchasing Organizations (GPOs) in the US at fixed prices that

are lower than the list prices we charge wholesalers. When the GPOs purchase our products through wholesalers at these reduced prices, the wholesaler charges us for the difference between the price the wholesaler paid to us and the price at which they sold the products to the GPO. Accruals for wholesaler charge backs closely approximate actual results because charge back amounts are fixed at the date of purchase by the GPOs. As the charge backs are settled within a short time of incurring the liability, the outstanding accruals are relatively low.

We offer rebates primarily in connection with attainment of sales targets by wholesalers and large retailers in contractually agreed percentages. The rebates are accrued as the underlying sales transactions are recognized and are based on reasonable estimates on the attainment of the sales targets.

Returns

Returns that reduce our gross product revenue may arise from the following:

- Customers return of products defective upon delivery;
- Specific right of return in accordance with contractual terms; and
- Returns via the normal distribution channels if the product is in good condition, pursuant to local law in certain jurisdictions.

In 2008, returns amounted to € 791 (2007: € 1,200) or approximately 0.4% (2007: 0.7%) of our net product sales.

The following table shows the percentage of products returned as a percentage of the gross product sales per country during 2008 based on the country from which the products were originally sold.

Country	Returns 2008	Returns 2007	Returns 2006
Spain	3.0%	2.5%	1.7%
Italy	1.1%	1.4%	0.1%
Switzerland	0.1%	0.1%	0.7%
US	2.1%	1.9%	0.9%
Sweden	0.9%	0.1%	0.2%
Korea	—	—	—
Netherlands	—	—	—

Roll-forward information

The table below shows the roll-forward information of our discounts, rebates, and product returns:

In thousands of Euro

	Accrual for discounts and rebates	Accrual for returns	Total
January 1, 2008	(190)	(1,117)	(1,307)
Additions – current period	(945)	(791)	(1,736)
Actual returns/credits – current period	762	240	1,002
Actual returns/credits – prior period	160	975	1,135
Release of accruals – current period	—	—	—
Release of accruals – prior period	—	—	—
Effect of movements in exchange rates	24	18	42
December 31, 2008	(189)	(675)	(864)

Discounts and rebates

We base our estimates for discounts and rebates primarily on historical experience and contractual agreements, supplemented by management's judgment. In 2008, our estimates for rebates based on historical experience did not differ materially from actual results. With respect to discounts, we have limited uncertainties in determining our estimates, because these deductions generally occur within a short time frame of incurring the liability.

For calculating our rebates estimates we make use of quantifiable contractual rebates data. In general, our rebates are based on fixed rebate percentages on product sales to customers that have been granted rebates.

Returns

We base our estimates of product returns on the percentage of returns that we have experienced historically. We may adjust these return estimates if we are aware of other factors that we believe could meaningfully impact our expected return percentages. For example, in respect of our influenza vaccine, we specifically take into account the development of the flu season, in particular, the number and impact of outbreaks. While we do not have a formula that estimates the impact of the

number and impact of outbreaks on the level of the accrual for returned vaccines, an increased number of outbreaks will generally result in a lower accrual for returned influenza vaccines, because it becomes more unlikely that vaccines will be returned. Alternatively, a lower number of outbreaks can result in a higher accrual, because it becomes more likely that influenza vaccines will be returned unused at the end of a mild flu season.

In addition, in our estimates of returns, we take into account other information, such as media coverage of vaccination programs, estimates of inventory levels of our product in the distribution channel, vaccine shelf life and known sales and market trends. These are reflected in the accruals by means of management's judgment.

Increased media coverage of vaccination programs, either by advertising campaigns or coverage of flu outbreaks, results in an increased public awareness. Consequently, this may lead to an increased number of flu vaccinations and fewer unsold doses with our customers, which limits the level of accruals for product returns.

Relatively high levels of inventory of our product in the distribution channel and short shelf life of product sold can be indicators for an increased level of returns.

Sales and market trends are taken into account by reference to the life cycle phase of products. If product sales show a decreasing revenue pattern over time, this can be an indicator for an increased level of returns. We do not rely on quantitative externally sourced information in our calculation of returns estimates. We are not aware of any available external quantitative information or other quantifiable data that would provide us the benefit of a more reliable estimate.

The rate of product returns is quantifiable. We monitor returns primarily on a per country basis based on the country from which the product was sold because our accruals are determined at this level. Within the individual countries, we monitor the returns on a product-by-product basis. In 2008, our estimates for returns did not differ materially from actual results.

Tabular disclosure of contractual obligations

Future minimum payments for all contractual obligations for years subsequent to December 31, 2008 are as follows:

In thousands of Euro

	Total	Less than one year	1-3 years	3-5 years	More than 5 years
Contractual obligations					
Debt obligations (excluding finance lease obligations)	40,225	22,677	2,239	861	14,448
Finance lease obligations ⁽¹⁾	20,526	2,777	6,381	7,911	3,457
Interest payments on debt obligations	12,580	2,105	3,512	2,314	4,649
Derivative financial instruments ⁽²⁾	45,560	45,560	—	—	—
Accounts payable	59,205	59,205	—	—	—
Other liabilities	21,114	20,523	591	—	—
Recognized obligations	199,210	152,847	12,723	11,086	22,554
Commitments					
Operating lease obligations ⁽³⁾	24,662	3,830	6,575	3,498	10,759
Capital expenditure commitments ⁽⁴⁾	20,380	16,163	4,217	—	—
Total commitments	45,042	19,993	10,792	3,498	10,759
Total recognized obligations and commitments	244,252	172,840	23,515	14,584	33,313

⁽¹⁾ Finance lease obligations

Certain of the Group's fixtures and equipment are finance leases. The finance leases relate to equipment for the new production facility in Leiden, the Netherlands and to the filling line in Spain. Interest rates are fixed at the contract date. All leases are on a fixed repayment basis and no arrangements have been entered into for contingent rental payments.

⁽²⁾ Derivative financial instruments are foreign exchange contracts. The contractual obligations are € 45,060. The corresponding receivables are € 46,442.

⁽³⁾ Operating lease obligations

The operating lease obligations include rental obligations. CruCell concluded long-term rental agreements for premises in Sweden and the Netherlands. In addition, CruCell leases certain motor vehicles and items of machinery and equipment.

⁽⁴⁾ Capital expenditure commitments

The contractual commitments for purchases of property, plant and equipment as per December 31, 2008 amount to approximately € 20,380 (2007: € 4,696, 2006: € 11,693).

These commitments mainly relate to our new production facility in Incheon, Free Economic Zone, Korea.

See note '5.19 Short and long-term financial liabilities' in the notes to the financial statements for details on the maturity profile and the interest rate environment of our financial liabilities.

Off-balance sheet arrangements

As of December 31, 2008, we have no unconsolidated special purpose financing or partnership entities or other off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition or lead to changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources, that is material to investors.

The Group has investments in one associate and in one joint venture that are both non-consolidated companies. Details are provided in '5.9 Investments in associates and joint venture' in the financial statements.

Further details on our off-balance sheet arrangements such as our guarantees and covenants are disclosed in note 3 'Financial risk management' in our financial statements.

Quantitative and qualitative disclosure about market risk

Market risk is the risk of loss related to adverse changes in market prices, including currency risk, interest rate risk and risk of financial instruments. During the ordinary course of business, the Group is exposed to various financial market risks, primarily from foreign exchange, interest rates and credit risk. Details on our market risks are disclosed in '3 Financial risk management' in the financial statements.

Impact of inflation

CruCell does not operate subsidiaries in countries with hyperinflation. Sales to customers in hyperinflationary countries are made in hard currency, mainly Euro, US Dollar, Swiss Franc and Swedish Crown.