

Risk Factors

You should carefully consider all the information in this Annual Report, including these material risk factors. The risks we face are not limited to the risks listed here. Some risks are not yet known to us and some of the risks that we currently do not believe to be material to our operations could prove to be material at a later date. All of these risks can materially affect our business, financial condition and results of operations.

Risks related to our company

We have a history of net losses and we may not achieve or maintain profitability.

We have incurred net losses since our incorporation. At December 31, 2007, we had an accumulated deficit of € 293.8 million (2006: 247.9 million). We may have net losses and net cash outflows in the future. Achieving profitability will depend, in part, on:

- the rate of growth, if any, in our product sales and licensing revenues;
- our ability, in the longer term, to obtain approval for current pipeline products and to develop potential products either on our own or through partnerships, collaborations or strategic alliances; and
- the level of our expenses.

We may never generate sufficient revenues to achieve profitability. Growth of our revenues is dependent on expanding current product sales, obtaining approval of the products in our pipeline, the success of our technologies – in particular, PER. C6 – and on our success and that of our licensees in developing commercially successful products based on our technologies. Revenue growth related to our existing products may be dependent on factors beyond our control as discussed below under ‘— Our products may fail at any stage of development or after market introduction due to factors beyond our control.’ Further, we do not have control over the ability of our licensees to develop commercially successful products based on our technologies. We expect to continue to invest in research and development to enhance our technologies and develop potential products. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We have used substantial capital in our business in the past, and we may need to raise additional capital in the future. If we do not raise this additional capital, we may be unable to acquire other companies or assets we would like to or may have to scale back certain research and development activities.

In the past, we have had to raise additional funds to acquire other companies and assets and continue the research and development of our technologies and potential products. For example, to fund our research and development, we raised net proceeds of € 50.1 million in a private offering of our ordinary shares in 2005, to accelerate our product development, especially in the field of antibodies and therapeutic proteins. To make acquisitions, we have raised additional capital and issued new shares. In February 2006, we issued 16.7 million ordinary shares in connection with our acquisition of Berna Biotech and in November 2006, we raised gross proceeds of € 80 million in a private offering of our ordinary shares to fund the acquisition of SBL and BPC and repay outstanding mortgage loans previously incurred by Berna Biotech.

We expect that our future capital requirements will continue to be substantial. Changes may occur that would consume available capital resources significantly sooner than we currently expect. We may seek additional funding through public or private financing (including debt or equity financing), strategic alliances or other arrangements. We may not have access to additional financing and, if we do, it may not be on favourable terms. If we fail to raise sufficient funds, we may have to forego acquisitions, reduce our capital expenditures, scale back our potential product development, reduce our workforce and license potential products or technologies to others that we otherwise would seek to commercialize ourselves.

Our results fluctuate as a result of seasonality in our business, particularly with respect to our flu vaccine product.

Our influenza vaccine, Inflexal V, accounts for a significant proportion of net sales from our vaccines business. The market for flu vaccines is extremely seasonal. There is a narrow window of time for production, regulatory approval and marketing of flu vaccines. Possible delays in stock availability or marketing of the Inflexal V vaccine could have a significant negative effect on us, since a majority of the distribution and sales occurs during only a few weeks in the third and/or fourth quarter

of every year. Potential delays in any step of the regulatory approval, production and marketing process could result in a significant sales reduction for us. In addition, the antigen necessary to produce influenza vaccine is in limited supply, and we generally rely on a single source for our supply of this antigen. Any interruption or delay in our antigen supply could have a materially adverse effect on our sales of Inflexal V and negatively impact our earnings and financial position.

We may be unable to make desirable acquisitions or to integrate successfully any business we acquire.

Our future success may depend in part on the acquisition of business or technologies intended to complement, enhance or expand our current business or products or that might otherwise offer us growth opportunities. Our ability to complete such transactions may be hindered by a number of factors, including potential difficulties in obtaining financing or in issuing our own securities as payment in acquisitions. We expect any acquisitions we undertake would be expected to result in future growth benefits, cost savings and other benefits. However, our ability to successfully realize these benefits and the timing of their realization may be affected by a variety of factors, including:

- the challenges of integrating the businesses, management teams and workforce of the two companies;
- unexpected events including major changes in the vaccine industry; and
- aligning new priorities.

Given these and other risks related to the combination of Crucell and any business we acquire, there can be no assurance that the benefits we expect from any combination will be realized. If the expected benefits of any combination we undertake are not or only partially realized, our business, financial condition and results of operations may be materially and adversely affected.

Our products may fail at any stage of development or after market introduction due to factors beyond our control.

There are inherent risks in the business of biotechnological development and production in connection with the development of biological products. Pre-clinical testing, clinical research and regulatory approval of a pharmaceutical or medical product is a very lengthy and costly process, and

there is a significant risk of failure at each stage of the process, should issues arise with respect to the efficacy or safety of a product. In particular, pre-clinical and early clinical studies cannot ensure efficacy for humans, and human studies are thus required for vaccine development. Such studies may, however, fail to prove the efficacy of the product candidates and are at constant risk of suspension for posing unreasonable health risks. There can be no assurance that any product candidate in our pipeline will either reach or successfully complete the clinical research process. Although a product reaches a later stage of development and offers a reasonably high probability of success relative to products in earlier stages of development, the chances of failure remain significant. We have had products fail at later stages of development in the past. Any or all of our current later-stage products could fail to be proved sufficiently safe or effective to be brought to market or could fail to receive necessary regulatory approvals. Such failures could have a material adverse effect on our business and prospects.

Even if the products currently in later-stage development are introduced, there can be no assurance that a market for such products will develop or be sustained. If a market does develop, there can be no assurance that our existing facilities and resources will be sufficient to meet demand. Accordingly, there can be no assurance that we will realize any potential benefits that may be associated with our later-stage development product portfolio.

If we or our licensees or our partners do not develop commercially successful products, we may fail to realize significant sales and royalty revenues in future years.

Very little data exists regarding the safety and effectiveness of the type of potential products that we, our licensees and our partners are developing. All of our potential products, and those of our licensees and partners, including those based on our PER.C6 technology, are either in research or in pre-clinical or clinical development. We and our licensees may not succeed in developing commercial products that are safe and effective, meet applicable regulatory standards, are capable of being manufactured at reasonable cost, or can be marketed successfully.

Development of products requires significant investment, including pre-clinical and clinical testing, to demonstrate their effectiveness prior

to their commercial distribution. To a certain extent, we are dependent on the research and performance of third parties to bring potential products to market. We and our licensees and partners must conduct a substantial amount of additional research and development before any regulatory authority will approve any of our or their potential products. Our research and development or that of our licensees and/or partners may not establish that our technologies or our or their potential products are safe and effective, in which case regulatory authorities may not approve them. Further, our government and university licensees and collaborators may have goals, such as academic publication or data collection, that are not solely focused on producing marketable products. Problems frequently encountered in connection with the development and use of new and unproven technologies and the competitive environment in which we and our licensees and partners operate may further limit our and their ability to develop commercially successful products.

If our licensees or partners do not continue to use our potential products, PER.C6 technology or our other technologies, or if they terminate their agreements with us, we will earn less or no revenue from our agreements with them.

License, service and manufacturing revenues and government grants from our potential products, PER.C6 and other technologies have accounted for a substantial portion of our revenues in the past and we expect that they will continue to comprise a portion of our revenues for the foreseeable future. If our current or prospective partners or licensees do not continue to use our potential products or technologies, or if they terminate their relationship with us, we may not be able to continue to realize the revenues related to those partners or licensees. In particular, our current or prospective licensees or partners may use or develop alternative technologies or develop competing products or potential products independently or in collaboration with others, including our competitors. If any of our licensees or partners become involved in a business combination or other major corporate transaction, this could cause a strategic shift in their business focus and the technologies they use. Our agreements with our licensees do not routinely require them to dedicate resources to developing and distributing commercial products based on our technologies. Furthermore, our licensees or partners may generally terminate their agreements with us on short notice. If they do terminate their agreements with us, we may not

be able to enter into new arrangements with other parties to replace those agreements. During 2007, existing licenses with 18 licensees were not renewed.

We are dependent on a small number of products for a majority of our revenues and expect this dependence to continue for the foreseeable future.

We are dependent on a small number of products that account for the majority of our revenues. By the end of 2007, our core product portfolio consisted of six vaccines, namely Quinvaxem and Hepavax-Gene (paediatric vaccines), Inflexal V (influenza), Dukoral, Epaxal and Vivotif (travel vaccines). The aggregated revenues for our core product portfolio amounted to € 149.297 in 2007 and represent 84.1% of our total product sales. In particular, we will be dependent on sales of Quinvaxem and Inflexal V.

If these products were to become subject to any problem such as loss of patent protection, unexpected side effects, regulatory proceedings, publicity affecting doctor or patient confidence or pressure from competitive products, or if new, more effective treatments should be introduced, we could experience a significant decrease in revenues and an adverse effect on our financial results. The general demand for our travel vaccines is driven by the number of travelers and their travel pattern. A terrorist act, war or natural disaster could significantly negatively impact both number of travelers and travel pattern for travelers coming, which could have an adverse effect on our financial results.

We may have conflicts with our licensees that could make collecting payments due to us more difficult or that could negatively affect our relationship with our current and potential licensees.

We may have disagreements with our licensees over royalty payments due to us and may have difficulty in collecting these payments. Our existing license arrangements generally entitle us to receive royalty payments for any potential products developed using our technology. We depend on our licensees to inform us when they develop products using our technology. If our licensees fail to inform us of their progress in these developments, we may not know of payments to which we would be entitled. In addition, our licensees may have difficulties making payments to us given the current economic climate or other factors. We may also incur significant expenses in collecting payments or, in some instances, we may not succeed in collecting these payments at all.

Our licensees may dispute the scope of the licenses that we have granted them, which could negatively affect our relationships with them and other licensees and our ability to grant additional licenses to other companies. In addition, a recent U.S. Supreme Court decision has established that a party need not break or terminate a license agreement before seeking a court judgment that the patents underlying the license agreement are not valid, not enforceable or not infringed. Some commentators in the intellectual property field have expressed the opinion that, due to this decision, patent challenges by licensees in general will increase. If, in the future, we become subject to additional patent challenges, it would cause us to have to expend greater resources defending such challenges. Challenges decided adversely to us could cause us to forego royalty payments which could have a material adverse effect on our business, financial condition and results of operations.

A number of our license agreements provide that if more favourable royalty terms are granted to another licensee pursuant to a license of substantially the same scope, the initial licensee will also be entitled to the more favourable terms. A licensee may claim that other license agreements contain more favourable terms and that we should extend these terms to it. This may lead to a licensee disputing the amounts payable to us.

An inability to attract and retain qualified personnel could adversely impact our business.

We may not be able to recruit and retain the qualified personnel necessary to develop our core technologies and potential products and execute our business plan. There is currently a shortage of skilled executives, scientific personnel and intellectual property and regulatory experts in our industry, particularly in the markets in which we operate. We believe this shortage is likely to continue. As a result, competition for skilled personnel is intense. Competition for experienced executives, scientists, developers and manufacturers of pharmaceutical products, and other experts from numerous companies and academic and other research institutions may limit our ability to attract and retain qualified personnel on acceptable terms or may significantly increase our labour costs. The inability to attract and retain highly skilled personnel on acceptable terms could have a material adverse effect on our business, financial condition, results of operations and prospects.

A number of our research and product development programs depend on access to biological materials without which we would be unable to conduct certain research and development.

To continue to develop our core technologies and potential products, we will need access to biological materials, such as virus and tissue samples, which may be in limited supply. If we lose or do not obtain access to appropriate biological materials, or if tighter restrictions are imposed on their use or on information generated from them, we could be restricted or prevented from conducting certain research and product development. In addition, government regulations could result in restricted access to, or use of, human and other biological material samples.

We require a reliable supply of crucial materials for the production of our products and for our serum-free medium. Some of these supplies are provided by a limited number of third party suppliers and some of these supplies we produce or are planning to produce ourselves. Any interruption in certain supplies would interrupt our production and ability to conduct research and product development.

We and some of our licensees rely on third parties for the supply of the serum-free medium in which we grow our PER.C6 cells. We cannot guarantee this medium will be available in the future on an industrial or bulk scale. If supply problems force us to use a new medium, we would need to spend time and resources to adapt our technology and processes to that medium, and during this period of adaptation, our use of PER.C6 would be interrupted. Any such interruption or other failure of the serum-free medium upon which we currently rely could decrease the potential viability and profitability of our PER.C6 technology.

In addition, we rely on third-party suppliers including CSL and Novartis for the supply of crucial materials for the production of some of our marketed products or those under development, including starting materials as well as antigens present in the final product. This includes, but is not limited to, the supply of A-Singapore flu antigen for the production of the currently marketed hepatitis A vaccine Epaxal, flu antigen for the production of the currently marketed flu vaccine Inflexal V and DiTewPHiB antigen for the currently marketed pentavalent vaccine Quinvaxem. Any interruption or termination of these supply relationships may have adverse effects on our ability to produce and supply these products as well as on our ability to launch new products in development and thus on our overall results.

In addition, our agreement with CSL for the supply of flu antigen for the production of our flu vaccine Inflexal V will terminate as of December 31, 2009. Due to the shortage of antigen production capacity worldwide, we expect that it may be difficult to establish a new contract for the supply of flu antigen on the terms and conditions we currently have. We have explored the availability of alternative sources and believe sufficient antigen supplies will be available. However, if we are unable to establish a new supply agreement, or are only able to establish a new agreement on less favourable terms and conditions, it could increase our costs, and there is no guarantee that we would be able to pass on these increased costs to our customers.

The manufacture and distribution of our products is technically complex. Supply interruptions, product recalls or inventory losses caused by unforeseen events, cold chain interruption and testing difficulties may reduce sales, delay the launch of new products and adversely affect our operating results and financial condition.

Our products are manufactured and distributed using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes as well as strict company and government standards for the manufacture of our products subject us to production risks. For example, during the manufacturing process, defects in equipment or infrastructure may generate production delays. In addition, process deviations or unanticipated effects of approved process changes may result in these intermediate products not complying with stability requirements or specifications. Our vaccine products in particular are subject to the risk of manufacturing stoppages or the risk of loss of inventory because of the difficulties inherent to the aseptic processing of biological materials at this stage. Any of those circumstances may arise in our own production facility and those of our suppliers. Vaccine components cannot be sterilized nor can conservative agents be added to the manufactured vaccine. If our products were to be contaminated by micro-organisms, it could result in the rejection of entire batches of finished vaccine, which would result in lost sales and possibly product recall, if contaminated vaccines have been shipped to customers.

Most of our products must be stored and transported at temperatures within a certain range,

which is known as 'strict cold chain' storage and transportation. If these environmental conditions deviate, our products' remaining shelf-lives could be impaired or their efficacy and safety could even become so impaired that they are no longer suitable for use. Further, most of our products are subject to additional testing upon receipt, both by our customers and by governmental agencies that regulate drugs in the markets in which we sell our products. Due to significant lab-to-lab variability of certain type of tests, in particular tests on biological products such as ours, batches of products may not be cleared by customers or these agencies, despite our having successfully tested them at the end of the manufacturing process. Failed tests may of course lead to customers rejecting delivery of the product or government agencies not releasing the product for marketing.

The occurrence or suspected occurrence of production, distribution and testing difficulties can lead to lost inventories, and in some case product recalls, with consequential reputational damage and the risk of product liability. We may have significant product liability exposure, and our product liability insurance may be inadequate to cover product liability or other claims against us. The investigation and remediation of any identified problems can cause production delays, substantial expense, lost sales and the delay of new product launches.

We rely only on one manufacturing site for each of our products. The marketing and authorization of biologicals, in particular vaccines, is strongly linked with the production facility and the equipment used, which are part of the regulated manufacturing process. With the exception of the filling process all our products are produced only at one site in a dedicated building. As such we are vulnerable to any event that could interrupt our production. Transferring a production in a new site would take a long time which could not be overcome with our product on stock due to the short shelf life of biologicals.

We rely on our manufacturing facilities in Korea to produce all of our supplies of Quinvaxem, and any events or disputes concerning that facility that interrupt, reduce or terminate production there may harm our business.

Our manufacturing facility in Korea is our sole source of our supplies of our Quinvaxem vaccine. As such, we are vulnerable to any event there that interrupts, reduces or slows our production of

Quinvaxem. For example, we could experience natural disasters such as floods or storms or work slow-downs or work stoppages by our employees. In addition, we lease the property on which our factory is built from our landlord, Green Cross Holdings Corp under a lease that expires in 2010, and which can be extended for an additional five years at our election. We are the only party entitled to terminate the lease. Our landlord also provides our utilities, such as access to water and electricity, at the site. Over a somewhat longer term, we intend to relocate our facilities to another site in Korea and preparations for an eventual move to another site are ongoing.

Our landlord plans to surrender a portion of the land on which our Korean facility sits, to the local and regional authorities due to construction of a light railway and a subway line extension along with the potential urban development associated therewith. In 2007, we demolished a warehouse that was directly in the path of the construction of the subway line. Currently, none of our property is in the way of the construction projects. Our landlord has advised us it will stop providing utilities to us in early 2009. Furthermore, our landlord filed a complaint against us in November 2007, seeking the demolition of two more of our buildings at the Korean facility and delivery to them of the land on which those buildings are located. The suit alleges that there is an implied lease agreement for those buildings and the land on which they sit, which automatically terminated upon commencement of the subway line extension project. In January 2008, we submitted our answer to the Court, denying the landlord's allegations on the grounds that there was no new (whether implied or express) agreement to demolish the buildings and deliver the relevant land. Such an agreement would be inconsistent with the long-term lease agreement which we and the landlord executed in April 2000. We expect this court case to last several years. We are currently engaged in negotiations with the local and regional authorities to determine the exact impact of the construction projects on our facilities, as well as the exact nature of the compensation we are to receive. While we may be entitled to at least partial compensation for any of our leasehold that the authorities condemn, our predecessor signed certain waivers in relation to the right to receive such compensation, as a condition to receiving permission to build the facilities. We may not be able to successfully challenge these waivers in court and, in turn, may not be legally entitled to full

compensation for any condemnation by the authorities. We also prepare for utilities in our own right. We can not guarantee that we will be successful in connecting to such utilities, nor can we assure you that any possible compensation we receive from authorities or third parties will be sufficient to cover all of our expense.

If our lease were terminated prior to its expiration, we were forced to demolish additional buildings or we were otherwise forced to leave the land, we would have to interrupt production of Quinvaxem, manufacture it at another of our facilities, build another facility to manufacture it or find a third party to manufacture it. We would incur substantial costs if we were to have to either move production to a different facility or build a new facility without necessarily being compensated for those expenses. Further, there is no guarantee that we could find a suitable third party to manufacture our vaccine or that if we did find one, we could enter into an agreement with them on favourable terms or at all. If we were to suffer any interruption, including a permanent one at our Korean facility, this would reduce our sales of Quinvaxem, may increase our expenses and, in turn, have a material adverse effect on our business, financial condition and results of operations.

We cannot be certain that our licensing or other agreements are not in breach of applicable competition laws and will not be considered void.

In the past, we have not notified the European Commission competition authorities of any of our licensing or other agreements or sought clearance from any other competition authority. We take the view that these agreements are unlikely to be found to infringe European Union or other applicable competition regulations. It is possible, however, that our current or future similar agreements could be found to infringe applicable competition regulations. In this event, among other things, we may be subject to fines, claims of damages and our licensing or other agreements may be considered void and unenforceable. Under the 2004 Technology Transfer Block Exemption Regulation, or the Regulation, in the European Union we may be required to review and possibly amend existing license and technology transfer agreements in the future. For example, if certain market share thresholds will or have been reached in the relevant markets by those third parties that use our technologies to produce their products, the Regulation may require us to revise our agreements with those parties to

ensure the agreements are in compliance with European competition law. This review process may be costly and time consuming and may require renegotiation of certain portions of our licenses and other agreements, but we do not expect this process to have a material adverse effect on our license portfolio or results of operations.

Potential patent disputes with GlaxoSmithKline, if decided adversely to us, could cause us to lose a significant share of our future revenues.

Berna Biotech's subsidiary Green Cross Vaccine Corporation, currently operating under the name Berna Biotech Korea Corp., and our partner Novartis, lodged oppositions against a patent of GlaxoSmithKline (GSK) in Korea. The patent is concerned with multivalent vaccine formulations, such as our pentavalent vaccine Quinvaxem which is registered in Korea. In response to the opposition, the patent was revoked by the Korean Intellectual Property Office in December 2004 on the grounds that the subject-matter claimed in the patent lacks novelty. GSK appealed that decision before the Korean Patent Court. After a hearing which took place in April 2006, the Korean Patent Court dismissed the appeal in June 2006. GSK has appealed this decision. If the Korean Supreme Court were to reverse the decision of the Patent Court and if GSK were to decide to enforce its patent, Berna Biotech Korea Corp. could be found to have infringed or be infringing the patent. If we are found to be infringing, we may be forced to suspend, or even cancel, our commercial activities with this vaccine. As a consequence we would lose revenues and our business would be adversely affected.

In addition, production of Quinvaxem requires a particular vaccine component that may become the subject of a patent dispute between either GSK and us or GSK and our supplier of that component. The patent on that particular component, held by GSK, is currently under opposition before the European patent office and a definitive outcome on the validity of the patent is expected to take a number of years. A negative outcome of this opposition proceeding could lead to infringement proceedings between GSK and us or GSK and our supplier, although we believe that neither we nor our supplier would be held to have infringed or be infringing that patent. The outcome of legal disputes is invariably difficult to predict with accuracy, but in the event GSK were to prevail in infringement proceedings against us, this would adversely affect our business.

Risks related to our industry

We face competition in discovering, commercializing and licensing new technologies from biotechnology firms in Europe, the U.S. and elsewhere. This competition may limit our ability to derive revenues from our technologies and development programs.

The field of biotechnology is new and rapidly evolving, and we expect that it will continue to undergo significant and rapid technological change. We operate in highly competitive markets and we may experience competition from companies that have similar or other technologies, or other products or forms of treatment for the diseases we are targeting. We are aware of a number of commercial initiatives in the fields in which we operate that may result in marketable products with which we would compete. We also may experience competition from companies that have acquired or may acquire technology from companies, universities and other research institutions. As these companies develop their technologies, they may develop proprietary positions in the areas of our core technologies or obtain regulatory approval for alternative technologies or commercial products earlier than we or our licensees do. Other companies are developing products to address the same diseases and conditions that we and our licensees target and may have or develop products or potential products that are more effective than those based on our technologies. We also compete with our licensees in developing new potential products. It is possible that we will not be able to effectively compete with these or other entities, and such competition could hamper our ability to bring products to market or license and derive revenue from our technology. Such an inability to compete could have a material adverse effect on our business, results of operations and ability to achieve profitability.

We may have significant product liability exposure, and our product liability insurance may be inadequate to cover product liability or other claims against us.

Like other manufacturers active in the biopharmaceutical industry, we may be exposed to product liability and other claims if third parties allege that our technologies, potential products or future products have caused harm. If a third party successfully sues us for an injury caused by our products, potential products or products developed using our technologies, our liability could exceed our total assets. This risk may be more pronounced in the case of the prophylactic vaccines and blood-derived products, which constitute our marketed products, than with respect to other pharmaceutical and medicinal products generally. Suits against us arising out of clinical trials may increase as more licensees utilize our technologies or potential products, thereby lessening our control over the manner of use of such technologies and potential products. We maintain product liability insurance in respect of all marketed products. We may seek to obtain additional product liability insurance in the future, though such additional insurance may be prohibitively expensive, or may not cover all of our potential liabilities. If we are unable to obtain sufficient insurance coverage at an acceptable cost or if we are otherwise unable to protect ourselves against potential product liability claims, this could prevent or inhibit the commercialization of products that we or our licensees develop. We are currently involved in a small number of product liability cases related to products that our subsidiary Berna Biotech marketed in the past. While we cannot predict the outcome of these cases, we do not believe that, if decided against us, any of these matters would have a material adverse effect on our business, financial condition or results of operations.

If ethical, legal and social issues related to the use of genetic technology, human based materials and pre-clinical and clinical testing negatively affect regulatory approval, patentability or market acceptance of our core technologies and of the products developed using these technologies, we would not be able to generate revenues from those products or our technologies.

The use of genetic technology and materials derived from human foetal tissue, such as PER.C6 technology, raises many ethical, legal and social issues that could hinder regulatory approval, patentability or market acceptance of its

technologies and products developed using them. Further, public expressions of concern and adverse events involving new biopharmaceutical technologies or products (such as stem cells or genetically modified foods or organisms) could result in greater governmental regulation of its existing technologies and potential regulatory delays relating to the testing or approval of our own or our licensees' potential products. Any of these factors could generate negative publicity or other adverse consequences regarding its business or industry, and could reduce or eliminate the potential markets for our own or our licensees' potential products.

We cannot be certain that we will be successful in public tenders to provide national governments and supranational organizations with our vaccine products.

For the sale of our paediatric vaccines, we rely to a considerable extent on the public markets, which typically operate via a tender system. In a tender system, national governments or supranational organizations request proposals for the terms under which a vaccine manufacturer will provide a large quantity of one or more vaccines. The award of the tender is typically based on a number of factors, including price and other non-financial attributes such as supply reliability and quality. The tender is often for a period of one or more years, meaning that only the chosen manufacturer will be permitted to supply the subject vaccine for that length of time. Failure to win a tender therefore, may cause us to be ineligible to supply the relevant national government or supranational organization for one or more years, and in turn, have a material adverse effect on our business, results of operations and financial condition.

Third parties may bring claims relating to improper handling, storage or disposal of the hazardous materials we use in our business, which may require us to spend significant time and financial resources to defend against claims and to pay damages if we are found liable.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our BioSafety Level III (BSL-III) laboratory facilities allow us to work on-site with hazardous materials like West Nile virus. Our operations also produce hazardous waste products. Given the inherently dangerous nature of certain of the materials we may work with in our BSL-III laboratory facilities and other hazardous materials incident to our work, we cannot eliminate the risk of accidental

contamination or discharge and any resultant injury from these materials. Various laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages and significant adverse publicity in the event of an improper or unauthorized release of, or exposure of individuals to, hazardous materials. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may make us adopt more labour intensive, time-consuming or complicated practices or procedures in connection with our research, development or production activities.

We may be unable to obtain regulatory approval to manufacture and market our new products and may have regulatory approval of the manufacture and marketing of our existing products revoked.

Regulatory bodies such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), the European Commission and comparable authorities elsewhere regulate the market introduction of biopharmaceutical products, while non-governmental bodies such as the World Health Organization (WHO) evaluate biopharmaceutical products in order to (pre)qualify those products for purchase by national or regional governmental bodies and large non-governmental purchasing organizations. To be approved for market introduction, a product candidate must undergo extensive testing, which can take many years and require substantial expenditures. The costs of pursuing and securing regulatory approval are increasing, necessitating additional regulatory compliance expenditure on our part. Required testing and trials include a review of the underlying technologies (including the cell line on which companies produce biopharmaceuticals) and are particularly rigorous with respect to vaccines. Product development involving new technologies is highly uncertain. In addition, different regulatory authorities may impose different conditions upon the marketing of a given product or may refuse to grant, or require additional data before granting, an approval to market a product even though the product may have been approved by another regulatory authority. Finally, national and regional governments rely on the (pre)qualification and/or approval granted to biopharmaceutical products by evaluative bodies such as the WHO and, in some

cases, simply elect not to purchase products which have not been granted (pre)qualification of approval. These evaluative bodies also require extensive information about the product and its market introduction test results prior to granting approval or (pre)qualification. There can be no assurance that regulatory approvals will ultimately be obtained to manufacture and market any such product candidates in which we are, or may in the future be, interested. Further, there can be no assurance that evaluative body approval or (pre)qualification will be obtained.

Although the FDA allows PER.C6 cells to be used to produce clinical materials that are being used in clinical trials at this time, the FDA has in the past raised concerns over the history and some of the properties of PER.C6 cells. If we or our licensees are unable to satisfy regulatory authorities as to the history and properties of PER.C6 or its appropriateness as a system from which companies can produce biopharmaceuticals, new regulations could be adopted that would preclude use of PER.C6 cells in the future. If this were to occur, our licensing and other revenues from PER.C6 will suffer. Our other technologies have not yet been used in clinical trials, and may face significant hurdles in obtaining regulatory approval if and when such trials begin.

Once a product is approved, the manufacture and marketing of the product remains subject to periodic review. Changes in applicable regulations, breaches of regulatory requirements or the discovery of problems related to the manufacture, safety, quality, efficacy or stability of a product, as well as changes in the characteristic of a product inherent to his biological origin, may result in the imposition of fines or restrictions upon the manufacture and sale of such product, including in the worst case withdrawal of the product from the market and/or the revocation of the relevant regulatory approvals. If the relevant regulatory authorities do not approve products developed using our technologies, or revokes approval of our existing products, we may not receive any licensing or royalty revenues, which may have a material adverse impact on our business, financial condition, results of operations and prospects.

Any potential health risks associated with our products or products produced using our technologies may lead to significant adverse regulatory and market consequences.

The possibility of product failure or adverse side effects poses a variety of risks for manufacturers of pharmaceutical and medical products. These risks may be more pronounced in the case of the prophylactic vaccines that constitute our core products than with respect to other pharmaceutical and medical products generally. Because prophylactic vaccines are administered to healthy subjects, any adverse health consequences associated with such administration may be perceived as less tolerable than side effects associated with the treatment of disease. Accordingly, there can be no assurance that even relatively minor potential health risks associated with our products will not give rise to adverse regulatory action, and/or negative market perception of us and our products, resulting in a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, if even a few of our partners or licensees experience development difficulties or failures while using our technologies, such as PER.C6, AdVac, MAbstract or STAR, other market participants, including existing or potential partners or licensees, could consider such difficulties or failure a result of our technologies and cause such participants to end partnerships, terminate licenses or never enter into either with us.

Our efforts to protect our intellectual property rights or to defend ourselves against any claims of infringement may be costly and, if unsuccessful, we may be barred from using or licensing our technologies.

Our commercial success depends in part on our ability to obtain and maintain adequate protection of our intellectual property rights, including patents, in our technologies and potential products in Europe, the U.S. and elsewhere. However, the patent positions of technology-based enterprises like us are subject to complex factual and legal issues that may give rise to uncertainty as to the validity, scope and priority of a particular patent. There can be no assurance that we will develop products that are patentable, that patents will be granted under pending or future applications or that patents granted to us or our collaborators will be of sufficient breadth to provide adequate protection against competitors with similar technologies or products or will not be successfully challenged. If we do not

adequately protect our intellectual property, competitors may be able to use our technologies and any potential products we develop and erode our competitive advantage and/or erode the value of our technologies.

Our inability to adequately protect and/or enforce our products and technologies in emerging economies, such as India and China, may give rise to competition from and in those territories, which would have an adverse effect on our ability to sell products and/or maintain economically healthy price levels. In addition, our ability to sell products at economically viable price levels may be subject to imported competing products manufactured in low cost economies. We may not be able to use our intellectual property to prevent manufacture of competing products to underdeveloped or developing countries, because of WTO inspired compulsory licensing regimes.

Our commercial success also depends in part on not infringing patents and proprietary rights of third parties. Our work is in areas of technology where a large number of patent rights exist. As our activities in the biotechnology and biopharmaceutical markets expand and more patents are issued, the risk that our technologies and potential products may give rise to claims of alleged infringement increases. In addition, we may in the future wish to undertake activities which raise patent infringement issues.

We routinely monitor the public disclosures of other companies operating in our industry regarding their technological development efforts to ensure that we do not undertake activities that infringe their intellectual property rights and to monitor whether those companies' activities may infringe our intellectual property rights. Due to the inherent imperfections of patent searching, we can never be certain that our monitoring will be exhaustive, and it is possible there may be third party intellectual property rights of which we are not yet aware. If we determine that other companies' technological development efforts violate our intellectual property rights, we intend to take appropriate action. We are aware of a few patents held by third parties which are potentially relevant to our past, current or anticipated activities. We believe that our current activities do not infringe any valid claims of these patents. Third parties, however, may seek to enforce patents against us and a court may find against us. Enforcing intellectual property rights against others or defending ourselves against claims of

infringement can be very expensive, and any action in which we are involved could result in substantial costs and diversion of management and technical personnel and resources.

Other companies are and may become involved in proceedings regarding patents that cover technologies related to ours. The outcome of any intellectual property proceedings in which we or they are involved could effectively block our ability to further use or license our technologies or enter into co development arrangements. It could also impair our or our licensees' ability to develop and commercialize potential products or products, and could result in the award of substantial damages against us. In the event of an unfavourable outcome in litigation, we may need to obtain licenses or redesign our technologies or potential products to avoid infringement. In the event that we must cease using a technology, we could encounter delays in license revenue generation, milestone or royalty payments or product introductions while we attempt to develop alternative technologies or potential products. If we do not succeed in such attempts, we may be forced to cease operations. In addition, if litigation results in a successful challenge to one of our patents, then competitors could be free to use the subject matter covered by the patent, or we may need to license the technology to others in settlement of such litigation.

Oppositions are relatively straightforward proceedings where any third party can seek to have a patent revoked. The proceedings typically have a stage where the patent's opponents and proprietor may each file observations in writing, followed by oral proceedings. The decision, which may be a dismissal of the opposition, a revocation of the patent or a maintenance of the patent in more limited form, usually takes between two to three years from the start of the proceedings. In most jurisdictions the decision is subject to appeal by the adversely affected party or parties. If the oppositions against our PER.C6 and AdVac patents are successful we may lose some or all patent protection in Europe.

If we or our licensees are unable to obtain any necessary licenses from third parties for use of their intellectual property on acceptable terms, we or our licensees may be unable to develop or market products based on our technologies.

Before we can market some of our products or technologies, we may need to obtain licenses from third parties who have patents or other intellectual property rights. We may be unable to earn revenues from products based on our technologies or from our own potential products if a third party does not grant us or our licensees a necessary license or offers a license only on unacceptable terms. For example, in the patent context, others have filed, and in the future are likely to file, patent applications covering technologies that we may wish to use or products that are similar to products that may be developed using our technologies. If these patent applications result in issued patents, we may need to obtain a license from the proprietors to use their patented technology. These licenses may not be available, or may not be available on acceptable or commercially reasonable terms. Without these licenses, we may be required to alter our technologies or potential products, or to avoid or stop certain activities. Our licensees may face similar problems.

Risks related to the securities markets and ownership of our shares or ADSs

The protective measures included in our articles of association may prevent unfriendly action that might otherwise be in the best interests of our shareholders.

Our articles of association have, in accordance with the laws of the Netherlands, protective effects. Among other things, our articles of association provide that our Supervisory Board may make binding nominations for the election of its board members, and only a shareholders' resolution approved by an absolute majority of the votes cast, representing more than one-third of our outstanding shares, can set the nominations aside. Furthermore under Dutch law, we may issue preference shares to a foundation, Stichting Preferente Aandelen CruCell, or the Preferred Foundation, giving it preferred dividend rights and diluting the voting rights held by the holders of the other classes of shares. The Preferred Foundation has an option to acquire a number of preference shares equal to the number of our outstanding shares. The chairman of our Supervisory Board, Jan Oosterveld, and four independent members comprise the board of the

Preferred Foundation. These and other provisions in our articles of association may have the effect of delaying, deterring or preventing unfriendly action that might otherwise be in the best interest of our shareholders or offer them the opportunity to sell their ordinary shares or ADSs at a premium over the market price. See 'Other information' and 'Articles of Association and Share Capital' for additional information regarding the preference shares and our articles of association.

U.S. and other non-Dutch holders of our ordinary shares may not be able to exercise pre-emption rights.

In the event of an increase in our share capital, holders of our ordinary shares are generally entitled to certain pre-emption rights unless these rights are excluded by a resolution of the general meeting of shareholders or of our board of directors, if so designated by the general meeting of shareholders or pursuant to our articles of association. However, U.S. holders of our ordinary shares may not be able to exercise pre-emption rights unless a registration statement under the Securities Act is declared effective with respect to the shares issuable upon exercise of such rights or an exemption from the registration requirements is available. No assurance can be given that any registration statement will be filed or, that if filed, will be declared effective, or that any exemption from registration would be available to enable the exercise of a U.S. holder's pre-emption rights.

Our shareholders may have difficulty protecting their rights as a shareholder and in enforcing civil liabilities because we are a Dutch limited liability company.

Dutch law and our articles of association govern issues regarding the legal organization, internal constitution, corporate authority and the liability of members of our Management Board and Supervisory Board. Most of our offices and assets are located outside the U.S. In addition, a majority of the members of our Supervisory Board, all of the members of our Management Board and management team are residents of, and most of their assets are located in, jurisdictions outside the U.S. As a result, it may be difficult to serve process on us or these persons within the U.S. It may also be difficult to enforce a U.S. court judgment against them in a U.S. court or in a Dutch court or to enforce a Dutch court's judgment against them in a U.S. court. This can include actions under the U.S. securities laws. In addition, it may be difficult to

enforce, in original actions brought in courts in jurisdictions located outside the U.S., liabilities under the U.S. securities laws. For a more complete discussion of potential difficulties in protecting your rights, see 'Articles of Association and Share Capital — Enforcement of Civil Liabilities'.

Our ordinary shares and ADSs may have a highly volatile trading price. You may not be able to resell your ordinary shares or ADSs at or above the price you pay for them, the ADSs may vary in value, and our share price may render us vulnerable to a takeover bid.

Our ordinary shares are listed on NYSE Euronext Amsterdam's Eurolist by Euronext (also called the Amsterdam Stock Exchange) and on the SWX Swiss Exchange, while our ADSs are listed on the Nasdaq Global Select Market. An active trading market for our ordinary shares or ADSs may not continue to be sustained. The ADSs' low closing price during 2005, 2006 and 2007 has been \$ 12.30, \$ 17.27 and \$ 16.08 respectively, and the closing price as of April 25, 2008 was \$ 18.97. The trading prices of ordinary shares of biotechnology companies in general have experienced significant volatility in the past and are likely to continue to be volatile. In addition, any negative change in the public's perception of the prospects of biotechnology companies could depress our ordinary share or ADS price regardless of our results of operations. Other broad market and industry factors may affect the trading price of our ordinary shares and ADSs, regardless of our performance.

We believe that we were or may have been a passive foreign investment company before 2005, causing certain adverse U.S. tax rules to apply to U.S. holders that held our ordinary shares or ADSs before 2005.

Although we believe that we were not a 'passive foreign investment company' or 'PFIC' for U.S. tax purposes with respect to the year 2007 and also do not anticipate becoming a PFIC with respect to the year 2008 or thereafter, we believe that we were or may have been a PFIC with respect to the years before 2005. If we were a PFIC in the past, U.S. holders that held our ordinary shares or ADSs at any time during the years when we were treated as a PFIC and did not make a mark-to-market election or a qualified electing fund ('QEF') election will generally continue to be subject to certain adverse U.S. federal tax rules (the 'PFIC rules'), even though we later ceased to qualify as a PFIC. In order to avoid being subject to these rules in the future,

affected U.S. investors may wish to make a deemed sale election with respect to our ordinary shares or ADSs. The PFIC rules are extremely complex, and U.S. investors are urged to consult their own tax advisers regarding the potential consequences to them of making the deemed sale election. See 'Information for shareholders and investors – Taxation of U.S. Investors – Passive Foreign Investment Company Rules'.