



## **OCTOPLUS N.V.**

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

### **Admission to listing and trading of 211,806 newly issued ordinary shares which form part of a private placement of 3,232,106 newly issued ordinary shares**

On 18 December 2009, OctoPlus N.V. issued a total amount of 3,232,106 ordinary shares (the "New Shares") at a price of € 1.25 each (the "Private Placement") to new and existing investors, including Signet Healthcare Partners and Generis Capital Partners.

In this Prospectus, the "Company", "OctoPlus", "we", "our", "us" and similar terms refer to OctoPlus N.V. and, where appropriate, its subsidiaries. Any reference to "Shares" shall refer to ordinary shares of the Company, including the New Shares, outstanding from time to time.

**Our business and any investments in our Shares involve significant risks. These risks are described under "Risk Factors" beginning on page 7 of this Prospectus.**

The Shares outstanding immediately prior to the Private Placement are listed and traded on Euronext Amsterdam by NYSE Euronext ("Euronext Amsterdam") under the symbol "OCTO" and ISIN Code NL0000345718. 3,020,300 Shares which were issued in the Private Placement were admitted to listing and trading on Euronext Amsterdam on 21 December 2009 without a prospectus being required. We have applied for admission of the remaining 211,806 Shares issued pursuant to the Private Placement to listing and trading on Euronext Amsterdam and expect that trading in these Shares on Euronext Amsterdam will commence on or about 8 March 2010 (the "Listing Date").

This Prospectus does not constitute an offer to sell, or a solicitation of an offer to buy, any of the New Shares or any other securities issued by the Company.

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 were offered and sold (i) outside the United States in reliance on Regulation S under the Securities Act ("Regulation S") and (ii) inside the United States in reliance on Regulation D under the Securities Act ("Regulation D"). The New Shares may not be offered or sold within the United States or to, or for the account or benefit of, U.S. persons (as defined in Regulation S) except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act.

The issue price for the New Shares has been determined on the basis of the quoted share price of the Shares and certain other factors.

This Prospectus constitutes a prospectus for the purposes of Article 3 of the Directive 2003/71/EC (the "Prospectus Directive") and has been prepared pursuant to Article 5:2 of the Financial Markets Supervision Act (*Wet op het financieel toezicht* (the "Financial Supervision Act")) and the rules promulgated thereunder. This Prospectus has been approved by and filed with the AFM.

Prospectus dated 5 March 2010

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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 7 and our consolidated financial statements and the notes thereto that are incorporated by reference in this Prospectus.*

*Under laws in effect in the states within the European Economic Area, no civil liability will attach to us in respect of this Summary, 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

OctoPlus is a drug delivery service company that is globally renowned as a center of excellence in pharmaceutical development and drug delivery. We offer clients our proven expertise and reliable services in formulation development, analytical development, process development and GMP manufacturing in combination with the drug delivery technologies OctoDEX<sup>®</sup>, PolyActive<sup>®</sup> and SynBiosys<sup>™</sup> for the development of controlled release formulations of injectable compounds. Such depot formulation products have demonstrated strong potential for the improvement of side effect profiles, increased patient compliance and better efficacy. Our expertise is focused on formulation of biotech-derived compounds and small chemical molecules.

In October 2008, we made the strategic decision to focus exclusively on activities for which we are reimbursed. Such contracts include our well established contract formulation & manufacturing activities, but shall also relate to activities whereby we combine our proprietary drug delivery technologies with biopharmaceutical drugs or compounds of our partners in order to improve the properties of such product candidates. We have entered into several agreements for feasibility projects to develop such controlled release formulations, whereby our partners incur the development costs and we will be reimbursed for all or substantially all costs and will furthermore be entitled to potential future milestone and royalty payments. As a result of the change in strategy, the activities in the Products & Drug Delivery segment have been terminated. Existing product candidates have been and will be licensed to partners. We will continue to perform formulation, analytical and process development services and GMP manufacturing for some of these product candidates, such as Locteron on a fee-for-service basis. The organization structure has been simplified and the relevant departments have been integrated. As a result, the Company has only one business unit from October 2009 onwards.

The clinically most advanced product based on our proprietary drug delivery technology, Locteron<sup>®</sup> is being developed by Biolex, the holder of the commercial rights to Locteron, and is currently in Phase IIb clinical trials.

### Services

Our expertise is combining our drug delivery systems, including OctoDEX and PolyActive, to develop improved formulations of our partners' biopharmaceutical drugs or other therapeutics. The improved products provide controlled and prolonged release of a drug, so as to enable reduced dosing frequency and reduced side effects with comparable or better efficacy relative to immediate release drugs. Through the use of our controlled release technology, which is ideally suited for the controlled release of proteins, we believe that we can offer a significant differentiation to our partners' product candidates and other therapeutic products. Our technologies are designed to have the advantage of efficiently and gradually delivering a drug in its native form. We believe that products based on our technologies can be applied in many therapeutic areas. In particular, we have recently seen a significant increase in investment in the

field of biosimilars by the pharmaceutical industry. Biosimilars are the second generation of biological products which are being developed and marketed following patent expiry of the originator's product. Companies developing biosimilars are looking at how they can differentiate their product from the originator brand. Through the use of our controlled release technology, which is ideally suited for the controlled release of proteins, we believe that we can offer a significant differentiation to biosimilar products.

For some clients we also offer formulation services and manufacture clinical product without the use of our proprietary drug delivery technologies. We have successfully provided these services on a fee-for-service basis to a diverse and international group of more than 135 pharmaceutical and biotechnology companies, focusing mainly on protein therapeutics and to a lesser extent on small molecule drugs. 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 pharmaceutical formulations for therapeutic proteins. We believe that our capabilities in the contract formulation and manufacturing business are demonstrated by our high rates of repeat business.

### ***Clinical Candidates using our Delivery Technology***

Locteron is a proprietary controlled release formulation of interferon alfa for the treatment of chronic hepatitis C infection (HCV). Hepatitis C is a common disease, affecting over 170 million people worldwide. Locteron combines interferon alfa produced by 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. It is believed that an improved side effect profile, such as experienced with Locteron, will lead to enhanced patient compliance. In June 2009, Biolex completed patient recruitment in a Phase IIb trial with Locteron, which is expected to be completed in 2010.

### ***Our Strategy***

Key elements of our corporate strategy, which was redefined in October 2008, include:

- Continued involvement in Locteron through manufacturing revenues, milestones and ultimately royalties.
- Build a portfolio of licensed products based on our technology by winning feasibility projects, executing them successfully and converting them into licensing agreements.
- Continue to build revenues from all elements of the business including contract formulation, manufacturing and drug delivery.

### ***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 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 The Hague 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.octoplus.nl](http://www.octoplus.nl).

## Summary of Terms of the Private Placement

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.
Private Placement	The Private Placement consisted of a private placement to qualified investors in the Netherlands and certain other jurisdictions (the "Investors") of 3,232,106 New Shares at a price of € 1.25 each (the "Issue Price"), totaling an amount of € 4.0 million. The New Shares were offered and sold (i) outside the United States in reliance on Regulation S and (ii) inside the United States in reliance on Regulation D.
Anti-Dilution Right	The rights of holders of the New Shares and our existing Shares rank <i>pari passu</i> with each other, save for anti-dilution protection of (i) the Investors in respect of the New Shares and (ii) the investors who participated in the private placement of 25 February 2009 in respect of the Shares issued in that private placement, which protection applies until 1 September 2010 (see "Description of Share Capital and Corporate Governance – Ranking Holders of Shares – Anti-Dilution Provision").
Shares Outstanding	<p>Immediately prior to the Private Placement, we had 30,203,326 Shares outstanding (see "Description of Share Capital and Corporate Governance – Share Capital – Authorized and Issued Share Capital").</p> <p>Immediately following the Private Placement, we have 33,435,432 Shares outstanding.</p>
Share Ownership	Approximately 71% of our outstanding share capital is owned by Signet Healthcare Partners, Life Sciences Partners, S.R. One, Sodoro B.V., Innoven Partenaires S.A., and Fagus N.V. (the "Major Shareholders").
Listing Date	On or about 8 March 2010.
Use of Proceeds	We intend to use the net proceeds we have received from issuance of the New Shares, after deduction of the expenses related to the Private Placement, for general corporate purposes, including capital expenditures and working capital (see "Use of Proceeds").
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").
Share Trading Information	<p>ISIN Code: NL0000345718</p> <p>Common Code: 026668441</p>

Amsterdam Security Code: 34571

Euronext Amsterdam Symbol: OCTO

## **Summary Consolidated Financial Information**

*The summary consolidated financial information set forth below should be read in conjunction with “Operating and Financial Review”, “Selected Financial Information” and our consolidated financial statements and their related notes that are incorporated by reference in this Prospectus. The year-end consolidated financial information has been extracted from our consolidated financial statements for the years ended 31 December 2006, 2007 and 2008 that have been audited by Deloitte Accountants B.V., independent auditors. The six months consolidated financial information has been extracted from our unaudited condensed consolidated interim financial statements as of and for the six months periods ended 30 June 2008 and 30 June 2009. Our results for the six months period ended 30 June 2009 are not necessarily indicative of our results for the full year.*

*Our consolidated financial statements, from which the summary consolidated financial information set forth below has been derived, were prepared in accordance with IFRS endorsed/adopted by the European Union (EU). The summary consolidated financial information set forth below may not contain all of the information that is important to you.*

**Consolidated Statement of Comprehensive Income Information**

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Service revenues	€ 5,587	€ 4,586	€ 8,708	€ 3,569	€ 9,780
License and other revenues	332	326	8,160	132	223
Income from subsidies	132	282	55	37	-
<b>Total (consolidated) revenues</b>	<b>6,051</b>	<b>5,194</b>	<b>16,923</b>	<b>3,738</b>	<b>10,003</b>
Raw materials and auxiliaries	180	379	678	370	173
Cost of contracted work and other external charges	1,928	3,652	2,782	1,293	862
Employee benefits	6,140	7,881	8,946	4,460	4,905
Depreciation and amortization	1,060	1,122	1,607	724	1,075
Other costs	5,263	7,294	7,112	2,774	3,870
<b>Total operating costs</b>	<b>14,571</b>	<b>20,328</b>	<b>21,125</b>	<b>9,621</b>	<b>10,885</b>
<b>Operating loss</b>	<b>(8,520)</b>	<b>(15,134)</b>	<b>(4,202)</b>	<b>(5,883)</b>	<b>(882)</b>
Interest	(145)	(41)	(2,007)	(531)	(745)
<b>Result for the period</b>	<b>€ (8,665)</b>	<b>€ (15,175)</b>	<b>€ (6,209)</b>	<b>€ (6,414)</b>	<b>€ (1,627)</b>

**Segmented Income Statement Information\***

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Contract formulation and manufacturing gross revenues	€ 8,504	€ 8,983	€ 10,730	€ 5,808	€ 7,944
Operating costs	7,869	8,478	10,294	5,104	8,102
<b>Operating profit</b>	<b>635</b>	<b>505</b>	<b>436</b>	<b>704</b>	<b>(158)</b>
<b>Inter-segment (internal) revenues</b>	<b>2,927</b>	<b>4,547</b>	<b>3,237</b>	<b>2,240</b>	<b>36</b>
Products & Drug Delivery gross revenues	474	758	9,430	170	2,127
Operating costs	9,287	15,253	13,951	7,561	2,904
<b>Operating loss</b>	<b>(8,813)</b>	<b>(14,495)</b>	<b>(4,521)</b>	<b>(7,391)</b>	<b>(777)</b>
<b>Inter-segment (internal) revenues</b>	<b>-</b>	<b>-</b>	<b>312</b>	<b>-</b>	<b>32</b>
<b>Unallocated costs</b>	<b>(342)</b>	<b>(1,144)</b>	<b>(117)</b>	<b>804</b>	<b>53</b>
<b>Consolidated operating loss</b>	<b>€ (8,520)</b>	<b>€ (15,134)</b>	<b>€ (4,202)</b>	<b>€ (5,883)</b>	<b>€ (882)</b>

\* As a result of the change in strategy, the Contract Development and Products & Drug Delivery activities have been integrated into one business unit during the second half of 2009. Consequently, this disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment.

**Consolidated Statement of Financial Position Information**

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Intangible fixed assets	€ 1,766	€ 3,284	€ 3,044	€ 3,207	€ 2,874
Other fixed assets	7,366	10,399	22,039	18,688	21,845
Current assets	23,134	7,230	6,139	6,245	6,656
<b>Total assets</b>	<b>32,266</b>	<b>20,913</b>	<b>31,222</b>	<b>28,140</b>	<b>31,375</b>
Equity	21,142	6,667	575	328	8,811
Non-current liabilities	3,618	3,558	12,275	9,500	11,811
Current liabilities	7,506	10,688	18,372	18,312	10,753
<b>Total equity and liabilities</b>	<b>€ 32,266</b>	<b>€ 20,913</b>	<b>€ 31,222</b>	<b>€ 28,140</b>	<b>€ 31,375</b>

**Consolidated Cash Flow Statement Information**

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Result for the period	€ (8,665)	€ (15,175)	€ (6,209)	€ (6,414)	€ (1,627)
Depreciation and amortization	1,060	1,122	1,607	724	1,075
Changes in working capital	1,195	1,582	565	136	(1,406)
Cash flow from operating activities	(6,410)	(12,471)	(4,037)	(5,554)	(1,958)
Cash flow from investing activities	(13,588)	7,941	(6,698)	(4,045)	(1,039)
Cash flow from financing activities	17,821	(8)	7,338	3,371	5,393
<b>Net cash flow</b>	<b>(2,177)</b>	<b>(4,538)</b>	<b>(3,397)</b>	<b>(6,228)</b>	<b>2,396</b>
Cash at beginning of period	9,230	7,053	2,515	2,515	(882)
Cash at end of period	7,053	2,515	(882)	(3,713)	1,514
<b>Net cash flow</b>	<b>€ (2,177)</b>	<b>€ (4,538)</b>	<b>€ (3,397)</b>	<b>€ (6,228)</b>	<b>€ 2,396</b>

## 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

***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, we will not generate revenues and we may not be successful.***

An important part of our business is to establish and maintain collaborative arrangements with pharmaceutical and biotechnology companies for the development and commercialization of their product candidates based on our contract formulation and manufacturing expertise, or based on our drug delivery technologies PolyActive, OctoDEX, SynBiosys or OctoVAX. In February 2005, we entered into a collaboration agreement with Biolex Therapeutics, Inc. (“Biolex”) to develop and commercialize Locteron. Locteron combines our PolyActive drug delivery technology and Biolex’ proprietary BLX-883 interferon alfa. In October 2008, we entered into a product rights acquisition agreement with Biolex pursuant to which Biolex obtained all commercialization rights of Locteron. We have successfully completed our Phase II trial for OP-145 CSOM and are looking for a commercialization partner. In 2008 and 2009, we also entered into several collaboration agreements for feasibility projects to develop controlled release formulations for biotech and pharmaceutical companies.

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 the 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.

Our ability to predict the success of our collaborations is limited due to (amongst others) 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 may not be able to achieve any of the milestones provided for in our collaborative agreements or derive any royalty revenue with respect to these collaborations.

***A substantial part of our future commercial potential depends on Locteron, a product candidate which is still under development. If our licensee, Biolex, is unable to bring Locteron to market successfully, or if significant delays are experienced in doing so, our ability to generate revenue will be harmed.***

Locteron is in Phase IIb clinical trials, and two Phase IIa trials of Locteron have previously been completed. Our ability to generate future revenues from Locteron will depend on the successful development and commercialization by Biolex of Locteron. Locteron 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;
- it does not offer therapeutic or other improvements over existing or future drugs used to treat the same conditions;
- it is not capable of being produced in commercial quantities at acceptable costs;
- it is not accepted in the medical community or by third-party payors; or
- we are unable to manufacture such product candidate in sufficient quantities to conduct clinical testing, because our facilities and operations fail to meet the complex requirements of the European Medicines Evaluation Agency (the "EMEA"), the US Food and Drug Administration (the "FDA") and other regulatory agencies.

We do not expect Locteron to be commercially available until 2014 at the earliest, if at all. If Biolex and we are unable to make Locteron commercially available, we will not generate revenues and we may not be successful. Notwithstanding positive clinical results so far, the results of the clinical trials completed to date do not provide assurance that acceptable efficacy or safety will be adequately demonstrated in Phase III clinical trials.

***The production method for Locteron may not be approved by the regulatory authorities.***

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 bacterial cultures. We cannot assure you that the EMEA, the FDA or other regulatory authorities will approve Locteron, or its method of production. Neither Biolex nor we can assure you that Locteron will not be inferior to other interferon alfa products that have already been tested.

***Unanticipated side effects during clinical development of Locteron may result in an interruption, delay or halt in clinical trials and could result in the denial of regulatory approval by the EMEA, FDA or other regulatory authorities.***

The active agent in Locteron is interferon alfa, variants of which are currently marketed in Europe, the United States and elsewhere for treatment of chronic hepatitis C. Treatment of patients with interferon alfa has historically been associated with significant adverse side effects, including severe flu-like symptoms, depression, suicidal thoughts and attempts, fatigue, alopecia, bone marrow toxicity, endocrine disorders, hepatotoxicity, cardiovascular and pulmonary disorders, pancreatitis, worsening of auto-immune disorders, sleep disorders, arthralgia, myalgia and ophthalmologic disorders. A number of participants in the Phase IIa clinical trial for Locteron have experienced adverse events adjudicated or determined by trial investigators to be potentially attributable to Locteron, although most of these adverse events have been rated as mild and only two of such adverse events were rated as severe or serious. Future clinical trials conducted by Biolex may demonstrate that the gradual release of interferon alfa does not reduce the frequency, duration or severity of side effects commonly experienced by patients treated with currently marketed pegylated interferons or alternatives currently under development, such as Zalbin (formerly Albuferon).

***Because Locteron has only been tested in a limited number of patients over a short duration, we cannot assure you that Locteron's efficacy or safety and tolerability profile suggested to date will be replicated in the future.***

To date, Locteron has only been tested in a very limited number of patients. Furthermore, most of the adverse side effects observed in the two Phase IIa trials were based on symptoms that are measured

subjectively, as they are subject to both varying perceptions by the patients and varying interpretations by the clinical investigators, including by virtue of their characterization as mild, moderate, severe or serious and their varying effect on diverse patient populations. Accordingly, and because observed significant adverse effects have been associated with currently marketed variants of interferon alfa, we cannot assure you that the favorable safety and tolerability profile suggested by Locteron in the completed early-stage clinical trials will be replicated in larger, later-stage trials. In addition, a definitive comparison of Locteron with currently marketed drugs or other drugs in clinical development requires a controlled, head-to-head clinical trial. To date, the longest a patient has been dosed with Locteron in any completed clinical trial has been for 12 weeks. The anticipated dosing period for Locteron, if approved, is expected to be 24 to 48 weeks in the most prevalent genotype of hepatitis C patients. Accordingly, we cannot assure you that the results indicated by Locteron in early trials will be replicated in longer trials that will be required prior to any regulatory approval.

***Biolex may fail to devote sufficient resources towards the development and approval of Locteron or may terminate our collaboration agreement.***

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' proprietary BLX-883 interferon alfa. In October 2008, we entered into a product rights acquisition agreement with Biolex pursuant to which Biolex obtained all commercialization rights of Locteron. We are subject to a number of additional risks associated with our dependence on our relationship with Biolex including:

- Biolex could fail to devote sufficient resources towards the development and approval of Locteron. Such failure to devote sufficient resources shall affect our ability to generate revenues from this collaboration.
- Biolex may not be able to provide sufficient quantities of BLX-883 for incorporation into Locteron for commercial sale in a cost effective and timely manner.

Furthermore, Biolex may terminate our product rights acquisition agreement at will upon due notice, subject to the survival of certain obligations, or upon our material breach of the product rights acquisition agreement. If we do not perform our obligations under the product rights acquisition agreement, Locteron may not be successfully developed and commercialized. If our collaboration with Biolex were to be terminated, we would not be able to generate any further revenues from Locteron and our likelihood of success will be harmed.

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

To obtain the requisite regulatory approvals to market and sell any product candidates by our collaborators, it must be demonstrated through extensive pre-clinical and clinical trials, that such product candidates are 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 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.

The commencement and completion of clinical trials for 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 our collaborators 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 conducted by our collaborators;
- lower than anticipated retention rates of patients and volunteers in clinical trials conducted by our collaborators;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- negative or inconclusive results, which may require our collaborators to conduct additional pre-clinical or clinical trials or to abandon projects that we expect to be promising;
- poor efficacy 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 conducted by our collaborators could delay commercialization of the product candidates involved and may harm our business and financial condition. It is also possible that none of the product candidates (including Locteron) will complete clinical trials in any of the markets in which our collaborators intend to sell those product candidates. Accordingly, our collaborators would not receive the regulatory approvals needed to market such product candidates, which would harm our business and financial condition.

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

We aim to develop product candidates on behalf of our collaborators, which involve the combination of a marketed drug or similar compound with PolyActive, OctoDEX, SynBiosys or OctoVAX. As a result, we anticipate that it is not required to conduct some early stage tests concerning the safety and toxicology of the active pharmaceutical ingredient contained in some of such product candidates. We cannot assure you, however, that the EMEA, the FDA or other regulatory authorities will not require such tests. If it is required to conduct further pre-clinical or clinical trials, the costs will increase and that may affect the ability to progress such product candidates towards commercialization as rapidly as we and our collaborators expect.

***Our business faces intense competition.***

The pharmaceutical and biotechnology industries are highly competitive. Any product candidates that our collaborators 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 product candidates, which we develop for our collaborators.

These competitors may have substantially greater financial, technological, manufacturing, marketing, managerial and research and development resources and experience than we and our collaborators may have. These organizations may also have much more experience than we and our collaborators have in pre-clinical and clinical trials of new drugs and in obtaining regulatory approvals. Accordingly, these

competitors may succeed in developing competing technologies and products more rapidly than we and our collaborators do.

Locteron and our other product candidates if successfully developed by a future collaborator and approved for commercial sale, will compete with a number of drugs and therapies currently manufactured and marketed by major pharmaceutical and biotechnology companies. Such 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 the products of our collaborators. 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 and our collaborators do, our commercial opportunity will be reduced or eliminated.

In addition to product-based competition, we face competition in the area of the pharmaceutical contract formulation and manufacturing services we offer. There are many organizations in our sector which are actively engaged in offering similar services as we do to the same markets. These competitors may succeed in acquiring new projects more rapidly than we do and this will impact our ability to generate service revenues.

***Our business faces rapid technological change.***

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 the product candidates of our collaborators obsolete or non-competitive. For example, the current standard of care for HCV infection consists of a combination therapy using interferon alfa and ribavirin. 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.

***The product candidates of our collaborators may not gain market acceptance.***

Even if the product candidates of our collaborators 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 the product candidates of our collaborators.

Physicians may elect not to recommend, and patients may elect not to use, such 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 such product candidates fail to achieve market acceptance, we may not be able to generate significant revenue, if any.

***Our collaborators have significant product liability exposure, which may also harm our business and our reputation.***

Our collaborators face an inherent risk of product liability lawsuits related to the testing of product candidates, and will face an even greater risk if such product candidates are introduced commercially. An individual may bring a liability claim against a collaborator if one of its product candidates causes, or merely appears to have caused, an injury. If our collaborators cannot successfully defend themselves against a product liability claim, they may incur substantial liabilities, which may also harm our business and reputation.

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

***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 the products of our collaborators 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 exposed to complex production issues.***

The formulation and manufacturing services that we offer can be highly complex. From time to time, issues may arise in the formulation laboratory or manufacturing facility, in both cases for a variety of reasons including equipment malfunction, failure to follow specific protocols and procedures, issues with raw materials, environmental factors and systematic failure of our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the

Internet. Such issues could affect the formulation success, the production of a particular batch or series of batches. This could, among other things, lead to increased costs, lost revenue, damage to customer relations, reimbursement to customers for lost active pharmaceutical ingredients, time and expense spent investigating the cause and, depending on the cause, similar losses with respect to other batches or products.

***Expenses related to our development and manufacturing capacity are largely fixed.***

The amount that the pharmaceutical and biotechnology industry spends on formulation development and manufacturing for clinical trials and commercial use and in particular how much it spends on outsourcing such activities may have a large impact on our revenues and profitability. For example consolidation in the industries in which our customers operate may have an impact on such spending as customers integrate acquired operations, including research and development departments and manufacturing. Also, additional competition may emerge and may, among other things, result in a decrease of the fees paid for services or a reduction in work for us. As a result, we may periodically experience overcapacity in terms of development resources and manufacturing resources which could affect our profitability as the costs related to these resources are largely fixed in the medium-term.

***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.***

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 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 Intellectual Property**

***Our success is dependent on intellectual property rights held by us, and third parties, and the value of such rights is complex and uncertain.***

Our success depends, in part, on our ability to obtain, maintain and enforce our intellectual property rights relating to our technologies and product candidates that are developed based on our drug delivery systems 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.

Patent positions, in particular those of pharmaceutical and biotechnology companies, including ours, involve complex legal and factual questions. Validity and enforceability of patents cannot be guaranteed. Patents may be challenged, invalidated, deemed unenforceable, or circumvented. The validity, enforceability and commercial value of patents are therefore highly uncertain.

We intend to apply for patents covering our technologies and when possible the combination of our technology 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 patent applications filed by us may not result in issued patents, or their validity may be challenged. Any 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 may 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 the value of 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 having a scope covering our technology or any of the product candidates that are developed based on our drug delivery systems in order to protect our rights, we may have to participate in expensive and time-consuming opposition proceedings, re-examination proceedings, or nullity proceedings, whichever is applicable, before the European Patent Office, the US Patent and Trademark Office (“USPTO”) or patent authorities in other jurisdictions. We cannot guarantee that there will be no claims from third parties alleging that such product candidates infringe their intellectual property rights. Third parties may assert that we or our collaborators are employing their proprietary technologies without authorization and they may resort to litigation to attempt to enforce their rights. Third parties may own or obtain patents relevant to our technology or the technology of our collaborators or the product candidates that are developed based on our drug delivery systems and claim that the use of this technology or any of these product candidates infringes their patents.

We may not be able to enter into collaboration agreements for the development or commercialization of our current product candidates due to third party patent protection. Our business may be harmed if we or our collaborators cannot negotiate a necessary or desirable license, can obtain such a license only on unattractive or unacceptable terms, or if we or our collaborators are unable to redesign our product candidates or processes to avoid actual or potential infringement of patents or other intellectual property. Our efforts and those of our collaborators to obtain, protect and defend our patents and other intellectual property rights, whether successfully or not, may be expensive and may require us or our collaborators to incur substantial costs, including the diversion of management and technical personnel. An unfavorable ruling in patent or intellectual property litigation could subject us or our collaborators to significant liabilities to third parties, require our collaborators to cease developing, manufacturing or selling the affected products or using the affected processes, require us or our collaborators to license the disputed rights from third parties, or result in awards of substantial damages against us or our collaborators. 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.

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

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 with 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 qualified management and scientific personnel.***

Our success depends on our ability to attract, retain and motivate highly qualified management and scientific personnel. In particular, we are highly dependent on Mr. Sturge, our Chief Executive Officer, and the other members of our Executive Board. If we are not able to retain these persons, we may not be able to successfully conduct our business. 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 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 may experience further growth in the number of our employees and the scope of our operations over the next several years. To manage 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 our collaborators 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. 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 our collaborators to incur additional costs and will cause significant delays. If the necessary regulatory approvals are not received, we will not be able to generate revenues and may not become profitable. Our collaborators may encounter significant delays in the regulatory process that could result in excessive costs that may prevent our collaborators from continuing to develop such product candidates in collaboration with us. 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.

***Product candidates which are developed by our collaborators will remain subject to ongoing regulatory review even if they receive marketing approval. If we and our collaborators fail to comply with continuing regulations, these approvals could be withdrawn and the sale of the products could be suspended.***

Even if regulatory approval to market a particular product candidate is received, the approval could be conditioned on conducting additional costly post-approval studies or could limit the indicated uses included in the labeling of products. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force our collaborators to withdraw it from the market or impede or delay the 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 the products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including restrictions on our manufacturing processes, civil or criminal penalties or fines, injunctions, voluntary or mandatory product recalls, suspension or withdrawal of regulatory approvals, and/or total or partial suspension of production. Any such sanction could severely harm our business and financial condition.

Our contract formulation and manufacturing business involves drug development and manufacture on behalf of third parties. Both of these activities, comprising decision making processes, manufacturing processes, procurement, manufacture, storage, shipping and recordkeeping, must comply with the FDA's cGMP regulations, among other requirements. FDA oversight, including facility inspections, is ongoing, and a failure to comply with applicable requirements can result in adverse publicity, warning letters, civil and criminal liability, and restrictions on and/or prohibitions against the performance of these activities, any of which may result in a loss of business.

***Our ability to generate revenue from any product candidate that may be developed by our collaborators will depend on reimbursement and drug pricing policies and regulations.***

Many patients will rely on governmental authorities, private health insurers and other third-party payors to pay for their medical needs. The ability to achieve acceptable levels of reimbursement for drug treatments by governmental authorities, private health insurers and other organizations will have an effect on the ability to successfully commercialize, and attract collaborative collaborators to invest in the development of the 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 co-develop, and any reimbursement that may become available may be decreased or eliminated in the future. Third-party payors increasingly are charging prices for pharmaceutical products, and many third-party payors may refuse to provide reimbursement for particular drugs when an equivalent generic or alternative non-generic drug is available. Even if improved efficacy or improved convenience of administration with the product candidate is shown, pricing of the existing drug may limit the amount which can be charged for the product. If reimbursement is not available or is available only at limited levels, our collaborators may not be able to successfully commercialize their product candidates, and we may not be able to generate satisfactory revenues from our collaborations.

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, it may be required to conduct a clinical trial that compares the cost-effectiveness of the product candidates to other available therapies. If reimbursement of such future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our collaborators may be unable to achieve or sustain profitability, which will affect our financial condition.

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 our collaborators may develop and could harm our revenues and profitability.

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

### ***We have incurred losses since 2002***

We are not profitable and have incurred losses in each year since 2002. Our net loss for the years ended 31 December 2008, 2007 and 2006 was € 6.2 million, € 15.2 million, and € 8.7 million, respectively, and € 1.6 million for the first six months of 2009. As of 30 June 2009, we had an accumulated deficit of € 41.8 million. Our losses, among other things, have caused our shareholders' equity and working capital to decrease. To date, we have derived a substantial portion of our revenues from our contract formulation and manufacturing business. We have also received government subsidies, a significant up-front fee from Biolex for the sale of the commercialization rights to Locteron and nominal licensing revenues through the out-licensing of certain technologies, i.e. the granting of rights to third parties to use our technologies in accordance with the scope of the license agreements entered into with such parties.

In October 2008, we received an up-front fee from Biolex for the sale of the commercialization rights to Locteron. We do not expect that we will generate revenues from the sale of products for the foreseeable future. We expect to become profitable within the foreseeable future. However, if Locteron or the other current product candidates that we intend to develop with current and future collaborators, fail in clinical trials or do not gain regulatory approval, or if such product candidates do not achieve market acceptance, we may never achieve profitability. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods.

### ***We may need 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 product development programs or commercialization efforts or cause us to discontinue our operations.***

We may need to raise additional capital to pursue our business strategy. Our future funding requirements will depend on many factors, including:

- our ability to continue to generate revenues from our contract formulation and manufacturing business;
- terms and timing of any collaborative, licensing and other arrangements that we may establish;
- cost, timing and outcomes of regulatory approvals;
- timing, receipt and amount of royalties, if any, from the 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; and
- 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.

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 curtail development programs and may be required to delay, scale back or eliminate certain of our activities, which would have a material adverse affect on our financial condition 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 offerings, debt financings and collaboration and licensing arrangements. To the extent that we raise additional capital through the issuance of Shares or convertible debt, 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 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 formulation and manufacturing business and, to a lesser extent, government subsidies and license revenues. Our customer base presently comprises approximately 40 clients who award us with work on a contract-by-contract basis. In 2008, our five largest clients accounted for 47% of our contract formulation and manufacturing 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 formulation and manufacturing 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. Some of our clients and target customers are loss making and as such will be dependent on external financing for their product development programs. If they fail to secure such external financing, they may not have the financial means to continue working with 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 the 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.***

We cannot predict the extent to which an active market for our Shares will develop or be sustained, 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 Issue Price was agreed between us and the Investors based on a number of factors, including market conditions in effect shortly prior to the Private Placement, which may not be indicative of future performance. The market price for our Shares may fall below the Issue Price. The market price of our Shares could fluctuate substantially due to factors described above and a number of other factors, including, but not limited to:

- 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;

- 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.

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

Signet Healthcare Partners, Life Sciences Partners, S.R. One, Sodoro B.V., Innoven Partenaires S.A., and Fagus N.V. (the "Major Shareholders") own approximately 71% of our Shares.

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.

***Our Executive Board has broad discretion over the use of the net proceeds received by us from the Private Placement 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 the New Shares. We intend to use the net proceeds from the Private Placement primarily for general corporate purposes, including capital expenditures and working capital (see "Use of Proceeds"). 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. 9,768,530 (approximately 29%) of our total Shares will be outstanding in addition to the 23,666,902 Shares currently owned by the Major Shareholders.

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

Although we believe that we are not a passive foreign investment company ("PFIC") for US 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 US 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 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.

***US 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, US 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 US 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 US 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.

***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.

***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. Under the terms of an agreement we intend to enter into with Stichting Continuïteit OctoPlus, in certain circumstances Stichting Continuïteit OctoPlus will be entitled 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. 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.

## **Important Information**

No person is or has been authorized to give any information or to make any representation in connection with 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. 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.

### **Notice to Investors**

The distribution of this Prospectus 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 a solicitation of an offer to buy, any of the New Shares or any other securities issued by the Company.

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

### **Presentation of Financial and Other Information**

Certain figures contained in this Prospectus 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 “US dollars”, “US\$” or “\$” are to the lawful currency of the United States.

Any financial information in this Prospectus that has not been extracted from our audited consolidated financial statements for the years 2006, 2007 and 2008 is unaudited.

### **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 US dollars at these rates.

The table below shows the high, low, average and end of period exchange rates expressed in US 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
			<b>(US Dollars per Euro)</b>	
2005 .....	1.3476	1.1667	1.2444	1.1842
2006 .....	1.3327	1.1860	1.2563	1.3197
2007 .....	1.4862	1.2904	1.3708	1.4603
2008 .....	1.6010	1.2446	1.4710	1.3919
2009.....	1.5100	1.2547	1.3935	1.4332

On 22 February 2010, the Noon Buying Rate for the euro was € 1.00 = \$ 1.3618.

### **Enforceability of Judgments**

We are a limited liability company incorporated under the laws of the Netherlands. Most 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 US 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 US Centers for Disease Control and Prevention, the Public Health Agency of Canada, the US National Institutes of Health, Datamonitor, Decision Resources, 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 relevant markets 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*) (in the Dutch and English language) and certain parts of our Annual Reports for the years ended 31 December 2006, 2007 and 2008 and our Condensed Consolidated Interim Financial Statements for the first six months ended 30 June 2009 (also including the 30 June 2008 figures), listed below, are incorporated by reference into this Prospectus. Our six months consolidated financial information is unaudited. No other documents or information form part of, or are

incorporated by reference into, this Prospectus. Copies of our Annual Reports for the years ended 31 December 2006, 2007 and 2008 and our Condensed Consolidated Interim Financial Statements for the six months ended 30 June 2009 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. All Annual Reports are also available via [www.octoplus.nl](http://www.octoplus.nl).

Annual Report for the year ended 31 December 2006	Incorporated by reference
• Consolidated balance sheet	page 26
• Consolidated income statement	page 27
• Consolidated statement of changes in equity	page 28
• Consolidated cash flow statement	page 29
• Notes to the consolidated financial statements	page 30-53
• Auditors' report	page 62
Annual Report for the year ended 31 December 2007	Incorporated by reference
• Consolidated balance sheet	page 28
• Consolidated income statement	page 29
• Consolidated statement of changes in equity	page 30
• Consolidated cash flow statement	page 31
• Notes to the consolidated financial statements	page 32-57
• Auditors' report	page 66-67
Annual Report for the year ended 31 December 2008	Incorporated by reference
• Consolidated balance sheet	page 28
• Consolidated income statement	page 29
• Consolidated statement of changes in equity	page 30
• Consolidated cash flow statement	page 31
• Notes to the consolidated financial statements	page 32-60
• Auditors' report	page 68-69

Consolidated Interim Financial Statements 30 June 2009

Incorporated by reference

(also including the 30 June 2008 figures)

- Consolidated statement of financial position page 8
- Condensed consolidated statement of comprehensive income page 9
- Condensed consolidated statement of changes in equity page 10
- Condensed consolidated statement of cash flows page 11
- Notes to the condensed consolidated interim financial statements page 12-16

## **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, 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 have raised € 4.0 million in gross proceeds from the issue of the New Shares. The net proceeds we have received from the Private Placement are estimated to be approximately € 3.8 million, after deducting the estimated commissions and expenses of € 275,000 payable by us. We intend to use the net proceeds we have received from the Private Placement primarily for general corporate purposes, including capital expenditures and working capital.

This expected use of net proceeds represents our current intentions based upon our present plans and business conditions. The amounts and timing of our actual expenditures depend on numerous factors. As a result, the Executive Board will retain broad discretion over the allocation of the net proceeds from the Private Placement. Pending use of the net proceeds of the Private Placement, 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 table below sets forth our unaudited consolidated cash and cash equivalents, capitalization and indebtedness as of 31 December 2009, on an actual basis including the proceeds of the Private Placement.

The financial information in the table below has been extracted or derived from our 31 December 2009 management accounts which have not been audited or reviewed and will not be published. You should read this table together with our consolidated financial statements incorporated by reference in this Prospectus, 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 31 December 2009.

<b>(€ in thousands)</b>	<b>31 December 2009 Unaudited</b>
<i>Capitalization</i>	
Current liabilities	8,082
Non-current liabilities	10,316
<b>Total financial indebtedness</b>	<b>18,398</b>
Share capital – ordinary shares	4,012
Share premium	49,686
Retained earnings (accumulated deficit)	(43,109)
Other reserves	754
<b>Total equity</b>	<b>11,343</b>
<i>Indebtedness</i>	
Cash and cash equivalents	2,984
Current restricted cash	340
<b>Liquidity</b>	<b>3,324</b>
Current portion of non-current liabilities	951
Bank overdrafts	11
Trade and other payables	7,120
<b>Current financial debt</b>	<b>8,082</b>
<b>Net current financial indebtedness</b>	<b>(4,758)</b>
Finance lease liabilities	10,316
<b>Non-current financial indebtedness</b>	<b>10,316</b>
<b>Net financial indebtedness</b>	<b>(15,074)</b>

No guarantees have been issued in respect of the current and non-current financial indebtedness as at 31 December 2009. An amount of € 2,193,000 of the non-current financial indebtedness and an amount of € 711,000 of the current financial indebtedness as at 31 December 2009 is secured by means of a right of pledge on the shares of OctoPlus Development B.V. pursuant to the lease facility with Amstel Lease Maatschappij N.V. An amount of € 11,000 of the current financial indebtedness as at 31 December 2009 is secured by means of a right of pledge over equipment, inventories and receivables of OctoPlus Development B.V. pursuant to the credit line facility with ABN AMRO Bank N.V. (see also Chapter "Operating and Financial Review – Liquidity and Capital Resources").

As at 31 December 2009, our net asset value per share was € 0.34 (unaudited).

As at 31 December 2009, our authorized capital amounted to € 9,600,000 and was divided into 40,000,000 ordinary shares and 40,000,000 preference shares, all with a nominal value of € 0.12 each.

As at 31 December 2009, 33,435,432 ordinary shares were outstanding and were fully paid up.

See "Operating and Financial Review – Contractual Obligations" for information about certain contingent obligations of ours. Please also refer to "General Information – Financial and Trading Position" for significant changes in our financial and trading position since 30 June 2009.

## Selected Financial Information

The selected consolidated financial information set forth below should be read in conjunction with "Operating and Financial Review", and our consolidated financial statements and their related notes that are incorporated by reference in this Prospectus. The year-end consolidated financial information has been extracted from our consolidated financial statements for the years ended 31 December 2006, 2007 and 2008 that have been audited by Deloitte Accountants B.V., independent auditors. The six months consolidated financial information has been extracted from our unaudited condensed consolidated interim financial statements as of and for the six months periods ended 30 June 2008 and 30 June 2009. Our results for the six months period ended 30 June 2009 are not necessarily indicative of our results for the full year.

Our consolidated financial statements, from which the selected consolidated financial information set forth below has been derived, were prepared in accordance with IFRS endorsed/adopted by the European Union (EU). The selected consolidated financial information set forth below may not contain all of the information that is important to you.

### Consolidated Statement of Comprehensive Income Information

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Service revenues	€ 5,587	€ 4,586	€ 8,708	€ 3,569	€ 9,780
License and other revenues	332	326	8,160	132	223
Income from subsidies	132	282	55	37	-
<b>Total (consolidated) revenues</b>	<b>6,051</b>	<b>5,194</b>	<b>16,923</b>	<b>3,738</b>	<b>10,003</b>
Raw materials and auxiliaries	180	379	678	370	173
Cost of contracted work and other external charges	1,928	3,652	2,782	1,293	862
Employee benefits	6,140	7,881	8,946	4,460	4,905
Depreciation and amortization	1,060	1,122	1,607	724	1,075
Other costs	5,263	7,294	7,112	2,774	3,870
<b>Total operating costs</b>	<b>14,571</b>	<b>20,328</b>	<b>21,125</b>	<b>9,621</b>	<b>10,885</b>
<b>Operating loss</b>	<b>(8,520)</b>	<b>(15,134)</b>	<b>(4,202)</b>	<b>(5,883)</b>	<b>(882)</b>
Interest	(145)	(41)	(2,007)	(531)	(745)
<b>Result for the period</b>	<b>€ (8,665)</b>	<b>€ (15,175)</b>	<b>€ (6,209)</b>	<b>€ (6,414)</b>	<b>€ (1,627)</b>

### Segmented Income Statement Information\*

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Contract formulation and manufacturing gross revenues	€ 8,504	€ 8,983	€ 10,730	€ 5,808	€ 7,944
Operating costs	7,869	8,478	10,294	5,104	8,102
<b>Operating profit</b>	<b>635</b>	<b>505</b>	<b>436</b>	<b>704</b>	<b>(158)</b>
<b>Inter-segment (internal) revenues</b>	<b>2,927</b>	<b>4,547</b>	<b>3,237</b>	<b>2,240</b>	<b>36</b>
Products & Drug Delivery gross revenues	474	758	9,430	170	2,127
Operating costs	9,287	15,253	13,951	7,561	2,904
<b>Operating loss</b>	<b>(8,813)</b>	<b>(14,495)</b>	<b>(4,521)</b>	<b>(7,391)</b>	<b>(777)</b>

<b>Inter-segment (internal) revenues</b>	-	-	312	-	32
<b>Unallocated costs</b>	(342)	(1,144)	(117)	804	53
<b>Consolidated operating loss</b>	€ (8,520)	€ (15,134)	€ (4,202)	€ (5,883)	€ (882)

\* As a result of the change in strategy, the Contract Development and Products & Drug Delivery activities have been integrated into one business unit during the second half of 2009. Consequently, this disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment.

#### **Consolidated Statement of Financial Position Information**

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Intangible fixed assets	€ 1,766	€ 3,284	€ 3,044	€ 3,207	€ 2,874
Other fixed assets	7,366	10,399	22,039	18,688	21,845
Current assets	23,134	7,230	6,139	6,245	6,656
<b>Total assets</b>	<b>32,266</b>	<b>20,913</b>	<b>31,222</b>	<b>28,140</b>	<b>31,375</b>
Equity	21,142	6,667	575	328	8,811
Non-current liabilities	3,618	3,558	12,275	9,500	11,811
Current liabilities	7,506	10,688	18,372	18,312	10,753
<b>Total equity and liabilities</b>	<b>€ 32,266</b>	<b>€ 20,913</b>	<b>€ 31,222</b>	<b>€ 28,140</b>	<b>€ 31,375</b>

#### **Consolidated Cash Flow Statement Information**

(€ in thousands)	Year ended 31 December			Six months ended 30 June	
	2006	2007	2008	2008	2009
				UNAUDITED	UNAUDITED
Result for the period	€ (8,665)	€ (15,175)	€ (6,209)	€ (6,414)	€ (1,627)
Depreciation and amortization	1,060	1,122	1,607	724	1,075
Changes in working capital	1,195	1,582	565	136	(1,406)
Cash flow from operating activities	(6,410)	(12,471)	(4,037)	(5,554)	(1,958)
Cash flow from investing activities	(13,588)	7,941	(6,698)	(4,045)	(1,039)
Cash flow from financing activities	17,821	(8)	7,338	3,371	5,393
<b>Net cash flow</b>	<b>(2,177)</b>	<b>(4,538)</b>	<b>(3,397)</b>	<b>(6,228)</b>	<b>2,396</b>
Cash at beginning of period	9,230	7,053	2,515	2,515	(882)
Cash at end of period	7,053	2,515	(882)	(3,713)	1,514
<b>Net cash flow</b>	<b>€ (2,177)</b>	<b>€ (4,538)</b>	<b>€ (3,397)</b>	<b>€ (6,228)</b>	<b>€ 2,396</b>

## Operating and Financial Review

*You should read the following in conjunction with the "Selected Financial Information" and our consolidated financial statements and their related notes that are incorporated by reference in this Prospectus. Our consolidated financial statements have been prepared in accordance with IFRS endorsed/adopted by the European Union (EU). Our six months consolidated financial information has been extracted from our unaudited condensed consolidated interim financial statements as of and for the six months periods ended 30 June 2008 and 30 June 2009. Our results for the six months period ended 30 June 2009 are not necessarily indicative of our results for the full year.*

*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 provide advanced drug formulation and clinical scale manufacturing services to biotechnology and pharmaceutical companies worldwide. We have provided our services to more than 135 clients that have progressed more than 40 products into clinical studies and six products on to the market. Since our establishment in 1995 through 30 June 2009, our contract formulation and manufacturing business has achieved € 70 million in cumulative gross (non-consolidated) revenues, or € 58 million of consolidated revenues, which excludes internal revenues generated from supporting our former drug development programs (our former Products and Drug Delivery Business). In 2008, approximately 57% of our revenues from this business originated in the European Union and approximately 36% of our revenues originated from clients in North America, while the remainder was sourced from other countries. In 2009 our revenues sourced from North America increased significantly as a result of manufacture of clinical trial material for the ongoing Locteron Phase IIb study for Biolex.

In addition to providing advanced drug formulation and clinical scale manufacturing services, we actively seek to develop, in collaboration with our partners, improved pharmaceutical products based on our proprietary drug delivery technologies that have fewer side effects, increased patient convenience and better efficacy than existing products.

The clinically most advanced product based on our technology, Locteron, is in Phase IIb clinical trials. Locteron is a novel therapy for the treatment of chronic hepatitis C infection, combining our proprietary PolyActive drug delivery technology with Biolex' interferon alfa. 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. In February 2005, we entered into a collaboration agreement with Biolex to develop and commercialize Locteron. In October 2008, we entered into a product rights acquisition agreement with Biolex pursuant to which Biolex obtained all commercialization rights of Locteron. Together with Biolex, we have completed patient treatment in a Phase IIa study of Locteron in Europe. We also initiated a separate Phase IIa study in the United States which was successfully completed earlier in 2009. In June 2009, Biolex completed patient recruitment in a Phase IIb clinical trial which it expects to complete in 2010. Biolex will present interim results after 12 weeks of treatment from its two Phase IIb studies for Locteron versus PEG-Intron® at the International Liver Congress in April 2010, organized by the European Association for the Study of the Liver (EASL). The data have been accepted for both oral and poster presentations. Under the strict rules of the conference, the results are currently embargoed until publication at the conference. The "SELECT-2" Phase IIb study is being conducted in the United States and Europe in 116 treatment-naïve, genotype-1, chronic hepatitis C patients. Patients have been randomized into one of four dosing cohorts, the 320, 480 or 640 µg dose of Locteron (administered once every two weeks) or a control arm consisting of PEG-Intron (administered every week), with all patients receiving weight-based ribavirin. Patients will be treated for 48 weeks and will be followed for an additional 24 weeks to determine the sustained virologic response (SVR) rate. The SELECT-2 Phase IIb clinical study started in April 2009, and patient enrollment was completed in June

2009. The second component of the planned Phase IIb trial program for Locteron, the "480 STUDY", is designed to provide clinical experience with the same Locteron configuration that is planned for use in Phase III trials. The 480 STUDY was also initiated last year, is being conducted in Europe and Israel, and will include at least 72 treatment-naïve hepatitis C patients with the genotype-1 variant of the virus. Locteron's expected product profile was tested by Biolex in extensive market research in the first half of 2009, and the research results suggested that the potential tolerability and dosing convenience advantages of Locteron support a substantial commercial opportunity. It is estimated that worldwide sales of interferon products for the treatment of hepatitis C will approach US\$6 billion by 2016<sup>1</sup>.

Our second clinical-stage product candidate is OP-145 CSOM, a novel proprietary peptide therapeutic for the treatment of chronic otitis media, also known as chronic middle ear infection, has successfully completed Phase II clinical trials. We intend to out-license OP-145 CSOM before further clinical studies commence. Furthermore, we have entered into several collaboration agreements for feasibility projects to develop controlled release formulations for biotech and pharmaceutical companies. Depending on the outcome of these feasibility projects our partners may decide to continue developing such product candidates requiring our ongoing involvement for the further formulation and manufacturing services as well as a license to our proprietary drug delivery technologies.

From 2006 to 2008, our annual Total (consolidated) revenues increased from € 6.1 million to € 16.9 million. In the first half of 2009, our Total (consolidated) revenues amounted to € 10.0 million.

At the end of 2008, we made the strategic decision to focus exclusively on formulation, development and manufacturing activities for which we are reimbursed. Such contracts further strengthen our well established contract formulation and manufacturing activities, but shall also relate to activities whereby we combine our proprietary drug delivery technologies with biopharmaceutical drugs or compounds of our partners in order to improve the properties of such product candidates. We have entered into several collaboration agreements for feasibility projects to develop such controlled release formulations, whereby our partners incur the development costs and we will be reimbursed for all or substantially all costs and will furthermore be entitled to potential future milestone and royalty payments. As a result of the change in strategy, the activities in the Products & Drug Delivery segment have been terminated. Existing product candidates have been and will be licensed to partners. We will continue to perform formulation, analytical and process development services and GMP manufacturing for some of these product candidates, such as Locteron on a fee-for-service basis. The organization structure has been simplified and the relevant departments have been integrated. As a result, the Company has only one business unit from October 2009 onwards. Consequently, disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

## **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 Formulation and Manufacturing Business\****

Since our establishment in 1995 through 30 June 2009, our contract formulation and manufacturing business has achieved € 70 million in cumulative gross (non-consolidated) service revenues, including € 12 million in Inter-segment (internal) revenues from our former Products and Drug Delivery business unit.

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<sup>1</sup> See press release dated 10 February 2010 of Biolex, which can be found at: <http://www.biolex.com/pdfs/Biolex%20Locteron%20EASL%20Presentation%20Acceptance%20-%202002-10-10.pdf>

\* On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

Since 2004, our contract formulation and manufacturing 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, peptides and other large molecules for our pharmaceutical and biotechnology clients. Annually, we commence work on approximately 10 - 20 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 formulation and manufacturing 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 formulation and manufacturing business typically experiences slower growth. Conversely, when financing is more readily available to fund development projects, our contract formulation and manufacturing business grows more rapidly. The growth of our contract formulation and manufacturing business is furthermore related to our ability to increase our capacity in terms of human and physical resources.

Our contract formulation and manufacturing 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 a significant impact on our results, particularly if not replaced quickly by other projects. In 2008, we generated approximately 47% of our Total (consolidated) revenues in the contract formulation and manufacturing business from our five largest clients. During the first half of 2009, 58% of our contract formulation and manufacturing revenues were generated from manufacturing Locteron clinical trial material for the ongoing Phase IIb study for Biolex.

### ***Products and Drug Delivery Business\****

In addition to revenues from our contract formulation and manufacturing business we have generated revenues based on certain development and licensing agreements concerning our product candidates and technologies. Our ability to generate additional royalty revenues will depend on the continued success of our existing collaborations, our ability to enter into further arrangements for the out-licensing of our technologies and OP-145 CSOM, and our ability to enter into future collaborations for the development of other product candidates.

In addition, we have received € 3.0 million in subsidies from the Dutch Ministry of Economic Affairs and the European Union. Certain projects were completed or discontinued without utilizing the full amount of the subsidy available. We remain eligible to receive a further € 0.8 million pursuant to these grants. We do not foresee any immediate change in our ability to secure and draw down subsidy revenues.

In 2004, we entered into an agreement with SurModics, Inc. ("SurModics") regarding the out-licensing of certain applications in the field of drug-eluting medical devices based on our OctoDEX and PolyActive technologies. This agreement was replaced in 2007 by an agreement for the out-licensing of certain applications in the field of drug-eluting medical devices based on our PolyActive technology only. In accordance with our agreement with SurModics, we have received up-front and licensing fees over the period of the agreement. SurModics terminated the license per 30 September 2009 and paid the cancellation fee as outlined in the agreement in September 2009.

In November 2006, we granted a license to Green Cross Corporation of South Korea for the co-development and exclusive commercialization of OP-145 CSOM in the South Korean market for the treatment of chronic middle ear infection. In accordance with our agreement with Green Cross Corporation, we have received a nominal up-front milestone payment and a nominal ongoing milestone

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\* On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

payment and may continue to receive additional ongoing milestone payments. In addition to these milestone payments, Green Cross Corporation will be obligated to pay us certain royalties based on gross receipts for sales of OP-145 CSOM by Green Cross Corporation. The exact royalty rate will be determined pursuant to a formula set forth in the agreement, which we anticipate to result in a low double digit royalty rate. Furthermore, we are entitled to 50% of any amounts that Green Cross Corporation receives from its sublicensees.

In October 2008, we sold the worldwide commercial rights for the further exclusive development and commercialization of Locteron to Biolex. In accordance with the product rights acquisition agreement with Biolex, we have received an up-front fee of \$11 million (€ 8.1 million) and may continue to receive ongoing milestone payments of \$138 million (approximately € 100 million). In addition to these milestone payments, Biolex will be obligated to pay certain royalties to us based on net sales of Locteron. The agreement with Biolex furthermore sees to our continued involvement as manufacturer of commercially produced Locteron. The sum of royalties and income from manufacturing equates to a low double digit royalty rate on net sales. We are currently holding 2,897,445 shares of common stock in Biolex and are entitled to the corresponding dividends thereon. We may receive an additional equity stake in Biolex of 2,897,445 common shares, subject to achievement of certain milestones.

Pursuant to the agreements with Biolex of 3 October 2008, we remain involved in the future formulation, development and manufacturing of Locteron, albeit on a fee-for-service basis. OctoPlus will receive a predetermined Euro hourly fee for all formulation and development activities plus an agreed price per batch manufactured.

## **Operating Costs**

Our operating costs consist of five categories: Raw materials and auxiliaries (primarily our polymers and active pharmaceutical ingredients); Cost of contracted work and other external charges (primarily related to services performed by contract research organizations); Employee benefits (primarily salaries and benefits); Depreciation and amortization; and Other costs (related to other personnel costs such as temporary personnel, recruitment fees and training expenditures, marketing expenditures, professional advisors, consumables and chemicals used in our manufacturing facility and our laboratory facilities and general overhead, such as premises costs and office expenses). While we do not separately account for research and development costs, we consider Raw materials and auxiliaries, Cost of contracted work and other external charges and Employee benefits, to represent the majority of our research and development costs. Our direct and indirect costs related to research and development in 2008, 2007 and 2006 amounted to € 12.0 million, € 15.3 million and € 9.3 million, respectively. These costs decreased significantly in 2009 as a result of our strategic change to adopt a service-based business model.

Raw materials and auxiliaries, as well as Cost 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 3% of our total 2008 operating costs were related to Raw materials and auxiliaries. Approximately 13% of our total 2008 operating costs were related to Cost of contracted work and other external charges. Approximately 42% of our total 2008 operating costs were related to Employee benefits. Approximately 8% of our total 2008 operating costs were related to Depreciation and amortization. Approximately 34% of our total 2008 operating costs were related to Other costs.

**Results of Operations for the Years Ended 31 December 2006, 2007, 2008 and the Six Months Ended 30 June 2008 and 2009**

**Six Months Ended 30 June 2008 and 2009**

<b>Revenues (in thousands)</b>	<b>Six months ended 30 June</b>		<b>Change</b>	
	<b>2008</b>	<b>2009</b>	<b>€</b>	<b>%</b>
	<b>(unaudited)</b>	<b>(unaudited)</b>		
Gross service revenues	€ 5,809	€ 9,848	€ 4,039	70%
Inter-segment (internal) revenues	(2,240)	(68)	2,172	(97)
Consolidated service revenues	3,569	9,780	6,211	174
License and other revenues	132	223	91	69
Income from subsidies	37	-	(37)	(100)
<b>Total (consolidated) revenues</b>	<b>€ 3,738</b>	<b>€ 10,003</b>	<b>€ 6,265</b>	<b>168%</b>

\* As a result of the change in strategy, the Contract Development and Products & Drug Delivery activities have been integrated into one business unit during the second half of 2009. Consequently, this disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment.

Gross service revenues increased by 70%. The Company sold and out-licensed its rights to its lead product Locteron to former co-development partner Biolex in October 2008. From that date onwards, OctoPlus is reimbursed for all process development for and manufacturing of clinical trial supplies of Locteron. This resulted in a significant increase in consolidated external revenues and it diminished inter-segment revenues as effectively the Products and Drug Delivery business unit ceased to exist. In total, Consolidated service revenues increased by 174%.

License and other revenues increased by 69% primarily as a result of increased payments by SurModics.

There was no Income from subsidies for the six months period ended 30 June 2009, as the study we were conducting with Utrecht University for a novel drug delivery technology is finalized.

<b>Operating Costs (in thousands)</b>	<b>Six months ended 30 June</b>		<b>Change</b>	
	<b>2008</b>	<b>2009</b>	<b>€</b>	<b>%</b>
	<b>(unaudited)</b>	<b>(unaudited)</b>		
Raw materials and auxiliaries	€ 370	€ 173	€ (197)	(53)%
Cost of contracted work and other external charges	1,293	862	(431)	(33)
Employee benefits	4,460	4,905	445	10
Depreciation and amortization	724	1,075	351	48
Other costs	2,774	3,870	1,096	40
<b>Total operating costs</b>	<b>€ 9,621</b>	<b>€ 10,885</b>	<b>€ 1,264</b>	<b>13%</b>

Raw materials and auxiliaries decreased by 53%. The Company sold and out-licensed its rights to its lead product Locteron to former co-development partner Biolex in October 2008. From that date onwards, the Company no longer incurs charges for pre-clinical and clinical trials for Locteron. Costs of contracted work and other external charges decreased by 33%. The Company sold and out-licensed its rights to its lead product Locteron to former co-development partner Biolex in October 2008. From that date onwards, the Company does no longer incur charges for pre-clinical and clinical trials for Locteron.

Employee benefits increased by 10%, mainly as a result of costs related to the re-structuring of the Company. Depreciation and amortization increased by 48%, mainly as a result of the Company's new manufacturing facility becoming operational in the first part of 2009.

Other costs increased by 40%, mainly as a result of significant one-off costs related to the Company's new manufacturing facility becoming operational in the first part of 2009.

**Years Ended 31 December 2007 and 2008**

<b>Revenues (€ in thousands)</b>	<b>Year ended 31 December</b>		<b>Change</b>	
	<b>2007</b>	<b>2008</b>	<b>€</b>	<b>%</b>
Gross service revenues	€ 9,133	€ 11,945	€ 2,812	31%
Inter-segment (internal) revenues*	(4,547)	(3,237)	1,310	(29)
Consolidated service revenues	4,586	8,708	4,122	90
License and other revenues	326	8,160	7,834	2,403
Income from subsidies	282	55	(227)	(80)
<b>Total (consolidated) revenues</b>	<b>€ 5,194</b>	<b>€ 16,923</b>	<b>€ 11,729</b>	<b>226%</b>

\* As a result of the change in strategy, the Contract Development and Products & Drug Delivery activities have been integrated into one business unit during the second half of 2009. Consequently, this disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment.

Gross service revenues increased by 31%, primarily as a result of a strong business environment for pharmaceutical services, increased capacity in our contract formulation and manufacturing business and the ongoing clinical study of Locteron for which we manufacture the final product. We also commenced work on 20 new projects during this period. Inter-segment (internal) revenues declined by 29% during this period, partly because as of October 2008 manufacture of Locteron is reimbursed by Biolex. In total, Consolidated service revenues increased by 90%.

License and other revenues increased more than twenty-fold as a result of the up-front fee paid by Biolex as part of the product rights acquisition agreement entered into by OctoPlus and Biolex in October 2008.

Income from subsidies declined because we completed a subsidized study we were conducting with Utrecht University for a novel drug delivery technology.

<b>Operating Costs (€ in thousands)</b>	<b>Year ended 31 December</b>		<b>Change</b>	
	<b>2007</b>	<b>2008</b>	<b>€</b>	<b>%</b>
Raw materials and auxiliaries	€ 379	€ 678	€ 299	79%
Cost of contracted work and other external charges	3,652	2,782	(870)	(24)
Employee benefits	7,881	8,946	1,065	14
Depreciation and amortization	1,122	1,607	485	43
Other costs	7,294	7,112	(182)	(2)
<b>Total operating costs</b>	<b>€ 20,328</b>	<b>€ 21,125</b>	<b>€ 797</b>	<b>4%</b>

Raw materials and auxiliaries increased by 79%, primarily due to increased development activities, also with regard to Locteron.

Cost of contracted work and other external charges decreased due to lower costs with respect to clinical trials for Locteron in general and is furthermore amplified by the fact that as of October 2008 we are no longer cost sharing partner of Biolex for the ongoing development of Locteron.

Employee benefits increased by 14%, due to higher wages and salaries.

Depreciation and amortization increased by 43% because we have commenced occupying our additional facilities early 2008.

### Years Ended 31 December 2006 and 2007

Revenues (€ in thousands)	Year ended 31 December		Change	
	2006	2007	€	%
Gross service revenues	€ 8,514	€ 9,133	€ 619	7%
Inter-segment (internal) revenues	(2,927)	(4,547)	(1,620)	55
Consolidated service revenues	5,587	4,586	(1,001)	(18)
License and other revenues	332	326	(6)	(2)
Income from subsidies	132	282	150	114
<b>Total (consolidated) revenues</b>	<b>€ 6,051</b>	<b>€ 5,194</b>	<b>€ (857)</b>	<b>(14%)</b>

\* As a result of the change in strategy, the Contract Development and Products & Drug Delivery activities have been integrated into one business unit during the second half of 2009. Consequently, this disaggregated information was no longer used by the Company for the remainder of 2009. On a going forward basis, the Company identifies only one (remaining) operating segment.

Gross service revenues increased by 7%, primarily as a result of the materials manufactured for the clinical study of Locteron. We commenced work on 14 new projects during this period. Inter-segment (internal) revenues increased by 55% during this period, primarily as a result of the materials produced for the Locteron clinical study.

Income from subsidies increased by 114% because of activities on a subsidized study we were conducting with Utrecht University for a novel drug delivery technology.

Operating Costs (€ in thousands)	Year ended 31 December		Change	
	2006	2007	€	%
Raw materials and auxiliaries	€ 180	€ 379	€ 199	111%
Cost of contracted work and other external charges	1,928	3,652	1,724	89
Employee benefits	6,140	7,881	1,741	28
Depreciation and amortization	1,060	1,122	62	6
Other costs	5,263	7,294	2,031	39
<b>Total operating costs</b>	<b>€ 14,571</b>	<b>€ 20,328</b>	<b>€ 5,757</b>	<b>40%</b>

Raw materials and auxiliaries increased by 111%, primarily due to increased development activities, in particular, with regard to Locteron.

Cost of contracted work and other external charges also increased due to greater activity involving the furtherance of the product candidates under development in 2007. In particular, we incurred greater costs from the contract research organizations managing the clinical and pre-clinical trial activities, primarily related to Locteron.

Employee benefits increased by 28%, due to an increase in the number of our employees from 139 as of 31 December 2006 to 170 as of 31 December 2007.

Other costs increased by 39%, partly due to greater overhead and equipment expenses as a result of an increase in our number of staff. Furthermore, we incurred additional expenses in relation to temporary personnel services and professional recruitment charges.

### Interest

#### Interest Costs

In April 2004, we acquired our main building, which we subsequently sold and leased back. A significant part of our interest costs in 2006 of € 391,000 relates to this finance lease contract. The

remaining part relates to interest associated with other finance lease contracts and interest related to the utilization of part of our € 2.0 million credit facility, which we obtained from ABN AMRO Bank N.V. in 2004.

Interest costs for 2007 amounted to € 436,000 and primarily reflect the interest expenses associated with the finance lease contract for our main building and other finance lease contracts for our property, plant and equipment.

In 2008, interest costs amounted to € 2,014,000 and comprises (i) € 859,000 related to the finance lease contracts for our property, plant and equipment (including the additional facilities that came available in the beginning of 2008) and some of the equipment used in the new facilities, (ii) € 330,000 through utilization of the € 2.0 million credit facility, which we obtained from ABN AMRO Bank N.V. in 2004 and other bank charges, (iii) € 458,000 related to interest charges on the convertible bridge loans provided by Life Sciences Partners, S.R. One and Biolex and (iv) an exchange loss of € 367,000 on the settlement of the convertible bridge loan with Biolex, for which we bore the currency exchange risk.

For the six months ended 30 June 2009, the interest costs of € 745,000 mainly related to the finance lease contracts for our property, plant and equipment and some of the equipment used in the new facilities.

### **Interest Income**

Interest income reflects interest earned on our deposits of cash in interest bearing accounts. Interest income for the years 2008, 2007 and 2006 amounted to € 7,000, € 395,000 and € 246,000, respectively. There was no interest income for the six months period ended 30 June 2009.

### **Liquidity and Capital Resources**

Our primary sources of liquidity have been our funds generated from our contract formulation and manufacturing business and, more recently, from our Products and Drug Delivery Business, plus equity and debt financing. We have also received some government subsidies. With our change of focus from Contract formulation and manufacturing to the development of proprietary product candidates using our drug delivery technologies from the year 2000 onwards, our capital requirements have increased and equity fund raising has been an increasingly important source of our liquidity. However, following the product rights acquisition agreement and the product development and supply agreement with Biolex, entered into in October 2008, our need for further capital was reduced considerably.

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 B.V. 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 B.V.'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 credit facility with ABN AMRO Bank N.V. As collateral for this facility, OctoPlus Development B.V. provided a pledge over its equipment, inventories and receivables. OctoPlus N.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 tangible net worth shall equal at least 25% of the balance sheet total, adjusted for certain items.

On 6 January 2010 we signed a credit agreement with Fortis Bank (Nederland) N.V., pursuant to which we will be granted a credit facility of up to € 2.0 million, which shall replace our existing credit facility with ABN AMRO Bank N.V. As collateral, OctoPlus N.V. and its subsidiaries will provide a pledge over their equipment, inventories, receivables and patents (with the exception of patents owned by PolyActive Sciences B.V.). In addition, the facility agreement contains a covenant that requires that OctoPlus N.V.'s

consolidated tangible net worth shall equal at least 25% of the balance sheet total, adjusted for certain items.

In January 2005, we issued 6,861,500 preference shares (which were converted into ordinary shares) and a subordinated convertible bond, raising a total of € 18.4 million. Investors in this round of financing included Life Sciences Partners, S.R. One, Innoven Partenaires S.A., Fagus N.V. /S.A., SurModics, 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 278,600 preference shares (which were converted into ordinary 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.

On 9 October 2006, we issued 4,301,076 ordinary shares pursuant to our Initial Public Offering (“IPO”) and raised € 20 million in gross proceeds.

In March 2008, we entered into a convertible bridge loan facility with Life Sciences Partners and S.R. One for a cumulative amount of € 4.0 million. Monies drawn under this facility carried 15% interest. This facility including the interest thereon was redeemed through the issuance of 5,996,249 ordinary shares on 25 February 2009.

In July 2008 we entered into a convertible bridge loan facility with Biolex for an amount of € 2.0 million which amount was increased by € 235,000 on 22 August, by € 115,000 on 25 August and by € 400,000 on 8 September 2008. This bridge loan including accumulated interest was set off against the up-front fee payable by Biolex under the product rights acquisition agreement of October 2008.

In April 2008, through our subsidiary OctoPlus Development B.V., we entered into a finance lease agreement with Amstel Lease Maatschappij N.V., pursuant to which Amstel Lease Maatschappij N.V. provides financing to OctoPlus Development B.V. by way of a sale and lease back of certain equipment with an investment value of € 3.7 million. The sale and lease back was executed in December 2008. As collateral for this lease facility, OctoPlus Development B.V. provided a pledge over its shares. In addition, the finance lease agreement contains a covenant that requires OctoPlus Development B.V.’s guaranteed capital to be at least equal to 30% of its total assets per 31 December 2009.

On 25 February 2009, we issued 13,996,250 ordinary shares pursuant to a private placement and raised € 10.5 million in gross proceeds. Part of this private placement related to the conversion of the bridge loan facility entered into with Life Sciences Partners and S.R. One in March 2008 for a total amount of € 4.5 million (including accumulated interest).

In December 2009, we completed the Private Placement issuing 3,232,106 New Shares and raising € 4.0 million in gross proceeds.

## **Cash Flows**

In 2006, we reported a negative net cash flow from operating activities of € 6.4 million. Investments in property, plant and equipment and intangible assets amounted to € 1.1 million and € 12.5 million of the IPO proceeds were invested in short-term and long-term deposits, resulting in a negative net cash flow from investing activities of € 13.6 million. The positive net cash flow from financing activities amounted to € 17.8 million, and all related to our IPO. As a result, the negative net cash flow from all operating, investing and financing activities in 2006 was € 2.2 million. Cash, cash equivalents, deposits and bank overdrafts increased from € 9.2 million to € 19.6 million during the year in 2006.

In 2007, we reported a negative net cash flow from operating activities of € 12.5 million. Investments in intangible and tangible assets amounted to € 4.6 million in total, of which € 1.25 million related to the additional patents acquired from IsoTis N.V. (“IsoTis”) in April 2007. Matured deposits amounting to € 12.5 million are also reflected in the cash flow from investing activities, resulting in a reported € 7.9 million positive net cash flow from investing activities for 2007. The cash flow from financing activities is cash

neutral in 2007. As a result, the total negative net cash flow from all operating, investing and financing activities in 2007 was € 4.5 million negative. Cash, cash equivalents, deposits and bank overdrafts decreased from € 19.6 million to € 2.5 million during the year.

In 2008, we reported a negative cash flow from operating activities of € 4.0 million. Investments in property and plant and equipment and intangible assets amounted to € 6.7 million. The positive net cash flow from financing activities amounted to € 7.3 million, and is related to the convertible bridge loans provided by Life Sciences Partners and S.R. One for € 4.0 million in total, a finance lease agreement with Amstel Lease Maatschappij N.V. for € 3.7 million in total and repayments on finance lease liabilities of € 0.4 million. As a result, the negative net cash flow from all operating, investing and financing activities in 2008 was € 3.4 million. Cash, cash equivalents, deposits and bank overdrafts reduced from € 2.5 million to € 0.9 million negative during the year in 2008, thereby utilizing some of the ABN AMRO Bank N.V. € 2.0 million credit facility.

In the first half of 2009, we reported a negative net cash flow from operating activities of € 2.0 million. Investments in intangible and tangible assets amounted to € 1.0 million in total, of which a significant part relates to the final payments for the new manufacturing facility and the validation of this facility. We reported a positive cash flow from financing activities of € 5.4 million for the first half of 2009. This relates to our private placement of 25 February 2009, where we raised € 10.5 million in gross proceeds. As part of this private placement, the bridge loans received from Life Sciences Partners and S.R. One in March 2008 for a total amount of € 4.5 million (including accumulated interest) were converted into ordinary shares. As a result, we received € 6.0 million in (gross) proceeds. The total positive net cash flow from all operating, investing and financing activities in the first half of 2009 was € 2.4 million. Cash, cash equivalents and bank overdrafts increased from € (0.9) million to € 1.5 million during the first half of 2009.

Since 2002, our expenses in technology and product development have exceeded net operating profits from our contract formulation and manufacturing business. Following our strategic focus on a service based business model, we expect to be able to achieve a positive cash flow from operating activities in the foreseeable future.

### ***Principal Investments***

In 2006, our investments in plant and equipment and intangible assets amounted to € 1.1 million. Approximately 50% relates to equipment for our laboratories and manufacturing plant. The remaining amount is almost equally divided over computers and software on the one hand and costs for design of the manufacturing plant for the new building.

In 2007, our investments in plant and equipment and intangible assets amounted to € 4.6 million in total, of which € 1.25 million related to the additional patents acquired from IsoTis in April 2007. The remaining amount is primarily related to the design of our new manufacturing facility.

In 2008, our investments in plant and equipment and intangible assets amounted to € 6.7 million in total, nearly all of which is related to the design of our new manufacturing facility.

In the first half of 2009, our investments in plant and equipment and intangible assets amounted to € 1.0 million in total, nearly all of which is related to the design and validation of our new manufacturing facility.

### ***Working Capital Statement***

Our current cash resources, together with our existing financing facilities, do provide us with sufficient working capital for at least the next 12 months following the date of this Prospectus. This working capital statement covers us and all our current subsidiaries.

## 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. We have sold and leased back our headquarters for a period of twenty years and a significant part of the equipment used in our new manufacturing facility for a period of five years, and together with some other less significant finance lease obligations, this has resulted in total finance lease obligations of € 7.2 million as of 31 December 2006, € 6.9 million as of 31 December 2007 and € 21.7 million as of 31 December 2008. The 2008 increment is caused by the long-term finance lease contract with the owner of our headquarters for the expanded office, laboratory and manufacturing facilities. We have a total of approximately 5,250 m<sup>2</sup> of offices, laboratories and manufacturing facilities available under long-term lease contracts to accommodate our anticipated growth. In 2008, our total finance lease and operating lease payments approximated € 1.3 million. Approximately € 1.0 million of this amount was related to the lease of our headquarters, and € 0.3 million was related to finance lease payments for other property, plant and equipment, mainly laboratory and production equipment.

The following table sets out our payment obligations under contracts as of 30 June 2009 that provide for fixed and determinable payments over the periods indicated.

€	July – Dec 2009	2010	2011 and 2012	2013 and later
Finance leases	€ 979,000	€ 1,915,000	€ 3,828,000	€ 14,684,000
Royalty obligations	-	-	-	-
Other operating commitments	153,000	-	-	-
Operating leases	60,000	94,000	189,000	1,404,000
<b>Total</b>	<b>€1,192,000</b>	<b>€2,009,000</b>	<b>€4,017,000</b>	<b>€16,088,000</b>

In addition, other amounts that we may be obligated to pay under our existing contractual relationships that are not currently fixed and determinable include royalty and milestone payments under our agreements with Leiden University Medical Center (“LUMC”), Utrecht University, IsoTis and Theratechnologies, Inc. (“Theratechnologies”). Pursuant to our license agreement with LUMC for OP-145 CSOM we may be obligated to pay royalties on future sales. 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 undertake commercialization of a final product, or on royalties received from third parties. Pursuant to our agreement with IsoTis, IsoTis is entitled to royalty payments on our revenues from the sale of products using the PolyActive technology acquired from IsoTis and milestone payments we receive related to product candidates using such PolyActive technology. The up-front payment as received from Biolex in October 2008 did not result in any royalty payment to be made to IsoTis. Payments under this agreement continue until the end of the life of the patents currently in the PolyActive patent portfolio. On 29 October 2007, US based company Integra Life Sciences Holdings Corporation (“Integra”) acquired all issued and outstanding shares of IsoTis and any potential royalties will therefore need to be paid to Integra.

Pursuant to our agreement with Theratechnologies, Theratechnologies is entitled to multiple development, regulatory and sales milestone payments for each product incorporating the licensed technology. Currently we do not expect to enter into a partnership to develop such a product.

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. As we have discontinued this project, we anticipate that we will not have to repay the “soft loan”.

We expect to be able to meet these contractual obligations from our anticipated revenues, as well as from the proceeds of the Private Placement. A significant part of our contractual obligations are contingent upon reaching various milestones, including commercialization milestones.

## **Outlook**

Our prime focus is on restructuring OctoPlus and building our business into a cash flow positive and profitable organization in the medium-term. We believe that this can be achieved by successfully fulfilling the contractual obligations and other service activities currently anticipated under the product rights acquisition agreement and the development and supply agreement with Biolex and by realizing further growth of our contract formulation and manufacturing activities.

The expected cash flow calculations do not include future milestone and royalty payments by Biolex. If the activities and the resulting cash flows associated with the product rights acquisition agreement or the product development and supply agreement are substantially less than currently expected due to changes in the scope or the rate of product development or uncured material breach by OctoPlus, this could have a significant negative impact on our cash flow from operations.

Based on the current contract formulation and manufacturing order book, together with the ongoing discussions with our existing clients and potential clients, we believe that we will continue to witness further growth for our non-Locteron contract formulation and manufacturing activities in 2010. We will be able to meet increased demand from our customers by utilizing our expanded facilities in Leiden and making some further modest investments, predominantly in equipment.

In addition to our contract formulation and manufacturing activities, we have started a number of feasibility projects for the development and formulation of controlled release pharmaceuticals, which combine the proprietary product of our partners with our proprietary drug delivery technologies. We are reimbursed for our activities under these projects. Revenues from these projects are relatively modest. However, depending on the outcome of these feasibility projects (which on average run up to 6 - 12 months), our partners may decide to continue developing their product candidate, requiring our ongoing investment for further formulation and manufacturing services as well as a license to our proprietary drug delivery technologies. We have, save for our agreement with Biolex, not yet entered into such a development agreement with a partner. Our goal is that on average one out of five of these feasibility projects will result in a development agreement, generating ongoing development and manufacturing revenues as well as license revenues and potentially royalty income at a later stage.

## **Off Balance Sheet Arrangements**

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

## **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 endorsed/adopted by the European Union (EU). 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 that 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 incorporated by reference in this Prospectus. 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 that reflect specific risks relating to the relevant segment.

## **Convertible Loans**

In 2008, the Company obtained convertible bridge loans up to € 4.0 million (excluding accumulated interest) from Life Sciences Partners and S.R. One. This bridge financing is classified as a financial liability as it will or may be settled in the entity's own equity instruments and is a non-derivative for which the entity is or may be obliged to deliver a variable number of the entity's own equity instruments. The loan part and the option to convert are treated as two separate transactions. Both parts are initially booked at fair value and classified within short-term financial liabilities, as the loan might be repaid or converted within 12 months. The estimated future cash outflows for us in case of actual conversion are expected to be close or equal to zero. The value of the conversion option is therefore also close or equal to zero and the conversion option does not have impact on the 2008 financial statements.

On 25 February 2009, we issued 13,996,250 ordinary shares pursuant to a private placement and raised € 10.5 million in gross proceeds. Part of this private placement related to the conversion of the bridge loan facility entered into with Life Sciences Partners and S.R. One for a total amount of € 4.5 million (including accumulated interest).

## **Corporate Income Taxes**

We have a history of tax losses and recognize 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 utilized by the fiscal unity. Our management's judgment is that sufficient convincing other evidence is not currently available and a deferred tax asset is therefore only recognized to the extent that a fiscal unity has sufficient taxable temporary differences.

## **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, known as the Binomial method, which considers, 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.

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.

## **Revenue 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 Other Revenues***

License and other revenues include amounts earned from third parties with licenses and/or options to our intellectual property. License and other 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 other 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.

## **Lease Accounting**

Evaluating the substance of a lease agreement involves complex accounting judgments under International Accounting Standards (IAS) 17. For our existing lease agreements, we have evaluated whether or not significant risks and rewards have been transferred and have accounted for leases, especially with regard to land and buildings, on that basis.

At the end of 2009, OctoPlus decided to change the accounting policy for the land part which was subject to the sale and leaseback transaction in 2004. Following a re-evaluation of the substance of this transaction the land part will be treated as an operating lease under IAS 17. The change in accounting treatment will result in the de-recognition of the land in property, plant and equipment and the de-recognition of the related financing under the non-current finance lease liabilities for an amount of € 1.1 million. The change of accounting policy has no effect on shareholders' equity and result for the year.

## Business

### Overview

OctoPlus is a drug delivery service company that is globally renowned as a center of excellence in formulation development and drug delivery. We offer clients our expertise in combination with the drug delivery technologies OctoDEX, PolyActive and SynBiosys for the development of controlled release formulations of injectable compounds. Such depot formulation products have demonstrated strong improvement of side effect profiles, increased patient compliance and better efficacy. In addition, we offer proven and reliable services in formulation development, analytical development, process development and GMP manufacturing. Our expertise is focused on formulation of biotech-derived compounds and small chemical molecules.

Since its establishment in 1995, OctoPlus has provided advanced drug formulation and clinical scale manufacturing services to biotechnology and pharmaceutical companies worldwide. We have provided our services to more than 135 clients that have progressed more than 40 products into clinical studies and six products on to the market. In 2008 approximately 69% of our revenues from this business originated in the European Union and approximately 27% of our revenues originated from clients in North America, while the remainder was sourced from other countries. In 2009 our revenues sourced from North America increased significantly as a result of our development work and manufacture for Biolex. Since our establishment in 1995 through 30 June 2009, we have achieved € 58 million of consolidated revenues. In 2008, approximately 57% of our contract formulation and manufacturing revenues originated in the European Union and approximately 36% of our revenues originated from clients in North America, while the remainder was sourced from other countries. In 2009 revenues sourced from North America increased significantly as a result of manufacturing services clinical trial material for the ongoing Locteron Phase IIb study for Biolex.

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. We believe that products based on our technologies can be applied in many therapeutic areas. There is currently one product in clinical development under a license and development agreement. In addition, we have entered into several collaboration agreements for feasibility projects to develop controlled release formulations for biotech and pharmaceutical companies. Depending on the outcome of these feasibility projects our collaborators may decide to continue developing such product candidates, requiring our ongoing involvement for the further formulation and manufacturing services as well as a license to our proprietary drug delivery technologies.

The clinically most advanced product candidate based on our proprietary drug delivery technology, Locteron, is being developed by Biolex, the holder of the commercial rights to Locteron, and is currently in Phase IIb clinical trials. Locteron is a novel therapy for the treatment of chronic hepatitis C infection, combining our proprietary PolyActive drug delivery technology with Biolex' interferon alfa. Locteron is designed to require less frequent administration and to cause fewer side effects than marketed forms of interferon alfa that currently represent the standard of care for this illness.

We have one other proprietary clinical-stage product candidate which is OP-145 CSOM, a novel proprietary peptide therapeutic for the treatment of chronic otitis media, also known as chronic middle ear infection. This product has successfully completed Phase II clinical trials. We intend to seek a licensing partner responsible for future costs, before continuing any further development activities in respect of OP-145 CSOM.

In October 2008 we redefined our strategy. We will focus exclusively on formulation, development and manufacturing activities for which we are reimbursed. Such contracts can further strengthen our well established contract formulation and manufacturing activities, but shall also relate to activities whereby we combine our proprietary drug delivery technologies with biopharmaceutical drugs or compounds of our partners in order to improve the properties of such biopharmaceutical drugs. We have entered into

several collaboration agreements for feasibility projects to develop controlled release formulations for biotech and pharmaceutical companies, whereby our partners incur the development costs and we will be reimbursed for all or substantially all costs and will furthermore be entitled to potential future milestone and royalty payments.

Our Executive Board has many years of experience in the areas of drug delivery, pharmaceutical formulation and manufacturing, business development and finance. Our facilities are located in Leiden, the Netherlands, and include a cGMP manufacturing facility, laboratories and offices, which we all lease under long-term contracts. As of 31 December 2009, we employed 132 people, all of which are located in Leiden.

## History

OctoPlus was founded in 1995 by Joost Holthuis, Ph.D., who served on the Executive Board until August 2009, and Prof. Daan Crommelin, Ph.D., who served as the chairperson of our Scientific Advisory Board until mid 2009. Initially, we focused on providing pharmaceutical and biotechnology companies with advanced drug formulation and clinical scale manufacturing services. Starting in 1996, we entered into a number of agreements with Utrecht University by which we received a worldwide exclusive license to the OctoDEX technology. While we continued to successfully grow our contract formulation and manufacturing 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.

In 2001, we raised € 3 million 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 B.V. from IsoTis.

In 2005, Life Sciences Partners, S.R. One, Innoven Partenaires, Fagus, SurModics and certain other parties invested € 18.4 million in OctoPlus, which allowed us to fund further development of our proprietary technologies and the portfolio of product candidates we were developing.

In October 2006, we completed our IPO on Euronext Amsterdam raising € 20 million in gross proceeds, which allowed us to continue our drug development efforts.

In April 2008, we obtained € 4.0 million bridge financing from Life Sciences Partners and S.R. One that allowed us to fund our operations. In July and September 2008, our partner Biolex provided working capital totaling € 2.75 million under materially the same terms and conditions as Life Sciences Partners and S.R. One.

In October 2008, we signed a product rights acquisition agreement with Biolex for the sale and out-licensing of our commercial rights to Locteron to Biolex in exchange of \$149 million in up-front and milestone payments plus further royalties on sales revenues. This agreement marked the start of OctoPlus' new service-oriented strategy, moving away from developing product candidates at our own expense towards out-licensing our proprietary drug delivery technologies and co-developing products with partners.

In February 2009, we completed a private placement of Shares raising € 10.5 million in gross proceeds, which allowed us to make the final investments in OctoPlus' new production facility and continue to implement our new service-based strategy. Part of this private placement related to the conversion of the bridge loans provided by Life Sciences Partners and S.R. One for a total amount of € 4.5 million (including accumulated interest).

In December 2009, we completed the Private Placement raising € 4.0 million in gross proceeds, which we will use primarily for general corporate purposes.

## Strategy

Key elements of our corporate strategy, which was redefined in October 2008, include;

- **Continue to grow our contract formulation and manufacturing business.** We intend to further grow our globally renowned activities in the field of drug delivery, formulation development, analytical development, process development services and GMP manufacturing for our clients.
- **Build a portfolio of licensed products based on our proprietary technology by winning feasibility projects, executing them successfully and converting them into licensing agreements.** We intend to expand the number of feasibility projects in which we combine our drug delivery technologies with our clients' biopharmaceutical drugs or other therapeutics in need of clinical improvement. We intend to primarily apply our proprietary drug delivery technologies to those product opportunities where our partners can capitalize on the known safety, efficacy and often established drug development history of existing drugs. 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, strong side effects and/or limited efficacy. Depending on the outcome of these feasibility projects our collaborators may decide to continue developing such product candidates, requiring our ongoing involvement for the further formulation and manufacturing services as well as a license to our proprietary drug delivery technologies.

## Contract Formulation and Manufacturing<sup>\*</sup>

Our Contract Formulation & Manufacturing business is operated by our subsidiary OctoPlus Development B.V. Over the last 14 years, we have become a leading European 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 formulation and manufacturing business are performed in our dedicated facilities in Leiden, the Netherlands, where we operate a cGMP manufacturing facility for manufacture of final product for pre-clinical and clinical trials, and for small-scale commercial use. 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 expertise in parenteral formulations and especially biotech-derived and low-soluble compounds. Our cGMP manufacturing facility allows us to offer our customers a full range of sterile pharmaceutical production options, including freeze-drying.

We have successfully provided the services of our contract formulation and manufacturing business on a fee-for-service basis to a diverse and international group of more than 135 pharmaceutical and biotechnology companies, focusing mainly on protein therapeutics and to a lesser extent on small molecule drugs. Since our establishment in 1995 through 30 June 2009, we have achieved € 70 million in cumulative gross (non-consolidated) revenues from this business, including inter-segment (internal) revenues of € 12 million from our Products and Drug Delivery business. 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 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 formulation and manufacturing business are demonstrated by our high rates of repeat business.

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<sup>\*</sup> On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

## ***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 other formulations, such as 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 formulation and manufacturing 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 formulation and manufacturing business are set out below:

- **Characterization.** We have 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, formulations using liposomes, and the solubilization of low soluble compounds. Our capabilities include the ability to freeze-dry clinical batches and small-scale commercial batches of therapeutic products. 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;
- **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 or have manufactured a wide range of liquid and semi-solid biopharmaceutical products, including injectable, 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 the opening of our expanded manufacturing facility in June 2009, our manufacturing capacity increased from 3,000 units per batch to 10,000 units per batch. Therefore, we cannot only produce sufficient materials for toxicology, Phase I and Phase II clinical trials, but we can also manufacture small-scale commercial products;
- **Stability studies.** We perform stability studies in accordance with the International Conference on Harmonization guidelines.

## ***Our Customer Base***

Since establishment, our contract formulation and manufacturing business has provided services to more than 135 clients in a total of approximately 250 projects. We have contributed to over 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 40 clients, which are located worldwide 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 2008, our five largest clients represented 47% of our contract formulation and manufacturing business revenues. In the same year, approximately 57% of our contract formulation and manufacturing revenues originated in the European Union and approximately 36% of our revenues originated from clients in North America, while the remainder was sourced from other countries. In 2009 revenues sourced from North America increased significantly as a result of manufacturing clinical trial material for the ongoing Locteron Phase IIb study for Biolex.

### **Drug Delivery Technologies and Product Candidates<sup>\*</sup>**

Our Drug Delivery and technology activities, including any activities associated with product candidates are operated by our subsidiaries OctoPlus Technologies B.V., Chienna B.V., OctoPlus Sciences B.V. and OctoPlus PolyActive Sciences B.V.

Our expertise is combining our drug delivery technologies with our partners' biopharmaceutical drugs or other therapeutics that are in need of clinical improvement. We have recently seen a significant increase in investment in the field of biosimilars by the pharmaceutical industry.<sup>2</sup> Biosimilars are the second generation of biological products which are being developed and marketed following patent expiry of the originator's product. It is viewed by many that the biosimilars market will be very different from the existing and well known generic model for traditional small molecule based pharmaceutical products. The fundamental difference lies in the size and complexity of protein based products which, with present technology, do not allow companies or regulatory agencies to quantify that one product is identical to another, hence the term biosimilar. The consequence to this is that developers of biosimilars need to undertake an extensive clinical development programme for their product and marketing of the product has to be as a distinct entity, not as a replacement for the existing branded product. With this significant development investment in mind a number of companies who are investing in biosimilars, are looking at how they can differentiate their product from the originator brand and how they can use their marketing skills to gain market share. Through the use of our controlled release technology, which is ideally suited for the controlled release of proteins, we believe that we can offer a significant differentiation to biosimilar products.

It is by using this technology that we aim to leverage our broad expertise in formulation development and drug delivery in order to develop pharmaceutical products that improve existing approaches to the treatment of serious illnesses. We do not expect, anymore, to invest significantly in product development at our own expense but to use our technology in the context of a commercial collaboration, whereby our partners incur the development costs and we will be reimbursed for all or substantially all costs and will furthermore be entitled to future milestone and royalty payments too.

The following table summarizes key information about the product candidates currently being developed, based on our proprietary technology or active pharmaceutical ingredient. In addition, we have entered into several collaboration agreements for feasibility projects to develop controlled release formulations for biotech and pharmaceutical companies.

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<sup>\*</sup> On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

<sup>2</sup> <http://www.business-standard.com/india/news/intas-biopharma-to-focus-developing-biosimilars-for-us-eu/384189/>, <https://www.espicom.com/Prodcat.nsf/Search/00000012?OpenDocument>, [http://www.sandoz.com/site/enproduct\\_range/more\\_about\\_biosimilars/index.shtml](http://www.sandoz.com/site/enproduct_range/more_about_biosimilars/index.shtml).

<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	Phase IIb ongoing	Out-licensed and transferred to Biolex <sup>1</sup>	Biolex to complete Phase IIb trial in 2010
OP-145 CSOM	Chronic Middle Ear Infection	Phase II completed	Co-development with Green Cross Corporation <sup>2</sup>	Out-licensing in 2010

<sup>1</sup> In October 2008, we concluded a product rights acquisition agreement with Biolex for the development and exclusive commercialization of Locteron by Biolex.

<sup>2</sup> In November 2006, we concluded an out-licensing agreement with Green Cross Corporation of South Korea for the co-development of OP-145 CSOM and the exclusive commercialization of OP-145 CSOM in the South Korean market.

### **Locteron for Chronic Hepatitis C**

Locteron is a proprietary controlled release formulation of interferon alfa for the treatment of chronic hepatitis C infection (HCV). Hepatitis C is a common disease, affecting over 170 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 the hepatitis C virus and are replaced by scar tissue. Resulting damage to the liver can lead to impaired liver function, liver cancer and ultimately death.

Locteron combines interferon alfa produced by 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 for the treatment of HCV are dosed once-every-week. 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. These high initial levels of interferon alfa contribute to the acute flu-like symptoms commonly associated with the current standard of care for HCV. Locteron aims to provide at least the same therapeutic benefit to HCV patients with fewer, less severe and less frequent side effects and a more convenient dosing schedule. It is believed that an improved side effect profile will lead to enhanced patient compliance. The expected intended superior side effect profile of Locteron may attract and maintain patients on therapy who currently delay or refuse treatment, in particular in light of the current 48-week treatment period for HCV genotype 1, the HCV variant most prevalent in Western countries.

### **Locteron Clinical Development**

In 2006, OctoPlus and Biolex completed a Phase I clinical study in which 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.

In 2007, OctoPlus and Biolex completed a 12-week Phase IIa clinical trial to evaluate the safety, tolerability and preliminary efficacy of Locteron administered once-every-two-weeks in combination with ribavirin in treatment-naïve hepatitis C patients. Results of the study showed that Locteron was generally safe and well tolerated. In addition, the results showed that 12 weeks of treatment with Locteron in combination with ribavirin was effective in reducing hepatitis C virus levels.

In 2008, OctoPlus and Biolex commenced a separate Phase IIa clinical study in order to generate clinical and regulatory experience with Locteron in the United States and to make a direct comparison with the current standard of care in HCV. This separate Phase IIa clinical study was completed successfully earlier in 2009.

In June 2009, Biolex completed patient recruitment in Phase IIb trials with Locteron, which are expected to be completed in 2010. Biolex will present interim results after 12 weeks of treatment from its

two Phase IIb studies for Locteron versus PEG-Intron® at the International Liver Congress in April 2010, organized by the European Association for the Study of the Liver (EASL). The data have been accepted for both oral and poster presentations. Under the strict rules of the conference, the results are currently embargoed until publication at the conference.

### ***Locteron Manufacturing***

BLX-883, the interferon alfa ingredient in Locteron, is produced by Biolex in accordance with cGMP guidelines at its facilities in North Carolina. We are manufacturing Locteron by combining our PolyActive microspheres with BLX-883 for the Phase IIb clinical studies in our licensed manufacturing facility in Leiden, the Netherlands and are performing scale-up activities for which we are reimbursed by Biolex.

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

OP-145 CSOM is our novel, proprietary peptide therapeutic 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. 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 eradicated easily using common antibiotics. However, a more serious condition may develop 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 CSOM 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 CSOM 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 CSOM interacts with lipid components on the surface of bacteria typically associated with chronic middle ear infection. By binding to these surface components, OP-145 CSOM destabilizes the cell membrane leading to bacterial cell death. In light of these two characteristics, we believe that OP-145 CSOM may offer benefits for patients with chronic middle ear infection that cannot be treated adequately with current therapies.

### ***OP-145 CSOM clinical development***

Based on the anticipated advantages of OP-145 CSOM, 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.

In April 2006, we completed a Phase I/IIa safety and tolerability study comprising a dose-ranging assessment in 16 therapy-resistant patients who had an average disease duration of 17 years. Results from this study showed that OP-145 CSOM was safe and well tolerated, and gave an early indication of efficacy.

In a double-blind, placebo-controlled Phase II study completed in 2008, we have successfully demonstrated the safety and efficacy of OP-145 CSOM.

We intend to seek a licensing partner responsible for future costs, before continuing any further development activities.

### **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.

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.

We have successfully used OctoDEX for the controlled delivery of several therapeutic proteins in a number of in vitro, in vivo and clinical 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.

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 manufacturing facility, enabling us to supply materials for clinical development.

### **PolyActive**

PolyActive is our drug delivery system based on a series of biodegradable polyethers and polyesters. We acquired the PolyActive drug delivery technology as part of our acquisition of Chienna B.V. from IsoTis in 2003. PolyActive was first introduced as a biomaterial over 15 years ago. Since then, it has been used in medical devices for orthopedic and wound repair applications in over 5,000 patients, and two medical devices based on PolyActive polymers have received FDA approval to date. We have access to a detailed safety and toxicity file concerning the PolyActive polymer that was prepared by IsoTis, the former owner of the PolyActive technology, and was filed with the FDA for the use of PolyActive in medical devices.

We focus on the use of PolyActive to create injectable and biodegradable microspheres that enable the controlled release of biopharmaceuticals. 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.

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 manufacturing facility, using a well-established procedure based on a double-emulsion protocol.

## 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 trademarks 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 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, together with our collaboration partners, 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.

OctoPlus' current patent portfolio consists of 202 granted patents and 66 patent applications, which are divided into 29 patent families, of which 7 relate to OctoDEX and OctoVAX, 7 to PolyActive and the remainder to other technologies and products, including OP-145 CSOM and OP-286 CR. OctoPlus has recently disbanded, or plans to disband in the near future, a number of patents and patent applications lacking commercial prospects resulting in an easier to manage patent portfolio and lower maintenance costs. Many of these patents have been filed in our own name, while for certain others we hold exclusive licenses. Certain of our patents and patent applications are jointly held with our collaboration partners. One of our main collaboration partners is Biolex with whom we share ownership of certain patents.

OCTOPLUS is a registered trademark in the European Union. OCTODEX is a registered trademark in the Benelux countries. POLYACTIVE is a registered trademark in the United States, the European Union, Australia, Japan and Norway.

### ***Intellectual Property of our Drug Delivery Technologies***<sup>\*</sup>

Our OctoDEX delivery technology platform, along with its variants and potential technology extensions, is covered by 7 patent families. These patents were filed between 1996 and 2008. It is therefore expected that these patents will expire between 2016 and 2028. 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 US patent US 6,303,148, and the European patent EP 910 412 and the corresponding US patents US 6,497,903 and US 7,060,296, in respect of which we have an exclusive license from Utrecht University. Corresponding patent applications are still pending in Japan. These patents cover the fundamental chemical (polymers, substituents, spacers and crosslinking methods), physical (hydrogels, microspheres and drug-containing

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<sup>\*</sup> On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

compositions), and engineering features (methods for making microspheres) of our OctoDEX drug carriers. They are expected to expire in 2016/2017.

The other OctoDEX patent families relate to potential improvements and extensions of our technology platform, some of which are currently under feasibility investigations and which may also in certain cases have applicability for our other drug delivery technologies. Granted patents relating to these improvements include EP 1 183 016, EP 1 255 534, US 6,395,302, EP 1 306 127, EP 1 750 679 and US 7,468,151. Patent applications in this category include the regional/national applications following from the international patent applications WO 98/00170, WO 98/22093, WO 00/48576 (pending in the US and Japan), WO 01/60339 (pending in Japan), WO 2003/035244 (pending in Canada), WO 2005/110377 and WO 2008/018796.

Our PolyActive drug delivery technology platform is covered by 7 patent families. These patents were filed between 1996 and 2002 and it is therefore expected that these patents will expire between 2016 and 2022.

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 US patent US 5,980,948, which are expected to expire in 2016/2017. 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.

As a result of the product rights acquisition agreement between OctoPlus and Biolex, OctoPlus transferred to or co-owns with Biolex 3 patent families. Biolex has the exclusive rights in the Biolex field from these patents, while OctoPlus retains exclusively all other rights subject to certain non-compete provisions. These patents include, EP 830 859, EP 1 247 522, US 5 980 948, EP 1 843 749, WO 2006/085747 and EP 1 306 127. The Biolex field concerns the controlled release formulations of interferon alfa by using our PolyActive technology.

### ***Intellectual Property of our Products***

In 2006, we filed an international patent application WO 2006/085747 related to the formulation of Locteron which is based on a combination of interferon (including interferon alfa) with our PolyActive delivery technology. Any European, US and other national patents that may issue based on this international patent application may cover controlled release interferon compositions, and may potentially cover both Locteron and comparable products involving the delivery of interferon by microspheres. In the event that these patents are granted, they could provide patent protection for Locteron (and the production thereof) until at least 2026. In 2009, EP 1 843 749 has been granted in all the member states of the European Union for a method for the preparation of microparticles comprising interferon.

We have exclusively licensed WO 2004/067563 from LUMC and have jointly with the LUMC filed international patent application WO 2006/011792 covering OP-145 CSOM and its therapeutic applications in several important jurisdictions. If these applications lead to granted patents, they could provide exclusive protection until at least 2025. Thus far, patents derived from WO 2004/067563 have been granted in Europe, India, South Africa, Singapore, South Korea, New Zealand and the Russian Federation. A patent derived from WO 2006/011792 has been granted in Singapore. In many other jurisdictions examination is in progress.

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 October 2008, we entered into a product rights acquisition agreement and a product development and supply agreement with Biolex following earlier agreements of 2005 and 2003 for the co-development of Locteron. Pursuant to these agreements, Biolex has obtained all commercialization rights, while we continue to provide development services and remain involved as manufacturer of Locteron. We will participate in any revenues from the commercialization of Locteron through milestone payments and royalties on net sales.

Biolex can terminate the product rights acquisition agreement for cause or at will by providing written notice. In the event of a termination at will by Biolex: (i) all the licenses granted to Biolex (other than cross-licenses to certain jointly owned intellectual property) will terminate, (ii) the non-compete obligations applicable to OctoPlus will terminate, (iii) Biolex will assign to OctoPlus its interest in certain intellectual property assigned to Biolex in connection with the execution of the 2008 agreement and (iv) certain license granted from Biolex to OctoPlus with respect to intellectual property retained by Biolex will become effective upon termination. In the event of a termination by Biolex for cause, i.e. because of an uncured material breach by OctoPlus: (i) all the licenses granted to Biolex (other than cross-licenses to certain jointly owned intellectual property) will terminate, (ii) the non-compete obligations applicable to OctoPlus will terminate and (iii) Biolex will assign to OctoPlus its interest in certain intellectual property assigned to Biolex in connection with the execution of the 2008 agreement. The scope of the intellectual property that will be assigned back to us in the event of a termination by Biolex for cause is more limited than in the event of a termination at will by Biolex,

In the event of the termination of the product rights acquisition agreement by either OctoPlus or Biolex, either party will have the right to also terminate the product development and supply agreement, subject to certain phase out arrangements and, in certain circumstances, transition arrangements for the transfer of manufacturing to Biolex.

Under the product development and supply agreement, OctoPlus may be subject to penalties of up to \$4 million in the event OctoPlus fails to meet certain performance standards with respect to the supply of products to Biolex.

In conjunction with the above agreements, Biolex and we entered into an agreement pursuant to which intellectual property rights used in our collaboration have been transferred to OctoPlus PolyActive Sciences B.V., a 100% subsidiary of the Company. We have to refrain from certain actions which may affect the rights of Biolex under these agreements. In case of a material breach we will be subject to a penalty of € 8 million.

### ***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 for internal research purposes. 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 November 2006, we licensed OP-145 CSOM for the treatment of chronic middle ear infection to Green Cross Corporation for the exclusive sale and distribution in South Korea of products based thereon. In addition, we have agreed to perform development work for Green Cross Corporation with respect to the formulation of an OP-145 CSOM product and provide the active ingredients necessary for Green Cross Corporation to perform the studies for registration of the OP-145 CSOM product in South Korea free of charge. After we have found a commercial partner for this product, an international multicenter clinical Phase III program is scheduled to commence in which Green Cross Corporation will be responsible for conducting the clinical trials in South Korea.

Green Cross Corporation is required to pay us a number of nominal milestone payments. Future milestone payments are due upon the grant of a certain patent, upon submission for approval of the clinical study in South Korea and upon the commercial launch of the product based upon OP-145 CSOM. Green Cross Corporation is required to pay us royalties based on gross receipts for sales of OP-145 CSOM by Green Cross Corporation. Furthermore, we are entitled to 50% of any amounts that Green Cross Corporation receives from its sublicensees.

The agreement shall remain in effect until the expiration of the last valid patent relating to the OP-145 CSOM technology licensed or, if later, 15 years after the launch of the product in South Korea. The agreement may be terminated by either party upon a specified notice period or by either party at any time for unremedied default.

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

In August 2004, we entered into an agreement with InnoCore Technologies B.V. ("InnoCore") 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. OctoPlus and InnoCore will collaborate on identifying potential third parties whose compounds may benefit from the application of the SynBiosys technology. OctoPlus and InnoCore will share any payments received from third parties based on a pre-determined formula. This agreement terminated in August 2009 and we are currently negotiating terms for renewal.

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

We have had a partnership with IsoTis since 1999. Through our acquisition in 2003 of Chienna B.V., a subsidiary of IsoTis, we acquired from IsoTis patents and licenses to patents relating to the PolyActive technology. The license agreement with IsoTis was terminated in April 2007 and replaced by a new agreement. Under the 2007 agreement, we acquired the patents not then owned by us relating to the PolyActive technology, except for the patent family covering IsoTis' SynPlug™ product. In connection with the acquisition of the patents relating to the PolyActive technology, we took over IsoTis' rights as licensor of these patents. Furthermore, the 2007 agreement provided for the transfer to us of the PolyActive name and trademarks. IsoTis retains an exclusive, world-wide, royalty-free license with a right to grant sub-licenses to make, use, sell, market and develop any PolyActive rights relating to osseouschondral and/or osteochondral plugs, fillers, cement restrictors (including IsoTis' product SynPlug) and an exclusive, world-wide, royalty-free license with a right to grant sub-licenses to make, use, sell, market and develop any PolyActive rights owned by us related to the use of the PolyActive technology in a medical device to be used to measure and/or monitor blood glucose.

Under the 2007 agreement, IsoTis is entitled to a low single-digit royalty on our revenues of PolyActive-based products. In addition, we will owe Technologiestichting STW, a non-profit organization associated with the Netherlands Ministry of Economic Affairs and the Ministry of Education and Science providing research grants, a low single-digit royalty on the revenues of PolyActive-based products for the duration of the base patent, which expires in 2016. The term of the 2007 agreement is until the expiration of the last valid patent rights licensed to IsoTis.

Pursuant to our supply agreement with IsoTis, we have long-term access to a continued supply of PolyActive polymers. We also have access to updates of the Device Master File provided to the FDA and as maintained by IsoTis. IsoTis transferred the production equipment of PolyActive polymers to PolyVation B.V. In the event IsoTis wishes to sell the production equipment, we have a first right of refusal to purchase the production equipment at a predetermined price. In the event we do not purchase this equipment, IsoTis is obligated to ensure uninterrupted supply of PolyActive to us by the third party supplier under the same terms and conditions as the current arrangement.

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

In 2002, we entered into a co-operation and license agreement with LUMC for OP-145 CSOM. Pursuant to that agreement, we were granted rights to develop OP-145 CSOM 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 CSOM for all indications.

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

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

### ***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. In February 2007, we entered into an agreement with SurModics amending the 2004 agreement, regarding the out-licensing of certain applications in the field of drug-eluting medical devices based on our PolyActive technology only. As a result of the 2007 amendment, certain royalty payment obligations under the old agreement were renegotiated and replaced by fixed annual license payments for the period until 31 March 2012 with the potential for sales based royalties. Thereafter, SurModics will pay certain minimum annual royalty payments. SurModics terminated the license per 30 September 2009 and paid the cancellation fee as outlined in the agreement in September 2009.

### ***Theratechnologies, Inc.***

In September 2007, we concluded a license agreement with Theratechnologies pursuant to which we were granted a worldwide exclusive license to certain GLP-1 analogues, comprising a number of different compounds. In consideration for the license granted under this agreement, we have granted to Theratechnologies options to acquire 200,000 Shares (see "Description of Share Capital and Corporate Governance – Share Capital – Outstanding Options").

Under the license agreement, multiple development, regulatory and sales milestone payments are due for each product incorporating the licensed technology. The sum of these milestone payments amounts to € 35.7 million per product if all milestones are met, with the milestone payments increasing as the development of the product progresses. The regulatory and sales related milestone payments account for approximately 80% of the total milestone payments. We have the right to satisfy developmental milestone payments of up to € 7.7 million per product by issuing Shares to Theratechnologies with a value equal to the amount of the required payment. This right is subject to certain conditions and limitations. In addition to milestone payments, we are required to make low single-digit royalty payments based on sales of products incorporating the licensed technology. The term of the agreement is until the expiration of the last patent; however, the agreement may be terminated for unremedied breach. Currently, we do not expect to enter into a partnership to develop a product based on this licensed technology.

## ***Utrecht University***

Starting in 1996, we executed several agreements with Utrecht University, whereby Utrecht University 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.

## **Competition**

The pharmaceutical and biotechnology industries are highly competitive and subject to rapid technological change. Any product candidates that we successfully develop in collaboration with partners 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 product candidates which we develop for our partners. Many of these entities have financial and other resources substantially greater than those of our partners. 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, programs we develop for our partners. Moreover, there can be no assurance that such competitors will not obtain patent protection or other intellectual property rights that would make it difficult or impossible to market products we develop for our partners. As a result, there can be no assurance that we will be able to compete effectively against these companies or their products.

The ability to compete successfully will depend largely on the joint ability of our partners and us to:

- provide ongoing superior expertise on the field of formulation development, analytical development, process development and GMP manufacturing;
- successfully collaborate with pharmaceutical and biotechnology companies in the discovery, development and commercialization of new products;
- obtain intellectual property protection for such products and technologies; and
- attract and retain qualified personnel.

We have noted below existing and potential competition for our contract formulation and manufacturing business and the main products under development, Locteron and OP-145 CSOM, as well as for our drug delivery technologies. In addition to these competitors, the product candidates under development may also face competition from existing or new products we and our partners are currently unaware of.

## ***Contract Formulation and Manufacturing Business***

Our contract formulation and manufacturing 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. and MP5 s.a.r.l. 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.

## **Products**

*Locteron*

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

Biolex and 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, Biolex and we are aware of other long-acting interferon alfa treatments currently in active clinical development, including Zalbin (formerly Albuferon) (in development by Human Genome Sciences, Inc. in collaboration with Novartis AG) as well as product candidates from Flamel Technologies SA, Intarcia Therapeutics, Inc. and Zymogenetics, Inc. (in collaboration with Bristol-Myers Squibb Company).

#### *OP-145 CSOM*

We anticipate that OP-145 CSOM, 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.

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

There are many other companies developing controlled release drug delivery systems, some of which may compete with us in respect of our products in the future.

#### **Facilities**

Our registered main place of business is located at Zernikedreef 12, 2333 CL Leiden, the Netherlands. These approximately 5,250 m<sup>2</sup> facilities comprise laboratories, a cGMP manufacturing facility and offices. We entered into a long-term lease for these premises with a remaining period of 14 – 18 years.

In 2006, we opened a business development office in Cambridge, Massachusetts, United States, where we leased approximately 125 m<sup>2</sup> of office space. Our presence in the Cambridge office was discontinued as per September 2009 and the personnel that was employed in Cambridge was relocated to our offices in Leiden.

#### **Employees**

We believe that our success will depend on our ability to attract, retain and motivate key employees. At the end of 2006, 2007 and 2008, we had 139, 170 and 144 employees, respectively. As of 31 December 2009, we had a total of 132 employees, all of which were located in the Netherlands (representing 122 full-time employees).

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

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\* On a going forward basis, the Company identifies only one (remaining) operating segment: formulation, drug delivery and manufacturing activities.

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, Scientific Advisory Board 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. See “Description of Share Capital and Corporate Governance”.

### 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. One of the members of the current Executive Board, our Chief Business Officer, has been appointed for an indefinite period of time. Our CEO has been appointed for a period ending 31 December 2011, and our CFO will be nominated for appointment for a term of four years at the next General Meeting of Shareholders. 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 reappointed 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***

At our Annual General Meeting of Shareholders of 6 November 2008, Mr. Simon Sturge was appointed Chief Executive Officer and Mr. Gerben Moolhuizen was appointed Chief Business Officer. As per August 2009, Mrs. Susan Swarte was hired, and was nominated to be appointed as Chief Financial Officer at the next General Meeting of Shareholders.

The Executive Board is composed of the following members:

<b>Name</b>	<b>Age</b>	<b>Position</b>	<b>Member Since</b>	<b>Term</b>
Simon Sturge	50	Chief Executive Officer	6 November 2008	31 December 2011
Susan Swarte	41	Chief Financial Officer	To be appointed	Four years
Gerben Moolhuizen	43	Chief Business Officer	6 November 2008	Indefinite

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

#### *Simon Sturge – Chief Executive Officer*

Mr. Sturge obtained a Bachelor's Degree (Hons.) in Biology from Sussex University. He has over 20 years of experience in the pharmaceutical industry. From 1980 to 1988, he worked as a Division Manager for NAPP Laboratories Ltd. After that, he joined the Celltech Group (now part of UCB), where he held several positions. In 1997, he founded RiboTargets, when it was spun out from the Medical Research Council's Laboratory of Molecular Biology. He remained Chief Executive Officer of RiboTargets Holdings until 2003. He also held a non-executive directorship with Metalogic Systems Ltd. until 2005. From 2003 till 2008, Mr. Sturge has been Chief Executive Officer of Vernalis Group plc. He is also a non-executive director of the Bio Industry Association.

#### *Susan Swarte – Chief Financial Officer*

Mrs. Swarte obtained a Master's Degree in Business Economics from Erasmus University in Rotterdam and she is a registered controller (RC), which qualification she obtained from VU University Amsterdam. She has over 16 years of experience in financial and strategic management. She worked at Unilever and Numico (now Danone), two large, international and publicly listed companies, where she was responsible for financial, logistic and reporting aspects. From 2003 to 2006, Mrs. Swarte was Senior Business Controller at the Numico Baby Division. At Numico she professionalized the finance function in China and most recently she was responsible for all financial aspects of the export business of Danone Baby Nutrition as Finance Director, Global Export.

#### *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.) as Vice-President, Business Development in 1999. He joined us in 2001, as senior manager, Business Development. He became Chief Business Officer in January 2006.

## **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, provided that as long as Signet Healthcare Partners, in its capacity as general partner and manager of Life Sciences Opportunities Fund L.P. and Life Sciences Opportunities Fund (Institutional) L.P., holds at least 10% of our total issued ordinary share capital, one member of the Supervisory Board shall be appointed from a nomination, drawn up by Signet Healthcare Partners. A nomination drawn up by Signet Healthcare Partners containing the names of at least two persons shall be binding, provided that the General Meeting of Shareholders may deprive such nomination of its binding character by a resolution adopted by a majority of not less than two thirds of the votes cast, representing more than half of the total issued share capital.

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, provided that, as long as Signet Healthcare Partners holds at least 10% of our total issued ordinary share capital, any resolution to suspend or dismiss a member of the Supervisory Board, who is appointed from a nomination drawn up by Signet Healthcare Partners, other than on the proposal of Signet Healthcare Partners, may only be adopted with a majority of not less than two thirds of the votes cast, representing more than half of total issued share capital. 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 composed of the following members:

<b>Name</b>	<b>Age</b>	<b>Position</b>	<b>Member Since</b>	<b>Term</b>
Hans Stellingsma	53	Chairperson	1 April 2001	2010
Philip Smith <sup>1</sup>	60	Member	19 January 2005	2013
René Kuijten <sup>2</sup>	45	Member	19 January 2005	2012
Paul Toon <sup>3</sup>	41	Member	19 January 2005	2011
Frans Eelkman Rooda	57	Member	6 November 2008	2012

James Gale<sup>4</sup>

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Member

23 April 2009

2013

- 1 Mr. Smith was until December 2008 General Partner of S.R. One, one of our Major Shareholders, and therefore until that date he was not independent within the meaning of the Dutch Corporate Governance Code.
- 2 Mr. Kuijten is General Partner of Life Sciences Partners, one of our Major Shareholders, and therefore not independent within the meaning of the Dutch Corporate Governance Code.
- 3 Until June 2007, Mr. Toon has been Director of Innoven Partenaires S.A., manager of Innoven Europe 2, which is one of our Major Shareholders. Until that date he was not independent within the meaning of the Dutch Corporate Governance Code.
- 4 Mr. Gale is General Partner of Signet Healthcare Partners, being the general partner and manager of Life Sciences Opportunities Fund L.P. and Life Sciences Opportunities Fund (Institutional) L.P., together one of our Major Shareholders, and therefore not independent within the meaning of the Dutch Corporate Governance Code.

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 from Utrecht University and a postgraduate degree (M.Phil.) from Glasgow University. He attended the Advanced Management Program at Harvard Business School. 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. between 1993 and 1996. From 1996 to 1998, he was 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 the Managing Partner at Arthur D. Little in the Netherlands and a Senior Partner with Monitor, both global strategy consulting firms (1999 – 2004). Currently, Mr. Stellingsma is self-employed and serves on the supervisory boards of MTel B.V., Simac Techniek N.V., De Sleutels van Zijl en Vliet and Twinning Holding B.V.

#### *Philip Smith – Member*

Mr. Smith obtained a Bachelor's Degree in Chemistry from the University of Maine, and a 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, where he has been a General Partner from January 2003 until December 2008. In the past five years, Mr. Smith held board positions at Avantium Holding B.V., Onyvax Ltd, Redpoint Bio Corp., Cydex, Inc. and Trinity Biosystems, Inc.

#### *René Kuijten – Member*

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, where he was co-leader of the European Pharmaceuticals and Healthcare Practice. He joined Life Sciences Partners in 2001 as a General Partner. Mr. Kuijten was a board member of the McKinsey Alumni Association and the Max Geldens Society. 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., Hybrigenics S.A., Trinity Biosystems, BMEYE, Nexstim, Ipsat and Syntaxin. Mr. Kuijten is currently board member of the NVP (Nederlandse Vereniging van Participatiemaatschappijen) and the Stichting Steun Emma Kinderziekenhuis. He has participated in a committee of the Royal Netherlands Academy of Sciences advising the Dutch government on gene patenting.

#### *Paul Toon – Member*

Mr. Toon holds a Bachelor's Degree (Hons.) from Oxford University and has 17 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 led the acquisition of a French venture capital fund management company, Innoven Partenaires S.A. in 2004, and served as a Managing Partner until June 2007. He subsequently became Head of Unquoted Investments at Noble Fund Managers before founding a new French venture capital fund in 2008, Generis Capital Partners, where he is a Managing Partner. He was also a board member of 20/10 Perfect Vision Optische Geraete GmbH and CMC Biopharmaceuticals A/S. Currently, Mr. Toon is a board member of Alba Cosmetics, Ltd and Generis Capital Partners SAS.

#### *Frans Eelkman Rooda –Member*

Mr. Eelkman Rooda obtained a Master's Degree in Econometrics from Erasmus University Rotterdam and a Master's Degree in Business Administration from Dartmouth College. In 1977, he started his career with Esso Nederland B.V. and was subsequently employed by Esso Europe Inc. After that, he held positions of increasing responsibility at McKinsey and Company from 1982 to 1987 and 1989 to 1997. From 1987 to 1989, he worked as Department Manager Securities and Syndicates for the Algemene Bank Nederland (ABN) N.V. From 1997 to 2008, he was Chief Financial Officer of OPG Groep N.V. Currently, Mr. Eelkman Rooda is Chief Financial Officer of Wessanen N.V. He is also a member of the supervisory board of De Lage Landen International B.V.

#### *James Gale –Member*

Mr. Gale obtained a Master's Degree in Business Administration from Chicago Booth School of Business. In 1977 he started his career with E.F. Hutton & Co and Home Insurance Co. Prior to co-founding Signet Healthcare Partners in 1998, he was head of principal investment activities and head of investment banking for Gruntal & Co. Mr. Gale is a board member of AlpexPharma SA (chairman), Cedarburg Pharmaceuticals Inc., Cydex Pharmaceuticals Inc. (chairman), Paladin Laboratories Inc., IGI Labs, Inc., Pfenex, Inc. and SpePharm Holding B.V. During the past five years, Mr. Gale held board positions at Avantium Holding B.V., Relm Wireless Corp., Indevus Pharmaceuticals, Inc., Molecular Medicine Biosciences and Abrika Pharmaceuticals, Inc. Mr. Gale resigned from the board of Indevus Pharmaceuticals, Inc. early this year upon the completion of the sale to Endo Pharmaceuticals Inc.

### **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 Mr. Eelkman Rooda (chairperson), Mr. Kuijten and Mr. 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 the 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, and the proposals for appointments and reappointments. It also assesses the functioning of individual members of the Supervisory Board and the Executive Board.

The Remuneration and Nominating Committee consists of Mr. Stellingsma (chairperson), Mr. Smith and Mr. 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 remuneration of the members of the Supervisory Board consists of a fixed cash remuneration, which is determined by the General Meeting of Shareholders.

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). The remuneration system is based on achieving performance criteria that are determined on a yearly basis.

## **Executive Board**

The total remuneration we paid to or for the benefit of (former) members of our Executive Board in 2009 amounted to approximately € 838,000. The following table denotes the breakdown in remuneration of (former) members of the Executive Board in 2009.

<b>Name</b>	<b>Base Salary</b>	<b>Bonus<sup>3</sup></b>	<b>Pension Contributions</b>	<b>Other Payments</b>	<b>Total Remuneration</b>
Simon Sturge	€ 375,000		--	€ 26,000	€ 401,000
Joost Holthuis <sup>1</sup>	€174,000		€ 13,000	€ 2,000	€ 189,000
Hans Pauli <sup>2</sup>	€ 50,000		€ 2,000	€ 1,000	€ 53,000
Gerben Moolhuizen	€ 175,000		€ 12,000	€ 8,000	€ 195,000
<b>Total</b>	<b>€ 774,000</b>		<b>€ 27,000</b>	<b>€ 37,000</b>	<b>€ 838,000</b>

1 Mr. Holthuis (former Chief Scientific Officer) has left the Company as per 1 September 2009.

2 Mr. Pauli (former Chief Financial Officer) has left OctoPlus as per 31 March 2009. Mr. Pauli was replaced by Mrs Swarte per the 1<sup>st</sup> of August 2009, who will be proposed for nomination as an Executive Board member in the next annual General Meeting of Shareholders.

3 The bonus amounts for 2009 have not been decided yet.

Remuneration totals for members of our Executive Board in 2009 do not include the value of share options.

### **Share ownership**

The number of Shares currently owned by members of our Executive Board are as follows:

	<b>Number of Shares Owned</b>
Simon Sturge .....	133,333
Gerben Moolhuizen.....	22,500
	<hr/>
<b>Total.....</b>	<b>155,833</b>

The numbers of options currently owned by members of our Executive Board are described below.

### **Supervisory Board**

The remuneration of the members of the Supervisory Board is determined by the General Meeting of Shareholders. As of 1 January 2008, the chairperson of the Supervisory Board receives an annual remuneration of € 31,250 and the other members of the Supervisory Board receive an annual remuneration of € 25,000 each. In addition, each member of the Supervisory Board who serves in one or more of its committees receives € 5,000 for such membership(s).

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 and Supervisory Board 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.

Mr. Stellingsma served as Chief Operating Officer of Bikkair B.V. until February 2009. Bikkair B.V. was declared bankrupt on 4 February 2009.

Mr. Smith served on the board of Descartes Therapeutics, Inc and Scion Pharmaceuticals, Inc which were liquidated in December 2008 and May 2005 respectively.

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

Other than the fact that two 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 or Supervisory Board and their duties and responsibilities to us.

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

## **Option Plans**

### ***2003 Option Plan***

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 2004 and 2006, we granted options pursuant to a standard share option agreement. The exercise period of the options granted thereafter is 60 months. The exercise prices of the options granted by us in the respective years are: between € 3.43 and € 4.34 (2004) and between € 2.70 and € 4.55 (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.

### ***2006 Option Plan***

With a view to the listing of our Shares in October 2006, we adopted a new share option plan which entered into force following our listing. The share option agreements entered into prior to that date remain in place.

Under the 2006 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. The granting of options to the Executive Board can be made subject to the approval of the General Meeting of Shareholders.

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, permanent disability or retirement, we may force that employee to disgorge a specified portion of any profits realized from the exercise of those options. The Executive Board has the authority to decide, in favor of the respective employee, to deviate from the above described terms.

We will not grant options to our employees and members of the Executive Board, which if exercised, would represent more than 7.5% of our issued share capital, unless the General Meeting of Shareholders approves otherwise. Following approval of the General Meeting of Shareholders on 6 November 2008, Mr. Sturge has been granted 1,215,500 options in addition to the aforementioned option pool, which at the time of the grant amounted to 7.5% of our issued share capital.

### ***Options Granted to the Executive Board and Other Parties***

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

Name	Currently Outstanding Options	Options Granted in 2004	Options Granted in 2006	Options Granted in 2008	Options Granted in 2010	End of Exercise Period of 2004 Options	End of Exercise Period of 2006 Options	End of Exercise Period of 2008 Options	End of Exercise Period of 2010 Options	Average Exercise Price of All Outstanding Options
Simon Sturge	1,615,500	-	-	1,215,500 <sup>1</sup>	400,000 <sup>2</sup>	n.a.	n.a.	2013	2014-2018	1.00
Susan Swarte	334,000	-	-	-	334,000 <sup>2</sup>	n.a.	n.a.	n.a.	2014-2018	1.41
Gerben Moolhuizen	385,411	-	51,411	-	334,000 <sup>2</sup>	n.a.	2011	n.a.	2014-2018	1.58
Other employees	505,290	-	36,000	-	469,290	n.a.	2011	n.a.	2014	1.60
Consultants and former employees <sup>3</sup>	302,622	136,600	166,022	-	-	2011-2014	2011-2014	n.a.	n.a.	3.03
<b>Total</b>	<b>3,142,823</b>	<b>136,600</b>	<b>253,433</b>	<b>1,215,500</b>	<b>1,537,290</b>					<b>€ 1.41</b>

- 1 The number of options Mr. Sturge from the options granted in 2008 depends on the future development of the price of our Shares and is indicated in the table below:

Average Value per Share during 2 Months prior to 31 December 2012	Percentage of Options that Vest
€ 2.00 - 2.99	20%
€ 3.00 - 3.99	40%
€ 4.00 - 4.99	60%
€ 5.00 - 5.99	80%
€ 6.00 - 6.99	100%

- 2 50% of the options granted to the members of our Executive Board in 2010 are conditional: 1/3 is dependent upon certain pre-defined performance criteria for the relevant employee's 2010 performance, 1/3 is dependent upon certain pre-defined performance criteria for the relevant employee's 2011 performance and 1/3 is dependent upon certain pre-defined performance criteria for the relevant employee's 2012 performance.
- 3 Consultants and former employees include options held by Mr. Holthuis (150,370), our co-founder who no longer works for OctoPlus.

## Employment Agreements

We have employment agreements with each of the members of the Executive Board. All employment agreements have an indefinite term and can be terminated, subject to the statutory notice period, which is one to two months for the employee and three to four months for us, dependent on the number of years of service.

Save for the employment agreement with Mr. Sturge and Mrs. Swarte, our employment agreements do not provide for severance payments in the event of termination. If we terminate the employment agreement with Mr. Sturge or Mrs. Swarte (save for urgent cause, long-lasting illness or non-extension of the terms of appointment by the General Meeting of Shareholders), we are obliged to pay a severance amount equal to 1.5 times the monthly salary per year of service, up to a maximum of a full year salary. Furthermore, if the employment agreement with Mr. Sturge or Mrs. Swarte is terminated by either party within six months after a change of control, resulting in a substantial adverse change in the position, tasks and responsibilities of Mr. Sturge or Mrs. Swarte, Mr. Sturge or Mrs. Swarte is entitled to a severance amount of 1.5 times his monthly salary inclusive of the average bonus payment received over the three years preceding the change of control, up to a maximum of a full year salary inclusive of the average bonus received.

## **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, 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 defense (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. From 1 February 2006, we have had a defined contribution plan, which replaced our defined benefit plan, which was closed on 31 January 2005.

For some of our employees, including one of 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 management 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.

## Major Shareholders

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. This information is sourced from the public online register of the AFM.

Shareholder	Shares owned	
	Total	%
Signet Healthcare Partners <sup>1</sup>	5,280,000	15.8
Life Sciences Partners	5,196,645	15.5
S.R. One <sup>2</sup>	5,096,846	15.2
Joost Holthuis / Sodoro B.V. <sup>3</sup>	2,998,044	9.0
Innoven Partenaires S.A. <sup>4</sup>	2,812,861	8.4
Fagus N.V.	2,282,506	6.8
Others <sup>5</sup>	9,768,530	29.3
<b>Totals</b>	<b>33,435,432</b>	<b>100.0</b>

1. Signet Healthcare Partners acts as general partner and manager of Life Sciences Opportunities Fund II, L.P. and Life Sciences Opportunities Fund (Institutional) II, L.P.
2. S.R. One is an investment fund wholly owned by GlaxoSmithKline Inc.
3. All shares in Sodoro B.V. are held by Joost Holthuis, our co-founder.
4. Innoven Partenaires S.A. acts as management company of various FCPI Funds (*Fonds Commun de Placement dans l'Innovation*).
5. Others include Mr. Sturge, our Chief Executive Officer, and Gerben Moolhuizen, our Chief Business Officer.

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

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.

## Related Party Transactions

Except as disclosed in “Management and Employees” and except as disclosed below, the members of the Executive Board, the members of the Supervisory Board, and the Major Shareholders have had no interest in any transactions to which we were a party since 1 January 2006, or in any transactions which we entered into prior thereto and under which we or the other parties still have ongoing obligations.

In April 2008, we entered into a convertible loan agreement with Life Sciences Partners and S.R. One, two of our Major Shareholders, as a result of which Life Sciences Partners and S.R. One provided a convertible loan of € 2.0 million each. The convertible loan carried 15% interest. This convertible loan agreement including the interest thereon was redeemed through the issuance of 5,996,249 New Shares to Life Sciences Partners and S.R. One on 25 February 2009 at € 0.75 per share.

On 25 February 2009, Mr. Sturge acquired 133,333 ordinary shares as part of a private placement at € 0.75 per share. Mr. Sturge is not entitled to the anti-dilution protection to which the Investors are entitled (see “Ranking Holders of Shares – Anti-Dilution Provision”).

On 18 December 2009, we raised € 4.0 million in gross proceeds in the Private Placement. Signet Healthcare Partners and Generis Capital Partners participated in the Private Placement. Mr. James Gale, a member of our Supervisory Board, is managing partner at Signet Healthcare Partners and Mr. Paul Toon, also a member of our Supervisory Board, is managing partner at Generis Capital Partners. As a result of their involvement in the financing, Mr. Gale and Mr. Toon did not have voting rights during the Supervisory Board meeting in which the Private Placement was authorized.

## 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. We were incorporated on 29 May 1997 under Dutch law, under the name OctoPlus B.V. On 4 October 2006, we converted OctoPlus B.V. into OctoPlus N.V. a limited liability company under Dutch law. We trade under the name OctoPlus. We are registered with the Trade Register of the Chamber of Commerce for The Hague, 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](mailto:octoplus@octoplus.nl), or through our website which is [www.octoplus.nl](http://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 29 April 2009, before Mr. D.F.M.M. Zaman, civil law notary in Rotterdam, the Netherlands. The certificate of no objection of the Ministry of Justice for that amendment was granted on 25 April 2009, under number N.V. 597.465.

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 (the "Articles of Association").

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 (bio)medical 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 share capital amounts to € 9,600,000, divided into 40,000,000 ordinary shares and 40,000,000 preference shares, each with a nominal value of € 0.12. As a result of the Private Placement there are 33,435,432 ordinary shares issued and outstanding.

The following table sets forth information about our issued share capital as of the date of this Prospectus.

	<u>As of the date of this Prospectus</u>
Ordinary shares	33,435,432
Preference shares	-
Options <sup>1</sup>	<u>3,342,823</u>
Total	<u>36,778,255</u>

<sup>1</sup> 3,142,823 options issued under our share option plans and 200,000 options issued under our agreement with Theratechnologies (see "Description of Share Capital and Corporate Governance – Share Capital – Outstanding Options" below).

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.

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

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

### **Outstanding Options**

On various occasions in 2004, 2006, 2008 and 2010, we entered into share option agreements with employees. Pursuant to these option agreements, a total of 1,393,323 unconditional options are currently outstanding. Each option entitles its holder to acquire an ordinary share for an exercise price, depending on the calendar year in which the option was granted, between € 3.43 and € 4.34 (2004; only options with an exercise price of € 3.43 currently outstanding), between € 2.70 and € 4.55 (2006), € 0.87 (2008) and € 1.41 (2010). Except for the exercise price and the exercise period, all option agreements have identical terms (see "Management and Employees – Option Plans – 2003 Option Plans").

On 26 September 2007, we granted options to Theratechnologies to acquire 200,000 Shares at an exercise price of € 3.95 per Share, equal to the average closing price of the Shares for the ten trading days immediately prior to the date of our license agreement with Theratechnologies. These options are exercisable at any time until the earlier of ten years following date of execution or the fifth anniversary of the date of termination of the agreement with Theratechnologies.

On 6 November 2008, we granted options to Mr. Sturge, our Chief Executive Officer, to acquire 1,215,500 Shares at an exercise price of € 0.87 per Share, equal to the closing price on 6 November 2008. These options are exercisable at any time until 6 November 2013. However, the number of options Mr. Sturge may exercise depends on the average value per Share which shall be calculated on the basis of the closing price per Share on the relevant stock exchange, during a period of 2 months prior to 31 December 2012. To the extent the options granted do not vest, such options will lapse.

On 1 January 2010, we granted conditional options to Mr. Sturge, Mrs. Swarte and Mr. Moolhuizen to acquire in total 534,000 Shares at an exercise price of € 1.41 per Share (which is the closing price for the Shares on 31 December 2009). The number of unconditional options each person will receive depends

on certain pre-defined performance criteria for each person in the years 2010, 2011 and 2012, with 1/3 of the conditional options related to each of the three years. Each unconditional option granted can be exercised in the period between 36 months after the date of grant and 60 months after the date of grant.

### ***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 designate the Executive Board, for a period of five years from 4 October 2006, as the corporate body authorized to issue ordinary shares and preference shares, and/or to limit or exclude pre-emptive rights in relation to an issuance of shares with the prior approval of our Supervisory Board. This designation 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 designation 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 designate the Executive Board, for a period of five years from 4 October 2006, as the corporate body authorized to grant rights to subscribe for shares, with the prior approval of our Supervisory Board. This designation 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 designation 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 from the meeting of shareholders which was held on 23 April 2009, 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 cancelling 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 period 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.

Furthermore, the corporate body authorized to issue ordinary shares and preference shares, and/or to limit or exclude pre-emptive rights in relation to an issuance of shares, and/or to grant rights to subscribe for shares, shall be authorized to resolve that in respect of any issuance of shares and/or granting of rights for shares, the nominal value of these shares shall be paid up on account of our equity, to the extent it exceeds the aggregate of the paid in and called up part of our share capital and the reserves which must be maintained pursuant to the law and to resolve that pre-emptive rights in respect of such issuance or granting are restricted or limited.

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*).

### **Stichting Continuïteit OctoPlus and Preference Shares and Inquiry Proceedings**

On 29 March 2007 we incorporated Stichting Continuïteit OctoPlus (the “Foundation”). The purpose of the Foundation is 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 consists of two A board members and one B board member. Emile Job Leonardus Bakker and Rudolf van Dam are serving as A board members and Jan Willem Termijtelen is serving as B board member. The A board members are appointed by the board of the Foundation, whilst the B board member are appointed by the Supervisory Board upon proposal of the Executive Board.

Under the terms of an agreement we intend to enter into with the Foundation, we will grant to the Foundation a call option (the “Call Option”) entitling it, in certain circumstances, 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. The Call Option can be exercised in one or more tranches. Furthermore, under the terms of that same agreement, we will grant to the Foundation the right to initiate inquiry proceedings with the Enterprise Chamber of the Amsterdam Court of Appeal (*Ondernemingskamer van het Gerechtshof te Amsterdam*, the “Enterprise Chamber”).

Our preference shares and the Foundation’s right to initiate inquiry proceedings will be instruments of protection against hostile takeovers and other possible influences that could threaten our continuity, independence or corporate identity.

In line with guidance from the Dutch Corporate Governance Code, we believe that the issuance of preference shares or the outcome of inquiry proceedings may help us to determine our position in relation to a bidder and its plans or other possibly threatening influences, 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.

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 an exercise of the Foundation's right to initiate inquiry proceedings. 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 intends to 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 thirtieth 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.

### **Ranking Holders of Shares – Anti-Dilution Provision**

The rights of holders of the New Shares and our existing Shares rank *pari passu* with each other, save for anti-dilution protection until 1 September 2010, which has been granted to (i) the Investors in respect of the New Shares and (ii) the investors who participated in the private placement of 25 February 2009 in respect of the Shares issued in that private placement.

If we issue new ordinary shares or securities convertible into or exchangeable or exercisable for ordinary shares (“Dilutive Event”) at a price lower than the issue price (such price as adjusted from time to time, the “Dilutive Price”) prior to 1 September 2010, each Investor shall be entitled to receive simultaneously with such issuance – in the form of a bonus issue – for no additional consideration, such an additional number of ordinary shares that such investor would have obtained in the private placement (combined with the Shares that such investor acquired in the private placement) if the issue price had been the Dilutive Price.

If a Dilutive Event has occurred, the Dilutive Price shall be decreased to the price at which the securities have been issued during the Dilutive Event and such adjusted price will be the Dilutive Price for the purpose of the next Dilutive Event during the anti-dilution period, if any. In calculating the number of bonus shares to be issued at such next Dilutive Event, the number of the bonus shares issued in any previous Dilutive Event will also be taken into account.

The granting of options, or the issuance of new ordinary shares pursuant to an exercise of options granted under our employee option plan existing on the date hereof (see "Management and Employees – Option Plans – 2006 Option Plan") shall not constitute a Dilutive Event.

### **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. With effect from 1 January 2009, the Dutch corporate governance code has been amended by the Frijns Committee (Code Frijns). The Dutch Corporate Governance Code contains 22 principles and 129 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 fully support the principles and best practice provisions of 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.

### ***Exceptions in the application of the Dutch Corporate Governance Code***

II.1.1 An Executive 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.

Our Chief Business Officer, Gerben Moolhuizen, has been appointed to the Executive Board in November 2008, for an indefinite period, in line with his labour agreement. The other members of the Executive Board have or will be appointed for a period of maximum four years, irrespective of the term of their labour agreement. It is our intent to apply this provision for any future member of the Executive Board.

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 six members. Two members are not independent as they are employed by Signet Healthcare Partners and Life Sciences Partners, both of which have more than 10% Shares in OctoPlus. This situation came into existence from the need to raise funds, which were made available under the condition of a Supervisory Board seat.

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 that 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, in view of our size, initially not appoint an internal auditor.

### **Disclosure of Information**

As a Dutch company listed on Euronext Amsterdam, 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. In addition, we will also be obliged to publish interim management statements (*inter alia* containing an overview of important transactions and their financial consequences) in the period starting ten weeks after and six weeks before the first and second half of each financial year, or, alternatively, we are obliged to publish quarterly financial statements.

We must also make public certain inside information by means of a press release. Pursuant to the Financial Supervision Act, inside information is knowledge of concrete information directly or indirectly relating to the issuer or the trade in its securities which has not been made public and publication of which could significantly affect the trading price of the securities. The Financial Supervision Act contains specific rules intended to prevent insider trading.

### **Obligations of Shareholders to Make a Public Offer**

The European Directive on Takeover Bids (2004/25/EC) has been implemented in Dutch legislation in the Financial Supervision Act. Pursuant to the Financial Supervision Act, a shareholder who has acquired 30% of our shares or of our voting rights has the obligation to launch a public offer for all shares and depositary receipts issued for shares. The legislation also applies to persons acting in concert who jointly acquire substantial control.

### **Squeeze Out Procedures**

Pursuant to section 2:92a of the Dutch Civil Code, a shareholder who for his own account contributes at least 95% of our issued capital may institute proceedings against our other shareholders jointly for the transfer of their shares to the claimant. The proceedings are held before the Enterprise Chamber and can be instituted by means of a writ of summons served upon each of the minority shareholders in accordance with the provisions of the Dutch Code of Civil Procedure (*Wetboek van Burgerlijke Rechtsvordering*). The Enterprise Chamber may grant the claim for squeeze out in relation to all minority shareholders and will determine the price to be paid for the shares, if necessary upon advice of one or three experts. Once the order to transfer becomes final before the Enterprise Chamber, the person acquiring the shares shall give written notice of the date and place of payment and the price to the holders of the shares to be acquired whose addresses are known to him. Unless the addresses of all of them are known to him, he shall also publish the same in a newspaper with a national circulation.

The offeror under a public offer is also entitled to start a squeeze out procedure, within three months after the public offer, if following the public offer he contributes at least 95% of the class of shares and represents at least 95% of the total voting rights attached to these shares. A mandatory offer price is in principle deemed to be a reasonable price, which has to be accepted by minority shareholders. In the

event of a voluntary public offer, the offered price is considered reasonable as long as 90% of the shares have been acquired.

The same legislation also entitles each remaining minority shareholder to demand a squeeze out if the offeror has acquired at least 95% of the class of shares held by him, representing at least 95% of the total voting rights in that class. This procedure must be initiated with the Enterprise Chamber within three months after the end of the period for tendering shares in the public offer. With regard to price, the same procedure as for squeeze out proceedings initiated by the offeror applies.

### **Notification of Holdings of Voting Rights and Capital Interest**

Pursuant to the Financial Supervision Act, certain notification requirements apply to us as well as to holders of our shares due to the fact that we are a listed company. The notification requirements are summarized below.

Pursuant to the Financial Supervision Act, each person whose holding of voting rights and/or capital interest, directly or indirectly, amounts to 5% or more must notify the AFM without delay by means of a standard form or through the automated notification system of the AFM. Any person who, directly or indirectly, acquires or disposes of an interest in our share capital or voting rights must without delay give written notice to the AFM, if, as a result of such acquisition or disposal, the percentage of capital interest or voting rights held by such person, directly or indirectly, reaches, exceeds or falls below the following thresholds: 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 60%, 75% and 95%.

We are required to notify the AFM of any changes in our share capital and voting rights. More specifically, we are required to notify the AFM without delay of any changes in our share capital if our share capital has changed by 1% or more compared to the previous disclosure in respect of our share capital. We are also required to notify the AFM without delay of any changes in the voting rights, insofar as it has not already been notified at the same time as a related change in our share capital. Changes in our share capital and voting rights of less than 1% must also be notified; these changes can be notified at any time but at the latest within eight days after the end of each calendar quarter. The AFM will publish such notifications in a public register. If, as a result of such change, a person's direct or indirect interest in our share capital or voting rights passively reaches, exceeds or falls below the abovementioned thresholds, the person in question must give notice to the AFM no later than the fourth trading day after the AFM has published the change in our share capital and/or voting rights in the public register.

In addition, annually within four weeks after the end of the calendar year, every holder of 5% or more of our shares or voting rights whose interest has changed in the period after his most recent notification to the AFM, which change relates to the composition of the notification as a result of certain acts (e.g., the exchange of shares (an actual interest) for depositary receipts for shares (which is a potential interest) or the exercise of a right to acquire shares (pursuant to which the potential interest becomes an actual interest)) must notify the AFM of such changes.

A person is deemed to hold the interest in our share capital or voting rights that is held by its controlled undertakings as defined in the Financial Supervision Act. The controlled undertaking does not have a duty to notify the AFM because the interest is attributed to the undertaking in control, which as a result has to notify the interest as an indirect interest. Any person, including an individual, may qualify as an undertaking in control for the purposes of the Financial Supervision Act. A person who has a 5% or larger interest in our share capital or voting rights and who ceases to be a controlled undertaking for purposes of the Financial Supervision Act must without delay notify the AFM. As of that moment, all notification obligations under the Financial Supervision Act will become applicable to the former controlled undertaking.

For the purpose of calculating the percentage of capital interest or voting rights, amongst others, the following interests must be taken into account: (i) shares or depositary receipts for shares or voting rights directly held (or acquired or disposed of) by any person, (ii) shares or depositary receipts for shares or voting rights held (or acquired or disposed of) by such person's controlled undertakings or by a third party for such person's account or by a third party with whom such person has concluded an oral or written

voting agreement (including a discretionary power of attorney), and (iii) shares or depositary receipts for shares or voting rights which such person, or any controlled undertaking or third party referred to above, may acquire pursuant to any option or other right held by such person (including, but not limited to, on the basis of convertible bonds). As a consequence, the notification should indicate whether the interest is held directly or indirectly, and whether the interest is an actual or a potential interest.

A holder of a pledge or right of usufruct in respect of shares or depositary receipts for shares can also be subject to the reporting obligations of the Financial Supervision Act, if such person has, or can acquire, the right to vote on the shares or, in the case of depositary receipts for shares, the underlying shares. If a pledgee or usufructuary acquires the voting rights on the shares or depositary receipts for shares, this may trigger a corresponding reporting obligation for the holder of the shares or depositary receipts for shares. Special rules apply with respect to the attribution of shares or depositary receipts for shares or voting rights which are part of the property of a partnership or other community of property.

The Financial Supervision Act contains detailed rules that set out how its requirements apply to certain categories of holders, including but not limited to (managers of) investment funds, investment managers, custodians, market makers, clearing and settlement institutions, brokers and credit institutions.

Pursuant to the Financial Supervision Act, members of our Executive Board and Supervisory Board must notify the AFM of their interest in our share capital and voting rights within two weeks of their appointment as a member of our Executive Board or our Supervisory Board. Any subsequent change of their interest in our share capital and voting rights must be notified to the AFM without delay.

The notifications referred to in this paragraph should be made in writing by means of a standard form or electronically through the notification system of the AFM.

### **Market Abuse Regime**

The rules on preventing market abuse set out in the Financial Supervision Act are applicable to us, the members of our Executive Board and Supervisory Board, other insiders and persons performing or conducting transactions in our securities. Certain important market abuse rules set out in the Financial Supervision Act that are relevant for investors are described hereunder.

We are required to make inside information public. Inside information is information that is specific and pertains directly or indirectly to us or our shares or the trading thereof: (a) which information has not been made public and (b) where disclosure of such information could have a significant effect on the price of our shares or derivatives of our shares. We must also provide the AFM with this inside information at the time of publication. Furthermore, we must without delay publish the inside information on our website and keep it available on our website for at least one year.

It is prohibited for any person to make use of inside information within or from the Netherlands or a non-European Union member state by conducting or effecting a transaction in our shares. In addition, it is prohibited for any person to pass on inside information to a third party or to recommend or induce, on the basis of inside information, any person to conduct a transaction. Furthermore, it is prohibited for any person to manipulate the market, for instance by conducting transactions which could lead to an incorrect or misleading signal of the supply of, the demand for or the price of the securities.

Our insiders within the meaning of the Financial Supervision Act are obliged to notify the AFM when they carry out or cause to be carried out, for their own account, a transaction in our shares or in securities the value of which is at least in part determined by the value of our shares. Insiders within the meaning of the Financial Supervision Act in this respect are: (i) members of our Executive Board and our Supervisory Board, (ii) other persons who have a managerial position and in that capacity are authorized to make decisions which have consequences for our future development and business prospects and who, on a regular basis, can have access to inside information relating, directly or indirectly, to us, and (iii) certain persons closely associated with the persons mentioned under (i) and (ii) designated by the Dutch Market Abuse Decree (*Besluit marktmisbruik Wft*).

This notification must be made no later than the fifth business day after the transaction date on a standard form drawn up by the AFM. This notification obligation does not apply to transactions based on a discretionary management agreement as described in section 8 of the Dutch Market Abuse Decree. Under certain circumstances, the notification may be delayed until the date on which the value of the transactions amounts to € 5,000 or more in the calendar year in question.

If a member of our Executive Board or Supervisory Board has notified a transaction to the AFM under the Financial Supervision Act as described above under "Notification of Holdings of Voting Rights and Capital Interest", such notification is sufficient for purposes of the Financial Supervision Act as described in this paragraph.

We have adopted an internal code on inside information in respect of the holding of and carrying out of transactions in our shares by the members of our Executive Board and Supervisory Board and our employees. Further, we have drawn up a list of those persons working for the Company who could have access to inside information on a regular or incidental basis and we have informed the persons concerned of the rules on insider trading and market manipulation including the sanctions which can be imposed in the event of a violation of those rules.

## **Market Information**

### **Euronext Amsterdam**

Our Shares are listed and traded on Euronext Amsterdam. We are subject to Dutch securities regulations and supervision by the relevant Netherlands 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 and compliance with financial reporting requirements. It also supervises financial intermediaries and investment advisers. Since the implementation of the Prospectus Directive on 1 July 2005, the AFM is furthermore 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. Due to the implementation of the Market Abuse Directive and related Commission Directives on 1 October 2005, the AFM has taken over from Euronext Amsterdam its supervisory powers with respect to publication of inside information by listed companies. The surveillance unit of Euronext Amsterdam continues to monitor and supervise all trading operations.

## Taxation

*The following 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 tax adviser for more information about the tax consequences of acquiring, owning and disposing of Shares in his particular circumstances.*

### Dutch Taxation

This taxation summary solely addresses the principal Dutch tax consequences of the acquisition, ownership and disposal of Shares. It does not consider 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. 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 be the meaning to be attributed to the equivalent Dutch concepts under Dutch tax law. This summary 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 law of the Netherlands (unpublished case law not included) as it stands at the date of this Prospectus. The law upon which this summary is based is subject to change, perhaps with retroactive effect. Any such change may invalidate the contents of this summary, which will not be updated to reflect such change.

Where in this section “Dutch Taxation” reference is made to “your Shares”, that concept includes, without limitation, that:

1. you own one or more Shares and in addition to the title to such Shares, you have an economic interest in such Shares;
2. you hold the entire economic interest in one or more Shares;
3. you hold an interest in an entity, such as a partnership or a mutual fund, that is transparent for Dutch tax purposes, the assets of which comprise one or more Shares; or
4. you are deemed to hold an interest in Shares, as referred to under 1. to 3., pursuant to the attribution rules of article 2.14a, of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*), with respect to property that has been segregated, for instance in a trust or a foundation.

### 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” applies only 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 following tests:

- 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 any benefits derived or deemed to be 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 any one or more of the following circumstances is present:

1. You - either alone or, in the case of an individual, together with your partner (*partner*), if any – own, or pursuant to article 2.14a, of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*) are deemed to own, directly or indirectly, either a number of Shares in us representing five per cent. 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, representing five per cent. or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of our Shares), or profit participating certificates (*winstbewijzen*) relating to five per cent. or more of our annual profit or to five per cent. or more of our liquidation proceeds.
2. Your Shares, profit participating certificates or rights to acquire Shares or profit participating certificates in us have been acquired by you or are deemed to have been acquired by you under a non-recognition provision.
3. Your partner or any of your relatives by blood or by marriage in the direct line (including foster-children) or of those of your partner has a substantial interest (as described under 1. and 2. above) in us.

If you are entitled to the benefits from Shares or profit participating certificates (for instance if you are a holder of a right of usufruct) you are deemed to be a holder of Shares or profit participating certificates, as the case may be, and your 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., but do not satisfy test c. and/or test d., 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 following tests:

- i. you are a corporate entity (*lichaam*), 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;
- ii. you are resident, or deemed to be resident, in the Netherlands for Dutch corporation tax purposes;
- iii. 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
- iv. you are not an investment institution (*beleggingsinstelling*) as defined in article 28 of the Dutch Corporation Tax Act 1969 (*Wet op de vennootschapsbelasting 1969*).

If you are not an individual and a holder of Shares and if you do not satisfy any one or more of these tests, with the exception of test ii., your Dutch corporation tax position is not discussed in this Prospectus. If you are not an individual and a holder of Shares that does not satisfy test ii., please refer to the section “Dutch Taxation – Taxes on Income and Capital Gains – Non-Resident Holders of Shares”.

*Dutch Individuals Deriving Profits or Deemed To Be Deriving Profits from an Enterprise*

If you are a Dutch Individual and if you derive or are deemed to derive any benefits from your Shares, including any capital gain realized on the disposal of such Shares, 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 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 your Shares, including any gain realized on the disposal of such Shares, 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, or be deemed to derive, benefits from Shares that are taxable as benefits from miscellaneous activities in the following circumstances:

- a. if your investment activities go beyond the activities of an active portfolio investor, for instance in the case of use of insider knowledge (*voorkennis*) or comparable forms of special knowledge; or
- b. if you hold Shares, whether directly or indirectly, and any benefits to be derived from such Shares are intended, in whole or in part, as remuneration for activities performed by you or by a person who is a connected person to you as meant by article 3.92b, paragraph 5, of the Dutch Income Tax Act 2001 (*Wet inkomstenbelasting 2001*).

#### *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 are taxed annually as a benefit from savings and investments (*voordeel uit sparen en beleggen*). Such benefit is deemed to be four per cent per annum of the average of your “yield basis” (*rendementsgrondslag*) at the beginning and at the end of the year, to the extent that such average exceeds the “exempt net asset amount” (*heffingvrij vermogen*) for the relevant year. The benefit is taxed at the rate of thirty per cent. The value of your Shares forms part of your yield basis. Actual benefits derived from your Shares, including any gain realized on the disposal of such Shares, are not as such subject to Dutch income tax.

#### *Attribution Rule*

Benefits derived or deemed to be derived from certain miscellaneous activities by, and yield basis for benefits from savings and investments of, a child or a foster child who is under eighteen years of age are attributed to the parent who exercises, or to the parents who exercise, authority over the child, irrespective of the country of residence of the child.

#### *Dutch Corporate Entities*

If you are a Dutch Corporate Entity, any benefits derived or deemed to be derived by you from your Shares, including any gain 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 (*Wet op de Vennootschapsbelasting 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” applies only 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 following tests:

- 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 any benefits derived or deemed to be derived from such Shares have no connection with your past, present or future employment or membership of a management board (*bestuurder*) or a supervisory board (*commissaris*);
- 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 (*Wet inkomstenbelasting 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 (*Wet op de Vennootschapsbelasting 1969*).

See the section “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 any one or more of tests b., c., and d., 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 any benefits derived or deemed to be derived by you from your Shares, including any capital gain realised on the disposal thereof, except if

1. (i) you derive profits from an enterprise, as an entrepreneur (*ondernemer*) or pursuant to a co-entitlement to the net value of such enterprise, other than as a shareholder, if you are an individual, or other than as a holder of securities, if you are not an individual and (ii) such 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, and (iii) your Shares are attributable to such enterprise; or
2. you are an individual and you 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.

#### *Attribution rule*

Benefits derived or deemed to be derived from certain miscellaneous activities by a child or a foster child who is under eighteen years of age are attributed to the parent who exercises, or the parents who exercise, authority over the child, irrespective of the country of residence of the child.

## **Dutch Taxation – Dividend Withholding Tax**

### **General**

We are generally required to withhold Dutch dividend withholding tax at a rate of fifteen per cent. 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 repurchase or 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 holder of Shares 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 (a) the general meeting of our shareholders has resolved in advance to make such repayment and (b) 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**

A Dutch Individual (other than an individual who is not resident or deemed to be resident in the Netherlands, but who has elected to be treated as a resident of the Netherlands for Dutch income tax purposes) or a Dutch Corporate Entity generally can credit Dutch dividend withholding tax against his Dutch income tax or its Dutch corporation tax liability, as the case may be, and generally is entitled to a refund in the form of a negative assessment of Dutch income tax or Dutch corporation tax, as the case may be, insofar as such dividend withholding tax, together with any other creditable domestic and/or foreign taxes, exceeds his aggregate Dutch income tax or its aggregate Dutch corporation tax liability, as the case may be, provided that, in the case of a Dutch Corporate Entity, (i) the dividends distributed by us in respect of which such dividend withholding tax is withheld are included in its taxable profits and (ii) it has timely and duly filed a corporation tax return. In the case of a Dutch Corporate Entity for which dividends distributed by us are not included in its taxable profits, the dividend withholding tax withheld thereon is refunded upon a timely and duly filed request.

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, reduction or refund of, or credit for, dividend withholding tax, 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.

An individual who is not resident or deemed to be resident in the Netherlands, but who has elected to be treated as a resident of the Netherlands for Dutch income tax purposes, may be eligible for relief from Dutch dividend withholding tax on the same conditions as an individual who is a Non-resident holder of Shares, as discussed below.

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 taxation 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. 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 and the Tax Arrangement for the Kingdom (*Belastingregeling voor het Koninkrijk*).

In addition, a Non-resident holder of Shares that is not an individual is entitled to an exemption from dividend withholding tax, provided that the following tests are satisfied:

1. it is, according to the tax law of a Member State of the European Union or a state designated by ministerial decree, that is a party to the Agreement regarding the European Economic Area, resident there and it is not transparent according to the tax law of such state;
2. any one or more of the following threshold conditions are satisfied:
  - a. at the time the dividend is distributed by us, it holds Shares representing at least five per cent. of our nominal paid up capital; or
  - b. it has held Shares representing at least five per cent. of our nominal paid up capital for a continuous period of more than one year at any time during the four years preceding the time the dividend is distributed by us, provided that such period ended after 31 December 2006; or
  - c. it is connected with us within the meaning of article 10a, paragraph 4, of the Dutch Corporation Tax Act 1969 (*Wet op de Vennootschapsbelasting 1969*); or
  - d. an entity connected with it within the meaning of article 10a, paragraph 4, of the Dutch Corporation Tax Act 1969 (*Wet op de Vennootschapsbelasting 1969*) holds at the time the dividend is distributed by us, Shares representing at least five per cent. of our nominal paid up capital;
3. it is not considered to be resident outside the Member States of the European Union or the states designated by ministerial decree, that are a party to the Agreement regarding the European Economic Area under the terms of a double taxation treaty concluded with a third State; and
4. the holder of Shares does not perform a similar function as an investment institution (*beleggingsinstelling*) as meant by article 6a or article 28 of the Dutch Corporation Tax Act 1969 (*Wet op de Vennootschapsbelasting 1969*).

The exemption from dividend withholding tax is not available if pursuant to a provision for the prevention of fraud or abuse included in a double taxation treaty between the Netherlands and the country of residence of the Non-resident holder of Shares, such holder would not be entitled to the reduction of tax on dividends provided for by such treaty. Furthermore, the exemption from dividend withholding tax will only be available to the beneficial owner of dividends distributed by us. If a Non-resident holder of Shares is resident in a Member State of the European Union with which the Netherlands has concluded a double taxation treaty that provides for a reduction of tax on dividends based on the ownership of the number of voting rights, the test under 2.a. above is also satisfied if such holder owns five per cent. of the voting rights in us.

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 – 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 – Non-Resident Holders of Shares” for a description of the term Non-resident holder of Shares.

### **Dutch Taxation – Gift and Inheritance Taxes**

If a holder of Shares disposes of Shares by way of gift, in form or in substance, or if a holder of Shares who is an individual dies, no Dutch gift tax or Dutch inheritance tax, as applicable, will be due, unless:

- (i) the donor is, or the deceased was, resident or deemed to be resident in the Netherlands for purposes of Dutch gift tax or Dutch inheritance tax, as applicable; or
- (ii) 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 of 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, other than court fees, is payable in the Netherlands by the holder of Shares in respect of or in connection with (i) the subscription, issue, placement, allotment, delivery of Shares, (ii) the delivery and/or enforcement by way of legal proceedings (including the enforcement of any foreign judgment in the courts of the Netherlands) of the documents relating to the issue of Shares or the performance by us of our obligations under such documents, or (iii) the transfer of Shares.

## General Information

### Available Information

We will be required to publish our annual accounts, accompanied by an annual report and an auditor's certificate, 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. In addition, we are also obliged to publish interim management statements.

Our Annual Reports (comprising our annual accounts, an annual report and an accountants' certificate) and our half-yearly figures and interim management statements upon their publication 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.

Copies of our Annual Reports for the years ended 31 December 2006, 2007 and 2008, our Condensed Consolidated Interim Financial Statements for the six months ended 30 June 2009 (also including the 30 June 2008 figures), 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. These Annual Reports and Half Year Reports are also available on [www.octoplus.nl](http://www.octoplus.nl) for the life of this Prospectus.

This Prospectus will be available to investors on the website of the AFM at [www.afm.nl](http://www.afm.nl) and through the NYSE Euronext website at [www.euronext.com](http://www.euronext.com). Alternatively, this Prospectus will be available at no cost upon simple request from the Company, by sending an e-mail to: [IR@octoplus.nl](mailto:IR@octoplus.nl)

### Share Trading Information

The Shares are traded through the book-entry facilities of Euroclear Netherlands, only. The address of Euroclear Netherlands is: Herengracht 459-469, 1017 BS Amsterdam.

The Shares are traded under the following characteristics:

ISIN Code: NL0000345718  
Common Code: 026668441  
Amsterdam Security Code: 34571  
Euronext Amsterdam Symbol: OCTO

### Paying Agent

Fortis Bank (Nederland) N.V. is the Paying Agent with respect to our Shares. The address of the Paying Agent is:

Fortis Bank (Nederland) N.V.  
Rokin 55  
1012 KK Amsterdam  
The Netherlands

## Organizational Structure

We are a holding company of a number of directly held operating companies. Our subsidiaries and holdings are:

<u>Name</u>	<u>Percentage</u>	<u>Country of Incorporation</u>
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.	100%	The Netherlands
OctoPlus PolyActive Sciences B.V.	100%	The Netherlands
OctoPlus Inc.	100%	United States (Delaware)

## Advisors

Loyens & Loeff N.V. acted as our Dutch counsel in connection with the Private Placement and this Prospectus.

## Independent Auditors

Our audited consolidated financial statements as of and for each of the years in the three-year period ended 31 December 2006, 2007 and 2008, incorporated by reference in this Prospectus, have been audited by an auditor of Deloitte Accountants B.V., independent auditors, as stated in their report thereon appearing elsewhere herein. The auditor is a member of the Royal Netherlands Institute of Chartered Accountants (*Koninklijk Nederlands Instituut voor Registeraccountants*).

## Legal Proceedings

There are no governmental, legal or arbitration proceedings, including any such proceedings pending or threatened of which we are aware, during a period covering at least the past 12 months which may have, or have had in the recent past, significant effects on our financial position or profitability.

## Financial and Trading Position

Since 30 June 2009, the following significant changes to the financial and trading position of OctoPlus have occurred:

- In September 2009, we announced that as a result of further efficiency measures we were able to reduce our work force by approximately 25% while retaining our revenue guidance for the year.
- In November 2009, we announced a positive operating result (EBIT) for the third quarter, driven by strong third quarter revenues and cost savings.
- In December 2009, we completed the Private Placement raising € 4.0 million in gross proceeds and € 3.8 million in net proceeds. The New Shares were issued at € 1.25 per share. The gross proceeds were received on 18 December 2009.
- In December 2009, we agreed on a contract to obtain a new credit facility at more favourable conditions from Fortis Bank (Nederland) N.V. of up to € 2.0 million, which shall replace our existing credit facility. The contract was signed on 6 January 2010.

**ISSUER**

**OctoPlus N.V.**  
*Business Address*  
Zernikedreef 12  
2333 CL Leiden  
The Netherlands

**LEGAL ADVISORS TO THE ISSUER**

**Loyens & Loeff N.V.**  
Weena 690  
3012 CN Rotterdam  
The Netherlands

**INDEPENDENT AUDITORS**

**Deloitte Accountants B.V.**  
Orlyplein 10  
1043 DP Amsterdam  
The Netherlands