



Quarterly Review

Volume 1, No. 3- October 15, 2004

The investor newsletter with the latest news and views from Crucell

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Latest News

- [Crucell Reports Third Quarter 2004 Results](#)
- [Crucell Initiates Legal Proceedings Against CEVEC Over PER.C6® Patent Infringement](#)
- [Crucell Receives Two European Patents Covering its PER.C6® and AdVac® Technology](#)
- [Aviva / Delta Lloyd Acquires 5.09% Interest in Crucell](#)
- [Crucell Grants IAVI Exclusive License to use AdVac® Technology for AIDS Vaccine](#)
- [PER.C6®-produced HIV Vaccine Progresses Towards Next Phase](#)
- [Crucell and Harvard Medical School Announce Promising Results for Novel Vaccine Technology \(AdVac®\)](#)

Upcoming Events

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

- CFO Leon Kruimer will present at the Rodman & Renshaw Techvest 6th Annual Healthcare Conference in New York, October 26-28, 2004
- Analyst Meeting, New York, November 16, 2004. A webcast will be available via www.crucell.com
- Crucell will attend the Euronext Small and Midcap Event in Paris, November 17, 2004
- ING 4th Annual European Healthcare Conference, London, December 7, 2004
- Year End 2004 Results, January 24, 2005. A video webcast will be available via www.crucell.com
- The Company visit set for December 7 is now full. The next Company visit day for Investors will take place at our headquarters in Leiden on

In perspective

Crucell and its partners have made big strides in core programs during 2004. Just as significantly, we are also adding strings to our bow. Earlier in the year, Aeras, the Global TB Vaccine Foundation, agreed to fund Crucell's early-stage TB vaccine development right up to the clinic. Now, during the third quarter, we have signed a license agreement with IAVI, the International Aids Vaccine Initiative, to develop an AIDS vaccine based on our AdVac® technology. By adding this to our support of Merck's PER.C6®-based HIV vaccine candidate, our technologies are now supporting two major programs in the fight against AIDS. With HIV joining our efforts on flu, Ebola, malaria, TB and West Nile, we are now involved in virtually every important vaccine initiative worldwide. Clearly, Crucell is quickly demonstrating how seriously it takes its mission: to become the leading biotechnology company developing products to prevent and treat infectious diseases. As the current crisis regarding the supply of flu vaccines in the US emphasizes, new players and new technologies are sorely needed. Crucell's technology looks increasingly likely to play a significant role in shoring up human defences against disease where it is most needed. Many people stand to benefit from our growth, not least of all, of course, our investors.

Jaap Goudsmit
Chief Scientific Officer

INVESTOR SURVEY – win a copy of Jaap Goudsmit's new book!

With this issue of Crucell's Quarterly Review we are including a short survey for investors to complete. Clearly, it is very important to Crucell that our investors are given the opportunity to provide feedback regarding the quality of information and service we provide, and such

March 15, 2005

Financial snapshot

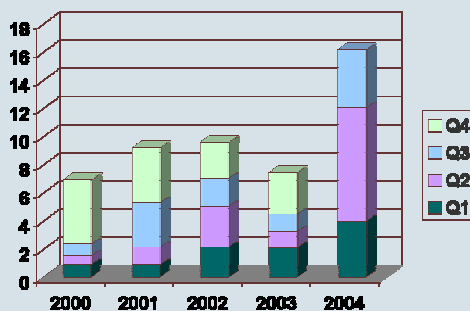
Key figures Third Quarter 2004 (€ million, except net loss per share)

	Q2 2004	% Change	Q2 2003
Revenues	4.1	242%	1.2
Net loss	(5.5)	24%	(7.2)
Net loss per share (basic and diluted) (0.15)	25%	(0.20)	

Cash and cash equivalents on:

September 30, 2004	81.5
December 31, 2003	87.2

Revenues per quarter (€ million)



feedback is helpful in informing and improving our efforts in the future.

The survey is an easy-to-complete online form and will require less than 5 minutes of your time. It can be accessed by clicking on the following link: <http://survey.crucell.com>. Each respondent before November 1st will also go into a draw to win one of five signed copies of Jaap Goudsmit's new book, [Viral Fitness](#).

Leon Kruimer: A Strong Third Quarter

As this week's third quarter results showed, Crucell is on course for the strongest financial year in its history. Revenues are up and cash burn has been revised downward for the second successive quarter. CQR asked Leon Kruimer, Chief Financial Officer, to explain what lies behind these trends.



CQR: Leon, this has been a financially successful quarter. Why did revenues increase so significantly?

LK: The increase results from an increase in licensing revenues and service fees from collaborative agreements. This is a reflection of our core business model which focusses on growing our licensing revenue while also pursuing the selective partnership initiatives we have secured for the majority of our programs. This has put external funding behind our programs and also pooled our expertise with that of our collaborators, shoring up our financial position while simultaneously boosting the progress of development. In addition, the third quarter also saw Crucell receive more subsidies than it did in the same period in 2003.

CQR: Why did you revise your cash burn guidance?

LK: Our strong revenues to date and modestly increasing costs caused our investment in the business to be much lower than projected. That is why we revised our cash burn estimate at mid-year for the first time and why we now revise it for a second time.

CQR: Why did Crucell revise its cash burn again so soon? Couldn't you have foreseen this at the

first half results?

LK: Our revenues result from deals we sign with licensees and partners we work with. Product development agreements in particular tend to be complex multi-year deals. Often, we can only predict the revenues and cash flows associated with these deals once they are in the final stages of negotiation. We have signed a number of these deals this year. We tend to be conservative in our projections to the market, but we feel that the results to date warrant this positive revision.

CQR: Why did R&D expenses decrease compared to the third quarter last year? One would expect these to be higher, given your progress towards the clinic and broadening of the number of programs running.

LK: We initially expected the costs for research conducted externally to be higher, but we managed to get a higher-than-expected proportion reimbursed or carried out by others. Again, we have been successful during 2004 in attracting external partners who have committed to funding a significant portion of our development costs leading up to the clinic. Crucell is very strongly positioned as a result.

CQR: Given Crucell's continuing strong financial performance and the ongoing expansion and progress of your development programs, are you satisfied with the Company's current share price?

LK: Share price is for the market to determine. Certainly, 18 months ago our shares traded at about 50% of cash value, a situation not uncommon in Biotech, but it was a valuation we were not happy with. It wasn't a fair reflection of our progress, but since then the value of the Company has increased more than four-fold. Clearly, that's a better reflection of what we've achieved. We aim to keep the investment community well-informed of our progress so it can make up its own mind as to our value. As long as our performance continues to impress, and we intend to ensure that it does, it will no doubt be reflected by the market.

Meeting the AIDS Vaccine Challenge

A highlight of Crucell's third quarter was the license agreement signed with IAVI for the development of an AIDS vaccine based on our AdVac[®] technology. IAVI is a donor-funded, not-for-profit organization devoted to accelerating the development of a vaccine to

prevent HIV infection and AIDS. It also works to ensure that a vaccine will be accessible to everyone who needs it. In the past five years, IAVI has helped advance five different AIDS vaccine candidates from the concept stage to human trials.

There are a number of reasons why a vaccine for AIDS has been so difficult to develop. HIV is one of the most complicated viruses ever identified. It continually mutates and recombines, and it is not yet known whether a single universal vaccine to protect against all subtypes is possible. HIV infects helper 'T' cells, the immune cells that orchestrate the immune response, thereby targeting and destroying the very immune system that a vaccine traditionally triggers. Further, researchers lack an ideal animal model for testing, and do not know what constitutes an effective immune response to HIV. It may be antibodies, activated immune cells, a third immune response or even a combination of immune responses.

There are a number of programs underway globally for the development of an HIV vaccine. Of these, VaxGen's gp120 recombinant subunit vaccine recently completed Phase III efficacy trials but unfortunately failed to demonstrate efficacy. Aventis' canary pox recombinant viral-vectored vaccine is also undergoing efficacy trials in Thailand at present, using VaxGen's gp120 in a prime-boost regimen.

Merck's adenovirus-vectored vaccine produced on Crucell's PER.C6[®] is the other vaccine to have progressed beyond phase I trials. The use of adenovirus vectors shows considerable promise in this field. As such, Crucell's AdVac[®] technology is an important tool as it has demonstrated the ability to overcome the problem of pre-existing immunity that has hampered vaccines employing the most commonly used vector, serotype 5. Crucell is proud to be able to contribute to the fight against HIV and is confident that with IAVI and Merck, our technologies now support two major programs well positioned to bring an AIDS vaccine to market.

What's the fuss about flu?

Influenza vaccines are big news at the moment. With the US suffering a high-profile crisis of short supply last season, Chiron, the second largest manufacturer of flu vaccines, had its license suspended this month on the eve of the

new season. The US is now facing the annual influenza epidemic having lost almost 50% of its vaccine supplies.

While there is very little information regarding the cause of the contamination of Chiron's vaccine batch, the incident has once again brought to the fore discussions of alternative technologies for flu vaccine production. Primarily, this involves a new generation of vaccines based on mammalian cell lines, such as PER.C6®.

Crucell's PER.C6® production technology makes use of human cells to grow the influenza virus in large bioreactors. The virus is then inactivated and purified for use in a vaccine. The current



flu vaccine process is essentially the same, except chicken eggs are the approved substrate. The use of a fully human technology such as PER.C6® may lead to a purer product of higher quality, and a more stable production process. Also, cell-based production could cut weeks from production schedules that currently require more than six months to get the product to market.

The global market leader for Flu vaccines is Aventis Pasteur, which holds a market share of about 40%. Clearly, Aventis-Pasteur wants to stay on top of the latest developments and make use of the most modern technologies available. The fact that the number one producer of egg-based influenza vaccines has chosen to work with Crucell's human cell production technology is recognition of the fact that future demands and improving technologies will both require and enable improvements to egg-based production.

While much work needs to be done before influenza vaccines based on PER.C6® – or any other cell based technology – can be commercialized, a key component will be compliance with FDA requirements, which have yet to be fully identified. Crucell and Aventis will provide an update on the progress of the flu program at the Crucell Analyst Meeting to be held in New York on November 16.

Questions from the Quarter

Q. What is CRXL's patent strategy?

A. On October 6, Crucell was granted two European patents for its PER.C6[®] and AdVac[®] technologies. This brought our European patent position in line with our already strong position in the US. Subsequently, the Company initiated legal proceedings against CEVEC, a German company that has attempted to establish a human cell line similar to PER.C6[®]. Crucell contends that an infringement of our PER.C6[®] patent has occurred.

Crucell has a strategy of improving our technology and then applying for patents on these improvements. By continually applying for new patents, we add to the depth and length of the protection around our technologies. We employ an in-house team of intellectual property specialists that continuously build, manage and defend our patent portfolio, and provide full support to its value extraction by employing strategies of licensing, partnering or, if necessary, lawful enforcement.

Q. You claim that products have advanced toward the clinic. What progress has there been in product development?

A. We have made progress in all product programs this quarter. For example, we now know that the candidate flu strains for the coming season grow well on PER.C6[®] cells. We plan to disclose our plans and progress in more detail during the Analyst Meeting to be held in New York on November 16. This event will be webcast at 8.30 am EST in the US / 14.30 pm CET. The webcast will be accessible via the home page of the Crucell website:

www.crucell.com.

Don't forget to complete the Investor Survey!

<http://survey.crucell.com>



Questions, Suggestions, Remarks? Please contact Crucell

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