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**Latest News**

[Crucell Equity Offering Priced at €14.50 per Share; €52.2 Million Raised](#)

[Single-shot Outbreak Vaccine Provides Full Protection Against Ebola According to Results of New Animal Studies](#)

[Crucell Announces First Quarter 2005 Results](#)

[Crucell and NIH Sign €21.4 Million Ebola Vaccine Manufacturing Contract](#)

[Crucell Receives US Patent Covering its STAR™ Technology](#)

[Crucell's Cell-Culture Technology to be Part of Major US Government Influenza Pandemic Vaccine Program](#)

[AFM Completes Investigation into Exercising of Options by Crucell Management](#)

[Crucell Secures Exclusive Patent License from NIH to Commercialise Ebola Vaccines](#)

[Crucell and NIH Extend Ebola Vaccine Agreement](#)

[Crucell Receives Patents Covering PER.C6® for Protein Production](#)

[Crucell Confirms Selection for Amsterdam Midkap Index on Euronext](#)

[Crucell Fully Compliant](#)

[Crucell Announces 2004 Annual Results](#)

[Crucell Joins Influenza Vaccine Supply \(IVS\) International Task Force](#)

[Crucell Announces Evaluation by Genentech of STAR™ Technology](#)

[Crucell Receives European Patent Covering PER.C6® for Vaccine Production](#)

**In perspective**

Crucell had a big year in 2004 and booked a number of successful deals. A quick look at the list of highlights in our Annual Results press release in January demonstrated just how much was achieved during the year, and it's clear that 2005 is set to be an even more crucial year in the evolution of Crucell. Three of our core vaccine programs are expected to enter clinical trials this year. This is what we have been working towards since we made our transition to a product-focused company, and in many ways it also marks the point where formal drug development begins.

We live in a world where our focus on infectious diseases is becoming increasingly relevant. Recent weeks have seen this emphasized once again with an outbreak in Angola of the deadly hemorrhagic fever Marburg, a close relative of Ebola. Of 337 cases, 311 have been fatal. This comes at a time when Crucell's Ebola, Marburg and Lassa vaccine collaboration with the VRC and USAMRIID has been extended and boosted by positive new study results and the signing of a US\$ 27.6 million manufacturing contract with the NIH. Crucially, we have also secured an exclusive license to certain patents of the NIH for the development and commercialization of recombinant vaccines against Ebola.

The Marburg crisis follows hard upon the death of a number of people in South-East Asia from the deadly H5N1 bird flu, which is considered a significant pandemic threat (see article later in this newsletter for further details). Also, consecutive flu seasons in the northern hemisphere have seen the supply of vaccines substantially compromised. In 2004 we began with the development of PER.C6®-based vaccines for epidemic and pandemic flu with Sanofi Pasteur. In 2005 we find ourselves in a fast-growing flu market where cell-based competition is taking shape. Our human-cell production system appears to have a number of important advantages over other cell-based systems in terms of manufacturing characteristics. While risk is inherent in our industry, we believe we have reduced that risk by working together with the world leader in flu vaccines, as evidenced by the recent \$97 million grant the Sanofi-Crucell collaboration received from the HHS in the US. Our emphasis on developing our production process has also set us apart from our competitors, and we have prepared ourselves carefully each step of the way. Now, together with our efforts on Ebola and West Nile virus, work on our flu program is entering a critical phase. We believe we are well prepared, and it promises to be a challenging and rewarding year for Crucell.

Ronald Brus  
President & CEO

## Latest Licensing Deals

[Crucell and DSM Announce PER.C6® License Agreement with Ferring Pharmaceuticals](#)

[Crucell Announces PER.C6® Licensing Agreement with Vascular Biogenics](#)

[Crucell and DSM Announce PER.C6® Licensing Agreement with Mitsubishi Pharma for Protein Production](#)

[Crucell Signs Commercial PER.C6® License Agreement with SingVax for Vaccines Against Japanese Encephalitis](#)

[Crucell and DSM Announce PER.C6® Licensing Agreement with JCR Pharmaceuticals for Protein Production](#)

[Crucell and DSM Announce PER.C6® Licensing and Service Agreement with Roche for Protein Production](#)

## Upcoming Events

We keep a current listing of important shareholder news and events at [www.crucell.com](http://www.crucell.com), in the [Investors section](#). Here are just a few of note in coming months:

- CFO Leon Kruimer will be presenting at the Fourth Annual Needham & Company Biotechnology Conference in New York on May 26, 2005, at 9.30 AM. A live webcast of his presentation will be available via [www.crucell.com](http://www.crucell.com).

- Crucell's [Annual General Meeting](#) of Shareholders will convene on June 2, 2005, at 14.00, Hilton Hotel, Apollolaan 138-140, Amsterdam.

- Crucell will be presenting at the Biotechnology and Pharmaceuticals forum in New York on June 15, 2005. Click [here](#) for details.

- Crucell's Q2 Results will be announced on July 18, 2005, at 2 pm CET. A conference call will take place 30 minutes later, and a live audio webcast will be available via the home page of the [Crucell website](#).

- Upcoming Company visit days for investors will take place at our Leiden headquarters on 9 June, 14 June (full), 13 September (full) and 13 December. Please contact Femke van Egmond ([f.vanegmond@crucell.com](mailto:f.vanegmond@crucell.com)) if you are interested in attending.

[Read more>>>](#)

## Leonard Kruimer: Forward thinking

Crucell's Full-Year Annual Results announced on January 24 marked 2004 as the strongest year in the Company's four years as a public company. Revenues reached € 22.6 million (US\$ 30.9 million), a three-fold increase on 2003, and cash burn hit an all-time low of 10.5 million (US\$ 14.3 million). The announcement of the Company's Q1 results in April constituted a strong start to the new year. CQR asked Chief Financial Officer Leonard Kruimer what lies ahead as Crucell looks to continue its success in 2005.



**CQR:** You well-and-truly met your 2004 cash burn guidance of € 10-15 million in 2004, as revised at Q3, and now you have recorded a positive cash flow in Q1 2005. Looking ahead, what is your guidance for cash burn in 2005?

**LK:** We expect cash burn in 2005 to increase over the level of 2004, driven by our progress in clinical development. While this is the case, it remains our intention to maximize cash receipts from licensing, service fees, partnerships and grants. Consequently we expect cash burn to be in the range of € 15 to 20 million.

**CQR:** What impact are clinical trials likely to have on future financial results?

**LK:** It is reasonable to expect costs to increase once clinical trials begin. We've included this in our cash burn guidance for 2005, and we have financing in place to achieve this in 2005.

**CQR:** What impact will the Company's inclusion in the Euronext Midkap index have on the company in 2005?

**LK:** Our candidacy for this index is based on full-year 2004 turnover of shares in euros, so it's another reflection of the strength of our performance in 2004. The reward will be that Crucell can expect to get more attention from the market and the media as a result of a Midkap index listing.

**CQR:** IFRS reporting standards come into effect in 2005. How do you envisage this will impact Crucell's reporting?

**LK:** We don't expect to see much impact, as we've always reported under US GAAP and the differences between US GAAP and IFRS are minimal. We will continue to report under US GAAP.

**CQR:** Crucell issued 3.6 million new shares on May 10. What will the money be used for?

**LK:** The cash reserves we have are allocated to finance the development of our existing vaccines (flu, West Nile, malaria and Ebola) over the next few years and will enable us to reach cash break-even. If we take money out of those reserves to fund other programs, it creates extra risk for successful vaccine development later on.

We raised new money to fund development of certain proteins and our antibodies, and to accelerate the development of our STAR™ technology. Now we are in a position to decide on in-house development, rather than give a large part of the upside away to a partner. The funds have significantly strengthened our cash position and balance sheet, and have therefore reduced our risk. We were able to bring new large long-term value-oriented investors in as shareholders.

[Click here>>>](#) to listen to Leonard Kruimer's presentation at the 4th Annual Needham & Company Biotechnology Conference in New York today, May 26, 2005, at 9.30 AM Eastern time (3.30 PM CET). The webcast of this presentation will be archived for a period of 90 days.

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#### **Crucell Fully Compliant**

Crucell pro-actively requested the Netherlands Authority for the Financial Markets (AFM) to investigate the exercising of options by members of Crucell's Management and Supervisory Boards on January 18, 2005, after press publications questioned the fact that this had occurred during a closed period.

The AFM's investigation did not reveal that insider trading had occurred. The decision to exercise had in fact been made on November 11, 2004, two months before the expiration of the options in question and prior to the closed period, as dictated by Crucell's internal code and all applicable securities laws and regulations in the Netherlands and the US.

While this is the case, and despite Crucell's full compliance with legislation governing the exercising of options during closed periods, the Company has decided, with the benefit of hindsight, to eliminate future doubts by deciding against the exercising of options during any subsequent closed periods.

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#### **Bird flu: Why is it a pandemic threat?**

International influenza experts have long suggested that a flu pandemic is inevitable, and in recent years their warnings have focused on outbreaks of Avian (bird) flu in Asia. In fact, we've heard such predictions of pandemic catastrophe so frequently now that there is a danger of becoming blasé about them.

The signs, however, would seem to indicate that it certainly doesn't pay to be complacent about bird flu. In the 16 months since January 2004, 97 cases of the Avian Influenza A strain known as H5N1 have been recorded in Thailand, Vietnam and Cambodia, with 53 resulting in death – a 55%

mortality rate.

Almost all cases to date have been traced back to direct contact with infected birds, and the spread of the disease has been curtailed by the culling of millions of chickens, ducks and other birds throughout Asia. However, the fear is that the virus will mutate into a form capable of human-to-human transmission. Should this occur, the world could be confronted with a threat of pandemic proportions.

All type A influenza viruses are perpetually undergoing change, necessitating the annual update of flu shots to cover prevailing strains. But they can also swap or "reassort" genetic material and merge with other subtypes, including those from different species, resulting in a new subtype to which populations have no immunity. Historically, this has resulted in pandemics such as the 'Spanish Flu' outbreak of 1918-19, which killed as many as 40 million people worldwide. The event scientists now fear is the infection with H5N1 of an individual also infected with a human strain of influenza. A hybrid strain, able to be directly transmitted between humans, could then result. Pigs are also susceptible to both mammalian and avian viruses, and may serve as a "mixing vessel" for the emergence of a novel influenza subtype.

Recent alarming reports from Thailand suggest human-to-human transmission may already have happened in at least one isolated case last fall. An 11-year-old girl appears to have passed the disease to her mother and her aunt. Both the mother and daughter died.

While at this point there is no real way of knowing how lethal H5N1 might become if it adapted for human transmission, governments around the world are being urged to take steps for pandemic preparedness. The preparation of vaccines is clearly a major priority in this regard, and the limitations of current flu vaccine production are cause for concern. New vaccines that can be easily and quickly produced for all flu virus strains are urgently needed.

Cell-based production could play an important role in meeting the demand that a pandemic will create – a demand that egg-based production cannot meet. For the Crucell-Sanofi Pasteur collaboration on PER.C6®-based epidemic and pandemic flu vaccines, 2005 promises to be a significant year, with clinical trials for our vaccine candidates set to begin in Q3. In furthering our programs, we aim to make a major contribution to the world's defences against a possible flu pandemic.

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### **Questions from shareholders**

**Q.** Why is Dinko Valerio not joining the Supervisory Board?

**A.** It was jointly concluded that, rather than be subject to the restrictions of a formal role as a member of the Supervisory Board, Dinko Valerio's contribution to the Company's growth would best be served in an advisor's capacity. He has now been appointed in an advisory role for a period of four years.

**Q.** I have heard that CRXL shares are subject to 'Passive Foreign Investment Company' (PFIC) tax rules for US investors. Apparently, to avoid the PFIC taxation regime, I need to elect Crucell as a 'Qualified Electing Fund'. Could you provide the necessary details?

**A.** We do believe we are a PFIC in the year 2004. The required PFIC statement regarding Crucell N.V. and its subsidiaries for the fiscal year ended December 31, 2004 is available on the Crucell website in the Investors section, under 'Shareholder Services'. Shareholders are recommended to consult their tax advisor before taking any action concerning PFIC rules.

**Book Winners!**

In the last issue of Crucell's Quarterly Review we offered subscribers the chance to win signed copies of Jaap Goudsmit's Viral Fitness. Congratulations to the following readers:  
L. Potash; H. Keyner; B. Greydanus; P. de Gier.



**Questions, Suggestions, Remarks? Please contact Crucell:**

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This newsletter 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 February 27, 2004, and the section entitled "Risk Factors". The company prepares its financial statements under generally accepted accounting principles in the United States (US GAAP).

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