



## PRESS RELEASE

### **Crucell Announces Profits for Full Year 2008**

Net profit in 2008 was €14.6 million compared to a net loss of €42.9 million in 2007. Total revenue and other operating income increased by 33% to €283.3 million compared to €213.1 million in 2007.

Positive cash flow of €7.7 million increased the year-end cash position to €171 million. Gross margin for the year improved to 45% (from 34% last year).

**Leiden, The Netherlands (February 5, 2009)** – Dutch biopharmaceutical company Crucell N.V. (Euronext, Nasdaq: CRXL; Swiss Exchange: CRX) today announced its financial results for the fourth quarter and full year 2008, based on International Financial Reporting Standards (IFRS). These financial results are unaudited.

#### **Highlights:**

- Crucell achieved profitability for the fourth quarter as well as for the full year; net profit in 2008 was €14.6 million, compared to a net loss of €42.9 million in 2007. This amounted to €0.22 net profit per share, compared to a net loss per share of €0.66 in 2007.
- On January 7th, 2009 Crucell announced that it was in friendly discussions with Wyeth regarding a potential combination of the two companies. On January 26th, 2009 Crucell announced that Wyeth withdrew from these discussions.
- In 2008 Crucell more than doubled the production of its pentavalent children's vaccine Quinvaxem<sup>®</sup>. In 2008 supranational organizations awarded Crucell additional contracts for supplies of Quinvaxem<sup>®</sup> and Hepavax-Gene<sup>®</sup> for the period 2008 - 2009, bringing the total for the period 2007 - 2009 to \$0.5 billion.
- Crucell announced that Chinese authorities have approved Hepavax-Gene<sup>®</sup> for use in the private vaccine market in China.
- Crucell announced that its monoclonal antibody (mAb) directed against a broad range of influenza virus strains has strongly outperformed oseltamivir, an anti-influenza drug, in preclinical tests.
- In 2008 Crucell's human monoclonal antibody combination against rabies and novel vaccine against tuberculosis both entered into Phase II clinical testing.
- In 2008 DSM and Crucell announced a series of important advances in antibody production using PER.C6<sup>®</sup> technology platform. For example, a PER.C6<sup>®</sup> human cell line and proprietary XD<sup>™</sup> technology were employed to achieve a record yield of over 27 grams per liter of IgG antibodies.
- Crucell announced that its PER.C6<sup>®</sup> technology licensee Ark Therapeutics has entered a Phase III study with its product Trinam. Ark Therapeutics is



the first licensee to enter into a Phase III study with a product produced on Crucell's PER.C6<sup>®</sup> human cell line.

- Crucell signed new license agreements with several parties, including CSL Ltd. and GlaxoSmithKline, as well as a second exclusive license agreement with Talecris Biotherapeutics.

#### **Financial Highlights Fourth Quarter 2008:**

- Combined total revenue and other operating income for the fourth quarter were €93.7 million, compared to €75.9 in the same quarter of 2007. The increase of 23% (22% in constant currencies<sup>1</sup>) was driven by strong sales of paediatric vaccines, travel and endemic vaccines as well as higher license revenues.
- Milestone payments for Crucell's rabies monoclonal antibody combination accounted for the increase of license revenues
- Gross margins of 50%, compared to 34% in the fourth quarter of 2007. Gross margins were positively influenced by a large increase in product sales, license revenues and a positive currency impact as well as significant improvements in production performance.
- Net profit in the fourth quarter of 2008 was €19.2 million versus a net loss of €4.0 million in the same quarter of 2007.
- Net cash from operating activities in the fourth quarter of 2008 was €61.5 million, compared to €51.5 million in the same quarter of 2007.
- Overall, the net increase in cash and cash equivalents in the fourth quarter amounted to €67.0 million, versus €56.3 million in the fourth quarter of 2007.
- In anticipation of the expected further growth of Quinvaxem<sup>®</sup> in 2009, Crucell continued to build stock of Quinvaxem<sup>®</sup> in the fourth quarter of 2008.

#### **Financial Highlights Full Year 2008:**

- Combined total revenue and other operating income for the full year 2008 of €283.3 million, compared to €213.1 in 2007. The increase of 33% (38% in constant currencies<sup>1</sup>) was largely driven by strong sales of paediatric vaccines, travel and endemic vaccines as well as higher license revenues.
- Crucell achieved profitability for the full year 2008, reporting a net profit of €14.6 million, compared to a net loss of €42.9 million reported 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.
- Operating cash flow of minus €0.3 million for the year, compared to €22.2 million in 2007, due to inventory build-up of Quinvaxem<sup>®</sup> for sales in 2009.
- Cash and cash equivalents increased by €7.7 million during the year to €171.0 million at year-end 2008.

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<sup>1</sup> Constant currencies = EUR/USD rate of 1.38



**Key Figures 2008:**

(€ million, except net result per share)

Fourth quarter			Full Year 2008		
2008	2007	Change	2008	2007	Change
93.7	75.9	23%	283.3	213.1	33%
Total revenues and other operating income					
19.2	(4.0)		14.6	(42.9)	
Net result					
0.29	(0.06)		0.22	(0.66)	
Net result per share (basic)					
Cash & cash equiv.:					
- Dec 31, 2008			171.0		
- Dec 31, 2007			163.2		

Crucell's Chief Executive Officer Ronald Brus said:

"I am very proud that for the first time in the history of our company, we achieved profitability for the year. Together with our strong revenue growth and cash position, we were able to end the year on a historic high.

Our core business is stronger than ever and, with a clear strategy for sustainable growth and more focused research and development activities, we continue to increase the number of people we can protect from infectious diseases.

For 2009, we expect another good year for Crucell. Our sense of shared purpose is stronger than ever, and we look forward to ongoing growth of our product sales as well as further progress of our pipeline programs."

**Product and Business Update**

**Product Update:**

Product sales in the fourth quarter of 2008 amounted to €76.5 million and represent sales of paediatric vaccines (51%), travel and endemic vaccines (23%), respiratory vaccines (17%) and other products (9%).

For the full year 2008, product sales were €226.1 million, representing sales of paediatric vaccines (49%), travel and endemic vaccines (25%), respiratory vaccines (14%) and other products (12%).



### Paediatric

Sales of our paediatric vaccines showed strong growth in the fourth quarter and the year 2008, mainly driven by Quinvaxem®.

- **Quinvaxem®**: Fully liquid pentavalent vaccine against five important childhood diseases.
- **Hepavax-Gene®**: Recombinant vaccine against hepatitis B.
- **Epaxal® Junior**: Paediatric dose (0.25mL) of Epaxal®, the only aluminum-free vaccine against hepatitis A for use in children. The product is currently registered in selected countries worldwide. Sales in South America are progressing well and a European launch is planned this year.
- **MoRu-Viraten®**: Vaccine for protection against measles and rubella (for all age groups).

### Travel and Endemic

Our travel and endemic portfolio showed solid growth in 2008. We continue to see significant untapped demand and potential for geographical expansion of our travel portfolio.

- **Epaxal®**: The only aluminum-free vaccine against hepatitis A.
- **Vivotif®**: The only oral vaccine against typhoid fever.
- **Dukoral®**: The only oral vaccine against cholera and diarrhea caused by ETEC (enterotoxigenic E. coli).

### Respiratory

In the fourth quarter of 2008, sales of our flu vaccine Inflexal® V were slightly down, compared to the same quarter of 2007 due to phasing into the third quarter of 2008.

- **Inflexal® V**: A virosomal adjuvanted vaccine against influenza (for all age groups). Due to the seasonality of the product, we build inventory in the first half of the year to sell flu vaccines in the second half of the year.

### Pipeline Update:

- **Flavimun® - Live Attenuated Yellow Fever Vaccine**: Registration submission of the Yellow Fever vaccine in Switzerland and Germany is expected in the first quarter of 2009.
- **Influenza - Seasonal Flu Vaccine** (FluCell collaboration with sanofi pasteur): This seasonal influenza vaccine is being developed by Crucell's partner sanofi pasteur, using PER.C6® technology. Phase II testing of the cell based influenza vaccine was initiated in the U.S. in November 2007. In the third quarter of 2008, Crucell received a milestone payment from sanofi pasteur for progress of the Phase II trials involving healthy adult volunteers in the U.S. The trials focus on the safety profile and immunogenicity of the cell-based vaccine.



- **Rabies Human Monoclonal Antibody Combination (CL 184):** Crucell's monoclonal antibody combination against rabies is being developed in close collaboration with sanofi pasteur using Crucell's PER.C6<sup>®</sup> manufacturing technology. In 2008 Crucell initiated two Phase II studies in the U.S. and in the Philippines. Promising Phase I data in 2007 showed no serious adverse effects and demonstrated the expected rabies neutralizing activity upon administration. The rabies human monoclonal antibody combination was granted a Fast Track designation by the FDA Department of Health and Human Services. Under the terms of the collaboration agreement with sanofi pasteur, Crucell will be responsible for manufacturing of the final product and has retained exclusive distribution rights in Europe, co-exclusive distribution rights in China and the rights to sell to supranational organizations such as UNICEF, while sanofi pasteur will have exclusive distribution rights for all other territories and co-exclusive distribution rights in China.  
This antibody combination is to be used in combination with a rabies vaccine for post-exposure prophylaxis (PEP) against this fatal disease.
- Positive preliminary results of our Phase II US study were presented to rabies experts at the 19th annual RITA meeting in Atlanta on October 1, 2008. These results triggered another milestone payment from sanofi pasteur at the end of September, as part of the total eligible amount of €66.5 million.
- A second phase II clinical study evaluating the monoclonal antibody combination in combination with a vaccine in healthy children and adolescents was conducted in the Philippines from May to October 2008. The completion of this study triggered another milestone payment from sanofi pasteur, at the end of October. Final data from this study are expected to become available in the first half of 2009.
- An additional phase II study in healthy adults evaluating Crucell's monoclonal antibody in combination with another major rabies vaccine is scheduled to start in India in the second quarter of 2009.
- **Tuberculosis Vaccine based on AdVac<sup>®</sup>/PER.C6<sup>®</sup> Technologies:** Development of the candidate vaccine AERAS-402/Crucell Ad35 is being carried out in collaboration with the Aeras Global TB Vaccine Foundation. Data from all AERAS-402/Crucell Ad35 trials support the immunogenicity and acceptable safety profile of the TB vaccine candidate at all dose levels evaluated.

#### Phase I:

- US Phase I trial in healthy adults not previously immunized with Bacille Calmette-Guérin (BCG), the traditional TB vaccine, has been completed and has demonstrated that AERAS-402/Crucell Ad35 is safe in this population.
- Results of a second study in South Africa showed encouraging results, notably CD8-cell immune responses that are much higher than those seen in humans in any previous TB vaccine study.
- A phase I study in healthy adults in St. Louis, USA focuses on the immunogenicity and safety of two AERAS-402/Crucell Ad35 boost doses administered at three to six month intervals after BCG priming in



healthy adults. Data from this study specifically indicate that two injections of AERAS-402/Crucell Ad35 are immunogenic with an acceptable safety profile when used with a BCG-prime/AERAS-402/Crucell Ad35 boost interval of 84 days in BCG vaccinated healthy adults. This immune response is greater than that detected in the absence of BCG prime, supporting the possible utility of AERAS-402/Crucell Ad35 as a booster vaccine. BCG prime alone shows limited efficacy.

- An ongoing study in St. Louis, USA is evaluating a longer prime-boost interval. The study has been fully enrolled and has discovered no safety issues. Immunological data is expected to be available in the first half of 2009.
- In October 2008, a Phase I clinical trial of the jointly developed TB vaccine was started in Kenya. The study is being conducted by the KEMRI/Walter Reed Project-Kisumu at their Kombewa Clinical Trials Center near Kisumu, in Western Kenya. Its main objective will be to test the safety of the candidate vaccine in BCG-vaccinated adults with or without latent tuberculosis. This study is fully enrolled and now in its follow-up segment, with no safety issues identified.

#### Phase II:

- In October 2008 enrollment for the first Phase II study of AERAS-402/Crucell Ad35 in Cape Town, South Africa was started. The study is being conducted by the University of Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Initiative. The candidate is being tested in 82 adults who have had active TB. No evidence of an unacceptable safety issue has been found in its dose escalation design.
- **Malaria Vaccine based on AdVac<sup>®</sup>/PER.C6<sup>®</sup> Technologies:** Crucell and its collaborator, the US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), are conducting a Phase I trial in the U.S. The study is being carried out at two sites, Vanderbilt University in Nashville, Tennessee and Stanford University in Palo Alto, California. The first three cohorts have been enrolled and ongoing safety monitoring has revealed no significant safety concerns to date, but formal analysis awaits unblinding of the data. Enrollment for the fourth and final group of volunteers is ongoing. Preliminary results of the first three cohorts are expected before the end of the first quarter of 2009. Further updates on this program will be communicated in our first quarter 2009 results.
- **Multivalent Filovirus (Ebola & Marburg) Vaccine based on AdVac<sup>®</sup>/PER.C6<sup>®</sup> Technologies:** In October 2008 Crucell announced that it has secured a NIAID/NIH contract aimed at advancing the development of Ebola and Marburg vaccines, ultimately leading to a multivalent filovirus vaccine. The contract provides funding of up to \$30 million, with additional options that may be triggered at the discretion of the NIH worth a further \$40 million. The Phase I study of an adenovirus 5 (Ad5)-based Ebola vaccine, being developed in partnership with the Vaccine Research Center (VRC) of the NIAID/NIH, showed safety and



immunogenicity at the doses evaluated. Based on these results, a second Phase I study of an Ebola and/or Marburg vaccine is anticipated. This will use alternative adenovirus vectors that are able to by-pass pre-existing immunity against Ad5.

- **HIV Vaccine based on AdVac<sup>®</sup>/PER.C6<sup>®</sup> Technologies:** The Investigational New Drug Application (IND) for Phase I of the trial with Harvard Medical School (supported by the NIH) was approved by the FDA in January 2008. In April, Crucell announced the start of a Phase I clinical study of the novel recombinant HIV vaccine, using adenovirus serotype 26 (rAd26) as vector, that Crucell is jointly developing with the Beth Israel Deaconess Medical Center. The rAd26 vector is specifically designed to avoid the pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5). The phase I clinical study is being conducted at the Brigham and Women's Hospital in Boston, USA and is focused on assessing the safety and immunogenicity of the vaccine. Enrollment is ongoing and involves 48 healthy volunteers. Dose escalation has proceeded without difficulty and the third cohort ( $10^{11}$  vp/dose) is currently enrolling subjects.
- **Alternative Adenovirus Serotype Technologies:** In November 2008, leading scientific journal *Nature* published a study that demonstrated the value of Crucell's alternative adenovirus serotype technologies. Using Crucell's AdVac<sup>®</sup> vaccine technology and PER.C6<sup>®</sup> manufacturing technology, scientists engineered the rare adenovirus serotypes Ad26 and Ad35 to express a protein of SIV, the non-human primate equivalent of HIV. Rare serotype adenoviral vectors – such as rAd26 and rAd35 vectors – have been developed by Crucell to provide more potent prime-boost vaccine regimens. The study, which investigated the immunogenicity and protective efficacy of different vaccination regimes using rAd26, rAd35 or rAd5 as a prime, followed by a boost with rAd5, showed that in particular the rAd26/rAd5 combination elicits a strong T-cell immune response and provides protection against the HIV-like virus in non-human primate models. Crucell has several vaccines in development using alternative rAd26 and rAd35 vectors, including vaccines against malaria and tuberculosis.
- **Human Monoclonal Antibodies against a broad range of Influenza:** Crucell's scientists discovered a set of human monoclonal antibodies that provides immediate protection and neutralizes the broadest range of H5N1 strains in preclinical models. When tested in preclinical models for prevention or treatment of a potentially lethal H5N1 infection, this antibody was shown to prevent death and cure the disease. In a preclinical study, Crucell's mAb CR6261 was compared with the anti-influenza drug oseltamivir in terms of their value for flu prevention and treatment. In December 2008 Crucell announced that its monoclonal antibody had strongly outperformed the most current anti-influenza drug in these tests. The results were presented at IBC's 19th Annual International Conference on Antibody Engineering in San Diego, USA.



The flu strains tested included the 'bird flu' strain H5N1, which, experts fear, has the potential to cause a pandemic, and H1N1, which is similar to the strain responsible for the devastating pandemic in 1918.

Importantly, the study showed that CR6261 provides immediate protection against the influenza virus, suggesting that it will be able to prevent disease spread. In contrast, oseltamivir was less efficacious and in some cases not effective at all. The characterization of the antibody was described in the online journal PLoS ONE on December 16, 2008.

- **Blood Coagulation Factor V<sup>L/c</sup>**: Preclinical work on this program continues but conclusive proof of concept is not expected in the near future.

#### **Korean Production Facility:**

- **Crucell** announced in October 2008 that an agreement was reached to relocate Crucell's Korean production facility from the Shingal site in Yongin City, Korea to the Incheon Free Economic Zone, Korea. All parties involved have agreed on the time line and conditions of this relocation, enabling a smooth transition to the new production facility. Construction activities at the new site have started and are well on track. The new facility will enable the further growth and efficient production of Quinvaxem<sup>®</sup> and Hepavax-Gene<sup>®</sup>. The investments in the new facility are expected to total approximately €50 million, with the majority of spend in 2009.

#### **Etna Biotech Srl:**

- **Crucell** announced in November 2008 the sale of its fully-owned subsidiary Etna Biotech Srl (Catania, Italy) to **Zydus Cadila** (Ahmedabad, India). The sale results in net proceeds for Crucell of several hundred thousand Euros. This transaction is in line with Crucell's increased focus on the strengths of its core business.

#### **The Crucell Ambition:**

In 2008, The Crucell Ambition program was rolled out throughout the whole organization and the management board has met with more than 60% of Crucell's employees from different parts of the organization. The Crucell Ambition is a strategic program encompassing coordinated efforts in four priority areas, which were carefully defined after a thorough review of Crucell's operations, objectives and potential. These are:

1. **ORGANIZATION & PEOPLE.** Development of our organization and our people is the foundation for achieving our ambition as a company. Multiple measures are being implemented to achieve this.
2. **FOCUS.** Crucell is clearly focused on its mission to protect lives from infectious diseases by bringing innovation to global health. We are building



on our strengths by prioritizing those programs that are in line with this ambition and that contribute to our strategic and financial objectives.

3. OPERATIONAL EXCELLENCE. Crucell launched its 'Healthy Ambition' operational excellence program at the start of 2008 and is now implementing the validated plans drawn up in the first half of the year. By streamlining and optimizing our business processes, the program is expected to generate cost savings of €30 million by the end of 2009.

4. DELIVER ON PROMISES. Crucell has set its sights high and is firmly committed to delivering on its ambitious promises. Evidence-based target setting and a company-wide emphasis on organization and people focus and operational excellence will enable us to do so.

Crucell's operational excellence program 'Healthy Ambition' was rolled out in 2008. The program is targeting savings of €30 million by the end of 2009; initial net cost savings of €5 million were achieved in the second half of 2008. The Operational Excellence program has positively contributed to the results through improved yields in our Korean production facility, savings in overhead and several other 'quick wins' delivered in 2008.

#### **Manufacturing & Licensing Agreements:**

- **Crucell** announced a non-exclusive PER.C6<sup>®</sup> research license agreement with Australian-based **Arana Therapeutics, Ltd.** for the production of monoclonal antibodies. Financial details of the agreement were not disclosed. [October 2008]
- **Crucell** announced a non-exclusive PER.C6<sup>®</sup> research license agreement with Australian-based **Abraxis Bioscience, Inc.**, for the production of proteins. Financial details of the agreement were not disclosed. [October 2008]
- **Crucell** today announces a non-exclusive PER.C6<sup>®</sup> research license agreement with Canada-based **Cangene Corporation** for the development of several undisclosed antibodies. Financial details of the agreement were not disclosed. [October 2008]
- **Crucell** announced a non-exclusive manufacturing, sales and distribution agreement with Berlin-based **Biochrom AG** related to the PERMEXCIS™ cell culture medium developed by Crucell for PER.C6<sup>®</sup> cells. Biochrom will manufacture the medium, and in addition will market and sell it in the European Union, Switzerland, Turkey, Russia and Israel. Financial details of the agreement were not disclosed. [November 2008]
- **DSM Biologics** and **Crucell** announced that Hungary-based **Gedeon Richter Plc.** signed a commercial license agreement allowing Gedeon Richter to develop and produce certain biopharmaceuticals on the PER.C6<sup>®</sup> platform. Other terms of the agreement were not disclosed. [November 2008]



- **Crucell** today announces a non-exclusive PER.C6<sup>®</sup> research license agreement with Netherlands-based **Synthon B.V.** for the production of biosimilar proteins. Financial details of the agreement were not disclosed. [November 2008]
- **Crucell** today announces a non-exclusive PER.C6<sup>®</sup> research license agreement with Norway-based **Affitech AS** for the development of several undisclosed antibodies. Financial details of the agreement were not disclosed. [November 2008]
- **Crucell** announced a second exclusive commercial license agreement with North Carolina-based **Talecris Biotherapeutics** for an undisclosed and specific protein and the exclusive rights to produce that protein using a PER.C6<sup>®</sup> cell line.  
Crucell will receive an upfront payment of \$1.5 million following the execution of the agreement and will be eligible for milestone payments of approximately \$20 million. Further financial details of the agreement were not disclosed. [December 2008]
- **DSM Biologics** and **Crucell** announced that Australia-based **CSL Ltd.** signed a license agreement allowing CSL to develop protein therapeutics for multiple undisclosed disease targets on the PER.C6<sup>®</sup> platform. Under the terms of the agreement, CSL is responsible for the development of protein and antibody products resulting from this alliance. Financial terms of the agreement were not disclosed. [December 2008]
- **DSM Biologics** and **Crucell** announced that **GlaxoSmithKline (GSK)** signed a research license agreement allowing GSK to research a recombinant protein on the PER.C6<sup>®</sup> platform. Financial terms of the agreement were not disclosed. [December 2008]
- **Crucell** today announces a non-exclusive PER.C6<sup>®</sup> commercial license agreement with Australian-based **Elm Biotech Pty Ltd**, managed by pharmaBank Pty Ltd, for the production of an adenovirus-vectored Gene Therapy product. Financial details of the agreement were not disclosed. [December 2008]
- **Crucell** today announces two non-exclusive PER.C6<sup>®</sup> commercial license agreements with Netherlands-based **ProFibrix B.V.** for the development of recombinant fibrinogen and a second undisclosed recombinant protein. Financial details of the agreement were not disclosed. [December 2008]



#### **Patents:**

In Q4 2008 Crucell was granted a total of 51 patents, including patents for:

- Different aspects of improved adenoviral AdVac<sup>®</sup> vectors and AdVac<sup>®</sup> technology, in New Zealand, Eurasia, and the U.S.
- Rabies virus–neutralizing antibodies, in Europe
- PER.C6<sup>®</sup> protein expression technology, in Japan and the U.S.
- Improved materials for use in MAbstract<sup>®</sup> technology, in Canada
- Improvements in PER.C6<sup>®</sup> expression technology, in Europe
- Virus purification technology, in Europe
- Antiviral compound screening using PER.C6<sup>®</sup> technology, in Europe

#### **Post Balance Sheet Events:**

- **Crucell** announced a non-exclusive STAR<sup>®</sup> research and commercial license agreement with Pennsylvania-based **Centocor, Inc.** for the production of monoclonal antibodies. Financial details of the agreement were not disclosed. [January 2009]
- On January 7th, 2009 **Crucell** announced that it was in friendly discussions with **Wyeth** regarding a potential combination of the two companies. On January 26th, 2009 Crucell announced that Wyeth withdrew from these discussions.

### **Financial Review**

#### **Total Revenue and Other Operating Income**

Total revenue and other operating income was €93.7 million for the fourth quarter of 2008, an increase of 23% compared to the same quarter of 2007 (22% in constant currencies<sup>2</sup>). The increase was driven by continued strong sales of paediatric, travel and endemic vaccines, as well as higher license revenues.

For the full year ending December 31, 2008, total revenue and other operating income was €283.3 million. In constant currencies this would have been €293.0 million.

Increase of license revenues was mainly driven by milestone payments for Crucell's rabies monoclonal antibody combination.

Product sales for the fourth quarter amounted to €76.6 million and represent sales of paediatric vaccines (51%), travel and endemic vaccines (23%), respiratory vaccines (17%) and other products (9%).

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<sup>2</sup> Constant currencies = EUR/USD rate of 1.38



License revenues were €9.1 million in the fourth quarter, an increase of €2.9 million compared to the same quarter of 2007. License revenues consist of initial payments from new contracts as well as milestones and other payments on existing contracts.

Service fees for the quarter were €4.0 million, compared to €5.0 million last year. Service fees represent revenue for product development activities performed under contracts with partners and licensees.

Other operating income was €4.1 million for the quarter, compared to €1.3 million in the fourth quarter of 2007.

#### **Cost of Goods Sold**

Cost of goods sold for the fourth quarter of 2008 amounted to €44.8 million, €42.6 million of which represents product costs and €2.2 million the cost of service and license activities.

Gross margins of 50%, compared to 34% in the fourth quarter of 2007. Gross margins in the fourth quarter of 2008 were positively influenced by an increase in product sales, license revenues and a positive currency impact as well as significant improvements in production performance.

#### **Expenses**

Total expenses consist of research and development (R&D) expenses, marketing and sales (M&S) and general and administrative (G&A) expenses. Total expenses for the fourth quarter were €36.6 million, representing an €1.7 million increase over the same period in 2007 (€34.9 million).

R&D expenses for the fourth quarter amounted to €19.1 million, which represents a €0.8 million increase versus the fourth quarter of 2007.

SG&A expenses for the quarter were €17.2 million, which represents a €0.8 million increase versus the fourth quarter of 2007.

Net financial income and expenses in the fourth quarter of minus €2.0 million were the result of foreign exchange losses mainly caused by fluctuations in the EUR/USD exchange rate.

The company recorded a €8.8 million income tax gain in the fourth quarter as a result of tax benefits in Korea and previously unrecognized carry forward losses in Switzerland.

#### **Net Result**

Net profit of €19.2 million was reported in the fourth quarter of 2008, compared to a net loss of €4.0 million in the same period of 2007. This amounted to €0.29 net result per share, compared to a net loss per share of €0.06 in the fourth quarter of 2007. The company reported a net profit of €14.6 million for the full year 2008 compared to a net loss of €42.9 million in the same period of 2007. This amounted to €0.22 net result per share, compared to a net loss per share of €0.66 for the full year of 2007.



### **Balance Sheet**

Tangible fixed assets amounted to €151.2 million on December 31, 2008. Intangible assets, representing assets through acquisitions, amounted to €79.0 million. This figure includes acquired in-process research and development, developed technology, patents and trademarks, and the value of customer and supplier relationships.

Investments in associates and joint ventures amounted to €9.2 million and mainly represent investments in AdImmune and the PERCIVIA PER.C6<sup>®</sup> Development Center. Crucell's investment in Galapagos NV is classified under available-for-sale investments.

Total equity on December 31, 2008 amounted to €453.5 million. A total of 65.8 million ordinary shares were issued and outstanding on December 31, 2008.

Investment in working capital increased significantly, mainly due to build-up of paediatric vaccine inventory, in anticipation of strong 2009 sales.

### **Cash Flow and Cash Position**

Cash and cash equivalents increased by €67.0 million in the fourth quarter to €171.0 million. Increase of cash flow and working capital in the fourth quarter was due to strong product sales and license revenues.

Net cash from operating activities in the fourth quarter of 2008 was €61.5 million. Overall investments in net working capital increased mainly due to inventory build-up of Quinvaxem<sup>®</sup> in anticipation of the significant growth of Quinvaxem<sup>®</sup> expected in 2009. Net cash used in investing activities in the fourth quarter amounted to €4.5 million. Net cash from financing activities in the fourth quarter amounted to €9.4 million.

### **Outlook 2009<sup>3</sup>**

- Crucell expects its combined full-year 2009 total revenue and other operating income to grow by 20% in constant currencies.
- Operating profit for 2009 is expected to improve significantly compared to 2008.
- Furthermore, the Company expects solid cash flow despite significant investments in the new facility being built in Korea. These investments are expected to total approximately €50 million, with the majority of spend in 2009.
- Crucell does not expect its businesses to be affected by the difficult markets envisaged in 2009.

**Phasing:** We expect revenues throughout 2009 to be phased similarly to those in 2008. The phasing of cash flow and working capital are expected to significantly deteriorate in the first half of 2009, which is normal due to the seasonality of our business. We build inventory in the first half of the year to sell our respiratory and travel vaccine products in the second half of the year.

<sup>3</sup> Guidance currency = EUR/USD rate of 1.35



## **Annual Report**

Crucell N.V. is currently finalizing the financial statements for the year ended December 31, 2008. We expect to be able to file our 2008 Annual Report on Form 20-F with the U.S. Securities and Exchange Commission as well as publish our Statutory Annual Accounts for the year 2008 before the end of April 2009. The consolidated balance sheet of Crucell N.V. as of December 31, 2008, the related consolidated statements of operations and consolidated statements of cash flows for the year ended December 31, 2008, and all quarterly information as presented in this press release are unaudited.

## **Forward-looking statements**

*This press release contains forward-looking statements that involve inherent risks and uncertainties. We have identified certain important factors that may cause actual results to differ materially from those contained in such forward-looking statements. For information relating to these factors please refer to our Form 20-F, as filed with the U.S. Securities and Exchange Commission on May 7, 2008, in the section entitled 'Risk Factors'. The Company prepares its financial statements under International Financial Reporting Standards (IFRS).*

### **Conference Call and Webcast**

At 14:00 Central European Time (CET), Crucell's management will conduct a conference call, which will also be webcast. To participate in the conference call, please call one of the following telephone numbers 15 minutes prior to the event:

+44 203 003 2666 for the UK;  
+1 646 843 4608 for the US; and  
+3120 794 8426 for the Netherlands

Following a presentation of the results, the lines will be opened for a question and answer session.

The live audio webcast can be accessed via the homepage of Crucell's website at [www.crucell.com](http://www.crucell.com) and will be archived and available for replay following the event.

## **About Crucell**

Crucell N.V. (Euronext, NASDAQ: CRXL; Swiss Exchange: CRX) is a global biopharmaceutical company focused on research development, production and marketing of vaccines, proteins and antibodies that prevent and/or treat infectious diseases. Its vaccines are sold in public and private markets worldwide. Crucell's core portfolio includes a vaccine against hepatitis B, a fully-liquid vaccine against five important childhood diseases and a virosome-adjuvanted vaccine against influenza. Crucell also markets travel vaccines, such as the only oral anti-typhoid vaccine, an oral cholera vaccine and the only aluminum-free hepatitis A vaccine on the market. The Company has a broad development pipeline, with several product candidates based on its unique PER.C6<sup>®</sup> production technology. The Company licenses its PER.C6<sup>®</sup> technology and other technologies to the biopharmaceutical industry. Important partners and licensees include DSM Biologics, sanofi-aventis, Novartis, Wyeth, GSK, CSL and Merck & Co. Crucell is



headquartered in Leiden, the Netherlands, with subsidiaries in Switzerland, Spain, Italy, Sweden, Korea and the U.S. The Company employs over 1000 people. For more information, please visit [www.crucell.com](http://www.crucell.com).

**Financial Calendar**

6 May 2009	Q1 Results 2009
5 June 2009	Annual General Meeting of Shareholders
11 August 2009	Q2 Results 2009
3 November 2009	Q3 Results 2009
9 February 2010	Q4 Results 2009

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## CONSOLIDATED STATEMENTS OF OPERATIONS

in EUR '000 (except per share data)

	12 months ended		Fourth Quarter	
	December 31,			
	2008	2007	2008	2007
	unaudited	unaudited	unaudited	unaudited
Product sales	226,055	177,569	76,539	63,529
License revenues	30,202	12,211	9,089	6,164
Service fees	10,900	14,006	3,965	4,981
<b>Total revenue</b>	<b>267,157</b>	<b>203,786</b>	<b>89,593</b>	<b>74,674</b>
Cost of product sales	-138,790	-124,557	-42,567	-45,857
Cost of service and license fees	-6,965	-10,327	-2,199	-3,429
<b>Total cost of goods sold</b>	<b>-145,755</b>	<b>-134,884</b>	<b>-44,766</b>	<b>-49,286</b>
<b>Gross margin</b>	<b>121,402</b>	<b>68,902</b>	<b>44,827</b>	<b>25,388</b>
Government grants	5,380	7,086	2,005	1,458
Other income	10,772	2,244	2,100	-184
<b>Total other operating income</b>	<b>16,152</b>	<b>9,330</b>	<b>4,105</b>	<b>1,274</b>
Research and development	-70,229	-63,995	-19,113	-18,291
Selling, general and administrative	-64,350	-61,752	-17,242	-16,454
(Reversal of) impairment	4,888	-171	-266	-171
<b>Total other operating expenses</b>	<b>-129,691</b>	<b>-125,918</b>	<b>-36,621</b>	<b>-34,916</b>
<b>Operating profit/(loss)</b>	<b>7,863</b>	<b>-47,686</b>	<b>12,311</b>	<b>-8,254</b>
Financial income & expenses	-2,662	1,378	-1,973	-199
Results investments non-consolidated companies	1,442	1,190	431	2,372
Disposal of subsidiaries	-367	0	-367	0
<b>Profit/(loss) before tax</b>	<b>6,276</b>	<b>-45,118</b>	<b>10,402</b>	<b>-6,081</b>
Income tax	8,310	2,208	8,797	2,062
<b>Profit/(loss) for the period</b>	<b>14,586</b>	<b>-42,910</b>	<b>19,199</b>	<b>-4,019</b>
Net profit/(loss) per share - undiluted	0.22	-0.66	0.29	-0.06
Weighted average shares outstanding - undiluted	65,593	65,103	65,778	65,324



## CONSOLIDATED BALANCE SHEETS

in EUR '000

	December 31	September 30	December 31
	2008	2008	2007
	unaudited	unaudited	unaudited
<b>ASSETS</b>			
<b>Non-current assets</b>			
Plant and equipment, net	151,206	150,220	145,525
Intangible assets	79,004	80,530	94,045
Goodwill	46,076	44,568	44,377
Investments in associates and joint ventures	9,239	8,515	9,070
Net pension asset	8,612	6,304	7,397
Available-for-sale investments	4,922	5,267	10,009
Other financial assets	14,920	13,960	16,153
	<u>313,979</u>	<u>309,364</u>	<u>326,576</u>
<b>Current assets</b>			
Cash and cash equivalents	170,969	103,923	163,248
Financial assets, short-term	1,761	0	0
Trade accounts receivables	40,108	64,826	47,563
Inventories	91,847	97,863	67,233
Other current assets	17,633	26,489	25,218
	<u>322,318</u>	<u>293,101</u>	<u>303,262</u>
<b>TOTAL ASSETS</b>	<b><u>636,297</u></b>	<b><u>602,465</u></b>	<b><u>629,838</u></b>
<b>LIABILITIES AND EQUITY</b>			
<b>Equity attributable to equity holders of the parent</b>			
Share capital	15,800	15,767	15,685
Other reserves	746,315	744,580	743,918
Translation reserve	-33,251	-37,387	-28,542
Accumulated deficit	-275,372	-294,571	-289,958
Total equity	<u>453,492</u>	<u>428,389</u>	<u>441,103</u>
<b>Non-current liabilities</b>			
Long-term financial liabilities	35,297	33,304	28,030
Long-term provisions	4,647	4,636	4,573
Deferred tax liabilities	16,985	27,703	29,267
Other non-current liabilities	7,645	8,889	12,123
	<u>64,574</u>	<u>74,532</u>	<u>73,993</u>
<b>Current liabilities</b>			
Accounts payable	59,205	45,903	50,970
Short-term financial liabilities	26,333	19,477	24,765
Other current liabilities	28,405	32,657	37,897
Tax payable	2,777	827	349
Short-term provisions	1,511	680	761
	<u>118,231</u>	<u>99,544</u>	<u>114,742</u>
<b>Total liabilities</b>	<b>182,805</b>	<b>174,076</b>	<b>188,735</b>
<b>TOTAL LIABILITIES AND SHAREHOLDER'S EQUITY</b>	<b><u>636,297</u></b>	<b><u>602,465</u></b>	<b><u>629,838</u></b>



## CONSOLIDATED STATEMENTS OF CASH FLOW

in EUR '000

	12 months ended		Fourth Quarter	
	December 31,			
	2008	2007	2008	2007
	unaudited	unaudited	unaudited	unaudited
<b>Cash flows from/(used in) operating activities</b>				
Profit/(loss) for the period	14,586	-42,910	19,199	-4,019
Reversal of non-cash items				
Tax	-8,310	-2,208	-8,797	-2,062
Results investments non-consolidated companies	134	996	-431	-186
Unrealized financial income and expenses	3,957	-1,378	3,346	28
Depreciation	16,629	14,453	4,670	3,766
Amortization	11,674	11,894	2,951	2,763
(Reversal of) Impairment	-4,888	171	266	171
Fair value write-down on Inventory	1,165	8,493	229	2,337
Change in long-term liabilities, receivables and provisions	-5,309	7,591	-2,939	10,462
Gain on disposal of non-current assets	-1,304	-2,236	445	-2,170
Stock based compensation	5,053	6,817	1,460	2,032
	<b>33,387</b>	<b>1,683</b>	<b>20,399</b>	<b>13,122</b>
Change in net working capital				
Trade accounts receivable	-912	8,583	16,223	1,146
Inventories	-37,121	-6,128	3,565	18
Other current assets	5,103	-615	7,489	-2,488
Trade accounts payable	15,978	16,274	20,884	34,581
Other current liabilities	-14,080	8,247	-6,912	5,395
Short-term provisions	654	-1,191	647	39
Interest paid	-2,684	-2,152	-898	-80
Income taxes paid	-576	-1,545	65	-497
Payments out of provisions	-3	-962	85	294
<b>Net cash from/(used in) operating activities</b>	<b>-254</b>	<b>22,194</b>	<b>61,547</b>	<b>51,530</b>
Cash flows from/(used in) investing activities				
Purchase of property, plant and equipment	-15,787	-27,043	-3,287	-8,594
Subsequent adjustments to goodwill	-237	0	-237	0
Proceeds from disposal of intangible assets	0	0	0	-11
Proceeds from disposal of Joint ventures	0	6,081	0	6,081
Acquisition/Disposal of subsidiaries net of cash	118	0	118	0
Proceeds from/(investments in) financial assets	2,604	-8,553	-2,639	-176
Interest received	4,395	5,274	1,561	797
<b>Net cash from/(used in) investing activities</b>	<b>-8,907</b>	<b>-24,241</b>	<b>-4,484</b>	<b>-1,903</b>
Cash flows from/(used in) financing activities				
Proceeds from issue of share capital	3,230	2,281	1,171	681
Proceeds from financial liabilities	35,732	10,309	10,569	7,931
Repayment of financial liabilities	-22,336	-1,346	-2,376	86
<b>Net cash from (used in) financing activities</b>	<b>16,626</b>	<b>11,244</b>	<b>9,364</b>	<b>8,698</b>
Effects of exchange rate on cash and cash equivalents	256	-3,786	619	-2,060
<b>Net increase/(decrease) in cash and cash equivalents</b>	<b>7,721</b>	<b>5,411</b>	<b>67,046</b>	<b>56,265</b>
Cash and cash equivalents at beginning of period	163,248	157,837	103,923	106,983
<b>Cash and cash equivalents at end of period</b>	<b>170,969</b>	<b>163,248</b>	<b>170,969</b>	<b>163,248</b>