

# OCTOPLUS N.V.

*(a limited liability company incorporated under the laws of the Netherlands, with its corporate seat in Leiden)*

## **Offering of up to €25 million in newly issued ordinary shares with a nominal value of €0.12 per Share.**

We are offering (the “Offer”) up to €25 million in newly issued ordinary shares (the “New Shares”). The Offer consists of a public offering in the Netherlands and an international offering to institutional investors in certain other jurisdictions. Prior to the Offer, there has been no public market for our Shares. Preferential treatment will be given to our employees if they subscribe for New Shares pursuant to the Offer. There is no fixed percentage of the Offer reserved for such preferential treatment.

In this document (the “Prospectus”), the “Company”, “OctoPlus”, “we”, “our”, “us” and similar terms refer to OctoPlus N.V. and, where appropriate, its subsidiaries.

**Our business and any investments in our Shares involve significant risks. These risks are described under “Risk Factors” beginning on page 9 of this Prospectus.**

We intend to apply for admission of our ordinary shares, including the New Shares (the “Shares”), to trade on the stock market of Euronext Amsterdam N.V. (“Euronext”) and to list the Shares on Eurolist by Euronext Amsterdam (“Euronext Amsterdam”) under the symbol “OCTO”. We expect that trading in our Shares on Euronext Amsterdam will commence on or about 4 October 2006 (the “Listing Date”) on an “as-if-and-when-issued” basis and that delivery will take place on the third trading day following the Listing Date (the “Settlement Date”) on or about 9 October 2006.

If closing of the Offer does not take place on the Settlement Date or at all, the Offer will be withdrawn, all subscriptions for the New Shares will be disregarded, any allotments made will be deemed not to have been made, any subscription payments made will be returned without interest or other compensation and all transactions in our Shares on Euronext Amsterdam will be cancelled. All dealings in our Shares prior to settlement and delivery are at the sole risk of the parties concerned. Euronext does not accept any responsibility or liability for any loss or damage incurred by any person as a result of the listing and trading of our Shares on an “as-if-and-when-issued” basis as from the Listing Date until the Settlement Date.

**Offer Price: expected to be in the range of €4.65 to €5.50 per Share (the “Price Range”).**

**The New Shares have not been and will not be registered under the United States Securities Act of 1933, as amended (the “Securities Act”). The New Shares are being offered and sold in the United States in reliance on Rule 144A under the Securities Act (“Rule 144A”) or another available exemption from the registration requirement of the Securities Act. Prospective purchasers that are “qualified institutional buyers” (“QIBs”) are hereby notified that sellers of the New Shares may be relying on the exemption from the provisions of Section 5 of the Securities Act provided by Rule 144A. The New Shares are being offered and sold outside the United States in reliance on Regulation S under the Securities Act (“Regulation S”). For a description of restrictions on offers, sales and transfers of the Shares and the distribution of this Prospectus in other jurisdictions, see “Selling Restrictions” and “Transfer Restrictions”.**

We have granted to Cowen International Limited (“Cowen”), Fortis Bank (Nederland) N.V. (“Fortis”) and Kempen & Co N.V. (“Kempen & Co”, and together with Cowen and Fortis, the “Underwriters”) an option (the “Overallotment Option”) exercisable within 30 calendar days after the Allotment Date pursuant to which the Underwriters may require us to issue additional New Shares at the Offer Price for an amount up to 15% of the amount of the Offer.

Delivery of the New Shares is expected to take place on or about 9 October 2006 through the book-entry facilities of Nederlands Centraal Instituut voor Giraal Effectenverkeer B.V. (“Euroclear Netherlands”) only, in accordance with its normal settlement procedures applicable to equity securities and against payment for the New Shares in immediately available funds.

We reserve the right to change the Price Range and to increase the amount offered prior to the Allotment Date, which we expect will be on or about 4 October 2006. Any change of the Price Range on the day prior to the Allotment Date will result in an extension of the timetable for the Offer by at least one full trading day. Any change in the Price Range will be announced in a press release prior to the Allotment Date.

The Offer Price and the actual number of New Shares offered in the Offer will be determined after taking into account the conditions described under “The Offer” and by reference to the factors set forth on pages 120 and 121, and will, together with the Offer proceeds, be incorporated in a pricing statement which will be deposited with the Dutch Authority for the Financial Markets (*Autoriteit Financiële Markten*) (the “AFM”) on or about 4 October 2006 and published in the Daily Official List of Euronext Amsterdam (*Officiële Prijscourant*) (the “Daily Official List”) and in a national newspaper distributed daily in the Netherlands, subject to acceleration or extension of the timetable of the Offer. The pricing statement will also be placed on our website at [www.octoplus.nl](http://www.octoplus.nl) and you should access this information as soon as it is available. The contents of our website are expressly not incorporated by reference into this Prospectus.

Any acceleration or extension of the timetable for the Offer will be announced in a press release, in the event of an accelerated timetable for the Offer, at least three hours before the proposed expiration of the accelerated timetable for the Offer or, in the event of an extended timetable for the Offer, at least three hours before the expiration of the then-current timetable for the Offer. Any extension of the timetable for the Offer will be for a minimum of one full trading day.

This Prospectus constitutes a prospectus for the purpose of Article 3 of the Directive 2003/71/EC (the “Prospectus Directive”) and has been prepared in accordance with Article 3 of the Dutch Securities Act 1995 (*Wet toezicht effectenverkeer 1995*), as amended on 23 June 2005, and the rules promulgated thereunder. This Prospectus has been approved by and filed with the AFM.

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*Joint Global Coordinators and Joint Bookrunners*

**Cowen International Limited**

**Fortis**

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*Co-Manager*  
**Kempen & Co**

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## SUMMARY

*This summary provides an overview of selected information contained elsewhere in this Prospectus and should be read as an introduction to this Prospectus. Any decision to invest in our Shares should be based on consideration of this Prospectus as a whole by you. You should carefully read the Prospectus in its entirety before investing in our Shares, including the information discussed under “Risk Factors” beginning on page 9 and our consolidated financial statements and the notes thereto that appear elsewhere in this Prospectus. Unless otherwise stated, all the information in this Prospectus assumes that the Underwriters will not exercise the Overallotment Option.*

*Under laws in effect in the states within the European Economic Area, no civil liability will attach to us in respect of this Summary, including the Summary of Terms of the Offer and the Summary Consolidated Financial Data included herein, or any translation thereof, unless it is misleading, inaccurate or inconsistent when read together with the other parts of this Prospectus. Where a claim relating to information contained in this Prospectus is brought before a court in a state within the European Economic Area, the plaintiff investor may, under the national legislation of the state where the claim is brought, be required to bear the costs of translating this Prospectus before the legal proceedings are initiated.*

### **Summary of our Business**

We are a product-oriented biopharmaceutical company committed to the development of improved pharmaceutical products that are based on our proprietary drug delivery technologies and have fewer side effects, increased patient convenience and better efficacy than existing products.

We currently have five product candidates in development, of which three are in clinical trials. Our lead product candidate, Locteron™, is a novel interferon alfa combined with our proprietary PolyActive™ drug delivery technology for the treatment of chronic hepatitis C infection. Locteron is designed to require less frequent administration and cause fewer side effects than marketed forms of interferon alfa which currently represent the standard of care for this illness. We intend to commence Phase IIa clinical trials of Locteron in the fourth quarter of 2006. Our second clinical-stage product candidate is OP-145, a novel proprietary peptide therapeutic that is currently in Phase II clinical trials for the treatment of chronic otitis media, also known as chronic middle ear infection. Our third product candidate in clinical development is hGH-OctoDEX™, a novel formulation of recombinant human growth hormone for growth hormone deficiency. hGH-OctoDEX is in Phase I clinical trials and is based on our proprietary OctoDEX technology. We are also developing single shot vaccines based on our proprietary OctoVAX™ platform. HBV-OctoVAX for hepatitis B vaccination and JEV-OctoVAX for Japanese encephalitis vaccination are currently in pre-clinical trials.

### ***Our Lead Product Candidates***

*Locteron for Chronic HCV Infection.* Locteron is a proprietary controlled release formulation of interferon alfa currently entering Phase IIa clinical trials. The primary indication for Locteron is the treatment of chronic infection by the hepatitis C virus (“HCV”), which affects over 180 million people worldwide. Locteron combines interferon alfa produced by our co-development partner, Biolex Therapeutics, Inc. (“Biolex”), with our proprietary PolyActive microspheres. This product is designed to gradually release its active pharmaceutical ingredient over a 14-day period after a single injection. Currently marketed pegylated interferons circulate over a seven-day period after a single injection. By releasing interferon alfa in the body in a gradual manner, Locteron’s PolyActive microspheres avoid the high initial blood levels of interferon alfa which we believe cause many of the acute flu-like symptoms commonly associated with the current standard of care. We believe that the severity of these flu-like symptoms leads many patients to suspend or avoid treatment, despite the often serious nature of HCV infection.

Based on the results of our Phase I trial, we believe that Locteron will offer patients a once-every-two-weeks alternative for the treatment of chronic HCV infection because of the following advantages over currently marketed pegylated interferons:

- More convenient dosing schedule;
- Fewer, less severe and less frequent side effects; and
- Potentially improved efficacy.

We plan to initiate a Phase IIa trial of Locteron in the fourth quarter of 2006. If successful, we intend to commence a Phase IIb trial at the end of 2007. We have conducted a pre-IND meeting with the FDA and data collected in our planned Phase IIb trials of Locteron may form the basis of a regulatory submission to initiate a pivotal Phase III trial in the United States.

*OP-145 for Chronic Middle Ear Infection.* OP-145 is our novel, proprietary peptide therapeutic for the treatment of chronic middle ear infection, administered locally through an eardrop formulation. It is currently in Phase II clinical development. Chronic middle ear infection is a very common disease, affecting approximately 15% of all children. It is the most frequently recorded diagnosis for children in the United States and is the most common reason for a child being prescribed oral antibiotics. This disease is also prevalent in adults.

Acute middle ear infections are caused by a range of microbes. However, when toxic microbial degradation products linger in the mucus of the middle ear a chronic infection may develop. Antibiotics are rarely effective in treating chronic cases. Surgery is only effective in a minority of chronic patients.

OP-145 has been designed to neutralize toxic degradation products at the site of chronic infection, thereby restoring the body's natural clearance mechanism. OP-145 also has anti-microbial effects as it destabilizes the cell membrane of bacteria. We have demonstrated these two characteristics of OP-145 in pre-clinical studies. We recently completed a Phase I/IIa study in 16 therapy-resistant patients who had an average disease duration of 17 years. Patients in this study received OP-145 for two weeks. This study demonstrated that OP-145 was safe and well tolerated. Furthermore, at a 12-week follow-up examination, nine out of the 16 patients showed either full recovery or a meaningful improvement.

We are currently enrolling a placebo controlled Phase II study in 52 patients to evaluate the safety and efficacy of OP-145. We expect to receive data from this trial in the fourth quarter of 2007.

*hGH-OctoDEX for Growth Hormone Deficiency.* This product candidate is our controlled release formulation of human growth hormone ("hGH") designed to be administered once-weekly, in contrast to current hGH products which require daily injections. The primary indication for hGH-OctoDEX will be growth hormone deficiency in pediatric and adult patients.

Approximately one in 5,000 children and one in 10,000 adults are affected by growth hormone deficiency. In children, a deficiency of growth hormone can result in stunted growth and can eventually lead to short stature. In adults, low levels of hGH are frequently associated with various other metabolic disorders. The burden of daily injections over many years often leads to reduced compliance (particularly in children) or reluctance to initiate therapy (particularly in adults). We believe that a once-weekly formulation of hGH will contribute to improved compliance and improved clinical efficacy, and will potentially encourage patients who are reluctant to initiate hGH therapy to seek treatment.

We completed a proof-of-concept Phase I study with an earlier formulation of hGH-OctoDEX in 2004. An improved version of hGH-OctoDEX will be tested in a further Phase I trial, which we expect to start in the fourth quarter of 2007.

### ***Our Proprietary Drug Delivery Technologies***

Our major technology platforms, OctoDEX and PolyActive, have been developed to deliver active compounds in a more convenient, safe and effective manner than conventional formulations. Depending on the individual properties of a candidate compound, we select the technology platform with the highest potential for achieving an attractive product profile. Our OctoDEX-based products consist of injectable microspheres based on dextran polymers that enable the controlled release of biopharmaceuticals. We have also developed a modified version of our OctoDEX technology, OctoVAX, as a basis for an innovative, single-shot approach to

prophylactic vaccines. Our PolyActive drug delivery system is based on biodegradable co-polymers. These co-polymers have been used in medical devices for orthopedic and wound repair applications in over 5,000 patients.

### ***Our Contract Development Business***

We are a leading provider of advanced drug formulation and clinical scale manufacturing services to the pharmaceutical and biotechnology industries, with a focus on difficult to formulate active pharmaceutical ingredients in non-oral formulations. Our cGMP pilot plant allows us to offer our customers a full range of sterile pharmaceutical production options, including freeze drying. The expertise that we derive from rendering formulation and manufacturing services helps to support us in our own drug development programs.

### ***Our Strategy***

We aim to leverage our broad expertise in pharmaceutical development and drug delivery in order to develop pharmaceutical products that improve existing approaches to the treatment of serious illnesses. Key elements of our corporate strategy include:

- Advance the development of our lead product candidates;
- Continue to expand and advance our product candidate portfolio by combining our drug delivery technologies with known biopharmaceutical drugs or other therapeutics in need of clinical improvement;
- Capture value by entering into partnerships with large pharmaceutical or biotechnology companies for our product candidates;
- Further expand the potential applications of our drug delivery platforms; and
- Continue to grow our profitable Contract Development Business.

### ***Risks Associated with Our Business***

Our business is subject to numerous risks, such as risks related to our business and strategy, our dependence on third parties, our intellectual property, our employees and growth, regulatory approval and other government regulations, and our financial condition. These risks are more fully described in the section entitled “Risk Factors” immediately following this Prospectus summary.

### ***Corporate Information***

We are a public company with limited liability incorporated under the laws of the Netherlands and are registered with the Trade Register of the Chamber of Commerce of Rijnland under number 28075073 and we have our corporate seat in Leiden, the Netherlands. Our business address is Zernikedreef 12, 2333 CL Leiden, the Netherlands and our website is [www.octopus.nl](http://www.octopus.nl).

## Summary of Terms of the Offer

Issuer	OctoPlus N.V., a public company with limited liability incorporated under the laws of the Netherlands, with its corporate seat in Leiden, the Netherlands.
New Shares	We are offering New Shares for an amount of up to €25 million, subject to any change by reference to the factors set forth on page 121 assuming no exercise of the Overallotment Option. The actual number of New Shares will be published in a pricing statement and placed on our website on or about 4 October 2006, subject to acceleration or extension of the timetable for the Offer. The rights of holders of the New Shares and our existing Shares will rank pari passu with each other.
Shares Outstanding	<p>Immediately prior to the Offer, and assuming the Capital Restructuring has taken place, we will have 11,862,500 Shares outstanding, see “Description of Share Capital and Corporate Governance – Share Capital – Authorized and Issued Share Capital”.</p> <p>Immediately after the Offer, we expect to have 16,788,608 Shares outstanding, assuming we raise €25 million in the Offer, no exercise of the Overallotment Option and an Offer Price of €5.08, the mid-point of the Price Range.</p>
Share Ownership	Immediately after the Offer, assuming we raise €25 million in the Offer, no exercise of the Overallotment Option and an Offer Price of €5.08, the mid-point of the Price Range, we expect approximately 59.9% of our outstanding share capital will be owned by Holthuis-Bernaerts Holding B.V., Innoven Partenaires S.A., S.R. One, Ltd., Life Sciences Partners III B.V. / C.V., SurModics, Inc., and Fagus N.V. (the “Major Shareholders”), excluding any New Shares which may be acquired by any of the Major Shareholders pursuant to the Offer, see “Major Shareholders”.
Offer	The Offer consists of a public offering in the Netherlands and an international offering to institutional investors in certain other jurisdictions. The Offer includes an offer of New Shares in the United States in reliance on Rule 144A or another available exemption from the registration requirement of the Securities Act. The New Shares are being sold outside the United States in reliance on Regulation S.
Preferential Allotment	Preferential treatment will be given to our employees if they subscribe for New Shares pursuant to the Offer. There is no fixed percentage of the Offer reserved for such preferential treatment. See “The Offer – Allotment”.

Offer Price	The Offer Price, which applies to the New Shares, will be determined by reference to the factors set forth on pages 120 and 121 and will be published in a pricing statement and placed on our website on or about 4 October 2006, subject to acceleration or extension of the timetable for the Offer.
Pricing Date	Expected to be on or about 3 October 2006, subject to acceleration or extension of the timetable for the Offer.
Allotment Date	Expected to be on or about 4 October 2006, before the start of trading of the Shares on Euronext Amsterdam, subject to acceleration or extension of the timetable for the Offer.
Listing Date	Expected to be on or about 4 October 2006, subject to acceleration or extension of the timetable for the Offer.
Settlement Date	Expected to be on or about 9 October 2006, which is the third trading day following the date on which trading is expected to commence on Euronext Amsterdam, subject to acceleration or extension of the timetable for the Offer.
Joint Global Coordinators and Joint Bookrunners	Cowen and Fortis.
Overallotment Option	We have granted to the Underwriters an option, exercisable within 30 calendar days after the Allotment Date, pursuant to which the Underwriters may require us to issue additional New Shares at the Offer Price for an amount up to 15% of the amount of the Offer. The Underwriters may exercise this option at their discretion for any purpose in accordance with applicable law, including covering short positions created in the initial allotment of New Shares or in subsequent transactions.
Use of Proceeds	We intend to raise up to €25 million of gross proceeds from the issue of New Shares in the Offer. We intend to use the net proceeds we receive from the Offer, after deduction of the underwriting fees and commissions and our expenses related to the Offer, primarily for the development of our product candidates, working capital, capital expenditures, acquisitions if and when they present themselves and other general corporate purposes, as described under “Use of Proceeds”.



Lock-up Arrangements

Pursuant to certain “lock-up” agreements, we and all of our current shareholders, optionholders and warrant holders have agreed, subject to certain exceptions, not to dispose in any way of any Shares and securities convertible into or exchangeable or exercisable for or repayable with Shares for a minimum period of 365 days from the date of the underwriting agreement, unless Cowen has given its prior written consent thereto, see “Underwriting – Lock-Up Arrangements”.

Withdrawal of the Offer

If closing of the Offer does not take place on the Settlement Date or at all, the Offer will be withdrawn, all subscriptions for the New Shares will be disregarded, any allotments made will be deemed not to have been made, any subscription payments made will be returned without interest or other compensation and all transactions in the Shares on Euronext Amsterdam will be cancelled. All dealings in the Shares on Euronext Amsterdam prior to settlement and delivery are at the sole risk of the parties concerned.

Euronext does not accept any responsibility or liability for any loss or damage incurred by any person as a result of a withdrawal of the Offer and/or the related annulment of any transaction on Euronext Amsterdam.

Dividends

We do not anticipate paying any dividends for the foreseeable future. See “Dividend Policy”.

Voting Rights

Holders of the Shares will be entitled to one vote per Share at General Meetings of Shareholders. See “Description of Share Capital and Corporate Governance – General Meetings of Shareholders and Voting Rights”.

Payment, Delivery, Clearing and Settlement

Payment for the New Shares, including any New Shares issued upon exercise of the Overallotment Option prior to the Settlement Date, will take place on the Settlement Date. Delivery of the New Shares is expected to take place on or about 9 October 2006 through the book-entry facilities of Euroclear Netherlands only, in accordance with its normal settlement procedures applicable to equity securities and against payment for the New Shares in immediately available funds. Settlement of trades on Euronext Amsterdam is expected to take place on or about 9 October 2006.

Share Trading Information

ISIN Code: NL0000345718

Common Code: 026668441

Amsterdam Security Code: 34571

Euronext Amsterdam Symbol: OCTO

Listing and Paying Agent

Fortis Bank (Nederland) N.V.



### Summary of Consolidated Financial Data

The summary consolidated financial data set forth below should be read in conjunction with “Operating and Financial Review”, “Selected Financial Information” and our consolidated financial statements and notes thereto that appear elsewhere in this Prospectus. The year-end consolidated financial data are extracted from our consolidated financial statements that have been audited by Deloitte Accountants B.V., our independent auditors. The six-month consolidated financial data are based upon our unaudited condensed interim consolidated financial accounts for the six-month periods ended 30 June 2005 and 30 June 2006. The condensed interim consolidated financial data for the sixth month period ended 30 June 2006 have been reviewed by Deloitte Accountants B.V. See “Interim Financial Report – Review Report”.

Our results for the six-month period ended 30 June 2006 are not necessarily indicative of results for the full year. Our consolidated financial statements for the years ended 2005, 2004 and 2003, from which the summary consolidated financial data set forth below have been derived, were prepared in accordance with IFRS, which may differ from US GAAP in certain significant respects as they relate to us, most in particular regarding finance leases and intellectual property rights. For a discussion of the most significant differences between IFRS and US GAAP as they relate to us, see “Summary of Significant Differences between IFRS and US GAAP”. The summary consolidated financial data set forth below may not contain all of the information that is important to you.

#### Consolidated Income Statement Data

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Contract research . . . . .	€5,043	€4,924	€6,563	€3,300	€3,156
Royalties and license revenues . . . . .	–	60	60	30	30
Income from subsidiaries . . . . .	818	708	394	236	92
Other income . . . . .	–	26	–	–	1
Total revenues . . . . .	<u>5,861</u>	<u>5,718</u>	<u>7,017</u>	<u>3,566</u>	<u>3,279</u>
Raw materials and auxiliaries . . . . .	36	70	237	47	100
Costs of contracted work and other external charges . . . . .	639	307	1,390	416	1,147
Employee benefits . . . . .	3,450	3,597	4,758	2,155	2,920
Depreciation and amortization . . . . .	668	860	863	451	512
Other costs . . . . .	3,275	2,667	4,213	1,962	2,597
Total operating costs . . . . .	<u>8,068</u>	<u>7,501</u>	<u>11,461</u>	<u>5,031</u>	<u>7,276</u>
Operating income (loss) . . . . .	(2,207)	(1,783)	(4,444)	(1,465)	(3,997)
Interest . . . . .	(29)	(394)	(118)	(27)	(104)
Net income (loss) before taxes . . . . .	<u>€(2,236)</u>	<u>€(2,177)</u>	<u>€(4,562)</u>	<u>€(1,492)</u>	<u>€(4,101)</u>

**Segmented Income Statement Data**

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Contract Development income . . . . .	€5,123	€5,444	€6,804	€3,438	€4,111
Operating costs . . . . .	5,106	4,631	6,086	3,066	3,853
Operating income (loss) . . . . .	17	813	718	372	258
Inter-segment revenues . . . . .	356	772	366	204	955
Drug Delivery & Products income . . . . .	1,094	1,046	579	332	122
Operating costs . . . . .	3,318	3,642	5,776	2,169	4,339
Operating income (loss) . . . . .	(2,224)	(2,596)	(5,197)	(1,837)	(4,217)
Unallocated costs . . . . .	-	-	35	-	(38)
Consolidated operating income (loss) . . . . .	<u>€(2,207)</u>	<u>€(1,783)</u>	<u>€(4,444)</u>	<u>€(1,465)</u>	<u>€(3,997)</u>

**Consolidated Balance Sheet Data**

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Intangible fixed assets . . . . .	€1,401	€1,421	€1,705	€1,579	€1,725
Other fixed assets . . . . .	3,132	6,054	6,289	6,170	6,363
Current assets . . . . .	1,659	1,879	12,506	15,337	8,762
Total assets . . . . .	6,192	9,354	20,500	23,086	16,850
Equity (deficit) . . . . .	1,151	(1,356)	11,751	14,755	8,456
Long-term debts . . . . .	917	4,345	3,738	3,782	3,711
Current debts . . . . .	4,124	6,365	5,011	4,549	4,683
Total equity and liabilities . . . . .	<u>€6,192</u>	<u>€9,354</u>	<u>€20,500</u>	<u>€23,086</u>	<u>€16,850</u>

**Consolidated Cash Flow Statement Data**

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Net income (loss) from operations . . . . .	€(2,236)	€(2,177)	€(4,562)	€(1,492)	€(4,101)
Depreciation and amortization . . . . .	668	860	863	451	512
Changes in working capital . . . . .	1,927	2,265	(1,037)	(996)	(1,090)
Cash flow from operating activities . . . . .	359	948	(4,736)	(2,037)	(4,679)
Cash flow from investment activities . . . . .	(2,218)	(944)	(1,218)	(725)	(606)
Cash flow from financing activities . . . . .	(48)	(923)	16,860	17,040	29
Net cash flow . . . . .	(1,907)	(919)	10,906	14,278	(5,256)
Cash at beginning of period . . . . .	1,150	(757)	(1,676)	(1,676)	9,230
Cash at end of period . . . . .	(757)	(1,676)	9,230	12,602	3,974
Net cash flow . . . . .	<u>€(1,907)</u>	<u>€(919)</u>	<u>€10,906</u>	<u>€14,278</u>	<u>€(5,256)</u>

## RISK FACTORS

*Investing in the Shares involves a high degree of risk. You should carefully consider the risks described below and all of the other information set forth in this Prospectus before deciding to invest in any of our Shares. If any of the events or developments described below occurs, our business, financial condition or results of operations could be negatively affected. In that case, the trading price of the Shares could decline, and you could lose all or part of your investment in the Shares.*

*Although we believe that the risks and uncertainties described below are our most material risks and uncertainties, they are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also have a material adverse effect on our business, results of operations or financial condition and could negatively affect the price of the Shares.*

### **Risks Related to Our Business and Strategy**

***Our success depends substantially on our most advanced product candidates, which are still under development. If we are unable to bring any or all of these product candidates to market, or experience significant delays in doing so, our ability to generate product revenue and our likelihood of success will be harmed.***

Our three most advanced product candidates are in Phase I or Phase II clinical trials. Locteron is entering Phase IIa trials, OP-145 is in Phase II trials and hGH-OctoDEX is in Phase I trials. Our ability to generate product revenue in the future will depend on the successful development and commercialization of these product candidates. Our other product candidates are in various stages of pre-clinical development. Any of our product candidates could be unsuccessful if it:

- does not demonstrate acceptable safety and efficacy in pre-clinical or clinical trials or otherwise does not meet applicable regulatory standards for approval;
- does not offer therapeutic or other improvements over existing or future drugs used to treat the same conditions;
- is not capable of being produced in commercial quantities at acceptable costs; or
- is not accepted in the medical community or by third-party payors.

Our lead product candidate, Locteron, uses interferon alfa produced through a plant-based expression system. This method of production is different from that used for other interferon alfa products currently on the market, which are produced through mammalian or bacterial cultures. We cannot assure you that the European Medicines Evaluation Agency (the “EMA”), the United States Food and Drug Administration (the “FDA”) or other regulatory authorities will approve this interferon alfa product, known as BLX-883, or its method of production. For Phase III trials, we intend to use a different strain of the expressing plant which we believe produces a more consistent interferon alfa than that used for our Phase I trials. We cannot assure you that this interferon alfa will not be inferior to the interferon alfa that we have already tested. Our Phase I study for our hGH-OctoDEX product candidate gave rise to local tolerability concerns in some of the subjects, leading to a decision not to initiate repeat dosing studies with the same formulation. Although we have reformulated the hGH-OctoDEX product candidate to use a different form of recombinant hGH and we have improved our polymer and microsphere manufacturing process to address these concerns, we cannot assure you that our efforts were successful.

We do not expect any of our current product candidates to be commercially available until 2012 at the earliest, if at all. If we are unable to make our product candidates commercially available, we will not generate product revenues and we will not be successful. The results of our clinical trials to date do not provide assurance that acceptable efficacy or safety will be shown upon completion of Phase III clinical trials.

***Any failure or delay in commencing or completing clinical trials for our product candidates could severely harm our business.***

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive pre-clinical and clinical trials, that the product candidate is safe and effective in humans. Pre-clinical and clinical trials are expensive, can take many years and have an uncertain outcome. A failure of one or more of our clinical trials could occur at any stage of testing.

Positive or timely results from pre-clinical and early clinical trials do not ensure positive or timely results in late stage clinical trials or product approval by the EMEA, the FDA or any other regulatory authority. Product candidates that show positive pre-clinical or early clinical results often fail in later stage clinical trials.

We have limited experience in conducting the clinical trials required to obtain regulatory approval. We may not be able to conduct clinical trials at preferred sites, enlist clinical investigators, enroll sufficient numbers of patients, or begin or successfully complete clinical trials in a timely fashion, if at all. Any failure to perform may delay or terminate the trials.

To date, we have not completed all clinical trials required for the approval of any product candidate. The commencement and completion of clinical trials for our product candidates may be delayed, suspended or terminated as a result of many factors, including:

- our inability or the inability of our collaborators or licensees to manufacture or obtain from third parties materials sufficient for use in pre-clinical and clinical trials;
- the delay or refusal of regulators or institutional review boards to authorize us to commence a clinical trial at a prospective trial site;
- delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- lower than anticipated retention rates of patients and volunteers in clinical trials;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- negative or inconclusive results, which may require us to conduct additional pre-clinical or clinical trials or to abandon projects that we expect to be promising;
- poor effectiveness of product candidates during clinical trials;
- unforeseen safety issues or side effects;
- unfavorable governmental or regulatory inspection and review of a clinical trial site or records of any clinical or pre-clinical trial; and
- governmental or regulatory delays and changes in regulatory requirements, policies and guidelines.

Any delay in commencing or completing clinical trials for our product candidates would delay commercialization of our product candidates and severely harm our business and financial condition. It is also possible that none of our product candidates will complete clinical trials in any of the markets in which we or our collaborators intend to sell those product candidates. Accordingly, neither we, nor our collaborators, would receive the regulatory approvals needed to market our product candidates, which would severely harm our business and financial condition.

***The EMEA, the FDA and other regulatory agencies may require additional pre-clinical and Phase I clinical data for our product candidates.***

Many of our product candidates involve the combination of a marketed drug or similar compound with OctoDEX, OctoVAX or PolyActive. As a result, we anticipate that we will not need to conduct some early stage tests concerning the safety and toxicology of the active pharmaceutical ingredient contained in some of our product candidates. We cannot assure you, however, that the EMEA, the FDA or other regulatory authorities will

not require such tests. If we are required to conduct further pre-clinical or Phase I trials, our costs will increase and we will not be able to progress our product candidates towards commercialization as rapidly as we expect.

***We may fail to select or capitalize on the most scientifically, clinically or commercially promising or profitable product candidates.***

We have limited technical, managerial and financial resources to determine which of our product candidates should proceed to initial clinical trials, later stage clinical development and potential commercialization. We may make incorrect determinations in this regard. Our decisions to allocate our research, management and financial resources toward particular product candidates or therapeutic areas may not lead to the development of viable commercial products and may divert resources from better opportunities. Similarly, our decisions to delay or terminate drug development programs may also be incorrect and could cause us to miss valuable opportunities.

***We face intense competition.***

The pharmaceutical and biotechnology industries are highly competitive. Any product candidates that we successfully develop will compete with existing and future therapies. There are many organizations, including pharmaceutical companies, biotechnology companies, academic laboratories, research institutions, governmental agencies and public and private universities, which are actively engaged in developing products that target the same markets as our product candidates.

Many of these competitors have substantially greater financial, technological, manufacturing, marketing, managerial and research and development resources and experience than we do. Many of these organizations also have much more experience than we do in pre-clinical and clinical trials of new drugs and in obtaining regulatory approvals. Accordingly, our competitors may succeed in developing competing technologies and products more rapidly than we do.

Our product candidates, if successfully developed and approved for commercial sale, will compete with a number of drugs and therapies currently manufactured and marketed by major pharmaceutical and biotechnology companies. Our product candidates may also compete with new products currently under development by others. These new products may turn out to be safer or may work better, or be as effective but cheaper, than our products. If our competitors develop and market product candidates that are safer, more effective or cheaper, or develop, obtain regulatory approval and market such product candidates earlier than we do, our commercial opportunity will be reduced or eliminated.

***We face rapid technological change.***

Our success depends, in part, on maintaining a competitive position in the development of products and technologies in a rapidly evolving field. Within the pharmaceutical and biotechnology industries, major technological changes can happen quickly. The rapid technological change, or the development by competitors of technologically improved or different drug delivery systems or products, could render our platform technologies or product candidates obsolete or non-competitive. For example, the current standard of care for HCV infection consists of a combination therapy using interferon alfa and ribavirin. Our lead product candidate, Locteron, is designed to be an improved interferon alfa component of this therapy. In the event that a new standard of care emerges that does not use interferon alfa, Locteron could become obsolete.

***Our product candidates may not gain market acceptance.***

Even if our product candidates are ultimately approved, they may not gain market acceptance among physicians, patients and others in the medical community.

Sales of medical products depend on physicians' willingness to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe and effective from a therapeutic and cost perspective relative to competing treatments. We cannot predict whether physicians will make this determination as it relates to our product candidates.

Physicians may elect not to recommend, and patients may elect not to use, our products for a variety of reasons, including:

- lower demonstrated clinical safety and efficacy compared to other products;
- prevalence and severity of side effects;
- advantages of alternative treatment methods;
- ineffective marketing and distribution support;
- lack of availability of reimbursement from managed care plans and other third-party payors;
- lack of cost-effectiveness; and
- timing of market introduction of competitive products.

If any of our product candidates fails to achieve market acceptance, we may not be able to generate significant revenue, if any.

***We have significant product liability exposure, which may harm our business and our reputation.***

We face an inherent risk of product liability lawsuits related to the testing of our product candidates, and will face an even greater risk if our product candidates are introduced commercially. An individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we cannot successfully defend ourselves against the product liability claim, we may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- significant litigation costs;
- substantial monetary awards to, or costly settlements with, patients;
- product recalls;
- loss of revenue;
- the inability to commercialize our product candidates; and
- the diversion of management's attention from managing our business.

We are highly dependent upon market perceptions of us, our brands and the safety and quality of our products. We could be adversely affected if we or our brands are subject to negative publicity. We could also be adversely affected if any of our products or any similar products distributed by other companies prove to be, or are asserted to be, harmful to consumers. Also, because of our dependence upon market perceptions, any adverse publicity associated with illness or other adverse effects resulting from consumers' use or misuse of our products or any similar products distributed by other companies could have a material adverse impact on our results of operations.

We are also exposed to similar liability risks due to the provision of pharmaceutical development and manufacturing services by our Contract Development Business.

Some of our collaboration and customer supply agreements contain liability and/or indemnification provisions under which we may claim damages from our counterparties and under which our counterparties may claim damages from us, including damages caused by product defects. In the event we need to claim damages from a counterparty, we may not receive payments covering in full our damages, either because the applicable provision limits the payment to a certain amount, is unenforceable for any reason or because the counterparty is

unable to pay (due to insolvency or otherwise). Although in many cases we try to limit our liability, such limitations may not be effective in the event that we need to pay damages and we nevertheless could become liable to make substantial payments.

We have clinical trial and other liability insurance, which we currently believe is adequate to cover liabilities we may incur. However, our current or future insurance coverage may prove insufficient to cover any liability claims brought against us. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for our product candidates. Because of the increasing costs of insurance coverage, we may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy any liability that may arise.

***The success of Locteron depends heavily on our collaboration with Biolex, which involves a complex sharing of decisions, responsibilities, costs and benefits. A loss of Biolex as a partner, or any adverse developments in the collaboration, would materially harm our business.***

In February 2005, we entered into a collaboration agreement with Biolex to develop and commercialize Locteron. Locteron combines our PolyActive drug delivery technology and Biolex's proprietary BLX-883 interferon alfa product.

We are subject to a number of additional risks associated with our dependence on our collaboration with Biolex, including:

- We and Biolex could disagree as to development plans, including clinical trials or regulatory approval strategy, or as to which additional indications for Locteron should be pursued. Disputes regarding the collaboration agreement that delay or terminate the development, receipt of regulatory approvals or commercialization of Locteron would harm our business and could result in significant litigation or arbitration.
- Biolex could fail to devote sufficient resources towards the development and approval of Locteron. After the time periods stated in the collaboration agreement, Biolex could shift its research and development resources to other product opportunities.
- Biolex may not be able to provide us with sufficient quantities of BLX-883 for incorporation into Locteron for commercial sale in a cost effective and timely manner.

Furthermore, Biolex may terminate our collaboration agreement at will upon due notice, subject to the survival of certain obligations, or upon our material breach of the collaboration agreement.

We do not currently have the resources necessary to develop Locteron on our own. If either we or Biolex do not perform our respective obligations under, or devote sufficient resources to, our collaboration, or if we and Biolex do not work effectively together, Locteron may not be successfully developed and commercialized. If our collaboration were to be terminated, we would need to establish an alternative arrangement and may not be able to do so on acceptable terms or at all.

***No product manufactured using Biolex's novel plant-based expression technology has yet been approved.***

Biolex produces BLX-883, the active pharmaceutical ingredient in Locteron, in genetically engineered lemna, a clonal higher order plant species. To date, none of Biolex's lemna-based compounds have been approved for sale in the European Union, the United States or any other jurisdiction. Moreover, to our knowledge, no product produced in any plant-based expression system has been submitted to the EMEA, the FDA or any other regulatory agency for final regulatory approval.

If unforeseen technological, regulatory or other challenges associated with Biolex's plant-based expression system materialize, we will not be able to use BLX-883 and we would have great difficulty in sourcing interferon alfa for use in Locteron, and our ability to develop and commercialize this product will be severely disrupted.



***Our information technology systems could face serious disruptions that could adversely affect our business.***

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions in our service to customers, delays in our research and development work or the loss or delay of client relationships.

***We do not have large-scale manufacturing experience.***

Although we have manufactured certain product candidates on a small scale for use in clinical trials, we cannot assure you that we can successfully manufacture our products under current Good Manufacturing Practices (“cGMP”) and applicable laws and regulations in sufficient quantities for clinical trials, or in a timely or economical manner. We have not yet produced any biopharmaceutical products on a large scale or in commercial quantities and do not have the facilities and staff required for commercial production of any products that require large-scale manufacturing. To obtain such resources, we may seek to enter into collaborative arrangements with other parties. There can be no assurance that we will be able to obtain such capabilities through arrangements with others on acceptable terms, if at all.

***We are vulnerable to natural and other types of disaster, which could cause damage to our facilities and equipment and require us to cease or curtail operations.***

Substantially all of our facilities are located within a single facility in Leiden, the Netherlands. We are vulnerable to damage from natural and other types of disasters, including power loss, attacks from extremist organizations, fire, floods and similar events. If any disaster were to occur, our ability to operate our business could be seriously impaired. In addition, the nature of our research activities and of much of our equipment could make it difficult for us to recover from this type of disaster. We currently may not have adequate insurance to cover our losses resulting from disasters or other similar significant business interruptions, and we do not plan to purchase additional insurance to cover such losses due to the cost of obtaining such coverage. Any significant losses that are not recoverable under our insurance policies could seriously impair our business and financial condition.

## **Risks Related to Our Dependence on Third Parties**

***We need to enter into collaborative relationships to further develop our business and if we fail to enter into such agreements, or if we, or any of our collaborators, terminate or fail to perform any obligations under our collaborative agreements, the development and commercialization of our product candidates could be delayed or terminated.***

A material component of our business strategy is to establish and maintain collaborative arrangements with pharmaceutical and biotechnology companies, research institutions and foundations and private and public universities and to seek grants from the Dutch government and the European Union, to fund research and possible development and commercialization of our product candidates. We also intend to establish collaborative relationships to obtain domestic or international sales, marketing and distribution capabilities if any of our product candidates receive regulatory approval.

The process of establishing collaborative relationships is difficult, time-consuming and involves significant uncertainty. Moreover, even if we establish collaborative relationships, it may be difficult to maintain or perform under such collaboration arrangements, as funding resources may be limited or our collaborators may seek to renegotiate or terminate their relationships with us due to unsatisfactory clinical results, a change in business strategy, a change of control or other reasons. If we or any of our collaborators fail to fulfill any responsibilities in a timely manner, or at all, contractual disputes may arise and our research, clinical development or commercialization efforts related to that collaboration could be delayed or terminated. Additionally, it may become necessary for us to assume responsibility for activities that would otherwise have been the responsibility

of our collaborators. Further, if we are unable to establish and maintain collaborative relationships on acceptable terms, we may have to delay or discontinue further development of one or more of our product candidates, undertake development and commercialization activities at our own expense or find alternative sources of funding.

Our ability to predict the success of our collaborations is limited due to the complexity and uncertainty of these arrangements. Our collaborations typically involve a complex allocation of responsibilities, costs and benefits. Collaboration agreements may provide for milestone payments upon the achievement of specified clinical and regulatory milestones. They may also provide royalty-based revenue if product candidates are successfully commercialized. We will rely on our collaborators to provide resources to develop new product candidates and to potentially achieve these milestones and commercialize any new products. We may not be able to achieve any of the milestones provided for in our collaborative agreements or derive any license or royalty revenue with respect to these collaborations.

***We depend on third parties for active pharmaceutical ingredients.***

None of our drug delivery systems can be commercialized as a stand-alone therapeutic product. They must be combined with an active pharmaceutical ingredient. To develop new proprietary product candidates based on our drug delivery systems, we must obtain the active pharmaceutical ingredient from another party. This active pharmaceutical ingredient may not be available to us on acceptable terms, if at all. Our arrangements with developers and manufacturers of active pharmaceutical ingredients are critical to our success in developing our product candidates and bringing our products to the market. For example, we rely on Biolex to provide us with BLX-883, their proprietary version of interferon alfa, for use in Locteron. Should Biolex terminate its arrangements with us, we would have great difficulty in finding another supplier of interferon alfa that would enable Locteron to be a commercially viable product. As another example, we will also need to secure supply of 191 amino acid recombinant hGH for our hGH-OctoDEX product candidate in the short term in order to continue our clinical trials with this product candidate as planned.

Our current and future suppliers may not be able to supply us with the quantity of active pharmaceutical ingredients we require, particularly in the quantities required for commercialization of any product. Manufacturers of active pharmaceutical ingredients typically can terminate their agreements at will, in which case we will be required to identify an alternative manufacturer. Taking into account the limited number of manufacturers for certain active pharmaceutical ingredients, identifying and utilizing additional or replacement manufacturers may not be accomplished quickly, if at all. This could result in significant additional costs or limit our ability to develop and commercialize product candidates.

***We rely on third parties to conduct our pre-clinical and clinical trials. If these third parties do not perform as contractually required or expected, we may not be able to obtain regulatory approval for or commercialize our product candidates.***

We do not have the ability to independently conduct pre-clinical and clinical trials for our product candidates, and we must rely on third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories, to conduct our pre-clinical and clinical trials. We have, in the ordinary course of business, entered into agreements with these third parties. Nonetheless, we are responsible for confirming that each of our pre-clinical and clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the EMEA, the FDA and other regulatory agencies require us to comply with regulations and standards, commonly referred to as good clinical practices, for conducting, recording and reporting the results of pre-clinical and clinical trials to ensure that data and reported results are credible and accurate and that trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. If these third parties do not successfully carry out their contractual duties or regulatory obligations or meet expected deadlines, if the third parties need to be replaced or if the quality or accuracy of the data they obtain is compromised due to the failure to adhere to our pre-clinical and clinical protocols or regulatory requirements or for other reasons, our pre-

clinical or clinical trials may be extended, delayed, suspended or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, our product candidates.

***We currently rely on single source suppliers for the provision of essential materials incorporated in certain of our product candidates, and we have no arrangements in place for the commercial supply of any of our product candidates.***

For many of the essential materials incorporated into our product candidates, we rely on a single supplier. Any disruption in the supply of these materials could adversely affect our ability to successfully complete the clinical trials and other studies of our product candidates, delay submissions of our regulatory applications or adversely affect our ability to commercialize our product candidates in a timely manner, or at all.

We do not currently have any agreements to manufacture our product candidates on a commercial scale. In order to commercialize our product candidates, our existing suppliers will need to scale up their manufacturing of essential materials incorporated in our product candidates. We may be required to fund capital improvements to support scale-up of manufacturing and related activities. Our existing manufacturers may not be able to successfully increase their manufacturing capacity of materials essential for any of our product candidates for which we obtain marketing approval in a timely or economic manner, or at all. We may need to engage other manufacturers to provide commercial supplies of our product candidates. It may be difficult for us to enter into commercial supply arrangements on a timely basis or on acceptable terms, which could delay or prevent our ability to commercialize our product candidates. If our existing manufacturers are unable or unwilling to increase their manufacturing capacity or we are unable to establish alternative arrangements, the development and commercialization of our product candidates may be delayed or there may be a shortage in supply.

***If we are unable to enter into agreements with third parties to market and sell our product candidates, we may be unable to generate product revenue.***

As we have no marketing, sales or distribution capabilities, if our product candidates receive marketing authorization we will have to enter into arrangements with third parties to market, sell and distribute our product candidates. If we are not able to enter into such arrangements, we will have difficulty commercializing our product candidates, which would adversely affect our business and financial condition.

## **Risks Related to Our Intellectual Property**

***Our success is dependent on intellectual property rights held by us, and third parties, and our interest in such rights is complex and uncertain.***

Our success depends, in part, on our ability to obtain, maintain and enforce our intellectual property rights for our technologies and product candidates, and to preserve our trade secrets and other proprietary information. Our success also depends, in part, on the ability of our licensors to obtain, maintain and enforce their intellectual property rights to the extent that we rely on those rights.

The patent positions of pharmaceutical and biotechnology companies, including our patent positions, involve complex legal and factual questions and, therefore, validity and enforceability cannot be predicted with certainty. Patents may be challenged, deemed unenforceable, invalidated or circumvented. The validity, enforceability and commercial value of these rights, therefore, are highly uncertain.

We intend to apply for patents covering our technologies and product candidates as we deem appropriate. We may fail to apply for patents on important technologies or products in a timely fashion, or at all, and in any event, the applications filed by us may be challenged and may not result in issued patents. Any future patents obtained by us may not be sufficiently broad to prevent others from using our technologies or from developing competing products. Furthermore, others may independently develop similar or alternative technologies or design around our patented technologies. In addition, if challenged, our patents may be declared invalid. Even if valid, our patents may fail to provide us with any competitive advantages.

Any adverse outcome we may experience while attempting to obtain, maintain or enforce our intellectual property rights could have a material adverse effect on our business and financial condition.

***Litigation or third party claims of intellectual property infringement could require substantial time and money to resolve. Unfavorable outcomes in these proceedings could limit our intellectual property rights and our activities.***

We may need to resort to litigation to enforce or defend our intellectual property rights, including any patents issued to us. If a competitor or collaborator files a patent application claiming technology also invented by us, in order to protect our rights, we may have to participate in an expensive and time-consuming opposition proceeding before the European Patent Office, the United States Patent and Trademark Office or patent authorities in other jurisdictions. We cannot guarantee that there will be no claims from third parties alleging that our product candidates infringe their intellectual property rights. Third parties may assert that we are employing their proprietary technologies without authorization and they may resort to litigation to attempt to enforce their rights. Third parties may have or obtain patents in the future and claim that the use of our technology or any of our product candidates infringes their patents. We may not be able to develop or commercialize product candidates because of patent protection others have. Our business will be harmed if we cannot obtain a necessary or desirable license, can obtain such a license only on terms we consider to be unattractive or unacceptable, or if we are unable to redesign our product candidates or processes to avoid actual or potential patent or other intellectual property infringement. Our efforts to obtain, protect and defend our patent and other intellectual property rights, whether we are successful or not, can be expensive and may require us to incur substantial costs, including the diversion of management and technical personnel. An unfavorable ruling in patent or intellectual property litigation could subject us to significant liabilities to third parties, require us to cease developing, manufacturing or selling the affected products or using the affected processes, require us to license the disputed rights from third parties, or result in awards of substantial damages against us. During the course of any patent litigation, there may be public announcements of the results of hearings, motions and other interim proceedings or developments in the litigation. If securities analysts or investors regard these announcements as negative, the market price of our Shares may decline. General proclamations or statements by key public figures may also have a negative impact on the perceived value of our intellectual property.

There can be no assurance that we would prevail in any intellectual property infringement action or will be able to obtain a license to any third party intellectual property on commercially reasonable terms, successfully develop non-infringing alternatives on a timely basis, or license non-infringing alternatives, if any exist, on commercially reasonable terms. Any significant intellectual property impediment to our ability to develop and commercialize our products could have a material adverse effect on our business and prospects.

***Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.***

In our activities, we rely substantially upon proprietary materials, information, trade secrets and know-how to conduct our research and development activities, and to attract and retain collaborators, licensees and customers. We take steps to protect our proprietary rights and information, including the use of confidentiality and other agreements with our employees and consultants and in our academic and commercial relationships. However, these steps may be inadequate, agreements may be violated, or there may be no adequate remedy available for a violation of an agreement. We cannot assure you that our proprietary information will not be disclosed or that we can meaningfully protect our trade secrets. Our competitors may independently develop substantially equivalent proprietary information or may otherwise gain access to our trade secrets, which could adversely affect our ability to compete in the market.

## **Risks Related to Our Employees and Growth**

*We rely significantly on the skills and experience of our chief executive officer and other key executives and the loss of these individuals could harm our business.*

Our success depends on our ability to attract, retain and motivate highly qualified management and scientific personnel. In particular, we are highly dependent on Joost Holthuis, Ph.D., our Chief Executive Officer, and the other principal members of our executive and scientific teams. If we are not able to retain these persons, we may not be able to successfully develop or commercialize our product candidates. We do not maintain “key person” insurance in relation to any of our employees.

*Our future success depends on our ability to attract, retain and motivate qualified personnel.*

Recruiting and retaining qualified personnel is critical to our success. We may not be able to attract and retain qualified personnel on acceptable terms given the competition among pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research, clinical development and commercialization strategy. Our consultants and advisors may be employed by third parties or may have commitments under consulting or advisory contracts with third parties that may limit their availability to us.

*We may encounter difficulties in managing our growth.*

We expect to experience significant growth in the number of our employees and the scope of our operations over the next several years. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, and continue to recruit and train additional qualified personnel. Due to our limited resources, we may not be able to effectively manage the expansion of our operations or to recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans, which would adversely affect our results.

## **Risks Related to Regulatory Approval and Other Government Regulations**

*The regulatory approval process is costly and lengthy and we may not be able to successfully obtain all required regulatory approvals.*

The pre-clinical development, clinical trials, manufacturing, marketing and labeling of pharmaceuticals and medical devices are all subject to extensive regulation by numerous governmental authorities and agencies in the European Union, the United States and other jurisdictions. We or our collaborators must obtain regulatory approval for product candidates before marketing or selling any of them. The approval process is typically lengthy and expensive, and approval is never certain. It is not possible to predict how long the approval processes of the EMEA, the FDA or any other applicable regulatory agency will take or whether any such approvals ultimately will be granted. The EMEA, the FDA and other regulatory agencies have substantial discretion in the drug and medical device approval process, and positive results in pre-clinical or early clinical trials provide no assurance of success in later phases of the approval process. Generally, pre-clinical and clinical trials of products and medical devices can take many years and require the expenditure of substantial resources, and the data obtained from these trials can be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. The risks associated with the approval process include delays or rejections in the regulatory approval process based on the failure of clinical or other data to meet expectations, or the failure of the product or medical device to meet a regulatory agency’s requirements for safety and efficacy. In addition, regulatory approval, if obtained, may significantly limit the indicated uses for which a product may be marketed.

Additional clinical trials may be required if clinical trial results are negative or inconclusive, which will require us to incur additional costs and significant delays. If we do not receive the necessary regulatory

approvals, we will not be able to generate product revenues and may not become profitable. We may encounter significant delays in the regulatory process that could result in excessive costs that may prevent us from continuing to develop our product candidates. In addition, the failure to comply with applicable regulatory requirements may result in criminal prosecution, civil penalties, product recalls, withdrawal of product approval, mandatory restrictions and other actions that could impair our ability to conduct our business.

***Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we fail to comply with continuing regulations, we could lose these approvals and the sale of our products could be suspended.***

Even if we receive regulatory approval to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could limit the indicated uses included in the labeling of our products. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, the manufacturer of the product and its facilities will continue to be subject to regulatory review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing approval, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping related to the product will remain subject to extensive regulatory requirements.

If we fail to comply with applicable regulatory requirements, or previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on our products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties or fines;
- injunctions;
- product seizures, detentions or import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

Any such sanction could severely harm our business and financial condition.

***Our ability to generate revenue from any products that we may develop will depend on reimbursement and drug pricing policies and regulations.***

Many patients may be unable to pay for any products that we may develop. Many patients will rely on governmental authorities, private health insurers and other third-party payors to pay for their medical needs. Our ability to achieve acceptable levels of reimbursement for drug treatments by governmental authorities, private health insurers and other organizations will have an effect on our ability to successfully commercialize, and attract collaborative partners to invest in the development of, our product candidates. We cannot be sure that reimbursement in the European Union, the United States or other jurisdictions will be available for any products that we may develop, and any reimbursement that may become available may be decreased or eliminated in the future. Third-party payors increasingly are challenging prices charged for pharmaceutical products, and many third-party payors may refuse to provide reimbursement for particular drugs when an equivalent generic or non-generic drug is available. Even if we show improved efficacy or improved convenience of administration with



our product candidate, pricing of the existing drug may limit the amount we will be able to charge for our product candidate. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize our product candidates, and may not be able to obtain a satisfactory financial return on products that we may develop.

In addition, in some countries, particularly those in the European Union, prescription drug pricing is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

In recent years, the pricing of prescription drugs has been a subject of focus in many of the major pharmaceutical markets. Any future regulatory changes regarding the healthcare industry or third-party coverage and reimbursement may affect demand for any products that we may develop and could harm our sales and profitability.

### **Risks Related to Our Financial Condition**

***We have incurred losses since 2002 and anticipate that we will continue to incur losses for the foreseeable future. We may not achieve or sustain profitability again.***

We are not profitable and have incurred losses in each year since 2002. We do not currently have any products that have been approved for marketing, and we continue to incur research and development and general and administrative expenses related to our operations. Our net loss for the six months ended 30 June 2006 and the years ended 31 December 2005, 2004 and 2003 was €4.1 million, €4.6 million, €2.2 million, and €2.2 million, respectively. As of 30 June 2006, we had an accumulated deficit of €14.5 million. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our research activities and conduct development of, and seek regulatory approvals for, our product candidates, and commercialize any approved drugs. Our losses, among other things, have caused and will continue to cause our shareholders' equity and working capital to decrease. To date, we have derived a substantial portion of our revenues from our Contract Development Business. We have also received government subsidies and have generated nominal licensing revenues through the outlicensing of certain technologies. We do not anticipate that we will generate revenues from the sale of products for the foreseeable future. If our product candidates fail in clinical trials or do not gain regulatory approval, or if our product candidates do not achieve market acceptance, we may never again achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

***We will need substantial additional funding in the future, which may not be available to us on acceptable terms, or at all, and which could force us to delay, reduce or eliminate our product development programs or commercialization efforts or cause us to discontinue our operations.***

We will need to raise substantial additional capital to pursue our business strategy and continue the development of our product candidates. Our future funding requirements will depend on many factors, including:

- scope, rate of progress, results and cost of our pre-clinical and clinical trials and other research and development activities;
- terms and timing of any collaborative, licensing and other arrangements that we may establish;
- cost, timing and outcomes of regulatory approvals;
- number and characteristics of product candidates that we pursue;



- cost and timing of establishing sales, marketing and distribution capabilities;
- cost of clinical and commercial supplies of our product candidates and any products that we may develop;
- timing, receipt and amount of sales or royalties, if any, from our potential products, or any up-front or milestone payments during their development phase;
- the cost of preparing, filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the extent to which we acquire or invest in businesses, products or technologies, although we currently have no commitments or agreements relating to any of these types of transactions; and
- our ability to continue to generate revenues from our Contract Development Business.

Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may:

- terminate or delay pre-clinical and clinical trials for one or more of our product candidates;
- delay our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates; or
- curtail development programs.

If required, additional funds are not available on a timely basis, we may be required to delay, scale back or eliminate certain of our activities and commercialization efforts, which would have a material adverse affect on our financial condition and ability to develop our product candidates or cause us to discontinue our operations.

***Raising additional capital by issuing securities or through collaboration and licensing arrangements may cause dilution to existing shareholders, restrict our operations or require us to relinquish proprietary rights.***

We may seek the additional capital necessary to fund our operations through public or private equity offers, debt financings and collaboration and licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms of such securities may include liquidation or other preferences that adversely affect your rights as a shareholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us.

***We face the potential loss of significant revenue from the loss, modification or delay of large contracts or the inability to secure new contracts.***

To date, our principal sources of revenue have been our Contract Development Business and, to a lesser extent, government subsidies. Our customer base presently comprises approximately 35 clients who award us with work on a contract-by-contract basis. In 2005, our five largest clients accounted for 55% of our Contract Development Business revenues. Our clients may resolve, on relatively short notice, to suspend or terminate the development activities that we conduct on their behalf. We have in the past experienced such project suspensions or terminations with significant clients. We expect that a small number of clients will continue to represent a significant part of our contract development revenues. In addition, our clients and target customers, as they try to reduce costs as a result of budgetary limits or changing priorities, may proceed without or with decreased assistance of biopharmaceutical services companies like us. The loss, modification or delay of a large contract or of multiple contracts, or the inability to secure new contracts, could have a material adverse effect on our operating results.

## Risks Related to this Offer

*There has been no prior public market for our Shares, the price of our Shares may be volatile and you may not be able to sell our Shares at or above the price you pay for them.*

Prior to this Offer, there has been no public market for our Shares. We intend to apply for admission of our Shares to listing and trading on Euronext Amsterdam. We cannot predict the extent to which an active market for our Shares will develop or be sustained after this Offer, or how the development of such a market might affect the market price for our Shares. An illiquid market for our Shares may result in lower trading prices and increased volatility, which could adversely affect the value of your investment.

The Offer Price will be agreed between us and the Underwriters based on a number of factors, including market conditions in effect at the time of the Offer, which may not be indicative of future performance. The market price for our Shares may fall below the Offer Price. The market price of our Shares could fluctuate substantially due to a number of factors, including, but not limited to:

- adverse results or delays in our clinical trials;
- the timing of achievement of our clinical, regulatory, partnering and other milestones, such as the commencement of clinical development, the completion of a clinical trial, the receipt of regulatory approval or the establishment of a partnership for one or more of our product candidates;
- announcement of EMEA, FDA or other regulatory authorities' approval or non-approval of our product candidates or delays in their review processes;
- actions taken by regulatory authorities with respect to our product candidates, our clinical trials or our sales and marketing activities;
- the commercial success of any approved product;
- regulatory developments in the European Union, the United States and other jurisdictions;
- disruption of the manufacturing of essential materials that are incorporated in our product candidates;
- changes in the structure of healthcare payment systems;
- any actual or threatened intellectual property infringement lawsuit or cancellation proceeding involving us;
- announcements of technological innovations or new products by us or our competitors;
- a decline in our Contract Development Business;
- market conditions for, or developments affecting, the biotechnology or pharmaceutical industries in general or certain companies within these industries;
- changes in financial estimates or recommendations by securities analysts;
- sales of large blocks of our Shares;
- sales of our Shares by our executive officers, directors and significant shareholders;
- restatements of our financial results and/or material weaknesses in our internal controls;
- the loss of any of our key personnel;
- publication of research reports about us or the biopharmaceutical industry by securities or industry analysts;
- failure to meet or exceed securities analysts' expectations relating to our financial results;
- speculation in the press or investment community generally;

- general economic conditions, particularly as they impact consumer spending patterns; and
- war, acts of terrorism and other man-made or natural disasters.

The stock markets in general, and the markets for biopharmaceutical stocks in particular, have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. These broad market fluctuations may adversely affect the trading price of our Shares.

***If closing of the Offer does not take place on the Settlement Date or at all, subscriptions for our Shares will be disregarded and transactions effected in our Shares will be annulled.***

We intend to apply for admission of our Shares to listing and trading on Euronext Amsterdam under the symbol “OCTO”. We expect that our Shares will first be admitted to listing on a provisional basis (voorlopige notering) and that trading in such Shares will commence on the Listing Date which is expected to occur on or about 4 October 2006 (T). The Settlement Date, on which the closing of the Offer is scheduled to take place, is expected to occur on or about 9 October 2006, the third trading day following the date on which trading is expected to commence (T+3). The closing of the Offer may not take place on the Settlement Date or at all if certain conditions or events referred to in the underwriting agreement (see “Underwriting”) are not satisfied or waived or occur on or prior to such date. Such conditions include the receipt of officers’ certificates and legal opinions and such events include the suspension of trading on Euronext Amsterdam or a material adverse change in our financial condition or business affairs or in the financial markets. Trading in our Shares before the closing of the Offer will take place subject to the condition subsequent (ontbindende voorwaarde) that, if closing of the Offer does not take place on the Settlement Date or at all, the Offer will be withdrawn, all subscriptions for our Shares will be disregarded, any allotments made will be deemed not to have been made, any subscription payments made will be returned without interest or other compensation and transactions on Euronext Amsterdam will be annulled. All dealings in our Shares prior to settlement and delivery are at the sole risk of the parties concerned. Euronext does not accept any responsibility or liability for any loss incurred by any person as a result of a withdrawal of the Offer and/or (the related) annulment of any transactions on Euronext Amsterdam.

***The ownership of our Shares will continue to be highly concentrated and your interests may conflict with the interests of our existing shareholders.***

Joost Holthuis, our co-founder and CEO, together with Prof. Daan Crommelin, our co-founder, Hans Pauli, our CFO, and our Senior Management, will beneficially own approximately 21.8% of our Shares upon completion of the Offer (excluding any New Shares that may be purchased by them in the Offer and assuming we raise €25 million in the Offer, no exercise of the Overallotment Option and an Offer Price at the mid-point of the Price Range). The other Major Shareholders will also continue to own a significant number of our Shares following the Offer. Accordingly, these shareholders, when acting as a group, will continue to have significant influence over the outcome of corporate actions requiring shareholder approval, including the election of members of our Supervisory Board and Executive Board, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transaction. These shareholders could delay or prevent a change of control of our company, even if such a change of control would benefit our other shareholders. The significant concentration of share ownership may adversely affect the trading price of our Shares due to investors’ perception that conflicts of interest may exist or arise.

Life Sciences Partners, S.R. One and Innoven Partenaires have each nominated members to our Supervisory Board. All of these individuals will remain on the Supervisory Board after the Offer. Through these individuals and as a result of their significant holdings, Life Sciences Partners, S.R. One and Innoven Partenaires may pursue corporate actions that may conflict with interests of our other shareholders.

***Our Executive Board has broad discretion over the use of the net proceeds received by us from the Offer and may not apply the net proceeds effectively or in ways with which you agree.***

Our Executive Board has broad discretion over the use of net proceeds from the sale of New Shares in the Offer. We intend to use the net proceeds from the Offer primarily for the further development of our product

candidates. In addition, we may use a portion of the net proceeds to in-license or acquire additional product candidates or technologies.

You will not have an opportunity, as part of your investment decision, to assess whether the net proceeds received by us are being used appropriately. We cannot assure you that our Executive Board will apply the net proceeds effectively or that the net proceeds will be invested to yield a favorable return.

***Future sales, or the possibility of future sales, of a substantial amount of our Shares may depress the price of our Shares.***

Future sales of our Shares, or the perception that such sales will occur, could cause a decline in the market price of our Shares. Upon completion of the Offer, 6,734,408 of our total Shares will be outstanding in addition to the 10,054,200 Shares currently owned by the Major Shareholders, assuming we raise €25 million in the Offer, no exercise of the Overallotment Option and an Offer Price at the mid-point of the Price Range. In connection with the Offer, we and the current shareholders, optionholders and warrant holders have agreed to certain restrictions on the sale or other disposition of our Shares or securities exchangeable or convertible into, or exercisable for, or repayable with our Shares for a period of at least 365 days from the date of the underwriting agreement, except with the prior written consent of Cowen, and certain other exceptions. We cannot predict whether substantial numbers of our Shares will be sold in the open market following the expiry of the 365-day period. In particular, there can be no assurance that, after this period expires, the current shareholders will not reduce their holdings of our Shares. Future sales of our Shares could be made by us, the Major Shareholders, other shareholders or through a capital increase undertaken by us for additional working capital, to fund an acquisition or for another purpose. A sale of a substantial number of our Shares, or the perception that such sale could occur, could materially and adversely affect the market price of our Shares and could also impede our ability to raise capital through the issue of equity securities in the future.

***We could become a passive foreign investment company for United States federal income tax purposes.***

Although we believe that we are not a passive foreign investment company ("PFIC") for United States federal income tax purposes, this determination is based upon the best judgment of management as to the fair market value of our assets, including our intangibles. We have not sought or obtained an independent appraisal of our assets and business. No assurance can be offered that our conclusions as to the values of our assets will not be challenged by the United States Internal Revenue Service or that a court might not ultimately sustain such a challenge. Although we do not believe that we are now, nor do we expect to become, a PFIC, this conclusion is a factual determination that generally cannot be determined until the close of the taxable year in question and is made annually (based in part upon the value of our assets and ordinary shares) and thus may be subject to change. If we were to be a PFIC in any year, materially adverse consequences as described below under "Taxation – Taxation in the United States – Passive Foreign Investment Company Considerations" could result for holders of our Shares that are subject to taxation in the United States. Such investors are urged to consult their own tax advisers regarding the possibility of our being classified as a PFIC and the potential tax consequences arising from the ownership and disposition of an interest in a PFIC.

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

In the event of an increase in our share capital, holders of our 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 the Executive Board, if so designated by the General Meeting of Shareholders or pursuant to our Articles of Association.

In particular, U.S. holders of our 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. We intend to evaluate at the time of any rights issue the cost and potential liabilities associated with any such registration statement, as well as the indirect benefits and costs to us of enabling the exercise by U.S. holders of their pre-emption rights for our

Shares and any other factors considered appropriate at the time. We will then make a decision as to whether to file such a registration statement, although currently we do not expect that any registration statement would be filed. No assurance can be given that any registration statement would be filed or that any exemption from registration would be available to enable the exercise of a U.S. holder's pre-emption rights.

***If securities or industry analysts do not publish research or reports about our business, or if they change their recommendations regarding our Shares adversely, the price and trading volume of our Shares could decline.***

The trading market for our Shares will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us or our industry downgrade our Shares, the market price of our Shares would likely decline. If one or more of these analysts ceases coverage of us or fails to regularly publish reports on us, we could lose visibility in the financial markets, which could cause the market price of our Shares or trading volume to decline.

***As a new investor, you will experience immediate and substantial dilution in the net tangible book value of your Shares.***

The Offer Price of our Shares is considerably more than the net tangible book value per Share of our outstanding Shares. Accordingly, investors purchasing Shares in the Offer will pay a price per Share that substantially exceeds the value of our assets after subtracting liabilities.

***We do not intend to pay dividends for the foreseeable future.***

We do not intend to pay any dividends for the foreseeable future. Payment of future dividends to shareholders will effectively be at the discretion of the Executive Board, subject to the approval of the Supervisory Board after taking into account various factors including our business prospects, cash requirements, financial performance and new product development. In addition, payment of future dividends may be made only if our shareholders' equity exceeds the sum of our called up and paid-in share capital plus the reserves required to be maintained by law and by our Articles of Association. Accordingly, investors cannot rely on dividend income from our Shares and any returns on an investment in our Shares will likely depend entirely upon any future appreciation in the price of our Shares. We can provide no assurance that the price of our Shares will appreciate after the Offer or that the market price for our Shares will not fall below the Offer Price.

***Dutch law and our Articles of Association permit anti-takeover provisions that may prevent or discourage takeover attempts that may be favorable to shareholders.***

Our Articles of Association allow us to implement anti-takeover measures that may have the effect of preventing, discouraging or delaying a change of control. We intend to incorporate Stichting Continuïteit OctoPlus which upon incorporation will be entitled to acquire from us, and we may demand that Stichting Continuïteit OctoPlus acquires from us, preference shares up to a maximum of 100% of our total issued and outstanding share capital, excluding issued and outstanding preference shares. The issuance of preference shares in this manner would cause substantial dilution to the voting power of any shareholder, including a shareholder attempting to gain control of us, and could therefore have the effect of preventing, discouraging or delaying a change of control that might have otherwise resulted in an opportunity for shareholders to sell our Shares at a premium to the then-prevailing market price. This anti-takeover measure may have an adverse effect on the market price of our Shares.

***No minimum amount for the Offer.***

We have the right to proceed with the Offer even if we raise substantially less than we currently intend. No minimum number of Shares in the Offer has been set. The actual number of offered Shares will be confirmed in the financial press in the Netherlands (including in the Daily Official List) together with the Offer Price. Therefore, (i) a reduced number of Shares could be available for trade on the market, which could limit their

liquidity and (ii) our financial capacity might be reduced in view of our stated use of proceeds. We might therefore reduce our level of investment or have to seek for further external funding.

## IMPORTANT INFORMATION

No person is or has been authorized to give any information or to make any representation in connection with the offer or sale of the New Shares, other than as contained in this Prospectus, and, if given or made, any other information or representation must not be relied upon as having been authorized by us or the Underwriters. The delivery of this Prospectus at any time after the date hereof will not, under any circumstances, create any implication that there has been no change in our affairs since the date hereof or that the information set forth in this Prospectus is correct as of any time since its date.

OctoPlus N.V. accepts responsibility for the information contained in this Prospectus. Having taken all reasonable care to ensure that such is the case, OctoPlus N.V. further declares that the information contained in this Prospectus is, to the best of its knowledge, in accordance with the facts and contains no omission likely to affect its import.

**In connection with the Offer, the Underwriters through Fortis or its affiliates or agents as stabilization manager may over-allot or effect transactions that stabilize or maintain the market price of the Shares at levels above those which might otherwise prevail in the open market. Such transactions may be effected on Euronext Amsterdam in the over-the-counter market or otherwise. There is no assurance that such stabilization will be undertaken and, if it is, it commences as early as the Listing Date, may be discontinued at any time and will end no later than 30 calendar days after the Listing Date.**

### Notice to Investors

The distribution of this Prospectus and the offering and sale of the New Shares offered hereby may be restricted by law in certain jurisdictions. Persons in possession of this Prospectus are required to inform themselves about and to observe any such restrictions. This Prospectus may not be used for, or in connection with, and does not constitute, any offer to sell, or an invitation to purchase, any of the New Shares offered hereby in any jurisdiction in which such offer or invitation would be unlawful.

The New Shares have not been approved or disapproved by the United States Securities and Exchange Commission, any State securities commission in the United States or any other United States regulatory authority, nor have any of the foregoing passed upon or endorsed the merits of the Offer or the accuracy or adequacy of this Prospectus. Any representation to the contrary is a criminal offence in the United States.

NEITHER THE FACT THAT A REGISTRATION STATEMENT OR AN APPLICATION FOR A LICENCE HAS BEEN FILED UNDER CHAPTER 421-B OF THE NEW HAMPSHIRE REVISED STATUTES WITH THE STATE OF NEW HAMPSHIRE NOR THE FACT THAT A SECURITY IS EFFECTIVELY REGISTERED OR A PERSON IS LICENSED IN THE STATE OF NEW HAMPSHIRE CONSTITUTES A FINDING BY THE SECRETARY OF STATE OF NEW HAMPSHIRE THAT ANY DOCUMENT FILED UNDER RSA 421-B IS TRUE, COMPLETE AND NOT MISLEADING. NEITHER ANY SUCH FACT NOR THE FACT THAT AN EXEMPTION OR EXCEPTION IS AVAILABLE FOR A SECURITY OR A TRANSACTION MEANS THAT THE SECRETARY OF STATE OF NEW HAMPSHIRE HAS PASSED IN ANY WAY UPON THE MERITS OR QUALIFICATIONS OF, OR RECOMMENDED OR GIVEN APPROVAL TO, ANY PERSON, SECURITY OR TRANSACTION. IT IS UNLAWFUL TO MAKE, OR CAUSE TO BE MADE, TO ANY PROSPECTIVE PURCHASER, CUSTOMER OR CLIENT, ANY REPRESENTATION INCONSISTENT WITH THE PROVISIONS OF THIS PARAGRAPH.

### Presentation of Financial and Other Information

Our consolidated financial information in the Prospectus has been prepared in accordance with International Financial Reporting Standards (“IFRS”). IFRS differ in certain significant respects from US GAAP as they relate to our consolidated financial information. In making an investment decision, investors must rely upon their own examination of us, the terms of the Offer and the financial information provided herein. Potential investors should consult their own professional advisors for an understanding of the differences between IFRS and US GAAP. For a discussion of the main differences between IFRS and US GAAP as they relate to us, see “Summary of Significant Differences between IFRS and US GAAP”.



Certain figures contained in this Prospectus (not including financial figures mentioned in the “Summary – Summary of Consolidated Financial Data”, “Selected Financial Information” and in the tables in “Operating and Financial Review”) have been subject to rounding adjustments. Accordingly, in certain instances the sum of the numbers in a column or a row in tables contained in this Prospectus may not conform exactly to the total figure given for that column or row.

All references in this Prospectus to “euros” or “€” are to the currency introduced at the start of the third stage of the Economic and Monetary Union, pursuant to the Treaty establishing the European Economic Community, as amended by the Treaty on the European Union. All references to “U.S. dollars”, “US\$” or “\$” are to the lawful currency of the United States.

Any financial data in this Prospectus that has not been extracted from our audited financial statements 2003, 2004 and 2005 is unaudited. The figures relating to our consolidated financial statements for the first half of 2005 and 2006 are unaudited. However, the figures relating to our consolidated financial statements for the first half of 2005 and 2006 have been reviewed pursuant to the International Standard on Review Engagement 2410 by our auditor, Deloitte Accountants B.V. Unaudited financial information in addition to aforementioned unaudited financial statements for the period ended 30 June 2005 and 2006, has been indicated throughout this Prospectus.

Unless the context otherwise requires or it is expressly provided to the contrary, this Prospectus assumes no exercise of the Overallotment Option and an Offer Price of €5.08, the mid-point of the Price Range set forth on the front cover of this Prospectus and total Offer proceeds of €25 million.

## Exchange Rates

We publish our consolidated financial statements in euros. The exchange rates below are provided solely for information and convenience. No representation is made that the euro could have been, or could be, converted into U.S. dollars at these rates.

The table below shows the high, low, average and end of period exchange rates expressed in U.S. dollars per €1.00 for the years given, using the noon buying rate in New York City for cable transfers in foreign currencies as certified for customs purposes by the Federal Reserve Bank of New York (the “Noon Buying Rate”) for the periods indicated.

Year ended 31 December	High	Low	Average	End of Period
	(U.S. dollars per euro)			
2002 . . . . .	1.0485	0.8594	0.9458	1.0485
2003 . . . . .	1.2597	1.0361	1.1323	1.2597
2004 . . . . .	1.3625	1.1801	1.2441	1.3538
2005 . . . . .	1.3476	1.1667	1.2444	1.1842
2006 (through 31 August 2006) . . . . .	1.2953	1.1842	1.2424	1.2793

The table below shows the high and low Noon Buying Rates expressed in U.S. dollars per €1.00 for the first eight months of 2006.

	High	Low
	(U.S. dollars per euro)	
January 2006 . . . . .	1.2287	1.1842
February 2006 . . . . .	1.2100	1.1860
March 2006 . . . . .	1.2197	1.1886
April 2006 . . . . .	1.2624	1.2091
May 2006 . . . . .	1.2888	1.2607
June 2006 . . . . .	1.2953	1.2522
July 2006 . . . . .	1.2822	1.2500
August 2006 . . . . .	1.2914	1.2735

On 11 September 2006, the Noon Buying Rate for the euro was €1.00 = \$1.2699.

## **Enforceability of Judgments**

We are a limited liability company incorporated under the laws of the Netherlands. Substantially all of the members of our Executive Board and Supervisory Board are resident outside the United States, and a substantial portion of our assets and the assets of such persons are located outside the United States. As a result, it may not be possible for investors to effect service of process within the United States upon us or such persons, or to enforce against them in the Netherlands or elsewhere judgments obtained in U.S. courts, including judgments predicated on the civil liability provisions of the securities laws of the United States or any state or territory within the United States.

## **Market Data and Other Information from Third Parties**

All references to market data, industry statistics and industry forecasts in this Prospectus consist of estimates compiled by The World Health Organization, the United States Centers for Disease Control and Prevention, the Public Health Agency of Canada, the United States National Institutes of Health, Datamonitor, Reuters, Intercontinental Marketing Services, equity research analysts, other biopharmaceutical companies and ourselves. Industry publications generally state that their information is obtained from sources they believe reliable but that the accuracy and completeness of such information is not guaranteed and that the projections they contain are based on a number of significant assumptions. Although we believe these sources are reliable, as we do not have access to the information, methodology and other bases for such information, we have not independently verified the information and therefore cannot guarantee its accuracy and completeness.

In this Prospectus, we make certain statements regarding our competitive position, the expected size of the markets for which we are developing our products and the side effects or efficacy of current treatments for the relevant diseases. We believe these statements to be true based on market data and industry statistics which are in the public domain, but we have not independently verified the information and therefore cannot guarantee its accuracy and completeness.

The information in this Prospectus that has been sourced from third parties has been accurately reproduced and, as far as we are aware and able to ascertain from the information published by that third party, no facts have been omitted that would render the reproduced information inaccurate or misleading. Although we believe these sources are reliable, as we do not have access to the information, methodology and other bases for such information, we have not independently verified the information and therefore cannot guarantee its accuracy and completeness.

## **Documents Incorporated by Reference**

Our Articles of Association (statuten) as they will read after the execution of the Deed of Amendment and Conversion are incorporated by reference into this Prospectus. See “Description of Share Capital and Corporate Governance – General”. No other documents or information form part of, or are incorporated by reference into, this Prospectus.

## **FORWARD-LOOKING STATEMENTS**

This Prospectus contains forward-looking statements, including statements about our beliefs and expectations. These statements are based on our current plans, estimates and projections, as well as our expectations of external conditions and events. In particular the words “expect”, “anticipate”, “predict”, “estimate”, “project”, “may”, “could”, “should”, “would”, “will”, “intend”, “believe” and similar expressions are intended to identify forward-looking statements. Forward-looking statements involve inherent risks and uncertainties and speak only as of the date they are made. We undertake no duty to and will not necessarily update any of them in light of new information or future events, except to the extent required by applicable law. We caution investors that a number of important factors could cause actual results or outcomes to differ materially from those expressed in any forward-looking statements. These factors include, but are not limited to those discussed under “Risk Factors”.

## **DIVIDEND POLICY**

We currently intend to retain future earnings, if any, to finance the growth and development of our business. As a result, we do not anticipate paying any dividends for the foreseeable future.

Our dividend policy will, however, be reviewed from time to time and payment of any future dividends will be effectively at the discretion of the Executive Board, subject to approval of the Supervisory Board, after taking into account various factors including our business prospects, cash requirements, financial performance, new product development, the payment on our preference shares, to the extent any are issued, in accordance with our Articles of Association (see “Description of the Share Capital and Corporate Governance – Dividends and Other Distributions”) and the requirements of Dutch law. Under Dutch law, payment of dividends may be made only if our shareholders’ equity exceeds the sum of our called up and paid-in share capital plus the reserves required to be maintained by law and by our Articles of Association.

## USE OF PROCEEDS

We expect to raise approximately €25 million of gross proceeds from the issue of New Shares in the Offer. The net proceeds we will receive from the issue of New Shares in the Offer are estimated to be approximately €22.25 million after deducting the estimated underwriting fees and commissions and expenses payable by us, assuming no exercise of the Overallotment Option. We intend to use the net proceeds we receive from the Offer primarily for general corporate purposes, including:

- Locteron development activities, including the Phase IIa study and subsequent clinical studies and manufacturing and material costs;
- OP-145 development activities, including completion of the currently ongoing Phase II study and further studies needed to progress OP-145 to regulatory approval, as well as manufacturing and material costs;
- hGH-OctoDEX development activities, including a further Phase I clinical trial and subsequent clinical trials, as well as manufacturing and material costs;
- pre-clinical research and development activities for both OctoVAX product candidates, HBV-OctoVAX and JEV-OctoVAX, as well as subsequent clinical studies and manufacturing and material costs;
- in-licensing or acquiring of additional product candidates or technologies; and
- other general corporate purposes, including capital expenditures and working capital.

This expected use of net proceeds of this Offer represents our current intentions based upon our present plans and business conditions. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from clinical trials and other studies for Locteron, OP-145 and hGH-OctoDEX, as well as the development of our pre-clinical product portfolio and research being carried out, any collaborations we may enter into with third parties for our product candidates, and any unforeseen cash needs. As a result, the Executive Board will retain broad discretion over the allocation of the net proceeds from this Offer. We do not expect the net proceeds from this Offer to be sufficient to fund the completion of the development of any of our product candidates, and we expect that we will need to raise additional funds prior to being able to market any products.

Pending use of the net proceeds of this Offer, we intend to invest the net proceeds in accordance with our investment policy guidelines, which currently provide for investment of funds in cash equivalents, government obligations, high grade and corporate notes and commercial paper.

## CAPITALIZATION AND INDEBTEDNESS

The tables below set forth our unaudited consolidated cash and cash equivalents, capitalization and indebtedness as of 30 June 2006, as follows:

- on an actual basis; and
- on a pro forma basis, as adjusted to reflect our receipt of the estimated net proceeds from the issue of the New Shares in the Offer, after deducting the estimated underwriting fees and commissions and expenses payable by us, based on gross proceeds from the Offer of €25 million, an Offer Price of €5.08, the mid-point of the Price Range, and no exercise of the Overallotment Option, and after giving effect to (1) the conversion of the three classes of our shares in existence on the date of this Prospectus into one class of Shares, (2) conversion of the convertible subordinated loan into Shares (see “Related Party Transactions”) and (3) certain other elements of the Capital Restructuring (see “Description of Share Capital and Corporate Governance – Share Capital – Authorized and Issued Share Capital”), all of which will occur immediately prior to settlement on the Settlement Date.

The financial data are extracted or derived from our unaudited condensed interim consolidated financial statements reviewed by Deloitte Accountants B.V. (see “Interim Financial Report – Review Report”). You should read this table together with our consolidated financial statements and the related notes thereto, as well as the information under “Operating and Financial Review” appearing elsewhere in this Prospectus. The table below is prepared for illustrative purposes only and, because of its nature, may not give a true picture of our financial condition following the Offer. For a summary of our principal contractual obligations and commercial commitments over the next four years and thereafter, see “Operating and Financial Review – Contractual Obligations”.

	30 June 2006	
	Actual	Pro forma as adjusted
	(in thousands)	
Cash and cash equivalents <sup>(1)</sup> . . . . .	€ 4,960	€27,210
Share capital – ordinary shares . . . . .	€ 47	€ 2,015
Share capital – preferred shares . . . . .	71	–
Share premium . . . . .	18,483	42,985
Retained earnings (accumulated deficit) <sup>(2)</sup> . . . . .	(14,487)	(14,367)
Convertible subordinated loan . . . . .	4,149	–
Other reserves . . . . .	193	193
Total equity . . . . .	8,456	30,826
Total capitalization . . . . .	€16,850	€39,100

(1) The increase in cash and cash equivalents reflects the estimated net proceeds based on gross proceeds from the Offer of €25 million and estimated underwriting fees and commissions and expenses payable by us of €2.75 million.

(2) Out of the €2.75 million estimated underwriting fees and commissions and expenses payable by us, an estimated €120,000 is already included in the 30 June 2006 retained earnings (as also reflected under “current liabilities”).

As of 30 June 2006, our net asset value per share was €71.42 (unaudited).

As of 30 June 2006, our authorized capital amounted to €500,000 and was divided into 150,000 class AP Shares, 50,000 class BP Shares and 300,000 class C Shares, all with a nominal value of €1 each.

Prior to the closing of the Offer, the following steps will be taken: (i) the conversion of each of our issued class AP, class BP and class C shares into the same number of ordinary shares, (ii) a split of each of these ordinary shares into 100 ordinary shares with a nominal value of €0.01 each, and (iii) an increase in the nominal value of the ordinary shares to €0.12 each, which shall be charged against our share premium reserve in an amount of €1,304,875.

	<b>30 June 2006</b>	
	<b>Actual</b>	<b>Pro forma as adjusted</b>
	<b>(in thousands)</b>	
Cash and cash equivalents <sup>(1)</sup> . . . . .	<u>€4,960</u>	<u>€27,210</u>
Non-current liabilities . . . . .	€3,711	€3,711
Current liabilities . . . . .	<u>4,683</u>	<u>4,563</u>
Total liabilities . . . . .	<u>€8,394</u>	<u>€8,274</u>

(1) The increase in cash and cash equivalents reflects the estimated net proceeds based on gross proceeds from the Offer of €25 million and estimated underwriting fees and commissions and expenses payable by us of €2.75 million.

Of the non-current liabilities and current liabilities, €0 and €1.0 million, respectively, was secured by a pledge over the inventory and receivables of OctoPlus Development B.V. No guarantees have been issued by others in respect of any of these liabilities. See “Operating and Financial Review – Contractual Obligations” for information about certain contingent obligations of ours.



## SELECTED FINANCIAL INFORMATION

*Our selected consolidated financial data set forth below should be read in conjunction with “Operating and Financial Review” and our consolidated financial statements and notes thereto that appear elsewhere in this Prospectus. Our year-end consolidated financial data are extracted from our consolidated financial statements that have been audited by Deloitte Accountants B.V., independent auditors. Our six-month consolidated financial data are based upon our unaudited condensed consolidated interim financial accounts for the six-month periods ended 30 June 2005 and 2006. Our results for the six-month period ended 30 June 2006 are not necessarily indicative of results for the full year. Our financial statements and accounts from which the selected consolidated financial data set forth below have been derived were prepared in accordance with IFRS, which may differ from US GAAP in certain significant respects. For a discussion of the most significant differences between IFRS and US GAAP as they relate to us, in particular regarding finance leases and intellectual property rights, see “Summary of Significant Differences between IFRS and US GAAP”. Our selected consolidated financial data set forth below may not contain all of the information that is important to you.*

### Consolidated Income Statement Data

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Contract research . . . . .	€5,043	€4,924	€6,563	€3,300	€3,156
Royalties and license revenues . . . . .	–	60	60	30	30
Income from subsidiaries . . . . .	818	708	394	236	92
Other income . . . . .	–	26	–	–	1
Total revenues . . . . .	<u>5,861</u>	<u>5,718</u>	<u>7,017</u>	<u>3,566</u>	<u>3,279</u>
Raw materials and auxiliaries . . . . .	36	70	237	47	100
Costs of contracted work and other external charges . . . . .	639	307	1,390	416	1,147
Employee benefits . . . . .	3,450	3,597	4,758	2,155	2,920
Depreciation and amortization . . . . .	668	860	863	451	512
Other costs . . . . .	<u>3,275</u>	<u>2,667</u>	<u>4,213</u>	<u>1,962</u>	<u>2,597</u>
Total operating costs . . . . .	<u>8,068</u>	<u>7,501</u>	<u>11,461</u>	<u>5,031</u>	<u>7,276</u>
Operating income (loss) . . . . .	(2,207)	(1,783)	(4,444)	(1,465)	(3,997)
Interest . . . . .	<u>(29)</u>	<u>(394)</u>	<u>(118)</u>	<u>(27)</u>	<u>(104)</u>
Net income (loss) before taxes . . . . .	<u>€(2,236)</u>	<u>€(2,177)</u>	<u>€(4,562)</u>	<u>€(1,492)</u>	<u>€(4,101)</u>

### Consolidated Balance Sheet Data

	2003	2004	2005	Six months ended 2005	Six months ended 2006
				(unaudited)	(unaudited)
			(in thousands)		
Intangible fixed assets . . . . .	€1,401	€1,421	€1,705	€1,579	€1,725
Other fixed assets . . . . .	3,132	6,054	6,289	6,170	6,363
Current assets . . . . .	<u>1,659</u>	<u>1,879</u>	<u>12,506</u>	<u>15,337</u>	<u>8,762</u>
Total assets . . . . .	<u>6,192</u>	<u>9,354</u>	<u>20,500</u>	<u>23,086</u>	<u>16,850</u>
Equity (deficit) . . . . .	1,151	(1,356)	11,751	14,755	8,456
Long-term debts . . . . .	917	4,345	3,738	3,782	3,711
Current debts . . . . .	<u>4,124</u>	<u>6,365</u>	<u>5,011</u>	<u>4,549</u>	<u>4,683</u>
Total equity and liabilities . . . . .	<u>€6,192</u>	<u>€9,354</u>	<u>€20,500</u>	<u>€23,086</u>	<u>€16,850</u>

## OPERATING AND FINANCIAL REVIEW

*You should read the following in conjunction with the “Selected Financial Information” and our consolidated financial statements and the related notes thereto that appear elsewhere in this Prospectus. Our financial data have been prepared in accordance with IFRS, which may differ from US GAAP in certain significant respects as they relate to us, in particular regarding finance leases and intellectual property rights. For a discussion of the most significant differences between IFRS and US GAAP as they relate to us, see “Summary of Significant Differences between IFRS and US GAAP”.*

*In addition to historical information, the following review includes forward-looking information that involves risks, uncertainties and assumptions. Our actual results and the timing of events could differ materially from those anticipated by these forward-looking statements as a result of many factors, including those discussed below and elsewhere in this Prospectus, particularly under “Risk Factors” and “Forward-Looking Statements”.*

### Overview

We operate a synergistic business model. We were founded in 1995 to provide advanced formulation and manufacturing services to the pharmaceutical and biotechnology industries (the “Contract Development Business”). This business is operated by our subsidiary, OctoPlus Development B.V. In 1997 and 2003, we entered into exclusive licenses for access to proprietary controlled release technologies and these technologies became the basis of our own product portfolio (the “Drug Delivery and Product Business”). This business is operated by our subsidiaries, OctoPlus Technologies B.V., OctoPlus Sciences B.V. and Chienna B.V.

Over the course of the last 11 years, we have become a recognized expert in the field of the formulation of complex protein and peptide based active pharmaceutical ingredients into injectable pharmaceutical products. To date, we have achieved €39 million in cumulative revenues from this business and we have realized a positive operating result from these activities in all but one year since our establishment. We have provided our services to approximately 100 clients that have progressed more than 40 products into clinical studies and six products on to the market. Currently, approximately 70% of our revenues from this business originate in Europe, while the remainder is sourced from clients in North America, the Far East and Australia.

Our second business line focuses on the proprietary development of controlled release formulations of large molecule therapeutics. We added this business line through the exclusive in-licensing of the OctoDEX controlled release technology from Utrecht University in 1997 and our acquisition of Chienna B.V. in 2003, when we gained exclusive rights to the PolyActive technology for drug delivery applications.

For the period 2003 to 2005, our consolidated revenues increased from €5.9 million to €7.0 million. For the six months ended 30 June 2006, consolidated revenues amounted to €3.3 million, compared to €3.6 million for the same period in 2005. In each of these periods, income from clients exceeded 85% of the total revenues generated. The remaining consolidated revenues were provided by government grants and subsidies. More specifically, through the development of novel controlled release pharmaceuticals employing our drug delivery technologies, we have attracted support from the Dutch Ministry of Economic Affairs, as well as from the European Union. Since our establishment, we have been awarded a total of €7.2 million in subsidies, of which we have received approximately €2.5 million to date. As certain of our projects were completed without utilizing the full amount of the subsidy available, we remain eligible to receive a further €2.4 million pursuant to these grants.

In 2001, we issued shares to two Dutch investors, raising a total of €3 million. A further €18.4 million was raised in January 2005, when a group of European and North American funds invested €18.0 million in us. As part of this financing round, certain members of our management also invested €0.4 million in us. In June 2006, a second closing took place related to this financing, raising an additional €0.7 million.

## **Material Factors Affecting our Results of Operations and Financial Condition**

We believe that the factors described in the following paragraphs have had and are expected to continue to have a material effect on our operational results and financial condition.

### **Revenues**

#### ***Contract Development Business***

Since our establishment in 1995 through 30 June 2006, our Contract Development Business has achieved €38 million in revenues.

Since 2003, our Contract Development Business has provided active pharmaceutical formulation and manufacturing services in relation to at least 30 different projects per year. These services typically include formulation, scale-up, manufacturing and stability testing of proteins, lipids and other large molecules for our pharmaceutical and biotechnology clients. Annually, we commence work on approximately ten new projects and we have benefited to a significant extent from repeat business from our existing client base. Revenues per project generally range from approximately €25,000 to €1.5 million. Typically, our clients are charged on an employee man/hour basis for our development services, while manufacturing is charged on a lump-sum basis.

Our Contract Development Business is dependent on the overall development activity in the pharmaceutical and biotechnology sectors. In particular, in times when financing conditions for biotechnology companies are less favorable, our Contract Development Business typically experiences slower growth. Conversely, when financing is more readily available to fund development projects, our Contract Development Business grows more rapidly.

In addition, the growth of our Contract Development Business is related to our ability to increase our capacity in terms of human and physical resources. If we were able to recruit a greater number of qualified personnel, we believe we would be able to grow our business more rapidly. During the period under review, we have experienced an excess of demand for our Contract Development Business.

Our Contract Development Business revenues tend to be concentrated, with a limited number of large customer assignments generating a significant percentage of revenues in any given year. Our largest customers do, however, tend to change over time, as our large projects tend to last from two to five years on average, and are often then replaced by projects for different customers. Nevertheless, the loss of a large project can have an impact on our results, particularly if not replaced quickly by other projects. In 2005, we generated approximately 55% of our total consolidated revenues in the Contract Development Business from our five largest clients.

#### ***Drug Delivery and Product Business***

In addition to revenues from our Contract Development Business, since our establishment through 30 June 2006, we have received €2.5 million in subsidies from the Dutch Ministry of Economic Affairs and the European Union, as discussed above under “Overview”. We do not foresee any immediate change in our ability to secure and draw down subsidy revenues.

In addition, we have generated nominal revenues based on certain development agreements concerning our product candidates and technologies. Our ability to generate additional license revenues will depend on the continued success of our existing collaborations and our ability to enter into further arrangements for the out-licensing of our technologies and product candidates.

In 2004, we entered into an agreement with SurModics, Inc. regarding the out-licensing of certain applications in the field of drug eluting medical devices based on our OctoDEX and PolyActive technologies. In accordance with our agreement with SurModics, we have received and will continue to receive certain up-front and ongoing licensing fees. In addition to these licensing fees, from 1 July 2008 SurModics will be obligated to pay us certain royalties based on commercialization of our technology, including annual minimum royalty payments, for the term of the agreement. See “Business – Collaborations – SurModics, Inc.”.

In June 2006, we entered into a non-binding term sheet with Green Cross Corporation (“Green Cross”) of South Korea setting forth our understanding of the main commercial terms for the licensing of OP-145 for the treatment of chronic otitis media, or chronic middle ear infection, in the South Korean market. In the event that we enter into a binding agreement, under the proposed terms, we would receive nominal up-front license and milestone payments.

### **Operating Costs**

Our operating costs consist of five categories: Raw Materials and Auxiliaries (primarily our polymers and active pharmaceutical ingredients); Costs of Contracted Work and Other External Charges (primarily related to services performed by contract research organizations); Employee Benefits (primarily salaries, training and benefits); Depreciation and Amortization; and Other Costs (primarily related to professional advisors and general overhead). As a matter of policy, we consider Raw Materials and Auxiliaries and Costs of Contracted Work and Other External Charges to represent the majority of our research and development costs, along with a portion of our Employee Benefits cost. Our direct and indirect costs related to research and development in 2005, 2004 and 2003 amounted to €5.8 million, €3.7 million and €3.3 million, respectively, including research and development activities sponsored by us.

Raw Materials and Auxiliaries, as well as Costs of Contracted Work and Other External Charges, are allocated to our two business units as they are incurred. Employee Benefits, Depreciation and Amortization and Other Costs are allocated to our two business units on the basis of the number of full time employees in each business unit.

Approximately 2% of our total 2005 operating costs were related to Raw Materials and Auxiliaries. We anticipate that these costs will increase in line with our expanded clinical development activities.

Approximately 12% of our total 2005 operating costs were related to Costs of Contracted Work and Other External Charges. We anticipate that these costs will increase in line with our expanded clinical development activities.

Approximately 41% of our total 2005 operating costs were related to Employee Benefits.

Approximately 8% of our total 2005 operating costs were related to Depreciation and Amortization.

Approximately 37% of our total 2005 operating costs were related to Other Costs, of which costs related to property and equipment were the single largest factor. In connection with the planned expansion of our facilities, we anticipate that Other Costs will increase considerably in 2008. As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. For example, as a result of becoming a public company, we intend to appoint one additional member to our Supervisory Board, and to hire a company secretary and adopt additional policies regarding internal controls and procedures. In addition, we will incur increased costs associated with public company reporting requirements in the Netherlands.

## Results of Operations 2003, 2004, 2005 and Six Months Ended 30 June 2005 and 2006

### Six Months Ended 30 June 2005 and 2006

#### Revenues

	Six Months Ended 30 June		Change	
	2005 (unaudited) (in thousands)	2006 (unaudited) (in thousands)	€	%
Gross Service Revenues . . . . .	€3,504	€4,111	€607	17%
Inter-Segment Revenues . . . . .	(204)	(955)	(751)	368
Consolidated Service Revenues . . . . .	3,300	3,156	(144)	(4)
Royalty and License Revenues . . . . .	30	30	–	–
Income from Subsidies . . . . .	236	92	(144)	(61)
Other Income . . . . .	–	1	1	n.a.
Total Revenues . . . . .	€3,566	€3,279	€(287)	(8)%

Gross Service Revenues increased by 17%, primarily as a result of increased capacity in our Contract Development Business due to additional hirings. This additional capacity was entirely absorbed by Inter-Segment Revenues, which reflects work carried out for our Drug Delivery and Products Business by the Contract Development Business in furtherance of our clinical development programs. Consolidated Service Revenues decreased by 4% as a result of enhanced activity involving our Locteron product candidate, which utilized resources that otherwise would have been available for third party projects.

Income from Subsidies decreased, primarily as a result of the completion of subsidized activities related to the development of hGH-OctoDEX in the first quarter of 2005.

#### Operating Costs

	Six Months Ended 30 June		Change	
	2005 (unaudited) (in thousands)	2006 (unaudited) (in thousands)	€	%
Raw Materials and Auxiliaries . . . . .	€ 47	€ 100	€ 53	113%
Contracted Work and Other External Changes	416	1,147	731	176
Employee Benefits . . . . .	2,155	2,920	765	35
Depreciation and Amortization . . . . .	451	512	61	14
Other Costs . . . . .	1,962	2,597	635	32
Total Operating Costs . . . . .	€5,031	€7,276	€2,245	45%

Raw Materials and Auxiliaries increased by 113%, primarily due to increased development activities. In particular, we purchased increased amounts of raw materials for our drug delivery technologies.

Contracted Work and Other External Charges also increased due to greater activity involving the development of our clinical candidates. In particular, we incurred greater costs from the contract research organizations that were managing our clinical and pre-clinical trial activities, largely related to Locteron.

The number of our employees increased from 99 to 125, resulting in an increase of Employee Benefits of 35%. The increase in the number of our employees also resulted in a 14% increase in Depreciation and Amortization, largely due to the purchase of new equipment for these employees.

Other Costs increased by 32%, primarily as a result of expenditures related to our conversion from Dutch GAAP to IFRS accounting standards and improvements to our IT infrastructure.

**Years Ended 31 December 2004 and 2005**

*Revenues*

	Year Ended 31 December		Change	
	2004	2005	€	%
		(in thousands)		
Gross Service Revenues . . . . .	€5,717	€6,929	€1,212	21%
Inter-Segment Revenues . . . . .	(793)	(366)	427	(54)
Consolidated Service Revenues . . . . .	4,924	6,563	1,639	33
Royalty and License Revenues . . . . .	60	60	-	-
Income from Subsidies . . . . .	708	394	(314)	(44)
Other Income . . . . .	26	-	(26)	(100)
Total Revenues . . . . .	€5,718	€7,017	€1,299	23%

Gross Service Revenues increased by 21%, primarily as a result of a strong business environment for pharmaceutical services and increased capacity in our Contract Development Business. We also commenced work on 11 new projects during this period. Inter-Segment Revenues declined by 54% during this period, primarily due to our decision to terminate a pre-clinical research project at the end of 2004. In total, Consolidated Service Revenues increased by 33%.

Royalty and License Revenues in 2004 and 2005 reflects ongoing payments from SurModics pursuant to our license agreement covering the use of certain of our technologies in the area of drug eluting medical devices.

Income from Subsidies declined because we completed subsidized work related to the hGH-OctoDEX project in the first quarter of 2005. Furthermore, a pre-clinical research project was terminated in the first quarter of 2005, which involved subsidies from the Dutch Ministry of Economic Affairs.

*Operating Costs*

	Year Ended 31 December		Change	
	2004	2005	€	%
		(in thousands)		
Raw Materials and Auxiliaries . . . . .	€ 70	€ 237	€ 167	239%
Contracted Work and Other External Charges . . . . .	307	1,390	1,083	353
Employee Benefits . . . . .	3,597	4,758	1,161	32
Depreciation and Amortization . . . . .	860	863	3	0
Other Costs . . . . .	2,667	4,213	1,546	58
Total Operating Costs . . . . .	€7,501	€11,461	€3,960	53%

Cost associated with Raw Materials and Auxiliaries increased by 239%, primarily due to increased development activities, in particular, due to the purchase of interferon alfa.

Contracted Work and Other External Charges also increased due to greater activity involving the development of our clinical candidates. In particular, we incurred greater costs from the contract research organizations managing our clinical and pre-clinical trial activities, largely related to Locteron.

The number of our employees increased from 93 to 110, resulting in an increase of Employee Benefits of 32%. In addition, certain of our employees received benefit increases in 2004, in line with local employment trends.

Other Costs increased by 58%, partly due to greater overhead and equipment expenses as a result of an increase in our number of staff. Furthermore, we increased manufacturing activity in our pilot plant and we incurred additional expenses in relation to temporary personnel services and professional recruitment charges.

#### *Years Ended 31 December 2003 and 2004*

##### *Revenues*

	Year Ended 31 December		Change	
	2003	2004	€	%
		(in thousands)		
Gross Service Revenues . . . . .	€5,399	€5,717	€318	6%
Inter-Segment Revenues . . . . .	(356)	(793)	(437)	123
Consolidated Service Revenues . . . . .	5,043	4,924	(119)	(2)
Royalty and License Revenues . . . . .	–	60	60	n.a.
Income from Subsidies . . . . .	818	708	(110)	(13)
Other Income . . . . .	–	26	26	n.a.
Total Revenues . . . . .	€5,861	€5,718	€(143)	(2)%

Gross Service Revenues were relatively constant. Inter-Segment Revenues increased by 123%, primarily due to services provided to the Drug Delivery and Product Business related to the pre-clinical development project that was later terminated. Consolidated Service Revenues were relatively constant.

Royalty and License Revenues in 2004 reflect our agreement concluded that year to license certain of our technologies to SurModics.

Income from Subsidies declined by 13% due to a decrease in subsidized activities relating to the hGH-OctoDEX project. This decrease was partly offset by increased subsidized activities relating to the pre-clinical development project that was later terminated.

##### *Operating Costs*

	Year Ended 31 December		Change	
	2003	2004	€	%
		(in thousands)		
Raw Materials and Auxiliaries . . . . .	€ 36	€ 70	€ 34	94%
Contracted Work and Other External Charges . . . . .	639	307	(332)	(52)
Employee Benefits . . . . .	3,450	3,597	147	4
Depreciation and Amortization . . . . .	668	860	192	29
Other Costs . . . . .	3,275	2,667	(608)	(19)
Total Operating Costs . . . . .	€8,068	€7,501	€(567)	(7)%

Costs associated with Raw Materials and Auxiliaries increased by 94%, primarily due to increased development activities in relation to the pre-clinical development project that was later terminated.

Contracted Work and Other External Charges decreased by 52%, primarily due to a reduction in clinical and pre-clinical development activities related to the hGH-OctoDEX project following the completion of a Phase I clinical trial.



Depreciation and Amortization increased by 29%, primarily due to our decision to acquire, and subsequently enter into a sale and leaseback transaction related to, our property in Leiden, the Netherlands.

Other Costs decreased by 19% because expenses associated with the acquisition of Chienna were fully absorbed in 2003 and the relocation of Chienna employees to more economical facilities in Leiden was carried out during the first quarter of 2004.

## ***Interest***

### ***Interest Costs***

In 1998, we obtained a credit facility from ING Bank N.V. with a total capacity of €681,000. In 2003, this facility was increased to €981,000. As of 31 December 2003 we had drawn down €777,000 under this facility. This loan was originally provided at a variable interest rate, which as of April 2003 was converted to a fixed rate at 4.8%. We also borrowed funds from certain of our shareholders and related parties and as of 31 December 2003, these borrowings amounted to €411,000. In addition to interest owing on these borrowings, in 2003 we made periodic payments to IsoTis in relation to our acquisition of Chienna. These periodic payments were subject to an interest charge. As a result, total interest paid in 2003 amounted to €106,000.

In 2004, a new credit facility was negotiated with ABN AMRO Bank N.V., which raised our available credit to €2.0 million and replaced our earlier credit facility with ING. Furthermore, in April 2004 we acquired our main building, which we subsequently sold and leased back. As a result, a significant part of our annual rental costs are now accounted for as interest. As a result, total interest expense increased to €412,000 in 2004.

Following a capital increase in 2005, all amounts drawn down under our credit facility with ABN AMRO were fully repaid, though the facility remains available to us. As a result, interest costs for 2005 reflect primarily the interest expenses associated with the finance lease contracts for our property, plant and equipment, amounting to €405,000.

### ***Interest Income***

Interest income reflects interest earned on our deposits of cash in interest bearing accounts.

## **Liquidity and Capital Resources**

Our primary sources of liquidity have been our funds generated from our Contract Development Business' operations and equity and debt financing. We have also received some government subsidies and have generated limited license revenues. With our change of focus from contract development to the development of proprietary product candidates using our drug delivery technologies, our capital requirements have increased and equity fund raising has been an increasingly important source of our liquidity.

Following our incorporation in 1995, we completed our first equity financing round in December 2001, when two Dutch based venture capital investors, NPM Capital N.V. and 7X Life Sciences B.V. purchased ordinary shares for €3.0 million. The proceeds of this financing round were utilized to develop our proprietary technology platforms, OctoDEX and PolyActive.

Our acquisition of Chienna in March 2003 had a significant impact on our capital resources, due to the up-front costs of the acquisition as well as costs due to Chienna's ongoing operating expenses.

In September 2004, through our subsidiary OctoPlus Development B.V. we increased amounts available under our credit facilities from €981,000 to €2.0 million through entering into a new facility. This credit line remains available to us. As collateral for this facility, OctoPlus Development B.V. provided a pledge over its equipment, inventories and receivables. OctoPlus International Holding B.V. is jointly and severally liable for the debt. In addition, the facility agreement contains a covenant that requires that OctoPlus Development B.V.'s shareholders equity shall equal at least 25% of its total assets.

In January 2005, we issued 68,615 preference shares and a subordinated convertible bond, raising a total of €18.4 million. Investors in this round of financing included Life Sciences Partners B.V., S.R. One, Limited, Innoven Partenaires S.A., Fortis N.V./S.A., SurModics, Inc. and several members of our management team. The stated use of proceeds of the 2005 financing included the further development of our proprietary technologies and our portfolio of product candidates.

In June 2006, we issued a further 2,786 preference shares and a subordinated convertible bond as part of a second closing related to the January 2005 financing round. As a result we raised an additional €0.7 million, which was received in July 2006.

### **Net Cash Used**

In 2003, we reported operating cash flows of €359,000. However, due to the acquisition of Chienna and further investments in plant and equipment, we reported negative cash flows from investment of €2.2 million. Cash flows from financing activities were neutral. As a result we posted a net negative cash flow in 2003 of €1.9 million.

In 2004, operating activities generated cash flow amounting to €948,000. As a result of investments in plant and equipment we reported negative cash flows from investment of €944,000, while the redemption of various borrowings resulted in a further €923,000 cash reduction. As a result we posted a net negative cash flow in 2004 of €919,000.

In 2005, we reported negative cash flows from operating activities of €4.8 million. Investments in plant and equipment and intangible assets amounted to €1.2 million, resulting in a total cash out flow of €6.0 million. Net cash flow from all financing activities, including the issue of equity and a subordinated convertible bond, repayment of finance lease obligations and repayment of borrowings outstanding under our credit facility amounted to €16.9 million. As a result, the positive net cash flow from all operational, investment and financing activities in 2005 was €10.9 million.

In the first half of 2006, we reported negative cash flows from operating activities of €4.7 million. Investments in tangible and intangible assets amounted to €606,000, and net cash flow from all financing activities was neutral. As a result, the total negative net cash flow from all operational, investment and financing activities was €5.3 million.

As from 2002 onwards, expenses in technology and product development exceeded net operating profits from our Contract Development Business. For the next several years, we expect expenses for technology and product development to significantly exceed the net cash flow from our Contract Development Business. We believe the costs for the pre-clinical and clinical trials of our product candidates will exceed our income from subsidies and license revenues, if any. In addition to a consolidated net operating loss we expect to make significant investments in equipment for expanding our new facilities.

Our current cash resources, together with our existing financing facilities, do not provide us with sufficient working capital for the next 12 months following the date of this Prospectus. However, we do have sufficient working capital until May 2007. If the Offer should be withdrawn, we require additional funds of approximately €3 million to cover the deficit in our working capital for the next 12 months following the date of this Prospectus. In that event, we intend to request our current shareholders to provide us with the requisite funds. Several of our current shareholders have already confirmed their willingness to provide us with such funds. We are, therefore, confident that any deficit in our working capital occurring in the next 12 months following the date of this Prospectus will be remedied in time. If the Offer is completed, the expected net proceeds of the Offer plus our current cash resources together with our existing financing facilities provide us with sufficient working capital for at least the next 12 months following the date of this Prospectus.

### **Contractual Obligations**

It is our policy to lease our property, plant and equipment in order to reduce the substantial cash outlay associated with investments in property, plant and equipment. Due to the sale and leaseback of our headquarters

for a period of twenty years, our total lease obligations increased from €169,000 in 2003 to €7.7 million in 2004. In 2005 our total lease obligation declined to €7.5 million.

In 2005, our total lease payments approximated €751,000, of which approximately €390,000 was related to the lease of our headquarters. In addition to this facility, we rent neighboring facilities. These facilities can, at our option, be vacated at short notice.

We have contracted with the owner of our headquarters to expand this facility and to lease an additional 3,513 m2. Following completion of the planned construction works, which are scheduled to conclude in the fourth quarter of 2007, we will have a total of at least 5,238 m2 of offices, laboratories and pilot plant space available to accommodate our anticipated growth.

The following table sets out our payment obligations under contracts that provide for fixed and determinable payments over the periods indicated, which we expect can be sourced from working capital.

	2006	2007	2008 and 2009	2010 and later
	(in thousands)			
Finance lease . . . . .	€503	€477	€1,537	€10,838
Operating lease . . . . .	247	249	14	100
Royalty obligations . . . . .	–	38	38	–
Total	<u>€750</u>	<u>€764</u>	<u>€1,589</u>	<u>€10,938</u>

Although most of the subsidies we have received from the Dutch Ministry of Economic Affairs and the European Union are provided without repayment obligations, the subsidy related to the hGH-OctoDEX project was provided on the basis of a “soft loan”, pursuant to which monies borrowed are repaid on the basis of revenues generated from this project. 35% of the revenues we generate from hGH-OctoDEX, either in the form of sales, royalties or license fees in the period from 27 February 2005 to 27 February 2015, will be used to redeem the soft loan. In the event that insufficient revenues are generated from this project by 27 February 2015, the loan will be forgiven. We received a total of €1.4 million under this soft loan arrangement. To date, we have not received any revenues in the form of sales, royalties or license fees related to this project and accordingly we have not made any payments against this soft loan.

Upon entering into the license agreement regarding the OctoDEX technology with Utrecht University, we agreed that we would pay royalties on either net sales of products in the event that we undertook final commercialization of final product, or on royalties received from third parties.

Pursuant to our agreement to purchase its subsidiary, Chienna, IsoTis is entitled to a portion of the cumulative net profits we derive from products based on Chienna’s technology. The size of future payments depends on the cumulative profitability of the products developed based on the PolyActive technology during the lifetime of the patents which we acquired or in-licensed from IsoTis. Payment under this profit sharing scheme falls due at the end of the life of the acquired PolyActive patent portfolio. However, to the extent that the accumulated profits of Chienna exceed its accumulated losses, we are required to make annual payments in the form of advances to IsoTis on the basis of the arrangement described above.

As a result of our license agreement with LUMC for OP-145, we may be obliged to pay further license payments amounting to €75,000 as well as royalties on future sales.

#### **Off Balance Sheet Arrangements**

We have no off balance sheet obligations other than those presented above.

## **Share Based Payment**

In January 2005, we granted Fortis, one of the Underwriters, 204 class AP shares as partial remuneration for services provided as placement agent during our January 2005 financing round (See “Underwriting – Other Relationships”).

## **Critical Accounting Policies and Estimates**

Our discussion and analysis of our financial position and results of operations are based on our consolidated financial statements, which have been prepared in accordance with IFRS. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates based on historical experience and make various assumptions which we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

A summary of our significant accounting policies is contained in our consolidated financial statements, which are included in this Prospectus beginning on page F-4. We consider the following accounting policies to be critical to the understanding of the results of our operations.

### ***Impairment Test of Goodwill and Patents***

In performing impairment testing of goodwill and patents, we make significant judgments and estimates to determine whether the cash flows we believe can be generated on the basis of these patents exceed the carrying value of our patents and goodwill. Determining cash flows requires the use of judgments and estimates that have been included in our strategic plans and long-term forecasts. The data necessary for performing the impairment tests are based on our estimates of future cash flows. The discount rates used are estimated pre-tax rates which reflect specific risks relating to the relevant segment.

### ***Pensions***

For the calculation of the present value of the pension obligation and the net cost, actuarial assumptions are made about demographic variables (such as mortality) and financial variables (such as future increases in salaries). The discount rate is determined by reference to market rates of high-quality corporate bonds. Any changes in these assumptions will impact the carrying amount of our pension obligations.

### ***Share-Based Payments***

Share options granted to our employees are measured at the fair value of the equity instruments granted (indirect method of measurement). Fair value is determined through the use of an option-pricing model considering, among others, the following variables:

- The exercise price of the option;
- The expected life of the option;
- The current value of the underlying Shares;
- The expected volatility of the share price, calculated considering the effect of dividends on the share price;
- The dividends expected on the Shares; and
- The risk-free interest rate for the life of the option.

For our share option plans, we believe that the binomial method is most appropriate for determining fair values as this method allows accounting for non-transferability, vesting conditions and early exercise. As long as

we are not listed, there is no published share price information. Consequently, we needed to estimate the fair value of our Shares and the expected volatility of that value, for which we have used the historical weekly volatility of our peers.

The result of the share option valuations and the related compensation expense is dependent on the model and input parameters used. Even though we consider the fair values reasonable and defensible based on the methodologies applied and the information available, others might derive at a different fair value for each of our share option plans.

### ***Revenues Recognition***

#### *Service Revenues*

Sales of services are recognized in the accounting period in which the services are rendered, by reference to the stage of completion of the specific transaction when the outcome of a transaction can be estimated reliably. The stage of completion is assessed on the basis of the actual service provided as a proportion of the total services to be provided.

#### *License and Royalty Revenues*

License and royalty revenues include amounts earned from third parties with licenses and/or options to our intellectual property. License and royalty revenues are recognized when earned in accordance with the substance and under the terms of the related agreements and when it is probable that the economic benefits associated with the transaction will flow to the entity and the amount of the revenue can be measured reliably. In situations where we have continuing performance obligations, revenues related to license fee payments are deferred and the related revenue is recognized in the period of expected performance.

#### *Multiple Element Arrangements*

In certain circumstances, it is necessary to apply the recognition criteria to the separately identifiable components of a single transaction in order to reflect the substance of the transaction. Conversely, the recognition criteria are applied to two or more transactions together when they are linked in such a way that the commercial effect cannot be understood without reference to the series of transactions as a whole.

We offer arrangements whereby a customer licenses the right to use our intellectual property and purchases research and development services under one arrangement. When such multiple element arrangements exist, an element is accounted for as a separable element if it has value to the customer on a stand-alone basis and the fair value can be determined objectively and reliably.

When license revenues and service revenues are identified as separable elements in a multiple element transaction, the license revenue recognized is determined based on the fair value of the license in relation to the fair value of the arrangement taken as a whole and is recognized in accordance with the accounting policy for license and royalty revenues as discussed above. The revenue relating to the service element, which represents the fair value of the servicing arrangement in relation to the fair value of the arrangement, is recognized over the service period. The fair values of each element are determined based on the current market price of each of the elements when sold separately.

## BUSINESS

### Overview

We are a product-oriented biopharmaceutical company committed to the development of improved pharmaceutical products that are based on our proprietary drug delivery technologies and have fewer side effects, increased patient convenience and better efficacy than existing products.

We currently have five product candidates in development, of which three are in clinical trials. Our lead product candidate, Locteron, is a novel interferon alfa combined with our proprietary PolyActive drug delivery technology for the treatment of chronic hepatitis C infection. Locteron is designed to require less frequent administration and cause fewer side effects than marketed forms of interferon alfa which currently represent the standard of care for this illness. We intend to commence Phase IIa clinical trials of Locteron in the fourth quarter of 2006. Our second clinical-stage product candidate is OP-145, a novel proprietary peptide therapeutic that is currently in Phase II clinical trials for the treatment of chronic otitis media, also known as chronic middle ear infection. Our third product candidate in clinical development is hGH-OctoDEX, a novel formulation of recombinant human growth hormone for growth hormone deficiency. hGH-OctoDEX is in Phase I clinical trials and is based on our proprietary OctoDEX technology. We are also developing single shot vaccines based on our proprietary OctoVAX platform. HBV-OctoVAX for hepatitis B vaccination and JEV-OctoVAX for Japanese encephalitis vaccination are currently in pre-clinical trials.

We are using our proprietary drug delivery systems OctoDEX and PolyActive to develop products that provide controlled and prolonged release of a drug, which enables reduced dosing frequency and reduced risk of side effects with comparable or better efficacy relative to immediate release drugs. Rather than seeking to discover novel drug candidates through early stage research activities, we focus on the development of long-acting, controlled-release versions of known protein therapeutics and other drugs. In contrast to certain other approaches to improve the clinical benefit of protein therapeutics, such as chemical modification (including pegylation and polymer conjugates) or protein engineering (including changes in primary structure and fusion), our technologies have the advantage of efficiently and gradually delivering a drug in its native form. Four of our five products under development are based on either OctoDEX or PolyActive. Although our OctoDEX and PolyActive technologies can be applied for many diseases, our current product focus is primarily directed at improving the treatment or prevention of viral and bacterial infections as well as treatment of metabolic disorders.

In addition to developing our own proprietary products, we provide advanced drug formulation and manufacturing services to biotechnology and pharmaceutical companies worldwide. Since our establishment in 1995, we have achieved €39 million in cumulative revenues from this business and we have realized a positive operating result from this business in all but one year. The earnings and expertise that we derive from rendering formulation and manufacturing services support us in our own drug development programs.

Our Executive Board and Senior Management have many years of experience in the areas of clinical development, drug delivery, pharmaceutical formulation and manufacturing, business development and finance. Our main facilities are located in Leiden, the Netherlands, and consist of 1,725 m<sup>2</sup> of laboratories, a small-scale cGMP manufacturing plant and offices. We opened a business development office in Cambridge in the United States in July 2006. As of 31 August 2006, we employed 130 people, one of whom is located in our office in Cambridge, the United States.

### History

We were founded in 1995 by Joost Holthuis, Ph.D., our CEO, and Prof. Daan Crommelin, Ph.D., the chairman of our Scientific Advisory Board.

Initially, we focused on providing pharmaceutical and biotechnology companies with advanced drug formulation and manufacturing services. Starting in 1996, we entered into a number of agreements with Utrecht University by which we received a worldwide exclusive license to our OctoDEX technology.



While we continued to successfully grow our contract development business, we made the strategic decision in early 2000 to start to exploit our expertise in the drug delivery area and the versatility of our OctoDEX platform by expanding into the development of proprietary products. We raised €3 million in 2001 from NPM Capital N.V. and 7X Life Sciences B.V. in order to progress OctoDEX-based product candidates into clinical trials. In 2003, we were able to broaden our technology base by gaining access to a second drug delivery system, PolyActive, through the acquisition of Chienna from IsoTis N.V.

In 2005, Life Sciences Partners B.V., S.R. One, Ltd., Innoven Partenaires S.A., Fortis Bank N.V./S.A., SurModics, Inc. and certain other parties invested €18.4 million in us, which allowed us to fund pre-clinical and clinical trials of our most advanced product candidates.

## Strategy

We aim to leverage our broad expertise in pharmaceutical development and drug delivery in order to develop pharmaceutical products which improve existing approaches to the treatment of serious illnesses. Key elements of our corporate strategy include:

- **Advance the development of our lead product candidates.** Our primary focus is on the aggressive development of our most advanced product candidates so that they may eventually be submitted for regulatory approval. We currently have three product candidates in clinical trials. We are preparing our lead product candidate Locteron for a Phase IIa clinical trial for the treatment of chronic HCV infection. We expect to receive the results from this study in the second quarter of 2007. If this trial is successful, we plan to initiate a Phase IIb clinical trial late in 2007. In addition, we are conducting a Phase II clinical trial of OP-145, our novel peptide for the treatment of chronic otitis media. The results from this study are expected in the fourth quarter of 2007. In relation to our third product candidate, hGH-OctoDEX, we anticipate initiating a further Phase I trial in the fourth quarter of 2007. In this study, we will use an improved hGH-OctoDEX product as compared to a prototype version, which we used in a previously completed Phase I study.
- **Continue to expand and advance our product candidate portfolio by combining our drug delivery technologies with known biopharmaceutical drugs or other therapeutics in need of clinical improvement.** We primarily intend to apply our proprietary drug delivery technologies to those product opportunities where we can capitalize on the known safety, efficacy and often established drug development history of existing drugs. At the same time, we believe that our technologies may allow us to improve the performance of many of these known biopharmaceutical drugs, of which drawbacks may include frequent or inconvenient dosing schedules, injection site reactions, strong side effects and/or limited efficacy. Our goal is to initiate one new program per year.

We intend to gain access to biopharmaceuticals or other molecules for combination with our drug delivery technologies in a variety of ways. If a product is patent-protected, we intend to gain access to such molecule via a joint development partnership with a company that has freedom to operate for this product (for example, based on an alternative manufacturing process, as is the case for the interferon alfa molecule of our partner Biolex that is used in Locteron), or via an originator. In the event that the existing drug is off-patent, we will seek to secure the supply of the molecule from a commercial manufacturer (as we are currently pursuing for hGH), or via an originator.

More opportunistically, we also intend to acquire or in-license product candidates that are in pre-clinical or clinical development and which we believe have clear potential for an improved clinical profile upon combination with one of our controlled release technologies. We would require such development programs to be synergistic with our then existing product portfolio.

- **Capture value by entering into partnerships with large pharmaceutical or biotechnology companies for our product candidates.** We intend to create value by licensing our product candidates for further development and commercialization at a stage where the risk/reward balance would make such partnership attractive for us. In most cases, this would typically occur with the completion of Phase



II clinical trials. For product candidates that target smaller markets, we may decide to complete the development process ourselves and establish a commercial infrastructure to directly commercialize such products in certain territories.

- **Further expand the potential applications of our drug delivery platforms.** We believe that our proprietary drug delivery technologies have broad applicability. We continually seek to improve and find new applications for our OctoDEX and PolyActive platforms in order to remain competitive in developing controlled release formulations of many classes of drugs and therapeutic proteins. As an example, we have developed a modified version of our OctoDEX technology, OctoVAX, as a basis for an innovative, single-shot approach to prophylactic vaccines. We may also broaden our drug delivery base by acquiring or in-licensing other technologies that are complementary to our existing platforms. We believe that OctoDEX and PolyActive can be used to enhance the performance of a range of medical devices and other applications that are outside of our core areas of focus. We therefore may leverage our technologies by entering into selective collaboration agreements in these non-core areas. As an example, we have entered into a collaboration agreement with SurModics, Inc. to apply our OctoDEX and PolyActive technologies to the development of drug-eluting medical devices.
- **Continue to grow our profitable Contract Development Business.** We plan to grow our Contract Development Business, thereby focusing on knowledge-intensive activities in order to secure higher-margin projects. We will continue to offer our clients advanced services from formulation development through to manufacturing of material for clinical trials. We believe that there is a high degree of operational synergy between our Contract Development Business and our activities involving the development of our own product candidates. We will therefore continue to invest in this business for the benefit of both our external customers and our internal drug development activities. Furthermore, the profits we generate from this business allow us to offset certain of the costs associated with our own product development programs.

## Our Product Candidates

The following table summarizes key information about our product candidates.

<i>Product Candidate</i>	<i>Indication</i>	<i>Stage of Development</i>	<i>Partner Status</i>	<i>Next Expected Development Milestone</i>
Locteron	Chronic HCV Infection	Entering Phase IIa	Co-development with Biolex	Receive Phase IIa data in Q2:2007
OP-145	Chronic Middle Ear Infection	Phase II	None <sup>(1)</sup>	Receive Phase II data in Q4:2007
hGH-OctoDEX	Growth Hormone Deficiency	Phase I	None	Commence further Phase I study in Q4:2007
HBV-OctoVAX	Prophylactic Hepatitis B	Pre-clinical	Co-development with SciGen <sup>(2)</sup>	Commence Phase I study in Q4:2007 Vaccination
JEV-OctoVAX	Prophylactic Japanese Encephalitis Vaccination	Pre-clinical	Co-development with SingVax	Commence Phase I study in H1:2008

(1) In June 2006, we concluded a non-binding term sheet with Green Cross Corporation of South Korea for the co-development of OP-145 and the commercialization of OP-145 in the South Korean market. We intend to complete a formal agreement with Green Cross by the fourth quarter of 2006.

(2) In June 2005, we entered into a non-exclusive collaboration agreement with SciGen Ltd. If our proof-of-concept study is successful, we and SciGen may agree to continue with the development and commercialization of HBV-OctoVAX, based on our respective technologies, on an exclusive basis.

We may be required to perform additional clinical studies for Locteron, OP-145 and hGH-OctoDEX, even if the clinical development plans we currently expect to conduct are completed successfully.

We have not yet sought regulatory approval for any product candidate in the United States or any country outside of Europe. All of our current clinical trials are being conducted in Europe. Together with our co-development partner for Locteron, Biolex, we have held discussions with the FDA in relation to our clinical development plan for Locteron in the United States and Europe. We intend to commence clinical trials in the United States for Locteron after the completion of our Phase IIa and Phase IIb clinical trials in Europe in the event that these trials return positive clinical results.

We anticipate that data from our current and future studies in Europe will form a substantial part of the applications for marketing approval required to be filed in the United States with the FDA and various regulatory agencies in other parts of the world.

For an explanation of the various phases of pre-clinical and clinical development, see “Business – Government Regulation and Product Approval”.

### Locteron for Chronic Hepatitis C

Our lead product candidate is Locteron, a proprietary controlled release formulation of interferon alfa currently entering Phase IIa clinical trials. The primary indication for Locteron is the treatment of chronic infection by the hepatitis C virus (“HCV”). Hepatitis C is a common disease, affecting over 180 million people worldwide. Infection by HCV is a very serious medical condition that can lead to cirrhosis of the liver, a

condition where healthy liver cells are killed by infection with HCV and are replaced by scar tissue. Resulting damage to the liver can lead to impaired liver function, liver cancer and ultimately death.

The current standard of care for the treatment of HCV infection consists of a combination of ribavirin with one of two currently approved pegylated interferon alfa products, PEG-Intron marketed by Schering-Plough Corporation or Pegasys marketed by Roche. However, this treatment approach is frequently characterized by severe acute side effects that hamper widespread use and result in poor patient compliance. We believe that Locteron has the potential to offer substantial improvements in the management of chronic HCV infection.

Locteron combines interferon alfa produced by our co-development partner, Biolex, with our proprietary PolyActive microspheres. This product is designed to gradually release its active pharmaceutical ingredient over a 14 day period after a single injection. Currently marketed pegylated interferons circulate over a seven day period after a single injection. By releasing interferon alfa in the body in a gradual manner, our PolyActive microspheres avoid the high initial blood levels of the active drug that characterize the current standard of care. We believe that these high initial levels of interferon alfa contribute to the acute flu-like symptoms commonly associated with the current standard of care. Locteron aims to provide at least the same therapeutic benefit to HCV patients with fewer, less severe and less frequent side effects.

We believe that an improved side effect profile will lead to enhanced patient compliance which in turn will result in superior therapeutic outcomes. We also believe that Locteron's intended superior side effect profile may attract and maintain patients on therapy who currently delay or refuse treatment.

We have recently completed a Phase I clinical study where the safety, pharmacokinetics and pharmacodynamics of Locteron were investigated in healthy volunteers. Results of this Phase I clinical trial showed that a single dose of Locteron was safe and well tolerated. In particular, groups receiving Locteron reported fewer, less severe and shorter lasting flu-like symptoms than those subjects receiving PEG-Intron, a commonly prescribed pegylated interferon.

The data from this trial indicate that Locteron could be dosed once-every-two-weeks, which is a substantial improvement over currently used pegylated interferons that require weekly injections. We believe there is a strong correlation between reducing the dosing frequency of interferon therapy and improving patient compliance, in particular in light of the current 48 week treatment period for HCV genotype 1, the HCV variant that is the most prevalent in Western countries.

### **Disease Background, Limitations of Existing Products and Market Opportunity**

Hepatitis C is a disease of the liver caused by infection with HCV. Proper function of the liver is essential to human health. The liver removes or neutralizes unwanted substances from the blood, aids in the absorption of nutrients, produces immune agents to control infection, and removes microbes from the blood. It makes proteins that regulate blood clotting and produces bile to help absorb fats and fat-soluble vitamins.

HCV infects liver cells and can cause the liver to become inflamed. Over time, such infection can lead to cirrhosis, a condition where scar tissue replaces normal, healthy liver tissue, causing a deterioration in liver function. Damage to the liver due to HCV infection can lead to liver cancer or outright liver failure. Initial exposure to HCV elicits an immune response directed against the infected liver cells. However, most patients infected with HCV are unable to generate an immune response sufficient to eradicate the virus entirely, resulting in chronic infection with HCV. Patients may not realize that they have been infected with HCV until 10 to 30 years after initial exposure, in part because of the lack of obvious symptoms.

The World Health Organization (the "WHO") estimates that 180 million people globally are infected with HCV, with 3 to 4 million new infections per year. Approximately 70% of these cases will not resolve during the acute stage of infection and will result in chronic disease. Of these patients who progress to chronic hepatitis, according to the WHO, 10-20% will develop cirrhosis within 20 years, while some 30% of cirrhotic patients develop clinical liver decompensation over a period of ten years. HCV infection is the leading cause of liver transplantations in the United States where approximately 10,000 deaths per year are attributed to complications resulting from HCV infection. The Centers for Disease Control (the "CDC") of the United States National

Institutes of Health (the “NIH”) estimates that 5% of HCV infected patients will eventually develop end-stage liver failure requiring a liver transplant in order to survive. Published reports indicate that the number of liver cirrhosis and cancer cases due to HCV infection will further increase in the coming 10 to 20 years. The population of patients with chronic HCV infection in Europe and the United States is estimated at 6 million and 3.2 million, respectively.

There are at least six different strains of HCV, known as genotypes. Of those, genotype 1 is most commonly found in the United States and most parts of Europe. Genotype 1 is considered to be least responsive to treatment and requires the longest time on therapy. Large-scale clinical trials have demonstrated that the current standard of care induces a successful response in approximately 50% of patients.

The relative treatment rate for HCV infection is very low. It is estimated that only 22% of chronically infected HCV carriers in the United States receive treatment. In other developed countries it is estimated that only 12-13% of infected patients receive treatment. This undertreatment is caused by a number of factors, including absence of symptoms indicating infection, absence of sufficiently serious inflammatory damage to the liver to warrant treatment and the unpleasant and lengthy nature of treatment with interferon for chronic HCV infection.

The current standard of care for chronic HCV infection in developed countries involves a combination of pegylated interferon alfa and a generic anti-viral drug known as ribavirin. Interferon alfa is an anti-viral glycoprotein naturally produced by the human immune system in response to a viral infection. While interferon alfa is known to contribute to the eradication of the invading virus, it is also believed to be the source of many of the symptoms that cause discomfort during a viral infection. These are often referred to as “flu-like symptoms” and include tiredness, drowsiness, weight loss, dizziness, muscle ache, nausea, vomiting, loss of taste, diarrhea and headache.

In order to stimulate and assist the immune system in its response to chronic HCV infection, pegylated interferon alfa is given to patients on a weekly basis. However, interferon alfa causes flu-like symptoms, and this therapy results in severe side effects in a large majority of patients. Many patients with chronic HCV infection experience no hepatitis-related symptoms and therefore are more likely to discontinue therapy when confronted with the severe side effects of the current standard of care. According to a recent study conducted by the Public Health Agency of Canada, adverse events associated with interferon therapy resulted in a 21% cessation rate in HCV patients undergoing the 48 weeks of treatment.

Until 1998, Schering-Plough’s Intron A, a non-modified interferon alfa, was the standard of care for the treatment of chronic HCV infection. However, the introduction of pegylation technology saw a rapid shift away from this product to new versions of interferon alfa which were combined with this drug delivery technology. Pegylation is a technique that involves the attachment of large polyethylene glycol (“PEG”) polymers to each interferon molecule, thereby lengthening its circulation time in the body. As a result, a more convenient dosing schedule was achieved (once per week versus three times per week) and longer blood circulation of interferon at clinically relevant levels resulted in greater efficacy. However, the flu-like symptoms associated with standard interferon therapy continue to apply to therapy with pegylated interferons albeit with less frequency as such side effects typically manifest themselves within a short period after dosing. Pegylated versions of interferon were introduced in 2001. Between 2001 and 2005 the market for interferon alfa almost doubled. Pegylated versions of interferon now account for approximately 88% of the interferon sales.

Combination therapy with pegylated interferon and ribavirin is expensive. In the United States, a 48 week course of interferon alfa therapy costs approximately \$16,000. Worldwide sales for hepatitis C therapeutics in 2005 have been estimated at \$4 billion.

Analysts have forecasted that the market for HCV therapeutics will grow at 9–12% per year through 2010. This growth is expected to be driven by the following factors:

- **Increased Diagnosis Rates and Enhanced Public Education Campaigns.** An increasing number of patients who have been chronically infected with HCV for periods often in excess of 15 years will present with advanced liver disease, necessitating therapeutic intervention. Furthermore, diagnostic tests

for the detection of HCV are expected to become more widely available. In addition, public health authorities have launched education campaigns to encourage high risk groups to seek diagnosis and treatment.

- **Development of Improved and/or Novel Therapies.** New treatment options which are safer and more effective should increase the number of patients that seek or are referred for treatment. We believe that these advanced therapies will overcome currently high levels of patient apathy which result from the limited efficacy and severe side effects of current therapies.
- **Treatment of Non-Responders.** With the development of new and improved therapeutics for chronic HCV infection, patients who did not respond to standard therapy will undergo further treatment with new products. Large-scale clinical trials have demonstrated that approximately 50% of HCV patients with chronic genotype 1 infection respond to the current standard of care.

### **Anticipated Advantages of Locteron**

Locteron is designed to be a best-in-class therapeutic for patients with chronic HCV infection.

We believe that Locteron will offer patients an effective and more convenient treatment for chronic HCV infection because of the following advantages over currently marketed pegylated interferons:

- **More Convenient Dosing Schedule.** We have demonstrated in pre-clinical studies that Locteron gradually releases interferon alfa over a two week period. This profile was confirmed in a single dose clinical study in healthy volunteers. If clinical efficacy with this dosing interval is confirmed in larger clinical studies, we may be able to market Locteron as a once-every-two-weeks therapy as opposed to current weekly therapy. This would reduce the burden on patients and we believe would likely lead to greater patient compliance with therapy schedules.
- **Fewer, Less Severe and Less Frequent Side Effects.** By releasing interferon gradually over a two week period, Locteron is able to avoid the high initial blood concentrations of interferon that are associated with administration of pegylated proteins. By avoiding these high blood levels we believe that the number, severity and duration of severe side effects can be reduced. The reduction in side effects is aided by the once-every-two-weeks dosing schedule, as the most severe flu-like symptoms occur shortly after injection.
- **Potentially Improved Efficacy.** We believe that Locteron may provide patients with longer periods of exposure of infected tissues to clinically relevant levels of interferon when compared to pegylated interferons. Furthermore, Locteron may increase patient compliance due to more convenient dosing schedules. Unlike currently marketed pegylated interferons, Locteron's interferon alfa is not chemically modified by conjugation with PEG. We believe that Locteron's interferon more closely mimics naturally occurring interferon as it is produced by the body. We believe each of these factors may lead to improved efficacy.

### **Locteron Development Activities and Strategy**

In April 2006 we completed a single escalating dose Phase I clinical study of Locteron in healthy volunteers. We are currently preparing for Locteron to enter a Phase IIa study in HCV patients in the fourth quarter of 2006.

#### ***Locteron Phase I Study***

The Locteron Phase I study was a double-blind, randomized, placebo-controlled, single-dose escalation study in healthy volunteers designed to evaluate the safety, pharmacokinetics and pharmacodynamics of Locteron in comparison with PEG-Intron, a pegylated interferon marketed by Schering-Plough.

In this study, a single administration of Locteron was given at three different dose levels, 20 $\mu$ g, 80 $\mu$ g and 320 $\mu$ g. These doses were anticipated to fall within the clinically relevant dose range of Locteron and were

compared to controls consisting of the delivery vehicle (our PolyActive product alone, without any interferon), a placebo and PEG-Intron.

In total, 27 healthy male volunteers participated in this study and were split into three groups. In each group, four persons received Locteron, two received PolyActive only, two received PEG-Intron and one received a suspension vehicle. Phase I results showed that a clinically relevant amount of Locteron, given as a single dose to healthy volunteers, was safe and well tolerated. The clinical results confirmed a gradual release of interferon alfa after injection, thus avoiding high peak blood levels frequently associated with pegylated interferon therapy and resulting in a prolonged circulation.

Flu-like symptoms among those subjects receiving Locteron in the study were reported to be fewer, less severe and of shorter duration than in the subjects receiving PEG-Intron. Even at the highest Locteron dosage, both the intensity and duration of flu-like symptoms were less in the Locteron group than in the PEG-Intron group. It is important to note that the PEG-Intron dose given to healthy volunteers in this study was 80 $\mu$ g, the dose at which PEG-Intron is registered as monotherapy. The registered dose of PEG-Intron when it is used in combination therapy with ribavirin is 120 $\mu$ g, which we believe could likely lead to stronger flu-like symptoms in those patients receiving combination therapy.

We believe that the pharmacokinetic and pharmacodynamic profiles of Locteron that were demonstrated in this Phase I study support a once-every-two-weeks dosing schedule for this product candidate.

As part of our Phase I clinical trial of Locteron, we measured a number of biomarkers that are believed to correlate to the performance of interferons in the target patient population. The level of an enzyme known as 2'5'-oligoadenylate synthetase ("OAS") in peripheral blood is a biological marker for the activity of interferon alfa. The OAS biomarker has been used in multiple clinical trials where the efficacy of interferon alfa has been examined.

From our Phase I study of Locteron, we observed that a single injection of Locteron resulted in a sustained increase in OAS levels for 14 days at all three dosages of Locteron used in the Phase I trial.

Similarly, in our Phase I study of Locteron we examined levels of neopterin, an early indicator of cell-mediated immunity. It is generally accepted that elevated levels of neopterin indicate that an immune response has been induced by the presence of interferon in the blood stream. Neopterin levels have been examined in various clinical trials designed to study the anti-viral efficacy of potential therapies, including for infections by HIV and HCV.

Results obtained from the measurement of neopterin in the blood of subjects receiving Locteron indicated that at all three doses a sustained immune response had been induced by the presence of Locteron, with the highest dose achieving a sustained immune response for a period of 14 days.

None of the subjects receiving Locteron reported any serious adverse events at any dosage level. Common non-severe injection site reactions were noted in some subjects, that we believe are related to the presence of the PolyActive material under the skin after administration and have been reported for other polymer-based controlled-release formulations.

We believe that the results obtained from our Phase I study support further testing of Locteron in a Phase IIa clinical study in patients with chronic HCV infection.

### ***Planned Locteron Phase IIa Study***

On the basis of the results of the Phase I study, we are entering a Phase IIa study in treatment-naïve, genotype 1 chronic HCV patients.

Our Phase IIa Locteron study is designed as a multi-center, open label study. The goal of this study is to test the safety and preliminary efficacy of Locteron over a course of multiple injections and to select doses to be tested in a subsequent Phase IIb study which will be designed to examine the potential efficacy of Locteron. A total of 32 patients will be enrolled in the Phase IIa study. Each subject will be treated for 12 weeks (therefore



receiving six injections of Locteron in accordance with our proposed once-every-two-weeks dosing schedule). In addition to examining standard safety and efficacy endpoints, we will also assess OAS and neopterin levels.

Initially, doses of 160 $\mu$ g, 320 $\mu$ g and 480 $\mu$ g are planned to be given to three cohorts consisting of eight patients each. If the 480 $\mu$ g dose is well tolerated, a fourth cohort will receive 640 $\mu$ g of Locteron per injection. In the event that the 480 $\mu$ g dose is not well tolerated, the remaining eight patients of the fourth cohort may be randomized over the two other dose levels or may receive another, not yet tested dose. All patients at all dosage levels of Locteron will also receive ribavirin in accordance with standard combination therapy practices for the use of pegylated interferons.

As part of this clinical trial, we intend to measure the safety and tolerance of Locteron in patients over a 12-week period followed by an analysis at week 12 of early viral response (“EVR”). Following this initial 12-week period, all patients at all dosages of Locteron will cease treatment with Locteron and will then be administered PEG-Intron in accordance with the clinical investigators’ discretion. We expect to receive regulatory approval to commence this trial in the fourth quarter of 2006, which would allow us to begin enrolling patients and dosing with Locteron shortly thereafter. Results from this study are expected in the second quarter of 2007.

### ***Planned Locteron Phase IIb Study***

In the event that we receive positive results from our Phase IIa study of Locteron, we plan to accumulate further data about the clinical benefits of Locteron by progressing to a Phase IIb study. Unlike the Phase IIa study, the Phase IIb study will directly seek to examine the efficacy of Locteron in comparison to PEG-Intron, in addition to observing its safety and tolerability profile in a larger group of patients.

Clinical trial activities conducted in the United States or in accordance with United States regulations (regardless of the geography of the actual trial sites) are conducted under the auspices of an Investigational New Drug (“IND”) application.

We held a so-called “pre-IND” meeting with the FDA to discuss the Chemistry, Manufacturing and Controls (“CMC”) package, the pre-clinical safety program and the intended design of our Phase IIb trial. A pre-IND meeting allows innovators of new pharmaceutical products to discuss and receive feedback from the FDA about the nature, size, scope and duration of a planned clinical trial. At the meeting, we received in-principle agreement from the FDA for our plans for the Phase II study. We plan to file an IND with the FDA shortly, but in any event before commencement of a Phase IIb study.

We have discussed with the FDA our intended design for the Phase IIb trial. We plan to conduct a multi-center, double blind trial of Locteron, testing three separate doses in treatment-naïve patients for 48 weeks, the typical treatment period for patients suffering from chronic HCV infection with genotype 1 virus. These three Locteron patient cohorts will be compared with one equally sized cohort of patients receiving PEG-Intron. All four patient cohorts will receive ribavirin treatment contemporaneously with interferon therapy. The 12-weeks response data from this study are expected to provide significant guidance regarding the clinically appropriate dose of Locteron.

### **Manufacturing**

BLX-883, the interferon alfa ingredient in Locteron, is produced in accordance with cGMP by our co-development partner, Biolex, at its facilities in North Carolina. BLX-883 is produced in genetically engineered lemna, a clonal higher aquatic plant system. Biolex will be responsible for the manufacture of all future supplies of BLX-883, both for clinical trials and for eventual commercial supply.

We plan to manufacture finished Locteron product by combining our PolyActive microspheres with BLX-883 for both Phase II clinical studies in our licensed pilot plant facility in Leiden, the Netherlands. As we plan to out-license Locteron after completion of Phase II clinical trials, the manufacturing of Locteron required for Phase III clinical trials and for any future commercial supply will be decided in conjunction with a future commercialization partner.



## **Marketing and Sales**

We and Biolex intend to enter into one or more commercial partnerships with third parties, under which such third parties would assume responsibility for Phase III clinical trials, registration and commercialization of Locteron in all major markets. As part of that commercial partnership, we and/or Biolex may decide to retain certain rights for the co-promotion of Locteron in certain geographic areas.

## **Other Indications for Locteron**

In addition to the treatment of chronic HCV infection, interferon alfa is registered or in development for the treatment of a number of other diseases, such as hepatitis B, AIDS-related Kaposi's sarcoma and malignant melanoma. We may consider seeking approval for Locteron for the treatment of these or other additional indications at some point in the future. We anticipate that separate clinical development programs will need to be undertaken in order to gain approval of Locteron for these additional indications.

### **OP-145 for Chronic Middle Ear Infection**

OP-145 is our novel, proprietary peptide therapeutic in Phase II clinical development for the treatment of chronic middle ear infection (also referred to as chronic otitis media), administered locally through an eardrop formulation. Chronic middle ear infection is one of the most common childhood chronic infectious diseases worldwide. It is the most frequently recorded diagnosis for children in the United States and is the most common reason for a child being prescribed oral antibiotics. We believe that worldwide approximately 200 million people have a chronic middle ear infection. Approximately 60% of those suffering from chronic middle ear infection experience some degree of hearing impairment as a result of infection.

Acute middle ear infections are caused by a range of microbes, including bacteria and various fungi. These acute infections are usually easily eradicated by the use of common antibiotics. However, a more serious condition may occur when certain toxic microbial degradation products linger in the mucus of the middle ear after the eradication of the microbes associated with an acute infection. In these circumstances, we believe the presence of these toxins contributes to chronic middle ear infection.

The toxins associated with chronic middle ear infection are unresponsive to traditional antibiotics. Often, surgical procedures are required to treat these chronic infections and clear the degradation products from the site of infection.

OP-145 is designed to neutralize these toxins at the site of infection and to locally restore the body's natural clearance mechanism. We have demonstrated in pre-clinical studies that OP-145 binds to and clears two important bacterial toxins known as lipopolysaccharide ("LPS") and lipoteichoic acid ("LTA"). Both LPS and LTA are common constituents in the cell walls of bacteria and are released into the middle ear when the various bacteria that cause middle ear infection are destroyed by the immune system or by antibiotics.

In addition, we have demonstrated in pre-clinical studies that OP-145 interacts with lipid components on the surface of bacteria typically associated with chronic middle ear infection. By binding to these surface components, OP-145 destabilizes the cell membrane leading to bacterial cell death.

In light of these two characteristics, we believe that OP-145 may offer benefits for patients with chronic middle ear infection that cannot be treated adequately with current therapies.

We recently completed a Phase I/IIa safety and tolerability study comprising a dose-ranging assessment in 16 therapy-resistant patients who had average disease duration of 17 years. Results from this study show that OP-145 was safe and well tolerated.

We are currently enrolling a double blind, placebo-controlled Phase II study in 52 patients. The clinical endpoints of the study are safety and efficacy.

Given the dual mechanism of action of OP-145, we believe there is potential to expand into other indications where LPS and LTA are also implicated in disease progression, such as chronic sinusitis.

## **Disease Background, Market Opportunity, Limitations of Existing Products**

The middle ear is a hollow chamber in the bone of the skull. A thin membrane, the eardrum or tympanic membrane, separates the middle ear from the outside world. The Eustachian tube, a narrow passage, connects the middle ear to the back of the nose. The Eustachian tube is closed until a swallowing movement pulls it open and allows air to flow from the nose into the middle ear. The fresh air balances pressure inside the middle ear and outside the head. Normally, the pressure difference arises from oxygen absorption by the cells lining the middle ear.

If the Eustachian tube becomes blocked, the air pressure in the middle ear cannot equalize properly. Negative pressure develops and if the obstruction is prolonged, fluid may be drawn into the air space of the middle ear from surrounding tissue. Many infections may give rise to this situation, including infection with the common cold or a flu virus. The common cold is a frequent cause of acute middle ear infections in children. Acute middle ear infections typically resolve without treatment, but may in certain circumstances require a course of antibiotics or steroids. Acute middle ear infections are a common reason for the placement of artificial tubes in the eardrums of children and adults in order to release pressure and promote the discharge of debris.

If the blockage of the Eustachian tube persists, negative pressure in the middle ear or alternating periods of negative, normal and positive pressure may deform the eardrum. These changes may cause hearing loss and a sensation of pressure. In chronic infections, a majority of patients will develop severely distorted eardrums that will eventually become perforated. When there is a hole in the eardrum, the natural protection of the middle ear from the environment is lost. Water and bacteria can enter the middle ear from the ear canal causing inflammation and infection.

Acute infections in the middle ear can lead to a vicious cycle of inflammatory reactions which leads to chronic middle ear infection. As a result of incomplete recovery from an initial bacterial infection, tissue in the middle ear may become inflamed. As a result of this inflammation, this tissue becomes more susceptible to recurrent and persistent re-infection by the same or other infectious microbes. During these infections, bacterial toxins such as LPS and LTA play a large role in continuing the vicious process of infections. These toxins can induce an inflammatory reaction in the middle ear and can induce injury to the tissue lining the middle ear, the so-called mucous membrane. Initially, mucous secretions become thicker, and therefore less likely to drain, if at all. Subsequently, the membranes themselves begin to thicken and become inflamed. The natural defense mechanisms of the Eustachian tube and middle ear begin to fail and are unable to restore a healthy balance.

Chronic local inflammation can cause erosion of the ossicles and the walls of the middle and inner ear. Patients with chronic middle ear infection may experience hearing loss, imbalance, or weakness of facial movement on the affected side.

Most patients with infections of the middle ear are treated initially with antibiotics. These can be either systemically applied or delivered directly into the ear through the use of liquid drops. However, antibiotic treatment of chronic middle ear infection has limited efficacy. As antibiotics do not assist in the removal or degradation of LPS and LTA, there is a risk of infection re-emergence. When bacteria are not fully eradicated from the middle ear and inflammatory conditions persist due to the presence of LPS and LTA there is a considerable risk of the development of antibiotic-resistant bacteria colonizing the middle ear. The use of additional antibiotics typically does not assist in the clearance of these resistant bacteria nor will they assist in the removal of bacterial toxins such as LPS and LTA.

In the event that patients do not respond to multiple courses of antibiotic treatment, surgery on the middle ear is often performed in a bid to clear the mucus of toxins and thereby alleviate recurrent inflammation. Unfortunately, a significant number of patients do not benefit from surgery and will experience recurrent infection after this interventional procedure.

Chronic middle ear infection is one of the most common childhood chronic infectious diseases worldwide. It is the most frequently recorded diagnosis for children in the United States and is the most common reason for a child being prescribed oral antibiotics. We believe that worldwide approximately 200 million people have a chronic middle ear infection. Approximately 60% of those suffering from chronic middle ear infection

experience some degree of hearing impairment. We believe that approximately \$400 million is spent on antibiotic treatment of chronic middle ear infection annually.

### **Anticipated Advantages of OP-145**

We have demonstrated in pre-clinical studies that OP-145 has a different mechanism of action than currently approved treatments for chronic middle ear infection. Anticipated advantages of OP-145 include:

- **Dual Mechanism of Action.** We believe that we may be able to achieve better outcomes for patients as a result of the dual mechanism of action of OP-145 that combines antibacterial traits with anti-inflammatory effects as levels of the toxins LPS and LTA are reduced in the mucus of the middle ear.
- **Reduced Risk of Resistance.** The antibacterial activity of OP-145 targets constituent elements of the surface of bacterial cells which are integral to bacterial survival and inherently less subject to mutation, thereby reducing the risk of resistant strains of bacteria developing. Furthermore, the clearance activity of OP-145 is not expected to be subject to resistance.
- **Alternative to Continued Antibiotic Treatment and Surgery.** OP-145 is administered by patients and delivered via liquid drops and could serve as an alternative therapy to continued treatment with antibiotics or eventually surgery.

### **Development Activities and Strategies**

Based on the anticipated advantages of OP-145, we intend initially to focus on chronic middle ear infection patients who do not respond to current treatment approaches, including patients who have recurrent chronic middle ear infection despite having undergone surgery. All patients in our past and planned clinical trials have perforated eardrums.

In the pre-clinical studies of OP-145 that we have conducted to date, such as the typical tests used to examine the toxicological profile of new therapeutic agents, we did not see evidence of skin or lasting eye irritation in animal models.

#### ***OP-145 Phase I/IIa Clinical Study in Chronic Middle Ear Infection***

We have completed a Phase I/IIa safety and tolerability study that included a dose-ranging assessment in 16 therapy-resistant patients with average disease duration of 17 years. Certain patients in this study had also undergone surgery for treatment of resistant chronic middle ear infection without a successful clinical outcome. All patients had perforated eardrums. OP-145 was delivered via liquid drops into the ear canal and was administered twice a day for two weeks. Four different dosages were tested: 0.25mg/mL, 0.5mg/mL, 1.0mg/mL and 2.0mg/mL.

This study assessed the safety and tolerability of OP-145 through an examination of hearing levels and serum analysis. In addition, we also examined the efficacy of OP-145, though this was not a statistical endpoint of the trial. Efficacy was measured through the application of a mucosal endoscopic score, which gauged the level of inflammation of the mucus in the middle ear of all patients.

The results of this study demonstrated that OP-145 was safe and well tolerated at all dose levels. In addition, nine out of 16 patients showed either full recovery or a meaningful improvement after the two week course of therapy. In particular, seven of the 16 subjects participating in this study reported dry ears (indicating a complete response) 12 weeks after commencing therapy, the end of the patient follow-up period. No antibodies to OP-145 were detected in the serum of patients in this study.

Based on these results, we have decided to further develop OP-145 and have commenced a Phase II clinical study specifically designed to assess efficacy. Based on our Phase I/IIa study of OP-145, we selected a 0.5mg/mL concentration for further clinical trials.

### ***OP-145 Phase II Clinical Study in Chronic Middle Ear Infection***

Our Phase II clinical trial of OP-145 is enrolling patients and will be a double blind, placebo-controlled study in 52 patients. The clinical endpoints of the study are safety and efficacy of OP-145. This Phase II study will be carried out in at least three clinical centers in the Netherlands. Results from this Phase II study are expected in the fourth quarter of 2007.

### **Expansion into Other Indications**

Given its mechanism of action, we believe that there is potential to expand OP-145 into other indications where the persistent infection of body cavities exposed to the external environment may give rise to chronic ailments. In particular, we are considering further development of OP-145 for the treatment of chronic sinusitis. Chronic sinusitis is a very common disease affecting 33 million patients in the United States per year, for which there is no currently approved therapy. In addition, periodontitis (infection at the interface between the teeth and the gums) and a range of eye infections fall within the potential scope of OP-145, as bacterial infection of mucous membranes is involved in these conditions.

### **Manufacturing**

The initial supply of OP-145 for clinical trials was provided by our licensor of OP-145, the Leiden University Medical Center (“LUMC”). We have entered into an agreement with a commercial peptide manufacturer for the larger scale production of OP-145 for advanced clinical trials and, if OP-145 is approved, commercial sale. Optimization of the formulation of OP-145 may involve a switch in salt form, switch in excipients and the execution of a pre-clinical or clinical bridging trial. This decision shall be taken in light of pending pre-clinical data and regulatory feedback.

### **Marketing and Sales**

We intend to make a decision regarding our commercialization strategy for OP-145 upon completion of our Phase II clinical trials. We may decide to complete the development of OP-145 ourselves and commercialize the product in certain territories. We have recently signed a non-binding term sheet with Green Cross to enter into an agreement for the co-development and commercialization of OP-145 for the treatment of chronic middle ear infection in South Korea.

### **hGH-OctoDEX for Growth Hormone Deficiency**

hGH-OctoDEX is our controlled release formulation of recombinant human growth hormone (“hGH”) based on OctoDEX, one of our drug delivery technologies.

hGH-OctoDEX is designed to be administered once-weekly for the controlled release of recombinant hGH. The primary indication for hGH-OctoDEX will be growth hormone deficiency in pediatric and adult patients, which indications generated sales of hGH in excess of \$2.3 billion in 2005 based on reported revenues of existing products. We are developing hGH-OctoDEX as a controlled release formulation of hGH that requires less frequent administration and may therefore offer patients and physicians a more convenient option and improved compliance compared with current growth hormone products that are generally recommended to be injected on a daily basis. As hGH-OctoDEX incorporates an unaltered version of approved hGH, which is a well-known molecule with an established safety and efficacy profile, we believe that hGH-OctoDEX may represent less development risk than other biopharmaceutical products at a similar stage of development.

It is estimated that approximately one in 5,000 children and one in 10,000 adults are affected by growth hormone deficiency. In children, a deficiency of growth hormone can result in stunted growth and can eventually lead to short stature. In adults, low levels of hGH are frequently associated with various other metabolic disorders. The burden of daily injections for patients being treated with hGH therapy often leads to reduced compliance (particularly in children) or a reluctance to initiate therapy (particularly in adults). We believe that a

once-weekly formulation of hGH will contribute to improved compliance and improved clinical efficacy, and will potentially encourage those patients who are reluctant to initiate hGH therapy to seek treatment.

Currently approved recombinant human growth hormone is also used to treat certain other growth related disorders, including Turner Syndrome, Prader Willi Syndrome, chronic renal insufficiency, idiopathic short stature, children born small for gestational age, short bowel syndrome and muscle wasting associated with HIV infection. While we are currently focusing our development plans of hGH-OctoDEX for growth hormone deficiency, we might consider pursuing some of these additional indications at a later stage.

We completed a proof-of-concept Phase I study with a prototype version of hGH-OctoDEX in 2004. Based on the results of this trial, we decided to improve the product and we anticipate initiating a further Phase I trial with an improved hGH-OctoDEX product in the fourth quarter of 2007.

### **Disease Background, Market Opportunity, Limitations of Existing Products**

Growth hormone, also known as somatotropin, is synthesized and secreted by the pituitary gland and stimulates growth and cell reproduction in humans. The release of growth hormone is stimulated by growth hormone releasing factor and ghrelin.

A key role of growth hormone is related to the stimulation of bone elongation and growth in children. Growth hormone stimulates the production of insulin-like growth factor 1 (“IGF-1”), which has growth-stimulating effects on a wide variety of tissues. Growth hormone also contributes to proper bone density and plays an important role in various metabolic functions, including lipid breakdown, protein synthesis and insulin regulation.

Abnormalities in the pituitary gland can result in growth hormone deficiency. The major manifestations of growth hormone deficiency in children are growth failure and short stature. In adults, the effects of deficiency are more subtle, and may lead to increased fat mass, decrease in lean body mass, decrease in bone density, metabolic alterations that include changes in lipid metabolism, and decrease in muscle strength. Patients with growth hormone deficiency are typically treated with growth hormone replacement therapy.

In 2005, total global sales of marketed hGH products exceeded \$2.3 billion. The market for hGH grew by a compound annual growth rate of approximately 29% between 2002 and 2005, based on reported sales.

Frequent injections of hGH present a considerable burden for both pediatric and adult patients and often lead to poor compliance rates. In the case of adult hGH deficiency, the inconvenient route of hGH administration may also lead to a reluctance to initiate therapy. The standard course of treatment for pediatric growth hormone deficient patients typically lasts approximately six years and some 2,000 injections. Faced with this protracted treatment regime, pediatric patients often take “days off” and as a result skip required treatment. For adults with growth hormone deficiency, the benefits of hGH treatment are more subtle as they relate to metabolic function and organ health rather than increased height. As a consequence, and in contrast to hGH deficient children, many adults with growth hormone deficiency do not initiate hGH therapy, and many of those who do fail to continue treatment.

### **Anticipated Advantages of hGH-OctoDEX**

We believe that hGH-OctoDEX will represent an appealing treatment option for the management of growth hormone deficiency in both pediatric and adult settings. In particular, we believe hGH-OctoDEX will offer the following benefits:

- **Improved Convenience and Compliance.** Current medical guidelines generally recommend that existing hGH products be injected on a daily basis. Particularly in pediatric indications, we believe that these frequent injections are a high burden and significantly impact quality of life for both children and their parents, who typically are responsible for administering therapy. In adult settings, daily injections often lead to reduced compliance or reluctance to initiate therapy. By offering a once-weekly alternative,

we believe that hGH-OctoDEX will provide a significant convenience benefit, which may result in improved patient compliance.

- **Enhanced Effectiveness of Therapy.** hGH-OctoDEX releases hGH from our proprietary OctoDEX microspheres continuously over a prolonged period, resulting in sustained patient exposure to hGH. We believe that by virtue of its convenient dosing regimen, its ability to maintain elevated levels of hGH and its improved compliance, the application of hGH-OctoDEX has the potential to result in better long-term clinical outcomes than existing once-daily therapies that result in high initial levels of hGH followed by a rapid decline and therefore require frequent dosing.

## Development Activities and Strategies

### *Proof-of-Concept Phase I Clinical Study*

In 2004, we completed a randomized, single dose, double blind, placebo controlled proof-of-concept Phase I clinical study that was carried out in 18 elderly male volunteers. In this study, ten volunteers received hGHvar-OctoDEX, a controlled release formulation based on an earlier generation of the OctoDEX polymer incorporating a 190 amino-acid variant of hGH (“hGHvar”). Six volunteers received empty OctoDEX microspheres as a placebo control and two received a saline control. In the active hGHvar-OctoDEX arm, recombinant human growth hormone was dosed at 0.2mg hGHvar/kg. After a single injection of hGHvar-OctoDEX, we established that the pharmacokinetic release profile of hGHvar from OctoDEX microspheres was favorable, with elevated serum concentrations of growth hormone achieved for a period of ten days. No burst release effect (involving high initial concentrations of hGHvar followed by a rapid decline) was observed at the time of injection, implying that practically all hGHvar in hGHvar-OctoDEX will be available for sustained release. Furthermore, results from this study in humans showed a strong correlation with data generated by us in previous animal studies and in laboratory experiments.

The functional activity of the hGHvar protein released from the OctoDEX microspheres was confirmed during a subsequent 38-day period after administration during which we measured increased levels of two well-established biomarkers for hGH activity, IGF-1 and IGF-binding protein-3.

Side effects observed during this study included initial swelling and redness at the injection sites, and persistent palpable subcutaneous nodules. With hGHvar-OctoDEX, mild to moderate pain was reported in more than half of the subjects. In three out of ten subjects receiving hGHvar-OctoDEX more serious tolerability issues were observed. As such issues were not observed in any of the subjects receiving empty OctoDEX microspheres, we believe the most likely explanation for these issues was an inflammatory reaction against the 190-amino acid derivative of hGH used in hGHvar-OctoDEX.

Following our proof-of-concept Phase I study examining hGHvar-OctoDEX, we have undertaken a number of actions to further optimize the hGH-OctoDEX formulation:

- **Access to Current Standard hGH.** For our first Phase I trial of hGHvar-OctoDEX we used hGHvar, a recombinant variant of hGH consisting of 190 amino acids. Naturally occurring human growth hormone consists of 191 amino acids and hGH assembled from 191 amino acids reflects the current standard of care in treating growth hormone deficiency. In our improved formulation of hGH-OctoDEX, we will use hGH consisting of 191 amino acids, for which we are in advanced negotiations to secure a long-term supply agreement with a well-established manufacturer. We believe that the use of naturally occurring 191 amino acid hGH will improve the local tolerability of hGH-OctoDEX by reducing the chances for immune-mediated inflammatory reactions.
- **Increased hGH Loading of Microspheres.** In order to reduce the total volume of hGH-OctoDEX administered per injection, we altered the composition of our OctoDEX microspheres. Specifically, we managed to increase the loading of each microsphere from approximately 10% hGH to approximately 20-25% hGH by weight. As a result, each microsphere is now able to deliver a greater amount of hGH



into the circulation, which allows us to administer the same amount of hGH while reducing the total volume of OctoDEX microspheres administered to patients.

We are currently preparing pre-clinical studies for a Phase I clinical study of our improved hGH-OctoDEX product candidate, which we expect to commence in the fourth quarter of 2007

### ***hGH-OctoDEX Phase I Clinical Study – Design***

Our Phase I clinical study with the improved hGH-OctoDEX product candidate will be a randomized, single dose, double blind, placebo controlled study. Male volunteers will receive a subcutaneous dose of hGH-OctoDEX, empty OctoDEX microspheres or a placebo control using a suspension vehicle. Concentrations of growth hormone will be measured to determine the pharmacokinetic and pharmacodynamic properties of hGH-OctoDEX. In addition, profiles of IGF-1 and IGF-binding protein-3 will be measured as biomarkers for hGH activity.

### **Manufacturing**

We are in advanced negotiations to secure an agreement with a well-established manufacturer for the supply of bulk 191 amino acid hGH approved by regulatory authorities in all major countries for pre-clinical development, clinical trials and commercial use. Although we believe that we could source hGH from a number of potential suppliers, there can be no assurance that we will be able to conclude a suitable supply agreement. hGH-OctoDEX microspheres for use in Phase I and II clinical trials will be manufactured at our pilot production plant. The manufacturing of hGH-OctoDEX for late-stage clinical trials and commercialization may be outsourced to a contract manufacturing organization or carried out by a future licensee.

## **OctoVAX for Hepatitis B and Japanese Encephalitis**

### **Background**

Vaccines play an essential role in the prevention of many wide-spread and communicable diseases, such as hepatitis B, pneumococcal infection and polio. By providing immunity to large segments of the population, prophylactic vaccines have had a major impact on the course of human health in both the developed and developing world. Prophylactic vaccines are used either in broad immunization programs, aimed at protecting whole populations from a particular disease, or are targeted towards specific populations considered to be at particular risk of contracting certain infectious diseases, including international travelers, immunocompromised patients and healthcare workers.

Many vaccines require multiple injections over several weeks or months in order to induce a sufficient immune response that will engender long-term protection. Due to this inconvenient vaccination schedule, a significant portion of the intended target population does not finish the complete regimen of required injections, does not finish the regimen in time or does not start the vaccination process at all, leading to sub-optimal protection. Development of vaccination regimens that require fewer doses is expected to have a significant impact on overall vaccination coverage and vaccination compliance rates.

When administering vaccinations, the first injection is referred to as a “prime” and subsequent injections are referred to as “boosts”. Many of the current efforts aimed at developing new vaccines or improving the efficacy of existing vaccines focus on improving the active ingredients in the vaccine, which in many cases will still require multiple injections in order to be effective.

### **Our Approach**

Our vaccine approach is focused on developing a new generation of more patient-friendly vaccines which are designed to induce a long-term immune protection based on one single injection. More specifically, we have modified our proprietary OctoDEX technology for vaccine applications (“OctoVAX”), which we use in combination with the vaccine component to develop vaccine products with a view to generate both an immediate



“prime” effect as well as subsequent “boosts” via a single shot. We believe that the convenience offered by our single shot approach to vaccine therapy could greatly improve the rates of effective immunization by simplifying and enhancing patient compliance.

The key advantage of our proprietary OctoVAX technology over other vaccination approaches is that our method has the potential for combining a prime and a boost release in one-single shot. In pre-clinical studies in mice, we have demonstrated that a single injection of a vaccine delivered with our OctoVAX technology generated a prime and a delayed release of the therapeutic protein, and resulted in a similar antibody response as compared to two injections of the same vaccine given several weeks apart. Based on these results, we believe that using our OctoVAX technology we can design our microspheres to control the initiation and the rate of the release of the therapeutic component of our vaccine product. Currently, we intend to use a widely-used adjuvant, aluminum hydroxide, which we believe can maintain its desired immune stimulation effect weeks after injection, as a separate component of our single-shot vaccines.

We believe that our OctoVAX technology may be applied to develop a range of single-shot vaccination products for the following reasons:

- **Flexible Carrier Mechanism.** Our proprietary microspheres have the ability to entrap proteins with a molecular weight as low as ten kilodaltons (kDa), as well as whole particles, such as live or attenuated viruses. This proprietary system is therefore able to encapsulate a broad range of viral particles and is well suited for innovative vaccine applications.
- **Flexible, Non-Disruptive Manufacturing and Loading Process.** The biological activity of the relevant protein or virus should be maintained during our proprietary manufacturing process which loads the protein or virus into our microspheres. As a result, we anticipate that the biological activity of the delivered material will be maintained upon injection and at the time of its release into the blood stream.

Based on the pre-clinical results to date, we intend to initiate clinical trials with our first single shot vaccine candidate in the fourth quarter of 2007.

## **Market Opportunity**

In 2002, the market for prophylactic vaccines was worth an estimated \$5 billion to \$7 billion. Worldwide vaccine sales are expected to grow to over \$11 billion by 2010, almost exclusively driven by new product innovation.

Currently, a considerable number of major vaccines, including the pneumococcal, human papillomavirus, hepatitis B and anthrax vaccine, require multiple injections over several weeks or months in order to induce a sufficient immune response and thereby to convey long-term protection. As a consequence, a significant number of those receiving the initial prime injection for protection against these diseases do not finish the complete regimen or do not finish it in a timely manner, leading to sub-optimal protection.

## **Our OctoVAX Product Candidates**

Although our technology may be applicable to a wide variety of vaccines, we have decided to focus initially on market opportunities in the areas of hepatitis B and Japanese encephalitis.

### ***HBV-OctoVAX for Hepatitis B vaccination***

The WHO describes hepatitis B as one of the major diseases of mankind and a serious global public health problem. Of the 2 billion people who have been infected with the hepatitis B virus, more than 350 million people have chronic infections. About 90% of infants infected during the first year of life and 30-50% of children infected between one and four years of age develop chronic infection. In persons over the age of five years, approximately 6% of infected individuals become chronic carriers of the hepatitis B virus. These chronic carriers of the hepatitis B virus are at high risk of developing hepatic necrosis, cirrhosis, and liver cancer, diseases that result in about one million deaths annually. Prophylactic vaccines for hepatitis B infection are

available and can prevent the development of chronic infections and thereby reduce associated morbidity and mortality. The worldwide market for hepatitis B vaccines is estimated at over \$1 billion. Although vaccination against infection by hepatitis B is part of a national immunization program in many countries, still large numbers of individuals born prior to the implementation of these programs are unvaccinated and are at risk of the disease. Furthermore, the current technology employed in marketed hepatitis B vaccines necessitates that subjects receive multiple shots over a six-month period, leading to poor patient compliance with dosing regimens. According to a survey of U.S. adolescents and adults published by the CDC, only 53% of those who received the first dose of hepatitis B vaccine received the second dose, and only 30% received the third. We believe that compliance rates in other countries are similarly low. In addition, most of the current hepatitis B vaccines have a substantial non-response rate which means that such individuals are not fully immunized when injected by such vaccines.

Through the development of a single shot hepatitis B vaccine, we intend to initially focus on meeting the high medical needs of travelers to areas where hepatitis B is endemic, to non-responders to the currently marketed vaccines, healthcare workers, emergency response personnel and immunocompromised individuals. These niche groups are at increased risk of becoming chronic carriers of the hepatitis B virus and will benefit most from an improved hepatitis B vaccine, which is conveniently administered in a single shot. In the longer term, having attempted to address the needs of these niche groups, we may also decide to expand our focus to participate in childhood immunization programs.

#### *Status of Development*

We have an ongoing pre-clinical program to test several different hepatitis B vaccines in combination with OctoVAX for the development of a single shot product. We have entered into a non-exclusive feasibility agreement with SciGen, Ltd., which has developed and manufactures a proprietary, multi-shot hepatitis B vaccine under the brand name Sci-B-Vac, which is marketed in the Philippines, Hong Kong, Singapore and Vietnam. In contrast to most currently marketed hepatitis B vaccines, which are produced through recombinant technology in yeast and contain only one epitope, Sci-B-Vac is produced in mammalian cell culture and has three epitopes. Sci-B-Vac is more immunogenic than yeast-derived vaccines, leading to faster onset of protection and a higher percentage of successfully immunized subjects.

In a proof-of-concept study in mice, we showed that a single shot of our mammalian-based HBV-OctoVAX formulation with aluminum hydroxide adjuvant had a stronger immunological response than two separate injections of yeast-based vaccine with the same adjuvant and in a comparable aggregate dose. With HBV-OctoVAX, antibody titers on the 56th day of the study were approximately twice as high compared with the sequentially dosed yeast vaccine.

Upon completion of our pre-clinical development program, we intend to select a hepatitis B antigen for use with our OctoVAX technology for further development. In the event that we and SciGen decide to continue the program with the Sci-B-Vac antigen, we intend to commence clinical trials in the fourth quarter of 2007.

#### ***JEV-OctoVAX for Japanese Encephalitis Vaccination***

Japanese encephalitis is a severe mosquito-borne viral infection caused by the Japanese encephalitis virus (“JEV”) that results in encephalitis (inflammation of the brain) in humans. Mild infection may result in headache and fever, whereas severe cases lead to high fevers, seizures, paralysis, coma and potentially death. According to the WHO, approximately 50,000 cases are reported in Asia annually, with approximately 15,000 deaths attributed directly to infection with JEV.

Approximately 3 billion people live in JEV-endemic areas. In addition, the virus presents a threat to travelers from non-endemic countries visiting endemic areas. With the rapid and continued growth of international travel, the number of people potentially exposed to JEV is expected to increase.

There is currently a marketed Japanese Encephalitis vaccine available, known as JE-VAX. It is produced by the Research Foundation for Microbial Diseases of Osaka University and is marketed by sanofi-pasteur, the vaccine business of sanofi-aventis SA. JE-VAX is known to have a number of important limitations. Firstly, this

vaccine requires three separate injections over a period of one month, and has been shown to be protective in 75-90% of subjects, which is a relatively low response rate for a prophylactic vaccine. Furthermore, as JE-VAX is derived from mouse brains, the manufacturing costs of the product are relatively high. There are also concerns about the safety of JE-VAX as severe side effects including neurological reactions have been observed. As a result, subjects receiving the vaccine for JEV infection are advised to remain within close proximity of medical care for ten days after receiving the vaccine.

Through the combination of a new JEV antigen derived from a human cell line with our OctoVAX technology, we intend to develop a single-shot vaccine product for travelers to areas where JEV is endemic. In addition, the use of a new antigen may improve the safety and the efficacy profile as compared to JE-VAX.

#### *Status of Development*

We have entered into an exclusive co-development agreement with SingVax Pte. Ltd. for the development of JEV-OctoVAX. SingVax has obtained a license to a human cell line based on the PER.C6 technology of Crucell N.V. for the manufacturing of bulk JEV product. Under the terms of our agreement, SingVax will be responsible for the supply of bulk antigen based on inactivated whole cell Japanese encephalitis virus, and we will be responsible for incorporating these antigens within our OctoVAX microspheres and manufacturing the final product. We and SingVax will jointly carry out pre-clinical, clinical and regulatory activities.

We are currently performing pre-clinical experiments with SingVax to select the most promising formulation for further development. We anticipate that clinical trials of JEV-OctoVAX will commence in the first half of 2008.

### **Our Proprietary Drug Delivery Technologies**

Our major technology platforms, OctoDEX and PolyActive, have been developed to deliver active compounds in a more convenient, safe and effective manner than conventional formulations. They are particularly suitable for injectable products incorporating drugs and larger molecules. By combining our technologies with such compounds, we aim to create novel drugs with superior performance characteristics. One of the key features of both technology platforms is that they are capable of controlling the release of the incorporated compounds, resulting in long-acting products with systemic and/or local effectiveness. Moreover, we believe that controlled release systems based on OctoDEX and PolyActive are competitive as they can be designed to exhibit predictable, sustained release profiles of the pharmaceutical agent without any significant burst effect.

Depending on the individual properties of a candidate compound, we select the technology platform with the highest potential for achieving an attractive product profile. We frequently observe a strong correlation between the release characteristics obtained *in vitro* and *in vivo*, which helps us in evaluating the suitability of our drug delivery systems as a carrier for a specific compound at an early stage.

#### ***OctoDEX***

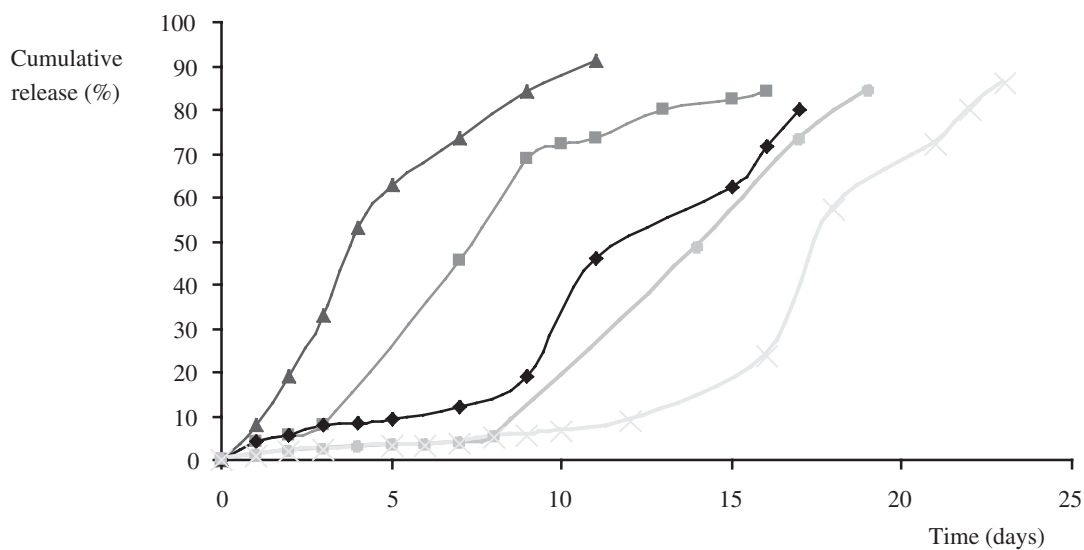
OctoDEX is our drug delivery system based on cross-linked, dextran-derived polymers. The technology was originally invented at Utrecht University, and has been further developed by us. Our OctoDEX-based products consist of injectable, biodegradable microspheres based on dextran polymers that enable the controlled delivery of biopharmaceuticals. In the preparation of the polymeric microspheres, we modify the dextrans in such a way that the products are biodegradable into non-toxic substances in a physiological environment.

Applying our proprietary, all-aqueous emulsion process, we use the OctoDEX polymers to create hydrogel microspheres incorporating biopharmaceutical ingredients. We believe that, due to the hydrophilic nature of the carrier and the absence of potentially harmful organic solvents in the manufacturing process, OctoDEX microspheres are compatible with a large number of biopharmaceuticals. As our drug-loaded OctoDEX microspheres can be suspended in a small liquid volume, they can be administered by subcutaneous injection.

The manufacture of OctoDEX microspheres involves the preparation of an emulsion in which an aqueous solution of a modified dextran and a drug substance is dispersed as fine droplets within an aqueous solution of polyethylene glycol. Polyethylene glycol is used as an excipient in this process and is not involved in any chemical conjugation. Upon cross-linking of the dextran, the droplets solidify as microspheres, incorporating the active ingredient within their polymeric network. We then remove excess reactants from the resulting suspension, after which drug-filled, gel-type microspheres remain. We have successfully scaled-up this process under cGMP conditions in our small-scale manufacturing facilities, enabling us to supply materials for clinical development.

As is shown in the next figure, OctoDEX microspheres are capable of releasing their incorporated drug substance over a period of several days to several weeks, depending on the individual design of the microspheres and the properties of the incorporated product. To date, we have not observed a significant burst effect, where high amounts of an incorporated drug substance are released immediately following administration, for any of our OctoDEX-based products.

**Figure: Cumulative in-vitro release profile of IgG from OctoDEX microspheres of varying composition. Water content of 60% and degree of substitution (DS) 3 (▲); Water content of 50% and DS 3 (■); DS 6 (◆); DS 8 (●) and DS 11 (X).**



We have successfully used OctoDEX for the controlled delivery of several therapeutic proteins in a number of in vitro and in vivo studies. Our proprietary microspheres have the ability to entrap proteins with a molecular weight as low as ten kilodaltons (kDa), as well as whole particles, such as live or attenuated viruses.

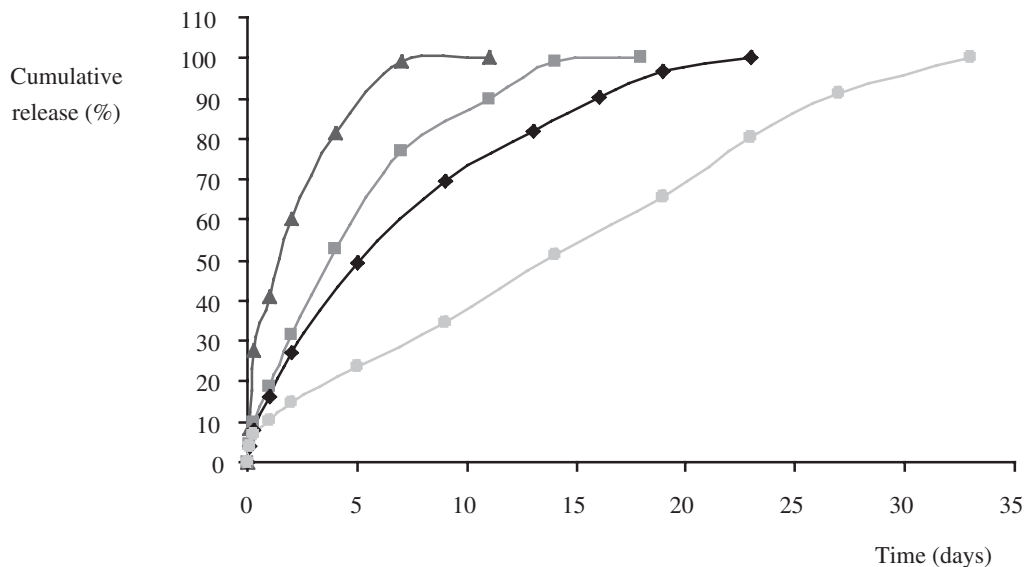
### ***PolyActive***

PolyActive was first introduced as a biomaterial over 15 years ago. Since then, the PolyActive polymer, which consists of a series of segmented polyethers and polyesters, has been used in medical devices for orthopedic and wound repair applications in over 5,000 patients. Two medical devices based on PolyActive polymers have received FDA approval to date. PolyActive can be used to make gels, implantable rods, wafers and coatings on medical devices. We focus on the use of PolyActive to create injectable and biodegradable microspheres that enable the controlled release of biopharmaceuticals. We acquired the PolyActive drug delivery technology as part of our acquisition of Chienna from IsoTis in 2003.

In chemical terms, PolyActive refers to polyetheresters comprising blocks of polybutylene terephthalate and polyethylene glycol. By varying the length and composition of these PolyActive polymers we can tailor the drug release profile of our product candidates.

Similarly to OctoDEX, we have tested various compositions of PolyActive in order to establish different in vitro release profiles of our PolyActive platform. Depending on the design and composition of the PolyActive-based microspheres, we have obtained release profiles ranging from one week to several months. An example is shown in the next figure.

**Figure: Cumulative in-vitro release profile of IFN $\alpha$ -2b from PolyActive microspheres: influence of polymer composition and formulation.): 1500/80/20, standard formulation ( $\blacktriangle$ ); 1500/80/20, optimized formulation ( $\blacksquare$ ); 1500/77/23 ( $\blacklozenge$ ), 1500/75/25 ( $\bullet$ ).**



We have successfully used PolyActive for controlled release of several therapeutic biopharmaceuticals in a number of in vitro and in vivo studies. Attractive candidates that could potentially be delivered by PolyActive microspheres include therapeutic proteins, peptides and small lipophilic molecules.

We are capable of manufacturing PolyActive microspheres under cGMP conditions in our small-scale manufacturing facilities, using a well-established four-step procedure based on a double-emulsion protocol.

We have access to a detailed safety and toxicity file concerning the PolyActive polymer that was prepared by IsoTis and was filed with the FDA for the use of PolyActive in medical devices.

### Contract Development

Our Contract Development Business is operated by our subsidiary OctoPlus Development B.V. Over the last 11 years, we have become a leading provider of advanced drug formulation and clinical scale manufacturing services to the pharmaceutical and biotechnology industries, with a focus on difficult to formulate active pharmaceutical ingredients. All activities within our Contract Development Business are performed in our dedicated facilities in Leiden, the Netherlands, where we operate a cGMP pilot plant for manufacturing and release of final product for clinical trials. As of 31 August 2006, we employed 59 people in our Contract Development Business. We offer a comprehensive range of services, including formulation, analytical development and production of both biological products, such as peptides, proteins and DNA, as well as conventional synthetic small molecules. We have strong experience in parenteral formulations. Our cGMP pilot plant allows us to offer our customers a full range of sterile pharmaceutical production options, including freeze drying. We believe we have a specific expertise in the area of low-soluble compounds.

We have successfully provided the services of our Contract Development Business on a fee-for-service basis to a diverse and international group of approximately 100 pharmaceutical and biotechnology companies, focusing mainly on protein therapeutics and to a lesser extent on small molecule drugs. To date, we have achieved €39 million in cumulative revenues from this business and we have realized a positive operating result from this business in all but one year since its establishment. Typically, our clients are charged on an hourly basis for our development services, while manufacturing is charged on a lump-sum basis.

We have established a strong competitive position in the market for contract formulation and manufacturing of clinical-grade products, particularly in the area of complex pharmaceutical formulations for therapeutic proteins. We were among the first independent companies to be active in this specific segment in Europe, allowing us to build significant in-house expertise in formulation and manufacturing processes. We believe that our capabilities in the Contract Development Business are demonstrated by our high rates of repeat business.

### *Our Expertise*

Our goal is to deliver successful outcomes to our customers by providing the highest quality of service, flexibility and expertise. We have well-established capacities and expertise in the fields of product manufacturing and state-of-the-art formulation techniques. For example, we have developed various protein formulations, including freeze-dried proteins, liposomal and other lipid-based products, micro/nanoparticles, immunotherapeutic formulations, as well as DNA-containing formulations for our clients. Primarily, we formulate products that are intended for parenteral administration. In addition, we have successfully developed a pulmonary liposome formulation, a protein product for colon targeting, protein-containing gels as well as pulmonary and topical formulations of oligonucleotides. We believe our achievements in the Contract Development Business have made us well-known to the pharmaceutical and biotechnology industries as a quality service provider for the development of critical and complex formulations.

The capacities of our Contract Development Business are set out below:

- **Characterization.** The Contract Development Business has an analytical group capable of characterizing the therapeutic substance provided by our clients and analyzing the formulated products. Our characterization capacities include the analysis of biopharmaceuticals for which we use state-of-the-art technologies.
- **Pre-formulation and formulation.** We have developed specialized formulation technologies based on liposomes, lipid complexes, emulsions and microspheres. Our core competencies in this area include the formulation of proteins using liposomes, and the solubilization of low soluble compounds. Our capabilities include the ability to freeze dry small-scale clinical batches of therapeutic proteins. We can formulate high-potency compounds, such as cytostatics and hormones, on a laboratory scale.
- **Drug delivery systems.** We use our expertise in drug delivery systems as an integral part of our formulation services. These systems include off-patent technologies based on liposomes, micelles and dispersions, as well as our proprietary systems based on sugar glasses and specialized dispersions. These technologies do not involve the use of our proprietary OctoDEX and PolyActive systems.
- **Analytical development and validation.** We apply commonly used procedures in the biopharmaceutical industry for analytical development and validation. In order to maintain and strengthen our position we also develop and evaluate novel analytical techniques.
- **Clinical manufacturing.** We have the capacity to manufacture a wide range of liquid and semi-solid biopharmaceutical products, including injectible, oral, dermal and pulmonary formulations, for use in clinical trials. Our facilities comprise a fully equipped production area for aseptic filling of liquid formulations, freeze drying and colloidal preparations. In addition, we are capable of formulating solid pharmaceuticals on a laboratory scale. With a current manufacturing capacity of 3,000 units per batch, we can produce sufficient materials for toxicology, Phase I and Phase II clinical trials. We intend to increase our manufacturing capacity in 2008 to a maximum of 15,000 units per batch.



- **Stability studies.** We perform stability studies in accordance with the International Conference on Harmonisation guidelines.

### ***Our Customer Base***

Since establishment, our Contract Development Business has provided services to approximately 100 clients in a total of approximately 250 projects. We have contributed to approximately 40 different products that have been progressed by our clients into clinical development, and to six products that have received regulatory approval. Currently, our active customer base comprises around 35 clients, which are located world-wide and include small, medium and large biotechnology as well as pharmaceutical companies. Contracts with our customers vary in size and duration, ranging from projects lasting only a few months to several years. Historically, revenues generated from individual contracts have generally been in the range of €25,000 to €1.5 million. In 2005, our five largest clients represented 55% of our Contract Development Business revenues. In the same year, we generated approximately 70% of the revenues of our Contract Development Business from Europe, while the remainder was sourced from North America, the Far East and Australia.

### **Intellectual Property**

We consider patents and other intellectual property rights to be vital to the success of our business. It is our policy to actively seek patent protection for our know-how, technologies, products, and their uses. Therefore, we analyze the results of our research and development activities to identify patentable subject-matter and file new patent applications as appropriate. In addition, we will continue to evaluate and potentially acquire externally generated intellectual property to further improve our competitive position.

Patents are the cornerstone of our proprietary protection, but we may also seek other registered intellectual property rights such as trade marks or utility models. In addition, we make use of trade secrets whenever indicated. In an effort to maintain the ownership of our proprietary information, we require our consultants, advisors and collaborators to execute confidentiality and invention assignment agreements. With respect to our employees, under Dutch law, employers own the intellectual property rights of inventions made by their employees during the course of their employment.

It is our intention to seek protection for any of our inventions that hold future value for in-house development or out-licensing. We file and maintain our patents in countries and jurisdictions which we consider most important to our business. These typically include the major European jurisdictions, the United States, often also Japan and, depending on the invention, other attractive markets or countries playing an important role in the pharmaceutical industries.

According to our patent strategy, we aim at building strong patent portfolios to protect our know-how broadly on the drug delivery technology level as well as on the more specific product level in order to maximize the strength and duration of protection. Consequently, we expect that every major product based on one of our proprietary delivery technologies will eventually be covered by at least one delivery platform patent and at least one product-specific patent.

At present, we hold 23 patent families comprising 183 granted national patents and 58 pending national and international patent applications. Many of these patents have been filed in our own name, while for certain others we hold exclusive licenses. A small number of our patents are jointly held with our collaboration partners.

OCTO PLUS is a registered trademark in the European Union. CHIENNA is a registered trademark in the European Union, the United States and in Japan. OCTODEX is a registered trademark in the Benelux countries. POLYACTIVE is a registered trademark of IsoTis in the United States, the European Union and in Japan, and as part of our license agreement with IsoTis we have the right to use the PolyActive name in drug delivery applications on a worldwide basis.



### ***Drug Delivery Technologies***

Our OctoDEX delivery technology platform, along with its variants and potential technology extensions, is covered by nine patent families. These patents were filed between 1997 and 2006. It is therefore expected that these patents will expire between 2017 and 2026. Key patents covering the basic principles behind our OctoDEX technology as it is presently employed in our product development programs include the granted European patents EP 941 068, EP 1 371 364, and the corresponding United States patent US 6,303,148 and the patent EP 910 412 and the corresponding United States patents US 6,497,903 and US 7,060,296, which we have exclusively licensed from Utrecht University. These patents cover the fundamental chemical (polymers, substituents, spacers and crosslinking methods), physical (hydrogels, microspheres and drug-containing compositions), and engineering features (methods for making microspheres) of our OctoDEX drug carriers. They are expected to expire in 2017.

The other OctoDEX patent families relate to potential improvements and extensions of our technology platform, some of which are currently under feasibility investigations. Patents which have been granted to us in relation to these improvements include EP 1 183 016, EP 1 255 534 and US 6,395,302. Among the pending patents in this group are the international patent applications WO 2003/035244, WO 2005/054318, WO 2005/087201, WO 2005/110377 and WO 2006/071110, and corresponding local applications in various countries.

When we purchased Chienna from IsoTis in 2003, we obtained exclusive worldwide access to the portfolio of patent rights and exclusive licenses relating to the PolyActive drug delivery technology. The portfolio of patent rights includes all of IsoTis' intellectual property that was licensed to Chienna in July 2002, consisting of over 90 patents and patent applications for drug delivery and tissue engineering.

The polyetherester copolymers which form the basis of the PolyActive technology platform were known for a number of years before their usefulness for drug delivery applications was discovered. Therefore, our patent protection in this area focuses on basic physical and pharmaceutical features, and in particular on the uses of the copolymers as drug carriers. Among the patents which play a key role in the PolyActive portfolio are the granted European patents EP 830 859 and EP 1 247 522, and the corresponding granted United States patent US 5,980,948, which are expected to expire between 2016 and 2018. We own certain further patents and patent applications that relate to specific manufacturing methods, medical devices and components as well as other extensions of the PolyActive technology.

### ***Products***

We have filed an international patent application WO 2006/085747 covering the formulation of Locteron which is based on the PolyActive delivery technology. We expect that European, United States and other national patents based on this international patent application will cover Locteron and comparable products involving the delivery of interferon alfa by microspheres. In the event that these patents are granted, they could provide exclusive protection for Locteron until 2026.

Jointly with the LUMC, we have filed two international patent applications WO 2004/067563 and WO 2006/011792 covering OP-145 and its therapeutic applications in certain important jurisdictions. If these applications lead to granted patents, they could provide exclusive protection until at least 2024.

In spite of our efforts, it is possible that our patent applications will not be granted, or that the scope of protection allowed under any issued patent may not provide adequate protection for our technologies and products. In addition, it is possible that any of our patents may be challenged and invalidated by third parties. Competitors may find means to circumvent patents held by us or our licensors. We may not be able to enforce any of our patents against infringers in any country or region important to our business.

Even though we believe that we are free to commercialize our technologies and products with respect to their major envisioned uses, there is a risk that we may inadvertently infringe prior or future patents owned by others. We may need to acquire licenses for patents held by third parties to re-establish or maintain our freedom to operate, possibly on unfavorable terms.

## **Collaborations**

We have entered into several collaborative arrangements with other biopharmaceutical companies and certain academic institutions. Our most important collaborations are summarized below.

### ***Biolex Therapeutics, Inc.***

In February 2005, we entered into an exclusive co-development agreement with Biolex for the development of Locteron, continuing a cooperation that started at the end of 2003. Locteron combines our proprietary PolyActive drug delivery technology with BLX-883, a proprietary interferon alfa produced by Biolex.

Pursuant to the agreement, all external costs are shared equally by the parties. In the event that the Phase II trials of Locteron are successful, we and Biolex intend to seek one or more development and commercialization partners for this product to assist us in gaining regulatory approval and sales access in our key markets, primarily North America, Europe and Japan. We will share any profits from the commercialization of Locteron on an equal basis with Biolex. Either of us may decide to retain co-marketing rights for Locteron in certain jurisdictions.

Our agreement with Biolex provides both parties with a right to terminate the agreement at will at pre-determined points. Furthermore, either party can terminate the agreement at will at any other time by providing written notice. In the event that one party decides to terminate the agreement at will, residual obligations and rights may exist for the terminating party, including an obligation to manufacture its respective component of the Locteron product or to grant a royalty-bearing license for the manufacture of this component. In addition, either party may terminate the agreement in the event that the parties have not entered into a commercialization agreement for Locteron within a predetermined period after regulatory approval. We and Biolex have agreed to indemnify each other against certain liabilities, but these indemnities are limited in scope and amount.

### ***Erasmus University***

In September 2004, we entered into a research and development agreement with the Thorax Center of Erasmus University Medical Center (the "Thorax Center") in Rotterdam, the Netherlands, for a novel treatment of myocardial (cardiac muscle) regeneration. Under the agreement, we will own all intellectual property resulting from the study and the Thorax Center will receive a non-exclusive, royalty-free license to this intellectual property. We will also pay a royalty to the Thorax Center based on our total revenues in respect of licenses we grant to third parties, subject to an overall cap. Either party may, with due notice, terminate this research and development agreement at will. This collaboration is subsidized by the Dutch Ministry of Economic Affairs.

### ***Green Cross Corporation***

In June 2006, we entered into a non-binding term sheet with Green Cross Corporation of South Korea setting forth our understanding of the main commercial terms for the licensing of OP-145 for the treatment of chronic middle ear infection in the South Korean market.

Although we must still enter into a binding license agreement with Green Cross, our term sheet already describes the proposed contractual provisions. Under these proposed terms, Green Cross would obtain access to all of our intellectual property and know-how related to OP-145 to the extent that it is required for the registration and commercialization of OP-145 in the South Korean market for use in the treatment of chronic middle ear infection.

Green Cross would be responsible for the Phase III development of OP-145 in South Korea and would bear related registration costs for the South Korean market. We believe that we would be able to use the results from this Phase III trial when registering OP-145 in other countries, although we will still need to conduct our own Phase III trials.

In the event that we enter into this agreement, under the proposed terms, we would receive nominal up-front license and milestone payments from Green Cross. In addition, Green Cross would pay us royalties on future sales at rates to be agreed.

#### ***InnoCore Technologies B.V.***

In August 2004, we entered into an agreement with InnoCore Technologies B.V. to collaborate on the development of a system for pharmaceutical drug delivery called SynBiosys, based on certain InnoCore polymers that can be used to encapsulate active ingredients. We believe that certain aspects of the SynBiosys system are complementary to our OctoDEX and PolyActive delivery technologies. We and InnoCore will collaborate on identifying potential third parties whose compounds may benefit from the application of the SynBiosys technology. We and InnoCore will share any payments received from third parties based on a pre-determined formula. To date, we have not identified any third parties for this collaboration. After an initial five-year term, the agreement is automatically renewed for successive one-year periods, unless terminated by either party. The agreement may be terminated sooner if we do not obtain sufficient third party engagements before August 2007.

#### ***IsoTis N.V.***

In 1999, we established a partnership with IsoTis to jointly develop and commercialize PolyActive for controlled drug delivery applications. IsoTis took a strategic decision to divest these activities through the sale of its subsidiary, Chienna B.V., in July 2002. In March 2003, we acquired Chienna from IsoTis for an aggregate consideration of € 2.8 million, thereby acquiring rights to the intellectual property portfolio relating to drug delivery applications of the PolyActive technology. As part of this transaction, we granted IsoTis an exclusive, royalty-free license, with a right to sub-license, to all future Chienna technology for any of the following uses: (i) use in the orthopedic field (therapeutic application to the musculoskeletal system, including bone, cartilage, joints, related connective tissues, ligaments, tendons and nerves); (ii) use as a medical device not containing a biologically active agent; and (iii) use as a material provided with living mammalian cells other than secretory cells. Secretory cells are defined as cells specialized for secretion, usually epithelial cells or endocrine cells in glands, such as Langerhans cells secreting insulin, and not comprising connective tissue cells, chondrocytes or bone marrow cells.

Under the agreement, IsoTis is entitled to a portion of the cumulative net profit derived from products based on Chienna technology. The size of future payments depends on the cumulative profitability of the products developed based on the PolyActive technology during the lifetime of the patents which we acquired or licensed from IsoTis. Payment under this profit sharing scheme falls due at the end of the life of the acquired PolyActive patent portfolio. However, to the extent that the accumulated profits of Chienna exceed its accumulated losses, we are required to make annual payments in the form of advances to IsoTis on the basis of the arrangement described above. In addition, we will owe Technologiestichting STW a low single digit royalty on the revenues of PolyActive based products for the duration of the base patent, which expires in 2016.

Pursuant to a supply agreement with IsoTis concluded in May 2003, we secured long-term access to a continued supply of PolyActive polymers. We were also granted access to updates to the device master file, as provided to the FDA and maintained by IsoTis. The supply agreement will end in July 2007, after which date it will be automatically extended for a subsequent period of five years. In the event that the supply agreement is terminated by IsoTis, we have the right to purchase the production facilities for the manufacture of PolyActive at book value.

#### ***Leiden University Medical Center***

In 2002, we entered into a co-operation and license agreement with Leiden University Medical Center (“LUMC”) for OP-145. Pursuant to that agreement, we were granted rights to develop OP-145 for the treatment of chronic middle ear infection and chronic infections of the upper respiratory tract. In March 2006, we amended our agreement with LUMC, so that we now have rights to develop OP-145 for all indications.

We have paid a nominal up-front license fee to LUMC and will pay nominal minimum royalties for the first two years of our development program. We will owe LUMC royalties based on net sales of OP-145. We have also agreed to pay LUMC a certain percentage of any sub-license revenues we receive in relation to OP-145.

The license agreement provides LUMC with certain termination rights if we do not pursue the development of OP-145 for a specified period of time. Furthermore, if we are responsible for a delay in the commercialization of OP-145 in a specific territory and for a specific indication, LUMC may terminate our rights to OP-145 as they relate to that territory and indication.

#### ***SciGen Ltd.***

In June 2005, we entered into a non-exclusive feasibility agreement with SciGen, which has developed and manufactures a proprietary, multi-shot hepatitis B vaccine under the brand name Sci-B-Vac, which is marketed in the Philippines, Hong Kong, Singapore and Vietnam. Pursuant to our agreement, we will study the feasibility of developing a single-shot hepatitis B vaccine based on Sci-B-Vac; HBV-OctoVAX. If our proof of concept study is successful, we and SciGen may decide to continue with the development and commercialization of a single-shot vaccine for hepatitis B on an exclusive basis, based on our respective technologies. We and SciGen have agreed to indemnify each other against certain liabilities, but these indemnities are limited in scope and amount. Either party may terminate this agreement at will upon notice.

#### ***SingVax Pte. Ltd.***

In September 2005, we entered into an exclusive co-development agreement with SingVax for the development of a single-shot vaccine for Japanese encephalitis.

Under our agreement, SingVax is responsible for a range of vaccine development activities, including development and production of JEV particles and cGMP manufacturing of the attenuated Japanese encephalitis virus.

In connection with the manufacturing of bulk JEV product, SingVax has obtained a license to the PER.C6 technology of Crucell N.V. Under the arrangement between SingVax and Crucell, Crucell has a right of first negotiation for the sale of any traveler's vaccine produced by SingVax that uses the PER.C6 technology for territories outside of the Asia Pacific region.

Pursuant to the terms of our agreement with SingVax, we are responsible for formulation development and cGMP manufacture of JEV-OctoVAX. We will share equally with SingVax all external and production costs and profits associated with the development of JEV-OctoVAX.

Our agreement with SingVax provides both parties with a right to terminate the agreement at will at pre-determined points. In the event that one party decides to terminate the agreement for convenience, residual obligations and rights may exist for the terminating party, including an obligation to manufacture its respective component of the JEV-OctoVAX product or to grant a royalty-bearing license for the manufacture of this component. In addition, either party may terminate the agreement in the event that the parties have not entered into a commercialization agreement for JEV-OctoVAX within a predetermined period after regulatory approval. We and SingVax have agreed to indemnify each other against certain liabilities, but these indemnities are limited in scope and amount.

#### ***SurModics, Inc.***

In June 2004, we provided SurModics with a worldwide exclusive license for the use of PolyActive and OctoDEX in the development of site-specific, local acting, drug-eluting implants, such as stents and ophthalmic devices.

We have received and will continue to receive certain up-front and ongoing licensing fees. We are also entitled to royalties on sales of products incorporating our technologies made by SurModics and on royalty payments received by SurModics pursuant to third party license agreements relying on our technology, including

annual minimum royalty payments, for the term of the agreement (See “Operating and Financial Review – Revenues – Drug Delivery and Product Business”). SurModics may, with due notice, terminate the license at will.

### *Utrecht University*

Utrecht University has granted us an exclusive license to all patents related to the OctoDEX technology. Pursuant to the relevant agreements, Utrecht University is entitled to receive royalties from us based either on our own sales of products that use the OctoDEX technology or on royalties that we receive from third parties, based on the sale of products using the OctoDEX technology. In addition, as part of our agreement with Utrecht University, we sponsor a Ph.D. position in the Department of Pharmaceutics and costs associated with this sponsorship can be offset against any royalties owed by us.

## **Government Regulation and Product Approval**

Our business is subject to extensive government regulation. Regulation by governmental authorities in the European Union, the United States and other jurisdictions is a significant factor in the development, manufacture and marketing of drugs and in ongoing research and development activities. All of our product candidates will require regulatory approval by governmental agencies prior to commercialization. In particular, pharmaceuticals are subject to rigorous pre-clinical and clinical trials and other pre-marketing approval requirements by the EMEA, the FDA and other regulatory authorities in the European Union, United States and other jurisdictions.

### *Regulation in the United States*

The testing, manufacturing, labeling, advertising, promotion, distribution, export and marketing of our product candidates are subject to extensive regulation by governmental authorities in the United States. The FDA, under the Federal Food, Drug and Cosmetic Act, regulates the approval and marketing of pharmaceutical drugs in the United States. The steps required before a drug may be approved for marketing in the United States generally include, among others:

- pre-clinical laboratory models and tests, including animal testing;
- the submission to the FDA of an Investigational New Drug Application (“IND”) for human clinical testing, which must become effective before human clinical trials commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug;
- the submission to the FDA of a new drug application (“NDA”);
- satisfactory completion of an FDA inspection of the manufacturing facilities at which the drug is made to assess compliance with current cGMP and, at the FDA’s option, an FDA audit of the clinical trial sites that generated the data in support of the NDA; and
- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources, and the receipt, timing, and conditions of any approval are uncertain. Pre-clinical studies include laboratory evaluations of the product candidate, model studies to assess the potential safety and efficacy of the product candidate, and testing in animals. The results of the pre-clinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which must become effective before clinical trials may be commenced.

### *Clinical Trial Approval*

Clinical trials involve the administration of the product candidates to patients or healthy volunteers under the supervision of a qualified principal investigator. Further, each clinical trial must be reviewed and approved by an independent institutional review board at or servicing each institution at which the clinical trial will be

conducted. The independent institutional review board will consider, among other things, ethical factors, the safety of human subjects and the possible liability of the institution.

Clinical trials typically are conducted in three sequential phases prior to approval, but the phases may overlap. These phases generally include the following:

- *Phase I.* Phase I clinical trials involve the initial introduction of the drug into human subjects, frequently healthy volunteers. These studies are designed to determine the safety and tolerability of the drug in humans, the adverse effects associated with increasing doses and, if possible, to gain early evidence of effectiveness. In Phase I, the drug is usually tested for safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism, excretion and pharmacodynamics.
- *Phase II.* Phase II clinical trials usually involve studies in a limited patient population to (i) determine dosage tolerance and optimal dosage; (ii) identify possible adverse effects and safety risks and (iii) evaluate the efficacy of the drug for specific, targeted indications. Although there are no statutory or regulatory definitions for Phase IIa and Phase IIb, Phase IIa is commonly used to describe a Phase II clinical trial evaluating, adverse effects, safety risks and preliminary efficacy; and Phase IIb is commonly used to describe a subsequent Phase II clinical trial that also evaluates dosage tolerance and optimal dosage.
- *Phase III.* If a compound is found to be potentially effective and to have an acceptable safety profile in Phase II studies, the clinical trial program will be expanded to further demonstrate clinical efficacy, confirm optimal dosage and safety within an expanded patient population at geographically dispersed clinical trial sites. Phase III studies usually include several hundred to several thousand patients.
- *Phase IV.* Phase IV clinical trials are studies required of or agreed to by a sponsor that are conducted after the FDA has approved a drug for marketing. These studies are used to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations. If the FDA approves a drug while a company has ongoing clinical trials that were not necessary for approval, a company may be able to use the data from these clinical trials to meet all or part of any Phase IV clinical trial requirement. These clinical trials are often referred to as Phase III/IV post approval clinical trials. Failure to promptly conduct Phase IV clinical trials could result in withdrawal of approval for drugs approved under accelerated approval regulations.

In the case of drugs for the treatment of severe or life threatening diseases, the initial clinical trials are sometimes done in patients rather than in healthy volunteers. Since these patients are afflicted already with the target disease, it is possible that such clinical trials may provide evidence of efficacy traditionally obtained in Phase II clinical trials. These trials are referred to frequently as Phase I/II clinical trials. We, the FDA or an independent review board may suspend clinical trials at any time on various grounds, including a finding that the patients or volunteers are being exposed to an unacceptable health risk.

### *Marketing Approval*

The results of pre-clinical and clinical trials, together with detailed information on the manufacture and composition of the drug and proposed labeling, are submitted to the FDA in the form of an NDA requesting approval to market the drug. In its review of NDA submissions, the FDA has broad discretion to require an applicant to generate additional pre-clinical and clinical data related to the product candidate's safety and efficacy.

Before approving an NDA, the FDA will inspect the facilities at which the drug is manufactured, whether ours or our third party manufacturer's, and will not approve the drug unless the manufacturing facility complies with cGMP. Once the NDA submission has been accepted for filing, the FDA typically takes one year to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied, require additional testing or information and/or require post-marketing testing and



surveillance to monitor safety or efficacy of a drug. FDA approval of any NDA submitted by us will be at a time the FDA chooses. Also, if regulatory approval of a drug is granted, such approval may entail limitations on the indicated uses for which such drug may be marketed. Once approved, the FDA may withdraw the drug approval if compliance with pre or post-marketing regulatory requirements and conditions of approvals is not maintained or if problems occur after the drug reaches the marketplace. In addition, the FDA may require post-marketing studies, referred to as Phase IV studies, to monitor the effect of approved drugs and may limit further marketing of the drug based on the results of these post-marketing studies.

If we obtain regulatory approval for a drug, this clearance will be limited to those diseases and conditions for which the drug is safe and effective, as demonstrated through clinical trials. Even if this regulatory approval is obtained, a marketed drug, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA for compliance with cGMP and other regulatory requirements. Discovery of previously unknown problems with a medicine, device, manufacturer or facility may result in restrictions on the marketing or manufacturing of an approved drug, including costly recalls or withdrawal of the drug from the market. Further, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the Internet. Upon approval, a drug may only be marketed for the approved indications in the approved dosage forms and at the approved doses. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. In addition, if there are any modifications to the drug, including changes in indication, labeling, or manufacturing processes or facilities, we may be required to submit and obtain FDA approval of a new or supplemental NDA. The FDA has broad post-market regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall drugs, withdraw approvals, enjoin violations and institute criminal prosecution.

#### *Pharmaceutical Pricing and Reimbursement*

Our ability to commercialize successfully and attract strategic partners for our product candidates depends in significant part on the availability of adequate coverage and reimbursement from third-party payers, including, in the United States, governmental payers such as the Medicare and Medicaid programs, managed care organizations, and private health insurers. Third-party payers are increasingly challenging prices charged for drugs and services and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the cost effectiveness of any future drugs. Even with studies, our product candidates may be considered less safe, less effective or less cost effective than existing drugs, and third-party payers therefore may not provide coverage and reimbursement for our product candidates, in whole or in part.

Political, economic and regulatory influences are subjecting the healthcare industry in the United States to fundamental changes. There have been and we expect there will continue to be a number of legislative and regulatory proposals to change the healthcare system in ways that could significantly affect our business. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”), among other things, established a new Part D prescription drug benefit that began on 1 January 2006 and changed coverage and reimbursement for drugs and devices under existing benefits. We anticipate that the United States Congress, state legislatures and the private sector will continue to consider and may adopt healthcare policies intended to curb rising healthcare costs. These cost-containment measures include:

- controls on government-funded reimbursement for medical drugs and services;
- controls on healthcare providers;
- challenges to the pricing of medical drugs and services or limits or prohibitions on reimbursement for specific drugs and therapies through other means;
- reform of drug importation laws; and



- expansion of use of managed care systems in which healthcare providers contract to provide comprehensive healthcare for a fixed cost per person.

We are unable to predict what additional legislation, regulations or policies, if any, relating to the healthcare industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation, regulations or policies would have on our business. Any cost containment measures, including those listed above, or other healthcare system reforms that are adopted could have a material adverse effect on our ability to operate profitably.

Drug pricing may also be affected materially by the approval of generic drugs by the FDA. Generic drugs may be approved upon the expiration of applicable patents and periods of regulatory exclusivity. They require the submission of an abbreviated new drug application, which must contain, among other things, studies showing the comparability of the generic product to the pioneer product approved pursuant to an NDA. The entry of a generic competitor typically results in a substantial reduction in effective pricing.

### ***Regulation in the European Union***

Clinical trials, the regulatory approval process, and safety monitoring of drugs and drug manufacturers in the European Union proceed in much the same manner as they do in the United States. Therefore, many of the concepts discussed above under “ – Regulation in the United States” apply similarly in the context of the European Union. In addition, drugs are subject to extensive price and reimbursement regulation of the European Union member states.

#### *Clinical Trial Approval*

Pursuant to the Clinical Trials Directive 2001/20/EC, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, approval must be obtained from the competent national authority of a European Union member state in which it is intended to conduct the study. Furthermore, a clinical trial may only be started after a competent ethics committee has issued a favorable opinion on the clinical trial application which must be supported by an investigational medicinal product dossier with supporting information prescribed by the Clinical Trials Directive and further detailed in applicable guidance documents.

#### *Marketing Approval*

Drug marketing approval in the European Union member states proceeds under one of four approval procedures: a centralized approval procedure, a mutual recognition procedure, a decentralized procedure or a national procedure.

Certain drugs defined as medicinal products developed by means of biotechnological processes must undergo the centralized approval procedure for marketing approval, which, if granted, is automatically valid in all European Union member states. The EMEA and the European Commission administer the centralized marketing approval process. This procedure is mandatory for biotechnological DNA and gene therapy products, products containing new active substance for the treatment of acquired immune deficiency syndrome (AIDS), cancer, neurodegenerative disorder or diabetes, orphan drugs and, starting 20 May 2008, also for pharmaceutical products containing a new chemical substance for the treatment of auto-immune diseases, other immune dysfunctions and viral diseases.

The centralized approval procedure is optional for new medicinal products containing a new active substance and other medicinal products that are sufficiently innovative in the eyes of the EMEA. The applicant has to show that the medicinal product concerned shows a significant therapeutic, scientific or technical innovation or that the granting of authorization is in the interest of patients at a Community level.

Under the centralized approval procedure, the EMEA’s Committee for Medicinal Products for Human Use (“CHMP”) serves as the scientific committee that renders opinions about the safety, efficacy and quality of human product candidates on behalf of the EMEA. The CHMP is composed of experts nominated by each

member state's national drug authority, one of them to be appointed to act as rapporteur for the co-ordination of the evaluation with the possible assistance of a further member of the Committee acting as a co-rapporteur. CHMP has 210 days, or longer if additional information is requested, to give its opinion to the EMEA as to whether a marketing approval should be granted. This process is complex and involves extensive consultation with the regulatory authorities of member states and a number of experts.

If the centralized procedure is not mandatory, there are three alternative procedures. If marketing authorization in only one member state is preferred, an application can be filed with the national competent authority of a member state. The other two options are a mutual recognition by European Union member states and the decentralized procedure.

If an authorization has been granted by one member state (the "Reference Member State"), an application may be made for mutual recognition in one or more other member states (the "Concerned Member State(s)"). Before submitting the application for mutual recognition, the holder of the authorization requests the Reference Member State to prepare an assessment report or update an existing report in respect of the drug concerned. The assessment report has to be provided, as well as forwarded, to the Concerned Member State(s) within 90 days of the receipt of the request. The holder of the marketing authorization also files the application(s) with the EMEA. Unless a member state considers that there are grounds for supposing that the applied for marketing authorization may present a risk to public health, each Concerned Member State recognizes the marketing authorization granted by the Reference Member State within 90 days of receipt of the application and the assessment report.

If the member states have not reached an agreement within said time limit they shall directly refer the matter to the EMEA. The Committee for Proprietary Medicinal Products ("CPMP"), which is a part of the EMEA, shall review the matter and issue a reasoned opinion within 90 days. If several applications have been made for a particular drug and member states have adopted divergent decisions concerning the authorization of the drug or its suspension or withdrawal, a member state, the European Commission or the marketing authorization holder may refer the matter to the CPMP. In that case, the 90-day period may be extended. The procedure before the CPMP is a form of arbitration.

After the CPMP has heard both sides of the argument, the Committee forwards its final opinion to the European Commission. The European Commission prepares a draft of the decision to be taken in respect of the application, taking into account European Union law, within 30 days of the receipt of the opinion.

The fourth option is the decentralized procedure. For all other pharmaceutical drugs for which no marketing authorization has been granted in a member state, a marketing authorization can be obtained from the competent member state authorities through a decentralized procedure. A marketing authorization may only be granted to an applicant established in the European Union. A member state has to ensure that the procedure for granting an authorization is completed within 210 days of the submission of a valid application. Authorizations are valid for five years and are renewable for consecutive five-year periods.

When appropriate, we may seek accelerated approval for our drug candidates. We cannot predict whether any of our drug candidates will obtain such designations, or the ultimate impact, if any, of such designations on the timing, conditions, or likelihood of EMEA approval.

After a drug has been approved and launched, it is a condition of maintaining the marketing approval that all aspects relating to its quality, safety and efficacy must be kept under review. Sanctions may be imposed for failure to adhere to the conditions of the marketing approval. In extreme cases, the approval may be revoked resulting in withdrawal of the product from sale.

Even if a drug has received marketing approval, national pricing and reimbursement rules will apply, which may delay, or effectively prevent, commercialization or make commercialization substantially less profitable than anticipated, or even uneconomical.

### *Manufacturing*

The manufacturing of approved drugs – for which a separate manufacturer’s license is mandatory – must be conducted in strict compliance with the EMEA’s cGMP and comparable requirements of other regulatory bodies, which mandate the methods, facilities, and controls used in manufacturing, processing, and packaging of drugs to assure their safety and identity. The EMEA enforces its cGMP requirements through mandatory registration of facilities and inspections of those facilities. Failure to comply with these requirements could interrupt supply and result in delays, unanticipated costs and lost revenues, and subject the applicant to potential legal or regulatory action, including but not limited to warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil and criminal penalties.

### *Marketing and Promotion*

The EMEA also regulates the marketing and promotion of approved drugs, including industry-sponsored continuing medical education, direct-to-consumer, advertising, and direct physician sales, to ensure that information provided by applicants regarding their products is truthful, balanced, and accurately reflects the safety and efficacy claims approved by the EMEA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties.

### *Manufacturers’ License*

A manufacturers’ license is a legal prerequisite for a pharmaceutical product that has received a marketing authorization for offering for sale within the European Union. Manufacture must be in accordance with cGMP, and sites are subject to inspection. Sanctions (including suspension of manufacturing) are applicable if requirements are not met.

### *Regulatory Data Protection and Marketing Exclusivity*

Without prejudice to the law on the protection of industrial and commercial property, all applications for marketing approval submitted on or after 20 November 2005, receive an 8+2+1 protection regime. This regime consists of a regulatory data protection period of eight years plus a marketing exclusivity of ten years plus an additional marketing exclusivity of one further year if, during the first eight years of those ten years, the marketing approval holder obtains an approval for one or more new therapeutic indications which, during the scientific evaluation prior to their approval, are determined to bring a significant clinical benefit in comparison with existing therapies. Under the current rules, a third party may reference the pre-clinical and clinical data of the original sponsor beginning eight years after first European approval, but can only market a generic version after ten (or 11) years have lapsed.

### *Pricing and Reimbursement*

Regulatory approval of pricing and reimbursement is required in most countries other than the United States. Regulators in some European countries condition their reimbursement of a drug on the agreement of the seller not to sell the drug for more than a specified price or in more than specified quantities per year in their countries. In some cases, the price established in any of these countries may serve as a benchmark in the other countries. As a result, the price approved in connection with the first approval obtained in any of these European countries may serve as the maximum price that may be approved in the other European countries. Further, a price approved in one of these European countries that is lower than the price previously approved in the other European countries may require a reduction in the prices in those other European countries. In such event, the resulting prices may be insufficient to generate an acceptable return on investment in the drug, or the product could be imported from a country where it is cheaper.

### *Regulation in Other Countries*

Approval of a drug by comparable regulatory authorities may be necessary in other countries prior to the commencement of marketing of the drug in those countries, whether or not U.S. or European Union approval

has been obtained. The approval procedure varies among countries and can involve requirements for additional testing. The time required may differ from that required for approval in the United States or the European Union. In general, each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

The Japanese approval agency requires that tests be conducted on Japanese subjects to determine appropriate dosages for Japanese patients. In particular, the Japanese approval agency may request dedicated clinical bridging studies to prove comparability of clinical results between non-Japanese and Japanese patients. Also, other parts of the clinical program may need to be repeated in Japan. This may therefore result in a delay in introducing a drug developed outside of Japan to the Japanese market.

## **Competition**

The pharmaceutical and biotechnology industries are highly competitive and subject to rapid technological change. Any product candidates that we successfully develop will compete with existing and future therapies. There are many organizations, including pharmaceutical companies, biotechnology companies, academic laboratories, research institutions, governmental agencies and public and private universities, which are actively engaged in developing products that target the same markets as our product candidates. Many of these entities have financial and other resources substantially greater than our own. In addition, many of our competitors have significantly greater experience in manufacturing, pre-clinical testing, conducting clinical trials, obtaining regulatory approvals and marketing than we do. These entities also compete with us in recruiting and retaining qualified scientific and management personnel, as well as in acquiring products and technologies complementary to, or necessary for, our programs. Moreover, there can be no assurance that our competitors will not obtain patent protection or other intellectual property rights that would make it difficult or impossible for us to market our products. As a result, there can be no assurance that we will be able to compete effectively against these companies or their products.

Our ability to compete successfully will depend largely on our ability to:

- advance the development of our product candidates, including the enrollment of patients for our clinical trials;
- demonstrate the safety, convenience of use and clinical efficacy of our product candidates;
- obtain regulatory approval for our product candidates in their respective indications;
- commercialize our product candidates successfully based on potential advantages of our products over alternative treatment methods;
- successfully collaborate with pharmaceutical and biotechnology companies in the discovery, development and commercialization of new products;
- obtain intellectual property protection for our products and technologies; and
- attract and retain qualified personnel.

We have noted below existing and potential competition for each of our products under development, as well as for our drug delivery technologies and our Contract Development Business. In addition to these competitors, our product candidates under development may also face competition from existing or new products we are currently unaware of.

### ***Products***

#### ***Locteron***

We believe that in the near to medium term interferon alfa will remain a principal element in the treatment of HCV.

We anticipate that Locteron, if approved, would compete with two approved pegylated interferon alfa products for the treatment of chronic HCV infections. These two products are Pegasys (marketed by Roche) and PEG-Intron (marketed by Schering-Plough). In addition, Locteron would face competition from conventional, unmodified forms of interferon, including Roferon-A (marketed by Roche), Intron A (marketed by Schering-Plough), and Infergen (marketed by Valeant Pharmaceuticals International and Astellas Pharma Inc.). In addition, we are aware that Human Genome Sciences, Inc. (in collaboration with Novartis AG), Flamel Technologies SA and Intarcia Therapeutics, Inc., have all progressed potentially competitive long-acting interferon alfa therapies into various stages of clinical development. In addition, we understand that Maxygen, Inc., (in collaboration with Roche), and Nautilus Biotech S.A., have progressed novel variants of interferon alfa into late pre-clinical development.

#### *OP-145*

We anticipate that OP-145, if approved, would compete with other products that are currently marketed for the treatment of chronic middle ear infection. The current standard of care for the treatment of chronic middle ear infection involves the use of antibiotics, which are delivered either systemically or as eardrops to destroy bacteria and corticosteroids which reduce inflammation of the mucus of the middle ear. For patients who become refractory to this therapy, a surgical intervention may be necessary in order to remove resistant infectious material and inflamed mucus. Antibiotics prescribed for chronic middle ear infection include Cipro HC Otic, a combination of ciprofloxacin hydrochloride and hydrocortisone otic suspension that is marketed by Alcon, Inc., and Floxin Otic (ofloxacin otic), which is marketed by Daiichi Sankyo, Inc. We are aware that Kyoto Pharmaceutical Industries is currently seeking Japanese registration of ceftizoxime alapivoxil, a product that inhibits bacterial cell wall synthesis to treat bacterial infections including chronic middle ear infection. In addition, we understand that Arriva Pharmaceuticals Inc. and ProMetic Life Sciences are jointly developing a product for otitis media and other indications.

#### *hGH-OctoDEX*

We anticipate that hGH-OctoDEX, if approved, would compete with currently approved versions of human growth hormone marketed by Eli Lilly and Company, Novo Nordisk A/S, Pfizer, Inc., Genentech, Inc., Ipsen SA, Serono SA, Ferring International S.A., Teva Pharmaceutical Industries Ltd., Sandoz AG, and BioPartners GmbH. In addition, we are aware that hGH-OctoDEX might compete with novel forms of hGH in clinical development by certain of these companies and by others. Companies that are also seeking to develop a long-acting, once-weekly hGH therapy include BioPartners and Altus Pharmaceuticals, Inc. We may also face competition from products that take advantage of alternative routes of administration of hGH, such as oral or inhaled formulations, as well as from engineered variants of hGH that have been optimized for improved drug characteristics.

#### *HBV-OctoVAX*

We anticipate that HBV-OctoVAX, if approved, would face competition from currently marketed hepatitis B vaccines, all of which require multiple injections in order to induce immunity. These vaccines include Engerix-B, marketed by GlaxoSmithKline plc, and Recombivax, marketed by Merck & Co, Inc. Twinrix, marketed by GlaxoSmithKline, is a combined hepatitis A and B vaccine specifically marketed to international travelers who may be exposed in endemic areas. In addition to these marketed products, we are aware that Dynavax Technologies Corporation has two vaccine candidates for hepatitis B in late stage clinical development.

#### *JEV-OctoVAX*

We anticipate that JEV-OctoVAX, if approved, would face competition from JE VAX, a three dose vaccine marketed by sanofi-pasteur, the vaccines business of sanofi-aventis SA. We are also aware of two other Japanese Encephalitis vaccines that are manufactured in China, primarily for domestic use. We are further aware of two JEV vaccines in Phase III clinical development by Intercell AG (in collaboration with Novartis) and Acambis plc.

### ***Drug delivery technologies***

There are many other companies developing controlled release drug delivery systems. Our most direct competitors are active in the area of parenteral controlled release delivery systems for biopharmaceuticals, and include Alkermes, Inc., Altus Pharmaceuticals, ALZA Corporation (a division of Johnson & Johnson), Atrix Laboratories, Inc., Debio S.A., DURECT Corporation, Elan Corporation, Ethypharm S.A., Flamel Technologies, MGI Pharma, Inc. and SkyePharma plc.

### ***Contract Development Business***

Our Contract Development Business faces competition from companies that are active in providing formulation and clinical trial manufacturing services. A number of large contract manufacturing organizations offer development services and manufacturing of clinical trial material as part of an extensive service package. In addition, we face significant competition from smaller, more specialized firms such as Aptuit Ltd., Evotec AG, Formatech, Inc., MedPharm Ltd., MP5 s.a.r.l. and Patheon, Inc. These firms typically focus on a specific part of the formulation market, such as biopharmaceuticals, low soluble compounds, oral drug delivery or pulmonary drug delivery. Such firms may offer formulation development services in combination with proprietary drug delivery technologies or bulk manufacturing capacity.

### **Facilities**

Our registered main place of business is located at Zernikedreef 12, 2333 CL Leiden, the Netherlands. This 1,725 m<sup>2</sup> facility comprises of a small-scale production plant, a number of laboratories as well as offices. We entered into a long-term lease for these premises with a remaining period of almost 18 years. We rent two additional facilities in Leiden, consisting of 340 m<sup>2</sup> of office space and 535 m<sup>2</sup> of laboratory and office space. Both these facilities can be vacated at short notice. To accommodate our anticipated growth, we have entered into an agreement to rent a purpose-built facility of 3,513 m<sup>2</sup>, which will be built adjacent to our current main facility. We intend to occupy this building towards the end of 2007.

We recently opened a business development office in Cambridge, MA, United States, where we lease approximately 125 m<sup>2</sup> of office space.

### **Legal Proceedings**

In 2004, we commenced opposition proceedings against a European patent application filed by Schering-Plough covering the administration of interferon alfa for the treatment of HCV within a specific dosing range. Although we believe Locteron will fall outside the claimed dosing range, we intend to continue our opposition proceedings in order to preserve flexibility in our further development activities. Schering-Plough currently holds a granted United States patent comparable in its coverage to the European patent application we are opposing. If Locteron is formulated with a dose of interferon alfa that falls within the covered range, we could be precluded from commercializing Locteron in the United States. In such event, we would consider commencing legal proceedings to invalidate the United States patent.

### **Employees**

We believe that our success will depend on our ability to identify, attract and retain key employees. At the end of 2003, 2004 and 2005, we had 91, 93 and 110 employees, respectively. As of 31 August 2006, we had 130 employees, of whom 129 were located in the Netherlands and one was located in the United States, representing 119 full-time employees. Of these employees, 59 worked for the Contract Development Business and 34 worked for the Drug Delivery and Product Business. A further 37 employees were not specifically assigned to either business unit.

We believe that relations with our employees are good. None of our employees is represented under a collective bargaining agreement. As required by Dutch law, we have established a works council. We believe that relations with our works council are good (see "Management and Employees – Works Council").



## MANAGEMENT AND EMPLOYEES

### General

Set out below is a summary of relevant information concerning our Executive Board, Supervisory Board, Senior Management and other employees. In addition, we set out a brief summary of certain significant provisions of Dutch corporate law and our Articles of Association in respect of our Executive Board and Supervisory Board as they will read after the expected execution of the Deed of Amendment and Conversion. See “Description of Share Capital and Corporate Governance - General”.

The numbers of Shares and other securities and exercise prices set forth in this chapter are based on the assumption that the Capital Restructuring has been completed. See “Description of Share Capital and Corporate Governance – Share Capital – Authorized and Issued Share Capital”.

### Management Structure

We have a two-tier board structure, consisting of an Executive Board (*Directie*) and a Supervisory Board (*Raad van Commissarissen*).

### Executive Board

#### *Powers, Composition and Function*

The Executive Board is responsible for the day-to-day management of our operations under the supervision of the Supervisory Board. The Executive Board is required to keep the Supervisory Board informed, consult with the Supervisory Board on important matters and submit certain important decisions to the Supervisory Board for its approval, as more fully described below.

The Executive Board may perform all acts necessary or useful for achieving our corporate purpose, save for those acts that are prohibited by law or by our Articles of Association. The Executive Board as a whole is authorized to represent us, as are any two members of the Executive Board acting jointly.

Our Articles of Association provide that the number of members of the Executive Board will be determined by the Supervisory Board, and that the Executive Board will consist of at least one member. In the event that the Executive Board comprises two or more members, the Supervisory Board may attribute specific titles to individual members of the Executive Board, such as “Chief Executive Officer”, “Chief Financial Officer” and “Chief Operating Officer”.

Members of the Executive Board are appointed by the General Meeting of Shareholders following a proposal by the Supervisory Board. The current members of the Executive Board have been appointed for an indefinite period of time. In view of the Dutch Corporate Governance Code, our Articles of Association provide (i) that new members of the Executive Board are appointed for a maximum term of four years, unless provided otherwise in the resolution to appoint such member and (ii) that a retiring member of the Executive Board can be re-appointed immediately for a term of not more than four years at a time.

The General Meeting of Shareholders may suspend or dismiss Executive Board members at any time. The Supervisory Board may also suspend Executive Board members at any time.

Under our Articles of Association, the following decisions of the Executive Board must be approved by the Supervisory Board:

- the acquiring, alienating, encumbering, leasing, letting and in any other way obtaining and giving the use or benefit of registered property;
- entering into agreements, whereby bank credit is granted to us;
- lending and borrowing money, with the exception of acquiring money under a credit already granted to us by a bank;



- entering into agreements by which we bind ourselves as guarantor or as severally liable co debtor, or otherwise bind ourselves as security for a debt of a third party;
- adoption of our annual budget;
- our operational and financial objectives;
- our long-term strategic policy and business plans and the parameters to be applied in relation to our strategy, for example in respect of our financial ratios;
- strategic issues and alliances;
- the sale or disposition of all, or an essential part of our assets;
- the issuance and acquisition of shares and debentures chargeable against us or chargeable against a limited partnership, or a general partnership of which we are a fully liable partner;
- petition for quotation, or withdrawal of quotation from a price list of any stock exchange of any listed securities;
- entering into or terminating long-term co-operation by us with another legal entity, company, or with a limited partnership or general partnership of which we are the fully liable partner, if such co-operation or termination of co-operation is of major significance to us;
- participating by us in the capital of another company;
- investments requiring an amount equal to at least one fourth of our issued capital plus reserves, according to our balance sheet and explanatory notes;
- a proposal to dissolve us, a proposal for a legal merger or a legal split-up, within the meaning of Title 7, Book 2 of the Dutch Civil Code, a proposal to decrease our issued capital, and a proposal to amend our Articles of Association;
- filing a petition for bankruptcy or for suspension of payments;
- a significant change in the employment conditions of a substantial number of our employees and a termination of the employment of a considerable number of our employees simultaneously or within a short period of time;
- the entering into and changing of employment agreements, whereby a remuneration is granted which exceeds the annual maximum amount determined by the Supervisory Board and notified to the Executive Board in writing;
- the entering into and termination of employment agreements with (proposed) members of our management;
- establishing pension plans and granting pension rights in excess of those arising from existing arrangements;
- adoption of employee stock-option plans;
- appointing staff members as officer with the general or limited power to represent us and determining their authority and title; and
- being a party to legal proceedings, including conducting arbitration proceedings, with the exception of taking legal measures that cannot be delayed, and making settlements.

The Supervisory Board may determine that a resolution as referred to above shall not require its approval if the amount involved does not exceed a value fixed by the Supervisory Board and notified to the Executive Board in writing. The Supervisory Board shall be entitled to require further resolutions of the Executive Board in addition to those listed above to be subject to their approval. Such further resolutions shall be clearly specified

and notified to the Executive Board in writing. The absence of approval of the Supervisory Board shall not affect the authority of the Executive Board or its members to represent the Company.

Furthermore, the Executive Board shall at least once a year inform the Supervisory Board in writing of the key elements of our strategic policy, our general and financial risks and our management and control system.

***Members of the Executive Board***

The Executive Board is currently composed of the following two members:

<u>Name</u>	<u>Age</u>	<u>Position</u>	<u>Member Since</u>	<u>Term</u>
Joost Holthuis . . . . .	52	Chief Executive Officer	20 July 1995 <sup>(1)</sup>	Indefinite
Hans Pauli . . . . .	46	Chief Financial Officer	22 December 2004	Indefinite

- (1) From 20 July 1995 until 1 June 2004, Mr. Holthuis served as our Managing Director through his management company Holthuis-Bernaerts Holding B.V.

The business address of both members of the Executive Board is Zernikedreef 12, 2333 CL Leiden, the Netherlands.

*Joost Holthuis – Chief Executive Officer and Co-Founder*

Mr. Holthuis graduated from the University of Leiden with a Master’s Degree in Pharmacy in 1980. After obtaining his Ph.D. and working as an Assistant Professor at Utrecht University, in 1988 he became the Director of Analytical Laboratories and Product Development at the Dutch subsidiary of Chiron Corporation. He is also co-chairman of the board of the Netherlands Biotechnology Association (NIABA), chairman of the BioPartner Center Foundation, member of the executive board of the foundation “Stichting Top Institute Pharma” as well as a member of the board of the “Adviescommissie IS” of the Dutch Ministry of Economic Affairs. Mr. Holthuis is also a member of the Netherlands Academy of Technology and Innovation. During his academic career, Mr. Holthuis published more than 50 scientific publications.

*Hans Pauli – Chief Financial Officer*

Mr. Pauli holds a B.A. degree (Hons) in Business Studies from Ealing College, London, where he received the Keith Wilshire Memorial Prize, and a Master’s Degree in Fiscal Economics from the University of Amsterdam. He began his career at Staal Bankiers N.V. in 1985 and joined Rabobank Nederland in 1987, where he served as manager of the New Issue and Syndication Department. He became Senior Manager, Investment Banking at Barclays de Zoete Wedd Nederland N.V. in 1988 and joined Nationale Investeringsbank N.V. as a Senior Manager, Investment Banking in 1992. From 1996 to 1999, Mr. Pauli served as CFO of Pharming Group N.V., during which period he was responsible for various financing activities, eventually leading to that company’s initial public offering. Since 1999, Mr. Pauli has held positions as CFO at various other companies, including RING!Rosa Products N.V., Secon Group B.V. and PamGene B.V. He joined us in 2003. Mr. Pauli is also chairman of the supervisory board of Henzo International Holding B.V. and member of the supervisory board of each of BAC B.V. and MedSciences II B.V.

**Supervisory Board**

***Powers, Composition and Function***

The Supervisory Board is responsible for supervising the conduct of and providing advice to the Executive Board and supervising our business generally. In performing its duties, the Supervisory Board is required to act in the interests of our business as a whole. The members of the Supervisory Board are not, however, authorized to represent us in dealings with third parties.

Our Articles of Association provide that the number of Supervisory Board members will be determined by the Supervisory Board.

Our Articles of Association provide that the General Meeting of Shareholders appoints the members of the Supervisory Board following a proposal by the Supervisory Board. The current members of the Supervisory Board have been appointed for the term set out in the table below. In view of the Dutch Corporate Governance Code, the Articles of Association will provide that any newly appointed member of our Supervisory Board will serve for a maximum of four years, unless provided otherwise in the resolution to appoint the Supervisory Board member in question, and may only be reappointed twice. The General Meeting of Shareholders appoints a chairperson and the Supervisory Board appoints a deputy chairperson from amongst its members.

Under our Articles of Association, the General Meeting of Shareholders may suspend or dismiss Supervisory Board members at any time. The Articles of Association provide that the Supervisory Board members shall retire periodically in accordance with a rotation plan to be drawn up by the Supervisory Board.

Under the Articles of Association, the Supervisory Board can only adopt resolutions by an absolute majority of the total number of votes to be cast in a meeting where the majority of the Supervisory Board members then in office are present or represented. Each member of the Supervisory Board shall be entitled to one vote.

### ***Members of the Supervisory Board***

The Supervisory Board is currently composed of the following members:

<u>Name</u>	<u>Age</u>	<u>Position</u>	<u>Member Since</u>	<u>Term Expires</u>
Hans Stellingsma . . . . .	49	Chairperson	1 April 2001	2010
René Kuijten . . . . .	42	Member	19 January 2005	2008
Philip Smith . . . . .	57	Member	19 January 2005	2009
Paul Toon . . . . .	38	Member	19 January 2005	2007

All members of the Supervisory Board were initially appointed for an indefinite term. However, in our Extraordinary General Meeting of Shareholders held on 1 September 2006, it was determined, subject to the execution of the Deed of Amendment and Conversion, that pursuant to a roster to be adopted by the Supervisory Board, the terms of the different members of the Supervisory Board were limited as described in the above table.

Mr. Stellingsma was reappointed by a written resolution of the General Meeting of Shareholders on 19 January 2006.

The business address of all members of our Supervisory Board is Zernikedreef 12, 2333 CL Leiden, the Netherlands.

#### *Hans Stellingsma – Chairperson*

Mr. Stellingsma obtained a Master’s Degree in Electronics from the Delft University of Technology and a post graduate degree (M.Phil.) from Glasgow University. He has held numerous senior positions at a range of businesses in the Netherlands. In particular, he has served as a Managing Director at Microsoft’s Dutch subsidiary and as senior vice president at KPN N.V. He was also a member of the managing board of Origin N.V. and then he became the chief executive officer of Content N.V. He was also a managing partner at Arthur D. Little in the Netherlands and a senior partner with Monitor, a consulting firm. Currently, Mr. Stellingsma is a partner at Quintel, a strategic consultancy and serves on the supervisory boards of Nova Media Holding B.V., Vergouwen Overduin B.V., MTel B.V. and Fenestrae B.V.

#### *René Kuijten*

Mr. Kuijten obtained his Medical Doctor degree from Utrecht University, having obtained additional training at Harvard Medical School and the Mayo Clinics. He completed his Ph.D. at the University of

Pennsylvania, where he published, among others, in The New England Journal of Medicine and Cancer Research. He received research awards from the World Health Organization and the International Union Against Cancer, and was honored with the Talma Eijkman Prize and the U-Gen Research Award for his scientific endeavors. He received an MBA from INSEAD in Fontainebleau, France. From 1992 to 2000, Mr. Kuijten was a senior consultant at McKinsey & Company and co-leader of the European Pharmaceuticals and Health Care Practice. He joined Life Sciences Partners in 2001 as a General Partner. On behalf of Life Sciences Partners, he serves or has served on the supervisory boards or as a Non-Executive Director of KuDOS Ltd., DNage B.V., Kreatech Holding B.V. and Hybrigenics S.A. Mr. Kuijten is a jury member of New Venture, a business plan competition, and board member of the McKinsey Alumni Association and the Max Geldens Society. He recently participated in a committee of the Royal Netherlands Academy of Sciences advising the Dutch government on gene patenting.

*Philip Smith*

Mr. Smith obtained his B.S. in Chemistry from the University of Maine, and his Master's Degree and Ph.D. in Medicinal Chemistry/Pharmacology from Northeastern University. He was an Assistant Professor at the University of Kansas Medical Center from 1981 to 1985. From 1986 to 2002, Mr. Smith held positions of increasing responsibility within the Pharmaceutical Development Group at SmithKline Beecham/GlaxoSmithKline, where he led an international group responsible for the identification and recommendation of internal drug delivery technologies for product development. In June 2002, Mr. Smith joined S.R. One, Limited, where he has been a General Partner since January 2003. He is currently on the board of directors of Cydex Inc., Linguagen Inc., Onyx Ltd., Trinity Biosystems, Inc. and Avantium B.V., and is an observer on the board of directors of Scynexis, Inc.

*Paul Toon*

Mr. Toon holds a B.A. degree (Hons) from Oxford University and has over 12 years experience in advising, investing in and managing life science and technology companies. He began his career at Merrill Lynch in the European Mergers & Acquisitions Group, focusing primarily on healthcare. He subsequently joined a drug development consultancy, developing a healthcare M&A practice over the course of six years. Mr. Toon then co-founded, and was COO, of an information technology start up company, completing two fundraising rounds to create a proprietary software platform to manage R&D investment. Subsequently, he invested in, and became COO and Commercial Director of a neuroscience biotechnology company leading two private funding rounds. He joined Innovent Partenaire in 2004, where he serves as a Managing Partner. Mr. Toon is a board member of Alba Cosmetics, Ltd., CMC Biopharmaceuticals A/S and 20/10 Perfect Vision Optische Geraete GmbH.

Messrs. Kuijten, Smith and Toon were appointed by our General Meeting of Shareholders upon nomination by Life Sciences Partners, S.R. One and Innovent Partenaire, respectively, pursuant to the shareholders agreement dated 19 January 2005. This shareholders agreement will be terminated upon completion of the Offer. We anticipate that these members of our Supervisory Board will not be independent members within the meaning of the Dutch Corporate Governance Code after the completion of the Offer.

## **Senior Management**

Our Executive Board is supported by the following members of the management team ("Senior Management"):

*Leo de Leede – Director, Pre-Clinical Development*

Mr. de Leede studied pharmacy at the University of Leiden and became a registered pharmacist in 1979. He received his Ph.D. from the University of Leiden in 1983. Mr. de Leede began his career as a scientist and group leader at the Department of Pharmaceutical R&D of N.V. Organon. In 1986, he became a manager of the central R&D facilities of Gist-brocades N.V., responsible for the biopharmaceutical and pharmacological research of the pharmaceutical division. In 1991, he joined Yamanouchi Europe B.V. where he served as plant manager, senior

project leader, senior manager of the European pharmaceutical research and development facilities, and Senior Director, Pre-Clinical Development Europe. Mr. de Leede joined us in 2001 and he became Director, Pre-Clinical Development in 2006. He is also a board member of FIGON (Netherlands Federation for Innovative Drug Research). Mr. de Leede is the author or co-author of over 35 scientific publications.

*Gerben Moolhuizen – Chief Business Officer*

Mr. Moolhuizen received a Master's Degree in medical biology from Utrecht University in 1991, studied at Tohoku University, Sendai, Japan and received an MBA from the Erasmus University of Rotterdam School of Management. He then joined Pharming Group N.V. where he held positions in Business Development, eventually becoming Director, Business Development. In 1997, Mr. Moolhuizen joined ASD B.V. (currently Primagen B.V.) where he became Vice-President, Business Development in 1999. He joined us in 2001, as Senior Manager, Business Development and Director, OctoPlus Products. He became Chief Business Officer in January 2006.

*Ellen Tjebbes – Director, Quality Assurance*

Mrs. Tjebbes obtained a Master's Degree in pharmacy from Utrecht University in 1990. She started her career as a pharmacist at the Pharmacy Department of the West Suffolk Hospital, Bury St. Edmunds, United Kingdom in 1990. In 1991, she joined Merck, Sharpe & Dohme B.V. where she was Validation Specialist and became QA Pharmacist, Supervisor Microbiology Laboratory in 1993. In 1995, Mrs. Tjebbes became Manager, Production and Packaging at Katwijk Farma B.V. and Project Manager in 2000. She joined Genzyme B.V. in 2002 as Clinical Pharmacist. Since September 2005, Mrs. Tjebbes has served as our Director, Quality Assurance.

*Alexander Willemse – Director, Contract Development*

Mr. Willemse obtained a Master's Degree in chemical technology from the Delft University of Technology in 1994, where he also received a Ph.D. in chemical process technology in 1998. Subsequently, he joined the Product Development Department of N.V. Organon where he briefly served as a Process Technologist and became Group Leader, Solids in 1998 and Senior Group Leader, Solids in 2002. In 2002, Mr. Willemse was a member of the Technical Committee of the 4th World Congress on Particle Technology in Sydney, Australia. He joined us in February 2003, and became Director, Contract Development in 2006. Mr. Willemse is the author or co-author of approximately 20 scientific publications.

*Ewoud-Jan van Hoogdalem – Chief Medical Officer*

Mr. van Hoogdalem obtained a Master's Degree in pharmacy from the University of Leiden in 1983. He received a Ph.D. in Pharmacology from the University of Leiden in 1989. Mr. van Hoogdalem joined Gist-brocades N.V. in 1989, where he served as a Research Scientist and joined Brocades Pharma B.V. in 1991 also as a Research Scientist. In 1994, he joined Yamanouchi Europe B.V., where he served as Head of the Biopharmaceutical Department, Head of the Section, Bioanalysis & Drug Metabolism of the Clinical Pharmacology Department and European Project Leader of the Project Management Department. In 2000, he joined pharmaceutical research operations of Johnson & Johnson, where he served as Associate Director, Clinical Drug Evaluation (Netherlands/United Kingdom) and Director, Experimental Medicine and Lead Scientist, Internal Medicine (Belgium). Mr. van Hoogdalem joined us in January 2006 as Chief Medical Officer. He is also a board member of the foundation "Organization Anselmus Colloquium" and the foundation "Organization EACPT2007". Mr. van Hoogdalem is the author or co-author of approximately 30 scientific publications.

## **Supervisory Board Committees**

Our Supervisory Board has appointed from among its members an Audit Committee and a Remuneration and Nominating Committee. These committees prepare the decision making of the Supervisory Board.

### *Audit Committee*

Our Audit Committee assists the Supervisory Board in monitoring our systems of internal controls, the integrity of our financial reporting process and the contents of our financial statements and reports. The Audit Committee also assists the Supervisory Board in assessing and mitigating our business and financial risks.

The Audit Committee shall meet at least twice a year and shall also meet each time we propose to issue a press release containing our financial figures.

The Audit Committee consists of René Kuijten (chairman) and Hans Stellingsma.

### *Remuneration and Nominating Committee*

Our Remuneration and Nominating Committee advises the Supervisory Board on the remuneration of the members of the Executive Board and monitors our remuneration policy, which covers bonus plans for our Senior Management and members of the Executive Board. The Remuneration and Nominating Committee further advises on the selection criteria and appointment procedures for members of the Executive Board and members of the Supervisory Board, the proposals for appointments and reappointments, and the policy of the Executive Board on selection criteria and appointment procedures for our Senior Management. It also assesses the functioning of individual members of the Supervisory Board and the Executive Board.

The Remuneration and Nominating Committee consists of Hans Stellingsma (chairman), Philip Smith and René Kuijten.

### **Remuneration Policy**

According to our Articles of Association, the General Meeting of Shareholders adopts the remuneration policy in respect of the remuneration of the Executive Board. The Supervisory Board establishes the remuneration of the individual members of the Executive Board, taking into account the policy adopted by the General Meeting of Shareholders, provided that arrangements in the form of Shares or rights to subscribe for Shares are subject to the approval of the General Meeting of Shareholders. Such a proposal must include the number of Shares or rights to subscribe for Shares that may be granted to the members of the Executive Board and which criteria apply to a grant or modification.

The objective of our remuneration policy is to ensure a high direct involvement and to encourage high performance by our personnel (including members of the Executive Board and Senior Management). The remuneration system is based on achieving performance criteria that are determined on a yearly basis.

### *Executive Board and Senior Management*

The total remuneration we paid to or for the benefit of members of our Executive Board and our Senior Management in 2005 amounted to approximately €404,000 and €280,000, respectively. The following table denotes the breakdown in remuneration of members of the Executive Board and Senior Management in 2005.

<u>Name</u>	<u>Base Salary</u>	<u>Bonus</u>	<u>Pension Contributions</u>	<u>Medical and other Benefits</u>	<u>Other Payments</u>	<u>Total Remuneration</u>
Joost Holthuis . . . . .	€175,000	€41,000	€20,000	€2,000	€20,000	€258,000
Hans Pauli <sup>(1)</sup> . . . . .	125,000	11,000	10,000	-	-	146,000
Senior Management . . . . .	225,000	16,000	25,000	2,000	12,000	280,000
Total . . . . .	<u>€525,000</u>	<u>€68,000</u>	<u>€55,000</u>	<u>€4,000</u>	<u>€32,000</u>	<u>€684,000</u>

(1) Until 1 February 2006, Hans Pauli was engaged on an 80% basis by OctoPlus.

Remuneration totals for members of our Executive Board and Senior Management in 2005 do not include the value of share options.



The number of Shares, including depositary receipts for Shares (see “Description of Share Capital and Corporate Governance – Share Capital – Depositary Receipts”), but excluding options and warrants to purchase our Shares (see “Management and Employees – Option Plans” and “Management and Employees – Warrants”) currently owned by the members of our Executive Board and Senior Management were as follows:

	<b>Number of Shares Owned</b>
Joost Holthuis <sup>(1)</sup> . . . . .	3,091,900
Hans Pauli . . . . .	46,500
Leo de Leede . . . . .	34,000
Gerben Moolhuizen . . . . .	22,500
Alexander Willemse . . . . .	15,000
Total . . . . .	<u>3,209,900</u>

(1) Shares are held through his management company, Holthuis-Bernaerts Holding B.V.

***Supervisory Board***

The remuneration of the members of the Supervisory Board is determined by the General Meeting of Shareholders. The remuneration of the chairperson of the Supervisory Board was €15,000 for 2005. The other members of the Supervisory Board did not receive any remuneration in 2005.

None of the members of the Supervisory Board owns Shares or options to acquire Shares.

**Other Information**

Except as indicated below, none of the members of the Executive Board, Supervisory Board and Senior Management is, or has been, subject to (i) any convictions in relation to fraudulent offences in the last five years, (ii) any bankruptcies, receiverships or liquidations of any entities in which such members held any office, directorships or senior management positions in the last five years, or (iii) any official public incrimination and/or sanctions of such person by statutory or regulatory authorities (including designated professional bodies), or disqualification by a court from acting as a member of the administrative, management or supervisory bodies of an issuer or from acting in the management or conduct of the affairs of any issuer for at least the previous five years.

Hans Pauli is chairman of the Supervisory Board of Henzo International Holding B.V. One of the subsidiaries of Henzo International Holding B.V. filed for bankruptcy as part of a corporate restructuring in April 2006.

Paul Toon served as a Director of SeedMarkets (Holding) Ltd., which entered into a voluntary liquidation in March 2002.

**Administrative, Management and Supervisory Bodies Conflicts of Interest**

Other than the fact that three of the members of our Supervisory Board may not be “independent” for the purposes of the Dutch Corporate Governance Code as described in “Description of Share Capital and Corporate Governance – Dutch Corporate Governance Code” and except as disclosed in “Related Party Transactions”, we are not aware of any potential conflict of interest between the private interests or other duties of the members of our Executive Board, Supervisory Board or Senior Management and their duties and responsibilities to us.

No family ties exist among the members of our Executive Board, Supervisory Board and Senior Management.



## Option Plans

### *Pre-Offer Option Plans*

In 2003, we adopted our share option plan as one of the elements of our remuneration policy for senior personnel (see “Management and Employees – Remuneration Policy”). In 2003, 2004 and 2006, we granted options pursuant to a standard share option agreement. The terms and conditions of these options are similar, except for the exercise period and exercise price of the options granted. The exercise period of the options granted prior to July 2004 was 37 months. These options have been exercised or lapsed. The exercise period of the options granted thereafter is 60 months. After taking the Capital Restructuring into account, the exercise prices of the options granted by us in the respective years are: €3.58 (2003), between €3.43 and €4.34 (2004) and €2.70 (2006), subject to customary adjustment provisions. In addition, the exercise prices of the options will be adjusted if we issue shares below the applicable exercise price of the options, subject to certain conditions.

### *Post-Offer Option Plan*

With a view to the listing of our Shares, we have drawn up a new share option plan which will enter into force following the Offer. The share option agreements entered into prior to that date will remain in place.

Under the new share option plan, the Supervisory Board has a discretionary power to grant options to our employees. The criteria for the granting of options, as well as the exercise price, will be determined by the Supervisory Board. The exercise period of the options shall be 60 months following the date of grant. Options can only be granted to members of the Executive Board following approval from the General Meeting of Shareholders. Options granted to members of the Executive Board or Senior Management can be exercised after satisfaction of conditions precedent set out in the grant letter pertaining to those options and in any event, at least five years after their grant. We will not issue options which, if exercised, would represent more than 7.5% of our issued share capital, unless the General Meeting of Shareholders approves otherwise.

All unexercised options held by an employee will lapse if we terminate that person’s employment or that person resigns, except in cases of death, permanent disability or retirement. In the event that the option holder ceases to be an employee for any reason other than death or permanent disability, we may force that employee to disgorge a specified portion of any profits realized from the exercise of those options.

### *Options Granted to the Executive Board, Senior Management and Other Parties*

The options indicated in the table below were granted to members of the Executive Board, Senior Management and other employees and consultants for the periods indicated.

Name	Currently Outstanding Options	Options Granted in 2004	Options Granted in 2005	Option Granted in 2006	End of Exercise Period of 2004 Options	End of Exercise Period of 2005 Options	End of Exercise Period of 2006 Options	Average Exercise Price of All Outstanding Options
Joost Holthuis . . . . .	80,600	73,500	–	7,100	2009	n.a.	2011	3.12
Hans Pauli . . . . .	56,800	49,600	–	7,200	2009	n.a.	2011	3.37
Leo de Leede . . . . .	81,100	77,100	–	4,000	2007/2009	n.a.	2011	3.46
Gerben Moolhuizen . . .	24,600	10,000	–	14,600	2009	n.a.	2011	2.99
Alexander Willemse . .	19,500	14,000	–	5,500	2009	n.a.	2011	3.22
Ewoud van Hoogdalem	10,000	–	–	10,000	n.a.	n.a.	2010	2.70
Other employees . . . .	60,300	9,500	–	21,500	2007	n.a.	2011	3.33
Consultants . . . . .	40,200	24,500	–	15,700	2009	n.a.	2011	3.14
Total . . . . .	<u>373,100</u>	<u>258,200</u>	<u>–</u>	<u>85,600</u>				<u>3.31</u>

Immediately prior to the Offer, our Executive Board, Senior Management and other employees and consultants held options to acquire a total of 373,100 Shares, which would, if exercised, represent approximately 2.2% of our total issued share capital immediately after the Offer, assuming we raise €25 million in the Offer, an Offer Price of €5.08, the mid-point of the Price Range, and no exercise of the Overallotment Option.

### **Warrants**

In 2003 and 2004, we granted warrants to Hans Pauli (1,260 warrants), Ton Holthuis (840 warrants), Henrik Luessen (560 warrants) and 7X Life Sciences B.V. (1,260 warrants) in connection with loans provided by them to us in 2003 and 2004 (see “Related Party Transactions”). These warrants entitle the holders thereof to acquire 100 Shares for each warrant during the period from 1 June 2004 to 30 November 2008 at an exercise price of €5.50 per Share, subject to customary adjustment provisions. To date, no warrants to purchase our Shares have been exercised.

### **Employment Agreements**

We have employment agreements with each of the members of the Executive Board and Senior Management. These employment agreements have an indefinite term and can be terminated, subject to the statutory notice period, which is one month for the employee and one to four months for us, dependent on the number of years of service. In the employment agreement with Mr. Willemse, the notice period is two months for both parties.

Our employment agreements do not provide for severance payments in the event of termination.

### **Directors Indemnification and Insurance**

In order to attract and retain qualified and talented persons to serve as members of the Executive Board or the Supervisory Board, in respect of a sector, region, product group or other internal company structure or segment, we provide such persons with protection through a directors’ and officers’ insurance policy.

Furthermore, we provide indemnification for members of our Executive Board and Supervisory Board against (i) substantiated costs made within the bounds of reasonableness with respect to conducting a defence (including lawyers fees), at law and otherwise, against third party claims for reimbursement of damages, or payment of fines, (judicially imposed) penalty payments and the like; and (ii) financial consequences of court rulings and resolutions of governmental authorities and amounts due relating to settlements that actually and in reasonableness have been paid by such member to third parties, due to an act or failing to act in the performance of his duties as member of the Executive Board or Supervisory Board or any other function he performs at our request, save where such act or the failing to act could be characterized as seriously culpable, or to the extent the loss of capital is covered by an insurance.

### **Pension Plan and Other Benefits**

We provide our employees with a collective pension plan. In the past, we have operated a defined benefit plan pursuant to which we made specified contributions to a large pension insurance company in the Netherlands in return for such company assuming the responsibility to make payments under the plan. This plan was closed on 31 December 2005. We are currently in the process of implementing a defined contribution plan, which will replace our defined benefit plan with a proposed effective date of 1 January 2006. We have paid contributions to the proposed administrator of this new plan in an amount we believe will be sufficient to cover our expected obligations to date under the new plan.

For some of our employees, including the members of the Executive Board, individual defined contribution pension plans apply.

We provide our employees with collectively negotiated health and retirement benefits in line with market practices in the Netherlands.

**Works Council**

As required by Dutch law, we have established a works council. Works councils in the Netherlands have the authority to advise on certain company decisions proposed by the General Meeting of Shareholders or the Executive Board, including but not limited to a change of control. Employers are also required to submit certain statutory defined matters that are viewed as ‘social policy’ (affecting employment terms and conditions) to the works council for prior approval. Our works council has given positive advice on our proposed listing of our Shares on Euronext Amsterdam.

## MAJOR SHAREHOLDERS

### Holdings Prior to and After the Offer

The following table presents information about the ownership of our Shares as of the date of this Prospectus for each existing shareholder we know to beneficially own 5% or more of our Shares, our management and employees as a group, and the aggregate number and percentage of Shares owned by others, assuming that the Capital Restructuring has taken place (see “Description of Share Capital and Corporate Governance – Share Capital”).

Shareholder	Shares owned immediately after the Offer <sup>(1)</sup>					
	Shares owned prior to the closing of the Offer		Without exercise of the Overallotment Option		With full exercise of the Overallotment Option	
	Total	%	Total	%	Total	%
Holthuis-Bernaerts Holding B.V. <sup>(2)</sup>	3,091,900	26.1	3,091,900	18.4	3,091,900	17.6
Innoven Partenaires S.A.	1,547,200	13.0	1,547,200	9.2	1,547,200	8.8
S.R. One, Limited	1,444,200	12.2	1,444,200	8.6	1,444,200	8.2
Life Sciences Partners III B.V. / C.V. <sup>(3)</sup>	1,650,100	13.9	1,650,100	9.8	1,650,100	9.4
SurModics, Inc.	1,160,400	9.8	1,160,400	6.9	1,160,400	6.6
Fagus N.V. <sup>(4)</sup>	1,160,400	9.8	1,160,400	6.9	1,160,400	6.6
Others <sup>(5)</sup>	1,631,100	13.7	1,631,100	9.7	1,631,100	9.3
Management & employees <sup>(6)</sup>	177,200	1.5	177,200	1.1	177,200	1.0
<b>Totals</b>	<b>11,862,500</b>	<b>100.0</b>	<b>11,862,500</b>	<b>70.7</b>	<b>11,862,500</b>	<b>67.7</b>

- (1) Based on an offer of 4,926,108 New Shares, assuming we raise €25 million in the Offer and an Offer Price of €5.08, the mid-point of the Price Range, and excluding any New Shares acquired by any of the existing shareholders pursuant to the Offer.
- (2) All shares in Holthuis-Bernaerts Holding B.V. are held by Joost Holthuis, our Chief Executive Officer.
- (3) Life Sciences Partners III B.V. (LSP III B.V.) and Life Science Partners III C.V. (LSP III C.V.) operate as one joint investment fund. Pursuant to their fund terms LSP III B.V. and LSP III C.V. may provide co-investment opportunities related to the Shares held by LSP III B.V. and LSP III C.V. prior to the closing of the Offer.
- (4) Fagus N.V. is a joint venture between European Investment Fund and Fortis Private Equity Belgium NV. Fortis Private Equity Belgium NV is an affiliate of Fortis, one of the Underwriters.
- (5) Others include, inter alia, FormFarm Holding B.V. (the investment company of our co-founder, Daan Crommelin), NPM Capital B.V. and 7X Life Sciences B.V.
- (6) Not including the Shares held by Joost Holthuis (see note 2). Hans Pauli, our Chief Financial Officer, holds 46,500 Shares.

Certain members of our Executive Board and Senior Management hold warrants and options to purchase Shares. We describe these options and warrants in more detail in “Management and Employees – Option Plans” and “Management and Employees – Warrants”.

Except as disclosed above, we are not aware of any person who, as of the date of this Prospectus, directly or indirectly, has a beneficial interest in 5% or more of our Shares. Our Major Shareholders have the same voting rights as other holders of the Shares.

### **Intentions to Subscribe**

S.R. One, Life Sciences Partners, Innoven Partenaires and SurModics have expressed the intention to subscribe for New Shares in the Offer up to a total amount of at least €5 million.

## RELATED PARTY TRANSACTIONS

Except as disclosed below, the members of the Executive Board and the Supervisory Board, Senior Management and the Major Shareholders have had no interest in any transactions to which we were a party since 1 January 2003 or which were entered into by us prior thereto and under which we or the other parties still have ongoing obligations.

We entered into a shareholders agreement with all our shareholders in January 2005 in connection with our second private equity round (see “Operating and Financial Review – Material Factors Affecting our Results of Operations and Financial Condition – Liquidity and Capital Resources”). This agreement will be terminated upon completion of the Offer.

Fagus N.V., a joint venture between the European Investment Fund and Fortis Private Equity Belgium NV, purchased Shares in January 2005 as part of this private placement. Fortis, an affiliate of Fortis Private Equity Belgium NV and one of the Underwriters, acted as placement agent in connection with this private placement. As part of its compensation for these services, Fortis received 204 class AP Shares, which immediately prior to the Offer will convert into 20,400 shares.

In January 2005, in conjunction with our second private equity round of financing, funds associated with Innoven Partenaires extended a number of subordinated loans to OctoPlus Technologies B.V. with an aggregate principal amount of approximately €4.0 million. These loans were replaced by subordinated convertible bonds in June 2005. In connection with the Offer, these convertible bonds will be redeemed on a non-cash basis as their value will be added to the share premium reserve as it relates to the shares held in us by Innoven Partenaires.

Prior to April 2004, we rented our operating facilities at market rates from OctoShed B.V., then a wholly-owned subsidiary of Holthuis-Bernaerts Holding, the personal holding company of our Chief Executive Officer. In April 2004, we acquired OctoShed and in the context of that transaction our facilities were valued at €3.7 million. In May 2004, we entered into a sale and leaseback arrangement with Fortress B.V., a real estate developer. Pursuant to this arrangement, we sold our facilities for €3.7 million to Fortress and a special purpose vehicle controlled by persons affiliated with Fortress. We hold a small beneficial interest in this special purpose vehicle. We entered into this arrangement as Fortress was in a position to finance an expansion of our facilities.

Prior to 2005, Holthuis-Bernaerts Holding and Joost Holthuis provided various loans to us at market rates. In January 2005, the outstanding balance of these loans was converted into equity at the valuation applicable to our second private equity round of financing. In addition, in consideration for providing these loans to us, Mr. Holthuis received 735 options with an exercise price of €342.50 (entitling the holder to acquire 73,500 Shares at an exercise price of € 3.43 per Share following the Capital Restructuring).

In November 2003, our Chief Financial Officer, Hans Pauli, provided a €150,000 guarantee to ING Bank in support of an increase of our credit facility. The guarantee expired in August 2004. In addition to receiving a monthly fee of 0.5% of the guaranteed amount, Mr. Pauli also received 1,260 warrants with an exercise price of €550 (entitling the holder to acquire 126,000 Shares at an exercise price of € 5.50 per Share following the Capital Restructuring). The warrants mature on 30 November 2008. Furthermore, in August 2004, Mr. Pauli provided us with a loan of €75,000. In addition to receiving monthly interest of 0.5%, Mr. Pauli also received 236 options with an exercise price of €342.50 (entitling the holder to acquire 23,600 Shares at an exercise price of € 3.43 per Share following the Capital Restructuring). This loan was paid back in December 2004.

In November 2003, Hans Stellingsma, the chairperson of our Supervisory Board, provided a €150,000 guarantee to ING Bank in support of an increase of our credit facility. The guarantee expired in June 2004. Mr. Stellingsma received a monthly fee of 1.0% of the guaranteed amount.

In November 2003, Ton Holthuis, a brother of our Chief Executive Officer, Joost Holthuis, provided a subordinated loan of €100,000, which was paid back in May 2004. In addition to receiving monthly interest of 0.5%, Mr. Holthuis also received 840 warrants with an exercise price of €550 (entitling the holder to acquire 84,000 Shares at an exercise price of € 5.50 per Share following the Capital Restructuring). The warrants mature on 30 November 2008.



## DESCRIPTION OF SHARE CAPITAL AND CORPORATE GOVERNANCE

### General

Our business was commenced by a company incorporated under Dutch law as a private company with limited liability (*besloten vennootschap met beperkte aansprakelijkheid*), by deed executed on 20 July 1995 under the name OctoPlus B.V., which is currently named OctoPlus Development B.V. and is one of our 100% subsidiaries. Our current name is OctoPlus International Holding B.V. and we were incorporated on 29 May 1997 under Dutch law. We trade under the name OctoPlus. We are registered with the Trade Register of the Chamber of Commerce for Rijnland, the Netherlands under number 28075073. Our corporate seat is in Leiden, the Netherlands and our office address is Zernikedreef 12, 2333 CL Leiden, the Netherlands. We can be contacted by telephone on + 31 (0)71 5244044, by fax on +31 (0)71 5244048 by email at octoplus@octoplus.nl, or through our website which is www.octoplus.nl. The contents of our website are expressly not incorporated by reference into this Prospectus.

Our articles of association were last amended by deed of amendment, executed on 19 January 2005, before Mr. T.H. Liem, civil law notary in Amsterdam, the Netherlands. The certificate of no objection of the Ministry of Justice for that amendment was granted on 11 January 2005, under number BV 597.465. We shall further amend our articles of association and convert our company into a public company with limited liability (*naamloze vennootschap*) prior to the Settlement Date.

On 16 August 2006, our Executive Board issued a notice calling an Extraordinary General Meeting of Shareholders, which was held on 1 September 2006. The purpose of the Extraordinary General Meeting of Shareholders was, amongst others, to consider and to resolve in favor of an amendment to our articles of association and our conversion into a public company with limited liability, subject to completion of the Offer. The deed of amendment and conversion (the “Deed of Amendment and Conversion”) is available for inspection by our shareholders at our offices in Leiden. The main objects of the Deed of Amendment and Conversion are (i) to restructure our share capital, by the abolition of our classes of AP, BP and C shares and any rights related thereto, the creation of preference shares and the redenomination of our ordinary shares, (ii) to change our name (from OctoPlus International Holding B.V. to OctoPlus N.V.), (iii) to introduce the right of our Supervisory Board to (a) withhold approval for an issuance of shares or the granting of rights to subscribe for shares (including the designation of the authority to do so) and the limitation or exclusion of pre-emptive rights in relation to such issuance (including the right to designate the authority to do so), (b) withhold approval for an acquisition or disposal of our own shares, (c) withhold approval for a reduction of issued share capital, (d) propose candidates for Executive Board vacancies, (e) withhold approval for certain Executive Board resolutions and (f) propose candidates for Supervisory Board vacancies, among other rights, and (iv) to update our articles of association as a result of changes in the Dutch Civil Code and to comply with the Dutch Corporate Governance Code.

The closing of the Offer on the Settlement Date and the amendment of our articles of association through the execution of the Deed of Amendment and Conversion are inter-conditional. The closing of the Offer will not occur if the articles of association are not amended.

Set out below is a summary of certain relevant information concerning our share capital, certain significant provisions of Dutch corporate law and a brief summary of certain provisions of our articles of association as they will read after the expected execution of the Deed of Amendment and Conversion (the “Articles of Association”). When we refer to our Articles of Association in this Prospectus, we refer to the Articles of Association, as amended.

This summary does not purport to give a complete overview and should be read in conjunction with the Articles of Association, together with relevant provisions of Dutch law, and does not constitute legal advice regarding these matters and should not be considered as such.

## Corporate Objects

Pursuant to Article 3 of our Articles of Association, our corporate objects are:

- to incorporate, to participate in any way whatsoever in, to manage and to supervise businesses and companies, in particular, but not limited to those involved in the pharmaceutical and biomedical industries, and, more in particular, those involved in the development and exploitation of pharmaceutical and biomedical processes and products and the rendering of research and development services;
- to develop and trade in patents, trade marks, licenses, know-how and other intellectual property rights;
- to render advice and services to businesses and companies with which we form a group and to third parties;
- to borrow, to lend and to raise funds, including the issue of bonds, promissory notes or other securities or evidence of indebtedness, as well as to enter into agreements in connection with the aforementioned activities;
- to grant guarantees, to bind ourselves and to pledge our assets for obligations of businesses and companies with which we form a group and on behalf of third parties;
- to acquire, dispose of, manage and exploit registered property and items of property in general; and
- to do all that is connected therewith or may be conducive thereto, all to be interpreted in the broadest sense.

## Share Capital

### *Authorized and Issued Share Capital*

At the date of this Prospectus, our authorized capital amounts to €500,000 and is divided into 150,000 class AP shares, 50,000 class BP shares and 300,000 class C shares, each with a nominal value of €1. Following the execution of the Deed of Amendment and Conversion, our authorized share capital will amount to €8,640,000, divided into 36,000,000 ordinary shares and 36,000,000 preference shares, each with a nominal value of €0.12. The separate classes of AP shares, BP shares and C shares will be abolished upon execution of the Deed of Amendment and Conversion.

Furthermore, the execution of the Deed of Amendment and Conversion will result in (i) a conversion of each of our issued class AP, class BP and class C shares into the same number of ordinary shares, (ii) a split of each of these ordinary shares into 100 ordinary shares with a nominal value of €0.01 each, and (iii) an increase in the nominal value of the ordinary shares to €0.12 each, which shall be charged against our share premium reserve (the “Capital Restructuring”). The execution of the Deed of Amendment and Conversion will, furthermore, result in the creation of a class of preference shares. Consequently, we will have two classes of shares, ordinary shares (referred to as the Shares elsewhere herein) and preference shares.

Immediately prior to the Offer, assuming that the Capital Restructuring has been effected, we will have 11,862,500 ordinary shares issued and outstanding. In addition, warrants and options outstanding prior to the Capital Restructuring will also be adjusted for the split, resulting in warrants for 392,000 ordinary shares and options for 373,100 ordinary shares.

The following table sets forth information about our issued share capital as of the date of this Prospectus, after the Capital Restructuring, and following completion of the Offer.

	As of the date of this Prospectus	After the Capital Restructuring	Following completion of the Offer <sup>(1)</sup>
Class AP shares . . . . .	55,929	-	-
Class BP shares . . . . .	15,472	-	-
Class C shares . . . . .	47,224	-	-
Ordinary shares . . . . .	-	11,862,500	16,788,608
Preference shares . . . . .	-	-	-
Warrants . . . . .	3,920	392,000	392,000
Options . . . . .	3,731	373,100	373,100
<b>Total . . . . .</b>	<b>126,276</b>	<b>12,627,600</b>	<b>17,553,708</b>

(1) Based on an offer of 4,926,108 New Shares, assuming we raise €25 million in the Offer and an Offer Price of €5.08, the mid-point of the Price Range.

Currently, neither we nor any of our subsidiaries hold any of our shares. All shares that are outstanding as of the date of this Prospectus are fully paid up.

Immediately following completion of the Offer, based on an offer of 4,926,108 New Shares, assuming we raise €25 million in the Offer and an Offer Price of €5.08, the mid-point of the Price Range, and no exercise of the Overallotment Option, we expect to have 16,788,608 ordinary shares issued and outstanding. The percentage of immediate dilution resulting from the Offer is 29.3% and amounts to €25 million.

### ***Form and Trading of Shares***

Our ordinary shares are in registered form (aandelen op naam) and will be traded through the book-entry facilities of Euroclear Netherlands. No share certificates will be issued. We are responsible for keeping a shareholders' register.

### ***Outstanding Warrants and Options***

In 2003 and 2004, we entered into warrant agreements with Hans Pauli, our Chief Financial Officer, and three other parties. Pursuant to these warrant agreements, a total of 3,920 warrants are currently outstanding. Each warrant entitles its holder to acquire a class C share for an exercise price of €550 (see "Management and Employees – Warrants"). As part of the Capital Restructuring, the warrants will be adjusted so that each warrant will entitle its holder to acquire 100 ordinary shares at an exercise price of €5.50.

The Offer does not constitute or trigger a termination of, or automatic right to exercise, any warrants. We have furthermore not entered into any agreements with the holders of the warrants to that effect. The warrants therefore shall remain in existence and in full force and effect after the Offer.

In addition, on various occasions in 2003, 2004 and 2006, we entered into share option agreements with employees. Pursuant to these option agreements, a total of 3,731 options are currently outstanding. Each option entitles its holder to acquire a class C share for an exercise price, depending on the calendar year in which the option was granted, of €358.00 (2003), between €342.50 and €433.63 (2004) or €270.00 (2006). Except for the exercise price and the exercise period, all option agreements have identical terms (see "Management and Employees – Option Plans – Pre-Offer Option Plans"). As part of the Capital Restructuring, the options will be adjusted so that each option will entitle its holder to acquire 100 ordinary shares at exercise prices varying between €2.70 and €4.34.

The Offer does not constitute or trigger a termination of, or automatic right to exercise, any option. We have furthermore not entered into any agreements with the holders of the options to that effect. The options shall therefore remain in existence and in full force and effect after the Offer.

We have drawn up a new employee share option plan in accordance with the Dutch Corporate Governance Code. Any options granted following the Offer shall be subject to our new option plan, (see “Management and Employees – Option Plans – Post-Offer Option Plan”).

### ***Depository Receipts***

As of 31 August 2006, out of the 47,224 currently issued class C shares, 305 are held by Stichting Administratiekantoor OctoPlus International Holding (the “Administration Office”). For the class C shares held by the Administration Office, it has issued depository receipts to certain of our employees following the exercise of their options. The Administration Office shall terminate the administration of all shares held by it subject to completion of the Offer. Pursuant to the termination of the administration, the depository receipts will be cancelled and the corresponding shares (following conversion into Shares pursuant to the Capital Restructuring) will be transferred to the holders of the cancelled depository receipts.

### ***Issue of Shares and Pre-emptive Rights***

In general, each holder of our ordinary shares shall have a pre-emptive right to subscribe for newly issued ordinary shares, pro rata to the aggregate amount of that holder’s ordinary shares. Such pre-emptive rights do not apply, however, in respect of (i) ordinary shares issued for a non-cash contribution, and (ii) ordinary shares issued to our employees. Holders of ordinary shares do not have pre-emptive rights to subscribe for an issue of preference shares.

Our Articles of Association will delegate the authority to issue ordinary shares and preference shares, and/or to limit or exclude pre-emptive rights in relation to an issuance of shares, to the Executive Board, with the prior approval of our Supervisory Board, for a period of five years, ending five years after the Deed of Amendment and Conversion becoming effective. This delegation may be extended, either by an amendment to the Articles of Association, or by a resolution of the General Meeting of Shareholders, for a period not exceeding five years in each case. A delegation pursuant to a resolution of the General Meeting of Shareholders shall require the proposal of the Executive Board, which is subject to the prior approval of the Supervisory Board.

Designation of the Executive Board as the corporate body with these authorities by the Articles of Association may be revoked by an amendment of the Articles of Association. Designation of the Executive Board as the corporate body with these authorities by the General Meeting of Shareholders cannot be revoked, unless determined otherwise at the time of designation.

Following termination of the Executive Board’s authority to issue ordinary shares and preference shares and/or to limit or exclude pre-emptive rights in relation to an issue of shares, the General Meeting of Shareholders shall be authorized to do so, unless it has delegated these authorities to another corporate body.

No resolution of the General Meeting of Shareholders or the Supervisory Board is required for an issue of shares pursuant to the exercise of a previously granted right to subscribe for shares.

The preference shares are further discussed below.

### ***Granting of Rights to Subscribe for Shares***

Our Articles of Association delegate the authority to grant rights to subscribe for shares to the Executive Board, with the prior approval of our Supervisory Board, for a period of five years after the Deed of Amendment and Conversion becoming effective. This delegation may be extended, either by an amendment to the Articles of Association, or by a resolution of the General Meeting of Shareholders, for a period not exceeding five years in each case. A delegation pursuant to a resolution of the General Meeting of Shareholders shall require a proposal by the Executive Board, which is subject to prior approval of the Supervisory Board.

Designation of the Executive Board as the corporate body with the authority to grant rights to subscribe for shares by the Articles of Association may be revoked by an amendment of the Articles of Association.

Designation of the Executive Board as the corporate body with the authority to grant rights to subscribe for shares by the General Meeting of Shareholders cannot be revoked, unless determined otherwise at the time of designation.

Following termination of the Executive Board's authority to grant rights to subscribe for ordinary shares and preference shares, the General Meeting of Shareholders shall be authorized to do so, unless it has delegated these authorities to another corporate body.

### ***Acquisition of Shares in Our Capital***

We may acquire our own fully paid shares at any time for no consideration (om niet). Furthermore, subject to certain provisions of Dutch law and our Articles of Association, we may acquire fully paid shares in our own capital if (i) our shareholders' equity less the payment required to make the acquisition, does not fall below the sum of the paid-in and called-up share capital plus the reserves as required to be maintained by Dutch law or by our Articles of Association (such excess, the "Distributable Equity") and (ii) we and our subsidiaries would thereafter not hold shares or hold a pledge over our shares with an aggregate nominal value exceeding 10% of our issued share capital.

Other than those shares acquired for no consideration, shares may only be acquired subject to a resolution of the Executive Board, which is approved by the Supervisory Board, and authorized by the General Meeting of Shareholders. Such authorization from the General Meeting of Shareholders for the acquisition of our shares shall specify the number and class of these shares that may be acquired, the manner in which these shares may be acquired and the price range within which shares may be acquired. Such authorization may be valid for no more than 18 months.

The General Meeting of Shareholders has authorized the Executive Board to acquire a maximum of 10% of our issued ordinary shares for a period of 18 months, ending 18 months after the Deed of Amendment and Conversion becoming effective, at a purchase price between the nominal value of the shares and 110% of the average price of our ordinary shares during five trading days before the repurchase.

No authorization from the General Meeting of Shareholders is required for the acquisition of fully paid shares for the purpose of transferring these shares to employees pursuant to our share option plan. Any shares we hold in our own capital may not be voted or counted for voting quorum purposes.

### ***Reduction of Share Capital***

The General Meeting of Shareholders may, at the proposal of the Executive Board, which proposal is subject to the approval of the Supervisory Board, resolve to reduce our issued and outstanding share capital by canceling our shares, or by amending our Articles of Association to reduce the nominal value of our shares.

### **Dividends and Other Distributions**

We may only make distributions to our shareholders in so far as our shareholders' equity exceeds the Distributable Equity.

Under our Articles of Association, a dividend shall first, if possible, be paid on the preference shares out of the profits (the positive balance of the profit and loss accounts) made in the most recently elapsed financial year. The dividend payable on the preference shares shall, if possible, be equal to the average twelve-month EURIBOR (Euro Interbank Offered Rate), weighted for the number of days to which the distribution pertains, increased by 1%, calculated over the paid up part of the nominal value of those shares. The dividend on the preference shares shall, if the respective shares have been issued in the course of the financial year, be calculated pro rata, to the payment of the year they have been outstanding.

If twelve-month EURIBOR shall no longer be published at any time, the dividend payable on the preference shares shall be equal to the mathematical average of the average effective return on the five Dutch government bonds with the longest maturity, as drawn up by the Central Bureau of Statistics and published in

the Daily Official List, over the 20 trading days preceding the issue, increased by a surcharge to be determined by the Executive Board, subject to the approval of the Supervisory Board, such surcharge to be between 0.25% and 1%, calculated over the paid up part of the nominal value of those shares.

The resolution to issue the preference shares may specify that if the profits of any financial year do not permit a distribution of dividends on the preference shares, the deficit shall be distributed from our Distributable Equity and, if this is also insufficient, from the profits of any subsequent years (i.e. cumulative preference shares).

After distribution of dividends on the preference shares (including any outstanding distribution on cumulative preference shares), the Executive Board may, subject to the approval of the Supervisory Board, determine which part of the profits shall be reserved. The part of the profit remaining after reservation shall be distributed as a dividend on the ordinary shares.

Under our Articles of Association, we may only make a distribution of dividends to our shareholders if our statutory annual accounts demonstrate that such distribution is legally permitted. The Executive Board may, however, subject to the prior approval of the Supervisory Board, declare an interim dividend. The General Meeting of Shareholders may, furthermore, upon the proposal by the Executive Board, with the prior approval of the Supervisory Board, resolve that a distribution is made from the Distributable Equity and that a distribution of dividends on the ordinary shares shall not be paid in whole or in part in cash, but in shares.

Claims to dividends and other distributions not made within five years from the date that such dividends or distributions became payable, will lapse and any such amounts will be considered to have been forfeited to us (verjaring).

#### **Preference Shares and Stichting Continuïteit OctoPlus**

We intend to incorporate Stichting Continuïteit OctoPlus (the “Foundation”). The purpose of the Foundation will be to safeguard our interests and those of our enterprise and to protect, insofar as possible, our continuity, our independence and our corporate identity. The board of the Foundation will consist of two board members A and one board member B. We have found Jan Willem Termeijtelen prepared to accept the position of board member B and are seeking to find two suitable candidates to accept a position of board member A. As soon as practically possible after we have found those two candidates, we will incorporate the Foundation. Once the Foundation is incorporated, the board members A will be appointed by the board of the Foundation, whilst the board member B will be appointed by the Supervisory Board upon proposal of the Executive Board. All board members are independent within the meaning of Appendix X of the Euronext Rule Book, Book II.

Our preference shares will be an instrument of protection against hostile takeovers. In line with guidance from the Dutch Corporate Governance Code, we believe that the issuance of preference shares may help us to determine our position in relation to a bidder and its plans, and to seek alternatives. The issue of preference shares is intended to be temporary. Unless the preference shares have been issued by a vote of the General Meeting of Shareholders, our Articles of Association require that a General Meeting of Shareholders be held no later than two years after the issue of preference shares to consider their redemption or cancellation. If the General Meeting of Shareholders does not resolve to redeem or cancel the preference shares, another General Meeting of Shareholders will be held within two years. Until the preference shares have been redeemed or cancelled, a General Meeting of Shareholders to consider a redemption or cancellation of the preference shares will be held within two years of the previous meeting.

Under the terms of an agreement which we will enter into with the Foundation, we will grant the Foundation a call option (the “Call Option”) entitling it to acquire from us preference shares up to a maximum of 100% of our total issued and outstanding share capital (excluding issued and outstanding preference shares) at the time the Foundation exercises the Call Option. Under the terms of another agreement to be entered into by the Foundation and us, the Foundation will grant us a put option (the “Put Option”) entitling us to issue preference shares to the Foundation up to a maximum of 100% of our total issued and outstanding share capital



(excluding issued and outstanding preference shares) at the time we exercise the Put Option. The Call Option as well as the Put Option can be exercised in one or more tranches.

No resolution of the General Meeting of Shareholders or the Executive Board is required for an issue of preference shares pursuant to the exercise of the Call Option or the Put Option. However, an issue of preference shares pursuant to a resolution of a corporate body other than the General Meeting of Shareholders, through which an amount of preference shares shall be issued that exceeds 100% of the outstanding amount of ordinary shares, is only permitted with prior approval of the General Meeting of Shareholders given for that specific instance. In the event of an issue of preference shares pursuant to a resolution of a corporate body other than the General Meeting of Shareholders, through which an amount of preference shares shall be issued that does not exceed 100% of the outstanding amount of ordinary shares, a General Meeting of Shareholders shall be convened and held within four weeks after the issue, at which meeting the reasons for the issue shall be explained.

Upon the issue of preference shares to the Foundation, the Foundation must pay at least 25% of the nominal value of the preference shares. The Foundation will enter into a credit facility agreement with a bank in order to finance such payment.

A transfer of preference shares (save for a transfer of preference shares to us) requires the prior approval of the Executive Board.

### **General Meetings of Shareholders and Voting Rights**

The annual General Meeting of Shareholders shall be held within six months after the end of each financial year. Our financial year is equal to a calendar year.

An Extraordinary General Meeting of Shareholders may be convened, whenever our interests so require, by the Executive Board or the Supervisory Board. Shareholders representing alone or in aggregate at least one-tenth of our issued and outstanding share capital may, pursuant to the Dutch Civil Code and our Articles of Association, request the district court to authorize such shareholder to convene a General Meeting of Shareholders.

The notice convening any General Meeting of Shareholders shall be sent no later than the 15th day prior to the meeting and shall include an agenda stating the items to be dealt with. Holders of shares (including holders of the rights conferred by law upon holders of depositary receipts issued with a company's cooperation for shares in its capital) who, alone or in the aggregate, own shares representing at least 1% of our issued and outstanding capital have the right to request the Supervisory Board or the Executive Board to place items on the agenda of the General Meeting of Shareholders. If such proposals are submitted to the Executive Board or the Supervisory Board in time for the Executive Board to put these proposals on the agenda for the next meeting, or announce them prior to the meeting by means of a supplementary notice with due observance of the aforementioned notice period, the Executive Board or the Supervisory Board shall be obliged to do so, provided that no important interest (zwaarwichtig belang) we have dictates otherwise.

All notices of General Meetings of Shareholders, all announcements concerning dividend and other distributions, and all other announcements to holders of shares (including holders of rights conferred by law upon holders of depositary receipts issued with a company's cooperation for shares in its capital), shall be effected by means of a publication in a nationally distributed daily newspaper, in the Daily Official List and on our website.

The Executive Board shall be authorized to determine a record date to establish which shareholders are entitled to attend and vote in the General Meeting of Shareholders. Such record date may not be set for a date prior to the seventh day before that of the meeting.

Each of our preference shares and ordinary shares is entitled to one vote. Shareholders may vote by proxy. The voting rights attached to any of our shares held by us are suspended as long as they are held in treasury.

Decisions of the General Meeting of Shareholders are taken by an absolute majority of votes cast, except where Dutch law provides for a qualified majority.

### **Amendment of Our Articles of Association and Change of Our Corporate Form**

The General Meeting of Shareholders may resolve to amend our Articles of Association, subject to a proposal by the Executive Board, which requires the approval of the Supervisory Board.

The General Meeting of Shareholders may furthermore resolve to change our corporate form. A change of our corporate form shall require a resolution to amend our Articles of Association, subject to a proposal by the Executive Board, which requires the approval of the Supervisory Board.

### **Statutory Merger and Statutory Demerger**

The General Meeting of Shareholders may resolve that we enter into a statutory merger or demerger (which term includes both a split-up and a spin-off), subject to a proposal by the Executive Board, which requires the approval of the Supervisory Board. In the event we are the acquiring company, the Executive Board may resolve to enter into a statutory merger or demerger, unless one or more shareholders representing at least 5% of our issued share capital request the Executive Board within one month of the announcement of the merger or demerger, to convene a General Meeting of Shareholders.

### **Dissolution and Liquidation**

We may only be dissolved by a resolution of the General Meeting of Shareholders subject to a proposal by the Executive Board, which requires the approval of the Supervisory Board.

In the event of a dissolution, our business will be liquidated in accordance with Dutch law and our Articles of Association, and the members of the Executive Board will (unless otherwise determined by the General Meeting of Shareholders) become liquidators, acting under supervision of the Supervisory Board. During liquidation, the provisions of our Articles of Association will remain in force to the extent possible.

The balance remaining after settlement of debts shall firstly be distributed to the holders of preference shares up to the amount of the outstanding dividends payable on the preference shares. Thereafter, an amount equal to the nominal paid-up amount of the preference shares shall be paid on each preference share. Any balance remaining after such payments shall be transferred to the holders of ordinary shares, in proportion to the aggregate nominal amount of their ordinary shares.

### **Dutch Corporate Governance Code**

On 9 December 2003, the Dutch Corporate Governance Committee, also known as the Tabaksblat Committee, released the Dutch Corporate Governance Code. The Dutch Corporate Governance Code contains 21 principles and 113 best practice provisions for executive boards, supervisory boards, shareholders and general meetings of shareholders, financial reporting, auditors, disclosure, compliance and enforcement standards.

Dutch companies listed on a government-recognized stock exchange, whether in the Netherlands or elsewhere, are required under Dutch law to disclose in their annual reports whether or not they apply the provisions of the Dutch Corporate Governance Code that relate to the executive board or supervisory board and, if they do not apply, to explain the reasons why. The Dutch Corporate Governance Code provides that if a company's general meeting of shareholders explicitly approves the corporate governance structure and policy and endorses the explanation for any deviation from the best practice provisions, such company will be deemed to have applied the Dutch Corporate Governance Code.

We acknowledge the importance of good corporate governance. The Executive Board and Supervisory Board have reviewed the Dutch Corporate Governance Code, generally agree with its basic provisions, and have taken and will take any further steps they consider appropriate to implement the Dutch Corporate Governance Code.

We support the Dutch Corporate Governance Code and will apply with the relevant best practice provisions of the Dutch Corporate Governance Code, subject to the exceptions set out below.

### *Non-Compliance with the Dutch Corporate Governance Code*

II.1.1 A management board member is appointed for a maximum period of four years. A member may be reappointed for a term not more than four years at a time.

The current members of the Executive Board have been appointed for an unlimited period and we do not consider it appropriate to renegotiate the existing agreements, in so far as this would be possible given the mandatory provisions of Dutch labor law. Any future appointments of members of the Executive Board will be in compliance with this provision.

II.1.3 The company shall have a suitable internal risk management and control system. It shall, in any event, employ as instruments of the internal risk management and control system:

- risk analyses of the operational and financial objectives of the company;
- a code of conduct which should, in any event, be published on the website;
- guides for the layout of the financial reports and the procedures to be followed in drawing up the reports; and
- a system of monitoring and reporting.

We do not yet have a code of conduct, but intend to adopt such a code in due course.

II.2.1 Options to acquire shares are a conditional remuneration component, and become unconditional only when the management board members have fulfilled predetermined performance criteria after a period of at least three years from the grant date.

The currently outstanding warrants and options have been granted unconditionally. We shall not amend these existing agreements. Considering that we are still in a relatively early stage of development of our products and that the setting of credible predetermined performance criteria at a term of at least three years is not practical at this stage, we shall not fully apply this provision.

II.2.6 The supervisory board shall draw up regulations concerning ownership of and transactions in securities by management board members, other than securities issued by their 'own' company. The regulations shall be posted on the website. A management board member shall give periodic notice, but in any event at least once a quarter, of any changes in his holding of securities in Dutch listed companies to the compliance officer or, if the company has not appointed a compliance officer, to the chairman of the supervisory board. A management board member who invests exclusively in listed investment funds or who has transferred the discretionary management of his securities portfolio to an independent third party by means of a written mandate agreement is exempted from compliance with this last provision.

We believe that the restrictions under Dutch securities law are sufficient to govern the ownership of and transactions in securities by members of the Executive Board. Implementing additional restrictions would potentially harm our ability to attract and ensure the continued services of the members of the Executive Board and we therefore believe that applying this best practice provision is not in our best interest.

III.2.1 The supervisory board members, with the exception of not more than one person, shall be independent within the meaning of best practice provision III.2.2.

Our Supervisory Board consists of four members, of which three were appointed by our General Meeting of Shareholders upon nomination by Life Sciences Partners, S.R. One and Innoven Partenaire, pursuant to the shareholders agreement dated 19 January 2005. If these shareholders decide to subscribe for New Shares in the Offer, and subject to the number of New Shares to be acquired by such shareholders, the supervisory directors nominated by such shareholders may not be independent within the meaning of the Dutch Corporate Governance

Code. We do not intend to terminate their respective appointments as we believe they are currently the best qualified persons available to us.

III.4.3 The supervisory board shall be assisted by the company secretary. The company secretary shall see to it that correct procedures are followed and that the supervisory board acts in accordance with its statutory obligations and its obligations under the articles of association. He shall assist the chairman of the supervisory board in the actual organization of the affairs of the supervisory board (information, agenda, evaluation, training program, etc.). The company secretary shall, either on the recommendation of the supervisory board or otherwise, be appointed and dismissed by the management board, after the approval of the supervisory board has been obtained.

We are in the process of determining the exact profile of the company secretary. As soon as we have determined this profile, we shall seek a suitable candidate. We expect to appoint a company secretary after the Offer.

III.7.3 The supervisory board shall adopt a set of regulations containing rules governing ownership of and transactions in securities by supervisory board members, other than securities issued by their 'own' company. The regulations shall be posted on the website. A supervisory board member shall give periodic notice, but in any event at least once a quarter, of any changes in his holding of securities in Dutch listed companies to the compliance officer or, if the company has not appointed a compliance officer, to the chairman of the supervisory board. A supervisory board member who invests exclusively in listed investment funds or who has transferred the discretionary management of his securities portfolio to an independent third party by means of a written mandate agreement is exempted from compliance with this last provision.

We believe that the restrictions under Dutch securities law are sufficient to govern the ownership of and transactions in securities by Supervisory Board members. Implementing additional restrictions would potentially harm our ability to attract and ensure the continued services of Supervisory Board members and we therefore believe that applying this best practice provision is not in our best interest.

IV.3.1 Meetings with analysts, presentations to analysts, presentations to investors and institutional investors and press conferences shall be announced in advance on the website and by means of press releases. Provision shall be made for all shareholders to follow these meetings and presentations in real time, for example by means of web casting or telephone lines. After the meetings, the presentations shall be posted on the company's website.

Considering our size, it would create an excessive burden to provide facilities which enable shareholders to follow in real time the meetings and presentations referred to in the best practice provision. We will, however, ensure that presentations are posted on our website immediately after the meetings in question.

V.3.1 The external auditor and the audit committee shall be involved in drawing up the work schedule of the internal auditor. They shall also take cognizance of the findings of the internal auditor.

We feel that our financial reporting will be sufficiently monitored by our audit committee and will initially not appoint an internal auditor.

### **Disclosure of Information**

We will be required to publish our annual accounts within four months after the end of each financial year and our half-yearly figures within two months after the end of the first six months of each financial year.

We shall also disclose forthwith all new facts relating to our business that are not publicly known and could materially affect the market price of our Shares.

## **Obligations of Shareholders to Make a Public Offer**

Currently there is no obligation under Dutch law for a shareholder whose interest in a company's share capital or voting rights passes a certain threshold to launch a public offer for all or part of the outstanding shares in the share capital of that company. However, when the EU Takeover Directive is implemented in the Netherlands, a shareholder who has acquired a certain percentage of our Shares and/or of our voting rights, will be obliged to launch a public offer for all Shares. The draft bill for the implementation of the EU Takeover Directive issued by the Dutch Ministry of Finance proposes to set such threshold at 30% of shares and/or of voting rights and to apply this obligation to shareholders acting in concert. The expected implementation date of the provisions of that bill is January 2007.

## **Obligations of Shareholders to Disclose Holdings**

Holders of our Shares may be subject to reporting obligations under the Act on Disclosure of Voting Rights and Capital Interest in Listed Companies (*Wet melding zeggenschap en kapitaalbelang in effectenuitgevende instellingen*) (the "Act on Disclosure"), the 1996 Act on Disclosure of Major Holdings in Listed Companies (*Wet melding zeggenschap in ter beurze genoteerde vennootschappen 1996*) (the "Disclosure of Holdings Act") and/or the Dutch Act on the Supervision of Securities Transactions 1995 (*Wet toezicht effectenverkeer 1995*) (the "Dutch Securities Act").

On 3 July 2006, a legislative proposal was adopted to replace the Disclosure of Holdings Act with the Act on Disclosure. Pursuant to the Decree of 25 August 2006, the Act on Disclosure will partly come into force as per 1 October 2006 and the remainder will come into force as per 1 November 2006. Until the Act on Disclosure has entirely come into force, the relevant provisions of the Disclosure of Holdings Act shall remain in force and effect.

### ***Disclosure of Holdings Act***

Under the Disclosure of Holdings Act, any person who, directly or indirectly, acquires or disposes of an interest in the capital and/or the voting rights of a public limited liability company incorporated under Dutch law with an official listing on a stock exchange within the European Economic Area shall give written notice of such acquisition or disposal if, as a result of such acquisition or disposal, the percentage of the capital interest and/or voting rights held by such person enters within a different specified percentage range to that held by such person prior to such acquisition or disposal.

The percentage ranges referred to in the Disclosure of Holdings Act are 0% to 5%, 5% to 10%, 10% to 25%, 25% to 50%, 50% to 66\_% and over 66\_%. Notification shall be given to us and to the AFM upon the occurrence of specified events, which includes the passing of any percentage threshold.

Each person whose holding of capital interest or voting rights amounts to 5% or more at the time of admission of our ordinary shares to listing on Euronext Amsterdam, shall notify us and the AFM within four weeks after such admission.

The AFM keeps a public register of all notifications made pursuant to the Disclosure of Holdings Act and publishes all such notifications it receives.

### ***Act on Disclosure***

The Act on Disclosure shall implement part of the Transparency Directive (2004/109/EC). The Act on Disclosure shall introduce more extensive notification obligations for listed companies with respect to changes in their issued share capital and the voting rights that can be exercised in respect of their shares.

On implementation of the Act on Disclosure, the following material changes shall be made to the notification obligations of any person who, directly or indirectly, acquires or disposes of an interest in the capital and/or the voting rights of a public limited liability company incorporated under Dutch law with an official listing on a stock exchange within the European Economic Area:

- As is the case in the Disclosure of Holdings Act, such person is required to notify the AFM forthwith, by means of a standard form, if it acquires or disposes of an interest in such company's capital or voting rights and, as a result thereof, the percentage of capital interest or voting rights held by such person meets, exceeds, or falls below any of the thresholds indicated by the Act on Disclosure. The Act on Disclosure sets these thresholds at: 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 60%, 75% and 95%.
- A notification obligation shall also apply if a person's capital interest or voting rights meet, exceed or fall below one of the thresholds as a consequence of a change in the company's share capital or voting rights. The notification shall be made forthwith, and in any event no later than on the fourth trading day, after the AFM's publication of the company's notification of such event.
- If an interest has changed due to an amendment in the composition of the capital interest (a potential interest has for instance been converted in an actual interest) and it was not obliged to notify this amendment, such person must update its notification within four weeks after the end of the calendar year as long as it holds at least 5% of the capital interest.

As per 1 October 2006, under the provisions of the Act on Disclosure, we shall be obliged to notify the AFM forthwith if our share capital or voting rights change by 1% or more as a result of changes in our share capital or voting rights since our previous notification. The AFM will publish such notifications in a public register. We may also notify the AFM of any other amendments in our share capital at any time, but we must at least notify the AFM of such amendments periodically. Pursuant to the Decree on Disclosure of Voting Rights and Capital Interest in Listed Companies (*Besluit melding zeggenschap en kapitaalbelang in effectenuitgevende instellingen*), dated 5 August 2006, 'periodically' should be read as 'each quarter'. In this respect, we are obliged to notify the AFM of any amendments in our share capital which have occurred during the past quarter within 8 days after the calendar quarter has ended.

### ***Dutch Securities Act***

Pursuant to the Dutch Securities Act, which has been amended by the Market Abuse Act of 23 June 2005, which came into force on 1 October 2005 (*Wet marktmisbruik*) implementing the Market Abuse Directive 2003/6/EC and related Commission Directives 2003/124/EC, 2003/125/EC and 2004/72/EC, members of our Executive Board and Supervisory Board and any other person discharging day-to-day co-managerial responsibilities or having the authority to make decisions affecting our future developments and business prospects and having regular access to inside information relating, directly or indirectly, to us (for the purpose of this paragraph, a "Relevant Person"), are required to notify the AFM of the existence of transactions conducted for their own account in our Shares or in securities issued by us, the value of which is determined by the value of our Shares.

Persons designated by the governmental decree pursuant to the Dutch Securities Act dated 14 September 2005 (*Besluit marktmisbruik*) (the "Securities Act Decree") who are closely associated with our members of the Executive Board, Supervisory Board or any of the Relevant Persons are required to notify the AFM of the existence of any transactions conducted for their own account in our Shares or in securities issued by us, the value of which is determined by the value of our Shares. The Securities Act Decree determines that following categories of persons are considered closely associated: (i) the spouse or any partner considered by national law as equivalent to the spouse, (ii) dependent children, (iii) other relatives who have shared the same household for at least one year at the relevant transaction date, (iv) any legal person, trust or partnership, amongst other things, whose managerial responsibilities are discharged by a person referred to under (i), (ii) or (iii) above.

The AFM shall be notified of transactions relating to our Shares or securities, which have a value which is determined by reference to the value of our Shares, within five days following the transaction date. Notification may be postponed until the date the value of the transactions amounts to €5,000 or more per calendar year.

### ***Regulations on Insider Trading and Disclosure***

We are required to apply a code of conduct in respect of the applicable insider trading rules and reporting obligations in respect of transactions in our securities and to draw up a list of persons working for us, under a contract of employment or otherwise, who could have access to inside information on a regular or incidental basis, to regularly update this list of persons and to inform persons on this list about the relevant prohibitions and sanctions in respect of insider knowledge (voorwetenschap) and market abuse. We shall adopt such a code of conduct and insider list prior to the Listing Date.

The AFM keeps a public register of all notifications made pursuant to the Dutch Securities Act.

### ***Non-compliance***

Non-compliance with the notification obligations under the Disclosure of Holdings Act, the Act on Disclosure and the Dutch Securities Act could lead to criminal fines, administrative fines, imprisonment or other sanctions. In addition, non-compliance with the Disclosure of Holdings Act and the Act on Disclosure may lead to civil actions, which may include the suspension of voting rights and the prohibition of further acquisitions of shares in the capital of the company concerned.



## **MARKET INFORMATION**

### **Euronext Amsterdam**

We intend to apply for the admission of all our Shares to listing and trading on Euronext Amsterdam. Upon listing and trading our Shares on Euronext Amsterdam, we will be subject to Dutch securities regulations and supervision by the relevant Dutch authorities.

### **Market Regulation**

The AFM is the market regulator in the Netherlands and supervises market conduct of the parties active on the securities markets. The AFM has supervisory powers with respect to the application of takeover regulations. It also supervises financial intermediaries (such as credit institutions and investment firms) and investment advisers. Pursuant to the implementation of the Prospectus Directive 2003/71/EC in the Netherlands on 1 July 2005, the AFM is the competent authority for approving all prospectuses published for admission of securities to trading on Euronext Amsterdam (except for prospectuses approved in other European Economic Area states that are used in the Netherlands in accordance with applicable passporting rules) and due to the implementation of the Market Abuse Directive and related Commission Directives on 1 October 2005, the AFM has taken over from Euronext its supervisory powers with respect to publication of inside information by listed companies.

## TAXATION

*This is a general summary and the tax consequences as described here may not apply to a holder of Shares. Any potential investor should consult his own tax adviser for more information about the tax consequences of acquiring, owning and disposing of Shares.*

### **Taxation in the Netherlands**

This taxation summary solely addresses the principal Dutch tax consequences of the acquisition, the ownership and disposition of Shares. Where in this summary English terms and expressions are used to refer to Dutch concepts, the meaning to be attributed to such terms and expressions shall therefore be the meaning to be attributed to the equivalent Dutch concepts under Dutch tax law. It does not discuss every aspect of taxation that may be relevant to a particular holder of Shares under special circumstances or who is subject to special treatment under applicable law. It also assumes that we are organized, and that our business will be conducted, in the manner outlined in this Prospectus. A change to such organizational structure or to the manner in which we conduct our business may invalidate the contents of this summary, which will not be updated to reflect any such change.

This summary is based on the tax laws of the Netherlands as they are in force and in effect on the date of this Prospectus. The laws upon which this summary is based are subject to change, possibly with retroactive effect. A change to such laws may invalidate the contents of this summary, which will not be updated to reflect any such changes.

### **Dutch Taxation - Taxes on Income and Capital Gains**

#### ***Resident Holders of Shares***

##### *General*

The summary set out in this section “Dutch Taxation – Taxes on Income and Capital Gains – Resident Holders of Shares” only applies to a holder of Shares who is a “Dutch Individual” or a “Dutch Corporate Entity”.

For the purposes of this section you are a “Dutch Individual” if you satisfy the tests that (a) you are an individual; (b) you are resident, or deemed to be resident, in the Netherlands for Dutch income tax purposes, or you have elected to be treated as a resident of the Netherlands for Dutch income tax purposes; (c) your Shares and income or capital gains derived therefrom have no connection with your past, present or future employment, if any; and (d) your Shares do not form part of a substantial interest (*aanmerkelijk belang*) or a deemed substantial interest in us within the meaning of Chapter 4 of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*).

Generally, if a person holds an interest in us, such interest forms part of a substantial interest or a deemed substantial interest in us if (i) such person alone or, if he is an individual, together with his partner (*partner*, as defined in Article 1.2 of the Dutch Income Tax Act 2001), if any, has, directly or indirectly, the ownership of Shares in us representing 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our Shares), or rights to acquire, directly or indirectly, Shares, whether or not already issued, that represent 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our Shares), or the ownership of profit participating certificates (*winstbewijzen*) that relate to 5% or more of our annual profit or to 5% or more of our liquidation proceeds; (ii) such person’s Shares, profit participating certificates or rights to acquire Shares or profit participating certificates in us have been acquired by him or are deemed to have been acquired by him under a non-recognition provision; and/or (iii) such person’s partner or any of his relatives by blood or by marriage in the direct line (including foster-children) or of those of his partner has a substantial interest (as described under (i) and (ii) above) in us.

A person who is entitled to the benefits from Shares or profit participating certificates (for instance a holder of a right of usufruct) is deemed to be a holder of Shares or profit participating certificates, as the case may be, and his entitlement to benefits is considered a share or profit participating certificate, as the case may be.

If you are an individual and a holder of Shares and if you satisfy test (b) above, but do not satisfy test (c) and/or test (d) above, your Dutch income tax position is not discussed in this Prospectus. If you are an individual and a holder of Shares who does not satisfy test (b), please refer to the section “Dutch Taxation – Taxes on Income and Capital Gains – Non-Resident Holders of Shares”.

For the purposes of this section you are a “Dutch Corporate Entity” if you satisfy the tests that (1) you are a corporate entity (including an association that is taxable as a corporate entity) that is subject to Dutch corporation tax in respect of benefits derived from its Shares; (2) you are resident, or deemed to be resident, in the Netherlands for Dutch corporation tax purposes; (3) you are not an entity that, although in principle subject to Dutch corporation tax, is, in whole or in part, specifically exempt from that tax; and (4) you are not an investment institution (*beleggingsinstelling*) as defined in the Dutch Corporation Tax Act 1969 (*Wet op de vennootschapsbelasting 1969*).

If you are a corporate entity and a holder of Shares and if you do not satisfy any one or more of these tests, with the exception of test (2) directly above, your Dutch corporation tax position is not discussed in this Prospectus. If you are a corporate entity and a holder of Shares that does not satisfy test (2) directly above, please refer to the section “Dutch Taxation – Taxes on Income and Capital Gains – Non-Resident Holders of Shares”.

#### *Dutch Individuals Deriving Profits from an Enterprise*

If you are a Dutch Individual and if you derive or are deemed to derive any benefits from Shares, including any capital gains realized on the disposal thereof, that are attributable to an enterprise from which you derive profits, whether as an entrepreneur (*ondernemer*) or pursuant to a co-entitlement to the net value of an enterprise, other than as an entrepreneur or a shareholder, such benefits are generally subject to Dutch income tax at progressive rates.

#### *Dutch Individuals Deriving Benefits from Miscellaneous Activities*

If you are a Dutch Individual and if you derive or are deemed to derive any benefits from Shares, including any gain realized on the disposal thereof, that constitute benefits from miscellaneous activities (*resultaat uit overige werkzaamheden*), such benefits are generally subject to Dutch income tax at progressive rates.

If you are a Dutch Individual you may, *inter alia*, derive benefits from Shares that are taxable as benefits from miscellaneous activities in the following circumstances:

- your investment activities go beyond the activities of an active portfolio investor, for instance in the case of the use of insider knowledge (*voorkennis*) or comparable forms of special knowledge; or
- you make Shares available or you are deemed to make Shares available, legally or in fact, directly or indirectly, to a related party as described in Articles 3.91 and 3.92 of the Dutch Income Tax Act 2001 under circumstances described there.

#### *Other Dutch Individuals*

If you are a Dutch Individual and your situation has not been discussed before in this section “Dutch Taxation – Taxes on Income and Capital Gains – Resident Holders of Shares”, benefits from your Shares will be taxed as a benefit from savings and investments (*voordeel uit sparen en beleggen*). Such benefit is deemed to be 4% per annum of the average of your “yield basis” (*rendementsgrondslag*) at the beginning and at the end of the year, insofar as that average exceeds the “exempt net asset amount” (*heffingvrij vermogen*). The benefit is taxed at the rate of 30%. The value of your Shares forms part of your yield basis. Actual benefits derived from your Shares, including any capital gains realized on the disposal thereof, are not as such subject to Dutch income tax.

### *Dutch Corporate Entities*

If you are a Dutch Corporate Entity, any benefits derived or deemed to be derived by you from Shares, including any capital gains realized on the disposal thereof, are generally subject to Dutch corporation tax, except to the extent that the benefits are exempt under the participation exemption as laid down in the Dutch Corporation Tax Act 1969.

### *Non-Resident Holders of Shares*

The summary set out in this section “Dutch Taxation – Taxes on Income and Capital Gains – Non-Resident Holders of Shares” only applies to a holder of Shares who is a “Non-Resident Holder” of Shares.

For the purposes of this section, you are a Non-Resident Holder of Shares if you satisfy the tests that (A) you are neither resident, nor deemed to be resident, in the Netherlands for purposes of Dutch income tax or corporation tax, as the case may be, and, if you are an individual, you have not elected to be treated as a resident of the Netherlands for Dutch income tax purposes; (B) your Shares and income or capital gains derived therefrom have no connection with your past, present or future employment, if any; (C) your Shares do not form part of a substantial interest or a deemed substantial interest in us within the meaning of Chapter 4 of the Dutch Income Tax Act 2001, unless such interest forms part of the assets of an enterprise; and (D) if you are not an individual, no part of the benefits derived from your Shares is exempt from Dutch corporation tax under the participation exemption as laid down in the Dutch Corporation Tax Act 1969.

See “Dutch Taxation – Taxes on Income and Capital Gains – Resident Holders of Shares” for a description of the circumstances under which Shares form part of a substantial interest or a deemed substantial interest in us.

If you are a holder of Shares and you satisfy test (A), but do not satisfy test (B) and/or test (C), your Dutch income tax position or corporation tax position, as the case may be, is not discussed in this Prospectus.

If you are a Non-Resident Holder of Shares you will not be subject to any Dutch taxes on income or capital gains (other than the dividend withholding tax described below) in respect of benefits from Shares, including any capital gains realized on the disposal thereof, except in the following circumstances:

- if you derive profits from an enterprise, whether as an entrepreneur (ondernemer) or pursuant to a co-entitlement to the net value of such enterprise, other than (i) as a shareholder, if you are an individual, or (ii) as a holder of securities, if you are not an individual, which enterprise is either managed in the Netherlands or carried on, in whole or in part, through a permanent establishment or a permanent representative in the Netherlands provided that your Shares are not attributable to such enterprise;
- if you are an individual, provided that you do not derive benefits from Shares that are taxable as benefits from miscellaneous activities in the Netherlands.

See the section “Dutch Taxation – Taxes on Income and Capital Gains – Resident Holders of Shares” for a description of the circumstances under which the benefits derived from Shares may be taxable as benefits from miscellaneous activities, on the understanding that such benefits will be taxable in the Netherlands only if such activities are performed or deemed to be performed in the Netherlands.

## **Dutch Taxation - Dividend Withholding Tax**

### *General*

We are generally required to withhold Dutch dividend tax at the rate of 25% from dividends distributed by us.

The concept “dividends distributed by us” as used in this section “Dutch Taxation – Dividend Withholding Tax” includes, but is not limited to, the following:

- distributions in cash or in kind, deemed and constructive distributions and repayments of capital not recognized as paid-in for Dutch dividend withholding tax purposes;

- liquidation proceeds and proceeds of redemption of Shares in excess of the average capital recognized as paid-in for Dutch dividend withholding tax purposes;
- the par value of Shares issued by us to a shareholder or an increase of the par value of Shares, as the case may be, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- partial repayment of capital, recognized as paid-in for Dutch dividend withholding tax purposes, if and to the extent that there are net profits (zuivere winst), unless: (i) the general meeting of our shareholders has resolved in advance to make such repayment; and (ii) the par value of the Shares concerned has been reduced by an equal amount by way of an amendment to our articles of association.

### ***Dutch Individuals and Dutch Corporate Entities***

Dutch Individuals and Dutch Corporate Entities generally can credit Dutch dividend withholding tax against their Dutch income tax or Dutch corporation tax liability, as the case may be, and generally are entitled to a refund of Dutch dividend withholding tax insofar as such tax, together with any other creditable domestic and/or foreign taxes, exceeds their aggregate Dutch income tax or Dutch corporation tax liability. Pursuant to domestic rules to avoid dividend stripping, Dutch dividend withholding tax will only be creditable by or refundable to the beneficial owner (*uiteindelijk gerechtigde*) of dividends distributed by us. A holder of Shares who receives proceeds therefrom shall not be recognized as the beneficial owner of such proceeds if, in connection with the receipt of the proceeds, it has given a consideration, in the framework of a composite transaction including, without limitation, the mere acquisition of one or more dividend coupons or the creation of short-term rights of enjoyment of Shares (*kortlopende genotsrechten op aandelen*), whereas it may be presumed that (i) such proceeds in whole or in part, directly or indirectly, inure to a person who would not have been entitled to an exemption from, or who would have been entitled to a smaller reduction or refund of, or credit for, dividend withholding tax than the actual recipient of the proceeds; and (ii) such person acquires or retains, directly or indirectly, an interest in Shares or similar instruments, comparable to its interest in Shares prior to the time the composite transaction was first initiated.

See the section “Dutch Taxation – Dividend Withholding Tax – General” for a description of the concept “dividends distributed by us”.

See the section “Dutch Taxation – Taxes on Income and Capital Gains – Resident Holders of Shares” for a description of the terms Dutch Individual and Dutch Corporate Entity.

### ***Non-Resident Holders of Shares***

If a Non-Resident Holder of Shares is resident in the Netherlands Antilles or Aruba or in a country that has concluded a double tax treaty with the Netherlands, such holder may be eligible for a full or partial relief from the dividend withholding tax, provided such relief is timely and duly claimed. In addition, a qualifying parent company within the meaning of the EU Parent Subsidiary Directive (Directive 90/435/EEC, as amended) is, subject to certain conditions, entitled to an exemption from dividend withholding tax. Pursuant to domestic rules to avoid dividend stripping, dividend withholding tax relief will only be available to the beneficial owner of dividends distributed by us. The Dutch tax authorities have taken the position that this beneficial ownership test can also be applied to deny relief from dividend withholding tax under double tax treaties, the Tax Arrangement for the Kingdom (*Belastingregeling voor het Koninkrijk*) and the EU Parent Subsidiary Directive.

See the section “Dutch Taxation – Dividend Withholding Tax – Dutch Individuals and Dutch Corporate Entities” for a description of the term beneficial owner.

See the section “Dutch Taxation – Taxes on Income and Capital Gains – Non-Resident Holders of Shares” for a description of the term Non-Resident Holder of Shares.

### ***United States Holders of Shares***

Under the convention of 18 December, 1992, between the Kingdom of the Netherlands and the United States of America for the Avoidance of Double Taxation and the Prevention of Fiscal Evasion with respect to Taxes on Income (the “US/NL Income Tax Treaty”), the Dutch dividend withholding tax rate on dividends distributed by us to a Non-Resident holder of Shares who is resident in the United States and who is entitled to the benefits of the US/NL Income Tax Treaty will generally be reduced to 15%. The US/NL Income Tax Treaty provides for an exemption for dividends received by exempt pension trusts and exempt organizations, as defined therein. Except in the case of exempt organizations, the reduced dividend withholding tax rate under the US/NL Income Tax Treaty may be available at source, upon payment of a dividend in respect of such Shares, provided that the holder thereof or, if applicable, the paying agent, has supplied us with the appropriate Dutch tax forms in accordance with the Dutch implementation regulations under the US/NL Income Tax Treaty. If such forms are not duly and timely supplied, we generally will be required to withhold the dividend withholding tax at the Dutch statutory rate of 25%. In such case, a Non-Resident holder of Shares, who is resident in the United States and who is entitled to the benefits of the US/NL Income Tax Treaty may obtain a refund of the difference between the amount withheld and the amount that the Netherlands was entitled to levy in accordance with the US/NL Income Tax Treaty by filing the appropriate forms with the Dutch tax authorities within the term set therefore.

### **Dutch Taxation - Gift and Inheritance Taxes**

If you acquire Shares as a gift (in form or in substance) or if you acquire or are deemed to acquire Shares on the death of an individual, you will not be subject to Dutch gift tax or to Dutch inheritance tax (as the case may be), unless:

- the donor is, or the deceased was, resident or deemed to be resident in the Netherlands for purposes of gift or inheritance tax (as the case may be); or
- the Shares are or were attributable to an enterprise or part of an enterprise that the donor or deceased carried on through a permanent establishment or a permanent representative in the Netherlands at the time of the gift or of the death of the deceased; or
- the donor made a gift of Shares, then became a resident or deemed resident of the Netherlands, and died as a resident or deemed resident of the Netherlands within 180 days after the date of the gift.

### **Dutch Taxation - Other Taxes and Duties**

No Dutch registration tax, transfer tax, stamp duty or any other similar documentary tax or duty will be payable in the Netherlands in respect of or in connection with the subscription, issue, placement, allotment or delivery of the Shares.

### **Taxation in the United States**

United States Internal Revenue Service Circular 230 Notice: To ensure compliance with Internal Revenue Service Circular 230, prospective investors are hereby notified that: (a) any discussion of U.S. federal tax issues contained or referred to in this Prospectus or any document referred to herein is not intended or written to be used, and cannot be used by prospective investors for the purpose of avoiding penalties that may be imposed on them under the United States Internal Revenue Code; (b) such discussion is written for use in connection with the promotion or marketing of the transactions or matters addressed herein; and (c) prospective investors should seek advice based on their particular circumstances from an independent tax advisor.

The following summary describes the material United States federal income tax consequences of the purchase, ownership and disposition of our Shares as of the date of this prospectus.

Except where otherwise stated, this summary deals only with Shares held as a capital asset by a holder who is a United States holder (as defined below), purchases the Shares in the Offer, and does not own (directly or by attribution) 10% or more of the voting power of all our outstanding Shares).

A “United States holder” is a beneficial owner of our Shares that is, for United States Federal income tax purposes:

- a citizen or resident of the United States;
- a corporation or other entity treated as a corporation for US federal income tax purposes created or organized in or under the laws of the United States or any states within the United States or the District of Columbia;
- an estate the income of which is subject to United States federal income taxation regardless of its source; or
- a trust if it is subject to the primary supervision of a court within the United States and one or more United States persons have the authority to control all substantial decisions of the trust, or has a valid election in effect under applicable United States Treasury regulations to be treated as a United States person.

If a partnership (or other entity treated as a partnership for U.S. federal income tax purposes) holds Shares, the tax treatment of a partner will generally depend upon the status of the partner and the activities of the partnership. If you are a partner of a partnership that acquires the Shares, you should consult your tax advisor.

United States taxation is often dependent on the taxpayer’s particular situation, and each United States holder is encouraged to consult his or her own tax advisor. This summary does not address all the tax consequences that may be relevant to holders that are subject to special tax treatment, such as:

- dealers in securities or currencies;
- financial institutions;
- tax-exempt investors;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons liable for alternative minimum tax;
- insurance companies;
- real estate investment trusts;
- regulated investment companies;
- persons holding Shares as part of a hedging, conversion, integrated or constructive sale transaction;
- persons holding ordinary shares as part of a straddle; or
- United States holders whose functional currency is not the United States dollar.

This summary is based on the Internal Revenue Code of 1986, as amended (the “Internal Revenue Code”), the Treasury Regulations promulgated under the Internal Revenue Code and administrative and judicial interpretations. These income tax laws, regulations and interpretations, however, may change at any time, possibly with retroactive effect. This summary is also based upon our determination that we are not a passive foreign investment company (“PFIC”). The determination that we are not a PFIC is based upon the best judgment of management as to the fair market value of our assets, including our intangibles. We have not sought or obtained an independent appraisal of our assets and business. No assurance can be offered that our conclusions as to the values of our assets will not be challenged by the United States Internal Revenue Service (“IRS”) or that a court might not ultimately sustain such a challenge. We have neither sought nor obtained any advance ruling from the IRS regarding the United States federal income tax consequences of any of the transactions described in this prospectus.



This summary does not address state, local, foreign or other tax laws. This summary is not intended to be, nor should it be construed to be, legal, business or tax advice to any particular shareholder. Accordingly, United States holders should consult their own tax advisors with respect to the United States federal, state, and local tax consequences and the foreign tax consequences to them of the ownership of Shares.

### ***Disposition of Shares***

In general, subject to the “Passive Foreign Investment Company Consideration” below and unless an exception set forth in the Internal Revenue Code applies, a sale or exchange of our Shares will give rise to taxable capital gain or loss equal to the amount by which the adjusted tax basis of the Shares sold or exchanged is less or more than the amount realized by the United States holder on the disposition. Capital gains of non-corporate taxpayers on dispositions of Shares held for more than one year generally will be subject to tax at a maximum rate of 15% if such gain is recognized prior to 1 January 2011. Any gain or loss on Shares held by a United States holder for less than one year will be treated as short-term capital gain or loss, with gain generally taxed at ordinary income rates. The tax basis of the Shares will be the amount of cash paid to acquire them.

### ***Dividends on Shares***

Dividends from a “qualified foreign corporation” are currently taxable in the United States at the maximum rate of 15% for non-corporate taxpayers if certain conditions are satisfied (including certain holding period requirements and that the corporation not be a PFIC). That rate is scheduled to expire at the end of 2010, after which dividends will be taxed at the same rate as ordinary income. We believe that we are a qualified foreign corporation; however, we have not sought or received an opinion of counsel or a ruling from the IRS to that effect. No assurance can be given that a court would not ultimately determine that we are not a qualified foreign corporation. If we were not a qualified foreign corporation, our dividends would be taxable as ordinary income at rates up to 35%.

Subject to the “Passive Foreign Investment Company Considerations” below, for United States federal income tax purposes, distributions paid by us will be taxable as dividends to the extent of our current and accumulated earnings and profits. Such dividends generally will be foreign source income. Any further distributions are first treated as tax-free return of basis and then as capital gain. If the dividend has been subject to withholding taxes in the country of origin, the United States holder may be able to claim a credit for such taxes or may be able to claim a deduction in lieu of such credit. Special rules apply in determining the foreign tax credit limitation with respect to dividends that are subject to the maximum 15% tax rate. The United States holder will be required to include in income its amount of foreign taxes withheld. The dividend will not be eligible for the dividends received deduction generally allowed to U.S. corporations in respect of dividends received from other U.S. corporations. United States holders should consult their own tax advisors with respect to the appropriate U.S. federal income tax treatment of any distribution received from us.

### ***Passive Foreign Investment Company Considerations***

A corporation organized outside the United States generally will be classified as a “passive foreign investment company” or a PFIC, for United States federal income tax purposes in any taxable year in which, after applying certain look-through rules, either: (i) at least 75% of its gross income is “passive income,” or (ii) on average, at least 50% of the gross value of its assets is attributable to assets that produce “passive income” or are held for the production of passive income. Passive income for this purpose generally includes dividends, interest, royalties, rents, annuities, the excess of gains over losses from commodities and securities transactions, and the excess of gains over losses from the disposition of assets which produce passive income. For purposes of applying the foregoing tests, the assets and gross income of a company’s significant direct, and indirect, subsidiaries are attributed to the company. We do not believe that we are now, nor do we expect to become, a PFIC, but this conclusion is a factual determination that generally cannot be determined until the close of the taxable year in question and is made annually (based in part upon the value of our assets and ordinary shares) and thus may be subject to change. If we were to be a PFIC in any year, materially adverse consequences as described below could result for United States holders. United States holders are urged to consult their own tax

advisers regarding the possibility of us being classified as a PFIC and the potential tax consequences arising from the ownership and disposition of an interest in a PFIC.

If we were a PFIC in any year during which a United States holder owned Shares and the United States holder did not make, or have in effect, one of the elections described below, the United States holder would generally be subject to special rules (regardless of whether we continued to be a PFIC) with respect to (i) any “excess distribution” (generally, distributions received by the United States holder in a taxable year in excess of 125% of the average annual distributions received by that United States holder in the three preceding taxable years, or, if shorter, the United States holder’s holding period), and (ii) any gain realized on the sale, retirement or other disposition of Shares. Under these rules, (a) the excess distribution or gain would be allocated ratably over the United States holder’s holding period, (b) the amount allocated to the current taxable year and any taxable year prior to the first taxable year in which we were a PFIC would be taxed as ordinary income, and (c) the amount allocated to each of the prior taxable years would be subject to United States federal income tax at the highest rate of tax in effect for the taxpayer for that year plus an interest charge on the amount of tax deemed to be deferred.

Certain elections enable the Shareholder in a PFIC to avoid these consequences. A United States holder makes a Qualified Electing Fund (“QEF”) election for a taxable year by properly filing and completing a Form 8621 with its tax return for such year. The effect of such election is that the United States holder generally will be currently taxable on its pro rata share of a company’s ordinary earnings and net capital gains (at ordinary income and capital gains rates, respectively) for each taxable year of such company in which it is classified as a PFIC, even if no dividend distributions are received by such United States holder, unless such United States holder makes an election to defer such taxes.

A QEF election may only be made by a United States holders of Shares if we provide such holders with certain information that allows such holders to report and pay any current or deferred taxes due with respect to their pro rata shares of our net ordinary earnings and net capital gains for such taxable year. If we determine that we are a PFIC for a taxable year, we may or may not provide such information. United States holders should consult their tax advisors concerning the merits and mechanics of making a QEF election and other relevant tax considerations if we are a PFIC for any taxable year.

If a United States holder does not make a QEF election for the first year that a company is a PFIC, the United States holder may later elect QEF status, as described above, and if it does so, may also elect to “purge” such company’s PFIC taint. A United States taxpayer’s “purge election” must be made as to its PFIC shares held as of the qualification date (see below) by also attaching a Form 8621 to the tax return for the United States holder’s taxable year that includes the qualification date. The qualification date is the first day of the United States holder’s taxable year for which it elects to treat the PFIC as a QEF. The election may cause the United States holder to recognize taxable gain as if the ordinary shares had been sold.

If we were a PFIC, a United States holder who does not make a QEF election may be able to avoid taxation and interest charges under the PFIC regime by making a mark-to-market election with respect to their Shares, provided that the Shares are regularly traded on a qualifying securities exchange within the meaning of the applicable Treasury Regulations. The mark-to-market election requires a United States holder to include as ordinary income each taxable year an amount equal to the excess, if any, of the fair market value of the ordinary shares at the close of the tax year over the shareholder’s adjusted basis in the ordinary shares. Similarly, an electing United States holder may deduct the excess, if any, of the United States holder’s adjusted basis in the ordinary shares over their fair market value at the close of each tax year. However, the United States holder’s deduction is limited to the net mark-to-market gains (reduced by any prior deductions) that the United States holder has included in income from the ordinary shares in previous tax years. United States holders should consult their tax advisers regarding the availability and consequences of a mark-to-market election.

### ***Information Reporting and Backup Withholding***

For a non-corporate United States holder, information reporting requirements, on IRS Form 1099, generally will apply to:

- payments of dividends or other taxable distributions made within the United States; and
- the payment of proceeds from the sale of Shares effected at a United States office of a broker.

Additionally, backup withholding may apply to these payments if the non-corporate United States holder fails to provide an accurate taxpayer identification number or certification of exempt status or fails to report all interest and dividends required to be shown on its U.S. federal income tax returns.

Payment of the proceeds from the sale of Shares effected at a foreign office of a broker generally will not be subject to information reporting or backup withholding. However, a sale of Shares that is effected at a foreign office of a broker will be subject to information reporting and backup withholding if:

- the proceeds are transferred to an account maintained by the holder in the United States;
- the payment of proceeds or the confirmation of the sale is mailed to the holder at a United States address; or
- the sale has some other specified connection with the United States as provided in Treasury Regulations;

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or the holder otherwise establishes an exemption.

In addition, a sale of Shares effected at a foreign office of a broker will be subject to information reporting if the broker is:

- a United States person;
- a controlled foreign corporation for United States tax purposes;
- a foreign person 50% or more of whose gross income is effectively connected with the conduct of a United States trade or business for a specified three-year period; or
- a foreign partnership, if at any time during its tax year, one or more of its partners are “U.S. persons”, as defined in Treasury Regulations, who in the aggregate hold more than 50% of the income or capital interest in the partnership; or such foreign partnership is engaged in the conduct of a United States trade or business;

unless the broker does not have actual knowledge or reason to know that the holder is a United States person and the documentation requirements described above are met or the holder otherwise establishes an exemption. Backup withholding will apply if the sale is subject to information reporting and the broker has actual knowledge or reason to know that the holder is a United States person.

The backup withholding tax is imposed at a rate of 28%. Backup withholding is not an additional tax and will be credited against the United States holder’s United States federal income tax liability or refunded to the United States holder, provided that the required information is furnished to the IRS.

**The above summary of United States federal income tax consequences is for general information only and is not intended to constitute a complete analysis of all United States income tax consequences relating to United States holders of their acquisition, ownership and disposition of the Shares. All prospective purchasers should consult their tax advisers as to the particular tax consequences to them of owning the Shares, including the applicability and effect of state, local, foreign and other tax laws and possible changes in tax law.**

## THE OFFER

### Introduction

The Offer consists of an offering of up to €25 million in New Shares by us. We intend to apply for the admission of our Shares to listing and trading on Euronext Amsterdam.

The Offer consists of a public offering in the Netherlands and an international offering to institutional investors in certain other jurisdictions. Preferential treatment will be given to our employees if they subscribe for New Shares pursuant to the Offer. There is no fixed percentage of the Offer reserved for such preferential treatment (see under “Allotment”).

The New Shares will be issued on the Settlement Date.

The rights of holders of Shares will rank *pari passu* with each other.

We have granted to the Underwriters an option, exercisable within 30 calendar days after the Allotment Date, pursuant to which the Underwriters may require us to issue additional New Shares at the Offer Price for an amount up to 15% of the amount of the Offer. For more information on the Overallotment Option, see “Underwriting – Overallotment Option”.

Prior to the Offer, there has been no public market for our Shares.

### Timetable

The timetable below lists certain expected key dates for the Offer.

Event	Time and Date
Beginning of subscription period in the Netherlands . . . . .	09:00 (Amsterdam time) 18 September 2006
End of subscription period in the Netherlands . . . . .	16:00 (Amsterdam time) 3 October 2006
Expected allotment of New Shares . . . . .	4 October 2006
Listing Date . . . . .	4 October 2006
Settlement Date . . . . .	9 October 2006

The timetable for the Offer is subject to acceleration or extension.

Any acceleration or extension of the timetable for the Offer will be announced in a press release (together with any related revision of the expected dates of pricing, allocation and closing), in the event of an accelerated timetable for the Offer, at least three hours before the proposed expiration of the accelerated timetable for the Offer or, in the event of an extended timetable for the Offer, at least three hours before the expiration of the original timetable for the Offer. Any extension of the timetable for the Offer will be for a minimum of one full trading day.

### Offer Price and Change of Price Range

Prior to the Offer there has been no public market for any of our Shares. The Offer Price will be determined by negotiations between us and the Underwriters. In addition to prevailing market conditions and a qualitative assessment of demand for the New Shares, the factors to be considered in these negotiations will include:

- the history of, and prospects for, our company and the industry in which we operate and compete;
- our past and present financial condition;
- an assessment of our management, our past and present operations and the prospects for, and timing of, our future revenues;
- the present state of our development; and

- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

We reserve the right to change the Price Range prior to the Allotment Date. Any change in the Price Range on the day prior to the Allotment Date will result in an extension of the timetable for the Offer by at least one full trading day. Any change in the Price Range will be announced in a press release prior to the Allotment Date.

The Offer Price will be published in a pricing statement on or about 4 October 2006 which will be deposited with the AFM and be published in the Daily Official List and in a national newspaper distributed daily in the Netherlands. The pricing statement will also be placed on our website at [www.octoplus.nl](http://www.octoplus.nl) and you should access this information as soon as it is available.

### **Offer Size and Number of Shares**

The Offer consists of an offering of up to €25 million in New Shares. The actual number of Shares offered in the Offer will depend on the Offer Price and the amount we raise pursuant to the Offer and will be determined after taking into account market conditions, and criteria and conditions such as those listed below:

- demand for the New Shares; and
- general economic and market conditions, including those in the debt and equity markets.

We reserve the right to raise less than €25 million pursuant to the Offer.

The Offer Price, the Offer proceeds and the actual number of New Shares offered in the Offer will be published in a pricing statement on or about 4 October 2006 which will be deposited with the AFM and be published in the Daily Official List and in a national newspaper distributed daily in the Netherlands. The pricing statement will also be placed on our website at [www.octoplus.nl](http://www.octoplus.nl) and you should access this information as soon as it is available.

### **Subscription**

The subscription period for prospective investors is expected to begin on 18 September 2006 at 09:00 Amsterdam time and end on 3 October 2006 at 16:00 Amsterdam time.

Subscriptions can be submitted at the branches of the Underwriters, as described in more detail below, at no cost to the investor. Subscriptions are not binding upon us if they are not accepted, as discussed in more detail under “Allotment” below. Investors wishing to subscribe through intermediaries other than the Underwriters should request details of the costs which these intermediaries may charge and which they will have to pay themselves.

Only one application form per investor will be accepted. If Cowen or Fortis determines, or has reason to believe, that a single investor has submitted several orders, through one or more institutions, it may disregard such orders.

Investors are invited to introduce their orders as soon as possible with the Underwriters. Except in the event where an amendment to this Prospectus were to be published prior to the closing of the Offer, subscriptions cannot be withdrawn.

### **Retail Investors**

Retail investors must indicate in their orders the number of New Shares they commit to subscribe to. Retail investors can only subscribe for the New Shares at the Offer Price, see “The Offer – Offer Price and Change of Price Range”. Retail investors can submit their subscriptions to Fortis through their own admitted institution.

## **Institutional Investors**

Institutional investors must indicate in their orders the number of New Shares they commit to subscribe for, and the price (within the Price Range) at which they are making such orders. Institutional investors can submit their subscriptions to the Underwriters.

## **Allotment**

The allotment is expected to take place on the Allotment Date, which is expected to be on or about 4 October 2006, and which will be before the start of trading on Euronext Amsterdam on the Listing Date, which is expected to be on or about 4 October 2006, subject to acceleration or extension of the timetable for the Offer. There will be a preferential allotment to our employees. Employees who subscribe for New Shares will receive the number a New Shares subscribed for. Other investors may receive a smaller number of New Shares than subscribed for, or non at all. The Underwriters may, at their own discretion and without stating the grounds, reject any subscriptions of investors wholly or partly. In the event that the New Shares are oversubscribed, preferential treatment may be given to orders submitted by investors at the branches of the Underwriters rather than through other financial intermediaries.

We expect to announce the Offer Price, the Offer proceeds and the numbers of New Shares allocated to investors under the Offer on or about 4 October 2006. Concurrently with such announcement, we will publish a pricing statement which will state the Offer Price and the aggregate number of New Shares to be issued by us in the Daily Official List and in a national newspaper distributed daily in the Netherlands. The pricing statement will also be placed on our website at [www.octoplus.nl](http://www.octoplus.nl) and you should access this information as soon as it is available.

Investors will be informed by their intermediaries of the number of New Shares allotted to them shortly after the Allotment Date.

## **Joint Global Coordinators and Joint Bookrunners**

Cowen and Fortis are acting as Joint Global Coordinators and Joint Bookrunners in connection with the Offer.

## **Listing Agent and Paying Agent**

Fortis Bank (Nederland) N.V. is the Listing Agent and Paying Agent with respect to the listing and trading of our Shares on Euronext Amsterdam. The address of the Listing and Paying Agent is:

Fortis Bank (Nederland) N.V.  
Rokin 55  
1012 KK Amsterdam  
The Netherlands

## **Payment, Delivery, Clearing and Settlement**

Payment for the New Shares, and payment for any New Shares subject to the Overallotment Option provided this option has been exercised prior to the Settlement Date, will take place on the Settlement Date.

The Shares will be ordinary shares in registered form (*aandelen op naam*) which are entered into the collection deposit (*verzameldepot*) and/or giro deposit (*girodepot*) on the basis of the Securities Giro Act (*Wet Giraal Effectenverkeer*). Application has been made for the Shares to be accepted for clearance through the book-entry facilities of Euroclear Netherlands.

Delivery of the New Shares is expected to take place on or about 9 October 2006 (the Settlement Date) through the book-entry facilities of Euroclear Netherlands only, in accordance with its normal settlement procedures applicable to equity securities and against payment for the New Shares in immediately available funds.

There are certain restrictions on the transfer of our registered book-entry shares, as detailed in “Selling Restrictions” and “Transfer Restrictions”.

### **Ranking and Dividends**

Should the Executive Board decide in the future to grant a dividend, the rights of holders of the Shares will rank pari passu with each other. See “Dividend Policy”.

### **Listing and Trading of our Shares**

In order to seek to increase the liquidity of our Shares and raise our investor profile, we intend to apply for the admission of our Shares to listing and trading on Euronext Amsterdam under the symbol “OCTO”.

We expect that listing and trading in our Shares on Euronext Amsterdam will commence on or about 4 October 2006 (the Listing Date) on an “as-if-and-when-issued” basis. The Settlement Date on which the closing of the Offer and delivery of the New Shares is scheduled to take place, is expected to be on or about 9 October 2006, the third trading day following the Listing Date (T+3).

Investors who wish to enter into transactions in our Shares prior to the Settlement Date, whether such transactions are effected on Euronext Amsterdam or otherwise, should be aware that the closing of the Offer may not take place on the Settlement Date or at all if certain conditions or events referred to in the Underwriting Agreement (see “Underwriting”) are not satisfied or waived or occur on or prior to such date. Such conditions include the receipt of officers’ certificates and legal opinions and such events include the suspension of trading on Euronext Amsterdam or other international market or a material adverse change in our financial condition or business affairs or in the financial markets. If closing of the Offer does not take place on the Settlement Date or at all, the Offer will be withdrawn, all subscriptions for the New Shares will be disregarded, any allotments made will be deemed not to have been made, any subscription payments made will be returned without interest or other compensation and all transactions in our Shares on Euronext Amsterdam will be cancelled. All dealings in our New Shares on Euronext Amsterdam prior to settlement and delivery are at the sole risk of the parties concerned.

Euronext does not accept any responsibility or liability for any loss or damage incurred by any person as a result of the listing and trading on an “as-if-and-when-issued” basis as from the Listing Date until the Settlement Date.



## UNDERWRITING

We and the Underwriters are expected to enter into an underwriting agreement no later than at the Pricing Date, which is expected to take place on 3 October 2006 with respect to the New Shares being offered. Subject to the terms and conditions of the underwriting agreement, each Underwriter is expected to severally agree to purchase from us the percentage of New Shares set forth opposite its name below. Cowen International Limited and Fortis Bank (Nederland) N.V. are Joint Global Coordinators and Joint Bookrunners and acting as the representatives of the Underwriters.

Underwriter	Percentage of the Offer
Cowen International Limited . . . . .	50%
Fortis Bank (Nederland) N.V. . . . . .	35%
Kempen & Co N.V. . . . . .	15%
Total . . . . .	100%

The Offer consists of an initial public offering in the Netherlands and an international offering to institutional investors in certain other jurisdictions. Cowen International Limited, Fortis Bank (Nederland) N.V. and Kempen & Co N.V., through their respective selling agents, Cowen & Company, LLC, Fortis Securities LLC and Kempen & CO USA Inc., propose to resell New Shares in the United States to QIBs in reliance on Rule 144A and may resell New Shares to certain other investors in reliance on another available exemption from the registration requirement of the Securities Act. Any offers or sales of New Shares in reliance on Rule 144A or another available exemption will be made by broker-dealers registered as such under the United States Securities and Exchange Act of 1934, as amended (the “Exchange Act”).

The underwriting agreement provides that, upon the occurrence of certain events, such as a suspension or material limitation in trading in securities generally on the New York Stock Exchange, the Nasdaq Global Market, the London Stock Exchange or Euronext Amsterdam, a material loss or interference with our business any change or development in or affecting our condition (financial or otherwise), the results of our operations, our assets, our management or our business in a material adverse way, or certain other conditions, the Underwriters have the right, collectively but not individually, not to proceed with the consummation of the Offer.

The Underwriters have agreed, severally and not jointly, to purchase all of the New Shares sold under the underwriting agreement if any of these New Shares are purchased, other than those New Shares covered by the Overallotment Option described below. If an Underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting Underwriters may be increased or the underwriting agreement may be terminated.

We have agreed that we shall indemnify and hold harmless each Underwriter, its directors, officers, managers, members, employees, representatives, agents, controlling persons and affiliates, against any loss, claim, damage, expense or liability whatsoever (or any action, investigation or proceeding in respect thereof), joint or several, to which such person may become subject under applicable securities laws or otherwise insofar as such loss, claim, damage, expense, liability, action, investigation or proceeding arises out of or is based upon, amongst others, an untrue statement or omission, or alleged untrue statement or omission, of a material fact in this Prospectus.

The Underwriters are offering the New Shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The Underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

## **Overallotment Option**

The Underwriters may require us to issue additional New Shares at the Offer Price for an amount up to 15% of the amount of the Offer, less underwriting fees and commissions. This option is exercisable for a period of 30 days after the Allotment Date. The Underwriters may exercise this option for any purpose in accordance with applicable law, including for purposes of covering Overallotments, if any, made in connection with the sale of New Shares offered hereby or in subsequent transactions. To the extent that the Underwriters exercise this option, the Underwriters will purchase additional New Shares from us in approximately the same proportion as shown in the table above.

## **Fees and Commissions**

We will pay the Underwriters a commission of 4.75% of the gross proceeds from the Offer and from the sale of additional New Shares pursuant to the Overallotment Option. In addition, we may, in our sole discretion, pay to the Underwriters an incentive fee of up to 1.25% of the gross proceeds from the Offer and from the sale of additional New Shares pursuant to the Overallotment Option.

We estimate that the total expenses of the Offer, excluding underwriting fees and commissions, will be approximately €1.5 million and are payable by us.

The Underwriters propose to offer the New Shares at the Offer Price.

## **Stabilization**

In connection with the Offer, the Underwriters, through Fortis acting as stabilization manager or its affiliates or agents, may engage in stabilizing transactions, Overallotment transactions, syndicate covering transactions, penalty bids and purchases to cover positions created by short sales.

- Stabilizing transactions consist of various bids for any purchases of Shares made by the Underwriters in the open market during the stabilization period, and are engaged in for the purpose of preventing or retarding a decline in the market price of the Shares while the Offer is in progress.
- Overallotment transactions involve sales by the Underwriters of Shares in excess of the number of Shares the Underwriters are obligated to purchase. This creates a syndicate short position which may be either a covered short position or a naked short position. In a covered short position, the number of Shares over-allotted by the Underwriters is not greater than the number of Shares that they may purchase in the Overallotment option. In a naked short position, the number of Shares involved is greater than the number of Shares in the Overallotment Option. The Underwriters may sell Shares in excess of the Overallotment Option as discussed above up to a maximum of 5% of the number of Shares initially purchased in the Offer, creating a naked short position. The Underwriters may close out any short position by exercising their Overallotment Option and/or purchasing Shares in the open market.
- Syndicate covering transactions involve purchases of Shares in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of Shares to close out the short position, the Underwriters will consider, among other things, the price of Shares available for purchase in the open market as compared with the price at which they may purchase Shares through exercise of the Overallotment Option. If the Underwriters sell more Shares than could be covered by exercise of the Overallotment Option and, therefore, have a naked short position, the position can be closed out only by buying Shares in the open market. A naked short position is more likely to be created if the Underwriters are concerned that after pricing there could be downward pressure on the price of the Shares in the open market that could adversely affect investors who purchase in the Offer.
- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the Shares originally sold by that syndicate member are purchased in stabilizing or syndicate covering transactions to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our Shares or preventing or retarding a decline in the market price of our Shares. As a result, the price of our Shares in the open market may be higher than it would otherwise be in the absence of these transactions. Neither we nor the Underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of our Shares. These transactions may be effected on the Euronext Amsterdam, in the over-the-counter market or otherwise and, if commenced, may be discontinued at any time.

### **Lock-Up Arrangements**

Pursuant to certain “lock-up” agreements, we and all of our current shareholders, optionholders and warrant holders have agreed, subject to certain exceptions listed below, not to offer, sell, assign, transfer, pledge, contract to sell, announce any intention to sell or otherwise dispose of, enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of, directly or indirectly, any Shares or securities convertible into or exchangeable or exercisable for or repayable with any Shares currently owned, without the prior written consent of Cowen, for a period of 365 days from the date of the underwriting agreement. The 365-day restricted period will be automatically extended if (i) during the last 17 days of the 365-day restricted period we issue an earnings release or material news or a material event relating to us occurs or (ii) prior to the expiration of the 365-day restricted period, we announce that we will release earnings results or become aware that material news or a material event will occur during the 16-day period beginning on the last day of the 365-day restricted period, in either of which case the restrictions described above will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

The exceptions to the lock-up provision permit us, among other things and subject to restrictions, to: (a) issue Shares or options pursuant to employee benefit plans, (b) issue Shares upon exercise of outstanding options or warrants, or (c) issue securities in connection with acquisitions or similar transactions. The exceptions permit parties to the “lock-up” agreements, among other things and subject to restrictions, to: (a) participate in tenders involving the acquisition of a majority of our Shares, (b) participate in transfers or exchanges involving Shares or securities convertible into Shares or (c) make certain gifts. In addition, the lock-up provision will not restrict broker-dealers from engaging in market making and similar activities conducted in the ordinary course of their business.

The exceptions to the lock-up provision which apply to our current shareholders, optionholders and warrant holders, permit them, among other things and subject to restrictions, to: (a) make transfers in respect of the acceptance of a general tender offer for no less than a majority of our Shares and (b) make certain transfers for no consideration, including gifts to family members in the case of an individual or distributions to equity owners or transfers to affiliates in the case of a legal entity.

### **Other Relationships**

Certain of the Underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they received, and may in the future receive, customary fees.

Fortis, one of the Underwriters, acted as placement agent in connection with a private placement of our Shares conducted in January 2005 (which had a second closing in June 2006). As part of its compensation for these services, Fortis received 204 class AP Shares, which immediately prior to completion of the Offer will convert into 20,400 Shares. In January 2005, as part of this private placement, Fagus N.V., a joint venture between the European Investment Fund and Fortis Private Equity Belgium NV, purchased 11,604 class AP Shares, which immediately prior to the Offer will convert into 1,160,400 Shares. Fortis Private Equity Belgium NV is the global private equity business of Fortis Group. Fortis Private Equity Belgium NV is an affiliate of Fortis. You should be aware that the interests of Fortis and its affiliate as shareholders of ours could lead to potential conflicts with our interests and the interests of Fortis as an Underwriter.

Fortis Bank (Nederland) N.V. is acting as Listing Agent and Paying Agent with respect to the listing and trading of our Shares on Euronext Amsterdam.

*Electronic Offer, Sale and Distribution of Shares.* A Prospectus in electronic format may be made available on restricted portions of the websites maintained by one or more of the Underwriters or selling group members, if any, participating in the Offer, and one or more of the Underwriters participating in the Offer may distribute Prospectuses electronically. The Representative may agree to allocate a number of Shares to Underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the Underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the Prospectus in electronic format, the information on these websites is not part of this Prospectus, has not been approved or endorsed by us or any Underwriter in its capacity as underwriter, and should not be relied upon by investors.

#### **No Public Offering Outside The Netherlands**

No action has been or will be taken in any jurisdiction other than the Netherlands that would permit a public offering of the New Shares, or the possession, circulation or distribution of this Prospectus or any other material relating to us or the New Shares in any jurisdiction where action for that purpose is required. Accordingly, the New Shares may not be offered or sold, directly or indirectly, and neither this Prospectus nor any other offering material or advertisements in connection with the New Shares may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Purchasers of the New Shares may be required to pay stamp taxes and other charges in accordance with the laws and practices of the country of purchase in addition to the Offer Price.

## SELLING RESTRICTIONS

### European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive (each, a “Relevant Member State”), with effect from and including the date on which the Prospectus Directive was implemented in that Relevant Member State (the “Relevant Implementation Date”) no New Shares have been offered or will be offered pursuant to the Offer to the public in that Relevant Member State prior to the publication of a prospectus in relation to the New Shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in the Relevant Member State, all in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, offers of New Shares may be made to the public in that Relevant Member State at any time:

- to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- to any legal entity which has two or more of (i) an average of at least 250 employees during the last financial year; (ii) a total balance sheet of more than €43 million; and (iii) an annual turnover of more than €50 million as shown in its last annual or consolidated accounts;
- to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the Underwriters; or
- in any other circumstances that do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive,

and each person who initially acquires any New Shares or to whom any offer is made under the Offer will, unless under bullet point three above, be deemed to have represented, acknowledged and agreed that it is a “qualified investor”, within the meaning of Article 2(1)(e) of the Prospectus Directive.

For the purpose of the expression an “offer of any New Shares to the public” in relation to any New Shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer of any New Shares to be offered so as to enable an investor to decide to purchase any New Shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State.

In the case of any New Shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, such financial intermediary will also be deemed to have represented, acknowledged and agreed that the New Shares acquired by it in the Offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to persons in circumstances which may give rise to an offer of any New Shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the Underwriters has been obtained to each such proposed offer or resale. We, the Underwriters and their affiliates, and others will rely upon the truth and accuracy of the foregoing representation, acknowledgement and agreement. Notwithstanding the above, a person who is not a qualified investor and who has notified the Underwriters of such fact in writing may, with the consent of the Underwriters, be permitted to subscribe for or purchase New Shares in the Offer.

### United Kingdom

This Prospectus is for distribution only to persons who (i) have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (as amended, the “Financial Promotion Order”), (ii) are persons falling within Article 49(2)(a) to (d) (“high net worth companies, unincorporated associations etc”) of the Financial Promotion Order, (iii) are outside the United Kingdom, or (iv) are persons to whom an invitation or inducement to engage in

investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000) in connection with the issue or sale of any New Shares may otherwise lawfully be communicated or caused to be communicated (for the purpose of this paragraph, all such persons together “relevant persons”). This document is directed only at relevant persons and must not be acted on or relied on by persons who are not relevant persons. Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

### **Italy**

The contents of this Prospectus have not been approved by the Commissione Nazionale Per La Società E La Borsa (“Consob”) nor any other authority in Italy. The offering of the New Shares is exempt from registration with the Consob pursuant to section 100, first paragraph, letter (a) of legislative decree no. 58 of 24 February 1998 .

The offer, sale or delivery of the New Shares or distribution of copies of this Prospectus in the republic of Italy may only be made (a) by an investment firm, bank or financial intermediary permitted to conduct such activities in the republic of Italy in accordance with legislative decree no. 385 of 1 September 1993 (“decree no. 385”), legislative decree no. 58 of 24 February 1998, Consob regulation no. 11971 of 14 May 1999 and any other applicable laws and regulation; (b) exclusively to professional investors as defined in section 30, second paragraph of legislative decree no. 58 of 24 February 1998 and section 31, 2nd paragraph of Consob regulation no. 11522 of 1 July 1998 and subsequent amendments; (c) in compliance with any other applicable notification requirement or limitation which may be imposed by Consob or any other Italian regulatory authority.”

### **United Arab Emirates**

This Prospectus does not constitute a public offer or a solicitation of securities within the territory of the United Arab Emirates and accordingly should not be construed as such. This Prospectus is not for circulation to the general public in the United Arab Emirates, nor will New Shares be offered to the general public in the United Arab Emirates. To the extent that this Prospectus is circulated within the territory of the United Arab Emirates, it is being done so in relation to a private placement (i.e. a limited circle of investors) only. Accordingly, the Offer and this Prospectus have not been filed with, reviewed by or approved by the United Arab Emirates Central Bank, the Emirates Securities and Commodities Authority, or any other United Arab Emirates governmental regulatory body or securities exchange. This Prospectus must not be copied or otherwise distributed by the recipient to others.

### **Kuwait**

By receiving this Prospectus, the person or entity to whom it has been issued or provided understands, acknowledges and agrees that this Prospectus has not been approved by the Kuwait Central Bank or the Kuwait Ministry of Commerce and Industry or any authorities in Kuwait, nor have we or any of our representatives received authorization or licensing from the Kuwait Central Bank or the Kuwait Ministry of Commerce and Industry or any authorities in Kuwait to market or sell the New Shares within Kuwait. Therefore, the New Shares will not be marketed or sold from within Kuwait and no services relating to an offering, including the receipt of applications or this Prospectus or both, will be rendered within Kuwait by us or any of our representatives. The New Shares are being offered for sale only to qualified institutional investors and sophisticated, high-net-worth individuals. Neither the New Shares nor the private offering have been licensed by Kuwait Central Bank, the Kuwait Ministry of Commerce and Industry or any other relevant Kuwaiti government agency. No Underwriter or any other party involved in the Offer is licensed in Kuwait.

### **Bahrain**

Any marketing of New Shares to investors in Bahrain is done by way of private placement only. It is not subject to the regulations of the Bahrain Monetary Agency that apply to public offerings of securities and the extensive disclosure requirements and other protections that these regulations contain. This Prospectus is



therefore intended only for “professional clients” or “market counterparties” as defined by the Bahrain Monetary Agency.

The New Shares offered pursuant to this Prospectus, may only be offered in minimum subscriptions of \$250,000 (or equivalent in other currencies).

The Bahrain Monetary Agency assumes no responsibility for the accuracy and completeness of the statements and information contained in this Prospectus and expressly disclaims any liability whatsoever for any loss howsoever arising from reliance upon the whole or any part of the contents of this Prospectus.

### **Qatar**

No general offering of the New Shares will be made in Qatar, and any New Shares may only be placed with a limited number of targeted investors in Qatar.

### **Lebanon**

All prospective investors in Lebanon whose investment authority is subject to legal restriction should consult their legal advisors to determine whether and to what extent the New Shares constitute legal investments under those restrictions. The New Shares are suitable only as an investment for, and are being offered only to, persons who have, directly or through qualified representatives, the ability to evaluate the merits and risks of an investment in the New Shares and the ability to assume all the risks involved in such an investment. In addition, investment in the New Shares requires the financial ability and willingness to accept the risks inherent in an investment in the New Shares, the knowledge and experience in financial and business matters to be capable of evaluating a prospective investment in the New Shares, and the financial ability to bear the risks of such an investment.

The acceptance of this Prospectus shall constitute the agreement of the recipient that: (a) it will hold this Prospectus and all related enclosures, documents and information in the strictest confidence; (b) it will not reproduce or use this Prospectus for any purpose other than in connection with a decision to purchase New Shares; (c) it will not transmit to or discuss this Prospectus with persons other than its authorized representatives and advisors who agree to hold the same subject to the provisions of this paragraph; (d) it will not utilize the contents of this Prospectus in any manner detrimental to the interests of the selling agents; and (e) it will return this Prospectus to the Underwriters or their selling agents immediately upon request.

### **Jordan**

Any marketing of New Shares to Jordanian investors is done by way of private placement only.

### **Israel**

This Prospectus may not be distributed to any individual (for the purpose of this paragraph, the “Israel Public”) in Israel or used, or considered by any member of the Israel Public as, an offer to the Israel Public to sell the New Shares, or a solicitation of an offer from any person to the Israel Public, to buy or subscribe for the New Shares. Any such offer or solicitation to the Israel Public may only be made in a prospectus published in Israel in accordance with a permit granted by the Israel Securities Authority (for the purpose of this paragraph, the “Securities Authority”) pursuant to the provisions of the Securities Law, 5728-1968, of Israel (the “Israel Securities Law”), after examination and approval of this Prospectus by the Securities Authority. This Prospectus and the New Shares hereby offered have not been submitted to, approved by or registered with the Securities Authority, nor has a permit been requested or granted, pursuant to the provisions of the Israel Securities Law.



## TRANSFER RESTRICTIONS

### Rule 144A Shares

Each purchaser of New Shares within the United States pursuant to Rule 144A, by accepting delivery of this Prospectus will be deemed to have represented, agreed and acknowledged that:

- It is (a) a qualified institutional buyer within the meaning of Rule 144A (“QIB”), (b) acquiring such New Shares for its own account or for the account of another QIB and (c) aware, and each beneficial owner of such New Shares has been advised, that the sale of such New Shares to it is being made in reliance on Rule 144A.
- It understands that such New Shares have not been and will not be registered under the Securities Act and may not be offered, sold, pledged or otherwise transferred except (a) in accordance with Rule 144A to a person that it and any person acting on its behalf reasonably believe is a QIB purchasing for its own account or for the account of another QIB, (b) in an offshore transaction in accordance with Rule 903 or Rule 904 of Regulation S or (c) pursuant to an exemption from registration under the Securities Act provided by Rule 144 thereunder (if available), in each case in accordance with any applicable securities laws of any State of the United States.
- It understands that such New Shares, if certificated, will bear a legend substantially to the following effect unless otherwise determined by us in accordance with applicable law:

THIS SHARE HAS NOT BEEN AND WILL NOT BE REGISTERED UNDER THE UNITED STATES SECURITIES ACT OF 1933 (THE “SECURITIES ACT”) OR WITH ANY SECURITIES REGULATORY AUTHORITY OR ANY STATE OR OTHER JURISDICTION OF THE UNITED STATES AND MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED EXCEPT (1) IN ACCORDANCE WITH RULE 144A UNDER THE SECURITIES ACT TO A PERSON THAT THE HOLDER AND ANY PERSON ACTING ON ITS BEHALF REASONABLY BELIEVE IS A QUALIFIED INSTITUTIONAL BUYER WITHIN THE MEANING OF RULE 144A PURCHASING FOR ITS OWN ACCOUNT OR FOR THE ACCOUNT OF ANOTHER QUALIFIED INSTITUTIONAL BUYER, (2) IN AN OFFSHORE TRANSACTION IN ACCORDANCE WITH RULE 903 OR RULE 904 OF REGULATION S UNDER THE SECURITIES ACT OR (3) PURSUANT TO AN EXEMPTION FROM REGISTRATION UNDER THE SECURITIES ACT PROVIDED BY RULE 144 THEREUNDER (IF AVAILABLE). IN EACH CASE IN ACCORDANCE WITH ANY APPLICABLE SECURITIES LAWS OF ANY STATE OF THE UNITED STATES. NO REPRESENTATION CAN BE MADE AS TO THE AVAILABILITY OF THE EXEMPTION PROVIDED BY RULE 144 UNDER THE SECURITIES ACT FOR REALES OF THIS SHARE.

- We, the Underwriters and their affiliates, and others will rely upon the truth and accuracy of the foregoing acknowledgements, representations and agreements. If it is acquiring any New Shares for the account of one or more QIBs, it represents that it has sole investment discretion with respect to each such account and that it has full power to make the foregoing acknowledgements, representations and agreements on behalf of each such account.

**You are hereby notified that sellers of the New Shares may be relying on the exemption from the provisions of Section 5 of the Securities Act provided by Rule 144A.**

### Other Shares Sold in the United States

Each purchaser of New Shares within the United States that is not a QIB and purchases the New Shares pursuant to an available exemption from the registration requirements under the Securities Act other than Rule 144A will be required to execute and deliver a letter addressed to us and the Underwriters containing certain acknowledgements, representations, warranties and covenants prior to any purchase by them of the New Shares.

Such acknowledgements, representations, warranties and covenants will include, among others, those to the effect that:

- The New Shares are being sold to them pursuant to an exemption from the registration requirements of the Securities Act.
- They are of such a status so as to be eligible to purchase the New Shares pursuant to such an exemption.
- The New Shares purchased by them will be subject to restrictions on transfer and may not be offered, sold, pledged or otherwise transferred by them except in an offshore transaction in accordance with Rule 903 or 904 of Regulation S, and that such New Shares, if certificated, will bear a legend to the foregoing effect unless otherwise determined by us in accordance with applicable law.

## GENERAL INFORMATION

### Available Information

Annually, within five months of the end of our fiscal year, unless the General Meeting of Shareholders has extended this period (which it may do for up to a maximum of six months due to special circumstances), the Executive Board is required to prepare annual accounts, accompanied by an annual report and an accountants' certificate. The annual accounts must be signed by all members of the Executive Board and the Supervisory Board. The annual accounts, annual report and accountant's certificate can be inspected by our shareholders without charge at our head office in Leiden during regular business hours from the day of notice convening the annual General Meeting of Shareholders. Our annual accounts and annual report will also be available from our website: [www.octoplus.nl](http://www.octoplus.nl).

Copies of our annual accounts for the years ended 31 December 2003, 2004 and 2005, our deed of incorporation and our Articles of Association may be obtained free of charge for the life of this Prospectus by sending a request in writing to us at our business address: Zernikedreef 12, 2333 CL Leiden, the Netherlands.

This Prospectus will be available to investors at no cost upon simple request from Fortis, Rokin 55, 1012 KK Amsterdam, the Netherlands, telephone number +31 (0)20 527 2467. Alternatively, this Prospectus is also available for Dutch residents, for informational purposes only, through our website at [www.octoplus.nl](http://www.octoplus.nl) and the website of Euronext at [www.euronext.com](http://www.euronext.com).

### Provision of Information

We have agreed that, for so long as any of the Shares are outstanding and are "restricted securities" within the meaning of Rule 144(a)(3) under the Securities Act, we will, during any period in which we are neither subject to Section 13 or 15(d) of the Exchange Act nor exempt from reporting pursuant to Rule 12g3-2(b) thereunder, provide to any holder or beneficial owner of such restricted Shares or to any prospective purchaser of such restricted Shares designated by such holder or beneficial owner, upon the request of such holder, beneficial owner or prospective purchaser, the information required to be provided by Rule 144A(d)(4) under the Securities Act.

We are not currently subject to the periodic reporting and other informational requirements of the Exchange Act.

### Share Trading Information

The Shares will be traded through the book-entry facilities of Euroclear Netherlands, only. The address of Euroclear Netherlands is: Damrak 70, 1012 LM Amsterdam.

The Shares will be traded under the following characteristics:

ISIN Code: NL0000345718

Common Code: 026668441

Amsterdam Security Code: 34571

Euronext Amsterdam Symbol: OCTO

### Corporate Resolutions

On 1 September 2006, the General Meeting of Shareholders resolved to issue such number of New Shares to the extent necessary for this Offer and to exclude the related pre-emptive rights of the existing holders of Shares in the Company, subject to the listing of the Shares on Euronext and the Deed of Amendment and Conversion becoming effective. The issue price and the conditions will be determined by the Executive Board, which will be approved by the Supervisory Board no later than on the Pricing Date.

The Executive Board is designated in our Articles of Association as the corporate body competent to issue Shares and to limit or exclude the pre-emptive rights for a period of five years after the Deed of Amendment and Conversion becoming effective. See “Description of Share Capital and Corporate Governance” – “Share Capital – Issue of Shares and – Granting of Rights to Subscribe for Shares”.

### Organizational Structure

We are a holding company of a number of directly held operating companies. Our subsidiaries and holdings are:

Name	Percentage	Jurisdiction
OctoPlus Development B.V. . . . . .	100%	The Netherlands
OctoPlus Technologies B.V. . . . . .	100%	The Netherlands
Chienna B.V. . . . . .	100%	The Netherlands
OctoPlus Sciences B.V. . . . . .	100%	The Netherlands
OctoShare B.V. <sup>(1)</sup> . . . . .	100%	The Netherlands
OctoPlus Inc. . . . . .	100%	Delaware (United States)
Zernike Investment Beheer B.V. <sup>(2)</sup> . . . . .	90%	The Netherlands

- (1) OctoShare B.V., a directly held 100% subsidiary of OctoPlus International Holding B.V., merged into the Company on 1 September 2006. Subsequently, OctoShed B.V., another 100% subsidiary of the Company changed its name into OctoShare B.V. pursuant to a deed of amendment of its articles of association.
- (2) Pursuant to voting restrictions in the articles of association of Zernike, we can only exercise 33% of the voting rights on the entire issued share capital and do therefore disclaim control of this company.

### Advisors

Loyens & Loeff N.V. acts as our Dutch counsel in connection with the Offer and this Prospectus. Our United States counsel is Hughes Hubbard & Reed LLP. The Underwriters are being represented by Houthoff Buruma N.V. with respect to matters of Dutch law and Ashurst with respect to matters of United States law.

### Independent Auditors

Our audited consolidated financial statements as of and for each of the years in the three-year period ended 31 December 2003, 2004 and 2005, appearing in this Prospectus have been audited by Deloitte Accountants B.V., independent auditors, as stated in their report thereon appearing elsewhere herein. Deloitte Accountants B.V. is a member of the Royal Netherlands Institute of Chartered Accountants (*Koninklijk Nederlands Instituut voor Registeraccountants*). Our interim condensed consolidated financial statements for the six month period ended 30 June 2005 and 30 June 2006 have not been audited, but have been reviewed by Deloitte Accountants B.V. as stated in their report appearing elsewhere herein.

### Legal Proceedings

Except as described in the section “Business – Legal Proceedings”, we are not involved, nor have been involved during the past 12 months, in any governmental, legal or arbitration proceedings which may have or have had significant effects on our financial position or profitability.

### Financial and Trading Position

Since 30 June 2006, no significant changes in our financial or trading position have occurred.

## SUMMARY OF SIGNIFICANT DIFFERENCES BETWEEN IFRS AND US GAAP

Our consolidated financial statements and our subsidiaries as of 31 December 2005, 2004 and 2003 and for the years then ended have been prepared in accordance with the International Financial Reporting Standards as adopted by the European Union (“IFRS”), which differ in certain significant respects from accounting principles generally accepted in the United States of America (“US GAAP”). We have not prepared the financial statements included in this Prospectus in accordance with US GAAP. A brief description of principal differences between our stated accounting policies in Note 2 to our consolidated financial statements and US GAAP is outlined below. These differences have not been quantified. In making an investment decision, you must rely upon your own examination of us, the terms of this Prospectus and the financial and other information contained in this Prospectus. You should consult your own advisors for an understanding of the differences between IFRS and US GAAP and how those differences could affect the financial information contained herein.

The following is a summary of certain differences between IFRS and US GAAP as of the dates of our financial statements included in this Prospectus. We are responsible for preparing the summary below. You should not take this summary to be an exhaustive list of all differences between IFRS and US GAAP. The following discussion does not purport to identify all disclosure, presentation or classification differences that would affect the manner in which transactions, events, or results are presented in our consolidated financial statements or the notes thereto. We have not prepared a complete reconciliation of our financial statements and related footnotes disclosures between IFRS and US GAAP and have not quantified such differences. Had we undertaken any such quantification or preparation or reconciliation, other potentially significant accounting and disclosure differences may have come to our attention which are not identified below. Accordingly, we can provide no assurance that the identified differences in the summary below represent all of the principal differences relating to our financial position, operations and cash flows. Furthermore, no attempt has been made to identify future differences between IFRS and US GAAP as the result of prescribed changes in accounting standards, transactions or events that may occur in the future. Regulatory bodies that promulgate IFRS and US GAAP have significant projects ongoing that could affect future comparisons such as this one. Future developments or changes in either IFRS or US GAAP may give rise to additional differences between IFRS and US GAAP, which could have a significant impact on us.

### **Business Combinations**

Under IFRS, if part of the purchase consideration is contingent on a future event, an estimate of the amount must be included as part of the cost at the date of the acquisition where it is probable that it will be paid and it can be reliably measured. Any revision to the estimate is subsequently adjusted against goodwill. Under US GAAP, contingent purchase considerations are generally excluded from the initial purchase price. The additional cost is not recognized until the contingency is resolved or the amount is determinable beyond a reasonable doubt. Any additional revision to the estimate is recognized as an adjustment to goodwill.

Under IFRS, acquired in-process research and development (R&D) is recognized as a separate intangible asset if it meets the definition of an intangible asset and its fair value can be measured reliably. Non-identifiable intangible assets are subsumed within goodwill. US GAAP similarly requires acquired in-process R&D to be valued at fair value. However, the acquired in-process R&D is expensed immediately unless it has an alternative future use.

Under IFRS, the acquiree’s contingent liabilities must be recognized separately at the acquisition date as part of allocating the cost, provided their fair values can be measured reliably. Under US GAAP, pre-acquisition contingencies are included in the allocation of the purchase price if their fair value can be determined during the allocation period. If the fair value cannot be determined, the contingent liability must be included if it is probable and reasonably estimable.

Under IFRS, liabilities for termination or reducing the activities of the acquiree are only recognized as liabilities on acquisition when the acquiree has, at the acquisition date, an existing liability for restructuring recognized. Any liabilities arising as a result of decisions made by the acquirer are dealt with as post-acquisition

costs. Under US GAAP, such liabilities related to restructuring of the acquiree are recognized as a liability in the purchase price allocation of the acquirer, if as of the acquisition date, management, having the appropriate level of authority, began assessing and formulating a plan to exit an activity of the acquiring entity. The plan must be completed in detail as soon as possible, but no more than one year after the consummation date and management must communicate the termination or relocation arrangements to the employees of the acquired company.

Prior to issuance of IFRS 3, “Business Combinations”, IFRS required that the excess of fair value of net assets acquired over the acquisition costs be recognized as negative goodwill. This negative goodwill was subsequently taken into income either (1) in the periods when future losses occurred to the extent that the negative goodwill related to expectations of future losses or (2) on a systematic basis over the remaining weighted-average useful life of the acquired assets for amounts of negative goodwill that did not exceed the fair values of acquired identifiable non-monetary assets or (3) immediately for amounts of negative goodwill that exceeded the fair values of acquired non-monetary assets. From 1 January 2003, upon adoption of IFRS 3, “Business Combinations,” negative goodwill resulting from business combinations is to be immediately recognized in income. Furthermore, according to the standards transition rules, any existing negative goodwill was to be derecognized with a corresponding adjustment to the opening balance of retained earnings. Under US GAAP, the excess of fair value of net assets over the acquisition costs is allocated on a pro-rata basis to reduce the carrying amounts of certain acquired non-financial assets, with any excess recognized as an extraordinary gain.

### **Goodwill**

Under IFRS, goodwill was amortized until 31 December 2002 on a systematic basis over its estimated useful lives, generally not to exceed twenty years, subject to impairment reviews in the event facts and circumstances indicate that the recorded value of the assets may not be recoverable. Effective 1 January 2003, goodwill is no longer amortized but, instead, is tested for impairment annually, or more frequently based upon facts and circumstances. Under IFRS, goodwill resulting from a business combination needs to be allocated to each of the acquirer’s cash-generating units, or groups of cash-generating units, that are expected to benefit from the synergies of the combination. The carrying amount of a cash-generating unit, or group of cash generating units, including goodwill allocated, is then compared with the recoverable amount, defined as the higher of fair value less cost to sell or the value in use. If the carrying amount exceeds the recoverable amount, an impairment charge is recorded to reduce the carrying amount of the cash-generating unit (group of units) to its recoverable amount. The impairment charge is recognized to first reduce the carrying amount of goodwill allocated to the cash-generating unit (group of units) under review to zero. In a second step, the carrying amount of the remaining individual assets of the cash-generating unit (group of units) are reduced on a pro rata basis, however, not below the higher of their fair values less costs to sell, their values-in-use or zero.

Under US GAAP, goodwill amortization ceased effective 1 January 2002. Subsequently, goodwill was required to be tested for impairment annually at a reporting unit level, or more frequently based upon facts and circumstances. Under US GAAP, the goodwill impairment test involves a two-step approach. In step one, the fair value and carrying amount of a reporting unit including goodwill are compared. If the fair value of the reporting unit is less than its book value, goodwill is considered to be impaired. In step two, the goodwill impairment amount is measured as the excess of its carrying amount over its implied fair value (i.e., fair value of the reporting unit minus fair value of individual identifiable assets and liabilities).

### **Impairment of Long Lived Assets**

Under IFRS, when events or changes in circumstances indicate possible impairment, the sum of expected discounted future cash flows is compared to the carrying amount of the respective assets. If the carrying amount of the asset exceeds the sum of the discounted future cash flows, an impairment loss exists and a write-down is necessary. The impairment loss is based on the recoverable amount (the higher of the asset’s value-in-use and net selling price). Subsequent reversal of an impairment loss is required if certain criteria are met.

Under US GAAP, when events or changes in circumstances indicate possible impairment, the sum of expected undiscounted future cash flows, related to the fixed asset (or group of assets) being measured, is compared to the carrying amount of the respective assets. Estimates of future cash flows to test the recoverability of a long-lived asset group should include only the future cash flows that are directly associated with and are expected to arise as a direct result of the use and eventual disposition of that asset group. If the carrying amount of the asset exceeds this value, an impairment loss exists and a write-down is necessary. The impairment charge is measured as the excess of carrying value over fair value. Fair value may be measured using quoted market prices in active markets, if available or using discounted future cash flows. Impairment losses cannot be reversed.

### **Deferred taxes**

Generally, both IFRS and US GAAP follow the liability method to account for deferred taxes. As such, deferred tax assets and liabilities need to be recorded for all temporary differences between the tax basis and the carrying amount recorded in the consolidated financial statements that reverse in future periods.

IFRS requires recognition of the effects of a change in tax laws or rates when the change is “substantially” enacted. Thus, recognition may precede actual enactment. US GAAP requires recognition of the effects of a change in tax laws or rates upon the actual enactment date.

Under IFRS, a deferred tax liability for taxable temporary differences associated with investments in subsidiaries, branches and associates is not recognized to the extent that (a) the parent, investor or venturer is able to control the timing of the reversal of the temporary difference, and (b) the temporary difference will not reverse in the foreseeable future. Under US GAAP, a deferred tax liability for such taxable temporary differences is generally recognized unless the earnings in the foreign subsidiary are considered permanently invested.

IFRS requires that deferred tax assets initially be recognized when it is probable, defined as more likely than not, that taxable profits will be available against which the deferred tax asset can be utilized. Furthermore, the carrying amount of a deferred tax asset is reduced subsequently to the extent that it is no longer probable that sufficient taxable profits will be available to utilize the deferred tax asset. Under US GAAP, a deferred tax asset is initially recognized in full but is then reduced by a valuation allowance if it is more likely than not that some portion, or all, of the deferred tax asset will not be realized.

IFRS also prohibits the recognition of deferred taxes for temporary differences relating to non taxable government grants. US GAAP requires recognition of deferred taxes for temporary differences related to non taxable government grants.

IFRS requires deferred tax assets and liabilities to be classified as non-current. Under US GAAP, however, the classification of deferred tax assets and liabilities as current and non-current is determined by the classification of the underlying asset or liability to which the temporary difference relates.

### **Pension Liabilities**

IFRS and US GAAP have similar fundamental approaches to accounting for employee benefit plans. The net obligation in respect of defined benefit pension plans and similar obligations is calculated using the projected unit credit method. Differences, however, can arise due to a number of differences in the details of the relevant standards, especially in respect of the additional minimum liability, the recognition of prior service costs and the amortization of actuarial gains and losses.

Under US GAAP, if the accumulated benefit obligation exceeds the fair value of plan assets, an additional minimum liability that is at least equal to the unfunded accumulated benefit obligation, is recorded. Also, under US GAAP, an equal amount is capitalized as an intangible asset up to the amount of any unrecognized net transition obligation plus the unrecognized prior service costs, with the remainder charged against shareholders' equity as a component of other comprehensive income. Under IFRS, there are no such requirements for the immediate recognition of an additional minimum pension liability.



Under IFRS, the vested portion of past service cost, which is the increase in the present value of the obligation due to changes in the benefit entitlement that is allocated to prior period's service, is recognized immediately in full. Under US GAAP, both the vested and the unvested portions are amortized on a straight-line basis over the average future service lives of the active participants.

Under US GAAP, actuarial gains and losses are recognized as income or expense if the net cumulative unrecognized actuarial gains and losses at the end of the previous reporting period exceeded the greater of 10% of the present value of the projected benefit obligation at that date (before deducting plan assets) or 10% of the fair value of any plan assets at that date. In accordance with IFRS actuarial gains and losses may be recognized even if they fall within the aforementioned limits.

Under IFRS, net pension assets are limited to the lower of (a) the asset resulting from applying the standard, and (b) the net total of any unrecognized actuarial losses and past service costs and the present value of any available funds from the plan or reduction in future contributions to the plan. This concept of an asset limitation does not exist under US GAAP.

### **Provisions and Contingencies**

Under IFRS, provisions for contingencies are measured at the best estimate to settle the obligation which generally involves the expected value method (discounting is required) if it is more likely than not that an outflow of resources embodying economic benefits will be required to settle the obligations. Where there is a range of possible outcomes, IFRS requires a provision for the expected value of the obligation to be made, weighting all possible outcomes by their associated probabilities.

Under US GAAP, a provision can only be discounted if the amount and the timing of payments are fixed or reliably determinable (considering the nature of provisions, this means that it can be difficult to account for a provision on a discounted basis). The Financial Accounting Standards Board ("FASB") Interpretation ("FIN") 14, "Reasonable Estimation of the Amount of a Loss" requires that if any outcome within the range is more likely, then that outcome should be accrued. If no amount within the range is a better estimate than any other, then the minimum amount should be accrued.

### **Revenue Recognition**

IFRS focuses on the transfer of significant risk and rewards and the probability that the economic benefits associated with the transaction will flow to the entity and that the revenue and costs can be measured reliably. Under US GAAP, revenue recognition is, in principle, similar to IAS. However there are four key criteria that must be present in order to recognize revenue under US GAAP. These four criteria are (a) the seller's price to the buyer is fixed or determinable, (b) collectibility of payment is reasonably assured, (c) there must be persuasive evidence that an arrangement exists and (d) delivery must have occurred or services must have been rendered.

Under IFRS, revenue for services is recognized in accordance with the percentage of completion method. Under U.S. GAAP, revenue for services is generally recognized ratably over the contractual term of the arrangement.

### **Leases**

Under IFRS, a lease is classified as a finance lease if the risks and rewards incident to ownership lie with the lessee. There are only narrative thresholds for useful life (described as major part) and present value test (described as substantially all of). Classifying a lease depends upon the substance of transaction rather than the form of the contract. Under US GAAP, if any one of the following four criteria applies to a lease agreement, then the lessee must clarify the lease as a finance (or capital) lease:

- The lease transfers ownership of the leased assets to the lessee at the end of the lease term.
- The lease contains a bargain purchase option.

- The lease term is greater than or equal to 75% of the economic useful life of the leased asset.
- The present value of the minimum lease payments is greater than or equal to 90% of the fair value of the leased asset.

Another difference between IFRS and US GAAP relates to build to suit leases. These situations arise when a party enters into a lease agreement with a lessor while the asset that is the subject of the lease is still under construction. Under IFRS capitalization occurs upon commencement of the lease. Under US GAAP, the applicable guidance may require the capitalization of the asset under construction on the books of the future lessee prior to the lease commencement date.

### **Sale and leaseback transactions**

IFRS and US GAAP generally require that any gain or loss on a sale and leaseback transaction be deferred and amortized over future periods if the resulting lease is a capital or finance lease. However, IFRS require that the deferred amount be amortized over the lease term, while US GAAP requires that the deferred amount be amortized in proportion to the amortization of the leased asset.

IFRS require immediate profit or loss recognition for a sale and leaseback transaction classified as an operating lease if the sale transaction is established at fair value because, in those situations, the sale transaction is deemed to be a normal sale transaction that would typically result in profit or loss being recognized immediately. If the sale price is less than the property's fair value, IFRS require immediate loss recognition unless the loss is compensated by future rentals at a below-market price, in which case the loss is deferred and amortized in relation to the rental payments over the period that the asset is expected to be used. If the sale price is above fair value, IFRS require that the excess over fair value be deferred and amortized over the period for which the asset is expected to be used. US GAAP generally require profit or loss deferral on a sale and leaseback transaction that is classified as an operating lease.

Under US GAAP specific strict criteria are considered if the sale and leaseback transaction involves real estate. Furthermore, under US GAAP specific rules apply for sale and leaseback transactions relating to continuing involvement and transfer of risks and rewards of ownership.

Under US GAAP, sale and leaseback transactions with continuing involvement in sold properties are accounted for as a financing. Accordingly, the seller-lessee continues to depreciate the asset as if the transaction had not occurred and the sales proceeds are recognized as a financing obligation which is amortized via the effective interest method based upon lease payments due under the "lease". When the prohibited form of continuing involvement no longer exists, the sale is recognized and the related asset and obligation are removed with any difference recognized as a gain. Gains of the seller-lessee are generally deferred and amortized over the lease term if the leaseback is classified as an operating lease, or in proportion to the amortization of leased asset if leaseback is classified as a finance (or capital) lease. Losses of the seller lessee are recognized immediately when the fair value of the asset is less than its carrying amount.

### **Stock-Based Compensation**

Prior to the issuance of IFRS 2 "Share-Based Payments" in February 2004, IFRS required disclosure of stock based compensation plans but did not require or provide guidance on the recognition and measurement of compensation expense. IFRS did not require disclosure of the fair value of the stock options granted, contrary to US GAAP.

IFRS 2, which was effective as of January 1, 2005, requires an entity to measure the goods or services received, and the corresponding increase in equity, directly, at the fair value of the goods or services received, unless that fair value cannot be estimated reliably. If the entity cannot estimate reliably the fair value of the goods or services received, the entity is required to measure their value, and the corresponding increase in equity, indirectly, by reference to the fair value of the equity instruments granted. Fair value is estimated using a valuation technique to estimate what the price of those equity instruments would have been on the measurement date. For employees and others providing similar services, the fair value of the equity instruments granted is

measured at grant date. For transactions with parties other than employees, the fair value is measured at the date the entity obtains the goods or the counterparty renders service. The Company early adopted IFRS 2 effective January 1, 2003.

Under US GAAP, prior to the effective date of FAS 123(R), the Company can elect to follow the accounting prescribed by either Accounting Principles Board Opinion 25, "Accounting for Stock Issued to Employees", (APB 25) or SFAS No 123, "Accounting for Stock-Based Compensation" (SFAS 123).

Under US GAAP, compensation is recorded for the cost of providing the warrants and options to the employee over the relevant service period. The costs can be determined based on either the intrinsic value method (APB 25) or the fair value method (SFAS 123). Under the intrinsic value method, the compensation cost is the difference between the market price of the stock at the measurement date and the price to be contributed by the employee (exercise price). Under the intrinsic method, the measurement date is the first date on which the employee knows the number of shares that such employee is entitled to receive and the exercise price. The measurement date is often the grant date; however, it may be later than the grant date in plans with variable terms that depend on events which occur after the grant date. These terms may be variable by design, may become variable due to their modification after the date of grant, or may be considered variable due to their relationship to other stock option features. In such cases, compensation is measured at the end of each reporting period until the measurement date or, in some cases, until the stock option's exercise, forfeiture, or expiry.

Under the fair value method, the cost associated with warrants and options is based on the fair value at the date of grant. Cost is estimated using an option-pricing model. If an entity chooses to follow the intrinsic value method, it must make pro-forma disclosures of net income and earnings per share as if the fair value method had been applied.

Under US GAAP, warrants and options granted to non-employees for services performed are accounted for at fair value. The fair value is measured at the earlier of the completion of the services or the date when the company receives a commitment of performance.

In December 2004, the FASB issued FASB Statement No. 123(R), Share-Based Payment (FAS 123(R)). FAS 123(R) requires companies to (i) use fair value to measure stock-based compensation awards and (ii) cease using the "intrinsic value" method of accounting, which APB 25 allowed and resulted in no expense for many awards of stock options for which the exercise price of the option equaled the price of the underlying stock at the grant date. FAS 123(R) is effective for non-public companies as of 1 November 2006.

### **Research and Development Costs**

Under IFRS, research costs should be expensed as incurred. An intangible asset arising from development (or from the development phase of an internal project) should be recognized as an intangible if, and only if, an enterprise can demonstrate all of the following:

- The technical feasibility of completing the intangible asset so that it will be available for use or sale;
- Its intention to complete the intangible asset and use or sell it;
- Its ability to use or sell the intangible asset;
- How the intangible asset will generate probable future economic benefits. Among other things, the enterprise should demonstrate the existence of a market for the output of the intangible asset or the intangible asset itself or, if it is to be used internally, the usefulness of the intangible asset;
- The availability of adequate technical, financial and other resources to complete the development and to use or sell the intangible asset; and
- Its ability to reliably measure the expenditure attributable to the intangible asset during its development.

The ability to use the intangible asset is assessed primarily on the probability of obtaining regulatory approval.

Under US GAAP, all research and development costs are expensed as incurred.

### **Other Comprehensive Income**

Generally under IFRS, items such as cumulative translation adjustments and revaluations of available-for-sale marketable securities are recorded directly in equity.

Under US GAAP, such items are recorded in Other Comprehensive Income, which must be disclosed as a separate primary statement or as a category highlighted within the primary statement of change in Shareholders' equity.

### **Disclosure Differences between IFRS and US GAAP**

In addition to the summary of certain differences between IFRS and US GAAP, which may affect consolidated income and total shareholders' equity, there are a number of significant disclosure differences.

Compared to IFRS, the financial statement disclosures required under US GAAP can be more comprehensive in many areas including taxes, retirement and other post-retirement benefits, leasing, segment information, and related party disclosures. No attempt has been made to identify all disclosure differences or future disclosure differences as the result of prescribed changes in accounting standards. In addition, this description is not intended to address all differences in presentation, including classification, disclosure and display of financial information contained therein.

## GLOSSARY OF SELECTED TERMS

**Biomarkers:** Biomarkers are anatomic, physiologic, biochemical, or molecular parameters associated with the presence and severity of specific disease states. Biomarkers are detectable and measurable by a variety of methods including physical examination, laboratory assays and medical imaging.

**Biopharmaceutical/biologic:** A biological molecule used as a drug, usually a protein.

**cGMP:** Formal standards of a manufacturing facility's cleanliness, process, quality controls and documentation set out and periodically monitored by the main medicines control agencies to which a company has to conform in order to manufacture quantities of a medicinal product for clinical-phase testing.

**Clinical trials:** Trials of a new drug, device or drug indication in humans, divided into phases that examine safety and efficacy. Subject to the scrutiny of the results from such trials, the governing body may give approval for marketing.

**Depot injection:** The injection of a substance in a formulation that tends to keep it at the site of injection, slowing release into the body.

**EMA:** The European Medicines Evaluation Agency which oversees the approval process for a new drug or device to be marketed.

**Epitope:** A unique shape or the part of an antigen molecule which contacts the antigen binding site of an antibody or T-cell receptor, carried on an antigen's surface that triggers a corresponding antibody response.

**FDA:** The United States of America's Food and Drug Administration, responsible for overseeing the approval process for a new drug or device to be marketed.

**Genotype:** The genotype is the specific genetic makeup (genome) of an individual, in the form of DNA. Together with the environmental variation that influences the individual, it codes for the phenotype of that individual.

**Hepatitis C Virus (HCV):** A contagious viral disease that causes inflammation of the liver. A chronic carrier state occurs in some individuals and may result in life-threatening liver damage, cirrhosis, and/or liver cancer. HCV is spread mainly via contaminated blood products or shared needles. There is no standard treatment or vaccine.

**hGH (Human Growth Hormone):** Growth hormone is a powerful anabolic hormone that occurs naturally in the human body. It is produced by the pituitary gland in the brain and stimulates the growth of muscle, cartilage, and bone.

**IFN:** An abbreviation for Interferon. Interferons are cytokines that can induce cells to resist viral replication. Interferon-a and interferon-b are produced by leukocytes and fibroblasts respectively as well as by other cells.

**In vitro:** Pertaining to experiments or reactions occurring in the artificial environment of a laboratory test tube. Literally meaning "in glass".

**IND/pre-IND:** Investigational New Drug (IND) is the status of an experimental drug after the FDA agrees that it can be tested in people. After completing preclinical testing, a company files an IND with the FDA to begin to test the drug in humans. The IND becomes effective if the FDA does not disapprove it within 30 days. Pre-IND is the status prior to this agreement.

**Interferon alfa:** Interferons are any of a group of glycoproteins that are produced by different cell types in response to various stimuli, such as exposure to a virus, bacterium, parasite, or other antigen, and that prevent viral replication in newly infected cells and, in some cases, modulate specific cellular functions. There are three types of Interferons. Alfa and beta Interferons are produced by white blood cells and a type of connective tissue cell called a fibroblast.

**Japanese Encephalitis:** Japanese Encephalitis is a disease that is spread to humans by infected mosquitoes in Asia. It is one of a group of mosquito-borne virus diseases that can affect the central nervous system and cause severe complications and even death.

**Otitis Media:** Middle ear infection (otitis media) is an infection of the part of the ear inside the ear drum. It causes ear pain and fever, is most common in children, and often follows a cold.

**New drug application (NDA):** An application submitted by the manufacturer of a drug to the FDA, after clinical trials have been completed, for license to market the drug for a specified indication.

**OctoDex:** Our proprietary delivery system for the controlled release of therapeutic proteins. The technology is based on cross linked dextran microspheres, prepared without organic solvents. OctoDEX based products can be used for both subcutaneous and intramuscular administration.

**Parenteral:** Delivery of a drug not through the alimentary canal, but by injection through some other route such as subcutaneous, intravenous, or intramuscular.

**Pegylated interferon:** The chemical addition of polyethylene glycol (PEG) to interferon. This acts as a slow release formulation since the long chain PEG molecules degrade slowly giving a steady release of interferon.

**Peptide:** A substance which consists of a chain of two or more amino acids. A functional peptide is commonly referred to as a protein.

**Pharmacodynamics:** The study of a drug's action in the body over time, this includes absorption, distribution, localization, transformation, and excretion (in simple terms, what the drug does in the body).

**Pharmacokinetics (PK):** The study of absorption, distribution, metabolism, and excretion of drugs (what the body does to the drug).

**Phenotype:** The observable character of a cell or an organism, the physical manifestation of the genotype.

**PLGA:** Polylactic-co-glycolic acid is an FDA approved copolymer which is used in a host of therapeutic devices, owing to its biodegradability and biocompatibility.

**PolyActive:** A biodegradable polymeric drug delivery system. It controls the release of proteins and lipophilic small molecules. Products based on PolyActive can be used for both local and systemic administration, and have applications in pharmaceuticals and medical technology.

**Prophylactic vaccine:** A vaccine for the prevention of, or protective treatment for disease. This vaccine creates an immunological barrier at the portal of entry.

**Recombinant:** A microbe, or strain, that has received chromosomal parts from different parental strains. Often used to denote the insertions of a sequence of DNA, by chemical or biological means, into the DNA of a recipient organism with the objective of producing therapeutically useful products.

**Sustained release:** A way of formulating a medicine so that it is released into the body steadily, over a long period of time, thus reducing the dosing frequency.

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**OctoPlus International Holding B.V.**

**FINANCIAL STATEMENTS**

**31 December 2005, 2004 and 2003**

**Deloitte Accountants B.V.**

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Date  
August 31, 2006

From  
J. Verloop

Reference  
HV/mv/1-2ra/  
3100101130-007  
Your reference

Subject  
Independent Auditor's Report

## Introduction

We have audited the accompanying consolidated and Company-only balance sheets of OctoPlus International Holding B.V., Leiden, as of 31 December 2003, 2004 and 2005, and the related statements of income, changes in equity and cash flows and the notes thereon (F-5 to F-51) for the years then ended. These financial statements are the responsibility of the company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

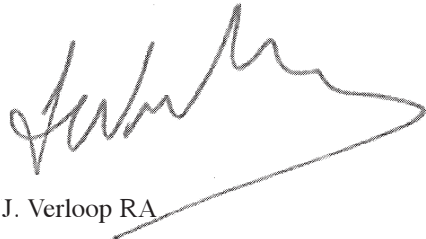
## Scope

We conducted our audit in accordance with auditing standards generally accepted in the Netherlands. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

## Opinion

In our opinion, the financial statements give a true and fair view of the financial position of the company as of 31 December 2003, 2004 and 2005 and the results of its operations and its cash flows for the years then ended in accordance with International Financial Reporting Standards, as published by the International Accounting Standards Board and adopted by the E.U.

Deloitte Accountants B.V.



J. Verloop RA

**CONSOLIDATED FINANCIAL STATEMENTS**

**31 December 2005, 2004 and 2003**

## CONSOLIDATED BALANCE SHEET

		At 31 December		
	Note	2005	2004	2003
		(in thousands)		
<b>ASSETS</b>				
<b>Non-current assets</b>				
<i>Intangible assets</i>				
Goodwill	6	€ 243	€ 243	€ 213
Patents	6	1,167	1,167	1,167
Other intangible assets	6	295	11	21
		1,705	1,421	1,401
<i>Property, plant and equipment</i>				
Land and buildings	7	3,246	3,364	–
Machines and installations	7	2,499	2,208	1,619
Other equipment	7	528	466	605
		6,273	6,038	2,224
Financial assets carried at cost	8	16	16	–
Receivables from related parties	10	–	–	908
		7,994	7,475	4,533
<b>Current assets</b>				
Inventories	9	15	15	15
Trade receivables	10	1,345	1,174	775
Receivables from related parties	10	–	3	95
Social security and other taxes	10	255	49	176
Other receivables, prepayments and accrued income	10	1,165	556	578
Cash and cash equivalents	11	9,726	82	20
		12,506	1,879	1,659
<b>Total assets</b>		20,500	9,354	6,192
<b>EQUITY</b>				
Shareholders' equity	12	7,766	(1,356)	1,151
Convertible subordinated loan	13	3,985	–	–
<b>Total group equity</b>		11,751	(1,356)	1,151
<b>LIABILITIES</b>				
<b>Non-current liabilities</b>				
Deferred corporate income tax liabilities	14	–	353	–
Pension liabilities	15	89	131	122
Borrowings	16	–	–	554
Finance lease liabilities	16	3,649	3,670	80
Debt to related parties	17	–	161	161
Other non-current liabilities	17	–	30	–
		3,738	4,345	917
<b>Current liabilities</b>				
Current portion of non-current liabilities	16	142	120	189
Bank overdrafts	16	496	1,758	777
Trade payables	17	1,491	1,079	909
Debt to related parties	17	–	–	150
Social security and other taxes	17	239	221	99
Other current liabilities	17	2,643	3,187	2,000
		5,011	6,365	4,124
<b>Total liabilities</b>		8,749	10,710	5,041
<b>Total equity and liabilities</b>		€20,500	€ 9,354	€ 6,192

The notes on pages F-9 to F-46 are an integral part of these consolidated financial statements.

## CONSOLIDATED INCOME STATEMENT

	Note	Year ending at 31 December		
		2005	2004	2003
		(in thousands)		
Service revenues . . . . .		€ 6,563	€ 4,924	€ 5,043
Royalty and license revenues . . . . .		60	60	–
Income from subsidiaries . . . . .	18	394	708	818
Other income . . . . .	18	–	26	–
<b>Total revenues</b> . . . . .		<b>€ 7,017</b>	<b>€ 5,718</b>	<b>€ 5,861</b>
Raw materials and auxiliaries . . . . .	19	€ 237	€ 70	€ 36
Cost of contracted work and other external charges . . . . .	19	1,390	307	639
Employee benefits . . . . .	20	4,758	3,597	3,450
Depreciation and amortisation . . . . .	6,7	863	860	668
Other costs . . . . .	21	4,213	2,667	3,275
<b>Total operating costs</b> . . . . .		<b>€11,461</b>	<b>€ 7,501</b>	<b>€ 8,068</b>
<b>Operating loss</b> . . . . .		(4,444)	(1,783)	(2,207)
Interest income . . . . .	23	287	18	77
Interest costs . . . . .	23	(405)	(412)	(106)
<b>Result before corporate income taxes</b> . . . . .		<b>(4,562)</b>	<b>(2,177)</b>	<b>(2,236)</b>
Corporate income taxes . . . . .	24	353	(353)	–
<b>Result for the year</b> . . . . .		<b>(4,209)</b>	<b>(2,530)</b>	<b>(2,236)</b>
<b>Attributable to:</b>				
Equity holders of the Company . . . . .		<b>€(4,209)</b>	<b>€(2,530)</b>	<b>€(2,236)</b>
<b>Result per share for result attributable to the equity holders of the Company during the year</b> (expressed in Euro per share)				
– basic . . . . .	25	(37.59)	(53.91)	(47.64)
– diluted . . . . .	25	(37.59)	(53.91)	(47.64)

The notes on pages F-9 to F-46 are an integral part of these consolidated financial statements.

## CONSOLIDATED STATEMENT OF CHANGES IN EQUITY

	Note	Attributable to equity holders of the Company					Total equity
		Share capital	Share premium reserve	Other reserves	Retained earnings	Convertible loan	
(in thousands)							
Balance at 1 January 2003		€ 47	€ 4,746	€ –	€ (1,411)	€ –	€ 3,382
Income/(expense) recognised directly in equity		–	–	–	–	–	–
Result for the year		–	–	–	(2,236)	–	(2,236)
Total recognised income for 2003		–	–	–	(2,236)	–	(2,236)
Employees share option scheme:							
– value of employee services	12	–	–	5	–	–	5
		–	–	5	–	–	5
Balance at 31 December 2003		47	4,746	5	(3,647)	–	1,151
Balance at 1 January 2004		47	4,746	5	(3,647)	–	1,151
Income/(expense) recognised directly in equity		–	–	–	–	–	–
Result for the year		–	–	–	(2,530)	–	(2,530)
Total recognised income for 2004		–	–	–	(2,530)	–	(2,530)
Employees share option scheme:							
– value of employee services	12	–	–	23	–	–	23
		–	–	23	–	–	23
Balance at 31 December 2004		47	4,746	28	(6,177)	–	(1,356)
Balance at 1 January 2005		47	4,746	28	(6,177)	–	(1,356)
Income/(expense) recognised directly in equity		–	–	–	–	–	–
Result for the year		–	–	–	(4,209)	–	(4,209)
Total recognised income for 2005		–	–	–	(4,209)	–	(4,209)
Employee share option scheme:							
– value of employee services	12	–	–	132	–	–	132
Issue of share capital	12	69	13,130	–	–	–	13,199
Convertible subordinated loan	13	–	–	–	–	3,985	3,985
		69	13,130	132	–	3,985	17,316
Balance at 31 December 2005		€116	€17,876	€160	€(10,386)	€3,985	€11,751

The notes on pages F-9 to F-46 are an integral part of these consolidated financial statements.



## CONSOLIDATED CASHFLOW STATEMENT

	Note	Year ending at 31 December		
		2005	2004	2003
		(in thousands)		
<b>Cash flows from operating activities</b>				
Result before corporate income taxes . . . . .		€(4,562)	€(2,177)	€(2,236)
Adjustments for:				
– Depreciation and amortisation . . . . .	6,7	863	860	668
– Share-based payments . . . . .	20	132	23	5
– (Gain)/loss on sale of property, plant and equipment . . . . .	27	–	(26)	–
– Interest costs . . . . .		405	412	106
– Interest income . . . . .		(287)	(18)	(77)
– Change in pension provision . . . . .		(42)	9	65
Changes in working capital: . . . . .				
– Trade receivables . . . . .		(171)	(399)	286
– Receivables from related parties . . . . .		3	1,000	16
– Social securities and other taxes . . . . .		(206)	127	(49)
– Other receivables, prepayments and accrued income . . . . .		(609)	22	135
– Trade payables . . . . .		412	170	610
– Other liabilities and accruals . . . . .		(556)	1,339	859
Cash generated from operations . . . . .		(4,618)	1,342	388
Interest received . . . . .		287	18	77
Interest paid . . . . .		(405)	(412)	(106)
Corporate income taxes paid . . . . .		–	–	–
Net cash used in/generated from operating activities . . . . .		(4,736)	948	359
<b>Cash flows from investing activities</b>				
Acquisition of subsidiaries, net of cash acquired . . . . .	30	–	–	(1,481)
Purchases of property, plant and equipment . . . . .	27	(924)	(924)	(710)
Proceeds from sale of property, plant and equipment . . . . .	27	–	26	–
Purchases of intangible assets . . . . .	6	(294)	(30)	(27)
Purchases of financial assets carried at cost . . . . .	8	–	(16)	–
Net cash used in investing activities . . . . .		(1,218)	(944)	(2,218)
<b>Cash flows from financing activities</b>				
Proceeds from issuance of shares . . . . .	12	13,038	–	–
Proceeds from issuance of convertible subordinated loan . . . . .	13	3,985	–	–
Proceeds from and repayment of finance lease liabilities . . . . .	27	(163)	(219)	(90)
Proceeds from borrowings . . . . .		–	–	150
Repayments of borrowings . . . . .		–	(704)	(108)
Net cash generated from/used in financing activities . . . . .		16,860	(923)	(48)
<b>Cash, cash equivalents and bank overdrafts</b>				
Net increase/(decrease) during the year . . . . .		10,906	(919)	(1,907)
Balance at beginning of the year . . . . .		(1,676)	(757)	1,150
Balance at end of the year . . . . .	11	€ 9,230	€(1,676)	€ (757)

The notes on pages F-9 to F-46 are an integral part of these consolidated financial statements.

## NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

### 1. General information

OctoPlus International Holding B.V. ("the Company") and its subsidiaries (together "the Group") are engaged in providing services for life sciences companies in the field of drug formulation. Furthermore, the Group develops a product portfolio based on its proprietary drug delivery technology.

The Company is a limited liability company incorporated and domiciled in the Netherlands. The address of its registered office is Zernikedreef 12, 2333 CL Leiden, the Netherlands.

These consolidated financial statements are subject to approval by the General Meeting of Shareholders.

### 2. Summary of significant accounting policies

The principal accounting policies applied in the preparation of these consolidated financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

#### *2.1 Basis of preparation*

The Group has adopted International Financial Reporting Standards ("IFRS"), including International Accounting Standards ("IAS") and interpretations issued by the International Accounting Standards Board ("IASB") as adopted by the EU ("EU-IFRS"), as its primary accounting basis for the consolidated financial statements as from 1 January 2005 (see Note 33 for the impact of adopting IFRS). For the Group, there are no differences between EU-IFRS and IFRS. The Group's transition date to IFRS is 1 January 2003. The Group prepared its opening balance sheet on the basis of IFRS at that date. With reference to the company-only income statement of the Company, use has been made of the exemption pursuant to Section 402 of Book 2 of the Netherlands Civil Code.

The consolidated financial statements have been prepared under the historical cost convention. Furthermore, the consolidated financial statements are presented in euros and all values are rounded to the nearest thousand except when otherwise indicated.

The preparation of financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgement in the process of applying the Group's accounting policies. The areas involving a higher degree of judgement or complexity or areas where assumptions and estimates are significant to the consolidated financial statements are disclosed in Note 4.

#### *2.2 Consolidation*

The Company is the holding company of a group of companies. The other consolidated group companies ("subsidiaries") are:

- OctoShare B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Development B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Technologies B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Sciences B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoShed B.V., 100%, having its legal seat in Leiden, the Netherlands
- Chienna B.V., 100%, having its legal seat in Bilthoven, the Netherlands
- OctoPlus Inc., 100%, having its legal seat in Delaware, United States of America

#### *Subsidiaries*

Subsidiaries are all entities over which the Group has the power to govern the financial and operating policies, generally accompanied by a shareholding of more than one half of the voting rights. The existence and

effect of potential voting rights that are currently exercisable or convertible are considered when assessing whether the Group controls another entity. Subsidiaries are fully consolidated from the date on which control is transferred to the Group. They are de-consolidated from the date that control ceases.

The purchase method of accounting is used to account for the acquisition of subsidiaries by the Group. The cost of an acquisition is measured as the fair value of the assets given, equity instruments issued and liabilities incurred or assumed at the date of exchange, plus costs directly attributable to the acquisition. Identifiable assets acquired and liabilities and contingent liabilities assumed in a business combination are measured initially at their fair values at the acquisition date, irrespective of the extent of any minority interest. The excess of the cost of acquisition over the fair value of the Group's share of the identifiable net assets acquired is recorded as goodwill. If the cost of acquisition is less than the fair value of the net assets of the subsidiary acquired (also after re-assessment), the difference is recognised directly in the income statement.

Inter-company transactions, balances and unrealised gains on transactions between group companies are eliminated. Unrealised losses between group companies are also eliminated, however, these are considered to be an impairment indicator of the asset transferred. Accounting policies of subsidiaries have been changed where necessary to ensure consistency with the policies adopted by the Group.

### ***2.3 Segment reporting***

A business segment is a group of assets and operations engaged in providing products or services that are subject to risks and returns that are different from those of other business segments. A geographical segment is engaged in providing products or services within a particular economic environment which are subject to risks and returns that are different from those of segments operating in other economic environments.

### ***2.4 Foreign currency translation***

#### *(a) Functional and presentation currency*

Items included in the financial statements of each of the Group's entities are measured using the currency of the primary economic environment in which the entity operates ("the functional currency"). The consolidated financial statements are presented in euros, which is the Company's functional and presentation currency.

#### *(b) Transactions and balances*

Foreign currency transactions are translated into the functional currency using the exchange rates prevailing at the dates of the transactions. Foreign exchange gains and losses resulting from the settlement of such transactions and from the translation at year-end exchange rates of monetary assets and liabilities denominated in foreign currencies are recognised in the income statement.

### ***2.5 Intangible assets***

#### *(a) Goodwill*

Goodwill represents the excess of the cost of an acquisition over the fair value of the Group's share of the net identifiable assets of the acquired subsidiary at the date of acquisition. If the cost of acquisition is less than the fair value of the net assets of the subsidiary acquired (also after re-assessment), the difference is recognised directly in the income statement.

Separately recognised goodwill is tested annually for impairment and carried at cost less accumulated impairment losses. Impairment losses on goodwill are not reversed. Gains and losses on the disposal of an entity include the carrying amount of goodwill relating to the entity sold.

Goodwill is allocated to cash-generating units for the purpose of impairment testing. The allocation is made to those cash-generating units or groups of cash-generating units that are expected to benefit from the business combination in which the goodwill arose.

*(b) Patents*

Acquired patents have a definite useful life and are carried at cost less accumulated amortisation and impairment losses. Amortisation is calculated using the straight-line method to allocate the cost of patents over their estimated useful lives (generally 10 years unless a patent expires prior to that date). Amortisation begins when an asset is available for use. However, in the years presented in these financial statements, no amortisation on patents is recorded since the technology which the patents relate to is not yet available for use.

*(c) Computer software*

Acquired computer software is capitalised on the basis of the costs incurred to acquire and bring to use the specific software. These costs are amortised over their estimated useful lives (generally three years).

*(d) Research and development*

Research expenditure is recognised as an expense as incurred. Costs incurred on development projects are recognised as intangible assets when it is probable that the project will be a success considering its commercial and technological feasibility, generally when filed for regulatory approval for commercial production and costs can be measured reliably. Other development expenditures are recognised as an expense as incurred. Development costs previously recognised as an expense are not recognised as an asset in a subsequent period. Development costs with a finite useful life that have been capitalised are amortised from the commencement of the commercial production of the product on a straight-line basis over the period of its expected benefit.

**2.6 Property, plant and equipment**

Property, plant and equipment comprise the land and building in Leiden, leased under a financial lease agreement, and machinery and other equipment. All property, plant and equipment is stated at historical cost less depreciation. Historical cost includes expenditures that are directly attributable to the acquisition of the items.

Subsequent costs are included in the asset's carrying amount or recognised as a separate asset, as appropriate, only when it is probable that future economic benefits associated with the item will flow to the Group and the cost of the item can be measured reliably. All other repairs and maintenance charges are expensed in the financial period in which these are incurred.

Depreciation is calculated using the straight-line method to allocate the cost of the assets to their residual values over their estimated useful lives. Land is not depreciated; other items are depreciated as follows:

- Buildings 20 years
- Machinery and installations 3-10 years
- Other equipment 3-5 years

The assets' residual values and useful lives are reviewed, and adjusted if appropriate, at each balance sheet date.

An asset's carrying amount is written down immediately to its recoverable amount if the asset's carrying amount is greater than its estimated recoverable amount (also refer to 2.7).

Gains and losses on disposals are determined by comparing proceeds with carrying amount. These are included in the income statement.

*Finance leases*

The Group leases certain property, plant and equipment. Leases of property, plant and equipment where the Group has substantially all the risks and rewards of ownership are classified as finance leases. Finance leases are capitalised at the commencement of the lease at the lower of the fair value of the leased property and the present value of the minimum lease payments.

Each lease payment is allocated between the liability and finance charges so as to achieve a constant rate on the finance balance outstanding. The corresponding rental obligations, net of finance charges, are included in

“finance lease liabilities”. The interest element of the finance cost is charged to the income statement over the lease period so as to produce a constant periodic rate of interest on the remaining balance of the liability for each period. The property, plant and equipment acquired under finance leases is depreciated over the shorter of the useful life of the asset or the lease term.

#### *Borrowing costs*

Borrowing costs incurred for the construction of any qualifying asset are capitalised during the period of time that is required to complete and prepare the asset for its intended use. Other borrowing costs are expensed.

### **2.7 Impairment of non-financial assets**

Goodwill and other assets not subject to amortisation are reviewed for impairment at least annually. Assets subject to amortisation or depreciation are reviewed for impairment whenever events or changes in circumstances indicate that the carrying amount may not be recoverable. An impairment loss is recognised for the amount by which the asset’s carrying amount exceeds its recoverable amount. The recoverable amount is the higher of an asset’s fair value less costs to sell and value-in-use (i.e. the present value of the future cash flows to be generated by an asset from its continuing use in the business). For the purpose of assessing impairment, assets are grouped at the lowest levels for which there are separately identifiable cash flows (cash-generating units). Non-financial assets other than goodwill that suffered impairment are reviewed for possible reversal of the impairment at each reporting date.

### **2.8 Financial assets**

The Group has financial assets in the two categories “loans and receivables” and “financial assets carried at cost”. In the years presented in these financial statements, the Group did not purchase or hold any derivative financial assets.

#### *(a) Loans and receivables*

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. They are included in “current assets”, except for maturities greater than 12 months after the balance sheet date, which are classified as “non-current assets”. Loans and receivables are carried at amortised costs using the effective interest method.

#### *(b) Financial assets carried at cost*

Financial assets carried at cost (less accumulated impairment losses) are unquoted equity instruments that are not carried at fair value because their fair value cannot be reliably measured. They are included in non-current assets unless management intends to dispose of the investment within 12 months of the balance sheet date. These financial assets are subsequently carried at cost.

Regular purchases and sales of investments are recognised on trade-date; the date on which the Group commits to purchase or sell the asset. Investments are initially recognised at fair value plus transaction costs. Investments are derecognised when the rights to receive cash flows from the investments have expired or have been transferred and the Group has transferred substantially all risks and rewards of ownership.

The Group assesses at each balance sheet date whether there is objective evidence that a financial asset or a group of financial assets is impaired. If there is objective evidence that an impairment loss has been incurred on an unquoted equity instrument that is not carried at fair value because its fair value cannot be reliably measured, the amount of the impairment loss is measured as the difference between the carrying amount of the financial asset and the present value of estimated future cash flows discounted at the current market rate of return for a similar financial asset.

### **2.9 Inventories**

Inventories are stated at the lower of cost and net realisable value. Cost is determined using the first-in, first-out (FIFO) method. Net realisable value is the estimated selling price in the ordinary course of business, less applicable variable selling expenses.

## ***2.10 Trade receivables***

Trade receivables are recognised initially at fair value and subsequently measured at amortised cost using the effective interest method, less provision for impairment. A provision for impairment of trade receivables is established when there is objective evidence that the Group will not be able to collect all amounts due according to the original terms of receivables. Significant financial difficulties of the debtor, probability that the debtor will enter bankruptcy or financial reorganisation, and default or delinquency in payments are considered indicators that the trade receivable is impaired. The amount of the provision is the difference between the asset's carrying amount and the present value of estimated future cash flows, discounted at the effective interest rate. The amount of the provision is recognised in the income statement within "other costs".

## ***2.11 Cash and cash equivalents***

Cash and cash equivalents includes cash-in-hand, current accounts, deposits held at call with banks, other short-term highly liquid investments with original maturities of three months or less, and bank overdrafts. Bank overdrafts are shown separately within current liabilities on the balance sheet.

## ***2.12 Equity***

Ordinary shares and preference shares are classified as equity.

A financial instrument or its component parts are classified on initial recognition as a financial liability, a financial asset or an equity instrument in accordance with the substance of the contractual arrangement and the definitions of a financial liability, a financial asset and an equity instrument. An equity instrument is defined as any contract that evidences a residual interest in the assets of an entity after deducting all of its liabilities. Based on these principles, the Group's subordinated convertible loan is classified as equity.

Incremental costs directly attributable to the issue of new shares or options are shown in equity as a deduction from the proceeds, net of tax.

## ***2.13 Deferred corporate income taxes***

Deferred corporate income tax is recognised, using the liability method, on temporary differences arising between the tax bases of assets and liabilities and their carrying amounts in the consolidated financial statements. Deferred corporate income tax is determined using tax rates (and laws) that have been enacted or substantially enacted by the balance sheet date and are expected to apply when the related deferred corporate income tax asset is realised or the deferred corporate income tax liability is settled. Deferred corporate income tax assets are recognised to the extent that it is probable that future taxable profit will be available against which the temporary differences can be utilised.

Deferred corporate income tax is not accounted for if it arises from initial recognition of an asset or liability in a transaction other than a business combination that at the time of the transaction affects neither accounting nor taxable profit or loss.

## ***2.14 Borrowings***

Borrowings are recognised initially at fair value, net of transaction costs incurred. Borrowings are subsequently stated at amortised cost; any difference between the proceeds (net of transaction costs) and the redemption value is recognised in the income statement over the period of the borrowings using the effective interest method.

Borrowings are classified as "current liabilities" unless the Group has an unconditional right to defer settlement of the liability for at least 12 months after the balance sheet date ("non-current liabilities").

## ***2.15 Employee benefits***

### ***(a) Pension obligations***

The Group operates a collective defined benefit pension plan for nearly all employees funded through payments to an insurance company. This plan includes an average pay part and a defined contribution surplus

salary part. The Group also operates some individual defined contribution pension plans. A defined contribution plan is a pension plan under which the Group pays fixed contributions into a separate entity. The Group has no legal or constructive obligations to pay further contributions if the fund does not hold sufficient assets to pay all employees the benefits relating to employee service in the current and prior periods. A defined benefit plan is a pension plan that is not a defined contribution plan. Typically, defined benefit plans define an amount of pension benefit that an employee will receive on retirement, usually dependent on one or more factors such as age, years of service and compensation.

The liability recognised in the balance sheet in respect of defined benefit pension plans is the present value of the defined benefit obligation at the balance sheet date less the fair value of plan assets, together with adjustments for unrecognised actuarial gains or losses and past service costs. The defined benefit obligation is calculated annually by an independent actuary using the projected unit credit method. The present value of the defined benefit obligation is determined by discounting the estimated future cash outflows using a discount rate determined on basis of corporate bonds, adjusted for the duration of the liability.

Actuarial gains and losses arising from experience adjustments and changes in actuarial assumptions in excess of the greater of 10% of the value of plan assets or 10% of the defined benefit obligation are charged or credited to the income statement over the employees' expected average remaining working lives.

Past-service costs related to changes to the pension plan are recognised immediately in the income statement, unless the changes to the pension plan are conditional on the employees remaining in service for a specified period of time (the "vesting period"). In this case, the past-service costs are amortised on a straight-line basis over the vesting period.

For defined contribution plans, the Group pays contributions to pension insurance plans on a contractual basis. The Group has no further payment obligations once the contributions have been paid. The contributions are recognised as employee benefit expense when they are due. Prepaid contributions are recognised as an asset to the extent that a cash refund or a reduction in the future payments is available.

*(b) Share-based compensation*

The Company operates an equity-settled, share-based compensation plan. The costs of employee share option plans are measured by reference to the fair value of the options at the date at which the options are granted using a Binomial option model.

The costs of these options, which reflect the services rendered by employees in exchange for the grant of the options, are recognised in the income statement, together with a corresponding increase in equity during the vesting period. The total amount to be expensed over the vesting period is determined by reference to the fair value of the options granted, excluding the impact of any non-market vesting conditions (for example, profitability and sales growth targets).

Estimates of forfeitures are included in assumptions about the number of options that are expected to become exercisable. At each balance sheet date, the Company revises its estimates of the number of options that are expected to become exercisable. It recognises the impact of the revision of original estimates, if any, in the income statement, with a corresponding adjustment to equity. The income statement charge or credit for a period represents the movement in cumulative expense recognised at the beginning and end of that period.

The proceeds received net of any directly attributable transaction costs are credited to share capital (nominal value) and share premium when the options are exercised.

*(c) Profit-sharing and bonus plans*

The Group recognises a liability and an expense for bonuses and profit-sharing plans if contractually obliged or if there is a past practice that has created a constructive obligation.



## **2.16 Provisions**

Provisions are recognised when: The Group has a present legal or constructive obligation as a result of past events; it is more likely than not that an outflow of resources will be required to settle the obligation; and the amount can be reliably estimated. Provisions are not recognised for future operating losses.

Provisions are measured at the present value of the expenditures expected to be required to settle the obligation using a pre-tax rate that reflects current market assessments of the time value of money and the risks specific to the obligation. The increase in the provision due to passage of time is recognised as interest expense.

## **2.17 Revenue recognition**

Revenue comprises the fair value of the sale of goods and services, and is shown net of value-added tax, rebates and discounts and after eliminated sales within the Group. The Group's revenues primarily consist of sales of services, license and royalty revenues and subsidies (see 2.18). These revenues are recognised as follows:

### *(a) Service revenues*

Sales of services are recognised in the accounting period in which the services are rendered, by reference to the stage of completion of the specific transaction when the outcome of a transaction can be estimated reliably. The stage of completion is assessed on the basis of the actual service provided as a proportion of the total services to be provided.

### *(b) License and royalty revenues*

License and royalty revenues include amounts earned from third parties with licenses and/or options to the Group's intellectual property. License and royalty revenues are recognised when earned in accordance with the substance and under the terms of the related agreements and when it is probable that the economic benefits associated with the transaction will flow to the entity and the amount of the revenue can be measured reliably. In situations where the Group has continuing performance obligations, revenues related to license fee payments are deferred and the related revenue is recognised in the period of expected performance.

### *Multiple element arrangements*

In certain circumstances, it is necessary to apply the recognition criteria to the separately identifiable components of a single transaction in order to reflect the substance of the transaction. Conversely, the recognition criteria are applied to two or more transactions together when they are linked in such a way that the commercial effect cannot be understood without reference to the series of transactions as a whole.

The Group offers arrangements whereby a customer licenses the right to use the Group's intellectual property and purchases research and development services under one arrangement. When such multiple element arrangements exist, an element is accounted for as a separable element if it has value to the customer on a stand-alone basis and the fair value can be determined objectively and reliably.

When license revenues and service revenues are identified as separable elements in a multiple element transaction, the license revenue recognised is determined based on the fair value of the license in relation to the fair value of the arrangement taken as a whole and is recognised in accordance with the accounting policy for license and royalty revenues as discussed above. The revenue relating to the service element, which represents the fair value of the servicing arrangement in relation to the fair value of the arrangement, is recognised over the service period. The fair values of each element are determined based on the current market price of each of the elements when sold separately.

## **2.18 Income from subsidies**

The Group receives certain subsidies, which support the Group's research efforts in defined research and development projects. These subsidies generally provide for reimbursement of approved costs incurred as defined in various grants. Subsidies are recognised at their fair value when there is a reasonable assurance that the subsidy will be received and the Group will comply with all attached conditions.

The Group includes income from subsidies under “income from subsidies” in the income statement in order to enable comparison of its income statement with companies in the life sciences sector. Companies in the life sciences sector generally present governmental subsidies as income, as these subsidies often are a significant source of income. Furthermore, research and development expenses would, generally, be incurred to the same amount if no governmental contributions would be granted.

The WBSO (“afdrachtvermindering speur- en ontwikkelingswerk”) is a fiscal facility that provides subsidies to companies, knowledge centres and self-employed people who perform research and development (as defined in the WBSO Act). Under this Act, a contribution is paid towards the labour costs of employees directly involved in research and development. The contribution is in the form of a reduction of payroll taxes and social security contributions.

Subsidies relating to labour costs (WBSO) are deferred and recognised in the income statement as negative labour costs over the period necessary to match them with the labour costs that they are intended to compensate.

### ***2.19 Operating leases***

Leases in which substantially all the risks and rewards of ownership are retained by the lessor are classified as operating leases. Payments made under operating leases (net of any incentives received from the lessor) are charged to the income statement on a straight-line basis over the period of the lease.

### ***2.20 Dividend distribution***

Dividend distribution to the Company’s shareholders is recognised as a liability in the Group’s financial statements in the period in which the dividends are approved by the Company’s shareholders.

## **3. Financial risk management**

### ***3.1 Financial risk factors***

The Group is exposed to a variety of financial risks: Market risk, credit risk, liquidity risk and cash flow and fair value interest rate risk. The Group’s overall risk management program seeks to minimise potential adverse effects of these financial risk factors on the Group’s financial performance.

#### *(a) Market risk*

Foreign exchange risk arises from future commercial transactions and recognised assets and liabilities in foreign currencies. In the years presented, the Group had no significant outstanding receivables or payables in currencies other than euros.

The Group is not exposed to equity securities price risk, since it does not hold any such investments, or commodity price risk.

#### *(b) Credit risk*

The five largest external partners generate approximately 55% of total revenues in 2005. The outstanding receivables with these parties comprise of 55% of the total trade receivables at 31 December 2005. Management does not believe that this results in major credit risks since all customers are companies of good reputations. The Group has policies in place to ensure that contracts are only signed with customers with an appropriate credit history.

#### *(c) Liquidity risk*

Prudent liquidity risk management implies maintaining sufficient cash and marketable securities plus the availability of funding through an adequate amount of committed credit facilities. Due to the dynamic nature of the underlying businesses, the Group aims to maintain flexibility in funding by keeping committed credit lines available. Management considers the existing funding to provide sufficient time to create shareholder value before a next financing round is carried out.

*(d) Cash flow and fair value interest rate risk*

As the Group has no significant long-term interest-bearing assets or debts, the Group's income and operating cash flows are not significantly impacted by changes in market interest rates.

**3.2 Estimation fair value of financial instruments**

The Group does not hold any financial instruments traded in active markets. Financial assets consist of loans and receivables and an unquoted equity investment, which is not carried at fair value because its fair value cannot be reliably measured.

**4. Critical accounting estimates and judgements**

Estimates and judgements are continually evaluated and are based on historical experience and other factors, including expectations of future events that are believed to be reasonable under the circumstances.

The Group makes estimates and assumptions concerning the future. The resulting accounting estimates will, by definition, seldom equal the related actual results. The estimates and assumptions that have a significant risk of causing a material adjustment to the carrying amounts of assets and liabilities within the next financial year as well as critical judgements in applying the Group's accounting policies are discussed below.

*(a) Impairment test of goodwill and patents*

Goodwill and intangible assets not yet available for use are not amortised but are subject to an annual impairment test or more frequent testing whenever events or changes in circumstances indicate that the carrying amount may be not be recoverable. For the purpose of the impairment testing, goodwill is allocated to cash-generating units. In the years presented, all goodwill recognised relates to the acquisition of Chienna B.V. in the year 2003 and is allocated to the Group's Drug delivery & products unit. The technology that the patents acquired as part of the acquisition of Chienna B.V. relates to, are not yet available for use. These patents were also allocated to the Group's Drug delivery & products unit and are tested for impairment as part of this cash-generating unit. The recoverable amount of the applicable cash-generating unit is determined based on value-in-use calculations by using the discounted cash flow model.

In performing impairment testing of goodwill and patents, management must make significant judgements and estimates to determine whether the cash flows generated by the cash-generating unit the assets belong to are less than the unit's carrying value (see Note 6). Determining cash flows requires the use of judgements and estimates that have been included in the Group's strategic plans and long-term forecasts. The data necessary for performing the impairment tests are based on management estimates of future cash flows. The discount rates used are estimated pre-tax rates which reflect specific risks relating to the relevant segment.

*(b) Corporate income taxes*

The Group, which has a history of recent tax losses, recognises deferred tax assets arising from unused tax losses or tax credits only to the extent that the relevant fiscal unity has sufficient taxable temporary differences or there is convincing other evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilised by the fiscal unity. Management's judgement is that sufficient convincing other evidence is not available and a deferred tax asset is therefore only recognised to the extent that a fiscal unity has sufficient taxable temporary differences.

*(c) Pensions*

For the calculation of the present value of the pension obligation and the net cost, actuarial assumptions are made about demographic variables (such as mortality) and financial variables (such as future increases in salaries). The discount rate is determined by reference to market rates of high-quality corporate bonds. Any changes in these assumptions will impact the carrying amount of the Group's pension obligations. Additional information on these assumptions is included in Note 15.

*(d) Share-based payments*

Share options granted to employees are measured at the fair value of the equity instruments granted (indirect method of measurement). Fair value is determined through the use of an option-pricing model considering, among others, the following variables:

- a) The exercise price of the option;
- b) The expected life of the option;
- c) The current value of the underlying shares;
- d) The expected volatility of the share price, calculated considering the effect of dividends on stock price;
- e) The dividends expected on the shares; and
- f) The risk-free interest rate for the life of the option.

For the Company's share option plans, management's judgement is that the Binomial method is most appropriate for determining fair values as this method allows accounting for non-transferability, vesting conditions and early exercise. Since the Company is not listed, there is no published share price information. Consequently, the Company needs to estimate the fair value of its shares and the expected volatility of that value. These assumptions and estimates are further discussed in Note 12 to the consolidated financial statements.

The result of the share option valuations and the related compensation expense is dependent on the model and input parameters used. Even though Management considers the fair values reasonable and defensible based on the methodologies applied and the information available, others might derive at a different fair value for each of the Company's share option plans.

*(e) Capitalisation of development costs*

Costs incurred on development projects are recognised as intangible assets when it is probable that a project will be a success considering its commercial and technological feasibility. Management's judgement is required in determining when the Group should start capitalising of development costs. Management determined that commercial and technological feasibility is, in general, probable when the Group files for regulatory approval for commercial production and costs can be measured reliably. At 31 December 2005, the Group has not filed for regulatory approval for its proprietary drug delivery technology. Based on Management's assessment of commercial and technological feasibility, no development costs have been recognised as intangible assets in the consolidated financial statements.

## **5. Segment information**

*Primary reporting format – business segments*

At 31 December 2005, the Group is organised into two main business segments:

- (1) Providing development services for life sciences companies in the field of drug formulation ("Contract development unit"); and
- (2) Development of a product portfolio based on the Group's proprietary drug delivery technology ("Drug delivery & products unit").

The segment results for the year ending 31 December 2005 are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Total gross segment revenues . . . . .	€6,804	€ 185	€ –	€6,989
Inter-segment revenues . . . . .	(366)	–	–	(366)
Subsidies and other income . . . . .	–	394	–	394
Revenues . . . . .	<u>6,438</u>	<u>579</u>	<u>–</u>	<u>7,017</u>
Operating result . . . . .	718	(5,197)	35	(4,444)
Finance costs – net . . . . .				(118)
Result before corporate income tax . . . . .				<u>(4,562)</u>
Corporate income taxes . . . . .				353
Result for the year . . . . .				<u>€(4,209)</u>

The segment results for the year ending 31 December 2004 are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Total gross segment revenues . . . . .	€5,418	€ 359	€ –	€5,777
Inter-segment revenues . . . . .	(772)	(21)	–	(793)
Subsidies and other income . . . . .	26	708	–	734
Revenues . . . . .	<u>4,672</u>	<u>1,046</u>	<u>–</u>	<u>5,718</u>
Operating result . . . . .	813	(2,596)	–	(1,783)
Finance costs - net . . . . .				(394)
Result before corporate income tax . . . . .				<u>(2,177)</u>
Corporate income taxes . . . . .				(353)
Result for the year . . . . .				<u>€(2,530)</u>

The segment results for the year ending 31 December 2003 are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Total gross segment revenues . . . . .	€5,123	€ 276	€ –	€5,399
Inter-segment revenues . . . . .	(356)	–	–	(356)
Subsidies and other income . . . . .	–	818	–	818
Revenues . . . . .	<u>4,767</u>	<u>1,094</u>	<u>–</u>	<u>5,861</u>
Operating result . . . . .	17	(2,224)	–	(2,207)
Finance costs - net . . . . .				(29)
Result before corporate income tax . . . . .				<u>(2,236)</u>
Corporate income taxes . . . . .				–
Result for the year . . . . .				<u>€(2,236)</u>

Unallocated costs represent corporate expenses. Inter-segment transfers or transactions are entered into under the normal commercial terms and conditions that would also be available to unrelated third parties.

Other segment items included in the income statement are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
<b>Year ending 31 December 2005</b>				
Depreciation and amortisation . . . . .	€633	€230	€–	€863
<b>Year ending 31 December 2004</b>				
Depreciation and amortisation . . . . .	€644	€216	€–	€860
<b>Year ending 31 December 2003</b>				
Depreciation and amortisation . . . . .	€492	€176	€–	€668

The segment assets and liabilities **at 31 December 2005** and capital expenditure for the year then ending are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Assets . . . . .	€9,499	€6,061	€4,940	€20,500
Liabilities . . . . .	7,722	11,373	(10,346)	8,749
Capital expenditure (Note 6 and 7) . . . . .	559	271	552	1,382

The segment assets and liabilities **at 31 December 2004** and capital expenditure for the year then ending are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Assets . . . . .	€5,450	€1,717	€2,187	€9,354
Liabilities . . . . .	4,169	5,571	970	10,710
Capital expenditure (Note 6 and 7) . . . . .	1,147	124	3,423	4,694

The segment assets and liabilities **at 31 December 2003** and capital expenditure for the year then ending are as follows:

	<u>Contract development</u>	<u>Drug delivery and products</u>	<u>Unallocated</u>	<u>Group</u>
	(in thousands)			
Assets . . . . .	€3,094	€1,167	€1,931	€6,192
Liabilities . . . . .	2,354	3,452	(765)	5,041
Capital expenditure (Note 6 and 7) . . . . .	617	1,513	88	2,218

## Secondary reporting format – geographical segments

The Group's customers are mainly located in Europe and North-America as shown below:

<b>Revenues</b>	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
European Union . . . . .	€3,543	€4,141	€4,362
North-America . . . . .	2,222	1,088	688
Other countries . . . . .	1,252	489	811
	<u>€7,017</u>	<u>€5,718</u>	<u>€5,861</u>

Revenues are allocated based on the country in which the customer is located. All of the Group's assets and capital expenditure (as disclosed per business segment above) are located in the Netherlands.

## 6. Intangible assets

	<u>Goodwill</u>	<u>Patents</u>	<u>Other intangibles</u>	<u>Total</u>
		(in thousands)		
<b>At 1 January 2003</b>				
Cost . . . . .	€ –	€ –	€ 11	€ 11
Accumulated amortisation . . . . .	–	–	(6)	(6)
Net book amount . . . . .	<u>–</u>	<u>–</u>	<u>5</u>	<u>5</u>
<b>Year ending 31 December 2003</b>				
Opening net book amount . . . . .	–	–	5	5
Additions . . . . .	–	–	27	27
Acquisition of subsidiary . . . . .	213	1,167	–	1,380
Amortisation charge . . . . .	–	–	(11)	(11)
Closing net book amount . . . . .	<u>213</u>	<u>1,167</u>	<u>21</u>	<u>1,401</u>
<b>At 31 December 2003</b>				
Cost . . . . .	213	1,167	38	1,418
Accumulated amortisation . . . . .	–	–	(17)	(17)
Net book amount . . . . .	<u>213</u>	<u>1,167</u>	<u>21</u>	<u>1,401</u>
<b>Year ending 31 December 2004</b>				
Opening net book amount . . . . .	213	1,167	21	1,401
Additions (related to 2003 acquisition) . . . . .	30	–	–	30
Amortisation charge . . . . .	–	–	(10)	(10)
Closing net book amount . . . . .	<u>243</u>	<u>1,167</u>	<u>11</u>	<u>1,421</u>
<b>At 31 December 2004</b>				
Cost . . . . .	243	1,167	38	1,448
Accumulated amortisation . . . . .	–	–	(27)	(27)
Net book amount . . . . .	<u>243</u>	<u>1,167</u>	<u>11</u>	<u>1,421</u>
<b>Year ending 31 December 2005</b>				
Opening net book amount . . . . .	243	1,167	11	1,421
Additions . . . . .	–	–	294	294
Amortisation charge . . . . .	–	–	(10)	(10)
Closing net book amount . . . . .	<u>€243</u>	<u>€1,167</u>	<u>€295</u>	<u>€1,705</u>



	<u>Goodwill</u>	<u>Patents</u>	<u>Other intangibles</u>	<u>Total</u>
	(in thousands)			
<b>At 31 December 2005</b>				
Cost . . . . .	€ 243	€ 1,167	€ 332	€ 1,742
Accumulated amortisation . . . . .	—	—	(37)	(37)
Net book amount . . . . .	<u>€ 243</u>	<u>€ 1,167</u>	<u>€ 295</u>	<u>€ 1,705</u>

Other intangibles consist of acquired software.

The items included under “acquisition of subsidiary” relate to the acquisition of Chienna B.V. at 1 March 2003.

#### *Patents*

In the years presented in these financial statements, no amortisation on patents is recorded since the technology which the patents relate to are not yet available for use. However, the Group estimates at the end of each annual reporting period the recoverable amount of these patents, irrespective of whether there is any indication that it may be impaired.

#### *Impairment test of goodwill and patents*

For the purpose of the impairment testing, goodwill and patents have been allocated to a cash-generating unit since these assets do not generate cash inflows that are largely independent of those from other assets. In the years presented, all goodwill and patents recognised relate to the acquisition of Chienna B.V. in 2003 and are allocated to the Group’s Drug delivery & products unit (see Note 5 on segment information). This business segment is treated as one cash-generating unit.

The recoverable amount of this cash-generating unit is determined based on a value-in-use calculation (i.e. the present value of the future cash flows expected to be derived from the Drug delivery & products unit). The calculation uses cash flow projections based on financial plans and existing and potential new customer contracts. No impairment loss has been recognised as a result of the impairment testing of goodwill and patents.

For executing the impairment testing, Management considered the relevant current contracts with its licensing partners, as well as ongoing discussions with potential parties to the extent these contracts provide access to the PolyActive technology the Group obtained when acquiring Chienna B.V.

Management reviewed the contracted licensing revenues, the possibility of such revenues actually occurring and the timing thereof. The expected cash flow from this agreement has been discounted against a risk-adjusted discount rate of 35%. Management has also evaluated the likelihood of successfully completing one of the ongoing discussions regarding out-licensing of the PolyActive technology based on the proposed terms and conditions. The envisaged cash flow is adjusted for probability of success and value of time.

The sum of both calculations results in a recoverable amount of the Drug delivery & products unit that significantly exceeds the unit’s carrying value, so impairment of goodwill and patents is not considered to be necessary.

## 7. Property, plant and equipment

	Land	Buildings	Machines & installations (in thousands)	Other equipment	Total
<b>At 1 January 2003</b>					
Cost . . . . .	€ -	€ -	€2,948	€ 927	€3,875
Accumulated depreciation . . . . .	-	-	(1,311)	(494)	(1,805)
Net book amount . . . . .	-	-	1,637	433	2,070
<b>Year ending 31 December 2003</b>					
Opening net book amount . . . . .	-	-	1,637	433	2,070
Additions . . . . .	-	-	428	282	710
Acquisition of subsidiary . . . . .	-	-	-	101	101
Disposals . . . . .	-	-	-	-	-
Depreciation charge . . . . .	-	-	(446)	(211)	(657)
Closing net book amount . . . . .	-	-	1,619	605	2,224
<b>At 31 December 2003</b>					
Cost . . . . .	-	-	3,376	1,310	4,686
Accumulated depreciation . . . . .	-	-	(1,757)	(705)	(2,462)
Net book amount . . . . .	-	-	1,619	605	2,224
<b>Year ending 31 December 2004</b>					
Opening net book amount . . . . .	-	-	1,619	605	2,224
Additions . . . . .	1,084	2,364	1,111	105	4,664
Disposals . . . . .	-	-	-	-	-
Depreciation charge . . . . .	-	(84)	(522)	(244)	(850)
Closing net book amount . . . . .	1,084	2,280	2,208	466	6,038
<b>At 31 December 2004</b>					
Cost . . . . .	1,084	2,364	4,466	1,415	9,329
Accumulated depreciation . . . . .	-	(84)	(2,258)	(949)	(3,291)
Net book amount . . . . .	1,084	2,280	2,208	466	6,038
<b>Year ending 31 December 2005</b>					
Opening net book amount . . . . .	1,084	2,280	2,208	466	6,038
Additions . . . . .	-	-	814	274	1,088
Disposals . . . . .	-	-	-	-	-
Depreciation charge . . . . .	-	(118)	(523)	(212)	(853)
Closing net book amount . . . . .	1,084	2,162	2,499	528	6,273
<b>At 31 December 2005</b>					
Cost . . . . .	1,084	2,364	5,280	1,689	10,417
Accumulated depreciation . . . . .	-	(202)	(2,781)	(1,161)	(4,144)
Net book amount . . . . .	€1,084	€2,162	€2,499	€ 528	€6,273

The items included under “acquisition of subsidiary” relate to the acquisition of Chienna B.V. at 1 March 2003.

In 2004 an item of property, plant and equipment in the category “machines & installations” was sold for € 26. The historical cost of the item was € 21 and it was fully depreciated at the time of sale. Accordingly both “cost” and “accumulated depreciation” at 31 December 2004 are reduced by € 21.

*Acquisition of the assets and liabilities of OctoShed B.V. in 2004*

At 31 December 2003, OctoShed B.V., a 100% subsidiary of Holthuis-Bernaerts Holding B.V., was the direct parent of OctoPlus International Holding B.V.

In 2004, it was decided that the Company should acquire the building as well as the other assets and liabilities of OctoShed B.V. On 15 April 2004, OctoShed B.V. sold its shares in OctoPlus International Holding B.V. to Holthuis-Bernaerts Holding B.V. On the same date, a subsidiary of the Company, OctoShare B.V. acquired the OctoShed B.V. shares held by Holthuis-Bernaerts Holding B.V. Consequently, OctoShed B.V. became a new group company.

This transaction is not considered a business combination but an acquisition of individual assets and liabilities. In the Group’s accounts, the cost of the acquisition of assets and liabilities of OctoShed B.V. is allocated between the individual identifiable assets and liabilities based on their relative fair values at the date of acquisition, obtained through an independent third party valuation. This resulted in € 1,084 being allocated to the land, € 2,364 being allocated to the building and € 1,007 being allocated to other equipment (clean rooms).

Shortly after the acquisition of the assets and liabilities of OctoShed B.V., on 28 May 2004, the Company entered into a sale and leaseback transaction with two external parties named Zernike Investments Beheer B.V. (“Zernike”) and Fortress Participations B.V. (“Fortress”) for both the permanent ground lease of the land and the building, whereby a distinction was made between the sale of the Zernikedreef building and the land it is built on (Zernike) and the sales of the land next to the Zernikedreef building (Fortress). However, Zernike and Fortress are two subsidiaries of the same company. From OctoPlus’ perspective, the entire sale and leaseback agreement is therefore entered into with one external party. The selling price for the building and the land in this transaction was equal to the selling price in the prior transaction with OctoShed B.V.

The lease of the building is accounted for as a finance lease. Furthermore, as a result of the Group’s continuing involvement in the land, the land is not derecognised from the balance sheet. Accordingly, the amount received in relation to the land is considered to be financing and included within “finance lease liabilities” on the balance sheet.

*Finance leases and securities*

Property, plant and equipment includes the following amounts where the Group is a lessee under finance leases:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Cost – capitalised finance leases . . . . .	€4,261	€4,097	€357
Accumulated depreciation . . . . .	(585)	(358)	(200)
Net book amount . . . . .	<u>€3,676</u>	<u>€3,739</u>	<u>€157</u>

Finance lease liabilities are secured on the assets held under finance leases as the rights to the leased assets revert to the lessor in the event of default. Bank overdrafts are secured on other property, plant and equipment with book value at 31 December 2005 of € 2,419 (2004: € 2,366 and 2003: € 2,097) (Note 16).

## 8. Financial assets carried at cost

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Beginning of the year . . . . .	€16	€-	€-
Additions . . . . .	<u>-</u>	<u>16</u>	<u>-</u>
End of the year . . . . .	16	16	-
Non-current portion . . . . .	<u>(16)</u>	<u>(16)</u>	<u>-</u>
Current portion . . . . .	<u>€-</u>	<u>€-</u>	<u>€-</u>

Financial assets carried at cost relate to the investment in Zernike Investments Beheer B.V. Following the acquisition of OctoShed B.V. and the subsequent disposal of the property (see Note 7), a Group company became to hold all preference shares (90% of issued share capital) of Zernike Investment Beheer B.V. having its legal seat in Maassluis, the Netherlands. This Group company is entitled to a pre-defined share of the profit of Zernike Investment Beheer B.V. However, the Group has no significant influence on Zernike Investment Beheer B.V.'s business and operating policy.

## 9. Inventories

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Raw materials . . . . .	€15	€15	€15

## 10. Trade and other receivables

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Trade receivables . . . . .	€1,387	€1,216	€834
Provision for impairment of receivables . . . . .	<u>(42)</u>	<u>(42)</u>	<u>(59)</u>
Trade receivables – net . . . . .	<u>1,345</u>	<u>1,174</u>	<u>775</u>
Receivables from related parties (Note 31) . . . . .	-	3	1,003
Non-current portion: . . . . .	<u>-</u>	<u>-</u>	<u>(908)</u>
Current receivables from related parties . . . . .	<u>-</u>	<u>3</u>	<u>95</u>
Corporate income taxes . . . . .	-	6	123
VAT to be received . . . . .	255	43	-
Prepaid social security costs . . . . .	<u>-</u>	<u>-</u>	<u>53</u>
Social security and other taxes . . . . .	<u>255</u>	<u>49</u>	<u>176</u>
Prepaid expenses . . . . .	351	181	34
Accrued income . . . . .	484	319	401
Other amounts to be received . . . . .	<u>330</u>	<u>56</u>	<u>143</u>
Other receivables, prepayments and accrued income . . . . .	<u>€1,165</u>	<u>€556</u>	<u>€578</u>

Accrued income includes € 113 (2004: € 218 and 2003: € 183) related to subsidies.

The nominal value less impairment provision of trade and other receivables are assumed to approximate their fair values.

Additions to and releases from the provision for impaired receivables are included in “other costs” in the income statement. However, there was no movement in the provision for impairment of receivables during 2005.

## 11. Cash and cash equivalents

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Cash at bank and in hand . . . . .	€ 226	€82	€20
Short-term bank deposits . . . . .	9,500	–	–
	<u>€9,726</u>	<u>€82</u>	<u>€20</u>

The effective interest rate on short-term bank deposits was 2.1% in 2005; these deposits have an average maturity of 30 days.

Cash, cash equivalents and bank overdrafts include the following for the purposes of the cash flow statement:

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Cash and cash equivalents . . . . .	€9,726	€ 82	€ 20
Bank overdrafts . . . . .	(496)	(1,758)	(777)
Net cash and cash equivalents . . . . .	<u>€9,230</u>	<u>€(1,676)</u>	<u>€(757)</u>

## 12. Shareholders' equity

### Share capital

	<u>Number of issued shares</u>			<u>Share capital</u>			
	<u>Ordinary shares</u>	<u>Class AP</u>	<u>Class BP</u>	<u>Ordinary shares</u>	<u>Class AP</u>	<u>Class BP</u>	<u>Total</u>
					(in thousands)		
At 1 January 2003 . . . . .	€46,934	€ –	€ –	€ 47	€ –	€ –	€ 47
New shares issued . . . . .	–	–	–	–	–	–	–
At 31 December 2003 . . . . .	46,934	–	–	47	–	–	47
New shares issued . . . . .	–	–	–	–	–	–	–
At 31 December 2004 . . . . .	46,934	–	–	47	–	–	47
New shares issued . . . . .	–	53,752	14,863	–	54	15	69
At 31 December 2005 . . . . .	<u>€46,934</u>	<u>€53,752</u>	<u>€14,863</u>	<u>€47</u>	<u>€54</u>	<u>€15</u>	<u>€116</u>

The total authorised number of ordinary (“class C”) shares is 234,760 shares (2004 and 2003: 234,760 shares) with a par value of € 1.00 per share (2004 and 2003: € 1.00 per share). All issued ordinary shares are fully paid.

The non-convertible AP shares (“class A preference shares”) and the BP shares (“class B preference shares”) were issued on 19 January 2005 and have a par value of € 1.00 per share. The class BP shares were granted on the condition that the holder provided the Group with a subordinated loan of € 268.13 multiplied by the number of Class BP preference shares received (total of € 3,985). The contribution paid in excess of the nominal value of the Class AP preference shares is recorded as share premium. All issued preference shares are fully paid.

The AP shares are non-redeemable and have the same voting and dividend entitlements as the ordinary class C shares. The BP shares are non-redeemable and have the same voting entitlements as the ordinary class C shares. Out of the profits earned in the past financial year, first, if possible, an amount shall be paid to the holders of BP shares at a rate of one per cent (1%) of the nominal value of those shares. Any remaining profit is added to each of the profit reserves AP and C in proportion to the total nominal values of the issued classes of shares AP and C. In addition to these rights, the holders of the class AP and BP shares are entitled to be repaid their initial investments in the Company before any proceeds from a sale of the Company are allocated between the shareholders. Furthermore, the class AP and BP shareholders are prioritised over holders of ordinary shares in the event of liquidation of the Company.

No shares are held as treasury shares at 31 December 2003, 2004 and 2005.

#### *Share premium*

The total addition to share premium in 2005 amounts to € 13.1 million. The share premium paid by the Class AP shareholders amounts to € 14.4 million (€ 268.13 multiplied with 53,752 Class AP shares). This amount is reduced by € 1.2 million of expenses related to the issuance of the preference shares and € 0.1 million related to capital tax on issuance of share capital.

#### *Other reserves*

The costs of share options to employees and Management are recognised in the income statement, together with a corresponding increase in equity during the vesting period, taking into account (deferral of) corporate income taxes. The accumulated expense of share options recognised in the income statement is shown separately in the equity category “other reserves” in the “consolidated statement of changes in equity”. In the years presented in these financial statements, the Company did not have any legal or other types of reserves.

#### *Share options*

As part of the shareholders agreement dated 29 December 2004 between the Company and its shareholders, it was agreed to reserve 4,283 ordinary shares for the Company’s stock option plan. Under this plan, 3,314 stock options are outstanding at 31 December 2005 (31 December 2004: 3,765 and 31 December 2003: 1,756).

The exercise price of the granted options is higher than the market price of the shares on the date of the grant. Options are conditional on the employee completing a pre-defined number of years service (“the vesting period”). Each instalment of the Company’s graded vesting awards is treated as a separate share option grant. Consequently, the vesting periods for the individual instalments of the Company’s graded vesting awards vary between 1 and 4 years for options granted after 1 December 2004 and between 0 and 5 years for options granted before 1 December 2004. The options are exercisable from the grant date, but employees that have exercised options and leave the Company during the vesting period are obliged to sell the shares which they are entitled to. Furthermore, the proceeds (“the award”) that the employees receive will have to be partially repaid to the Company if the date of leaving is within the vesting periods.

The Group has no legal or constructive obligation to repurchase or settle the options in cash.

Movements in the number of share options outstanding and their related weighted average exercise prices are as follows:

	2005		2004		2003	
	Average exercise price in € per share	Number of options	Average exercise price in € per share	Number of options	Average exercise price in € per share	Number of options
At 1 January . . . . .	€350.06	3,765	€358.00	1,756	€358.00	1,295
Granted . . . . .	–	–	347.70	2,562	358.00	486
Forfeited . . . . .	358.00	(116)	358.00	(273)	358.00	(25)
Exercised . . . . .	–	–	–	–	–	–
Lapsed . . . . .	358.00	(335)	358.00	(280)	–	–
At 31 December . . . . .	€348.98	3,314	€350.06	3,765	€358.00	1,756

Share options outstanding at the end of the year have the following expiry year and exercise prices:

Expiry year	Exercise price in € per share	Share options		
		2005	2004	2003
2004 . . . . .	358.00	–	–	620
2005 . . . . .	358.00	65	491	590
2006 . . . . .	358.00	407	432	546
2007 . . . . .	371.41	490	490	–
2008 . . . . .	–	–	–	–
2009 . . . . .	342.50	2,352	2,352	–
		3,314	3,765	1,756

For further details on the options with an expiry date in 2005 but still included as outstanding options at 31 December 2005, reference is made to Note 32.

No options were granted during 2005. The fair value of options granted during 2004 determined using the Binomial valuation model was € 320 (2003: € 85). The significant inputs into the model for the options granted in 2004 were share prices in the range € 269.13 – 284.14 (2003: € 285.39 – 299.16) at the grant dates, annual risk-free interest rates between 2.92% and 3.15% (2003: 3.09% and 3.21%), volatility between 87% and 94% (2003: between 95% and 106%) and no expected dividend yields. The historical volatility used is based on the average of the historical weekly volatility of the peers over a period that agrees with the period of maturity. The exercise prices and option lives are disclosed above.

Since the Company is not listed, the share price is not readily available at the valuation date of the share option. The share prices used at the grant dates in 2003 and 2004 have been estimated by Management on basis of two valuations that were performed in conjunction with two venture capital rounds. The respective estimated share prices at the dates of these valuations were € 314.17 per share in December 2001 and € 269.13 per share in December 2004. These valuations were not performed contemporaneously with the option grants, but Management believes that the share price at the grant date is appropriately estimated by assuming the share price of the Company decreased linearly between December 2001 and December 2004.

#### *Warrants*

In 2003 and 2004 various parties (including employees and Management) guaranteed a loan made by a bank to the Group in a total amount of € 400 and provided loans to the Group totalling € 250. As part of the agreements, these parties had the option to receive an interest of 1.0% per month (based on the amount guaranteed or loan provided) or the lower interest of 0.5% per month and 140 warrants per € 100 per month.

In total 3,920 warrants have been granted as part of this arrangement (2003: 560 and 2004: 3,360). The warrants can be exercised between 1 June 2004 and 30 November 2008. The exercise price of these warrants was determined at € 550.00. No warrants have been exercised until 31 December 2005.

### **13. Convertible subordinated loan**

Following the shareholders' agreement on 29 December 2004, on 19 January 2005, a group of venture capital investors participated in the Company for an amount of € 18,250. In addition to the preference shares issued (see note 12), € 3,985 was provided to the Group as a subordinated convertible loan. The Company does not have an obligation to redeem the loan or to pay interest/dividends, except when normal dividends are paid to the other shareholders. The loan issuer is only entitled to collect any sums pursuant to the loan agreement if and to the extent the (other) investors receive any sums pursuant to their ownership of Class AP shares in the Company. The total amount of the subordinated convertible loan is therefore classified as equity in the consolidated financial statements.



#### 14. Deferred corporate income taxes

Deferred corporate income tax assets and liabilities are offset when there is a legally enforceable right to offset current tax assets against current tax liabilities and when the deferred corporate income taxes relate to the same fiscal authority. The offset amounts are as follows:

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Deferred corporate income tax assets: . . . . .			
– Deferred tax assets to be recovered after 1 year . . . . .	€–	€ –	€–
– Deferred tax assets to be recovered within 1 year . . . . .	–	–	–
	<u>–</u>	<u>–</u>	<u>–</u>
Deferred corporate income tax liabilities: . . . . .			
– Deferred tax liabilities to be recovered after 1 year . . . . .	–	353	–
– Deferred tax liabilities to be recovered within 1 year . . . . .	–	–	–
	<u>–</u>	<u>353</u>	<u>–</u>
Net deferred tax balance at the end of the year . . . . .	<u>€–</u>	<u>€353</u>	<u>€–</u>

The movement on the recognised deferred corporate income tax liability is as follows:

	<u>2005</u>	<u>2004</u> (in thousands)	<u>2003</u>
Beginning of the year . . . . .	€353	€ –	€–
Income statement charge/(credit) (Note 24) . . . . .	(353)	353	–
End of the year . . . . .	<u>€ –</u>	<u>€353</u>	<u>€–</u>

Deferred corporate income tax assets and liabilities are measured at the (substantially) enacted tax rates that are expected to apply to the period when the asset is realised or the liability is settled. For the Group's deferred corporate tax assets and liabilities, realisation is not expected before 2007 and therefore a corporate tax rate of 29.1% is used to calculate the deferred corporate tax assets and liabilities at 31 December 2005 (31 December 2004: 30.0% and 31 December 2003: 34.5%).

The movement in deferred corporate tax assets and liabilities during the year, without taking into consideration the offsetting of balances within the same tax jurisdiction, is as follows:

Deferred corporate tax liabilities:	<u>Deferral of gains on sale of PPE</u>	<u>Other</u> (in thousands)	<u>Total</u>
At 1 January 2003 . . . . .	€ –	€ –	€ –
Charged /(credited) to the income statement . . . . .	<u>–</u>	<u>–</u>	<u>–</u>
At 31 December 2003 . . . . .	–	–	–
Charged/(credited) to the income statement . . . . .	<u>481</u>	<u>14</u>	<u>495</u>
At 31 December 2004 . . . . .	481	14	495
Charged /(credited) to the income statement . . . . .	<u>(15)</u>	<u>7</u>	<u>(8)</u>
At 31 December 2005 . . . . .	<u>€466</u>	<u>€21</u>	<u>€487</u>

The deferral of gains on sale of property, plant and equipment (“*herinvesteringsreserve*”) relates to the taxable profit in the fiscal unity OctoPlus International Holding B.V. from the sale of a building in 2004. This building was subsequently leased back by the Group (see Note 7).

Deferred corporate tax assets:

	<u>Tax losses carried forward</u>	<u>Other</u> <u>(in thousands)</u>	<u>Total</u>
At 1 January 2003 . . . . .	€ –	€ –	€ –
Credited/(charged) to the income statement . . . . .	–	–	–
At 31 December 2003 . . . . .	–	–	–
Credited/(charged) to the income statement . . . . .	83	59	142
At 31 December 2004 . . . . .	83	59	142
Credited/(charged) to the income statement . . . . .	298	47	345
At 31 December 2005 . . . . .	€381	€106	€487

Deferred corporate income tax assets are recognised for tax loss carry-forwards to the extent that the realisation of the related tax benefit through the future taxable profits is probable. Currently, there is no expiry date in Dutch tax law related to tax loss carry-forwards. The total amounts of tax losses carried forward and corporate deferred tax assets as well as the amounts of recognised and unrecognised corporate deferred taxes per fiscal unity are as follows:

	<u>Tax losses carried forward</u>	<u>Deferred tax asset</u>	<u>Recognised</u>	<u>Not recognised</u>
	<u>(in thousands)</u>			
<b>At 31 December 2003</b>				
OctoPlus International Holding B.V. <sup>(1)</sup> . . . . .	€ 5	€ 2	€ –	€ 2
OctoShare B.V. <sup>(2)</sup> . . . . .	2,563	884	–	884
Chienna B.V. <sup>(3)</sup> . . . . .	1,646	558	–	568
	<u>4,214</u>	<u>1,454</u>	<u>–</u>	<u>1,454</u>
<b>At 31 December 2004</b>				
OctoPlus International Holding B.V. . . . .	277	83	83	–
OctoShare B.V. . . . .	2,971	891	–	891
Chienna B.V. . . . .	2,900	870	–	870
	<u>6,148</u>	<u>1,844</u>	<u>83</u>	<u>1,761</u>
<b>At 31 December 2005</b>				
OctoPlus International Holding B.V. . . . .	2,689	781	298	483
OctoShare B.V. . . . .	2,971	864	–	864
Chienna B.V. . . . .	4,911	1,429	–	1,429
	<u>€10,571</u>	<u>€3,074</u>	<u>€298</u>	<u>€2,776</u>

(1) At 1 March 2004 the fiscal unity OctoShare B.V. was merged with OctoPlus International Holding B.V., forming the fiscal unity OctoPlus International Holding B.V. OctoShed B.V. entered the fiscal unity on 16 April 2004 and since this date the Company constitutes a fiscal unity with all of its subsidiaries except for Chienna B.V.

(2) Deferred tax losses prior to 1 March 2004

(3) Chienna B.V. was acquired on 1 March 2003

## 15. Pension liabilities

The amounts recognised in the balance sheet for the defined benefit plan are determined as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Present value of funded obligations . . . . .	€924	€712	€526
Fair value of plan assets . . . . .	(794)	(566)	(386)
	130	146	140
Unrecognised actuarial losses . . . . .	(41)	(15)	(18)
Liability in the balance sheet . . . . .	<u>€ 89</u>	<u>€131</u>	<u>€122</u>

The amounts recognised in the income statement for the defined benefit plan are as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Current service cost . . . . .	€ 62	€ 83	€ 70
Interest cost . . . . .	45	39	30
Expected return on plan assets . . . . .	(40)	(31)	(23)
Other costs . . . . .	73	80	75
Total expense, included in "employee benefits" (Note 20) . . .	<u>€140</u>	<u>€171</u>	<u>€152</u>

The actual return on plan assets in 2005 was a loss of € 6 (2004: gain of € 2 and 2003: loss of € 14).

The movement in the liability recognised in the balance sheet is as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Beginning of the year . . . . .	€ 131	€ 122	€ 57
Total expense charged to the income statement . . . . .	140	171	152
Contributions (incl. other costs paid) . . . . .	(182)	(162)	(87)
End of the year . . . . .	<u>€ 89</u>	<u>€ 131</u>	<u>€122</u>

The principal actuarial assumptions used were as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
Discount rate . . . . .	5.00%	5.50%	5.75%
Expected return on plan assets . . . . .	5.00%	5.50%	5.75%
Rate of salary increases . . . . .	2.00%	2.00%	2.00%
Rate of pension benefit increases . . . . .	1.00%	1.50%	1.75%

Assumptions regarding future mortality experience have been set based on published statistics used by Dutch insurance companies ("collectief '93").

## 16. Borrowings and finance lease liabilities

	2005	2004	2003
		(in thousands)	
Non-current portion . . . . .	€ –	€ –	€ 554
Current portion . . . . .	–	–	109
Borrowings . . . . .	–	–	663
Non-current portion . . . . .	3,649	3,670	80
Current portion . . . . .	142	120	80
Finance lease liabilities . . . . .	3,791	3,790	160
ABN Amro Bank N.V., current account (see Note 11) . . . . .	496	1,758	–
ING Bank N.V., current account (see Note 11) . . . . .	–	–	777
Bank overdrafts . . . . .	€496	€1,758	€777

### *Borrowings*

The amount included under borrowings at 31 December 2003 is a Euro loan issued by ING Bank N.V. This loan was guaranteed by the Dutch government for 90% of the nominal amount. The duration was 12 years and the interest was fixed. As from April 2003 the interest was fixed at 4.8%. The redemption was € 28 per quarter, starting at 1 October 2001. The total remaining loan balance was early redeemed in 2004.

### *Finance lease liabilities*

Finance lease liabilities – minimum lease payments:

	2005	2004	2003
		(in thousands)	
No later than 1 year . . . . .	€ 500	€ 467	€ 81
Between 1 and 5 years . . . . .	1,693	1,632	88
Later than 5 years . . . . .	5,311	5,615	–
	7,504	7,714	169
Future finance charges on finance leases . . . . .	(3,713)	(3,924)	(9)
Present value of finance lease liabilities . . . . .	€3,791	€3,790	€ 160

The present value of finance lease liabilities is as follows:

	2005	2004	2003
		(in thousands)	
No later than 1 year . . . . .	€ 142	€ 120	€ 80
Between 1 and 5 years . . . . .	384	322	80
Later than 5 years . . . . .	3,265	3,348	–
	€3,791	€3,790	€160

Lease liabilities are effectively secured by the lessor as the rights to the leased asset revert to the lessor in the event of default.

### *Bank overdrafts*

The Company's subsidiary OctoPlus Development B.V., utilises a current account lending facility with ABN Amro Bank N.V. amounting to € 2.0 million for working capital and investment purposes. The following securities have been provided by OctoPlus Development B.V.:

- Pledge on equipment (book value at 31 December 2005: € 2,419 and 31 December 2004: € 2,366);
- Pledge on inventories and receivables (book value at 31 December 2005: € 1,360 and 31 December 2004: € 1,158);
- Joint and several liability of OctoPlus International Holding B.V.;
- In addition, the financing agreement included a covenant which required the shareholders' equity of OctoPlus Development B.V. to exceed 25% of its balance sheet total. No breaches of this covenant have occurred during 2003, 2004 and 2005.

The carrying amounts of short-term borrowings (bank overdrafts) approximate their fair values.

### *Effective interest rates and borrowing facilities*

The effective interest rates at the balance sheet date were as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
Bank overdrafts . . . . .	4.5%	4.5%	3.1%
Finance lease liabilities . . . . .	9.1%	8.9%	5.7%

At 31 December 2003, the Group utilised a current account lending facility with ING Bank N.V. amounting to € 831. The Group's only borrowing facility at 31 December 2004 and 2005 is the current account lending facility of OctoPlus Development B.V. amounting to € 2.0 million referred to above. The undrawn borrowing facility at the balance sheet date was as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
Undrawn borrowing facility (at floating rate) . . . . .	€1,504	(in thousands) €242	€54

## 17. Trade and other payables

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Trade payables . . . . .	€1,491	€1,079	€ 909
Non-current amounts due to related parties (Note 31) . . . . .	–	161	161
Current amounts due to related parties (Note 31) . . . . .	–	–	150
Debt to related parties . . . . .	–	161	311
Corporate income taxes . . . . .	2	–	–
Wage taxes . . . . .	204	194	78
Accrued social security costs . . . . .	33	27	21
Social security and other taxes . . . . .	239	221	99
Subsidies received in advance (Note 18) . . . . .	853	821	–
Deferred income . . . . .	147	766	551
Prepayments by customers . . . . .	745	844	320
Accrued expenses . . . . .	831	641	592
Other amounts to be paid . . . . .	67	145	537
	<u>2,643</u>	<u>3,217</u>	<u>2,000</u>
Non-current portion: Deferred income . . . . .	–	(30)	–
Other current liabilities . . . . .	<u>€2,643</u>	<u>€3,187</u>	<u>€2,000</u>

## 18. Income from subsidies and other income

### *Income from subsidies*

OctoPlus Technologies B.V. started a development project in the year 2001 of which the expected cost approximate € 7,432. For this project, SenterNovem, the department of the Ministry of Economic Affairs responsible for subsidies, has granted a technical development credit of 35% of the amounts spent between 30 January 2001 and 31 March 2005, which equals an amount of € 2,601. The partnership with SenterNovem for this project has been terminated in 2005 and the Group will finance the remaining amounts internally.

Further conditions with regard to the repayment of the technical development credit have been stipulated by SenterNovem and are dependent of net turnover resulting from this development project. Based on the contract with SenterNovem, the following redemption conditions have been agreed:

- Annually before 27 February of the following calendar year, during the development period and further from 2005 and during a maximum of 10 calendar years, an amount equal to 35% of the royalty fees and entrance fees resulting or derived from the development project.
- Within four weeks after receiving the final decision concerning the magnitude of the grant: 35% of the proceeds obtained by sale or otherwise of a null series, prototype, parts hereof or from other assets that have been financed by this grant.
- Within four weeks after receiving the final decision concerning the magnitude of the grant: 35% of the value of the assets financed with the grant and still can be used and are not used for the production of rendering services resulting from the grant.

The contract described above is the only subsidy contract of any OctoPlus legal entity with redemption conditions; i.e. a part of potential future revenues needs to be paid to SenterNovem. The total subsidy received

has been recognised as “income from subsidies” since it is non-refundable. A liability for the royalty fees will only be recognised when such payments become probable.

In 2002 a development project was commenced in association with Diatos S.A. (France). OctoPlus Technologies’ share of the estimated costs amounts to € 1,925. SenterNovem has granted € 1,155 subsidy for this project. The Group will finance the remainder.

In 2003 a development project was initiated in association with CytImmune Sciences Inc. (USA). OctoPlus Technologies’ share of the estimated cost amounts to € 2,007. SenterNovem has granted € 1,204 subsidy to this project. The Group finances the remainder of these costs. On 22 December 2004 OctoPlus and CytImmune Sciences Inc. agreed to terminate their collaboration in this project.

In 2004 in collaboration with the Thorax Centre of Erasmus University (Rotterdam, the Netherlands) OctoPlus Technologies B.V. commenced a 3-year research project for a novel approach to treat myocardial regeneration. Total costs of this project approximate € 3,250. SenterNovem has granted a subsidy of € 2,000 in order to relieve OctoPlus Technologies B.V.’s and Erasmus University’s burden in the costs. OctoPlus will finance the costs that exceed the € 2,000 subsidy. An advance of 25% of the total subsidy (€ 500) was received by OctoPlus in December 2004 and is recorded as “subsidies received in advance” under “other current liabilities” on the balance sheet at 31 December 2004 and 31 December 2005 (Note 17).

In 2004, OctoPlus Technologies B.V., in partnership with Utrecht University (Utrecht, the Netherlands), initiated a study for a second-generation drug delivery technology. For this study, a total subsidy of € 1,413 has been granted of which € 897 is allocated to OctoPlus Technologies B.V. (being 70% of its estimated expenditures) and € 516 is allocated to Utrecht University (being 60% of its estimated expenditures). The project is expected to run over a period of 3 years. An advance of 25% of the total subsidy (€ 353) was received by OctoPlus in December 2004 and is recorded as “subsidies received in advance” under “other current liabilities” on the balance sheet at 31 December 2004 and 31 December 2005 (Note 17).

In 2005, a development project was carried out in association with InnoCore Technologies B.V. The total estimated project costs amount to € 122 and OctoPlus Technologies B.V.’s share of the total project costs was € 54. SenterNovem granted in total € 50 in subsidy to this project.

#### *Other income*

Other income of € 26 in 2004 relates to a gain on sale of property, plant and equipment. No items were recorded as other income in 2003 and 2005.

### **19. Raw materials and auxiliaries and costs of contracted work**

The costs included in raw materials and auxiliaries are the materials used in production for customers. Costs of contracted work and other external charges include costs related to clinical studies, toxicology studies and other purchased research and development costs.

### **20. Employee benefits**

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Wages and salaries . . . . .	€3,994	€3,063	€2,938
Social security costs . . . . .	462	318	349
Share options granted to directors and employees (Note 12) . .	132	23	5
Pension costs – defined contribution plans . . . . .	30	22	6
Pension costs – defined benefit plans (Note 15) . . . . .	140	171	152
	<u>€4,758</u>	<u>€3,597</u>	<u>€3,450</u>
Number of employees at 31 December . . . . .	110	93	91

The wages and salaries are net of WBSO subsidies of € 337 (2004: € 312 and 2003: € 320).



## 21. Other costs

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Housing costs . . . . .	€ 540	€ 485	€ 785
Production costs . . . . .	957	663	758
Office expenses . . . . .	224	153	189
Selling & Marketing costs . . . . .	715	550	358
General expenses . . . . .	538	385	683
Other personnel costs . . . . .	1,239	431	502
	<u>€4,213</u>	<u>€2,667</u>	<u>€3,275</u>

In general, other costs have increased due to an increase in staff and activities of the Company. This is shown in particular in other personnel costs in 2005 by an increase of costs related to temporary employees, recruiting and training of personnel.

Housing costs in 2003 were significantly higher than in 2004 and 2005 as the company owning the building (OctoShed B.V.) was not part of the Group. The resulting operating lease charges are included under housing costs. Following the sale and leaseback transaction in 2004, as described under note 7, the Group entered into a finance lease agreement and the monthly rental charges for the building are recorded under depreciation and amortisation and interest charges from then onwards.

For leases where the Group is a lessee under operating leases, lease rentals amounting to € 233 (2004: € 109 and 2003: € 22) are included in “other costs” in the 2005 income statement.

## 22. Research and development costs

The costs directly attributable to research and development (as required disclosed under the Group’s accounting policies) recognised as costs in the income statement were as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Direct research and non-capitalised development costs . . . . .	€3,378	€2,261	€1,945

The Group’s total costs related to research and development including indirect costs are € 5.8 million (2005), € 3.7 million (2004) and € 3.3 million (2003).

## 23. Interest income and interest costs

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
<b>Interest income:</b>			
– Bank deposits . . . . .	€ 287	€ –	€ –
– Current accounts . . . . .	–	18	77
	<u>287</u>	<u>18</u>	<u>77</u>
<b>Interest expense:</b>			
– Bank borrowings, overdrafts and other debt . . . . .	(44)	(200)	(94)
– Finance leases . . . . .	(361)	(212)	(12)
	<u>(405)</u>	<u>(412)</u>	<u>(106)</u>
Finance costs – net . . . . .	<u>€(118)</u>	<u>€(394)</u>	<u>€(29)</u>

## 24. Corporate income taxes

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Current corporate income taxes . . . . .	€ -	€ -	€ -
Deferred corporate income taxes (Note 14) . . . . .	353	(353)	-
Tax (charge)/income . . . . .	<u>€353</u>	<u>€(353)</u>	<u>€ -</u>

The tax on the Group's profit before tax differs from the theoretical amount that would arise using the statutory corporate income tax rate in the Netherlands of 31.5% (2004 and 2003: 34.5%) to profits of the consolidated companies as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Result before corporate income tax . . . . .	€(4,562)	€(2,177)	€(2,236)
Tax calculated at domestic tax rates applicable to profits . . . . .	1,437	751	771
Income not subject to tax . . . . .	-	-	-
Expenses not deductible for tax purposes . . . . .	-	-	-
Deferred tax liability on fiscal reserve for re-investments . . . . .	481	(481)	-
Utilisation of previously unrecognised tax losses . . . . .	-	-	-
Deferred income tax assets not recognised (tax losses) . . . . .	(1,565)	(623)	(771)
Tax (charge)/income . . . . .	<u>€ 353</u>	<u>€ (353)</u>	<u>€ -</u>

## 25. Earnings per share

### Basic

Basic earnings per share is calculated by dividing the profit attributable to equity holders of the Company by the weighted average number of shares outstanding during the year.

The class AP and BP shares issued in 2005 are non-convertible preference shares with a par value of € 1.00 per share (i.e. the same par value as the existing class C ordinary shares). The holders of these shares do not have right to fixed preference dividends. However, out of the profits earned in the past financial year, first, if possible, an amount shall be paid to the holders of BP shares at a rate of one per cent (1%) of the nominal value of those shares. In addition the holders of the BP shares will receive interest on the subordinated convertible loan if and to the extent dividends are paid to the holders of class AP shares. Therefore the total amounts received by the holders of class BP shares become identical to the dividend percentage received by the class AP shareholders.

Class AP and BP shares have been included in the weighted average number of shares from 19 January 2005 (see Note 12).

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Result attributable to equity holders of the Company . . . . .	€ (4,209)	€(2,530)	€(2,236)
Weighted average number of ordinary class C shares . . . . .	46,934	46,934	46,934
Weighted average number of class AP shares . . . . .	50,954	-	-
Weighted average number of class BP shares . . . . .	14,089	-	-
	<u>€111,977</u>	<u>€46,934</u>	<u>€46,934</u>
Basic earnings per share (€ per share) . . . . .	€ (37.59)	€(53.91)	€(47.64)

### *Diluted*

Diluted earnings per share is calculated by adjusting the weighted average number of ordinary shares outstanding to assume conversion of all dilutive potential ordinary shares. The convertible subordinated debt does not represent potential ordinary shares since the holder is not entitled to ordinary shares in addition to the class BP shares issued in 2005 (Note 12). The Company has therefore two categories of dilutive potential ordinary shares: Share options and warrants.

For all years included in these financial statements, the share options and warrants are not included in the diluted earnings per share calculation as the Group was loss-making and the share options and warrants were “out-of-the-money” for all three years (i.e. the exercise prices are higher than the estimated average price of the ordinary shares). Consequently basic and diluted earning per share are the same.

## **26. Dividends per share**

The Company did not declare dividends for any of the years presented in these consolidated financial statements.

## **27. Cash flow statement**

In the cash flow statement, purchases of property, plant and equipment comprise:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		<i>(in thousands)</i>	
Additions according to Note 7 . . . . .	€1,088	€ 4,664	€710
Of which finance leases (non-cash) . . . . .	(164)	(3,740)	–
Purchases of property, plant and equipment . . . . .	<u>€ 924</u>	<u>€ 924</u>	<u>€710</u>

In the cash flow statement, proceeds from sale of property, plant and equipment comprise:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		<i>(in thousands)</i>	
Net book amount (Note 7) . . . . .	€ –	€ –	€ –
Gain on sale of property, plant and equipment . . . . .	–	26	–
Proceeds from sale of property, plant and equipment . . . . .	<u>€ –</u>	<u>€26</u>	<u>€ –</u>

In the cash flow statement, proceeds from issuance of shares comprise:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		<i>(in thousands)</i>	
Issue of share capital . . . . .	€13,199	€ –	€ –
Converted loan from Statutory Director (Note 31) . . . . .	(161)	–	–
Proceeds from issuance of shares . . . . .	<u>€13,038</u>	<u>€ –</u>	<u>€ –</u>

## **28. Contingencies**

### *Contingent consideration*

As a result of the acquisition of Chienna B.V. in 2003, the Group is obliged to make certain milestone payments up to 3 years after the acquisition date (1 March 2003) and has profit-sharing obligations during the patents terms. Up to 31 December 2005, milestone payments amounting to € 30 have been made. This resulted in a corresponding adjustment of goodwill in 2004. No profit-sharing payments have been made up to 31 December 2005. If and when profit-sharing payments have to be made during the remainder of the patents terms is uncertain and dependent on the commercial success of the Chienna technology.

### *Subsidies*

For the development project which started in 2001 (expected cost approximates € 7,432), repayment of the technical development subsidy from SenterNovem is dependent on the net turnover resulting from this development project. Further details on these conditions are provided in Note 18.

### *Royalties*

The Group is obliged to pay royalties to Utrecht University for revenues received based on the OctoDEX technology platform. Such royalties shall not exceed 2% of such revenues. Furthermore, Leiden University Medical Centre is entitled to certain royalty revenues. Depending on the cumulative revenues, the royalties vary from 30% for cumulative revenues less € 15 million to 12.5% once cumulative revenues have exceeded € 30 million.

## **29. Commitments**

### *Capital commitments*

At the balance sheet dates 31 December 2003, 2004 and 2005 there are no capital expenditures contracted for but not yet incurred.

### *Operating lease commitments*

The Group leases various plant and machinery under operating lease agreements. The lease expenditure charged to the income statement during the year is disclosed in Note 7.

The future aggregate minimum lease payments under non-cancellable operating leases are as follows:

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
No later than 1 year . . . . .	€165	€209	€509
Later than 1 year and no later than 5 years . . . . .	35	72	57
Later than 5 years . . . . .	93	100	–
	<u>€293</u>	<u>€381</u>	<u>€566</u>

## **30. Business combinations**

There were no business combinations effected during the years ending 31 December 2004 and 2005. For the business combination effected in 2003, please refer to Note 33 on “adoption of IFRS”.

## **31. Related-party transactions**

### *a) Shareholders*

At 31 December 2003, OctoShed B.V. was the direct parent of the Company (holder of 68% of the shares) and Holthuis-Bernaerts Holding B.V. the ultimate controlling party (holder of 100% of the shares in OctoShed B.V.). On 15 April 2004, OctoShed B.V. sold its shares in OctoPlus International Holding B.V. to Holthuis-Bernaerts Holding B.V.

Following the changes in shareholders in 2005, no individual party controls the Company. However, Holthuis-Bernaerts Holding B.V. has significant influence over the Company (27% of the voting rights). For further details on the changes in shareholders in 2005, reference is made to Note 12 and 13.

The following transactions were carried out with the shareholders:

<b>Transactions</b>	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Sale of services, royalty and license revenues . . . . .	€60	€ 60	€ –
Purchases of goods and services . . . . .	€ –	€140	€481

The “purchases of goods and services” relate to rental of office space from the direct parent of the Company, OctoShed B.V., until 15 April 2004. At this date the Company purchased the building from OctoShed B.V. For further details on this transaction, reference is made to Note 7.

Services are negotiated with related parties on an arm’s length basis.

<b>Receivables</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>
		(in thousands)	
Loan to OctoShed B.V. . . . . .	€ –	€ –	€908
Current account OctoShed B.V. . . . . .	–	–	94
Current account Holthuis-Bernaerts Holding B.V. . . . . .	€ –	€ 3	€ 1

As a part of the restructuring of the group in 2004, OctoShed B.V. has become a new group company (Note 7). Accordingly, the loan included in the balance sheet at 31 December 2003 has become an intra-group loan, which was eliminated upon consolidation.

<b>Loans from Shareholders</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>
		(in thousands)	
7X Life Science Fund B.V. (Note 17) . . . . .	€ –	€ –	€150

7X Life Sciences Fund granted the Company a loan that was redeemable per 30 November 2004 and carried 5% interest per annum. The loan was fully redeemed in 2004. As additional compensation for this loan, 7X Life Science Fund B.V. received 1,260 warrants in the Company (see Note 12).

*b) Supervisory Directors and Statutory Directors*

The remuneration of the Supervisory Directors amounts to € 15 (2004: € 40 and 2003: 39). The remuneration of the individual members of the Supervisory Board is set out in the table below:

	<b>Base salary</b>	<b>Other</b>	<b>2005 Total</b>	<b>2004 Total</b>	<b>2003 Total</b>
			(in thousands)		
H. Stellingsma (Chairman) . . . . .	€15	€ –	€15	€11	€11
R. Kuijten . . . . .	–	–	–	–	–
P. Toon . . . . .	–	–	–	–	–
Ph. Smith . . . . .	–	–	–	–	–
Former members . . . . .	–	–	–	29	28
	<b>€15</b>	<b>€ –</b>	<b>€15</b>	<b>€40</b>	<b>€39</b>

Mr. Stellingsma guaranteed a loan made by a bank to the Group in a total amount of € 150 from 1 December 2003 to 31 May 2004. This guarantee terminated on 31 May 2004. As compensation for this guarantee, Mr. Stellingsma received an interest rate of 1.0% per month.

The remuneration of Statutory Directors amounts to € 263 (2004: € 199 and 2003: € 180). The remuneration of the individual members of the Board of Management is set out in the table below:

	<b>Base salary</b>	<b>Bonus</b>	<b>Pensions</b>	<b>Other</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>
				(in thousands)			
J.J.M. Holthuis, CEO . . . . .	€175	€41	€20	€22	€258	€199	€180
J.C.H.L. Pauli, CFO . . . . .	125	11	10	–	146	122	63
	<b>€300</b>	<b>€52</b>	<b>€30</b>	<b>€22</b>	<b>€404</b>	<b>€321</b>	<b>€243</b>

Mr. Pauli was appointed to Statutory Director on 22 December 2004. The remuneration of Mr. Pauli in 2003 and 2004 was therefore not received in the position of Statutory Director of the Company.

The remuneration of Statutory Directors results in the following costs in the income statement related to key management compensation:

	2005	2004	2003
		(in thousands)	
Salaries and other short-term employee benefits . . . . .	€443	€321	€264
Post-employment benefits . . . . .	30	20	5
Share-based payments . . . . .	56	4	1
	€529	€345	€270

#### Loans from Statutory Directors

	2005	2004	2003
		(in thousands)	
J.J.M. Holthuis, Chief Executive Officer . . . . .	€ –	€161	€161

The loan provided by Mr. Holthuis was converted into 598 preference shares with a share price of € 269.13 as part of the private offering of the Company's securities in 2005 (see Note 12 and below).

#### Statutory Directors' interests in the Company

The Statutory Directors' own shares and have share options and warrant rights in the Company as follows:

	Shares	Options	Warrants
		(in thousands)	
<b>At 31 December 2003</b>			
J.J.M. Holthuis, CEO . . . . .	€30,172	€ –	€ –
J.C.H.L. Pauli, CFO . . . . .	–	200	210
	30,172	200	210
<b>At 31 December 2004</b>			
J.J.M. Holthuis, CEO . . . . .	30,172	735	–
J.C.H.L. Pauli, CFO . . . . .	–	571	1,260
	30,172	1,306	1,260
<b>At 31 December 2005</b>			
J.J.M. Holthuis, CEO . . . . .	30,895	735	–
J.C.H.L. Pauli, CFO . . . . .	379	571	1,260
	€31,274	€1,306	€1,260

#### Shares

Mr. Holthuis holds 30,895 shares in the Company through Holthuis-Bernaerts Holding B.V. (100% owned by Mr. Holthuis) and Mr. Pauli holds 379 shares in the Company at 31 December 2005 (2004 and 2003: 0 shares).

#### Share options

J.J.M. Holthuis, CEO, holds 735 share options (31 December 2004: 735 and 31 December 2003: 0 share options) in the Company at an exercise price of € 342.50. These options expire on 29 December 2009.

J.C.H.L. Pauli, CFO, holds share options in the Company as follows:

	2005		2004		2003	
	Average exercise price in € per share	Number of options	Average exercise price in € per share	Number of options	Average exercise price in € per share	Number of options
At 1 January . . . . .	€347.93	571	€358.00	200	€358.00	200
Granted . . . . .		–	342.50	371		–
Forfeited . . . . .		–		–		–
Exercised . . . . .		–		–		–
Lapsed . . . . .		–		–		–
At 31 December . . . . .		<u>571</u>	<u>€347.93</u>	<u>571</u>	<u>€358.00</u>	<u>200</u>

The outstanding share options held by Mr. Pauli expire as follows: 75 options on 31 January 2006, 125 options on 24 December 2006 and 371 options 29 December 2009. On 31 January 2006 Mr. Pauli exercised 75 share options with an exercise price of € 358.00 per share (Note 32).

### Warrants

In addition to stock options, Mr. Pauli holds a total of 1,260 warrants (31 December 2004: 1,260 and 31 December 2003: 210) in the Company at an exercise price of € 550. Mr. Pauli guaranteed a loan made by a bank to the Group in a total amount of € 150 during the period 1 December 2003 to 31 May 2004. This loan was repaid on 31 May 2004. As compensation for this guarantee, Mr. Pauli received an interest rate of 0.5% per month and a total of 1,260 warrants in the Company (see Note 12).

### 32. Events after the balance sheet date

#### *Equity transactions*

In 2005, 65 share options with an exercise price of € 358.00 per share were exercised. However, the formal registration of the share issuance did not take place until 1 March 2006. The related 65 share options have therefore been included as outstanding options at 31 December 2005 (Note 12).

In addition, 225 share options with an exercise price of € 358.00 per share were exercised on 31 January 2006. However, the formal registration of the share issuance has not yet taken place.

### 33. Adoption of IFRS

The Group has adopted International Financial Reporting Standards (“IFRS”), including International Accounting Standards (“IAS”) and interpretations issued by the International Accounting Standards Board (“IASB”) as adopted by the EU (“EU-IFRS”), as its primary accounting basis for the consolidated financial statements as from 1 January 2005. For the Group, there are no differences between EU-IFRS and IFRS since the carve-out sections are not applicable to the Group.

Until 2004, the Group prepared its consolidated financial statements in accordance with Generally Accepted Accounting Principles in the Netherlands (“Dutch GAAP”). Since the Group has decided to provide comparative figures for 2003 and 2004, the transition date to IFRS is 1 January 2003. The Group converted the 2003 and 2004 financial information in the consolidated financial statements to IFRS for comparison purposes.

#### *Transition to IFRS: IFRS 1 exemptions and exceptions*

IFRS 1, First-time Adoption of International Financial Reporting Standards requires the Group to determine its accounting policies according to IFRS and apply these retrospectively to determine its consolidated opening balance sheet under IFRS at the date of transition (1 January 2003). However, IFRS 1 allows a number of optional exemptions as well as requires the application of a number of mandatory exceptions to this general



principle. The exemptions and exceptions are set out below, including a short description of the choices made by the Group.

*Employee benefits (IAS 19)*

The Group elected the exemption not to retrospectively recalculate the pension liabilities under IAS 19 Employee Benefits. Accordingly all cumulative actuarial gains and losses in relation to the employee benefit plan were recognised directly in equity at 1 January 2003.

*Share-based payments (IFRS 2)*

In accordance with IFRS 1, the Group has only expensed share options that are granted after 7 November 2002 and vested after 1 January 2005. For other options granted, only additional disclosures have been provided.

*Other IFRS 1 exemptions and exceptions*

The following exemptions in IFRS 1 regarding retrospectively application of the Group's accounting policies under IFRS, were not applied by or are not applicable to the Group:

- Business combinations (IFRS 3);
- Fair value or revaluation as deemed cost (IAS 16);
- Cumulative translation differences (IAS 21);
- Compound financial instruments (IAS 32/39);
- Transition dates for subsidiaries, associates and joint ventures (IAS 28/31);
- Designation of previously recognised financial instruments (IAS 32/39);
- Insurance contracts (IFRS 4);
- Comparatives for financial instruments (IAS 32 and IAS 39);
- Changes in existing decommissioning, restoration and similar liabilities included in the cost of property, plant and equipment (IFRIC 1);
- Arrangements containing leases (IFRIC 4);
- Fair value measurement of “no active market” financial assets and financial liabilities (IAS 32/39); and
- Exploration and evaluation assets (IFRS 6).

IFRS 1 prohibits retrospective application of some aspects of other IFRS standards relating to:

- Derecognition of financial assets and financial liabilities (IAS 32/39);
- Hedge accounting (IAS 32/39);
- Estimates (IAS 8) ; and
- Assets classified as held for sale and discontinued operations (IFRS 5).

In accordance with the IFRS 1 provision regarding estimates, which is the only of the four mandatory exceptions applicable to the Group, estimates under IFRS at the date of transition to IFRS (1 January 2003) are consistent with estimates made for the same date under Dutch GAAP. Both existing estimates under Dutch GAAP and new estimates under IFRS reflect conditions that existed at the date of transition to IFRS and do not reflect any subsequent new information.

*Key Impact on 2003 and 2004 financial information*

Reconciliation of the result for 2004 and 2003 reported in the Dutch GAAP consolidated financial statements to the result for the year under IFRS:

	2004	2003
	(in thousands)	
Result for the year (before changes in accounting policies) . . . . .	€(1,083)	€(1,421)
Business combinations . . . . .	146	60
Intangible assets . . . . .	(188)	(67)
Revenue recognition . . . . .	(165)	(131)
Employee benefits . . . . .	(24)	–
Leases . . . . .	–	(1)
Share-based payments . . . . .	(23)	(5)
Corporate income taxes . . . . .	(1,193)	(671)
Result for the year (after changes in accounting policies) . . . . .	<u>€(2,530)</u>	<u>€(2,236)</u>

Reconciliation of the Group's shareholders' equity as reported in the consolidated financial statements under Dutch GAAP to its shareholders' equity under IFRS at 1 January 2003 and 31 December 2003 and 2004:

	31 Dec. 2004	31 Dec. 2003	1 Jan. 2003
	(in thousands)		
Equity (before changes in accounting policies) . . . . .	€ 1,243	€2,326	€3,747
Business combinations . . . . .	159	60	–
Intangible assets . . . . .	(582)	(394)	(327)
Revenue recognition . . . . .	(42)	123	254
Employee benefits . . . . .	(75)	(51)	(51)
Leases (incl. sale and leaseback transaction) . . . . .	(509)	(3)	(2)
Corporate income taxes . . . . .	(1,550)	(910)	(239)
Equity (after changes in accounting policies) . . . . .	<u>€(1,356)</u>	<u>€1,151</u>	<u>€3,382</u>

#### *Presentation*

In general, adoption of IFRS did not result in significant changes to the presentation of the Consolidated balance sheet, Income statement, Cash flow statement or the Consolidated statement of changes in equity.

However, the presentation and classification of accrued service revenue has changed under IFRS compared to Dutch GAAP. The revenue from services included in the line item "Change in Work in Progress" in the Dutch GAAP financial statements has been reclassified to "Service revenues" in the IFRS financial statements. Furthermore, the work in progress balance regarding the rendering of services, as presented under Dutch GAAP, is effectively a receivable (accrued revenues) from the customers and not inventory. Therefore, the work in progress balance in the IFRS balance sheet is presented under accrued revenues (within "other receivables, prepayments and accrued income") or deferred revenues (within "other current liabilities") in the IFRS financial statements and not under "Inventory".

#### *Business combinations*

The business combination effected in 2003 (Chienna B.V.) has been accounted for in accordance with IFRS 3, Business Combinations. Based on IFRS 3, the acquirer shall, at the acquisition date, allocate the cost of a business combination by recognising the acquiree's identifiable assets, liabilities and contingent liabilities that satisfy the recognition criteria at their fair values at that date. The purchase price allocation performed on basis of IFRS 3 resulted in an additional amount of € 167 being allocated to patents (in process research and development). Consequently, the amount of patents is € 167 higher and the amount of goodwill € 167 lower, at the acquisition date 1 March 2003, under IFRS compared to Dutch GAAP.

Under Dutch GAAP, the acquisition of OctoShed B.V. in 2004 was accounted for as a business combination. Under IFRS, the acquisition does not represent a business combination based on the criteria in IFRS 3 (see Note 7). The cost of the acquisition is allocated between the individual identifiable assets and liabilities based on their relative fair values at the date of acquisition and no goodwill is recorded. The goodwill

initially recognised (€ 165) and the goodwill amortisation recorded in 2004 (€ 23) under Dutch GAAP are therefore reversed under IFRS.

Under Dutch GAAP, acquired goodwill is capitalised and amortised. IFRS 3 requires goodwill not to be amortised, but to be subject to impairment testing annually, or more frequently if events or changes in circumstances indicate that the asset might be impaired. As a result, the goodwill amortisation recorded under Dutch GAAP amounting to € 122 in 2004 and € 60 in 2003 has been reversed under IFRS.

The Group conducted an impairment test of the goodwill at 31 December 2003, 31 December 2004 and 31 December 2005 in accordance with IAS 36, Impairment of Assets. No impairments were identified.

#### *Intangible assets*

Under IFRS, the expenses incurred to register patents, even though paid to an external party, are not considered the separate acquisition of a patent. The registration costs for patents are part of the expenditures for the research and development project they relate to. Therefore, registration costs for patents must be expensed as incurred as long as the research and development project does not yet meet the criteria for capitalisation. Consequently, the book values of patents amounting to € 575 at 31 December 2004, € 379 at 31 December 2003 and € 304 at 1 January 2003 have been reversed.

The expenses for formation of a company or issuance of shares cannot be distinguished from the cost of developing the business as a whole. Therefore, such items do not qualify as intangible assets as defined in IAS 38 and should not be capitalised. This resulted in an IFRS adjustment amounting to € 7 at 31 December 2004, € 15 at 31 December 2003 and € 23 at 1 January 2003.

#### *Revenue recognition*

Under Dutch GAAP, revenues from the sales of certain services were recognised based on the percentage of completion with zero profit method. Under IFRS, revenues on all services are recognised based on the percentage of completion method. As a result, accrued income at 31 December 2004 was increased by € 48, at 31 December 2003 by € 123 and at 1 January 2003 by € 254 compared to Dutch GAAP. Consequently, revenues for 2004 under IFRS are reduced by € 75 and revenues for 2003 by € 131 compared to Dutch GAAP.

Furthermore, under Dutch GAAP, an up-front payment for an option to use the Group's technology was recognised as revenue immediately. In line with the Group's IFRS policies when there are future support requirements or deliverables, revenue is recognised using a proportional performance basis over the term of the option period. Consequently, revenue amounting to € 90 recognised in 2004 under Dutch GAAP was deferred under IFRS and recognised over the option period (€ 60 in 2005 and € 30 in 2006). This results in € 90 higher deferred revenues in the balance sheet at 31 December 2004 and € 30 higher deferred revenue in the balance sheet at 31 December 2005.

#### *Employee benefits*

In accordance with IAS 19, the Group recognises the unfunded part of defined benefit obligations with respect to pensions and post-employment benefits. At the transition date 1 January 2003, the difference between the unfunded part of the IFRS employee benefit obligations and the pension provisions under Dutch GAAP was € 51, and is charged directly to equity in the IFRS opening balance. Furthermore, the pension provision at 31 December 2003 is increased by € 51 and the pension provision at 31 December 2004 is increased by € 75 compared to Dutch GAAP.

Under IFRS, the 2004 pension charge including interest expenses is € 24 higher than under Dutch GAAP. In 2003, the pension charge under IFRS is unchanged compared to Dutch GAAP.

#### *Share-based payments*

Under Dutch GAAP, the Group did not record any charges for employee share options since all of the options granted to employees were issued at an exercise price equal to the price of the Company's shares on the date of grant (the options were granted "at the money") or a higher exercise price.

In accordance with IFRS 2, Share-based Payment, the Group recognises compensation charges in its income statement for all employee share options using “the fair value method”. The compensation charges are recognised over the vesting period of the options, based upon the fair values of the options granted to the employees, with a corresponding increase in shareholders' equity. This resulted in an additional expense of € 23 in 2004 and € 5 in 2003 compared to Dutch GAAP. However, this has no impact on total equity since the recognition of an expense results in a corresponding increase directly in equity.

*Leases (incl. sale and leaseback transaction)*

Under IFRS, the acquisition of OctoShed B.V. in 2004 does not represent a business combination based on the criteria in IFRS 3. The cost of the acquisition is allocated between the individual identifiable assets and liabilities based on their relative fair values at the date of acquisition and no goodwill is recorded. The goodwill initially recognised under Dutch GAAP is therefore reversed. In addition, the book values of the building and other items of property, plant and equipment are lowered to the allocated cost that was actually paid for the acquisition of OctoShed B.V. These IFRS adjustments resulted in € 507 lower equity at 31 December 2004.

The related impact on the income statement for 2004 is presented in the line “business combinations” in the reconciliation of the result for 2004 (€ 47 lower costs compared to Dutch GAAP, of which reversal of the amortisation of goodwill amounts to € 23).

In addition some of the Group's lease contracts have been reclassified from operational leases to finance leases, which did not result in any significant impact on equity or the result for the years presented.

*Taxation*

Under Dutch GAAP, the Group recognised deferred corporate income tax assets amounting to € 1,640 at 31 December 2004, € 910 at 31 December 2003 and € 246 at 1 January 2003.

Under IFRS, the existence of unused tax losses is strong evidence that future taxable profit may not be available. Therefore, when an entity has a history of recent losses, the entity recognises a deferred tax asset arising from unused tax losses or tax credits only to the extent that the entity has sufficient taxable temporary differences or there is convincing other evidence that sufficient taxable profit will be available against which the unused tax losses or unused tax credits can be utilised by the entity. Management has concluded that sufficient “convincing other evidence” is not available and has therefore only recognised deferred tax assets to the extent that the fiscal unities have taxable temporary differences.

As described in the paragraph above regarding leases, the acquisition of OctoShed B.V. does not qualify as a business combination. Since the acquisition does not affect accounting or taxable profit either, no deferred tax liability is accounted for under IFRS. However, the subsequent sale and leaseback transaction did result in a taxable gain. The tax effect on this gain was deferred by creating a fiscal provision (“herinvesteringsreserve”). The deferred tax liability from this transaction is valued against 30% at 31 December 2004 (since it will be settled after 2007) and not discounted. Therefore, a deferred tax liability of € 481 was recognised, which was partly offset with the deferred tax asset from tax losses carried forward in the same fiscal unity. This resulted in a net deferred tax liability of € 353 recognised in the IFRS balance sheet at 31 December 2004, and a tax expense in the IFRS income statement for 2004 of € 353 (2003: € 0).

The remaining deferred corporate income tax assets recognised under Dutch GAAP, for which the Group does not have taxable temporary differences available, have been reversed in the IFRS financial statements. The related impact on the income statement for 2004 is a reversal of deferred tax income amounting to € 1,193 (2003: € 671).

In addition, the IFRS conversion has resulted in temporary differences between the carrying amount of assets and liabilities and their tax bases. However, this did not result in a tax effect on the IFRS opening equity at 1 January 2003 since the Group only recognises deferred tax assets to the extent that the fiscal unities have taxable temporary differences available to net these with. This was not the case at 1 January 2003.

## COMPANY-ONLY FINANCIAL STATEMENTS

### Balance sheet of OctoPlus International Holding B.V.

	Note	At 31 December		
		2005	2004	2003
		(in thousands)		
<b>ASSETS</b>				
<b>Non-current assets</b>				
Land and buildings . . . . .	E	€ 3,246	€ 3,364	€ –
Receivables from related parties . . . . .	F	1,062	1,062	1,062
		<u>4,308</u>	<u>4,426</u>	<u>1,062</u>
<b>Current assets</b>				
Receivables from related parties . . . . .		12,163	3,977	–
Social security and other taxes . . . . .		308	14	11
Other receivables, prepayments and accrued income . . . . .		187	45	8
Cash and cash equivalents . . . . .		8,618	–	3,015
		<u>21,276</u>	<u>4,036</u>	<u>3,034</u>
<b>Total assets</b> . . . . .		<u>25,584</u>	<u>8,462</u>	<u>4,096</u>
<b>EQUITY</b>				
Issued share capital . . . . .	G	116	47	47
Share premium reserve . . . . .	G	17,876	4,746	4,746
Convertible subordinated loan . . . . .	G	3,985	–	–
Other reserves . . . . .	G	160	28	5
Retained earnings . . . . .	G	(10,386)	(6,177)	(3,647)
Total equity . . . . .		<u>11,751</u>	<u>(1,356)</u>	<u>1,151</u>
<b>LIABILITIES</b>				
<b>Non-current liabilities</b>				
Deferred corporate income tax liabilities . . . . .		–	353	5
Provisions for group companies . . . . .	H	9,985	5,022	2,853
Finance lease liabilities . . . . .		3,557	3,616	–
		<u>13,542</u>	<u>8,991</u>	<u>2,858</u>
<b>Current liabilities</b>				
Current portion of non-current liabilities . . . . .		58	54	–
Trade payables . . . . .		80	85	81
Debt to related parties . . . . .		–	649	–
Social security and other taxes . . . . .		89	18	–
Other current liabilities . . . . .		64	21	6
		<u>291</u>	<u>827</u>	<u>87</u>
Total liabilities . . . . .		<u>13,833</u>	<u>9,818</u>	<u>2,945</u>
<b>Total equity and liabilities</b> . . . . .		<u>€25,584</u>	<u>€8,462</u>	<u>€4,096</u>

**Income statement of OctoPlus International Holding B.V.**

	Note	Year ending 31 December		
		2005	2004	2003
Income from subsidiaries after taxes . . . . .		€(4,963)	€(2,169)	€(2,216)
Other results of OctoPlus International Holding B.V. after taxes . . . . .		754	(361)	(20)
Net result . . . . .		<u>€(4,209)</u>	<u>€(2,530)</u>	<u>€(2,236)</u>

## NOTES TO THE COMPANY-ONLY FINANCIAL STATEMENTS

### A. General

The company-only financial statements are part of the 2005 financial statements of OctoPlus International Holding B.V.

With reference to the company-only income statement of OctoPlus International Holding B.V., use has been made of the exemption pursuant to Section 402 of Book 2 of the Netherlands Civil Code.

#### *2. Principles for valuation and determination of the result*

For setting the principles for the recognition and measurement of assets and liabilities and determination of the result for its company-only financial statements, OctoPlus International Holding B.V. makes use of the option provided in Section 2:362 (8) of the Netherlands Civil Code. This means that the principles for the recognition and measurement of assets and liabilities and determination of the result (hereinafter referred to as “accounting policies”) of the company-only financial statements of OctoPlus International Holding B.V. are the same as those applied for the consolidated EU-IFRS financial statements. These consolidated EU-IFRS financial statements are prepared according to the standards laid down by the International Accounting Standards Board and adopted by the European Union. Please see the notes to the consolidated financial statements for a description of these principles.

Investments in subsidiaries are in the company-only financial statements stated at net asset value if the Company effectively exercises influence of significance over the operational and financial activities of these investments. The net asset value is determined on the basis of the accounting principles applied by the Company. In case the net asset value of an investment in subsidiaries is negative, a provision for group companies has been set up. By setting up a provision in these cases, reconciliation is maintained between the Group’s and the Company’s equity.

### B. Change in accounting policies

As a result of the application of the accounting policies used in the consolidated financial statements in the company-only financial statements, the Company has implemented a change in accounting policies in the company-only financial statements. This change in accounting policies is the result of applying the option in Section 2:362 (8) of the Netherlands Civil Code. By applying this option, reconciliation is maintained between the Group’s and the Company’s equity.

The company-only financial statements were previously prepared in compliance with accounting policies referred to in Part 9, Book 2 of the Netherlands Civil Code and Dutch GAAP. The change in accounting policies, which is treated retrospectively, has had an effect on equity and results. Comparative figures have been adjusted on the basis of the changed valuation principles.



### C. Effect of change in accounting policies on the income statement

The table below reconciles result for the year before and after changes in accounting policies for 2003 and 2004:

	<u>2004</u>	<u>2003</u>
	(in thousands)	
Result for the year (before changes in accounting policies) . . . . .	€(1,083)	€(1,421)
Changes in accounting policies:		
Group companies . . . . .	(1,478)	(816)
OctoPlus International Holding B.V. . . . .	31	1
Total changes . . . . .	<u>(1,447)</u>	<u>(815)</u>
Result for the year (after changes in accounting policies) . . . . .	<u>€(2,530)</u>	<u>€(2,236)</u>

For a detailed discussion of the changes, reference is made to the consolidated financial statements.

### D. Effect of change in accounting policies on equity

The table below reconciles the equity before and after changes in accounting policies for 2003 and 2004:

	<u>31 Dec. 2004</u>	<u>31 Dec. 2003</u>	<u>1 Jan. 2003</u>
	(in thousands)		
Equity (before changes in accounting policies) . . . . .	€ 1,243	€2,326	€3,747
Changes in accounting policies:			
Group companies . . . . .	(2,362)	(1,160)	(365)
OctoPlus International Holding B.V. . . . .	(237)	(15)	–
Total changes . . . . .	<u>(2,599)</u>	<u>(1,175)</u>	<u>(365)</u>
Equity (after changes in accounting policies) . . . . .	<u>€(1,356)</u>	<u>€1,151</u>	<u>€3,382</u>

For a detailed discussion of the changes, reference is made to the consolidated financial statements.

### E. Property, plant and equipment

Land and buildings are the only items of property, plant and equipment owned by OctoPlus International Holding B.V. For further details, reference is made to note 7 of the consolidated financial statements.

### F. Receivables from related parties

	<u>2005</u>	<u>2004</u>	<u>2003</u>
	(in thousands)		
OctoShed B.V. . . . .	€ 908	€ 908	€ 908
OctoPlus Sciences B.V. . . . .	154	154	154
	<u>€1,062</u>	<u>€1,062</u>	<u>€1,062</u>

The loan to OctoShed B.V. was issued in 1999, and the loan to OctoPlus Sciences B.V. was issued in 2003. These loans are liable to 6% interest per year and have to be fully redeemed at 1 June 2008.

### G. Shareholders' equity

The Company has applied Section 2:362 (8) of the Netherlands Civil Code, and therefore the reconciliation is maintained between the Group's equity and the Company's equity. For details of the movements in and

components of equity, reference is made to the “Statement of changes in equity” and Note 12 and 13 of the consolidated financial statements.

The convertible subordinated loan of € 3,985 was provided to OctoPlus Technologies B.V. under terms and conditions allowing this convertible subordinated loan to be accounted for in the Company’s equity. Further details are provided in Note 13 of the consolidated financial statements

No part of the Company’s equity is classified as legal reserves.

For details of the movements in stock options, reference is made to Note 12 of the consolidated financial statements.

#### **H. Provisions for group companies**

This relates to a provision for 100% participation in the issued and fully paid-up capital of OctoShare B.V., Leiden.

	<u>2005</u>	<u>2004</u>	<u>2003</u>
		(in thousands)	
Provision at 1 January . . . . .	€5,022	€2,853	€ 637
Loss current year . . . . .	4,963	2,169	2,216
Provision at 31 December . . . . .	<u>€9,985</u>	<u>€5,022</u>	<u>€2,853</u>

#### **I. Remuneration of Directors and Supervisory Directors**

The remuneration of the Supervisory Directors amounts to € 15 (2004: € 40 and 2003: € 39). For further details, reference is made to Note 31 of the consolidated financial statements.

The remuneration of Statutory Directors amounts to € 404 (2004: € 321 and 2003: € 180). For further details, reference is made to Note 31 of the consolidated financial statements.

## OTHER INFORMATION

### Statutory arrangement concerning the appropriation of the profit

In article 32 of the articles of association, the following has been stated concerning profits:

- 32.1 The company shall maintain separate profits reserves for the benefit of the holders of the relevant classes of shares, namely, (i) a profit reserve C for the holders of the C shares, and (ii) a profit reserve AP for the holders of the AP shares.

Out of the profits earned in the past financial year, first, if possible, an amount shall be paid to the holders of BP shares at a rate of one per cent (1%) of the nominal value of those shares.

The profits of the company remaining after the previous sentence shall be added to each of the profit reserves AP and C in proportion to the total nominal values of the issued classes of shares AP and C.

If AP shares are converted into C shares, an amount pro rata the number of converted shares in relation to the total number of issued AP shares before the conversion shall be transferred from the profit reserve AP to the profit reserve C, provided however that in case the amount to be added from profit reserve AP to profit reserve C per AP share to be converted shall be lower than the amount of profit reserve C divided by the total number of C shares issued prior to the conversion, and no distribution out of profit reserve C will be made to take away the difference, then the Company will earmark such portion of profit reserve C such that the remaining amount of profit reserve C shall be equal to the amount to be added from profit reserve AP to profit reserve C per AP share to be converted multiplied by the number of class C shares issued prior to the conversion, which earmarked amount will be exclusively reserved for distribution to the holders of these class C shares already issued.

- 32.2 The company can only make distributions to the extent its equity exceeds the paid and called up part of the capital increased with the reserves, which must be maintained pursuant to the law.
- 32.3 With due observance of the provisions of paragraph 2, the general meeting may resolve to make distributions out of the profit reserves, provided that payment to the holders of C shares can only be made out of profit reserve C after the entire profit reserve AP has been paid to the holders of AP shares. Such a resolution shall at all times require the approval of the APBP Meeting, by which the resolution to approve must be passed by a two-thirds (2/3) majority of the valid votes cast in the APBP Meeting.
- 32.4 The general meeting may, with due observance of the provisions of paragraphs 2 and 3, resolve to pay, wholly or partly, dividends other than in cash, provided that such a resolution requires at all times the prior approval of the APBP Meeting, by which the resolution must be passed by a two-thirds (2/3) majority of the valid votes cast in the APBP Meeting.
- 32.5 For the calculation of the amount to be distributed on the shares, the shares held by the company in its own capital shall not be taken into account.
- 32.6 A claim of a shareholder to receive a distribution expires after five years.

### Proposed result appropriation for the financial year 2005

The General Meeting of Shareholders will be proposed to debit retained earnings with the loss for 2005 of € 4,209. The financial statements reflect this proposal.

**Events after balance sheet date***Equity transactions*

In 2005, 65 share options with an exercise price of € 358.00 per share were exercised. However, the formal registration of the share issuance did not take place until 1 March 2006. The related 65 share options have therefore been included as outstanding options at 31 December 2005 (Note 12).

In addition, 225 share options with an exercise price of € 358.00 per share were exercised on 31 January 2006.

**Adoption and approval of the annual accounts 2005**

The annual accounts 2005 have been approved by the shareholders on April 21st, 2006.

**OctoPlus International Holding B.V.**

**INTERIM FINANCIAL REPORT**

**30 June 2006 and 2005**

Date  
August 31, 2006

From

Reference  
HV/mv/1-2ra/  
3100101130-006

## Review report

### Introduction

We have reviewed the condensed consolidated balance sheets of OctoPlus International Holding B.V. as of 30 June 2006 and 31 December 2005, and the related condensed consolidated income statement for the six-month periods ended 30 June 2006 and 2005, the condensed statement of changes in equity and the condensed cash flow statement and the notes thereon (F-57 to F-64) for the six-month periods ended 30 June 2006 and 2005. These interim financial statements are the responsibility of the Company's management. Our responsibility is to issue a report on these interim financial statements based on our review.

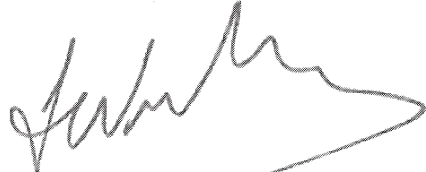
### Scope

We conducted our review in accordance with the standard for review engagements published by the International Auditing and Assurance Standards Board. These standards require that we plan and perform the review to obtain moderate assurance about whether the interim financial statements are free of material misstatement. A review is limited primarily to inquiries of company personnel and analytical procedures applied to financial data and therefore provides less assurance than an audit conducted in accordance with International Auditing Standards and the standards generally accepted in the Netherlands. We have not performed an audit and, accordingly, we do not express an audit opinion.

### Opinion

Based on our review, nothing has come to our attention that causes us to believe that the interim financial statements do not comply with IAS 34 Interim Financial Reporting.

Deloitte Accountants B.V.



J. Verloop RA

**CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**  
**30 JUNE 2006 AND 2005**



**CONDENSED CONSOLIDATED BALANCE SHEET**  
**AT 30 JUNE 2006 AND 31 DECEMBER 2005**

	Note	At 30 June 2006	At 31 December 2005
		(in thousands)	
Intangible fixed assets . . . . .		€ 1,725	€ 1,705
Property, plant and equipment . . . . .		6,347	6,273
Financial fixed assets . . . . .		16	16
		<u>8,088</u>	<u>7,994</u>
Cash and cash equivalents . . . . .	3	4,960	9,726
Other current assets . . . . .	4	3,802	2,780
		<u>8,762</u>	<u>12,506</u>
<b>Total assets</b> . . . . .		<u><u>16,850</u></u>	<u><u>20,500</u></u>
Equity . . . . .	5	8,456	11,751
Non-current liabilities . . . . .		3,711	3,738
Current liabilities . . . . .		4,683	5,011
<b>Total equity and liabilities</b> . . . . .		<u><u>€16,850</u></u>	<u><u>€20,500</u></u>

**CONDENSED CONSOLIDATED INCOME STATEMENT FOR THE PERIOD ENDED  
30 JUNE 2006 AND 2005**

	Note	Six months ending 30 June	
		2006	2005
		(in thousands)	
Service revenues . . . . .		€ 3,156	€ 3,300
Royalty and license revenues . . . . .		30	30
Income from subsidiaries . . . . .	6	92	236
Other income . . . . .		1	–
<b>Total revenues</b> . . . . .		3,279	3,566
Raw materials and auxiliaries . . . . .		100	47
Cost of contracted work and other external charges . . . . .	7	1,147	416
Employee benefits . . . . .	8	2,920	2,155
Depreciation and amortisation . . . . .		512	451
Other costs . . . . .	9	2,597	1,962
<b>Total operating costs</b> . . . . .		7,276	5,031
<b>Operating loss</b> . . . . .		(3,997)	(1,465)
Interest . . . . .	10	(104)	(27)
<b>Result before corporate income taxes</b> . . . . .		(4,101)	(1,492)
Corporate income taxes . . . . .	11	–	353
<b>Result for the year</b> . . . . .		(4,101)	(1,139)
<b>Attributable to:</b>			
Equity holders of the Company . . . . .		(4,101)	(1,139)
<b>Result per share for result attributable to the equity holders of the Company during the year (expressed in € per share)</b>			
– basic . . . . .		(35.47)	(10.51)
– diluted . . . . .		€(35.47)	€(10.51)

**CONDENSED CONSOLIDATED STATEMENT OF CHANGES IN EQUITY FOR THE PERIOD  
ENDED 30 JUNE 2006 AND 2005**

	Note	Attributable to equity holders of the Company					
		Share capital	Share premium reserve	Other reserves	Retained earnings	Convertible loan	Total equity
(in thousands)							
Balance at 1 January 2005		€ 47	€4,746	€ 28	€(6,177)	€ –	€(1,356)
Result for 6 month period ending 30 June 2005		–	–	–	(1,139)	–	(1,139)
Total recognised income for 6 month period ending 30 June 2005		–	–	–	(1,139)	–	(1,139)
<b>Employee share option scheme:</b>							
– value of employee services		–	–	66	–	–	66
Issue of share capital	5	69	13,130	–	–	–	13,199
Convertible subordinated loan	5	–	–	–	–	3,985	3,985
		69	13,130	66	–	3,985	17,250
Balance at 30 June 2005		116	17,876	94	(7,316)	3,985	14,755
Balance at 1 July 2005		116	17,876	94	(7,316)	3,985	14,755
Result for 6 month period ending 31 December 2005		–	–	–	(3,070)	–	(3,070)
Total recognised income for 6 month period ending 31 December 2005		–	–	–	(3,070)	–	(3,070)
<b>Employee share option scheme:</b>							
– value of employee services		–	–	66	–	–	66
Issue of share capital	5	–	–	–	–	–	–
Convertible subordinated loan	5	–	–	–	–	–	–
		–	–	66	–	–	66
Balance at 31 December 2005		116	17,876	160	(10,386)	3,985	11,751
Balance at 1 January 2006		116	17,876	160	(10,386)	3,985	11,751
Result for 6 month period ending 30 June 2006		–	–	–	(4,101)	–	(4,101)
Total recognised income for 6 month period ending 30 June 2006		–	–	–	(4,101)	–	(4,101)
<b>Employee share option scheme:</b>							
– value of employee services		–	–	33	–	–	33
Issue of share capital	5	2	607	–	–	–	609
Convertible subordinated loan	5	–	–	–	–	164	164
		2	607	33	–	164	806
Balance at 30 June 2006		€118	€18,483	€193	€(14,487)	€ 4,149	€8,456

**CONDENSED CONSOLIDATED CASH FLOW STATEMENT FOR THE PERIOD ENDED  
30 JUNE 2006 AND 2005**

	Note	Six months ending 30 June	
		2006	2005
		(in thousands)	
<b>Cash flows from operating activities</b>			
Result before corporate income taxes . . . . .		€ (4,101)	€ (1,492)
Adjustments for: . . . . .			
– Depreciation and amortisation . . . . .		512	451
– Share-based payments . . . . .		33	66
– Change in pension provision . . . . .		37	(62)
– Changes in working capital . . . . .		(1,160)	(1,000)
Net cash used in operating activities . . . . .		(4,679)	(2,037)
<b>Cash flows from investing activities</b> . . . . .		(606)	(725)
<b>Cash flows from financing activities</b> . . . . .	5	29	17,040
<b>Cash, cash equivalents and bank overdrafts</b>			
Net (decrease)/ increase in cash and cash equivalents . . . . .		(5,256)	14,278
Cash and cash equivalents at 1 January . . . . .		9,230	(1,676)
Cash and cash equivalents at 30 June . . . . .	3	€ 3,974	€ 12,602

## NOTES TO THE CONDENSED CONSOLIDATED FINANCIAL STATEMENTS FOR THE PERIOD ENDED 30 JUNE 2006 AND 2005

### 1. Summary of significant accounting policies

The principal accounting policies applied in the preparation of these condensed consolidated interim financial statements are set out below. These policies have been consistently applied to all the years presented, unless otherwise stated.

#### *1.1 Basis of preparation*

The condensed consolidated interim financial statements have been prepared in accordance with International Accounting Standard (IAS) 34, Interim Financial Reporting.

The condensed consolidated interim financial statements have been prepared under the historical cost convention. Furthermore, the condensed consolidated interim financial statements are presented in euros and all values are rounded to the nearest thousand except when otherwise indicated.

The preparation of condensed consolidated financial statements in conformity with IFRS requires the use of certain critical accounting estimates. It also requires management to exercise its judgement in the process of applying the Groups' accounting policies. The areas involving a higher degree of judgement or complexity or areas where assumptions and estimates are significant to the condensed consolidated financial statements are disclosed in the notes to the annual report 2005.

The accounting policies adopted are consistent with those followed in the preparation of the Group's annual financial statements for the year ended 31 December 2005.

#### *1.2 Consolidation*

- The Company is the holding company of a group of companies. The other consolidated group companies ("subsidiaries") are:
- OctoShare B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Development B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Technologies B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoPlus Sciences B.V., 100%, having its legal seat in Leiden, the Netherlands
- OctoShed B.V., 100%, having its legal seat in Leiden, the Netherlands
- Chienna B.V., 100%, having its legal seat in Bilthoven, the Netherlands
- OctoPlus Inc., 100%, having its legal seat in Delaware, United States of America

## 2. Segment information

The segment results for the six month period ending 30 June 2006 are as follows:

	Contract development	Drug delivery and products	Unallocated	Group
	(in thousands)			
Total gross segment revenues . . . . .	€ 4,111	€ 30	€ –	€ 4,141
Inter-segment revenues . . . . .	(955)	–	–	(955)
Subsidies and other income . . . . .	–	92	1	93
Revenues . . . . .	<u>3,156</u>	<u>122</u>	<u>1</u>	<u>3,279</u>
Operating result . . . . .	258	(4,217)	(38)	(3,997)
Finance costs – net . . . . .				(104)
Result before corporate income tax . . . . .				(4,101)
Corporate income taxes . . . . .				–
Result for the year . . . . .				<u>€ (4,101)</u>

The segment results for the six month period ending 30 June 2005 are as follows:

	Contract development	Drug delivery and products	Unallocated	Group
	(in thousands)			
Total gross segment revenues . . . . .	€ 3,438	€ 96	€ –	€ 3,534
Inter-segment revenues . . . . .	(204)	–	–	(204)
Subsidies and other income . . . . .	–	236	–	236
Revenues . . . . .	<u>3,234</u>	<u>332</u>	<u>–</u>	<u>3,566</u>
Operating result . . . . .	372	(1,837)	–	(1,465)
Finance costs – net . . . . .				(27)
Result before corporate income tax . . . . .				(1,492)
Corporate income taxes . . . . .				353
Result for the year . . . . .				<u>€ (1,139)</u>

## 3. Cash and cash equivalents

Cash, cash equivalents and bank overdrafts include the following for the purposes of the cash flow statement:

	At 30 Jun 2006	At 31 Dec 2005	At 30 Jun 2005
	(in thousands)		
Cash and cash equivalents . . . . .	€4,960	€9,726	€13,200
Bank overdrafts . . . . .	(986)	(496)	(598)
Net cash and cash equivalents . . . . .	<u>€3,974</u>	<u>€9,230</u>	<u>€12,602</u>

## 4. Current assets

The increase in other current assets relates to the issuance of new AP and BP shares (see note 5 below) on 29 June 2006 for an amount of approximately €750. The related funds were not received until 4 July 2006 and the €750 is therefore classified under other current assets.

## **5. Equity**

The non-convertible AP shares (“class A preference shares”) and the BP shares (“class B preference shares”) were issued on 19 January 2005 and have a par value of €1.00 per share. The class BP shares were granted on the condition that the holder provided the Group with a subordinated loan of €268.13 multiplied by the number of Class BP preference shares received (amounting to €4,149 per 30 June 2006). The contribution paid in excess of the nominal value of the Class AP preference shares is recorded as share premium. All issued preference shares are fully paid. The net proceeds of the issuance of these shares and subordinated loan amounted to € 17,040.

The number of outstanding shares per December 31, 2005 was 115,549, comprising of 46,934 Ordinary shares, 53,752 Class AP preferred shares and 14,863 Class BP preferred shares.

As a result of the January 2005 investment agreement, additional shares were issued in June 2006. As a consequence, the number of Class AP preferred shares increased with 2,177 shares to 55,929 shares per 30 June 2006 and the number of Class BP preferred shares increased with 609 shares to 15,472 shares per 30 June 2006.

Because of exercising options in the first six months of 2006, the number of ordinary shares increased with 65 shares to 46,999 per 30 June 2006.

As of 31 January 225 options with an exercise price of € 358.00 per share were exercised. Since the issuance of these shares has not taken place yet, these shares are not taken into the number of outstanding shares as of 30 June 2006.

## **6. Income from subsidies**

Income from subsidies decreased from €236 for the first six months of 2005 to €92 for the first six months of 2006 as a result of completion of subsidised activities related to the development of hGH-OctoDEX in the first quarter of 2005.

## **7. Cost of contracted work**

Cost of contracted work increased as a result of greater activity involving the development of our clinical candidates. In particular, we incurred greater costs from the contract research organisations that were managing our clinical and pre-clinical trial activities, largely related to Locteron.

## **8. Employee benefits**

The increase in employee benefits is caused by an increase in staff from 99 employees per 30 June 2005 to 125 employees per 30 June 2006.

## **9. Other costs**

The increase in other costs is mainly related to cost of advice and administrative support in connection with our conversion from Dutch GAAP to IFRS accounting standards and improvements to our IT.

## **10. Interest**

The increase in interest expenses is related to the lower cash and cash equivalent balances in the first six months of 2006 compared to the first six months of 2006.

## **11. Corporate income taxes**

The €353 recorded under corporate income taxes for the six month period ending 30 June 2005 is related to the €353 corporate income taxes expense recorded in 2004. At 1 March 2004, the fiscal unity OctoShare B.V. was merged with OctoPlus International Holding B.V. forming the fiscal unity OctoPlus International Holding B.V. OctoShed B.V. entered the fiscal unity on 16 April 2004 and since that date the Company constitutes a



fiscal unity with all of its subsidiaries except for Chienna B.V. The fiscal unity OctoPlus International Holding B.V. reported a profit over the year 2004. The related corporate income taxes expense is reversed in the first six months of 2005 as a result of the loss making position.

## **12. Contingent liabilities**

As a result of our license agreement with LUMC for OP-145, effective as of 1 March 2006, we are obliged to pay further license payments amounting to €75 as well as royalties on future sales.

## **13. Events after balance sheet date**

On 29 August 2006, a contract was signed by OctoPlus International Holding B.V. with Fortress Participations B.V. with regard to the lease of approximately 3.513 m<sup>2</sup> of office and laboratory space at Zernikedreef 12, 2333 CL Leiden, the Netherlands. This contract is an amendment to the current lease contract for our Leiden premises and includes the planned expansion of our Leiden facilities to facilitate the anticipated growth of the Company. The contract has been signed for a period of 20 years, starting at 1 December 2007 for an annual lease charge of €752.

In September 2006, OctoShare B.V., a directly held 100% subsidiary of OctoPlus International Holding B.V., will be merged with OctoPlus International Holding B.V. Subsequently, OctoShed B.V., another 100% subsidiary of OctoPlus International Holding B.V., will change its name into OctoShare B.V., pursuant to a deed of amendment of its articles of association.

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