



Quarterly Review

Vol. 2, No. 2 - Sept. 20, 2005

The investor newsletter with the latest news and views from Crucell

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Latest Licensing Deals

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In perspective

In 2003, Crucell successfully completed its transition from an enterprise focussed on technology to a company dedicated to the development of its own vaccine and antibody products. It was a significant progression for our business, and one that was further consolidated during 2004 as we secured a number of important partnerships across our vaccine development portfolio.

But as our mission statement suggests, vaccines are only one part of the Crucell story. In 2004, our Antibody Discovery Group announced two important achievements with the discovery of antibodies for protection against both SARS and rabies. We have just announced our development plans for our rabies antibody product, which combines two human monoclonal antibodies, and in the meantime we've been able to announce the discovery of an antibody against West Nile virus, complementing our West Nile vaccine program.

These are all exciting developments and they represent one part of our business set to benefit from the institutional share placement of May 10, which raised more than € 50 million. Crucell's existing cash reserves were committed to taking our vaccine programs through clinical trials. New opportunities, no matter how promising, should not compromise this stated commitment. Now, however, we believe we are even better positioned to take full advantage of these and other exciting new developments at Crucell. We are able to fully realise the potential of our expanding product and technology portfolio.

Crucell is an ambitious company. Part of our strength comes from our dedicated focus on fighting infectious diseases and our commitment to taking each of our existing core product programs to market. Now, we are in a position to further expand and strengthen our business and fulfil the potential offered by our technologies without distilling that core focus. As we look ahead it promises to be an exciting and rewarding time to follow Crucell's progress, and we thank you for your support.

Ronald Brus
President & CEO

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 coming months:

- Crucell will be presenting at the UBS Global Life Sciences Conference in New York between 26-29 September, 2005. [Click here](#) for further details.

- Crucell's Q3 Results will be announced on October 17, 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](#).

- Demand for placements at Crucell's Investor Visit days is high and all places for 2005 are now fully booked. We endeavour to fulfil all requests for participation and new dates for 2006 will be announced on [the website](#) as soon as possible.

Financial snapshot

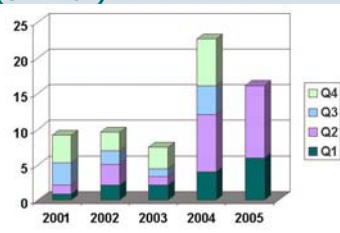
Key Figures First Half 2005 (€ million, except net loss per share)

	H1 2005	% change	H1 2004
Revenue	16.1	34%	12.0
Net loss	(8.7)	(4%)	(9.1)
Net loss per share (basic and diluted)	(0.23)	(8%)	(0.25)

Cash and cash equivalents on:

June 30, 2005	120.3
December 31, 2003	76.7

Revenues per quarter (€ million)



Leonard Krumer: Half-year 2005

Crucell's Q2 results, [announced on 18 July](#), continued to demonstrate the strong growth in revenue achieved throughout 2004 and Q1 2005. CQR asked Chief Financial Officer Leonard Krumer to elaborate on the Company's first half-year success.



CQR: Revenues for the first half of 2005 were up € 4.1 million on the first half of 2004. Where is this growth coming from?

LK: It's happening across the board, as you can see our licensing revenues and government grants both experienced some growth in the first six months of this year. However, the biggest revenue increase comes from the € 3 million increase in service fees, which climbed to € 5.1 million for the half-year. That is related to the increased level of development activities we perform for partners in return for payment.

CQR: Excluding the proceeds of the May share placement, second quarter cash burn exceeded € 10 million, but you still maintain guidance for a € 15 – 20 million cash burn for the full year. Does this mean you foresee a limited cash burn for the second half of 2005?

LK: Our guidance for cash burn of € 15-20 million compares to a cash burn of just over € 10 million last year. That increase reflects a much higher level of development work. However, we get paid for a lot of that work, such as our work with Sanofi on flu and the US Army on Ebola. Looking ahead, this level of activity will remain high, and is likely to increase if anything. It also remains our intention to maximize cash receipts from licensing, service fees, partnerships and grants. We will likely decide to step up our work on antibodies and proteins. If we do we may exceed our original estimate, but that will be funded by the May share placement. As such, we're still comfortable with our stated cash burn guidance.

CQR: Did the second quarter results include any inflow from the flu and Ebola contracts?

LK: No. The way those contracts work is basically that we get payment from our partners based on the work that we do. Essentially, we act as a subcontractor. As such, the way to look at a grant such as that won by Sanofi Pasteur for flu is to look at it as a sort of letter of credit from the US government that can be called upon if you have performed work. So, it's not something that will come in evenly over time, but rather it will come 'piecemeal' for work performed, which is very attractive from a revenue perspective as it adds to our revenues over a substantial period of time.

CQR: The Q2 results included reference to a second milestone from the DSM alliance. Are there any more milestones pending in the second half of 2005?

LK: There will be no further DSM milestones this year. This was a milestone for achievements under an existing contract.

West Nile Virus: Here to Stay?

Before 1999, West Nile virus was just another neglected tropical disease that had never been encountered in the western hemisphere. But in the space of five seasons it spread from the east coast of the US to the west, with human cases reported in practically all of the mainland states. It is transmitted to humans and some animals via the bite of mosquitoes that have fed on infected birds, which act as the reservoir for the virus – hence the rather foreboding demise of birdlife that heralds the arrival of a new West Nile season. Season 2005 has now begun.

While 80 percent of people infected with the virus will show no symptoms at all, 20 percent will develop 'West Nile Fever', a disorder including fever, headache, body aches, skin rash and swollen lymph glands. One in every 150 will develop more severe forms of the illness known as West Nile encephalitis or meningitis, inflammations of the brain that can result in tremors, convulsions, paralysis, coma and, in the worst cases, death. Will West Nile virus disappear as quickly as it arrived in the US, or is it here to stay?

Since it first hit the headlines in New York in the summer of 1999, more than 17,000 Americans have been reported as suffering from mild or severe disease, with the death toll now approaching 700. The vast majority of cases have occurred in the past three seasons. More than 250 deaths occurred in both 2002 and 2003, and while that figure dropped to 100 in 2004, health authorities are now bracing themselves for another possibly difficult year. More than 800 cases have already been reported this season, including 18 deaths, with California and Louisiana being among the hot spots. California's State Department of Health Services reports that more mosquitoes are infected with the virus than last year, when the state was the most heavily affected in the country.

The drop in cases reported during 2004 may indicate that Americans are learning the important lessons of West Nile prevention: wearing insect repellent, installing screens on doors and windows and removing any standing water around houses that may afford mosquitoes the sites they need to lay their eggs. But with little to indicate that the virus is on its way out, the development of vaccines and medicines to prevent and treat the disease is still a top priority. It is a point

further emphasised by the first signs of the disease emerging in Europe. Cases reported in France in recent seasons were followed by Britain's first travel-related cases last year, with two Irish tourists to Portugal's southern Algarve region bringing West Nile home. Evidence that the virus is present in UK birds has also recently emerged for the first time.

In June, Crucell announced that it has discovered an antibody for protection against West Nile virus. This adds to the existing vaccine program that is heading towards clinical trials. While the vaccine will be targeted at preventing infection in the elderly population most at risk of developing the most severe form of the disease, the antibody may be applied post-infection in specific cases to prevent the potentially fatal onset of encephalitis. Crucell believes these complementary programs can make an important contribution in countering this emerging threat.

What is AdVac®?

Crucell's AdVac® technology has once again risen to prominence this month with two significant announcements. Firstly, Crucell's collaboration with Harvard Medical School, which has been focussing on the development of AdVac® for the past two years, received a US\$ 19.2 million grant from the National Institutes of Health (NIH) for the development of new AdVac®-based vaccines against HIV/AIDS. A fortnight later, a Cooperative Research and Development Agreement (CRADA) was signed with the US Navy for the development of biodefense vaccines against Anthrax and Plague. This agreement follows similar lines to the Ebola program conducted with the Vaccine Research Center (VRC) of the NIH.

AdVac® technology is already at the centre of Crucell's malaria vaccine program and was also licensed by the International Aids Vaccine Initiative (IAVI) last year for the development of AIDS vaccines. So, what exactly is AdVac® and what are its advantages?

AdVac® employs adenoviruses as 'vectors', or delivery agents for immunogenic material aimed directly at the immune system. Adenoviruses, a group of viruses causing upper respiratory diseases including the common cold, are particularly useful as vectors because they can be easily manipulated for the insertion of genetic material and can be easily and cheaply produced on a large scale for manufacturing. One or more genes from the virus are deleted and replaced by segments of DNA encoding proteins of the target disease. The result is a replication-incompetent vector in the guise of a virus capable of entering human cells. Antigens can then be introduced to the immune system without actual infection taking place.

Such an approach has been the most successful to date in providing hope for an AIDS vaccine. Merck has taken its adenoviral-vectored HIV vaccine, produced

using our PER.C6® technology, to Phase II clinical trials, making it the most advanced vaccine candidate at the present time. While they do not elicit the circulation of virus-neutralizing antibodies, vaccines such as Merck's prompt a high response from T-cells, the chief regulatory cells of the immune system. This sharply reduces the virus load and keeps the infection at bay. A similar effect is central to TB vaccine efficacy, and we have partnered with the Aeras Global TB Vaccine Foundation to put AdVac® to use in improving the existing TB vaccine.

AdVac®'s advantage is that it addresses the most important problem inherent in the use of adenoviruses as vectors. The most commonly used vector, known as serotype 5, has a high natural prevalence in human populations, in excess of 35% in the United States and Europe and as high as 90% in sub-Saharan Africa. This creates a pre-existing immunity to the vector, blunting immune responses and drastically reducing the efficacy of any vaccine based upon it. AdVac® technology gets around this problem by employing serotypes much less prevalent in humans, but equally suitable for harnessing as vectors.

Questions from the Quarter

Q: Crucell has recently added a paragraph entitled 'Crucell's Licensing Program Disclosure Policy' at the foot of press releases announcing PER.C6® licensing deals. Does this indicate some kind of change in the licenses or in the partnership with DSM?

A: No. Nothing has changed. This is merely intended to explain why Crucell feels it is obliged to report all licensing deals agreed with partners, regardless of the revenues potentially derived from the deals. It will become standard text in all licensing press releases.

Q: Is bioterrorism becoming increasingly important in the financing of Crucell's activities?

A: Crucell is proud to contribute to measures aimed at curbing the threat of bioterrorism. However, in the context of the Company's operations, agreements such as the recently announced CRADA with the US Navy are of greater strategic importance in terms of the experience they offer for the development of Crucell's technologies. The Company's main aim continues to be to bring vaccines and antibodies to market, and we are not dependent on bioterrorism to provide those markets. Whether or not Crucell products will benefit from initiatives such as the BioShield Act in the US, our experience in this field will broaden our knowledge regarding the capabilities of our technologies. This experience will pay off across our full array of development programs.

Questions, Suggestions, Remarks? Please contact Crucell

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